Abnormal Aortic Aneurysm: diagnosis and management

Consultation on draft guideline - Stakeholder comments table
16/05/2018 – 29/06/2018

Please note: because some similar themes were raised by multiple stakeholders, we have provided single responses to these at the foot of this document. References to this shared material are made throughout our responses to individual comments.

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SWAN (Screening Women for Abdominal Aortic Aneurysms)	Draft guideline	General	General	We have reviewed these NICE guidelines from the perspective of the work we have performed for the NIHR HTA. Most recently this was to construct and populate a discrete-event simulation model of AAA screening in women, the SWAN project (NIHR HTA 14/179/01). In the SWAN project we conducted comprehensive systematic reviews of the management of AAA in women and extensive modelling of AAA screening including clinical and cost-effectiveness outcomes. This work was built upon our work in a previous HTA project, RESCAN (NIHR HTA 08/30/02), in which we performed an individual patient data meta-analysis of small AAA surveillance and used the dataset to model varying surveillance intervals for small AAA.	Comment noted; thanks for the background.
SWAN (Screening Women for Abdominal Aortic Aneurysms)	Draft guideline	General	General	AAAs, from definition to care, are not well studied in women and it might be incorrect to apply the same guidelines for elective repair to men and women and more caution should be expressed. Similar reservations may apply when using sweeping recommendations across different ethnic groups.	Throughout guideline development, the committee gave consideration to areas in which their recommendations might apply differently to any subgroups of people, and they were especially careful to think about their impact on women. See Evidence reviews C, D and F for examples. We agree that the evidence-base is sparse, in this area. Wherever the committee made research recommendations, they considered whether there was likely to be a need for particular consideration of women with AAA. Where they thought there was, they specified that the research should be stratified appropriately to explore subgroup effects.
SWAN (Screening Women for	Draft guideline	3-4	40-49 (section 1.1.3)	The general screening 70-year women for AAA, using the NHS AAA Screening Programme model for men, is neither clinically effective nor cost-effective (need to screen 3900	The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two

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Abdominal Aortic Aneurysms)				women to avoid 1 AAA-death, estimated incremental cost-effectiveness ratio [ICER] £30,000 per quality-adjusted life-year [QALY] gained) [Sweeting et al Lancet 2018 in press]. This is particularly pertinent given the list of associated conditions and co-morbidities which are recommended to trigger opportunistic screening. Many of the associated conditions and co-morbidities are the very conditions which may render a woman unfit for elective open repair, which you recommend for repair of intact AAA, or increase the already unacceptably high operative mortality associated with elective open repair in women. Moreover, there is no direct evidence on the clinical effectiveness and cost-effectiveness of either targeted or opportunistic screening of 'higher risk' women. So this recommendation does not have sufficient evidence to support it,	is that with case finding, healthcare-seeking individuals are offered imaging rather than a screening programme actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. Our preliminary view of Sweeting et al.'s study (which has now published) is that it is not inconsistent with the committee's view of the evidence and recommendations. Although this study cannot be seen as supporting population-level screening, it does demonstrate that identifying AAA in women is likely to lead to net health gains. Moreover, if an indiscriminate population-level approach yields net health gains at a cost of between £20–30,000/QALY, it is very likely that the opportunistic approach the committee recommends will be somewhat more cost effective (because it does not incur the costs of screening women who are relatively unlikely to have AAA, and focuses on those who are at highest risk).
SWAN (Screening Women for Abdominal Aortic Aneurysms)	Draft guideline	7	124-127 (section 1.3.3)	We appreciate that the NICE committee wishes to harmonise the guidelines for the frequency of surveillance of detected AAAs. As the committee acknowledge, and as reported in Thompson et al Health Technology Assessment 2013; 17(41), uncertainty remains in the ICERs particularly due to the small absolute differences in expected QALYs and costs between the alternative surveillance options. Therefore a stepped approach to reducing surveillance intervals with a yearly scan for 4.0-4.4cm may be a safer, more cautious, option.	No evidence was identified looking at a stepped monitoring protocol, such that it would be difficult to support the suggested amendment. However, the committee agreed that this is an important area of uncertainty, and made a research recommendation that frequency of review and threshold for surgery should be considered, suggesting that a systematic review and economic model would be well placed to answer the question (an approach such as that adopted by the SWAN collaborators seems, on the face of it, well suited to answer these questions).

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SWAN (Screening Women for Abdominal Aortic Aneurysms)	Draft guideline	9	179-182 (sections 1.5.2 & 1.5.3)	The recent quality improvement programme to reduce the elective operative mortality for AAA repair set a target of <3.5%. By both these and international standards, elective open repair is not a safe operation in women, whereas elective EVAR is a much safer procedure in women. Data from a recent systematic review show that the 30-day mortality for elective open repair in women was 5.4% versus 2.3% for elective EVAR [Ulug et al Lancet. 2017 Jun 24;389(10088):2482-2491]. Recent data from both the UK National Vascular Registry and Hospital Episode Statistics (2010-2014) show similar results, with the National Vascular Registry reporting an in-hospital mortality of 6.9% for open repair versus 1.8% for EVAR in women [Sidloff et al Br J Surg. 2017 Nov;104(12):1656-1664]. The same pattern is observed in nationwide data from Germany (2005-13), where in women the in-hospital mortality for open repair was 5.0% in women versus 2.8% for EVAR [Trenner et al Br J Surg. 2018 Mar;105(4):379-387]. Therefore, elective EVAR should be the preferred treatment option for women.	The data from Sidloff et al. (2017) that you cite show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). The same is true of Trenner et al. (2018: RR=1.36 for OSR versus RR=1.9 for EVAR). Other publications based on large datasets have found the same (see, e.g., analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.
SWAN (Screening Women for Abdominal Aortic Aneurysms)	Draft guideline	10	183-185 (section 1.5.4)	Issues such as the quality of life, anxiety and depression and psychosocial considerations which might be associated with small AAA surveillance over a prolonged period and then an eventual refusal to offer repair at 5.5 cm because open repair is considered too risky and elective EVAR is not recommended have not been adequately studied. Further research is needed before EVAR is denied in this latter situation.	For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
Imperial College London - IMPROVE trial	Draft guideline	8	149-153 (sections 1.4.4 and 1.4.5)	We also are reassured to read that scoring systems should not be used to deny a patient emergency repair of AAA rupture. We have conducted a thorough investigation of this and tried to develop a new score which includes basic AAA morphology, but nothing allows for a score which reliably identifies patients	Thank you for your comment and endorsement of recommendations relating to risk assessment tools for people undergoing elective AAA repair. Unfortunately the proffered study by Sweeting et al. (2018) falls outside the scope of the guideline as it assess risk assessment tools for ruptured AAA.

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management committee				who would not benefit from a repair. See Sweeting et al https://doi.org/10.1002/bjs.10820	The NICE review was specific to risk assessment tools for unruptured AAA. As a result, the Study by Sweeting et al. cannot be considered for inclusion.
Imperial College London - IMPROVE trial management committee	Draft guideline	10	195-202 (section 1.6.1)	We are delighted to read that EVAR should be considered for repair of ruptured abdominal aortic aneurysm (AAA), especially in women. However, we have major concerns how future trainees and clinical teams will gain sufficient experience in EVAR (for which there is a considerable learning curve, which cannot be accomplished solely through the use of simulators) to be able to use EVAR in the emergency setting, unless EVAR is recommended for at least a proportion of elective AAA repairs. Using EVAR in the emergency setting requires additional skills to those required for elective repair, such as use of occlusion balloons. The urgent need to control the aorta and declining number of ruptures mitigate against either individual or team training being offered in the emergency setting.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Vascular Society of Great Britain and Ireland	Draft guideline	General	General	The Vascular Society of Great Britain & Ireland would like to thank the committee for their extensive work on this AAA management guideline. There are many recommendations that we agree with especially with regard to early detection, surveillance and risk factor optimisation for patients with AAA. Also, the initial emergency management of ruptured AAA. In these areas the guidance will be beneficial for our patients. We do however have a number of concerns regarding the recommendations relating to the form of repair (open or EVAR) for both unruptured and ruptured AAA. Also, the proposed EVAR surveillance recommendations. There is no specific provision in the recommendations for symptomatic AAA's and women with AAA which we feel is a significant omission.	Thank you for providing this summary of your comments, which we respond to fully where they are given in detail. We are also grateful for the work you have done to elicit the views of your individual members. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see rationale and impact section in the guideline for information on implementation issues and Theme 12 for a discussion of subgroups..

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				These recommendations will have a major impact on current UK practice with enormous implications for implementation. UK practice will be at odds with accepted practice elsewhere in the developed world and current international guidelines (Society of Vascular Surgery USA, European Society of Vascular Surgery). There is evidence that has not been considered by the committee which would allow a more balanced appraisal of current practice, outcomes and costs. A particular omission was the data on patient choice and preference. Also data to reflect more recent EVAR practice as opposed to that in the EVAR trials from 1999-2004. The committee state that the medium to long term view should be the focus. However this overlooks the short to medium term advantages of EVAR, especially in current practice. The data for long term outcomes (8-15 years) is limited, only 60 out of 1252 patients were available for follow up at the end of the EVAR 1 trial. When patients are informed about late complications they still express a preference for the short term gains of EVAR. The clinical reality is that we cannot ignore the short to medium term advantages of EVAR. There are also logistical and training issues raised by the recommendations which do not appear to have been considered. Assessment of anaesthetic and medical "fitness" is used as a fundamental binary indicator for open repair or no intervention. Yet virtually no guidance on how to make this fitness assessment is given. We provide evidence that in fact this is extremely difficult to do in real world practice. The delivery of EVAR to ruptured AAA patients is to be considered. The committee appear to have overlooked the implementation of this when elective practice is almost entirely open surgery or turn down for repair. Vascular teams will be	

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				deskilled in EVAR and unable to deliver challenging EVAR to ruptured AAA patients under local anaesthetic. Training the future workforce will also suffer from the same limitations. In summary therefore, there is much to welcome in this guidance but also significant areas where evidence has not been considered, omissions made, and issues of practical implementation have been overlooked. More details are provided in the following sections, but we strongly urge the committee to reconsider their recommendations in these important areas. We are certain that there is a better middle ground where EVAR is utilised for specified indications providing patients with the best care. We have surveyed our membership in the limited time available with 240 replies received (approximately 56% of total members) Their responses are included in the relevant sections below. Details of the survey can be given if required by the committee. The survey questions followed the recommendation statements in the guideline.	
The Vascular Society of Great Britain and Ireland	Draft guideline	General	General	**Ireland** The VSGBI represents members in the 4 home nations and Ireland. The Irish Vascular Society are unable to comment on these recommendations directly but they have made their views on the guidance known to the VSGBI. We feel we must summarise these as part of our response in order to truly represent our membership. Their main points are : A very narrow view has been taken of EVAR with too much emphasis on cost. Many of the conclusions are based on EVAR I and EVAR II which enrolled patients from 1999 – 2003. This was part of the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				learning curve of many units. There are no data in either trial regarding operator experience, compliance with IFU, number of cases done in these units before enrolling patients. These trials provide no data regarding the device used i.e. whether it had suprarenal fixation, whether CT sizing software was used, type of CT used. There appears to be complete exclusion of North American data, much of which is favourable to EVAR e.g. *Giles et al; Decrease in total aneurysm related deaths in the era of endovascular aneurysm repair: J Vasc Surg. 2009; 49(3): 543–551.* No attempt is made to discuss anatomic suitability for EVAR, or compliance with device IFU. There will be a reduction in elective AAA repair for many patients of moderate risk with a corresponding increase in ruptures. Also a probable further reduction in the number of patients offered surgery for either unruptured or ruptured AAA.: *Thresholds for Abdominal Aortic Aneurysm Repair in England and the United States, Alan Karthikesalingam, et al N Engl J Med 2016;375:2051-9.* *Mortality from ruptured abdominal aortic aneurysms: clinical lessons from a comparison of outcomes in England and the USA. Alan Karthikesalingam et al: Lancet 2014* 15;383(9921):963-9	The American OVER RCT was included in the evidence-base on which the consultation draft was based and contributed to the estimates of perioperative and long-term mortality adopted in the HE model's base case. When it comes to observational data, a substantial majority of the included evidence in our post-consultation review of casemix-adjusted perioperative mortality data for infrarenal AAA originates from the USA (30 out of 40 studies). As detailed in **Theme 2** and **Theme 9**, the committee were confident that these analyses validated their initial conclusions. Giles et al.'s study (2009) is not amongst these: it mostly focuses on ruptured AAA, and none of its analyses adjust for casemix.

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				A new generation of Vascular Surgeons who will be neither trained in or comfortable with either open repair or EVAR. A very serious manpower crisis in our speciality. We would therefore feel that the conclusions are seriously flawed.	
European Society for Vascular Surgery (ESVS)	Draft guideline	General	General	The European Society for Vascular Surgery has confidence in and agrees with many of the recommendations in the NICE document. However, we share the concerns of the Vascular Society and are particularly concerned about the restrictive nature of interpretation of the evidence on EVAR. Changing UK practice (and many other European Countries) for AAA repair over the last 10-15 years has led to lower 30-day mortality rates. A significant part of this improvement is due to the use of EVAR. For patients, this has led to earlier discharge and lower complication rates. Patients and their doctors have recognised that choice of procedure is a balance between anatomical suitability, patient morbidities, expectation of life and the durability of graft (and mode of delivery) chosen for repair. Considerable changes in graft technology have taken place in the last 10 years and long-term outcomes are not yet available for some of these. Patients' expectation is that the procedure chosen for elective repair will be based on balancing the evidence, but also take account of areas where evidence is not yet available or mature enough to provide these longer-term results. Patient choice, should they wish to have surgery, is understandably biased towards the safer intervention, which, in the early years, is EVAR. Longer-term results for EVAR, especially for newer technology, will inevitably 'lag' behind the earlier grafts used in	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. See Theme 2 for further information on perioperative mortiality. It is clearly true that, for patients with infrarenal AAA, both OSR and EVAR are technically possible but OSR is more dangerous in the short term. However, the review of the evidence found that EVAR is the more expensive approach (even when one factors in generous estimates of postoperative cost-savings that may be associated with EVAR – see **Theme 6**), andrequires more reinterventions than OSR, even if the rate of reintervention may have decreased somewhat over time (see **Theme 8**). Tthe committee also concluded from randomised and observational evidence that

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				the Trials. By removing this choice today, (when both procedures are technically possible, but one is clearly more dangerous), patients will be denied both the early benefit and the possibility of continued protection from newer grafts in later years.	EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**. Accordingly, when the short-term benefits of EVAR are balanced against its costs and its long-term harms, the committee were clear that OSR should be seen as the preferred approach.
European Society for Vascular Surgery (ESVS)	Draft guideline	General	General	The EVAR trial data have recently been reviewed by Prof R Greenhalgh, (Society for Vascular Surgery, Boston, June 2018, oral presentation) – longer follow up with specific analyses of the causes of serious endoleaks leading to sac expansion and rupture were presented. Most patients were found not to require long follow up beyond 2 years, if surveillance had shown no leak or expansion; a small number needed intervention and follow up for longer, to prevent fatal ruptures. This analysis should be reviewed by the Committee, as it alters the cost-benefit assessment of this trial.	We are unable to comment on unpublished data; however, the authors of the research to which you refer have provided us with some details in their own consultation response. The committee agreed that the postoperative surveillance of people who have undergone EVAR could be optimised – hence, they made a research recommendation in this area. However, without any evidence as to the empirical performance of an (on average) less intensive follow-up regimen, there is a real danger that bias will be introduced to our analysis by assuming that the costs of surveillance can be minimised without compromising patient safety – see **Theme 11**.
European Society for Vascular Surgery (ESVS)	Draft guideline	General	General	The European Society (ESVS) wish to inform the Committee that ESVS is in the final phase of publishing its 2018 revised ESVS Guidelines on treatment of AAA. They will be E-published in September and paper-published in the European Journal of Vascular and Endovascular Surgery (EJVES) in January 2019. The ESVS Guideline committee, the Writing Committee (WC) of the ESVS Guidelines and the WC of the NICE GL base their recommendations on much of the same evidence. It is the view of the Executive Committee of the ESVS that National GL	Thank you for your comment. The committee were aware of current and impending guidelines from European and American specialist societies, The NICE method requires committees to independently consider the best available evidence of effectiveness and cost effectiveness and develop recommendations based on that evidence taking account of a range of issues (including any

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				(such as NICE) should take into account these imminent European Guidelines, before the NICE GL are published, so that unnecessary confusion from any conflicting recommendations can be avoided	ethical issues, social value judgements, equity considerations and inequalities in outcomes.
Bristol Bath Weston Vascular Network (North Bristol NHS Trust)	Draft guideline	General	General	**General remarks** As a network we support the majority of the recommendations contained within these AAA guidelines. Our concerns, as vocalised by one of our patients under small AAA surveillance, focuses on '*removing the choice of having an endovascular repair*'. We also provide our rationale for our adopting a post-EVAR surveillance programme in which CT angiography is combined with Duplex ultrasound, performed by vascular scientists. **Background to our AAA service** By way of background, as a network from 2007-14 we treated 234 elective patients with standard EVAR. We participate in the NHS AAA Screening Programme and host the local programme team. We provide complex endovascular repairs for the South West region, and from 2014 to 2017 and have seen a year on year increase in these referrals as individual units are choosing to send their patients to our specialist unit. We have network pathways with our ambulance Trust for the management of symptomatic or ruptured AAA, including a bypass policy to bring patients direct to the arterial centre. Our vascular nurse specialists see men with AAA detected by the NHS AAA Screening Programme and all new men and women who are referred with incidentally discovered small AAA (< 5.5cm) to provide health and life-style advice.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Thank you for the contextual information about your service.

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Bristol Bath Weston Vascular Network (North Bristol NHS Trust)	Draft guideline	General	General	**Impact of the proposed changes on current practice and available resources** An unforeseen consequence of the NICE guidelines may be further centralisation of vascular services. Reduced volume of EVAR (a major index procedure which has been a key factor driving unit sustainability) across vascular units as a consequence of turning down higher risk patients will be inevitable. Further re-organisation of vascular services would be necessary and this has proved difficult to deliver to date. We anticipate significant service implications as a result of the increased use of open repair Critical care bed capacity remains at a premium (especially in hospital trusts with a major trauma unit). There is a significant risk of a delay to definitive AAA repair (delays due to ICU bed availability) and an impact on the length of hospital stay Post-operative EVAR surveillance in our network is primarily delivered by Duplex ultrasound (one stop assessment). CT angiography usually requires an additional visit to hospital is more costly and potentially increases renal risk and is associated with significant cumulative radiation dose. In our network robust processes are in place for the recall of patients and Duplex has been locally validated against CT angiography for sac size measurement and endoleak detection (see below).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline. . In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks – see **Theme 11**.

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				Significant cost implications We would like to highlight the following as cost implications for commissioners: CT scanning in place of Duplex ultrasound Length of ICU stay and hospital stay Open AAA surgery is associated with a large incision and frequent gastrointestinal (ileus, pain, weight loss) and abdominal wall complications (wound infection, incisional hernia). These complications are common and costly. The impact is significant and was poorly captured within the large RCTs. We anticipate that more patients will seek assistance from non-vascular services such as primary care, ED and gastrointestinal surgery.	As discussed in Evidence review W, the adoption of CT-led post-EVAR surveillance does not – even under extremely conservative asssumptions – meet NICE's definition of a substantial resource impact (i.e. >£1m per year). For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**. The suggestion that the RCTs underestimated long-term reinterventions associated with OSR had been addressed in the HE model reported in the consultation draft. As noted in HE.2.2.9.1, the EVAR-1 investigators were mindful of this criticism, and retrospectively obtained data on hernia interventions required following EVAR and OSR. These were reported in the long-term follow-up report (Patel et al., 2016); these rates are incorporated in the base-case HE model. We also incorporated other laparotomy-related complications recorded by in US registry data (Schermerhorn et al., 2015) that had not been retrospectively included in the EVAR-1 reintervention data.
Association of British HealthTech Industries (ABHI)	Draft guideline	9-11	179-206	**Guidance does not support application of clinician judgment.** The evidence on EVAR versus open surgery shows that any advantage for one over the other is driven largely by the patient's individual circumstances, including age, gender, smoking status, co-morbidities, and anatomic complexity. This draft guidance makes definitive	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				recommendations in favour of open surgery and does not encourage physicians to take these patient factors into account when discussing treatment options with patients. The strength of the recommendations in favour of open surgery and the consequences on availability of EVAR are not in keeping with the NICE charter and goals for shared decision making. NICE Charter 2017 "…our recommendations are not intended to replace the professional expertise and clinical judgement of health professionals, as they discuss treatment options with their patients." NICE Shared Decision Making website "We've updated all of our guidelines to highlight the importance of balancing professional judgment and expertise with the needs and wishes of people receiving care." We recommend allowing physicians to use their best judgment on the best treatment for individual patients depending on their individual circumstances	whilst supporting individualised care around which interventions are appropriate. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**. We do not agree with your suggestion that the evidence on EVAR versus OSR shows that outcomes depend on patient's individual circumstances. On the contrary, the available evidence on unruptured infrarenal AAA shows that, on average, OSR leads to better net outcomes than EVAR, does not identify any subgroups of patients in which better net outcomes can be expected with EVAR (see **Theme 12**), and shows that there are no tools that reliably predict which individual patients might face a different balance of risks and benefits (see Evidence review H).
Association of British HealthTech Industries (ABHI)	Draft guideline and Economic Appendix and Model	10-11	203-206	**[This section concerns ruptured complex AAA repair.] There currently is no model for emergency (ruptured)-complex cases.** This is based on the rationale that for complex cases will always have to be treated with customised devices. However, if the anatomy is suitable and the patient hemodynamically stable, Complex EVAR with off-the-shelf devices might be a suitable alternative to open surgical repair (OSR), resulting in potentially better health outcomes and acceptable additional costs. The guideline in this regard will need to consider this device type for emergency (ruptured)-	It is important to understand the 'burden of proof' required of treatments considered by NICE's decision-making committees, as set out in Developing NICE guidelines (2014). NICE guidelines recommend courses of action when there is credible evidence that they are associated with net health gain for patients at a cost that does not compromise care for other NHS service users. In the case of complex EVAR for ruptured AAAs, the committee found no evidence to support a positive

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				complex cases. In addition, we recommend the committee analyse most recent Patient Level Information & Costing Systems (PLICS) data to gain further insight into contemporary resource utilisation. We recognize that the guideline committee has no health-economic data for repair of ruptured complex AAAs. However, in many clinical settings, if the anatomy is suitable and if the hemodynamic parameters make endovascular repair possible, more and more ruptured complex AAAs can be treated with certain readily available EVAR devices that do not have to be customised. We have concerns that the guidance regarding the repair of ruptured complex AAAs has been developed without taking current real-world evidence into consideration. Further, in the absence of definitive RCT evidence, we suggest the committee consider recommending reliance on clinical judgement about the decision to use EVAR on a case-by-case basis.	recommendation; indeed, there are no data of even very low quality to estimate the safety and effectiveness of such an approach. Therefore, they recommended the collection of reliable data to inform future guidance. Without any estimate as to the safety and effectiveness of the approach, resource-use data alone are of limited relevance to decision-making. However, we would note that we have reviewed the PICS data and would have difficulties applying them to the case in hand, as coding anomalies make them difficult to interpret.
The Vascular Society of Great Britain and Ireland	Draft guideline	11-12	221-226	**Recommendations 1.7.3 ; 1.7.4 ; 1.7.5 EVAR surveillance** Use CT to detect endoleak and sac expansion. Use CEUS when CT is contraindicated. Also, "do not use colour duplex ultrasound as the main imaging technique to detect endoleaks in people who have had an EVAR" We would like some clarification on the wording of recommendation 1.7.5. Does this mean do not use colour duplex at all, or does the term "as the main imaging technique" imply that there is a role for colour duplex in combination with other modalities? Lines 333-341, evidence review W, suggest there is a role for duplex but it is not made clear.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour

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				Many surveillance programmes use a combination of modalities and would argue that an initial CT is used to exclude type 1 and 3 endoleaks, significant stent kinking, stenosis or malposition. Surveillance is then continued with duplex ultrasound +/- plain film x-ray with the primary aim of monitoring sac size and stent migration but also detecting endoleaks. Significant sac size increase on duplex would lead to repeat CT assessment. The recent SVS guidelines on AAA management include recommendations for a combined modality CT and duplex approach to EVAR surveillance which achieves the goal of detecting clinically significant type 1 endoleak using CT with also the pragmatic use of duplex to reduce excess patient exposure to CT. The aim of such an approach is to reduce costs related to CT scans and reduce clinical harm from contrast renal injury and radiation exposure. The committee discuss the safety aspects of CT surveillance in evidence review W, lines 424 – 434. Concern relating to long term CT radiation exposure leading to an increase in malignancies is rejected on the basis that patients post EVAR have a short life expectancy. This is however at odds with the committees' statement that AAA management should be based on the medium to long term view (evidence review K, lines 596-7). Also, the considerable weight given to the evidence from the EVAR 1 trial at 8-15 years follow up. There is inconsistency in the committees' arguments here. If our focus is to be on "medium to long term outcomes" then the long term impact of repeat CT radiation and contrast must be considered. The recommendations in this guideline do not do this.	duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about

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				In fact the long term EVAR 1 trial data does show an excess of malignancy related deaths in the EVAR group. Numbers are small, but it is difficult to justify a CT dominated surveillance recommendation in the light of these findings. Evidence review W, line 262 – refers to "resultant potential for harm" arising from the use of colour duplex in surveillance. We are unaware of any evidence for this and would request that this statement is evidenced. Evidence review W, line 370 – 73. – "recommending CEUS over duplex ultrasound would generate downstream resource savings, by avoiding false-negative endoleak diagnoses. Similarly, the committee agreed that recommending CTA over CEUS would generate downstream savings, due to its superior diagnostic accuracy, offsetting the higher cost per scan to some degree". Again, we are unaware of any evidence to support these statements. What level of cost savings are involved? We support the views of the Society of Vascular Technology, a professional society affiliated with the Vascular Society. In addition to the pragmatic arguments above they offer evidence to suggest CTA is not the gold standard for endoleak detection. Implementation of CEUS has practical considerations also. We would therefore advocate a more pragmatic combined modality approach to EVAR surveillance along the lines of the SVS guideline. This approach will reduce costs and optimise patient safety. **Ref**	costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.

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				Chaikof EL J Vasc Surg 2018 : 67 ; 2-77 (EVAR surveillance section pages 51-52)	
Association of British HealthTech Industries (ABHI)	Draft guideline And Economic Appendix and Model	9-10	172-182	**[This and the following four comments concern unruptured infra-renal AAA repair.]** We believe that the evidence used to derive the recommendations for unruptured elective cases (open repair in all suitable cases, do not offer EVAR) is incomplete and not contemporary. We will comment on three key areas that if updated would likely result in a comparable if not better clinical EVAR performance, compared to OSR, at acceptable additional costs.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see responses below.
Association of British HealthTech Industries (ABHI)	**Draft guideline and Economic Appendix and Model**	**9-10**	**172-182**	**Peri-operative (Short-term) Mortality. The peri-operative mortality was modelled in the cost-effectiveness analysis via an EVAR baseline mortality (0.4% for infra-renal and 3.6% for complex cases, taken from 2016 NVR data, Watson et al., 2017) that was, per the health economics appendix "consistent with the experience of the guideline committee". However, the actual effect measure was derived from a Cochrane meta-analysis (Paravastu et al., 2014) of randomised controlled trials that was dominated by EVAR-1 (62% weight in a fixed-effects model).** **EVAR-1 recruited from 1999 to 2004 when OSR was more common in routine clinical practice than EVAR. EVAR performance might have been hampered by relative surgical inexperience (compared to later time periods) and, in some cases, by possibly suboptimal fitting of the device due to less developed imaging techniques (both of which have improved since). Further, pre-2004 EVAR devices were used.**	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. Having reviewed a new review of casemix-adjusted observational evidence on perioperative mortality, the committee agreed that their decision to place primary reliance on randomised evidence of perioperative mortality was well validated – see **Theme 2**.

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				There are highly relevant data from a large registry (Vascunet, reporting on over 83,000 patients) that compared the real-world performance of EVAR and OSR over time (2005-2009 vs 2010-2013, Budtz-Lilly et al., 2017). While peri-operative mortality for EVAR fell from 1.5 to 1.1% (p=0.0001), OSR mortality increased from 3.9 to 4.4% (p=0.008); these changes were driven by high-volume centres for EVAR and by low-volume centres for OSR and might be even larger. There are two observations that can be derived from this study: **1) the even older EVAR-1 data (where first-generation EVAR devices where used compared to second- or third-generation devices after 2004) might inaccurately represent the current relative performance in terms of the odds ratio for EVAR and OSR; and** **2) In the Vascunet registry, low-volume OSR centres, in the second time period, had a mortality of 5.4%. If This data should be taken into consideration when assessing the potential impact of the recommendation implementation. See Table 1 and Figure 1 below.** **In the current health-economic model, calculations are performed based on a peri-operative mortality of 0.4% for EVAR and 1.3% for OSR (difference 0.9%) – an effect size assumption that differs markedly from contemporary real-world evidence. 2016 data from the NVR suggests an EVAR peri-operative mortality of 0.4% vs. 2.9% for OSR, a difference of 2.5%. These data are in line with evidence from other studies (e.g., in VQI: peri-operative mortality 0.7% for EVAR vs 4.0% for OSR in the non-ruptured infrarenal group, a difference of 3.3%). Moreover, the OSR patients were likely younger and possibly also healthier.**	The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to support decision-making – see **Theme 3a**. The committee also agreed that Budtz-Lilly et al.'s (2017) analysis of unadjusted registry data reflecting AAAs with heterogeneous anatomical complexity was of limited relevance to its decision-making for infrarenal AAA – see **Theme 3b**.

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				Because these differences affect all subsequent long-term mortality projections, their accuracy is essential for the correct estimation of an incremental cost-effectiveness ratio (ICER). **While the NICE model provides for exploration of the NVR parameter set, it does so only in a sensitivity analysis. The base case assumes an effect size that is two-thirds (1.4%) lower than the contemporary evidence from the NVR. We therefore suggest that NICE, instead of the meta-analysis-derived odds ratio from old trials, considers effect size calculations based on contemporary evidence for the base case. This might include NVR data only or a meta-analysis including NVR and other contemporary data.**	
Association of British HealthTech Industries (ABHI)	Draft guideline and Economic Appendix and Model	9-10	172-182	**Post Peri-operative (Long-term) Mortality.** The post peri-operative mortality was modelled in the health-economic model via different approaches. These included adjusted general population estimates (base case) and several different fitted parametric survival models. The EVAR-1 trial is the main evidence used which, again, is a concern, for several reasons. First, there is evidence that newer EVAR devices are associated with fewer complications than older devices (e.g., Verzini et al., 2014 reported seven-year complication rates of 14.4% vs 25.8% for EVAR devices before and after 2004, p=0.015). Consequently, newer devices might be associated with a lower aneurysm-related long-term mortality than those reported in the EVAR-1 trial. Of note, the adjusted hazard ratio	While the EVAR-1 trial is the largest trial in the assembled evidence, we would not agree with the description that it is 'main evidence used' in estimating long-term mortality – in the base case, it is 1 of 3 trials from which evidence is synthesised, all of which show a similar pattern (note that I^2=0% in figure HE97). The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of

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				(HR) for all-cause mortality only became borderline-significant in the EVAR-1 trial after more than eight years (HR=1.25; 95% confidence interval: 1.00 to 1.56; p=0.484 as per Patel et al., 2018; see Table 2 and Figures 2 and 3 below). This, in conjunction with the current peri-operative mortality assumptions, leads to model-projected survival in favour of OSR after a period of just three years – which is in disagreement even with the very dated and conservative EVAR-1 data (as detailed above).	operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as recommended by you and other stakeholders. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 8**. However,we would not agree with your use of Verzini et al.'s finding (2014) that reintervention rates are lower with more modern grafts cannot be cited, as evidence that long-term survival is also likely to be more favourable, when this is something the study explicitly looks at, finding no evidence of longer survival with newer grafts (p=0.308 for aneurysm-related survival; p=0.537 for overall survival; both over 7 years' follow-up). We do not accept that modelled survival is at odds with that observed in EVAR-1. In fact, as can be seen in the Kaplan–Meier graph you cite, the short-term survival advantage associated with EVAR only persists around 2 years into the trial. You are correct to emphasise that perioperative mortality parameters are critical in defining the point at which the balance of long-term deaths will begin to favour OSR. In our base-case model, this comes at around 3 years; however, if we directly use the perioperative mortality data from EVAR-1 instead, the modelled crossover point comes at 7 years.

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					We also note that survival favouring OSR after a period of 3 years or less is a feature of several of the propensity-matched Kaplan–Meier curves identified in our review of observational evidence (e.g. Huang et al., 2015; Mark et al., 2013; Symonides et al., 2018).
				Second, in the base case, the health-economic model employs a Cox (proportional hazard regression) survival model. However, as Patel et al., 2018 have demonstrated, EVAR has a survival advantage in the first six months, for the next 7.5 years there is no statistically significant difference, and only after eight years, a borderline statistically significant difference emerged. It appears that using the hazard ratios for the entire duration of the model is questionable given that the proportional hazard assumption has neither been tested nor is likely fulfilled based on the data cited above. As a result, the base case can be expected to compute a survival gain that is too conservative for EVAR and too high for OSR. In consequence, QALY calculations can be expected to not accurately reflect clinical reality. This issue is further amplified when discounting is applied.	As shown in **Theme 9a**, an argument against a proportional hazards assumption based simply on the statistical significance of piecewise hazards is not valid. The simple model of perioperative benefit for EVAR followed by constant post-perioperative risk can be shown to fit empirical data extremely well. Consequently, the committee had no hesitation in endorsing this model for the base-case HE model, although they were also interested in alternative approaches as sensitivity analyses (parametric curve-fitting to EVAR-1 alone; use of a piecewise hazard). However, if there were a bias in favour of OSR in our long-term projections, this would be attenuated, not amplified, by discounting, because the long-term phase in which OSR's advantage becomes apparent would have less weight in the analysis.
				On the basis of these observations, we propose the committee consider using a constant hazard ratio of 1.0 for the long-term mortality. This might reflect the uncertainty around long-term mortality that has emerged since EVAR-1. One important data point will be the long-term follow-up of the OVER trial, which according to the study authors is expected to be published in the next few weeks. An alternative assumption could be explored, where the mortality increases after 12 years as per Patel et al., 2018 (see Figure 2 below).	No evidence is cited that EVAR is associated with a constant HR of 1.0, compared with OSR, and there is plenty of evidence that it is not (see **Theme 9**). We do not agree with the suggestion of a 12-year starting-point for long-term survival effects. If a piecewise hazard is to be adopted, then – per your argument 2 paragraphs above – the significant effect must be applied from year 8 onwards. This approach – which was detailed as a sensitivity analysis in

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					the consultation draft – results in EVAR becoming even less cost effective, compared with OSR, in both infrarenal and complex models – see **Theme 9a**.
Association of British HealthTech Industries (ABHI)	Draft guideline and Economic Appendix and Model	9-10	172-182	**Costs and Resource Utilisation.** Assumptions about periprocedural resource utilisation and unit costs have a significant impact on total cost by strategy. In fact, around 67% of the total EVAR strategy costs in the modelled base case for elective (unruptured) infrarenal aneurysm repair are defined by the perioperative cost component, and 79% of the total OSR strategy costs. As such, these cost assumptions arguably play an important role in defining incremental costs between the strategies, and thereby incremental cost-effectiveness calculations. This relevance is further amplified by the – comparably – small QALY differences observed in the infrarenal model, which mean that relatively small changes in costs might have a pronounced impact on ICERs. We appreciate the committee's consideration of available data sources, including reference costs. As the committee states *"However, they were identified as being potentially unreliable, with a lack of clarity regarding the extent to which both repair devices and procedure complexity are captured."* The committee ultimately settled on using data from the EVAR-1 study, which collected periprocedural data in the period 1999-2004, around 15-20 years ago. **Length of stay calculations** For the infrarenal model, total length of stay for EVAR is assumed to be 9.76 days (Preoperative stay 1.81 days,	We agree that perioperative resource use has an important role in defining the net costs with which EVAR and OSR are associated. Naturally, it is critical that the HE model used to support decision-making should have as accurate an estimate of these figures as possible. We have reviewed resource use in all relevant categories – including all those raised in this comment – and made revisions to the base-case model used to support the committee's decision-making. Details are provided below. We have reviewed evidence on length of stay following AAA repair, and provide comments below.

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				postoperative stay 6.53 days, ITU stay 0.59 days, HDU stay 0.83 days). More current data do not support these assumptions and range from 2.54 to 3.79 days:	We note, however, that your comments relate exclusively to resource use associated with EVAR, and how that appears to have changed since the EVAR-1 trial. Of course, from a health economic perspective, the cost implications of a given technology can only be assessed in comparison with an alternative approach. In this case, this means that it is very important to consider how resource use with OSR may also have changed over time, in order to arrive at the best estimate possible of the incremental costs associated with EVAR.
				National Vascular Registry (NVR): For EVAR, the latest National Vascular Registry data (2016 data, published in 2017) reports a median total length of stay of 3 days. Over 60% of patients were returned to a normal hospital ward after surgery. Among those admitted to either level 2 or 3 critical care, the median length of stay was 1 day. These data suggest a dramatic change from the EVAR-1 assumptions.	We have obtained means and SDs for these data for EVAR and OSR from the NVR. These show that resource use with EVAR and OSR have reduced by a very similar amount since the EVAR-1 trial, with the result that – far from being a dramatic change – the difference between the 2 is essentially unchanged. Details are provided in **Theme 6a**.
				Hospital Episode Statistics (HES) and PLICS data: 2016/17 Hospital Episode Statistics published by the NHS report a mean length of stay (excluding intensive care days) of 2.54 days (for procedure code YR04Z - Endovascular Repair of Abdominal Aortic Aneurysm).	For the reasons stated in the consultation draft (as you have cited above), we consider NHS Reference Costs, from which the 2.54-day mean is drawn are not, in this case, reliable. However, if we were to use these data, then we should also use the analogous figure for OSR, which is 4.46 days – this would represent a much smaller difference between EVAR and OSR than was assumed in the base-case model reported in our consultation draft.
				2013/14 PLICS data, which report critical care costs, report an average of £545 of critical care costs for this procedure code.	We find it challenging to reconcile PLICS data with evidence reported elsewhere. Nevertheless, we note that, in the

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				On the basis of a 90%/10% split between HDU and ITU utilisation (based on NVR data) and cost assumption of £718 and £1,017, per the NICE model, this results in approx. 0.73 days in critical care – for total resulting length of stay estimate of 3.27 days.	2014/15 findings, the total average finished consultant episode costs are £14,214 for EVAR and £11,228 for OSR, a difference of £3,000, which is somewhat more than estimated in the HE model reported in the consultation draft.
				Preliminary analysis of the most recent HES data year (April 2017 to March 2018) reports a mean length of stay for elective (unruptured) cases of 3.0 days (Diagnosis code I714 - Abdominal Aortic Aneurysm, without mention of rupture; procedure codes L271 - Endovascular insertion of stent graft for infrarenal abdominal aortic aneurysm or L281 - Endovascular insertion of stent for infrarenal abdominal aortic aneurysm), including critical care time of 0.79 days.	As noted above, we are concerned about the trustworthiness of HES data, in this area. In any event, the absence of comparative data showing how the same datasource estimates OSR resource use makes it impossible to use these data.
				Additional sources These general trends in EVAR length of stay reductions are convincingly documented through other data as well.	As explained above, the relevant question is not whether postoperative EVAR resource use has reduced – we accept that it has; it is whether EVAR resource use has reduced to a greater extent than postoperative OSR resource use – it appears that it has not.
				Medtronic's publicly available regulatory submission to the U.S. Food and Drug Administration (FDA) in 2008 states a mean length of stay of 3.6 days, compared to a historical control (SVS) of 8.2 days. Since, then, procedure and device improvement can be expected to have further contributed to reductions in length of stay to durations	These data do not provide any comparison with OSR, so are irrelevant for this purpose.
				Length of stay reported in the Dutch Surgical Aneurysm Audit 2014 That audit found EVAR to be associated with mean ward	The data cited by Burgers et al. (2016) are unpublished figures from the Dutch Surgical Aneurysm Audit. Whilst we have no way of checking their provenance, they appear to be

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				stay of 3.70 days and critical care stay of 0.27 days (Burgers et al., 2016).	unadjusted registry data. The EVAR numbers are similar to those reported in the NVR (3.89 days and 0.42 days, respectively); the analogous OSR figures are also similar (2.7 days' critical care and 8.8 ward bed-days, compared with 3.4 days and 7.1 days in the NVR).
				More recent data from the Global Registry for Endovascular Aortic Treatment (GREAT) registry (not yet published but made available through study sponsor and ABHI member W.L. Gore & Associates) report on a subset of n=1,479 subjects treated with the Gore Excluder with C3 for abdominal aortic aneurysms. The mean hospital stay for these subjects was 3.79 days (total length of stay including any critical care)	These data do not provide any comparison with OSR, so are irrelevant for this purpose.
				Potential impact of using contemporary LOS estimate: Using the 2016/17 HES data-derived EVAR length of stay instead of the base case assumptions would lead to an approximate reduction in EVAR costs of more than £2,000.	This is only true if the estimates for EVAR are altered in an attempt to reflect current-day practice while the estimates for OSR are fixed at their historical level. Using 2016/17 HES data-derived length of stay for **both** EVAR and OSR would lead to an **increase** in net additional costs associated with EVAR.
				Theatre Time	
				The base case assumes 191 minutes of EVAR and 215 minutes of OSR theatre time. The cost per hour of theatre time is estimated at £831. The 2008 FDA submission based on Medtronic TALENT found a mean procedure duration of 166 minutes, compared to historical control (SVS) of 225 minutes. Again, this suggests a trend with newer devices and increased procedural experience that likely has evolved further between 1999-2004, 2008, and now current practice in 2018. Data from the Dutch Surgical Aneurysm Audit 2014 (referenced in	For a discussion of intraoperative resource use, please see **Theme 5**. In exactly the same way as for length of stay, it is insufficient to assert that intraoperative resource-use with EVAR has reduced; rather, it is critical to establish how the **difference** in intraoperative resource-use between EVAR and OSR may have changed since the detailed, balanced data collection in the RCTs.

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				Burgers, Vahl et al., 2016) reported mean procedure duration of 146 minutes. Data from the European C3 Module of the Global Registry for Endovascular Aortic Treatment (GREAT) (Verhoeven et al., 2014) report a median procedure time of 120 minutes, based on a sample of n=400 patients treated.	Non-comparative data such as Medtronic's FDA submission and the GREAT registry are therefore not useful. The Dutch estimates provided by Burgers et al. (2016) are referenced to both the unpublished Dutch Surgical Aneurysm Audit and to 'expert opinion' – it is impossible to tell what these numbers represent. However, we have explored their impact in sensitivity analysis – see **Theme 5**. The PLICS data to which you direct our attention above suggest that mean theatre-time for EVAR in 2014/15 was around 237 minutes. Equally, however, this source suggests that OSR operation times have risen similarly (to around 300 minutes), although we think this category is likely to include complex AAA anatomy, where the EVAR numbers are not.
				Potential impact of using contemporary theatre time estimate: Just relying on the TALENT data of 2008 would reduce EVAR procedure cost by an additional £400. If the more recent Dutch data are considered, these additional savings would amount to more than £620. Using the median data from the GREAT registry would result in an even higher savings estimate of £983.	Again, we would argue that it is invalid to adjust one side of the equation but not the other.
				We suggest NICE consider more recent data than EVAR-1 also for this parameter, in an attempt to reflect current practice parameters as closely as possible.	As detailed in **Theme 5**, we conclude that there are no relevant, contemporary, casemix-adjusted data for this parameter. In our base case, we retain our reliance on randomised evidence, as these data at least reflect reliably matched cohorts in a UK setting, and there are no more current data with these advantages. However, we explore the impact of more contemporary, albeit methodologically less

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					reliable, data in sensitivity analysis and find that it has no material impact on model outcomes – see **Theme 5**.
				In addition, the National Vascular Registry suggests 6.8% of OSR patients had to return to the theatre, vs. 2.0% for EVAR patients. The NICE model does not seem to take return to theatre into account. Inclusion would arguably benefit EVAR when considering incremental costs.	We understand that, depending on the precise timing of these episodes, they should be accounted for in either the estimates of intraoperative resource use from the RCTs or in reintervention rates. Therefore, applying an additional provision for such cases would double-count the costs with which they are associated.
				Rehabilitation Costs	
				The economic model did not formally consider rehabilitation, use of rehab could be expected to be higher in the OSR cohort than the EVAR cohort, and the degree of resource utilisation (length in days, if rehab is used) would be higher. In turn, this could be expected to lead to additional incremental costs (or savings) that are currently not explored in the model.	The committee broadly accepted this hypothesis, as it chimed with members' own experience. They noted, however, that there are few data available to explore the issue in the HE model. Nevertheless, using casemix-adjusted comparative observational evidence from a US setting and combining this with descriptive UK data and evidence on resource-use from the emergency setting (IMPROVE), we were able to estimate a best-case scenario for the cost-savings that might be achieved with EVAR, in this area. Although the amounts estimated were nontrivial, they did not make anough difference to bring EVAR close to cost effectiveness, compared with OSR. For details, see **Theme 6b**.
				Reinterventions	
				The committee has noted they are not aware of any evidence supporting the notion that the rate of reinterventions has decreased with newer EVAR stent graft generations, compared to older EVAR devices.	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of

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				However, one paper that supports such a conclusion is Verzini, Isernia et al., 2014. In this single-centre retrospective observational study, n=882 newer devices (Endurant, Zenith, second-generation Excluder, and second-generation Anaconda) were compared with n=530 old devices (AneurRx, Talent, first-generation Excluder, first-generation Anaconda, and Fortron). Even though in the newer device group the AAA diameter was larger (55.7 vs. 53.2 mm, p<0.0001) and the patients were older (p<0.0001), freedom from reintervention after 7 years was different between the two groups (83.6% vs. 74.2%, respectively, p=0.015). We believe that the model needs to reflect these observed reductions in reintervention rates. The Verzini et al. 2017 study, subsuming evidence from older and newer generation devices, reports 83.5% freedom from reintervention at six years. The contemporary data from the GREAT registry (made available through W.L. Gore & Associates) report 93.5% freedom from reintervention at 6 years, suggesting further reductions in reintervention rates in current practice. Potential impact of using contemporary reintervention estimate Of note, the NICE model, in its elective (unruptured) infrarenal based case, assumes freedom from reintervention of 64% (based on model tracker "patients who have not experienced a serious AAA-related reintervention"). This suggests the NICE model calculation might overestimate reinterventions by more than 50%. Based on the NICE model-provided estimate of £4,719 of reintervention costs (incl. hernias), this suggests further that actual reintervention costs might be more than £2,000 lower than the model-projected reintervention costs.	operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 8**. Thank you for pointing out this anomaly. Having explored the issue, we accept that there was inconsistency in the way reintervention rates were calculated in the model made available at consultation. This has been revised better to reflect the evidence from EVAR-1; see **Theme 8**. The result of this revision and the application of a reduced rate of reinterventions for EVAR to reflect contemporary practice (see above) is that the difference in reintervention costs between EVAR and OSR has, indeed, fallen by an amount approaching

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					£2,000. However, this is insufficient to rebalance the analysis in favour of EVAR: OSR remains the dominant option.
Association of British HealthTech Industries (ABHI)	Draft guideline And Economic Appendix and Model	9-10	172-182	**Inclusion of our recommended assumptions would yield an ICER below the NHS Threshold** Our internal analyses suggest that the combination of changes in peri-operative mortality and post-perioperative (long-term) mortality to the outlined updated parameters would lead to an overall QALY gain for EVAR in the order of 0.17 QALYs (as opposed to -0.16 QALYs in the current model). Consideration of the outlined cost updates (including, but not limited to approx. £500 reductions in theatre time costs, £2,000 in length-of-stay-related costs, and £2,000 in reintervention costs, for total of £4,500) would yield an ICER well below the willingness-to-pay threshold of £20,000 per QALY gained, rendering EVAR cost-effective compared to OSR. Importantly, consideration of all factors might lead to additional savings that would render EVAR dominant, i.e. associated with improved outcomes at lower overall cost.	The committee accepted some of the criticisms that you and other stakeholders have made of the parameters reported in the consultation draft, and the analysis has been revised accordingly. However, the cCommittee did not accept your suggested use of some other parameters, as they concluded that theyse had little or no empirical basis. We respond to each of your suggestions, in turn, where they appear in detail. We would also note that we are not the only investigators to conclude that EVAR represents poor value for money in the infrarenal elective setting. As outlined in HE.4.1.4.1, every analysis performed from an NHS prerpective concludes that EVAR is associated with an ICER considerably in excess of £20,000/QALY, when compared with OSR, and several of these other analyses share our conclusion that the most likely net result is that EVAR is not only more expensive than OSR; it is also associated with worse net outcomes.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	3	40	There is no evidence for population screening of women for abdominal aortic aneurysms in the same way as the programme for men (Thompson SG et al, NIHR HTA 14/179/01, report in press). There is no robust evidential basis on which to base a recommendation of targeted or opportunistic screening of at-risk women over the age of 70; in fact we would be concerned that the selected screening of women over the age of 70 with COPD, coronary, cerebrovascular or peripheral arterial disease is likely to deliver a cohort of women with AAAs, the majority of whom are then not sufficiently fit to tolerate open repair as recommended in these draft guidelines.	The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging rather than a screening programme actively inviting people who are at risk for imaging. The committee considered that this approach of opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed.

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Bedford Hospital NHS Trust	Draft guideline	4	56,57	A 5cm aneurysm should be scanned every 3 months. They are likely to miss there scan If they are seen in the clinic 12 weeks after the referral. Guidelines also make no distinction between a 5cm and 5.4cm aneurysms. We would suggest that the any patient with an aneurysm of 5 cm or more is seen within 4 weeks of referral.	Thank you for your comment. The committee drafted recommendations to reflect current expectations in the NHS AAA screening programme. In the screening programme, aneurysms 5.5 cm or larger are referred to be seen by a vascular specialist within 2 weeks of diagnosis. Aneurysms less than 5.5 cm in diameter are not referred to a regional vascular service but are seen by a vascular nurse in the screening programme (who is also member of a regional vascular service) to obtain some clinical input/advice. This clinical input is usually obtained within 12 weeks of diagnosis. The committee were mindful that women with smaller aneurysms are not seen by the screening programme or referred to the regional vascular service. Therefore, there is some need for clinical input. This logic underpinned their recommendations.
The Vascular Society of Great Britain and Ireland	Draft guideline	7	127	A surveillance interval of 2 years does not allow for the detection, and referral, of rapid expansion in size as defined. (>1cm /year). This anomaly needs to be resolved. Rapid expansion of a small AAA (<4.5cms) is an extremely rare indication for AAA repair. The rapid growth criteria could be limited to the >4.5 cm AAA's who are being scanned every 3 months.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend

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					that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	7	126	We note that the committee propose to recommend that AAA measuring between 3.0cm and 4.4cm be ultrasound scanned every 2 years, with the frequency increasing to 3 monthly for AAA measuring between 4.5cm and 5.4cm. This is presumably to align more closely with NAAASP intervals, although we are not aware of any robust evidence to support such a proposal; in fact, we understand that NAAASP are considering lengthening the surveillance intervals from 3 months for patients with 4.5cm AAA. Our unit currently scans AAA patients with diameters of 3.0cm to 4.4cm on a 12 monthly basis, moving to an interval of 6 months for 4.5cm to 4.9cm, and then 3 monthly only at 5.0cm. We would anticipate that the proposed change in the surveillance protocol would result in a significant increase in the number of surveillance scans we would need to perform, having an impact on our vascular scanning department capacity, costs and service.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"

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Rouleaux Club	Draft guideline	9	181-182	Currently UK trainees have less open experience and greater endovascular exposure, with less than a third of all infra-renal AAA repairs that trainees are involved in undergoing open surgical repair (Rouleaux Club/VERN trainee survey, 2017). In contrast, implementation of the guidelines will mean that future trainees will struggle to gain the necessary skills and experience to be able to perform EVAR in the emergency setting to a competent level due to the loss of elective EVAR training. Simulation based training is a good adjunct but not a replacement for clinical experience.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	9 26	179 624	We accept the committee's assertion that there is no evidence that EVAR for people with an unruptured infrarenal AAA provides long-term benefit compared with open surgical repair. We would contest that the published literature does not, however, support the contrary argument. The trials on which this assertion is based were not sufficiently powered to derive these long-term conclusions. The early iteration stent devices that were used in the original EVAR trials have been superseded with improved technology, overcoming many of the issues that led to stent failure and the necessity for secondary interventions in the early study	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Nevertheless, it is the committee's confident interpretation of randomised and observational evidence that EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**. For specific comments on the statistical power of the elective RCTs to identify differences in long-term survival, please see **Theme 9b**. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				populations. In addition, vascular specialists are now far more experienced and proficient at planning and performing EVAR than when the original stents were implanted, and as a collective we are generally no longer on the primary "learning curve". As evidenced by the National Vascular Registry, the 30-day mortality rate for EVAR patients has dropped in the UK since the original trials were conducted and to a far greater extent than the fall in mortality for open repair (30-day mortality in EVAR1: 1.8% EVAR, 4.3% open repair; in-hospital NVR 2017: 0.4% EVAR, 2.9% open repair). Furthermore, many of the indications for re-intervention in the early EVAR experience have now been recognised by modern vascular practice as benign, all of which results in a compounded reduction in long term complications, secondary intervention and associated costs. It should also be considered that vascular practice has evolved since the original EVAR trials were conducted. Post-EVAR lengths of stay are now far shorter than in the trials, and there is no routine requirement for post-operative care in an environment other than a level 0 surgical ward, meaning that the in-hospital care costs are much reduced in modern vascular practice.	The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to support decision-making – see **Theme 3a**. The committee accepted that modern practice features fewer reinterventions following EVAR than were observed in the RCTs. The model developed to support their decision-making has been revised accordingly – see **Theme 8**. For discussion of perioperative resource use associated with EVAR and OSR, please see **Theme 6**.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	9 10	179 196	The NICE guidance will effectively preclude EVAR for the treatment of unruptured AAAs (recommending open repair unless there are anaesthetic or medical contraindications, not offering EVAR if open repair is suitable and not offering EVAR if open repair is unsuitable), yet the guidance recommends considering EVAR for patients with ruptured infrarenal AAA. We are concerned that from a training perspective this will not be a sustainable model beyond the current generation of vascular specialists who are already well-versed and	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				experienced in planning and delivering elective EVAR. We struggle to see how a vascular specialist in the future will become sufficiently proficient and experienced at planning and performing EVAR if the procedure is only recommended for the most unwell patients in the direst of clinical situations (notwithstanding that the NICE guidance will inevitably lead to a greater number of patients presenting with ruptured AAA). It is difficult for us to see how vascular specialists will be trained in this emergency procedure in the absence of any elective EVAR practice.	
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	9	179	We are disappointed that there has not been any patient and public involvement in generating the proposed guidance for the management of unruptured AAA. We would anticipate a significant psychological and emotional impact for patients diagnosed with AAA measuring 5.5cm or greater, not fit for open repair, for whom the NICE guidance would recommend no intervention. We would advocate that the views be considered of patients with non-treated AAAs and also the views of patients who have undergone intervention, so that this could fully inform a quality of life assessment.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. . The guidance committee included 2 patient representatives: people diagnosed with AAA who underwent elective repair procedures. During guideline development, these individuals were routinely consulted and actively involved in discussions to gain valuable insights on a patients' perspectives on diagnosis, monitoring and treatment of AAAs. The draft guideline consultation also allowed an opportunity for patients groups to feedback and inform the revision of the recommendations. In addition, see Theme 13 for further information on the impact on quality of life of living with an untreated AAA.

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University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	9 10 27	179 181 183 637	We note that the committee do not recommend EVAR for unruptured AAA in patients who are not fit for open surgical repair, primarily because it cannot be considered an effective use of NHS resources. We are concerned that individual patients may, however, consider EVAR to be personally cost-effective, particularly if the alternative is to wait for their AAA to rupture before they can be treated. This could drive a two-tier system where patients who can afford to finance their own care will be able to pay for EVAR privately; those who cannot afford private treatment will be left to await AAA rupture before they can then be treated on the NHS. In addition to the psychological effect on individual patients, we are concerned about how this two-tier system will be perceived by the public more widely.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the potential impact on quality of life of living with an untreated AAA, please see **Theme 13**.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	9 7	177 126	The guidelines suggest that patients who have AAA measuring greater than 4.0cm, with an increase in diameter of greater than 1.0cm in 1 year, be considered for intervention. However, up to 4.4cm the guidelines recommend a surveillance interval of 2 years; we are unclear, therefore, how an annual increase of 1.0cm will be detected.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than

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					specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
The Vascular Society of Great Britain and Ireland	Draft guideline	10	183	**Recommendation 1.5.4.** The Vascular Society has a number of concerns relating to recommendation 1.5.4. We believe this will have the biggest impact on current practice and be the most challenging to implement. This recommendation severely limits the use of EVAR in the elective repair of an AAA. People with an AAA will be offered open surgical repair (OSR) or no intervention. This is a major change from current practice in the UK where 70% of AAA repairs are performed using EVAR (NVR 2017 report). In 2008 the UK was a major outlier in the Vascunet report on AAA repairs from Europe and Canada. The UK open elective mortality was 7.9%, the next worse was Denmark at 4.5%. A hugely successful AAA quality improvement programme was undertaken, led by the Vascular Society, and we have seen a fall in open AAA mortality to 2.9% in 2016. A number of factors have led to this improvement but of greatest importance has been the availability of EVAR in addition to OSR to tailor intervention to the needs of the patient. To lose this clinical choice totally will lead to an increase in the UK open AAA mortality taking us back towards where we were in 2008. We agree with the committee that there are no validated fitness tests, risk models or scoring systems (recommendation 1.4.3) that can predict which patients are suitable for OSR on	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual

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				anaesthetic or medical grounds. But recommendation 1.5.4 suggests that this can be done and patients fall clearly into 2 groups for OSR or no intervention. A recent study on fitness testing highlights that this is not the case with up to 60% of patients having "indeterminate fitness" (Rose GA 2018). This was despite the use of cardiopulmonary exercise testing. Data has been submitted to the committee from University Hospital Warwick in response to this consultation showing that survival is not predicted by CPEX testing, and patients turned down for repair have much worse survival than those with AAA repair. The current recommendations risk repeating these poor outcomes for patients turned down after their fitness test on a national scale. Repair would offer better survival. This inability to accurately determine fitness for AAA repair creates 2 major clinical issues. Firstly, there will be high risk patients who undergo OSR. Currently these patients are treated with EVAR. The mortality rate in this cohort of higher risk patients undergoing OSR will be significantly higher than the current 2.9% (NVR report 2017). Secondly patients will be turned down for intervention when in fact they are fit enough for a repair. This uncertainty was evident in the EVAR 2 trial where the no intervention arm of the trial had a 34% crossover rate with successful outcomes. Fitness "inflation" was seen where enlargement of the AAA in the no intervention arm, led to patients being declared fit for repair.	has to be judged by vascular MDTs in the light of their comorbidities. The relevance of the cited publication by Rose et al. (2018) is unclear, as it review risks factors for colorectal surgery. The authors' conclusion that CPET metrics cannot be used as a sole criterion to identify a population for whom surgery is suitable is one that our reviews share. As you note, the predominant evidence underpinning the committee's decision-making is the EVAR-2 RCT, which stipulated that fitness for OSR should be decided at the local level, but provided some guidelines as to likely contraindications for open surgery (Brown et al. 2004). The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). We are unable to make detailed comments on the unpublished data submitted (from Coventry, rather than Warwick) without access to a full description of its methods and results. However, we would note that it is inevitable that people who are deemed ineligible for any repair (regardless of CPET result) would have worse survival than their fitter counterparts; this would be the case whether the fitter people underwent EVAR or not. This does not help us to understand the balance of benefits and harms of EVAR among people for whom OSR is unsuitable, but for whom EVAR would currently be considered.

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					Nevertheless, in view of these uncertainties, the committee agreed that future guidance would be much improved if more specific recommendations could be given regarding people to whom repair should be offered. They were mindful of this when making 2 research recommendations: 1 regarding optimal thresholds for repair (which may vary between people whose comorbidities and life expectancy imply a different balance of risks and benefits) and 1 regarding the role of EVAR in people from whom OSR is unsuitable because of their comorbidities (see below).
				We argue that between "fit" and "very unfit" there is a large middle group of patients who benefit from EVAR. To deny them any intervention relies entirely on the assumption in this guidance that the cohort of patients in the EVAR 2 trial are representative of the whole population and the results therefore translate to the clinical setting today. Studies of Medicare patients (Giles et al, JVS 2009, Egarova JVS 2009) and VSGNE and VQI (Eslami JVS 2017, 2018) have failed to identify a subset of patients currently undergoing EVAR with perioperative mortality similar to that seen in the EVAR-2 trial other than Egarova et al who found that < 1% of all Medicare patients undergoing EVAR from 2000-2006 had a predicted operative risk similar to that seen in EVAR-2. EVAR 2 patients were selected in the larger vascular units of the day, proficient in EVAR, and therefore able to take part in the trial. The results reflect that select practice, and do not necessarily translate to all vascular units in the UK. In the "evidence review K, lines 562-571" the committee acknowledge the limitations of the EVAR 2 trial. For example,	On discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria regarding the people for whom OSR should be deemed unsuitable can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They amended their recommendation to state that EVAR should only be offered in this population as part of an RCT comparing EVAR with no intervention, and made a new research recommendation noting that such a study would be helpful.

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				patients not receiving their allocated treatment, 34% crossovers, high EVAR mortality rate (9%). We strongly believe that this dated trial from 19 years ago does not provide us with enough evidence to abandon EVAR altogether. The EVAR 2 trial authors were also of the same opinion. In our member survey 158/240 (67%) disagreed with the recommendation "do not offer EVAR when OSR is not suitable". Given these uncertainties we believe that EVAR should still be retained as an option for AAA repair when open surgery is not suitable. These should be on IFU and criteria can be set to prevent inappropriate use of EVAR. The Vascular Society would be able to work with the committee to help define these criteria. We would strongly support fitness testing and risk modelling as research recommendations for this guidance. Currently however, we lack a credible evidence base which would allow us to segregate patients into OSR or no AAA repair. **Refs** Rose G et al., British Journal of Anaesthesia 120(6): 1187-94, 2018. Vascunet 2008 report https://www.vascularsociety.org.uk/_userfiles/pages/files/Document%20Library/ESVS_VASCUNET_REPORT_2008_BW.pdf Giles KA et al J Vasc Surg 2009 : 50 (2) ; 256-62 Egorova N et al J Vasc Surg 2009 : 50 (6) ; 1271-9 Eslami MH et al J. Vasc. Surg. 2017 : 65 (1) ; 65-71 Eslami MH et al J. Vasc. Surg. 2018 : 67 (1) ; 143-50	

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European Society for Vascular Surgery (ESVS)	Draft guideline	10	183	Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition. We agree with the Advice submitted by the UK Vascular Society	Comment noted.
Bristol Bath Weston Vascular Network (North Bristol NHS Trust)	Draft guideline	10	183	**Recommendation 1.5.4.** **'Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition'** Implementation of recommendation 1.5.4 will result in a significant proportion of patients being turned down for AAA repair by our network MDT. These are patients who we would currently consider as benefitting for EVAR, fully cognisant of the longer term risks of re-interventions and late rupture. We recognise the breath of the sensitivity analyses performed in the incremental cost effectiveness analyses. These models recognise the poor long term-survival of patients in whom EVAR has been utilised. However, not all anaesthetic and medical conditions are associated with reduced long-term survival. Such patients can represent a real challenge for open AAA surgery. The following patient groups we consider to have high peri-operative risk for open surgical repair, but might benefit from endovascular repair at an acceptable cost: Hostile abdomen (including previous peritonitis, stoma formation and incisional hernia). Previous aortic surgery	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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				Inflammatory AAA	
Association of British HealthTech Industries (ABHI)	Draft guideline	10	183 - 185	**Guidance will lead to patients identified with life threatening aneurysm being turned down for treatment.** The national screening programme (Public Health England) has been highly effective in the UK, reducing the numbers of patients being admitted for ruptured aneurysms. ABHI believe it is perverse to subject individuals to screening and then turn them down for treatment (if they are not suitable for OSR), hence leaving them without a treatment option and burdening them with the anxiety of a potential rupture. There is no data to support this screening strategy without commissioned EVAR procedures and the psychological impact has not been investigated in any trial setting.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
Rouleaux Club	Draft guideline	10	183-185	Our job is also to counsel and inform patients of often complex treatment options. These guidelines will leave doctors to explain to their patients that although they may be unfit for open repair, but fit for EVAR, they will be refused elective treatment. But they may then be eligible for EVAR in the case of rupture. Patients should be informed of this at initial consultation, rather than in the emergent setting and this should be reflected in the recommendation.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For information on the impact on quality of life of living with an untreated AAA see Theme 13.

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					The committee agreed that it is important that patients with AAA are aware of the care pathway and the options that are likely to be suitable for them.
The Vascular Society of Great Britain and Ireland	Draft guideline	10	186	**Complex EVAR as part of a RCT in patients fit for OSR.** We agree that robust data does not exist in relation to complex EVAR. Further study is required in this area. The term "complex EVAR" needs some clarification. This is a term used for the endovascular treatment of aortic aneurysms using fenestrations and branches because the AAA is close to or involves renal and visceral arteries. Open surgery for these AAA's is also more complicated with clamping required above renal and visceral arteries depending upon the extent of the aneurysm (juxta renal, suprarenal, type 4 thoraco-abdominal AAA). There is therefore a range of open and EVAR requirements for these aneurysms that needs specific consideration. The reported open surgical mortality rates vary considerably which may reflect the varying mix of "complex" AAA's treated in each series. Better mortality rates from juxtarenal, worse for type 4 repairs. Determining precise open mortality rates for each AAA type is difficult since procedural coding is not always well reported. Current data from the NVR reports an open mortality rate of 18.4% for complex AAA versus 3.5% for EVAR. Whilst we acknowledge that these will be open repairs largely where EVAR was felt not to be possible for anatomical reasons, and therefore a select group, the open mortality rate is still alarmingly high. An analysis of HES data for suprarenal AAA repair in England reports an open mortality rate of 14%(Karthikesalingam A 2013). In the evidence review K (lines 788 – 809) the committee decide that these high mortality rates are not representative but offer no data to support that view. In the absence of good data, the	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. For discussion of evidence available of perioperative mortality with EVAR and OSR for complex AAA, please see **Theme 4**. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				above reports of high open mortality have to be taken into consideration, and cannot simply be ignored. A major concern with the recommendation that no complex EVAR should be preformed outside of a randomised controlled trial, is the lack of surgical equipoise to randomise to open repair, knowing the high associated mortality rate. This is particularly so with open surgery beyond juxtarenal. We are aware that the NIHR-funded UK COMPASS registry with 5-year follow-up is designed to provide better data on these procedures. A recommendation to make entry into such a registry mandatory for complex EVAR would be a more pragmatic way of gaining more much needed data on the outcomes and costs of these procedures. Refs Karthikesalingam A et al 2013 PLoS ONE 8(5): e64163. doi:10.1371/journal.pone.0064163	
Association of British HealthTech Industries (ABHI)	Draft guideline	10	186	**FEVAR, off-label use of EVAR devices, physician-modified devices and various combinations of chimney and snorkel techniques are all different and should be stratified separately.** Complex EVAR is a term used for the endovascular treatment of aortic aneurysms using fenestrations and branches because the AAA is close to or involves renal and visceral arteries. Open surgery for these AAA's is also more complicated with clamping required above renal and visceral arteries depending upon the extent of the aneurysm. There is therefore a range of open and EVAR requirements for these aneurysms that needs specific consideration and clarification.	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. An exploratory analysis from the HE model focusing on fEVAR alone was deemed possible as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details.
Bristol Bath Weston Vascular	Draft guideline	10	186	**Recommendation 1.5.5**	We agree that future research should distinguish between different complex AAA anatomies and the types of endovascular approach that each demands, and we have

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Network (North Bristol NHS Trust)				**Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.** Along with many other vascular networks we now rarely perform open supra-renal AAA repair due to the high mortality and morbidity. At least in the short- to medium- term patients treated using complex endovascular techniques regain a better quality of life. Any trial must differentiate juxta-renal aneurysms (i.e. those with an infra-renal aortic neck of 10 mm or less) and para-renal aneurysms (i.e. those involving the renal ostium) from true thoraco-abdominal aortic aneurysms that involve the mesenteric origins and would require a supra-coeliac aortic clamp for open repair. The **GLOBALSTAR** registry is collecting valuable data and the NIHR-funded **UK COMPASS** registry with 5-year follow-up is designed to provide better data on these procedures. It is perhaps preferable to collect long term, high-quality, data from these patient registries than embark on an RCT for which there is no equipoise.	added detail to our research recommendation to emphasise this. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Association of British HealthTech Industries (ABHI)	Draft guideline And Economic Appendix and Model	10	186-188	**[This and the following two comments concern unruptured complex AAA repair.]** As a preface, we recognize that not all complex cases can be treated with EVAR devices but only those who have a suitable anatomy. Consequently, section 1.5.5 only applies to those patients who are amenable to endovascular treatments, and where therefore a decision has to be made whether these particular patients should be treated with either OSR or EVAR. It is also important to highlight that not all complex devices	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				have to be custom-made and some EVAR device types can treat some, but not all, complex cases. We also understand that the clinical evidence comparing repairs of complex AAA is currently still somewhat limited compared to evidence on infrarenal EVAR, as complex cases volume is lower overall	We have undertaken a rapid review of casemix-adjusted observational publications to supplement the evidence-base available to the committee – for details, see **Theme 4b**. While it is true that there are fewer cases of complex AAA than infrarenal, the volume is sufficient that meaningful research is possible – over 2,000 procedures were reported to the NVR in 2014–16.
Association of British HealthTech Industries (ABHI)	Draft guideline and Economic Appendix and Model	10	186-188	**A single cost assumption for all customised and non-customised complex EVAR devices is unreasonable.** In the health-economic model, a relatively high EVAR device price £15,686 is being assumed for all complex cases. While the broad range of devices which include, in current practice, customised and non-customised devices, makes it challenging to assess a realistic base case cost estimate, we suggest NICE explore the effects of variation in this input parameter using the full range of costs for EVAR technologies currently used in complex endovascular AAA repair. Further, the committee might want to consider, in subset analyses, the different types of complex cases with their different anatomic challenges, and how these affect respective device and resource utilisation.	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. Figure HE59 in the HE appendix of the consultation draft showed the relationship between average complex EVAR device cost and cost–utility results. We have updated this analysis in Figure HE133. It is important to emphasise that this analysis should not be interpreted as identifying the threshold device cost below which it would be cost effective to offer EVAR in any individual case. It is likely that cases in which relatively inexpensive endovascular grafts can be used are also those that would accrue lower costs if OSR were used. Therefore, it must be understood that this analysis shows the threshold cost below which the average EVAR device would have to fall before it could be cost effective to adopt a model in which all complex AAAs received EVAR. There was only 1 area in which data that could potentially be used to inform a subgroup-specific analysis were identified – juxtarenal/pararenal AAAs that are amenable to fenestrated EVAR. An exploratory analysis from the HE model focusing on

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					fEVAR alone was presented to the committee as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details.
Association of British HealthTech Industries (ABHI)	Draft guideline and Economic Appendix and Model1	10	186-188	**It is unreasonable to assume that the cost of complex OSR is equal to the cost of infra-renal open surgical repair** For OSR costs, the current base case mentioned in the health economic model assumes procedure costs of £10,921, same as the infra-renal model. We could not identify any evidence that supports this assumption made by the committee. In should be noted that some complex cases repaired openly do require the same left medial visceral surgical exposure with supra-visceral clamping, renal artery bypass, and/or re-implantation with consequent more severe (or even repeated) physiological insult which might not just impact the peri-operative mortality but also translate to longer lengths of stay, short-term complications including more wound healing problems and acute kidney injury, or even higher long-term mortality. Contrary to the current assumption, service level reporting at the Liverpool Heart and Chest Hospital (the highest volume complex open aortic centre in the UK) demonstrated that the cost for open repair of a suprarenal/extent IV aneurysm in 2012 was £27,111, equating to £31,046 in 2018 once adjusted for inflation (personal communication: Mr. Donald Adam, Consultant Vascular Surgeon). Data from NHS Scotland for the National Thoracoabdominal Aortic Aneurysm Service included information on some	On reviewing stakeholder comments including this one, the committee agreed that its decision-making would benefit from additional exploration of perioperative costs related to complex AAA repair – both EVAR and OSR. Therefore, potentially relevant evidence on intraoperative and postoperative resource-use, including registry data and observational publications, was reviewed and its impact on cost–utility results explored (see **Theme 5** and **Theme 6**, respectively). We also accounted for the need for rehabilitation (see **Theme 6b**). The assumptions that were made in revising the HE model all favoured EVAR, some to a degree that the committee considered palpably unrealistic – for example, using unadjusted length-of-stay data from the NVR when it reflects a small number of highly selected OSR cases that are almost certain to be disproportionately complex. The result of these revisions was to increase our estimate of costs for a primary complex OSR procedure by around 50% – from £10,662 (see table HE52) to £15,705 (see table HE113), while our estimate for complex EVAR did not meaningfully change (rising by <1%). Even though the committee agreed that the analysis was optimistic for EVAR, it did not result in an ICER, compared with OSR, that could be considered to represent an effective use of NHS resources.

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				procedures that are relevant to the scope of this guideline (National Health Service Scotland, 2007). In the Scottish centre, over 59% of procedures were performed for complex AAA which were reported as suprarenal and extent IV aneurysms but, from the fact that the majority did not have a renal artery bypass or re-implantation, it is reasonable to assume that some of these would have been considered to be para-renal AAA. The cost of complex OSR (excluding extent I-III/V TAAA) in the centre can be ascertained from a subsequent publication (Richards et al., 2010). Using the data in the publication to represent the average patient and applying the English reference costs used by NHS Scotland in 2007, the crude cost per case in 2007 was £24,666 which equates to £33,188 in 2018 after inflation, a figure remarkably similar to the actual cost observed in Liverpool. The original and subsequent funding for the National TAAA Service in Scotland has been based on cost calculations such as these with the service currently receiving over £1 million per annum to treat 25-30 patients by open surgery, resulting in mean costs in the region of £40,000 per case (Chalmers, 2012). Given that the published or other available evidence points towards higher OSR procedure costs for complex cases, it seems reasonable to revisit this assumption not just in sensitivity analyses but importantly also for the base case, as it might have a pronounced effect onto the calculated incremental cost-effectiveness ratio.	These data represent the best-available evidence-based estimate of the average cost of EVAR and OSR for complex AAAs. However, because complex AAA is a heterogeneous category (see **Theme 10**), there will inevitably be a broad range of costs associated with more and less intricate procedures. Citing anecdotal evidence as to the expenses incurred with OSR in the most complex cases does not – in the absence of any counterfactual data regarding the costs of EVAR in directly analogous cases – help us to understand what the incremental costs associated with the approaches might be. Most thoracoabdominal aneurysms are outside the scope of this guideline, so the cited Scottish experience is of limited relevance. Those cases that would have fallen within our remit are obviously likely to fall in the upper end of complexity and cost, with the implications noted above. Having reviewed Chalmers & Nimmo's paper (2012), we note that the service described also provided EVAR for type IV thoracoabdominal aneurysms; therefore, the cited total budget does not tell us anything about the relative costs of different approaches.
The Vascular Society of Great Britain and Ireland	Draft guideline	10	189	**Recommendation 1.5.6. Do not offer Complex EVAR to patients unfit for OSR**	There are no data to suggest that people with complex AAA have worse outcomes when receiving no intervention than people with infrarenal AAAs. On the other hand, there is evidence that people receiving complex EVAR are at higher

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				This recommendation is made using the same rational as recommendation 1.5.4. However unlike, 1.5.4 there is no actual randomised trial, such as EVAR 2, to base this recommendation on. We have similar concerns to those expressed above in comment 3. Furthermore with more extensive AAA's, the determination of "fitness" on anaesthetic and medical grounds will be even more demanding. In reality the bar will be set higher for a juxtarenal/suprarenal open AAA repair than for an infrarenal repair. Patients will need to be fitter to be accepted for the open procedure. Patients deemed unfit for complex open repair will not have the same level of co-morbidities that led to patients being deemed unfit for open repair in the EVAR 2 trial. We have a different population. We cannot assume the EVAR 2 no intervention mortality rate applies to patients turned down for open complex AAA repair. The obvious concern is that these patients will in fact be allowed to die from AAA rupture and we have no robust data to justify that. Again use of a registry to gain more data on the outcomes for these patients treated with Complex EVAR will help to define the role of EVAR in this cohort going forward.	risk of perioperative mortality than those undergoing infrarenal EVAR, even when some attempt is made to adjust for potential confounding factors (e.g. Ultee et al., 2017). We also know that complex EVAR procedures are substantially more expensive than infrarenal ones. The committee considered it appropriate that, in cases in which anatomical complexity raises the risk of short-term harms, the balance with putative long-term gains might be different. As a consideration, this should apply regardless of mode of repair though, naturally, the technique under consideration may imply different levels of short-term risk.
Association of British HealthTech Industries (ABHI)	Draft guideline And Economic Appendix and Model	10	195-202	**[This and the following comment concern ruptured infra-renal AAA repair.]** We recognize that there are cases where EVAR is not possible for anatomical or hemodynamic reasons. We agree with the committee's assessment that EVAR might provide higher incremental benefit in older patients. We are concerned, however, that the clinical recommendation and the health-economic findings do not align. The main health-economic result from the model is that the clinical benefit of EVAR is not limited to the patient group above 70 years.	We are unsure on what basis you assert that the 'main health-economic result from the model is that the clinical benefit of EVAR is not limited to the patient group above 70 years'. As shown in HE.3.2.1.3 (and in HE.9.2.1.3 in the updated results), there was clear evidence of subgroup effects in our HE model, with women of all ages and men over 70 tending to accrue more net benefit with EVAR; however, OSR was the preferred option in men under 70.

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				Therefore, the committee might want to revisit their recommendation regarding age groups. **The odds ratio for long-term mortality between EVAR and OSR appears to be too high** In addition, we want to bring another concern to the committee's attention. This relates to the odds ratio for long-term mortality between EVAR and OSR which we believe is too high meaning that the EVAR effect is underestimated. Specifically, in the NICE model, the relative effect measure (i.e., the odds ratio) was taken directly from a Cochrane meta-analysis (Badger et al., 2017) that pooled the results of several large randomised controlled trials (RCTs) of emergency (ruptured) AAA repair studies (IMPROVE, AJAX, ECAR, and Hinchcliffe et al., 2006). The odds ratio (OR), 0.88 (95% confidence interval [CI]: 0.66-1.16), was driven by the IMPROVE trial with a weight of 71%. IMPROVE was a pragmatic RCT where the intention-to-treat analysis showed no statistical significant difference (OR: 0.92; 95% CI: 0.66-1.28). In light of this, we believe it would have been more appropriate to model the per-protocol analysis, especially since the model considers conversion to open repair with the subsequent effectiveness taken from the OSR arm. Using this different approach, we believe that clinical effectiveness projections would be more accurate and could be expected to very likely lead to different clinical and economic effectiveness findings in favour of	We believe that the comment should refer to short-term, not long-term, mortality. While it is correct to state that, as the largest trial, IMPROVE has the largest weight in the Cochrane meta-analysis, it should be noted that estimates from the other 3 included trials are consistent with the estimate from IMPROVE (I^2=0%), so it cannot be concluded that this trial has 'driven' the pooled result. As noted in Evidence review T, the committee agreed that the design of IMPROVE 'reflected the decision problem at a commissioning level – that is, whether a service should offer emergency EVAR where possible' and was accordingly ideally designed for the committee's decision-making purposes. Throughout the HE model, we refer to the competing strategies as 'OSR only' and 'EVAR where possible', to emphasise the mutually exclusive options under consideration. Finally, we can can confirm that the model does not use effectiveness data from the OSR arm to simulate the 'EVAR where possible' strategy: the analyses are based on the intention-to-treat data throughout.
The Vascular Society of Great Britain and Ireland	Draft guideline	10	196	**Recommendation 1.6.1 Consider EVAR or OSR for ruptured AAA repair.** We agree with the committee that EVAR has benefits to certain patient groups with a ruptured AAA. The implementation of this will however be very difficult when	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				elective practice is restricted to only a limited number, if any, of EVAR cases. Units will not be able to maintain the required skills in all their staff. We will develop a deskilled workforce. Training future surgeons and interventional radiologists to deliver emergency EVAR successfully will also be impossible in the absence of any elective practice. We therefore fully support the views of the JCST and Vascular SAC that these recommendations will lead to major training and recruitment difficulties. Workforce surveys show that there will be a demand for more vascular specialists in the future and a high number of current practitioners are predicted to retire in 5 – 10 years. The variety of modern treatment options for vascular disease is one of the attractions of the speciality. This backward step in AAA therapy will seriously hamper the ability to recruit into the specialty and meet future workforce requirements. There is also the concern that more trained surgeons and interventionists will leave and practice abroad, than currently do. These recommendations are therefore a major threat to the future viability of vascular surgery as a surgical specialty. For obvious reasons of rapid patient access, ruptured AAA repair is not a service that can be delivered in a small number of tertiary centres. It will need to be available in all the arterial centres of the vascular networks. However individually they will have little elective EVAR practice. The cost-effective gains of EVAR for RAAA that the committee wishes to achieve will therefore not be realised due to the restriction on overall EVAR practice. A further issue is maintaining consignment stock in units for emergency cases when the overall EVAR practice (elective	whilst supporting individualised care around which interventions are appropriate.

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				plus ruptures) is drastically reduced. Companies will no longer see this as financially viable. EVAR for ruptured AAA, and EVAR training will all be facilitated by a more measured approach to the use of EVAR as suggested in comment 1. The Vascular Society would be able to work with the committee to define the scope of this use.	
Bristol Bath Weston Vascular Network (North Bristol NHS Trust)	Draft guideline	10	196	**Recommendation 1.6.1** **Consider EVAR or OSR for ruptured infra-renal abdominal aortic aneurysm (AAA).** There will be a significant impact on the delivery of care for patients' presenting with ruptured AAA. We anticipate it will be difficult, if not impossible, to provide an endovascular first strategy for ruptured AAA in units not performing elective procedures. The IMPROVE Ruptured AAA Trial on which most of the evidence for ruptured AAA in the draft NICE guidance is based only included accredited vascular centres. These vascular centres had to demonstrate inter-disciplinary team working and expertise in the endovascular management of ruptured AAA to include a minimum number of elective and emergency EVAR. We believe that it will be difficult to sustain the current expertise in the endovascular management of ruptured AAA with little or no elective EVAR activity. It will not prove possible to offer a 24/7 EVAR for ruptured AAA service in many areas of the country. The availability of large amounts of expensive endovascular stock for infrequent emergency EVAR may be very difficult to justify in vascular centres.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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Rouleaux Club	Draft guideline	10	199-200	There are ~1000 ruptured AAA in the UK each year. As only ~70% of these are appropriate for EVAR this means each vascular practitioner (Surgeon/Radiologist) is likely to only perform 1-2 EVAR's a year. Maintaining current EVAR skills & quality will be difficult and developing these skills will be very difficult for current/future trainees.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	10 10	183 196	The committee recommend that EVAR not be offered to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition. However, the recommendation for people with a ruptured infrarenal AAA is that EVAR be considered, with no caveat offered on their medical or anaesthetic condition. We predict there will be an inevitable increase in the incidence of ruptured AAA, effectively transferring patients who are currently pre-emptively treated by EVAR into a group presenting as emergencies with ruptured AAA. The treatment of this latter group is likely to be more costly overall and difficult than pre-emptive EVAR because some patients who would have been suitable for elective EVAR will inevitably need open repair. Furthermore, and regardless of treatment modality, more of these emergency patients will require intensive care unit admission and will have increased lengths of hospital stay. We are concerned about the impact of this change of practice on our local critical care and inpatient resources. Many vascular specialists view the EVAR 2 trial as flawed, not least due to the excessive crossovers between the two study groups, and the evidence upon which the committee has	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture. However, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group. People who were randomised to no intervention were much more likely to die with – rather than from – their AAA. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in

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				generally based this recommendation is recognised as low quality.	this area. They made a research recommendation noting that such a study would be helpful.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	11	219	We believe that basing the frequency of surveillance imaging post-EVAR on the person's risk of graft-related complications is a laudable aim, but the draft recommendations do not give any insight as to how to achieve this. We are unaware of any current evidence upon which to base such a targeted and tailored surveillance programme.	Thank you for your comment. There was a dearth of evidence to support specific recommendations about tailoring surveillance after EVAR. In the absence of evidence, the committee discussed whether it was possible to specify which complications would warrant changing surveillance protocols. They noted that endoleak was the main complication that clinicians would be most mindful of; however, other potential risks included aneurysm neck angle, diameter, shape and length, graft kinks and the potential for graft slippage. The committee also acknowledged that comorbidities could lead to alterations to surveillance protocols. With so many situations in which surveillance protocols could be amended, it was agreed that it is not possible to make extensive recommendations on every possible scenario. As a result, the committee considered it important to highlight that imaging frequencies should be amended at the discretion of treating physicians.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	11 12	221 223 226	We would find it difficult to implement the recommended surveillance imaging modalities. In keeping with the majority of large UK vascular units, our post-EVAR surveillance is ultrasound-based. This is because most type 2 endoleaks can be considered benign, providing there is no sac size increase; ultrasound is a proven method for accurately, safely and reproducibly measuring sac diameter, without the requirement for repeated exposure to ionising radiation and intravenous contrast. Type 1 and type 3 endoleaks present on EVAR completion will be detected by intraoperative angiography and their *de novo* development later on during surveillance would ordinarily give rise to an increase in sac size, as well as being	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour

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				visible on ultrasound scanning. Therefore, in our opinion, post-EVAR surveillance should primarily be aimed at measuring changes in sac size and observing large high flow endoleaks, rather than at detecting the presence of subtle endoleaks *per se*. Where there are changes in sac size found during surveillance, we would at that stage advocate further imaging with either CT or contrast-enhanced ultrasound. It has been postulated that an increased incidence of malignancies in patients undergoing EVAR surveillance could be the result of repeated CT scanning. At best, this could be explained by the untargeted screening that CT affords, revealing pathologies that might otherwise never have clinically manifest. However, the possibility can't be overlooked that repeated exposure to the ionising radiation associated with multiple CT scans could have a causative effect. We feel this needs further consideration before recommending a change from a non-ionising imaging modality to an ionising one. On a practical level locally, in the last 12 months our vascular scientists performed 743 scans as part of our EVAR surveillance programme - we would struggle to incorporate this additional CT burden. Furthermore, we are unclear why ultrasound surveillance is considered satisfactory for pre-procedure surveillance, but unsatisfactory post-EVAR.	duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about

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					costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	12	238	We feel the term "complex EVAR" should also include branched stent grafts (either visceral or iliac).	The definition of complex EVAR that was adopted for this guideline was any endovascular stategy that is outside the instructions for use of aortic stent–grafts; this would include branched grafts.
Bristol Bath Weston Vascular Network (North Bristol NHS Trust)	Draft guideline	12 16	226 336	**Recommendation 1.7.5** **Do not use colour duplex ultrasound as the main imaging technique to detect endoleaks in people who have had an EVAR.** As a network we use CT surveillance for an initial ('reference') scan and again if there is concern that a patient is either at higher-risk for requiring re-intervention or if there is concern raised on annual plain film and Duplex surveillance. The change to Duplex surveillance was based on a number of considerations No additional IV contrast (nephro-toxicity) No additional radiation exposure Duplex ultrasound is easier to deliver in local Trusts, and is cheaper Vascular labs have processes in place to recall patients for surveillance imaging (i.e. small AAA surveillance), few if any radiology departments or vascular services have the same administrative structures in place.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The recommendation now outlines that colour duplex ultrasound should not be used alone as a definitive tool for excluding the presence of endoleaks. This is because the identified evidence revealed that the pooled sensitivity of CDUS-alone for was not sufficient enough for clinicians to decisively rule out the occurrence of some types of endoleak. Since the evidence also demonstrated that CDUS had a satisfactory sensitivity and specificity for identifying changes in

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				We recognised the paucity of good data on the safety and efficacy of surveillance strategies following EVAR. In most published series compliance with follow up has been poor; in the EVAR 1 trial only 22% of patients were being followed up by the end of the extended follow up period. We therefore validated adding Duplex to our surveillance pathway by looking at dual modality reporting at a single centre (Bristol Royal Infirmary) between January 2012 and January 2014. Data was collected prospectively. 106 paired scans (68 patients) were performed. Endoleaks were detected in 18 patients (26%); 4 Type I and 14 Type II. When compared to CT aortogram a non-contrast Duplex ultrasound performed by a qualified vascular scientist achieved sensitivity, specificity, positive predictive value and negative predictive value for detecting endoleaks of 90%, 92%, 71% and 98%. The same values for the detection of Type I endoleak were 100%, 100%, 100% and 100%. There was a highly significant correlation in maximum aortic sac size between the two modalities (r=0.950, p<0.0005). The sensitivity, specificity, positive predictive value and negative predictive value for detecting a sac size increase of >= 3mm were 78%, 97%, 70% and 98% respectively. Ultrasound is well tolerated by patients as part of their surveillance pathway, as is plain film ultrasound, we consider it a retrograde step without good evidence to remove these two modalities from post-EVAR surveillance pathways. We consider compliance with a pathway as important as the imaging modality (Schanzer A. et al. Follow-Up Compliance After Endovascular Abdominal Aortic Aneurysm Repair in Medicare Beneficiaries. J Vasc Surg 2015;61(1), 16-22.	sac size (which is suggestive of an endoleak) the committee agreed that it was a reasonable to use ultrasound surveillance, so long as any abnormalities are subsequently explored with contrast-enhanced CTA or CEUS to exclude the presence of endoleaks. The two studies listed in your response are outside the scope of this guideline and therefore cannot be considered for inclusion in our evidence reviews. Thank you for your endorsement of our research recommendation on postoperative surveillance.

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				Jones W. B. et al. Lost to follow-up: A potential under-appreciated limitation of endovascular aneurysm repair. J Vasc Surg 2007;46(3), 434-40). We support the research recommendation regarding **Surveillance after endovascular aneurysm repair.** We believe this should be based on risk-stratification methodologies and should evaluate the role of ultrasound.	
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	11 12	221 - 222 226 - 227	Using USS, with CT if there is concern regarding potential complications, is the current standard of care for long-term EVAR follow up. The main purpose of USS surveillance is to measure sac diameter, which the committee accepts for size measurement in the screening of AAA (514). Rupture of a non- expanding aneurysm without flow on Duplex is an exceptionally rare event in the literature. If CT is the primary follow up modality this will increase cost along with accrued radiation dose for individual patients, with induced malignancies becoming a real risk in our follow up patients.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on

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					their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	28	677 - 686	The authors carefully avoid the issue of patient choice. Patients should be able to choose EVAR, accepting a widely accepted 5 – 10% re-intervention and a < 1 % long-term rupture rate, but gaining a very significant initial > threefold increase in survival. (EVAR I trial). Our patients do when presented this option (EVAR) choose it every time with very few exceptions.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				Being forced into performing open surgery, knowing that this high risk procedure will result in unnecessary deaths, and having experienced the exceptional safety of minimally invasive surgery (EVAR) since 2006, will affect the morale of our staff at CHS and weigh heavily on all our consciences. Our patients will vote with their feet and potentially travel to Scotland, or other European countries, to avoid open surgery. This will introduce a system of effectively patients "unsuitable or not" with the "money to travel" benefiting from EVAR, and the "unsuitable" patients, with limited financial means sitting at home to await their death by rupture. We feel that these guidelines are a threat to the social cohesion in Sunderland and the country as a whole. They are not compatible with the basic principles of equal access to healthcare across the UK, independent of financial means and free at the point of delivery, as laid down in the NHS constitution.	
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	8 and 9	181 - 185	The authors would appear to have only accepted evidence from randomised controlled trials, conducted over a decade ago, to the exclusion of any other sources or levels of evidence. This inevitably means that there is no information from modern or contemporary practice informing these discussions and potential guidance.	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	8 and 9	181 - 185	For recommendations 1.5.3 to 1.5.6 the authors use the term 'unsuitable' when differentiating between patients to be offered AAA repair or no intervention at all. There is no attempt to clarify the meaning of "unsuitable" in terms of actual risk profiling for individual patients and is a blanket term that is clinically not usable and very subjective. It is likely that this term arises from the UK EVAR II trial. Most participating centres interpreted this as patients unfit for any surgery, a	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				highly selective group and even in this a significant crossover occurred. Denying a minimally invasive operation (EVAR) with exceptionally low mortality to all patients, regardless of the individual operative mortality risk, and disregarding aneurysm size as a predictor of potential benefit of EVAR is an approach not in line with any modern concepts of surgery. It will result in a surgical practice not seen in this country since the 1960s	The inference that the committee's consideration of people who are unsuitable for OSR was driven by the EVAR-2 RCT is broadly correct. That trial stipulated that fitness for OSR should be decided at the local level, but provided some guidelines as to likely contraindications for open surgery (Brown et al. 2004). The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). Data from EVAR-2 show that, contrary to your suggestion, aneurysm size is not a significant predictor of long-term survival in people randomised to EVAR or no intervention (see Table HE37).
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline and economic model	9-10	179-189	The recommendation for open repair only of an intact aneurysm Despite a significant open aortic practice in our institution we cannot implement the proposed recommendations. Such an increase in open cases would require a large increase in inpatient beds and critical care beds and we do not have that capacity within our institution. Even with additional external investment (which seems unlikely) we are unlikely to see a significant increase – especially in critical care beds; as we are	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Following consultation a number of amendments were made to the resource costs used in the model. These additional

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				unable to recruit sufficient levels of nursing staff. This is in common with the majority of NHS Vascular Hubs. This is an important point, as it is one of several points which renders the economic evaluation invalid. Key assumptions of the economic model are that ward and critical care beds carry a known cost, this is an unlimited resource and that the cost of these beds is constant as the number used is increased. All of these assumptions are untrue within our institution and I am sure within the NHS as a whole. As we are unable to increase this bed capacity and both ward and critical care are working at maximum capacity then the cost of implementation of the recommendations is the death of the incremental AAA patient or the opportunity cost must be considered. This will be the inability to treat another patient requiring either inpatient vascular surgical or critical care. This will involve the loss of life and limb of other vascular patients or patients outside the speciality such as those undergoing cancer surgery or major trauma for instance. This will carry significant costs and consequences which have not been included in the model.	analyses are reported in the addendum of the Health Economic appendix.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline and Economic analysis	9-10	179-189	The recommendation for open repair only of an intact aneurysm The majority of the analysis is based upon the results of the EVAR 1 and 2 trials. There are important reasons why these are not applicable to contemporary practice. They were performed around 20 years ago by teams early on the learning curve with regard to assessment of patient fitness,	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				suitability, planning and deployment. Practice has changed significantly in all of these areas to refine the outcome. The grafts used in the trial are no longer used and grafts of that quality and design would not be contemplated in modern practice. Grafts were inserted via open cut down invariably under a general anaesthetic. This inflated both the risks of complications and the morbidity of the procedure when compared with modern percutaneous access. Patient's length of stay and HDU/ICU use is completely inconsistent with modern practice. We do not use any HDU/ICU at all for infrarenal EVAR. Practice is moving toward next day or even same day discharge. The decision to reintervene and the method of this has changed also. Surveillance was by serial CT – as suggested by the present guidelines. This has been associated with increasing renal dysfunction and will inflate all cause mortality when compared with contrast enhanced ultrasound – which is increasingly prevalent practice. We have not seen EVAR related complications which were not anticipated from our ultrasound based surveillance and have a static population so such cases would not have presented elsewhere in significant numbers. Experience with and therefore the results following open repair are considerably lower in vascular surgical units now than	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**. It is clearly true that EVAR is associated with a lower probability of critical care for the average candidate than OSR, though NVR data show that it cannot be avoided in every case. In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks – see **Theme 11**.

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				when this study was performed. They may be significantly worse now, especially with regard to complex repair. There is no current level 1 evidence which can be used with confidence to support the superiority of OSR over modern EVAR practice. We note that these points are likely to invalidate any confidence in the economic analysis as the best case scenario for open repair (which may not be reproducible in current NHS conditions), is being compared with the worst case endovascular scenario, which is inconsistent with modern experience and data. These factors may explain some of the findings of the economic model which lack face validity with modern experience such as the fact that despite a 750% increase in perioperative death and worse quality of life for up to 3 years post open repair, the model concludes that open surgical repair is associated with the highest number of QALYs.	
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline and Economic analysis	9-10	179-189	Assuming that EVAR is removed from the treatment paradigm for intact aneurysms, this would increase the business costs for industry in providing all of the other vascular and non-vascular products to each trust. This would likely increase the costs to the provider of all of these products on a background of UK hospitals already facing higher costs than in most large health economies. This increase in the costs of provision of other vascular and non vascular services has not been accounted for in the economic models.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Hull and East Yorkshire Hospitals	Draft guideline and	9-10	179-189	The recommendation for open repair only of an intact aneurysm	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations

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Vascular and Endovascular Service	Economic model			The implementation of this guideline nationally will be hampered by a number of other factors: Many units have dramatically reduced the numbers of open procedures. Volume outcome relationships have demonstrated that this is likely to be associated with a reduction in high quality outcomes. This is even more true for complex repair. Similarly the exposure of vascular trainees to high quality training in open repair nationally is significantly reduced and in many cases almost absent. It is challenging to turn the clock back 20 years overnight, which will be the implications of publication of these guidelines. With the likely stakes of misjudgement of this issue, it could be argued that it is irresponsible to initiate such wide sweeping changes without a deliverable national strategy for re-training, mentorship and redesign of the vascular training system, which will need to be designed, validated and in place, to mitigate severe consequences. Failure to address this may lead to an increase in adverse treatment outcomes and cost; and/or greater numbers of untreated deaths as units exercise caution to protect their published results. The impact of this on any models should be explored.	related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of volume–outcome dynamics see **Theme 3b**.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline			Question 3: What would help users overcome any challenges: There are two crucial challenges about defining and determining "fitness" and "treatment thresholds" for elective AAA surgery. Need of validated risk-assessment tools for patients and more evidence for the correct treatment threshold.	Thank you for your comment. The committee were in agreement that there was no evidence that risk assessment tools had sufficient discriminatory power at predicting postoperative outcomes. In the absence of evidence to inform thresholds for AAA repair, the committee made a recommendation to encourage research in this area which will inform future updates of the guideline.

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The Northern Vascular Centre	Draft guideline			We would like to congratulate the committee on their hard work and efforts in producing this much needed updated guidance, we acknowledge the time and energy of all parties involved. The guidelines offer a framework upon which to build a safer, more efficient and higher quality service for our patients with abdominal aortic aneurysm. We would like to offer our feedback on recommendations detailed in Guideline 1.5 that we feel will have the biggest impact on practice and would be the most challenging to implement, most notably; 1.5.2 O*ffer open surgical repair unless there are anaesthetic or medical contraindications.* 1.5.3 *Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is suitable* 1.5.4 *Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition* In principle we support the recommendation of offering open surgical repair where appropriate as a first line treatment of infra-renal AAA. This aligns with the current practice in our unit and that of most reputable major vascular centres in the UK. However we have several concerns that we wish to highlight:	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
The Northern Vascular Centre	Draft guideline			The guidelines do not take into account the importance of shared decision making. EVAR is a well-established practice and patients are well educated on this technique and its associated risks. To remove EVAR as a treatment option risks contravening patient autonomy thus impairing our ability to practice non-maleficence.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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The Northern Vascular Centre	Draft guideline			We have concern over our patients who are deemed anaesthetically/medically "fit" for open repair, have technical reasons why open repair would be a high risk option and have a safe endovascular option. Examples include patients with hostile abdomen and those with highly challenging juxta/supra-renal aneurysms. To require open repair for the management of these patients would likewise result in poorer outcomes.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
The Northern Vascular Centre	Draft guideline			The implementation of a national aneurysm screening programme was welcomed by our unit. Despite our policy of offering open repair as a first line option where appropriate, one-third of our screen-detected patients are deemed high risk for open repair and successfully undergo EVAR. Without this option the programme might be devalued, as a large proportion of patients will be screened for a condition for which we have no recommended treatment option. This adds significant psychological morbidity.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future.

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					For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
The Northern Vascular Centre	Draft guideline			Acknowledging the evidence based benefits of EVAR versus open repair in an emergency setting (1.6.1) and abandoning an elective stent graft programme significantly risks de-skilling practitioners in this technique. This will render EVAR less efficacious and thus unlikely to uphold the enhanced outcomes seen in the evidence upon which this recommendation was based (IMPROVE 2017). This further contravenes patient safety as de-skilled endovascular surgeons will favour open repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline	General		This response is from the Vascular Research Group at ScHARR, University of Sheffield. Members of the group have been closely involved with some of the previous research relating to the management of aneurysm, including the economic modelling carried out for the NICE technology appraisal of endovascular repair (TA167). The group is currently carrying out a programme of research funded by NIHR relating to the provision of vascular services (RP-PG-1210-12009). This programme has involved a number of areas of research utilising mixed-methods research methodologies over the past 5 years and is due for completion in May 2019. The areas of research that are relevant to this guideline include detailed analysis of routinely collected hospital episodes statistics (HES) relating to vascular services, including emergency and elective abdominal aortic aneurysm (AAA) repair, qualitative and quantitative studies relating to patient outcomes and preferences in relation to AAA, and further modelling of vascular services for AAA. Some of this work forms the basis of our responses and we would be happy to provide further details and copies of relevant draft papers or	Thank you for your helpful response and the information on the work ScHARR is undertaking. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				other information if this would be helpful to the Guideline Committee. Our analysis of HES is currently unpublished, as we are awaiting recent data from NHS Digital to update our models. However, our conclusions are based upon analysis of routinely collected NHS information and should, thus, be available to NICE. We would be happy to share our methodology if the committee wishes to confirm the estimates of parameters through their own analysis. In summary, our main concerns relate to the recommendations regarding the place of endovascular aneurysm repair (EVAR) in clinical practice. The limitations in the modelling discussed below have resulted in a failure to adequately model the cost effectiveness for clinically relevant subgroups of patients and are not, therefore, a sound basis for rejecting the findings of the modelling carried out for TA167, which suggested that there are subgroups of patients based upon features such as age, fitness, and aneurysm size, for whom EVAR represents a cost-effective use of NHS resources (comments 2, 5-15, 17-20). The committee appear not to have adequately investigated and considered evidence of potential benefits of EVAR that fail to be captured in the cost–utility analysis and are relevant to review question 12. In particular, this includes the strong patient and societal preferences for the less invasive process of care offered by EVAR, which is not captured in QALY calculations and may be taken into account in line with the NICE methods guidance (comment 16).	

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				The positive recommendation for EVAR in the emergency situation is likely to be both impractical to implement and unlikely to result in the predicted cost effectiveness in the absence of an elective EVAR practice (comment 3). The recommendation that EVAR should only be used for complex aneurysm in the context of a randomised controlled trial is impractical to implement, since no such trial exists and it is unlikely that such a trial would be feasible (comment 21).	
Cardiovascular and Interventional Radiology Society of Europe	Draft guideline	General	General	We read with concern the recent draft guidelines on EVAR proposed by NICE	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
				The NICE recommendations are based on 4 randomised controlled trials of reasonable quality but with the usual limitations of RCTs.	All 4 RCTs were judged to be at low risk of bias in the Cochrane review that underpinned the evidence review for unruptured AAA in people for whom EVAR and OSR are options. Other stakeholders argue that, despite their high internal validity, the age of the RCTs renders them of limited value to present-day decision-making. The committee concluded that this concern was overstated (see **Theme 1**); however, the evidence-base was widened to include casemix-adjusted observational data. This was seen to corroborate the RCTs and validate the committee's conclusions.

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				NICE proposes that: All patients with AAA that satisfy current criteria for treatment should be offered open surgery. Patients suitable for open surgery should not undergo EVAR. Patients who are not fit for open surgery should not undergo EVAR. Patients with complex AAA should be offered open surgery. Patients who are not fit for open surgery should not undergo FEVAR or other complex EVAR techniques unless they are part of a RCT comparing complex EVAR with open surgery. Patients with ruptured AAA may be treated by open surgery or EVAR. All patients who undergo (or who have previously undergone) EVAR should be followed up by CTA or contrast US if CTA is contraindicated. Patients who undergo EVAR should not be followed up by duplex ultrasound as sole imaging modality.	We agree that this is a reasonable summary of some of the recommendations on which consultation comments were sought.
				We agree that EVAR is a maturing technology that needs continued assessment. However, the new NICE guidelines, if adopted, would sound the death knell for EVAR and minimally invasive interventions for AAA.	The committee agreed that, although their confident interpretation of best-available evidence was that the current preponderance of EVAR over OSR is not in patients' best interests, there are areas in which EVAR should retain a key role, if possible – especially when it comes to ruptured AAAs.
				Interestingly, the European Society of cardiology (ESC) produced guidelines in 2014 that were based on the same data and delivered different recommendations: If a large aneurysm is anatomically suitable for EVAR, either open or endovascular repair is recommended in patients with an acceptable surgical risk If a large aneurysm is unsuitable for EVAR, open aortic repair is recommended.	

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				In patients with asymptomatic AAA who are unfit for open repair, EVAR, along with best medical treatment, may be considered Similarly, the Society of Vascular Surgeons (SVS) produced updated EVAR guidelines in Jan 2018 building on 2009 guidelines (which were supportive of EVAR) and came to different conclusions: Elective EVAR should be performed in Hospitals that perform at least 10 EVAR procedures per year, with a documented mortality and conversion to open surgical repair rate of 2% or less. Open AAA repair should be performed in hospitals that perform at least 10 open repairs per year, with a mortality rate less than 5%. Endovascular repair is preferred over open surgical repair for the treatment of ruptured aneurysms if anatomically feasible We feel that new NICE draft guidelines are completely at odds with current practice and current guidelines. We would suggest the following for patients with AAA; EVAR should only be offered to patients within IFU documentation. Patients fit for surgery should be offered Operative repair or EVAR as first line management with full disclosure of the short and long-term risks associated with each. Patients who are unfit for surgery should be offered EVAR Patients with complex AAA and who are fit for open surgery should be offered OR as first line management.	We note your suggested recommendations; however, it is unclear on what evidence they are founded.

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				Patients with complex AAA and who are unfit for open surgery but have at least 5 years expectancy should be offered EVAR with one of the complex endograft iterations that are currently available (fenestrated EVAR, branched EVAR, chimney EVAR). Centres, which offer these complex endograft procedures, should provide this service within a clear framework of clinical governance, multidisciplinary team and research context. Moreover, robust data collection should be entered into a well-designed multicentre registry or be part of research trials. There should be a call for a new well-designed trial to investigate the effects of new endograft and ancillary technology in EVAR, addressing the limitations of previous trials and benefiting from lessons learned. We agree with NICE recommendations that the outcomes of complex endografts for complex AAA should be documented. Ideally, this would be in a UK randomised controlled trial. However, comprehensive data collection in a UK registry would also be sufficient. EVAR should only be performed in high volume centres with a multidisciplinary approach where all options for management and subsequent follow up are available.	The committee agreed that trials in this area are extremely desirable – see below. The committee – mindful of prevailing beliefs by which EVAR and OSR are preferred in complex AAAs, with little overlap between the 2 – agreed that registry data are very unlikely to provide clear evidence as to which approach(es) should be preferred. Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline.
JCST- Joint Committee on Surgical Training and the Vascular Specialty	Draft guideline	General	General	The Vascular SAC are primarily concerned about the major impact these guidelines will have on patient care and patient choice with regards to the management of abdominal aortic aneurysms (AAA) in the UK. In addition, and as a consequence of these guidelines, the Vascular SAC is very concerned of the significant impact they will have on the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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Advisory Committee				recruitment and training of vascular surgeons in the United Kingdom, both now and in the future. Good patient care is what matters most to us all and it is the view of the Vascular SAC that these guidelines have taken too narrow a view of the randomized data available, and that too much emphasis has been placed on cost.	
				It seems that no consideration has been taken into account of the Quality Improvement Framework which achieved a significant reduction in abdominal aortic aneurysms (AAA) repair mortality, which was in part due to the greater number of endovascular abdominal aortic aneurysm repairs (EVAR) being performed electively in the UK.	For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.
				In addition, these guidelines do not consider problematic patients with hostile abdomens, synchronous cancers, bowel stomas etc., where EVAR is a safer option than open AAA surgery.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
				Implementation of these guidelines will lead to increased numbers of open AAA's being performed and this will almost certainly increase early post-operative AAA mortality in the UK. These guidelines, as they stand, would abolish patient choice and surgeon discretion and would lead to a reduced number of AAAs being repaired overall and subsequently this will mean that AAA rupture rates might correspondingly increase.	For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
				Endovascular repair of infrarenal abdominal aortic aneurysms, is currently one of the first line treatments that patients are	We note that, in the current Vascular Surgery Curriculum, endovascular techniques are level 2 or 3 competencies (that

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				offered when they present with an AAA of greater than 5.5cm. This has been widely adopted in all major vascular units in the UK. For a surgeon to become competent to perform an EVAR they must learn detailed anatomy of the aorta and its branches, understand the devices available and their limitations, develop wire and catheter skills, know how the devices are deployed safely and learn how to recognize and manage the potential complications. This takes many years and whilst some of these skills can be learnt on simulators, these are not readily available nationwide, have significant limitations and are no substitute for real live cases. The elective infrarenal EVAR gives the perfect opportunity for the trainee to learn planning, specific wire and catheter skills (that cannot be learnt in the angiography suite doing lower limb angioplasty) and deployment of devices and cannulation, in a controlled, calm operating environment. In order for a vascular trainee to gain their Certificate of Completion of Training (CCT) they have to be competent in all of these areas in order to be independent vascular surgeon. A vascular surgeon and interventional radiologist can only become competent at treating patients with ruptured AAA with EVAR, if they have gained significant experience with elective EVAR. These emergency cases are not planned, can occur at any time, and are highly pressurized situations, which are not ideal for training. In addition, the number of ruptured AAA's has reduced nationally since the introduction of aneurysm screening and hence there are not the number of cases available to train, the current workforce in the UK, the competencies they require to be adept at treating patients with ruptured AAA with percutaneous EVAR. Should these guidelines be implemented we will not be able to train	is, activities that people completing the programme should be competent to do with assistance), whereas OSR is a level 4 requirement (that is, activities that can be done without assistance).

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				surgeons or radiologists to perform EVAR for ruptured aortic aneurysms. This can only be possible if they are exposed to training in elective EVAR. If these guidelines are implemented the following will occur: Vascular Trainees and Interventional radiology trainees will not be trained in elective infrarenal EVAR. They will not be equipped to treat ruptured AAA with EVAR, as they have not gained the necessary skills required. As a consequence, their preference will be for open repair which will probably lead to reduced survival from ruptured AAA, increased ITU bed utilization and increase length of stay. With a rise in elective open AAA surgery there will be an increase utilization of ITU beds. This will put a significant strain on ITU's around the country and inevitably will lead to cancellation of cases and thus there will be lost training opportunities. Elective mortality for abdominal aortic aneurysms will increase. With an increase in the number of open AAA's performed there will be a cohort of patients who will be deemed high risk. Given that vascular surgeons now submit all cases to the National Vascular Registry and their results are publicly scrutinized, there is a real concern that surgeons will become risk averse, newer consultants will perform the case themselves and the training opportunities for open repair will decrease. As the trainees will have limited experience of EVAR by the completion of training they will not be equipped to perform more complex EVAR of juxtarenal or suprarenal aneurysms. To gain the necessary competent skills they would probably require an overseas fellowship for at least twelve months. The	

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				concern is that many trainees may not return from such fellowships and gain employment outside of the UK. The significant effect that these guidelines will have on the morale of trainees cannot be underestimated. The current senior trainees have spent a large proportion of their time training in EVAR, many of whom are now considering their options such as working outside of the UK. Vascular Surgery has struggled to recruit new trainees, like many surgical specialties, over the last few years. The introduction of these guidelines will: a. reduce training opportunities for foreign surgeons and hence fewer will come to the UK; and b. UK trainees will no longer perceive vascular surgery in the UK, to be innovative and technologically driven and will opt for other surgical specialties, this will ultimately lead to a reduction in recruitment of new vascular trainees and lead to a workforce shortage of trained vascular surgeons in the future. Vascular surgery became a separate specialty from general surgery in 2012, and the first vascular trainees commenced their training in 2013, many of whom will be looking for Consultant Vascular Surgeon posts in 2019. The main driver for this separation was the increasing use of endovascular techniques to treat vascular disease and in particular endovascular repair of aortic aneurysms. The UK has been at the forefront of this development internationally, and this has attracted many trainees into our specialty. The implementation of these guidelines will put us out of kilter with the rest of Europe, North America and Australasia. The UK will be left behind as technological advances improve the management of aortic aneurysm throughout the rest of the world. These guidelines are seen as a retrospective step by both the Vascular SAC members and Vascular trainees and will have a	

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				detrimental effect on patient choice, patient care, vascular trainee recruitment and training. In the long term, the specialty itself, should it fail to recruit into its training programs, will be at risk. This will have a major impact on the management of patients with vascular disease in the UK.	
South Wales Vascular Surgery Network	Draft guideline	General	General	Endovascular stent grafts in the EVAR 1 , DREAM, OVER and ACE trials have now been superseded. Each manufacturer has gone through at least 1 generation of stent graft since these trials took place. Graft porosity, flexibility, seals and longevity have all been improved. The basis of the evidence for EVAR in this guidance is now historical.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	General	General	The Vascular Anaesthesia Society of Great Britain & Ireland (VASGBI) would like to thank the NICE Committee for producing this guideline on the diagnosis and management of abdominal aortic aneurysms. We agree with many of the recommendations and acknowledge the extensive amount of work done by the Committee. Our main concerns: According to the recommendation assessment of "fitness" would be the primary factor determining whether a patients has elective open repair or no surgery. The NICE document provides no guidance on how anaesthetists would make this fitness assessment. Implementation of the guideline would ask our vascular anaesthetists to make significant decisions on patient fitness for elective open abdominal aortic aneurysm (AAA) surgery	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				without reference to any framework or indeed to tools developed in large populations such as the ACS NSQIP calculator. In our view the lack of a framework for risk stratification would increase the risk of substantial variation in practice between vascular centres and contradict the aims of the recently published GIRFT for vascular surgery. If the guideline is implemented in its current form, patients deemed unfit for elective open AAA repair, would not be offered less invasive elective endovascular aneurysm repair (EVAR). This recommendation will have a major impact on current UK practice (where 70% of elective AAA repairs are EVAR) and if implemented will be disparate with guidelines and practice in the rest of Europe (European Society of Vascular Surgery). There is a lack of evidence about the "treatment threshold" for elective AAA repair especially for high-risk patients with larger more high-risk aneurysms. The studies that inform treatment thresholds do so with particular reference to the treatment of small aneurysms and cannot be used to inform the management of large aneurysms in higher risk patients. Current recommendations are based on the older EVAR trials (before 2004). There is a need for more high quality evidence from modern EVAR practice to inform treatment thresholds. Significant abandoning of elective EVAR surgery will affect skills and training of vascular teams, including theatre staff, anaesthetic trainees and surgical trainees. This will have practical implications for the delivery of EVAR for ruptured AAA's. There seems to be no allowance for patient choice with regards to elective abdominal aortic aneurysm (AAA) repair and the NICE document provided no data on patient	

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				preference. In modern practice patient choice is important for consent and the shared decision-making process. We asked for comments from the VASGBI membership in the limited timeframe. We also asked current and previous members of the VASGBI Committee to comment. Their responses are included in this document.	
Royal College of Physicians and Surgeons of Glasgow	Draft guideline	general	general	The College welcomes this Quality Standard in an important area. Abdominal Aortic Aneurysms are significant causes of mortality and morbidity. The acute situation requires admission to hospital requiring critical care support with high mortality. The draft guideline was sent to reviewers in two vascular different centres Both centres take the view that the guideline begins by rightly promoting changes which increase identification Abdominal Aortic Aneurysm (AAA) by an extension of "screening". However, it ends by, indirectly, recommending a reduction in access to treatment. This is because the guideline recommends open operation for asymptomatic patients rather than Endovascular Aneurysm. Patients should be given a choice. Many asymptomatic patients will be less fit for open surgery and therefore deemed unsuitable for repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
British Society of Endovascular Therapy (BSET)	Draft guideline	General	General	Endovascular Aneurysm Repair (EVAR) has been an option for abdominal aortic aneurysm (AAA) treatment for nearly 25 years. Over that time, devices and techniques have evolved to enable treatment in a greater proportion of patients. The research involved and relationship with industry have rightly been labelled as an excellent example of innovation with translational benefits to offer minimally invasive treatment to	Thank you for this summary of the context in which your comments should be interpreted. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				patients and increase efficiency within the wider health service. This has allowed a reduction in length of stay (LoS) and critical care use with a greater proportion of patients being discharged directly to home who then enjoy a much faster return to normality. The adoption of appropriate EVAR use has been partly responsible for a significant reduction in 30 day mortality since 2007 when Vascunet figures revealed a UK mortality of >7% compared with 2% now. This was fundamental in the development of the national AAA screening programme.	whilst supporting individualised care around which interventions are appropriate.
British Society of Endovascular Therapy (BSET)	Draft guideline	General	General	Implications for training the next generation of vascular surgeons That the removal of EVAR would reduce the training opportunities in endovascular skills of trainees significantly. There may be global ramifications if this that are not envisaged in terms of translatable skills from EVAR to other endovascular procedures, most obviously the skills involved in complex endografting which requires a baseline competence in EVAR. Equally there will be a significant effect on the technical skills of the operator and non technical skills of the team, and in the scenario of ruptured AAA we cannot begin to expect the same outcomes as were observed in the improve trial. Lastly there may we'll be effects on technical and non technical skills in endovascular intervention in other territories such as the lower limb. A potential strategy would be that of skills training on simulators and team training in theatre of fully immersive endovascular suites to maintain skills ready for the ruptured AAA case. Skills training is effective but will add a huge cost burden to the NHS of teams are to be trained regularly.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We note that, in the current Vascular Surgery Curriculum, endovascular techniques are level 2 or 3 competencies (that is, activities that people completing the programme should be competent to do with assistance), whereas OSR is a level 4 requirement (that is, activities that can be done without assistance).

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				We are aware that the operative skills of trainees have reduced as a result of a number of factors including the European working time directive, patient expectation, and increase in minimally invasive techniques and pressure on operating time. This will have the effect of drawing consultants to operate in pairs or teams in most units in the UK we envisage. The practice of the NVR to list individual consultant mortality figures will only strengthen this desire for dual consultants operating. This comes at a cost which is not calculated in any cost effectiveness model.	
British Society of Endovascular Therapy (BSET)	Draft guideline	General	General	Patient & Public Involvement It is not clear from the guidelines how much patient & public engagement has been sought in their preparation. The recommendation to not offer EVAR ignores patient choice (Key principal 4 of the NHS Constitution) and removes a treatment option available in the majority of healthcare system in the developed world. - A number of publications support the notion that patients prefer EVAR (e.g. Winterborn et al. J Vasc Surg 2009; Reise et al. EJVES 2010) - The psychological impact of being turned down for repair and impact over what could be many years of living with an aneurysm are unknown and ignored in these recommendations. The deleterious psychological effects of being diagnosed with an aneurysm are reported (Bath et al. Br J Surg 2018)	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. As recorded in guideline documentation, the committee included 2 lay members who provided patient perspective and had equal status in all discussions and conclusions. For discussion of the potential impact on quality of life of living with an untreated AAA, please see **Theme 13**.

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				A recent meeting of the Liverpool Aneurysm PPI group reported the following headlines: Patients strongly prefer to be informed of all of the treatment techniques and as detailed information as possible regarding supporting evidence. Recommendation or offer of 'one best' treatment based on evidence and / or guidelines was not considered adequate counselling. Patients take different choices under the same circumstances, with the same information. Patients understand the importance to the NHS of treatment costs. Patients expect treatment costs to play no role in selection or offer of treatments.	
UHCW NHS Trust Coventry	Draft guideline	General	General	*Trauma* Being unable to stent elective patients will seriously impact on our ability to look after thoracic aortic trauma	Thoracic aortic trauma is outside the scope of this guideline.
UHCW NHS Trust Coventry	Draft guideline	General	General	Finally, we feel that we should treat both the patient and the AAA, and a personalised or individualised approach is key when treatment options are discussed with the patient. Increasing the proportion of patients offered open aortic surgery is appropriate but absolute exclusion of elective EVAR is not.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that based on the evidence reviewed there are no methods that reliably predict short-term outcomes of AAA repair, and also

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					found that no individual characteristics are associated with better outcomes for EVAR. See **Theme 12**.
UHCW NHS Trust Coventry	Draft guideline	General	General	**Summary** We hope the panel see our comments as an attempt to offer a constructive critique of the proposed NICE Guidelines for AAA. We feel, as articulated, the current guidelines represent a positive appraisal of the vascular specialty's failure to treat the whole patient as opposed to just the AAA, but the proposed AAA guidelines are, in our opinion, actually disjointed and potentially unsafe in their approach.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
UHCW NHS Trust Coventry	Draft guideline	General	General	**Specifics** Our own unit's experience of a high mortality associated with poor results from open repair was published in Peri-operative Medicine: https://perioperativemedicinejournal.biomedcentral.com/track/pdf/10.1186/2047-0525-2-10 ***Risk stratification by pre-operative cardiopulmonary exercise testing improves outcomes following elective abdominal aortic aneurysm surgery: a cohort study*** ***Abstract*** ***Background****: In 2009, the NHS evidence adoption center and National Institute for Health and Care Excellence (NICE) published a review of the use of endovascular aneurysm repair (EVAR) of abdominal aortic aneurysms (AAAs). They recommended the development of a risk-assessment tool to help identify AAA patients with greater or lesser risk of*	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Thank you for summarising your published study; this was not included in evidence review G, as the protocol stipulated that only prospective cohort studies would be deemed eligible. However, other included evidence looked at a very similar cutoff for VO_2 at anaerobic threshold (10.2 ml/kg/min) on CPET, with comparable conclusions (Grant et al., 2015). The committee concluded that, *while CPET may provide healthcare professionals valuable objective information on the fitness of people prior to elective AAA repair, the evidence was not robust enough to make strong recommendations for the use of*

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				operative mortality and to contribute to mortality prediction. A low anaerobic threshold (AT), which is a reliable, objective measure of pre-operative cardiorespiratory fitness, as determined by pre-operative cardiopulmonary exercise testing (CPET) is associated with poor surgical outcomes for major abdominal surgery. We aimed to assess the impact of a CPET-based risk-stratification strategy upon perioperative mortality, length of stay and non-operative costs for elective (open and endovascular) infra-renal AAA patients. ***Methods****: A retrospective cohort study was undertaken. Pre-operative CPET-based selection for elective surgical intervention was introduced in 2007. An anonymized cohort of 230 consecutive infra-renal AAA patients (2007 to 2011) was studied. A historical control group of 128 consecutive infra-renal AAA patients (2003 to 2007) was identified for comparison. Comparative analysis of demographic and outcome data for CPET-pass (AT ≥ 11 ml/kg/min), CPET-fail (AT < 11 ml/ kg/min) and CPET-submaximal (no AT generated) subgroups with control subjects was performed. Primary outcomes included 30-day mortality, survival and length of stay (LOS); secondary outcomes were non-operative inpatient costs.* ***Results****: Of 230 subjects, 188 underwent CPET: CPET-pass n = 131, CPET-fail n = 35 and CPET-submaximal n = 22. When compared to the controls, CPET-pass patients exhibited reduced median total LOS (10 vs 13 days for open surgery, n = 74, P < 0.01 and 4 vs 6 days for EVAR, n = 29, P < 0.05), intensive therapy unit requirement (3 vs 4 days for open repair only, P < 0.001), non-operative costs (£5,387 vs £9,634 for open repair, P < 0.001) and perioperative mortality (2.7% vs 12.6% (odds ratio: 0.19) for open repair only, P < 0.05). CPET-stratified (open/endovascular) patients exhibited a mid-term survival benefit (P < 0.05).* ***Conclusion:*** *In this retrospective*	*the test as a decisive arbiter of fitness. Moreover, the committee agreed that individual CPET parameters should not be used in isolation to decide whether a patient should have surgery or not, but instead, may be used to inform shared decision making in context of medical history and examination.* We are unable to provide detailed comments on your unpublished data without access to a full description of its methods and results. We would note, however, that it is inevitable that people who are deemed ineligible for any repair (regardless of CPET result) would have worse survival than their fitter counterparts; this would be the case whether the fitter people underwent EVAR or not. This does not help us to understand the balance of benefits and harms of EVAR among people for whom OSR unsuitable, but for whom EVAR would currently be considered.

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				cohort study, a pre-operative AT > 11 ml/kg/min was associated with reduced perioperative mortality (open cases only), LOS, survival and inpatient costs (open and endovascular repair) for elective infra-renal AAA surgery. We found a selective approach based upon fitness for surgery and anatomical configuration reduced both the LOS, substantially reduced perioperative mortality and non-operative in hospital costs. Our 'conservative practice' is to use EVAR devices predominantly on IFU. Further follow up data on this cohort has now been obtained and we have undertaken a combined 'EVAR 1 / EVAR 2' analysis. It should be noted patients were NOT randomised. ***Ten year follow data on open surgical repair, EVAR and conservative treatment registry at UHCW NHS Trust*** *Total patients included with valid CPET 316. 129 Open surgical repair (OSR), 119 EVAR, 65 not operated* ***CPET results*** *The patients not offered surgical intervention had a mean AT of 11.64ml/kg/min. The EVAR group can be split into 2 subgroups; patients whom were physiologically eligible for OSR (i.e AT>11ml/min/kg) this subgroup contained 82 patients with a mean AT of 14.03ml/kg/min. This was significantly higher than those who were not offered surgery (P<0.001). The second subgroup is of those whom were deemed ineligible for OSR (AT<11ml/min/kg). This group was composed of 37 patients with a mean AT of 9.58ml/min/kg. This was significantly lower than those not offered surgery*	

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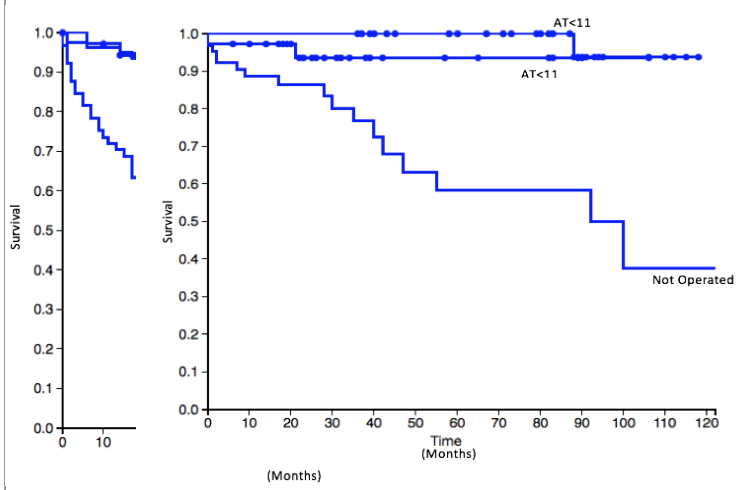
				(p=0.003). When considered as a whole the EVAR group had a mean AT of 12.64ml/kg/min (p=0.03). ***Long term Survival*** *Mean survival: OSR 97 months, EVAR 94 months, Non-operated 59 months. Vs non-operated all EVAR HR=0.34 CI=0.19-0.61 (P<0.01). Reported as mean as we cannot calculate median survival due to not having reached 50% mortality in the OSR and EVAR groups.* ***Mortality: EVAR (split by AT) vs non operated***  	

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				All Cause *Aneurysm Specific* ***Re-interventions*** *19 re-interventions were undertaken in 18 patients. Mean time from EVAR to first intervention was 19 months (range 0-77). Only one patient required a second re-intervention at 50 months post EVAR. 6 re-interventions were surgical and 13 radiological. There were 15 documented endograft complications that have not required intervention to date, the most common of these being thrombus within the main body or limb(s) of the graft. Persistent endoleak without sac expansion was also noted in 5 patients all of these were type 2 or 3. Significant complications of spinal cord ischaemia and buttock claudication secondary to bilateral internal iliac occlusions occurred in one patient each.*	

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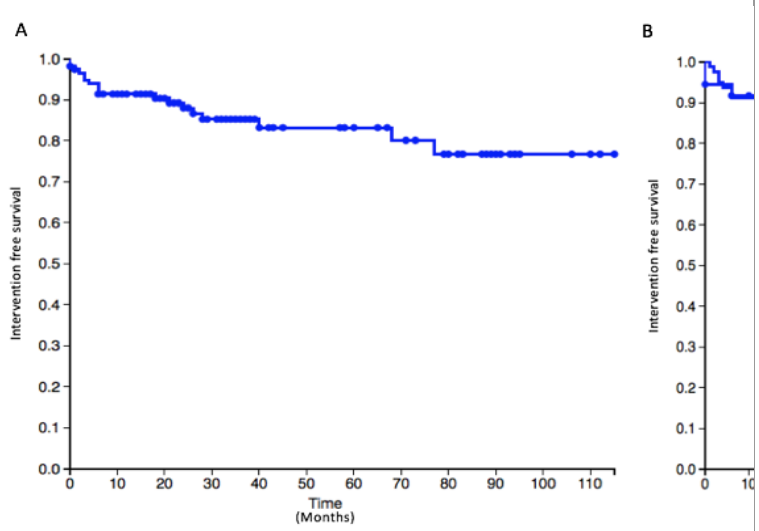
				Intervention free survival  *Combined EVAR by AT* *Split* In this preliminary data, we feel that some of the concerns expressed by NICE based upon datasets that are 20+ years old are not substantiated. Key points:	

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				A. Aneurysm specific deaths as far out as 120 months in the EVAR group is low and this appears to be independent of cardiovascular fitness. B. Re-intervention in the EVAR group is also relatively low. C. Cost differences need to be recalculated to bring them up to date. LOS for EVAR in the original study was 4-6 days and is now 1-2. Open surgery LOS has also fallen but only to about 8 days.	See **Theme 9** for updated discussion of long-term survival for people undergoing EVAR and OSR. We would also note that it is extremely difficult to draw conclusions regarding AAA-specific mortality, especially in the context of people with significant comorbidities. This is shown by the EVAR-2 RCT, in which participants randomised to no intervention experienced significantly higher AAA-related mortality than people receiving EVAR. However, there was significantly **lower** non-AAA-related mortality in the no-intervention group (even when assessed using appropriate methods to account for competing hazards of death). The combination of these countervailing findings is why the trial showed no overall survival benefit for EVAR. The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice, and advised that the HE model should be revised to address this issue. Full details are provided in **Theme 8**. Resource implications of in-hospital care with EVAR and OSR have been updated in the HE model – for details, please see **Theme 6a**.
South East and South West London Vascular Networks	Draft guideline	General	General	The South London Vascular Network would like to thank NICE for the opportunity to comment on the draft AAA diagnosis and management guidelines. The network team fully support responses submitted by the clinical teams at St George's University Hospital NHS Trust and Kings Health Partners (Guy's and St Thomas' NHS Trust and Kings College Hospital NHS Trust).	Thank you for your acknowledgement of the committee's work, and for providing contextual information about your comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care

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				In many areas the draft guidance will enhance practice. However, we are concerned that the draft guidance will not improve patient access in the intended fashion, and conversely will restrict access to potentially beneficial care for patients with abdominal aortic aneurysms, due to the focus on open repairs. Adopting these guidelines could have a significant impact on capacity at arterial centres and the running of networked regional vascular services. This will impact on quality of care for patients. The length of stay of aneurysm patients will increase, as EVAR is normally performed as an overnight stay. Predominantly providing open repair with associated longer lengths of stay will reduce capacity in vascular services, limiting care to patients with aneurysms and other vascular conditions. The ICU/ITU usage for AAA repair will increase. Most EVAR do not use ITU, and these comprise 70% of current AAA repairs in the UK. Adoption of these guidelines could increase the number of cancellations due to reduced capacity within vascular services and ICUs/ITUs through the increased use of open aneurysm repair. Aortic rupture rates will increase, as many currently treated patients will not be offered elective repair under this guidance, and will consequently present with aortic rupture, burdening emergency services and intensive cares. AAA identified through the NAAASP might not be eligible for treatment. We are concerned about offering screening to patients who might not be treated.	around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. . The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk

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					factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
Addenbrookes Hospital	Draft guideline	general	general	Addenbrookes hospital in a high volume tertiary hospital for the management of patients with aortic aneurysmal disease. In total over the last 5 years we have treated 700 patients for an infrarenal AAA (529 patient elective – 106 open repair / 433 endovascular repair). the mean age of the EVAR cohort (all comers – elective and emergency) was 77years and for open repair (all comers) was 70 years. Within the same time period / cohort of patients, our median length of stay for EVAR was 2 days and for open repair 9 days. Our vascular network covers a population of over 1.5 million people covering 6 hospitals (including Papworth hospital). In keeping with being the tertiary unit for the eastern region we also are the major centre in the region for trauma, transplantation (including being the UK centre for multi-visceral transplantation) , major upper GI oncological resection and neurosurgery. We have xx intensive care beds and a further xx level 2 beds. An inability to use EVAR at all in the elective setting we feel would have the following consequences for our population of patients: There would be a significant proportion of patient who would be denied treatment for their AAA with a technique that would likely be of benefit to them. While there are recognised	Thank you for the contextual information about your service. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				reintervention rates following EVAR, there are still significant number of patients who have their EVAR with no long-term complications. We accept that we need to better identify patients who will do well with EVAR bit feel complete withdrawal of this treatment is a somewhat draconian measure that is at odds with all current recommendations from throughout the world and will ultimately lead to a return to the high mortality rates associated with AAA repair seen a decade or so ago. The current NICE guidance would bring with it significant dilemmas for the clinician given that he / she would be advising a course of treatment against what he / she feels would be the most appropriate for that patient. This not only has ethical / legal issues but also goes against the NHS constitution and against the dogma of patient choice that has been placed as a central facet within the NHS at present. As we are a high volume unit, given the figures presented above, if we have a 25% turn down rate, this would equate to a further 60 open repairs a year – at best a further 420 extra bed days per year. However, it is likely that these patients would be less fit than the cohort we are performing open repair on at present and so we would expect higher ITU / HDU use and longer overall length of stays. Further, all patients undergoing an open repair would need a high dependency bed post op and given the tertiary nature of the general work performed at Addenbrookes and the finite resources with regard to high dependency bed will no doubt result in cancellations of operations. The consequence of the guidance is that the turn down rate for elective repair for AAA will increase. This is probably	

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				appropriate for some patients but not for all. The likely consequence of this will be an increase in the number of patients presenting with a ruptured AAA and a significant proportion of these will be offered repair at this stage. This will place further strain on ITU / HDU beds and overall longer length of stays and no doubt in those who do survive will leave them with more significant complications and a poorer quality of life following intervention in this cohort of patients. The NICE recommendations fail to give any guidance on what they deem to be an unfit patient. Further they state that we should not be using scoring systems to aid in our decision-making. We need clarity from the NICE panel as to what they define as a fit and unfit patient so that both locally and nationally, centres will be treating patients the same – ie equity in decision making throughout centres and a lack of a postcode lottery with regard to management of patients.	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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Addenbrookes Hospital	Draft guideline	General	General	As we are a high volume unit we have a number of EVAR patients under surveillance. Over the last three years we have performed between 375 and 450 ultrasound scans post EVAR per year (2015: 428, 2016: 386, 2017: 423) on the Addenbrookes site only. There are also large volumes of USS EVAR surveillance scans done in our spoke hospitals. The guidance that we should change to CT imaging for surveillance will have significant consequences for our hospital. This will result in approximately a further 400 CT scans a year, which at the best estimate equates to at least 6 weeks continual use of a CT scan (9-5pm) within Addenbrookes. Further, at a time when interventional radiology are struggling to recruit trainees / consultants, this would add further workloads to our already stretched interventional service.	In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks – see **Theme 11**.
Addenbrookes Hospital	Draft guideline	General	General	We have recently (January 2016) had built an endovascular theatre at an overall outlay of £1.5million. This was with the predominant aim of providing high quality imaging for EVAR. These guidelines would make the theatre hardware significantly redundant and mean that we will not recoup the financial outlay put in place. This is likely to be the same for nearly all vascular surgery units within England.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Addenbrookes Hospital	Draft guideline	General	General	We fully endorse the recommendation for the use of EVAR in patients presenting with a ruptured AAA. We have excellent outcomes in patients attending with a ruptured AAA with low turn down rates. This is related in part to high use of EVAR in this cohort of patients. These are often the most complex patients and the expertise of the whole team has been built on the back of the structures put in place by our elective EVAR protocols. A consequence of not undertaking EVAR in an	Thank you for your endorsement of these recommendations. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				elective setting will be a reduction in the use of EVAR in an emergency setting with ultimate poorer outcomes in patients.	
Addenbrookes Hospital	Draft guideline	General	General	While the NICE document provides guidance for patients deemed unfit for open repair, there is no guidance for patients who may be medically fit for open surgery, but have a hostile abdomen, with previous operations or a stoma. Nor is there any comment about patients with dual pathologies such as aortic aneurysm disease with bowel cancer. In these circumstances, there is a strong rationale for endovascular repair in these patients as open surgery may be excessively risky, or may jeopardise / delay subsequent cancer surgery.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
Addenbrookes Hospital	Draft guideline	General	General	Patient choice is a core component of modern healthcare and a pledge in the NHS constitution. When given the choice between treatment options (including the risks), some patients may choose endovascular intervention, particularly as this has been the mainstay of treatment for many years. This guidance may remove that choice.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Addenbrookes Hospital	Draft guideline	General	General	While we recognise that NICE guidance must be based on evidence of the highest quality, the evidence used in this guidance has numerous flaws and limitations. Most notably, selection bias, where patients deemed to have an unequivocal benefit for endovascular treatment were never randomised in clinical trials. Therefore, a broad recommendation that endovascular stenting should not be offered to large groups of patients completely fails to appreciate this enormous limitation of the evidence. Adherence to this guidance as it stands will mean that patients will be denied intervention despite the fact that the vast majority of specialists believe that endovascular stenting should be performed (such as a patient with a 10cm	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. 'Selection bias' – where the internal validity of a study is compromised by which participants got which treatment(s) – is an inappropriate term for the kind of challenge to external validity you hypothesise, here. Nonetheless, indirectness of

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				aortic aneurysm, with good anatomy for endovascular stenting, who has had 2 previous laparotomies and a stoma). This will raise major ethical concerns.	evidence is an important component of our appraisal of the strength of evidence. However, we have uncovered no evidence – either in the RCTs on which the consultation draft focused or in the casemix-adjusted observational evidence we have now included – that a population population exists for whom an 'unequivocal benefit for endovascular treatment' can be assumed. Furthermore, as you do not specify the characteristics of such people, it is not possible to confirm whether they are included in evidence at the committee's disposal. As noted above, the committee agreed that people with abdominal copathology may preferto EVAR OSR where either is possible.
W.L. Gore and Associates	Draft guideline	General	General	**Guidance does not support application of clinician judgment.** The evidence on EVAR versus open repair shows that any advantage for one over the other is driven largely by the patient's individual circumstances, including age, gender, smoking status, co-morbidities, and anatomic complexity. This draft guidance makes definitive recommendations in favour of open repair and does not encourage physicians to take these patient factors into account when discussing treatment options with patients. As utilization of EVAR decreases, centres will stop performing the procedure, and turn down for EVAR will become more and more common. The strength of the recommendations in favour of open repair and the consequences on availability of EVAR are not in keeping with the NICE charter and goals for shared decision making. NICE Charter 2017	For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**. We do not agree with your suggestion that the evidence on EVAR versus OSR shows that outcomes depend on patient's individual circumstances. The available evidence on unruptured infrarenal AAA shows that, on average, OSR leads to better net outcomes than EVAR, does not identify any subgroups of patients in which better net outcomes can be expected with EVAR (see **Theme 12**), and shows that there are no tools that reliably predict which individual patients might face a different balance of risks and benefits (see Evidence review H).

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				"…our recommendations are not intended to replace the professional expertise and clinical judgement of health professionals, as they discuss treatment options with their patients." NICE Shared Decision Making website "We've updated all of our guidelines to highlight the importance of balancing professional judgment and expertise with the needs and wishes of people receiving care."	
W.L. Gore and Associates	Draft guideline	General	General	**Guidance would effectively end innovation in EVAR.** EVAR technology has been evolving and improving since it was introduced in the 1990s. Multiple studies suggest that outcomes have improved as the devices have evolved. If this guidance were implemented, it would effectively end EVAR innovation in the UK. While newer and more effective devices would continue to be available in other countries, the UK will be focused on open repair. Newer and improved EVAR devices may not be introduced into the UK market by manufacturers. This is true both for infrarenal and complex EVAR, as the RCT recommended for complex EVAR would likely not permit the use of different devices over time because it would make the results less reliable. This lack of focus on innovation is not in keeping with the government's "Strategy for UK Life Sciences," which states that the UK will help "bring innovation to market earlier and more easily, making the UK the location of choice for investment." The lack of ability to use technologically advanced treatments for patients will also deter doctors from practicing this specialty in the UK and further exacerbate the current recruitment crisis.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. NICE's position on the value of innovation is as stated in our Social value judgements (2012), as cited in Developing NICE guidelines (2014). We say that *Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the intervention as an effective use of NHS resources will specifically take account of…* *[w]hen the intervention is an innovation that adds demonstrable and distinct substantial benefits that may not have been adequately captured in the measurement of health gain.*

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					As the ICER of an intervention increases in the £20,000 to £30,000 range, an advisory body's judgement about its acceptability as an effective use of NHS resources should make explicit reference to the relevant factors considered above. Above a most plausible ICER of £30,000 per QALY gained, advisory bodies will need to make an increasingly stronger case for supporting the intervention as an effective use of NHS resources with respect to the factors considered above. It was the committee's view that EVAR fails to meet this test on 2 grounds: (a) in the infrarenal elective case, our best estimate is that it is dominated by OSR (that is, it causes net patient harm alongside additional NHS costs) and, in complex elective cases and those for whom OSR is unsuitable, it is associated with ICERs far above the levels referred to, here; (b) we have no evidence that EVAR adds demonstrable and distinct benefits that we have not captured (the HE model incorporates best-available evidence on patients' quality of life and on the resource impact of EVAR compared with OSR, including postoperative bed-days and likelihood of discharge to home, as well as the implications for short- and long-term survival and reintervention). We are unsure what evidence is available for a 'recruitment crisis': the Royal College of Surgeons report a 'high competition ratio of 14:1' for vascular surgical trainee positions.
W.L. Gore and Associates	Draft guideline	General	General	**Gore supports additional research on the effectiveness of EVAR.** W.L. Gore and Associates thanks NICE for the opportunity to comment on this draft guidance. While we have significant concerns regarding some of the inputs and assumptions in the economic model and the impacts of this	Thank you for your acknowledgement of the work undertaken by the committee. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect

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				guidance, we appreciate NICE's thorough approach and use of a public review process. We feel strongly that the question of the cost effectiveness of EVAR for AAA repair has not been answered due to the use of outdated and incorrect input assumptions, and that the full impact of the implementation of the guidance has not been considered. We want to ensure the right patients receive the right procedure in accordance with instructions for use (IFU). We strongly support additional research that assesses long-term outcomes from appropriate on-label use of modern EVAR devices. We hope to be able to continue to innovate and help to improve EVAR outcomes over time.	the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see the Health Economic appendix which reports extensive sensitivity analyses for the inputs included in the model. We provide full responses to the comments summarised here where they appear in full detail, below.
Royal College of Anaesthetists	Draft guideline	General	General	The draft guidance ignores the role of the peri-operative physician in assessing and mitigating risk in the management of patients with abdominal aortic aneurysms. It is a significant omission not to include referral to a peri-operative physician or to ensure that decisions on patient management are not considered by a multidisciplinary team that includes peri-operative physicians and anaesthetists.	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Although the guideline does not make specific recommendations about the role of perioperative physicians, committee discussions about perioperative patient management and shared-decision making are described in individual evidence reviews.
Royal College of Anaesthetists	Draft guideline	General	General	It would be sensible to state clearly that this guidance is restricted to abdominal aortic aneurysms and does not consider thoracic, thoracoabdominal aneurysms and associated procedures (open surgery, TEVAR or hybrid procedures). This may require repetition. For example the recommendations regarding open or endovascular procedures may be very different if thoracic aneurysms are included.	Thank you for your comment. The scope of this guideline is specific to treatment and management of abdominal aortic aneurysms, and does not consider other types of aneurysms. This will be outlined in an introductory webpage, as well as at the beginning of each evidence review.
Royal College of Anaesthetists	Draft guideline	General	general	Is there any evidence of an effect of diabetes type or duration of disease has any effect on incidence, risk factors, research	Thank you for your comment. In the evidence review assessing risk factors for aneurysm

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				recommendations etc? The draft guideline treats diabetes as a single entity, whereas in practice it is not.	growth or rupture (Evidence review C) studies were identified which indicated that people with diabetes had lower odds of having an AAA. Unfortunately no other evidence was identified exploring whether the type or duration of diabetes influenced the risk of AAA presence, growth or rupture. As a result, the committee were unable to make specific recommendations according to type of diabetes.
The British Society of Interventional Radiology	Draft guideline	General	General	The BSIR would like to thank NICE for the extensive work that they have done on this recommendation. There are many areas that we agree with but some areas have caused us concern.	Thank you for your comment and endorsement of the guideline. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Individual comments have been responded to where they appear.
Association of British HealthTech Industries (ABHI)	Draft guideline	General	General	**Guidance would effectively end innovation in EVAR.** EVAR technology has been evolving and improving since it was introduced in the 1990s. Multiple studies suggest that outcomes have improved as the devices have evolved. This is documented in other sections within the response (Comment 19). If this guidance were implemented, it would effectively end EVAR innovation in the UK. While newer and more effective devices would continue to be available in other countries, the UK will be focused on open repair. Newer and improved EVAR devices may not be introduced into the UK market by manufacturers. This is true both for infrarenal and complex EVAR, as the RCT recommended for complex EVAR would likely not permit the use of different devices over time because it would make the results less reliable. This lack of focus on innovation is not in keeping with the government's	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence and Theme 1. NICE's position on the value of innovation is as stated in our Social value judgements (2012), as cited in Developing NICE guidelines (2014). We say that

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				"Strategy for UK Life Sciences," which states that the UK will help "bring innovation to market earlier and more easily, making the UK the location of choice for investment."	*Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the intervention as an effective use of NHS resources will specifically take account of…* *[w]hen the intervention is an innovation that adds demonstrable and distinct substantial benefits that may not have been adequately captured in the measurement of health gain.* *As the ICER of an intervention increases in the £20,000 to £30,000 range, an advisory body's judgement about its acceptability as an effective use of NHS resources should make explicit reference to the relevant factors considered above. Above a most plausible ICER of £30,000 per QALY gained, advisory bodies will need to make an increasingly stronger case for supporting the intervention as an effective use of NHS resources with respect to the factors considered above.* It was the committee's view that EVAR fails to meet this test on 2 grounds: (a) in the infrarenal elective case, our best estimate is that it is dominated by OSR (that is, it causes net patient harm alongside additional NHS costs) and, in complex elective cases and those for whom OSR is unsuitable, it is associated with ICERs far above the levels referred to, here; (b) we have no evidence that EVAR adds demonstrable and distinct benefits that we have not captured (the HE model incorporates best-available evidence on patients' quality of life and on the resource impact of EVAR compared with OSR, including postoperative bed-days and likelihood of discharge

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					to home, as well as the implications for short- and long-term survival and reintervention).
South Tees NHS Trust	Draft guideline	General	General	We agree with the guidance recommendations on diagnosis, identifying asymptomatic, symptomatic and ruptured aortic aneurysms, Imaging technique is also appropriate and evidence based.	Thank you for your endorsement of these aspects of the draft guidance. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. Guidelines from other jurisdictions were not part of the scope for this update so they have not been reviewed by the committee.
				However, these guidelines contradict existing Guidelines of the European Society for Vascular Surgery and International Guidelines from the Society for Vascular Surgery (SVS). It has wide implication for future training and distribution of skills to perform this procedure and could potentially put some vascular units that do not perform large volume open surgery at risk. In addition CCGs may use such a document to withhold funding for EVAR based on faulty and inadequate evidence and solely on the 'opinion' of a Panel. After successful Quality Improvement Programme outcomes in vascular surgery, why has NICE decided to publish guidelines that contradict the central premises of the vascular QIP bearing in mind that vascular QIP has meant that AAA repair in the UK is now the safest it has ever been and is more evidence based than it has ever been?	For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.

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				These guidelines do not mention the most important (and consistent) risk factor for rupture in AAA which is AP diameter. There are no guidelines regarding intervention based on size beyond moving from surveillance to treatment. This leaves a large grey area unaddressed.	The committee were unable to identify any evidence that, once a person's AAA has reached the size at which repair is indicated, its diameter should play any part in subsequent decision-making. In particular, as noted in HE.2.3.6.1, AAA diameter was not a significant predictor of long-term mortality in the EVAR-2 cohort. This was also the case in the no intervention arm alone (either per protocol or ITT with an adjustment for crossover).
East of Scotland Vascular Network	Draft guideline	general	general	We are concerned that the implementation of these guidelines will have a detrimental effect on patient care and vascular practice in the UK. Elective endovascular aneurysm repair (EVAR) is an important option for the management of abdominal aortic aneurysms (AAA) and should be offered to appropriately selected patients. We believe the clinical evidence supports this. The recommendations to remove elective EVAR as a patient choice are based on cost. Patients and clinicians will find it difficult to accept this restriction on practice. EVAR has evolved over decades of development in technology and improvement in practice and abandoning it will impact on recruitment and training within vascular surgery and interventional radiology. This will have further effects on service provision and patient care. There will be a question over the validity of the national AAA screening programme. We recognise that there are aspects of AAA management that should be improved:	Thank you for providing this summary of your comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We respond in detail to your agruments regarding clinical evidence below. For discussion of the evolution of EVAR since the RCTs, see **Theme 1**.

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				The pendulum has swung too far towards EVAR and away from open repair in younger, fit patients. There are some patients who are high risk with comorbidities and limited life expectancy who will not benefit from AAA repair. We need to improve our assessment of these patients who are best managed conservatively and should not be offered EVAR.	
				The boundaries of anatomical suitability for EVAR have been pushed too far. Emphasis should be placed on practice within IFU.	The committee agreed that current practice in the area of complex EVAR has little foundation in reliable evidence. However, because people with complex AAAs face a higher absolute risk of perioperative mortality, it is not implausible that complex EVAR may be associated with a better balance of benefits, harms and costs than OSR in such cases, although current best-available evidence does not support this conclusion. This is why the committee recommended research should be carried out in this population. In contrast, having reviewed randomised and observational evidence and original HE modelling based on this research, the committee concluded that it is in the 'on-IFU' population of people with infrarenal AAA that evidence is strongest that OSR should be preferred to EVAR.
				A structured multi-disciplinary team approach to managing AAAs where both open repair and EVAR can be offered to appropriately selected patients will continue to provide the best short and long term outcomes for our patients. Informed consent, patient choice and clinical judgement should be of paramount importance.	Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that there are no methods that reliably predict short-term outcomes of AAA repair, and also found that no individual characteristics are associated with better outcomes for EVAR at a cost that represents effective use of NHS resources. See **Theme 12**.

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East of Scotland Vascular Network	Draft guideline	general	general	**Likely effects of implementation of the guidelines** Vascular surgery and interventional radiology are interesting and rapidly developing specialties. The improvement in endovascular technology and techniques has played a significant role in this. The implementation of these guidelines will be a retrograde step, with the main restriction on practice being seen as one of cost. These two specialities will become less attractive to UK and overseas clinicians and trainees. This will impact on recruitment, training, retention and service provision. The negative effect that the implementation of these guidelines will have on UK Vascular practice cannot be underestimated. Patient care will suffer. Overall aneurysm related mortality will increase in the UK as a result of higher peri-operative mortality and a reduction in intervention rates. The development in UK vascular surgery that has resulted from becoming a separate specialty as well as the benefits seen from the advances in endovascular technology, the AAA improvement programme and the national AAA screening programme will be set back decades.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
Leeds Teaching Hospitals NHS Trust	Draft guideline	General	General	We are most grateful to the NICE guidelines committee for the incredible amount of work they have put into creating these draft guidelines and re-appraising the existing evidence. Given the complexity and scope of the guidelines, however, we believe a longer consultation period would have been appropriate	Thank you for providing this summary of your comments, which we respond to fully where they are given in detail, below. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and the individual.

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				The principal theme in the guidance for repairing unruptured aortic aneurysm (1.5) is about a dichotomy of patients that are "suitable" for open repair and those that are not. This is a critical distinction in the proposed guidelines as it determines who should be offered an elective repair. However, the crucial part missing is any guidance on how this selection should be made. Whilst we recognize the paucity of evidence in this area, in the absence of any guidance on selection, the consideration of which treatments to offer is flawed. We are concerned that the guidelines may be interpreted as suggesting clinical decisions are black and white whereas in reality each case needs to be assessed on risks and potential benefits, together with the patients expressed views. Current clinical practice aims to identify those who are clearly unlikely to benefit from any intervention. There are also those who are younger and fitter, with a low peri-operative risk, who are likely to benefit from open repair. There is however a much larger group in the middle who have a likely higher peri-operative risk from open repair, but may still benefit from increased life expectancy from intervention on their AAA (either open or EVAR), especially if they have a larger aneurysm with a higher annualised risk of rupture. These cases form a grey area, or "group of uncertainty", which is arguably different to the historical EVAR 2 trial cohort. We strongly believe that the risks and benefits of EVAR, open repair and non-operative treatment need further clarification and would welcome a call from the NIHR for clinical trials in this area. There has been no recognition of the size of AAA when considering the risk to benefit ratio of undergoing repair in the 'physiologically unsuitable for OR group'. The decision to	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The predominant evidence underpinning the committee's decision-making is the EVAR-2 RCT, which stipulated that fitness for OSR should be decided at the local level, but provided some guidelines as to likely contraindications for open surgery (Brown et al. 2004). The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful. The committee were unable to identify any evidence that, once a person's AAA has reached the size at which repair is indicated, its diameter should play any part in subsequent

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				operate on a patient that is physiologically unsuitable for OR with a 5.5 cm AAA is different from the same patient, but with an 8 cm aneurysm. It is clear that the patient's risk of rupture is much greater in the latter case and that repair is much more likely to be beneficial. Furthermore, the patient's physiological status means that long-term, 15-year survival is unlikely to be their primary objective; they may benefit from a better short-term outcome and recovery. The recent success of the HTA funded ETTA study highlights the potential value of studying the outcome of patients who are managed conservatively and similar national data collection for patients with conservatively managed AAAs may provide important contemporary information on rupture rates.	decision-making. In particular, as noted in HE.2.3.6.1, AAA diameter was not a significant predictor of long-term mortality in the EVAR-2 cohort. This was also the case in the no intervention arm alone (either per protocol or ITT with an adjustment for crossover). We cautiously agree with this point, insofar as it pertains to AAA rupture rates in people who have been selected for conservative management. However, we would caution against the use of such data as a basis for the explicit or implicit comparison of other long-term outcomes – especially survival – between people who do and do not undergo repair. It is to be expected that people who are selected for conservative management have much shorter life expectancy than those selected for treatment, and this would be the case regardless of approach to their AAA.
All-Party Parliamentary Group on Vascular and Venous Disease	Draft guideline	26-29	623 - 693	The rationale given for the decision to limit access to EVAR for unruptured aneurysms is that there is no evidence that EVAR for people with an unruptured infrarenal AAA provides long-term benefit compared to open surgical repair. It also states that this will minimise harm by reducing long-term mortality, as well as the reduction in reintervention requirements. The APPG is concerned, however, that the data that supports this assertion is outdated; the EVAR-1 trial. This trial was initiated in 1999 and completed in 2004. Since then, the technologies used in this procedure have advanced,	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				which is likely to have an impact on long-term patient outcomes, with fewer complications. For example, the Verzini et al. study in 2014 reported seven-year complication rates of 14.4% versus 25.8% for EVAR devices before and after 2004. Furthermore, clinical techniques have clearly evolved and developed since 1999. This does not seem to have been accounted for within the current draft guideline. The APPG is also aware of a number of upcoming studies which are likely to have a significant impact on the draft guideline; in particular the OVER Study. The consultation deadline should be extended so that promising economic data and data from the OVER Study, which is embargoed until after the deadline, can be included. The APPG is eager to ensure that all relevant data and trials, including relevant registry data, has been reviewed within this context of this draft guideline review and consultation. Currently, by prioritising decade old, outdated trial data ahead of real world data collected in recent years – and about to be released - NICE has reached a decision that is contrary to current clinical practice and a large section of clinician opinion.	Evidence from Verzini et al. (2014) was used in revisions to the HE model, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 8**. 8-year outcomes from OVER are included in the evidence-base on which the guideline relies; while we agree that further follow-up would be interesting, it is expected to be in line with the pattern of outcomes so far. Inevitably, we are compelled to set a cut-off date for inclusion of evidence, and anything that post-dates this will be considered as part of our ongoing surveillance processes.
Association of British HealthTech Industries (ABHI)	Draft guideline And Economic Appendix and Model	9-11	172 - 206	**The economic analysis and subsequent recommendations do not account for the impacts on capacity from additional open surgeries.** Open surgery demands significantly additional utilisation of ward beds, intensive therapy units (ITU), and high dependency units (HDU) compared to EVAR. If the guidance is implemented, it will result in reduced availability of surgical theatres and ITU and HDU beds.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				Based on NVR assumptions 4,000 annual AAA repair patients, eliminating EVAR as an option, and using 2016 NVR data on resource use, an additional 10,439 ward bed days, 7,520 ITU bed days, and 5,666 HDU bed days would be needed. This would lead to increased wait times for AAA repair, as well as other conditions requiring use of theatres, bed days, ITUs, and HDUs. The cost of this has not been considered in the guidelines nor the impact on the patient experience.	
Medtronic UK	Draft guideline	9-11	172 - 206	**The updated Guidance contradicts the aims and recommendations of the Vascular Surgery Get if Right First Time (GIRFT) Programme** The Vascular Surgery GIRFT Programme National Specialty Report 2018 (Horrocks, 2018) provides recommendations to improve the way vascular surgery is organised and delivered in NHS England to enable patients to receive urgent surgery sooner, reduce length of stay and readmissions, reduce theatre time, increase availability of beds, increase availability of staff and improve data collection. The following statements are lifted from the report to highlight that the draft guidance is heavily misaligned against this government-backed GIRFT initiative: "Average wait times for elective abdominal aortic aneurysm (AAA) repair currently range from 35 days (5 weeks) to 145 days (21 weeks). This surgery is designed to avoid the AAA rupturing; the longer the delay,the greater the risk of rupture." (p6) "When wait times were discussed with providers, a range of factors was identified as contributing, from	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We support the aim of the GIRFT programme to provide timely, efficient and safe treatment to people with AAA.

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				lack of available facilities (theatres, beds, CT scanners) to lack of staff. The latter not only refers to surgeons but also the wider team: vascular interventional radiologists, anaesthetists, nurses and physiotherapists." (p18) "Where AAA surgery takes place, there are two main methods: open surgery and EVAR. As both involve repair to the aorta, both are complex, high-risk procedures; however, EVAR is less invasive and recovery times are typically shorter. As a result, around 75% of elective AAA surgery is now conducted by EVAR, with only one provider below the 50% mark." "Setting standard parameters for consultants' workload helps with workforce planning at trust level. However, trusts can only recruit from the available vascular surgery workforce and concerns about whether or not this is sufficient have been long documented. In 2014, the Vascular Society published a Workforce Report 7 that highlighted a range of issues. At present, in England there are approx. seven radiologists per 100,000 of the population (most of these will be non-interventional) and one vascular surgeon per 137,000. These figures are much lower than our international counterparts. Demand is rising and it is known that many vascular surgeons are expected to retire in the next decade." (p26) "When examining length of stay for vascular surgery, it is important to recognise the vast differences between procedure types and the recovery times associated with them. For AAA, EVAR procedures typically last a couple of hours and patients may be discharged within a day or two. Open surgery may	

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				take three or four hours to complete and patients may need to stay in for a week. Furthermore, in some cases, surgeons opt to undertake a staged closure following open repair of a ruptured aneurysm – meaning the patient receives two procedures, thus extending their stay." (p27)	
Medtronic UK	Draft guideline And Economic Appendix and Model	9-11	172-206	**NHS Capacity:** Open surgical repair requires much greater resource utilization of ward beds, intensive therapy units (ITU), and high dependency units (HDU) than EVAR. If the guidance is implemented, it will result in reduced availability of surgical theatres and ITU and HDU beds which will impact not only on capacity for AAA repairs but on all therapy areas that share theatre, critical care and bed space within a hospital. Based on the modest assumption that 4,000 AAA repairs are performed annually, eliminating EVAR as an option, and using 2016 NVR data on resource use, an additional 10,439 ward bed days, 7,520 ITU bed days, and 5,666 HDU bed days would be required. The national shortage of critical care beds has been heavily covered by the press recently (https://www.theguardian.com/society/2018/mar/07/patients-turned-away-intensive-care-lack-beds-shortage-hospitals) and we are concerned that the current draft guidance will only add to the widespread problem.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Medtronic UK	Draft guideline	9-11	179-206	**Decision of EVAR or OSR should be made on an individual patient basis.** The short- and long-term outcomes achieved in EVAR and OSR are heavily driven by the patient's individual characteristics (e.g. age, gender, smoking status, co-morbidities, and anatomy). This draft guidance makes definitive recommendations in favour of open surgery and	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				does not encourage physicians to make decisions on a tailored patient-by-patient basis: NICE Charter 2017 "…our recommendations are not intended to replace the professional expertise and clinical judgement of health professionals, as they discuss treatment options with their patients."	The available evidence on unruptured infrarenal AAA shows that, on average, OSR leads to better net outcomes than EVAR, does not identify any subgroups of patients in which better net outcomes can be expected with EVAR (see **Theme 12**), and shows that there are no tools that reliably predict which individual patients might face a different balance of risks and benefits (see Evidence review H). For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	10-11	195-203	**1.6.1 and 1.6.2** Offering EVAR to patients with ruptured, as opposed to elective infra-renal aneurysms poses risks: - Practitioners will find it difficult to maintain the skills required for emergency EVAR if they are not performing routine elective EVAR. Training our juniors to perform EVAR will be practically impossible. - It is unlikely that stent graft manufacturers will agree to maintain stock in hospitals for the sole purpose of emergency EVAR - The guidance on the optimal method for treating patients with acute symptomatic aneurysms, that the committee concedes are at high-risk of rupture, is confused. Elsewhere in the draft, the committee suggests that these patients should be managed as elective cases, notwithstanding the fact that the evidence used to justify the recommendation pertains only to RCTs in truly elective asymptomatic AAA. This implies that patients presenting with non-ruptured, but acutely	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]).

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				symptomatic AAAs will be denied EVAR – a stance that materially endangers the significant subset of this group that are unfit/less than ideally fit for open AAA repair. It implies also that such patients will have to wait for the moment of frank rupture to be allowed access to EVAR. This apparent ambiguity requires urgent explanation and resolution.	We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.
UHCW NHS Trust Coventry	Draft guideline	11-12	221-116	*CT angiography* CT angiography as the main form of surveillance is in our opinion inappropriate and unnecessary. Again, an issue of patient choice.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. This amendment also allows for patient choice. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when

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					compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline Evidence review H	7-8 23-24 12	130-147 536-556 198-205	The committee considered that the predictive tests and tools identified in evidence reviews G and H, other than cardiopulmonary exercise testing, were not of sufficient discriminatory power to be useful in decision-making and "They agreed that individual variables (as opposed to risk models) can be still useful for making judgments of an individual's risk of postoperative morbidity and mortality." Having accepted that cardiopulmonary exercise testing and some individual factors could be used to predict risk, it seems that the modelling of cost effectiveness could have considered such factors in assessing the cost effectiveness of the different treatment options in subgroups with known risk profiles.	The committee's conclusion was that it would be inappropriate to rely on any test or tool as an arbiter of fitness for repair. Adopting quantitative evidence from Evidence reviews G and H as an input to the HE model would result in exactly that kind of judgement being applied on the basis of evidence about which the committee's uncertainties are clear. The committee agreed that, clearly, clinicians do and should take the risk factors to which people are subject into account when engaging in shared decision-making. However, they were clear that this is a qualitative process, and we currently do not have any reliable ways of predicting surgical outcome

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				Furthermore, the exclusion of eGFR, which was shown to be a predictor of improved outcomes after EVAR, on the basis that no clear threshold could be determined, seems unnecessary as the creation of a dichotomy based upon a threshold is not required if the test is used as part of an overall risk assessment and, along with other measures of risk. Such analysis might have allowed suitable thresholds or subgroups to be identified through the economic modelling.	that would be appropriate to use in hard-and-fast decision-rules.
All-Party Parliamentary Group on Vascular and Venous Disease	Draft guideline	9 - 10	172 – 191	The APPG is concerned that the removal of EVAR and reliance on open surgery would significantly increase the workload of surgeons. This would also add an increased burden on clinical resource – including cath lab capacity and bed days - which this will risk patient safety. Assuming there are 4,000 AAA repairs annually in the NHS, eliminating EVAR as an option, and using 2016 NVR data on resource use, an additional 10,439 ward bed days, 7,520 ITU bed days, and 5,666 HDU bed days would be needed to adopt the draft recommendations. This would lead to increased wait times for AAA repair, as well as other conditions requiring use of theatres, bed days, ITUs, and HDUs. This decision contradicts and undermines the aims and recommendations within the Vascular Get It Right First Time (GIRFT) programme, which highlights EVAR as helpful to reducing bed stays. This initiative has the close backing of the Government.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We support the aim of the GIRFT programme to provide timely, efficient and safe treatment to people with AAA.

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Medtronic UK	Draft guideline	9-10	172-206	**Innovation:** The government's strategy for UK Life Sciences has made it clear that they wish the country to be open for innovation and progress by bringing "innovation to market earlier and more easily". However a guideline that turns the clock back 20 years for the treatment of AAAs is completely counter to this strategy and sends a serious message to health care companies that the reverse is in fact true.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence.
Bradford Teaching Hospitals NHS Foundation Trust	Draft guideline	9-10	179-191	Section 1.5 Repairing unruptured aneurysms The draft recommendation states that open repair is to be offered as the primary treatment, and that EVAR should not be offered if a patient is suitable for open surgical repair. The vast majority of AAA is treated with EVAR, both in the UK, and within Europe. Recommending open repair as a first line treatment for repair would place the UK at odds with standard practice within both the EU and also with North America. A change towards offering more open repair, and less EVAR, is likely to have a significant impact on Vascular Surgeons (who would have to undertake more open surgical procedures), and Vascular Interventional Radiologists (who would undertake less EVAR procedures). Much of the guidance sited in the recommendations relates to EVAR 1 and 2 trial information, which is based on evidence from cohorts of patients recruited between 1994 and 2004. As per the consultation documents, the trials show a reduced 30	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				day mortality from EVAR versus open repair, but this advantage was lost towards the end of the study period due to endograft failures. Nonetheless, there was no significant difference in all cause mortality between the two approaches, and thus EVAR is considered a safe procedure. Endograft failures *were* a feature of early EVAR. However, graft technology has changed significantly in the intervening 14 years. Most notably, all grafts now include a graft anchoring system, that is deployed either above the renal arteries (supra renal fixation), or below the renal arteries (infra renal fixation). These systems prevent graft migration in instances of continued neck dilation. Furthermore, there are a number of devices that are now available that can contend with more tortuous and short necked aneurysms. This larger array of available devices means that an appropriately sized graft can be chosen, based on aneurysm geometry, and reduce the likelihood of graft failure.	In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 8**.
				The assessment of suitability for EVAR or open repair occurs in an MDT setting, which takes into account the anaesthetic risk posed to the patient by both EVAR and open repair. The anaesthetic risk of mortality is lower in patients undergoing EVAR. Therefore, with the proposed guideline, there is a risk that patients with a higher operative mortality will be offered open repair rather than EVAR, with a consequent rise in early mortality.	The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
				In terms of patient selection, over and above anaesthetic exclusions, there are instances in which EVAR is desirable over open surgery. Such instances include: Patients with coincident diagnosis of cancer, where there is a rapid need to	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual

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				start treatment for their cancer (surgical; chemotherapy or radiotherapy); the hostile abdomen (previous surgery; including previous aortic surgery); inflammatory AAA, where the surgical approach would be prolonged and potentially hazardous. There is likely to be a significant disbenefit to these patients if they were not offered EVAR. The patient consent process involves a discussion that outlines the techniques available, and their relative advantages and disadvantages. The draft guidelines do not outline the course of action to be taken when a patient gives a preference for EVAR over open repair. It is therefore possible that patients may decide to decline open surgical repair, and would be precluded from choosing EVAR as an alternative.	abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	9-10	181-191	We are particularly concerned about the proposed recommendations regarding the effective elimination of EVAR in the treatment of elective patients and restriction of complex EVAR to the setting of randomised control trials: "*1.5.3 Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is suitable.* *1.5.4 Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.* *1.5.5. Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.* *1.5.6 Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.*"	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				We observe that, while no relevant new Level 1A evidence is available, this draft nonetheless represents the complete reversal of previous NICE guidance on this topic (TA 167, 2009), whose guidance starts: *"*1.1 *Endovascular stent–grafts are recommended as a treatment option for patients with unruptured infra-renal abdominal aortic aneurysms, for whom surgical intervention (open surgical repair or endovascular aneurysm repair) is considered appropriate.* *The decision on whether endovascular aneurysm repair is preferred over open surgical repair should be made jointly by the patient and their clinician after assessment of a number of factors including: aneurysm size and morphology; patient age, general life expectancy and fitness for open surgery; the short- and long-term benefits and risks of the procedures including aneurysm-related mortality and operative mortality."* It is also at absolute variance with guidance issued by other august authorities, notably the North American SVS guidelines (Journal of Vascular Surgery, January 2018) and European ESVS guidelines (European Journal of Vascular & Endovascular Surgery, September 2011). Furthermore, in its current form, the current draft NICE guidance does not represent our collective understanding of the available literature and is disconnected from current daily international clinical practice. We contend therefore, that the conclusions and draft recommendations are so seriously flawed as to cast doubt on NICE Guidance processes and	For discussion of how additional literature has been reviewed, and how it was interpreted by the committee, please see **Theme 1**, **Theme 2**, **Theme 4**, **Theme 5**, **Theme 6**, **Theme 7** and **Theme 9**.

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				credibility and, if implemented, represent a direct risk to patients with abdominal aortic aneurysms.	
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	9-10	179-189	The recommendation for open repair only of an intact aneurysm Aside from the associated additional morbidity, this is condemning patients overall to a minimal increase in the risk of periprocedural death by 750%. This represents a best case scenario as the comparative data available are related either to patients where there was equipoise as to which was best, or patients underwent a procedure tailored to their unique medical condition and risks. The real world data of a blanket application of this policy to a modern population is unknown, but will almost certainly be worse than this. The proposed recommendations therefore represent an untried experiment in a predominantly western population.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. It is not clear whence you have drawn your estimate of excess perioperative mortality; we infer that it may have been from unadjusted data from the National Vascular Registry. While the committee recognised the value of the NVR as a snapshot of current practice, they rejected it as a valid source of evidence as to the relative risks and benefits of EVAR and OSR, owing to the critical selection biases to which it is subject – see **Theme 3a**.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	4-5		Recommendation of Aortic USS as first choice in detecting ruptured or symptomatic AAA. There is no convincing evidence presented of the sensitivity and specificity of USS for the detection of a ruptured AAA in the hands of a non expert ED physician in a spoke hospital out of hours. This seems to be based upon opinion.	Thank you for your comment. Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. Since no evidence was identified relating to diagnostic imaging of people with suspected ruptured AAA, the committee extrapolated data from people with symptomatic unruptured AAA and drafted consensus recommendations based on their skills and experience. The majority of studies assessed bedside FAST ultrasound, which is often used in emergency settings, and can be performed simultaneously with resuscitative efforts. The speed at which bedside FAST ultrasound can be performed, combined with its availability and utility in emergency settings, led the committee

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					to recommend the technique for assessing people with suspected symptomatic or ruptured AAA. The committee were mindful of the possibility of false-negative ultrasound result, and therefore also recommended that clinicians should immediately contact a regional vascular service if a clinical suspicion of symptomatic or ruptured AAA remains in the absence of ultrasound confirmation of AAA presence.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	1	1&2	We feel the title of this guideline should reflect its contents and be amended to include surveillance.	Thank you for your comment. While recommendations have been drafted relating to opportunistic case finding, the committee were in agreement that this did not constitute surveillance or screening. Since surveillance (such as the National AAA screening programme) is outside the scope of this guideline, the title will remain the same.
Independent Vascular Services	Draft guideline	1	1-2	We feel the title of this guideline should reflect its contents and be amended to include surveillance.	Thank you for your comment. While recommendations have been drafted relating to opportunistic case finding, the committee were in agreement that this did not constitute surveillance or screening. Since surveillance (such as the National AAA screening programme) is outside the scope of this guideline, the title will remain the same.
NHS abdominal aortic screening programmes: England, Scotland, Northern	Draft guideline	3	27	1.1.1 Response: This is consistent with AAA screening procedures, but may increase the number of men who self-refer in the short term.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging rather than a screening programme actively inviting people who are at risk for imaging. The committee took the view that opportunistic case finding of men 66 years and

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Ireland and Wales.					over was likely to be cost effective, as the recommendations allow for more people with AAAs to be identified early, before complications or rupture arise.
NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	Draft guideline	3	30	1.1.2. Response: This is consistent with AAA screening procedures, but may increase the number of men who self-refer in the short term.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging rather than a screening programme actively inviting people who are at risk for imaging. The committee took the view that opportunistic case finding of men 66 years and over was likely to be cost effective, as the recommendations allow for more people with AAAs to be identified early, before complications or rupture arise.
South East and South West London Vascular Networks	Draft guideline	3	40	A large NIHR-funded study has drawn the conclusion that screening women is not clinically or cost effective. We understand this evidence is about to be published in the Lancet demonstrating that 3900 women aged 70 would need to be screened to prevent 1 death.	Thank you for your comment. We noted that the study you have highlighted is related to population-based screening. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed.

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NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	Draft guideline	3	40	1.1.3. Response: Screening women is not part of any population programmes, and would have to be arranged through GP services.	Thank you for your comment. The committee acknowledges that recommendation 1.1.3 is aimed at health services other than the national screening programme, such as GP services. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men.
Royal College of Anaesthetists	Draft guideline	3	40	Section 1.1.3. I am not convinced there is enough evidence to make a firm recommendation for screening in women at age 70. It seems to be based on one study (Singh et al 2001) that is over 20 years old	Thank you for your comment. The committee agreed that the evidence from Singh et al 2001 was of moderate quality and sufficient to incorporate 70 years as the age cut-off in which women were at higher risk off AAA. The results of the study were in agreement with the committee's clinical experience; that women tend to have AAA at later ages than men. Since the evidence was not particularly strong, the committee agreed it was only appropriate to make this recommendation at the 'consider' level. 'Consider' reflects a weaker recommendation compared to 'offer'.
NHS England Specialised Commissioning – Specialised Vascular	Draft guideline	3	whole	the section on Identifying people at risk of abdominal aortic aneurysms is relevant to primary care, but will need an awareness raising campaign possibly through PHE that will require resources. (*Dr Raj Patel, Deputy National Medical Director for Primary Care)*	Thank you for your comment. The committee noted the importance of raising awareness within the clinical community however they did not recommend an awareness campaign. They acknowledged that this would initially require some resources; however, they believed that

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Clinical Reference Group					the recommendations would lead to down-stream cost savings as more people with AAAs would be identified early, before complications or rupture arise.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	3		Screening The viability of the NAASP programme should be considered as a greater number of AAA are likely to rupture based upon these recommendations. This may be an opportunity to consider targeted screening of first degree relatives of patients outside of NAAASP.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. As result, they considered that the recommendations would have little impact on the screening programme. This is further supported by a consultation comment from the screening programme. Recommendation 1.1.2 outlines that a family history of AAA is an important risk factor indicating the need for men aged 66 or over to self-refer to NAAASP. Furthermore, as women are not routinely seen by NAAASP, recommendation 1.1.3 also highlights that a family history of AAA is an important risk factor indicating the need of aortic imaging in women aged 70 or over.
NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	Draft guideline	4	51	1.1.4. Response: This should not impact on screening services, and does ensure surveillance on people with small and medium AAA.	Thank you for your comment and endorsement of the guideline recommendation. The committee believed that the recommendation will not directly impact on screening services because it is related to opportunistic case finding. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that this approach would help identify

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					individuals with aneurysms who are not already seen by the screening programme.
Royal College of Anaesthetists	Draft guideline	4	54-55	Section 1.1.4 The recommendation for patients with an AAA>5.5 should be seen within 2 weeks of diagnosis within a regional clinic does not seem to be based on much evidence and might have significant resource implications. Whereas the UK small aneurysm trial and others showed 5.5cm to be an important threshold, the annual risk of rupture increases significantly with size. At 5.5cm the actual risk is quite small, but is much higher at 9cm for example. Is there consensus to stratify the recommendations by AAA size i.e. support a short referral period for larger aneurysms but a more relaxed period for smaller aneurysms?	Thank you for your comment. The recommendations ensure that the time within which people with newly identified aneurysms are seen by regional vascular services is proportional to the risk of rupture. The committee specified 2 weeks as this time period reflects current expectations within the NHS AAA Screening Programme.
Royal College of Anaesthetists	Draft guideline	4	61-68	Section 1.1.6. This is a very important section. It needs emphasis and in my opinion needs revision. Why do the risk factors listed here differ from the risk factors in 1.1.2? The evidence base is identical and arguably urgent diagnosis even more important because the time available for intervention is minutes or hours rather than days or weeks. In particular the presence of a family history is very important. I appreciate the evidence about this is mixed but the 'low quality' studies encompasses studies of > 3 million patients, and there is moderate quality evidence in a study of >1300 patients. It would also be a 'no-brainer' to a patient, their family or a coroner to consider AAA in anyone with a family history presenting to ED with back pain.	Thank you for your comment. Recommendations 1.1.2 and 1.1.6 were derived from evidence identified in 2 separate reviews (evidence reviews A and N); one assessing risk factors for presence, and another assessing risk factors for aneurysm rupture. The recommendations reflect the risk factors identified in each review taking into consideration the quality of the studies reporting each risk factor.
Royal College of Anaesthetists	Draft guideline	4	61-68	Section 1.1.6. You could consider whether or not to stratify this a little more. Abdominal/back pain can mean 'tender' or impending rupture aneurysm, whereby shock or LOC imply it has already happened.	Thank you for your comment. The committee considered your suggestion and agreed that that level of stratification was not necessary. This is because they believed that in any of these circumstances a patient will

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					need urgent medical attention, and evaluation of risk would be down to the discretion of the clinician.
Royal College of Anaesthetists	Draft guideline	4	61-68	Section 1.1.6. Renal colic is a very common mimic of AAA and the two are often confused. Though this is mentioned in Evidence review N, Appendix A, it is not the sort of thing amenable to an RCT but is known by every vascular and urological surgeon and experienced vascular anaesthetist/intensivist and ED doctor. I would suggest adding this as a 'red flag' consideration and adding to 1.1.6 Similarly I would promote obesity as an early indication for imaging, not because of the association with AAA but because diagnosis is often more difficult in the obese patient	Thank you for your comment. The recommendations are intended to highlight risk factors that suggest an aneurysm has ruptured or is about to. As a result, the committee agreed that it was not necessary to change the recommendations because this would take away from their intended message.
Royal College of Anaesthetists	Draft guideline	4	69	I would suggest adding a line to the effect that 'although the incidence is lower in women…more likely to rupture if present'	Thank you for your comment. Upon consideration of your comment, the committee agreed not to amend the recommendation. However the following is presented in the context section of the guideline instead: 'Although the incidence of abdominal aortic aneurysms is approximately 6 times lower in women, the rate of aneurysm rupture is significantly higher'.
Society and College of Radiographers	Draft guideline	5	70	Can further clarification be given as to setting? The patient may not be in hospital where bedside ultrasound is a possibility.	Thank you for your comment. The committee drafted the recommendation to considering all settings. They recommended that immediate bedside ultrasound (FAST ultrasound) should be offered for symptomatic or suspected ruptured AAA to accommodate hospital settings. They were mindful that in community settings, as well as some hospital settings, ultrasound devices may not be available. As a result the recommendation

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					highlights that clinicians should discuss the patient immediately with a regional vascular service if the ultrasound is not immediately available.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	5	70	**1.1.8** The recommendation for bedside ultrasound for suspected ruptured AAA is impractical, of questionable clinical relevance and likely to cause diagnostic delay risking death: - Referring hospitals are unlikely to have appropriately trained operators to reliably perform immediate bedside ultrasound for AAA - The IMPROVE trial (Br J Surg 2014;101:216) investigators recommended CT, an imaging modality readily available in modern UK hospitals, for all patients suspected to have ruptured AAA to avoid diagnostic error.	Thank you for your comment. Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. Since no evidence was identified relating to diagnostic imaging of people with suspected ruptured AAA, the committee extrapolated data from people with symptomatic unruptured AAA and drafted consensus recommendations based on their skills and experience. The majority of studies assessed bedside FAST ultrasound, which is often used in emergency settings, and can be performed simultaneously with resuscitative efforts. The speed at which bedside FAST ultrasound can be performed, combined with its availability and utility in emergency settings, led the committee to recommend the technique for assessing people with suspected symptomatic or ruptured AAA. The committee were mindful of the possibility of false-negative ultrasound result, and therefore also recommended that clinicians should immediately contact a regional vascular service if a clinical suspicion of symptomatic or ruptured AAA remains in the absence of ultrasound confirmation of AAA presence. The committee discussed whether CT could be recommended for diagnosing symptomatic or unruptured AAA. Although it is the best imaging technique, recommending a CT scan for all patients who are symptomatic (whether as the sole test or as a subsequent test to the FAST ultrasound) was not considered safe as it may unnecessarily delay the transfer of patients to the regional vascular service for treatment. Furthermore,

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					performing a CT scan in all patients would also incur considerable costs.
Nottingham University Hospital	Draft guideline	5	70	Suspected rupture, bedside ultrasound often unhelpful, availability and expertise variable CT angiogram much more useful in confirming diagnosis and showing whether emergency EVAR is possible i.e. flexibility required on which investigation appropriate depending on local circumstances.	Thank you for your comment. Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. The committee discussed whether CT could be recommended for diagnosing symptomatic or ruptured AAA. Although it is the best imaging technique, recommending a CT scan for all patients who are symptomatic (whether as the sole test or as a subsequent test to the FAST ultrasound) was not considered safe as it may unnecessarily delay the transfer of patients to the regional vascular service for treatment. Furthermore, performing a CT scan in all patients would also incur considerable costs. The committee also discussed the role of CT angiography in patients who have been transferred to a regional vascular service, and are being considered for emergency repair. They expressed the view that it would be bad practice to undertake emergency EVAR without performing CT angiography. However, they also acknowledged that, where a patient's condition is critically unstable, a vascular specialist may need to rely on a strong clinical diagnosis coupled with ultrasound imaging to inform their decision to attempt open surgical repair. Therefore, the committee agreed it would be unsafe to recommend that CT should always be undertaken and, instead, agreed that it should be considered in each case.
The Society of Vascular Technology Great Britain	Draft guideline	5	70 - 72	Although immediate bed side Aortic ultrasound is fundamental in initial rapid diagnosis this requires training for medical & surgical personnel. This is currently in their curriculum for them to be able to measure an AAA using ultrasound. SVTGB&I are currently working with vascular society to	Thank you for making us aware of these developments.

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& Ireland (SVTGB&I)				discuss how this could be implemented. Implementation of this training will begin next year.	
Independent Vascular Services	Draft guideline	5	70-72	Although immediate bed side Aortic ultrasound is fundamental in initial rapid diagnosis this requires training for medical & surgical personnel. NICE should recommend that ultrasound training is curricular based with assessments of competency for vascular surgeons in training.	Thank you for your comment. It is not within the remit of the committee to specify training curricula for vascular surgeons in training.
Society and College of Radiographers	Draft guideline	5	77	The AAA screening programme uses an inner to inner measurement as the research that led to screening used this. Its use is more variable in ultrasound examinations undertaken outside of the screening programme where outer to outer measurements are often used. It would be good if there was advice on further alignment of measurement techniques. Vascular surgeons base their surveillance and surgical intervention criteria on outer to outer measurements. Measurements of inner to inner tend to be approx. 4mm smaller than outer to outer measurement and this factor needs to be taken in to account as surgical intervention may be delayed or a person may not be included in a surveillance programme if the measurement was just under the guidelines. The SCoR feels there should probably be standardisation across the board so that vascular labs, sonographers, NAAASP are all doing the same thing and that surveillance/surgical criteria should be based on whichever method is adopted.	Thank you for your comment. Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. The committee were in agreement that there are variations in measurement planes and parameters, with is preferred measurement approach used across practice. The committee considered that inner arterial edge has a clearer line from which to measure, suggesting that measurement from the inner to inner edge may be more reproducible. In the absence of any evidence to make a recommendation, the committee agreed that the potential for reproducibility supported a recommendation for setting the anterior-posterior inner-to-inner diameter as the standard measurement parameter. Taking an inner-to-inner measurement reflects current practice of the NHS AAA Screening Programme, and therefore will maintain a standardised approach across the NHS.
NHS abdominal aortic	Draft guideline	5	77	1.1.9. Response: This method is consistent with screening programme methodology.	Thank you for your comment and endorsement of the guideline recommendation.

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screening programmes: England, Scotland, Northern Ireland and Wales.					
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	5	77 - 80	The SVTGB&I recognise the method for ultrasound measurement anterior-posterior inner to inner dimensions in accordance with NAAASP. However the SVTGB&I recognises that there is research to support all methods of Ultrasound measurement including outer to outer diameters and therefore the NICE guidelines in relation to ultrasound measurement should stipulate AAA ultrasound measurements done in individual labs should be done on well defined evidence based protocol's and method of measurement should be stated on reports The SVTGB&I feels NICE should go further in its guidance and recommend safe levels of inter-observer agreement like NAAASP, and define what is meant by an increase in sac size but also recommend a inter-modality difference threshold for comparison to CT like NAAASP. This will ensure accurate and consistent measurements. The SVTGB&I feel that this recommendation should be made despite there being conclusive evidence. While the SVTGB&I realises that 5.5 cm is the current threshold based on UKSAT study [1] it should be noted that the MASS study used outer to outer diameters [2] Therefore,	Thank you for your comment. The committee made the recommendation for inner-to-inner measures to reflect current standards within the NHS AAA screening programme which takes two anterior–posterior measurements of the maximum aortic diameter, recorded in centimetres, measured across the lumen from/to the inside of the ultrasound-detected aortic wall. The committee made the recommendation to ensure a standardised approach is used for measuring aneurysms across the whole NHS. The committee were mindful that additional measurements could be potentially useful. Thus, they also stated in the recommendation that any additional measurements should be documented clearly. In relation to your comment about the lack of clarity of the recommendation, the recommendation has now been reworded. Finally the committee chose, to retain the wording "anterior-posterior" as this is the wording used by the NHS AAA screening programme.

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				the decision to refer to vascular services at 5.5cm using an inner to inner measure is inconsistent with the original trial. As CT is often measured via an outer-to outer method a tolerance measure (5 mm) should be applied when comparing ultrasound with CT. Alternative it may be appropriate to measure an AAA using both inner to inner and outer to outer methods providing these are documented correctly within the report. *Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants.* Lancet, 1998. **352**(9141): p. 1649-55. Ashton, H.A., et al., *The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial.* Lancet, 2002. **360**(9345): p. 1531-9 Additionally There are two ways interpreting "report anterior-posterior inner-to-inner diameter as a minimum." Need to clarify whether or not this means quoting the diameter as a minimum (smallest) measurement for the aorta, or if this is the minimum amount of information to be given about the vessel. Antero-posterior is the correct term (not anterior-posterior.)	
Independent Vascular Services	Draft guideline	5	77-80	IVS Ltd agree that the recommended method for ultrasound is anterior-posterior inner to inner dimensions in accordance with NAAASP. However, IVS Ltd feels NICE should go further in its guidance and recommend safe levels of inter-observer agreement like NAAASP but also recommend a inter-modality	Thank you for your comment. The committee made the recommendation for inner-to-inner measures to reflect current standards within the NHS AAA screening programme which takes two anterior–posterior

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				difference threshold for comparison to CT like NAAASP. This will ensure accurate and consistent measurements. IVS Ltd feel that this recommendation should be made despite their being conclusive evidence. While IVS Ltd realises that 5.5 cm is the current threshold based on UKSAT study [1] it should be noted that the MASS study used outer to outer diameters [2] Therefore, the decision to refer to vascular services at 5.5cm using an inner to inner measure is inconsistent with the original trial. As CT is often measured via an outer-to outer method a tolerance measure (5 mm) should be applied when comparing ultrasound with CT. Alternative it may be appropriate to measure an AAA using both inner to inner and outer to outer methods providing these are documented correctly within the report. *Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants.* Lancet, 1998. **352**(9141): p. 1649-55. Ashton, H.A., et al., *The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial.* Lancet, 2002. **360**(9345): p. 1531-9	measurements of the maximum aortic diameter, recorded in centimetres, measured across the lumen from/to the inside of the ultrasound-detected aortic wall. The committee made the recommendation to ensure a standardised approach is used for measuring aneurysms across the whole NHS. The committee were mindful that additional measurements could be potentially useful. Thus, they also stated in the recommendation that any additional measurements should be documented clearly. In relation to your comment about the lack of clarity of the recommendation, the recommendation has now been reworded. Finally the committee chose, to retain the wording "anterior-posterior" as this is the wording used by the NHS AAA screening programme.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	5	81 - 86	A tolerance for the discrepancy between ultrasound and CT should be adopted from NAAASP. The guideline should also describe how Aortic diameter should be measured by CT such that there is a standard guideline.	Thank you for your comment. The committee made the recommendation for inner-to-inner measurement to reflect current standards within the NHS AAA screening programme which takes two anterior–posterior measurements of the maximum aortic diameter, recorded in

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					centimetres, measured across the lumen from/to the inside of the ultrasound-detected aortic wall. The committee made the recommendation to ensure a standardised approach is used for measuring aneurysms across the whole NHS. The committee were mindful that additional measurements could be potentially useful. Thus, they also stated in the recommendation that any additional measurements should be documented clearly. In relation to your comment about the lack of clarity of the recommendation, the recommendation has now been reworded. Finally the committee chose, to retain the wording "anterior-posterior" as this is the wording used by the NHS AAA screening programme.
Independent Vascular Services	Draft guideline	5	81-86	A tolerance for the discrepancy between ultrasound and CT should be adopted from NAAASP. The guideline should also describe how Aortic diameter should be measured by CT such that there is a standard guideline – such as anterior-posterior inner to inner for ultrasound.	Thank you for your comment. The committee made the recommendation for inner-to-inner measurement to reflect current standards within the NHS AAA screening programme which takes two anterior–posterior measurements of the maximum aortic diameter, recorded in centimetres, measured across the lumen from/to the inside of the ultrasound-detected aortic wall. The committee made the recommendation to ensure a standardised approach is used for measuring aneurysms across the whole NHS. The committee were mindful that additional measurements could be potentially useful. Thus, they also stated in the recommendation that any additional measurements should be documented clearly. In relation to your comment about the lack of clarity of the recommendation, the recommendation has now been reworded. Finally the committee chose, to retain the wording

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					"anterior-posterior" as this is the wording used by the NHS AAA screening programme.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline	5 6 8	89-92 93-96 148-153	These recommendations regarding the selection of patients for transfer or treatment of emergency AAA raise the danger of discriminatory practice – our evidence suggests practice variation in that more women are turned down for surgery, even after adjustment for age and co-morbidities (Aber et al. Gender differences in the rates of repair of emergency abdominal aortic aneurysm. BSET Annual Meeting 2018). Although there is a case for implementing end-of-life care for patients unlikely to survive, we need to be aware that decisions by non-experts not to transfer patients may result in exacerbation of potentially discriminatory practice due to preconceptions about likelihood of survival – for example there is some evidence from HES data which suggests that certain centres routinely turn down patients for treatment based upon age (Michaels et al. Cost and outcome implications of the organisation of vascular services. Health Technol Assess 2000; 4(11) p21). Whilst we would agree that formal risk assessment tools do not provide an adequate basis for selecting patients with ruptured aneurysm for transfer or treatment, this is because the underlying clinical parameters are poor predictors of outcome in these cases. Clinicians, particularly those less familiar with the treatment of AAA, should also be wary of informal methods for making these choices, to avoid unjustifiably denying potentially life-saving treatment on the basis of poorly founded preconceptions about predicted risks.	Thank you for your comment and bringing these issues to our attention. Evidence review O provides a detailed overview of the committee's deliberations with the aim to reduce discriminatory practice.
Hull and East Yorkshire	Draft guideline	5		Ultrasound measurement inner to inner.	Thank you for your comment.

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Hospitals Vascular and Endovascular Service				This is not consistent with the evidence base which established the treatment threshold in the first place. There are considerable issues with this. These include where the callipers should be placed; On the inside of the wall? The thrombus? There can be a significant amount of judgment in this. Where will the sonographers actually place the callipers irrespective of any recommendations? Neither of these measurements are applicable to the evidence base relating to rupture risk. What is the recommendation for CT? Is practice to be changed with regard to CT with no evidence? The evidence quoted in the present paper makes the point commonly found in practice, that USS underestimates size. If this is compounded by inner to inner measurements then intervention will not be offered until the AAA has grown to a size significantly greater than the evidence based threshold, with an increased risk of rupture in surveillance.	Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. The committee were in agreement that there are variations in measurement planes and parameters, with no preferred measurement approach used across practice. The committee considered that inner arterial edge has a clearer line from which to measure, suggesting that measurement from the inner to inner edge may be more reproducible. In the absence of any evidence to make a recommendation, the committee agreed that the potential for reproducibility supported a recommendation for setting the anterior-posterior inner-to-inner diameter as the standard measurement parameter. Taking an inner-to-inner measurement reflects current practice of the NHS AAA Screening Programme, and therefore will maintain a standardised approach across the NHS.
South East and South West London Vascular Networks	Draft guideline	6	104 - 111	We agree that transfer protocols for urgent and ruptured AAA should be agreed and formalised to encourage timely transfer to regional vascular units and should include recommendations regarding immediate CT angiography and case planning with 3D reconstruction. These protocols should be led by the arterial centres and network clinical leads. Use of imaging linking technology such as IEP should be explicitly encouraged to improve communication between district hospitals and arterial centres.	Thank you for your comment and endorsement of the guideline recommendations about patient transfer. The committee noted the importance of the points made in your comment; however, they believe that it is not within their remit to be explicit about how transfer protocols should be developed and implemented. They believe that these details should be determined by local service providers within the context of the facilities, equipment and other resources available to them.
Guy's & St. Thomas' and King's College Hospitals -	Draft guideline	6	113	**1.2.6** The recommendation for permissive hypotension is not supported by current evidence. The IMPROVE trial (Br J Surg 2014;101:216) found better survival in patients who had a higher blood pressure, although the trial was not designed to compare outcomes after permissive compared with	Thank you for your comment. Evidence review O provides a detailed account of the committee's discussion about permissive hypotension. Briefly, no evidence from RCTs was identified relating to the use of

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King's Health Partners Vascular Unit				normotensive resuscitation. Further studies, designed specifically to address this question, are needed before any recommendation is made (Moreno Cochrane Database Syst Rev 2018).	permissive hypotension in people with ruptured AAA. As a result, the committee agreed that it was appropriate to make consensus recommendations by adapting recommendations drafted in the NICE guideline for assessment and treatment of major trauma (NNG 39). This was because they considered that the rationale underpinning the use of restrictive fluid resuscitation in people after major trauma was applicable to people with ruptured AAAs.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	7	117 – 122	We feel that medical optimisation is crucial for AAA patients and the guideline should go further than just smoking cessation and hypertension modification.	Thank you for your comment. When assessing risk factors for aneurysm growth or rupture the committee agreed that modifiable risk factors were most important as they could influence the management of people with known AAAs. Smoking cessation and hypertension modification were considered 2 fundamental components of medical optimisation in people identified as having an AAA. When the committee discussed how to improve operative outcomes in people with AAA, they cross-referred to other NICE guidelines (in recommendation 1.4.6) that they believed would facilitate medical optimisation in this population. These guidelines included the NICE guidelines on medicines optimisation, lipid modification, diabetes management, and antiplatelet therapy.
Independent Vascular Services	Draft guideline	7	117-122	We feel that medical optimisation is crucial for AAA patients and the guideline should go further than just smoking cessation and hypertension modification.	Thank you for your comment. When assessing risk factors for aneurysm growth or rupture the committee agreed that modifiable risk factors were most important as they could influence the management of people with known AAAs. Smoking cessation and hypertension modification were considered 2 fundamental components of medical optimisation in people identified as having an AAA. When the committee discussed how to improve operative

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					outcomes in people with AAA, they cross-referred to other NICE guidelines (in recommendation 1.4.6) that they believed would facilitate medical optimisation in this population. These guidelines included the NICE guidelines on medicines optimisation, lipid modification, diabetes management, and antiplatelet therapy.
NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	Draft guideline	7	118	1.3.1 and 1.3.2. Response: Men in surveillance are seen by specialist nurses and given guidance on healthy living (including smoking cessation). They are advised to attend their GPs for secondary prevention.	Thank you for your comment. We appreciate your experience of how patients are managed in the screening programme and feel that this is in line with the committee recommendations for the wider NHS.
Independent Vascular Services	Draft guideline	7	124	We feel the guideline should identify the normal size of the AAA. Recent work by Oliver-Williams et al (2018) has noted that the size of the native normal aorta has decreased in size. Oliver-Williams, C., et al., *Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme.* Br J Surg, 2018. **105**(1): p. 68-74.	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Unfortunately, identification of the size of the native normal aorta was not an issue included within the scope of the guideline, and therefore it was not possible for any recommendations to be made on this topic.
University Hospitals of the North Midlands (UHNM)	Draft guideline	7	124	1.3.3 Scanning patients with USS every 2 years rather than every year represents a change of practice. There is a subset of aneurysms which progress more rapidly within that time frame and therefore could be at greater risk of rupture. (see ref1.5.1)	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm

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					and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	7	124	We feel the guideline should identify the normal size of the AAA. Recent work by Oliver-Williams et al (2018) has noted that the size of the native normal aorta has decreased in size. Oliver-Williams, C., et al., *Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme.* Br J Surg, 2018. **105**(1): p. 68-74.	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Unfortunately, identification of the size of the native normal aorta was not an issue included within the scope of the guideline, and therefore it was not possible for any recommendations to be made on this topic.
NHS abdominal aortic screening programmes: England, Scotland,	Draft guideline	7	124	1.3.3.. Response: This is inconsistent with current screening programmes standard operating procedure. The new NICE recommendation was made following level 1 research evidence that prolonging surveillance intervals in men with small AAA (3-4cm) is safe. Additional evidence from surveillance in NAAASP is that men with AAA just below the referral threshold have a low rupture risk, and that 5.5cm	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm

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Northern Ireland and Wales.				remains the appropriate referral threshold. Further research may prove that it may be safe to increase the surveillance interval to 6 monthly in men with medium AAA (4.5-5.4cm). Screening programmes are presently planning changes to surveillance intervals based on updated data that are likely to match this NICE guidance.	and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Cardiovascular and Interventional Radiology Society of Europe	Draft guideline	7	126	Monitoring aneurysms between 4.5cm and 5.4cm every 3 months is evidence based but for slow growing aneurysms < 5.0cm (minimal change after 6 months surveillance), this can safely be extended to 6 month intervals	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the

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					committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Independent Vascular Services	Draft guideline	7	127	This is a large group of AAA sizes. The guideline fails to account for rapidly growing AAAs in recommending surveillance intervals. Those who are growing rapidly and measure 4.4cm at initial diagnosis would not be seen for 2 years (as we do not know they are rapidly growing). This could result in sac measurements of up to 6.4 cm at the second scan – 2-year interval. However, they would be likely to have ruptured before then. One yearly surveillance scans would capture this. We would recommend scanning intervals of: Every 5 years if the AAA is 2.6 – 2.9 cm Every 2 years if the AAA is 3.0 – 3.9 cm Annually if the AAA is 4.0 – 4.4 cm Every 3 months if the AAA is 4.5cm to 5.4cm The committee acknowledges the lack of evidence (Evidence document D) in this area in addition to appreciating that this is currently the widely accepted standard nationally. Given the clinical risk and lack of evidence surely clinical risk must take priority over cost-effectiveness until such evidence is available that suggests an amended protocol is safe?	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an

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					asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	7	127	This is a large group of AAA sizes. The guideline fails to account for rapidly growing AAAs in recommending surveillance intervals. Those who are growing rapidly and measure 4.4cm at initial diagnosis would not be seen for 2 years (as we do not know they are rapidly growing). This could result in sac measurements of up to 6.4 cm at the second scan – 2-year interval. However, they would be likely to have ruptured before then. One yearly surveillance scans would capture this. We would suggest examples of appropriate scanning intervals are: Every 5 years if the AAA is 2.6 – 2.9 cm Every 2 years if the AAA is 3.0 – 3.9 cm Annually if the AAA is 4.0 – 4.4 cm Every 3 months if the AAA is 4.5cm to 5.4cm The committee acknowledges the lack of evidence (Evidence document D) in this area in addition to appreciating that this is currently the widely accepted standard nationally. Given the clinical risk and lack of evidence surely clinical risk must take priority over cost-effectiveness until such evidence is available that suggests an amended protocol is safe? There should also be provision in a local protocol to allow for the natural history of any person's AAA, and patient preference for a scanning interval.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Hull and East Yorkshire Hospitals	Draft guideline	7		Surveillance – 2 yearly for AAA 3-4.4cm.	Thank you for your comment. Evidence review D provides a detailed description of the

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Vascular and Endovascular Service				This is at odds with the recommendation to consider repair of an intact AAA >4cm with a growth of >1cm/year. Whereas the arbitrary choice of 3 months for 4.5-5.4cm would double the number of scans we do for patients 4.5-4.9cm. It is acknowledged in the document that these are not evidence based recommendations, so why make them at all? Consider making the range of reasonable options acceptable.	committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Royal College of Anaesthetists	Draft guideline	8	137	The draft guidance's out-of-hand dismissal of the value of risk assessment tools in the shared decision-making that must underpin patient care ignores their value in relative risk evaluation. The absolute numbers produced by these tools may not have the accuracy that would satisfy the statisticians producing this guidance. However, their results will serve to inform discussion with patients and between healthcare professionals, and it is counterproductive to list tools that should not be used rather than explain the way in which they could be used. It is widely accepted that all risk assessment	Thank you for your comment. To clarify the statement that risk assessment tools are not commonly used outside research: the committee noted that risk assessment tools were routinely used in many clinical areas but, in their experience, they were not widely used outside research when it came to the context of AAA. The committee had little confidence about the clinical utility of risk assessment tools because they could not see how using tools with c-statistics of around 0.70 would lead to appropriate decisions about patient management and prognostic

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				tools must be used in conjunction with clinical judgement and this assertion could be usefully incorporated into the guidance. Furthermore, we are not at all sure that the data on CPET implies that it should be recommended as part of a shared decision-making process over some of the available risk assessment tools. For example, a systematic review published in 2016 (Moran et al, British Journal of Anaesthesia) identified only four studies evaluating the use of CPET in around 1500 patients undergoing aortic aneurysm surgery and was modest in its recommendations for use. However, the British Aneurysm Repair Score (Grant et al) was developed and validated using bootstrapping methods on over 11,000 patients from the UK's own vascular registry, and demonstrated acceptable (AUC 0.72) discrimination. It is particularly disingenuous to recommend a test (CPET) for use which only a proportion of UK hospitals have access to, while dismissing risk assessment tools which could be used sensibly, in conjunction with clinical experience and judgement, by clinicians at every bedside and in every clinic. Further to that, it is also incorrect and contrary to the efforts of other perioperative improvement endeavours (e.g. the National Emergency Laparotomy Audit) to state that risk assessment tools are not commonly used outside research, given that there are national recommendations from Royal Colleges and national audits which recommend the use of an objective risk assessment tool alongside clinical judgment. Finally, if proposing that the available evidence on risk assessment tools is not currently sufficient to make positive	outcomes. The committee considered that use of risk assessment tools with insufficient discriminatory power could have potentially harmful effects on patient care. This is because such tools could result in the decision to operate on a patient who shouldn't be operated on, or vice versa. The committee discussed decision-making without the use of risk assessment tools. They noted that most of the clinical data used to derive risk assessment tools are commonly collected and are already available before surgery. They agreed that individual variables (as opposed to risk models) can be still useful for making judgments of an individual's risk of postoperative morbidity and mortality. The committee decided against making a research recommendation because extensive research into risk assessment tools for AAA surgery has already been performed over recent decades and further research in this area is unlikely to be viewed as a priority. In relation to CPET, the committee noted that, while CPET may provide healthcare professionals valuable objective information on the fitness of people prior to elective AAA repair, the evidence was not robust enough to make strong recommendations for the use of the test as a decisive arbiter of fitness. Moreover, the committee agreed that individual CPET parameters should not be used in isolation to decide whether a patient should have surgery or not, but instead, may be used to inform shared decision making about treatment options in context of medical history and examination. The committee agreed that it was only appropriate to make this recommendation at the 'consider' level because the evidence was not particularly strong.

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				recommendations over which ones (if any) to use, the guidance should recommend future research on this topic.	
South East and South West London Vascular Networks	Draft guideline	8	149	This point in the guidance is inconsistent with Point 1.2.2, with which we agree. Cardiac arrest and prolonged loss of consciousness are signs/symptoms and should be taken account of.	Thank you for your comment. The committee made recommendation 1.3.2 (previously 1.2.2) to raise awareness that people with a confirmed ruptured AAA who have a cardiac arrest and/or have a persistent loss of consciousness (in the emergency department or during transfer) have a negligible chance of surviving AAA repair. The guideline then highlights (in 1.4.4) that it is not appropriate to rely on any single symptom, sign or risk factor to determine suitability for AAA repair. Overall, this means that cardiac arrest and loss of consciousness should be considered in combination with other factors to determine whether aneurysm repair is suitable.
Leeds Teaching Hospitals NHS Trust	Draft guideline Evidence Review H	8 24 11 13	152 551 142 211	"*Do not use patient risk assessment tools (scoring systems) to determine whether aneurysm repair is suitable for a person with a ruptured AAA."* *"None of the risk assessment tools had a high enough predictive accuracy at predicting post-op outcomes…..not improve decision making and could potentially lead to inappropriate decisions about patient care".* Determining fitness for surgery is at the heart of these guidelines. Whilst we recognise the limitations of the evidence surrounding risk assessment tools and scoring systems as reviewed in detail in evidence review H; there is no guidance on what <u>should</u> be used. It is helpful that specific tools have been identified not to be used, but we would welcome the opportunity to use or develop the remaining tools to aid in patient selection. The authors appear to support this in evidence review H "*The committee did not want to preclude development of tools for assessing postoperative outcomes of*	Thank you for your comment. The committee had little confidence about the clinical utility of risk assessment tools because they could not see how using tools with insufficient discriminatory power would lead to appropriate decisions about patient management and prognostic outcomes. They discussed decision-making without the use of risk assessment tools and noted that most of the clinical data used to derive risk assessment tools are commonly collected and are already available before surgery. It was agreed that individual variables (as opposed to risk models) can be still useful for making judgments of an individual's risk of postoperative morbidity and mortality, and therefore inform the decision to operate. The committee decided against making a research recommendation because extensive research into risk assessment tools for AAA surgery

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				AAA surgery. Thus, the committee chose to specify risk assessment that should not be used rather than state that risk assessment tools should not be used, in general." But this does not appear to be reflected in the recommendations for patients "suitable for open repair". We are concerned that "clinician intuition" or even an MDT is unlikely to stand up well either to statistical scrutiny of its predictive value. Risk assessment tools as part of a holistic assessment within the framework of an MDT should improve consistency in decision-making for these patients which is currently subject to variation both between and within centres.	has already been performed over recent decades and further research in this area is unlikely to be viewed as a priority.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	8	154 - 171	We feel the guideline falls short of recommending supervised exercise optimisation prior to elective surgical repair or EVAR. Selective exercise programmes can improve CPEX results prior to surgery and thus improve surgical outcome. Particular benefit would be seen in those patients that have 4.5 – 5.0 cm AAA as time is available for optimisation.	Thank you for your comment. The committee considered that the identified evidence on preoperative exercise interventions was not robust enough to support a recommendation. Although the identified evidence for most outcomes were graded as being low-to-moderate in quality, the committee felt that the small sample sizes and relatively short follow-up periods of included studies precluded any confidence in the reported outcomes. The committee made a research recommendation on preoperative exercise to encourage research that will inform future updates of the guideline.
Independent Vascular Services	Draft guideline	8	154-171	We feel the guideline falls short of recommending supervised exercise optimisation prior to elective surgical repair or EVAR. Selective exercise programmes can improve CPEX results prior to surgery and thus improve surgical outcome. Particular benefit would be seen in those patients that have 4.5 – 5.0 cm AAA as time is available for optimisation.	Thank you for your comment. The committee considered that the identified evidence on preoperative exercise interventions was not robust enough to support a recommendation. Although the identified evidence for most outcomes were graded as being low-to-moderate in quality, the committee felt that the small sample sizes and relatively short follow-up periods of included studies precluded any confidence in the reported outcomes. The committee

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					made a research recommendation on preoperative exercise to encourage research that will inform future updates of the guideline.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	Page 8	137 – 147	We agree with the Committee that there are currently no validated risk assessment tools to predict "fitness" and suitability for open AAA surgery. However, the recommendation 1.5.4 (page 10, 183) suggests that this is possible and that patients can be categorised into two distinct groups, either "fit for open AAA repair" or "no intervention". There is no robust evidence for this. VASGBI would support means of fitness testing and developing validated risk models as a research recommendation for this guidance. A post-hoc analysis of the patients in the EVAR1 (fit for open repair) and EVAR2 (unfit for open repair) studies indicated that there was very substantial overlap between the risk profiles of the two groups.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a

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					research recommendation noting that such a study would be helpful.
University Hospitals of the North Midlands (UHNM)	Draft guideline	9	172	1.5.1 It will be impossible to determine the growth of an aneurysm of more than 1cm per year in some cases and offer treatment if the frequency of assessment with USS is reduced to every two years (See ref 1.3.3)	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Cardiovascular and Interventional Radiology Society of Europe	Draft guideline	9	172-191	The recommendations for repairing unruptured aneurysms are the most concerning and contentious in the entire document. They are primarily based on early RCTs comparing EVAR to open repair, which showed an early survival benefit for EVAR in all trials, a mid-term catch up to equivalent survival (although the OVER Trial reported a survival benefit trend	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				favouring EVAR) and a late survival advantage in one trial (EVAR 1) favouring open repair, not reported in other trials. The re-intervention rate and overall health costs are significantly higher for EVAR in all studies. The major concerns of the recommendations for the treatment of unruptured aneurysms are as follows: 1. The EVAR RCT trials on which the recommendations are based used old devices, procedures and interventional techniques. It has been clearly demonstrated that the frequency of major complications (and consequently interventions) such as type 1 and type 3 endoleaks, iliac artery access complications, limb occlusions have all significantly reduced with newer generation devices. Device costs have reduced in relative terms as volume and commercial competition have increased. Moreover, the reduced reintervention rates (a major contributor to cost) have further reduced EVAR costs. 2. The proposal places a major emphasis on the assessment of peri-operative risk. It implies the decision "fit for surgery" is a binary and relatively straightforward one. This is far from the case. Multidisciplinary meetings assessing peri-operative risk continue to evolve and any protocol that relies only on peri-operative risk will see a great variability in patients being treated across the United Kingdom.	whilst supporting individualised care around which interventions are appropriate. We found that all 3 RCTs that report long-term survival have closely comparable findings (see figure HE07 and figure HE97 in the HE report, which reports an I^2 of 0% for post-perioperative HRs, suggesting that there is no between-study variation over and above that which would be expected by sampling error). For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Device costs used in the HE evaluation reflect current prices. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to

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					offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				3. The recommendation not to offer EVAR to patients if open repair is suitable (1.5.3) or to patients considered high risk for open repair due to anaesthetic and medical issues (1.5.4) are of major concern on many grounds. They deny patients the opportunity to benefit from new technological advances. Patient groups who are considered to be high risk for open repair (including those with hostile abdomens) would be deprived of any treatment under these recommendations. The recommendations take no account of the stress and quality of life reduction suffered by many patients once they are aware that they have an aneurysm. Once patients know that they have an aneurysm, they can't "unknow" this and for many patients, the "timebomb" they have in their abdomen greatly reduces their quality of life. It makes no sense for these recommendations to allow EVAR in complex anatomy as part of ongoing trials and to totally exclude patients who have straightforward anatomy for EVAR, who do not choose open repair	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.

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NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	Draft guideline	9	173	1.5.1. Response: Current screening programme standard operating procedure indicates that intervention is not specifically indicated if an AAA grows by 1cm in a year. This would depend on previous size (i.e. more concerning if 4.3 to 5.3cm than 3.1 to 4.1cm). Screening programmes rely on individualised advice from programme clinical leads. This recommendation does not take into account the fact that in future small AAA will only undergo surveillance every 2 years. The 4-nations groups has grappled with this issue and found it impossible to offer generalised advice.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
NHS abdominal aortic screening programmes: England, Scotland, Northern	Draft guideline	9	173	1.5.1 to 1.5.6. Response: This section has the biggest potential to affect NHS AAA screening programmes. This restriction on the use of EVAR in men unfit for open repair is expected to reduce the number of men who can be offered AAA repair after it has been detected by screening. It could affect QoL if a man is in surveillance for years, finally reaches 5.5cm, is referred urgently, but then turned down for treatment. The only logical conclusion is that some measure of	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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Ireland and Wales.				fitness for open repair would need to be introduced for men in surveillance. Those unfit for open repair would be discharged from surveillance. The problem is that there is no clear way of assessing fitness for open aneurysm repair. Men with screen-detected AAA who are of borderline fitness for open repair could be accepted for surgery, with a resulting increase in mortality following elective open AAA repair. Other points More men turned down for surgery, ultimately means more men will die of ruptured AAA (screening less effective at preventing death from AAA rupture) Lack of patient choice More open surgery means increased need for critical care, and longer hospital stays	The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
South East and South West London Vascular Networks	Draft guideline	9	173-178	This point is inconsistent with Point 1.3.3. It is not possible to detect an aneurysm that is 'larger than 4.0cm and has grown by more than 1cm in 1 year' if screening is only 'every 2 years if the AAA is 3.0-4.4cm.'	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals

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					because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Nottingham University Hospital	Draft guideline	9	176	No mention of differences in size threshold between men and women	Thank you for your comment. Evidence review F provides a detailed account of the committee's discussions about thresholds for surgery. Upon review of the identified evidence it was noted that women were underrepresented in the included studies and no evidence of differences between genders were explored. Since there was no robust evidence to confirm the optimum threshold for considering surgery in women, the committee were reluctant to recommend a different threshold from the widely accepted 5.5 cm threshold used for men. The committee also discussed whether the size threshold may vary according to age but acknowledged that there was no available evidence indicating that the size and resultant risk of rupture was dependent on age.
South Tees NHS Trust	Draft guideline	9	177	This recommendation is at odds with the previous guidance on time intervals for aneurysm surveillance as an increase in an aneurysm of >1cm in 1 year in aneurysms of less than 4.4cm	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to

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				will be missed. Although, we agree that the incidence of this is likely to be extremely small.	monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	9	177 &178	By their nature AAA do not grow rapidly consistently. On the whole AAAs remain stable or slow growing for long periods and then can enter a phase of accelerated growth. If you have an AAA that measures 4.0 cm and has been slow growing would not be seen for 2 years. However, could grow significantly, greater than 1cm/year in that 2 year period with an increased risk of rupture. This population would not be detected and therefore would not be repaired as per the guideline recommendation.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of

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					rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Independent Vascular Services	Draft guideline	9	177-178	By their nature AAA do not grow rapidly consistently. On the whole AAAs remain stable or slow growing for long periods and then can enter a phase of accelerated growth. If you have an AAA that measures 4.0 cm and has been slow growing would not be seen for 2 years. However, could grow significantly, greater than 1cm/year in that 2 year period with an increased risk of rupture. This population would not be detected and therefore would not be repaired as per the guideline recommendation.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following:

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					"Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
University Hospitals of the North Midlands (UHNM)	Draft guideline	9	179	1.5.2 Mortality argument: - We accept there may be increased rates of re intervention for EVAR vs open repair and therefore an increased mortality beyond 10 years. However, EVAR has a lower mortality compared with surgery (**1.7% EVAR vs. 4.2% OSR: EVAR 1**). Accepting a higher mortality rate by not offering EVAR would be contrary to VASQIP guidance (3.5%mortality accepted per unit). Performing open repair only therefore, may lead to unacceptably high AAA related early mortality rates. In our unit, we looked at mortality for patients having an elective EVAR who were over 80 years old between 2009 and 2018. There were **173** cases with **2** deaths (**1.15% mortality**). This suggests that mortality rates are, in fact, lower even in this more comorbid group of patients from endovascular repair at 30 days in hospital. We speculate that this difference in observed real world practice in the elderly comorbid patients compared with EVAR 1 trial data may be due to the fact that earlier generation devices were used in these older trials and the subsequent increased expertise in performing EVAR.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. Thank you for giving us details of your experience; please see **Theme 3c**. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. There are, in fact, 4 RCTs included in our systematic review (OVER and ACE as well as EVAR-1 and DREAM).

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				Whilst we recognise that the only randomised control data that are available are from the EVAR and DREAM trials we would question the relevance of this data in today's modern endovascular practice.	
				It may be helpful to include real world registry data in this analysis from the National vascular and Eurostar Registries. We acknowledge the limitations from registry data which include voluntary submission and lack of long term outcomes. In our practice, confirmed by the data submitted to the NVR database, the mortality for elective open repair in the last 7 years is higher than elective EVAR (**OSR 5.7% vs EVAR 0.5%**). This is real world, honest data from a balanced open/endovascular large vascular network performing more than 100 elective aneurysm procedures per year. This is contrary to the published data. These draft guidelines, if implemented, would potentially increase the number of open repairs, which would increase the short term AAA related mortality in patients with aneurysmal disease. GIRFT and NAAASP recommend detection to treatment targets of eight weeks for patients with aneurysmal disease. A sea change in practice of this magnitude, in preference to open repair, would have huge implications on the delivery of AAA services nationwide. With increased open surgery we foresee increased delays to treatment timelines, more cancellations due to the general lack of critical care capacity in the UK, increased length of hospital stay and an increased risk of rupture and death whilst waiting.	For discussion of the use of NVR and other registries to estimate perioperative mortality, please see **Theme 3a** and **Theme 3b**. Thank you for giving us details of your experience; please see **Theme 3c**.

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				There is also the issue of deskilling of surgical and interventional radiology teams committed to providing a balanced endovascular practice. Moral argument There would be a cohort of patients who are deemed not fit for open surgery who are known to have an AAA from the screening program or from in-hospital surveillance. These patients, using the draft guidance as it currently stands, would be denied an elective EVAR and turned down for open surgery but potentially subsequently present in an emergency situation as a rupture. We are then morally obliged to offer them emergency EVAR, which seems perverse as they have been declined this option in an elective setting. A proportion of these patients would die before ever reaching care and the mortality from emergency endovascular repair remains disproportionally higher than in an elective setting even in these more comorbid patients.	The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. The evidence from EVAR-2 suggests that people with medical comorbidities of sufficient seriousness to contraindicate OSR face a substantially greater force of mortality from those factors than they do from AAA rupture. In other words, most participants who were randomised to no intervention died with – rather than from – their AAA. In the setting of ruptured AAA, there is obviously a different balance of benefits and harms associated with the decision between intervening or not. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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				Economic argument Our economic review of the supplied data appears somewhat confusing. The difference appears to be roughly the cost of the device with similar QALY. It may be worth looking at whether the device cost could be reduced. We appreciate that re-interventions were higher in the trial setting with EVAR and this undoubtedly increases the overall cost in the EVAR group. However, as before, these were older generation devices with greater device related complications.	NICE has no role in setting the price of medical devices. However, we do provide sensitivity analyses showing cost-effectiveness results at different graft prices in the HE report (see figure HE47, figure HE59, figure HE70, figure HE78, figure HE93 and figure HE94, updated in the revised results as figure HE116, figure HE117, figure HE118, figure HE133, figure HE134, figure HE135, figure HE136 and figure HE155). In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
				We also recognise that secondary re-interventions are higher when devices are used outside the manufacturer's instructions for use (IFU) and as such, this cavalier practice to endovascular repair for AAA disease should be discouraged and it is regrettable that NICE have not mentioned this as a draft recommendation. There is no long term data on re-interventions in patients undergoing open repair compared to EVAR and as such, long term cost comparisons cannot be made.	There is high-quality randomised evidence and additional casemix-adjusted observational evidence on re-interventions in patients undergoing OSR compared with EVAR. These data informed the committee's considerations and were used as inputs to the HE model.
				The draft economic argument regarding length of stay is based on EVAR trial data where length of stay following EVAR was 9.8 days; this included an in hospital CTA. Data from the NVR highlights a post EVAR in hospital stay of 2 days in our unit and 3 days nationally. It is not common practice to offer a post op CTA in current practice. We feel these two points contribute to the flaws in the economic argument.	We have revised postoperative resource-use inputs to the HE model, using data including estimates from the NVR; see **Theme 6a**.

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				We are also unsure as to whether the open surgical repair return to theatre costs and length of stay costs are included in the modelling which, of course, would alter the scenario.	Length of stay costs are included in the HE model; see **Theme 6a**. We understand that, depending on the precise timing of return-to-theatre episodes, they should be accounted for in either the estimates of intraoperative resource use from the RCTs or in reintervention rates. Therefore, applying an additional provision for such cases would double-count the costs with which they are associated.
British Society of Endovascular Therapy (BSET)	Draft guideline	9	179	The recommendations not to offer infrarenal EVAR are based on a "lack of long-term durability" for EVAR over open repair. Unfortunately, the evidence used to make these recommendations is fatally flawed. The mistake being made here is that the randomised trials on which the recommendations are based were never designed to look at long term durability. All of these trials had a sample size calculations based on comparing all cause mortality between EVAR and open surgery at 30 days and at a maximum 3 years where EVAR was still superior to open repair.[1] This means that longer term comparisons will be statistically dubious at best, but attrition rates were so high in these trials that 5 to 15 year comparisons between EVAR and open surgery based on these data are meaningless.[2] It is on the basis of these comparisons that the NICE committee are suggesting we actively withhold the most common treatment for infrarenal EVAR performed in the UK today.[3] The long-term results of these trials are still actively debated at scientific vascular meetings around the world, and there are strong, valid arguments over flaws in the way the long-term data are being presented and applied to modern practice.[4-6]	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. However, we disagree with the suggestion that the design of RCTs renders their results unreliable. The power of trials is relevant to the precision, but not the accuracy, of their findings – see **Theme 9b**. The finding that EVAR is associated with excess post-perioperative mortality is strongly supported by the review of casemix-adjusted observational evidence that we have conducted in response to stakeholders' criticism that the consultation draft placed too much weight on RCTs alone – see **Theme 9**. In fact, this evidence suggests that the trials may represent an underestimate of the true effect in real-world practice.

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				These include: a lack of long-term complication data in the open AAA group; the fact that EVAR devices have been updated since the devices used in the early 2000's and have significantly lower complication rates;[7] and the huge updates in understanding in anatomical suitability and application of EVAR which was lacking in these trials but has led to better patient selection and therefore outcomes since. All of these are valid arguments against EVAR being inferior to open repair in the long term, but are superseded by the simple fact that these trials were not designed for long terms comparisons between EVAR and open surgery and cannot be used to withhold EVAR as a result. Brown LC, Epstein D, Manca A, Beard JD, Powell JT, Greenhalgh RM. The UK Endovascular Aneurysm Repair (EVAR) trials: design, methodology and progress. Eur J Vasc Endovasc Surg. 2004 Apr;27(4):372-81. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM; EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. Lancet. 2016 Nov 12;388(10058):2366-2374. doi: 10.1016/S0140-6736(16)31135-7. https://www.vsqip.org.uk/reports/2017-annual-report/ 1: Dubois L, Mayer D, Rancic Z, Veith FJ, Lachat M. Debate: whether endovascular repair offers a survival advantage over open repair for ruptured abdominal aortic aneurysms. J Vasc Surg. 2015 Feb;61(2):546-55. doi: 10.1016/j.jvs.2014.11.042. PubMed PMID: 25619580. Mayer D, Rancic Z, Veith FJ, Lachat M. Part two: against the motion. EVAR offers no survival benefit over open repair for the treatment of ruptured abdominal aortic aneurysms. Eur J	Each of the issues raised by the literature cited has been well covered in the analyses undertaken for this guideline: • 'a lack of long-term complication data in the open AAA group': although it was not part of their original protocol, the EVAR trial investigators retrospectively incorporated hernia procedures to their reporting and we use those data in our HE model. We have also captured additional laparotomy-related procedures (lysis of adhesions and bowel resection), which are more prevalent following OSR, based on a matched comparison of US Medicare data (Schermerhorn et al., 2015). The particular resource use and quality of life implications of each of these complications are captured. • 'the fact that EVAR devices have been updated since the devices used in the early 2000's and have significantly lower complication rates': the HE model has been revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. The meta-analysis by Kent et al. (2018) was amongst the evidence considered, though the revised base-case relies on another study that is more favourable to EVAR (Verzini et al., 2014). Full details are provided in **Theme 7**. • 'the huge updates in understanding in anatomical suitability and application of EVAR which was lacking in these trials but has led to better patient selection and therefore outcomes since': while it is true that outcomes have improved for EVAR over the period since the RCTs recruited, the same is also true for OSR, with the net result that there is no evidence that the relative benefit for EVAR over OSR has grown over time – see **Theme 3** and **Theme 9**.

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				Vasc Endovasc Surg. 2015 Feb;49(2):119-27. doi: 10.1016/j.ejvs.2014.11.016. PubMed PMID: 25662727. Dubois L. Part one: for the motion. EVAR offers no survival benefit over open repair for the treatment of ruptured abdominal aortic aneurysms. Eur J Vasc Endovasc Surg. 2015 Feb;49(2):116-9. doi: 10.1016/j.ejvs.2014.11.015. PubMed PMID: 25662726. Kent F, Ambler GK, Bosanquet DC, Twine CP; BSET (British Society for Endovascular Therapy). The Safety of Device Registries for Endovascular Abdominal Aortic Aneurysm Repair: Systematic Review and Meta-regression. Eur J Vasc Endovasc Surg. 2018 Feb;55(2):177-183. doi: 10.1016/j.ejvs.2017.11.013.	
Royal College of Anaesthetists	Draft guideline	9	179	The use of the term "anaesthetic or medical contraindications" is inappropriate and may reveal a lack of understanding of the nature of risk in relation to these patients. There are no absolute contraindications to general anaesthesia. Rather, there are patient and surgical factors that may affect patient outcome after aneurysm repair under general anaesthesia. Some factors are open to mitigation; others are not. Risk in this context is a spectrum, and the decision of whether to offer a patient an open repair under general anaesthesia is one that should be taken by a multidisciplinary team that includes peri-operative physicians and anaesthetists.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	179	"*For people with unruptured AAAs meeting the criteria offer open surgical repair unless there are anaesthetic or medical contraindications*". We are concerned regarding this wording. We would prefer explicit recognition that is the surgery and surgical stress response that causes morbidity and mortality, which may be contributed to by medical comorbidities. Modern anaesthesia is incredibly safe and deaths attributable directly to	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				anaesthesia in the elective setting are extremely rare. Surgery however is inherently risky, especially major body cavity surgery including open AAA repair. Assessment of physiological reserve to be likely to withstand the insult of such major surgery is what is key here. Describing this as "fitness for anaesthesia" is misleading. Whilst accepting that a clinical useful guideline cannot consider every clinical eventuality, there is no guidance on the relatively common scenario of patients who are physiologically fit for an open repair but having a relative contraindication to surgery such as previous radiotherapy of abdominal surgery. Under this guideline recommendation no definitive treatment would be offered to these patients.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	9	179-180	Statement 1.5.2 this recommendation will be challenging as this is a dramatic change in clinical practice to what is currently offered throughout the UK. This has substantial impact upon funding and workforce and doesn't reflect outcomes being experienced. In addition there is a patient choice related to open v EVAR – with a substantial increase in morbidity for open procedures – this really is astonishing that a NICE guidance is recommending something so foreign and against much of the data. Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. [This text was identified as confidential so has been removed.]	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals of the North	Draft guideline	9	181	1.5.3 There are a subset of patients that are not suitable for open surgical repair for reasons other than comorbidity that may be suitable for EVAR e.g. patients with hostile abdomens, radiotherapy etc. Decreasing the number of overall EVARs	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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Midlands (UHNM)				would reduce expertise and make treating these patients more challenging with similar arguments as mentioned above.	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder comments like this, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR.See **Theme 14**.
University Hospitals Southampton – Wessex Vascular Network	Draft guideline	9	181	**Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is suitable.** The categorical nature of this statement appears unfair to our patients, removing patient choice and sacrificing significant short and medium term benefit to our patients. NICE appear to have made this definitive advice based on long term outcomes of the EVAR-1 trial- a study powered for outcomes up to 3 years. More astonishingly this long-term evidence is based on less than ½ of the original recruitment. University Hospitals Southampton currently perform 1/3 of aneurysm treatments using open repair. This leaves 2/3 of our current elective caseload treated by EVAR. Patients don't look at 10 year or 15 year data- they look at early outcomes, their own quality of Life [QoL] and time to return to normal activity. EVAR offers enormous advantages in each of these domains making denying patients this alternative unethical.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee's conclusions on the long-term risks associated with EVAR were not solely based on EVAR-1; rather they reflect a range of randomised and observational data. It was the committee's confident interpretation of this evidence that EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**. For specific comments on the statistical power of the elective RCTs to identify differences in long-term survival, please see **Theme 9b**. It is in the nature of long-term survival effects that they become most evident in the proportion of the cohort that lives the longest.

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				We are conscious that many other groups which UHS surgeons are part of will submit challenges to the poor quality evidence used to generate these draft AAA recommendations and errors in the Health economic modelling [BSET & Vascular Society]– thus we will not dwell on them. The shift towards an endovascular-dominated practice is multi-factorial, combining clinical factors, scientific progress and patient choice. When provided with the evidence, patients prefer EVAR because of the over-riding benefit in early survival and reduced risk of organ dysfunction. Patients are willing to travel to centralised units, to receive EVAR with the added incentives of survival and prompt restoration of quality of life. Endovascular sceptics often fall back on the argument of cost yet EVAR-1 presents an unfair and inaccurate comparison between EVAR and OR. There is no record of laparotomy-related complications and associated costs. Surveillance post EVAR has been rationalised to duplex and may yet become more patient-specific, reducing this burden further. EVAR has driven down our length of stay freeing up more beds and making our service more efficient. This has also reduced our need to use ITU and HDU beds. A move back to only OR will have enormous funding implications for our trust. This will be particularly more relevant as the number of patients, turned down for elective surgery, present for emergency repair and consume ITU resources for an extended period. We estimate that our trust would need to fund an extra ITU bed simply based on this recommendation.	Although it was not part of their original protocol, the EVAR trial investigators retrospectively incorporated hernia procedures to their reporting and we use those data in our HE model. We have also captured additional laparotomy-related procedures (lysis of adhesions and bowel resection), which are more prevalent following OSR, based on a matched comparison of US Medicare data (Schermerhorn et al., 2015). The particular resource use and quality of life implications of each of these complications are captured. In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks – see **Theme 11**.

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				EVAR represents the principle driver for reduced AAA mortality. Patients will vote with their feet and seek out EVAR rather than expose themselves to the unnecessary peri-operative risk associated with OR.	
Nottingham University Hospital	Draft guideline	9	181	This denies patient choice, in my experience many patients prefer a smaller operation and accept a greater risk of re-intervention. It is based on historical data with first generation devices with many devices being used outside manufacturers IFU (because of lack of alternatives). Modern results are likely to show much lower re-intervention rates, albeit still higher than open repair. Have NICE considered the knock on effect on other specialities, for example ITU bed demand and increased length of stay?	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
Countess of Chester Hospital	Draft guideline	9	181	Do Not Offer EVAR The effect of this blanket withdrawal of treatment will be to adversely impact on the outcomes for those with life expectancy of up to 8 years .	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				There will be an increase in perioperative mortality. The provision of ITU and HDU will be unable to meet the demands of elective OSR	Cohorts with lower-than-average life expectancy were amongst the subgroups that were considered in the HE model, in an attempt to identify population(s) for whom EVAR may be the optimal choice. However, we were unable to identify any groups that would benefit at a cost that can be considered an effective use of NHS resources. See **Theme 12**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
East of Scotland Vascular Network	Draft guideline	9	181	This recommendation (do not offer EVAR to people with un-ruptured infra-renal AAA) is not based on the evidence on clinical outcomes. Evolution in practice has not been recognised. Implementation will impact on patient care and overall aneurysm related mortality in the UK. **Clinical outcome evidence** The randomised trials have provided level 1 evidence supporting elective EVAR in terms of clinical outcomes. The UK endovascular aneurysm repair trial 1 (EVAR 1 trial) 15-year follow-up reported that the early mortality benefits of EVAR compared with open repair are offset by an increase in	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. The committee acknowledged the high-quality evidence that OSR is associated with worse perioperative mortality than EVAR. However, it was also the committee's interpretation of evidence – including but not limited to EVAR-1 – that EVAR has been and remains associated with excess mortality in the long term – see **Theme 9**.

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				late mortality. The aneurysm related mortality curves cross over between 6 years and 8 years and the total mortality curves diverge after 10 years. However there were no significant differences in the primary outcome of total mortality and the secondary outcome of aneurysm related mortality over the whole follow-up period [(1)]. The late increase in mortality in the EVAR group is predominantly due to secondary sac rupture. Few of these ruptures are spontaneous, without uncorrected complications identified during surveillance: type 1 and 3 endoleaks, type 2 endoleaks associated with sac size increase, graft migration and kinking [(2)]. These results highlight the importance of lifelong surveillance following EVAR and re-intervention when necessary [(1)]. The results do not support the abandonment of elective EVAR. The importance of the early survival benefit associated with EVAR should not be underestimated. The median survival of patients in the EVAR 1 trial was just over 8 years (8.7 years in the EVAR group and 8.3 years in the open group) [(1)]. The numbers at risk at 15 year's follow-up are small. The EVAR 1 trial was powered for 3 year follow-up for the primary outcome of all-cause mortality [(3)]. **Evolution of practice** Practice and technology have developed in the 15-20 years since the EVAR 1 trial patients were randomised and this should be acknowledged. Examples of this are: There have been significant advancements in imaging, allowing improved case planning and device selection. It is	The follow-up regimen mandated in the RCTs was relatively intensive – the committee agreed that current NHS practice often relies on less frequent use of less sensitive tests (and other stakeholders have supported this view in criticising our recommendation of CT-based follow-up). Therefore, the committee concluded that RCT results reflect an optimistic view of rates of late complication-related mortality and morbidity associated with EVAR – a conculsion that is apparently supported by observational data (see **Theme 11)**. For discussion of the statistical power of the EVAR-1 RCT, please see **Theme 9b**. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The evidence cited suggests that the performance of modern stent-grafts is superior to that of older devices only in the domain of reintervention rate. The committee acknowledged

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				now standard practice for all patients to have post-operative, pre-discharge imaging – this was not part of the trial protocol. A number of patients in the EVAR 1 trial had sac ruptures with no post-operative imaging or after having missed follow-up [2]. Improvements have been made in surveillance protocols and the importance of early re-intervention for complications has been recognised. Stent-graft technology has developed over decades. There is evidence that modern devices perform better than the older stent-grafts used in the trials [4]. None of the stent-grafts used in the EVAR 1 trial remain in clinical use in the UK without significant design modification (Cook Zenith, Gore Excluder) or have been withdrawn completely (Medtronic Talent and AneuRyx). The Talent and AneuRyx devices were used in 35% of patients in the EVAR 1 trial (32% and 3% respectively) [5]. These stent-grafts were designed with no active anatomical fixation (hooks, barbs) and have been associated with high rates of graft migration [6,7,8]. The EVAR 1 trial was not powered to compare outcomes of different stent-grafts. However, device-specific results were reported with relatively short follow-up (median 3.8 years). There were no statistically significant differences in secondary interventions and mortality, although the direction of results was in favour of Cook Zenith (active fixation) versus Medtronic Talent (no active fixation) [5]. Registries of modern stent-grafts are demonstrating efficacy in reducing endoleaks, graft migrations and aneurysm related mortality (Gore GREAT Registry and Medtronic ENGAGE Registry). The EVAR 1 and 2 trials have also provided evidence that adverse anatomy is associated with poorer long term	this finding, and considered revised HE modelling that used a lower reintervention rate for EVAR. However, this did not have a material influence on conclusions – see **Theme 7**. There is no evidence that the excess long-term mortality with which EVAR is associated has diminished similarly.

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				outcomes [9]. This and a plethora of similar data [10,11] should guide changes in clinical practice, in terms of patient selection. No account of this evidence has been taken in the draft guidelines. **Patient care and overall aneurysm related mortality** Implementation of the guidelines will have a significant impact on patient care. The Abdominal Aortic Aneurysm Quality Improvement Programme (AAAQIP) was initiated in 2009 by the Vascular Society (VSGBI) after the UK was identified as an outlier for peri-operative AAA mortality at 7.5% compared with the rest of Europe at 3.5%[12]. In 2012, The National Vascular Registry reported improved outcomes in the UK with a mortality rate of 2.4%, and this has now reduced to 1.5% [13]. The increase in elective EVAR in the UK (54% of elective repairs in 2009, 70% in 2017) has undoubtedly played a significant role in this reduction in peri-operative mortality. Much of this will be undone if the guidelines are implemented and elective EVAR is abandoned. The UK will again become an outlier with the rest of Europe, as well as with North America and Australasia. Experience in open aneurysm repair has declined in the UK. Peri-operative mortality will inevitably increase and there is likely to be a reduction in the number of AAAs being repaired with increased turn down rates. Overall aneurysm related mortality will increase in the UK as a result. There is evidence already that the lower rates of AAA intervention in the UK are associated with a higher rate of overall aneurysm related mortality than in the US [14]. Additionally, there is likely to be an increased ITU bed utilisation and increase length of in-patient stay which will impact on other areas of service provision and patient care.	For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.

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				Impact on practice, costs and challenges with implementation of the guidelines within the East of Scotland Vascular Network (ESVN) Over the 3 years, 2015-2017, 24% of our patients underwent open repair and 76% had EVAR (infra-renal and complex). We know that open repair is associated with longer in-patient stays and increased HDU and ITU bed utilisation. Implementation of the guidelines and abandonment of elective EVAR is highly likely to result in increased numbers of cancellations and have knock on effects on other areas of the service. We do not have additional capacity to deal with this change in workload. Other issues, such as double consultant scrubbing and available theatre capacity will present difficulties that we do not currently have the resources to address. We are likely to have an increase in elective cancellations as a result. Addressing these issues will have cost implications with staffing, theatre capacity, in-patient bed capacity and HDU/ITU resources. All our patients are discussed at a dedicated AAA MDT with vascular surgeons, radiologists and anaesthetists. We anticipate an increase in turn down rates if elective EVAR cannot be offered. We will be obligated to prospectively audit this, as will vascular services UK-wide. Our perioperative mortality rates will be recorded in the NVR. We have been given no guidance regarding the following situations: symptomatic patients, patients with hostile abdomens, stomas, inflammatory aneurysms, synchronous tumours, previous aortic surgery or previous EVAR.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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				1. Rajesh Patel, Michael J Sweeting, Janet T Powell, Roger M Greenhalgh, for the EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1	The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously 1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.

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				(EVAR trial 1): a randomised controlled trial. *Lancet* 2016; **388:** 2366-2374. 2. Thomas R. Wyss, MD, Louise C. Brown, PhD, Janet T. Powell, MD, and Roger M. Greenhalgh. Rate and Predictability of Graft Rupture After Endovascular and Open Abdominal Aortic Aneurysm Repair. Data From the EVAR Trials. *Ann Surg* 2010; **5:** 805-811. 3. L. C. Brown, D. Epstein, A. Manca, J. D. Beard, J. T. Powell, R. M. Greenhalgh. The UK Endovascular Aneurysm Repair (EVAR) Trials: Design, Methodology and Progress. *Eur J Vasc Endovasc Surg* 2004; **27:** 372–381. 4. Verzini F, Isernia G, De Rango P, et al. Abdominal aortic endografting beyond the trials: a 15-year single-center experience comparing newer to older generation stent-grafts. *J Endovasc Ther* 2014; **21:** 439–47. 5. The EVAR Trial participants. Secondary Interventions and Mortality Following EVAR: Device-specific Results from the UK EVAR Trials. Eur J Vasc Endovasc Surg 2007; **34:** 281-290. 6. Tonnessen B, Sternbergh W, Money S. Mid- and long-term device migration after endovascular abdominal aortic aneurysm repair: A comparison of AneuRx and Zenith endografts. *J Vas Surg* 2005; **42:** 392-401. 7. Spanos K, Karathanos C, Saleptsis V, Giannoukas AD. Systematic review and meta-analysis of migration after endovascular abdominal aortic aneurysm repair. Vascular 2015; **24**: 323-36. 8. Mannetje Y, Cuypers P, Saleem B, Bode A, Teijink J, van Sambeek M. Comparison of midterm results for the Talent and Endurant stent graft. *J Vascular Surgery* 2017; **66:** 735-742. 9. The influence of thrombus, calcification, angulation, and tortuosity of attachment sites on the time to the first graft -	

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				related complication after endovascular aneurysm repair. *J Vasc Surg* 2011; **54**: 965-971. 10. Schanzer A., Greenberg R.K., Hevelone N., Robinson W.P., Eslami M.H., Goldberg R.J., Messina L. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation* 2011; 123: 2848-2855. 11. Stather P.W., Sayers R.D., Cheah A., Wild J.B., Bown M.J., Choke E. Outcomes of Endovascular Aneurysm Repair in Patients with Hostile Neck Anatomy. *Eur J Vasc Endovasc Surg* 2012; **44**: 556-561. 12. Second Vascular Surgery Database Report 2008. European Society for Vascular Surgery. Eds: Gibbons C, Kinsman R, Walton P. Dendrite Clinical Systems Ltd 2008, ISBN 1-903968-21-6. 13. National Vascular Registry 2016 Annual Report. https://www.vsqip.org.uk 14. Karthikesalingam A, Vidal-Diez A, Holt P, Loftus I, Schermerhorn M, Soden P, Landon B, Thompson M. Thresholds for Abdominal Aortic Aneurysm Repair in England and the United States. N Engl J Med 2016; **375:** 2051-9.	
Leeds Teaching Hospitals NHS Trust	Draft guideline Evidence Review G Evidence Review H Evidence Review K	9 10 12 23	181 145 166 545	*"Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is suitable".* These recommendations are based on an analysis of EVAR 1, OVER and DREAM trials which showed a reduction in peri-operative mortality, hospital stay and recovery for patients undergoing EVAR but no difference in longer term mortality compared to open repair and an increased rate of re-interventions. We are concerned that short term outcomes and recovery are important in this group of older patients, for whom the recovery	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				from an open procedure may represent an important proportion of their remaining life expectancy. In addition they are often caregivers for spouses or partners. The comments in Evidence G and H would appear to support this: Evidence H page 166 - *"the outcomes which matter most are mortality and complications that occur within 30d of surgery"* Evidence G page 145 - "*The committee agreed that perioperative mortality, particularly 30-day mortality, was an important outcome. Identification of people at high risk of perioperative mortality allows healthcare professionals to judge whether surgery should be offered to people as well as plan care and support accordingly"* The statement in Evidence Review K "*outcomes that matter most are long-term survival*" would appear to contradict this. We are not aware of any evidence to support this statement. There is clearly an opportunity for the NICE to recommend further studies using Patient and Public Involvement (PPI) to address what really matters to patients rather than a view obtained from an MDT We feel it is the balance between the "up front" (peri-operative risk) and the potential increase in life expectancy (long term survival) that is important and the guidelines should reflect this for the decision-making for individual patients.	
Leeds Teaching	Draft guideline	9 14	181 217	We are concerned that outcomes from the trials considered to support this recommendation do not reflect current practice and outcomes. 30-day mortality for EVAR in EVAR 1 was	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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Hospitals NHS Trust	Evidence Review K			1.7% and 1.2% in DREAM. NVR 2017 (reflecting 2016 practice) demonstrates EVAR in hospital mortality of 0.4%. This is in line with our institution's practice; 30-day mortality since Jan 2015 is 0.52%. We do recognise that NVR data was used in the health economics model.	For discussion of the use of NVR to estimate perioperative mortality, please see **Theme 3a**. Thank you for giving us details of your experience; please see **Theme 3c**.
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	We are concerned that no consideration appears to be given to patient choice and shared decision-making within the document. Whilst we note the committee did include patient representatives; we would support wording that described a recommended of preferred option rather than exclusion of EVAR in this patient group. The Montgomery test has not been applied regarding patient choice '*an adult person of sound mind is entitled to decide which, if any, of the available forms of treatment to undergo, and his/her consent must be obtained before treatment interfering with his/her bodily integrity is undertaken"*. These guidelines explicitly exclude offering patients with an unruptured infra-renal AAA EVAR which is a widely available treatment option in the UK and Europe.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	Question 1: Our local audit data (2010-2015 – [This text was identified as confidential so has been removed.]) would indicate the adoption of these guidelines would lead to an additional 27 open infra-renal aortic aneurysm repairs per year in our unit. These are patients who were documented "fit for open repair" by the MDT who underwent EVAR (patient choice). This would impact on our theatre capacity and critical care bed usage. This may be a conservative estimate as these were patient documented "fit for open repair" by our MDT in the knowledge that EVAR was available. If EVAR was not an option it is possible more patients may be considered "fit for	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				open repair". Critical care bed availability is challenging for us already, especially during the winter months, and this is likely to impact on our ability to deliver aortic aneurysm repair within the timeframe required according to the National Aneurysm Screening Program. Potentially this places patients at increased risk of rupture. Furthermore, our local policy allows us to undertake EVAR without confirmation of level 1 bed availability (a bed will become available somewhere across the Trust during the day), however this is not possible when needing a level 2/3 bed – the availability of this resource cannot be guaranteed and therefore operating teams/facilities are left idle at significant (unfactored) cost whilst awaiting a bed decision.	
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	Question 2: We have not had opportunity within the timeframe for the consultation to undertake a cost analysis but the intra-operative costs (Theatre time, intensive care and ward stay) are likely to be higher for patients undergoing open repair. We currently perform more than 80% of EVARs as percutaneous procedures with an overnight stay, and have introduced a day case service for selected patients. The EVAR list runs parallel with a theatre list and uses radiology nurses, if these cases were performed as open repairs this would require theatre and theatre nurses who would not then be available for other open vascular cases (whereas there is a second radiology suite available for non-aneurysm vascular radiology cases)	We can confirm that the HE analysis accounts for theatre time, critical care and ward bed-days, and that EVAR is associated with lower resource-use in each of these categories. The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.

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Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	In EVAR 1 the length of stay (LOS) for EVAR was a median of 7 days. Our local data shows year-on-year reduction in median LOS, from 3.49 days in 2015, 2.29 days in 2016 to 1.65 days in 2017 (median 1 day). As mentioned above, in 2018 we have begun to undertake day case EVAR in a selected patient group. This reduction in LOS will not only have a quantifiable reduction in EVAR cost, but it will increase patient through-put in the healthcare system.	Thank you for giving us details of your experience; please see **Theme 3c**. It is certainly true to note that length of stay has decreased for EVAR – from a mean of 9.76 days in the EVAR-1 trial to a mean of 4.31 days in the 2017 NVR, a reduction of 5.45 days. However, it should also be noted that, over the same period, there has been a reduction in mean postoperative stay following OSR as well – from a mean of 15.76 days in the EVAR-1 trial to a mean of 10.50 days in the 2017 NVR, a reduction of 5.26 days. Therefore, the difference between the 2 has remained relatively constant. The HE analysis undertaken to support the committee's decision-making has been revised to rely on the current NVR data (although the committee had some hesitation about the potential for selection bias in these data). For further details, please see **Theme 6a**.
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	Cost Effectiveness. Van Bochave et al (JVS 2016) undertook a very similar review to that of this NICE committee. Despite including and analysing the same RCTs used to generate this guidance, they came to a very different conclusion. Like this guidance, they focused on costs per QALY gained as a primary outcome measure. They, like this committee, found that EVAR was not cost effective based on EVAR 1, DREAM and ACE trials. EVAR was, however cost effective when looking at the more recent OVER trial. Van Bochave et al state in their discussion '*the results of older studies may say very little about the current cost-effectiveness of EVAR vs OR because newer devices have better technical performance and physicians are more experienced resulting in lower complication rates'*. They go on to say '*the length of hospital stay has declined considerably over the years due to experience and better devices*'. Van Bochave et al report two	Van Bochave et al.'s systematic review (2016) includes evidence from a variety of healthcare settings and perspectives. All the studies they identified with a UK focus were included in our systematic review of cost–utility analyses – see HE.1.2. All UK evidence included in both reviews concludes that EVAR is unlikely to be considered cost effective for the average person with infrarenal AAA. The cited opinions of the authors do not appear to be based on any of their empirical findings.

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				studies that varied the patient's fitness, concluding that EVAR in less fit patients (higher surgical risk) is more likely to be cost-effective than EVAR in fit patients.	
Leeds Teaching Hospitals NHS Trust	Draft guideline	9	181	We note from the national GIRFT report that there is considerable variation in the cost of elective EVAR procedures nationally (£2251-£19,690) and seek reassurance that this has been considered in the Health Economic Modelling. Our institution pays >£1000 less per graft than the £6558 quoted in this document. Furthermore, the figure quoted is taken from a single commercial source [Marianna Stellino, W.L. Gore and Associates, 14 October 2015, personal communication] as being the "average" selling price of the EVAR device (across all manufacturers) in the UK. If we believe that the cost of EVAR is too high, could the committee recommend looking at ways of standardising or reducing the cost of EVAR rather than abandoning it. Patel et al (HTA No 22.5) report the overall mean costs over 14 years in the EVAR 1 trial, including aneurysm repair, aneurysm-related reinterventions, surveillance and follow-up, were £19,845 in the EVAR group and £16,307 in the OR group (mean difference £3538, 95% CI £2059 to £5018). This difference is relatively small and given that contemporary EVAR involves reduced LOS, reduced device cost, reduced re-intervention as well as reduced surveillance. We would recommend that the committee considers this data in any further recommendations	The cited cost of £6,558 was reported by Patel et al. (2018). The figure we use in our base-case HE model is similar to this – £6,500 – though we explore other plausible costs (see HE.2.2.11.1 and HE.8.1.8). We noted the variability of NHS Reference costs for EVAR (as quoted in the GIRFT report) in our draft documentation (see HE.2.2.11.1). While there undoubtedly is national variation in the true prices paid, it is clear that there is also substantial heterogeneity of practice among centres submitting data as regards what should be included in the total cost of the episode. For this reason, we considered NHS reference costs unreliable as an overarching source of procedure costs, and undertook our own microcosting to inform the HE model. We are aware that trusts are able to negotiate lower prices with manufacturers. However, according to Developing NICE guidelines (2014), *Analyses based on price reductions for the NHS will be considered only when the reduced prices are transparent and can be consistently available across the NHS, and when the period for which the specified price is available is guaranteed.* We are not in that situation, here. NICE has no role in setting the price of medical devices. However, we do provide sensitivity analyses showing cost-effectiveness results at different graft prices in the HE report

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					(see figure HE47, figure HE59, figure HE70, figure HE78, figure HE93 and figure HE94, updated in the revised results as figure HE116, figure HE117, figure HE118, figure HE133, figure HE134, figure HE135, figure HE136 and figure HE155). We cannot agree that £3,538 is a small amount of money, especially when scaled across some 4,000 infrarenal surgeries per year, implying a national resource impact of £14m per year. The HE analysis undertaken to support the committee's decision-making accounts for some of the features of contemporary EVAR resource-use that you cite (though, as noted above, we do not have any evidence of reduced device costs, and we do not believe it would be appropriate to assume low-intensity surveillance – see **Theme 11**). In its revised base case, the HE model estimates a net discounted lifetime cost difference of £3,023 per case – roughly equivalent to a national resource impact of £12m per year.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	9	181 & 182	This rationale does not consider patient age. Although open surgical repair offers definitive treatment it would not be appropriate in someone greater than 75. In this scenario the current guideline does not recommend EVAR to this patient group who are unruptured and infra-renal. The risk of rupture therefore shortens lifespan in this age group who could have a long and fulfilled life expectancy if they have EVAR. It is not appropriate to NOT offer EVAR to this patient group if they are not suitable for open surgical repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee reached a firm conclusion that it is not appropriate to make decisions about people's management based on their age alone. This argument is not supported by

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					the evidence. For example, the OVER RCT found that people aged 70 or older had greater long-term benefit from OSR compared with EVAR (while younger participants had the opposite profile). This phenomenon did not persist when an age-stratified analysis of long-term outcomes across all 4 RCTs was undertaken by the EVAR investigators (see Patel et al., 2018); however, this analysis provides no support for the belief that EVAR has greatest advantages over OSR in older patients.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	9	181-182	1.5.3 Again this is against current practice and limited evidence to support this – where has this come from? Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. Contact [This text was identified as confidential so has been removed.]	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	9	181-182	1.5.3 This is again wrong on a number of levels including patient choice.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Independent Vascular Services	Draft guideline	9	181-182	This rationale does not consider patient age. Although open surgical repair offers definitive treatment it would not be appropriate in someone greater than 75. In this scenario the current guideline does not recommend EVAR to this patient group who are unruptured and infra-renal. The risk of rupture	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				therefore shortens lifespan in this age group who could have a long and fulfilled life expectancy if they have EVAR. It is not appropriate to NOT offer EVAR to this patient group if they are not suitable for open surgical repair.	whilst supporting individualised care around which interventions are appropriate. The committee reached a firm conclusion that it is not appropriate to make decisions about people's management based on their age alone. This argument is not supported by the evidence. For example, the OVER RCT found that people aged 70 or older had greater long-term benefit from OSR compared with EVAR (while younger participants had the opposite profile). This phenomenon did not persist when an age-stratified analysis of long-term outcomes across all 4 RCTs was undertaken by the EVAR investigators (see Patel et al., 2018); however, this analysis provides no support for the bias that EVAR has greatest advantages over OSR in older patients.
South Tees NHS Trust	Draft guideline	9	181-185	We do not agree with this statement. The guidance is predominantly based on EVAR 1 and EVAR 2. Trials are 15 years old with much discussed flaws. Analysis of trials in the NICE guidance evidence states that trials are not high quality evidence and certainly not robust enough to merit such a strong recommendation. Mortality and reintervention rates in EVAR groups in EVAR 1 and EVAR 2 were well above current standards and predate the AAA QIP. In current times these trials would have been stopped due to excessive mortality and in fact the recommendation should be to repeat the trials post AAA QIP and with the technology and clinical far more extensive expertise.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. In the consultation draft, the evidence base for elective infrarenal repair comprised 4 RCTs (not just EVAR-1). In terms of their internal validity, we judged these RCTs to be at low risk of bias; when they were brought together, we had

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					high-quality evidence for all key outcomes and moderate-quality evidence for most others. The EVAR-2 RCT was judged to be at higher risk of bias, and it was the only evidence available for people for whom OSR is unsuitable. Therefore, evidence generated for that population ranged from moderate to very low quality. On discussing stakeholder feedback on this issue, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				In addition the technology has substantially progressed and improved with lower complication and re-intervention rates with the more modern stents.	In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
				This appears to be the opinion of the NICE Panel based on what they admit is poor evidence.	It is unclear on what basis you make this statement: it is the role of the committee to appraise and interpret the best-available evidence to inform recommendations. As noted above, the committee considered this evidence to be of higher quality in some areas than others.
				A significant proportion of patients who are deemed high risk for open surgery (50% of our AAA population undergoing EVAR) or who have got a concurrent diagnosis of cancer (which in our practice is 10-12% of the population) and/or have a hostile abdomen (8-10%) are best served with endovascular repair of an abdominal aortic aneurysm. This subgroup of patients was not represented in the EVAR 1 or EVAR 2 trials	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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				and the Panel guidelines appear to completely ignore this group of patients.	The presence of cancer would not, in and of itself, constitute a contraindication to OSR in every case. However, the committee agreed that it would be reasonable to include the presence of abdominal neoplasia that would make an open approach dangerous, or a hostile abdomen resulting from previous cancer surgery under this heading.
				Being able to assess preoperative risks objectively (based on CPEX in our practice) and offering these patients EVAR where appropriate within the MDT setting is one of the main reasons why mortality from AAA repair has dropped significantly in the last 20 years in the UK and worldwide. These guidelines will completely undo this improvement.	The committee did not recommend the use of tests and scores as a decisive arbiter of fitness for surgery; however, they recognised that there are situations in which CPET can help to clarify the benefits and harms to aid with shared decision-making (see Evidence reviews G and H). The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
				Modern practice has changed with DOSA (day of surgery admission) and the increased use of percutaneous EVAR with regional or local anaesthesia, requiring only an overnight ward stay (and in parts of Europe a 23 hour bed) and significantly decreased the cost of EVAR compared to the common expenses of doing an EVAR in these studies.	The costs of EVAR that were used in the HE analysis that was undertaken to support the committee's decision-making reflected contemporary use to the extent possible (see **Theme 5** and **Theme 6**). The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates

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					a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.
South Tees NHS Trust	Draft guideline	9	186-191	This guidance is purely the opinion of the NICE panel as there was no evidence considered (all published data discarded due to data quality). We disagree with these statements as there are currently no large scale randomised trials of this nature for units to immediately enter patients into and there is no evidence to suggest that the practice of complex EVAR has significantly different outcomes to open surgery, such that the practice should be stopped.	It is important to understand the 'burden of proof' required of treatments considered by NICE's decision-making committees, as set out in Developing NICE guidelines (2014). NICE guidelines recommend courses of action when there is credible evidence that they are associated with net health gain for patients at a cost that does not compromise care for other NHS service users. For these reasons, the committee concluded that it would be appropriate to encourage high-quality research in this area.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline	9 10	181-2 183-5	The major change in practice that would result from the implementation of the draft guidelines, relates to the recommendation not to use EVAR for the elective treatment of AAA. Due to constraints on our time and resources this response focuses primarily on this issue. EVAR is currently a common procedure for the elective treatment of AAA, having been recommended "as a treatment option for patients with unruptured infra-renal abdominal aortic aneurysms" by NICE in TA167. Since the recommendations of the appraisal were based upon economic modelling that used much of the same evidence as the current guideline, it is important to understand why such a different conclusion has	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Comment noted. Thank you for devoting the time you had available to providing your feedback on this issue. We do not accept that the HE model developed for this guideline did not allow for adequate exploration of subgroup effects, and we have provided more detail in our updated analyses (including probabilistic subgroup analyses, in line with your suggestion).

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				been reached. We believe that this is partly the result of the modelling techniques and parameters used in the modelling carried out for the guideline, which have not allowed adequate exploration of possible scenarios and subgroups of patients for whom EVAR might represent a cost-effective use of NHS resources. In common with previous economic modelling, including that carried out by the assessment group for TA167, the base case in the economic model suggests that the incremental cost effectiveness ratio (ICER) for EVAR, when using average costs and outcomes, falls above the usual NHS threshold for cost effectiveness. However, the appraisal modelling identified a series of scenarios based upon age, aneurysm size, patient fitness and suitability of EVAR, in which EVAR could be considered a cost-effective use of resources. Unfortunately, the appraisal committee were unable to provide clear guidance upon the situations in which EVAR was appropriate and left this open to interpretation by the clinical community, stating in their guidance that; - *The decision on whether endovascular aneurysm repair is preferred over open surgical repair should be made jointly by the patient and their clinician after assessment of a number of factors including:* *aneurysm size and morphology* *patient age, general life expectancy and fitness for open surgery* *the short- and long-term benefits and risks of the procedures including aneurysm-related mortality and operative mortality.* The result of this has been very variable uptake of EVAR, with recent data showing that the proportion of patients treated by	

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				EVAR in different centres varies from under 40% to over 90% (based upon the most recent NVR annual report). In general, there is much wider use of EVAR than was likely to be considered cost effective based upon the previous modelling. There are a number of reasons for this wide uptake of EVAR. These include patient and professional preferences for a new and less invasive procedure with lower immediate morbidity and mortality, perverse incentives related to pressures on bed and critical care facilities and the possible influences of far greater commercial interest in the endovascular procedure from the manufacturers of EVAR devices. It might be expected that, with their different remit and processes, the guideline committee would be better placed than the appraisal committee to define a set of clinical circumstances in which EVAR would be appropriate. However, the economic modelling has not identified subgroups or scenarios to support such recommendations and this may relate to some of the simplifications and parameter choices used in the modelling. Further specific details of some of the concerns are provided below, but we have some general comments about the modelling approach taken. The decision to treat the issue raised in review question 12 as two separate decision problems reflecting the EVAR 1 and EVAR 2 populations, with a dichotomous choice for each, is an over-simplification. In practice there is not a clear dichotomy between those who are fit and unfit for open surgery, but these are value judgements based upon the relative risks of different treatment options. The potential options available to a patient with AAA include open surgery, EVAR, watchful waiting (repeat ultrasound scan) and a	You are correct to suggest that the guideline committee was well placed to provide guidance about people for whom EVAR represents an effective use of NHS resources, when compared with OSR. However, having devoted substantial effort to identifying such subgroup(s), the committee concluded that none could be confidently identified (at least in the elective setting). We respond to your specific concerns about the modelling approach below. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice,

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				decision not to treat. The risk factors for procedure-related risk following open surgery or EVAR, general mortality, aneurysm related mortality for untreated AAA or that following treatment, and the likelihood of endoleak, all have potentially different risk factors.	albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that it would be valuable to generate new high-quality research in this area.
				The modelling for the appraisal included more detailed consideration of a number of relevant parameters, including aneurysm size, patient age and fitness, using a dynamic programming approach (HTA 2009; Vol13, No 48, p125). The more recent analysis of the cost effectiveness of screening in women (Sweeting J, Masconi KL, Jones E, Ulug P, Glover MJ, Michaels JA, Bown MJ, Powell J. Should we screen women for abdominal aortic aneurysm? Analysis of clinical benefit, harms and cost-effectiveness. *Lancet* 2018; In press) used discrete event simulation, due to the limitations of the simplified state transition model used in this case.	We do not agree that more elaborate modelling approaches are more suited to this topic area; on the contrary, we believe that it is a strength of our analyses that they describe natural phenomena in a parsimonious way, making maximal use of best-available evidence, and avoiding reliance on the kind of speculative assumptions and tenuous data that are always necessary to populate more convoluted models. The use of techniques such as dynamic programming and discrete event simulation represent ingenious solultions for problems that cannot be readily solved with more robust approaches. Primarily, this is a function of available evidence. It would, for example, be unnecessary to use such approaches to estimate the cost effectiveness of screening in women if there had been multiple high-quality trials in which women were randomised to different screening protocols and followed up for 15 years.
				Thus, the modelling does not include the separate consideration of different relevant subgroups of patients based upon age, gender, fitness for surgery, aneurysm size, anatomical suitability for EVAR etc. etc. The use of a series of one-way sensitivity analyses, scenario analysis based upon single alternative parameters or assumptions, and probabilistic	All HE analyses include a series of subgroup analyses exploring the joint effect of age, sex and AAA diameter – see HE.3.1.1.3, HE.3.1.2.3, HE.3.2.1.3, HE.3.3.1.3, HE.3.3.2.3 and HE.3.4.1.3. We have revised the way in which these are presented in our updated HE analysis, to make it clear that all 3 dimensions were considered simultaneously – see

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				sensitivity analysis (PSA) is inadequate to fully explore these issues.	HE.9.1.1.3, HE.9.1.2.3, HE.9.2.1.3, HE.9.3.1.3 and HE.9.4.1.3. Age, sex and AAA diameter were explored as potential effect modifiers as they are objective factors on which data are commonly available. Fitness for surgery is extremely difficult to capture in a quantitative way, as would be necessary in order to use it as a covariate of outcome. It would also be necessary to find a way to account for interactions between this factor and other, more objective variables (e.g. age, with which it is very likely to be correlated), as well as its interaction with repair approach (it is at least implicit in this and other stakeholder comments that fitness is expected to be a more important modifier of outcome in OSR than in EVAR case, and it would be necessary to account for that). As shown in Evidence review G and Evidence review H, the available tests and tools have limited predicitive validity when it comes to short-term (perioperative) effects. Their influence on longer-term outcomes, including interaction with other variables (including repair approach) is unknown. In the absence of a reliable, replicable way of quantifying patient fitness, we performed some speculative scenario analyses in which we artificially varied life expectancy to explore whether – if patients with a known life expectancy could be identified – they would have a different balance of benefits, harms and costs from the overall cohort.

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				Furthermore, the PSA confounds parameter uncertainty with patient specific factors that represent heterogeneity in the patient population, which will be known prior to treatment. Thus, for example, the choice of an average age and standard deviation for cohort age based upon the EVAR-1 trial (Table HE80) means that 95% of PSA simulations are between the age of 73.701 and 74.377, whereas in practice most patients will be outside this range. The specific parameters and values are discussed in more detail below.	'Anatomical suitability for EVAR' is also a factor that cannot be captured in detail using current evidence. Obviously, we at least make the distinction between infrarenal AAAs and those that require complex repairs. However, if your implication is that it would be illuminating to have a more granular analysis of the heterogeneous category of 'complex AAA', we agree. The committee, noting that no evidence is available to inform such an analysis, agreed that more evidence would be helpful for future decision-makers. The purpose of PSA is to explore parameter uncertainty, not patient-level heterogeneity. It is appropriate for these analyses to be parameterised using best-available cohort-level evidence – the uncertainty we are interested in, here, is our uncertainty about the **mean** age of people receiving AAA repair. It would be incorrect to inflate our parameter uncertainty by conflating it with patient-level heterogeneity; our approach is consistent with all relevant authorities on this point (see, e.g., Briggs et al., 2012) Notwithstanding this, we accept that probabilistic analysis of subgroup effects could be valuable. Therefore, to address your comment, we have undertaken additional analyses, so that likelihood of cost effectiveness can be quantified for each combination of covariates. Please see HE.9.1.1.3, HE.9.1.2.3., HE.9.2.1.3, HE.9.3.1.3 and HE.9.4.1.3.
Vascular Research Group, School of Health and Related	Draft guideline	9 10 10	181-2 183-5 196-202	There is a fundamental inconsistency in recommending EVAR for emergency but not for elective surgery. The IMPROVE trial, which is the basis of the recommendation regarding ruptured aneurysm, was limited to centres with an established and ongoing elective EVAR service. There must be considerable doubt about whether an emergency EVAR	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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Research (ScHARR), University of Sheffield				service would be feasible or obtain equivalent costs and outcomes if it was provided in centres without an elective EVAR service.	whilst supporting individualised care around which interventions are appropriate.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	9	173 (1.5.1)	Clarify whether or not diameters for repair refer to ultrasound inner to inner wall or CT measurement	Thank you for your comment. The diameters refer to the recommended ultrasound inner-to-inner wall measurement parameters. The committee did not think it was necessary to repeat the wording in the recommendation.
All-Party Parliamentary Group on Vascular and Venous Disease	Draft guideline	9	172 (1.5-1.5.6))	We are concerned that the removal of EVAR for people with an unruptured aneurysm would have a profound impact on patients. Long term outcomes of open surgery for a certain patient profile can be good. However, it is obviously traumatic for patients, requires a pro-longed stay in hospital and recovery time (3-6 months), and considerable time off work and an impact on the quality of life. EVAR means reduced time under anaesthesia, less pain after surgery, less blood loss and complications, a shorter stay in hospital and recovery time (2-4 weeks), as endorsed by the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Evidence-based estimates of the quality of life impacts of OSR and EVAR are incorporated in the analyses that supported the committee's decision-making. These show that, while OSR is associated with a greater decrement to quality of life than EVAR in the month following surgery, experience is similar by 3 months. One RCT (DREAM) found that long-term quality of life significantly favours OSR over EVAR; however, this has not been a universal finding (other trials show no difference), so we assume equivalent QoL beyond the initial impact of surgery in our analyses. These factors are also included in our analyses, both as regards their impact on patients and their implications for NHS costs.

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				recent GIRFT report on Vascular Surgery. EVAR is obviously popular with patients, which has been demonstrated through robust clinical trials. Moreover, the 30 day post-operative mortality following aneurysm repair is significantly lower with EVAR compared with open surgery (two thirds lower in the EVAR 1 trial).	The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. The GIRFT report focuses purely on short-term outcomes. We acknowledge that these tend to favour EVAR over OSR. However, it is equally unambiguous that EVAR is the more expensive approach (even when one factors in generous estimates of postoperative cost-savings that may be associated with EVAR – see **Theme 6**), and no one disputes that EVAR also requires more reinterventions than OSR, even if the rate of reintervention may have decreased somewhat over time (see **Theme 7**). It is also the committee's confident interpretation of randomised and observational evidence that EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**.
				A greater concern is that for the profile of patients who are not eligible for open surgery and hence are left with no treatment option. Elderly patients are often not eligible for open surgery given that the chances of surgical complications are too high. For these patients, then, there is no other treatment option, meaning that hundreds of patients each year will be left with no intervention at all, posing a significant risk to life. Allowing a slightly more elderly patient profile no treatment options when an evidenced and appropriate alternative is available surely beings into question age discrimination issues?	
				Women are also likely to be disadvantaged by the current draft guideline, which does not seem to have been accounted for.	The data from Sidloff et al. (2017) that you cite show that the effect of sex on perioperative mortality risk is greater for

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				Published evidence has shown that 1 in 15 women (6.9%) die during or shortly after the open surgical procedure whereas the short-term mortality risk for women undergoing EVAR is only 1.8% (Sex differences in mortality after abdominal aortic aneurysm repair in the UK, Sidloff et al, 2017).	people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.
				The draft guideline does not adequately cover recommendations for patients with symptomatic AAA who are assumed to be at high risk of rupture and therefore require urgent intervention. This patient group should be covered within the draft guideline, with adequate interventions recommended within it.	The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and

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				Patients should have the option of either open surgery or EVAR and should not be left with no treatment option or an option which is likely to provide higher risk to life.	OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.
Medtronic UK	Draft guideline Evidence Review K	10 30	179-180 872-875	**Gender Inequality:** As evidence has shown, the short-term mortality of Open Surgical Repair in women is higher versus men and versus EVAR: In 2017, Ulug et al reviewed the 30-day mortality in men and women undergoing EVAR and OSR by looking at nine studies (52 018 men, 11 076 women). The overall pooled estimate for EVAR was higher in women (2·3%) than in men (1·4%; OR 1·67, 95% CI 1·38–2·04). The overall estimate for open repair also was higher in women (5·4%) than in men (2·8%; OR 1·76, 95% CI 1·35–2·30). Sidloff et al. 2018 performed analysis of the NVR and Hospital Episode Statistics (HES) databases and found that for elective open AAA repair, the in-hospital mortality rate was 6·9 per cent in women and 4·0 per cent in men (odds ratio (OR) 1·48, 95 per cent ci. 1·08 to 2·02; P =0·014), whereas for elective endovascular AAA repair it was 1·8 per cent in women and 0·7 per cent in men (OR 2·86, 1·72 to 4·74; P <0·001); the results in HES were similar.	The data from Sidloff et al. (2017) that you cite show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.

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				Medtronic strongly suggest that this recent data is considered by the committee as it would be inequitable to recommend an intervention for women where up to 1 in 15 procedures would result in death when a much lower mortality is achievable with EVAR (Sidloff et al., 2018). We therefore recommend the committee consider the clinical evidence and adjust the evidence review, economic model and recommendations accordingly.	
South East and South West London Vascular Networks	Draft guideline	10	181-191	Evidence from patient engagement for the South East London Vascular Network suggests that patients prefer to be involved in the discussion about their options for surgery, and to participate in the decision making about the most suitable option for them. Some patients may choose not to have surgery at all and must be counselled about the risk of aneurysm rupture, and others might hold a preference for either open or endovascular repair. All these options should be discussed with the patient in an open way. The Network team would be willing to share the conclusions of this extensive patient engagement exercise, which was conducted in January 2018. Evidence exists that patients prefer EVAR and are also prepared to travel to access services that deliver EVAR routinely and have low peri-operative mortality rates. (Reise et al. EJVES 2010; 39:55-61, Holt et al BJS 2010;97:504-510, Winterborn et al J Vasc Surg. 2009;49(3):576-581).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals of the North Midlands (UHNM)	Draft guideline	10	183	1.5.4 In our unit, we have offered EVAR to patients who are less fit for open repair due to a lower initial mortality rate demonstrated in trials and registries. As mentioned above, our mortality for these more comorbid patients remains low (**173 cases with 1.15% mortality**).	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				The impact of not offering EVAR to these more comorbid patients would reduce the rate of aneurysm repair overall, and particularly in older patients. This may increase the rupture related mortality and have an impact on overall survival.	
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	10	183	This recommendation may imply abandoning the elective endovascular aneurysm repair (EVAR) service, a technology that has matured significantly over recent years. This is a significant change from current practice in the UK where about 70% of elective AAA repairs are done endovascularly (National Vascular Registry 2017 report). Furthermore this implementation would put the UK practice at odds with international guidelines and practice in the rest of the developed world, including Europe. We are concerned that there appears to be an assumption that vascular anaesthetists and surgeons would judge who will be "fit" for open repair, but validated tools for this are lacking and risk scores not allowed. There is no clear definition of what is meant by "fitness" for surgery. A middle road, which preserves some clinical options and patient choice, would be more acceptable. A recent study reported that up to 60% of patients fall in a grey area of intermediate fitness (Rose Ga et al., British Journal of Anaesthesia 120(6): 1187-94, 2018). It could be this large group of patients with "intermediate" fitness who might benefit from EVAR. A patient who is considered high risk because of multiple comorbidities may benefit from the treatment of a large AAA high risk of rupture e.g. >7.5cm. We note above that there are limited data to inform the management of such patients with much of the evidence on treatment thresholds relating to small	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice.

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				aneurysms. In such patients, if the risk of rupture is high, EVAR may prevent a significant number of fatal ruptures. We suggest that further research is required on the benefits of EVAR for large aneurysms in relatively unfit patients. Limiting elective EVAR and increasing open AAA repair would also impact on critical care resources. We expect a significant increase in the demand for critical care beds and this increase would likely be in the older, less robust patients, who would might need longer and higher dependency critical care stay. The UK National Vascular Registry (NVR) captures data on more than 90% of AAA procedures and would be able to provide data to support an economic analysis. *https://www.vascularsociety.org.uk/_userfiles/pages/files/Document%20Library/2017%20NVR%20Annual%20Report.pdf	Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful. The relevance of the cited publication by Rose et al. (2018) is unclear, as it reviews risks factors for colorectal surgery. The authors' conclusion that CPET metrics cannot be used as a sole criterion to identify a population for whom surgery is suitable is one that our reviews share. We have revised postoperative resource-use inputs to the HE model, using data including estimates from the NVR; see **Theme 6a**.
University Hospitals Southampton – Wessex Vascular Network	Draft guideline	10	183	**Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.** This statement can only be based on the EVAR-2 trial. A flawed study beset by inappropriate patient recruitment and cross-over. The committee has adopted a far too simplistic approach to the nuanced issue of fitness for surgery. It is simple to identify fit patients. Equally, identification of profoundly unfit patients can be straightforward. The majority	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee reached the firm conclusion that it not appropriate to base management decisions on any individual

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				of vascular patients fall somewhere in between. Their medical conditions, frailty or obesity demonstrate that they would be better served with a procedure of reduced physiological stress or morbidity. This recommendation fails to understand the challenging rehabilitation after open aortic surgery, where patients need up to 6 months to return to their base-line fitness. 6 months of life they will not get back. It would be more appropriate if NICE would recommend robust fitness assessments and provide thresholds that may indicate better outcomes. This would provide a better guideline and allow clinicians to turn-down patients with more evidence than simply the extrapolated study designed to asses outcomes at 3 years.	sign, symptom, test or risk score (see Evidence review G and Evidence review H). They agreed that, in the absence of risk models with adequate predictive validity, the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. As you note, the predominant evidence underpinning the committee's decision-making is the EVAR-2 RCT, which stipulated that fitness for OSR should be decided at the local level, but provided some guidelines as to likely contraindications for open surgery (Brown et al. 2004). The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity (for example, the problem of patient crossovers has been addressed using well established statistical techniques), its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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British Society of Endovascular Therapy (BSET)	Draft guideline	10	183	Clarification is required about technical issues (rather than "anaesthetic risk and medical condition") which may make a patient unsuitable for open repair regardless of fitness - secondary aneurysms, type 1a endoleak, hostile abdomen, inflammatory aneurysms as described in the study used by NICE (and possibly SR/extent IV in most of England). This applies to standard and complex. The term "fit for operation" is important in the NICE document, since this is clearly patient, situation, anatomy and surgeon dependent. One patient who is not "fit" for open elective surgery when the aneurysm is small clearly can be "fit" for operation when the aneurysm is larger and/or tender. An important group will be those refused procedures who later develop symptoms and if EVAR is not the preferred option this group will further impact on the services of the NHS. We require clarification as to how you would assess and determine patients' fitness for surgery.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agree with your position that judgements about the suitability of offering repair to people with AAAs involve the multidisciplinary consideration of many factors which may affect the likely benefits and harms. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity (for example, the problem of patient crossovers has been addressed using well established statistical techniques), its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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UHCW NHS Trust Coventry	Draft guideline	10	183	*Recommendation 1.5.4* *Inappropriate exclusion of high risk patients from EVAR* There is no clarification in the NICE AAA guidelines as to how we can treat symptomatic patients, hostile abdomen, inflammatory AAA, synchronous tumours, previous aortic surgery and EVAR.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where ~~unusual~~ abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach,

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					which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases. Inflammatory AAA was outside the scope of the guideline.
East of Scotland Vascular Network	Draft guideline	10	183	We recognise there is a subgroup of AAA patients who are high risk with comorbidities and limited life expectancy who will not benefit from AAA repair, and it is therefore not appropriate to offer EVAR. However, there are situations where clinical judgement has to be allowed – for example those with large AAAs and those who present with symptoms or sac size enlargement. Turning down such patients for elective repair but subsequently offering emergency EVAR if/when they rupture is not an acceptable pathway of patient care.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
Leeds Teaching Hospitals NHS Trust	Draft guideline Evidence Review K	10 14	183 237	The proposed recommendations state "*Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition*". These recommendations are based on a single randomised controlled trial (EVAR 2) undertaken 15 years ago. Whilst this is the only RCT to address this patient group, it has several well-described limitations including the size of the study (338 patients), cross-over rates (34%) and the reproducibility of the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. In recruitment for the EVAR trials, 1,880 patients were eligible for randomisation, of whom 457 were judged unfit for OSR,

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				fitness assessment. The EVAR 2 trial findings are not based on actual findings, but instead on statistical modelling (rank-preserving structural failure time). Currently in our unit 78% of elective infra-renal abdominal aortic aneurysms are performed as EVAR (GIRFT data 2016). A recent audit (presented VS 2016) of patients "unfit for open repair" (MDT decision) undergoing EVAR (40% of all EVAR patients (87 patients)) had a 30-day mortality of 1% with a one-year mortality of 10%. At a median of follow-up of 34 months the overall mortality was 26%. This compares to EVAR 2 data where unfit patients undergoing EVAR had a 30 day mortality of 9% and a 42% mortality at a median follow-up of 2.4years (29months). One possible explanation may be improved "best medical therapy" with antiplatelets and statins in comparison to the EVAR 2 group where only 40% of patients were on statins and 58% on aspirin. Our turn-down rate is 22% (local audit 2013-2015, presented Charing Cross 2018). The overall mortality for this group was 29% at a median on 17 months, with a 30% one-year mortality. This is more comparable to the EVAR 2 data. 50% of deaths in this group were aneurysm-related. . We acknowledge that there has been an element of "mission creep" with increasing numbers of elderly and frail patients being offered EVAR who may be better managed conservatively. We do, however believe there are a subset of patients who are best managed with endovascular repair. To recommend only intervening on patients who are fit for open repair, based on a single trial may well disadvantage a large number of patients. We would ask the committee to	and offered entry into EVAR-2 (see Brown et al., 2012). This represents 24% of the overall population; clearly, this is much closer to the turn-down rate you cite than the proportion of people who are considered eligible for repair but unsuitable for OSR in your practice. As you note, the outcomes of the EVAR-2 population appear to be comparable to those you have observed in people receiving no repair. This suggests that any 'mission creep' between the practice reflected in EVAR-2 and today perhaps reflects increasing unwillingness to consider people eligible for OSR rather than an increasing willingness to offer repair to people who may not benefit. As you note, the predominant evidence underpinning the committee's decision-making is the EVAR-2 RCT, which stipulated that fitness for OSR should be decided at the local level, but provided some guidelines as to likely contraindications for open surgery (Brown et al. 2004). The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity (for example, the problem of patient crossovers has been addressed using well established statistical techniques), its deliberately non-prescriptive

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				recommend the need for further studies to highlight this specific group, perhaps based upon data from the Carlisle Risk Model.	eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
Leeds Teaching Hospitals NHS Trust	Draft guideline	10	183	Question 1: It should be recognised that a dramatic reduction in elective endovascular repairs may impact on our ability to maintain competency and deliver a service for ruptured AAA, where EVAR remains the preferred modality (especially in those over 70 years old). This can be balanced against an improved exposure to open aneurysm repair both for maintaining competency and training. In our institution, the on-call rota which provides EVAR for ruptured AAAs has ten consultants. It would not be possible for ten operators to maintain the skills required perform EVAR for rupture without undertaking it electively. Furthermore, the ability to undertake EVAR for rupture relies on an on-site, immediately available range of stent grafts; it is inconceivable that Industry would support large consignment stocks of grafts for a small number of cases (uptake of EVAR for rupture still remains relatively low at approximately 30% according to NVR data).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	10	183-185	1.5.4 Why not – as you can perform EVAR under LA?? Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. [This text was identified as confidential so has been removed.]	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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					The committee's rationale for this recommendation is summarised in the short guideline and explained in detail in Evidence review K.
Medtronic UK	Draft guideline	10	183-185	**Screening:** The national screening programme has been highly effective in the UK, reducing the numbers of patients being admitted for ruptured aneurysms and this has been in a part due to the ability to offer patient choice regarding the treatment options available. A national screening programme, by definition, must be able to treat a disease process as well as identify patients at risk. It is perverse to subject individuals to screening and then turn them down for treatment, hence leaving them without a treatment option and burdening them with the anxiety of a potential rupture. There is no data to support this strategy and the psychological impact has not been investigated in any trial setting.	For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
University Hospitals Southampton – Wessex Vascular Network	Draft guideline	10	186	**Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.** At UHS we offer both complex open AAA repair and FEVAR. We see the huge morbidity associated with these most challenging cases, and we see how well our patients do after FEVAR. We would be very supportive of the long needed FEVAR trial and would hope that if this guideline were introduced that an NIHR funded study could be developed.	Thank you for the feedback.
East of Scotland Vascular Network	Draft guideline	10	186	We agree in concept that a randomised controlled trial comparing elective complex EVAR with open surgical repair should be encouraged but question whether this would be feasible, given the very small numbers of complex open repairs now being carried out in the UK [(1)]. We also question	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for

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				whether it would be ethical, given the very high peri-operative mortality associated with complex open repair (NVR 2016 report) [(1)]. Over several years, our own increasing experience and excellent results with complex EVAR and decline in open surgery [(2)] will make it very difficult for our MDT to be in equipoise and to consider randomising a large number of our patients with complex aneurysms. National Vascular Registry 2016 Annual Report. https://www.vsqip.org.uk *Burdess A, Orawiec P, Bhat R, Flett M, on behalf of the East of Scotland Vascular Network.* Establishing complex endovascular aneurysm repair (EVAR) in Scotland. An 8-year experience of fenestrated and branched EVAR. Presented at the British Society of Endovascular Therapy (BSET) Annual Meeting, June 2018.	a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Leeds Teaching Hospitals NHS Trust	Draft guideline	10	186	The proposed guidance states: *Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.* The recommendations on complex aortic repair are based on limited evidence from a single, non-UK trial of only 90 patients reporting only 30-day outcomes, together with National Vascular Registry (NVR) data. Very few centres entered patients with complex open repairs. We would welcome call for novel research proposals to address these complex issues whilst recognising the challenges of conducting conventional randomised clinical trials in this area. .	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. In addition, he evidence review undertaken for this chapter with a review of casemix-adjusted observational evidence.

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UHCW NHS Trust Coventry	Draft guideline	10	186, 189	*Complex AAA* We agree that complex stenting should only carried as be part of a trial/registry	Thank you for your comment.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	10	186-188	1.5.5 Currently there aren't any trials as outcome data published is good? Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. Contact [This text was identified as confidential so has been removed.]	Thank you for your offer for the shared learning database. Examples can be submitted via the webpage https://www.nice.org.uk/about/what-we-do/into-practice/shared-learning-case-studies
W.L. Gore and Associates	Draft guideline	10	186-188	**Model incorrectly assumes that open repair is a viable option for complex AAA.** The guidance recommends that patients with complex AAA that are suitable for both open repair and EVAR should be part of a randomized control trial. For patients with complex AAA, open repair is much less common than EVAR; almost 90 percent of complex AAA patients receive EVAR. Moreover, outcomes are much better for patients with complex AAA that receive EVAR compared to those receiving open repair. The NVR shows that postoperative morality is more than 5 times higher for open repair versus EVAR for complex AAA, and those receiving open repair are 3 times more likely to be readmitted to critical care and more than twice as likely to return to theatre. In addition, physicians are not prepared to conduct open repair for certain complex AAAs like suprarenal AAA. Given the evidence strongly in favour of better outcomes from EVAR, and the lack of training and preparation for increased open repair of complex AAA, the randomized control trial is inappropriate.	The committee was emphatic in its conclusion that NVR data should not be used to compare the relative effectiveness of EVAR and OSR for complex AAAs – a conclusion the authors of the report share (see **Theme 4a**). Furthermore, the committee noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that complex EVAR is associated with a large reduction in perioperative mortality, there should be equipoise about whether any such effect translates into net health gain over a patient's lifetime. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				NVR 2017 Annual Report Complex AAA repairs undertaken between January 2014 and December 2016: Open=217, EVAR=1,838 In-hospital postoperative mortality rate: Open=18.4, EVAR-3.5 Re-admission to critical care: Open=10.6, EVAR=3.2 Return to theatre: Open=17.1, EVAR=7.1	
Association of British HealthTech Industries (ABHI)	Draft guideline	10	186-188	**Evidence review, model and subsequent recommendations incorrectly assumes that open surgery is a viable option for complex AAA.** The guidance recommends that patients with complex AAA that are suitable for both open repair and EVAR should be part of a randomised control trial. For patients with complex AAA, open repair is much less common than EVAR; almost 90 percent of complex AAA patients receive EVAR. Moreover, outcomes are much better for patients with complex AAA that receive EVAR compared to those receiving open repair. The National Vascular Registry shows that postoperative mortality is more than 5 times higher for open repair versus EVAR for complex AAA, and those receiving open repair are 3 times more likely to be readmitted to critical care and more than twice as likely to return to theatre. Given the evidence strongly in favour of better outcomes from EVAR, and the lack of training and preparation for increased open repair of complex AAA, the randomised control trial is inappropriate. • 2017 NVR Annual Report • Complex AAA repairs undertaken between January 2014 and December 2016: Open=217, EVAR=1,838 • In-hospital postoperative mortality rate: Open=18.4, EVAR-3.5 • Re-admission to critical care: Open=10.6, EVAR=3.2 • Return to theatre: Open=17.1, EVAR=7.1	The committee was emphatic in its conclusion that NVR data should not be used to compare the relative effectiveness of EVAR and OSR for complex AAAs – a conclusion the authors of the report share (see **Theme 4a)**. Furthermore, the committee noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that complex EVAR is associated with a large reduction in perioperative mortality, there should be equipoise about whether any such effect translates into net health gain over a patient's lifetime In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate..

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				• HES data for suprarenal AAA repair in England reports an open mortality rate of 14% In the evidence review K (lines 788 – 809) the committee decide that these high OSR mortality rates are not representative but offer no data to support that view. In the absence of good data, the above reports of high open mortality have to be taken into consideration and cannot simply be ignored.	The supplementary review of casemix-adjusted observational evidence that we have undertaken in response to stakeholder comments now provides strong validation of the committee's firm belief that NVR data should not be used to compare the relative effectiveness of EVAR and OSR for complex AAAs – see **Theme 4b**.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	10	186-191	**1.5.5 and 1.5.6** Removing the option of complex endovascular repair outside of the setting of RCTs will deprive patients with more extensive aneurysms of a treatment that has been found safe and effective in large contemporary analyses. We note that this recommendation is based on a very highly selected reading of the available literature (*Donas KP, et. al. The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 2012; 56, 285-90*). A small report (90 patients), now 6 years since publication. By contradistinction, the following larger and more recent literature is available but has apparently been discarded by NICE: - The GLOBALSTAR registry (BSET Collab Circulation 2012), collating data on 318 patients from 14 centres in the UK performing FEVAR for juxta renal aneurysms, found a 4% peri-operative mortality rate and demonstrated a primary technical success rate of 99%, and intraoperative target vessel loss of just 0.6%. Overall survival was 94%, 91% and 89% 1, 2, and 3 years respectively.	In response to stakeholder comments such as this, we have now performed a more thorough review of the observational evidence available to inform estimates of the balance of benefits, harms and costs between EVAR and OSR for complex AAAs. See evidence review K2 for further details. Thank you for highlighting this evidence. We considered its eligibility for our supplementary review, with the following conclusions: • GLOBALSTAR (2012) is excluded as it is a non-comparative case series that does not provide any evidence on the relative effectiveness or safety of EVAR and OSR for complex AAAs • Gupta et al. (2017) is included in our review (though it is mostly superseded by other studies from the same dataset that use superior methods and/or have larger sample sizes)

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				- A more recent analysis of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database identified 535 patients who underwent complex (fenestrated) endovascular repair and 1207 who had open elective repair for abdominal aortic aneurysms that involved the visceral segment (Gupta et. al. J Vasc Surg 2017). Outcomes for FEVAR were better than those after open repair with a significantly shorter length of stay (2 vs 7 days, P<0.0001), fewer respiratory complications, lower rate of renal failure requiring dialysis, fewer cardiovascular events, less major transfusion requirements and a lower peri-operative mortality. - Analysis of the American College of Surgeons National Surgical Quality Improvement Program Targeted Vascular Module (Ultee et. al. J Vasc Surg 2017) demonstrated a lower peri-operative mortality (3.4% vs 6.6%, P<0.05), lower respiratory, cardiac and wound complications, shorter length of ITU (1.0 vs 4.7 days, P<0.001) and hospital (4.1 vs 11.3 days, P<0.001) stays after FEVAR compared with open aneurysm repair. - Haulon S, et. al., recently reported an 82% two year survival rate after FEVAR with a patency rate of 97% associated with renal fenestrations (Martin-Gonzalez et al. Eur J Vasc Endovasc Surg 2016). - At the King's Health Partners Vascular Unit, as part of our complex endovascular program, we have performed 79 FEVARS for juxtarenal aortic aneurysms since 2011, with a perioperative mortality of 1.3% and a median length of stay of 4 days.	• Ultee et al. (2017) is included in our review (though it mostly reports unadjusted comparisons and, with the exception of perioperative mortality, it does not provide casemix-adjusted estimates of any outcomes of interest). • Martin-Gonzalez et al. (2016) relates to thoraco-abdominal aneurysms that are mostly beyond the scope of this guideline, and compares 2 endovascular approaches, rather than providing evidence on the relative effectiveness or safety of EVAR and OSR. Aside from the 2 studies you identify that we considered to provide meaningful evidence on the relative benefits and harms of EVAR and OSR for complex AAA, we found 7 other papers from which evidence could be drawn. For details, please see the updated Evidence review K. Thank you for providing your experience; please see **Theme 3c**.

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				As to the question of Complex EVAR and RCTs: The vascular surgical community both in England and internationally does not have the equipoise required to allow the ethical randomisation of patients to either endovascular or open repair of thoracoabdominal aortic aneurysms. In fact, representatives from high-volume UK aortic centres used the RAND appropriateness methodology to examine this point and concluded that there was no clinical equipoise for treatment of suprarenal/extent IV TAAA. Furthermore, there was a consensus in favour of FEVAR for patients at moderate anaesthetic/medical risk who would require supra-renal clamping at open repair (Cross et. al. Br J Surg 2012). It is therefore improbable that such RCTs will ever be designed, funded or recruited. Rather than effectively banning the whole of the advance that has been made by complex EVAR over the last decade "by the back door", a more pragmatic solution is required.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
				Decisions as to the type of surgical repair of juxta-renal and thoraco-abdominal aortic aneurysms are currently made on a patient-by-patient basis according to patient fitness, the technical advantages/limitations of one type of repair over another and availability of resources. Each part of this decision-tree is informed by the international literature (some of which is quoted above) and by local experience and expertise. In our daily practise, it is our experience that a significant majority of patients are absolutely or relatively unfit for open juxta-renal or thoraco-abdominal aortic aneurysm repair but, while threatened by their aneurysms, do not have any obvious life-shortening pathology.	Your suggestion that a 'significant majority' of patients are unfit for OSR implies that the judgement is very different from that which was applied in recruitment of the EVAR trials, in which around 3/4 of potential participants were considered eligible for randomisation to EVAR or OSR. EVAR-1 (and other trials with similar eligibility criteria) have now generated evidence showing that OSR can not only be performed safely in this cohort, it is generates better net outcomes than EVAR.

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				The guidelines assume the same cost for infra-renal open repair and more complex open repair (£10,921). This is simply not correct. Open repair of complex aneurysms is likely to be associated with at least 4-fold higher cost than infra-renal.	We accept that this was an oversimplification in our model inputs. Our analysis has been revised to reflect additional information about postoperative resource use associated with complex AAA repair (both open and endovascular), with the result that the estimated costs of the primary admission for OSR have risen by a little under 50% from the value provided in the consultation draft. See **Theme 6** for details. We were unable to identify a reliable source of data for intraoperative resource use for complex OSR or EVAR; however, some tentative estimates are available from our review of casemix-adjusted observational evidence, and we explore these in sensitivity analysis. However, the statement that 'Open repair of complex aneurysms is likely to be associated with at least 4-fold higher cost than infra-renal' appears to be without foundation. The committee were emphatic in agreeing that a very inaccurate picture of the costs and harms of OSR for complex AAA has emerged because the approach is increasingly reserved in practice for extremely complex cases that are not typical of the average candidate. It may be relevant to note that most thoracoabdominal aortic aneurysms – which the committee believe are particularly likely to be associated with high costs – are beyond the scope of this guideline.
British Society of Endovascular Therapy (BSET)	Draft guideline	10	189	The NHSE a4 policy document on complex recommends consideration of complex EVAR if hostile abdomen or high anticipated blood loss. Another issue is cost of open complex which appears to be less than open standard. The committee have used a Cochrane RR multiplier of 0.33 for EVAR from NVR data to estimate risk of OR. For complex, there is an error in that 3.6% increases to 10.8% with 0.33 RR multiplier	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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				and not 10.1%. The multiplier gives a mortality of 1.2% for standard open repair and 10.8% for complex open but the cost of complex is estimated at about £200 less. If technical complexity is associated with mortality 10-fold higher than infrarenal then risk of complications will be also and this will be significantly more expensive than NICE estimate. This could close the cost gap for JRAAA. For SR/extent IV, it is quite different. An SLR from LHCH in 2012 was £27000 for these which equates to £31000 in 2018. This is less than the published cost from Edinburgh where over 60% of practice is SR/IV. This more accurate assessment of cost would make complex EVAR cost effective for SR/extent IV and perhaps supravisceral clamp for JRAAA (the majority in the Edinburgh series of SR/IV did not require renal bypass/implantation so are technically very similar in terms of physiological insult).	There is no error in the calculation of estimated mortality for OSR: the relative effect measure from the pooled trial data is an odds ratio, not a relative risk. On reviewing stakeholder comments including this one, the committee agreed that its decision-making would benefit from additional exploration of perioperative costs related to complex AAA repair – both EVAR and OSR. Therefore, potentially relevant evidence on intraoperative and postoperative resource-use, including registry data and observational publications, was reviewed and its impact on cost–utility results explored (see **Theme 5** and **Theme 6**, respectively). We also accounted for the need for rehabilitation (see **Theme 6b**). The assumptions that were made in revising the HE model all favoured EVAR, some to a degree that the committee considered palpably unrealistic – for example, using unadjusted length-of-stay data from the NVR when it reflects a small number of highly selected OSR cases that are almost certain to be disproportionately complex. The result of these revisions was to increase our estimate of costs for a primary complex OSR procedure by around 50% – from £10,662 (see table HE52) to £15,705 (see table HE113), while our estimate for complex EVAR did not meaningfully change (rising by <1%). Even though the committee agreed that the analysis was optimistic for EVAR, it did not result in an ICER, compared with OSR, that could be considered to represent an effective use of NHS resources.

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					These data represent the best-available evidence-based estimate of the average cost of EVAR and OSR for complex AAAs. However, because complex AAA is a heterogeneous category (see **Theme 10**), there will inevitably be a broad range of costs associated with more and less intricate procedures. Citing anecdotal evidence as to the expenses incurred with OSR in the most complex cases does not – in the absence of any counterfactual data regarding the costs of EVAR in directly analogous cases – help us to understand what the incremental costs associated with the approaches might be. Most thoracoabdominal aneurysms are outside the scope of this guideline, so the cited Scottish experience is of limited relevance. Those cases that would have fallen within our remit are obviously likely to fall in the upper end of complexity and cost, with the implications noted above. Having reviewed Chalmers & Nimmo's paper (2012), we note that the service described also provided EVAR for type IV thoracoabdominal aneurysms; therefore, the cited total budget does not tell us anything about the relative costs of different approaches.
				1.5.5 and 1.5.6 Removing the option of endovascular repair would deprive patients with more extensive aneurysms of a treatment that has been found effective in large, contemporary analyses. - The GLOBALSTAR registry (BSET Collab Circulation 2012), collating data on 318 patients from 14 centres in the UK performing FEVAR for juxta renal aneurysms, found a 4% peri-operative mortality rate and demonstrated a primary technical success rate of 99%, and intraoperative target vessel	Thank you for highlighting this evidence. We considered its eligibility for our supplementary review, with the following conclusions: • GLOBALSTAR (2012) is excluded as it is a non-comparative case series that does not provide any evidence on the relative effectiveness or safety of EVAR and OSR for complex AAAs • Gupta et al. (2017) is included in our review (though it is mostly superseded by other studies from the same dataset that use superior methods and/or have larger sample sizes)

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				loss of just 0.6%. Overall survival was 94%, 91% and 89% 1, 2, and 3 years respectively. - A more recent analysis of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database identified 535 patients who underwent complex (fenestrated) endovascular repair and 1207 who had open elective repair for abdominal aortic aneurysms that affected the visceral segment (Gupta et al. J Vasc Surg 2017). Outcomes for FEVAR were better than open repair with a significantly shorter length of stay (2 vs 7 days, P<0.0001), fewer respiratory complications, lower rate of renal failure requiring dialysis, fewer cardiovascular events, less major transfusion requirements and lower peri-operative mortality. - Analysis of the American College of Surgeons National Surgical Quality Improvement Program Targeted Vascular Module (Ultee et al. J Vasc Surg 2017) demonstrated a lower peri-operative mortality (3.4% vs 6.6%, P<0.05), lower respiratory, cardiac and wound complications, shorter length of ITU (1.0 vs 4.7 days, P<0.001) and hospital (4.1 vs 11.3 days, P<0.001) stays after fenestrated compared with open aneurysm repair. We acknowledge that certain endovascular techniques proposed for complex aneurysm repair (e.g. Endoanchors, parallel stenting) may have limited follow up to show efficacy but long term data now exist for fenestrated repairs as illustrated by points above and also by superior results related to work in centralised centres of excellence. Haulon et al, for example, recently reported an 82% two year survival rate after FEVAR with a patency rate of 97% associated with renal	• Ultee et al. (2017) is included in our review (though it mostly reports unadjusted comparisons and, with the exception of perioperative mortality, it does not provide casemix-adjusted estimates of any outcomes of interest). Aside from the 2 studies you identify that we considered to provide meaningful evidence on the relative benefits and harms of EVAR and OSR for complex AAA, we found 7 other papers from which evidence could be drawn. For details, please see the updated Evidence review K. The study by Martin-Gonzalez et al. (2016) compares 2 endovascular approaches, rather than providing evidence on the relative effectiveness or safety of EVAR and OSR. It is impossible to know whether, e.g., an 82% 2-year survival rate is good, bad or indifferent without reference to some form of counterfactual evidence, which this study does not provide.

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				fenestrations (Martin-Gonzalez et al. Eur J Vasc Endovasc Surg 2016). Emphasis should be placed on further centralising complex endovascular repairs into experienced centres, incorporating multi-disciplinary teams, to optimise outcomes rather than excluding this treatment all together. The vascular community would not have equipoise to randomise patients to other endovascular or open repair of thoracoabdominal aortic aneurysm. The vast majority of patients would be unsuitable for open repair owing to anaesthetic and/or medical concerns. Representatives from high-volume UK aortic centres used the RAND appropriateness methodology to conclude that there was no clinical equipoise for treatment of suprarenal/extent IV TAAA with consensus in favour of FEVAR for patients who require supra-renal clamping at open repair and those at moderate anaesthetic/medical risk for this open repair (Cross et al Br J Surg 2012).	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline	10	189-191	1.5.6 Why not – there is a significant reduction in morbidity. Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. Contact [This text was identified as confidential so has been removed.]	The rationale for this recommendation is summarised in the rationale and impact section; full detail of the committee's interpretation of the evidence is in Evidence review K.
Bradford Teaching Hospitals NHS Foundation Trust	Draft guideline	10	189-191	Graft technology and operative techniques are advancing at such a pace that complex EVAR, for example using graft fenestration, is a treatment that can be offered to patients with juxtarenal AAA. Section 1.5.6 states that complex EVAR should not be offered to patients who are judged unsuitable for open repair due to their anaesthetic or medical condition.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate

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				Whilst it is acknowledged complex EVAR may prolong anaesthetic time and case complexity, and so increase procedural risk, there are instances in which complex EVAR should be considered, such as those given above. In these cases, careful consideration should be given to offering complex EVAR, and the potential risks and benefits discussed at a specialist MDT.	
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	10	193	Recommendation 1.5.7 – consider epidural for open repair We agree that epidurals are commonly used for elective open repair, but this is too strong a recommendation without much evidence base. Furthermore, it leaves little room for exploring the benefits (compared to epidural analgesia) of developing regional anaesthesia techniques such as rectus sheath and wound catheters.	Thank you for your comment. As the evidence was not particularly strong, the committee agreed it was only appropriate to make this recommendation at the 'consider' level to ensure sufficient flexibility in decision making. 'Consider' reflects a weaker recommendation compared to 'offer'. No evidence was identified relating to the use of rectus sheath catheters to deliver analgesia in people undergoing repair of unruptured or ruptured AAA. Furthermore, the committee were not aware of this technique routinely being used during AAA surgery. As a result, the committee did not deem it appropriate to recommend their use as standard practice. This does not mean that they cannot be used at the discretion of the treating clinicians.
University Hospitals Southampton – Wessex Vascular Network	Draft guideline	10	193	**Consider epidural analgesia in addition to general anaesthesia for people having open surgical repair of an unruptured AAA.** This is not our local practice and we would dispute the evidence that NICE have reviewed. Complications from epidurals are not insignificant, they are not reliable, and can delay patient recovery. Our practice is to use rectus sheath catheters [RSC] instead of epidurals. There is randomised controlled trial evidence that RSC infusions in addition to	Thank you for your comment. As the evidence was not particularly strong, the committee agreed it was only appropriate to make this recommendation at the 'consider' level to ensure sufficient flexibility in decision making. 'Consider' reflects a weaker recommendation compared to 'offer'. No evidence was identified relating to the use of rectus sheath catheters to deliver analgesia in people undergoing repair of unruptured or ruptured AAA. Furthermore, the committee were not aware of this technique

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				patient controlled analgesia [PCA] provide superior analgesia when compared to PCA alone in surgery performed through a midline incision. There is also a randomised controlled trial in progress that is comparing analgesic quality of epidural infusions to RSC with PCA. We would ask NICE to consider recommending rectus sheath catheters as an adjunct to analgesia for patients undergoing elective and even more importantly emergency open aortic surgery.	routinely being used during AAA surgery. As a result, the committee did not deem it appropriate to recommend their use as standard practice. This does not mean that they cannot be used at the discretion of the treating clinicians.
Leeds Teaching Hospitals NHS Trust	Draft guideline	10	193	1.5.7 *Epidural for open repair* This is a strong recommendation but based on no evidence, although it probably reflects our current practice. However we are concerned that a didactic statement, without a strong evidence base, leaves little room for exploring the benefits (compared to epidural analgesia) of "newer" regional anaesthesia techniques such as wound catheters or rectus sheath catheters. We would welcome a call for a randomized controlled trial in this area.	Thank you for your comment. Evidence review L provides a detailed description of the committee's discussions about anaesthesia and analgesia during repair of ruptured or unruptured AAA. As the evidence was not particularly strong, the committee agreed it was only appropriate to make this recommendation at the 'consider' level to ensure sufficient flexibility in decision making. 'Consider' reflects a weaker recommendation compared to 'offer'. No evidence was identified relating to the use of rectus sheath catheters to deliver analgesia in people undergoing repair of unruptured or ruptured AAA. Furthermore, the committee were not aware of this technique routinely being used during AAA surgery. As a result, the committee did not deem it appropriate to recommend their use as standard practice. This does not mean that they cannot be used at the discretion of the treating clinicians.
Medtronic UK	Draft guideline	10	195-202	**Symptomatic AAA:** The scope for this clinical guideline stated that the following would be covered by the guideline committee:	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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				"Management of ruptured abdominal aortic aneurysms and **abdominal aortic aneurysms at high risk of rupture**" Medtronic do not believe that NICE have fully addressed the scope in relation to patients with symptomatic AAA whom are assumed to be at high risk of rupture and therefore require urgent intervention. Given the high procedural mortality, coupled with the risk of imminent rupture, we strongly believe that these patients should have access to EVAR (Peppelenbosch 2003, Sullivan 1990, Cambria 1994, Haug 2004, Fillinger 2002, Lederle 2002).	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.

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University Hospitals of the North Midlands (UHNM)	Draft guideline	10	196	1.6.1 This guidance suggests offering EVAR for ruptured aneurysms as opposed to open surgery. The implication would be that the numbers of elective EVARS reduce and expertise in performing EVAR for rupture would be lower and therefore likely to increase the mortality from ruptured aneurysms. From a governance and training perspective, we struggle to understand how NICE could justify performing a procedure only in an emergency setting and not in an elective situation. There is a fundamental flaw in the argument that ruptured aneurysms should be treated with EVAR in an emergency setting. The IMPROVE trial failed to demonstrate superiority of EVAR vs OR in ruptured AAA, nor was the trial powered for the subsequent subgroup analyses (women and local anaesthetic).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
South Wales Vascular Surgery Network	Draft guideline	10	196	To consider EVAR for ruptured AAA when EVAR is not to be contemplated in the elective setting seems poorly thought out. To perform an EVAR for rupture without training in the elective setting means that trainees and vascular surgeons of the future will not be adequately trained in performing EVAR	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	10	196	We agree with the recommendation that there are benefits for some patients with a ruptured AAA from EVAR. However, the implementation of this would be severely affected if elective EVAR surgery is restricted to only a small number of patients. There are concerns about the impact of the proposed changes in the elective service on retaining operating team skills. For	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which

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				example, how would teams carrying out mainly open AAA repair for planned elective daytime surgery, be able to switch to EVAR under local anaesthesia for emergencies ?	interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
University Hospitals Southampton – Wessex Vascular Network	Draft guideline	10	196	**Consider endovascular repair (EVAR) or open surgical repair for people with a ruptured infrarenal abdominal aortic aneurysm (AAA).** If EVAR is not indicated in the elective setting I cannot believe any unit would be able to deliver an emergency EVAR service. It would be impossible to provide the training or appropriate experience to deliver this recommendation. Emergency EVAR is incumbent on units holding a large consignment of grafts / grafts [as we do currently]; with no elective practice this would be impossible. We would recommend a softening on the NICE position to allow continued and regulated EVAR delivery in the elective setting to facilitate emergency EVAR delivery in large vascular centres.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
UHCW NHS Trust Coventry	Draft guideline	10	196	*Training* We will not be able to train juniors/new colleagues to perform EVARs in an emergency setting only.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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East of Scotland Vascular Network	Draft guideline	10	196	**Emergency EVAR, training and service sustainability** The guidelines recommend infra-renal EVAR for ruptured AAA. However, training in all the key steps of EVAR (patient selection, planning, device selection, implantation, follow-up, and re-intervention) requires exposure to elective EVAR in a controlled operating environment. Individuals will not become competent to treat patients with ruptured AAA with EVAR unless they have gained significant experience with elective EVAR. If the guidelines are implemented it will not be possible to train UK vascular surgeons and interventional radiologists to perform EVAR for ruptured aortic aneurysms. There will be similar implications for anaesthetists. Providing an emergency EVAR service for ruptured AAA, as recommended in the draft guidelines will become unsustainable.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	10 11	196 – 198 208 - 209	We agree with this conclusion but to recommend a surgical procedure only in the emergency setting but not electively is an unacceptable recommendation in any area of surgery especially such complex procedures as EVAR Performing ruptured EVAR is more demanding than elective repair due to the higher likelihood of dealing with the time pressures and adverse anatomy. This will create unsurmountable training issues affecting both new practitioners and current operators. A well organised theatre team that is maintaining high standards due to weekly elective EVAR, as at CHS, is not going to be available causing significant performance concerns	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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Bradford Teaching Hospitals NHS Foundation Trust	Draft guideline	10	196-198	The provision of emergency Ruptured EVAR (REVAR) requires a familiarity with graft sizing and implantation. This can only be achieved by day to day expertise of the provision of an elective EVAR service. If EVAR is limited to only ruptured aneurysm treatment, then it is unlikely that there will not be a large enough cohort of suitable trained specialists to provide a REVAR service. This is likely to have a significant impact on the delivery of a REVAR service and has training implications for Vascular Interventional Radiologists, who would have to maintain a skill base in the face of a declining elective caseload.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Medtronic UK	Draft guideline	10	196-206	**Training on the devices and availability:** Medtronic take robust steps to ensure that any new technology is introduced in a safe way. We have strict training in place for any new physicians wishing to use our devices. This includes online training, hands on simulator practice, classroom training with experts and then proctoring at the physicians' hospital and at a centre of excellence. If these guidelines were to be introduced, it would not be reasonable to train physicians for the rare occasions that they would require the devices for an emergency setting. In addition, Medtronic would have to seriously consider the implications of supply when the devices are only used in an emergency setting. The logistics and practical challenges to supply chain would potentially be impossible to manage	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
South Tees NHS Trust	Draft guideline	10	196-206	This statement has significant implications for training if the panel is suggesting that EVAR should not be offered in the elective, calm training environment but should be offered in the event of rupture. It also makes consultations with patients who have a frightening life threatening condition extremely complex and confusing – ' we will not treat your aneurysm and	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which

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				calm your fears with a stent as you are medically unfit for open surgery, but if you survive a rupture and make it to hospital we will have a go, even though we probably haven't done one in a few months…..', etc. There is a distinct concern about maintaining adequate expertise if the procedure of EVAR is only performed occasionally in a imminently life threatening and stressful setting of a rupture. Centralising these cases in the hopes of increasing numbers is entirely impractical as it would mean excessively prohibitive journey times for these dying patients.	interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. See also **Theme 13** for some relevant comments from the committee's discussion of consultations with people for whom surgical repair is unsuitable.
Nottingham University Hospital	Draft guideline	10	197	All very well to consider EVAR for rupture but if no elective cases being done, how do we train surgeons and radiologists in the technique? EVAR for rupture are not a good training cases.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	10	196 - 206	Consider EVAR for ruptures. It is inconsistent to assert that there has been no positive developments in planned EVAR for intact AAA from 20 years ago, but the improved results from a contemporary ruptured AAA trial should be applied. If the IMPROVE trial had been performed in the 1990s, then it is likely that the results for EVAR would have been worse than open repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee did not ascribe differences in the balance between EVAR and OSR in the elective and emergency settings to any differences in the technology or technique

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					used. Rather, they considered it plausible that the lesser physiological insult of EVAR would be of most value to an acutely ill patient in an immediately life-threatening setting. The committee retained the suspicion that EVAR repairs may prove to be less durable than OSR in the long run; however, it is less likely that any difference that emerges will be sufficient to outweigh the substantial short-term benefits that have been demonstrated, especially for women.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	10	196 - 206	Consider EVAR for ruptures. This carries challenges to implementation. If EVAR is not used for planned intact AAA it will be difficult to maintain skills in the procedure for existing staff and even more challenging to train new staff. There may well be a down grading in facilities due to the other recommendations which make emergency EVAR more difficult to deliver. Companies will be reluctant to place consignment stock with trusts purely for ruptures as they will see little profit and carry the liability of the losses due to shelf life. It is therefore likely that trust will be forced to purchase grafts and the associated additional costs of the expired stock and capital investment needs to be reflected in any economic model, as is the likely increase in adverse events associated with these points.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Vascular Research Group, School of Health and Related Research	Draft guideline	10	186-8	The recommendation that EVAR for complex aneurysms should only be carried out as part of a randomised clinical trials seems impractical. The modelling suggests that, although the best estimate of cost effectiveness is above the usual threshold, the best estimates of clinical effectiveness demonstrates a high likelihood that it has clinical benefits, although these may not be sufficient to justify the high costs.	You are correct to note that our base-case model estimates a fairly high likelihood that complex EVAR is associated with net QALY gains. However, in the absence of randomised evidence specific to this decision, this model relies on some broad assumptions that would tend to favour EVAR, especially as regards the generalisability of estimates from the infrarenal setting to complex cases. For example, we assume that, as for

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(ScHARR), University of Sheffield				Under such circumstances there is unlikely to be clinical equipoise and thus it would seem unethical to randomise patients, as well as being unlikely to recruit sufficient patients to such a trial. A recent value of information analysis (Ciani et al. Decision uncertainty and value of further research: a case-study in fenestrated endovascular aneurysm repair for complex abdominal aortic aneurysms. Cost Eff Resour Alloc (2018) 16:15) suggested that a cohort study may be sufficient to resolve the key uncertainties and that the cost of a prolonged RCT is not justified. The HTA Programme has considered this question and came to a similar conclusion, funding an observational study of this subject, which is ongoing (UK-COMPASS). It would seem perverse to undermine the completion of this NHS funded trial through guidance that prevents recruitment to the study.	infrarenal AAAs, people who have undergone EVAR face an increased hazard of post-perioperative death of 1.09. However, the only study in our review of casemix-adjusted observational evidence that reported post-perioperative data for complex AAAs reflected a much more substantial benefit for OSR over EVAR (HR = 2.03 [1.13 to 3.63]). When we configure our model to use this estimate, OSR becomes substantially dominant over EVAR. This shows that it is not appropriate to use the outputs of our model to question the equipoise in the decision between EVAR and OSR for complex AAAs – rather this work highlights the urgent need for reliable comparative evidence on this topic. Similarly, we are somewhat sceptical of the conclusions of Ciani et al.'s VoI analysis (2018). While this analysis is adequate to explore the value of research to improve the parameter estimates in their model, this uncertainty is dwarfed by the substantial structural uncertainty that is not part of their VoI calculations. Like ours, their model relies on substantial extrapolation from the infrarenal evidence-base for long-term mortality, reintervention rates and quality of life. Assessing the value of research to enhance the precision of these estimates overlooks the bigger problem that they are reasonably likely to be invalid for the decision problem. For this reason, we conclude that this analysis substantially understates decision uncertainty and therefore underestimates the value that would be provided by information that could assist with its resolution. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for

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					a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
British Society of Endovascular Therapy (BSET)	Draft guideline	11	204	NICE has not followed their scoping document by failing to provide specific advise on acute symptomatic high-risk for rupture cases which were to be assessed alongside rupture. There is one line to state the committee did not think they were any different from elective cases even though mortality in these acute cases is generally double that for elective as there is no time to assess risk and optimise.	Thank you for your comment. The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.

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University Hospitals of the North Midlands (UHNM)	Draft guideline	11	208	1.6.4 This is not a clear evidence based recommendation	Thank you for your comment. Evidence review L provides a detailed description of the committee's discussions about anaesthesia and analgesia during repair of ruptured or unruptured AAA. As the evidence was not particularly strong, the committee agreed it was only appropriate to make this recommendation at the 'consider' level to ensure sufficient flexibility in decision making. No evidence was identified relating to the use of rectus sheath catheters to deliver analgesia in people undergoing repair of unruptured or ruptured AAA. Furthermore, the committee were not aware of this technique routinely being used during AAA surgery. As a result, the committee did not deem it appropriate to recommend their use as standard practice. This does not mean that they cannot be used at the discretion of the treating clinicians.
University Hospitals of the North Midlands (UHNM)	Draft guideline	11	219	1.7.2 To our knowledge there is no validated risk assessment tool to detect complications following EVAR and from this draft guidance neither are these recommended for open repair. .	Thank you for your comment.
South Tees NHS Trust	Draft guideline	11	219	This statement is so vague as to not be guidance when compared to earlier statements	Thank you for your comment. The committee noted the frequency of EVAR surveillance is highly variable in practice. In the absence of evidence on how often imaging should be done, the committee agreed on a practical recommendation to tailor surveillance to the perceived risk of complication. This should maximise attention for those patients who are perceived to be at greatest risk, and help to identify complications earlier. The committee also recommended further research in this area due to the lack of evidence identified from literature searches.

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The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	11	219 & 220	We feel NICE should go further than just recommending the frequency of surveillance on the risk of graft related complications. The risk of graft related complications is a relatively unknow characteristic. We are not aware of any criteria that predict risk other than endoleak seen at completion. We would suggest NICE consider recommending the surveillance intervals similar to below; Completion imaging on deployment Pre-discharge standard duplex 1 or 3-month reference CT 6-month duplex with X-ray KUB Annual duplex with X-ray KUB unless known endoleak Every 6 months if known endoleak plus annual X-Ray KUB.	Thank you for your comment. The committee considered your proposal on surveillance intervals but felt it was not possible to make such a recommendation without strong evidence to support it. They believed that postoperative imaging modalities and intervals should be left to the discretion of treating clinicians taking into account the facilities and resources available to them.
Independent Vascular Services	Draft guideline	11	219-220	We feel NICE should go further than just recommending the frequency of surveillance on the risk of graft related complications. The risk of graft related complications is a relatively unknow characteristic. We are not aware of any criteria that predict risk other than endoleak seen at completion. We would suggest NICE consider recommending the surveillance intervals below; Completion imaging on deployment Pre-discharge standard duplex 1 or 3-month reference CT 6-month duplex with X-ray KUB Annual duplex with X-ray KUB unless known endoleak Every 6 months if known endoleak plus annual X-Ray KUB.	Thank you for your comment. The committee considered your proposal on surveillance intervals but felt it was not possible to make such a recommendation without strong evidence to support it. They believed that postoperative imaging modalities and intervals should be left to the discretion of treating clinicians taking into account the facilities and resources available to them.
Nottingham University Hospital	Draft guideline	11	221	Recommendation for CTA to detect AAA expansion /rupture is strange, much more expensive, gives ionising radiation and Duplex ultrasound provides excellent data on sac size/endoleak in the majority.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows:

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					1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is

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					important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Leeds Teaching Hospitals NHS Trust	Draft guideline	11	221	The committee recommends the use of CT angiography for the surveillance of patients post EVAR. In our institution Hammond et al (CVIR 2016) found acceptably low rates of delayed endoleaks in patients with a satisfactory CTA one-year post implantation and therefore we have convert our patients to annual ultrasound surveillance if their initial CTA is normal. In a study of 234 patients, 151 had normal first CTA. In this group only 9 went on to require secondary intervention (normal first CTA was 93% predictive of freedom from re-intervention) and of these 8 presented symptomatically. This evidence suggests that lifelong CTA surveillance in patients with a normal post-op CTA is unnecessary and inefficient. Could the committee quantify the cost implications of long term CT surveillance? The evidence for the significance of various endoleaks and their subsequent management is uncertain and we are less convinced that it is 'particularly important not to miss these complications'. This is the basis for recommending CTA for surveillance as a "gold-standard", but it is the least cost-efficient modality available. A reasonable alternative judgement would have been that we have no clear evidence that endoleaks undetectable on US are dangerous and	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little

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				therefore we should survey patients post EVAR with this modality given its zero-contrast load, zero radiation burden and low cost. The 15-year EVAR 1 follow-up showed an excess of cancer deaths in the EVAR group (50 vs 31) after 8 years (HR 1·87, 95% CI 1·19–2·96, p=0·0072). There is concern that this may relate to the use of annual CT surveillance in the EVAR arm. Furthermore, the committee's concern that ultrasound is operator dependent and unreliable should be addressed by recommending the implementation of a robust quality assurance programme to ensure scans are accurate and reproducible; the answer is not to simply reject this modality. .	evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	11	221 & 222	In 2018 it is wholly not appropriate to follow up EVAR with contrast-enhanced CT angiography when there are numerous papers that document the non-inferiority and even superiority of contrast-enhanced ultrasound (CEUS) to contrast-enhanced CT angiography [6-11]. The issue with the guideline is around its use of 'false positive' data and the assumption contrast-enhanced CT angiography is still the gold standard imaging	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking.

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				modality for endoleak. It is no longer appropriate to use CTA as a gold standard (see comment on evidence document W). A contrast-enhanced CT angiogram of a single area for EVAR will cost the Clinical Commissioning Groups approximately £90. The current cost of a standard vascular duplex is approximately £50 according to the 2018 Payment-By-Results Tariff. This effectively means that the cost of EVAR surveillance becomes 50% more expensive under this new guideline. This will move work from the Vascular Laboratory/Ultrasound units and adds to the workload of the Radiologists. Given the current shortfall in Radiologists and the lack of specialists able to perform resuscitative thrombectomy for stroke it would be more effective for the NHS if this work load to remain with the Vascular Scientist workforce. The movement to a contrast-enhanced CT angiogram based EVAR surveillance programme will have practical and resource related issues for Nurse-led surveillance. Additional resources will be needed to ensure CT scans are requested and reported by the radiologists prior to the patients seeing the nurse. In all reality it becomes unfeasible for Nurse-led EVAR surveillance to continue. Abbas, A., et al., *3D contrast enhanced ultrasound for detecting endoleak following endovascular aneurysm repair (EVAR).* Eur J Vasc Endovasc Surg, 2014. **47**(5): p. 487-92. Bredahl, K.K., et al., *Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair.* European Journal	1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used.

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				of Vascular and Endovascular Surgery, 2016. **52**(6): p. 729-734. Chung, J., et al., *Contrast-enhanced ultrasound (CEUS) versus computed tomography angiography (CTA) in detection of endoleaks in post-EVAR patients. Are delayed type II endoleaks being missed? A systematic review and meta-analysis.* J Ultrasound, 2015. **18**(2): p. 91-9. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5). Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72. Zimmermann, H., et al., *Value of high-resolution contrast-enhanced ultrasound in detection and characterisation of endoleaks after EVAR.* Clin Hemorheol Microcirc, 2014. **58**(1): p. 247-60.	As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Independent Vascular Services	Draft guideline	11	221-222	In 2018 it is wholly not appropriate to follow up EVAR with contrast-enhanced CT angiography when there are numerous papers that document the non-inferiority and even superiority of contrast-enhanced ultrasound (CEUS) to contrast-enhanced CT angiography [7-12]. The long-term effect of a lifetime of CT angiography surveillance on renal function in addition to radiation exposure (patients are living longer so radiation related cancer becomes a possibility) will not be cost effective. The issue with the guideline is around its use of 'false positive' data and the assumption contrast-enhanced CT angiography	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is

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				is still the gold standard imaging modality for endoleak. It is no longer appropriate to use CTA as a gold standard (see comment on evidence document W). A contrast-enhanced CT angiogram of a single area for EVAR will cost the Clinical Commissioning Groups £86. The current cost of a standard vascular duplex is £51 according to the 2018 Payment-By-Results Tariff. This effectively means that the cost of EVAR surveillance becomes 50% more expensive under this new guideline. This will move work from the Vascular Laboratory/Ultrasound units and adds to the workload of the Radiologists. Given the current shortfall in Radiologists and the lack of specialists able to perform resuscitative thrombectomy for stroke it would be more effective for the NHS if this work load to remain with the Vascular Scientist workforce. The movement to a contrast-enhanced CT angiogram based EVAR surveillance programme will have practical and resource related issues for Nurse-led surveillance. Additional resources will be needed to ensure CT scans are requested and reported by the radiologists prior to the patients seeing the nurse. In all reality it becomes unfeasible for Nurse-led EVAR surveillance to continue. Abbas, A., et al., *3D contrast enhanced ultrasound for detecting endoleak following endovascular aneurysm repair (EVAR).* Eur J Vasc Endovasc Surg, 2014. **47**(5): p. 487-92. Bredahl, K.K., et al., *Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair.* European Journal	contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the

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				of Vascular and Endovascular Surgery, 2016. **52**(6): p. 729-734. Chung, J., et al., *Contrast-enhanced ultrasound (CEUS) versus computed tomography angiography (CTA) in detection of endoleaks in post-EVAR patients. Are delayed type II endoleaks being missed? A systematic review and meta-analysis.* J Ultrasound, 2015. **18**(2): p. 91-9. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5). Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72. Zimmermann, H., et al., *Value of high-resolution contrast-enhanced ultrasound in detection and characterisation of endoleaks after EVAR.* Clin Hemorheol Microcirc, 2014. **58**(1): p. 247-60.	first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
South Tees NHS Trust	Draft guideline	11	221-227	Ultrasound follow up of EVAR has significantly reduced the cost of surveillance and is being increasingly used with plain Xray to triage those patients needing more expensive CTs with the increased radiation risk.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is

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					contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the

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					first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	11		CT surveillance unless contraindicated. This seems a strong recommendation based on evidence which may not reflect current practice. Consider a recommendation for validation of the contrast ultrasound surveillance system in each unit. The risk is that the stepwise hit in renal impairment and increased risk of cancer would reproduce the EVAR 1 findings. It could be argued that in the presence of a viable ultrasound solution, untargeted lifelong serial CT is contraindicated in anyone with kidneys or DNA.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication.

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					The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	12	223 - 227	The literature is clear that contrast-enhanced ultrasound is a superior imaging modality in relation to endoleak detection and cost-effectiveness [6-11]. In an ideal setting this should be the surveillance modality for EVAR. However, there is currently a skills shortage within the Vascular Scientist community. The cost and training implications are therefore massive when recommending a surveillance protocol using solely contrast-enhanced ultrasound, making it impractical at this stage. The learning curve for a Vascular Scientist to learn contrast-enhanced ultrasound assessments of EVAR is 20 paired cases with	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour

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				contrast-enhanced CT angiography. Also the implementation of these suggestions would expose patients to what we feel would be an unnecessarily regular and therefore unacceptable level of ionising radiation and nephrotoxic contrast agents. **See comments relating to Evidence Review W below** While the Vascular Scientist community becomes skilled in this modality the **Society for Vascular Technology (SVTGB&I) recommends the below infra-renal EVAR surveillance strategy** developed and in use by The University of Manchester, IVS Ltd and Wythenshawe Hospital (formally University Hospital of South Manchester NHS FT). This pathway has been followed for 2 years effectively and has been taught on multiple SVTGB&I contrast-enhanced ultrasound for EVAR training courses. <u>Suggested surveillance protocol:</u> 1) Standard Duplex follow up at discharge, 6-month, and 12 months then annually (coupled with X-Ray KUB (kidney, Ureter, and Bladder) for stent migration and fracture [12]) This is to detect expansion and complications. Despite lower sensitivity for endoleak the risk of complication is detected by expansion in diameter. 2) A reference CT angiogram should be performed at 3 months if necessary. 3) If the sac grows (as identified by duplex), a <u>new</u> type 2 endoleak is identified or a type 1 or 3 is identified perform a contrast-enhanced ultrasound scan. 4) Discuss the case at the next Multi-disciplinary team meeting - even if that Consultant is away.	duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about

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				5) A decision is made for back into standard duplex surveillance at 6-month intervals, urgent contrast-enhanced CT angiography for planning or direct to interventional radiology for coiling/embolization/relining or extension using catheter angiography. There is little research on the role of contrast-enhanced ultrasound for the assessment of complex EVAR [13, 14]. The SVTGB&I therefore do not have a position on its surveillance but suggests complex EVAR surveillance is by contrast-enhanced CT angiography in conjunction with contrast-enhanced ultrasound or standard duplex for complications and expansion. Abbas, A., et al., *3D contrast enhanced ultrasound for detecting endoleak following endovascular aneurysm repair (EVAR).* Eur J Vasc Endovasc Surg, 2014. **47**(5): p. 487-92. Bredahl, K.K., et al., *Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair.* European Journal of Vascular and Endovascular Surgery, 2016. **52**(6): p. 729-734. Chung, J., et al., *Contrast-enhanced ultrasound (CEUS) versus computed tomography angiography (CTA) in detection of endoleaks in post-EVAR patients. Are delayed type II endoleaks being missed? A systematic review and meta-analysis.* J Ultrasound, 2015. **18**(2): p. 91-9. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification*	costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details. The committee considered your proposal on surveillance intervals but felt it was not possible to make such a recommendation without strong evidence to support it. They believed that postoperative imaging modalities and intervals should be left to the discretion of treating clinicians taking into account the facilities and resources available to them.

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				after endovascular aneurysm repair. Journal of Vascular Surgery, 2017. **65**(5). Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72. Zimmermann, H., et al., *Value of high-resolution contrast-enhanced ultrasound in detection and characterisation of endoleaks after EVAR.* Clin Hemorheol Microcirc, 2014. **58**(1): p. 247-60. Harrison, G.J., et al., *Surveillance after EVAR based on duplex ultrasound and abdominal radiography.* Eur J Vasc Endovasc Surg, 2011. **42**(2): p. 187-92. Perini, P., et al., *Contrast-enhanced ultrasound vs. CT angiography in fenestrated EVAR surveillance: a single-center comparison.* J Endovasc Ther, 2012. **19**(5): p. 648-55. Gargiulo, M., et al., *Could Four-dimensional Contrast-enhanced Ultrasound Replace Computed Tomography Angiography During Follow up of Fenestrated Endografts? Results of a Preliminary Experience.* European Journal of Vascular and Endovascular Surgery, 2014. **48**(5): p. 536-542.	
Independent Vascular Services	Draft guideline	12	223-227	The literature is clear that contrast-enhanced ultrasound is a superior imaging modality in relation to endoleak detection and cost-effectiveness [7-12]. In an ideal setting this should be the surveillance modality for EVAR. However, there is currently a skills shortage within the Vascular Scientist community. The cost and training implications are therefore massive when recommending a surveillance protocol using solely contrast-enhanced ultrasound, making it impractical at this stage. The learning	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is

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				curve for a Vascular Scientist to learn contrast-enhanced ultrasound assessments of EVAR is 20 paired cases with contrast-enhanced CT angiography. While the Vascular Scientist community becomes skilled in this modality the IVS Ltd **recommends the below infra-renal EVAR surveillance strategy** developed and in use by The University of Manchester, IVS Ltd and Wythenshawe Hospital (formally University Hospital of South Manchester NHS FT). This pathway has been followed for 2 years effectively and has been taught on multiple SVTGB&I contrast-enhanced ultrasound for EVAR training courses. Suggested surveillance protocol: 1) Standard Duplex follow up at discharge, 6-month, 12 months then annually (coupled with X-Ray KUB for stent migration and fracture [12]) This is to detect expansion and complications. Despite lower sensitivity for endoleak the risk of complication is detected by expansion in diameter. 2) A reference CT angiogram should be performed at 3 months if necessary. 3) If the sac grows (as identified by duplex), a new type 2 endoleak is identified or a type 1 or 3 is identified perform a contrast-enhanced ultrasound scan. 4) Discuss the case at the next Multi-disciplinary team meeting - even if that Consultant is away. 4) A decision is made for back into standard duplex surveillance at 6-month intervals, urgent contrast-enhanced CT angiography for planning or direct to interventional radiology for coiling/embolization/relining or extension using catheter angiography.	contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the

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				There is little research on the role of contrast-enhanced ultrasound for the assessment of complex EVAR [14, 15]. IVS LTD therefore does not have a position on its surveillance but suggests complex EVAR surveillance is by contrast-enhanced CT angiography in conjunction with contrast-enhanced ultrasound or standard duplex for complications and expansion. Abbas, A., et al., *3D contrast enhanced ultrasound for detecting endoleak following endovascular aneurysm repair (EVAR).* Eur J Vasc Endovasc Surg, 2014. **47**(5): p. 487-92. Bredahl, K.K., et al., *Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair.* European Journal of Vascular and Endovascular Surgery, 2016. **52**(6): p. 729-734. Chung, J., et al., *Contrast-enhanced ultrasound (CEUS) versus computed tomography angiography (CTA) in detection of endoleaks in post-EVAR patients. Are delayed type II endoleaks being missed? A systematic review and meta-analysis.* J Ultrasound, 2015. **18**(2): p. 91-9. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5). Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72.	first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details. The committee considered your proposal on surveillance intervals but felt it was not possible to make such a recommendation without strong evidence to support it. They believed that postoperative imaging modalities and intervals should be left to the discretion of treating clinicians taking into account the facilities and resources available to them. Regarding your suggested list of references: Abbas et al (2014) was included in evidence review W Bredahl et al (2016) was excluded as no relevant outcomes were reported Chung et al (2015) was excluded as no primary studies or no new primary studies were extracted from this systematic review Lowe et al (2017) was included in evidence review W Ormesher et al (2014) was excluded as our evidence review considered postoperative imaging Zimmerman et al (2014) was excluded as no relevant outcomes were reported Harrison et al (2011) was excluded as it did not have a relevant study design Perini et al (2012) was included in evidence review W Gargiolo et al (2014) was included in evidence review W

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				Zimmermann, H., et al., *Value of high-resolution contrast-enhanced ultrasound in detection and characterisation of endoleaks after EVAR.* Clin Hemorheol Microcirc, 2014. **58**(1): p. 247-60. Harrison, G.J., et al., *Surveillance after EVAR based on duplex ultrasound and abdominal radiography.* Eur J Vasc Endovasc Surg, 2011. **42**(2): p. 187-92. Perini, P., et al., *Contrast-enhanced ultrasound vs. CT angiography in fenestrated EVAR surveillance: a single-center comparison.* J Endovasc Ther, 2012. **19**(5): p. 648-55. Gargiulo, M., et al., *Could Four-dimensional Contrast-enhanced Ultrasound Replace Computed Tomography Angiography During Follow up of Fenestrated Endografts? Results of a Preliminary Experience.* European Journal of Vascular and Endovascular Surgery, 2014. **48**(5): p. 536-542.	
Society and College of Radiographers	Draft guideline	12	226	"do not use Duplex ultrasound as the main …. In cases of EVAR". Can you clarify if that means it can be used at intervals? In xxxx we alternate between CT and US each year post EVAR.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging,

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					with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.

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South Tees NHS Trust	Draft guideline	12	233	The Panel does not seem to have provided any guidance for intervention of Type IV endoleaks.	Thank you for your comment. A detailed discussion of the committee's discussion about management of postoperative complications can be found in evidence review X. The committee noted that type IV endoleaks can occur after some EVAR procedures, due to the porosity of certain graft materials, but usually resolve on their own without the need for intervention. As a result, it was agreed that no recommendations were needed in relation to type IV endoleaks.
Independent Vascular Services	Draft guideline	13	259	NICE have not recommended further ultrasound-based research other than surveillance intervals for AAA. Would NICE consider adding the below recommendations as research priorities; Training for surgical and medical personnel of the correct technique for Point-Of-Care and FAST scanning of Aortic Aneurysms. NICE may wish to consider making this recommendation to HEE to include in the training competencies of vascular surgeons in training. Cost-effectiveness studies on the use of contrast-enhanced ultrasound in the surveillance of EVAR. The use of 3D & 4D ultrasound technology to further improve planning and surveillance of AAA pre and post EVAR. Including volumetric assessment. Computation Fluid Dynamics, Finite Element Analysis and other complex characteristics for the prediction of growth, rupture and complication risk. The use of Artificial Intelligence, Augmented Reality and mass data in surgical technique, risk prediction and imaging.	Thank you for your comment. Your comments relating to implementation of training and core competencies will be relayed to HEE as it is not within the remit of NICE to specify who should provide training and how it should be provided. In relation to post imaging surveillance: the committee made a research recommendation in the evidence review on tailored surveillance. The research recommendation specifically focusses on the risks, benefits, and cost implications of different imaging modalities and imaging intervals (including contrast enhanced ultrasound) in people who have undergone EVAR. In relation to advanced imaging technology (including post-processing techniques and CT angiography data analysis tools): The committee agreed that there were clear advantages of using advanced imaging tools because they can make assessment of aneurysm anatomy more accurate compared with estimations made when reviewing axial datasets without using these tools. The committee agreed that

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					the time associated with the use of these techniques is more than offset by the additional data and benefits that this analysis provides. This also remains true in emergency EVAR where this activity can be done in parallel with other acute patient preparation. As advanced imaging software packages are already widely embedded in clinical radiology practice, and now considered to be standard in most hospitals, the committee did not consider it necessary to make any research recommendations.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	13	259	VASGBI funds research in vascular anaesthesia and we are pleased about the recommendations for further research into some areas of our practice. However, there are further areas where we lack evidence: e.g. validated pre operative risk scoring and other methods to test fitness and inform the shared decision making process. Recent papers support the need for reappraisal of the current interpretation of cardiopulmonary fitness testing. We strongly recommend including this as a research recommendation in the guidance document.	Thank you for your comment. The committee decided against making a research recommendation because extensive research into preoperative risk scoring for AAA surgery has already been performed over recent decades and further research in this area is unlikely to be viewed as a priority. They noted that most of the clinical data used to derive risk assessment tools are commonly collected and are already available before surgery. They agreed that individual variables (as opposed to risk models) can be still useful for making judgments of an individual's risk of postoperative morbidity and mortality.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Draft guideline	13	259	The SVTGBI are disappointed to see that NICE have not recommended further ultrasound-based research other than surveillance intervals for AAA. The SVTGB&I would ask NICE to consider adding the below recommendations as research priorities; Training for surgical and medical personnel of the correct technique for Point-Of-Care and FAST scanning of Aortic Aneurysms. NICE may wish to consider making this	Thank you for your comment. Your comments relating to implementation of training and core competencies will be relayed to HEE as it is not within the remit of NICE to specify who should provide training and how it should be provided. In relation to post imaging surveillance: the committee made a research recommendation in the evidence review on tailored surveillance. The research recommendation specifically

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				recommendation to HEE to include in the training competencies of vascular surgeons in training. Cost-effectiveness studies on the use of contrast-enhanced ultrasound in the surveillance of EVAR. The use of 3D & 4D ultrasound technology to further improve planning and surveillance of AAA pre and post EVAR. Including volumetric assessment. Computation Fluid Dynamics, Finite Element Analysis and other complex characteristics for the prediction of growth, rupture and complication risk. The use of Artificial Intelligence, Augmented Reality and mass data in surgical technique, risk prediction and imaging.	focusses on the risks, benefits, and cost implications of different imaging modalities and imaging intervals (including contrast enhanced ultrasound) in people who have undergone EVAR. In relation to advanced imaging technology (including post-processing techniques and CT angiography data analysis tools): The committee agreed that there were clear advantages of using advanced imaging tools because they can make assessment of aneurysm anatomy more accurate compared with estimations made when reviewing axial datasets without using these tools. The committee agreed that the time associated with the use of these techniques is more than offset by the additional data and benefits that this analysis provides. This also remains true in emergency EVAR where this activity can be done in parallel with other acute patient preparation. As advanced imaging software packages are already widely embedded in clinical radiology practice, and now considered to be standard in most hospitals, the committee did not consider it necessary to make any research recommendations.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline	13	259+	The research recommendations do not include any suggestions as to studies that might help to identify suitable subgroups of patients for whom elective EVAR may be an effective and cost-effective option. As discussed in the previous comments, it seems likely that there are circumstances in which the risks, costs and benefits of EVAR are very different from the averages provided in the economic model. The NICE appraisal committee identified this in TA167 in 2009 and, since then about 20,000 EVAR procedures have been carried out in England. Had NICE made a 'coverage	Thank you for your comment. The detailed research recommendation relating to EVAR for unruptured AAA (available in appendix K of evidence review K) specifies that any analyses should stratified according to age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity) and ethnicity. The committee believed that such analyses would allow for identification of suitable subgroups of patients for whom elective EVAR may be an effective and cost-effective option.

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				with evidence' recommendation at that time, with collection of case mix and follow-up data being required to resolve these uncertainties, then we would be in a much better position to accurately identify the place of EVAR in current practice. If the committee are unable to define clear criteria for selecting a suitable subgroup of people for whom EVAR is an option, then such a research recommendation might be appropriate.	
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Draft guideline	17	362-363.	The wording appears the wrong way around, surely the primary aim of screening is to reduce AAA related mortality. Cost should come second. Rather than cost reduction, the remit of NICE is to study cost effectiveness. The very language of this draft suggests a bias towards a prioritisation of cost minimisation rather than a focus on patient safety, clinical effectiveness and cost effectiveness (+/- affordability) in that order of priority.	We state that encouraging appropriate people to seek screening is a good thing because it both reduces costs and improves outcomes. Nowhere in the guideline do we talk about cost without considering the relationship between expenditure and patient outcomes.
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Draft guideline	24	563	Question 1: We do not agree with the statement: "risk scoring tools are only used in research". In current practice, risk assessment tools are being used by consultant anaesthetists in preoperative assessment clinics to help aid discussions and to inform shared decision-making. However, these tools are used carefully and only as a guideline.	Thank you for your comment. To clarify the statement that risk assessment tools are not commonly used outside research: the committee noted that risk assessment tools were routinely used in many clinical areas but, in their experience, they were not widely used outside research when it came to the context of AAA.
Countess of Chester Hospital	Draft guideline	26	623	Which technique to use The reliance on EVAR2 data to extrapolate to current practice is flawed. Improvements in devices, device profile, access techniques, experience with endoleak management have therefore not been adequately costed in this model. Our early experience was to consider intervention for many type 2 endoleaks but this has changed significantly, most	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				require no intervention at all. The adjunctive techniques allow low cost and rapid intervention for type 1 and 3 endoleaks. Repeated interventions are incredibly rare. It is not true that OSR do not have late complications for example aneurysmal dilatation at anastomosis sites. We have seen a small but significant number of these cases and repeated open intervention is hazardous.	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice, and advised that the HE model should be revised to address this issue. Full details are provided in **Theme 7**. The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree. The guideline does not state that OSR does not have late complications; it states that it has fewer late complications than EVAR, which no one seriously disputes (even when we adjust our estimates to account for the reduced rate of EVAR reinterventions and take pains to include post-OSR procedures that have sometimes been overlooked). The evidence used for the HE model reflects the incidence of relatively rare life-threatening reinterventions as reported in the RCTs.
Vascular Research Group,	Draft guideline	26 27	623 to 639	The description of the reasons for reaching the decision that open repair should universally be preferred to EVAR for elective treatment does not adequately address the possibility	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations

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School of Health and Related Research (ScHARR), University of Sheffield				of relevant subgroups for whom different recommendations are relevant, as recommended by the methods guide (section 7.6). Unfortunately, many of the shortcomings of the modelling referred to above, mean that the committee was not presented with appropriate cost utility estimates for relevant subgroups, based upon factors such as age, sex, aneurysm size and comorbidities, or any threshold analysis on which they could potentially have identified a device acquisition cost at which the procedure would be cost effective (as was done for drug eluting coronary stents in TA152).	related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee was presented with cost–utility estimates for subgroups based on age, sex and AAA diameter. See **Theme 12**. Threshold analyses on device acquisition cost were also presented to the committee – see figure HE47, figure HE59, figure HE70, figure HE78, figure HE93 and figure HE94.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline	26 27	623 to 639	There is also no evidence that there was consideration of factors relevant to the decision that were not fully captured in the cost utility analysis. For example, there is evidence of strong preferences for the less invasive process of care involved with EVAR, which may not be captured in the outcome measurements used (e.g. see Winterborn et al. J Vasc Surg 2009;49:576-81 and Higgins et al Value in Health 2014;17:877-87). In NICE appraisals it is not unusual to consider aspects such as the convenience and route of treatment administration as a consideration in decision-making over and above the estimate of ICER, in keeping with the NICE advice on Social Value Judgements (see Methods Guide section 7.7). We have recently been carrying out a patient preference study using standard gamble methods to evaluate the strength of patient preference for various aspects outside standard measures of clinical effectiveness. Preliminary analysis of this work suggests that a majority of patients have a strong preference for EVAR and would be willing to trade an average	Thank you for drawing our attention to this literature, which other stakeholders have also cited. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We agree that convenience and route of treatment are good examples of the kinds of health gains that are unlikely to be captured by cost–utility analyses, and may be taken into account by decision-making committees when making judgements about technologies (especially those with ICERs in the range £20,000–30,000). However, in the infrarenal elective case, our best estimate is that it is dominated by OSR (that is, it causes net patient harm alongside additional NHS costs) and, in complex elective cases and those for whom

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				of 0.135 QALY for access to the treatment, independent of any QALY difference based upon clinical outcomes. There is also evidence that has demonstrated that there may be increasing preference for less invasive treatments with age (e.g. see Mazur DJ, Merz JF. How older patients' treatment preferences are influenced by disclosures about therapeutic uncertainty: surgery versus expectant management for localized prostate cancer. Journal of the American Geriatrics Society. 1996 Aug 1;44(8):934-7.). This, along with the higher peri-operative risk, likely greater difference in resource use and lower expected follow-up costs in older people, may be relevant in considering older subgroups of patients who may benefit from EVAR.	OSR is unsuitable, it is associated with ICERs far above the levels referred to in the cited methods. We are unable to comment on the preliminary findings of your unpublished work, other than to note that, while 0.135 QALYs is a large amount, it would still not be enough to overturn our base-case estimate that EVAR is associated with a net loss of 0.157 discounted QALYs, compared with OSR. Mazur and Merz's paper (1996) explores patient preferences for intervention versus no intervention, rather than different degrees of invasiveness. This evidence may have some relevance to decision-making about offering OSR or no intervention in older people; however, it does not directly inform the comparison of EVAR and OSR.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Draft guideline Health economics appendix	26 27 General	623 to 631	The decision to recommend against the use of EVAR in all cases is based upon a failure of the economic modelling to adequately consider all possible subgroups and scenarios in which EVAR may prove to be a cost-effective use of NHS resources. This represents a fundamental inconsistency in the guidance. In several places it is clear that the guidance identifies patient characteristics that are likely to be predictive of outcomes and costs. This includes the use of cardiopulmonary exercise testing (Short p7 132-4), eGFR (Short p23-24 554-547) and individual variables that are predictive of outcome (Evidence review H p12, 203-5). The entire basis of the modelling and of the EVAR 1 and 2 trials, which form the basis of much of the evidence, is predicated upon the assumption that clinicians are able to judge the fitness and suitability of individual patients for the different treatment options. It thus seems odd that there was no attempt to consider different scenarios relating to subgroups of	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. However, at no stage does the guideline recommend that any signs, symptoms, tests or tools should be used to make categorical decisions about a person's management; indeed it explicitly recommends the opposite. Adopting quantitative evidence from Evidence reviews G and H as an input to the HE model would result in exactly that kind of judgement being applied on the basis of evidence about which the committee's uncertainties are clear.

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				patients based upon aneurysm size, age, sex, fitness for surgery and general health. To only address these through a series of one-way sensitivity analyses, rather than considering realistic clinical scenarios fails to deal with the heterogeneity of clinical situations faced in practice.	For example, the committee's conclusion regarding CPET, as reported in the consultation draft, was that, *while CPET may provide healthcare professionals valuable objective information on the fitness of people prior to elective AAA repair, the evidence was not robust enough to make strong recommendations for the use of the test as a decisive arbiter of fitness. Moreover, the committee agreed that individual CPET parameters should not be used in isolation to decide whether a patient should have surgery or not, but instead, may be used to inform shared decision making in context of medical history and examination.* The committee was presented with subgroup analyses exploring the joint effects of age, sex and AAA diameter (see **Theme 12)**; however, fitness for surgery is more difficult to quantify (see relevant comments in **0**).
				It is clear there are some circumstances which present very different risks, such as the extreme case of patients with a hostile abdomen in whom open surgery carries very high risk. However, there are also common circumstances in which there is significant variation from the average. As an example, our logistic regression based upon the most recent NHS HES data that we have available, estimates the 30-day mortality for an 80-year-old male with COPD to be 0.914% with EVAR and 8.179% with open repair, the comparable figures for females being 1.809% and 9.809%. Since at this age the length of follow-up and potential for repeat treatments is much lower than average (it is questionable whether patients would be followed up as intensively as the modelling assumes into their 90's) there is likely to be a much greater benefit for such	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. It is difficult to comment on preliminary findings of your unpublished work in progress. Clearly, there are people who do not survive OSR who may have survived EVAR and, if such cases could reliably be predicted a priori, it is likely that it would be cost effective to offer them EVAR (though it is also possible that, if the characteristics that predict perioperative mortality with OSR overlap with the factors that clinicians were taking into account when randomising participants to EVAR-2,

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				patients. Given the greater surgical risks, there is also likely to be a much greater difference in resource use (an aspect not considered in the modelling), so that the ICER is likely to be more favourable to EVAR. We accept that this raises difficulties in providing clear guidance, due to the lack of a set of validated predictive models that could be used to identify such sub-groups, but it would seem appropriate to consider whether such sub-groups are likely to exists and, if so, either to make recommendations that might help to delineate them or, at least, to recommend further research to generate predictive models and decision aids that would allow more detailed advice to be provided in future (see comment 22). The detailed data that are already collected as part of the NVR, if combined with HES data for long term outcomes and re-treatment, should be suitable for the development of such models.	no intervention may be a superior approach). However, the committee had no confidence that any such prediction tools currently exist, and were mindful of the danger of denying patients a more durable repair on the basis of poorly predictive information. As previously emphasised, the committee considered carefully whether subgroups are likely to exist with a different balance of benefits, harms and costs from the average member of the cohort, and was unable to find plausible evidence that any such subgroups can be reliably identified – see **Theme 12**.
South Wales Vascular Surgery Network	Draft guideline	26	624 -	We, the South Wales Vascular Network, wish to raise our concerns regarding the draft guidance GID-CGWAVE0769; Abdominal aortic aneurysm: diagnosis and management. The 15-year follow-up of the EVAR 1 trial concluded: EVAR has an early survival benefit but an inferior late survival compared with OR, which needs to be addressed by lifelong surveillance of EVAR and re-intervention if necessary. In the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. This is a faithful summary of some features of the EVAR-1 RCT.

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				trial 626 patients were randomized to either EVAR or Open repair with a mean age at inclusion of 74. The authors report, as of June 2015 four patients were lost to follow up and 25 for re-intervention (five in the EVAR group and 20 in the OR group). Over the course of follow-up, a median of six CT scans (IQR 3-8) were done per patient in the EVAR group compared to three (IQR 1-6) in the OR group. This is now not in keeping with clinical practice. Follow up surveillance of EVAR is based on Ultrasound of the aorta with duplex. Only where increase in sac size of the AAA is found are CTs then performed thus limiting the number of CTs performed. As of September 2009, 728 patients had died, and their outcomes were assessed through Hospital Episode Statistics. Cause of death was based on death certificates not autopsy examination. Re-interventions for the EVAR group were higher. This is not in keeping with clinical practice. Type 2 endoleaks are not routinely re intervened upon unless there is evidence of an increasing sac size.	Recommendations made elsewhere in this guideline advise against reliance on duplex ultrasound as the primary screening modality for post-EVAR surveillance. Please see **Theme 11**. We infer that you make this comment to cast doubt on the accuracy of AAA-related mortality as an outcome. To some degree, we share this concern, which is one reason why the HE model that was developed to support this guideline did not, as some previous models in the same area have, attempt to distinguish between AAA-related and other-cause mortality. Instead, we use data on overall survival, which is much more likely to be robust. The committee did not agree with your suggestion that it is not in keeping with clinical practice for EVAR to be associated with more reinterventions than OSR. However, it did agree that reintervention rates for EVAR have reduced over the time the EVAR-1 trial has been going on. In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced

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					rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
				Open aortic aneurysm repair is associated with a 37% incisional herniation rate.[3] The EVAR 1 trial did not record incisional herniation and repair rates in the OR group, by its nature herniation does not occur in the EVAR group.	The committee certainly accepted that OSR is associated with a risk of hernia. The figure you cite is distinctly inflated, however (we note that it is based on a series of 27 patients published in 1988). More recent data from much larger datasets estimate the probability of reintervention for incisional hernia following OSR at 11.2% at 8 years (Schermerhorn et al., 2015; n=39,966). It is true that the EVAR-1 trial did not initially collect data on this outcome. However, the investigators were mindful of this criticism, and retrospectively obtained data on hernia interventions required following EVAR and OSR for all trial participants. These were reported in the long-term follow-up reports (Patel et al., 2016; Patel et al., 2018); these rates are incorporated in the base-case HE model. We also incorporated other laparotomy-related complications recorded in US registry data (Schermerhorn et al., 2015) that had not been retrospectively included in the EVAR-1 reintervention data. Therefore, we are confident that the HE model developed to support decision-making for this guideline does not underestimate the late complications of OSR.
				The authors conceded, that with a mean age of seventy-four at recruitment, 15 years later many patients still alive may have been frail and therefore interventions may not have been undertaken, therefore pushing up the rupture rate in the EVAR group	This finding is a simple reflection of clinical practice – indeed, it is likely that, owing to less intensive follow-up in practice than was mandated in the RCT, more late ruptures will occur in 'real world' data.

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All-Party Parliamentary Group on Vascular and Venous Disease	Draft guideline	28	677 - 686	Clinician skills will also become a significant issue. With the removal of EVAR as a treatment option for unruptured AAA, but the option still offered for patients with a ruptured AAA, there is a reliance on the ability, skill and training of clinicians in order to be able to perform this procedure in emergency cases, with very little real world practice. It does not seem to have been considered within the current draft guideline that, as with all interventions, the number of procedures a clinician performs correlates to improved outcomes. How can clinicians be expected to deliver life-saving results with a procedure they rarely carry out and within an emergency setting only? Many clinicians are likely to refuse to carry out the EVAR technique on emergency rupture patients as recommended by NICE if they have not been routinely doing this as preventative treatment, risking lives. .	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
All-Party Parliamentary Group on Vascular and Venous Disease	Draft guideline	28	677 - 686	The draft guideline recognises that the recommendations on EVAR will have a large impact on practice as EVAR is a widely performed procedure. Indeed, EVAR has become the standard of care for AAA repair. One of the objectives of the APPG – and indeed the Government – is to promote the adoption and use of innovation and technologies equitably across the country. This decision, therefore, marks a huge step backward for the NHS and, in reality, it is almost impossible to turn the clock back 15/20 years. A similar analogy would be to go back to cardiac surgery as the only treatment choice for coronary artery disease rather than balloon angioplasty.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				Disinvestment of this proven technology which is routinely used goes against the direction of travel in improving access to proven technologies. It could cost millions, make the NHS appear backwards internationally, drive away pioneering clinicians and is at odds with the NHS productivity agenda.	
Countess of Chester Hospital	Draft guideline	29	704	The absence of consideration of local and spinal anaesthesia as a standard for elective EVAR fails to identify the associated reduction in costs, morbidity and length of stay. In our consecutive series, 65 out of 66 cases were performed with a percutaneous approach, the majority under Local &/or Regional Anaesthesia. With experience this could be achieved in all centres. Day case elective EVAR is a real prospect for many patients. This must compare favourably with elective admission for OSR to high dependency areas which already lack capacity.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. In our revised HE modelling, inputs have been updated to reflect current-day perioperative resource-use data (drawn from 2017 NVR). This will reflect the degree to which the techniques you advocate have become widespread, and the extent to which they affect costs. The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.

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Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Short Economic model	9-10, 31	179-189, 763	Complex AAA should be treated by open repair. We note that a range of cases have been rolled under the subheading of "complex AAA". This hampers meaningful discussion. This group of patients will include patients requiring a suprarenal, but also those requiring a supracoeliac clamp and reimplantation of multiple vessels. Also although the guidance is for abdominal aneurysms, the commissioners will likely extrapolate to thoraco abdominal aneurysms, requiring thoracotomy as well. There is no evidence to suggest that a complex endovascular repair doesn't carry a survival advantage in such cases. Complex cases will present even greater challenges to many units if asked to perform open repair. This would likely lead to greater numbers of transfers and related deaths. Where is this accounted for in the economic model? It is incorrect to say that in a patient who would require complex EVAR to treat a ruptured AAA, open surgery is a safe and suitable option. Can a procedure with a 30-40% mortality (at least, probably much more if juxta/suprarenal) be described as "safe"?	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. However, it is clear that no such data exist. See **Theme 10** for discussion. We would agree with you that it would be inappropriate to extrapolate from this guidance to any situation beyond its scope, and NICE would advise commissioners against doing so. We are unaware of any evidence to confirm or quantify these speculative statements. Clearly, the safety of any course of action can only be judged against a reasonable counterfactual scenario. In the case of OSR for ruptured complex AAAs, 30–40% mortality is to be preferred to 100% mortality (which would be inevitable without intervention). The relative safety of complex EVAR, in such cases, is unknown, as are its long-term effects. In the IMPROVE RCT, there was 38% 30-day mortality among participants who were randomised to the EVAR-if-possible strategy but who underwent OSR because they were adjudged anatomically unsuitable for EVAR. This group probably stands as a reasonable proxy for people undergoing OSR for complex

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					ruptured AAAs. We cannot know how these people would have fared had complex EVAR been attempted. It is extremely unlikely that 30-day mortality would have been lower than the 27% that was recorded in members of the EVAR-if-possible cohort whose anatomy was propitious for infrarenal EVAR; indeed, the committee thought it would be certain to be substantially higher.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Short Economic model	9-10, 31	179-189, 763	Complex AAA should be treated by open repair. In the economic model complex EVAR is apportioned the cost for a custom endograft. Despite this the recommendations define complex as including ChEVAR, ChEVAS and I presume stapled infrarenal endograft. These carry much lower costs. This a a further point which renders the proposed analysis as invalid.	We are aware that the costs of EVAR grafts are extremely heterogeneous, as regards their list prices and – even more opaquely – the prices negotiated by individual trusts. Our base case, therefore, relies on our best estimate of the cost of a typical complex graft. However, in view of the uncertainty, we provide results that reflect a range of costs. Figure HE59 in the HE appendix of the consultation draft showed the relationship between average complex EVAR device cost and cost–utility results. We have updated this analysis in Figure HE133. It is important to emphasise that this analysis should not be interpreted as identifying the threshold device cost below which it would be cost effective to offer EVAR in any individual case. It is extremely likely that cases in which relatively inexpensive endovascular grafts can be used are also those that would accrue lower costs if OSR were used. Therefore, it must be understood that this analysis shows the threshold cost below which the average EVAR device would have to fall before it could be cost effective to adopt a model in which all complex AAAs received EVAR.
Countess of Chester Hospital	Draft guideline	33	817	Variable surveillance. We believe that insufficient weight has been given to look at best practice for EVAR surveillance. In vascular centres the	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the

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				expertise already exists to minimise contrast and radiation dose as well as cost by utilising a follow up regimen which minimises CT and CEUS while maximising the identification of complications. In our practice the correlation between Duplex Ultrasound and CT findings is excellent. We rely on Duplex Ultrasound and plain film for post EVAR surveillance. We are happy to share our follow up protocol and experience.	recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I

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					and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	26 and 27	629 – 639	Costs. We agree with the committee that elective EVAR incurs higher initial costs due to the costs of the devices. This is offset by the shorter length of stay and that the patients routinely do not require HDU/ITU care. Our current HDU/ITU usage for AAA care at CHS is negligible since the introduction of EVAR. The need for an HDU/ITU bed for open surgery will result in frequent cancellations leaving operating facilities under-utilised and, if available, reduces the availability of these beds for other patients in need of this level of care for their survival.	Thank you for your comment. For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**. It is clearly true that EVAR is associated with a lower probability of critical care for the average candidate than OSR, though it will clearly remain unavoidable in a small proportion of cases. Our analysis suggests that cost savings associated with reduced critical care and overall LoS attenuate, but do not eradicate, the cost difference associated with devices.
UHCW NHS Trust Coventry	Evidence review K	23	532	*Resources* We are not resourced re- ITU facilities and IP bed to suddenly stop performing elective EVARS.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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UHCW NHS Trust Coventry	Evidence review K	26	706-707	*Patient's wishes* We do not feel that we can ignore patient's wishes. To deny an effective treatment (our data) for AAA (EVAR) on a historical dataset is not acceptable. Patients undergoing any other treatment (such as breast cancer) would be given the option of making an informed decision based upon available data and patient choice.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues and Theme 15 for NICE's view on the importance of joint decision making between the clinician and the individual.
UHCW NHS Trust Coventry	Evidence review K	30	869-71	*Women* Outcome in women with AAA is worse in both elective and ruptures and equity of access differs. EVAR access to women needs to increased (Ulug P Lancet 2017). We disagree with the committee's statements on this issue.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Sidloff et al. (2017) show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR).

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Wirral University Teaching Hospital NHS Foundation Trust	Draft guideline	9	181	Do Not Offer EVAR The effect of this blanket withdrawal of treatment will be to adversely impact on the outcomes for those with life expectancy is upto 8 years . There will be an increase in perioperative mortality. The provision of ITU and HDU will be unable to meet the demands of elective OSR	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. This comment appears to assume that any post-perioperative benefit for OSR only accrues after 8 years, doubtless in reflection of piecewise survival results from EVAR-1. We do not think this is a correct interpretation of those data and others – see **Theme 9a**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
Wirral University Teaching Hospital NHS Foundation Trust	Draft guideline	26	623	Which technique to use The reliance on EVAR2 data to extrapolate to current practise is flawed.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				Improvements in devices, device profile, access techniques, experience with endoleak management have therefore not been adequately costed in this model. Our early experience was that we would intervene for many type 2 endoleaks this has changed significantly, most require no intervention at all. The adjunctive techniques allow low cost and rapid intervention for type 1 and 3 endoleaks. Repeated interventions are incredibly rare. It is not true that OSR do not have late complications for example aneurysmal dilatation at anastomosis sites.	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice, and advised that the HE model should be revised to address this issue. Full details are provided in **Theme 7**. The guideline does not state that OSR does not have late complications; it states that it has fewer late complications than EVAR, which no one seriously disputes (even when we adjust our estimates to account for the reduced rate of EVAR reinterventions). The evidence used for the HE model reflects the incidence of relatively rare life-threatening reinterventions as reported in the RCTs.
Wirral University Teaching Hospital NHS Foundation Trust	Draft guideline	29	704	The absence of consideration of local and spinal anaesthesia as a standard for elective EVAR fails to identify the associated reduction in costs, morbitity and length of stay. In our hands we have 65 out of 66 cases performed under percutaneous approach the majority under LA and or spinal anaesthesia. With experience this could be achieved in all centres. Day case elective EVAR is a real prospect for many patients. This must compare favourably with elective admission to high dependency areas which already lack capacity.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. In our revised HE modelling, inputs have been updated to reflect current-day perioperative resource-use data (drawn from 2017 NVR). This will reflect the degree to which the techniques you advocate have become widespread, and the extent to which they affect costs. The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with

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					enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.
Wirral University Teaching Hospital NHS Foundation Trust	Draft guideline	33	817	Variable surveillance. I believe that insufficient weight has been given to look at best practice for EVAR surveillance. In vascular centres the expertise already exists to minimise contrast and radiation dose as well as cost by utilising a follow up regimen which minimises CT and CEUS while maximising the identification of complications. In our vascular centre (South Mersey based at Countess of Chester) our correlation between doppler and CT findings is excellent. We rely on Doppler USS and plain film surveillance. We are happy to share our regimen and experiences.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on

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					their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Medtronic UK	N/A Response Reference List	General	General	**REFERENCES** Aggarwal S, Qamar A, Sharma V, Sharma A. Abdominal aortic aneurysm: A comprehensive review. Exp Clin Cardiol. 2011;16(1):11-5. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. N Engl J Med. 2000;342(25):1878-86. Broos PP, Stokmans RA, Cuypers PW, van Sambeek MR, Teijink JA. Effects of Anesthesia Type on Perioperative	Thank you for these references; we consider them where cited in your comments.

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Hull and East Yorkshire Hospitals Vascular and	Introductory comment	N/A	N/A	Our local population has high levels of social and health deprivation. The incidence of AAA on screening is much higher than the UK average and the levels of associated comorbidity higher also. We currently offer a very balanced	Thank you for providing this summary of your comments, which we respond to fully where they are given in detail. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of

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Endovascular Service				practice including both EVAR and open repair in large numbers. Patients who are unfit or due to their physical condition are unlikely to benefit from prophylactic AAA repair are not offered treatment. Patients of borderline fitness undergo treatment at a higher size threshold. For the majority of patients who are fit, they are offered open surgery or the best endovascular solution, unless there are compelling reasons for one over the other. An honest discussion is undertaken regarding the significant reduction in early morbidity and mortality with endovascular repair versus the requirement for surveillance and possible reintervention. Many of our younger and fitter patients elect to undergo open repair and these make up a significant part of our practice – more so than in other centres. Our feeling is that this approach represents the optimal interpretation of the available evidence and do not agree that the recommendations made in this draft document represent a reasonable or responsible appraisal of existing knowledge. Other than the significant improvement in early mortality we see little in common between our real world experience and the historical EVAR 1 trial which is pivotal to these draft recommendations. We have significant concerns regarding the basis for the recommendations and the profoundly negative impact we believe they will have on our patients and our service. In the evolution of endovascular treatment for aortic aneurysmal disease we have undergone the stages of initial proof of concept, early comparative trial (which demonstrated	the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				advantages and challenges) and a period of development of knowledge, skills and technology. Crucially it is now time for a reappraisal of what place this technology should have in contemporary management. To dismiss the technology altogether based upon the results of the early trials with no meaningful assessment of the impact of the last 20 years of development could be viewed as an extreme and unjustifiable action. Given the number and magnitude of concerns regarding the validity of the review, a more measured approach would be to embark on a series of NIHR supported studies to explore the very real evidence gaps, before conclusions are made. Whilst the temptation is to give a detailed referenced response, we have aimed to be concise, aware that there is likely to be a great number of responses for the NICE committee to process. We have not discussed the recommendations which are reasonable, evidence based or valid and welcome the clear view given in these areas.	
Cook Medical	Health economics appendix	98-161	General	**Sensitivity analysis** *As we disagree with many of the base case estimates, we similarly disagree with the plausible ranges of estimates for the variables and believe that the current sensitivity analysis gives false confidence in the results of the economic model (i.e., what we consider highly plausible falls outside the 95% confidence intervals).*	Comment noted. We have responded to each of the instances you raise in response to each relevant comment.
Cook Medical	Health economics appendix	59-62	General	**Monitoring costs**	The committee agreed that the postoperative surveillance of people who have undergone EVAR could be optimised – hence, they made a research recommendation in this area.

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				Elsewhere in the guidelines, the committee recommends that CT scans be recommended for EVAR follow-up. Recommendation 1.7.2 says "base the frequency of surveillance imaging on the person's risk of graft-related complications". The economic model base case assumes 1 outpatient consultation, followed by an outpatient CT 1 month later. Thereafter, 1 outpatient imaging appointment per year for 5 years. OSR patients attend an outpatient consultation after 2 months with no imaging and no additional follow-up. *Given that surveillance of imaging is recommended based on the person's risk of graft-related complications, there should be more justification provided for the selection of these model inputs – i.e., ideally information on what current practice is / compliance to guidance.*	However, without any evidence as to the empirical performance of an (on average) less intensive follow-up regimen, there is a real danger that bias will be introduced to our analysis by assuming that the costs of surveillance can be minimised without compromising patient safety – see **Theme 11**.
W.L. Gore and Associates	Health economics appendix	10	28	**The model does not account for the costs of post-discharge patients receiving rehabilitation care.** Patients receiving aneurysm repair, whether EVAR of open repair, often require rehabilitation, and these costs are not included in the model. Rehabilitation costs are considerable for patients receiving open repair. We recommend that post-discharge costs be added to the elective infrarenal model. We conservatively estimate post-discharge costs for EVAR at £146 (assumes 0.5 day in nursing home, 1 GP home visit and 1 nurse visit) and for open repair at £672 (assumes 3.5 days in nursing home, 2 GP home visits, and 2 nurse visits). These costs are based on estimates from the 2017 Costs of Health and Social Care	The committee considered and accepted this argument. They therefore advised that an estimate of rehabilitation costs should be incorporated into the base-case model. See **Theme 6b** for details. The resource-use estimate we have used is much less conservative than your estimate, as it is partially based on data from the emergency setting, where it is likely that people will require more extensive rehabilitation. Therefore, the analysis can now be viewed as estimating the largest possible benefit for EVAR, in this domain, and almost certainly represents an overestimate.

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				report from the University of Kent Personal Social Services Unit.	
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	13	1-17	The statement that two cost-utility models were built to address the review questions prioritised by the guideline committee is misleading. The review questions considered open repair, EVAR and non-surgical treatment (presumably including watchful waiting and no further intervention) of unruptured aneurysm (RQ12) and similar options for ruptured aneurysm (RQ23). The modelling has chosen to simplify the problem to consider only two options in arbitrarily defined subgroups; EVAR vs open repair for 'fit patients' and EVAR vs no treatment for 'unfit patients'. This essentially replicates the EVAR trials rather than accurately reflecting the review questions or the more complex choices facing patients and clinicians in clinical practice. For example, it precludes the possibility of considering watchful waiting with different threshold sizes depending upon fitness or comparing all options in patients with differing levels of fitness.	It is in the nature of HE modelling that it deals with simplified representations of decision problems that may be complicated at the individual level. In this instance, we accept that categorising people as fit or unfit for OSR is a sophisticated process that requires multidisciplinary discussion. However, there is currently no reliable way of doing this on an objective basis (see Evidence reviews G and H). In this context, the EVAR-2 trial provides invaluable information on the outcomes that can be expected for the sort of people whom clinicians tend to think of as contraindicated for OSR, even if there is no way of defining such people according to objective criteria. There are no empirical data on watchful waiting, and any simulation of such a strategy would be extremely speculative.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Health economics appendix	14	12	The economic analysis has not considered contemporary resource use very well. The evidence in the economic analysis is largely drawn from the recent analyses of the EVAR1 data. For example, critical care use is a major driver of cost. In EVAR1 mean critical care stay was 1.42 days for EVAR (Brown 2012) and this was used in the analysis here (Table HE26, page 58). It is now extremely rare for patients undergoing EVAR to require any critical care stay. Current resource use figures need to be determined and checked before finalizing the HE model.	It is true to say that perioperative resource use has reduced with EVAR, compared with the RCTs; however the same is true of OSR. On considering stakeholder comments such as this one, the committee agreed – on a balance of considerations – that we should revise model inputs to reflect contemporary evidence, even though they had misgivings about the presence of clear selection biases in those data. See **Theme 6** for details.

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University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Health economics appendix	16	2	The cohort parameters for contemporary elective AAA repair are incorrect. Median age at repair in the NVR is 71 years. The use of EVAR1 data is not justified when contemporary data are available; further evidence that the parameters for the HE model are incorrect and need to be updated to contemporaneous figures.	The mean age of people undergoing elective infrarenal AAA repair in the 2017 NVR is 73.8 – not very different from the 74.0 of people in EVAR-1. Nevertheless, we accept that this is strictly a more applicable estimate of the likely mean age of the cohort in our decision problem, and have updated model inputs accordingly.
W.L. Gore and Associates	Health economics appendix	17	17-32	**The model underestimates waiting time length and waiting time mortality.** The elective infrarenal model notes that in EVAR-1, the waiting period for EVAR was 60 days compared to 93 days for open repair, and waiting period mortality for EVAR was 1.9% versus 3.0% for open repair. The guidance states that this is most likely due to random chance and applies a pooled estimate for both the length of the waiting period (76 days) and waiting period mortality (2.4%). No evidence is provided to support use of the same waiting period length and mortality rate for EVAR and open repair, and this is the only data point from EVAR-1 that is assumed to be random rather than representing a real difference. This 2.4% figure from EVAR-1 for waiting period mortality is too high compared to current data. Use of this figure has significant impacts on perioperative and long-term mortality, as well as QALY calculations. If NICE is going to assume equal mortality for EVAR and open repair during the waiting period, we recommend the use of a 1% mortality rate for the waiting period in the elective infrarenal model.	As detailed in the paragraph to which you refer, it is impossible to hypothesise a reason why the **rate** of waiting list mortality would be different for people awaiting EVAR and OSR and, for this reason, the committee advised that a homogeneous risk should be used. This is obviously very different from any other phase of the trial, when participants had actually received the treatment to which they had been randomised. We are unaware of any data to substantiate your hypothesis that waiting list mortality rates are now lower than observed in the EVAR-1 RCT. We vary this value in sensitivity analysis; it does not make a material difference to model results. It should be remembered that the estimate used, here, defines all-cause mortality for this period, not merely AAA-related death. General population mortality is approximately 0.3% per month for a cohort of this age, to which is added not only the risk of rupture-related death but also some degree of additional background hazard to which this cohort is subject (doubtless owing to factors that are also associated with the development of AAAs). In this context, a monthly risk of death approaching 1% did not seem excessive to the committee.
Cook Medical	Health economics appendix	17	17-42	**Waiting time mortality**	We are unable to find the data you have cited in the 2017 NVR. The **modal** aneurysm size is reported in that document as 5.5 to 6.4 cm; we estimate that the mean of the distribution

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				The differential between EVAR and OSR complex mortality is further decreased by the committee's assumption that complex EVAR patients will wait 4 months for a graft (≈4% mortality) and OSR patients will wait 2 months (≈2% mortality). NICE bases the mortality risk on the EVAR-1 trial where the mean AAA diameter was 65mm (Patel, 2018) and the annual rupture risk was 12%. In a snapshot audit detailed in the NVR 2017 report, the mean diameter size range was 56-59mm (infrarenal and complex), so monthly mortality from rupture is likely to be less than 0.5% per month now. In addition, it should be noted that the reported wait times for aneurysms >64mm were the shortest, as expected. It is true that custom made grafts require a longer time to supply (Cook Medical is a manufacturer of these devices). However, not all complex devices are custom made devices. In the NVR 2017 snapshot audit of complex aortic conditions (covered a 6-month period from June 2016 to December 2016 of which 43 cases were open repair and 341 were endovascular procedures) it was reported that non-conventional endovascular devices were required in 41.9% of cases, and took on average 67 days to be obtained. Note: a clinician will also consider using other approaches with no delay if the AAA is considered large enough. Further, the NVR points out that referrals can increase wait time for complex OSR and EVAR patients: "one reason for the time from referral to treatment being increased can be the need for advice from doctors in other clinical specialties. A quarter of the open repairs required specialist opinion compared to 12.4% for endovascular repairs".	is likely to be around 6.3 cm – quite close to the 6.5 cm in EVAR-1. The point that not all complex AAAs require a custom-made graft is a fair one. We have revised our base case in reflection of this fact: instead of a 2-month additional wait for complex EVAR, we now assume a 1-month delay. This is consistent with the NVR data you cite (that is, 42% of cases waiting 67 days, implying a mean expected delay of 28 days across all cases). It should be remembered that the estimate used, here, defines all-cause mortality for this period, not merely AAA-related death. General population mortality is approximately 0.3% per month for a cohort of this age, to which is added not only the risk of rupture-related death but also some degree of additional background hazard to which this cohort is subject (doubtless owing to factors that are also associated with the development of AAAs). In this context, a monthly risk of death approaching 1% did not seem excessive to the committee.

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				Therefore, we consider that the mortality differential based on waiting times for complex devices is overstated and the inputs need to be adjusted to reflect current practice.	
East of Scotland Vascular Network	Health Economics Appendix	17 18 62	45-47 1-39 1	The draft NICE guidelines have taken a narrow cost based view of the trial evidence. No account has been taken of patient choice or clinical judgement. **Cost-utility model** We have concerns with assumptions made within the NICE cost-utility model for both infra-renal repair and complex repair. The peri-operative mortality for infra-renal repair within the model is assumed to be 0.4% for EVAR and 1.3% for open repair. This compares to the actual mortality rates in the 2016 National Vascular Registry (NVR) Report of 0.4% and 2.9% respectively [(1)]. We understand that these assumed mortality rates are intended to present an accurate baseline of real-world practice, using the NVR (2016) as a baseline for 30-day EVAR mortality and applying an odds ratio of 1/0.33 to obtain the mortality rates for open repair. The odds ratio is based on the meta-analysis of the EVAR trials undertaken by the Cochrane systematic review (2014) [(2)] and based heavily on the UK EVAR 1 trial. An assumption has been made that the same odds ratio remains applicable to today's real world	It is NICE's statutory responsibility to consider the balance between the benefits and costs of competing approaches to healthcare. However, in light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**. Having reviewed a new review of casemix-adjusted observational evidence on perioperative mortality, the committee agreed that their decision to place primary reliance on randomised evidence of perioperative mortality was extremely well validated – see **Theme 2**. The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to support decision-making – see **Theme 3a**. The committee also agreed that Budtz-Lilly et al.'s (2017) analysis of unadjusted registry data reflecting AAAs with heterogeneous anatomical complexity was of limited relevance to its decision-making for infrarenal AAA – see **Theme 3b**.

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				practice, despite the increasing experience and developments in EVAR and the UK wide decline in open repair experience. The data from the NVR does not support this assumption, nor does the data from the Vascunet report of outcomes in 11 European countries, including the UK (2010-2013, 61,826 patients 1.1% EVAR mortality and 4.4% open repair mortality) [(3)]. We don't believe this is a valid assumption on which to base the performance of EVAR within the cost-utility model. In the model, the mortality for elective complex repair is assumed to be 3.6% for complex EVAR and 10.1% for open repair. This compares to the 2016 NVR reported actual mortality rates of 3.6% and 19.6% for complex EVAR and open repair respectively [(1)]. The guideline committee's advice was that the complex open repair mortality of 19.6% within the NVR was not consistent with its own clinical experience and, as there is no randomised comparative data on complex EVAR, an assumption was made that the same historical odds ratio for infra-renal repair should be applied to complex repair. We don't agree that this is a reasonable assumption. There is no evidence to support it. There is another assumption in the cost-utility model that the total primary procedure peri-operative costs for complex open repair are the same as infra-renal open repair (£10,921). Again, we don't agree that this is a valid assumption. ITU utilisation, blood transfusion requirements and lengths of in-	The committee were also emphatic in their conclusion that NVR data should not be used to compare the relative effectiveness of EVAR and OSR for complex AAAs – a conclusion the authors of the report share (see **Theme 4a)**. In the absence of reliable comparative evidence, the strategy of combining real-world data for baseline probability with randomised comparative data from a closely analogous population was agreed by the committee to be a reasonable solution to explore an uncertain area. We have now undertaken a supplementary review of casemix-adjusted observational evidence in response to stakeholders' suggestion that it is unreasonable to rely on the infrarenal RCTs in this and other contexts. If we populate the HE model with data from that review, complex EVAR is substantially dominated by OSR (see **Theme 4b**). The HE model has been revised to reflect additional information about postoperative resource use associated with complex AAA repair (both open and endovascular), with the result that the estimated costs of the primary admission for OSR have risen by a little under 50% from the value provided

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				patient stay are obvious contributors to increased costs in these patients. Even with these assumptions on outcomes and costs, the model for elective complex repair has shown that complex EVAR is more effective than open surgery, although with a high (unacceptable to NICE and NHS England) cost per QALY of £95,815. However, for the reasons given above we don't agree that this is accurate. National Vascular Registry 2016 Annual Report. https://www.vsqip.org.uk Paravastu S, et al. Endovascular repair of abdominal aortic aneurysm (Review). www.cochranelibrary.com Budtz-Lilly J, et al. Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. Eur J Vasc Endovasc Surg 2017; 54:13-20.	in the consultation draft. See **Theme 6** for details. We were unable to identify a reliable source of data for intraoperative resource use (including blood transfusions) for complex OSR or EVAR; however, some tentative estimates are available from our review of casemix-adjusted observational evidence, and we explore these in sensitivity analysis. The base-case ICER for complex EVAR versus OSR has reduced substantially as a result of revisions to the analysis undertaken in response to stakeholder feedback; however, it remains very much higher than a level that could be judged to represent an effective use of NHS resources.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	17 to 18	44 to 39	The method used for calculating perioperative mortality by taking the most recent EVAR mortality rate from the National Vascular Registry (NVR) and estimating open mortality using the odds ratio (OR) from reviews of RCTs leads to some inconsistencies and difficulties. The estimate of 0.4% from NVR is the in-hospital mortality rather than 30-day mortality, as was assumed for perioperative mortality in the model. Due to the differences in stay length, this provides a variable estimate of 30-day mortality. Our analysis of HES data suggests that 30-day mortality is approximately 25% higher	Thank you for this information. In the absence of published data on this topic, we do not feel it would be appropriate to amend any quantitative data in our model. However, we now note the issue in our discussion of the parameter. We note that, according to your account of the issue, the NVR would tend to underestimate the 30-day risks of EVAR and overestimate the same figure for OSR. Accordingly, if this datasource is used to estimate relative effects (which we do

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				than in-hospital mortality for EVAR and slightly lower than in-hospital mortality for open repair. Due to the relatively small sample and wide confidence limits of the NVR estimate, it may have been more appropriate to use the 3-year averages, also provided in the NVR report. We would question the use of pooled RCT evidence from historical trials to provide the OR for estimating open surgery risks, ignoring the real-world data provided by sources such as HES, Vascunet and the NVR. It is clear from the rich data collected by NVR that EVAR is currently used in a population that is older and has increased comorbidity compared to the population undergoing open repair. Using regression models to correct for identifiable risk factors such as age and comorbidity, the data from HES, NVR or Vascunet, all suggest that the crude OR is an underestimate of the current adjusted OR. It is thus counter-intuitive and inconsistent with current evidence to use an OR that predicts less difference than is seen in current real-world evidence.	not support; see **Theme 3a**), this is a further reason why data are likely to be biased in favour of EVAR. We think that the 1,246 OSRs and 2,907 EVARs reported in the 2017 NVR represent a reasonable sample. Moreover, to the extent that sampling error introduces uncertainty to our estimates, it is appropriate to reflect this in PSA. For discussion of our reasons for preferring randomised data, and the ways in which we have validated this decision in response to stakeholder feedback, please see **Theme 1**. It is true that the NVR data show that – at least in infrarenal AAAs – EVAR tends to be offered to people who are older and have more comorbidities than those who receive OSR. However, the OSR cohort is more likely to be female and has larger AAAs (which the committee strongly suspected was a proxy for anatomical complexity more generally, even among those cases categorised as infrarenal). In the complex AAAs recorded in the NVR 'snapshot', there appear to be fewer comorbidities among people receiving EVAR. The net result of these countervailing selection biases is difficult to predict. However, we note that, in studies that make some attempt to account for casemix (either by randomisation or by risk-adjustment), only 1 small study has ever found that EVAR is associated with a perioperative mortality benefit of the magnitude implied by unadjusted NVR data – see **Theme 3a**.
Cook Medical	Health economics appendix	18	23-39	**Peri-operative mortality – Elective repair – Complex** The authors report that there is no RCT data comparing complex repair techniques. There is, however, NVR data	In the absence of reliable comparative evidence, the strategy of combining real-world data for baseline probability with randomised comparative data from a closely analogous

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				which reports 3.6% mortality for complex EVAR and 19.6% mortality for complex OSR (16% difference). The guideline committee advised that the NVR mortality rate for OSR was higher than its own clinical experience and they felt that complex EVAR repairs are "likely to be inherently less complex than open repairs reported as complex". Therefore, they apply the infrarenal Cochrane OR (0.33) to the NVR complex EVAR mortality to get a peri-operative mortality of 10.1% for OSR (reducing the difference between the two procedures to 6.5%). The sensitivity analysis (pg 117) models 7.4% vs 19.6% (12.2% difference) which reduces the ICER to below £30,000 per QALY. It also models 3.6% vs 20.9% (17.3% difference) which reduces the ICER to £18,554 per QALY, indicating that using unadjusted registry data could result in a recommendation supportive of EVAR. There may be justification for adjusting for bias within the registry data, and the NVR states that they are currently unsure of the level of case-ascertainment for complex procedures. However, the evidence of bias needs to be provided and the methodology for adjustment needs to be appropriate. The peri-operative mortality rate has a significant impact on the QALY differential and we believe that the mortality rate for OSR should not be effectively halved based only on the committee's clinical experience (patients also need to be able to understand why the reported NVR OSR mortality rate of 19.6% is not applicable to them). *Therefore, we recommend that further evidence be collected to support this critical input selection and there be greater acknowledgement of the uncertainty of the results (i.e. not just*	population was agreed by the committee to be a reasonable solution to explore an uncertain area. The evidence suggests that any effort to adjust observational data for confounders leads to results that make our base-case estimate, in this population, look unrealistically generous to EVAR – see **Theme 4b**. The committee were emphatic in their conclusion that NVR data should not be used to compare the relative effectiveness of EVAR and OSR for complex AAAs – a conclusion the authors of the report share (see **Theme 4a**). Furthermore, the committee noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that complex EVAR is associated with a large reduction in perioperative mortality, there should be real equipoise about whether any such effect translates into net health gain over a patient's lifetime.

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				limiting the use of complex devices to RCTs) and the importance of clinical judgement in this treatment area. Note: clinical outcomes and costs will be difficult to estimate in this patient population. There is a mixture of devices utilised (e.g. fenestrated vs chimney) and complex covers juxtarenal, suprarenal and according to NVR it also covers thoraco-abdominal disease (although the NICE definition does not mention thoraco-abdominal). Further stratification according to disease classification and/or device may be required.	
Cook Medical	Health economics appendix	18	39: Table HE13	**Peri-operative mortality – Elective repair – Infrarenal** The peri-operative mortality rate input for infrarenal OSR (1.3%) in the economic model is not reflective of either current global registry or clinical study data and therefore we disagree with it being used as the base case input. The authors calculated the peri-operative mortality for infrarenal OSR by applying the Cochrane review odds ratio for EVAR compared with OSR (0.33) to the 2016 UK National Vascular Registry (NVR) reported EVAR mortality rate (0.4%). This calculation effectively imagines that the scale of improvement seen in peri-operative mortality for EVAR patients also applies to OSR patients. However, data from Vascunet (pools information from 11 vascular registries) shows that while perioperative mortality has fallen for EVAR from 1.5% to 1.1%, it has increased for OSR from 3.9% to 4.4% (Budtz-Lilly, 2017). The 2016 NVR reported peri-operative mortality for OSR of 3.0%. Furthermore, the NVR notes that those undergoing OSR are, on average, slightly younger and have less comorbid disease than those	Registry data – including those from the NVR or from Vascunet – do not provide valid estimates of the relative effectiveness of EVAR and OSR. See **Theme 3a** and **Theme 3b**. It is true that the NVR data show that – at least in infrarenal AAAs – EVAR tends to be offered to people who are older and have more comorbidities than those who receive OSR. However, the OSR cohort is more likely to be female and has larger AAAs (which the committee strongly suspected was a proxy for anatomical complexity more generally, even among those cases categorised as infrarenal). In the complex AAAs recorded in the NVR 'snapshot', there appear to be fewer comorbidities among people receiving EVAR. The net result of these countervailing selection biases is difficult to predict. However, we note that, in studies that make some attempt to account for casemix (either by randomisation or by risk-adjustment), only 1 small study has ever found that EVAR is associated with a perioperative mortality benefit of the magnitude implied by unadjusted NVR data.

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				undergoing EVAR. Therefore, there is no justification for using a figure lower than 3.0%. The artificial OSR mortality figure of 1.3% reduces the difference in mortality between EVAR and OSR from 2.6% to 0.9% and has a significant impact on the QALY calculation due to less OSR death (note: the sensitivity analysis models perioperative mortality using EVAR-1 as the baseline which reduces the incremental QALYs to near zero). *We recommend that the NVR peri-operative mortality rates for both EVAR and OSR be used in the base case of the economic model, taking into consideration that those undergoing OSR are generally healthier and younger.*	All data sources that adjust for the selection biases that have increasingly contaminated observational data find that mortality for OSR has fallen at a similar rate to that for EVAR over time – see **Theme 2**.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	19	1 to 52	Limiting the effect modifiers to age, sex and AAA size misses a variety of known and predictable risk factors for both peri-operative and long-term mortality. Our own analysis of HES data has shown that there are a number of significant predictors on logistic regression, including renal disease, coronary disease, COPD and hepatic disease and the committee also identified significant risk factors (see comment 5).	Age, sex and AAA diameter were explored as potential effect modifiers as they are objective factors on which data are commonly available. We cannot comment on preliminary findings of your unpublished, unvalidated research. Clearly, there are people who do not survive OSR who may have survived EVAR and, if such cases could reliably be predicted a priori, it is likely that it would be cost effective to offer them EVAR (though it is also possible that, if the characteristics that predict perioperative mortality with OSR overlap with the factors that clinicians were taking into account when randomising participants to EVAR-2, no intervention may be a superior approach). However, the committee had no confidence that any such prediction tools currently exist, and were mindful of the danger of denying patients a more durable repair on the basis of poorly predictive information.

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				The way in which those modifiers that were identified (age, sex and AAA size) have been used in the PSA only considers the effect of these modifiers on the uncertainty of the central estimates of the EVAR cohort characteristics and does not consider the heterogeneity of patients undergoing treatment. Thus, for example, the 95% confidence interval (CI) for age in the PSA is 73.701 to 74.377, that for the proportion of males is 89 to 92.2% and the CI for AAA size is 6.414 to 6.517 cm. Since there has been no attempt to carry out PSA in relation to other scenarios, this only provides evidence in regard to the mean ICER's for the overall EVAR cohort and says nothing about the likelihood of cost effectiveness for patients with other baseline characteristics, for example an 80-year-old female with a 7 cm AAA and several comorbidities, may have very different costs and outcomes from the average case considered in the PSA.	We agree with your summary. The purpose of PSA is to explore parameter uncertainty, not patient-level heterogeneity. It is appropriate for these analyses to be parameterised using best-available cohort-level evidence – the uncertainty we are interested in, here, is our uncertainty about the mean age of people receiving AAA repair. It would be incorrect to inflate our parameter uncertainty by conflating it with patient-level heterogeneity(see, e.g., Briggs et al., 2012) In light of this comment, we have undertaken additional analyses that repeat our subgroup analyses in a probabilistic way, so that likelihood of cost effectiveness can be quantified for each combination of covariates. Please see HE.9.1.1.3, HE.9.1.2.3., HE.9.2.1.3, HE.9.3.1.3 and HE.9.4.1.3.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	26	2 and subsequent pages	The estimates of post-perioperative survival may be distorted by the confusion between 30-day and in-patient mortality referred to above. In view of the evidence that suggests divergence of survival curves beyond 8 years there is no contemporary evidence regarding long-term outcomes of more recent practice identified in the review. The reference used to support the statement that there is no difference in the safety and durability of newer devices (Hammond et al) is a single centre study without follow up beyond 8 years.	Comment noted. We note that, according to the argument you advance, any such distortions are most likely to bias the model in favour of EVAR. By definition, long-term evidence will only ever be available for treatment that happened a long time ago. However, we have now been able to supplement the RCTs with some more recent observational evidence that has similar results (though somewhat less favourable for EVAR). We do not agree that the difference in long-term survival among people undergoing EVAR or OSR only emerges after 8 years. Our research suggests that the data are extremely

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					well modelled using a parsimonious approach of assuming a proportional hazard at all times following the perioperative period – see **Theme 9a**. The post-perioperative survival data identified in our review of casemix-adjusted observational evidence covers follow-up periods ranging from 4 to 7 years. This duration of follow-up is easily sufficient to show a meaningful difference in hazard of death favouring OSR. There was little evidence of divergence from proportional hazards in any of the included studies. We accept that we placed disproportionate reliance on Hammond et al. (2016) in the consultation draft. On reviewing this and similar stakeholder comments, the committee accepted that further exploration of the implications of modern EVAR devices on likely reintervention rates was warranted. They agreed that, using evidence cited by stakeholders (Verzini et al., 2014), the original HE model should be configured to simulate a lower rate of reintervention with EVAR than had been used in the base-case model on which consultation comments were sought. This had the effect of substantially attenuating the excess costs associated with long-term follow-up following EVAR. However, this revision was insufficient to rebalance the analysis in favour of EVAR, which remained dominated in the infrarenal case and associated with a high ICER in the complex case. See **Theme 7** for details.
Cook Medical	Health economics appendix	26 & 54	4-10 3-10	**Post perioperative survival and reinterventions** The committee stated that there is no evidence to suggest newer-generation EVAR devices are associated with improvement in long-term mortality, safety and durability. The	We accept that we placed disproportionate reliance on Hammond et al. (2016) in the consultation draft. On reviewing this and similar stakeholder comments, the committee accepted that further exploration of the implications of modern EVAR devices on likely reintervention rates was warranted.

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				committee cites one single arm study (Hammond, 2016 – authored by a committee member) as supporting evidence. EVAR-1's survival data is thus considered transferrable to current UK practice and the model utilises EVAR-1 data as the main input for long term outcomes and the risk of complications requiring reintervention. It does not appear consistent that the committee recognised that over the past 15 years there has been an improvement in EVAR perioperative mortality but did not recognise that there has also been an improvement in post perioperative outcomes*. It should be noted that it is not only device design that impacts EVAR outcomes. Clinical experience, imaging methods, anaesthesia/drug management, monitoring, complication management etc. would also all contribute. The statement of "no evidence" for longer term outcome improvement is contrary to previous NICE committee guidance and the clinical literature. We therefore recommend that the committee undertake a wider literature review to inform the post perioperative survival and reintervention inputs (rate and type of treatments).* **NICE guidance** NICE technology appraisal guidance 167, published in February 2009, included the following considerations of the evidence: "4.3.3. The Committee heard from the clinical specialists that the rates reported in the trials for long-term aneurysm-related death, complications and re-intervention following EVAR were higher than those seen currently in UK clinical practice. The Committee	They agreed that, using evidence cited by stakeholders (Verzini et al., 2014), the original HE model should be configured to simulate a lower rate of reintervention with EVAR than had been used in the base-case model on which consultation comments were sought. This had the effect of substantially attenuating the excess costs associated with long-term follow-up following EVAR. However, this revision was insufficient to rebalance the analysis in favour of EVAR, which remained dominated in the infrarenal case and associated with a high ICER in the complex case. See **Theme 7** for details.

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				heard that these trials used older stent–grafts, and that the technology has significantly improved since the RCTs were carried out. In addition, clinical expertise both in assessing patients' suitability for EVAR and in undertaking the procedure has improved with more widespread use of the technology. The Committee was persuaded that the benefits of EVAR compared with OSR in current UK clinical practice were likely to be greater than those seen in the RCTs." "4.3.9. The Committee considered the hazard ratio used in the model for reintervention after EVAR (6.7) and noted that the ratio used by the Assessment Group had been obtained from the EVAR 1 trial. The Committee heard from the clinical specialists that clinicians are less inclined to re-intervene in current UK clinical practice than was the case during the RCTs. This was particularly true for type II endoleaks, which comprised the majority of re-interventions in the trials. The Committee concluded that it was appropriate to use a hazard ratio for reinterventions of 1.5 in the revised cost-effectiveness analysis." **Clinical literature** There is evidence to suggest that long term mortality and reinterventions rates have improved for EVAR. There is also strong debate about the applicability of EVAR-1 trial to current practice. For example: The EVAR-1 trial investigators themselves state that "EVAR devices are constantly being improved and sizing and imaging methods available for deployment are better now than they	

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				were between 1999 and 2004: a corollary is that experience in OSR repair is declining" (Patel, 2016). They reference another study which reported that 7-year complication rates decreased before and after 2004 from 25.8% to 14.4%, concluding "newer-generation endografts can perform substantially better than the older devices. In the long term, incidences of reintervention, conversion, and AAA growth are decreased in patients treated with devices currently in use. However, the need for continuous surveillance is still imperative for all endografts" (Verzini, 2014). An analysis of US Medicare data found that the outcomes of endovascular repair, including mortality and rate of reinterventions, improved over time for procedures undertaken from 2001 to 2008 (Schermerhorn, 2015). Note: this paper informs the economic model's assumption regarding hernia repairs as a percentage of serious graft-related reinterventions. Patients undergoing infrarenal EVAR between 2004 and 2010 at a single UK institution (St Georges) were studied prospectively by Holt et al. Ruptures and aneurysm-related deaths were lower than reported in EVAR 1 and the authors speculated that this was due to "improved preoperative planning and endograft implantation, whereas a more robust approach to treating complications associated with sac expansion might have reduced aortic rupture in the longer term" (Holt, 2012). In a critique of the EVAR 1 trial, Starnes et al. mention that "newer devices and better skills are being used. Criteria for re-interventions are better understood and interventional physicians have more experience performing EVAR and correcting potential complications… The limited experience of the operators in EVAR 1 and the use of early-generation	

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				devices negatively biased the results against EVAR. This is illuminated by the high incidence of early ruptures" (Starnes, 2011).	
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	32	6 to 8	Little information is provided on the way in which the effect modifiers for post-perioperative mortality were chosen and derived, but the decision not to use separate effect modifiers for EVAR and open surgery seems to lack face validity. Since a key driver in the economic model is the difference in post-perioperative mortality between EVAR and open surgery, and both age and aneurysm size are known to be risk factors for endoleak (e.g. Ward et al. Anatomic risk factors for type-2 endoleak following EVAR: a retrospective review of preoperative CT angiography in 326 patients. Cardiovascular and interventional radiology. 2014 Apr 1;37(2):324-8.) it seems likely that they would also be risk factors for post-perioperative mortality (and costs – see comment 13). Thus, the decision not to include age as an effect modifier for post-perioperative survival and not to separately consider risks for EVAR and open surgery seems questionable. Whilst the baseline age related mortality is addressed in the use of life table data, the difference in late mortality is a significant driver of cost effectiveness, so that any age-related effect on this may be relevant in considering subgroups.	As noted in the text of the report, we explored interactions – including between treatment and other covariates – in finding an optimal model for post-perioperative effect modification. We could not find any evidence of meaningful treatment × risk-factor interactions of the type that would be expected if the covariates acted differently on the 2 groups. We also explored polynomial terms for age, which would highlight any nonlinearity of effect (strictly: nonlinearity of log[effect]) in a way that would uncover any suggestion that age-related effects are more complex than can be reflected by assuming a constant relationship. Again, there was no evidence that the model was improved by the inclusion of these terms.
Cook Medical	Health economics appendix	58	1: Table HE26	**ALOS – Initial procedure** EVAR-1 data was used to inform the resource use for the primary intervention procedure. The length of stay reported in the trial was 9.76 days for EVAR and 15.76 days for OSR. However, ALOS has markedly decreased in the past 15 years. For example, the 2017 NVR reports: "For EVAR procedures,	We have reviewed evidence on length of stay following AAA repair and provide comments below. We note that your comments relate exclusively to resource use associated with EVAR, and how that appears to have changed since the EVAR-1 trial. Of course, from a health economic perspective, the cost implications of a given

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				over 60% of patients were returned to a normal hospital ward after surgery. Among those admitted to either level 2 or 3 critical care, the median length of stay was 1 day. The median length of the overall postoperative stay was 3 days. For patients undergoing open repair, 98% of patients were admitted to a level 2 or level 3 critical care unit. They typically remained there for 2 days, the median total postoperative stay was 8 days, and they had a comparatively high in-hospital mortality rate. Patients having open repair were more susceptible to respiratory complications, and the rate of return to theatre was also higher. The procedures had comparable 30-day readmission rates." The GIRFT report also looks at length of stay: "for AAA, EVAR procedures typically last a couple of hours and patients may be discharged within a day or two. Open surgery may take three or four hours to complete and patients may need to stay in for a week" (Horrocks, 2018). *Therefore, we recommend that further research is undertaken to inform the average length of stay input (for EVAR and OSR) so that it reflects current practice.*	technology can only be assessed in comparison with an alternative approach. In this case, this means that it is very important to consider how resource use with OSR may also have changed over time, in order to arrive at the best estimate possible of the incremental costs associated with EVAR. We have obtained means and SDs for these data for EVAR and OSR from the NVR. These show that resource use with EVAR and OSR have reduced by a very similar amount since the EVAR-1 trial, with the result that the difference between the 2 is essentially unchanged. Details are provided in **Theme 6a**.
Cook Medical	Health economics appendix	58	1: Table HE26	**Theatre time and return to theatre** The model assumes 191 minutes theatre time for an EVAR procedure and 215 minutes for OSR procedure (from EVAR-1). Recent evidence suggests that the theatre time has decreased for EVAR e.g. Burgers, 2016. Further, the GIRFT report mentions that when it comes to return to theatre, "for AAA repair, there are some providers	As detailed in **Theme 5**, we conclude that there are no relevant, contemporary, casemix-adjusted data for this parameter. In our base case, we retain our reliance on randomised evidence, as these data at least reflect reliably matched cohorts in a UK setting, and there are no more current data with these advantages. However, we explore the impact of more contemporary, albeit methodologically less reliable, data in sensitivity analysis and find that it has no impact on model outcomes – see **Theme 5**.

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				who deliberately conduct a staged second look operation repair for open surgery" (Horrocks, 2018). The NVR data also reports 6.8% return to theatre for OSR and 2% for EVAR. It is not clear if return to theatre is included in the current economic model. *We therefore recommend that further research is undertaken to inform the theatre time input so that it reflects current practice.*	We understand that, depending on the precise timing of return-to-theatre episodes, they should be accounted for in either the estimates of intraoperative resource use from the RCTs or in reintervention rates. Therefore, applying an additional provision for such cases would double-count the costs with which they are associated.
W.L. Gore and Associates	Health economics appendix	58	Table HE26	**The model overestimates the theatre time for EVAR procedures and underestimates the theatre time for open repair.** The elective infrarenal model assumes an operative time of 191 minutes for EVAR and 215 minutes for open repair. However, recent data suggest these figures are too high. Burgers 2016 shows an operative time of 146 minutes for EVAR and 228 minutes for open repair, while Verhoeven 2014 found that EVAR median procedure time is 120 minutes. In addition, a 2018 study from Roche-Nagle found that the switch to the percutaneous EVAR (or PEVAR) technique in a Canadian hospital reduced operative time from 133 minutes to 101 minutes. Based on the recent evidence, we recommend that the model utilize a theatre time for EVAR of 120 minutes. Verhoeven 2014 EVAR median procedure duration: 120 minutes Burgers 2016 EVAR mean operative time: 146 minutes Open repair mean operative time: 228 minutes Roche-Nagle 2018 PEVAR mean operative time: 101 minutes	As detailed in **Theme 5**, we conclude that there are no relevant, contemporary, casemix-adjusted data for this parameter. In our base case, we retain our reliance on randomised evidence, as these data at least reflect reliably matched cohorts in a UK setting, and there are no more current data with these advantages. However, we explore the impact of more contemporary, albeit methodologically less reliable, data in sensitivity analysis and find that it has no impact on model outcomes – see **Theme 5**.

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W.L. Gore and Associates	Health economics appendix	58	Table HE26	**The model overestimates fluoroscopy duration for EVAR.** The elective infrarenal model overestimates the duration of fluoroscopy for EVAR. The estimate of 25 minutes is taken from EVAR-1. However, fluoroscopy duration for EVAR has decreased in the time since EVAR-1 enrolled patients. A recent study of elective infrarenal EVAR patients found a mean fluoroscopy time of 5.7 minutes, with a confidence internal of 3.4 minutes. Based on this evidence, we recommend that the fluoroscopy duration for EVAR in the elective infrarenal model be reduced to a conservative estimate of 15 minutes. Ruz 2016 "A total of 128 patients underwent elective EVAR with a mean fluoroscopy time of 5.7 ± 3.4 min."	The committee did not accept that it was necessary to revise the model input for fluoroscopy duration. They noted that the evidence you cite is a small Canadian case-series. A contemporaneous Canadian case-series arrives at an estimate of 24 minutes (Brassard et al., 2015), and the RCT-based estimate is also supported by evidence from a slightly older UK study (22–28 minutes; Thakor et al., 2011).
W.L. Gore and Associates	Health economics appendix	58	Table HE26	**The model overestimates preoperative and postoperative length of stay.** The elective infrarenal model assumes a postoperative stay of 6.53 days for EVAR and 9.25 days for open repair. However, data from the NVR show a median postoperative length of stay of 3 days for EVAR and 8 days for open repair. Other studies have shown similar mean lengths of stay. In addition, the model includes estimates for preoperative hospital stays based on data from EVAR-1. However, preoperative stays are very rare today due to a lack of available beds. We found no evidence supporting inclusion of preoperative days for either EVAR or open repair. We recommend that the elective infrarenal model use the recent NVR data on postoperative length of stay (3 days for	The committee agreed with your experience that preoperative stays are extremely rare in current-day practice; accordingly, they advised that the model should be revised to omit this cost. We think you may have misinterpreted table HE26. The entries for postoperative stay, ITU stay and HDU stay are mutually exclusive; therefore, total LoS is the sum of the 3. This means that the EVAR-1 estimate is that people spent a total of 7.95 days in hospital after an EVAR procedure, compared with 13.60 days for OSR (omitting preoperative stay). We apologise for the ambiguity that made any misreading possible; we have made it clearer in our revised documentation.

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				EVAR and 8 days for open repair) and that preoperative stay be removed from the model. NVR 2017 Annual Report EVAR median postoperative length of stay: 3 days Open repair median postoperative length of stay: 8 days Burgers 2016 EVAR mean postoperative length of stay: 3.7 days Open repair postoperative mean length of stay: 8.8 days	We have obtained means and SDs for these data for EVAR and OSR from the NVR. These show that resource use with EVAR and OSR have reduced by a very similar amount since the EVAR-1 trial, with the result that the difference between the 2 is essentially unchanged. Details are provided in **Theme 6a**.
W.L. Gore and Associates	Health economics appendix	58	Table HE26	**The model overestimates critical care length of stay.** The elective infrarenal model assumes a high dependency unit (HDU) length of stay of 0.83 days and an intensive care unit (ITU) stay of 0.59 days for patients receiving EVAR, based on data from EVAR-1. However, since EVAR-1 enrolled patients, critical care use has declined post-EVAR due to a lack of available beds. Recent data from the NVR strongly suggests that the estimate for HDU and ITU is too high and should be lower. Only one in three elective infrarenal EVAR patients are admitted to HDUs and only 3.5% are admitted to ITUs. Based on NVR data, we recommend that the elective infrarenal model include an HDU stay of 0.66 days and an ITU stay of 0.07 days. NVR 2017 Annual Report EVAR Level 2 admissions: 33.4%; median length of stay for those admitted: 1 day (IQR: 0 to 1 days) EVAR Level 3 admissions: 3.5%; median length of stay for those admitted: 1 day (IQR: 1 to 2)	Please see **Theme 6a**. Again, the reduction in critical care time that has been observed with EVAR has been mirrored almost exactly following OSR: in EVAR-1 people undergoing EVAR spent 2.93 fewer days in critical care than people undergoing OSR. In the 2017 NVR dataset (means provided by authors), the difference is 2.95 days.

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W.L. Gore and Associates	Health economics appendix	58	Table HE26	**The model does not include accurate assumptions on post-procedure surveillance.** The elective infrarenal model does not account for changes in costs associated with improved post-procedure surveillance. In EVAR-1, patients were observed more closely to explore various unknowns related to patient health post-operation, and only a small number of patients were retained through long-term follow-up. Since EVAR-1, centres have developed an efficient and comprehensive means to effectively monitor patients that optimizes survival and reduces future complications. For example, the model assumes that EVAR patients receiving follow-up surveillance scans will receive CT scans. However, ultrasound is currently the most widely used surveillance modality. Overall, current surveillance is less intensive and costs are lower than were estimated in EVAR-1. We recommend the elective infrarenal model assume that surveillance is conducted via ultrasound rather than CT scan. Chambers 2009 The previous NIHR HTA acknowledged improvement in practice over time and accounted for this improvement. "Results are very sensitive to model assumptions. EVAR may be more cost-effective than open repair if the relative costs of the procedure have fallen, reinterventions are relatively less frequent, and follow-up surveillance is currently less intensive compared with the base-case assumptions." Parameters for this HTA were included as a sensitivity analysis in NIHR 2018 HTA (Patel), and found EVAR to be cost effective. Brown 2012	The committee agreed that the postoperative surveillance of people who have undergone EVAR could be optimised – hence, they made a research recommendation in this area. However, without any evidence as to the empirical performance of an (on average) less intensive follow-up regimen, there is a real danger that bias will be introduced to our analysis by assuming that the costs of surveillance can be minimised without compromising patient safety – see **Theme 11**. In contrast to Chambers et al.'s analysis (2009), surveillance intensity is not a major driver of the results of our model.

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				"The EVAR trial 1 required surveillance after AAA repair at 1 month and 3 months and yearly thereafter. However, this protocol may not reflect standard clinical practice, particularly after open repair…" Epstein 2014 "Surveillance policy after aneurysm repair differed across the trials." "In clinical practice, the frequency of surveillance depends on many variables; for example, patients with diagnosed, untreated complications may have more frequent surveillance and more costly scans, and the guidelines of the European Surgery Society for Vascular recommend duplex imaging at 5, 10 and 15 years after open repair… there is no difference in surveillance costs between EVAR and open repair after trial follow-up." (Relates to Chambers bullet 3 above) Roy 2017 "Historically, EVAR surveillance was undertaken using CT angiography (CTA)… Concerns over cost, use of potentially nephrotoxic contrast agent and repeated radiation exposure led to alternative imaging modalities being investigated and implemented in surveillance regimens. Colour duplex ultrasound scan (CDUS) is the most widely used imaging modality currently."	
Vascular Research Group, School of Health and Related Research (ScHARR),	Health economics appendix	58	Table HE26	Resource use figures are not in keeping with current practice. The 2017 NVR report appendices show that the majority of larger centres have a median stay of 3 days or less for EVAR with a median of 7 to 10 days being common for open repair. Unfortunately, the NVR data does not include mean stay, but we have analysed HES data in this respect and in the most recent year for which we have data (2014/15) the mean total LOS for EVAR and open are 5.2 and 11.2 days respectively	We have obtained mean and variance data from the NVR, and use these in our revised base case (see **Theme 6a**). Your unpublished analysis of HES data is extremely close to all other data. Indeed, for overall LoS, the difference between 11.2 days and 5.2 days (6.0 days) is identical to that observed in EVAR-1 (15.76 days − 9.76 days = 6.00 days). The

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University of Sheffield				and the mean critical care stay as recorded in HES is 0.74 vs 3.18 days respectively. It is also worth noting that the EVAR patients, as recorded in both HES and NVR data, are an older and higher risk population and thus a greater difference in these figures might be expected in a matched population or higher risk subgroups, an effect that we have confirmed in logistic regression.	difference in critical care days is 0.5 days less than was observed in EVAR-1. We did not find any evidence on the relationship between patient characteristics and resource use. EVAR patients have other features that make them lower risk (fewer women; smaller aneurysms). It is unclear what the dependent variable of the logistic regression you mention would be.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	59	42 to 47	The cost of EVAR devices is variable between centres and devices. We have carried out a freedom of information request to a number of trusts to try and find accurate device costs and have been given values ranging between £590 and £25,000. Several of the larger centres have failed to respond or suggested that the information is commercially sensitive. There is, however, data from the NHS Improvement Reference Cost Collection 2016-17 includes a Reconciliation Statement that provides a "Memorandum of high cost device costs included in relevant HRGs: provider data" (https://improvement.nhs.uk/resources/reference-costs/). This includes details of the expenditure on endovascular stent grafts by trust. This also suggests considerable variation with some of the trusts with higher activity apparently obtaining devices with average acquisition costs below £2000 per patient.	We agree that a 'true' cost of EVAR stent-grafts is extremely hard to identify. We examined the 'unbundled' costs in the reconciliation statement when exploring appropriate acquisition costs for EVAR grafts. We noted the variability you have highlighted. We were also concerned that the devices listed may have been used in procedures other than AAA repair: some – or, indeed, many – of the items included could reflect procedures outside the scope of this guideline (for example, repair of isolated iliac aneursyms or peripheral stent-grafts) that may be associated with very different costs. In view of these uncertainties, we provide one-way sensitivity analyses exploring the relationship between device cost and model results (see figure HE47, figure HE59, figure HE70, figure HE78, figure HE93, figure HE94).
Cook Medical	Health economics appendix	60	16: Table HE27	**Device cost** The base case uses the guideline committee's quotes for pricing of the devices. *It seems more appropriate that the NHS supply chain quote is used when available (i.e. £6,186 for infrarenal, not £6,500).*	It is extremely challenging to arrive at an accurate estimate for an average device cost. If there were a limited number of relevant devices in the NHS supply chain catalogue, and if their prices remained fairly stable, we would agree that this would be the best source of data. However, neither of these things is true: there are a heterogeneous range of devices and

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				We recognise that it will be difficult to estimate the cost of complex grafts because there are a wide variety of devices (so this should be addressed in the sensitivity analysis).	shifting costs. For these reasons, we relied on the committee's advice, while noting that it appears consistent with such data as can be gleaned from public sources. We also explored the impact of graft costs in detailed 1- and 2-way sensitivity analyses (see Figures HE116, HE117 and HE118).
Cook Medical	Health economics appendix	60	17: Table HE28	**Primary procedure costs** The HDU cost source is NHS XC07Z (Adult Critical Care, 0 Organ supported): £718 per day (2015/16 costs) The ITU cost source is NHS XC06Z (Adult Critical Care, 1 Organ Supported): £1017 per day (2015/16 costs) The NVR reports patients are admitted to either the ward or level 2 or 3 care after AAA surgery. The Guidelines for the Provision of Intensive Care Services (2015) provides the following definitions: Level 2: Patients requiring more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care Level 3: Patients requiring advanced respiratory support alone, or basic respiratory support together with support of at least two organ systems. This level includes all complex patients requiring support for multi-organ failure. Therefore, it appears that the ICU costs above (focusing only on 0-1 organs) could be an underestimation. Note: the recent NHS HTA (Patel, 2018) used an activity weighted average for adult critical care 0-6 organs supported = £1,142 per day (2014/15 costs).	Thank you for drawing our attention to this issue. We have revised our base case model to adopt the solution you highlight from Patel et al. (2018) – that is, assuming a single activity-weighted cost for all critical care, based on all levels of support required. We have also configured the model to explore alternative approaches to these parameters in sensitivity analyses.

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				We recommend that the HDU and ITU cost sources be checked as they may be underestimates (higher impact for OSR).	
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	62	Table HE29	There appears to be no attempt to apply effect modifiers to the procedure costs. Having established that age, sex, AAA size and various comorbidities are significant predictors of outcome (see comments 5, 8 and 10) it seems counter-intuitive to ignore them as potential drivers of cost. Our own cost estimates for aneurysm repair based upon a regression analysis of HES data and reference costs, suggests that there is currently little difference in the cost of the primary procedure between EVAR and open repair based upon the crude data and, after correcting for case mix, the total costs for EVAR (including the device acquisition cost) are less than for open repair. To not explore such possible effects in the modelling within an appropriate subgroup analysis (as is recommended in the NICE methods guidance) denies the committee the opportunity to identify subgroups in whom EVAR might be cost effective, or even cost saving.	The suggestion that perioperative costs should reflect patient-level predictors of resource use is, on the face of it, an attractive one. Unfortunately, we are not aware of any published, validated evidence that would help us to do that, and we do not have access to the kind of primary data that would allow us to derive our own estimates. As before, it is not possible for us to comment on your unpublished work in progress. It has not been our finding that EVAR is associated with lower primary procedure costs than OSR. Nor, to our knowledge, has any other economic evaluation found this outside a US setting (where costs of hospitalisation in general and critical care in particular are so high that the costs of the device are much more likely to be offset by savings in the immediate postoperative period). We note that your analysis relies on NHS reference costs, which we concluded were critically flawed, in this area (see HE.2.2.11.1). However, this our judgement is based on data that are available at the aggregate level. If you have been able to link reference costs with HES data at a more granular level, we can see how that might give you scope to address some of those problems.
University Hospitals of Leicester NHS Trust - Leicester	Health economics appendix	62	1	The committee needs to re-examine the economic evidence for EVAR and open repair. Whilst they have attempted to use contemporaneous data, the figures they derive are contrary to other economic analyses. We would suggest a delay in publishing guidelines until a formal health technology assessment can be completed. As an example, in the recently	All inputs to the original HE model developed to support the committee's decision-making have been reviewed in the light of stakeholder feedback, with substantive revisions in the areas of postoperative resource use (in-hospital and rehabilitation; see **Theme 6**) and reinterventions (see **Theme 7**).

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Vascular Institute				completed NIHR HTA SWAN project Thompson et al. (2018, in press) have re-costed EVAR and open repair for women from the EVAR trial data to modern practice. Using HES data for length of stay and outcomes it has been shown that the unit cost for elective EVAR has dropped by 24.2% compared to a drop of only 4.2% for open repair unit costs. This is contrary to the figures shown in table HE29. When combined with the flawed collection of re-intervention data in the EVAR1 trial influencing the economic analyses (comment above), this suggests the conclusions drawn by the committee are incorrect.	It is unfortunate that the SWAN project has not, as yet, published full details of its methods. The Lancet publication notes reliance on unpublished analysis of HES data; it is hard to comment on the applicability of that work to our decision context. Of course, the SWAN costs relate only to the provision of care to women. On the one hand, this may limit its relevance to the whole population under consideration. On the other, if resource use differs systematically between people with different characteristics, then it would be ideal to incorporate such data in our subgroup analyses; however, we have been unable to identify any published evidence that would enable us to undertake an analysis of this type. The figures you cite appear to be unpublished, and it is not clear what they are a 'drop' from and to. We do not believe there is any material inaccuracy in the reintervention data we have used in our analysis – see our response to your comment 432.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	64	7 to 27	The calculation of the difference in disutility associated with the procedures of open repair or EVAR may not be adequately captured by these calculations. It seems counter-intuitive that the more robust data for the disutility associated with laparoscopic hernia repair (p 67) suggest that there is considerably greater disutility associated with hernia repair than that associated with open AAA repair in the early months, whereas the latter is a far more extensive and invasive procedure.	We accept this point. Utility is notoriously difficult to measure following major surgery, and we accept it is likely that the perioperative period constitutes a greater impact on people's QoL than can be inferred from their measurements 3–4 weeks after surgery (which is all that is available in the evidence). In the absence of empirical data, we have amended the base-case model to make use of data on the amount of time people spend in critical care and in hospital generally. Because EVAR is associated with shorter durations of critical care and overall LoS than OSR, this revision reflects the greater insult of the open procedure (in addition to the empirical QoL loss,

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					measured after 1 month, that informs the remainder of the first 3 postoperative months, to reflect a more prolonged recovery following discharge). See **Theme 7** for details.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Health economics appendix	68	12	Many assumptions are incorrect. For example, "*New-generation EVAR devices and surgical techniques have not affected the relative safety and effectiveness of EVAR and OSR. Existing trials, with historic enrolment periods (e.g. 1999 to 2003 for the EVAR-1 study) are applicable for the present comparison."* – this is incorrect. EVAR has had a steadily reducing mortality/morbidity despite being applied to an increasingly comorbid population. These assumptions require ratification by clinicians familiar with the techniques before being used as the basis for economic modelling.	The assumptions included in the HE model were ratified by a multidisciplinary committee comprising 16 clinical and patient experts with expertise covering the whole pathway of care for people with AAA. The supplementary review of casemix-adjusted observational evidence undertaken in response to stakeholder feedback provided strong validation of the particular assumption you highlight, suggesting that the relative benefits and harms associated with EVAR and OSR have not changed materially over time. Nevertheless, the committee accepted that modern practice features fewer reinterventions following EVAR than were observed in the RCTs. The model developed to support their decision-making has been revised accordingly – see **Theme 7**.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	70	2-15	The model structure for the unfit population is an over-simplification that raises some fundamental concerns. The risk of aneurysm-related mortality is closely linked to aneurysm size and the failure to represent aneurysm size, potential enlargement and risk of rupture in the model, severely limits its applicability. Furthermore, the idea that the population with AAA can be dichotomised into 'fit' and 'unfit' for open surgery is inaccurate. In the EVAR-2 study a number of patients randomised to non-treatment subsequently underwent successful open repair. Fitness for surgery is, thus, a relative assessment as to whether the risks and benefits of intervention outweigh those of non-intervention.	Data from EVAR-2 show that aneurysm size is not a significant predictor, at a 95% confidence level, of long-term survival in people randomised to EVAR or no intervention (see Table HE37). However, the covariate is included in our subgroup analyses at its mean value, which suggests a somewhat increased hazard of death. In this instance, we accept that categorising people as fit or unfit for OSR is a sophisticated process that requires multidisciplinary discussion. However, there is currently no reliable way of doing this on an objective basis (see Evidence reviews G and H).

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				Finally, the choices available to a patient include non-treatment and watchful waiting with further scans to monitor AAA size, and the model does not allow consideration of different thresholds for treatment based upon patient factors and aneurysm size. For these reasons we are of the view that the modelling does not represent an adequate basis for addressing the review question.	In this context, the EVAR-2 trial provides invaluable information on the outcomes that can be expected for the sort of people whom clinicians tend to think of as contraindicated for OSR, even if there is no way of defining such people according to objective criteria. There are no empirical data on watchful waiting, and any simulation of such a strategy would be extremely speculative. The committee emphasised that further randomised research would be helpful. Any evidence generated in this way will help to clarify future guidance for people with different levels of fitness.
Vascular Research Group, School of Health and Related Research (ScHARR), University of Sheffield	Health economics appendix	72	20-49	Use of RPSFT in these circumstances to correct for cross overs is not valid in the absence of any consideration of aneurysm enlargement and symptoms. RPSFT has a strong assumption of non-interaction – i.e. if individuals have the same survival and treatment history then they are assumed to have same outcome if they had not crossed over. However, this is assumption is unlikely to be satisfied in EVAR 2, as cross over in some cases was likely to be the result of enlargement of the aneurysm or the development of symptoms. Both of these represent factors that are likely to significantly increase the risk of aneurysm rupture or aneurysm-related death, and this possibility is not taken into account in the way that RPSFT has been applied. The two extreme assumptions are that a patient who crosses over would have been expected to have the same outcome as comparable patients who did not non-cross over (the RPSFT assumption) or that cross over was due to imminent rupture and that all cross over patients would have been AAA ruptures or AAA related deaths! We might expect the base case to	We do not completely agree with your characterisation of the assumptions inherent in the RPSFT method; however, we accept that one could take issue with the 'common treatment effect' assumption, in this case. We did explore alternative methods of adjusting for crossover, including the use of inverse probability of censoring weights; however, this did not prove tractable, because we do not have access to the kind of longitudinal data that would potentially make it possible to fit a reasonable model of censoring. Your suggestion of an extreme-case sensitivity analysis, assuming that everyone who crossed over to the treatment arm of EVAR-2 would have died immediately had they not done so, is a good one. We have undertaken this analysis. Our finding was that EVAR would be associated with a QALY gain of 0.691 and an ICER of £18,314/QALY under this extreme assumption. The fact that this totally implausible scenario produces an ICER that is only just below £20,000/QALY is a very strong indication that the 'true' ICER

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				have been somewhere between these extremes, perhaps considering both in a sensitivity analysis. If there is a possibility that some cross overs were related to patients with aneurysm enlargement or symptoms, then the finding that correction using RPSFT results in a less favourable HR for EVAR seems counter-intuitive, bringing the face validity of this analysis into doubt.	must be very much higher, with no realistic prospect of representing an effective use of NHS resources. The finding that crossover is not associated with survival gain is only counterintuitive if you start from the assumption that treatment prolongs survival. Clearly, there was enough equipoise about this question to randomise people to EVAR or no intervention at the time, and the fact that the trial could not find any benefit for EVAR demonstrates that it is far from certain that net survival benefit exists. We think it is important to break down the survival results of the EVAR-2 trial. The finding that EVAR and no intervention are associated with similar overall survival is a function of 2 countervailing phenomena: that EVAR is associated with a significant advantage in AAA-related mortality and that it is associated with a significant disadvantage in other-cause death. When these endpoints are evaluated using a competing-hazards model (Fine–Gray approach), we estimate that the subhazard ratio for AAA mortality is 1.982 (1.244 to 3.159), whereas the subhazard ratio for non-AAA mortality is 0.412 (0.317 to 0.536). Broadly, we could say that EVAR leads to half the risk of AAA death and double the risk of other-cause death, in an analysis that accounts for the competing nature of these outcomes (that is to say: this finding cannot be explained by a suggestion that people who do not receive intervention die of their AAA before they have time to succumb to other causes). This is important. While it is plausible that crossover could have attenuated differences in people's AAA-related survival, it is less easy to explain why it should have exaggerated

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					differences in other-cause mortality (once competing hazards have been accounted for).
Cook Medical	Health economics appendix	74	3-10	**Peri-operative mortality – Elective repair – OSR not suitable – Infrarenal** The NVR does not record if those who underwent EVAR were or were not suitable for OSR. Therefore, the NVR perioperative mortality rate of 0.4% was not considered appropriate. Instead, EVAR-2 data was used (7.3%). It is reasonable to assume that OSR not suitable (i.e. frailer patients) would have a higher mortality rate than those that would be OSR suitable. However, 7.3% (i.e. 18 X 0.4%) is likely to be an overestimation of current practice outcomes given that a significant portion of those included in the NVR infrarenal EVAR data would be high risk patients. If it is assumed that low risk EVAR patients have 0% mortality and high risk have 7.3% mortality, a maximum 5.5% of NVR EVAR patients could be considered high risk for the group to have 0.4% mortality overall. *We would suggest that a more extensive literature review is undertaken to provide a perioperative mortality rate that reflects current practice.* For example, Adkar et al., 2017 analysed data from the 2005 to 2013 American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Participant Use Data Files and found that: "Among 24,813 patients undergoing EVAR, 12,043 (48%) patients were characterized as high risk (at least one impairment criterion); 12,770 (52%) patients were	We are uneasy about uncoupling the short- and long-term effects of the EVAR-2 RCT in our model. It has been a common theme of stakholder's response to this consultation that the population for whom OSR is unsuitable owing to medical comorbidities is poorly defined. We agree with this, noting that categorising people as fit or unfit for OSR is a sophisticated process that requires multidisciplinary discussion. However, there is currently no reliable way of doing this on an objective basis (see Evidence reviews G and H). In this context, the EVAR-2 trial provides invaluable information on the outcomes that can be expected for the sort of people whom clinicians tend to think of as contraindicated for OSR, even if there is no way of defining such people according to objective criteria. There are multiple reasons why the 'high-risk' cohort in Adkar et al.'s study (2017) is likely to represent a less impaired population than that studied in EVAR-2. The study population had not explicitly been identified as high-risk – much less unfit for OSR – by a vascular MDT; rather, it was retrospectively identified from a database on the basis of 1 or more characteristics that would tend to indicate high-risk status. The authors themselves argue that the publication of the EVAR-2 trial led to a more conservative approach to the management of people with comorbidities; if this is true, it would tend to limit

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				stratified as low risk. The 30-day mortality rate was 1.9% in the high-risk cohort compared with the 7.3% reported by EVAR 2, and it was higher in the high-risk cohort compared with the low risk cohort (1.9% vs 0.9%; P < .001)."	the 'high-risk' population in their database to people at the lower-risk end of that spectrum. The population that entered EVAR-2 was sufficiently unwell that they faced at least a 1.6% likelihood of death in any month in the first year of the trial (not just a month in which they underwent major surgery). We note that data provided in this consultation by Leeds Teaching Hospitals NHS Trust shows that survival of the EVAR-2 cohort is not very different from the survival expectation of people for whom no treatment is judged suitable in their recent experience. Despite these misgivings, we have configured the model to use the 1.9% mortality rate from Adkar et al. (2017) as a sensitivity analysis. This results in EVAR being associated with an ICER of £77,000/QALY. Indeed, in this population, EVAR still does not meet normal thresholds for defining reasonable valus for NHS money if it is associated with **no** perioperative mortality.
Cook Medical	Health economics appendix	74	11-22	**Peri-operative mortality – Elective repair – OSR not suitable – Complex** For complex repair, an estimated complexity odds ratio based on registry data (0.4% vs 3.6%) was calculated on the log scale and applied to the EVAR-2 perioperative rate of 7.3%. This resulted in a mortality calculation of 40.9% (or 42.1% in table HE36). "The guideline development committee advised that this figure is somewhat higher than their experience of clinical practice, but recognised the limited data in this population. Accordingly, we subject the figure to extreme value sensitivity analysis."	The substantial uncertainty in this estimate is acknowledged in the guideline. We provide extensive sensitivity analysis Beach et al.'s cohort (2018) is not selected for any features that imply high risk (other than complex aortic morphology). Comparing the population's characteristics with the EVAR-2 cohort shows that they are clearly younger and less comorbid. Even aside from those objections, it would not be sensible to base any absolute estimate of average NHS performance on numbers reported by the top-ranked cardiovascular programme in the USA.

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				We believe that this calculation of >40% perioperative mortality is unreasonable and should not be used as the base case input as it is highly misleading. As the committee discussed when interpreting the results, "the relatively high perioperative mortality rate associated with complex EVAR" can never offset the differences in long term survival. It should be noted again that a significant portion of patients in the NVR EVAR data, but particularly so for complex patients, would be high risk patients (GLOBALSTAR Registry, 2012). A slight adjustment to the complex EVAR registry figure (3.6%) might be reasonable, but an effective multiplication by a factor of 11 is not a slight adjustment! Although there are limitations to the existing data and no study is likely to align perfectly with the NICE definition of complex repair, we believe a wider literature review would provide a range of more appropriate estimates to model. For example, Beach et al., 2018 evaluated 1,091 patients at the Cleveland Clinic who underwent fenestrated and branched endovascular aortic repair from August 2001 to June 2015 for complex aortic aneurysms (CAAs). Operative mortality was 3.7% and CAA-related survival at 30 days was 96.8% in a "high risk population". Further, a multicentre prospective registry (WINDOW) was set up to evaluate f/b EVAR in high risk patients with para/juxtarenal AAA, and infradiaphragmatic and supradiaphragmatic TAAA. Thirty-day mortality and in-hospital mortality were 6.7% and 10.1% respectively in 268 patients (Marzelle, 2015).	Similarly, Marzelle et al. (2015) report a population that is younger and less comorbid than the EVAR-2 cohort. However, even if we assume complex EVAR is associated with 0% perioperative mortality in this population, it is associated with an ICER over £120,000/QALY, compared with no intervention. If we assume 0% mortality **and** assume that all 'crossovers' (i.e. people who were randomised to the no intervention arm but received repair at some point) would have instantly died without repair, the ICER only falls to £28,000.
Vascular Research Group, School of	Health economics appendix	75	1-16	The application of the Vascunet model for effect modifiers in this case makes no sense. The increasing risk of rupture and aneurysm-related death with increasing aneurysm size is the basis of the treatment of AAA and to apply estimates of effect	This is a misreading of our methods. This section relates to perioperative mortality only, and we only applied the Vascunet logistic regression model to estimate effect modification for people undergoing EVAR.

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Health and Related Research (ScHARR), University of Sheffield				modifiers from a study of treated patients to patients who have an untreated AAA ignores this fundamental relationship. There is considerable evidence of the relationship between aneurysm size and rupture rate that could have been used to populate a more sophisticated model (for example see; HTA 2009;13:48 Table 69 p122). The EVAR-2 trial itself provided evidence that the rupture rate in those with AAA >6 cm was 27 per 100 patient years compared to 10 per 100 patient years in those with AAA <6 cm. Both these figures were considerably lower than those provided by a meta-analysis of published papers (Powell et al, Ann Surg 2008;247: 173–179), which may relate to the selected population entering the trial, more intensive medical treatment of the trial population or censoring due to cross-overs.	Longer-term effect-modification is modelled using the Cox regression shown in table HE37. We did not find that AAA diameter is a significant predictor of long-term survival in the EVAR-2 dataset, at a 95% confidence level (although the covariate is included in our subgroup analyses at its mean value, which suggests a somewhat increased hazard of death).
W.L. Gore and Associates	Health economic appendix	General	General	**The economic model for elective infrarenal aneurysm repair uses incorrect inputs and assumptions.** Based on current evidence, we strongly believe that the economic model for elective infrarenal aneurysm repair uses incorrect figures for several input parameters, including waiting time, perioperative, and post perioperative mortality; complications and reinterventions; theatre time; fluoroscopy use; preoperative, postoperative, and critical care length of stay; rehabilitation stay; and follow-up scans. The figures in the model do not reflect current real-world experience and have a dramatic impact on the results of the model. We identified more recent figures for these input parameters, re-ran the economic model, and found an incremental cost effectiveness ratio (ICER) for endovascular aneurysm repair	We consider each of your suggestions in turn, below, detailing areas in which the committee agreed to revise our analyses or explore alternative approaches, and explaining why we have not done so where the committee did not agree with your suggestions. We comment on each of these in turn in response to the relevant comment.

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				(EVAR) of less than £15,000. These input parameters and a rationale for each are outlined in comments 2 through 13 below. All our recommended alternative input parameters are listed in a table at the end of this document. The extensive use of data from the EVAR-1 trial, which enrolled patients from 1999 to 2004, is the primary reason that the model's input assumptions are incorrect. In comments 17 through 20, we provide evidence of the evolution of EVAR devices, deployment systems, surgical technique, and patient selection since EVAR-1, which have resulted in significant improvements in EVAR outcomes.	Clearly, it is possible to use the HE model developed for this guideline to arrive at an answer that is more favourable for EVAR by manipulating inputs to that end. The committee accepted some of the criticisms that you and other stakeholders have made of the parameters reported in the consultation draft, and the analysis has been revised accordingly. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The critical question is not whether EVAR devices and outcomes have improved; it is whether they have improved in a way that outstrips progress in OSR. There is very limited evidence that they have.
W.L. Gore and Associates	Health economic appendix	General	General	**Model does not account for the impacts on resource use from additional open surgeries.** The NICE policy manual on guideline development states that NICE will "provide information on the resource impact of recommendations" in consultation with the resource impact assessment team. However, no assessment has been published to date on the resource impact of this draft guidance. We believe there will be significant impacts that will harm patients, and we strongly encourage NICE to conduct a complete resource impact assessment. The recent Vascular Surgery Getting It Right First Time (GIRFT) report, published by the NHS in March 2018, notes that a range of factors are currently driving long wait times for aneurysm repair, including a lack of available theatres and beds. Open repair demands significantly additional utilization of ward beds, theatres, ITUs, and HDUs compared to EVAR.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. .

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				Based on assumptions 4,000 annual AAA repair patients, eliminating EVAR as an option, and using 2016 NVR data on resource use, an additional 10,439 ward bed days, 7,520 ITU bed days, and 5,666 HDU bed days would be needed. This would lead to increased wait times for AAA repair, as well as other conditions requiring use of theatres, bed days, ITUs, and HDUs. Furthermore open repair has a mandatory requirement for the availability of post-operative ITU care- when this is not available on the day of surgery this will lead to cancellation and rescheduling of the procedure. The additional cost of this for open repair has not been accounted for in the model. This increased resource use will exacerbate the already strained capacity within the NHS. It will have a significant impact on wait times and turn down rates for aneurysm repair, as well as all other procedures within the NHS. Patient outcomes will suffer as a result.	
EVAR trial post-operative surveillance group	Health economic appendix	Page 15, Page 29 Page 99	Line 16 Line 15 Figure HE37	**The model assumes a constant post-perioperative hazard ratio for all-cause deaths after EVAR versus Open repair. This may overestimate the difference between treatments in the extrapolation beyond the RCT data (the tail of the survival curve).** The 15 year follow up from EVAR-1 found the hazard ratio for all-cause deaths was not constant over the study period (Patel et al. 2018, Page 26). Furthermore, the difference in deaths in the long term follow up was mainly due to AAA-related mortality.	As shown in **Theme 9a**, an argument against a proportional hazards assumption based simply on the statistical significance of piecewise hazards is not valid. The simple model of perioperative benefit for EVAR followed by constant post-perioperative risk can be shown to fit empirical data extremely well. Consequently, the committee had no hesitation in endorsing this model for the base-case HE model. Nevertheless, the committee were also interested in seeing alternative approaches that do not rely on a proportional hazards assumption as sensitivity analyses (parametric curve-fitting to EVAR-1 alone; use of a piecewise hazard). They saw

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				All cause mortality increases with age in the model, so applying a constant proportional hazard for EVAR versus open to this increasing mortality has the effect of widening the difference between the treatments in the tail of the survival curve. We believe this may have overestimated the difference in life years between the treatments in the NICE model. The estimated difference in survival (and hence QALYs) may be quite different if AAA related deaths and other cause deaths are modelled separately (see Patel et al. 2018, page 28, Figure 5). Our model published in Patel et al 2018 estimates that EVAR has a small gain in life years and QALYs compared with open repair, although with greater lifetime costs than open repair (see Patel et al 2018, page 49, Table 17). It does not appear cost-effective based on data from the large RCTs, but we hypothesise that EVAR could be made more effective and less costly with an evidence-based surveillance strategy.	that all such methods result in worse cost effectiveness for EVAR.
EVAR trial post-operative surveillance group	Health economic appendix	Page 13 and Page 44.		**The model estimates absolute mortality risk difference of EVAR versus Open repair at 30d to be 0.9% (1.3% Open – 0.4% EVAR). This may be an underestimate.** The modelled absolute risk difference is considerably less than the EVAR -1 RCT (4.2% Open - 1.6% EVAR, an absolute difference of 2.6%), and the (unadjusted) NVR data (3% Open – 0.4% EVAR, an absolute difference of 2.6%) (HE Appendix page 13 and 44). The model estimate is based on the assumption that 30d outcomes after open surgery would have improved since the	Having reviewed a new review of casemix-adjusted observational evidence on perioperative mortality, the committee agreed that their decision to place primary reliance on randomised evidence of perioperative mortality was extremely well validated – see **Theme 3**. See also Evidence review K2 for further information.

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				early 2000's at the same relative odds reduction as observed after EVAR, with 30d deaths falling from 4.2% to 1.3%. We believe that this is a modelling assumption where further investigation would be helpful (e.g. risk-adjusted analysis of the NVR data. Clearly, the overall lifetime difference in effectiveness between the treatments will depend to a large extent on the initial 30d difference.	
EVAR trial post-operative surveillance group	Health economic appendix	Page 59		**The model assumes no surveillance follow-up after 5 years. This underestimates the costs of EVAR and may be unsafe for patients.** The NICE economic model assumes that surveillance will continue for only 5 years (with 2 follow-ups in the first year) (HE appendix page 59). This is justified with reference to the draft clinical guidance, which notes "the rate of complication and re-intervention after 5 years is relatively small" though this guidance does not actually recommend that surveillance stops at 5 years (Appendix V). If patients are not followed-up, it will be impossible to detect asymptomatic complications and re-intervene appropriately. Hence the modelled rate of re-intervention after 5 years is inconsistent with the assumption that there are no scans after 5 years. Furthermore, if emerging complications are not corrected, the rate of secondary sac rupture will be greater than that observed in the EVAR-1 trial. If the model includes the rate of re-intervention and post perioperative deaths based on the EVAR-1 trial data, then the model should also include the corresponding costs of the	We agree that not following patients up would be unsafe. The committee recommended that all people who have undergone EVAR should be enrolled in a surveillance programme which uses CT to check for endolaeks. However, in simulating follow-up of people following EVAR, the model adopts a 5-year limit as a reasonable compromise, reflecting the fact that, across the pooled RCTs that define the simulated patients' follow-up, adherence to annual follow-up was imperfect. A sensitivity analysis is performed in which lifelong annual CTs are assumed for all patients; predictably, this makes EVAR look somewhat less cost-effective.

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				surveillance as used in the EVAR-1 trial (we estimated these as £1622 over 14 years, see Patel et al 2018, page 42). Clearly this will increase the estimated total cost of endovascular repair in the model.	
Vascular and Endovascular Research Network	General	General	General	Having read all associated documents with great interest, the UK Vascular and Endovascular Research Network (VERN) executive committee would like to provide some comments for consideration during the ongoing consultation phase. Given our national presence as a trainee-led cardiovascular research network, we have focussed our comments on research issues. We welcome the proposed future research areas. We believe, however, that the priority research areas identified recently through a national Delphi consensus process by the Vascular Society of Great Britain and Ireland (VSGBI) have not been taken into account in the draft NICE guidance (The VSGBI performed a Delphi consensus exercise nationwide in 2017 to identify important areas for future research – the Society's Research Committee has since circulated these research priority areas amongst its members). Additionally, there are important research areas relating to the diagnosis and management of AAA that have not been identified as future areas of focus, such as: 1) Management of cardiovascular risk of patients with AAA, both during AAA screening/surveillance as well as after their treatment. The vast majority of individuals with AAA will die or suffer major morbidity not due to their AAA but due to other cardiovascular causes as identified in large prospective cohort studies and confirmed in meta-analyses[1-6]. In fact, several patients suffered major cardiovascular events after AAA repair	Thank you for your comment. The committee were aware of a number of different areas for research proposed in other guidelines and noted that there was some overlap with the research recommendation made in the NICE AAA guideline. The research recommendation made in the NICE AAA guideline is based on significant gaps in high quality evidence identified during the guideline development process. The committee agreed that, where possible, their research recommendation should remain independent of those specified in other guidelines as duplicating research recommendations would preclude a thriving research environment in various areas that would improve the diagnosis and management of AAA. Please also note that NICE research recommendations are considered for funding by the NIHR.

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				in all the endovascular vs. open surgery trials during follow-up. Addressing cardiovascular risk is therefore of major importance in the future; however, this is not reflected in the draft NICE research recommendations at the moment. 2) Assessing fitness of individuals for AAA repair using objective quantitative and reproducible methods. The guideline recommends no specific method of assessing individuals for fitness before offering surgery, despite some sporadic non-randomised evidence supporting modalities such as cardiopulmonary exercise testing[7-13]. We believe future research should focus on assessing existing or novel methods of assessing fitness in national randomised studies, especially since most units in the UK are already using cardiopulmonary exercise testing despite the lack of randomised evidence. 3) The draft guidance does not fully address the issue about a future randomised trial comparing open and endovascular repair of complex AAA. This is an extremely important area, given the already ongoing COMPASS study (an NIHR-funded national cohort study). When should we investigate these two methods in a trial and is this even possible? We believe the expert NICE committee should offer their insight. 4) There is no mention of patient choice and Quality of Life (QoL) research in the NICE recommendations for future research. Thus far very little effort has been invested in investigating patient preferences in this clinical area. Overall, we found no patient-preference or QoL-related research recommendations in the draft documents. 5) Further to our position on the lack of training in, mostly open, AAA repairs, we believe that another essential area of future research is the role of simulation in vascular surgical training, especially for complex AAA.	

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				6) Finally, recent evidence, not fully explored in the NICE draft documents, has highlighted that post-operative complications, such are renal decline over the short and long-term, are not adequately addressed in ongoing post-repair surveillance programmes[14,15]. This is another potentially crucial area of future research. References 1. Freiberg MS, Arnold AM, Newman AB, Edwards MS, Kraemer KL, Kuller LH. Abdominal aortic aneurysms, increasing infrarenal aortic diameter, and risk of total mortality and incident cardiovascular disease events: 10-year follow-up data from the Cardiovascular Health Study. Circulation. 2008;117(8):1010-1017. 2. Forsdahl SH, Solberg S, Singh K, Jacobsen BK. Abdominal aortic aneurysms, or a relatively large diameter of non-aneurysmal aortas, increase total and cardiovascular mortality: the Tromso study. Int J Epidemiol. 2010;39(1):225-232. 3. Norman PE, Muller J, Golledge J. The cardiovascular and prognostic significance of the infrarenal aortic diameter. Journal of vascular surgery. 2011;54(6):1817-1820. 4. Saratzis A, Dattani N, Brown A, et al. Multi-Centre Study on Cardiovascular Risk Management on Patients Undergoing AAA Surveillance. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2017;54(1):116-122. 5. Bath MF, Saratzis A, Saedon M, et al. Patients with Small Abdominal Aortic Aneurysm are at Significant Risk of Cardiovascular Events and this Risk is not Addressed Sufficiently. European journal of vascular and endovascular	

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				surgery : the official journal of the European Society for Vascular Surgery. 2017;53(2):255-260. 6. Bath MF, Gokani VJ, Sidloff DA, et al. Systematic review of cardiovascular disease and cardiovascular death in patients with a small abdominal aortic aneurysm. The British journal of surgery. 2015;102(8):866-872. 7. Hollingsworth A, Danjoux G, Howell SJ. Cardiopulmonary exercise testing before abdominal aortic aneurysm surgery: a validated risk prediction tool? Br J Anaesth. 2015;115(4):494-497. 8. Barakat HM, Shahin Y, McCollum PT, Chetter IC. Prediction of organ-specific complications following abdominal aortic aneurysm repair using cardiopulmonary exercise testing. Anaesthesia. 2015;70(6):679-685. 9. Goodyear SJ, Yow H, Saedon M, et al. Risk stratification by pre-operative cardiopulmonary exercise testing improves outcomes following elective abdominal aortic aneurysm surgery: a cohort study. Perioper Med (Lond). 2013;2(1):10. 10. Hartley RA, Pichel AC, Grant SW, et al. Preoperative cardiopulmonary exercise testing and risk of early mortality following abdominal aortic aneurysm repair. The British journal of surgery. 2012;99(11):1539-1546. 11. Tang TY, Hayes PD, Boyle JR. Cardiopulmonary exercise testing provides a predictive tool for early and late outcomes in abdominal aortic aneurysm patients. Ann R Coll Surg Engl. 2012;94(5):373. 12. Becher G, Kinsella J. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing (Br J Surg 2007; 94: 966-969). The British journal of surgery. 2007;94(12):1575; author reply 1575-1576.	

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				13. Nugent AM, Riley M, Megarry J, O'Reilly MJ, MacMahon J, Lowry R. Cardiopulmonary exercise testing in the pre-operative assessment of patients for repair of abdominal aortic aneurysm. Ir J Med Sci. 1998;167(4):238-241. 14. Saratzis A, Bath MF, Harrison S, et al. Long-Term Renal Function after Endovascular Aneurysm Repair. Clin J Am Soc Nephrol. 2015;10(11):1930-1936. 15. Saratzis A, Bown MJ. Renal Injury After Endovascular Aneurysm Repair: An Overlooked Entity. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2016;51(3):325-326.	
UHCW NHS Trust Coventry	General	General	General	*We have several general concerns about the potential impact of the NICE AAA guidelines* We feel that the AAA screening program could be destabilised by these guidelines. Many countries view the NAAASP as a beacon of good practice.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. The committee noted that, currently, women with AAA are not referred to the NHS AAA Screening programme. Thus there would be no additional burden to the programme.
UHCW NHS Trust Coventry	General	General	General	*Costs* Costings: our own experience of the costs associated with EVAR and open surgery do not appear to reflect those alluded	Comment noted

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				in the NICE guidelines and we feel contemporary costings for both open and EVAR needs to be confirmed.	
UHCW NHS Trust Coventry	General	General	General	*Complication rates* We believe that apparent assumptions about open surgical complication rates – based upon recent NVR data - might not continue in the future if patients were only offered open surgery (without the option of EVAR in some patients).	Comment noted
Royal College of General Practitioners	General	General	General	There is no mention in the guidance about quality of life. A recent study suggested that screening for AAA does reduce mental QoL; however, this effect is transient (less than 12 months). Men diagnosed with AAA have a consistently worse physical QoL https://onlinelibrary.wiley.com/doi/abs/10.1002/bjs.10721	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. The impact of AAA open and endovascular repair on Quality of life was assessed in the NICE guideline. However, the impact of screening of quality of life was not an issue included within the scope of the guideline, and therefore it was not possible for any recommendations to be made on this topic.
Royal College of General Practitioners	General	General	General	Should patients presenting with AAA be screened for intracranial aneurysms? http://stroke.ahajournals.org/content/49/Suppl_1/A166	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Unfortunately, the co-existence of other aneurysms in people with AAA was not an issue included within the scope of the guideline, and therefore it was not possible for any recommendations to be made on this topic.
The Northern Vascular Centre	General	General	General	When justifying the financial calculations that led to the conclusion that EVAR constitutes a cost-inefficient treatment of AAA, NICE have used three randomised controlled trials; EVAR, DREAM and OVER. OVER is the only such trial that looked at all cause morbidity and subsequently concluded that open AAA repair is a more costly practice. EVAR and DREAM assessed only aneurysm related morbidity and hence reported	The overwhelming reason that the OVER analysis is alone in finding EVAR a reasonable use of resources is the extremely high cost of hospital stay and, in particular, critical care in the USA. Although it was not part of their original protocol, the EVAR trial investigators performed a thorough retrospective review of

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				results to the contrary. We acknowledge the panel's attempts to adjust for these factors but the evidence is floored by the larger trials (EVAR and DREAM) that looked exclusively at aneurysm only related morbidity, disregarding complications of laparotomy such as hernia formation and adhesional bowel obstruction.	HES data which enabled them to incorporate hernia procedures in their reporting. As noted in HE.2.2.9.1, we use those data in our HE model. In addition, we have also captured further laparotomy-related procedures (lysis of adhesions and bowel resection), which are more prevalent following OSR, based on a matched comparison of US Medicare data (Schermerhorn et al., 2015). The particular resource use and quality of life implications of each of these complications are captured.
The Northern Vascular Centre	General	General	General	An alternative approach to the one described by the proposed NICE guidelines would be to look at identifying those who do benefit from EVAR and refine our selection. No-one would argue that EVAR is perfect, but equally no one would argue that they have never seen a successful EVAR. Most patients derive benefit from the procedure, but a few do go on to require re-intervention and fewer still go on to rupture. Delineating the factors which lead to these poor outcomes should be a priority rather than abandoning the whole concept – "don't throw the baby out with the bathwater!" Many units offer a balanced approach to EVAR / open surgery, utilising the best of both techniques to the patient's advantage. A "one size fits all" approach is clumsy and should be avoided (both in terms of advocating EVAR and open surgery). There is substantial evidence that going away from manufacturers IFU leads to poorer outcomes. In addition, experience from large centres has determined that some anatomical anomalies are best overcome by moving the seal zone proximally, perhaps leading to the current expansion of complex EVAR that we are seeing. We accept that this in itself requires further research before firm conclusions can be made. Whilst the draft guidelines suggest this, limiting the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that there are no methods that reliably predict short-term outcomes of AAA repair, and also found that no individual characteristics are associated with better outcomes for EVAR at a cost that represents effective use of NHS resources. See **Theme 12**. It is commonplace, when new technologies are being introduced, for patients only to have access to them in the context of randomised research. The fact that complex EVAR has become relatively established in NHS practice does not change the urgent need to collect the kind of data that should have been available to mandate its introduction. Therefore, the

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				application of complex EVAR to research studies alone is neither ethical (how can we offer a treatment to patients only if they accept randomisation?) nor practical (currently no enrolment into an RCT for complex EVAR). We welcome your feedback on our concerns and wish the panel every success in producing guidelines that ensure we continue to offer our patients high quality, sustainable and safe treatment of their abdominal aortic aneurysms.	committee saw no reason why randomising patients presents any ethical complications.
Rouleaux Club	General	General	General	Rouleaux Club is an independent club of trainees, and non-consultant doctors, in Vascular Surgery within the UK. At the time of commenting we have 233 members of which 124 are registered as national training number trainees, making up approximately 80% of formal vascular surgery trainees. These comments were drafted by the executive committee of the Club and amended based on feedback from the membership. As doctors we have a responsibility to ensure our patients have a choice between evidence based, cost effective treatment options available to them. We should only offer to undertake treatments we are adequately trained in and can provide to a high standard. Rouleaux Club, as a trainee organisation, will only comment on the effect on training/trainee(s) that these guidelines will have. We anticipate that our training needs would change substantially following the implementation of the guidelines and feel that it is important to pre-emptively highlight the issues this could create in delivering the recommended care.	Thank you for your introductory comments. We are also grateful for the steps you have taken in seeking your members' views and summarising them for us.
The Rouleaux Club	General	General	General	The guidelines are not in line with current practice in Europe, America, Australasia and elsewhere in the world. The Rouleaux Club has concerns that if instigated in their current format there will be a cohort of UK vascular trainees who will	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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				require significant amendments to training and may not be able to obtain the endovascular skills to manage AAA disease in the elective and emergency setting. This will limit accessible care for UK patients. We await the final guidelines, which will likely necessitate an extensive overhaul of UK vascular training, with training objectives and opportunities altered to provide the recommended treatment for AAA patients. Trainees will require the appropriate additional support and resource to achieve this.	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Guidelines from other jurisdictions were not part of the scope for this update so they have not been reviewed by the committee.
NHS abdominal aortic screening programmes: England, Scotland, Northern Ireland and Wales.	General	General	General	Final point: screening programmes have introduced an 8 week pathway for investigation and treatment of men of average health with a standard AAA. This reduces the risk of interim rupture (that does occasionally occur in screened men). Although not evidence-based, it does mean vascular services have to streamline pathways, and improves the quality of care given to men with a large AAA. This is supported by ESVES guidelines, and also GIRFT, where is has been recommended to apply to all patients with a large AAA, screened or detected incidentally.	Thank you for your comment. The recommendations on referral times were drafted to reflect current expectations in the NHS AAA screening programme about the timeframes that people with aneurysms of different sizes should receive clinical input. The committee noted that the 8-week timeframe that you have mentioned is the expected time for treatment of large aneurysms in men of standard fitness. They did not think that it was necessary to specify this in the recommendations as the treatment time will be established once individuals had been seen by the regional vascular service.
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	We would question the accuracy of cost effectiveness stats as they underestimate the improvements in practice in recent years. Length of stay now <36hrs	According to the 2017 NVR, mean length of stay for infrarenal elective EVAR was 4.31 days in 2016. Although the committee had misgivings about the selection biases the NVR reflects, they agreed to incorporate these data into their HE analysis. See **Theme 6**.

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				Percutaneous day case becoming regular practice	The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.
				Duplex and Xray follow up in experienced hands is cost effective with a low radiation and contrast burden. CT follow up is the exception used only to answers specific issues. CEUS is also an additional tool in use for specific queries	In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks. Instead, it recommended CT-led surveillance. See **Theme 11**.
				Our reintervention rates are 6% We would be happy to share with NICE our follow up protocols and reintervention rates.	It is unclear over what period these are measured or what they relate to.
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	We believe that the impact of return to open AAA has not been sufficiently assessed in this guidance in particular the need for additional resources	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which

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					interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
				HDU /ITU bed requirement has not been factored into this guidance.	See **Theme 6a**.
				Dual Vascular Consultant operating required reducing productivity.	We are unaware of any recommendation that dual consultant operating is required for AAA repair. We do not believe it was used in the evidence-base that informed the committee's recommendations. Presumably, if this practice is being adopted, it is expected to lead to patient benefits that justify the additional resource, though we have not seen any evidence on this topic.
				All day list for OSR. Elective EVAR needs only ½ day list.	We have been unable to identify any contemporary evidence regarding duration of procedure for EVAR and OSR – see **Theme 5**. Although the committee accepted that EVAR procedures do take less time than OSRs, such evidence as is available suggests differences between the 2 that are measured in minutes rather than half-days.
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	We believe that the guidance has given insufficient consideration and guidance regarding	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
				Mortality rates of open repair, Vascunet 2008, 7.9% UK	For discussion of the Vascular Society's AAA Quality Improvement Programme that was instigated in response to the 2008 Vascunet report, please see **Theme 2a**.

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				Criteria for who to turn down Insufficient recognition that patients fall between the EVAR1 and EVAR2 groups	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They amended their recommendation to state that EVAR should only be offered in this population as part of an RCT comparing EVAR with no intervention, and made a new research recommendation noting that such a study would be helpful.
				Advice and information to patients who prefer EVAR or are turned down for open repair What happens to patients turned down for open who present later with symptomatic AAA	For discussion of the possible impact on quality of life of living with an untreated AAA, please see Theme **3**.

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				How will UK outcomes compare with European units	
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	Safety of rEVAR when there is no elective service. It is inconceivable that we can offer a rEVAR service providing a procedure done out of hours, in more challenging circumstances when they are not done routinely in hours. The experience of the whole team and new members of vascular teams will be severely depleted. Therefore the only option for rupture will be open with an identified poorer outcome. The rate of rupture will be increased as elective repairs for those who fall between the EVAR1 and EVAR2 groups will be reduced.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	There is genuine acceptance of the need to analyse benefits in for those who have increased risk for open repair. Age Comorbidities Life expectancy We contend that instead of abandoning EVAR in all elective cases we should commission more appropriate guidelines for those who lie between the EVAR 1 and EVAR 2 groups. Defined reproducible metrics should be used for defining those not suitable for EVAR or OSR to ensure equitable access to treatment.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that there are no methods that reliably predict short-term outcomes of AAA repair, and also found that no individual characteristics are associated with better outcomes for EVAR at a cost that represents effective use of NHS resources. See **Theme 12**.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					The committee also agreed that it would be valuable to generate new high-quality research in the area of optimal treatment for people whose comorbidities make OSR unsuitable. They made a research recommendation noting that such a study would be helpful.
Wirral University Teaching Hospital NHS Foundation Trust	General	General	General	We have concerns regarding the breadth of advice & evidence provided to committee – Were there any EVAR experienced surgeons included? Do the committee members have a AAA practice? Advice does not reflect our real world experience. Was there a patient representative included. Guidance is missing for when EVAR should be done, e.g. hostile abdomen, inflammatory AAA, prior aortic surgery	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. As detailed in guideline documentation, the committee included 3 experienced vascular surgeons, including – according to VSQIP data – by far the most active surgeon in the UK. All 3 have extensive experience of endovascular and open techniques. In addition, an interventional radiologist with EVAR practice was a core committee member. The committee also included 2 lay members who provided patient perspective and had equal status in all discussions and conclusions. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. Inflammatory AAA is outside the scope of this guideline.

<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer's response</th></tr>
<tr><td>Wirral University Teaching Hospital NHS Foundation Trust</td><td>General</td><td>General</td><td>General</td><td>I can see no evidence that the psychological effects have been considered of being given a AAA diagnosis but not an offer of repair .

Many patients with relatively high risks will have a reduced quality of life due to the uncertainty of a likely fatal aneurysm rupture.

The impact on our practice will be an increase in perioperative mortality as almost certainly we will undertake OSR in higher risk patients, due to patient choice and risk of fatal AAA rupture.</td><td>Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

For discussion of the possible impact on quality of life of living with an untreated AAA, please see Theme 13.</td></tr>
<tr><td>W.L. Gore and Associates</td><td>General</td><td>General</td><td>General</td><td>Input Parameters – NICE Model and Recommended Alternatives

<table>
<tr><th>Parameter</th><th colspan="2">NICE Model Base Case</th><th colspan="2">Recommended Alternative</th></tr>
<tr><td>Mortality</td><td>EVAR</td><td>OSR</td><td>EVAR</td><td>OSR</td></tr>
<tr><td>Waiting time mortality</td><td>2.40%</td><td>2.40%</td><td>1%</td><td>1%</td></tr>
<tr><td>Peri-operative mortality</td><td>0.4%</td><td>1.30%</td><td>0.4%</td><td>2.9%</td></tr>
<tr><td>Post peri-operative mortality</td><td></td><td>Hazard ratio=1.089</td><td></td><td>Hazard ratio=1.0</td></tr>
<tr><td>Serious Reintervention Rate</td><td></td><td></td><td></td><td></td></tr>
<tr><td>0-6months</td><td>7.30%</td><td>3.04%</td><td>3.04%</td><td>3.04%</td></tr>
<tr><td>6months – 4 yrs</td><td>8.71%</td><td>1.40%</td><td>1.40%</td><td>1.40%</td></tr>
<tr><td>4-8 yrs</td><td>5.18%</td><td>3.60%</td><td>3.60%</td><td>3.60%</td></tr>
<tr><td>8+ yrs</td><td>5.18%</td><td>3.60%</td><td>3.60%</td><td>3.60%</td></tr>
<tr><td>Resource Use</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Theatre time (mins)</td><td>191</td><td>215</td><td>120</td><td>215</td></tr>
</table></td><td>The committee reviewed these suggestions and, with a couple of exceptions, agreed that the figures would inappropriately and unrealistically bias the model in favour of EVAR.
To take each in turn:
• Waiting time mortality – There is no evidence for your suggestion.
• Peri-operative mortality – The committee were emphatic that unadjusted registry data do not provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR. For an explanation, please see Theme 3a
• Post peri-operative mortality – There is no evidence for your suggestion; the supplementary review of casemix-adjusted observational data shows that the base-case model may underestimate degree of excess late mortality with which EVAR is associated.
• Serious Reintervention Rate – There is no evidence for your suggestions; simply assuming that EVAR is associated with</td></tr>
</table>

<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer's response</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>Fluoroscopy duration (mins)</td><td>25</td><td>2</td><td>15</td><td>2</td></tr>
<tr><td>Preoperative stay (days)</td><td>1.81</td><td>2.16</td><td>0</td><td>0</td></tr>
<tr><td>Postoperative stay (days)</td><td>6.53</td><td>9.25</td><td>3</td><td>8</td></tr>
<tr><td>ITU stay (days)</td><td>0.59</td><td>2.47</td><td>0.07</td><td>2.47</td></tr>
<tr><td>HDU stay (days)</td><td>0.83</td><td>1.88</td><td>0.66</td><td>1.88</td></tr>
<tr><td>Post-discharge nursing home stay (days)</td><td>0</td><td>0</td><td>0.5</td><td>3.5</td></tr>
<tr><td>GP Home visits</td><td>0</td><td>0</td><td>1</td><td>2</td></tr>
<tr><td>Community Nurse visit</td><td>0</td><td>0</td><td>1</td><td>2</td></tr>
<tr><td>Follow-up Scans</td><td>CT</td><td>-</td><td>Ultrasound</td><td>-</td></tr>
<tr><td>Return to theatre – duration 120 mins</td><td>0</td><td>0</td><td>2.0%</td><td>6.8%</td></tr>
<tr><td>Total cost of procedure & post discharge care, per patient (infra-renal, elective)</td><td>£13,561</td><td>£10,921</td><td>£10,546</td><td>£10,828</td></tr>
</table>
</td><td>
the same amount of reinterventions as OSR is without foundation, even if rates have declined (as the committee accept). We have, however, reduced EVAR reintervention rates in an evidence-based way – see Theme 8.

Theatre time – We surmise that the authority you would cite for the number you would like us to rely on is Verhoeven et al. (2014). This is inappropriate as (a) that study is a non-comparative case-series that tells us nothing about the relative resource-use with EVAR and OSR, and (b) the figure cited is a median, which is certain to be substantially lower than the mean, which is what we need for HE purposes. See Theme 5.
Fluoroscopy duration – The small Canadian case-series you cite as evidence for your suggestion is contradicted by other evidence.
Preoperative stay – Although there is no evidence for this, the committee agreed that, in practice, preoperative inpatient care is no longer provided for either treatment so, as you have suggested, we have set these parameters to 0 in our base case.
Postoperative stay – Although the committee had misgivings about the biased nature of the evidence-base, we used NVR data to estimate these parameters in our revised base case, as you recommend. We were able to obtain means and SDs from the data-owners, so the estimates on which we rely are more accurate than these. See Theme 6a.
Post-discharge nursing home stay; GP Home visits; Community Nurse visit – No evidence for your suggestions. However, we have revised the model to include an evidence-based estimate of resource-use associated with

</td></tr>
</table>

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					rehabilitation, which is somewhat more favourable to EVAR than the numbers you suggest – see **Theme 6b**. • Follow-up Scans – Assuming ultrasound-based follow-up is inconsistent with both the evidence and the committee's recommendations – see **Theme 11**. Return to theatre –duration 120 mins – These episodes are already accounted for in the intra-operative resource-use data or reintervention rates (see Patel et al., 2018)
W.L. Gore and Associates	General	General	General	Input Parameters – NICE Model and Recommended Alternatives [See above table]	[This response relates to the above table] The committee reviewed these suggestions and, with a couple of exceptions, agreed that the figures would inappropriately and unrealistically bias the model in favour of EVAR. To take each in turn: • Waiting time mortality – There is no evidence for your suggestion. • Peri-operative mortality – The committee were emphatic that unadjusted registry data do not provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR. For an explanation, please see **Theme 3a** • Post peri-operative mortality – There is no evidence for your suggestion; the supplementary review of casemix-adjusted observational data shows that the base-case model may underestimate degree of excess late mortality with which EVAR is associated. • Serious Reintervention Rate – There is no evidence for your suggestions; simply assuming that EVAR is associated with the same amount of reinterventions as OSR is without foundation, even if rates have declined (as the committee accept). We have, however, reduced EVAR reintervention rates in an evidence-based way – see **Theme 8**. • Theatre time – We surmise that the authority you would cite

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					for the number you would like us to rely on is Verhoeven et al. (2014). This is inappropriate as (a) that study is a non-comparative case-series that tells us nothing about the relative resource-use with EVAR and OSR, and (b) the figure cited is a median, which is certain to be substantially lower than the mean, which is what we need for HE purposes. See **Theme 5**. • Fluoroscopy duration – The small Canadian case-series you cite as evidence for your suggestion is contradicted by other evidence. • Preoperative stay – Although there is no evidence for this, the committee agreed that, in practice, preoperative inpatient care is no longer provided for either treatment so, as you have suggested, we have set these parameters to 0 in our base case. • Postoperative stay – Although the committee had misgivings about the biased nature of the evidence-base, we used NVR data to estimate these parameters in our revised base case, as you recommend. We were able to obtain means and SDs from the data-owners, so the estimates on which we rely are more accurate than these. See **Theme 6a**. • Post-discharge nursing home stay; GP Home visits; Community Nurse visit – No evidence for your suggestions. However, we have revised the model to include an evidence-based estimate of resource-use associated with rehabilitation, which is somewhat more favourable to EVAR than the numbers you suggest – see **Theme 6b**. • Follow-up Scans – Assuming ultrasound-based follow-up is inconsistent with both the evidence and the committee's recommendations – see **Theme 11**. Return to theatre –duration 120 mins – These episodes are

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					already accounted for in the intra-operative resource-use data or reintervention rates (see Patel et al., 2018)
W.L. Gore and Associates	General	General	General	Bibliography Ambler GK, Mariam NBG, Sadat U, et al. Weekend effect in non-elective abdominal aortic aneurysm repair: Weekend effect in non-elective abdominal aortic aneurysm repair. *BJS Open*. 2017;1(5):158-164. doi:10.1002/bjs5.24 Brown L, Powell J, Thompson S, Epstein D, Sculpher M, Greenhalgh R. The UK EndoVascular Aneurysm Repair (EVAR) trials: randomised trials of EVAR versus standard therapy. *Health Technology Assessment*. 2012;16(9). doi:10.3310/hta16090 Budtz-Lilly J, Venermo M, Debus S, et al. Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years. *European Journal of Vascular and Endovascular Surgery*. 2017;54(1):13-20. doi:10.1016/j.ejvs.2017.03.003 Burgers LT, Vahl AC, Severens JL, et al. Cost-effectiveness of Elective Endovascular Aneurysm Repair Versus Open Surgical Repair of Abdominal Aortic Aneurysms. *European Journal of Vascular and Endovascular Surgery*. 2016;52(1):29-40. doi:10.1016/j.ejvs.2016.03.001 Castagno C, Varetto G, Quaglino S, et al. Acute kidney injury after open and endovascular elective repair for infrarenal abdominal aortic aneurysms. *Journal of Vascular Surgery*. 2016;64(4):928-933.e1. doi:10.1016/j.jvs.2016.02.048 Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *Journal of Vascular Surgery*. 2018;67(1):2-77.e2. doi:10.1016/j.jvs.2017.10.044 Chambers D, Epstein D, Walker S, et al. Endovascular stents	Thank you for these references; we consider them where cited in your comments.

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				for abdominal aortic aneurysms: a systematic review and economic model. *Health Technol Assess*. 2009;13(48):1-189, 215-318, iii. doi:10.3310/hta13480 England A, Mc Williams R. Endovascular Aortic Aneurysm Repair (EVAR). *Ulster Med J*. 2013;82(1):3-10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3632841/. Accessed June 26, 2018. Epstein DM, Sculpher MJ, Manca A, et al. Modelling the long-term cost-effectiveness of endovascular or open repair for abdominal aortic aneurysm. *BJS*. 2008;95(2):183-190. doi:10.1002/bjs.5911 Epstein D, Sculpher MJ, Powell JT, Thompson SG, Brown LC, Greenhalgh RM. Long-term cost-effectiveness analysis of endovascular versus open repair for abdominal aortic aneurysm based on four randomized clinical trials. *BJS*. 2014;101(6):623-631. doi:10.1002/bjs.9464 Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009)The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J*. 2009;30(19):2369-2413. doi:10.1093/eurheartj/ehp285 Haider S, Najjar SF, Cho J-S, et al. Sac behavior after aneurysm treatment with the Gore Excluder low-permeability aortic endoprosthesis: 12-month comparison to the original Excluder device. *Journal of Vascular Surgery*. 2006;44(4):694-700. doi:10.1016/j.jvs.2006.06.018 Hames H, Forbes TL, Harris JR, Lawlor DK, DeRose G, Harris KA. The effect of patient transfer on outcomes after rupture of an abdominal aortic aneurysm. *Can J Surg*. 2007;50(1):43-47. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2384251/. Hogg ME, Morasch MD, Park T, Flannery WD, Makaroun MS,	

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				Cho J-S. Long-term sac behavior after endovascular abdominal aortic aneurysm repair with the Excluder low-permeability endoprosthesis. *Journal of Vascular Surgery*. 2011;53(5):1178-1183. doi:10.1016/j.jvs.2010.11.045 Holt PJE, Karthikesalingam A, Poloniecki JD, Hinchliffe RJ, Loftus IM, Thompson MM. Propensity scored analysis of outcomes after ruptured abdominal aortic aneurysm. *BJS*. 2010;97(4):496-503. doi:10.1002/bjs.6911 IMPROVE Trial Investigators. Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: three year results of the IMPROVE randomised trial. *BMJ*. 2017;359:j4859. doi:10.1136/bmj.j4859 Khashram M, Williman JA, Hider PN, Jones GT, Roake JA. Systematic Review and Meta-analysis of Factors Influencing Survival Following Abdominal Aortic Aneurysm Repair. *European Journal of Vascular and Endovascular Surgery*. 2016;51(2):203-215. doi:10.1016/j.ejvs.2015.09.007 Langenberg JCM, Kluytmans JAJW, de Groot HGW, et al. Surgical Site and Graft Infections in Endovascular and Open Abdominal Aortic Aneurysm Surgery. Surgical Infections. 2018;19(4):424-429. doi:10.1089/sur.2017.302 Lederle FA, Freischlag JA, Kyriakides TC, et al. Long-Term Comparison of Endovascular and Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine*. 2012;367(21):1988-1997. doi:10.1056/NEJMoa1207481 Liang NL, Reitz KM, Makaroun MS, Malas MB, Tzeng E. Comparable perioperative mortality outcomes in younger patients undergoing elective open and endovascular abdominal aortic aneurysm repair. *Journal of Vascular Surgery*. 2018;67(5):1404-1409.e2. doi:10.1016/j.jvs.2017.08.057	

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				Maleux G, Claes H, Van Holsbeeck A, et al. Ten Years of Experience with the GORE EXCLUDER® Stent-Graft for the Treatment of Aortic and Iliac Aneurysms: Outcomes from a Single Center Study. *CardioVascular and Interventional Radiology*. 2012;35(3):498-507. doi:10.1007/s00270-011-0235-6 Michaels JA, Drury D, Thomas SM. Cost-effectiveness of endovascular abdominal aortic aneurysm repair. *BJS*. 2005;92(8):960-967. doi:10.1002/bjs.5119 Moore R, Nutley M, Cina CS, Motamedi M, Faris P, Abuznadah W. Improved survival after introduction of an emergency endovascular therapy protocol for ruptured abdominal aortic aneurysms. *Journal of Vascular Surgery*. 2007;45(3):443-450. doi:10.1016/j.jvs.2006.11.047 Mullenix PS, Starnes BW, Ronsivalle JA, Andersen CA. The impact of an interventional vascular specialty team on institutional endovascular aneurysm repair outcomes. *The American Journal of Surgery*. 2005;189(5):577-580. doi:10.1016/j.amjsurg.2005.01.037 NHS. Patient choice. Your choices in the NHS. https://www.nhs.uk/NHSEngland/patient-choice/Pages/your-rights-to-choice.aspx. Published August 16, 2017. Accessed June 26, 2018. NICE. Endovascular stent-grafts for the treatment of abdominal aortic aneurysms. February 2009. nice.org.uk/guidance/ta167. NICE. NICE Charter. 2017. https://www.nice.org.uk/media/default/about/who-we-are/nice_charter.pdf. NICE. Shared decision making. NICE Guidelines. https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/shared-decision-	

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				making. Patel ST, Haser PB, Bush HL, Kent KC. The cost-effectiveness of endovascular repair versus open surgical repair of abdominal aortic aneurysms: A decision analysis model. *Journal of Vascular Surgery*. 1999;29(6):958-972. doi:10.1016/S0741-5214(99)70237-5 Patel R, Sweeting MJ, Powell JT, Greenhalgh RM. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. The Lancet. 2016;388(10058):2366-2374. doi:10.1016/S0140-6736(16)31135-7 Perry RJT, Martin MJ, Eckert MJ, Sohn VY, Steele SR. Colonic ischemia complicating open vs endovascular abdominal aortic aneurysm repair. *Journal of Vascular Surgery*. 2008;48(2):272-277. doi:10.1016/j.jvs.2008.03.040 Picel AC, Kansal N. Essentials of Endovascular Abdominal Aortic Aneurysm Repair Imaging: Preprocedural Assessment. *American Journal of Roentgenology*. 2014;203(4):W347-W357. doi:10.2214/AJR.13.11735 Pratesi G, Piffaretti G, Verzini F, De Blasis G, Castelli P, Pratesi C. Ten-year outcome analysis of the Italian Excluder Registry with the Gore Excluder endograft for infrarenal abdominal aortic aneurysms. *Journal of Vascular Surgery*. 2018;67(3):740-746. doi:10.1016/j.jvs.2017.07.133 Roche-Nagle G, Hazel M, Rajan DK. Financial impact of PEVAR compared with standard endovascular repair in Canadian hospitals. *Journal of Interventional Radiology.* 2018;69:215-219. doi: 10.1016/j.carj.2017.08.003 Rudarakanchana N, Hamady M, Harris S, et al. Early outcomes of patients transferred with ruptured suprarenal aneurysm or dissection. *Ann R Coll Surg Engl*.	

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				2018;100(4):316-321. doi:10.1308/rcsann.2018.0014 Rudarakanchana N, Jenkins MP. Hybrid and total endovascular repair of the aortic arch. *Br J Surg*. 2018;105(4):315-327. doi:10.1002/bjs.10713 Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ*. 1996;312(7023):71-72. doi:10.1136/bmj.312.7023.71 Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. *New England Journal of Medicine*. 2015;373(4):328-338. doi:10.1056/NEJMoa1405778 Sidloff DA, Saratzis A, Sweeting MJ, Michaels J, Powell JT, Thompson SG, Bown MJ. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *British Journal of Surgery* 2017;104(12):1656-1664 Society of Vascular Surgeons. *VQI-Annual-Report 2016*.; 2016. Starnes BW, Tatum B, Singh N. Procedural and perioperative results in patients treated with fenestrated endovascular aneurysm repair planned by automated software in a physician-sponsored investigational device exemption trial of physician-modified endografts. *Journal of Vascular Surgery*. April 2018. doi:10.1016/j.jvs.2018.02.045 Tanski W, Fillinger M. Outcomes of original and low-permeability Gore Excluder endoprosthesis for endovascular abdominal aortic aneurysm repair. *Journal of Vascular Surgery*. 2007;45(2):243-249. doi:10.1016/j.jvs.2006.10.042 The United Kingdom EVAR Trial Investigators. Endovascular versus Open Repair of Abdominal Aortic Aneurysm. *New England Journal of Medicine*. 2010;362(20):1863-1871. doi:10.1056/NEJMoa0909305	

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				Ulug P, Sweeting MJ, von Allmen RS, Thompson SG. Morphological suitability for endovascular repair, non-intervention rates, and operative mortality in women and men assessed for intact abdominal aortic aneurysm repair: systematic reviews with meta-analysis. *Lancet* 2017;389(10088):2482-2491. doi:10.1016/S0140-6736(17)30639-6 Vallabhaneni R, Farber MA, Schneider F, Ricco J-B. Debate: Whether young, good-risk patients should be treated with endovascular abdominal aortic aneurysm repair. *Journal of Vascular Surgery*. 2013;58(6):1709-1715. doi:10.1016/j.jvs.2013.09.017 van Beek SC, Conijn AP, Koelemay MJ, Balm R. Editor's Choice – Endovascular Aneurysm Repair Versus Open Repair for Patients with a Ruptured Abdominal Aortic Aneurysm: A Systematic Review and Meta-analysis of Short-term Survival. *European Journal of Vascular and Endovascular Surgery*. 2014;47(6):593-602. doi:10.1016/j.ejvs.2014.03.003 van Bochove CA, Burgers LT, Vahl AC, Birnie E, van Schothorst MG, Redekop WK. Cost-effectiveness of open versus endovascular repair of abdominal aortic aneurysm. *Journal of Vascular Surgery*. 2016;63(3):827-838.e2. doi:10.1016/j.jvs.2015.10.055 Vascular Services Quality Improvement Programme. National Vascular Registry Annual Report. 2017. https://www.vsqip.org.uk/content/uploads/2018/05/2017-NVR-Annual-Report.pdf. Accessed June 26, 2018. Verhoeven ELG, Katsargyris A, Bachoo P, et al. Real-world Performance of the New C3 Gore Excluder Stent-Graft: 1-year Results from the European C3 Module of the Global Registry for Endovascular Aortic Treatment (GREAT). *European Journal of Vascular and Endovascular Surgery*.	

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				2014;48(2):131-137. doi:10.1016/j.ejvs.2014.04.009 Wilson J, Jungner G. Principles and Practice of Screening for Disease. 1968. http://www.who.int/ionizing_radiation/medical_radiation_exposure/munich-WHO-1968-Screening-Disease.pdf. Accessed June 18, 2018. Winterborn RJ, Amin I, Lyratzopoulos G, Walker N, Varty K, Campbell WB. Preferences for endovascular (EVAR) or open surgical repair among patients with abdominal aortic aneurysms under surveillance. *Journal of Vascular Surgery*. 2009;49(3):576-581.e3. doi:10.1016/j.jvs.2008.09.012 Zabrocki L, Marquardt F, Albrecht K, Kribben A, Herget-Rosenthal S. Permanent Decline of Renal Function after Infrarenal Abdominal Aortic Aneurysm Repair—Frequency and Risk Factors. *Annals of Vascular Surgery*. 2018;47:272-278. doi:10.1016/j.avsg.2017.09.009	
Royal College of Nursing	General	General	General	We welcome this NICE guideline	Thank you for your comment and endorsement of the guideline recommendations. Individual comments have been responded to where they appear.
Royal College of Nursing	General	General	General	To deliver care can equally be challenging post operatively particularly if it an emergency repair of AAA. Guidelines on post-operative care would have been useful as patients are at greater risk of: Respiratory failure due to HAP, ARDS, atelectasis. Cardiovascular collapse requiring careful fluid resuscitation and vasopressors AKI Ileus Abdominal compartment syndrome Management of pain Rehabilitation following critical care	Thank you for your comment. Unfortunately, postoperative care following repair of ruptured AAA was not part of the scope developed for this guideline, and therefore it is not possible to make any recommendations in this area.

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Imperial College NHS Trust	General	General	General	Individual patient groups are likely to be significantly affected adversely without access to EVAR: **Urgent, symptomatic patients:** these patients have a higher rate of mortality than standard elective patients, most likely because of a failure to optimise and plan surgery appropriately. It is very unlikely that any symptomatic patient was placed in the trial and therefore we would contest that there is any evidence at all to state categorically that EVAR should not be used for symptomatic aneurysms. Symptomatic patients often present with concurrent disease that, given time could be optimised and treated ensuring the patient is fit for surgery. However the symptomatic nature means repair must take place as an in-patient. Clearly this is case for EVAR, even if you accept that the long term outcomes are not as durable as open surgery.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides

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					some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.
				The **hostile abdomen** where open surgery confers a significant risk but where patients are fit Those awaiting surgical or medical treatments for **cancer** where the aneurysm can be treated effectively and quickly with an endovascular approach	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. The presence of cancer would not, in and of itself, constitute a contraindication to OSR in every case. However, the committee agreed that it would be reasonable to include the presence of abdominal neoplasia that would make an open approach dangerous, or a hostile abdomen resulting from previous cancer surgery under this heading.
				Women, whose open AAA repair mortality is high, and who form only 10% of patients in the EVAR trial. Assumptions on the best treatment for this group cannot be made from a trial largely composed of male participants	Data from Sidloff et al. (2017) show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.

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Bedford Hospital NHS Trust	General	General	General	AAA repair mortality has been as high as 7-8% in the past. The introduction of endovascular repair along with vascular society's Quality Improvement Framework has helped us to bring our mortality down to levels comparable to rest of Europe. Restrictions on our freedom to propose most suitable treatment for the patients may result in significant shift back to higher death rates after aneurysm repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See Theme 15 for NICE's view on the importance of joint decision making between the clinician and the individual. For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.
Bedford Hospital NHS Trust	General	General	General	We have serious concerns on the make-up of the committee and lack of endovascular expertise in the group. Though the integrity of the members' is beyond doubt we feel that unconscious bias in the choice and interpretation of evidence might have crept in. This is particularly evident in following: Comparing the outcomes of open versus Endovascular repair and drawing conclusions that "no treatment" is better than "endovascular repair". Drawing conclusions on "plausibility" of long term benefits and cost effectiveness based on historical data and ignoring the improvement in devices and enhanced expertise. Not taking into account the change in practice for example reduced length of stay and changes in operating team structure for both EVAR and open repair in cost effectiveness analyses. Not appreciating the impact on emergency endovascular provision if elective EVAR was to be abandoned. Not recognising the value of non-invasive surveillance modalities in guiding the selective use of contrast enhanced CT scan.	The guideline committee is a multidisciplinary group of vascular professional and lay members with a broad range of skills and expertise, including members with extensive experience in the use of EVAR for AAA. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. All points listed were discussed during the development and consultation phases of the guideline and are recorded in the committee discussion section of the relevant evidence reviews.

<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer's response</th></tr>
<tr><td></td><td></td><td></td><td></td><td>Not recognising the impact of CT scan surveillance on overall cost of EVAR for comparison.
Not appreciating the risk of kidney injury if contrast enhanced CT scan was adopted as surveillance modality when considering long term complications.</td><td></td></tr>
<tr><td>Association of British HealthTech Industries (ABHI)</td><td>General</td><td>General</td><td>General</td><td>Table 1: Data from Vascunet, Comparing EVAR and OSR Peri-Operative Mortality Over Time
<table>
<tr><td></td><td>2005-2009</td><td>2010-2013</td><td>p-value</td></tr>
<tr><td>Open repair</td><td></td><td></td><td></td></tr>
<tr><td>High volume</td><td>3.4%</td><td>3.4%</td><td>0.86</td></tr>
<tr><td>Low volume</td><td>4.35</td><td>5.4%</td><td>0.03</td></tr>
<tr><td>EVAR</td><td></td><td></td><td></td></tr>
<tr><td>High volume</td><td></td><td>1.1%</td><td>0.02</td></tr>
<tr><td>Low volume</td><td>1.3%</td><td>1.2%</td><td>0.56</td></tr>
</table></td><td>Thank you for submission of this information. See Theme 3a and Theme 3b.</td></tr>
<tr><td>Association of British HealthTech Industries (ABHI)</td><td>General</td><td>General</td><td>General</td><td>Table 2: EVAR-1 Mortality Over Time. From Patel et al., 2018
<table>
<tr><th>Total Mortality</th><th>EVAR (n=626) n/N (rate/100 person-years)</th><th>OR (n=626) n/N (rate/100 person-years)</th><th>Unadjusted hazard ratio (95% CI)</th><th>Adjusted hazard ratio (95% CI)</th><th>p-value</th></tr>
<tr><td>All patients</td><td>466/626 (9.3)</td><td>444/626 (9.0)</td><td>1.05 (0.92-1.19)</td><td>1.11 (0.97-1.27)</td><td>0.14</td></tr>
<tr><td>Time since randomization</td><td></td><td></td><td></td><td></td><td></td></tr>
</table></td><td>Thank you for submission of this information. See Theme 3a and Theme 3b.</td></tr>
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<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer's response</th></tr>
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<table>
<tr><td></td><td>0-6 months</td><td>26/626 (8.5)</td><td>45/626 (15.0)</td><td>0.57 (0.35-0.92)</td><td>0.61 (0.37-1.02)</td><td>0.06</td></tr>
<tr><td></td><td>6 months-4 years</td><td>126/600 (6.7)</td><td>116/581 (6.3)</td><td>1.07 (0.83-1.38)</td><td>1.13 (0.83-1.47)</td><td>0.035</td></tr>
<tr><td></td><td>4-8 years</td><td>135/474 (8.3)</td><td>129/464 (8.0)</td><td>1.03 (0.81-1.31)</td><td>1.07 (0.83-1.37)</td><td>0.62</td></tr>
<tr><td></td><td>>8 years</td><td>179-339 (14.9)</td><td>154/333 (12.7)</td><td>1.18 (0.95-1.47)</td><td>1.25 (1.00-1.56)</td><td>0.0484</td></tr>
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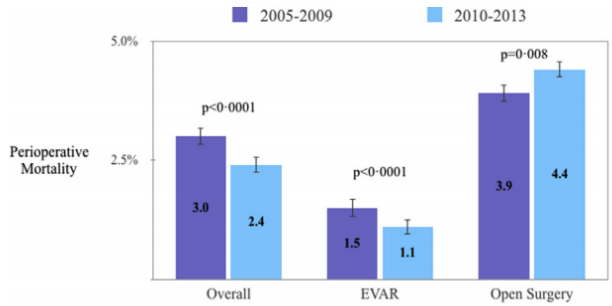
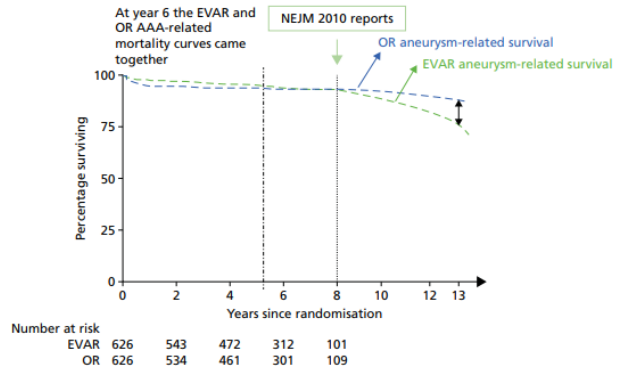
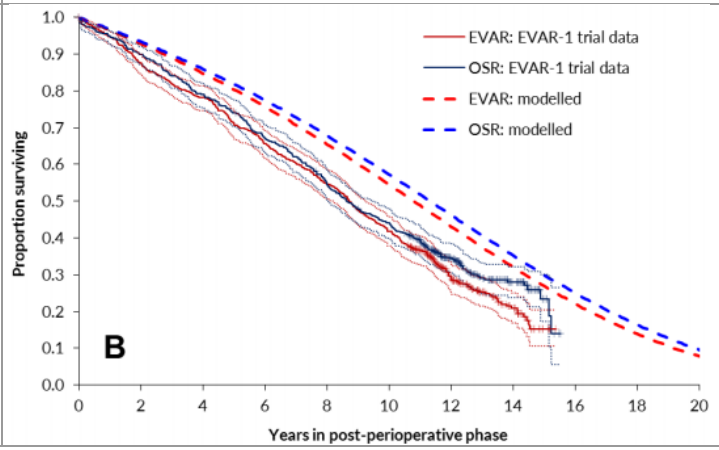
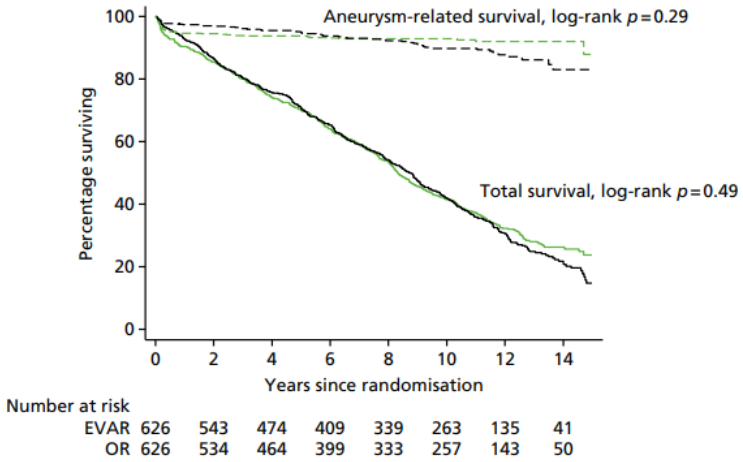
</td><td></td></tr>
<tr><td>Association of British HealthTech Industries (ABHI)</td><td>General</td><td>General</td><td>General</td><td>


Figure 1. Changes in peri-operative mortality in the Vascunet Registry between the two periods.

Figure 1: Data from Vascunet, Comparing EVAR and OSR Peri-Operative Mortality Over Time
</td><td>Thank you for submission of this information. See Theme 3a and Theme 3b.</td></tr>
</table>

Stakeholder	Document	Page No	Line No	Comments	Developer's response
Association of British HealthTech Industries (ABHI)	General	General	General	 **Figure 2: EVAR-1 Mortality Over Time. From Patel, Powell et al., 2018.** Note that this is aneurysm-related mortality, not all-cause mortality	Thank you for submission of this information. See **Theme 3a** and **Theme 3b**.
Association of British HealthTech Industries (ABHI)	General	General	General		Thank you for submission of this information. See **Theme 3a** and **Theme 3b**.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Figure 3: Actual EVAR-1 Survival vs Modelled Survival Models.	
Association of British HealthTech Industries (ABHI)	General	General	General	 **Figure 4: EVAR-1 Mortality Over Time. From Patel, Powell et al., 2018.**	Thank you for submission of this information. See **Theme 3a** and **Theme 3b**.

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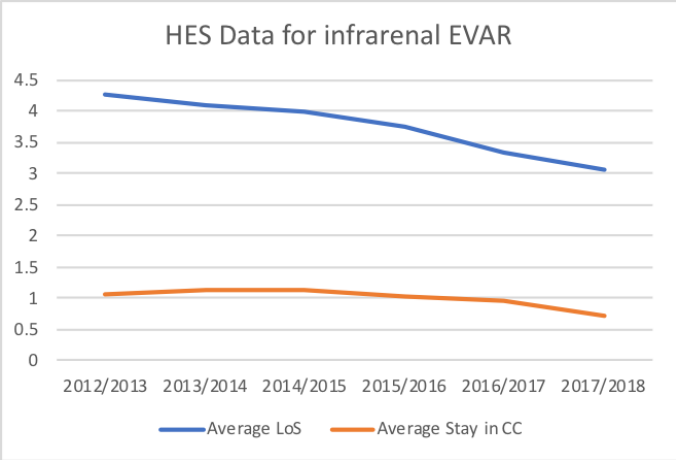
Medtronic UK	General	General	General	 Figure 1: Medtronic internal analysis of HES Database using the following procedure codes: L271 - Endovascular insertion of stent graft for infrarenal abdominal aortic aneurysm AND/OR L281 - Endovascular insertion of stent for infrarenal abdominal aortic aneurysm	Thank you for submission of this information. See **Theme 3a** and **Theme 3b**.
Countess of Chester Hospital	General	General	General	We are not convinced that the cost effectiveness analysis reflects current practice. We have seen improvements in our own EVAR practice over the last 5 years that includes; Length of stay is normally <36hrs	According to the 2017 NVR, mean length of stay for infrarenal elective EVAR was 4.31 days in 2016. Although the committee had misgivings about the selection biases the NVR reflects, they agreed to incorporate these data into their HE analysis. See **Theme 6**.

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				Percutaneous approach is regular practice, making true day case operating possible	The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.
				Routine follow up is with Duplex and Xray, with a low radiation and contrast burden CT follow up is the exception used only to address specific issues CEUS is used on occasion again to answer specific questions	In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks. Instead, it recommended CT-led surveillance. See **Theme 11**.
				Reintervention rates in our series are 6%, normally for type 1 or 3 endoleaks Good anatomy predicts good outcome We would be happy to share with NICE our follow up protocols and reintervention data.	It is unclear over what period these are measured or what types of reintervention they relate to.

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Countess of Chester Hospital	General	General	General	The impact of an increased volume of open surgical repair (OSR) has not been sufficiently assessed in this guidance. There will be a significant need for additional resources; The total HDU / ITU bed requirement has not been factored into this guidance. EVAR patients represent 80% of our AAA cases and are nursed routinely on the ward. There is already a significant rate of cancellation on the day for any Surgical case that requires a Critical Care bed. This is stressful for all concerned, especially the patient and we estimate an additional 400 bed days would be required in one year in our unit. Dual Vascular Consultant operating for OSR will reduce productivity and increase costs. OSR will occupy an all day operating list wheras elective EVAR needs only ½ day list.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. . We are unaware of any recommendation that dual consultant operating is required for AAA repair. We don not believe it was used in the evidence-base that informed the committee's recommendations. Presumably, if this practice is being adopted, it is expected to lead to patient benefits that justify the additional resource, though we have not seen any evidence on this topic. We have been unable to identify any contemporary evidence regarding duration of procedure for EVAR and OSR – see **Theme 5**. Although the committee accepted that EVAR procedures do take less time than OSRs, such evidence as is available suggests differences between the 2 that are measured in minutes rather than half-days.
Countess of Chester Hospital	General	General	General	The guidance has given insufficient consideration and guidance regarding mortality rates. We are concerned that	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations

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				NICE have recommended a trade off between mortality and cost; The Vascunet report of 2008 confirmed a 7.9% mortality in the UK compared to 3.5% in Europe, which marked a move to centralised units and increased uptake of EVAR What are the criteria for which patients will be turned down for repair? There is no recognition that some patients fall between the EVAR1 and EVAR2 groups	related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. It is not accurate to characterise the committee's recommendations as a trade off between mortality and cost. It would be more accurate to call them a trade off between short- and long-term survival prospects, with clear evidence that prevailing practices put undue emphasis on the former. For discussion of the Vascular Society's AAA Quality Improvement Programme that was instigated in response to the 2008 Vascunet report, please see **Theme 2a**. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive

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					eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				What advice and information will be given to patients who prefer EVAR or are turned down for open repair? How can we provide informed consent with the knowledge that a safer alternative exists that will not be funded? What role does 'patient choice' have? What will the outcome be for patients who were turned down for OSR but present later with symptomatic or ruptured AAA? How will UK outcomes compare with European units? Are we going back in time to 2008? We believe that these changes to practice will mean an increase in mortality for both elective and emergency repair. They will also increase the number of patients who present with ruptured AAA.	For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
Countess of Chester Hospital	General	General	General	We are very concerned that EVAR is recommended for ruptured AAA. This will not be safe if there is no elective service;	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				It is inconceivable that we would be able to offer an EVAR service for rupture, a procedure done out of hours, in more challenging circumstances when they are not done routinely in hours. The experience of the whole team and new members of the vascular team will be severely depleted. Therefore, the only option for rupture will be OSR with an identified poorer outcome. The rate of rupture will be increased as elective repairs for those who fall outside the EVAR1 group will be reduced.	whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Countess of Chester Hospital	General	General	General	We do believe that the increased uptake of EVAR has meant patients who are older &/or have more comorbidities have been treated where previously they may not have been offered surgery. There is a need to accurately predict which patients are truly 'EVAR 1' and 'EVAR 2' and analyse the benefit for those who have increased risk for open repair due to; Age Medical comorbidities Life expectancy	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that there are no methods that reliably predict short-term outcomes of AAA repair, and also found that no individual characteristics are associated with better outcomes for EVAR at a cost that represents effective use of NHS resources. See **Theme 12**.

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				We contend that instead of abandoning EVAR in all elective cases we should commission very clear and appropriate guidelines for those who lie outside the EVAR 1 group. Defined reproducible metrics should be used for identifying those not suitable for EVAR or OSR to ensure equitable access to treatment.	The committee also agreed that it would be valuable to generate new high-quality research in the area of optimal treatment for people whose comorbidities make OSR unsuitable. They made a research recommendation noting that such a study would be helpful.
Countess of Chester Hospital	General	General	General	We have concerns regarding the breadth of advice & evidence provided to the committee; Were there any EVAR experienced surgeons included? Do the committee members have a AAA practice? The advice does not reflect our real world experience. Was there a patient representative included?	As detailed in guideline documentation, the committee included 3 experienced vascular surgeons, including – according to VSQIP data – by far the most active surgeon in the UK. All 3 have extensive experience of endovascular and open techniques. In addition, an interventional radiologist with EVAR practice was a core committee member. The committee also included 2 lay members who provided patient perspective and had equal status in all discussions and conclusions.
Countess of Chester Hospital	General	General	General	It is not clear if the psychological effects have been considered of being given a AAA diagnosis and then not an offer of repair; Many patients who are relatively high risk will have a reduced quality of life due to the uncertainty of a likely fatal aneurysm rupture. The impact on our practice will be an increase in perioperative mortality as we will undertake OSR in higher risk patients, due to patient choice and risk of fatal AAA rupture.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.

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				Guidance is missing for when EVAR should be offered, e.g. hostile abdomen, inflammatory AAA, prior aortic surgery.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. Inflammatory AAA is outside the scope of this guideline.
City Hospitals Sunderland NHS Foundation Trust (CHS)	General	General	General	Our local experience in Sunderland shows that between January 2015 and March 2018 our MDT has stratified 44 consecutive high risk patients using CPEX, echo, PFT and Carlisle risk calculator, all with aneurysms larger than threshold for repair. The predicted 30-day mortality for open surgery for these patients was a median of 9% (range 5-27%). All underwent EVAR with a 30-day mortality of 0%. Under the draft guidelines most of these patients would have had to be denied EVAR.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Your experience serves to underline that existing risk-stratification tools have very poor predictive validity. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that it would be valuable to generate

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					new high-quality research in this area. They amended their recommendation to state that EVAR should only be offered in this population as part of an RCT comparing EVAR with no intervention, and made a research recommendation noting that such a study would be helpful.
University Hospitals Southampton – Wessex Vascular Network	General	General	General	Please find attached our response to the current draft AAA guidelines. It is clear that these recommendations will have a profound impact on our local service delivery. They will have a huge negative impact on patient choice, aneurysm-related mortality, and our local service delivery particularly length of stay and ITU utilisation	Thank you for providing this summary of your comments, which we respond to fully where they are given in detail. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues and Theme 15 on NICE's view of the importance of joint decision making between the clinician and individual.
Royal Derby Hospital	General	General	General	I enclose on behalf of the body of interventional radiologists and the vascular surgeons in Derbyshire, our agreed early views on the draft proposal. We reject this in its entirety as a poorly constructed and inflammatory proposal. Please withdraw this draft.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
British Society of Endovascular	General	General	General	Q1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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Therapy (BSET)				The impact on the NHS we would predict will be significant. The length of stay is significantly increased with open repair. The National Vascular Registry (NVR) 2017[1] shows 4,153 elective aortic aneurysms were repaired in 2016. Simplistically, with open repair having an average of 8 days stay, five longer than that of EVAR, if even 70% of the EVAR population were deemed "fit" for open surgery an additional 10,000 bed days would be required of vascular services, a significant number of these in HDU or ITU facilities. This will create a burden on ITU and HDU services and hospital wards that is unrealistic at this time. [1] Waton S, Johal A, Heikkila K, Cromwell D, Boyle J, Loftus I. National Vascular Registry: 2017 Annual report. London: The Royal College of Surgeons of England, November 2017. The true picture is most likely worse by a number of factors since the cohort that underwent EVAR are likely to have significant co-morbidity and stay longer for social reasons and have even more complications, further lengthening the stay. There is a significant risk on impacting waiting times for aneurysm repair. It is quite clear that the NHS services are a long way from meeting adequate waiting times. The current situation is that most patients wait 70 days between assessment and aneurysm repair, but in many units, a significant group of patients are waiting 140 days. To dismiss the clear benefits to patient care based on the fact that EVAR ultimately fails in the longer term in a small proportion of patients is a grave error. If this philosophy was extrapolated to other health care arenas, one would then have to question the benefit of chemotherapy for cancer as some	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. Randomised and casemix-adjusted observational evidence reports very similar results to the NVR, in this 1 area – see **Theme 6a**. This would tend to challenge the existence of selection effects such as those you hypothesise.

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				patients get recurrences and some die of metastatic disease. The concept of informed patients deciding between the upfront benefits of a more minimally invasive treatment compared with durability benefits of more invasive treatments are enshrined as patient choice considerations in many healthcare arenas. Rather than stop elective EVAR use, we must get better at selecting the patients that will benefit from EVAR, improve our ability to treat some less anatomically favourable cases with open surgery and finesse our ability to detect those patients who will not benefit from treatment by either modality. Recommending a wholesale abandonment of elective EVAR treatment is naive, unevidenced and could not be safely adopted within current UK vascular practice. The likely (perhaps unintended) consequences would be: a. An increase in AAA mortality, after years of improvement. This would be very visible within the NVR and in the public domain. b. An increase in LoS and critical care use at a time when NHS in-patient capacity is at an all-time low. c. An increase in emergency presentations from patients waiting longer for open surgery or from those turned down as 'unfit', but then present as emergencies. d. A lack of ability to treat emergency patients with EVAR as a result of reduced experience, training and consignment stock. e. A probable negative re-evaluation of the benefits of AAA screening.	Although an individualised approach to balancing risks and benefits is clearly desirable, the committee concluded that there are no methods that reliably predict short-term outcomes of AAA repair, and also found that no individual characteristics are associated with better outcomes for EVAR at a cost that represents effective use of NHS resources. See **Theme 12**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. Regarding AAA rupture in people for whom OSR is unsuitable, please see relevant comments in **Theme 13**. The rationale for this statement is unclear. If it is cost effective to screen people for AAA under current service patterns, then optimising the treatment pathway to deliver better health at

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					lesser cost can only make the screening programme more valuable.
				f. The UK being an outlier in global vascular healthcare. The lack of patient choice, potentially being a human rights infringement.	
				g. Increased social care required on discharge for elderly patients recovering from open surgery. There will also be pressure on bed based rehab, community physio and General Practice. These services are already under pressure with no additional capacity to deal with the extra workload.	The committee considered and accepted this argument. They therefore advised that an estimate of rehabilitation costs should be incorporated into the base-case model. See **Theme 6b** for details. The incorporation of this aspect into the HE analysis did not overturn the finding that OSR provides greater benefits at lower cost than EVAR.
				In addition, theatre time for open surgery is double that of EVAR and the length of stay is double and this has the potential to increase the waiting time because you will be able to do the maximum of two open surgical patients a day compared to three EVARs, with a high potential for cancellation on the day because of lack of critical care capacity which will have an impact on theatre utilisation. This would make it difficult to achieve the 8 week treatment pathway recommended by GIRFT.	There is no evidence that theatre time for OSR is double that of EVAR, although we have explored a range of values in our analyses – see **Theme 5**.
				This suggestion in the guidelines to remove the practice of elective EVAR is not in line with NHS practices of most other conditions that are seeking a minimally invasive approach and is a removal of a well-established therapy, not a recommendation on a new device. Since over 70% of patients with aneurysms are treated using EVAR in the UK, clearly there is a patient acceptance of this treatment. The impact of removing a treatment option for many patients, on and outside	For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.

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				the screening programme cannot be understated, as many patients will be denied treatment of their aneurysm despite having it monitored for many years, expecting endovascular stent placement. There has been a significant change with surgeon level outcome reporting in the UK over the last few years, a change of practice so vivid will impact the mortality figures for most if not all the surgeons and institutions in the UK, with consequences that may well lead to significant adverse publicity, a need to investigate and retrain a number of surgeons and most likely, a reluctance to offer repair in many cases, leading to a significant turn down rate – which will overall decrease the number of patients successfully treated for aneurysm repair. The rest of the world has embraced EVAR almost universally, including in financially deplete developing countries, as they recognise the benefits of EVAR for patients who have associated co-morbidity in the short term and that with developing technology it is likely that there is a significant improvement in the results of trials performed up to 15 years ago. A move to reduce EVAR to a few patients with ruptured abdominal aortic aneurysms has an Important National Health Service reputational impact, with a message of cost saving rather than an innovative, world class service. At the BSET Annual Meeting on 21st June, we surveyed the attendees. The questions and responses are below:	The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. Thank you for providing these data. While it is unsurprising to see that guidance that proposes limits on endovascular therapy would be poorly received by an organisation that exists to promote endovascular therapy (at a meeting sponsored by multiple manufacturers of endovascular

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				Do you think the current NICE proposals on AAA treatment could be safely adopted in your hospital in November 2018? Yes – 19% No – 74% Don't know – 6% **If adopted, would this lead to an increase or decrease in overall AAA mortality?** Increase – 92% Decrease – 8% **Do you think the AAA screening programme is viable if EVAR is not an option for treatment?** Yes – 50% No – 50% **Do you think patients should have the right to choose (where appropriate and with accurate information) between EVAR and open surgery?** Yes – 92% No – 8% **If you were not routinely performing elective EVAR in your hospital, would you be able to deliver an emergency EVAR service for rAAA as recommended?** Yes – 12% No – 88% **Does your hospital have enough critical care capacity to allow a switch to 100% open AAA surgery?** Yes – 5%	devices), it is instructive to have this evidence as to the challenges the guidance faces.

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				No – 85% **Do you believe the data discussed re EVAR for IRAAA can automatically be extrapolated to complex EVAR?** Yes – 2% No – 79% Not sure – 19%	
British Society of Endovascular Therapy (BSET)	General	General	General	Q2. Would implementation of any of the draft recommendations have significant cost implications? Implementation of these draft recommendations could potentially lead to: More ward bed days used because of the use of OSR resulting in a significantly longer length of stay post operatively than EVAR More critical care bed days used as an increasing number of patients will require critical care support because of the need for open surgery in all patients and the need for ventilation and temporary renal replacement therapy support (particularly for those undergoing surgery requiring a suprarenal or supracoeliac clamp). Higher return to theatre rate for open surgery – increased use of emergency theatres Increase cost of blood products as there is a higher blood product requirement for maximally invasive surgery Reduced capacity in theatre because standard OSR takes longer than EVAR and hence decreased theatre and departmental productivity (EVAR has a lower theatre cost per time) Increased cost of rehabilitation, social care and added burden to the GP and community services as open aortic surgery	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. We can confirm that all these issues have been considered by the committee and, in most cases, quantified in the analyses that supported their decision-making. See **Theme 5**, **Theme 6**, **Theme 6a**, **Theme 6b**, and **Theme 13**.

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				takes longer to recover from than EVAR and often means the patient does not reach baseline and requires ongoing support for activities of daily living for a longer period of time post operatively Potentially increased number of patients presenting with ruptured AAA requiring an increased resource for emergency treatment	
British Society of Endovascular Therapy (BSET)	General	General	General	Q3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) EVAR in 2018 is not the finished article and continues to evolve and improve. Much can be learned from where EVAR has not been so successful and it is recognised that some practice has not resulted in the outcomes hoped for: 1. Using devices outside the Instructions for Use (IFU) in unsuitable anatomy 2. The balance between profile and durability 3. Rapid adoption of sac sealing technology before sufficient evidence 4. Increasing focus on augmenting a proximal seal zone and achieving fixation, when the real problem is continual dilatation of the native neck We accept that there are flaws to current practice and that there is too much work done off IFU for EVAR, a reluctance to turn patients down for surgery and not enough open surgery for younger fitter patients. We feel that a pragmatic approach to this would be to set stricter criteria for endovascular	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that the suboptimal long-term outcomes of EVAR may be, in part, related to some of the challenges you outline. There is some evidence that – in relative terms – the people who derive **most** benefit from EVAR are the youngest and/or fittest (e.g. Brown et al., 2007; Lederle et al., 2012). However, having looked carefully for any subgroups of people who can be expected to derive sufficient benefit to outweigh long-term harms and justify additional costs, the committee concluded that none can be identified, on the basis of current evidence – see **Theme 12**).

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				treatment on IFU only. We would propose more stringent guidelines for controlled use of EVAR within IFU for all devices.	
Cook Medical	General	General	General	**Implementation issues - discussion of GIRFT report (Horrocks, 2018)** *We believe that the GIRFT report will be helpful in determining the feasibility of implementing the NICE recommendations.* The following recommendations and comments were provided in relation to AAA EVAR Repair in the GIRFT report, delivered in March 2018 by the Vascular Society of Great Britain and Ireland in partnership with the Royal National Orthopaedic Hospital NHS Trust and NHS Improvement: When it comes to wait time for surgery, data shows that many patients experience long waits for procedures that are clinically urgent, such as AAA repair. Among the factors contributing to delays, there were the lack of available facilities, the lack of staff and the lack of integration with other departments. Finally, and crucially, the majority of vascular surgery has become restricted to 'normal' working hours, immediately limiting the number of procedures that can be carried out per week. At present, just six NHS hospitals in England offer elective vascular surgery at weekends, even though they will have teams on call for the small number of emergencies they will face. Each year, approximately 43,000 vascular surgery procedures are carried out in England. The total number of procedures has gradually increased in recent years as new surgical techniques such as Endovascular Aneurysm Repair (EVAR) have been	Thank you for highlighting these views for us. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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				developed. Because these techniques are potentially less debilitating for patients, they have helped lower the threshold for surgical intervention and meant more unfit patients can receive surgery. EVAR is less invasive and recovery times are typically shorter. As a result, around 75% of elective AAA surgery is now conducted by EVAR. By contrast, approximately two-thirds of emergency AAA repairs are conducted by open surgery: though the number of emergency procedures is much lower, with only four providers undertaking more than 30 a year, the evidence suggests that hospitals are adhering to the more established approach in emergency care. In this regard, the GID-CGWAVE0769 guideline will bring in a challenging change in practice not only because of the bed capability, but also when it comes to surgeons' training needs: according to the GIRFT report (page 26), "at present, in England, there are approx. 7 radiologists per 100,000 of the population (most of these will be non-interventional) and one vascular surgeon per 137,000. These figures are much lower than our international counterparts. Demand is rising, and it is known that many vascular surgeons are expected to retire in the next decade. There is therefore a need to plan ahead and develop a workforce strategy – not just for surgeons but for all members of the vascular team. In particular, to ensure the workforce is sustainable, the numbers of vascular specialists in training will need to increase". Furthermore, according to the GIRFT report (page 39), "there is another key use of data that needs to be considered: data about individual surgeon	

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				performance. Data about the activity each surgeon conducts - in particular, the number of procedures they carry out and the procedural choices they make (e.g. EVAR or open surgery) - can help identify if surgeons appear to favour one method over another. While that in itself is not 'wrong', with different surgeons having different areas of expertise, it may also reflect a lack of knowledge or experience in a different method. Data about outcomes can also indicate a development need". When it comes to emergency readmissions (page 31), the report points out that "most emergency readmissions are a consequence of performing surgery on patients who are frail and have multiple co-morbidities … the variation in emergency readmissions is surprisingly broad. For AAA, the trust percentages range from below 5% to above 20%. There might be a link between the choice of procedure and the frequency of readmissions. Yet the data gathered to date does not support this; nationally, 10% of patients who underwent open repair for AAA were readmitted in an emergency within 30 days, compared to 11% of those who underwent EVAR. The views expressed during the GIRFT visits indicated that a high percentage of readmissions are due to non-surgical complications, usually related to co-morbidities. It should be possible to reduce these readmissions substantially, through better post-operative support and discharge planning, involving other disciplines as well as the vascular team. Physiotherapy can be invaluable here, as can home care, to support frail and elderly patients in their recovery. In general, it is often clear which patients are at greatest risk of readmission; it should be possible to provide such patients	

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				with a greater level of support, rather than providing a 'standard' level for all".	
Cook Medical	General	General	General	Adkar SS, Turner MC, Leraas HJ, et al., (2017). Low mortality rates after endovascular aortic repair expand use to high-risk patients. *J Vasc Surg*, 67 (2):424 – 432. Beach JM, Rajeswaran J, Parodi FE, et al., (2018). Survival affects decision making for fenestrated and branched endovascular aortic repair. *J Vasc Surg,* 67 (3):722 – 73. British Society for Endovascular Therapy and the Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair (GLOBALSTAR) Registry (2012). "Early results of fenestrated endovascular repair of juxtarenal aortic aneurysms in the United Kingdom, *Circulation*, 125:2707-2715. Budtz-Lilly J, Venermo M, Debus S, et al., (2017). Editor's Choice – Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years, *Eur J Vasc Endovasc Surg*, 54 (1):13-20. Burgers, LT, Vahl AC, Severens JL (2016). "Cost-effectiveness of Elective Endovascular Aneurysm Repair Versus Open Surgical Repair of Abdominal Aortic Aneurysms." *Eur J Vasc Endovasc Surg,* 52 (1):29-40. Hammond CJ, Shah AH, Snoddon A, et al., (2016). Mortality and rates of secondary intervention after EVAR in an unselected population: influence of simple clinical categories	Thank you for your comment and for this list of references. As a result of draft guideline stakeholder comments, the NICE guideline technical team has carried out an additional evidence review on the effectiveness of AAA repair based on data from oberservational studies. We will consider this list of references as part of this work where cited in your comments.

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				and implications for surveillance. *Cardiovasc Intervent Radiol,* 39: 815-23. Holt PJ, Karthikesalingam A, Patterson BO, et al., (2012). Aortic rupture and sac expansion after endovascular repair of abdominal aortic aneurysm, *Br J Surg,* 99 (12):1657-64. Horrocks, M, Vascular Surgery GIRFT Programme National Specialty Report 2018, Accessed at: http://gettingitrightfirsttime.co.uk/wp-content/uploads/2018/02/GIRFT_Vascular_Surgery_Report-March_2018.pdf Marzelle, J, Preseles E, and Becquemin JP, (2015) Results and Factors Affecting Early Outcome of Fenestrated and/or Branched Stent Grafts for Aortic Aneurysms, *Annals of Surgery*, 261 (1):197-206. NICE (2009). Endovascular stent–grafts for the treatment of abdominal aortic aneurysms. NICE Guideline [TA167]. Acessed at: https://www.nice.org.uk/guidance/ta167. Patel R, Sweeting MJ, Powell JT, et al., (2016). Endovascular versus open repair of 31 abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair 32 trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet,* 388: 2366-74. Patel R, Powell JT, Sweeting MJ, et al., (2018). The UK EndoVascular Aneurysm Repair (EVAR) randomised controlled trials: long-term follow-up and cost-effectiveness analysis. *Health Technol Assess,* 22(5).	

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				Schermerhorn ML, Buck DB, O'Malley AJ, et al., (2015). Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *New Eng J Med*, 373 (4):328-38. Royal College of Surgeons, Vascular Society, Healthcare Quality Improvement Partnership. National Vascular Registry 2016 Annual Report. Accessed at: https://www.vsqip.org.uk/reports/2016-annual-report/ Royal College of Surgeons, Vascular Society, Healthcare Quality Improvement Partnership. National Vascular Registry 2017 Annual Report. Accessed at: https://www.vsqip.org.uk/reports/2017-annual-report/ Vascular News, "EVAR reduces aneurysm-related mortality, fails to increase overall life expectancy in 15-year follow-up results of EVAR 2 trial", pg 21. Accessed at: https://vascularnews.com/vascular-news-charing-cross-eu-edition-2018/ Verzini, F, Isernia G, De Rango P, et al., (2014). Abdominal Aortic Endografting Beyond the Trials: A 15-Year Single-Center Experience Comparing Newer to Older Generation Stent-Grafts, *J Endovasc Ther,* 21: 439-447	
Aneurysm Repair Decision Aid (ARDA) Development Group	General	General	General	Dear Andrew, We were very interested to read the recently published draft AAA NICE guidelines and thank you and the team for your efforts in producing this comprehensive piece of work. We do however think that you should consider the following comments in relation to these draft guidelines.	Thank you for your comment. Data from the study you have suggested has now been included in the review, and the BAR score is now considered in the guideline. The committee noted that one study indicated that the BAR had excellent discriminatory power at predicting in-hospital mortality in a heterogeneous group of patients who

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				Firstly the guidelines state that risk prediction models should not be used to facilitate clinical decision making due to poor discriminative ability with AUC's of 0.70-0.74. As you are aware we have conducted extensive research on developing and validating risk prediction models for AAA surgery. The BAR model which we developed from over 11,000 patients data recorded in the National Vascular Database (NVD) is mentioned in the guidelines but excluded for a reason that is unclear. (1) The BAR score has consistently demonstrated good to excellent discriminatory ability in the setting of elective AAA repair on both original internal bootstrapped validation (0·77) and at least two subsequent external validations with excellent discriminatory performance. (2,3) In a recent systematic review published in the British Journal of Surgery the BAR score was described as the best model with regards to applicability and discrimination with a C-statistic of 0.83. (4) Clearly this level of discrimination is well within the QRISK2 discriminatory threshold of 0.77 and 0.84 which is mentioned as acceptable-to-excellent discrimination in the accompanying NICE AAA evidence review G document and comparable to models such as the logistic EuroSCORE which is widely used in cardiac surgery. As such, the BAR score can provide both clinicians and patients with important and accurate estimates of risk to help in shared decision making. Secondly it is surprising that the draft AAA NICE guidelines do conclude that CPET should be used when it will assist in shared decision making based on our much smaller studies conducted on data from two centres based in Manchester. While we agree that CPET has the potential to be a useful tool in shared decision making the CPET results have not been as extensively validated as is the case with the BAR score. In addition CPET does not provide patient specific estimates of	underwent endovascular or open surgical repair (AUC of 0.83). This was indeed at the same level as the QRISK2 tool that they used as a benchmark during their initial consideration of the evidence. Upon examination of treatment-specific AUCs, the BAR score only had acceptable discriminatory power at predicting in-hospital mortality in patients who only underwent endovascular repair (AUC of 0.75). The same was observed for patients who only underwent open repair (AUC of 0.70). In light of the variation between the overall and treatment-specific AUCs, the committee had little confidence in the discriminatory power of the BAR score at predicting in-hospital mortality. The committee agreed that this precluded the BAR score from being recommended as a tool that could be used in shared decision-making for repair of asymptomatic unruptured AAA.

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				risk. CPET does identify a high risk cohort of patients but the BAR score is certainly more useful in shared decision making for elective AAA than CPET at the present time. We therefore feel that this issue should be corrected in the full publication of the NICE guidelines and that the BAR score should as a minimum receive the same level of recommendation as CPET and that it should be considered as a tool for use in shared decision making for patients with AAA. Lastly we welcome the research recommendation to address 'what are the most effective and cost effective frequencies for monitoring people with unruptured asymptomatic abdominal aortic aneurysms (AAA) of different diameters, and what is the optimal threshold for repair?' As you are aware we addressed this question in our Health Technology Assessment funded project through the development of a discrete event simulation model the Anuerysm Repair Decision Aid (ARDA) and this was considered by the committee. (5) The ARDA demonstrated significant potential to help inform clinicians, patients and healthcare providers on the consequences of offering AAA repair to patients with unruptured symptomatic AAA at different size thresholds but the findings were limited by uncertainty around the model estimates. This was in part due to the lack of high quality data available to inform the model. A significant amount of data to inform the model had to be derived from historical data or registries that were not originally developed for this purpose. We therefore recommend that to achieve the research recommendation regarding optimal threshold for AAA repair the committee consider recommending improving the National Vascular registry to include detailed data on all aspects of the patient journey for patients with AAA, particularly detailed pre-operative data (including CPET data) and re-intervention data.	

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				Yours Sincerely Prof Charles McCollum and Mr Stuart Grant on behalf of the ARDA development group References Grant SW, Hickey GL, Grayson AD, Mitchell DC, and McCollum CN. National risk prediction model for elective abdominal aortic aneurysm repair. Br J Surg 2013;100:645-653. van Beek SC, Blankensteijn JD, Balm R; Dutch Randomised Endovascular Aneurysm Management (DREAM) trial collaborators. Validation of three models predicting in-hospital death in patients with an abdominal aortic aneurysm eligible for both endovascular and open repair. J Vasc Surg 2013;58:1452–1457 Grant SW, Hickey GL, Carlson ED, McCollum CN. Comparison of three contemporary risk scores for mortality following elective abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 2014;48:38–44. Lijftogt N, Luijnenburg TW, Vahl AC, Wilschut, ED, Leijdekkers, VJ, Fiocco MF et al. Systematic review of mortality risk prediction models in the era of endovascular abdominal aortic aneurysm surgery. Br J Surg 2017;104:964-976. Grant SW, Sperrin M, Carlson E, Chinai N, Ntais D, Hamilton M, et al. Calculating when elective abdominal aortic aneurysm repair improves survival for individual patients: development of the Aneurysm Repair Decision Aid and economic evaluation. Health Technol Assess 2015;19(32).	

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Imperial College NHS Trust	General	General	Impact on current services	70% of elective aortic aneurysms are currently treated by EVAR. EVAR patients have a shorter inpatient length of stay and level 1 beds. Open have a longer (8 vs 3) length of stay and require level 2 or 3 beds. At Imperial the additional burden on inpatient bed number and acuity would be problematic. In the wider NHS an additional 10,000 bed days would be required of vascular services, a significant number of these in HDU or ITU facilities	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**.
Imperial College NHS Trust	General	General	NICE methodology	The main reservation that we have as a vascular unit at Imperial College Healthcare NHS Trust is with the process used to reach the conclusions made. The evidence quoted for the statements regarding EVAR is based on randomised trial evidence (EVAR 1 and EVAR 2 trials) however: These trials are historical and since the treatment of these patients there has been significant increase in experience of treating physicians, graft design and accepted treatment pathways. We therefore believe that there is a necessity to examine contemporary AAA repair registry data in the analysis of AAA treatment. The evidence to produce these guidelines is based on evidence from pragmatic surgical trials and therefore a didactic conclusion from them is not possible. Patients were selected for trials based on whether the surgeon was in equipoise, and also the fitness for surgery was pragmatic. Therefore it is likely that there are groups not represented in the trials. Numbers remaining in the open and endovascular arms of the trial are now low and caution is needed in drawing strong clinical inferences	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The consultation draft was not based solely on the EVAR trials – when it came to elective infrarenal cases, the evidence comprised 4 RCTs. To respond to stakeholders' feedback that the draft placed disproportionate weight on the RCTs, the committee reviewed a new review of casemix-adjusted observational evidence and saw that it provided strong validation of the RCTs and the inference the committee had drawn from them. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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					The committee were emphatic in agreeing that unadjusted registry data should not be used to estimate the relative effectiveness of EVAR and OSR, as they are subject to critical selection biases – see **Theme 3a** and **Theme 3b**. It is in the nature of long-term survival effects that they affect the people who live the longest. As long as methods used to analyse the data appropriately capture the statistical uncertainty associated with these phenomena – and we are confident that they have, in this case – there is no reason to demand additional circumspection in interpreting findings.
Imperial College NHS Trust	General	General	Patient choice	This suggestion in the guidelines to remove the practice of elective EVAR is not in line with NHS practices of most other conditions that are seeking a minimally invasive approach and represents the withdrawal of a well established therapy, not a recommendation on a new device. Since over 70% of patients with aneurysms are treated using EVAR in the UK, clearly there is a patient acceptance of this treatment. The impact of removing a treatment option for many patients, on and off the screening programme cannot be understated, as many patients will be denied treatment of their aneurysm despite having it monitored for many years, expecting endovascular stent placement rather than open repair	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.
Imperial College NHS Trust	General	General	Reputational	EVAR has been adopted across the world, and the idea that we can return to 1991 whilst other healthcare systems continue to refine and improve the technology represents a major NHS reputational risk.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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					Please see the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence.
Imperial College NHS Trust	General	General	Surveillance	A recommendation to use CT scanning for surveillance is a significant change from current practice based on little evidence. This would have a significant impact on the NHS vascular services. The evidence provided is described to demonstrate CT evaluation as the most sensitive method of detecting endoleaks. However, almost universally the vascular community has adopted ultrasound evaluation may be less costly, and detects reliably an increase in size in aneurysm which can be used as a proxy to detect complications and a reduction in both cost and patient radiation exposure. There is significant evidence to suggest patients at low risk may be safely placed in a pathway of reduced surveillance [1], where ultrasound can be safely used. There should also be a recommendation for units to understand the lost to follow up numbers who should be on the surveillance programmes. These patients lost to follow up comprise a significant number of patients who have adverse	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of

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				late outcomes from EVAR. A reduction in these events may well further improve the results of this technology. 1. Early sac shrinkage predicts a low risk of late complications after endovascular aortic aneurysm repair. Bastos Gonçalves F, Baderkhan H, Verhagen HJ, Wanhainen A, Björck M, Stolker RJ, Hoeks SE, Mani K. Br J Surg. 2014 Jun;101(7):802-10.	complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Imperial College London - IMPROVE trial management committee	General	General	General	The draft NICE guidelines have been viewed from the perspective of the work we have performed for the National Institute of Health Research Health Technology Assessment (project 07/37/64) to identify whether endovascular repair (if morphologically feasible) provides a better option than open repair for ruptured abdominal aortic aneurysms.	Thank you for your comment. Individual comments have been responded to where they appear.
Hull and East Yorkshire Hospitals Vascular and	General	General	General	The publication of these recommendations in this format will lead to implementation by most if not all CCGs to decline to commission endovascular repair. This removal of treatment options which have been shown to be safe and highly clinically	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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Endovascular Service				effective is therefore inconsistent with the NICE charter which states "…our recommendations are not intended to replace the professional expertise and clinical judgement of health professionals, as they discuss treatment options with their patients."	whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
NHS England Specialised Commissioning – Specialised Vascular Clinical Reference Group	Draft guideline	General	General	**How will outcomes and cost (value) be affected by the change in guidance?** We believe that there would be an increase in 30 day mortality if the proposed guidelines were to be introduced. While we recognise that the variance in mortality narrows over two years between the two procedures, we do feel that clinicians are best placed to decide the most appropriate intervention in partnership with individual patients. We recognise the costs of follow up and potential device replacement etc will be reduced if more patients are directed towards open repair, we also believe that the proposed guidelines would see less patients undergoing AAA repair (due to comorbidities and surgical safety issues) and therefore a cost reduction, in relation to less procedures, could follow.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues and Theme 15 for NICE's view on the importance of joint decision making between clinician and individual.
NHS England Specialised Commissioning – Specialised Vascular Clinical Reference Group	Draft guideline	General	General	**What will be the effects on ITU bed usage and length of stay in the change in guidance?** Given that a significant proportion of open AAA repairs will need to spend some post-operative time in critical care units we would expect to see the use of such bed usage to increase if the guidelines were to be introduced. Currently critical care beds available across England are at a low level and it is difficult- due to wider healthcare pressures- to discharge patients from critical care. We would expect to see average	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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				length of stay for AAA repairs rise if the proposed guideline were introduced.	
NHS England Specialised Commissioning – Specialised Vascular Clinical Reference Group	Draft guideline	General	General	**How will the scope of hospitals commissioned and vascular networks be affected by the change in guidance?** This guidance suggests offering EVAR for ruptured aneurysms as opposed to open surgery. The implication would be that the numbers of elective EVARS reduce and expertise in performing EVAR for rupture would be lower. The present model for "complex" AAA (2.5 million population generating 25 EVARs per year) would become even more unsustainable, so there would need to be even larger populations covered (smaller number of centres), to allow for technical skills to be maintained, developed.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
University Hospitals of Leicester NHS Trust - Leicester Vascular Institute	Draft guideline	General	General	Stakeholder perspective: The Leicester Vascular Institute is a tertiary level vascular surgery unit covering the populations of Leicestershire, Rutland, Lincolnshire and Northamptonshire. In the last 5 years we have performed 431 AAA repairs. Our 5-year in-hospital mortality for elective open AAA repair is 2.0% and for elective EVAR is 0.6%. We have been conducting EVAR since the technique was started in the UK. Our experience includes homemade stents and all subsequent generations of commercially available devices including fenestrated and branched EVAR.	Thank you for the contextual information about your service. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals of Leicester NHS Trust - Leicester	Draft guideline	General	General	The draft guidelines are based in the most part on the EVAR1 trial data. The major flaw of the long-term outcome data for EVAR1 is that re-interventions (a major cost and disutility driver for EVAR) were reported by trial centres. There has been no attempt by the EVAR1 authors to validate their	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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Vascular Institute				methods or determine the accuracy of follow-up in the open repair arm. Since patients undergoing EVAR were routinely followed up and patients undergoing open repair were discharged it is highly likely that the re-intervention data strongly favours open repair because of a methodological failure rather than a true difference. To quote the EVAR1 HTA report: "Detailed hospital resource use data were not widely available from case record forms after 1 September 2009 because of loss to follow-up, **especially in patients in the OR group**." (Patel 2018). This has not been corrected for in the committee's economic analysis.	whilst supporting individualised care around which interventions are appropriate. Although it was not part of their original protocol, the EVAR trial investigators performed a thorough retrospective review of HES data which enabled them to incorporate hernia procedures in their reporting. As noted in HE.2.2.9.1, we use those data in our HE model. In addition, we have also captured further laparotomy-related procedures (lysis of adhesions and bowel resection), which are more prevalent following OSR, based on a matched comparison of US Medicare data (Schermerhorn et al., 2015). The particular resource use and quality of life implications of each of these complications are captured.
The Northern Vascular Centre	Draft guideline + Health Economic Appendix	150		We note the panel's financial justification for not recommending complex EVAR in patients deemed unfit for elective open repair, but are unsure as to the validity of this advice. In *HE.3.3.2.4 [Scenario analysis 10: Perioperative mortality – threshold analysis]* the panel estimates an operative mortality in this cohort of 40.9%. We acknowledge the comment in the Health Economic Appendix page 150 *"….development committee advised that our base-case EVAR mortality rate in this population (40.9%) may be relatively high."* From the subsequent threshold analysis (Figure HE85) it is clear that if complex EVAR has a 5% mortality the cost is around just £24,000. Our unit has an operative mortality for complex EVAR of just 2%. The national vascular registry shows operative mortality of 3.6%. We believe that if complex EVAR has a mortality of less than 5% then it would be associated with a cost below £20,000 and thus represents a cost effective treatment option.	This comment misinterprets figure HE85, which shows the relationship between baseline mortality rate (x-axis) and cost effectiveness (on the y-axis). However, you appear to have interpreted this as an ICER where, in fact, it is expressed in terms of incremental net monetary benefit. This is a rearrangement of the ICER calculation that is useful for situations like this where ICERs can become difficult to interpret. With INMB, any positive figure suggests that a treatment is cost effective. In a graph like this, the line would have to cross the x-axis for the treatment to represent reasonable value for money (it would be associated with an ICER of better than £20,000/QALY at that point). This means that, in this instance, complex EVAR has no prospect of being considered cost effective at any level of perioperative mortality (even 0).

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					We have introduced additional text to these graphs, explaining their correct interpretation
The Northern Vascular Centre	Draft guideline			Moving away from elective EVAR would place the UK at odds with the rest of the world's practice. This risks UK vascular centres/surgeons falling behind in a well-established internationally recognised procedure. We anticipate a large volume of surgeons (consultants and trainees) leaving UK practice, indeed our own units' dual trained consultants have intimated they would not work in a NHS were the guidelines to be accepted as written. This risks destabilising our already stretched provisions for delivering a modern vascular service both here in the North East and across the UK.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Northern Vascular Centre	Draft guideline			The evidence upon which these guidelines are based is historic. We have a 25 year established EVAR programme during which stent graft technology has advanced immeasurably, secondary prevention strategies in patients with vascular disease have vastly improved and national rates of smoking have decreased. These trials may no longer be representative of our current patient cohort; we raise concerns over adherence to guidelines based on such historic trials, in which mortality for EVAR was 4 times greater than latest reports (0.4% NVR / 1.6% EVAR-1), despite presumably many centres using EVAR when patients are deemed unfit for open surgery.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.
The Northern Vascular Centre	Draft guideline			Currently, national EVAR 30-day mortality for elective infra-renal AAA repair is 0.4%. Abandoning this safe practice will cause an increase in UK elective aneurysm death rates, at odds with those seen around the world. This data will be publically available. This risks subverting the reputation of UK vascular services, as it might appear that we are compromising patients' outcomes for financial incentive.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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					The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
The Northern Vascular Centre	Draft guideline			We would predict that a move away from EVAR for the management of patients with infrarenal AAA would result in an increase in 'turndown' rates, especially for those with significant co-morbities, but with at least a 2 year life expectancy. In this group, EVAR longevity is rarely an issue and treatment can reduce AAA related mortality. The natural sequela of turning down more patients for elective repair is an increase in the number of ruptured aneurysms. This results in poorer outcomes and places additional strain on our out-of-hours, on-call and intensive care services. Whilst we support strategies for providing a more cost-effective vascular service, we would have concerns regarding implementation of change that might result in poorer outcomes for our AAA patients. .	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Northern Vascular Centre	Draft guideline			Providing an elective open repair only service will place considerable logistical and financial constraints on our unit. We estimate the prolonged length of stay (4 additional bed days per patient) and additional requirement for intensive perioperative care necessitating funding two further level-3 care beds and two additional vascular level 1 bed. This places strain on an already overwhelmed service. This has implications for our ability to centralise additional arterial work from neighbouring peripheral vascular centres in accordance with recommendations from the Vascular Society of Great Britain and Ireland. NHS England is supporting change to	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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				patient care which results in a reduction in hospital bed day requirement. Implementation of this guidance would stall that development.	
The Northern Vascular Centre	Draft guideline			The panels' estimated costs of life threatening graft reintervention rates in EVAR patients of £17,089 are inexplicably high. The panel states this is extrapolated from the comparable cost for life threatening reintervention in patients who have undergone open surgical repair. We would express concern regarding this comparison and encourage the panel to expand on their definition of *life threatening re-interventions*. An open Hartmann's procedure for necrotic sigmoid colon is not analogous to deploying a proximal cuff, extending iliac limbs or re-lining an EVAR which are all life-saving procedures, performed endovascularly, using a percutaneous approach and at considerably less cost than those estimated in the Health Economics Appendix Table HE31. This challenges the economic argument that EVAR has a higher net cost compared with open repair.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Thank you for drawing our attention to this issue. We have revised our base-case analysis and explored them impact of alternative assumptions in our updated HE model. See **Theme 8a**.
Terumo Aortic	Draft guideline		General	Question 1: We feel that if these guidelines are put into practice then patients diagnosed with an aneurysm, whether infrarenal or juxtarenal and unsuitable for open repair, will be left untreated until the aneurysm ruptures which significantly increases the risk of death. With elective endovascular options currently accessible, there are viable and clinically proven treatment paths available which would be denied under these draft guidelines.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Terumo Aortic	Draft guideline		General	Question 2: There would be significant cost implications with regards to the degree of retraining required for practising physicians in this field. The guidelines aggressively challenge current practice with skill sets of current practising physicians	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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				lost and we feel that England would fall behind Europe and the rest of the world by shunning innovative endovascular treatments.	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Terumo Aortic	Draft guideline		General	Question 3: We feel that implementation of these draft guidelines would be immediately detrimental to a growing cohort of patients who are suitable for Fenestrated Endovascular Aneurysm Repair (FEVAR) with custom-made Fenestrated Anaconda devices. Such a patient cohort is deemed unsuitable for treatment by any other commercially available means with the majority physically not fit enough for open surgery or deemed too high risk to attempt open repair. Terumo Aortic's established custom device programme offers individualised solutions for such patients and has been providing such solutions on clinician request since 2011 with over 2500 successful implants in this time. Restricting use of FEVAR to the boundaries of a randomised clinical trial is not feasible due to the condition of many patients not being suitable for open repair and therefore no balance to ensure proper randomisation. We strongly recommend that the guidelines are reconsidered to allow clinicians the option to request a custom-made device to treat patients where they deem no other commercially available alternative options suitable for treatment. Such devices must comply with the essential regulatory requirements defined in the medical device directive with each device individually designed to provide the optimal treatment solution for that patient and there is growing evidence	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. There was only 1 area in which data that could potentially be used to inform a subgroup-specific analysis were identified – juxtarenal/pararenal AAAs that are amenable to fenestrated EVAR. An exploratory analysis from the HE model focusing on fEVAR alone was presented to the committee as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of

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				supporting the efficacy of FEVAR solutions as discussed below. We do not feel it appropriate to categorise custom-made devices bound by the requirements of the directive alongside other 'complex EVAR' solutions including off-label use of standard devices and physician modified devices as well as employing chimney/snorkel style techniques and strongly feel that modifying the guidelines to indicate custom devices as a viable option for patients unsuitable for open repair or indeed conventional EVAR would be the best course of action to ensure clinicians can continue to meet the challenging needs of such patients.	the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Terumo Aortic	Draft guideline		General	As the only stakeholder company with grafts for both open and endovascular repair, Terumo Aortic has a unique perspective with regards to the draft NICE guidelines. Terumo Aortic is not solely an endovascular product-based company, but has over 30 years experience in the design and manufacture of surgical grafts used in open repair. While we agree with some sentiments of the draft guidelines, we strongly disagree with the recommendation that patients not fit for open surgery should not be offered complex EVAR. We feel that the constantly evolving technology and benefits to such a wide cohort of otherwise untreatable patients mean that EVAR, and indeed FEVAR, should remain legitimate treatment options. Endovascular aneurysm repair (EVAR) has a distinct peri-operative mortality advantage over open repair for asymptomatic AAA [1]. In addition, benefits over open repair include shorter hospital stay, reduced surgical morbidity and earlier return to normal activities [2]. The greatest limitation to its more widespread use is unfavourable aneurysm anatomy.	The analysis that supported the committee's decision-making explicitly captured the factors you list (length of hospital stay, speed of recovery, etc.). It found no convincing evidence that complex EVAR is associated with perioperative survival gains, compared with OSR, and some evidence that it appears to be associated with substantial late excess mortality.

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				More specifically, a short (<15 mm) and angulated (>60°) proximal neck, a reverse conical neck, narrow access vessels and inclusion of important branch vessels by the aneurysm, are all factors which preclude its use. To circumvent this problem and enhance the applicability of EVAR to more complex aneurysms, fenestrated and branched stent grafts, which allow for the continued perfusion of renal and visceral vessels, were developed. The earliest of these devices was successfully deployed in 1999 [3]. Studies have demonstrated fenestrated stent grafts to have comparable peri-operative mortality rates to conventional EVAR, as well as high immediate and mid-term target vessel patency rates with a low rate of secondary interventions [4-6]. We feel that categorising FEVAR under the "complex EVAR" umbrella, grouping it alongside off-label use of EVAR devices, physician-modified devices and various combinations of chimney and snorkel techniques is not appropriate. Fenestrated Anaconda devices are only produced on request from clinicians and designed specifically as custom-made devices for individual use. These devices must comply with regulatory requirements defined by the Directive, Medical Device Regulations. With Fenestrated Anaconda, current technology allows for use of 3D printed models of the patient anatomy to aid in verification of the design and also offers clinicians the opportunity to test and evaluate proposed designs prior to implantation which has proven to be an excellent training tool and can also instil a degree of confidence prior to undertaking such complex procedures. Prototype testing is just one step in an established process to ensure the optimal design is realised for each request.	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. There was only 1 area in which data that could potentially be used to inform a subgroup-specific analysis were identified – juxtarenal/pararenal AAAs that are amenable to fenestrated EVAR. An exploratory analysis from the HE model focusing on fEVAR alone was presented to the committee as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The

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				Fenestrated stent-grafts are only requested because clinicians deem there are no available alternative solutions for their patients and restricting use of these devices to a randomised controlled trial, as the draft guidelines suggest, would immediately deny significant numbers of patients a sound treatment option. In effect, FEVAR allows for the repair of aneurysms that would otherwise not be treated. In fact, with the majority of these patients deemed physically not robust enough for open surgery, randomisation would simply not be feasible.	recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
				There was only one study used to support this statement for complex EVAR by the NICE committee, which was a single-centre, non-randomized trial of 90 patients with juxta renal AAA with 30-day outcomes reported. When mortality was compared with the open surgery group, endovascular mortality was 0% compared to 6.4% in the open surgery group. The data in this study were not interpreted in a favourable manner by the NICE committee, but to base a guideline on one small study does not seem to be an appropriate course of action.	In response to stakeholder comments such as this, we have now performed a more thorough review of the observational evidence available to inform estimates of the balance of benefits, harms and costs between EVAR and OSR for complex AAAs.
				The data formulating the basis of the guidelines also compares first generation EVAR (and complex EVAR) devices with long established open surgical repair. With significant research and development investment in recent years, EVAR devices have evolved significantly as has the experience and expertise of the operating clinicians during endovascular treatment. The degree of re-training required to switch back to a more 'open-centric' approach to AAA repair could also be detrimental to patient welfare, particularly in the short term. A growing number of endovascular specialists have fully	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				adopted endovascular technology since experiencing the benefits for many patients over equivalent open repair. Complex EVAR are treated in high volume centres in the UK for a very small cohort of patients with the average age of approximately 73. Utilising the latest FEVAR technologies provides a solution for patients who are simply not physically robust enough for open repair. Due to this being a patient-specific treatment, the relative numbers of patients are small which is reflected in the small numbers in studies published on this subject globally but there have been excellent results where Fenestrated Anaconda devices have been used with low morbidity, mortality and reintervention rates supporting continued use of the technology[7]. Terumo Aortic feels that patient choice should be paramount when discussing treatment with requesting physicians and the NHS has historically shared this view on personalised/individual care. By removing the option of complex EVAR, patient choice is effectively being denied since only treatment recommended by the NICE guidelines can be offered. We would strongly recommend that the draft guidelines are reconsidered both for EVAR and complex EVAR, particularly with regards to the use of custom-made devices. The custom-made Fenestrated Anaconda platform has allowed for successful treatment of over 2500 patients, many of whom were considered to be completely unsuitable for open repair. Should these guidelines be enforced in their current format,	The fEVAR publications that were included in our supplementary review of casemix-adjusted observational evidence comprised cohorts of similar age to the figure you cite (mean age 73 in Raux et al., 2014; 72 in Tinelli et al., 2016; a little younger at approximately 70 in Michel et al., 2015). These authors were able to provide a casemix-adjusted comparison of fEVAR with people with similar risk factors undergoing OSR. These analyses provide little evidence of a banefit for fEVAR (see **Theme 4**). The paper you cite is a non-comparative case series that can provide no insight as to the relative benefits, harms and costs of fEVAR and other approaches (be they OSR or conservative management).

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				then such patients would not be afforded any chance of intervention. **Reference List:** (1) Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010 May 20;362(20):1863-71. (2) Sandford RM, Bown MJ, Sayers RD, Fishwick G, London NJ, Nasim A. Endovascular abdominal aortic aneurysm repair: 5-year follow-up results. Ann Vasc Surg 2008 May;22(3):372-8. (3) Faruqi RM, Chuter TA, Reilly LM, Sawhney R, Wall S, Canto C, et al. Endovascular repair of abdominal aortic aneurysm using a pararenal fenestrated stent-graft. J Endovasc Surg 1999 Nov;6(4):354-8. (4) Greenberg RK, Haulon S, Lyden SP, Srivastava SD, Turc A, Eagleton MJ, et al. Endovascular management of juxtarenal aneurysms with fenestrated endovascular grafting. J Vasc Surg 2004 Feb;39(2):279-87. (5) Monahan TS, Schneider DB. Fenestrated and branched stent grafts for repair of complex aortic aneurysms. Semin Vasc Surg 2009 Sep;22(3):132-9. (6) Sun Z, Mwipatayi BP, Semmens JB, Lawrence-Brown MM. Short to midterm outcomes of fenestrated endovascular grafts in the treatment of abdominal aortic aneurysms: a systematic review. J Endovasc Ther 2006 Dec;13(6):747-53. (7) Colgan, F. Bungay, P. Burfitt, N. Hatrick, A. Clarke, M. Davies, A. Jenkins, M. Gerrard, D. Quarmby, J. Williams, R. (2016) operative and one year outcomes of the custom made	

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				fenestrated anaconda aortic stent graft- a UK multicentre study. Annals of Vasc Surg 10.1016/j.avsg.2017.05.027	
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	Appendix K	General	Given that the SVS and ESVS have drawn on the same body of literature to derive opposite conclusions, we opine that this distortion is a consequence of NICE's highly selective reading of the literature and the filling in of the inevitable data gaps by the "opinion of the committee". Indeed, the details of methodology outlined in Appendix K intimates as much. Data from randomised controlled trials/meta-analyses that recruited 15+ years ago have been given undeserved weight, while current registry data (particularly any analysis of current NVR data) and high-volume centre reports have been arbitrarily dismissed. The conclusion regarding the elective use of Complex EVAR appears to stand on a single, somewhat old report describing only 90 patients (*Donas KP, et. al. The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 2012; 56, 285-90*). Self-evidently,	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The committee's conclusion that unadjusted registry data cannot provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR was a principled judgement based on established methodological principles. Registries play an important role in describing current practice, but using them as evidence of relative effects of competing courses of action is inappropriate. Please see **Theme 3a** and **Theme 3b**. On reviewing stakeholder feedback, the committee accepted that it had been too stringent in only looking at prospective observational evidence (of which Donas et al., 2012, is the only published example). Therefore, a much broader evidence base was reviewed as part of the committee's post-consultation considerations. This comprises all casemix-adjusted observational evidence, including 9 studies looking at

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				a flawed analysis of the clinical data results in erroneous financial assumptions, irrespective of the quality of that tool. We are not equipped to question the financial model directly but observe significant variations in quoted cost of operations as recently exemplified in the recent GIRFT report (March 2018). We are therefore astonished at the committee's acceptance that an average cost for complex EVAR obtained from only three NHS Trusts would "adequately reflect a typical UK cost" (lines 766-8, Appendix K) and are left pondering the rigour of the process. Of course, we acknowledge the imperfections that characterise the medical literature in general. These limit the interpretation and generalisability of the EVAR literature as profoundly as they do most surgical fields, but a nihilistic exclusion of data and its replacement by uncredentialled opinion does not compensate for this weakness. It concerns us that, as demonstrated by this particular analysis, this flawed methodology has the potential for incorrect and dangerous assumptions. We all have to accept and work within the reality that randomised controlled data are not (and never were) "pure" or widely applicable. Those done too early in the evolution of a treatment do not test the mature version of that treatment. For all of these reasons (and more) RCTs have only ever acted as guides in the selection of treatments. Crucially, RCTs are only ethical in the setting of "clinical	the relative benefits, harms and/or costs of complex EVAR compared with OSR. Medical devices, unlike pharmaceuticals, are not subject to a national tariff. Therefore, it is extremely challenging to establish a nationally applicable cost for any type of endograft, even as regards their list prices, let alone the even more opaque prices negotiated by individual trusts. This problem is exacerbated yet further in the area of custom-made endografts for complex AAAs. Because of the clear uncertainty in this area, all economic analyses are reported with sensitivity analyses examining the impact of price on cost–utility results (see figure HE59 in the consultation draft, for the case of complex EVAR; this is updated as figure HE133 in the revised analysis). It is in the nature of long-term data that they can only reveal the long-term effects of treatment provided a long time ago. However, technologies cannot be recommended in the hope that they will provide superior results, over patients' whole lifetimes, especially when this would be a marked departure from all previous empirical findings. We trust that the supplementary review of casemix-adjusted observational evidence that has been undertaken in response to stakeholder feedback serves to temper your concern regarding the 'nihilistic exclusion' of data. Moreover, this additional work shows that it is not true that the 'only real new data' since TA167 are the 15-year outcomes from EVAR-1..

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				equipoise". Regarding EVAR, at its inception, equipoise existed. RCTs were done, reasonable conclusions drawn from those technologies in that era and guidelines (including NICE TA 167) were published and have become the backbone of guidance for aortic clinical practice. Since then, the only real new data are those arising from the 15-year outcomes of the EVAR1 trial. Despite the contentions of the clinicians involved in the NICE review process, these data do not represent current technology, expertise or clinical practice – and the dismissal of the possibility of improvement over time fails to acknowledge the several publications that clearly demonstrate the power of practice on outcomes in high volume units. As to denial of the value of improvement of technologies – we contend that "the absence of evidence is not the evidence of absence". It is unlikely that new randomised controlled trials to retest the conclusions of those that recruited between 1999 and 2008 will ever be done. Clinical equipoise no longer exists in the minds of the vast majority of aortic surgeons, the expense is prohibitive, and informed patient recruitment is improbable. New technologies will never be trialled against old ones or against open aortic surgery. We have to look to "big data" in the form of national registry data to determine whether current practice is safe and to see whether it compares with national data from the pre-EVAR/pre-AAA QIP era. We cannot rest on (revised) conclusions drawn from bygone eras, technologies and techniques. In drawing its financial conclusions, the NICE draft assumes a 0.9% difference between perioperative mortality after EVAR and open repair (0.4% vs 1.3%, respectively). However, the (ignored) large registry data (VASCUNET, 83,000 patients) suggests the contemporary difference to be 3.3% (1.1% EVAR vs 4.4%	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. For an explanation of why unadjusted registry data do not provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR, please see **Theme 3a** and **Theme 3b**. On the contrary, when attempts are made to adjust for the selection biases that compromise the relevance of observational data, investigators reach conclusions that are closely comparable with those found in RCTs. Moreover, there is no evidence that the balance of benefits and harms has changed over time – see **Theme 2**, **Theme 6** and **Theme 9**. We hope that our supplementary review addresses your concerns, in this area.

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				open repair, P<0.05) [Budtz-Lilly EJVES 2017]. Similarly, the UK National Vascular Registry data (2017) suggests a mortality difference of 2.5% (0.4% EVAR vs 2.9% open repair). This is not to say that EVAR is the first or best solution in the repair of all abdominal aortic aneurysms or in all patients. Open surgery has a significant role and it is important that the skills and infrastructure are maintained so that centralised, high volume units are able to offer the best treatment option to each individual patient. These individual patient decisions are legitimately based on the trade-off between speed (and quality) of recovery over the need for surveillance and possibly re-intervention as well as patient preference, and 30-day mortality risk. It is self-evident that patients with predictably short life-spans cannot benefit from AAA repair in any form. However, defining this group is difficult. Age alone is a poor guide and people now live long periods with active progressive pathologies that make them poor candidates for laparotomy, but low risk for EVAR. Some of these lives will be abbreviated unnecessarily by denying treatment of such patients with AAAs otherwise amenable to EVAR. There are good data to show that EVAR "off IFU" is associated with poor durability and we would agree that this is poor practice. It is however, not normal practice in high volume units able to offer all treatment options.	In reflection of these considerations, the committee agreed with your conclusion that there would be little point in repeating RCTs of EVAR versus OSR in elective infrarenal AAAs. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. It was also the committee's initial view that complex, off-IFU EVAR is not normal practice. However, it is notable that the 2017 NVR report an almost 10:1 preponderance of EVAR over OSR for complex AAAs in the period 2014–16. The committee concluded that this was at least partly reflective of substantially biased reporting (with anatomically identical cases much more likely to be labelled complex if addressed endovascularly), and they saw this as strong evidence of the invalidity of the NVR as a means to estimate the relative

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					effectiveness of the approaches. Nevertheless, it is clear that these data report almost 2,000 people who have undergone complex EVAR (invariably off-IFU) in the last 3 years for which data are available. As shown in this guideline, the evidence-base underpinning this activity is extremely weak.
British Geriatrics Society	Draft guideline	General		AAA is a common and potentially life-threatening condition which disproportionately affects older people. Forthcoming NICE Guidance recommends that open surgical repair (OSR) remains the treatment of choice for this condition. The BGS recommends that more attention is paid to multiprofessional assessment and management of older people with AAA to avoid real or perceived age discrimination in selection of patients for OSR.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee noted your concerns but were unable to make recommendations in the absence of evidence of systemic inequitable practice across the NHS. They noted that recommendation 1.1.8 outlines that non-experts should discuss all symptomatic or suspected ruptured AAAs with a regional vascular service. With this in mind, it was agreed that specialist input would inform the decision to transfer and operate. This would preclude any inappropriate decisions being made based on misplaced preconceptions about the likelihood of survival.
British Geriatrics Society	Draft guideline	General		AAA is one of many conditions which become increasingly common as people get older. Most people who have an AAA are completely unaware of it unless it ruptures, but those who suffer a ruptured AAA are very likely to die as a result. In recent years, screening for AAA by abdominal ultrasound has become established as an effective way of reducing mortality from this condition. People with a symptomless, unruptured	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				AAA can be offered surgical repair of the weakened arterial wall which greatly reduces the risk of a fatal rupture. Unfortunately, surgical AAA repair is and always has been a risky procedure. Despite great improvements in surgical and anaesthetic technique it still carries a significant risk of perioperative death and the potential for severe, often disabling, complications. In the assessment of suitability for surgery in people with a symptomless AAA, older people are at a number of disadvantages: AAA does not occur in isolation. It is commonly a result of high blood pressure, which also leads to strokes and kidney disease. These are risk factors for poor outcomes from surgery. Older people are more likely to have these risk factors simply through having had high blood pressure for longer. Many (but not all) older people have some degree of frailty. Frailty is a state of vulnerability due to a combination of physical, psychological and social impairments which combine to make a person less able to withstand traumatic events such as major surgery. Older age and frailty increase the risk of postoperative complications such as delirium and thus tend to increase resource use, for example through longer stay in Intensive Therapy Units (ITU). In a resource-constrained environment there may be tacit or even overt discrimination against older people based on utilitarian considerations (greatest good of the greatest number). Older people themselves may be reluctant to accept surgery, either because of self-perceived frailty or for	The committee reached a firm conclusion that it is not appropriate to make decisions about people's management based on their age alone. Such attitudes are not supported by the evidence. For example, the OVER RCT found that people aged 70 or older had greater long-term benefit from OSR compared with EVAR (while younger participants had the opposite profile). This phenomenon did not persist when an age-stratified analysis of long-term outcomes across all 4 RCTs was undertaken by the EVAR investigators (see Patel et al., 2018); however, this analysis provides no support for the belief that EVAR has greatest advantages over OSR in older patients.

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				altruistic motives – "spend the money on the young folk". In recent years people with AAA have been increasingly likely to be offered a minimally invasive "keyhole surgery" alternative to open AAA repair known as Endovascular Aortic Repair (EVAR). This appears to offer benefits, particularly in perioperative mortality, and is seen as being suitable for people not fit for open surgical repair (OSR). It has come to account for a large proportion of AAA repairs carried out in older people in particular. The NICE Guidance refers to a Cochrane review of EVAR and recommends that EVAR not be considered as a treatment option except as part of a formal research study. This represents a major change in current practice with the largest potential impact on older people with AAA. Senior BGS members with appropriate expertise having considered the evidence analysed in the Cochrane review, we find this recommendation justified on the available evidence.	
British Geriatrics Society	Draft guideline	General		It is therefore the Society's view that more attention must be paid to ensuring that older people with AAA are assessed fully and without age discrimination for their suitability for open surgical repair. Assessment must include senior anaesthetic and surgical review, optimisation of co-existing medical conditions and extensive discussion with the older person and, where appropriate, their family. Comprehensive Geriatric Assessment (CGA) by an experienced Geriatrician will be helpful in both pre-operative decision making and post-surgical care. Some older people may be willing to accept higher surgical risk than usually regarded as acceptable, whereas others may not wish to proceed even when risks are reasonably low.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee strongly agreed with these comments, again noting its recommendation that people should not be denied access to treatment on the basis of any individual sign, symptom or risk factor, which should certainly be understood to include age.

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				These views should form an important part of the decision-making process. When, after such an assessment, a person either does not wish to proceed to OSR or is deemed unfit for it, EVAR should not on current evidence be offered as an alternative simply on the basis that "something must be better than nothing". Open AAA repair is one of the most serious and high-risk surgical procedures for which an older person may be considered. As such, improved multidisciplinary assessment and management of this condition has the potential to act as a "trailblazer" for better surgical management of older people across the whole range of conditions for which surgery is an option.	
Royal Derby Hospital	Draft guideline	General	General	Patient choice issues and duty of candour are compromised. This is also against western and global practice.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Royal Derby Hospital	Draft guideline	General	General	Average quality of life in short term and medium term would be negatively affected with the proposed NICE guidance	The evidence shows that HRQoL is adversely affected by OSR, compared with EVAR, only in the short term. Two RCTs found that there is a significant advantage for EVAR at 3 weeks postoperatively (DREAM) and 4 weeks postoperatively (EVAR-1). However, both trials found that the benefit had disappeared by the 3rd postoperative month. One of these trials (DREAM) showed that, thereafter, OSR is associated

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					with significant **gain** in HRQoL, compared with EVAR, in the medium term; however, this finding was not replicated by EVAR-1 and OVER, both of which found there to be no difference in HRQoL beyond the short term. Therefore, the worst that can be said for OSR is that is is neutral for HRQoL in the medium term. Accordingly, this is the approach adopted in the HE model developed to support decision-making for this guideline.
Royal Derby Hospital	Draft guideline	General	General	EVAR 1 and 2 data is outdated and remaining patient numbers are so low to make this change in practice credible to involved clinicians. If EVAR is emergency only, competencies would be lost with poorer outcomes.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.
The Royal College of Radiologists	Draft guideline	General	General	The Interventional Radiology (IR) Committee at The Royal College of Radiologists' response to the draft AAA guidelines is specifically related to issues regarding the effects of these guidelines on training and maintaining clinical competency in interventional radiology. We know that many of the other issues relating to the evidence base around the availability of EVAR as a treatment option for patients with AAA will be addressed by other stakeholders. Hence the RCR IR	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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				Committee's main commentary in this area is in relation to training and maintenance of competencies. The draft guidelines are very explicit in outlining that EVAR should not be offered routinely to elective patients with AAA who are fit for open repair, but that it should be available and offered to patients in the context of a ruptured AAA. From an RCR perspective, this raises a number of issues:	
The Royal College of Radiologists	Draft guideline	General	General	Training in any interventional procedure requires a sequential and experiential pathway to gain the generic and specific competencies required to perform that procedure. This will commence with early experience gained in undertaking relatively simple and straightforward cases, moving on to progressively more challenging cases as experience is acquired, to advance and hone an individual's skills. This ensures trainees are able to build up their skills in a procedure whilst remaining within their sphere of competence. Such an approach is vital in maintaining patient safety and ensuring individuals are not practicing beyond their capabilities during training.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Royal College of Radiologists	Draft guideline	General	General	Once an individual has gained the competence to perform an interventional procedure, there is a need to maintain that competency, and this relies to some extent on having the sufficient caseload to retain their skills.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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The Royal College of Radiologists	Draft guideline	General	General	For anyone training to gain competencies in EVAR, there is a need to select patients carefully, taking into consideration the individual's competency and experience. For trainees, this would generally mean selecting cases with simple aortic anatomy related to their AAA. The vast majority of such anatomy is found in patients undergoing elective EVAR. To date, elective EVAR has provided the training ground to safely train the next generation of consultants in this procedure.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Royal College of Radiologists	Draft guideline	General	General	In the emergency setting of EVAR for ruptured aneurysm, the AAA anatomy is generally more challenging than in the elective setting. It would therefore be difficult for trainees to gain hands-on experience of EVAR solely utilising the case mix seen in the emergency setting. Indeed, due to this increased complexity, most trainees would not perform EVAR in the ruptured aneurysm patient until they reached the final months of their training, close to the time of completion of training.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Royal College of Radiologists	Draft guideline	General	General	There are fewer ruptured AAA cases seen clinically when compared to elective AAA. Even if all patients with ruptured AAA underwent EVAR, the volume of cases would be insufficient to enable all trainees to gain the skills to perform EVAR. There would also be an impact on the ability of existing consultants to perform sufficient numbers of cases to enable them all to continue to maintain competence in this procedure. This would mean that EVAR would no longer be available 24/7 for patients with ruptured AAA, compromising	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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				their chances of survival from a ruptured AAA. In reality, due to the more complex and challenging anatomy seen in the emergency setting, a greater proportion of patients are likely to be unsuitable for EVAR than in the elective setting, further limiting the pool of cases available for operators to gain and/or maintain competencies.	
The Royal College of Radiologists	Draft guideline	General	General	The vast majority of EVAR procedures in the UK are undertaken by interventional radiologists, although vascular surgeons are now also training to perform EVAR. The marked reduction in EVAR caseload that would result from implementation of the draft guidance would make it almost impossible for both groups of professionals to gain and maintain skills for EVAR. Given the comprehensive catheter and guidewire skills possessed by IRs, pragmatism would dictate that the limited number of EVAR cases would be performed by IRs, in order to concentrate expertise.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Royal College of Radiologists	Draft guideline	General	General	It is envisaged that the national AAA screening programme will reduce the AAA rupture rate in the future. In this scenario, and given the arguments above, it seems inconceivable that any vascular unit will be able maintain EVAR skills in enough individuals to enable them to continue offering EVAR for ruptured AAA.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
The Royal College of Radiologists	Draft guideline	General	General	The guidelines as they currently stand will result in loss of patient choice in the elective setting, where the NICE Committee have arbitrarily chosen improved long term	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations

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				outcomes seen with open repair to be more important than improved shorter term outcomes seen with EVAR; this in a population of patients for many of whom long term survival is not a realistic outlook and therefore irrelevant.	related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual. .
The Royal College of Radiologists	Draft guideline	General	General	The inevitable consequence of the removal of EVAR for the management of AAA in the elective setting will be a marked reduction in the number of practitioners able to train or maintain competence to perform the procedure. This will result in loss of patient choice in having EVAR in the emergency setting, with consequent direct increase in mortality in the ruptured AAA patient.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.
The Royal College of Radiologists	Draft guideline	General	General	In addition to many of the cogent arguments from other stakeholders which the NICE Committee will need to consider relating to the clinical aspects of elective EVAR, they also need to consider and outline how training and service provision of EVAR for ruptured AAA would be feasible in the absence of an elective EVAR programme within England and Wales.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.

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Gloucestershire Hospitals NHS Foundation trust	Draft guideline	General	General	We are concerned about the guidance; especially to suggest ''Not to Offer'' EVAR for patients not suitable for Open and to offer to it to those who rupture. First of all, this takes away the choice from patient. Second, there is absolutely no clarity about 'fit' or 'unfit' patient and 'how to measure fitness'. This is anybody's pick.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They a

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					research recommendation noting that such a study would be helpful.
				Third, we believe it was evidence based on older generation devices and outdated EVAR follow up programme and this would be different with the current treatment devices and follow up. Furthermore, the general skill level of Endovascular procedures is much higher than in the past and therefore the outcomes would be different to the EVAR trials.	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.
				Fourth, offering EVAR on an emergency basis is not feasible when elective EVAR is not offered due to lack of efficiency and declining skill.	
				Fifth, the whole economic analysis of cost-effectiveness may differ from draft guidance, if you take in to account the number of patients who require critical/allied medical services and the total duration of their stay, as there would be increased rupture AAA (if we do not offer treatment who are not fit for open; if we do not perform complex EVAR and also if the ruptures are predominantly treated by EVAR [because of not able to offer rupture EVAR service] and also because of poorer outcomes following open surgery due to reduced trainee exposure to Open in the current climate where more EVAR is performed). All this will lead to cost shifting from elective to emergency surgery and overall NOT good for the NHS.	The economic analysis that was undertaken to support the committee's decision-making took account of the categories of resource use to which you refer, where evidence was available (including length of stay, need for rehabilitation, costs and consequences of ruptures).
				Overall, we believe that the guidance is NOT appropriate and it is purely cost-centric and NOT patient-centric as NHS should be about providing right care to the patient based on patient preferences and choices.	It is NICE's statutory responsibility to consider the balance between the benefits and costs of competing approaches to healthcare, as it has in this case. For details of how the committee approached its responsibilities in respect of patient choice, please see Error! Reference source not found..

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				We sincerely hope the NICE team looks in to the all these factors before imposing death penalty for a lot of unfortunate patients who are not suitable for Open AAA repair.	On discussing stakeholder feedback on this issue, the committee agreed that, it would be valuable to generate new high-quality research in this area. They amended their recommendation to state that EVAR should only be offered in this population as part of an RCT comparing EVAR with no intervention, and made a new research recommendation noting that such a study would be helpful.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	General	General	We are deeply concerned that the proposed revised guidelines recommend the elimination of EVAR in the treatment of elective patients and restriction of complex EVAR to the setting of randomised control trials. As outlined in further detail below, the current NICE editing and then interpretation of the available international literature on this subject does not marry with our specialist knowledge and experience or with daily international practice. We are concerned that wholesale adoption of the current draft will result in the following adverse impacts: The identification of significant numbers of patients with AAAs (by the suggested more widespread application of screening in apparent risk groups – section 1 of the draft) who will have that fact brought to their attention only to be denied treatment (because they will be unable to access elective EVAR) is to cruelly impose anxiety for no purpose and represents a futile expense. The psychological impact of being turned down for repair and impact over what could be many years of living with an aneurysm are unknown and ignored in this draft guideline. The deleterious psychological effects of being diagnosed with an aneurysm have been reported (Bath et. al. Br J Surg 2018)	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**.

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				The rate of AAA rupture will rise as patients are refused surgery if they are not a "good risk" for open infra-renal AAA/Juxta-renal AAA repair.	The existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made aresearch recommendation noting that such a study would be helpful.
				The 30-day post-operative mortality for elective AAA repair will rise to pre QIP levels.	The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.
				A dramatic rise in open AAA repair will overwhelm ITU/HDU and ward facilities, ultimately resulting in longer waits for surgery and consequently a greater risk of pre-surgical aneurysm rupture. This is because in current practice, the majority of AAAs are repaired using EVAR techniques and most patients undergoing EVAR are managed without requiring ITU/HDU and with total hospital stays of a few days rather than a week or more.	For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**.

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				The limitation of EVAR to the setting of ruptured infra-renal AAA (a now relatively infrequent occurrence) disrupts the advantage of high volume routine elective surgery resulting in practiced surgeons and teams generating the best possible outcomes for emergencies. The little EVAR that will be sanctioned will therefore result in worse outcomes than is the case at present and the survival after RAAA will fall. Furthermore, given the rarity with which EVAR will be offered, it is unlikely that manufacturers will stock hospitals with a full range of devices – thereby ensuring that in practice open AAA repair once again becomes the only practical option. By these obvious mechanisms, the rate of AAA rupture will rise, and the associated mortality will rise also. As repeat RCTs to test the newer technologies and consequences of centralisation for elective infra-renal are unlikely to be planned, funded or to recruit, but NICE appears to reject any "lesser" evidence, there is a "Catch 22" which will ensure an absence or roll-back of clinical and technical progress in the management of aortic disease. If generalised, this manipulation will come to blight all similar technologically advancing surgical fields. In accordance with the "Duty of Candour", the unwritten outcome of the draft is that all patients who have had EVAR will have to be informed that they have received a treatment option that is no longer supported by NICE. Presumably a proportion will demand financial compensation and/or surgical redress. Acute NHS Trusts in England may seek financial redress to compensate for the tens of millions of pounds of capital	We hope some of your concerns will be allayed by the supplementary review of casemix-adjusted observational evidence that has been undertaken in response to stakeholder feedback. This shows that the committee's preference for randomised evidence is extremely well validated – see **Theme 2**, **Theme 6** and **Theme 9**.

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				investment, presumably now redundant in direct consequence of the current draft, that have been spent facilitating EVAR in consequence of the original NICE guidelines (TA 167, 2009). Either NICE will be seen as at variance with world professional opinion and discredited as an organisation and methodology, or those bodies that fund healthcare will seize upon the rationing opportunity that the draft embodies – in which case the malaise and its consequences will spread far beyond England. Overall, an identifiable subset of the population – retired men – will be singled out for disadvantage. The political consequences are unpredictable. In this regard, we note that we cannot find reference to any patient group involvement in the drafting of the current document. The removal of EVAR as a treatment option will be seen to be a violation of Key Principle 4 of the NHS constitution.	TA167 recommended EVAR as an option; it did not require vascular services to promote it as the predominant choice for AAA. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. As recorded in guideline documentation, the committee included 2 lay members who provided patient perspective and had equal status in all discussions and conclusions.
Guy's & St. Thomas' and King's College Hospitals - King's Health Partners Vascular Unit	Draft guideline	General	General	Emphasis should be placed on further centralising both complex open and endovascular aneurysm repair into experienced centres, incorporating multi-disciplinary teams, to optimise short- and long-term outcomes.	Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline.
Guy's & St. Thomas' and King's College Hospitals - King's Health	Draft guideline	General	General	This response represents the unanimous views of the Consultant Vascular Surgeons and Interventional Radiologists working in the 5 biggest London Vascular units, specifically those that have been providers of NAAASP screening. These units are represented by:	Thank you for the contextual information about your comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The

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Partners Vascular Unit				[This text was identified as confidential so has been removed.] The NVR database shows that these 5 units have submitted the following case-load between 1st January 2012 and 31st December 2017: Total Aortic Aneurysms (All anatomies, elective and emergency presenters, open and endovascular repair) 4903 with 333 deaths. Mortality rate 6.8% Total infra-renal AAAs (excluding complex EVARs) (All infra-renal cases, elective and emergency presenters, open and endovascular repair) 3105 with 176 deaths. Mortality rate 5.7% Total elective infra-renal AAAs (All elective infra-renal cases, elective presenters, open and endovascular repair) 2291 with 18 deaths. Mortality rate 0.8% We think that this is a considerable and current experience that lends weight and relevance to our concerns regarding the current NICE draft guideline: Abdominal aortic aneurysm, diagnosis and management, May 2018. It is our opinion that considerable revision is required.	recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**General comments** 1. The draft proposal is unsafe and dangerous to patients with aortic aneurysms. The proposal would prevent a cohort of patients with known aneurysms having any form of treatment until rupture occurs and necessitate another cohort being offered higher risk open repair with an increase in mortality, morbidity and consumption of healthcare resources, in	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				particular critical care beds. Overall, this will result in preventable premature death from ruptured aortic aneurysm in a population of patients whose pathology is actively looked for by a national screening programme thereby causing severe psychological stress until the terminal event occurs. 2. The committee have failed to consider that more deaths might have occurred in patients on the waiting list for OSR of AAA because they are more likely than EVAR patients to have their repair delayed because of a lack of critical care beds. In modern practice, critical care is rarely required for fit patients undergoing standard EVAR and consequently the procedure is rarely cancelled. 3. The committee estimate that 1% of patients with a 65mm AAA will rupture/die per month on the waiting list for their aneurysm repair. The NVR demonstrates that the mean AAA diameter for patients undergoing repair is currently 56-59mm which is associated with a significantly smaller monthly risk of rupture/death.	For discussion of the potential impact on quality of life of living with an untreated AAA, please see **Theme 13**. We are unable to find the data you have cited in the 2017 NVR. The **modal** aneurysm size is reported in that document as 5.5 to 6.4 cm; we estimate that the mean of the distribution is likely to be around 6.3 cm – quite close to the 6.5 cm in EVAR-1, from which we drew the estimate of 1% mortality per month. It should be remembered that the estimate used, here, defines all-cause mortality for this period, not merely AAA-related death. General population mortality is approximately 0.3% per month for a cohort of this age, to which is added not only the risk of rupture-related death but also some degree of additional background hazard to which this cohort is subject (doubtless owing to factors that are also associated with the development of AAAs). In this context, a monthly risk of death approaching 1% did not seem excessive to the committee.

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				4. The committee use the term 'average patient' in their conclusions. The committee should explain which groups of patients they consider are exceptional and fall outside 'average' as this is important to patients and clinicians. This group might include those with co-morbidities associated with an increased risk from OSR, a hostile operative field, where anticipated blood loss is high, or where OSR is not 'routine' and likely to be significantly more complex with correspondingly poor outcomes (patients requiring a supravisceral clamp, left visceral rotation, reno-visceral re-implantation or bypass, or a thoracoabdominal approach).	The committee considered carefully whether subgroups are likely to exist with combinations of risk factors – age, sex, AAA diameter – that represent a different balance of benefits, harms and costs from the average member of the cohort. They were unable to find plausible evidence that any such subgroups can be reliably identified – see **Theme 12**. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. However, the committee did not agree that it had seen any evidence that vascular anatomy alone is ever a reason for preferring EVAR over OSR. Most TAAAs are beyond the scope of this guideline (with the exception of extent IV, with regard to which no specific evidence was identified).
				5. With regards follow-up of patients after EVAR, routine CT is by and large not used in the UK. As yet contrast-enhanced USS is not established practice in the UK and as such there will be gaps in the skills, equipment and supply if its widespread introduction is recommended without strong evidence. It is thought to be important to distinguish type 1 from type 2 endoleaks but most of the latter are monitored with Duplex USS both for detection and growth and it is on the basis of growth that re-intervention is planned. There are studies supporting the use of Duplex USS for both endoleak detection and size monitoring. A more graduated approach to contrast-enhanced USS could be taken and there should	In its dedicated review on the topic of imaging modality for post-EVAR surveillance, the committee agreed the evidence shows that duplex ultrasound has insufficient sensitivity to be used as the primary screening tool for endoleaks – see **Theme 11**.

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				continue to be a role for duplex USS based on radiation-safety and pragmatism. 6. We have significant concerns about the binary nature of decision-making based on a person's fitness at a given moment being the major determinant of whether treatment with EVAR is permissible. For young men with a life-expectancy measured in decades a preference for OSR seems sensible (even though our screening programme is 60% OSR vs. 40% EVAR in 65 year old men). Some men are fit for OSR but one would expect them to be at more than average risk from OSR due to their co-existing conditions. There are survival advantages for EVAR during the first 7 years and so there would be good grounds to offer it to those patients with above average predicted mortality and morbidity from OSR and a life-expectancy beyond 7 years.	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). It is not clear whence you derive the assertion that there are survival advantages for EVAR during the first 7 postoperative years. We speculate it may reflect piecewise survival results from the EVAR-1 RCT, which demonstrate a significant survival advantage for OSR after 8 years. However, we do not agree that the difference in long-term survival among people undergoing EVAR or OSR only emerges after 8 years. Our research suggests that the data are extremely well modelled using a parsimonious approach of assuming a proportional hazard at all times following the perioperative period – see relevant comments in **Theme 9a**. The post-perioperative survival data identified in our review of casemix-adjusted observational evidence covers follow-up periods ranging from 4 to 7 years. This duration of follow-up is easily sufficient to show a meaningful difference in hazard of death favouring OSR. There was little evidence of divergence from proportional hazards in any of the included studies.

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					In the economic modelling that was undertaken to support guideline development, we explored scenarios in which people with lower life expectancy were simulated (see ' Post-perioperative mortality – identifying a less healthy population' in HE.3.1.1.4 and HE 3.1.2.4 [pre-consultation results], HE.9.1.1.4 and HE. 9.2.1.4 [post-consultation results]). In these analyses, it is necessary to specify an extremely high increased hazard of death for the population – in the order of 15 times that faced by the age-matched general population – before any results predict net QALY gain for people receiving EVAR. However, even under this scenario, the small amount of net benefit with which EVAR is associated comes at a cost tha could not be considered a reasonable use of NHS resources. Part of the reason for this is that any individual's survival prospects are notoriously difficult to predict – Henderson and Keiding (2005) provide a sobering summary. If clinicians are very skilled, they may be able to identify a population of people with a **mean** life expectancy of 7 years, but such a population would include many people who live substantially longer than that and, even if we restrict the excess mortality of EVAR to the post-8-year phase, enough people will live to accrue those benefits to offset the initial risk of OSR. On the other hand, we may try to identify a population in which a negligible proportion of people can expect to live beyond 7 years but, if we do that, we will end up with a population with a mean life expectation of only 2–3 years. In such a population, the balance of benefits, harms and costs is likely to favour no intervention.

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				7. Patients with infrarenal and complex AAA and a hostile operative field for OSR (defined by NHSE as previous abdominal pathology which is likely to have led to adhesions, or other factors which would make operative dissection difficult or predispose to significant blood loss) should be considered as a sub-group for EVAR as they have a higher risk of damage to adjacent structures and increased blood loss resulting in increased mortality and morbidity. Patients on dual antiplatelet therapy (after a recent percutaneous coronary stent or acute coronary syndrome) or long-term anticoagulation (for venous thromboembolic disease or prosthetic cardiac valve replacement) will be at increased risk of significant blood loss with OSR and should also be considered as a sub-group for EVAR. A reasonable body of vascular surgeons would concur with this advice.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**Management of infrarenal AAA** 1. The incidence of further interventions should be assessed according to the implantation and anatomy of the aneurysm, namely off-IFU or on-IFU use. There is considerable evidence that off-IFU implantation of infrarenal endografts is associated with significantly worse durability. NICE should recommend that elective infrarenal EVAR is only performed on-IFU and mechanisms are put in place to ensure this is occurs. 2. NICE have failed to consider the direct clinical and cost impact of the immediate and sustained increase in critical care beds which the NHS must provide for patients with	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. As noted in **Theme 7**, we are aware of contradictory evidence regarding whether complex EVAR – including off-IFU implantation of infrarenal grafts – is associated with a higher rate of reintervention. However, the recommendations in this guidance do not provide a mandate for any such procedures.

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				asymptomatic and acute symptomatic AAA who will require OSR instead of EVAR. This will have an indirect impact on the provision of critical care for other patients with other conditions.	
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**Patient preference** The committee claim that there are no publications assessing patient preference for the method of aortic aneurysm repair. Two publications from the UK have demonstrated an overwhelming patient preference for EVAR and this is consistent with the current status in the UK (Winterborn *et al*, Reise *et al*). **References** 1. Winterborn RJ, Amin I, Lyratzopoulos G, Walker N, Varty K, Campbell WB. Preferences for endovascular (EVAR) or open surgical repair among patients with abdominal aortic aneurysms under surveillance. J Vasc Surg. 2009;49:576-581. 2. Reise JA, Sheldon H, Earnshaw J, Naylor AR, Dick F, Powell JT, Greenhalgh RM. Patient preference for surgical method of abdominal aortic aneurysm repair: postal survey. Eur J Vasc Endovasc Surg. 2010;39:55-61.	Thank you for drawing this evidence to our attention. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**AAA screening** There is a recommendation to opportunistically screen women who are a) current or ex-smokers, b) of European descent (not Asian or Afro carribean women), c) have IHD, CVD, PVD, elevated lipids and hypertension, and d) those with a family history of AAA. The evidence for a cost-effective opportunistic screening programme as suggested is not strong and does not compare to the rigour of the MASS study. In our screening programme we screen 10,000 men aged 65 per annum. If, as suggested, we screen all the women who came into contact	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of

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				with healthcare who were between 70 and perhaps 80 years of age, then the 'at risk' group would be in the region of 90,000 women. The logistics of adding this to a clinical service are very challenging and it is unlikely that Public Health England would support running this through the National AAA Screening Programme. Furthermore, the guidance does not appear to be consistent with a recent report from Sweden (Johansson *et al*) suggesting that screening for AAA may cause more harm than benefit. **Reference** Johansson M, *et al*. Benefits and harms of screening men for abdominal aortic aneurysm in Sweden: a registry-based cohort study. Lancet 2018;391:2441-7.	AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. They also agreed that the recommendation was made at 'consider' level to ensure sufficient flexibility in decision making. The committee noted that, currently, women with AAA are not referred to the NHS AAA Screening programme. Thus there would be no additional burden to the programme.
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**Repair of complex abdominal aortic aneurysms** 1. The guideline committee admits that the assessment of complex EVAR was exploratory and validated by the expert panel who thought it was reasonable. This assessment was based on limited evidence (one non-randomised comparative study) and implicit assumptions extrapolated from treatment of infrarenal AAA. 2. Complex AAA are a heterogenous group of pathologies for which the physiological insult and risk of morbidity and mortality associated with OSR increases as the aneurysm complexity increases and the aortic clamp level moves from infrarenal to suprarenal to supramesenteric/supracoeliac. Despite this, the committee state that OSR is not made significantly more complicated (compared to infrarenal AAA) by the presence of a complex aneurysm. The majority of cardiovascular surgeons in the UK would disagree with this	This is an accurate summary. However, the committee saw a supplementary review containing a more extensive range of casemix-adjusted nonrandomised evidence in response to stakeholder feedback (see below) The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. The committee do not state that OSR is not made significantly more complicated by the presence of a complex aneurysm; they say that

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				statement. Assessment of complex AAA as a single entity is inappropriate.	*anatomical complexity is less problematic for open repair, during which a surgeon can tailor the graft to suit the anatomy during the procedure, and that this is not typically possible with EVAR, for which custom devices are built in advance of the procedure.* Naturally, the committee accepted that, with both OSR and EVAR, most complex AAAs are inherently more complicated than most infrarenal ones, and are associated with a higher degree of perioperative risk. For this reason, the committee thought it was reasonable to assume the same relative effect in perioperative mortality applied in infrarenal and complex cases, albeit at a higher absolute level of risk in the latter case.
				3. The only evidence presented for the assessment of complex EVAR is a low quality non-randomised comparative study describing 30-day outcomes in a small cohort of patients with primary JRAAA. Exclusions were suprarenal/extent IV TAAA requiring supramesenteric/supracoeliac clamping and sub-groups with JRAAA and a hostile operative field for OSR (failed EVAR with type Ia endoleaks, failed OR with proximal para-anastomotic aneurysms, and inflammatory and mycotic aneurysms).	On reviewing stakeholder feedback, the committee accepted that it had been too stringent in only looking at prospective observational evidence (of which Donas et al., 2012, is the only published example). Therefore, a much broader evidence base was reviewed as part of the committee's post-consultation considerations. This comprises all casemix-adjusted observational evidence, including 9 studies looking at the relative benefits, harms and/or costs of complex EVAR compared with OSR.
				The NHSE Clinical Commissioning Policy (NHSCB/A04/P/a) has advised that complex EVAR should be considered in patients with a hostile operative field defined as previous abdominal pathology which is likely to have led to adhesions, or other factors which would make operative dissection difficult or predispose to significant blood loss. The vast majority of vascular and cardiothoracic aortic surgeons in the UK and	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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				abroad would agree with this advice. NICE should demonstrate support for the NHSE recommendation that EVAR (standard and complex) can be considered where there are technical or surgical issues (as described by NHSE and in the publication which NICE have used as their evidence) which would put a patient at higher risk of mortality and morbidity from OSR. 4. The committee make an assumption that patients wait four months for complex EVAR devices. For patients with large AAA, complex EVAR devices are delivered within 4-6 weeks at the clinician's request. In addition, chimney EVAR (which is CE-marked and can be implanted according to IFU) can be performed with no delay for manufacture. The committee should re-consider their modelling assumptions in light of this evidence. 5. The committee make an assumption that the 30-day mortality of 3.6% for complex EVAR is consistent with the experience of the guideline development committee. Over the 5-year period ending December 2017, the 30-day mortality in our institution for complex EVAR (for complex AAA and TAAA) was approximately 1% which represents an OR of 0.1 compared to the estimated mortality for complex OSR which the committee have accepted as representative of UK practice. Contemporary data from at least two other high-volume complex EVAR centres in England demonstrate similar 30-day mortality rates for complex AAA. NHSE have previously recommended that complex EVAR should be performed in high-volume specialist complex EVAR centres where such low 30-day mortality rates (with OR 0.09 compared to OSR) will translate into a significant long-term	The committee agreed that this is a fair point. We have revised our base case to reflect the fact that not all complex AAAs require a custom-made graft: instead of a 2-month additional wait for complex EVAR, we now assume a 1-month delay. This is consistent with data from the 2017 NVR (42% of cases waiting 67 days, implying a mean expected delay of 28 days across all cases). In order to provide guidance for the NHS, the analyses used to support decision-making must provide the best possible estimate of the average results that would be expected across the system. The committee agreed that – though it has no faith at all in the NVR's ability to estimate a **relative** difference between EVAR and OSR using unadjusted data – the **absolute** level of mortality seen in the complex EVAR cohort provides a relevant reflection of current practice (this is a proper use of registry data; see **Theme 2**). Thank you for giving us details of your experience; please see **Theme 3c**. It may be relevant to note that most thoracoabdominal aortic aneurysms are beyond the scope of this guideline. It is unclear how you have derived the OR of 0.09 you cite. None of the casemix-adjusted evidence we have

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				survival advantage as clearly demonstrated by the survival curves in Figure HE18. NICE should demonstrate support for the NHSE recommendations to centralise complex EVAR in high-volume specialist centres.	now reviewed estimates an effect approaching this magnitude; in fact, it is not clear that EVAR provides any benefit in this evidence (see **Theme 4**). However, even if we assume 1% EVAR mortality and 10% for OSR (which we think may be your suggestion), the ICER for complex EVAR remain above £20,000/QALY in a model that makes multiple other assumptions that are optimistic about EVAR. Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline.
				6. The draft document estimates the mortality from OSR of complex AAA by using the NVR mortality for EVAR as baseline and employing a factor (0.33) from the Cochrane Collaboration Review of RCTs for EVAR versus OSR for infrarenal AAA. The 3.6% mortality for complex EVAR subjected to this factor estimates the mortality from OSR to be 10.1%. The committee implicitly assume that the relative mortality of EVAR compared with OSR for infrarenal AAA is transferrable to complex AAA patients in the setting of an RCT but provide no evidence to support this. In order to determine the effect of randomisation in a trial, a comparative study was undertaken by the Liverpool group (Canavatit *et al*) examining a heterogenous group of patients with complex AAA who were unsuitable for infrarenal EVAR according to the device IFU. Almost 40% of patients had a short-necked infrarenal AAA requiring an infrarenal clamp which the committee describe as 'routine for open surgery'. The proportion of patients requiring a supramesenteric/supracoeliac clamp was 7%. The mortality for complex OSR was 9.2% and for FEVAR was 3.7%, almost identical to the NVR mortality used by NICE. The risk-adjusted	This is an accurate summary of the methods used in the consultation draft. If there was evidence to show what the results of an RCT in complex AAA would be – for instance, an RCT in complex AAA – it would not be necessary to use such approximations. The review of casemix-adjusted observational evidence we have now undertaken suggests that using these data is very likely to overstate the benefits of EVAR; indeed, there is no evidence that EVAR is associated with any perioperative survival benefit in these studies. See **Theme 4b**. Canavati et al.'s study (2013) was excluded from the review because it does not use any valid methods to adjust for differences between the fEVAR and OSR cohorts – noting that the patients undergoing OSR had significantly larger AAAs and were significantly more likely to be women, both of which are known risk factors for perioperative mortality. Comparing observed outcomes to those predicted by a risk-scoring

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				mortality for the FEVAR cohort, if they had undergone OSR within an RCT, was 13.1% (OR 0.28). This UK study suggest that the estimated mortality reached by extrapolating RCT outcomes for infrarenal AAA may be a gross underestimate in the setting of an RCT of complex AAA. It is generally accepted that the absolute benefits of a minimally invasive treatment are proportionally greater as the risk of the maximally invasive comparator increases. This point is demonstrated in its most extreme form for extent I-III/V TAAA repair (which is not part of the NICE guidance) where the mortality for 128 patients undergoing OSR in the UK in the 6-years ending 2013 was 22.7% (Bottle *et al*) and for 59 patients undergoing OSR in Scotland over a decade ending 2011 was 18% (Chalmers *et al*). In the 5-year period ending December 2017, there was no 30-day mortality in our institution for elective complex EVAR for extent I-III/V TAAA. 7. The committee have provided no evidence for the patients suprarenal/extent IV thoracoabdominal aortic aneurysm (TAAA) requiring a supramesenteric/supracoeliac clamp. These aneurysms have more in common with extent I-III/V TAAA with regard to the complexity of repair, physiological insult and the relative volume of procedures and consequently, should be considered separately from JRAAA requiring only a suprarenal clamp: indeed the care of patients with these aneurysms is centralised in the Scottish National TAAA Service. It is not appropriate to extrapolate what evidence is available from infrarenal AAA repair to the management of this type of aneurysm. Our institution receives referrals for complex aneurysm repair from a significant proportion of the English population and over the 5-year period ending 2017, the estimated incidence of complex EVAR for this type of	system that is known to have poor predictive validity (see Evidence review H) is not a adequate substitute for methods that seek to control for confounding of treatment effect. As you note, type I–III/V TAAAs are outside the scope of this guideline. The only evidence identified including type IV TAAAs in our review is in the comparative cohort study reported by Michel et al. (2015, 2018), which includes a proportion of participants with 'infradiaphragmatic AAA'. The authors do not provide casemix-adjusted outcomes disaggregating this population from other AAAs, though we note that there was no difference in perioperative mortality between EVAR and OSR in a propensity-score matched analysis of the whole population. Cost-effectiveness results in the same study suggest TEVAR is dominated by OSR (that is, it both costs more and results in more deaths); however, this analysis was not casemix-adjusted.

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				aneurysm was 1.2 patients per million population per annum, a figure which is almost identical to data from the National TAAA Service in Scotland. This represents a very rare disease. Furthermore, an expert multidisciplinary consensus group from every high-volume UK aortic centre used the RAND appropriateness technique to demonstrate no clinical equipoise for treatment of suprarenal/extent IV TAAA with consensus in favour of FEVAR in patients with > 60 mm diameter aneurysms who were at low/mild/moderate risk (defined as < 5%, 5-10%, > 10% mortality, respectively) for OSR (Cross *et al*). An RCT in this sub-group of complex AAA would be unethical and undeliverable. 8. NICE have estimated the mortality for complex OSR to be approximately 8- to 9-fold higher than OSR for infrarenal AAA which would also translate into a significantly higher rate of major fatal and non-fatal adverse events, the treatment of which will consumed significantly more healthcare resources (planned and unplanned level 2 and 3 critical care, unplanned re-operation, increased blood transfusion requirement, etc.). Despite this, the committee have made an assumption that the cost of the complex OSR procedure and the peri-operative care is the same as for infrarenal AAA. For a model of OSR for AAA which is associated with a 10% 30-day mortality, Manecke *et al* demonstrate that major peri-operative complications will occur in 20% of patients who will have a 3-fold increased mortality, 2.5-fold increase in bed occupancy, and a 2.5-fold increase in costs compared to patients with no major complications. The 20% cohort with major complications increases the overall cost of the OSR cohort by almost 30% and the difference in cost for OSR with 1% mortality and 10% mortality is 2.8-fold. This assumption is particularly concerning	On reviewing stakeholder comments including this one, the committee agreed that its decision-making would benefit from additional exploration of perioperative costs related to complex AAA repair – both EVAR and OSR. Therefore, potentially relevant evidence on intraoperative and postoperative resource-use, including registry data and observational publications, was reviewed and its impact on cost–utility results explored (see **Theme 5** and **Theme 6**, respectively). We also accounted for the need for rehabilitation (see **Theme 6b**). The assumptions that were made in revising the HE model all favoured EVAR, some to a degree that the committee considered unrealistic – for example, using unadjusted length-of-stay data from the NVR when it reflects a small number of highly selected OSR cases that are almost certain to be disproportionately complex (probably including a disproportionate number of thoracoabdominal cases).

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				when one considers OSR for suprarenal/extent IV TAAA. Service Level Reporting from the Liverpool Heart and Chest Hospital (the highest volume complex open aortic centre in the UK) demonstrated that the cost of this procedure in 2012 was £27,111 (personal communication: Prof. Aung Oo, Professor of Cardiac Surgery, St Bartholomew's Heart Centre, London) which equates to £31,046 in 2018 prices. In 2007, data from NHS Scotland for the National TAAA Service demonstrated that the estimated crude cost per case for an open TAAA procedure (excluding pre-operative assessment and care during follow-up) was £32,115 using English reference costs. In 2016/17, the cost of an open TAAA procedure alone in the Scottish TAAA service was £31,000 (regardless of extent of repair) and this did not include the annual cost of delivering the service (total cost £1.2 million to treat 25-30 patients per annum) which would have increased the cost to over £45,000 per procedure. Approximately 60% of repairs in the Scottish TAAA service are for suprarenal/extent IV TAAA. NICE should make a more accurate assessment of cost of complex OSR as their assumption that the increased morbidity and mortality is cost neutral is not credible.	The result of these revisions was to increase our estimate of costs for a primary complex OSR procedure by around 50% – from £10,662 (see table HE52) to £15,705 (see table HE113), while our estimate for complex EVAR did not meaningfully change (rising by <1%). Even though the committee agreed that the analysis was optimistic for EVAR, it did not result in an ICER, compared with OSR, that could be considered to represent an effective use of NHS resources. These data represent the best-available evidence-based estimate of the **average** cost of EVAR and OSR for complex AAAs. However, because complex AAA is a heterogeneous category (see **Theme 10**), there will inevitably be a broad range of costs associated with more and less intricate procedures. Anecdotal evidence as to the expenses incurred with OSR in the most complex cases does not – in the absence of any counterfactual data regarding the costs of EVAR in directly analogous cases – help us to understand what the incremental costs associated with the approaches might be. Most TAAAs are beyond the scope of this guideline. Where type IV TAAAs (which are in scope) are concerned, we note Michel et al.'s finding (2016, 2018) that EVAR is associated with significantly higher costs than OSR – in excess of €20,000 greater hospital costs over the first 2 years. There was a similar finding in participants with s.
				8. The cost of complex EVAR estimated by the committee is inaccurate. Service Level Reporting in our Trust has demonstrated that the mean cost of the procedure and peri-operative care for patients undergoing fenestrated EVAR for	We have difficulty reconciling your estimate with evidence from elsewhere: our calculations suggest that the cost of theatre time alone amounts to very nearly £3,000 per procedure for any AAA. In a recently published cost–utility

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				complex AAA is £2693 (excluding the cost of the device). The committee have also made an assumption that it costs more for a bed on the vascular ward for a patient after complex EVAR than after OSR or standard EVAR. There is no evidence for this assumption and it is not the case in our institution. Using the cost of the device ascertained by the panel, the total cost of the procedure and peri-operative care is £18379: the committee have estimated the cost to be £4204 (23%) higher. NICE should consider employing a more accurate approach (perhaps using HES data) to the contemporary costings of complex EVAR (which they have overestimated) and complex OSR (which they have underestimated).	analysis, Ciani et al. (2018) calculated procedure costs for a fEVAR of £27,658 (somewhat higher than our estimate) and £13,529 for an analogous OSR proecure (somewhat lower than our estimate). We agree that it was not appropriate to assume different vascular bed costs for people following OSR and EVAR; we have revised this assumption in our updated analysis.
				9. The committee should be aware that, in specialist aortic centres, patients undergoing OSR for suprarenal/extent IV TAAA are followed up with annual CT scan due to the long-term risk of progressive aneurysm formation above the open surgical repair.	Information noted. Adding the cost of an annual CT to our model of the heterogeneous complex AAA population (and doing the same for EVAR, rather than ssuming surveillance stops at 5 years) does not have a material effect on outputs: the ICER reduces from £53,215 to £48,266.
				10. The committee should not consider life-threatening graft-related re-intervention as equal to emergency OSR as in real world practice it is not possible to explant a complex EVAR device. In reality, any such circumstances are managed by further endovascular intervention in the form of angioplasty or stent-grafting of the target vessels or proximal or distal EVAR extension pieces.	The committee agreed that revisions to the model were indicated, in this area. Please see **Theme 8a**.
				11. NICE claims that no device exists for complex EVAR which can be implanted on IFU. The Medtronic Endurant device is CE-marked and has an IFU to be used with a maximum of two chimney stent-grafts. Use of this device	There are no comparative data on the safety and effectiveness of chEVAR, which makes it impossible to arrive at an evidence-based conclusion as to its cost effectiveness.

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				should be considered in the analysis of complex EVAR as the cost of the procedure would be equivalent to the cost of standard EVAR plus two balloon expandable stent-grafts (estimated at £1000).	We present sensitivity analysis on graft cost in our model results (see figure HE59, HE60 and HE61 in the consultation draft, and updated equivalents in figures HE133, HE134, HE135 and HE136). If it were safe to assume that chEVAR has exactly average results for all complex AAAs, then it might be possible, using evidence like this, to infer a graft cost at which chEVAR could be considered reasonable value for money.
				12. The committee state that cases in the NVR recorded as "complex OSR" may be inherently *more complex* than the EVAR cases recorded as "complex" because OSR is not made significantly more complicated by the presence of a complex aneurysm. This is an incoherent statement as on the one hand they suggest that surgeons are putting more complex AAA in the complex OSR section of the NVR but state that a complex AAA does not make the OSR more complicated. On the contrary, the majority of practicing aortic surgeons would agree that a complex AAA requiring left visceral rotation and supravisceral clamping is more difficult to repair than a short-necked infrarenal AAA.	This is not the committee's argument. Their contention is that OSR cases will only get recorded as complex in the NVR if they are at the higher-risk end of the spectrum, whereas complex EVAR cases include a more benign range of anatomies. It is precisely their point that a complex AAA requiring left visceral rotation and supravisceral clamping will get reported as a complex OSR in the NVR, whereas a short-necked infrarenal OSR will not, though an equivalent EVAR may. This will lead to an exaggerated discrepancy between the 2. This is a secondary point, in any case: the main issue with NVR data for complex AAA is that they reflect selection practices that result in substantial asymmetry of risk between open and endovascular cases – see **Theme 4a**.
				13. The committee consider that procedure complexity of complex EVAR is likely to be influenced more than OSR by the presence of a complex aneurysm and consider it likely that an equivalent odds ratio from RCTs in complex aneurysms would be higher than the base-case figure of 0.33, rather than lower. As previously stated, in ours and other centres, complex EVAR can be delivered with a 30-day mortality in the region of 1% which represents an OR of 0.1 compared to OSR	The review of casemix-adjusted observational evidence we have now undertaken strongly supports the committee's intuition that generalising from the infrarenal to complex setting is very likely to overstate the benefits of EVAR; indeed, there is no evidence that EVAR is associated with any perioperative survival benefit in these studies. See **Theme 4b**.

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				in the NICE model. This represents the outcome of complex EVAR for patients who are suitable and unsuitable for OSR. In an RCT, patients would only be randomised if they were suitable for both interventions and so it is unlikely that the OR of 0.1 would change in specialist complex EVAR centres. The significant difference in early mortality (10-fold if the expert panel's estimate for OSR was used as an evidence-base compared with the outcome for complex EVAR in specialist complex EVAR centres) might have a significant negative impact on the probability of obtaining funding for an RCT and subsequently recruiting patients. 14. In conclusion, the 30-day mortality for complex EVAR in a specialist complex EVAR centre such as ours is in the region of 1% for all extent of complex aneurysms representing an odds ratio of approximately 0.1 compared with OSR in the NICE model. The cost of complex OSR used in the model has been underestimated for a procedure with such a high morbidity and mortality and there is evidence that the cost may exceed complex EVAR for patients requiring supravisceral clamping. The cost of complex EVAR used in the model has been overestimated. By using outcome data from specialist centres and more accurate costings in the model, there is a higher probability that complex EVAR will be cost-effective for a significant proportion of patients. NICE should support NHSE by recommending centralisation of complex EVAR services to deliver clinically effective care which will translate into cost-effective care for a lot of patients with complex aneurysms. 15. NICE have recommended that patients suitable for OSR and complex EVAR should be assessed in an RCT. This	The derivation of an odds ratio of 0.1 remains unclear and inconsistent with any evidence of which we are aware (see above). As noted above, we have revised our cost estimates for complex OSR to address some of the concerns you and other stakeholders have raised. We see no evidence that our estimate of the costs of complex EVAR is an overestimate – it is somewhat lower than equivalent numbers in the published literature (Michel et al., 2016 & 2018; Ciani et al., 2018). Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of

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				would be unethical in patients where there are surgical and technical reasons to favour an endovascular approach and those with aneurysms requiring a supramesenteric/supracoeliac clamp to perform OSR. This may have been possible in patients with primary short-necked infrarenal AAA and primary JRAAA which can be treated with OSR and an aortic clamp below the mesenteric vessels if it were not for the fact that a recent NIHR HTA call for research resulted in funding being awarded for a prospective registry to provide data to guide the use of complex EVAR for JRAAA in the UK. **References** 1. Canavati R, Millen A, Brennan J, Fisher RK, McWilliams RG, Naik JB, Vallabhaneni SR. Comparison of fenestrated endovascular and open repair of abdominal aortic aneurysms not suitable for standard endovascular repair. J Vasc Surg. 2013 Feb;57(2):362-7. 2. Bottle A, Mariscalco G, Shaw MA, *et al*. on behalf of the UK Aortic Forum. Unwarranted Variation in the Quality of Care for Patients with Diseases of the Thoracic Aorta. J Am Heart Assoc 2017 Mar 14;6(3). pii: e004913. doi: 10.1161/JAHA.116.004913. 3. Chalmers RTA, Nimmo AF. Scottish National TAAA Service: 10 year review paper http://www.taaareview.scot.nhs.uk/wp-content/uploads/2012/01/2012-03-16-TAAA-12-03-10-year-review-paper.pdf 4. Review of Thoraco-Abdominal Aortic Aneurysm Services within NHS Scotland: National Services Division, October 2007.	the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				http://www.nsd.scot.nhs.uk/publications/Servicereviews/Review%20of%20Thoraco-Abdominal%20Aortic%20Aneurysm%20Services%202007.pdf 5. Cross J, Raine R, Harris P, Richards T; FEVAR Consensus Working Group of the British Society of Endovascular Therapy. Indications for fenestrated endovascular aneurysm repair. Br J Surg. 2012;99:217-24. 6. Manecke GR, Asemota A, Michard F. Tackling the economic burden of postsurgical complications: would perioperative goal-directed fluid therapy help? Critical Care 2014;18:566.	
University Hospitals Birmingham & Heart of England Hospitals	Draft guideline	General	General	**Emergency treatment of AAA** 1. NICE recommend an EVAR-first approach to ruptured infrarenal AAA. While they make a passing reference to this, they have failed to grasp the profound problem which occurs by advocating cessation of any elective infrarenal EVAR practice in the UK. In the draft document, NICE provide no guidance as to how patients in England with ruptured AAA are going to receive safe level 1 evidence care if clinicians are unable to maintain skills and teach the next generation of specialists to continue to offer this treatment. 2. The committee has not followed their scoping document by failing to provide specific advice on patients with acute symptomatic aneurysms (infrarenal and complex) at high-risk of rupture which were to be assessed alongside rupture. The guidance on transfer and peri-operative management refer to this group of patients acknowledging the complexity of management but then fall short by failing to make a statement on their definitive repair. Elsewhere in the guidance, a statement is made to the effect that it was the opinion of the	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of

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				committee that this scenario was no different from elective cases - even though all of the RCTs have been in elective asymptomatic AAA. It is well recognised by the cardiovascular community that the mortality and morbidity in patients with acute unruptured aneurysms is significantly higher than elective repair as a) treatment is required urgently to prevent rupture and there is generally insufficient time to fully assess and medically optimise these patients, and b) the risk:benefit assessment shifts in favour of repair to save life in higher risk patients who might not have been candidates for elective repair,. This approach from NICE puts the clinician in the perverse situation of not being able to consider EVAR to treat a patient at high-risk of impending rupture until frank rupture occurs. 3. Despite providing no evidence, NICE has made recommendations on the use of complex EVAR in ruptured AAA and the requirement for an RCT in patients suitable for OSR. No mention is made about patients with ruptured complex AAA who are unsuitable for OSR. The committee consider complex EVAR in such emergency situations as speculative. However, high-volume aortic centres such as ours have reported world-class outcomes (with 1-year survival rates in excess of 70%) in haemodynamically stable patients treated with complex EVAR where OSR was not possible and no treatment would have been universally fatal (Mascoli *et al*). The committee should consider supporting specialist centres delivering such innovative treatment for a group of patients	the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases. The paper you cite deals with TAAAs, which are mostly beyond the scope of this guideline.

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				who would traditionally would have had no chance of surviving. **Reference** Mascoli C, Vezzosi M, Koutsoumpelis A, *et al*. Endovascular repair of acute thoraco-abdominal aortic aneurysms. Eur J Vasc Endovasc Surg. 2018;55:92-100.	
Cook Medical	Draft guideline	General	General	Cook Medical is a manufacturer of infrarenal and complex endovascular grafts used to treat abdominal aortic aneurysms. Cook Medical is a member of ABHI (Association of British HealthTech Industries Ltd.) and supports the comments in the ABHI submission. We appreciate that NICE invites organisations to comment on their draft recommendations. Our feedback focuses on the recommendations for elective repair (1.5.2-1.5.6) as these recommendations, if implemented, would impact the utilisation of endovascular grafts significantly. Most of our comments reference the health economics appendix. Key concluding comments for each section are in italics. NICE guidance aims to be "based on the best available evidence of what works, and what it costs". However, important inputs into the existing economic models do not appear to reflect current practice / the latest clinical evidence. We strongly believe that the assumptions being used in the economic models need to be thoroughly reviewed and the model associated recommendations adjusted accordingly. In summary, we have serious concerns about the following base case economic model inputs:	Thank you for your introductory comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. All inputs to the original HE model developed to support the committee's decision-making have been reviewed in the light of stakeholder feedback, with substantive revisions in several areas. Additional published evidence on the relative safety and effectiveness of EVAR and OSR has been reviewed, with the goal – among other things – of exploring the validity of model inputs. We respond to each of your detailed comments below.

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				Peri-operative mortality for OSR - for infrarenal (1.3% is too low) and complex (is uncertain) Peri-operative mortality for EVAR in patients where OSR is not suitable - for infrarenal (7.3% is too high) and complex (41% is too high) Post-operative mortality and reintervention rates for EVAR (too high) Waiting time mortality (too high for all but particularly complex EVAR) ALOS and theatre time for EVAR (too high) Unit bed price (too low) If the models were amended to reflect current data, it is likely that that the recommendations to not offer EVAR to unruptured AAAs would be amended. We believe that further research and guidance on patient selection (i.e., who is likely to benefit most from EVAR and who is likely to benefit most from OSR) and the appropriate monitoring / management of complications would be of most use to patients and clinicians.	
Association of British HealthTech Industries (ABHI)	Draft guideline	General	General	**Introduction and Contents** ABHI and its members would like to thank NICE for the opportunity to comment on this draft guideline. We are happy for any information contained within our response to be in the public domain. For the purpose of this consultation response, four device companies have developed an in-depth appraisal of the guideline appendices and the economic model assumptions; Medtronic, W.L Gore, Cook Medical and Terumo Aortic.	Thank you for your introductory comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. All inputs to the original HE model developed to support the committee's decision-making have been reviewed in the light

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				We first focus on the economic appendix and respective economic models. While we acknowledge the substantial amount of work that has been spent on the guideline development, we believe that many model assumptions are either inappropriate or need to be treated with a higher degree of uncertainty compared to the present state. Based on preliminary internal calculations, we believe that changing several key assumptions would result in actual changes in all of the economic models (elective-infrarenal [unruptured], elective-complex [unruptured], and emergency-infrarenal [ruptured]) and, consequently, in the related guideline. Most importantly for the elective infrarenal indication, there is significant concern that the committee's conclusion that EVAR is dominated by OSR is incorrect. Our internal calculations suggest that addressing the outlined concerns would rather lead EVAR being cost-effective, and possibly even dominant compared to OSR. Economic model for Unruptured Infra-renal AAA (Comments 2 – 6) Economic model for Unruptured Complex AAA (Comments 7 – 10) Economic model for Ruptured Infrarenal AAA (Comments 11) Economic model for Ruptured Complex AAA (Comment 12) The response then addresses other concerns and provides recommendations for the committee in relation to the following aspects of the draft guidance: Clinical judgement on an individual patient basis (Comment 13) Patient Choice (Comment 14)	of stakeholder feedback, with substantive revisions in several areas. Additional published evidence on the relative safety and effectiveness of EVAR and OSR has been reviewed, with the goal – among other things – of exploring the validity of model inputs. We respond to each of your detailed comments below.

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				Improvement in EVAR devices over time (Comments 15 – 17) Improvement in surgical technique over time (Comment 18) Improvement in device deployment over time (Comment 19) Impact on NHS capacity (Comment 20 - 21) Consideration of poor peri-procedural outcomes for women (Comment 22) Absence of guidance for acute symptomatic AAA (Comment 23) Patients turned down for treatment (Comment 24) Complex EVAR (Comments 25 – 26) References (Comment 27) As outlined in the response, we strongly believe there are many sources of data and evidence available that have not been considered by NICE for the development of this new clinical guideline. We feel that the heavy focus on outdated randomised clinical trials has led the committee to draw inaccurate conclusions and we urge NICE to consider the wide range of observational studies and registries available that back up our recommendations. We are aware of many clinical guidelines and technology appraisals that have used data other than RCTs to heavily inform the decision process and passionately recommend that, in this circumstance, inclusion of the evidence listed throughout this response is in the very best interest of NICE, the patients and the NHS.	
Association of British HealthTech Industries (ABHI)	Draft guideline	General	General	**The updated Guidance does not account for significant impact on increased capacity needed due to increased length of stay, increase in theatre time, training and availability of staff and associated infrastructure resources.**	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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				In March 2018, the Vascular Society of Great Britain and Ireland published the Vascular Surgery GIRFT Programme National Specialty Report 2018 (Horrocks, 2018). The report sets out recommendations to improve the way vascular surgery is organised and delivered in the NHS in England. Central goals include enabling patients to receive urgent surgery sooner, reducing length of stay and readmissions, reducing theatre time, availability of beds, training and availability of staff and data collection. The following recommendations and comments were provided in relation to AAA EVAR Repair: "Average wait times for elective abdominal aortic aneurysm (AAA) repair currently range from 35 days (5 weeks) to 145 days (21 weeks). This surgery is designed to avoid the AAA rupturing; the longer the delay, the greater the risk of rupture." (p6) "When wait times were discussed with providers, a range of factors was identified as contributing, from lack of available facilities (theatres, beds, CT scanners) to lack of staff. The latter not only refers to surgeons but also the wider team: vascular interventional radiologists, anaesthetists, nurses and physiotherapists." (p18) "Each year, approximately 43,000 vascular surgery procedures are carried out in England. The total number of procedures has gradually increased in recent years as new surgical techniques such as Endovascular Aneurysm Repair (EVAR) have been developed. Because these techniques are potentially less debilitating for patients, they have helped lower	whilst supporting individualised care around which interventions are appropriate.

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				the threshold for surgical intervention and meant more unfit patients can receive surgery." (p10) "Where AAA surgery takes place, there are two main methods: open surgery and EVAR. As both involve repair to the aorta, both are complex, high-risk procedures; however, EVAR is less invasive and recovery times are typically shorter. As a result, around 75% of elective AAA surgery is now conducted by EVAR, with only one provider below the 50% mark. By contrast, approximately two-thirds of emergency AAA repairs are conducted by open surgery: though the number of emergency procedures is much lower, with only four providers undertaking more than 30 a year, the evidence suggests that hospitals are adhering to the more established approach in emergency care." "Setting standard parameters for consultants' workload helps with workforce planning at trust level. However, trusts can only recruit from the available vascular surgery workforce and concerns about whether or not this is sufficient have been long documented. In 2014, the Vascular Society published a Workforce Report 7 that highlighted a range of issues. At present, in England there are approx. seven radiologists per 100,000 of the population (most of these will be non-interventional) and one vascular surgeon per 137,000. These figures are much lower than our international counterparts. Demand is rising and it is known that many vascular surgeons are expected to retire in the next decade." (p26) "When examining length of stay for vascular surgery, it is important to recognise the vast differences between	

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				procedure types and the recovery times associated with them. For AAA, EVAR procedures typically last a couple of hours and patients may be discharged within a day or two. Open surgery may take three or four hours to complete and patients may need to stay in for a week. Furthermore, in some cases, surgeons opt to undertake a staged closure following open repair of a ruptured aneurysm – meaning the patient receives two procedures, thus extending their stay." (p27) "For AAA repair, the variation is if anything broader still, though as noted above there are some providers who deliberately conduct a staged second look operation repair for open surgery. The variation needs to be examined and that should start locally. Trusts should review all returns to surgery at vascular mortality and morbidity meetings to identify whether there are common factors and address any issues of quality, whether during surgery itself or post-operative care." (p31) "The National Vascular Registry (NVR) has been a major asset to vascular surgery since it was originally established as the National Vascular Database by the Vascular Society. It provides an annual snapshot of the vascular surgery workload and how it is changing; it has been a crucial source of information for this report, particularly about procedure choice. However, the GIRFT process has also served to highlight the limitations of the NVR – particularly when NVR data is compared to the other key source of data used by the GIRFT team, Hospital Episode Statistics (HES)."	

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				We recommend that the future AAA guidance accounts for the capacity challenges and consequences faced by the NHS and continues with commissioned EVAR and OSR repair to reduce the burden on the NHS and improve patient experience.	
Association of British HealthTech Industries (ABHI)	Draft guideline	General	General	**References** D. Adams (2010): Personal Communication. S. Badger et al. (2017). "Endovascular treatment for ruptured abdominal aortic aneurysm." Cochrane Database of Systematic Reviews(5): CD005261. British Society for Endovascular Therapy and the Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair (GLOBALSTAR) Registry (2012). "Early results of fenestrated endovascular repair of juxtarenal aortic aneurysms in the United Kingdom." Circulation 125(22): 2707-2715. P. P. Broos et al. (2015). "Effects of Anesthesia Type on Perioperative Outcome After Endovascular Aneurysm Repair." J Endovasc Ther 22(5): 770-777. L. Brown et al. (2012): The UK EndoVascular Aneurysm Repair (EVAR) trials: randomised trials of EVAR versus standard therapy. Health Technology Assessment 16(9). J. Budtz-Lilly et al. (2017). "Editor's Choice - Assessment of International Outcomes of Intact Abdominal Aortic Aneurysm Repair over 9 Years." Eur J Vasc Endovasc Surg 54(1): 13-20. L. T. Burgers et al. (2016). "Cost-effectiveness of Elective Endovascular Aneurysm Repair Versus Open Surgical Repair of Abdominal Aortic Aneurysms." Eur J Vasc Endovasc Surg 52(1): 29-40. R. A. Cambria et al. (1994). "Symptomatic, nonruptured abdominal aortic aneurysms: are emergent operations necessary?" Ann Vasc Surg 8(2): 121-126.	Thank you for these references; we consider them where cited in your comments.

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Medtronic UK	Draft guideline	General	General	As outlined in the body of this response, Medtronic believe there are many sources of data and evidence available that have not been considered by NICE for the development of this new clinical guideline. The economic models and draft recommendations have been heavily informed by outdated randomised clinical trials which we firmly believe has led the committee to draw inaccurate conclusions. We therefore	Thank you for your introductory comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				recommend that NICE consider the wide range of observational studies and registries available because, although arguably lower level evidence vs. RCT, the data contained is more contemporary and the results reported are consistent across multiple studies. Many clinical guidelines and technology appraisals have previously used data other than RCTs to inform the recommendations made and we passionately believe that AAA patients, NHS staff and the wider NHS system will suffer if these guidelines remain.	All inputs to the original HE model developed to support the committee's decision-making have been reviewed in the light of stakeholder feedback, with substantive revisions in several areas. Additional published evidence on the relative safety and effectiveness of EVAR and OSR has been reviewed, with the goal – among other things – of exploring the validity of model inputs. We respond to each of your detailed comments below.
Lombard Medical Ltd	Draft guideline	General	General	**Practices** Conclusions drawn from implants placed from 1999 to 2004 (EVAR 1 Trial) must should reflect the following weaknesses in EVAR practice that have subsequently been substantially improved: 1)Imaging a) CT imaging used for planning was frequently performed with 10mm 'cuts' which were frequently not contiguous. This meant that the location of renal arteries sometimes had to be guessed. b) CT imaging was usually measured from films having 16 or 20 'cuts' per film. This resulted in the aorta being about 5mm in diameter on the film with the common iliacs being less than half that size. Accurate sizing and oversing could not be achieved with certainty. c) 3-D planning tools were basic and sparsely available. d) Intra-operative imaging was frequently performed with mobile C-arms. Some had limited image quality, particularly in larger patients. This substantially limited the ability to detect and treat intra-operative endoleaks.	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The critical question is not whether EVAR devices and outcomes have improved; it is whether they have improved in a way that outstrips progress in OSR. There is very limited evidence that they have. It is clear that many of the things that have contributed to improvement in EVAR outcomes have also contributed to similar progress in OSR. The developments in imaging technology you catalogue may be a good example: these would also have had benefits for the planning of OSR procedures. The contention that 'there is little data to indicate the extent of this improvement in terms of clinical outcomes [but it] is unarguably true… that contemporary results will be better than results in EVAR 1' is difficult to support. However, we have looked closely for evidence that would help to substantiate or refute your hypothesis. Such casemix-adjusted data as there are suggest that, when one focuses on a relative scale

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				e) Moreover, a few imaging machines did not have vascular software which meant they were unable to perform subtraction or to replay contrast runs from elecytonic memory. f) Modern CTs for EVAR planning are produced with 'cuts' of approximately 1mm, there are multiple software packages to assist EVAR planning and intra-operative imaging is frequently performed in hybrid operating theatres where the imaging allows clear visualisation of small, low density components such as Nitinol barbs. We assert that the changes in X-ray technology to assist planning and implantation will have substantially reduced the incidence of device mis-selection and mal deployment. We believe there is little data to indicate the extent of this improvement in terms of clinical outcomes. What is unarguably true is that contemporary results will be better than results in EVAR 1. 2) Devices a) During EVAR 1, 40% of the implants lacked active fixation (ie Talent, Aneurx, Lifepath, Bard, Endologix and Baxter. These devices were all associated with migration at the proximal neck leading to re-intervention to place cuffs or to treat Type Ia endoleaks. b) Modern devices have embraced active fixation, with the exception of the Nellix EVAS system. c) Delivery system profiles in EVAR 1 ranged between 6.7mm and 8.3mm. Frequently these sizes would have impacted on the intima of access vessels causing a degree of early re-interventions to treat stenosed or occluded external iliac arteries. The large sizes caused occlusion and ischemia of the limb and this caused high levels of discomfort which was one reason for using general anesthesia, which has its own risks and complications. Modern delivery systems have	assessing difference between EVAR and OSR, there has been very little change in the balance of benefits and harms offered by the 2 approaches.

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				smaller profiles of 4.6mm to 7.6mm. This reduces the risk of vascular complications and is a component in encouraging the greater use of local anethesia and day case discharge. We assert that the changes in implant technology have improved the safety of procedures and contributed to reducing the number of complications. We believe there is little data to indicate the extent of this improvement in terms of clinical outcomes. What is unarguably true is that contemporary results will be better than results in EVAR 1. **Complex EVAR** We find the definition of Complex EVAR in the draft is unusual and at times used inconsistently. We suggest that complex EVAR is defined in terms of anatomy and pathology and that the excellent point about avoiding off-label use should be stand alone. We are puzzled by the concern about Custom Devices which are usually seen in the context of humanitarian use. To this extent, the draft guidelines appear to have lost touch with humanity. **Conclusion**	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. The committee agreed that it would be ideal to define complex AAAs in purely anatomical terms; however, they believed that existing evidence does not do this, as cases that are termed 'complex' when approached endovascularly would not get that label if an open repair were planned. The committee's experience suggests that custom devices are used relatively routinely in current practice – indeed, 1 device manufacturer has boasted of 'over 2500 successful implants' of their custom-made endografts in reponse to this consultation. This does not suggest the kind of exceptional procedure that your comment suggests.

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				Many improvements have been made in EVAR devices and their use since performance of the EVAR 1 trial. We know that modern devices give better results and we therefore know that some of the quantitative conclusions of the EVAR 1 trial are no longer applicable. We believe it would be safer to implement a restricted set of your recommendations, with assessment, in order to assess whether or not they truly made a positive or negative impact on the practive of EVAR therapy.	
Liverpool Clinical Trials Unit	Draft guideline	K23	532	If the guidelines are implemented, there will be a substantial increase in the number of critical care and normal hospital bed-days occupied by AAA patients, accounting for all a factors that work both ways. There simply is not the capacity in the NHS to deliver this change. This is a major factor and merits formal impact estimation.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Liverpool Clinical Trials Unit	Draft guideline	K24	574	The only study included from literature search has no internal validity. There have been a number of other studies with much better internal validity eg. Incorporating risk stratification or propensity matching. This is suggestive of poor screening of literature. A number of papers with greater value have been largely ignored, most notably: HTA Technology Assessment Review of Fenestrated and Branched EVAR. Globalstar report. c. Window registry (French national study)	On reviewing stakeholder feedback, the committee accepted that it had been too stringent in only looking at prospective observational evidence (of which Donas et al., 2012, is the only published example). While we do not accept that this was a result of 'poor screening of literature' – we would say it was an unnecessarily restrictive review protocol – we do agree that it was necessary to explore a broader evidence-base to inform the committee's decision-making in more detail. Therefore, a supplementary review of casemix-adjusted observational data was undertaken to support the committee's post-consultation considerations. This includes 9 studies

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					looking at the relative benefits, harms and/or costs of complex EVAR compared with OSR. As regards the particular studies you cite: • The HTA Technology Assessment Review of Fenestrated and Branched EVAR found no evidence, and recommended that an RCT should be undertaken • The Globalstar report was excluded from our review because it is a non-comparative case-series that does not provide any information on the relative benefits, harms and costs of EVAR versus OSR. • One study was included in our review that is based on the French WINDOW registry (Michel et al., 2016)
Liverpool Clinical Trials Unit	Draft guideline	K24	580	The recommendation of an RCT in the area of Complex AAA is simplistic. Different research groups in the UK have worked on developing appropriate study designs for complex aneurysm management. All of them came to the same conclusion that an RCT would not be feasible. NIHR HTA have also come to the same conclusion independently. The reasons for this in the main are: A) There has been a consensus that endovascular techniques substantially reduce the risk of perioperative death compared to open repair, at all levels of operative fitness. This incremental benefit is believed to be much higher than what is seen in standard AAA. NVR data reinforces this view, despite its acknowledged limitations. Therefore, when approached, physicians have stated their unwillingness to randomise between open repair and FEVAR or FEVAR and 'Best Medical Therapy' alone.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee recognised that this view is probably the predominant one (though not universal, as can be seen in responses to this consultation). However, they disputed the safety of the view. Best-available evidence does not suggest that fEVAR has better short-term results than OSR, and suggests it may have substantially worse long-term outcomes. The committee find it hard to accept that we cannot randomise people because we are so certain of the superiority of a treatment that appears to have double the long-term mortality risk of its proposed comparator.

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				B) Both open repair and FEVAR operations come in a range of technical complexities. Vascular anatomies suitable for similar FEVAR configurations (with similar technical complexity of implantation) may require open surgical strategies of varying complexity, with cross clamp level ranging from infrarenal to supracoeliac, and therefore different operative risks. Similarly, juxtarenal AAAs that can be treated by open repair with the same level of aortic cross clamp may require FEVARs of varying complexity. There is also a potential for cluster effect, ie, some ecentres better at one technique than the other. These factors calls for randomisation protocols that would ensure that any one arm of a trial is not dominated by the most or the least favourable intervention. This creates implications for numbers needed to recruit, ensuring external validity as well as statistical analyses.	This is an excellent summary of some of the complexities that urgently need to be unpicked in a trial, because they are certain to result in very badly biased results when analysed using observational methods. We do not believe that any of these challenges would render a well designed RCT impractical, and they highlight exactly why a randomised design is necessary to generate unbiased results. In its research recommendation, the committee stipulated that any RCTs should be stratified in a way that will help to reveal any differences in the balance of benefits, harms and costs between EVAR and OSR according to AAA anatomy.
				C) In this context, the committee's view (line 790) "that anatomical complexity is less problematic for open repair ..." is not accurate. Surgeons who work as primary operators for both kinds of repairs (there are only a few of them) would disagree vehemently. Complexity is a major factor for either technique. It is for a reason why very high mortality rates are noted in NVR for complex aneurysms, notwithstanding limitations of NVR data.	We accept that this was clumsily phrased, and we have revised the text in the guideline. The committee's point was that the cases that are labelled as 'complex' OSRs in NVR submissions are disporoprtionately likely to feature the kinds of extremely complex anatomy that would result in a very high risk of perioperative mortality. This is a variant of the point you make above ('Vascular anatomies suitable for similar FEVAR configurations (with similar technical complexity of implantation) may require open surgical strategies of varying complexity, with cross clamp level ranging from infrarenal to supracoeliac, and therefore different operative risks'). The committee's strong inference was that the cases with lower operative risk may not get recorded as 'complex' in the NVR, under this circumstance.

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				The NIHR HTA has already commissioned and contracted a study: "A Risk-adjusted and Anatomically Stratified Cohort Comparison Study of Open Surgery, Endovascular Techniques and Medical Management for Juxtarenal Aortic Aneurysms:The UK COMplex AneurySm Study (UK-COMPASS) (ISRCTNISRCTN85731188)." This study is underway. Interim analysis is expected towards the end of 2018. This will provide an opportunity to examine the data to see if the study should continue as a cohort comparison study or in fact an RCT should be performed and if it could be feasible.	Thank you for highlighting this study. NICE are aware of the study aims.
Liverpool Clinical Trials Unit	Draft guideline	K25	635	The committee underestimated the incremental clinical benefit from EVAR; getting this right is crucial to accurate estimation of ICER. The model of taking baseline mortality of EVAR from NVR 2016 (0.4%) and estimating open repair mortality using odds ratio (0.33) derived from RCTs is arbitrary and wrong, despite its appearance to some of being acceptable. RCT simply does not have the external validity to extrapolate to population level data from NVR. Absolute risks were much higher in the RCTs and there is no reason to believe that risk reduction occurred 'uniformly' in both techniques during the time between RCT and 2016. In any case, such low operative death rates from open repair are unrealistic in UK, particularly if the 'safety valve' of EVAR is not available at the same time. Currently physicians are achieving excellent low mortality rates by best matching techniques to patients. For example, NVR 2016 also shows 3% mortality from open repair, a rate that was achieved by physicians confining open repair to the best risk patients, while offering EVAR to the rest. For example, the model used by the committee would also estimate that in 2016, if all EVAR patients (with a mortality of	The approach taken to estimating treatment effects in the economic model is not at all arbitrary: it is based on well established advice as to optimal methods for the parameterisation of decision-analytic models – see **Theme 2**. The committee took the opposite view to you: that selection biases reflected in the NVR are likely to overestimate the level of perioperative risk that should be achievable with a well organised open vascular programme. They noted that, once account is taken of casemix in observational evidence, measures of relative effect are estimated that are closely consistent with the outcomes of RCTs. The committee drew particular encouragement from recently published casemix-adjusted results from Poland (Symonides et al., 2018), that show perioperative mortality of 0.5% with OSR (at an OR of 0.33 compared with EVAR – i.e. exactly as estimated in the RCTs). This is not 1 centre of excellence in Poland, but the whole national, publicly funded system that is

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				0.4%) were to have undergone open repair instead, the total AAA postoperative deaths in 2016 would have been lower than the 3% actually observed after open repair. This is clearly unachievable and wrong. A more accurate modelling would have come from taking as baseline open repair death rates from a period before EVAR became widespread (perhaps accounting for less than 25% of total repairs) from NVR and estimating the lower EVAR death rates using the same odds ratio. This is no more or less arbitrary than the one used by the committee, which is designed to give the worst estimates of economic outcomes. Economic modelling was stated to have been based on patient-level data from EVAR trials. EVAR Trialists reported the estimated difference in cost between open repair and EVAR to be £3757 at 15 years (Ref: HTA 22:5:Jan 2018 ISSN 1366 -5278). I am unsure how using the same data the committee arrived at a cost difference of £ 6765.	reporting such excellent results. The committee saw no reason why the NHS should not aspire to similar outcomes. It would be inappropriate to use historical data for a baseline, when the evidence shows that – once account is taken of selection biases – both EVAR and OSR have improved at a similar rate over the past 2 decades. The model is not based on the EVAR trials alone; it incorporates evidence from all the published RCTs and some nonrandomised evidence. However, having revised model inputs in response to stakeholder feedback, our base-case estimate is now that EVAR is associated with a net lifetime discounted cost increase, relative to OSR, of £3,066 per patient. If we exclude our newly include estimate of rehabilitation costs (which the EVAR investigators do not account for), the difference becomes £3,711, which is closely comparable to the EVAR-1 estimate.
NHS Highland	Draft guideline	9 - 10	179 - 185	We are concerned that the NICE recommendations are a fundamental deviation from current best practice in the UK which is governed by Healthcare Quality Improvement Partnership (HQIP). The NVR annual report 2017 (https://www.vsqip.org.uk/content/uploads/2018/05/2017-NVR-Annual-Report.pdf) states that 70% of elective infrarenal aneurysm repairs were done using an endovascular procedure	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				(EVAR). Perioperative mortality and length of stay in hospital were significantly lower compared to open aneurysm repair. NICE seems to justify a return to open surgery as procedure of choice by highlighting adverse long term outcomes of EVAR procedures but ignoring the evolutionary process of an innovative, less invasive treatment option. We are deeply concerned that the NICE recommendations deny patients a choice of reasonable treatment options as advocated by GMC guidelines.	See the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.
Royal College of Physicians and Surgeons of Glasgow	Draft guideline	3	30/40	One of our reviewers notes that an increase in referrals to the aneurysm screening programme and/or referrals to vascular services will have resource and cost implication. It is logical that women identified with AAA should enter the screening programmes for surveillance.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. They also agreed that the recommendation was made at 'consider' level to ensure sufficient flexibility in decision making. The committee noted that, currently, women with AAA are not referred to the NHS AAA Screening programme. Thus there would be no additional burden to the programme.
Somerset & North Devon Vascular Network	Draft guideline	3	40	We are concerned that this recommendation is not cost effective, as suggested by the National AAA Screening programme, and that it will place considerable pressures on existing scanning resources	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to

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					population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. They also agreed that the recommendation was made at 'consider' level to ensure sufficient flexibility in decision making. The committee noted that, currently, women with AAA are not referred to the NHS AAA Screening programme. Thus there would be no additional burden to the programme.
Royal College of Physicians and Surgeons of Glasgow	Draft guideline	4	54-7	The timeline from referral to be seen by vascular services is stipulated but no timeline is given to treatment. With increasing numbers of open repair (as recommended) and the resource implications associated with this (ITU/Bed capacity/winter crisis), patients will wait on longer waiting lists and some will rupture during this time. This could lead to legal cases as mortality from rupture is not insignificant.	Thank you for your comment. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. They also agreed that the recommendation was made at 'consider' level to ensure sufficient flexibility in decision making. The committee noted that, currently, women with AAA are not referred to the NHS AAA Screening programme. Thus there would be no additional burden to the programme.

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Somerset & North Devon Vascular Network	Draft guideline	5	70	Bedside Ultrasound is sensitive to AAA, but not iliac aneurysm. Not sensitive for ruptures. Most units use Department based U/S hence might as well get a definitive CT scan which will diagnose cause of symptoms and presence or absence of AAA or iliac aneurysm rupture.	Thank you for your comment. Iliac aneurysms were not included in the scope of this guideline. As a result, the committee did not consider any evidence related to this type of aneurysm. The committee discussed whether CT could be recommended for diagnosing symptomatic or ruptured AAA. Although it is the best imaging technique, recommending a CT scan for all patients who are symptomatic (whether as the sole test or as a subsequent test to the FAST ultrasound) was not considered safe as it may unnecessarily delay the transfer of patients to the regional vascular service for treatment. Furthermore, performing a CT scan in all patients would also incur considerable costs. The committee also discussed the role of CT angiography in patients who have been transferred to a regional vascular service, and are being considered for emergency repair. They expressed the view that it would be bad practice to undertake emergency EVAR without performing CT angiography. However, they also acknowledged that, where a patient's condition is critically unstable, a vascular specialist may need to rely on a strong clinical diagnosis coupled with ultrasound imaging to inform their decision to attempt open surgical repair.
Royal College of Physicians and Surgeons of Glasgow	Draft guideline	7	123	Increased surveillance intervals for small AAAs could reduce overall costs.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA

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					screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Somerset & North Devon Vascular Network	Draft guideline	8	154	There is increasing evidence that holding ACEI prior to major surgery can reduce post op AKI.	Thank you for your comment. No evidence was identified relating to the preoperative use of ACE-inhibitors in people with AAA undergoing repair procedures. The committee noted that many people with AAA are likely to receive ACE inhibitors for treating other conditions. They agreed that the medication can have unpleasant side effects so clinicians would not prescribe it unless absolutely necessary (in line with their respective indications). As a result, the committee agreed that there was no need to make any specific recommendations on ACE inhibitors. Since most people with AAA are likely to be older people with some form of cardiovascular disease, the committee believed that optimisation of pre-existing medical conditions and minimisation of cardiovascular risks would increase the general health of people with AAA. As a result, the committee felt that general principles of secondary

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					prevention of cardiovascular disease, as outlined in other NICE guidelines, were applicable. The committee also agreed that it is important to reduce the risks of surgical site infections and venous thromboembolism in all people undergoing AAA repair. As result, recommendations were drafted cross-referring to other NICE guidance.
Somerset & North Devon Vascular Network	Draft guideline	9	179	We have considerable concerns over this statement. It is entirely too 'black or white'. There are clearly come patients in whom open repair is not ideal, but in whom life expectancy is reasonable and their anatomy is ideal for EVAR and there would be benefits to EVAR. Such a statement undermined credibility of the guidance.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR).
Somerset & North Devon Vascular Network	Draft guideline	9	179	To stop using EVAR would, for most hospitals, place increased demand on ITU services (which in many units is stretched to capacity – certainly throughout the South West), leading to more cancellations and the potential for interval	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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				ruptures. Increased operating time (can undertake 2 EVARs in same time as 1 open repair) will place increasing demands on already stretched theatre resources across the NHS	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. We have been unable to identify any contemporary evidence regarding duration of procedure for EVAR and OSR – see **Theme 5**. Although the committee accepted that EVAR procedures do take less time than OSRs, such evidence as is available suggests differences between the 2 that are measured in minutes rather than half-days.
Royal College of Physicians and Surgeons of Glasgow	Draft guideline	9	179-182	The Guidelines recommend open surgical repair over endovascular repair for unruptured aneurysms. One of our reviewers considers that randomised trials provide level 1 evidence supporting elective Endovascular Aneurysm Repair (EVAR) in terms of clinical outcomes. The UK Endovascular Aneurysm Repair Trial 1 (EVAR 1 trial) has a 15-year follow-up and shows that the early mortality benefits of EVAR compared with open repair are offset by an increase in late mortality.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. The committee acknowledged the high-quality evidence that OSR is associated with worse perioperative mortality than EVAR. However, it was also the committee's confident interpretation of evidence – including but not limited to EVAR-1 – that EVAR has been and remains associated with unignorable excess mortality in the long term – see **Theme 9**. The follow-up regimen mandated in the RCTs was relatively intensive – the committee agreed that current NHS practice

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				The total mortality curves diverge after 10 years, but there were no significant differences in the primary outcomes of total mortality and aneurysm related mortality over the whole follow-up period. The late increase in mortality in the EVAR group is predominantly due to secondary sac rupture. Very few of these ruptures are spontaneous – they occur in patients who have had (uncorrected) complications identified. These results highlight the importance of lifelong surveillance following EVAR and re-intervention when necessary. The results do not support the abandonment of elective EVAR. Our reviewer's opinion is that the draft NICE guidelines have taken a very narrow view of the trial evidence, predominantly based on cost. No account has been taken of patient choice. Patients and clinicians will find this very difficult to accept. The College views that working with patients and relatives as highly relevant to providing high quality care. The reviewer felt that the guidelines will have a significant impact on patient care as well as on recruitment, training and retention of surgeons in UK Vascular surgery. The Abdominal Aortic Aneurysm (AAA) Quality Improvement Framework has resulted in a significant decrease in peri-operative mortality in the UK, since 2008. At that time the UK was identified as an outlier for peri-operative AAA mortality within Europe (2008 report from the European Registry Group). The increase in elective EVAR has played a significant role in reducing peri-operative mortality. Much of this work will be undone if the guidelines are implemented.	often relies on less frequent use of less sensitive tests (and other stakeholders have supported this view in criticising our recommendation of CT-based follow-up). Therefore, the committee concluded that RCT results reflect an optimistic view of rates of late complication-related mortality and morbidity associated with EVAR – a conculsion that is apparently supported by observational data (see **Theme 11)**. It is NICE's statutory responsibility to consider the balance between the benefits and costs of competing approaches to healthcare, as it has in this case. For discussion of the implementation challenges that may be associated with a greater volume of OSR, please see **Theme 13**. For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**.

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				Peri-operative mortality will inevitably increase and there will be a reduction in the number of AAAs being repaired. There will be an increased ITU bed utilisation and increase length of in-patient stay. The UK will again become an outlier with the rest of Europe, as well as with North America and Australasia. The guidelines recommend EVAR for ruptured AAA. However, training in all the key steps of EVAR (patient selection, planning, device selection, implantation, follow-up, re-intervention) requires exposure to elective EVAR in a controlled operating environment. Individuals will not become competent to treat patients with ruptured AAA with EVAR, unless they have gained significant experience with elective EVAR. If the guidelines are implemented it will not be possible to train UK vascular surgeons and interventional radiologists to perform EVAR for ruptured aortic aneurysms. Vascular surgery is an interesting and rapidly developing specialty. The main driver for this has been the improvement in endovascular technology and techniques. The implementation of these guidelines will be a retrograde step, with the main restriction on practice being seen as one of cost. The specialty will become less attractive to UK and overseas trainees, impacting on recruitment, training and service provision. The significant negative effect these guidelines will have on UK Vascular Surgery cannot be underestimated. Another reviewer notes that patients are again recommended to have open surgery and not EVAR for unruptured AAA. This is a huge change and has "knock on implications". There will be an increase in open surgery with cost implications for beds/ITU etc. There will be an increased procedural mortality	For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a.**. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were

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				(open surgery more hazardous than EVAR). Fewer patients will be offered effective treatment (because they are unfit for surgery) so ruptures will increase - leading to possible resource implications if repair is then attempted.).	confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. The existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				The committee's objections to EVAR are based on "no long-term benefit" compared to surgery and increased costs. There is clear short-term benefit however and many patients choose this when offered. "Long term" is in any case an interesting concept in a patient population with a mean age probably in the eighth decade. EVAR internationally is currently regarded as the future of aneurysm care. In making this recommendation the UK will be making a retrograde step.	The average age of people in this population is around 74. In the general population, mean life expectancy is approximately 12 years for men and 14 years for women of this age, and the evidence suggests that people who survive OSR have very similar survival prospects (see figure HE05). This shows that the average candidate for AAA repair has ample opportunity to benefit from increased long-term survival prospects.

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East and North Herts NHS Trust	Draft guideline	9	181	Follow up data for EVAR is based on old stents. Newer stents inserted for aneurysms within the IFU have better long term outcomes (but one can not prove this for another few years).	It is only in the domain of reintervention rate that there is evidence that the performance of modern stent-grafts is superior to that of older devices. The committee acknowledged this finding, and considered revised HE modelling that used a lower reintervention rate for EVAR. However, this did not have a material influence on conclusions – see **Theme 8**. There is no evidence that the excess long-term mortality with which EVAR is associated has diminished similarly – see **Theme 9**.
East and North Herts NHS Trust	Draft guideline	9	181	Many patients choose an EVAR over an open repair for a standard AAA - based on current evidence and a quicker recovery. I am not sure if patient wishes / opinions have been included here. Majority of my patients choose EVAR over an open repair, even if they are fit for both procedures.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.
East and North Herts NHS Trust	Draft guideline	9	181	Fewer AAA procedures would get performed in the operating list, as standard open AAA take longer than standard EVARs, thus the theatre efficiency would reduce and potential waiting times for surgery increase.	We have been unable to identify any contemporary evidence regarding duration of procedure for EVAR and OSR – see **Theme 5**. Although the committee accepted that EVAR procedures do take less time than OSRs, such evidence as is available suggests differences between the 2 that are measured in minutes rather than half-days.
East and North Herts NHS Trust	Draft guideline	9	181	For patients with dual pathology, being able to perform an EVAR to stabilise the aneurysm, and then performing a laparotomy for the other pathology is beneficial as it avoids the need for 2 laparotomies (and associated complications of wound infections and adhesions). Such as when a AAA is found alongside a bowel cancer.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.

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City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	9	186 - 191	There are large data sets from registries and other non randomised large cohort studies published in peer reviewed journals which show consistently low mortalities of approximately 2 - 4 % or less for complex EVAR, with excellent long-term target vessel patency compared with real world outcomes of approximately 8 – 20% mortalities for open thoraco-abdominal aneurysm surgery. A randomised trial is highly likely to be stopped early, thus we question the morality of starting such a trial.	This comment demonstrates the potential danger in 'cherry-picking' sources of data that are known to suffer from critical biases. When investigators have attempted to provide risk-adjusted estimates of the relative benefits and harms of complex EVAR and OSR, they have not found that EVAR has better short-term results than OSR, and such evidence as is available for long-term outcomes suggests that EVAR may be substantially worse. The committee find it very hard to accept that we cannot randomise people because we are so certain of the superiority of a treatment that appears to have double the long-term mortality risk of its proposed comparator. Most thoracoabdominal aortic aneurysms are beyond the scope of this guideline.
Somerset & North Devon Vascular Network	Draft guideline	9	196	How can you offer a EVAR rupture service without the resources, consignment stock, practice, etc. available from having an elective EVAR service. This and the above are almost mutually exclusive	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
East and North Herts NHS Trust	Draft guideline	10	183	Many of our EVAR patients had an EVAR as their respiratory conditions / cardiac conditions / previous abdominal operations made them high risk for open AAA repair. They have had uneventful EVARs and continue to lead active lives, without the burden of having a 'ticking time bomb' inside them. The operation has reassured them that the AAA is unlikely to rupture, and so they have been able to live their normal lives	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				(including flying for holidays, driving etc). If they were not offered EVAR, and were too high risk for open repair, then we would be denying them an operation and limiting their lifestyles, and putting them at risk of ruptured AAA.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. The absence of counterfactual evidence makes anecdotal information regarding apparently successful EVAR procedures difficult to interpret. For discussion of the potential impact on quality of life of living with an untreated AAA, please see **Theme 13**. People for whom OSR is considered unsuitable owing to medical contraindications will face much more substantial restrictions on their lifestyles as a result of their comorbidities than they do from their AAA.
East and North Herts NHS Trust	Draft guideline	10	196	If EVARs are only used for emergency AAA (ruptured aneurysms), then outcomes will deteriorate as surgeons / radiologists will get de-skilled (as will the theatre scrub team who manage all the kit).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
Liverpool Clinical Trials Unit	Draft guideline	K 23	545	Risk of perioperative death is one of the factor that matters most, certainly to patients and the operating surgeon. This is reinforced by Liverpool Patient and Public Involvement group, whose additional opinions are summarised below.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for

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				Patients strongly prefer to be informed of all of the treatment techniques and as detailed information as possible regarding supporting evidence. Recommendation or offer of 'one best' treatment based on evidence and / or guidelines was not considered adequate counselling. Patients take different choices under the same circumstances, with the same information. Patients understand the importance to the NHS of treatment costs. Patients expect treatment costs to play no role in selection or offer of treatments.	NICE's view on the importance of joint decision making between the clinician and individual.
EVAR trial post-operative surveillance group	Draft guideline	28	677-686	NIHR Award 11/36/46 We are pleased to read that EVAR is now practiced worldwide and minimisation of harms and controlling costs is an important consideration. We would add that this is required now for those patients who have actually received an EVAR device and are at post-operative risk. We have available the paper "Predicting risk of rupture and rupture-preventing reinterventions utilising repeated measures on aneurysm sac diameter following endovascular abdominal aortic aneurysm repair" under consideration for publication. We may also have available a technical document comparing the health economic implications of different post-operative surveillance policies. We are currently modelling relationship between complications, reinterventions and secondary sac rupture with the aim of identifying a surveillance policy that will enable a subgroup of patients to be offered less frequent monitoring after EVAR whilst offering more frequent and/or more high-quality imaging in those more at risk of rupture. The aim is to identify an approach that facilitates more rapid identification	The committee made a research recommendation that is relevant to this work: • What are the risks, benefits and cost implications of different surveillance protocols in people who have undergone EVAR? The committee explicitly suggested that the need would be well met with systematic review of available evidence and statistical modelling of predicted costs and consequences. Your work in progress seems, on the face of it, well placed to fill this gap. We will pass this information to our surveillance team to help inform subsequent updates of this guideline.

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				and intervention for those with serious complications with a view to reducing AAA related mortality alongside reducing scan-related costs.	
Society and College of Radiographers	For information, patient safety related.			The SCoR was required to respond to the Berkshire coroner following the death of an 80 year old woman who suffered a ruptured thoracic aortic aneurysm. The patient was being followed up for what was thought to be a suprarenal abdominal aortic aneurysm. [This text was identified as confidential so has been removed.] The SCoR has also informed the Abdominal Aortic Aneurysm Screening Programme and the Royal College of Radiologists. The British Medical Ultrasound Society are also aware of this case.	Comment noted; thank you for the information. We have redacted information here that appeared to be confidential information.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review W	Specific to page119 but relevant to entire evidence review		The majority of the studies included in this forest plot are not representative of current ultrasound practice in the UK. 1. Many of these studies are more than 10 years old or are based on retrospective data analysis of scans conducted on equipment more than 10 years old. Ultrasound equipment has evolved significantly over this period with many of the biggest advances being in colour Doppler sensitivity. High resolution flow imaging techniques such as B-Flow, SMI and dynamic flow are now standard on the equipment used in the vast majority of Vascular ultrasound departments. SOR guidelines recommend equipment is reviewed every 4-6 years and that primary systems are replaced if there are significant advantages associated with the newer generation machines. For these reasons, including data collected on equipment more than 10 years ago in the meta analysis does not provide a scientifically valid representation of current practice.	Thank you for your comment. In light of your comment, a sensitivity analysis was performed to consider only studies published from 2008 onwards in which the presence of endoleaks was determined in real-time by the person who was performing the scan. This sensitivity analysis indicated a slight increase in the diagnostic accuracy of CDUS for detecting endoleaks, however the increase was not substantial enough to change the committee's conclusions. Please refer to evidence review W for further details about the committee's deliberations.

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				2. Several of the studies included were based on ultrasound images which were acquired by technicians and then reported retrospectively by radiologists. This is widely considered as sub-optimal practice and is not representative of how any SVT accredited Vascular Scientists work. EVAR surveillance is a real time dynamic study and it is no surprise that retrospective scan reporting by someone other than the person who performed the examination will result in a very poor sensitivity for endoleak detection. For this reason these studies should also be removed from the meta analysis. If you remove the studies which are more than 10 years old and those which relied on retrospectively reported scans, the list of papers identified in your initial literature search is as follows: Badri et al, 2009 Cantador et al, 2016 Demirpolat et al, 2011 Gray et al, 2012 Oikonomou et al, 2012 We have not conducted a further meta analysis based on this selection of relevant papers, but would like to draw your attention that **all of these papers report 100% detection rate of endoleaks which needed surgical or endovascular revision.** We would also like to highlight the fact that in some cases ultrasound is more sensitive to endoleaks than CTA and that	

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				small type 2 leaks with bidirectional flow patterns are often not identified on static CT images. This suggests that all these studies which consider CTA as the gold standard are fundamentally flawed. The only study we are aware of which compares both CTA and CDUS (Colour Doppler Ultrasound) with surgical findings actually found that CDUS was in fact more reliable than CTA at identifying endoleaks, which were in need of intervention. https://www.ncbi.nlm.nih.gov/pubmed/?term=endoleak+after+endovascular+repair+schmieder	
Medtronic UK	Evidence review T (Ruptured)	General	General	**Ruptured Infrarenal AAA**: Medtronic wish to provide our appraisal of the NICE evidence review for ruptured AAA (rAAA) as there are a number of reasons to believe that ruptured EVAR (rEVAR) outcomes are even better versus ruptured Open Repair (rOR) than what was reported in evidence review T: A major assumption of the committee is that EVAR for ruptured AAA (rAAA) is going to be more of a risk than OSR. In a literature review of 64 publications of studies of varying nature (prospective, retrospective, several RCTs, case study, etc), the authors conclude "rEVAR can now be considered a safe method of treating rAAA, and is at least equal to the well-established rOR method" (Patelis et al. 2016). Another review also had similar conclusions that rEVAR 30-day outcomes are non-inferior clinically and therefor rEVAR is preferred to rOR due to the minimal invasiveness of the technique and reduction of intensive care unit and hospital stay, need for mechanical ventilation, reduced blood loss and number of in-hospital reinterventions (van Beek, 2014).	We are unsure how you have reached this interpretation of the committee's decision-making: there is no suggestion that EVAR is more of a risk than OSR in the guideline documentation. On the contrary, the committee agreed that strategies that use EVAR where possible are associated with comparable short-term mortality (better short-term mortality for women) and improved medium-term survival compared with an OSR-only approach.

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				It is important to note that, in the IMPROVE trial, 110 of the 259 patients with ruptured AAA in the EVAR group actually received OSR (European Heart Journal 2015). However, the reported data was for the original ITT populations and so the small advantages shown for EVAR (faster discharge to home, QoL, etc) likely would have been even greater if the 42% OSR patients were not included with the EVAR treated patients. In a recent paper by Gupta et al. 2018, the authors also point out this problem with the IMPROVE trial, and noted that if the outcomes were compared for the treatments that the patients actually received (as-treated instead of Intent-to-treat), EVAR had superior 30-day mortality of 25% (46/186) compared to 38% (128/336) in the OAR group ($p<0.002$). The authors note the numbers from the IMPROVE trial (when reported by actual treatment received) are actually similar to the ones they have from the PHD database showing that the advantages of EVAR over OSR existed even back to the RCTs. The manuscript also mentions that 27 of the 110 open repairs in the EVAR group occurred in patients who were suitable for EVAR but because the endovascular suite was in use or they were inadequately staffed, the protocol was breached and OSR was used. This speaks to a potential lack of proper preparation for EVAR which could also have had a negative effect on the outcomes. Studies have shown that sites had improved outcomes after the implantation of an established EVAR protocol (Starnes, et al, 2015). It is also known that with increased operator experience/proficiency, EVAR outcomes are even better (Schermerhorn et al 2015, Dua et al. 2015).	This feature of IMPROVE's design was discussed by the committee: *The committee noted that, from a clinician's point of view, the design of the IMPROVE RCT could be considered confusing, as a large proportion of people with suspected ruptured AAA who were randomised to the 'EVAR' arm actually underwent open repair (because their AAA was anatomically unsuitable for standard EVAR). However, it agreed that this design reflected the decision problem at a commissioning level – that is, whether a service should offer emergency EVAR where possible – and, therefore, it would not be appropriate to downgrade the evidence for providing a biased estimate of effect.* Evidence review T, 'The quality of the evidence'

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				To challenge the assumption that rOR versus rEVAR studies may be subject to patient selection bias, that more stable patients might have been treated by EVAR compared to open repair or that the cases treated by EVAR might have been anatomically less challenging and less risky than the open cases, Mayer et al demonstrated that an "EVAR-ONLY" approach allowed for the treatment of nearly all presenting RAAA patients by EVAR with a low 30-day mortality rate (24%) and a minimal exclusion rate of 4%. Additionally, in this study a significantly lower 30-day mortality rate in favor of EVAR, with a more than 3-fold mortality risk for open repair during an EVAR/OPEN period was demonstrated. (Mayer, et al 2012)	This study suggests that some selection bias was present in these units in the EVAR/OPEN period era – with patients who received EVAR achieving lower mortality than the EVAR-ONLY cohort in subsequent years. In sum, the study shows that – if we assume the basic comparability of cohorts from different eras – the EVAR-ONLY policy achieves similar short-term results to a strategy that uses both approaches, presumably according to clinican discretion (24.3% versus 25.5% 30-day mortality). We would be cautious about assuming the equivalence of the strategies, however, as we know nothing about the long-term results of the repairs, and we know nothing about the costs with which the strategies were associated (and, while we have reasonable evidence that infrarenal EVAR is not associated with an unreasonable increase in costs, relative to its benefit, in the emergency setting, we also know that complex AAAs require more expensive endografting solutions, which is quite likely to tip the balance in favour of OSR). In view of these considerations, the committee recognised that, in view of the apparent superiority of EVAR for many people with ruptured infrarenal AAAs, it is possible that complex EVAR – to the extent this is possible using 'off-the-shelf' devices – could also provide some advantages. However, they agreed that, in view of the potential for substantial harm and significant extra costs, NHS activity should be limited to the setting of an RCT.
				In many geographies EVAR is now the more common choice for AAA repair than OR. In the US, in-hospital mortality rates	We are extremely cautious about these studies, which make no attempt to control for confounding factors. It would be

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				for both ruptured and unruptured cases fell by more than 50% during the 10 yr transition from OR to an EVAR/OSR therapy mix. Dua et al note that these lower mortality rates and shorter LOS despite a higher cost of care continues to justify the use of EVAR over OR. For patients with suitable anatomy, EVAR should be the preferred management of both ruptured and unruptured AAAs. (Dua, et al 2014) It can be argued that the goal of treatment for ruptured AAA is to get the patient past the initial physiological distress. If so, the 30-day mortality and morbidity data should be the primary measures of rAAA treatment success. Veith et al, using early generation device designs (prior to 2010) showed that 49 centres performing rEVAR whenever possible were shown to achieve an overall 30-day mortality after rAAA repair of 21.2%. (1037 patients), clearly less than of rOR only as reported in multiple studies,35% to 55%. The Veith study reported that rEVAR had a 30-day mortality rate of 19.7% (range: 0%–32%) for 680 rEVAR patients and 36.3% (range: 8%–53%) for 763 rOR patients (P _ 0.0001) (Veith, F, et al 2009) Other benefits of EVAR is that femoral access is less traumatic compared to midline laparotomy and results in less inflammatory response (Castelli et al 2005). The complete aortic cross clamp for OSR also leads to other hemodynamic (ex: left ventricular wall stress) and physiologic challenges whereas endovascular techniques results in lower hemodynamic shifts (Egorova et al 2008, Lachat and Steuer 2015). These benefits of the minimally invasive surgical implantation reduce additional trauma/stress to the body leading to better short term outcomes which is especially important when the body is already in a high stress state due to a ruptured AAA.	peculiar to place reliance on such evidence when there are contemporaneous RCTs.

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				In a very recent article by Gupta et al. 2018 the authors looked at patients with ruptured AAA entered into the Premier Healthcare Database from July 2009 to March 2015. 3164 patients were identified and after patient matching based on usual parameters like age, sex, race, etc. 1336 EVAR patients were compared with 1249 OAR patients. The benefit of this study is the large sample size which allows for appropriate power to the statistical analysis even after patient matching. Patients also received modern endografts in the contemporary period where physicians had already gone through the EVAR learning curve. The OAR patients had higher risks of mortality (1.68 odds ratio), cardiac complications (1.76 OR), pulmonary failure (1.82 OR), renal failure (1.94 OR), and bowel ischemia (2.64 OR) compared to the EVAR patients which were all significant at the 0<0.001 level. Mean length of stay in the EVAR group was significantly lower than OAR (8.4 days vs 12.6 days, p<0.001, non matched patient comparison) as was in hospital mortality (23.8% vs 36.3%, p<0.001, non-matched patients).	It is regrettable that, although Gupta et al. (2018) performed extensive matching on demographics and comorbidities, they have no data on anatomical characteristics of the AAAs. This makes it extremely likely that participants in the OSR cohort – even if they were comparable in non-vascular respects – had more extensive AAAs, of the type that would have been much more likely to be selected for OSR, certainly in the period in question. In this context, it is unsurprising that this analysis arrives at a similar estimate of benefit for EVAR over OSR to that which can be derived from the treatment-received analysis of IMPROVE (that is to say: if you compare a cohort of allcomers receiving OSR with a cohort of anatomically less complex cases receiving EVAR, the results will favour EVAR).
Royal Free London Foundation Trust - Department of Vascular Surgery	Evidence review K	Evidence for Complex Aneurysm	General	Please consider including Durability of branches in branched and fenestrated endografts. J Vasc Surg. 2013 April; 57(4): 926-33. (Mastracci et al). This study includes only group IV and juxtarenal aneurysms, and is the largest cohort study applicable to this guideline.	This is not a cohort study. It is an uncontrolled case series which provides no data on the comparative effectiveness of complex EVAR.
The Vascular Society of Great Britain and Ireland	Evidence review K	General	General	**Unsuitable for OSR for surgical reasons – not considered ?** The management of patients not suitable for OSR for surgical reasons is not clear from the recommendations. Hostile	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual

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				abdomens, incisional hernias, stomas, inflammatory AAA's, previous aortic surgery, previous EVAR, horseshoe kidneys in front of the AAA, overweight patients. Are these to be managed by EVAR ? When is the surgeon able to use their judgement relating to these "surgical" factors and change from OSR to EVAR in the patients' best interests? When patients have synchronous tumours with their AAA, EVAR is often used to treat the AAA and avoid rupture whilst their tumour treatment is completed. OSR is high risk in these patients. Clarification of the role of EVAR in all these clinical scenarios is required.	abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
W.L. Gore and Associates	Evidence review K	General	General	**The model does not account for costs associated with return to theatre.** The NVR clearly shows that open repair has a higher rate of return to theatre after aneurysm repair procedures compared to EVAR. The NVR shows a return to theatre rate of 6.8% for open repair versus 2.0% for EVAR. The additional costs associated with this additional theatre time are not accounted for in the elective infrarenal model. We recommend that return to theatre be added to the elective infrarenal model by increasing the procedure costs for open repair and EVAR based on the rate of return and the average costs associated with additional theatre use. NVR 2017 Annual Report EVAR return to theatre rate: 2.0% Open repair return to theatre rate: 6.8%	This statement is factually inaccurate. Depending on the precise timing of return-to-theatre episodes, they should be accounted for in either the estimates of intraoperative resource use from the RCTs or in reintervention rates (see Brown et al., 2012; Patel et al., 2018). Therefore, applying an additional provision for such cases would double-count the costs with which they are associated.

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W.L. Gore and Associates	Evidence review K	General	General	**The model does not account for changes in centre procedure volume.** Studies show that high volume centres have better EVAR outcomes compared to low volume centres, and this difference was not accounted for in the economic model. Given that EVAR was a new technology when the EVAR-1 study commenced, centres had little experience with the procedures. The study required that study centres had only performed a total of 20 EVAR procedures ever, which is a low threshold. EVAR procedures are now conducted in high volume centres as a result of the centralisation of vascular surgery, which has led to better outcomes compared to EVAR-1. In addition, if the guidance moves forward, open repair will be conducted in centres with little experience with the procedure, which will result in worse outcomes than are projected in the model. Holt 2010 "The management of AAA presents unique challenges and this study has suggested that these might best be managed within institutions with a large total aneurysm workload. Many factors may underpin this phenomenon in the elective setting, and these include higher volume specialist surgeons working within an environment surgery…" "Hospital volume-outcome relationships are known to exist for England elective arterial surgery and this relationship has been demonstrated to persist to long-term survival after EVAR for rAAA in the USA. Other studies have also found that EVAR for rAAA has a significant survival benefit, which was augmented by provision at higher volume institutions." "These data add weight to the case for centralization of vascular services. With centralization will come an increased use of EVAR and advanced endovascular techniques, which	Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline. Nevertheless, it is clearly true that the national service should be configured to deliver optimal evidence-based care; we believe that the evidence identified and synthesised in this guideline provides a clear baseline for this. See also related comments in **Theme 3b**.

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				will confer a significant survival advantage to patients with AAA." "The more AAA procedures done by a hospital, the lower the in-hospital mortality. This was significant for both rAAA and urgent groups, and for open repair and EVAR. Overall the best results were in hospitals performing 29 rAAA (OR 0.664) and 30 urgent (OR 0.352) repairs per annum."	
W.L. Gore and Associates	Evidence review K	General	General	**Model does not account for improvement in risk assessment and patient selection.** The proposed guidance overlooks the improved understanding and impact of risk assessment and patient selection in current practice. EVAR-1 and the other studies used as inputs in the economic model were randomized control trials. While the study only included patients for whom both open repair and EVAR were deemed appropriate, understanding of the risks for both procedures has evolved over time, and risk assessment tools are now used more widely. In practice today, patients are assessed on a broad range of factors and are recommended for either EVAR or open repair based on their assessment and appropriateness. This means that improved outcomes can be expected over what was seen in EVAR-1 and the other trials. In addition, the guidance does not recognize that about 50 percent of patients who are clinically assessed to not be fit for open repair receive EVAR due to risk factors such as medical comorbidities. These patients would no longer receive repair, resulting in increased deaths from rupture. Vallabhaneni 2013 "The consideration of a patient's risk factors includes physiologic, anatomic, and patient-specific risk factors. Patient	From its dedicated review on the subject (Evidence review H), the committee concluded that there are no preoperative risk assessment tools with adequate predictive validity, and explicitly recommended against their use. Clearly, there are people who do not survive OSR who may have survived EVAR and, if such cases could reliably be predicted a priori, it is likely that it would be cost effective to offer them EVAR (though it is also possible that, if the characteristics that predict perioperative mortality with OSR overlap with the factors that clinicians were taking into account when randomising participants to EVAR-2, no intervention may be a superior approach). However, the committee had no confidence that any such prediction tools currently exist, and were mindful of the danger of denying patients a more durable repair on the basis of poorly predictive information. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in

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				selection plays a critical role in determining outcomes for EVAR." "In addition, there seems to be a decrease in secondary interventions from EVAR as experience grows, advanced devices become available, and patient selection improves." Chaikof 2018 "Risk prediction models for aneurysm repair were first developed in the 1990s, largely derived from relatively small cohorts of several hundred patients treated by OSR. " Epstein 2014 "EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future…[In EVAR-1], preoperative imaging was rudimentary, rehearsal and simulation not standard, and hybrid suites not observed. Instructions for use were not always available."	current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful. The opinions of other authors are of limited relevance to the committee's decision-making, which is guided by objective appraisal of best-available evidence.
W.L. Gore and Associates	Evidence review K	General	General	**Model does not account for the need for re-training of surgeons performing EVAR to perform open repair**. The lack of training will lead to capacity issues for a period of time until clinicians can be re-trained. This will result in longer waiting times for patients, which may lead to increased ruptures and deaths. Moreover, the lack of experience with open repair among physicians newly trained for open repair will likely negatively impact outcomes. These impacts on outcomes have not been accounted for in the model. Holt 2010 "…studies have also found that EVAR for rAAA has a significant survival benefit, which was augmented by provision at higher volume institutions."	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline. Nevertheless, it is clearly true that the national

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				"Many factors may underpin [association between volume and outcomes] in the elective setting, and these include higher volume specialist surgeons…" Rudarakanchana 2018 "Despite centralisation of the provision of vascular care, not all areas in England and Wales are able to offer emergency treatment for patients with acute conditions affecting the aorta proximal to the renal arteries. While cardiothoracic centres have made network arrangements to coordinate care for the repair of type A dissections, a similar plan for vascular care is lacking." Patel 2016 "EVAR devices are constantly being improved and sizing and imaging methods available for deployment are better now than they were between 1999 and 2004: a corollary is that experience in open repair is declining" Vallabhaneni 2013 "OSR outcomes are particularly dependent on the surgeon's experience, and that has become extremely limited in recent years."	service should be configured to deliver optimal evidence-based care; we believe that the evidence identified and synthesised in this guideline provides a clear baseline for this. See also related comments in **Theme 3b**. The opinions of other authors are of limited relevance to the committee's decision-making, which is guided by objective appraisal of best-available evidence.
W.L. Gore and Associates	Evidence review K Health economics appendix	16-17 8	293-295 19-22	**Model does not account for improvements in health-related quality of life (HRQoL) instrument.** EVAR-1 utilized the EQ-5D-3L instrument, and the model incorporates utilities from this instrument. This instrument was replaced in 2009 by the EQ-5D-5L. The developer of the instruments, EuroQoL, describes the shortcomings of the 3L instrument and why it was replaced: "The number of levels of perceived problems per dimension was changed from 3 to 5, increasing the sensitivity and reducing the ceiling effect.	NICE's current position on the EQ-5D-5L is that it should not be used in preference to the EQ-5D-3L (see our Position statement). The predominant reason for this is the empirical finding that health states measured and valued using the EQ-5D-5L instrument and tariff have consistently higher values than those measured using the EQ-5D-3L, which has the effect of reducing differences between treatments (see Wailoo et al., 2017). Therefore, although we are unaware of any relevant EQ-5D-5L estimates for this population, it is almost certain that their use

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				The most severe label for the mobility dimension was changed from "confined to bed" to "unable to walk about", enhancing its applicability and increasing the sensitivity of the mobility dimension. The instructions for the EQ VAS task were simplified, making the task easier to complete and easier to score." The lower sensitivity in the 3L instrument may significantly impact the calculation of utilities, either underestimating or overestimating importance to the patient. No adjustments were made in the model to account for this potential.	would result in smaller estimated QoL differences – and therefore worse cost effectiveness – for EVAR.
European Society for Vascular Surgery (ESVS)	Evidence review K	26-27	714-6	'People with an unruptured infrarenal AAA for whom open surgical repair is a suitable option should be offered open surgical repair, and that EVAR should not be offered in such cases'. Again, interpretation of this recommendation by doctors and patients who are discussing surgery, is likely to lead to patients expecting to have choice – the word 'suitable' being open to individual interpretation by both groups in this discussion	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
W.L. Gore and Associates	Evidence review K	14	216-220	**The model underestimates perioperative mortality for open repair.** For EVAR perioperative mortality, the elective infrarenal model utilizes 2016 data from the National Vascular Registry (NVR), which shows a mortality rate of 0.4%. However, rather than using the same NVR data for open repair perioperative mortality, which shows a mortality rate of 2.9%, the model applies an odds ratio from the pooled data from the EVAR-1, OPEN, DREAM, and ACE trials in the Cochrane meta-analysis to derive a mortality rate of 1.3% and a difference in mortality of only 0.9%. The logic behind this decision to use the NVR for EVAR but not for open repair is	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The logic behind drawing baseline expectation of mortality from a current registry and applying a treatment effect drawn from high-quality randomised trials is that the approach is well established as the optimal method for estimating treatment effects in a given decision context (see Dias et al., 2011; Dias et al., 2011b; Kaltenhalter et al., 2013).

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				unclear. This decision has major implications for the subsequent calculation of long-term mortality and QALYs. Recent studies align with the NVR data and suggest a much larger difference than was used in the model. Vascular Quality Initiative (VQI) data from 2010-2016 and Vascunet data from 2010-2013 both show a mortality difference of 3.3%, which is a larger than the NVR difference of 2.5% and much larger than the 0.9% difference in the NICE model. The NVR data represent current experience with open repair, and NVR data is used for EVAR. The data from the four trials includes procedures that occurred between 1999 and 2008, and EVAR devices, deployment systems, risk assessment, surgical techniques have evolved significantly since that period. We recommend that more recent perioperative mortality rates from the NVR (0.4% for EVAR and 2.9% for open repair) be used in the elective infrarenal model for both EVAR and open repair rather than applying the odds ratio derived from the Cochrane meta-analysis pooled data. NVR 2017 Annual Report EVAR perioperative mortality: 0.4%; open repair perioperative mortality: 2.9% VQI 2016 Annual Report VQI data collected 2010-2016 EVAR perioperative mortality: 0.7%; open repair perioperative mortality: 4.0% Budtz-Lilly 2017 Vascunet data collected from 2010-2013	As we explained in the consultation draft, *the approach adopted utilises both the greatest strength of randomised evidence – informing the treatment effect OR while controlling for confounding factors – and the greatest strength of registry data – presenting an accurate baseline snapshot of real world practice.* Health economic appendix, HE.2.2.5.1 In adopting this approach, we strongly endorse Stephen Senn's (2004) exhortation to 'use the additive measure at the point of analysis and transform to the relevant scale at the point of implementation [using] auxiliary information on the level of background risk of the patient.' We use RCTs to derive our additive (log-odds) measure, and registry evidence to apply it in our decision space. Further, we use additional real-world evidence (from Vascunet) to estimate the influence of effect-modifying patient characteristics in our subgroup analyses. In all these respects, our analysis is consistent with best modelling practice. The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to estimate relative effects – see **Theme 3a**. they also agreed that Budtz-Lilly et al.'s (2017) analysis of unadjusted registry data reflecting AAAs with heterogeneous anatomical complexity was of limited relevance to its decision-making for infrarenal AAA – see **Theme 3b**. In contrast to biased estimates from unadjusted data, casemix-adjusted observational evidence strongly validates the committee's decision to place primary reliance on

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				EVAR perioperative mortality: 1.1%; open repair perioperative mortality: 4.4%	randomised evidence of perioperative mortality – see **Theme 2**.
W.L. Gore and Associates	Evidence review K	14	227-228	**The model does not accurately estimate post perioperative morality.** The elective infrarenal model uses long-term mortality estimates from EVAR-1 and adjusted life table data. EVAR-1 and DREAM are the only trials that have tracked mortality at long-term follow-up. In both trials, the mortality estimates for EVAR and open repair have wide 95 percent confidence intervals for their risk ratios that cross 1.0, meaning there is no statistically significant difference in mortality in either trial. This means the economic model assumes a difference in mortality that has not been demonstrated. In addition, the Cox model incorrectly assumes a constant hazard ratio, which is exacerbated by discounting. Because these studies show no difference in long-term mortality, we recommend that the elective infrarenal model use a hazard ratio of 1.00, which assumes equal long-term mortality for EVAR and open repair.	This comment contains a number of inaccuracies: • The model does not rely on EVAR-1 alone for long-term survival estimates • EVAR-1 and DREAM are not the only trials to have reported long-term follow-up: 8-year data are also available from OVER • Our economic model synthesises all of these estimates to provide its estimate of post-perioperative survival – see Figure HE07 and HE97. • Because we anticipated that some readers would prefer only to reflect 'significant' effects, the model was configured, as a scenario analysis, to adopt the assumption that differences in post-perioperative survival only emerge after 8 years (as per the significant piecewise hazard ratio in EVAR-1). This results in worse cost effectiveness for EVAR. • It is not incorrect to assume constant hazards in the post-perioperative phase – these data are extremely well modelled by such an approach. See **Theme 9a**. • If there were a bias in favour of OSR in our long-term projections, this would be attenuated, not amplified, by discounting, because the long-term phase in which OSR's advantage becomes apparent would have less weight in the analysis. The finding that EVAR is associated with excess post-perioperative mortality is strongly supported by the review of casemix-adjusted observational evidence that we have conducted in response to stakeholders' criticism that the

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					consultation draft placed too much weight on RCTs alone – see **Theme 9**. In fact, this evidence suggests that the trials may represent an underestimate of the true effect in real-world practice.
W.L. Gore and Associates	Evidence review K	14	229-231	**The model does not fully account for non-graft related complications resulting from open repair and the costs associated with these complications.** EVAR-1 has been widely criticized for not including the full range of complications resulting from open repair. While the elective infrarenal model does include estimates of laparotomy-related complications from a U.S. Medicare study, other non-graft related open repair complications not captured by EVAR-1 have not been estimated. These include acute kidney injury, respiratory complications, ischemic colitis, and major venous injuries. Moreover, patients with more comorbidities are currently much more likely to receive EVAR, leaving "healthier" patients for open repair. Complications are more likely in these more complicated patients that will be receiving open repair in lieu of EVAR if the guidance moves forward. We recommend that these other non-graft complications be estimated from other studies and added to the elective infrarenal model, in line with how laparotomy-related complications were added. Starnes 2011 "…the EVAR 1 authors admit that the incidence of complications related to open repair were significantly underestimated because readmission data were not collected	This is factually incorrect. In response to criticism that they have underreported complications of OSR, the EVAR trial investigators performed a thorough retrospective review of HES data which enabled them to incorporate hernia procedures in their reporting. We use these data in our HE model. In addition, as you note, we have also captured further non-vascular reinterventions, which are more prevalent following OSR, based on a matched comparison of US Medicare data (Schermerhorn et al., 2015). These data include estimates of bowel resection, which we assume relates to ischaemic colitis. We assume that acute kidney injury and respiratory complications are accounted for in the perioperative period, by reflecting the greater duration of critical care, longer hospital stay, lower quality of life and increased need for rehabilitation in people undergoing OSR. We also include a scenario analysis in which additional disutility and costs associated with pulmonary complications are applied, based on 1 RCT that found a raised incidence of these events with OSR (DREAM). Major venous injuries are included in the complications on which EVAR-1 collected data – see table 1 in Patel et al. (2018).

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				on reinterventions for abdominal wall hernias, bowel obstruction, or late wound complications resulting from OR." Castagno 2016 Incidence of acute kidney injury was significantly higher after open repair than EVAR (26.3% vs 5.5%; P < .001). "There is an urgent need of a common classification for AKI after aortic surgery." Zabrocki 2018 "Previous studies on AKI after iAAA [infrarenal abdominal aortic aneurysm] repair are limited as they have not or only incompletely applied the current and uniform AKI definition and staging. This may result in underestimation of AKI rate and severity." "AKI is frequent after iAAA repair. Importantly, the incidence of AKI was significantly lower in patients receiving EVAR as compared to OAR. Even after correction for demographic and clinical variables, EVAR was associated with a substantial lower rate..." The protective effect of EVAR in regard to the development of CKD may be indicated by the lower rate of eGFR loss which we found after 3 months." "AKI is significantly less frequent and severe in iAAA patients after EVAR as compared to OAR, and OAR patients demonstrate a higher CKD rate." Perry 2008 The overall incidence of colonic ischemia was 2.2% (1941 cases); however, the incidence for specific procedures was significantly higher after…open elective repair (1.9%) than after EVAR (0.5%; both P < .001) "Major venous injuries during open AAA reconstruction are uncommon but can negatively impact patient outcome.	

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				Venous injuries during open repair of ruptured AAA may result in irreversible shock in a patient with unstable hemodynamics." "large amount of intraoperative blood loss with associated hypotension results in systemic inflammatory response, acidosis, and hypothermia resulting in multiorgan failure" Liang 2018 "Open AAA repair … [has] a significantly higher rate of respiratory failure and renal failure requiring hemodialysis that reflect clinically significant differences" "open repair carries similar perioperative mortality risks compared with EVAR in highly select populations, such as those of younger age, although with a concomitantly higher rate of respiratory complications…"	
W.L. Gore and Associates	Evidence review K	14	229-231	**The model overestimates the reintervention rate for EVAR.** The EVAR reintervention rate of 9.3% in the elective infrarenal model is based on EVAR-1, which has been criticized for overestimating complications resulting from EVAR. More specifically, EVAR-1 showed an unusually high estimate of type 2 endoleaks, and classified all type 2 endoleaks as complications. However, newer guidelines from the Society for Vascular Surgery (SVS) do not consider these endoleaks to be complications and recommend a monitoring approach rather than reintervention. If type 2 endoleaks are removed from the EVAR-1 figure, the EVAR complication rate falls to 4.9%. Other evidence supports this figure. The Gore GREAT registry, which includes procedures from 2010 to present, shows a long-term device-related reintervention rate of 4.2% The GREAT registry data is unpublished, but Gore will make this data available to NICE for review. In addition,	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as recommended by other stakeholders. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. The suggestion that EVAR is associated with the same rate of graft-related reinterventions as OSR is not supported by any evidence. Like you, we note Schermerhorn et al.'s finding that

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				Schermerhorn 2015 shows a decline in reinterventions over time due to changing standards over reintervention for type 2 endoleaks. Based on this evidence, we recommend that the estimates for EVAR complications in the elective infrarenal model be reduced to match those estimates for open repair: 3.04% at 0-6 months, 1.40% at 6 months-1 year; 3.60% at 4-8 years, and 3.60% at 8+ years. Starnes 2011 "Complications were not well-defined in EVAR 1 and not applicable to current practice: The EVAR 1 trial was designed before the 2002 Society for Vascular Surgery reporting standards on EVAR were published." "The EVAR Trialists defined all endoleaks as complications, which is incontrovertibly not supported by the more recent Society for Vascular Surgery reporting standards. Type 2 endoleaks are often benign and may resolve on their own. The majority require observation, with intervention being reserved for patients with persistent endoleaks and residual aneurysm sac growth" In the EVAR 1 trial, there were a total of 288 patients with complications in the EVAR group versus 72 patients in the open group. Among all patients with complications, 156 were type 2 endoleaks (in 108 EVAR patients and 3 OR patients), which comprised 62% of all endoleaks. If one removed type 2 endoleaks as complications from the analysis, there were 180 remaining EVAR patients with complications versus 69 with OR, thus lessening the difference in complications between the groups Chaikoff 2018	the reduction in reinterventions in their year-by-year data was driven by a decreasing number of minor reinterventions.Therefore, our revised model, which reduces the rates of all post-EVAR reinterventions using evidence from Verzini et al. (2014) probably overestimates the true impact of the secular trend.

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				Treatment and surveillance protocols, both related and not related to aneurysm expansion, have further developed into guidelines for the standard of care post-op – including treatment of type I endoleaks, and surveillance of type 2 endoleaks not associated with aneurysm expansion Schermerhorn 2015 "The decline in reinterventions seemed to be driven by a decrease in the number of minor reinterventions, primarily coil embolization, which probably represents a more conservative attitude toward the management of type 2 (side branch) endoleak."	
Cook Medical	Evidence review K	14	232-247	**Post perioperative survival and reinterventions – not suitable for OSR** In the not suitable for OSR model, long term mortality data and event rates are informed by the "only relevant RCT": EVAR-2. The 'no intervention' group was adjusted for crossover as one third of patients in this trial arm received EVAR. The trial investigators noted that "the rate of crossover in the trial suggests that it may prove difficult to withhold endovascular repair in the future" (Greenhalgh, 2010). We believe that this has significant implications for the implementation of the NICE recommendations 1.5.4 and 1.5.6. Commenting more recently on the strengths and limitations of EVAR-2, Roger Greenhalgh (EVAR-2 principal investigator) noted, "Yes, there were limitations—it is all in the publication—but nevertheless, what you have to take away is that the re-interventions of today, the practice of today, even the devices of today could give a different result" (Vascular News, 2018).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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				We recommend that the long-term mortality data and event rates for the 'not suitable for OSR' model, should not be based solely on EVAR-2 as they do not reflect current practice.	
Medtronic UK	Evidence review K	22	495 - 501	***Committee statement: EVAR "has more long-term complications, and these complications mean that people will need further procedures"*** Reintervention rate in ENGAGE is nearly half of EVAR-1. (19·3% in EVAR-1 and 10·9% in ENGAGE through 4 years). The difference in need for reinterventions could be attributed to the better fixation provided by the improved design of the proximal end of the Endurant stent graft (Stokmans et al. 2012, Dijkstra et al., 2016). The six-year freedom from secondary interventions was 81.9% and 70.4% for open repair and endovascular cohorts, respectively in the DREAM trial (De Bruin et al. 2010). Despite having higher anatomic complexity, both the Endurant U.S. IDE trial (Singh et al 2016) and ENGAGE Post-market registry (Presented by Cuypers 2017 VEITH) demonstrated freedom from secondary interventions of 89% and 84.3% respectively through 5 years. This indicates that secondary procedures are far better with modern devices and possibly approaching the same level of OSR. Additionally, a more aggressive approach to the treatment of type II endoleaks post EVAR has evolved since the time of the EVAR 1 and DREAM RCTs. A more reserved approach to only treating type II endoleaks if associated with AAA expansion is utilized today (SVS 2018 AAA Guidelines). Therefore, both EVAR 1 and DREAM overestimate the reintervention risk associated with type II endoleak following EVAR as practiced today.	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as recommended by other stakeholders. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Nevertheless, it cannot be disputed that EVAR remains associated with a higher rate of reinterventions then OSR. Like you, we note Schermerhorn et al.'s finding that the reduction in reinterventions in their year-by-year data was driven by a decreasing number of minor reinterventions.Therefore, our revised model, which reduces the rates of all post-EVAR reinterventions using evidence from from Verzini et al. (2014) probably overestimates the true impact of the secular trend.

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				It is notable that open AAA surgical repair postoperative incision hernia has been reported to be as high as 32% at mean follow-up of 48 months and 37% at mean follow-up of 36 months (Raffetto, et al, 2003). Most comparisons of EVAR vs. OSR fail to take into account laparotomy related procedures most commonly associated with open surgical AAA repair due to incisional hernias and wound complications. In an 8 year follow-up of U.S. Medicare beneficiaries treated 2001-2008 (Schermerhorn et al 2017) and combining aneurysm-related interventions with laparotomy-related interventions, patients undergoing endovascular repair did have higher rates of reinterventions (25% vs 21% at 8 years, P < .001). But, a large percentage of the reinterventions after EVAR were only "minor" vascular reinterventions. Conversely, hospitalizations related to the aneurysm- or laparotomy related complications without intervention were lower after EVAR (18% vs 22%, P < .001).	
Medtronic UK	Evidence review K	22	495-501	***Committee Statement: "There is no evidence that elective EVAR for people with an unruptured infrarenal AAA provides long-term benefit compared with open surgical repair"*** It is true that long term data (10+ years) are only available on older generation devices; however, data from more recent devices with changes to delivery systems, stent graft material, fixation methods etc. show improved outcomes through 5 years. It is likely that mid-term trends will be sustained over long term timeframes since the stent graft designs have evolved specifically to address first generation durability issues. In a meta-analysis of the four RCTs cited by the committee, the authors of the 4 RCTs discussed how EVAR has an initial advantage over OSR but there is a "catch up" in mortality over	The finding that EVAR is associated with excess post-perioperative mortality is strongly supported by the review of casemix-adjusted observational evidence that we have conducted in response to stakeholders' criticism that the consultation draft placed too much weight on RCTs alone – see **Theme 9**. In fact, this evidence suggests that the trials may represent an underestimate of the true effect in real-world practice. Moreover, these data provide no evidence that the excess late mortality with which EVAR is associated has diminished, relative to OSR, over time. We also note that, Verzini et al.'s study (2014) that has been cited – and adopted by us – as evidence of reduced rates of reintervention with newer

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				time. The RCT authors identified ARM as one of the main factors contributing to the catch up in mortality as "ARM was five times higher in the EVAR group (mainly due to secondary rupture or reinterventions)" (Powell et al. 2017) The RCT authors also note that by "using more recent EVAR devices, according to the instructions for use, coupled with more rigorous surveillance, the continuing ARM in the EVAR group could be attenuated". This conclusion is supported by recent data such as in the ENGAGE registry where the KM curves show a 97.8% freedom from ARM through 5 years whereas in the EVAR-1 trial, the freedom from ARM in the OSR group at 4 years was 93% (EVAR trial investigators, 2005). By percentages, 2.0% (25/1263,table 21e) of patients in ENGAGE had ARM over 5 years compared to 6.4% (40/626) of EVAR-1 patients who had aneurysm-related death within 4 years of the study (EVAR trial investigators, 2010). This indicates that modern devices have reduced one of the main concerns of older generation grafts that contributed to the "catch up" in mortality. Medtronic recommend that the committee should focus more closely on the data reported in the National Vascular Registry 2017 annual report, version 2, May 2018: Overall in-hospital mortality rates were 3.1% for OSR and 0.6% for EVAR. They note that in 2008, mortality rate for elective infra-renal AAA repair in UK was 7% which fell to 2.4% by 2013. Their current estimate of 0.6% for patients treated from 2014 to 2016 shows the continued improvement of EVAR.	compared with older endografts also looked for evidence of differences in survival and found none. You do not mention that there has been a similar decrease in OSR mortality over the same period. When the selection biases that confound treatment effect in observational data are accounted for, there is no evidence that relative perioperative mortality has become more favourable for EVAR compared with OSR over this period – see **Theme 3**. The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to estimate relative effects – see **Theme 3a**.

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				EVAR patients were more likely to be returned to the normal hospital ward (60%) while the vast majority of OSR patients were admitted to level 2 or 3 critical care unit (98%). OSR patients spent longer (8 vs 3 days) in hospital, had more respiratory complications, and returned to theatre more often. In the OVER Trial results: The restricted mean survival was not significantly different between the Open and EVAR groups at 9 years (P=0.65). Survival was better with endovascular repair than with open repair among patients younger than 70 years of age (hazard ratio, 0.65; 95% CI, 0.43 to 0.98; P=0.04) (Lederle et al, 2012). It is our understanding that the long-term follow-up results of OVER are due to be published soon and we would recommend that NICE await this publication before making their final decision on recommendations.	All these findings are accounted for in the analyses that supported the committee's decision-making. The committee agreed that, from a patient's point of view, they should be seen as insufficient to outweigh the medium- and long-term benefits of OSR over EVAR. They also agreed that, from the perspective of NHS resource-allocation, the savings associated with these items do not offset the upfront cost of the grafts themselves. The OVER RCT is included in the synthesis of long-term survival outcomes we use to estimate post-perioperative mortality in the conomic model that was developed to support the committee's decision-making. We have contacted the authors of OVER who confirm that they are working on an updated publication; however, no publication date is yet available.
Medtronic UK	Evidence review K	22	502-508	***Committee statement: (regarding patients who are unsuitable for OSR for unruptured AAA) "for these people, the risks of their AAA rupturing, if no repair is attempted, have to be balanced against the perioperative risks and long-term complications associated with EVAR. The evidence shows that the average person receiving EVAR has an uncertain chance of a small net benefit, compared with the large and certain increase in costs"*** Medtronic believe that the comparison of EVAR with no intervention is potentially unethical. The progressive nature of AAA disease is well established and the growth rate of unruptured AAA is generally thought to be around 0.5cm per year although the expansion rate and risk for rupture is greater	We cannot accept that a trial that found no net difference in patient-relevant outcomes between the approaches it compared was unethical. EVAR-2 shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group.

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				for larger diameter aneurysms (Brown et al., 2003, Aggarwal et al. 2011). A more appropriate comparison should be unruptured EVAR vs. ruptured EVAR/OSR. The benefits of intervention before rupture is obvious, as ruptured AAA repair has 5x greater mortality, worse outcomes, etc (Sullivan et al.,1990) In a more recent study of patients ineligible for OSR who underwent EVAR repair, (Lim et al 2015) divided patients into a high risk cohort (those ineligible for OSR, used same criteria as EVAR2) and normal risk patients. They reported no difference in perioperative mortality, morbidity, late graft-related complications, or freedom from reintervention between the high risk and normal risk patients showing modern EVAR devices are successful in even high risk patients. Outcomes of both groups were also much improved from the EVAR2 results as well as showing improvements in outcomes since the time of the older generation EVAR devices. The committee is using results from the EVAR2 trial to make this claim that EVAR for those unsuited for open repair is not worth the risk which was mostly because of a 9% in-hospital mortality rate and 8% pre-procedural mortality for the EVAR group. Timaran et al. 2007 points out several key flaws of the EVAR2 trial including 9 of 14 preprocedural rupture deaths were likely due to long delays in receiving treatment (median time 57 days) and also issues with the numbers of patient crossovers (47 of 172) in the non-intervention group. Timaran et al. then show in their study of patients in the Nationwide Inpatient Sample database from 2001 to 2004, that the highest risk patients only had a 1.4x increased risk of in-hospital mortality and the rates ranged from 0.4% to 1.7% for those undergoing elective repair. The authors also emphasize the importance of elective EVAR as the in-hospital mortality for	Regarding the suggestion that EVAR-2 overestimated the risk of mortality that is associated with endovascular repair of AAA in people for whom OSR is unsuitable, we note that our analyses suggest that EVAR would not be cost effective, in this population, even if it were associated with no perioperative deaths (see figure HE151). However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.

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				elective EVAR was significantly lower than for urgent/emergent EVAR (0.9% vs 8.4%, p<0.001). In the high-risk patients there was a much lower in-hospital mortality than reported in EVAR2. Because EVAR is already used in high risk patients with much success, the authors argue that EVAR should not be denied to high-risk patients and EVAR should be offered as an elective procedure to avoid urgent/emergent repairs. Lee et al. 2004 compared perioperative outcomes of EVAR (2565 patients) vs OSR (4607 patients) using 2001 data from the same National Inpatient Sample database. The authors note that EVAR patients had more comorbidities than those undergoing open repair (most likely because EVAR is preferentially used in the high risk elderly who cannot tolerate open repair) but their perioperative mortality was still significantly lower than open repair (1.3% vs 3.8%, p<0.001).	
The Vascular Society of Great Britain and Ireland	Evidence review K	23	532	**Impact of the proposed changes on current practice and available resources.** To demonstrate the impact on practice and the challenge of implementation related to the change from elective EVAR to open surgery we can utilise NVR data from the 2017 (report available at https://www.vascularsociety.org.uk/_userfiles/pages/files/Document%20Library/2017%20NVR%20Annual%20Report.pdf) If we estimate that in future 75% of current elective EVAR's are undertaken as open repairs, (25% are turned down for intervention) then the following national figures apply per annum using NVR data. Extra bed days = 7101 Extra ICU days = 1420 Extra HDU days = 1420	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For additional analyses undertaken after consultation please see the addendum in the Health Economic appendix. Return-to-theatre events are not separately accounted for in our HE model. This is because, depending on the precise timing of a given episode, they should be accounted for in

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				Additional post operative deaths = 82 Additional returns to theatre = 120 This does not include the workload arising from increased ruptures in patients turned down for repair, many of whom will in fact be treated with open repair, with prolonged ITU stays. An accurate estimate of this additional workload is not possible, but it will all add to the above figures.	either the estimates of intraoperative resource use from the RCTs or in reintervention rates. Therefore, applying an additional provision for such cases would double-count the costs with which they are associated. As regards the additional postoperative deaths associated with OSR, again, we cannot reproduce your estimate. By our calculations, the total number of excess deaths in the scenario you put forward would be 51 ([1246 + 2907 * 75%] * 2.9% = 99, compared with 1246 * 2.9% + 2907 * 0.4% = 48). As detailed in **Theme 3a**, the committee rejected the argument that unadjusted NVR data can be used to project perioperative mortality, because of the selection effects with which those data are associated. Instead, the committee's preference was to rely on estimates of relative effect that attempt to provide a balanced comparison between similar cohorts. Having reviewed casemix-adjusted observational evidence, which would have revealed – but did not reveal – any important secular trends that would invalidate the RCTs for current-day decision-making, the committee remained confident that the best estimate of relative effect is to be found in the randomised trials that were specifically designed to estimate them (see **Theme 2**). Accordingly, the committee's view is that the number of additional short-term deaths that would be associated with their recommendations is lower than would be inferred from NVR data (applying the pooled odds ratio from RCTs to the scenario here would result in an estimate of 14 extra deaths).

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W.L. Gore and Associates	Evidence review K	23	535-536	**Guidance would end the viability of the National Abdominal Aortic Screening Programme (NAAASP), increasing ruptures and deaths.** Men aged 65 and older that screen positive for a large aortic aneurysm will face high turn down rates for aneurysm repair under the draft guidance due to the closure of EVAR centres and the lack of availability of open repair due to lack of facilities and trained professionals. This will result in people screening positive for AAA not being able to receive treatment, which is in violation of WHO standards for disease screening programs. The lack of available treatment will increase anxiety for patients in the immediate term. Over the longer term, the NAAASP will become non-viable and fewer aneurysms will be identified, ruptures will increase, and deaths will increase, and more lives will be lost. Wilson 1968 WHO principles and practice of screening for disease: (1) The condition sought should be an important health problem. (2) There should be an accepted treatment for patients with recognized disease. (3) Facilities for diagnosis and treatment should be available…" "Of all the criteria that a screening test should fulfil, the ability to treat the condition adequately, when discovered, is perhaps the most important. In adhering to the principle of avoiding harm to the patient at all costs (the *primum non nocere* of Hippocrates), treatment must be the first aim. For declared disease there is, of course, the ethical obligation to provide an accepted treatment whether or not this is of scientifically proved value")	The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**. If it is cost effective to screen people for AAA under current service patterns, then optimising the treatment pathway to deliver better health at lesser cost can only make the screening programme more valuable.

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Medtronic UK	Evidence Review K And Economic Appendix and Model	24	582 - 586	***Committee statement: "the committee found no evidence that newer devices perform better than their earlier counterparts and did not consider this to be a reason to reject the evidence reviewed"*** Budtz-Lilly et al. 2017 examined data from two periods of time in the Vascunet registry with 34k patients from 2005-2009 and 49k patients from 2010-2013. Some of the notable findings they had were that between the two periods of time, peri-operative mortality for EVAR decreased (odds ratio 0.59, P<0.0001). In contrast, peri-operative mortality for OSR increased between the two time points. In this study, it was clear that modern EVAR had better outcomes than older generation EVAR while OSR was trending in the opposite direction. Several studies have shown that Endurant has better outcomes and greater patient applicability than earlier generation Talent, Excluder, AneurX, and Zenith devices which were the major grafts used in EVAR-1 (Verzini et al 2014, Stokmans et al. 2012, Dijkstra et al. 2016) [This text was identified as confidential so has been removed.] Other temporal analyses show EVAR outcomes have improved over time. The Swedish Vascular Registry reports a linear improvement in EVAR outcomes over time for the four time periods in their analysis (Lilja et al, 2017). In a study of thoracic endografts, although not directly related to elective infrarenal repair, Matsumoto et al. concluded that temporal changes in device design, operator familiarity, and surrounding equipment improvement were noted to have contributed to the improvements in outcomes in the Valor and Valor II clinical studies (Matsumoto et al. *2014)*	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that Budtz-Lilly et al.'s (2017) analysis of unadjusted registry data reflecting AAAs with heterogeneous anatomical complexity was of limited relevance to its decision-making for infrarenal AAA – see **Theme 3b**. The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.

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				The DREAM trial (one of the original randomized control trials comparing OSR to EVAR) and the EUROSTAR registry included patients from the same region and in the same time period and showed comparable risk characteristics and outcomes. Since the research design methodologies led to similar results, the authors concluded that the registry offered a reliable source of real-world practice and justified future research comparisons using registry data (Leurs et al. 2007). Other reports have concluded well designed observational studies do not overestimate the magnitude of effect of treatments and can provide comparable data as RCTs (Concato et al 2000, Benson et al.2000). The RCTs that the committee proposes to compare modern EVAR devices to OSR are unlikely to occur . Thus it is important to understand real world registeries are reliable sources of data on current devices and their outcomes. In 2009 Chambers et al., assessed EVAR vs. OSR in advance of the NICE technology appraisal TA167. Within their methodology, the authors acknowledged the evolution of devices and surgical technique since EVAR-1 and consequently adjusted their parametric survival model. Medtronic would like to understand why this TA methodology is no longer acceptable within the modelling process for Clinical Guideline development?	
W.L. Gore and Associates	Evidence review K	24	582-586	**Model does not account for changes in devices over time.** The model assumptions on outcomes and cost and are based largely on results from the EVAR-1 study, which enrolled patients from 1999 to 2004. EVAR devices have evolved over the interim period, and outcomes have improved as a result. The device improvements and corresponding improvement in outcomes should be taken into account in the model.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				For example, the Gore Excluder® was used in EVAR-1, and a new version of the device was introduced in 2004 after EVAR-1 enrolment concluded. This new product utilized low permeability film, which studies show resulted in aneurysm sac size reduction compared to the previous Excluder model. In addition, the Zenith device manufactured by Cook was used in 55% of the procedures in EVAR-1, the Talent device from Medtronic was used in 32%, and the AneuRX from Medtronic was used in 3%. These Medtronic devices had poor outcomes and are no longer on the market. The Cook device has also been updated in the interim period. Epstein 2014 "EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future. EVAR devices used in these four trials were of an earlier technological generation..." "Endovascular technologies and their clinical applications are evolving rapidly. This indicates that EVAR should continue to be considered a research technology."	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.

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				England and McWilliams 2018 "What started as a series of devices constructed in the operating theatre has evolved into mass produced 'off-the-shelf' systems which can treat a range of patients. Not only has anatomical eligibility increased but other vascular diseases are now being treated using a stent-graft." "…we have seen huge developments in EVAR technologies and their applicability. Devices… are repositionable within the aorta and can conform to more challenging anatomy."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Liang 2018 "The current generation of endografts have been in use only for the past decade; long-term durability of these devices remains unknown but has a clear dependence on adherence to the device instructions for use"	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Patel 2016 "EVAR devices are constantly being improved and sizing and imaging methods available for deployment are better now than they were between 1999 and 2004…"	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Picel and Kansal 2014 "Stent-graft design continues to rapidly evolve as new devices are under development to address the shortcomings of the early stent-grafts."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Chambers 2009 The previous health technology assessment from the National Institute for Health Research (NIHR) acknowledged improvement in devices and practice over time and accounted for this improvement.	

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				"This apparent increase in the risk of death with time from EVAR may be confounded by evolution of devices and surgical technique, as those patients with the longest follow-up underwent EVAR with the oldest devices. We tried adjust for this by estimating parametric survival models, including a variable representing the year that the device was fitted..." Parameters for this HTA were included as a sensitivity analysis in NIHR 2018 health technology assessment (Patel), and found EVAR to be cost effective. Schermerhorn 2015 "The outcomes of endovascular repair have been improving over time." Across the Medicare population, the rate of total reinterventions at 2 years after endovascular repair decreased over time, from 10.4 in 2001 to 9.1 percent in 2007. These results were statistically significant due to the large sample size. "In a comparison of the results of repairs performed from 2005 through 2008 with those performed from 2001 through 2004, the overall survival rates were higher in the later period...." "The decline in perioperative mortality probably represents operators' increased familiarity with the procedure and improvements in endografts over time." While this is a U.S. study, the NICE guidance references other evidence from Medicare. Verhoeven 2014 "From 1998 to July 2004, the stent-graft was constructed with the original permeability (OP) e-PTFE fabric (n = 55; 45%); from July 2004 until the end of the study the stent-grafts	This study is included in our supplementary review of casemix-adjusted observational evidence. See **Theme 2** and **Theme 9** for comments. No quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts

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				incorporate a low-permeability (LP) e-PTFE fabric (n = 67; 55%)." "Technical success was achieved in 396/400 (99%) patients. Two patients needed intraoperative open conversion" "No patients required conversion to open repair during follow-up" "No stent-graft migration was noticed in any patient during follow-up" "Recently, the early results of the ENGAGE registry were published, showing promising real-world performance of the Endurant stent-graft (Medtronic Endovascular, Santa Rosa, CA, USA) in the short term. Early results of the C3 Excluder are comparable to the results of the ENGAGE registry in terms of initial technical success (both 99.0%)…" "Real-world performance as reflected by the European C3 module of GREAT indicates that the new C3 Excluder stentgraft offers excellent early and short-term outcome." Hogg 2011 The low porosity Excluder endograft (Excluder low-permeability endoprosthesis [ELPE]; W. L. Gore & Associates Inc, Flagstaff, Ariz) introduced in 2004…" "A sustained sac regression after AAA exclusion with ELPE is noted up to 5-year follow-up."	No quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts
W.L. Gore and Associates	Evidence review K	24	582-586	**Model does not account for changes in device deployment over time.** EVAR deployment systems have evolved since EVAR-1 enrolled patients, and outcomes have improved as a result. The changes in deployment and the corresponding improvement in outcomes should be taken into account in the model.	We do not agree with your hypothesis, which appears unsubstantiated.

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				For example, the Gore C3 Excluder®, introduced in 2010, included a new deployment system that allows for repositioning of the stent graft multiple times before deployment. Studies have shown that the C3 resulted in improved deployment accuracy and decreased use of unplanned proximal cuff-extenders relative to previous Excluder models. England 2018 "…we have seen huge developments in EVAR technologies and their applicability. Devices are now deployable on smaller delivery systems, are repositionable within the aorta and can conform to more challenging anatomy." Verhoeven 2014 "The C3 Gore Excluder stent-graft is a third-generation modern device featuring an original design with a flexible, catheter-mounted introduction, and active infrarenal attachment with barbs. The deployment mechanism has been modified into a three-step sequence, which enables positioning of the stent-graft up to three times prior to final release from the delivery catheter." "Early real-world experience shows that the new C3 delivery system offers advantages in terms of device repositioning resulting in high deployment accuracy." "This resulted in a high rate (96.2%) of accurate proximal deployment of the stent-graft and low use (4.8%) of unplanned proximal cuff-extenders, which was lower than older EVAR series."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making. No quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts
	Evidence review K	24	582-586	**Model does not account for improvement in surgical technique over time.** EVAR surgical technique has evolved	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and

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W.L. Gore and Associates				since EVAR-1 enrolled patients, and outcomes have improved as a result. An example is the increasing use of the minimally invasive percutaneous EVAR technique, which has been shown to reduce complications, operative time, and length of stay. The improvements in technique and corresponding improvement in outcomes should be taken into account in the model. Chambers 2009 The previous NIHR HTA acknowledged improvement in practice over time and accounted for this improvement. "This apparent increase in the risk of death with time from EVAR may be confounded by evolution of devices and surgical technique…. We tried adjust for this by estimating	appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 3 on secular trends and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.

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				parametric survival models, including a variable representing the year that the device was fitted..." Parameters for this HTA were included as a sensitivity analysis in NIHR 2018 HTA (Patel), and found EVAR to be cost effective.	
				Epstein 2014 "EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future… preoperative imaging was rudimentary, rehearsal and simulation not standard, and hybrid suites not observed. Instructions for use were not always available."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Schermerhorn 2015 "The outcomes of endovascular repair have been improving over time." Across the Medicare population, the rate of total reinterventions at 2 years after endovascular repair decreased over time, from 10.4 in 2001 to 9.1 percent in 2007. These results were statistically significant due to the large sample size. "In a comparison of the results of repairs performed from 2005 through 2008 with those performed from 2001 through 2004, the overall survival rates were higher in the later period...." "The decline in perioperative mortality probably represents operators' increased familiarity with the procedure…"	See **Theme 2** and **Theme 9** for comments.
				Roche-Nagle 2018 "AAA repair completed with the PEVAR approach demonstrates reduced operating time (101 minutes vs 133 minutes), length of stay (2.2 days vs 3.5 days), time in the	The guideline did not include a review of the costs and benefits of percutaneous access techniques for EVAR. However, we are aware that the claim is made that they reduce net resource consumption, including theatre time, critical care requirement and overall length of stay, with

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				recovery room (174 minutes vs 193 minutes), and postoperative complications (6% vs 30%)…" "…switching to the PEVAR approach in a Canadian hospital performing 100 AAA repairs annually would result in a potential cost avoidance of CAD$245,120."	enough savings to offset the nontrivial acquisition costs of the devices. As the revised economic model now reflects contemporary (NVR) data regarding length of stay and requirement for critical care, our analysis already incorporates a good proportion of any such benefit, to the extent that the approach is used in the UK. However, we do not include any costs. Therefore, this factor is likely to bias the analysis in favour of EVAR, to some degree.
Medtronic UK	Evidence review K	24	582-586	**Device Evolution:** Open surgical repair techniques and clinical outcomes evolved over a 20-25 year period leading to modern open surgical repair that has been utilized since the mid 1970s to today with known durability if patient survives the early morbidity and mortality associated with the invasiveness of open surgical repair. Endovascular repair was developed in an effort to make AAA treatment safer and allow repair for patients not able to withstand surgical repair. Since its initial introduction, EVAR has gone through a similar evolution curve. A lot has been learnt since late 1990's/early 2000's when initial devices became more widely available as treatment option for patients with abdominal aortic aneurysms. Modern EVAR devices have evolved to address earlier generation failure modes primarily related to loss of fixation and seal and AAA sac stabilization over time. Current designs as compared to the historical stent grafts used in the EVAR-1 trial are specifically engineered to reduce the rate of early and late failures (requiring secondary intervention) as seen in device generations used in EVAR 1, DREAM, and OVER. Medtronic wishes to explain some of these changes specific to Medtronic to help the committee understand that industry monitors for and does deep analysis into device failure modes.	The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Thank you for summarising for us the technical developments that may have led to lower reintervention rates.

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				The purpose of this is to continue to evolve device safety and efficacy. In the EVAR 1 study, 206 (40%) of implanted stent grafts lacked active fixation meaning that stent migration and loss of fixation and seal was a common reason for secondary intervention or device failure. During this time it was not universally established that 'active fixation' i.e. the provision of hooks or barbs intended to engage with the aortic wall would result in better patient outcomes. Currently available EVAR devices are now all provided with active fixation. The profile of the delivery systems has also reduced significantly since EVAR-1 when devices were between 20Fr and 25Fr (6.7mm to 8.3mm) which often resulted in the unwanted dilation of access vessels during introduction of the stent graft thus leading to stenosis or occlusion, requiring surgical revision after the EVAR procedure. Modern stent grafts now have lower profile delivery systems ranging in diameter from 4.7mm to 7.7mm to avoid access issues. Some early generation devices, including some used in EVAR-1, had issues with the permeability and abrasion of the stent fabric which consequently could lead to sac expansion. In the 3 generations of devices manufactured by Medtronic, we have seen improved sac stability with the 5 year rates of sac enlargement improving from 17.3% (AneuRx Clinical Update-Vol.-IV) with Aneurx to 4.2% with Endurant (Endurant Clinical Update 2016 Vol. VI) in the U.S. IDE trials. Older generation fabrics have evolved with denser weaves and processing to reduce permeability and improve resistance to abrasion that can lead to sac expansion. The use of improved	

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				fabrics combined with better device fixation and seal has contributed to more stability in AAA sac behavior. Significant sac shrinkage is a known marker for EVAR durability. (Gonçalves et al 2014). EVAR device design changes since EVAR 1 include: • Avoidance of oxide-coated Nitinol wire • Improvements in stent fabric permeability and suturing pattern of stents to improve abrasion resistance • Equal radial force across the stent and bifurcations • Increased sizing options available • Greater conformability for better anatomic fit • Improved deliverability and greater control during deployment Below we describe how the design features and benefits of Medtronic EVAR devices have evolved over time: **Device:** AnueRx **UK Launch:** 1997 (no longer commercialised) **Used in EVAR-1?** Yes, 3% **Design Features:** Modular stent graft, laser cut stents throughout, delivery system with runners and use of external machined handle to overcome high deployment forces, Low porosity graft material **Benefits vs. Previous Devices:** N/A **Device:** Talent **UK Launch:** 2000 (no longer commercialised) **Used in EVAR-1?** Yes, 32% **Design Features:** Suprarenal stent (No active fixation), Wire formed stents throughout. Coil trak delivery with integrated	

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				balloon, Larger stent grafts sizes >28mm to expand treatment options to patients with larger AAA necks. **Benefits vs. Previous Devices:** Lower rate of migration, Fewer balloon exchanges, Ability to treat more patients with larger necks. **Device:** Endurant **UK Launch:** 2008 **Used in EVAR-1?** No **Design Features:** Low profile delivery system, Suprarenal stent with anchor pins – active fixation, Proximal "m" shaped seal stent to enhance conformability and seal shorter and more angled AAA necks, Tip capture mechanism with more precise device placement accuracy. **Benefits vs. Previous Devices:** Broader patient applicability, Fewer access complications, Low rate of device migration, Low rate of proximal endoleaks, Precise deployment in short and challenging proximal necks. **Device:** Endurant II **UK Launch:** 2011 **Used in EVAR-1?** No **Design Features:** Reduced profile for 28mm SG, Longer limb lengths, Tip capture modifications, Increase opacity of contralateral gate **Benefits vs. Previous Devices:** Fewer access issues with most-commonly implanted 28mm SG, Treat longer anatomy with single limb and reduce number of distal extensions, Fewer delivery system removal issues, Easier gate cannulation for reduced fluoro and contrast utilization. **Device:** Endurant IIs	

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				UK Launch: 2014 **Used in EVAR-1?** No **Design Features:** Short bifurcation (3-piece system), Bifur legs equal diameter and radial force, In-situ sizing, 5 bifurcations options (compared to 31 for Endurant II), Main body diameter more consistent from seal stent to bifurcation **Benefits vs. Previous Devices:** Equal radial force in each bifurcation leg = reduction in limb issues, Increased sizing options for ipsilateral limb, In-situ sizing allows device to be customized to patient anatomy, 5 bifurcations improves inventory management and decision-making speed.	
Leeds Teaching Hospitals NHS Trust	Evidence review K	24	584	The current level 1 evidence questions the long-term outcomes after EVAR. The main perceived reason is graft failure. However, this data is based on old, out-of-date technology and a less experienced pool of operators (minimum of operator experience of 20 EVARs for EVAR 2 trial) with secondary interventions before 30 days more common in patients allocated EVAR (9.8% vs. 5.8%, p=0.02) . Current graft iterations may prove to be more robust in the long term with reduced degradation/migration/dislocation. There does not appear to have been consideration to past or on-going innovation and development. There are a number of emerging EVAR treatments and adjuncts. Whilst these need rigorous evaluation and undoubtedly some will fail to improve outcomes (such as the early iterations of the Nellix EVAS system); some can reasonably be expected to improve current practice. The worldwide practice of EVAR shows that rightly or wrongly, the aortic community believes in it. If these recommendations are accepted, The United Kingdom is in danger of becoming a single outlier in terms of aortic repair. We firmly believe in evidence-based practice and if our national practice is going to deviate significantly from other	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.

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				first-world norms we need to be very clear that this is in the best interests of our patients.	
Leeds Teaching Hospitals NHS Trust	Evidence review K	24	592	EVAR is recognised to have a re-intervention rate. There are a number of issues to consider here, some of which are contrary to one another. The committee states it believes one of the two most important outcomes is 'reduction in the need for re-intervention'. Given the low morbidity of EVAR (and reasonably expected to continue to improve) it can be argued that re-intervention is not always a disaster. When discussing repair options with patients in clinic, some may choose to have a lower morbidity better short-term outcome operation and accepting that they may need re-intervention in the future. This may be an opportunity for further PPI (Patient Public Involvement) research. Contrary to this, we do not have level 1 evidence to support re-intervention for many patients. The indications for re-intervention have changed since the EVAR 1 trial, when many patients underwent re-intervention for type 2 endoleak. As a vascular community, we are now far more conservative in our management of type 2 endoleaks unless there is sac expansion. This may also impact on the health economics modelling for EVAR. We agree this is another area where there is a paucity of quality evidence and clinical trials to answer some of these questions would be welcomed. There are new devices in development that aim to polymer fill the aneurysm sac (Nellix from Endologix and Arsenal from Medtronic) that may allow obliteration of type 2 endoleaks at the initial operation, again reducing re-intervention rates.	Comment noted. The committee agreed with this point. There is evidence that reintervention rates may have decreased since the time of the RCTs, but it tends to suggest that the decrease has been driven by relatively minor procedures, little change in the rate of complications requiring serious reinterventions. See **Theme 7**. Comment noted.

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European Society for Vascular Surgery (ESVS)	Evidence review K	24	572-3	'the committee agreed that complex EVAR should only be performed in the well-controlled environment of an RCT'. Where a patient is offered the opportunity to join a RCT, with one complex open procedure vs. a much less invasive operation, it is likely that they will not wish to take part in the trial, but will opt for a less invasive procedure. This is likely to prevent progress in evidence and a well-conducted Registry for expert centres may be more valuable. This would require the patient to be treated in centres where results for both procedures were excellent and follow up thorough.	The committee were mindful of the finding, from casemix-adjusted observational evidence, that there is no difference in perioperative mortality between complex EVAR and OSR. Moreover, they noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that it is associated with a large reduction in perioperative mortality, there should be equipoise about whether any such effect translates into net health gain over a patient's lifetime. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
The Vascular Society of Great Britain and Ireland	Evidence review K	24 26	584-6 667-8	**EVAR techniques and devices have not improved since the EVAR trials (relevance to recommendations 1.5.2 – 1.5.4)** The committee state that they could find no evidence that current EVAR devices performed better than those used in the EVAR trials. Reference is made to the single centre study of Hammond et al 2016 and the SwedVasc and Medicare registries. This is a change from the opinion expressed in the EVAR technology assessment 2009 (TA167) where "The Committee was persuaded that the benefits of EVAR compared with OSR in current UK clinical practice were likely to be greater than those seen in the RCTs".	On reviewing this and similar stakeholder comments, the committee accepted that further exploration of the implications of modern EVAR devices on likely reintervention rates was warranted. They agreed that, using the evidence cited here and by other stakeholders (Verzini et al., 2014), the original HE model should be configured to simulate a lower rate of reintervention with EVAR than had been used in the base-case model on which consultation comments were sought. This had the effect of substantially attenuating the excess costs associated with long-term follow-up following EVAR. However, this revision was insufficient to rebalance the analysis in favour of EVAR, which remained dominated in the infrarenal case and associated with a high ICER in the complex case. See **Theme 7** for details.

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				The study by Hammond is a single centre retrospective analysis of EVAR outcomes. All inserted after 2007 so not comparable with the EVAR trial period (1999-2004). In fact the older stent graft, Talent, does show inferior performance but it fails to reach statistical significance. This is likely to be a type 2 statistical error given the small study numbers. The devices used were Talent followed later by the Endurant, both products of Medtronic Inc. Data from the manufacturers registry (Engage) compared with the EVAR 1 trial outcomes shows a reduced re-intervention rate at 4 years with Endurant 2009-11 (19.3% in EVAR1 10.9 % in Engage) Verzini et al 2014 report outcomes of 530 old stent grafts (1997-2003) compared with 882 newer stent grafts (2004-11). These timeframes are closer to those of EVAR trials and post EVAR trials than the Hammond study. In adjusted analyses, the use of a new-generation device was a negative independent predictor of reintervention [hazard ratio (HR) 0.67, 95% confidence interval (CI) 0.49 to 0.93, p=0.015] and aneurysm growth (HR 0.63, 95% CI 0.45 to 0.89, p=0.010). With regards to the Medicare registry data, Schermerhorn ML 2015 reports a large propensity matched study of open and EVAR repairs (39,996 matched pairs). In this analysis the results of EVAR in terms of reinterventions were shown to improve between 2001 and 2007 (10,4% falling to 9.1%). The analysis also demonstrated improved perioperative outcomes for EVAR from 2001 to 2008. In Supplement Table 6, mortality decreased from 2.2% in 2001 to 1.4% in 2008, similarly conversion to open repair decreased from 2.2% to 0.3%, readmissions in 30 days decreased from 10.8% to 9.4%. The Supplement also includes a discussion of the	These data are considered in **Theme 7**. See also **Theme 2** for comments on year-by-year mortality data from this study. Restricted mean survival analysis is effectively a primitive form of the lifetime analysis of benefits that is available – integrated alongside a similarly thoroughgoing analysis of harms and costs – in the original HE model developed in support of this guideline. In our base case, we find that EVAR is associated with net QALY gains for around the first 7 years of the model (see Figure HE101); however, the cumulative difference begins to favour OSR as the model progresses. (We would

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				concept of restricted mean survival (RMS) analysis to account for the difference in area under the survival curves. This is appropriate when the proportional hazards assumption is violated as in the comparison of survival after EVAR and open AAA repair, where the survival curves eventually come together. In this RMS analysis the significant benefit of EVAR over open repair for survival persists for 7 years. We were unable to find references of an up to date analysis of the Swedvasc registry with results for current EVAR devices compared to 1999-2004. At the time of the EVAR trials, UK stenting was in its infancy. Planning often involved using hand held calipers on hard copy x-ray images, mobile theatre imaging with poor resolution and angulation. Limited operator experience. Higher use of uni-iliac devices and cross over surgery. Patients staying in hospital for 7-9 days post EVAR with a CT prior to discharge. Current practice has changed very significantly. 3D reformatted planning on digital workstations, increasing use of percutaneous EVAR, daycase or overnight stays with no immediate post procedure imaging. The new evidence provided above considered alongside the changes in clinical practice since the EVAR trials makes it extremely difficult to support and justify the statement that "the results of EVAR procedures and devices has not improved since the time of the EVAR trials". EVAR is now carried out in a more efficient way with low mortality and the results of the devices have improved compared with the time period of the EVAR trials. The modern	caution against the interpretation that EVAR is necessarily likely to provide greater benefits for people with a life expectancy less than 7 years, as the period over which benefit can be accrued will also be shorter in such people.) We accept that this reference was ambiguous; it has been removed as part of our comprehensive revisions reflecting the committee's updated consideration of this issue. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				use of EVAR, within IFU, needs to remain an option for patients meeting agreed criteria. Close evaluation of these procedures will inform us of the value of this approach and allow for better future decision making on the use of EVAR. Refs. Verzini F et al J Endovasc Ther. 2014 : 21 ; 439-47 Schermerhorn ML et al NEJM 2015 : 373 ; 328-38. Engage registry data provided by Medtronic Inc.	
Medtronic UK	Evidence review K	25	614-623	**"However, complex EVAR grafts are much more expensive than standard devices, so the difference in cost between EVAR and open surgical repair is even greater than in infrarenal AAAs. The committee also noted that the instructions for use of the grafts that are currently available do not cover complex AAAs."** The above statement (and subsequent economic analysis) indicates that there may be some confusion amongst the committee in terms of the range of endovascular devices that are encompassed by the phrase "complex EVAR". Medtronic received CE mark for Chimney EVAR in December 2016 when performed with our EVAR device, Endurant IIs. Please inform Medtronic if this CE mark documentation is required by the committee. These procedures do not require a bespoke fenestrated device and as a result are only a fraction of the price. Medtronic therefore believe that ChEVAR cannot be included within the same economic model as FEVAR because the current assumptions related to device cost (£15,686) and mortality risk due to device wait-time are not relevant to on-label, off-the-shelf ChEVAR procedures.	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. However, there are no comparative data on the safety and effectiveness of chEVAR, which makes it impossible to arrive at an evidence-based conclusion as to its cost effectiveness. We present sensitivity analysis on graft cost in our model results (see figure HE59, HE60 and HE61 in the consultation draft, and updated equivalents in figures HE133, HE134, HE135 and HE136). If it were safe to assume that chEVAR has exactly average results for all complex AAAs, then it might be possible, using evidence like this, to infer a graft cost at which chEVAR could be considered reasonable value for money.

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				Medtronic are extremely proud of the product training and expertise of our sales team, and we want to reassure the guideline committee that the teams are only promoting our devices for use following the mandated IFU.	
W.L. Gore and Associates	Evidence review K	26	704-712	**Guidance will result in reduced patient choice**. Patients strongly prefer EVAR over open repair. A recent study suggests that 84 percent would choose EVAR when presented with the risks and outcomes from EVAR versus open repair. However, the guidance removes the option for letting patients assess their own risks and make an informed choice regarding their care. This lack of patient choice for aneurysm repair will be in opposition to NICE's goals for patient shared decision making and the NHS's goals for strengthening patient choice. Moreover, the potential impacts on outcomes from patients making more informed decisions has not been accounted for in the model because the assumptions are derived from EVAR-1 (1999-2004), a randomized trial that did not permit patient choice. Winterborn 2009 84 percent of patients preferred EVAR when presented with the risks and outcomes from EVAR versus open repair. Most important concerns of patient preference for patients that need AAA repair include 4 of 5 areas where EVAR consistently outperforms open repair: pain, time to recovery of physical functioning, length of hospital stay, and body appearance. Burgers 2016 "EVAR is the more favorable option for patients who are eligible for both types of interventions, as EVAR and OSR are comparable in long-term effectiveness and EVAR leads to a	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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				reduction in costs. This study provides evidence that the use of EVAR in daily practice is justified" Chaikof 2018 "Several prediction models developed to estimate operative risk for open AAA repair and EVAR hold the promise of better informing patients of their individual risk of perioperative mortality and provide surgeons a useful tool to ensure an informed discussion with patients and their families." NICE Shared Decision Making website "We've updated all of our guidelines to highlight the importance of balancing professional judgment and expertise with the needs and wishes of people receiving care." NHS Patient Choice website "NHS England's goal is to significantly improve patient choice by 2020." "Our vision for patient choice by 2020 is that:"… "All GPs/referrers discuss the different treatment options available to patients, include them in shared decision making, and offer choice to patients"	
VASGBI (Vascular Anaesthesia Society of Great Britain & Ireland)	Evidence review K	26	706	There seem to be no allowance for patient choice with regards to elective abdominal aortic aneurysm (AAA) repair and the NICE document provided no data on patient preference. The committee stated that they were not aware of any evidence formally eliciting patient preference over EVAR and open surgery. However, there are some published studies on patient preference. One study reported that 46% of patients prefer EVAR vs 18% preferring open surgery (Reise JA et al., Eur J Vasc Endovasc Surgery 39: 55-61, 2010). Winterborn RJ et al (J Vasc Surg 49: 576-81, 2009) reported that 84% of patients expressed a preference for EVAR. Patient choice is important for consent and the shared decision-making process	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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				in modern practice and some allowance should be made for this.	
The Vascular Society of Great Britain and Ireland	Evidence review K	26	706-707	**Evidence for Patient Choice / Preference**. Recommendations 1.5.2-4 and 1.5.6 remove patient choice in the treatment of their AAA. Patient choice is now central to consent and the supported decision process. The committee were not aware of any evidence relating to patients' preferences for EVAR or open surgery. In fact two papers have addressed this issue, (Winterborn RJ 2009; Reise JA 2009). Factors that were important to patients with AAA when deciding on EVAR or OSR were mortality of the procedure, avoiding ITU, shorter hospital stay and shorter recovery time. These were graded as more important than risk of endoleak and unknown durability of the procedure. In one study 84% preferred EVAR, 13% OSR; in the other 46% EVAR, 18% OSR. The trial evidence (EVAR 1, DREAM, OVER, ACE) shows EVAR to be equivalent to OSR for 8 yrs. When given an explanation and information the majority of patients choose EVAR. There are also those patients with an AAA >6.5cms who are unable to drive under DVLA regulations. For those reliant on their ability to drive they lose some independence. No intervention is therefore a poor option for them and increases burden on their carers. This needs to be considered within the impact of these recommendations. A meeting of the Liverpool Aneurysm Public and Patient Information (PPI) group has been shown the NICE guidance. The summary of the discussions is as follows :	Thank you for drawing our attention to this literature, which other stakeholders have also cited. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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				Patients strongly prefer to be informed of all the treatment techniques and as detailed information as possible regarding supporting evidence. Recommendation or offer of 'one best' treatment based on evidence and / or guidelines was not considered adequate counselling. Patients take different choices under the same circumstances, with the same information. Patients understand the importance to the NHS of treatment costs. Patients expect treatment costs to play no role in selection or offer of treatments. The committee do briefly refer to the issue of patient choice (lines 710-11) stating that individual choice did not compel them to recommend treatment which is not cost effective. However this was before the available evidence on patient preference had been considered. Given the opportunity now to appraise the above evidence we feel this important issue should be re-considered. Some flexibility in access to EVAR would provide for informed decision making with patients. When asked in our membership survey, 183/233 (79%) supported informed patient choice in the decision for OSR or EVAR. **References** : Winterborn RJ et al J Vasc Surg 2009;49:576-81 Reise JA Eur J Vasc Endovasc Surg (2010) 39, 55-61	
Medtronic UK	Evidence review K	26	706-707	**The committee reported that there is no evidence relating to patient preference for EVAR over OSR.** Given that NICE highlight the importance of needs and wishes of people	Thank you for drawing our attention to this literature, which other stakeholders have also cited.

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				receiving care, Medtronic wish to provide information on published studies that have in fact addressed this key aspect: Reise et al. 2010 performed a survey in 2008 of patients' preference for EVAR vs OSR and concluded that 18% preferred OSR and 46% preferred EVAR. Notably, 40% said they would follow the advice of their physician. Respondents in this study prioritized having a shorter recovery time (50%), minimising ICU time (42%) with the least concern for scar size (10%) and impotence (27%). Winterborn et al. 2009 performed an interview on patients who had already been informed about EVAR vs OSR as they were potential candidates for the surgery. In this study, younger people were more likely to prefer OSR and some cited the concerns for lack of long term data on EVAR as the reason for this. However, an overwhelming number (84%) preferred EVAR and only 17% preferred OSR. In this study, risk of postoperative death and major organ failure were the main concerns while patients were least concerned about scarring and radiation exposure. Faggioli et al. 2011 looked at specific elements that differ between EVAR and OSR procedures such as local anesthesia for EVAR compared to general anesthesia for OSR. Patients in their PREFER study were then presented with a choice of hypothetical scenarios consisting of a combination of EVAR and OSR elements such as type of anaesthesia, time to return to normal activities, reintervention risk, risk of severe procedural complications etc. This method allowed them to assess specifically which defining characteristics were priorities to the patients and they reported that the risk of	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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				major complications, reinterventions, or mortality were the most important components in choosing EVAR or OSR. Return to daily activities was also important. Given that patients are predominantly asymptomatic when the decision to intervene is made, we are concerned that the prospect of an open surgical procedure will cause many patients to opt against AAA repair all together if their choice of EVAR or OSR is removed. This could have a detrimental impact on rupture rates in the UK.	
The Vascular Society of Great Britain and Ireland	Evidence review K	30	869-71	**Symptomatic AAA**. The committee decided that no specific recommendations were required for symptomatic AAA since the evidence for asymptomatic AAA would apply. However, it has been known for many years that patients treated on an urgent basis with a "symptomatic" AAA have higher procedural mortalities (Haug ES 2004). A symptomatic AAA is assumed to be at risk of rupture and treated within hours or a few days at most. Fitness assessment is limited. Optimising co-morbidities is limited. Also, faced with impending rupture, the surgeon and patient will aim for an intervention accepting higher risks. For all the above reasons the symptomatic AAA is a very different set of circumstances to the asymptomatic AAA. No RCT data exists for this cohort. Faced with higher procedural mortality, basic information on fitness, inability to optimise and need to avoid rupture surgeons should have access to EVAR for this group of patients. The committee do acknowledge (evidence review K, line 547) that there is a fundamental need to avoid AAA rupture. We argue that this particularly applies for the symptomatic AAA patient and specific	The evidence base for symptomatic AAAs is extremely sparse, as can be seen from the fact that the paper you cite is a Norwegian case series that recruited participants in 1983–1994. Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the

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				recommendations are required with EVAR the obvious solution given appropriate AAA anatomy. **Ref** Haug ES EJVES 2004 : 28 ; 612-8	studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.
The Vascular Society of Great Britain and Ireland	Evidence review K	30	872-875	**AAA Repair in Women**. The committee conclude that outcomes for women should not differ from men and therefore no recommendations specific to women are required. However elective open repair has a higher mortality in women (5.4% vs 2.8%) compared with men. This difference is reduced with EVAR (2.3% vs 1.4%). Women have higher ruptured AAA rates than men. We do feel that specific consideration does need to be given to the role of EVAR in women for unruptured repair. **Ref** Ulug P Lancet 2017 : 389 ; 2482-91.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The original HE modelling undertaken to support this review was configured to explore evidence of subgroup-specific cost effectiveness, including in those defined by sex. As noted in Evidence review K *The committee discussed whether the cost-effectiveness evidence suggested that there may be differences in the balance of benefits and harms between men and women, both when open surgical repair is a suitable option and when it is not, for the elective repair of unruptured infrarenal AAA. None of the preferred ICERs were sensitive to the sex of the cohort…* We have revised the section of committee discussion which prompted your comment to refer back to this evidence. See **Theme 12** for further discussion.

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W.L. Gore and Associates	Evidence review K	30	872-875	**Guidance does not address the disproportionate impact on women.** Women receiving open repair have significantly higher short-term mortality rates than men. Recent studies show that in-hospital mortality is about 50 percent higher and 30-day mortality is 76 percent higher in women than men after open repair. The guidance fails to address this disparity in mortality and the fact that aneurysm repair mortality will increase significantly for women if the guidance is implemented. Given this disproportionate impact, Gore believes that forcing women to receive open repair when EVAR has much better outcomes is unethical. We recommend that the committee consider the disproportionate impact on women and incorporate this impact into the model and recommendations. Ulug 2017 The overall pooled estimate [of 30-day mortality] for EVAR was higher in women (2·3%) than in men (1·4%; OR 1·67, 95% CI 1·38–2·04). The overall estimate for open repair also was higher in women (5·4%) than in men (2·8%; OR 1·76, 95% CI 1·35–2·30). Sidloff 2017 "For elective open AAA repair, the in-hospital mortality rate was 6·9 per cent in women and 4·0 per cent in men (odds ratio (OR) 1·48, 95 per cent ci. 1·08 to 2·02; P =0·014), whereas for elective endovascular AAA repair it was 1·8 per cent in women and 0·7 per cent in men (OR 2·86, 1·72 to 4·74; P <0·001)"	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The data from Sidloff et al. (2017) that you cite show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.

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Royal Free London Foundation Trust - Department of Vascular Surgery	Evidence review K	Line 794 – 798		Since 2014, the Royal Free London has invested considerable resource and time to ensuring >95% compliance with AAA data in the National Vascular Registry. This represents a real time and pragmatic reflection of our modern practice outcomes. WE believe that Registry Data is best placed to inform the practice within the current community. If the committee feels the Registry data input is biased due to reporting, they can refine the registry data to reflect only those centres with good compliance, or restrict practice to only those centres who contribute data. But ignoring the outcomes within the registry should not be an option.	The committee were emphatic in their conclusion that unadjusted registry data cannot provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR. This was a principled judgement based on established methodological principles. Registries play an important role in describing current practice, but using them as evidence of relative effects of competing courses of action is inappropriate. When it comes to the issue of perioperative mortality for complex AAA, the report's authors recognise this themselves. Please see **Theme 3a** and **Theme 4a**.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review W	139 - 140		The committee have used references as far back as 2002 in their identification of endoleak within Evidence W forest plot. The committee should consider that the contrast agents and ultrasound technology used in 2002 are vastly different to those used in 2017. This should be accounted for in any overall calculation of sensitivity and specificity. When assessing sensitivity, specificity, positive and negative likelihood in the use of 3D contrast enhanced ultrasound the committee have only included two studies (co-authored by our members). However, the SVTGB&I are aware of other papers [10]. Given the little published research on 3D and 4D ultrasound and that 4D ultrasound is effectively near real-time 3D ultrasound it may be prudent to include the paper by Gargiulo et al (2014) in with the same analysis [14]. Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72. Gargiulo, M., et al., *Could Four-dimensional Contrast-enhanced Ultrasound Replace Computed Tomography*	Thank you for your comment. Ormesher (2014) is out of scope of the evidence review because it compares 3D CEUS with standard catheter angiography (digital subtraction angiography), which is not a reference standard outlined in the review protocol. Gargiulo (2014) was already included in the evidence review W and considered during the committee's deliberations.

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				Angiography During Follow up of Fenestrated Endografts? Results of a Preliminary Experience. European Journal of Vascular and Endovascular Surgery, 2014. **48**(5): p. 536-542.	
Independent Vascular Services	Evidence review W	139-140		The committee have used references as far back as 2002 in their identification of endoleak within Evidence W forest plot. The committee should consider that the contrast agents and ultrasound technology used in 2002 are vastly different to those used in 2017. This should be accounted for in any overall calculation of sensitivity and specificity. When assessing sensitivity, specificity, positive and negative likelihood in the use of 3D contrast enhanced ultrasound the committee have only included two studies (co-authored by our staff). The committee should be aware of another paper [11]. Given the little published research on 3D and 4D ultrasound and that 4D ultrasound is effectively near real-time 3D ultrasound it may be prudent to include the paper by Gargiulo et al (2014) in with the same analysis [15]. Ormesher, D.C., et al., *Use of three-dimensional contrast-enhanced duplex ultrasound imaging during endovascular aneurysm repair.* J Vasc Surg, 2014. **60**(6): p. 1468-72. Gargiulo, M., et al., *Could Four-dimensional Contrast-enhanced Ultrasound Replace Computed Tomography Angiography During Follow up of Fenestrated Endografts? Results of a Preliminary Experience.* European Journal of Vascular and Endovascular Surgery, 2014. **48**(5): p. 536-542.	Thank you for your comment. Ormesher (2014) is out of scope of the evidence review because it compares 3D CEUS with standard catheter angiography (digital subtraction angiography), which is not a reference standard outlined in the review protocol. Gargiulo (2014) was already included in the evidence review W and considered during the committee's deliberations.
Independent Vascular Services	Evidence review W	16	67	Co-authors of the Lowe et al (2017) paper are current staff members of the IVS Ltd who would like to refer the committee to the use of reference test within this work. Whilst contrast-	Thank you for your comment. The committee recognised that the widespread use of CT

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				enhanced CT angiography remains the 'gold standard' the authors of this work have recognised the inferiority of CTa for the detection and classification of endoleak. This is why they have utilised the Multi-Disciplinary Team meeting as the gold standard. They do not feel it appropriate that the committee have used contrast-enhanced CT angiography as the gold standard index test in their analysis. It is well documented that contrast-enhanced ultrasound is superior than contrast-enhanced CT angiography for endoleak detection. Therefore, when using contrast-enhanced CT angiography as the index test the rate of false positive results by contrast-enhanced ultrasound is larger than it should be. This was addressed in the Lowe et al (2017) work by case presentation against catheter angiography. The misinterpretation of index tests for gold standards increases false positive ratios and results in a biased interpretation of the best modality for surveillance. In this case it is inappropriate to advise the use of contrast-enhanced CT angiography. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5).	angiography as a gold standard in the literature introduced bias, as an abnormality detected on another modality but not on CT would de-facto be defined as a false positive for that modality, rather than a false negative for CT. In practice the committee recognised that imaging modalities may be complimentary and the definition of a true reference standard is difficult, especially as the clinical significance of certain imaging findings remains unclear. Upon reconsideration of the evidence, the committee changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review W	16	67	Co-authors of the Lowe et al (2017) paper are current members of the SVTGB&I who would like to refer the committee to the use of reference test within this work. Whilst contrast-enhanced CT angiography remains the 'gold standard' the authors of this work have recognised the inferiority of CTA for the detection and classification of endoleak. This is why they have utilised the Multi-Disciplinary Team meeting as the gold standard. They do not feel it appropriate that the committee have used contrast-enhanced CT angiography as the gold standard index test in their analysis. It is well documented that contrast-enhanced ultrasound is superior than contrast-enhanced CT angiography for endoleak detection. Therefore, when using contrast-enhanced CT angiography as the index test the rate of false positive results by contrast-enhanced ultrasound is larger than it should be.	Thank you for your comment. The committee recognised that the widespread use of CT angiography as a gold standard in the literature introduced bias, as an abnormality detected on another modality but not on CT would de-facto be defined as a false positive for that modality, rather than a false negative for CT. In practice the committee recognised that imaging modalities may be complimentary and the definition of a true reference standard is difficult, especially as the clinical significance of certain imaging findings remains unclear. Upon reconsideration of the evidence, the committee changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking.

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				This was addressed in the Lowe et al (2017) work by case presentation against catheter angiography. The misinterpretation of index tests for gold standards increases false positive ratios and results in a biased interpretation of the best modality for surveillance. In this case it is inappropriate to advise the use of contrast-enhanced CT angiography. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5).	1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					contrast-enhanced ultrasound should be used.
Independent Vascular Services	Evidence review W	158		The committee have graded the works on 3D CEUS as having very serious bias. However, as documented in this publication 3D CEUS scans were paired with the index text of contrast-enhanced CT angiography and the vascular scientist performing the contrast-enhanced 3D ultrasound was blinded to the contrast-enhanced CT angiogram result. The authors of this work have removed bias from the protocol. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5).	Thank you for your comment. The relevant section has now been corrected.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review W	158		The committee have graded the works on 3D CEUS as having very serious bias. However, as documented in this publication 3D CEUS scans were paired with the index text of contrast-enhanced CT angiography and the vascular scientist performing the contrast-enhanced 3D ultrasound was blinded to the contrast-enhanced CT angiogram result. The authors of this work have removed bias from the protocol. Lowe, C., et al., *Three-dimensional contrast-enhanced ultrasound improves endoleak detection and classification after endovascular aneurysm repair.* Journal of Vascular Surgery, 2017. **65**(5).	Thank you for your comment. The relevant section has now been corrected.
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review D	9	114 - 117	The committee have only considered the cost analysis of surveying men. Does the same cost effectiveness relate to women?	As noted in the committee discussion, *The committee focused part of their discussion around specific surveillance intervals for women, after noting that the data suggest there may be a higher risk of AAA rupture in women. The committee noted that the results*

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					of the economic model presented were not sensitive to AAA rupture rates, and therefore believed that the same recommendation was appropriate for men and women. Evidence review D, 'Other factors the committee took into account'
Independent Vascular Services	Evidence review D	9	114-117	The committee have only considered the cost analysis of surveying men. Does the same cost effectiveness relate to women?	As noted in the committee discussion, *The committee focused part of their discussion around specific surveillance intervals for women, after noting that the data suggest there may be a higher risk of AAA rupture in women. The committee noted that the results of the economic model presented were not sensitive to AAA rupture rates, and therefore believed that the same recommendation was appropriate for men and women.* *Evidence review D, '*Other factors the committee took into account*'*
The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review B	7	38 & 39	Although imaging techniques have developed a lot since 2000 ultrasound techniques have developed significantly since 2010. Some references prior to 2010 may no longer be relevant in relation to ultrasound technology.	Thank you for your comment. In light of your comment, a sensitivity analysis was performed to consider only studies published from 2008 onwards in which the presence of endoleaks was determined in real-time by the person who was performing the scan. This sensitivity analysis indicated a slight increase in the diagnostic accuracy of CDUS for detecting endoleaks, however the increase was not significant enough to change the committee's conclusions. Please refer to evidence review W for further details about the committee's deliberations.

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Independent Vascular Services	Evidence review B	7	38-39	Although imaging techniques have developed a lot since 2000 ultrasound techniques have developed significantly since 2010. Some references prior to 2010 may no longer be relevant in relation to ultrasound technology.	Thank you for your comment. In light of your comment, a sensitivity analysis was performed to consider only studies published from 2008 onwards in which the presence of endoleaks was determined in real-time by the person who was performing the scan. This sensitivity analysis indicated a slight increase in the diagnostic accuracy of CDUS for detecting endoleaks, however the increase was not significant enough to change the committee's conclusions. Please refer to evidence review W for further details about the committee's deliberations.
Independent Vascular Services	Evidence review B	9	61	The below studies were missing from those used to reach a decision on measuring AAA diameter and should be included. There is no difference in terms of measuring diameter between those patients who do and do not have EVAR. Therefore, EVAR studies should have been included in this analysis. Bredahl, K., et al., *Reproducibility of ECG-gated ultrasound diameter assessment of small abdominal aortic aneurysms.* Eur J Vasc Endovasc Surg, 2013. **45**(3): p. 235-40. Bredahl, K., et al., *Three-dimensional Ultrasound Improves the Accuracy of Diameter Measurement of the Residual Sac in EVAR Patients.* European Journal of Vascular and Endovascular Surgery, 2013. **46**(5): p. 525-532. Ghulam, Q.M., et al., *Follow-up of Small Abdominal Aortic Aneurysms Using Three-dimensional Ultrasound: Volume Versus Diameter.* European Journal of Vascular and Endovascular Surgery, 2017. **53**(3): p. e17.	Thank you for your comment. Evidence review B assesses imaging techniques for the diagnosis of AAA, as opposed to post operative monitoring. Bredahl (2013_1) did not meet the protocol's inclusion criteria as it assesses inter operator variability of ultrasound measurements of different aneurysm planes. No comparisons were made with CT or other imaging techniques. Bredahl (2013_2) did not meet the protocol's inclusion criteria because it assesses inter technique variability for measuring sac diameter as opposed to aneurysm sizes in newly diagnosed aneurysms. Ghulam (2017) did not meet the protocol's inclusion criteria because it includes people who have undergone repair procedures. Furthermore, no comparisons have been made with other imaging techniques such as a CT or MRI reference standard.

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The Society of Vascular Technology Great Britain & Ireland (SVTGB&I)	Evidence review B	9	61	The below studies were missing from those used to reach a decision on measuring AAA diameter and should be included. There is no difference in terms of measuring diameter between those patients who do and do not have EVAR. Therefore, EVAR studies should have been included in this analysis. Bredahl, K., et al., *Reproducibility of ECG-gated ultrasound diameter assessment of small abdominal aortic aneurysms.* Eur J Vasc Endovasc Surg, 2013. **45**(3): p. 235-40. Bredahl, K., et al., *Three-dimensional Ultrasound Improves the Accuracy of Diameter Measurement of the Residual Sac in EVAR Patients.* European Journal of Vascular and Endovascular Surgery, 2013. **46**(5): p. 525-532. Ghulam, Q.M., et al., *Follow-up of Small Abdominal Aortic Aneurysms Using Three-dimensional Ultrasound: Volume Versus Diameter.* European Journal of Vascular and Endovascular Surgery, 2017. **53**(3): p. e17.	Thank you for your comment. Evidence review B assesses imaging techniques for the diagnosis of AAA, as opposed to post operative monitoring. Bredahl (2013_1) is out of scope assesses inter operator variability of ultrasound measurements of different aneurysm planes. No comparisons were made with CT or other imaging techniques. Bredahl (2013_2) is out of scope because it assesses inter technique variability for measuring sac diameter as opposed to aneurysm sizes in newly diagnosed aneurysms. Ghulam (2017) is out of scope because it includes people who have undergone repair procedures. Furthermore, no comparisons have been made with other imaging techniques such as a CT or MRI reference standard.
Hull and East Yorkshire Hospitals Vascular and Endovascular Service	Equality impact assessment			Has there been any consideration that socioeconomic status and deprivation will be important? Lifestyle risk factors for arterial disease, comorbidity and poor outcomes are linked to social deprivation. This will also have an important part to play in treatment as the wealthy will use private health to access what is seen globally as the gold standard treatment for AAA in many patients and minimise their early risk of mortality, however those who cannot afford this will be faced with the significantly greater risk of death and increased morbidity associated with open repair. There will be a perception that UK NHS patients are "second class citizens". Within those considered medically fit, patients with a background of deprivation remain higher risk of periprocedural adverse	Thank you for your comment. The committee considered various inequalities, including the role of socioeconomic status and deprivation, when they discussed each evidence review. The committee did not believe that their recommendations would prohibit access of lower socioeconomic groups to the best treatment options available within an NHS context, where equitable access to is a core principle of healthcare provision. Furthermore, they agreed that it was not within their remit to stipulate what treatments are available in private practice. In relation to risk factors, no direct evidence was identified demonstrating that socioeconomic status was associated with the presence of

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				events and a lower life expectancy and therefore may well see a greater benefit from EVAR.	AAA, as well as aneurysm growth or rupture. Although no evidence was identified demonstrating such associations, the committee considered that some of the identified risk factors have been proven to be associated with social deprivation and therefore will allow for more aneurysms to be identified in people from lower socioeconomic backgrounds.
The British Society of Interventional Radiology	Economic Appendix and Model	general		There is a real need for health economic modelling using data from current devices and modern techniques.	All inputs to the original HE model developed to support the committee's decision-making have been reviewed in the light of stakeholder feedback, with substantive revisions in several areas. Additional published evidence on the relative safety and effectiveness of EVAR and OSR has been reviewed, with the goal – among other things – of exploring the validity of model inputs.
Medtronic UK	Economic Appendix and model	General	General	**There is currently no model for emergency-complex cases**. This is based on the rationale that complex cases will always have to be treated with customized devices. However, if the anatomy is suitable, ChEVAR might be a suitable alternative to open surgical repair (OSR), resulting in potentially better health outcomes and acceptable additional costs. The guideline in this regard will need to consider this device type for emergency-complex cases.	The committee recognises that there are some instances in which it may be technically possible to offer complex EVAR to people with ruptured AAAs.
Medtronic UK	Economic Appendix and Model	General	General	**Model assumption for Waiting Time:** The economic model assumes a waiting time for both EVAR and OSR of 76 days and no evidence is cited to support this assumption. Medtronic have performed a HES data analysis and found that the average waiting time for infrarenal elective EVAR was 42.6 days (HES, 2017/18) which indicates that the model assumption overestimates the waiting time for EVAR which will have an impact on the pre-operative mortality and	Thank you for your comment. In the infrarenal case, the waiting time for both EVAR and OSR is assumed to be 2 months (not 76 days, which was the mean wait in EVAR-1 trial). The impact of this parameter is explored in sensitivity analysis.

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				consequently the overall QALY calculations. Medtronic recommend that NICE undertake this analysis for both EVAR and OSR to correct this assumption. We also predict that the waiting time for OSR will increase if the draft recommendations do not change because of bed-blocking resulting from longer ICU and ward stays post-OSR: **Admission Method:** Elective (including Daycase) **Number of Spells:** 1991 **Average spell duration:** 3.0 **Number of elective spells with completed waiting time:** 1,868 **Average (Mean Elective Waiting Time (Days):** 42.6	
Association of British HealthTech Industries (ABHI)	Economic Appendix and Model	10	189 - 191	**Peri-operative mortality – Elective repair – OSR not suitable – Complex** For complex repair, a complexity odds ratio was calculated based on registry data (0.4% vs 3.6%) and applied to the EVAR-2 perioperative rate of 7.3%. This resulted in a mortality calculation of 40.9%. This input does not reflect clinical studies, nor the experience of the committee so should not be used in the economic model. Rather, a broader searcher of the clinical literature should be undertaken to inform this input. Note: the GLOBALSTAR registry observed that a "a substantial proportion of patients undergoing f-EVAR in the United Kingdom appear to be in a high-risk category" (GLOBALSTAR Registry, 2012). Although, it is possible that NVR data for complex EVAR would slightly underestimate the mortality for OSR not suitable patients, it is a far more plausible estimate than the 41% calculation.	The substantial uncertainty in this estimate is acknowledged in the guideline. We provide extensive sensitivity analysis However, even if we assume complex EVAR is associated with 0% perioperative mortality in this population, it is associated with an ICER over £120,000/QALY, compared with no intervention. If we assume 0% mortality and assume that all 'crossovers' (i.e. people who were randomised to the no intervention arm but received repair at some point) would have instantly died without repair, the ICER only falls to £28,000. Clearly, although there is very real uncertainty in this area, that uncertainty does not encompass the question of whether complex EVAR can justify its expense, in this population.

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Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline	Complex EVAR Any endovascular strategy that is outside the 'instructions for use' of aortic stent–grafts, typically adopted because of an AAA's anatomical complexity. This includes using unmodified endografts outside	General	Please refine the definition of complex EVAR in this guideline as pertaining only to complex EVAR for AAA. This excludes any indication in thoracoabdominal aortic aneurysms, for which this guideline is not geared.	Thoracoabdominal aortic aneurysms were explicitly excluded from the scope of this guideline, with the exception of infradiaphragmatic (type IV) TAAAs.

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		their 'instructions for use', physician-modified endografts, customised fenestrated endografts, and 'snorkel' or 'chimney' 243 approaches with parallel covered stents.			
Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline	General	General	As vascular surgeons and anaesthetists, we interact daily with patients who have aneurysm disease. For many of these patients, the diagnosis of an aneurysm is a life-altering event. They are often the breadwinners or caregivers for many dependants, and need to return to the work force or family life with minimal morbidity. We have been able to deliver a service that results in most patients achieving this goal.	Thank you for providing the context for your individual comments; please see responses below. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Although the guidelines as written may reflect a sterile review of the literature, the ability to treat a patient based on best judgement and medical expertise has been removed from the decision making process. We feel this will have a negative impact on the patient experience, and disadvantage patients in the United Kingdom compared with their global counterparts. We strive to run a cost conscious and cost effective service at the Royal Free. We are open to any and all audits of that claim. As medical experts, we believe we have a better understanding of both the treatment of the disease, and the needs of the patients, and as such, feel strongly that these guidelines will be too restrictive for us to practice excellent care.	a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline	1.5.3 Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is	General	The randomized controlled trial data for EVAR were conducted using first generation devices (most of which have been removed from market) and did not anticipate the long term follow up required for patients who survived for >15 years.(EVAR 1 Trialists, NEJM 2010) Iterative improvement in devices since 1999 when the trial first began means that many issues leading to late failure have been improved. Additionally the practice has evolved to be more aware of predictors of late failure – thanks in large part to insights from the EVAR trial data{Wyss et al, JVS 2011} – so we no longer perform EVAR in patients who will predictably fail. The outcomes reported in EVAR-1 are not reflective of the practice in modern day. The EVAR-1 trial was powered to determine the safety, efficacy and cost-effectively of EVAR in the short term, with outcomes being all cause and aneurysm related mortality. However, the outcome data cited by the NICE guideline committee, namely the 15 year review, is a non-protocolized review of 711/1252	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.

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		suitable .		patients included in the trial.(Patel et al, Lancet 2016) During the 15 year course of follow up, patients undergoing EVAR had only 6/15 scans, and patients undergoing open surgery had only 3/15 scans that would be expected for annual review. This suggests the outcome data may suffer from both ascertainment bias, and significant statistical error from an incomplete data set. Larger administrative datasets have been reported, including a propensity analysis of 39,966 patients who underwent either open or endovascular repair. (Schermerhorn et al, NEJM 2015) The mortality was 1.6% with endovascular repair and 5.2% with open surgery. The clear perioperative benefit decreased with time, and longer, 8 year outcomes reveal that there is reintervention needed over time for both modalities of treatment. Although not a randomized controlled trial, these data reflect a more modern approach to disease and thus likely more accurately reflect the outcomes for EVAR We unequivocally believe that the evidence for EVAR has evolved over the last 25 years since its first report and early trials, and that we, as a field of vascular surgeons, have refined the indications for use of this modality to improve outcomes in a way that is better reflected in reports of modern practice. Many patients will have improved perioperative outcomes and increased longevity if EVAR can be judiciously used. We believe that surgeons should be allowed to judiciously apply endovascular technology on a patient-by-patient basis to treat anatomically suitable aneurysms, with mandatory public reporting of centre-specific results.	In response to stakeholders' suggestions that it may not be appropriate to rely on randomised evidence alone to estimate the short- and long-term relative effects of EVAR and OSR, the committee considered a new review of casemix-adjusted comparative observational studies presenting results for both techniques. This included the study you cite by Schermerhorn et al. (2015). This study found that perioperative mortality declined year-by-year with both EVAR and OSR, with no evidence of different rates of improvement between the 2 approaches. The authors also found that EVAR reintervention rates reduced somewhat over the period of study, although the reduction was relatively small and appeared to be driven by a decrease in minor procedures only – see **Theme 7**. The committee's conclusions on the long-term risks associated with EVAR were not solely based on EVAR-1; rather they reflect a range of randomised and observational data. It was the committee's confident interpretation of this evidence that EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**. For specific comments on the statistical power of the elective RCTs to identify differences in long-term survival, please see **Theme 9b**. It is in the nature of long-term survival effects that they become most evident in the proportion of the cohort that lives the longest. For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.

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Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline			The use of complex endovascular repair in patients with unruptured AAA has evolved over the years since early reports. Increasingly, patients have benefitted from greater coverage extent of coverage and the early risk of failure has decreased. (O'Callaghan et al, JVS 2015). The largest report of durability of fenestrated repair reported a 2% long term risk of aortic mortality after repair in 650 patients followed over 9 years (mean follow up 3 years). (Mastracci et al, JVS 2013). At the Royal Free hospital, we are able to offer complex endovascular repair with lower mortality that most global reported mortality: between October 2014 and March 2018, 124 Juxtarenal and group IV thoracoabdominal aneurysms were repaired. In this cohort, 82/124 patients had fenestrations for all 4 visceral arteries. Our mortality over this time period is 2/124, or 1.6%. As experts in aortic surgery, we do not believe there is sufficient equipoise in the field to ethically allow for the conduct of a randomized controlled trial in these patients. We do, however, recognize, that complex repair is a highly specialized practice that requires adequate volume to achieve good results.(Starnes et al, JVS 2016 and Rolls et al, EJVES 2016). Thus, we feel that the caution contained in the spirit of these guidelines would be best placed by recommending centralization of complex endovascular repair to high volume centres with mandatory reporting of centre specific results.	Thank you for highlighting these publications. As they both present uncontrolled case series, it is not possible to draw any inference about the relative benefits and harms of complex EVAR compared with OSR from these data. Thank you for giving us details of your experience; please see **Theme 3c**. The committee were mindful of the finding, from casemix-adjusted observational evidence, that there is no difference in perioperative mortality between complex EVAR and OSR. Moreover, they noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that it is associated with a large reduction in perioperative mortality, there should be real equipoise about whether any such effect translates into net health gain over a patient's lifetime. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for

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					a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Service delivery – especially as it relates to volume–outcome dynamics – was explicitly excluded from the scope of this guideline.
Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline	1.5.6 Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.		Although many patients with complex aneurysm disease may have a high rate of comorbidities that threaten their longevity moreso than their aneurysm, the high prevalence of respiratory conditions in the aneurysm population has a profound impact on rendering patients unsuitable for open surgery who would benefit from a minimally invasive approach. At Royal Free London, the ASA score of patients undergoing aneurysm surgery has increased over the last 5 years with no negative impact on outcomes.(https://www.royalfree.nhs.uk/services/services-a-z/aortic-surgery/outcomes/) We attribute this to the conduct of complex repairs with a highly specialized team with high volumes making the clinical decision making of the MDT one of the most valuable patient safety tools. Blanket recommendations, such as the one contained in 1.5.6, ignores the wisdom of the multidisciplinary team to adjudicate the best care for an individual patient, meaning that many patients who may benefit from a minimally invasive approach will be harmed by being rendered 'inoperable'.	We are sure you are right to emphasise the low risks with which you have been able to accomplish complex EVAR in people for whom OSR is unsuitable; however, the committee's decision-making had to acknowledge the absence of evidence that meaningful benefit is being provided in these cases. The evidence from EVAR-2 suggests that people with medical comorbidities of sufficient seriousness to contraindicate OSR face a substantially greater force of mortality from those factors than they do from AAA rupture. In other words, most participants who were randomised to no intervention died with – rather than from – their AAA. In the context of a treatment with known short-term risks and costs, and no evidence of extension of life expectancy, the committee agreed that the balance of benefits and harms favours conservative management. In the case of complex EVAR, the balance is pushed further in favour of no intervention, as the costs are unarguably higher (both the costs of complex, often custom-made grafts, and the increased resource use intraoperatively and postoperatively). For discussion of the relationship between NICE guidance and clinician judgement, please see **Theme 15**.
Medtronic UK	Draft guideline	9-10	172-182	For the purpose of consultation response to the economic models for this clinical guideline, four device companies have	Thank you for providing the context for your individual comments; please see responses below.

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	Health Economic Appendix			developed an in-depth analysis of the model assumptions via the Association of British Healthcare Industries (ABHI); namely Medtronic, W.L Gore and Associates, Cook Medical and Terumo Aortic. We confirm full support of all comments as provided in the joint industry submission from ABHI and request that NICE record all comments made as Medtronic submission also. The below responses are a Medtronic summary of that analysis. [This and the following comments (20-24) concern unruptured infra-renal AAA repair.] We believe that the evidence used to derive the recommendations for unruptured elective cases (open repair in all suitable cases, do not offer EVAR) is incomplete and not contemporary. We will comment on three key points, although there are several other areas that we believe deserve further detailed consideration by the committee. Changing the model assumptions to more appropriate ones for all three of the key comments will likely result in a comparable if not better clinical EVAR performance compared to OSR at acceptable additional costs.	
Medtronic UK	Draft guideline Health Economic Appendix	9-10	172-182	**The base case economic model assumes an effect size for peri-operative mortality that is much lower than contemporary evidence has shown.** The effect measure for the peri-operative mortality was modelled in the cost-effectiveness analysis via an EVAR baseline mortality (0.4% for infra-renal, taken from 2016 NVR data, Watson et al., 2017) and derived from a Cochrane meta-analysis (Paravastu et al., 2014) of randomized controlled trials that was dominated by the EVAR-1 trial and included three other historical trials. Recruitment for the EVAR-1 trial began in 1994 and was completed in 2004. Since this time	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee were emphatic in their conclusion that unadjusted registry data cannot provide a valid estimate of the relative benefits, harms and costs of EVAR and OSR. This

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				EVAR performance has improved significantly through increased surgical experience and vastly improved imaging technology and techniques. In the current health-economic model, calculations are performed based on a peri-operative mortality of 0.4% for EVAR and 1.3% for OSR (difference 0.9%). This effect size is smaller than the difference reported in contemporary real-world evidence. 2016 data from the NVR suggests an EVAR peri-operative mortality of 0.4% vs. 2.9% for OSR, a difference of 2.5%. These data are in line with evidence from other studies (e.g., in VQI: peri-operative mortality 0.7% for EVAR vs 4.0% for OSR in the non-ruptured infrarenal group, a difference of 3.3%). Moreover, the OSR patients were likely younger and possibly also healthier. Medtronic recommend that the model is re-run with these more representative assumptions for peri-operative mortality within the base case given that their accuracy is essential for the correct estimation of an incremental cost-effectiveness ratio (ICER). Further, we suggest the committee consider articulating more explicitly the previously observed gender differences relating to EVAR outcomes as described elsewhere in this response.	was a principled judgement based on established methodological principles. Registries play an important role in describing current practice, but using them as evidence of relative effects of competing courses of action is inappropriate. Please see **Theme 3a**. Having reviewed a new review of casemix-adjusted observational evidence on perioperative mortality, the committee agreed that their decision to place primary reliance on randomised evidence of perioperative mortality was extremely well validated – see **Theme 2**. Therefore, the committee did not alter its base-case approach to estimating the perioperative mortality that would be expected from a service that placed primary reliance on OSR for infrarenal AAAs. Despite this strong belief, the model is – and always has been – configured to explore the effect of alternative estimates. Using the unadjusted NVR data does not have a material impact on outputs.
Medtronic UK	Draft guideline Health Economic Appendix	9-10	172-182	**The base case assumes a long-term survival gain that is too conservative for EVAR and too high for OSR**. The post peri-operative mortality was modelled in the health-economic model via different approaches. These included adjusted general population estimates (base case) and several different fitted parametric survival models. The EVAR-	The finding that EVAR is associated with excess post-perioperative mortality is strongly supported by the review of casemix-adjusted observational evidence that we have conducted in response to stakeholders' criticism that the consultation draft placed too much weight on RCTs alone – see **Theme 9**. In fact, this evidence suggests that the trials

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				1 trial is the main evidence used which, again, is a concern, for several reasons. As previously described by the evidence (e.g., Verzini et al., 2014), newer EVAR devices are associated with fewer complications than older devices. Consequently, newer devices are highly likely to be associated with a lower aneurysm-related long-term mortality than those reported in the EVAR-1 trial. Of note, the adjusted hazard ratio (HR) for all-cause mortality only became borderline-significant in the EVAR-1 trial after eight years. The current cost-effectiveness analysis assumes that the model-projected survival of OSR overtakes that of EVAR after a period of just three years – which is in disagreement even with the very dated and conservative EVAR-1 data. As Patel et al., 2018 have demonstrated, EVAR has a survival advantage in the first six months, for the next 7.5 years there is no statistically significant difference, and only after eight years, a borderline statistically significant difference emerged, based on questionable follow-up data from only a very small number of trial participants. Medtronic feel it is inaccurate to assume a constant hazard ratio for the entire duration of the model given that the proportional hazard assumption has neither been tested nor is likely fulfilled based on the data cited above. As a result, we believe that the long-term survival gain is too conservative for EVAR and too high for OSR. In consequence, QALY calculations are not expected to accurately reflect clinical reality. This issue is further amplified when discounting is applied.	may represent an underestimate of the true effect in real-world practice. Verzini et al.'s paper (2014) cannot be cited as evidence that 'newer devices are highly likely to be associated with a lower aneurysm-related long-term mortality' when the study explores that very question and concludes the opposite. The proportional hazards model is extremely well supported by the data – see **Theme 9a**. However, if you prefer an approach that only applies differences when they are associated with significant p-values, or one that adopts a parametric, non-proportional-hazards approach, then they are available in the model. All such approaches produce estimates that are less favourable to EVAR than our base case. If there were a bias in favour of OSR in our long-term projections, this would be attenuated, not amplified, by discounting, because the long-term phase in which OSR's advantage becomes apparent would have less weight in the analysis. The committee firmly agreed that the assumption that EVAR is not associated with worse long-term survival cannot be supported on any objective appraisal of the evidence.

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				On the basis of these observations, we propose the committee consider using a constant hazard ratio of 1.0 for the long-term mortality. Alternatively, we recommend that a time-dependant hazard ratio is applied as used in the 2018 Health Technology Assessment for EVAR vs. OSR (Patel et al, 2018).	
Medtronic UK	Draft guideline Health Economic Appendix	9-10	172-182	**Data is available for the committee to make more accurate cost and resource utilization assumptions within the model.** Given that the model assumptions regarding periprocedural resource utilization have a significant impact on total cost by strategy, Medtronic wish to make some suggestions on how contemporary datasets could be utilized within the models' base case assumptions. This relevance is further amplified by the – comparably – small QALY differences observed in the infrarenal model, which mean that relatively small changes in costs are likely to have a significant impact on ICERs. We appreciate the committee's consideration of available data sources, however we do not believe that the committee's ultimate decision to use data from EVAR-1 is justified given that multiple data sources indicate that costs for EVAR have been overestimated. **Length of stay calculations** For the infrarenal model, total length of stay for EVAR is assumed to be 9.76 days (Preoperative stay 1.81 days, postoperative stay 6.53 days, ITU stay 0.59 days, HDU stay 0.83 days). More current data do not support these assumptions:	We certainly agree that perioperative resource use has an important role in defining the net costs with which EVAR and OSR are associated. Naturally, it is critical that the HE model used to support decision-making should have as accurate an estimate of these figures as possible. We have reviewed resource use in all relevant categories – including all those raised in this comment – and made revisions to the base-case model used to support the committee's decision-making. Details are provided below. We have reviewed evidence on length of stay following AAA repair, and provide comments below. We note, however, that your comments relate exclusively to resource use associated with EVAR, and how that appears to have changed since the EVAR-1 trial. From a health economic perspective, the cost implications of a given technology can only be assessed in comparison with an alternative approach. In this case, this means that it is very important to consider

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					how resource use with OSR may also have changed over time, in order to arrive at the best estimate possible of the incremental costs associated with EVAR.
				National Vascular Registry (NVR): For EVAR, the latest National Vascular Registry data (2016 data, published in 2017) reports a median total length of stay of 3 days. Over 60% of patients were returned to a normal hospital ward after surgery. Among those admitted to either level 2 or 3 critical care, the median length of stay was 1 day. These data suggest a dramatic change from the EVAR-1 assumptions. Medtronic recommend that the committee seek to obtain the mean (rather than the median) values from the NVR as per correct practice for cost-effectiveness analysis.	We have obtained means and SDs for these data for EVAR and OSR from the NVR. These show that resource use with EVAR and OSR have reduced by a very similar amount since the EVAR-1 trial, with the result that – far from being a dramatic change – the difference between the 2 is essentially unchanged. Details are provided in **Theme 6a**.
				Hospital Episode Statistics (HES) and PLICS data: 2016/17 Hospital Episode Statistics published by the NHS report a mean length of stay (excluding intensive care days) of 2.54 days (for procedure code YR04Z - Endovascular Repair of Abdominal Aortic Aneurysm).	For the reasons stated in the consultation draft, we consider NHS Reference Costs, from which the 2.54-day mean is drawn are not, in this case, reliable. However, if we were to use these data, then we should also use the analogous figure for OSR, which is 4.46 days – this would represent a much smaller difference between EVAR and OSR than was assumed in the base-case model reported in our consultation draft.
				2013/14 PLICS data, which report critical care costs, report an average of £545 of critical care costs for this procedure code. On the basis of a 90%/10% split between HDU and ITU utilization (based on NVR data) and cost assumption of £718 and £1,017, per the NICE model, this results in approx. 0.73	We find it challenging to reconcile PLICS data with evidence reported elsewhere. Nevertheless, we note that, in the 2014/15 findings, the total average finished consultant episode costs are £14,214 for EVAR and £11,228 for OSR, a

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				days in critical care – for total resulting length of stay estimate of 3.27 days. It is our understanding that, whilst more recent PLICS data is not yet published, NHS trusts continue to improve their cost-collection processes for PLICS and we therefore recommend that NICE obtain a more recent version of this dataset from NHS England. This data may also be available from individual trusts in case any have paid close attention to the accuracy of their PLICS data collection for vascular services. Internal analysis of the most recent HES data (April 2017 to March 2018) reports a mean length of stay for elective (unruptured) cases of 3.0 days (Diagnosis code I714 - Abdominal Aortic Aneurysm, without mention of rupture; procedure codes L271 - Endovascular insertion of stent graft for infrarenal abdominal aortic aneurysm or L281 - Endovascular insertion of stent for infrarenal abdominal aortic aneurysm), including critical care time of 0.79 days.	difference of £3,000, which is somewhat more than estimated in the HE model reported in the consultation draft.
				These general trends in EVAR length of stay reductions are convincingly documented through other data as well:	As explained above, the relevant question is not whether postoperative EVAR resource use has reduced – we accept that it has; it is whether EVAR resource use has reduced to a greater extent than postoperative OSR resource use – it appears that it has not.
				Our Medtronic regulatory submission to the U.S. Food and Drug Administration (FDA) in 2008 states a mean length of stay of 3.6 days, compared to a historical control (SVS) of 8.2 days (see publicly accessible 'Summary of Safety and Effectiveness' document). Since then procedure and device improvement can be expected to have further contributed to	These data do not provide any comparison with OSR, so are irrelevant for this purpose.

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				reductions in length of stay to durations similar to those reported in the recent UK NVR and HES data. The Dutch Surgical Aneurysm Audit 2014 (referenced in the Burgers et al., 2016 EVAR cost-effectiveness analysis conducted for the Dutch healthcare system) found EVAR to be associated with mean ward stay of 3.70 days and critical care stay of 0.27 days. Using the 2016/17 HES data-derived EVAR length of stay instead of the base case assumptions would lead to an approximate reduction in EVAR costs of more than £2,000. We also expect that efficiencies have also been achieved with open surgical repair since EVAR-1 however we are certain that these will not be to the extent of the efficiencies achieved with EVAR over the same 19-year time period. **Theatre Time** The base case assumes 191 minutes of EVAR and 215 minutes of OSR theatre time. The cost per hour of theatre time is estimated at £831. The 2008 FDA submission based on Medtronic TALENT found a mean procedure duration of 166 minutes, compared to historical control (SVS) of 225 minutes. Again, this suggests a trend with newer devices and increased procedural experience that likely has evolved further between 1999-2004, 2008, and now current practice in 2018. Data from the Dutch Surgical Aneurysm Audit 2014 (referenced in	The data cited by Burgers et al. (2016) are unpublished figures from the Dutch Surgical Aneurysm Audit. Whilst we have no way of checking their provenance, they appear to be unadjusted registry data. The EVAR numbers are similar to those reported in the NVR (3.89 days and 0.42 days, respectively); the analogous OSR figures are also similar (2.7 days' critical care and 8.8 ward bed-days, compared with 3.4 days and 7.1 days in the NVR). This is only true if the estimates for EVAR are altered in an attempt to reflect current-day practice while the estimates for OSR are fixed at their historical level. Using 2016/17 HES data-derived length of stay for both EVAR and OSR would lead to an increase in net additional costs associated with EVAR. For a discussion of intraoperative resource use, please see **Theme 5**. In exactly the same way as for length of stay, it is insufficient to assert that intraoperative resource-use with EVAR has reduced; rather, it is critical to establish how the **difference** in intraoperative resource-use between EVAR and OSR may have changed since the detailed, balanced data collection in the RCTs.

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				Burgers, Vahl et al., 2016) reported mean procedure duration of 146 minutes. Data from the European C3 Module of the Global Registry for Endovascular Aortic Treatment (GREAT) (Verhoeven et al., 2014) report a median procedure time of 120 minutes, based on a sample of n=400 patients treated.	Non-comparative data such as Medtronic's FDA submission and the GREAT registry are therefore not useful. The Dutch estimates provided by Burgers et al. (2016) are referenced to both the unpublished Dutch Surgical Aneurysm Audit and to 'expert opinion' – it is impossible to tell what these numbers represent. However, we have explored their impact in sensitivity analysis – see **Theme 5**. The PLICS data to which you draw our attention above suggest that mean theatre-time for EVAR in 2014/15 was around 237 minutes. Equally, however, this source suggests that OSR operation times have risen similarly (to around 300 minutes), although we think this category is likely to include complex AAA anatomy, where the EVAR numbers are not.
				Just relying on the TALENT data of 2008 would reduce EVAR procedure cost by an additional £400. If the more recent Dutch data are considered, these additional savings would amount to more than £620. Using the median data from the GREAT registry would result in an even higher savings estimate of £983.	Again, we must insist that it is invalid to adjust one side of the equation but not the other.
				We suggest NICE consider more recent data than EVAR-1 also for this parameter, in an attempt to reflect current practice parameters as closely as possible.	As detailed in **Theme 5**, we conclude that there are no relevant, contemporary, casemix-adjusted data for this parameter. In our base case, we retain our reliance on randomised evidence, as these data at least reflect reliably matched cohorts in a UK setting, and there are no more current data with these advantages. However, we explore the impact of more contemporary, albeit methodologically less

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					reliable, data in sensitivity analysis and find that it has no impact on model outcomes – see **Theme 5**.
				In addition, the National Vascular Registry suggests 6.8% of OSR patients had to return to the theatre, vs. 2.0% for EVAR patients. The NICE model does not seem to take return to theatre into account. Inclusion would arguably benefit EVAR when considering incremental costs.	We understand that, depending on the precise timing of these episodes, they should be accounted for in either the estimates of intraoperative resource use from the RCTs or in reintervention rates. Therefore, applying an additional provision for such cases would double-count the costs with which they are associated.
				Rehabilitation Costs	
				The committee have not formally considered rehabilitation due to the lack of evidence in this area however it should be a consideration for the committee.	The committee broadly accepted this hypothesis, as it chimed with members' own experience. They noted, however, that there are few data available to explore the issue in the HE model. Nevertheless, using casemix-adjusted comparative observational evidence from a US setting and combining this with descriptive UK data and evidence on resource-use from the emergency setting (IMPROVE), we were able to estimate a best-case scenario for the cost-savings that might be achieved with EVAR, in this area. Although the amounts estimated were nontrivial, they did not make anough difference to bring EVAR close to cost effectiveness, compared with OSR. For details, see **Theme 6b**.
				Reinterventions	
				The committee has noted they are not aware of any evidence supporting the notion that the rate of reinterventions has decreased with newer EVAR stent graft generations, compared to older EVAR devices. However, Verzini, et al., 2014 compared newer devices (Endurant, Zenith, second-generation Excluder, and second-	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of

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				generation Anaconda) with n=530 old devices (AneurRx, Talent, first-generation Excluder, first-generation Anaconda, and Fortron). Even though in the newer device group the AAA diameter was larger (55.7 vs. 53.2 mm, p<0.0001) and the patients were older (p<0.0001), freedom from reintervention after 7 years was different between the two groups (83.6% vs. 74.2%, respectively, p=0.015). We believe that the model needs to reflect these observed reductions in reintervention rates. NICE's unruptured infrarenal model assumes freedom from reintervention of 64% (based on model tracker "patients who have not experienced a serious AAA-related reintervention"). This suggests the NICE model calculation overestimates reinterventions. Based on the NICE model-provided estimate of £4,719 of reintervention costs (incl. hernias), this suggests further that actual reintervention costs might be more than £2,000 lower than the model-projected reintervention costs. Also important to note, the the elective infrarenal model assumes an EVAR reintervention rate of 9.3% which is heavily based on EVAR-1, which has been criticized for overestimating complications resulting from EVAR. More specifically, EVAR-1 showed an unusually high estimate of type 2 endoleaks and classified all type 2 endoleaks as complications. However, newer guidelines from the Society for Vascular Surgery (SVS) do not consider these endoleaks to be complications and recommend a monitoring approach rather than reintervention. If type 2 endoleaks are removed from the EVAR-1 figure, the EVAR complication rate falls to 4.9%.	operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Thank you for pointing out this anomaly. Having explored the issue, we accept that there was inconsistency in the way reintervention rates were calculated in the model made available at consultation. This has been revised better to reflect the evidence from EVAR-1; see **Theme 7**. The result of this revision and the application of a reduced rate of reinterventions for EVAR to reflect contemporary practice (see above) is that the difference in reintervention costs between EVAR and OSR has, indeed, fallen by an amount approaching £2,000. However, this is insufficient to rebalance the analysis in favour of EVAR: OSR remains the dominant option.

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Medtronic UK	Draft guideline Health Economic Appendix	9-10	172-182	**Inclusion of the recommendations outlined above would result in an ICER below £20,000 per QALY** Our internal analyses suggest that the combination of changes in peri-operative mortality and post-perioperative (long-term) mortality to the outlined updated parameters would lead to an overall QALY gain for EVAR rather than the QALY decrement of -0.16 in the current model. Consideration of the outlined cost updates would yield an ICER well below the willingness-to-pay threshold for NHS England. Importantly, consideration of all factors might lead to additional savings that would render EVAR dominant, i.e. associated with improved outcomes at lower overall cost.	Clearly, it is possible to use the HE model developed for this guideline to arrive at an answer that is more favourable for EVAR by manipulating inputs to that end. The committee accepted some of the criticisms that you and other stakeholders have made of the parameters reported in the consultation draft, and the analysis has been revised accordingly. However, in multiple suggestions, you are recommending that we discard robust data in favour of parameters with little or no empirical basis, and the committee could not accept the reasonableness of that. We respond to each of your suggestions, in turn, where they appear in detail. We would also note that we are not the only investigators to conclude that EVAR represents poor value for money in the infrarenal elective setting. As outlined in HE.4.1.4.1, every analysis performed from an NHS prerpective concludes that EVAR is associated with an ICER considerably in excess of £20,000/QALY, when compared with OSR, and several of these other analyses share our conclusion that the most likely net result is that EVAR is not only more expensive than OSR, it is also associated with worse net outcomes.
Association of British HealthTech Industries (ABHI)	Draft guideline Evidence review K	10 30	179 – 180	**The guideline committee did not consider the fact that women suffer far worse outcomes with open surgical repair.** As evidence has shown, the short-term mortality of Open Surgical Repair in women is higher versus men and versus EVAR. ABHI strongly believe that it would be unethical to recommend only open surgical repair to women where up to 1 in 15 procedures would result in death, especially when a much lower mortality is achievable with EVAR. We therefore	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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			872 - 875	recommend the committee consider the following clinical evidence and adjust the evidence review, economic model and recommendations accordingly: Ulug et al, 2017 The overall pooled estimate for EVAR perioperative mortality was higher in women (2·3%) than in men (1·4%; OR 1·67, 95% CI 1·38–2·04). The overall estimate for open repair also was higher in women (5·4%) than in men (2·8%; OR 1·76, 95% CI 1·35–2·30). Sidloff et al. For elective open AAA repair, the in-hospital mortality rate was 6·9 per cent in women and 4·0 per cent in men (odds ratio (OR) 1·48, 95 per cent ci. 1·08 to 2·02; P =0·014), whereas for elective endovascular AAA repair it was 1·8 per cent in women and 0·7 per cent in men (OR 2·86, 1·72 to 4·74; P <0·001); the results in HES were similar.	The data from Sidloff et al. (2017) that you cite show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.
Association of British HealthTech Industries (ABHI)	Draft guideline	10	195 - 202	**The recommendations do not fully address patients with acute symptomatic AAA who are at high risk of rupture.** The scope for this clinical guideline stated that the following would be covered by the guideline committee: "Management of ruptured abdominal aortic aneurysms and **abdominal aortic aneurysms at high risk of rupture**" The ABHI do not believe that NICE have fully addressed the scope in relation to patients with symptomatic AAA whom are assumed to be at high risk of rupture and therefore require urgent intervention. Given the high procedural mortality, coupled with the risk of imminent rupture, we feel passionately that these patients should have access to EVAR	The guideline recommends urgent investigation of people with symptomatic AAAs (1.1.9), swift transfer to a regional vascular centre (1.3.4 [previously [1.2.4] & 1.3.5 [previously 1.2.5]) and consideration for repair (1.5.1). Several of the studies identified in our review of casemix-adjusted non-randomised evidence include symptomatic (or 'emergent') cases. Among these, we identified 1 that reports results for symptomatic cases, though helpfully that is one of the few UK studies in the dataset. In univariable analysis across EVAR and OSR, Choke et al. (2012) found that symptomatic AAAs may be associated with a higher risk of perioperative death; however, at a 95% confidence level, the

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				(Peppelenbosch 2003, Sullivan 1990, Cambria 1994, Haug 2004, Fillinger 2002, Lederle 2002).	data are comfortably consistent with no difference (OR=1.94 [0.64 to 5.95]). We are not aware of any data exploring the possibility of interaction between symptomatic status and repair approach, which would be necessary to inform any specific recommendations regarding the relative benefit of EVAR and OSR, in these patients. However, as noted above, many of the studies included in our review of observational data included emergent cases, and the fact that pooled results from these studies are closely comparable to results from RCTs provides some validation for the committee's view that the balance of benefits and harms is unlikely to be very different in such cases.
Medtronic UK	Draft guideline Health Economic Appendix	10	195-202	**[This comment concerns ruptured infra-renal AAA repair.]** We believe the odds ratio for long-term mortality between EVAR and OSR is too high meaning that the EVAR effect is underestimated. Within the current NICE model, the relative effect measure (i.e., the odds ratio) was taken directly from a Cochrane meta-analysis (Badger et al., 2017) that pooled the results from IMPROVE, AJAX, ECAR, and Hinchcliffe et al., 2006. The odds ratio (OR), 0.88 was heavily driven by the IMPROVE trial which was a pragmatic RCT where the intention-to-treat analysis showed no statistical significant difference (OR: 0.92; 95% CI: 0.66-1.28). We therefore suggest it would have been more appropriate to model the per-protocol analysis, especially since the model considers conversion to open repair with the subsequent effectiveness taken from the OSR arm.	This comment reflects a misinterpretation of the model. The model does not 'conside[r] conversion to open repair with the subsequent effectiveness taken from the OSR arm'. At all stages, it presents an ITT analysis of an EVAR-if-possible strategy compared with an OSR-only approach, and we are careful to label all our results as such. The model only needs to track conversion to open repair in order to estimate graft costs for the proportion of people who do not undergo EVAR implantation. We believe this is the most applicable way of handling these data. The alternative you suggest – that is, using per-protocol data from IMPROVE – would result in a comparison of OSR for all AAAs versus EVAR for a subgroup of infrarenal AAAs, which is an unhelpful comparison for decision-making. If we were to use such data, we would only have to add extra modelling to simulate what happens to people with complex

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					AAAs who cannot have EVAR; if we did that job well, we would end up end up back at the ITT results of IMPROVE.
St George's University Hospital NHS Foundation Trust	Draft guideline	General	General	General Comments We thank NICE for seeking to update its guidance around the management of abdominal aortic aneurysm (AAA). This was a large and comprehensive task covering diagnosis, risk management, treatment and follow-up. The scale of the task is not underestimated, and in many areas the draft guidance will enhance practice; We are concerned that one clearly stated aim of the draft guidance was to improve access to care for patients diagnosed with AAA. We do not believe that the draft guidance will improve access in the intended fashion, and conversely will restrict access to the appropriate care for patients with abdominal aortic aneurysms. We believe that in a number of key areas the draft guideline is not underpinned by the most current data on which to base conclusions regarding the overall care of patients with AAA. This will have unintended consequences that we believe will be detrimental to patient care; The draft guidance has differences with all other key international guidelines on the diagnosis and management of AAA that are of a scale significant enough to raise concerns about aspects of this draft guideline. It is apparent that the SVS, ESVS, VSGB&I and other guidelines have had access to the same body of evidence, but drawn different conclusions; We are concerned that NICE may not have been aware of all relevant and most current literature, and the 'NICE process' being dominated by the use of, in this case, a very historical RCT alone has led to the wrong conclusions being drawn; Senior clinicians with a current aortic practice, and involvement in current aortic research, were under-	Thank you for your acknowledgement of the committee's work, and for providing a summary of your feedback; please see responses to individual detailed comments, below. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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				represented on the NICE panel. Consequently, the strength of position from which evidence-based judgements were made on the management of patients with abdominal aortic aneurysms is uncertain; Members of the panel who left early in the process, or contributed only limited amounts to the guidance, remain listed as contributors. This makes the panel, from an external standpoint, appear broader and more balanced than it may have been in practice; In general we have very considerable concerns about the make-up of the panel, which a Chair with no aortic practice or research contribution, and other experts who perform no EVAR themselves and have no current aortic research, or have small clinical practices. We do not find the following statement of the authors of the UK EVAR Trials in their recent NIHR HTA report, and on which this draft guideline is based, reflected in this guideline: "*Patients prefer EVAR, and today it is the method of choice for repair of AAA. EVAR devices improve constantly, and sizing and imaging for deployment is better than between 1999 and 2004: a corollary is that experience in OR is declining…. surveillance must be addressed in clinical guidelines: it should be diligent, regular, easy and avoid CT scanning where possible, perhaps concentrating on the sac diameter after EVAR by ultrasonography."* What the trial authors did not suggest was that EVAR should be terminated as a procedure. They suggested that the long-term trial results, for a trial powered only for 3-year mortality, not 15-year mortality, should act as a benchmark for future studies into EVAR, again not that this procedure should no longer be offered to patients. We have very significant concerns regarding the impact of these guidelines on the training of the next generation of	

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				vascular surgeons, and the impact of the guidelines of the future of vascular surgery as a specialty. There has been a step-change in the UK vascular curriculum in recent years, which now places great importance on the endovascular planning and treatment of AAA in a range of clinical settings. If the only time EVAR is to be used is in the setting of a rupture, this will seriously limit training opportunities and the competence of future surgeons to perform these extremely challenging procedures. The guideline will inevitably lead to surgeons entering consultant practice with insufficient experience of EVAR, placing patients at risk. This will have long-term consequences for the construct of on-call rotas, with more senior consultants needing to provide the cover for more junior colleagues. This will in turn have an impact on elective service delivery and access to care.	
The British Society of Interventional Radiology	Draft guideline	1.5.3/4		At a number of times in the guideline there is reference to if an aneurysm is "suitable" for open repair. As far as I am aware all aneurysms (infra-renal, juxta-renal, supra-renal and type IV thoracco-abdominal aneurysms all have an open surgical option. Thus if 1.5.3/4 are to be followed, then EVAR should only be offered where there is an significant contra-indication to open repair that is not co-,morbidity or anaesthetic related. That leaves probably those who have had a previous laparotomy, and that isn't an absolute contraindication to open repair.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
St George's University Hospital NHS	Draft guideline	General	General	The Committee have not overtly noted that the UK had the worst results for AAA surgery in the world only a few years ago (2008) with an elective AAA mortality of 8%. This was before the widespread adoption of EVAR which now comprise	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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Foundation Trust				70% of all elective case in UK. To adopt these draft guidelines will return the UK to the point of very poor outcomes that were experienced over the last decade. National mortality results for AAA are now 1%, and this is due to the widespread, and preferential, provision of EVAR and centralisation of arterial services. Our results are currently in line with, but even now do not exceed, other developed nations. NICE is aimed at delivering clinical excellence, which has been the aim of the Vascular Surgery Quality Improvement Framework, not palliation based on cost, which appears to be the aim of this guidance, and is not ethical.	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.
St George's University Hospital NHS Foundation Trust	Draft guideline	General	General	There is no clear discussion and advice surrounding centralisation for AAA surgery or the benefits of network formation in these guidelines, which have been shown to be associated with very great benefits in clinical outcomes for patients with AAA, exceeding the arguments presented regarding open vs endovascular aneurysm repair.	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Unfortunately, centralisation for AAA surgery or the benefits of network formation was not part of the scope developed for this guideline, and therefore it is not possible to make any recommendations in this area.
St George's University Hospital NHS Foundation Trust	Draft guideline	General	General	There will be a very significant effect on training within these guidelines. It is anticipated that vascular surgery will become very hard to recruit to following the introduction of such guidance. The delivery of training in open aortic repair will have very considerable implications for the current and future trainees in vascular surgery, and in the short term may not be feasible.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues.
St George's University	Draft guideline	General	General	No thought has been given to the management of existing patients on surveillance. If the evidence used in this guideline	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and

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Hospital NHS Foundation Trust				is accepted as current (and this is challenged), then a significant number of cases will need graft revisions. How will these graft revisions be performed now, and in the future, and who will have sufficient current expertise to perform them?	appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. The guideline looked for, but did not find, relevant evidence on the optimal methods for managing complications (see Evidence review X). We agree that the safe and effective provision of endovascular reintervention should be considered as part of any service reconfiguration that would be made necessary by the adoption of these guidelines.
St George's University Hospital NHS Foundation Trust	Draft guideline	General	General	There has been no consideration given to how to treat patients with a hostile abdomen, concurrent cancer that requires resection (chest or abdominal), overweight/obese patients, stomas all of whom are better served with EVAR than open repair.	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
St George's University Hospital NHS Foundation Trust	Draft guideline	9/10	173-185	Adopting the stance taken in 1.5.1 to 1.5.4 will have a significant impact on the running of regional vascular services: The length of stay of aneurysm patients will increase, as EVAR is normally performed as an overnight stay in the current era. This is a shorter length of stay than assessed in	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. As explained in **Theme 6a**, the reduction in length of stay with EVAR has been mirrored by an essentially identical reduction in postoperative resource use following OSR. Therefore, the

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				the historic clinical practice of the trials used in this draft guideline. This lower length of stay has a positive impact on the cost effectiveness of EVAR and calls into question the assumptions in the HE models used in reference to modern practice. Only providing open repair will effectively reduce capacity in vascular services, limiting care to patients with aneurysms and other vascular conditions. The ITU usage for AAA repair will dramatically increase in the UK in response to these guidelines. Most EVAR do not use ITU, and these comprise 70% of current AAA repairs in the UK. Therefore, there will be a very significant increase in ITU burden, with reciprocal limitation of access to other pathologies and treatments such as coronary artery bypass. Adoption of these guidelines will increase the number of cancellations due to reduced capacity within vascular services and ITUs through the increased use of open aneurysm repair. Cancellations expose patients to an increased risk of rupture through temporal delay, and stresses already overburdened services through the need to rebook patients. Aortic rupture rates will increase, as many currently treated patients will not be offered elective repair under this guidance, and will consequently present with aortic rupture, burdening emergency services and intensive cares. Alternatively they will simply be allowed to die, having had a condition that was absolutely treatable at the point of diagnosis. .	difference in costs between the 2 approaches, in this area, has remained consistent over time. For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**. The existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive

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					eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				Any benefit of the NAAASP will be negated as ruptures from patients with AAA turned down for elective repair will increase. We presume therefore that the guidance will be altered with direct communication to NHSE post-consultation to advise that there is no other conclusion than the NAAASP must be terminated as it is not ethical to screen for a condition for which no treatment will be offered (even if currently routinely and preferentially available)?	The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. For discussion of the possible impact on quality of life of living with an untreated AAA, please see **Theme 13**. If it is cost effective to screen people for AAA under current service patterns, then optimising the treatment pathway to deliver better health at lesser cost can only make the screening programme more valuable.
				Population aneurysm mortality rates will increase further above the already unacceptably high levels to the worst in the developed world. Costs will increase as treating aortic rupture is more expensive than elective aortic repair. Centres that offer fewer EVAR have much higher turndown rates (35%) for surgery than those offering EVAR (10%) (Karthikesalingam EJVES 2011;42:295-301, Thompson Ann R	Increased rupture rates can only be considered unacceptable if it is clear that treatment would have provided better survival prospects. In this case, the existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that

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				Coll Surg Engl 2011;93:474-481), limiting patient choice and withholding treatment. The NAAASP, shows huge discrepancies in turndown for surgery in screened patients, with centres offering higher proportions of EVAR having lower turndown rate than those with low EVAR rates (2% vs 25%). For clarity, this is for patients within the NAAASP. This proposed guideline will increase turndown through adoption, and drive risk aversion through its detail. Palliation for treatable conditions is topical in the national press and Gosport inquiry. The scale of what is proposed in this guidance will far outstrip the number of deaths seen in Gosport in a single year of implementation. The NICE process will be responsible for many entirely preventable deaths	intervention confers no net survival benefit for people in this group. While it is true that treating aortic rupture is more expensive than elective aortic repair, the total costs of a conservative strategy will be substantially lower, because a relatively small proportion of people will experience rupture and many more will die with, rather than from, their AAA. It seems unlikely that variation of practice of this degree can be explained on the basis of patients' presenting characteristics, so we would agree with your implication that there is likely to be avoidable harm to patients at one end or other af that spectrum. It is unclear, however, whether the units that manage high-risk candidates aggressively provide net benefit to them by doing so.
St George's University Hospital NHS Foundation Trust	Draft guideline	10/11	195-214	**Point 1.6** – We agree that local anaesthetic EVAR is a promising treatment for ruptured AAA. However, it is of concern to advise this in the context of the blanket ban the guidance is aiming to impose on the use of EVAR for elective/urgent cases. Experienced endovascular surgeons would confirm that there is no more demanding procedure	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact

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				than local anaesthetic treatment of aortic rupture, especially in the face of haemodynamic instability. This guidance will contribute to patients dying from ruptured aneurysm through a lack of current clinical exposure to endovascular techniques in an elective setting. There are particular and worrying implications in terms of training, if the only EVARs that surgeons in training are undertaking are for rupture. This guideline will effectively remove the option of EVAR for ruptured aneurysms, especially in the context of seeing more ruptured AAA due to points contained in 1.5 (ie the non-treatment of patients with large AAA electively). Industry are more likely than not to cease stocking centres with emergency stocks for aortic ruptures due to low numbers and it will not be cost efficient for them to maintain a rupture consignment. This will remove the option of EVAR for ruptured AAA. It is highly likely that the palliation rate for ruptured AAA will escalate despite being already high by international standards. This is completely unacceptable when these patients would have been treatable at the point of diagnosis electively.	section in the guideline for information on implementation issues.
St George's University Hospital NHS Foundation Trust	Draft guideline	11/12	221-227	**Point 1.7.3-5** – We absolutely disagree with these statements. It has been suggested that the excess deaths seen late in the EVAR trials may be related to cancers related to CT surveillance. The EVAR Trial authors commented in their HTA report: "*The significant late divergence of the survival curves in favour of OR can be partly explained through greater contribution to late mortality from … cancer deaths in the EVAR group, and the fact that these were elderly patients and the survival curves will inevitably start to converge in older ages.*"	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound.

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					1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after

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					EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
St George's University Hospital NHS Foundation Trust	Draft guideline	11/12	221-227	**Point 1.7.3-5** – Some EVAR patients have a gradual decline in renal function over the years post implantation, and it has been suggested that this could be due in part to the contrast given for CT surveillance. CT surveillance is one reason why there were higher costs in the EVAR groups in the clinical trials used in this draft guidance. Patients can also suffer life-threatening reactions to CT contrast, or suffer contrast induced nephropathy including acute renal failure. Whereas Duplex ultrasound is safe and effective. Where necessary contrast enhanced duplex can be employed, but it has not been shown to be clearly beneficial. Colour duplex is absolutely sufficient to monitor EVAR, safe and effective. If AAA sac size increases or a type 1/3 endoleak is found then further imaging is required. The appended review demonstrates that duplex has equivalent performance to CT in guiding reintervention, as well as having a better safety profile. Br J Surg. 2012 Nov;99(11):1514-23 – systematic review and meta-analysis of surveillance methods concluded both CEUS and DUS were specific for detection of types 1 and 3 endoleak. Estimates of their sensitivity were uncertain but there was no evidence of a clinically important difference. DUS detects types 1 and 3 endoleak with sufficient accuracy for surveillance after EVAR. Data from the EVAR trials in their HTA report confirm that only sac size needs monitoring, and that in fact the detection of endoleak is secondary. Ie sac shrinkage is safe, sac expansion needs further investigation. Duplex is sufficient to	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication.

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				detect most endoleaks, and absolutely sufficient to monitor sac size.	The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
St George's University Hospital NHS Foundation Trust	Draft guideline	3	40	**Point 1.1.3** - There is no evidence for population screening of women for AAA. A large NIHR-funded study has drawn the conclusion that screening women is not clinically or cost effective. This is about to be published in the Lancet demonstrating that 3900 women aged 70 would need to be screened to prevent 1 death.	Thank you for your comment. The noted that the study you have highlighted is related to population-based screening. The committee were in agreement that the recommendation is related to opportunistic case finding in women, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging whereas the screening programme involves actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men.

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					With this in mind the committee agreed that the recommendation should not be changed. They also agreed that the recommendation was made at 'consider' level to ensure sufficient flexibility in decision making.
St George's University Hospital NHS Foundation Trust	Draft guideline	5	70	**Point 1.1.8** - Patients with a suspected ruptured AAA should have an immediate CT angiogram, not a bedside ultrasound as advised in the draft guideline. This is particularly pertinent in light of later advice in this document that EVAR is the preferred modality of repair for many patients with a ruptured AAA. An ultrasound will lead to delays in accessing CT scanning, potentially increase the risk of death through delays to surgery, and isn't accurate in the diagnosis of rupture (it can diagnose an aneurysm, but not easily a rupture). CT is routinely available 24/7 in modern practice and is already the standard of care for the diagnosis of ruptured AAA, and other intra-abdominal catastrophes. CT scanning at the earliest stage of the management of a suspected ruptured AAA also facilitates appropriate case planning and reduces the possibility of misdiagnosis (e.g. aortic dissection, ischaemic or perforated bowel) that require different management strategies. The IMPROVE trial recommended that "*CT should be recommended for all patients with suspected ruptured aneurysms*." (BJS 2014;101:216-224). This went further to say *"Patients were entered into the trial on the basis of a clinical diagnosis of ruptured aneurysm made by a senior clinician…Approximately one in ten patients with a clinically suspected ruptured AAA was found to have an alternative pathology either at laparotomy or cross-sectional imaging, explaining their emergency presentation, even though the majority had an incidental diagnosis of AAA. Given that the patients were diagnosed by an experienced clinician and that*	Thank you for your comment. Evidence review B provides a detailed account of the committee's deliberations on imaging techniques for diagnosing AAAs. The committee discussed whether CT could be recommended for diagnosing symptomatic or ruptured AAA. Although it is the best imaging technique, recommending a CT scan for all patients who are symptomatic (whether as the sole test or as a subsequent test to the FAST ultrasound) was not considered safe as it may unnecessarily delay the transfer of patients to the regional vascular service for treatment. Furthermore, performing a CT scan in all patients would also incur considerable costs. The committee also discussed the role of CT angiography in patients who have been transferred to a regional vascular service, and are being considered for emergency repair. They expressed the view that it would be bad practice to undertake emergency EVAR without performing CT angiography. However, they also acknowledged that, where a patient's condition is critically unstable, a vascular specialist may need to rely on a strong clinical diagnosis coupled with ultrasound imaging to inform their decision to attempt open surgical repair. Therefore, the committee agreed it would be unsafe to recommend that CT should always be undertaken and, instead, agreed that it should be considered in each case.

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				some may have undergone ultrasound imaging…the diagnostic accuracy is likely to be significantly worse in everyday clinical practice… Patients should not undergo attempted repair of a suspected ruptured AAA without confirmatory imaging, usually CT."	
St George's University Hospital NHS Foundation Trust	Draft guideline	5	77/78	**Point 1.1.9** – We disagree that inner-to-inner diameter is the best measurement for AAA. This has been shown to systematically undersize aneurysms by 5mm when compared to CT scanning, the gold standard. Systematic under-sizing in surveillance will leave patients with a 55mm aneurysm exposed unnecessarily to aneurysm rupture, as they will have 60mm aneurysms by definition. Outer-to-outer diameter is the true indication of aneurysm size, correlates most closely with CT diameters, and therefore gives the best guidance regarding the true risk of rupture. Chiu et al. EJVES 2014;47(4):367-373 directly compared the accuracy of three methods of ultrasound measurement (inner-to-inner, leading edge to leading edge, outer-to-outer vs CT scanning). They concluded that "*inner to inner measurements undersized aortic diameter by 5mm on average. Outer-to-outer was the measurement that correlated most closely with CT scanning and was only 1mm undersized by ultrasound on average. The underestimations were highly statistically significant (p<0.0001)."* Advising a policy of systematic under-diagnosis is of questionable ethics and is against the NHS Constitution in which Key Principle 1 states: The service is designed to improve, prevent, **diagnose and treat** both physical and mental health problems with equal regard. It has a duty to each and every individual that it serves. Key Principle 3 states: The NHS aspires to the highest standards of excellence and professionalism – in the provision of **high quality care that is**	Thank you for your comment. The committee made the recommendation for inner-to-inner measurement to reflect current standards within the NHS AAA screening programme of taking two anterior–posterior measurements of the maximum aortic diameter, recorded in centimetres, measured across the lumen from/to the inside of the ultrasound-detected aortic wall. The committee made the recommendation to ensure a standardised approach is used for measuring aneurysms across the whole NHS. The committee were mindful that additional measurements could be potentially useful. Thus, they also stated in the recommendation that any additional measurements should be documented clearly.

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				safe. We would argue that both principles are breached in proposing a policy of under-diagnosis and in so doing leaving patients with large (>55mm on CT scanning) AAA untreated.	
St George's University Hospital NHS Foundation Trust	Draft guideline	5	77-86	**Point 1.1.9-11** – 3D reconstruction is essential to providing high quality EVAR. Not making a recommendation with respect to this suggests that limited advice was given to NICE on this point and its critical and now absolutely routine use in EVAR by advisors to the panel. At the time of the EVAR trials, this was not routinely available, as well as CT scanning being of rudimentary in nature by current standards, and of poor quality (10mm slices). Improvements in pre-operative imaging, and pre-operative planning using 3D reconstructions has greatly improved the accuracy and durability of EVAR and should be routine practice in all regional vascular centres. CT slices now are between 0.5 and 1mm with dual energy CT adding further information. ECG-gating and post-processing make CT scanning ever more accurate in sizing and planning EVAR, improving durability and reducing procedural complications.	Thank you for your comment. Evidence review I provides a detailed description of the committee's discussion about post-processing techniques. The committee agreed that post-processing techniques are an established part of clinical practice, and are commonly used at the clinician's discretion. They noted that most hospitals already have this technology available on their picture archiving and communication systems (PACS systems), and agreed that there was no need to make recommendations in this area. The committee were mindful that any recommendation stating that hospitals should "offer" post-processing techniques would be unjustified in the face of lack of evidence of their effect. They also considered that a recommendation to "consider" the use of post-processing techniques would also be meaningless given their already wide use.
St George's University Hospital NHS Foundation Trust	Draft guideline	6	104	**Point 1.2.5** - We agree that transfer protocols for urgent and ruptured AAA should be agreed and formalised to encourage timely transfer to regional vascular units and should include recommendations regarding immediate CT angiography of the entire thoraco-abdominal aorta for diagnosis and case planning with 3D reconstruction. CT scanning of the abdominal aorta alone is historical and should be abandoned as a practice. Use of imaging linking technology such as IEP should be explicitly encouraged in this guidance to improve communication between district hospitals and regional arterial centres.	Thank you for your comment and endorsement of the guideline recommendations about patient transfer. The committee noted the importance of the points made in your comment; however, they believe that it is not within their remit to be explicit about how transfer protocols should be developed and enacted. They believe that these details should be determined by local service providers within the context of the facilities, equipment and other resources available to them. The committee discussed whether CT could be recommended for diagnosing symptomatic or ruptured AAA. Although it is the best imaging technique, recommending a CT scan for all

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					patients who are symptomatic (whether as the sole test or as a subsequent test to the FAST ultrasound) was not considered safe as it may unnecessarily delay the transfer of patients to the regional vascular service for treatment. Furthermore, performing a CT scan in all patients would also incur considerable costs. The committee also discussed the role of CT angiography in patients who have been transferred to a regional vascular service, and are being considered for emergency repair. They expressed the view that it would be bad practice to undertake emergency EVAR without performing CT angiography. However, they also acknowledged that, where a patient's condition is critically unstable, a vascular specialist may need to rely on a strong clinical diagnosis coupled with ultrasound imaging to inform their decision to attempt open surgical repair.
St George's University Hospital NHS Foundation Trust	Draft guideline	6	113	**Point 1.2.6** – The evidence around permissive hypotension in ruptured AAA is poor and derived from trauma populations of younger patients with less co-morbidity. IMPROVE (BJS 2014;101:216-224) suggested that patient survival was better in patients who maintained a higher blood pressure (though there was insufficient power and the trial design was not to suggest that this was causal). There is therefore insufficient evidence to make this recommendation, and in many centres the policy is moving away from permissive hypotension.	Thank you for your comment. In the absence of evidence specific to the use of permissive hypotension in people with ruptured or symptomatic AAA the committee considered recommendations from the NICE guideline on assessment and initial management for major trauma (NG39). The committee recognised that populations experiencing haemorrhage after trauma and those experiencing haemorrhage due to ruptured AAA were likely to be demographically different (especially with respect to age). However, they agreed that the rationale underpinning the use of restrictive fluid resuscitation in people after major trauma was applicable to people with ruptured AAA, as both groups experience profuse bleeding. As a result, the committee considered it reasonable to adapt the recommendation from NICE guideline NG39 so it can be used within the context of AAA. The committee agreed that it was only appropriate to

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					make this recommendation at the 'consider' level because the evidence was not particularly strong and only partially applicable to people with ruptured AAA.
St George's University Hospital NHS Foundation Trust	Draft guideline	7	132	**Point 1.4.1** – there is no evidence to provide guidance that CPEX should be used to determine fitness for AAA surgery. This has been reviewed and published Young et al. EJVES 2012;44:64-71. This study concluded that there was a "*paucity of robust evidence which precluded the routine use of CPET in risk stratifying patients undergoing major vascular surgery*." Ultimately CPEX is a research tool at the current time and there is insufficient evidence to suggest its routine adoption.	Thank you for your comment. Evidence review G provides a detailed account of the committee's deliberations on tests for predicting outcomes after repair of unruptured abdominal aortic aneurysms. Recommendation 1.4.1 was drafted in the context of preoperative assessments. The committee noted that, while CPET may provide healthcare professionals valuable objective information on the fitness of people prior to elective AAA repair, the evidence was not robust enough to make strong recommendations for the use of the test as a decisive arbiter of fitness. Moreover, the committee agreed that individual CPET parameters should not be used in isolation to decide whether a patient should have surgery or not, but instead, may be used to inform shared decision making about treatment options in context of medical history and examination. The committee agreed that it was only appropriate to make this recommendation at the 'consider' level because the evidence was not particularly strong.
St George's University Hospital NHS Foundation Trust	Draft guideline	8	149	**Point 1.4.4** – This point in the guidance is inconsistent with Point 1.2.2, with which we agree. Cardiac arrest and prolonged loss of consciousness are signs/symptoms and should be taken account of.	Thank you for your comment. The committee made recommendation 1.3.2 (previously 1.2.2) to raise awareness that people with a confirmed ruptured AAA who have a cardiac arrest and/or have a persistent loss of consciousness (in the emergency department or during transfer) have a negligible chance of surviving AAA repair. The guideline then highlights (in 1.4.4) that it is not appropriate to rely on any single symptom, sign or risk factor to determine suitability for AAA repair. Overall, this means that cardiac

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					arrest and loss of consciousness should be considered in combination with other factors to determine whether aneurysm repair is suitable.
St George's University Hospital NHS Foundation Trust	Draft guideline	9	173-178	**Point 1.5.1** – This point is inconsistent with Point 1.3.3. It is not possible to detect an aneurysm that is 'larger than 4.0cm and has grown by more than 1cm in 1 year' if you only screen 'every 2 years if the AAA is 3.0-4.4cm.' The intervals suggested are not evidence based. If a rationalised surveillance is required to cut costs, we suggest biannual screens for AAA 3.0-4.0cm, annual screens 4.0-5.0, then optimise the patient for surgery through referral to the vascular team from surveillance at 5.0cm with continuing 3 monthly scans until the time of surgery at 5.5cm outer-to-outer measurement on ultrasound, validated by high-quality CT for procedural planning.	As detailed in Evidence review D, the intervals suggested in the consultation draft were evidence-based: they were predominantly based on evidence from the RESCAN project (Thompson et al., 2013). Upon further discussion, the committee were mindful that surveillance intervals specified by the NHS AAA screening programme may change in the future. As a result the recommendation (renumbered from 1.3.3 to 1.2.3) was changed to the following: "1.2.3 Offer surveillance with aortic ultrasound to people with an asymptomatic AAA. Base the frequency of surveillance on the intervals used by the NHS AAA screening programme"
St George's University Hospital NHS Foundation Trust	Draft guideline	9	173-178	We do not support the routine treatment of AAA of smaller than 5.5cm	Thank you for your comment. Evidence review F provides a detailed description of the committee's discussions about thresholds for repair. Upon review of the identified evidence, the committee noted that size was not the only criterion for determining whether aneurysms should be repaired. All identified studies also included symptomology (such as tenderness) and rapid growth rates as criteria for repairing aneurysms. As a result, the committee considered them important indicators of an increased risk of rupture.
St George's University Hospital NHS	Draft guideline	9	179-180	**Points 1.5.2** - We are concerned that the use of trials describing a historic practice have been used in the assessment of EVAR. The EVAR Trials do not reflect current treatment algorithms or endograft designs, and the relevance	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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Foundation Trust				of long-term data to modern aortic practices are highly questioned in the vascular community as a whole. We would agree that younger and fitter patients should have a discussion regarding the method of treatment that they would prefer, including conservative management, open repair and endovascular repair. However, data from the National Vascular Registry, and also the HES data, support the fact that young, fit patients perform well with either open repair or EVAR, and so it would not be correct to withhold this choice from them. These data sit with HQIP, David Cromwell at the RCS Clinical Effectiveness Unit and the Vascular Society of GB & Ireland Audit Committee. Patient choice appears not to have been considered in developing these draft guidelines. The same finding was found in all the clinical trials (EVAR, OVER, DREAM), and is known throughout the aortic surgeon community. The criticisms of infra-renal AAA repair with EVAR are unjustified and are based on historical evidence. The EVAR Trial papers are 20 years old and the Dutch DREAM study was underpowered. EVAR 1 was never powered to assess long term outcomes, being powered for mortality at 3 years at which time point EVAR was found to be both clinically and cost effective, and only 60 of 1252 patients remained in the trial at the end of the long-term follow-up period. To perform Kaplan-meier analysis for such a small number and proportion of patients from a trial is highly unusual and has attracted	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted registry data such as those from the NVR to support decision-making – see **Theme 3a**. It is not clear what 'same finding' you are alluding to in the 3 trials you cite. If it is that EVAR is associated with a lower risk of perioperative mortality, then the committee clearly acknowledged this fact; however, they were equally convinced that a broadening of horizon beyond the very short term leads to the unavoidable conclusion that, when compared with OSR, EVAR causes net harm across the population of people with infrarenal AAA. The suggestion that the design of RCTs renders their results unreliable is misguided. The power of trials is relevant to the precision, but not the accuracy, of their findings – see **Theme 9b**. We do not agree with the statement that survival analysis 'would normally have been stopped' at some point before later follow-up junctures. Statisticians commonly warn against the arbitrary exclusion of data from time-to-event analyses (see, e.g., Latimer 2011). Far from being 'highly unsual', it is

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				much criticism from clinicians and statisticians alike. Such analysis would normally have been stopped some years before with around 30% of patients remaining; Using these data for assessment ignores the very significant changes in treatment algorithms, case planning with 3D reconstruction, stentgraft design, implantation techniques, diagnostic and intra-procedural imaging in the last 20 years, all of which make EVAR safer and more durable than suggested by the trial results. Further, there is an increased understanding within the community that 'off IFU use' has worse durability than treating patients within instructions for use. The trials were performed of a technology in its infancy. The latest trials suggest EVAR is not only clinically and cost effective, but cheaper in real terms than open surgical repair (OVER and IMPROVE).	completely normal, recommended practice for survival analysis to be undertaken on the most complete datasets available. The committee looked for evidence that improvements in technology and technique have led to material improvements in patient-relevant outcomes. One possible area is in reduced hospital stays. They noted that, because (despite their misgivings about reliance on confounded data) they adopted unadjusted estimates of perioperative resource use from the NVR in the revised HE analyses, they were already accounting for this development. They also noted that OSR resource use has reduced by a very similar amount over the same period, so it is likely that that approach alos benefits from some of the same things (e.g. improvements in imaging), and there are also common contributors other than those you list (for example, those related to postoperative care). As far as long-term data are concerned, the committee were only able to find a suggestion that reintervention rates may have reduced. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. We should also note that some of the items you list as critical steps in the evolution of EVAR – for example, case planning with 3D reconstruction – are not included in our estimated costs of EVAR procedures. According to your argument, such innovations deliver benefits that we are already taking account

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					of (by using data from the NVR to estimate perioperative resource-use); we really ought to take account of their costs, as well. IMPROVE is not relevant to this discussion, as it solely included emergency surgery (in which setting, the committee agree that there is a definite role for EVAR, if an appropriate service can be implemented). OVER found that EVAR is cheaper than OSR for the primary admission because time in hospital – and, particularly, critical care – is so much more expensive in the USA. The OVER analysis estimated costs of over $40,000 for the index admission for people undergoing OSR whereas, in the UK, our analysis estimates costs of less than £10,000 under the same headings.
				The EVAR trials did not include any meaningful assessment or quantification of the laparotomy-related complications of open surgical repair, including incisional hernias, readmissions and surgery for adhesions and bowel obstruction. An attempt was made to address this is the latest report, but the validity of performing this retrospectively is highly questionable and simply will not be accurate. The rate of laparotomy-related complications after aneurysm repair is very much underestimated in the surgical community and is in the order of 25% at five-years post-surgery (Bensley et al. J Am Coll Surg 2-13;216(6):1159-1168). More recent trials have included the laparotomy-related complications of open aneurysm repair and found there to be no higher rate of reintervention in EVAR than in open repair (OVER and IMPROVE). The nature of reinterventions is different between open and endovascular aneurysm repair, but the rate is not. Unfortunately, this well-known fact has been placed to one side in this draft guidance.	It is true that the EVAR-1 trial did not initially collect data on this outcome. However, the investigators were mindful of this criticism, and retrospectively obtained data on hernia interventions required following EVAR and OSR for all trial participants, using HES data and medical record review. These data were reported in the long-term follow-up reports (Patel et al., 2016; Patel et al., 2018); consequently, these events are incorporated in the base-case HE model. We also incorporated other laparotomy-related complications recorded in US registry data (Schermerhorn et al., 2015) that had not been retrospectively included in the EVAR-1 reintervention data. Therefore, we are confident that the HE model developed to support decision-making for this guideline does not underestimate the late complications of OSR. IMPROVE is not relevant to this discussion, as it solely included emergency surgery. There is some ambiguity about

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					the rate of reinterventions in OVER. The NEJM paper (Lederle et al., 2012) finds no significant effect; however, the most recent publication (Lederle et al., 2016) shows a significantly raised risk with EVAR, as does the patient-level 5-year meta-analysis (Powell et al., 2016). Although we agree that the reinterventions associated with OSR have historically been understated, we have taken all necessary steps to ensure they are included in our analyses. However, it cannot reasonably be claimed that OSR is subject to a similar rate of reinterventions to EVAR – all relevant evidence shows clearly that EVAR has a higher overall rate of secondary procedures.
				Large population-based studies have confirmed that the benefit from the early mortality gain in EVAR is maintained until at least 8 years (NEJM 2015;373(4):328-338). This study showed very considerable levels of laparotomy-related reintervention and readmission in the open surgical cohort that were not apparent in the EVAR cohort. This is supported by UK data from the National Vascular Registry / HQIP / RCS CEU.	This study (Schermerhorn et al., 2015) is the source of evidence for laparotomy-related procedures that we incorporate in the HE model. The same study is also included in the casemix-adjusted observational data that was reviewed in response to stakeholder feedback. It shows a similar rate of post-perioperative excess mortality with EVAR as is seen in the RCTs.
				Both OVER and IMPROVE found EVAR to be cost-effective using traditional thresholds for assessing ICER. The long-term cost effectiveness of OVER is due to be published in the NEJM shortly and shows the cost effectiveness of EVAR.	As noted above, IMPROVE is not relevant to this discussion, and OVER's cost-effectiveness analyses are of little relevance to the UK setting, given the very much more expensive hospital care in the USA.
				EVAR 1 reported a number of post-EVAR ruptures. It is clear that many of these were attributable to a small number of centres with poor surveillance programmes and clinical algorithms that allowed type 1 and 3 endoleaks with sac	Annual CT-based surveillance of EVAR cases was mandated in EVAR-1 (and other RCTs), and other stakeholders have complained that such a follow-up protocol is too intensive to reflect current-day practice. We argue against this (see

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				expansion to be left untreated. This would not reflect current practice, and materially affects the interpretation of the trial. Re-analysis of the trial with major culprit centres excluded greatly extends the mortality benefit of EVAR. In EVAR 2, by the end of patient follow-up, 71 of 207 (34%) patients assigned to no intervention had undergone aneurysm repair making any interpretation of the data very difficult. There were also very long delays to treatment and some patients had surgery many years after randomisation, suggesting that the randomisation and inclusion of them in EVAR 2 was incorrect. However, significant differences were seen in aneurysm-related mortality in the long-term in EVAR 2 data showing a very significant benefit of EVAR to prevent aneurysm-related mortality. Open aneurysm repair in females carries a very high mortality (much higher than the 5% in men), and more in the region of 10% based on national data. Women have tended to be under-represented in all the clinical trials, except IMPROVE, suggesting lower population elective treatment rates and higher rupture rates in women. Females derive a very significant benefit from EVAR, both in lower mortality, and also	Theme 11); however, we do accept that more haphazard follow-up is currently the norm. The methods used to adjust for crossover in our analysis are well established. However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful. It is in the nature of the very unfit population of EVAR-2 that there would be some cases where intervention could not be achieved as speedily as has initially been planned. That is one reason why it was important for the investigators to report an ITT analysis starting from the moment of randomisation. Sidloff et al. (2017) show that the effect of sex on perioperative mortality risk is greater for people undergoing EVAR than it is for people undergoing OSR (OR=1.48 for OSR compared with OR=2.86 for EVAR). Other publications based on large datasets have found the same (see, e.g., Trenner et al., 2018, and analyses on the Vascunet database by Mani et al., 2015, and Budtz-Lilly et al., 2017). While Ulug et al. (2017) do not

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				in terms of reduced turndown, increasing access to care. EVAR should be the elective and emergency standard of care for all women to ensure equity of care.	replicate this finding, they do not find that the increase in risk is meaningfully greater for women undergoing OSR than those receiving EVAR (OR=1.76 for OSR versus OR=1.67 for EVAR). The issue of whether a different balance of benefits, harms and costs could be expected in women was explored in the original economic model. These analyses found no evidence of any subgroup effects of a sufficient magnitude to overturn the results in the wider cohort. See **Theme 12**.
				Clinical trials have demonstrated that younger, fitter males (with appropriate morphology) stand to gain the most from EVAR as compared to open repair. These patients also do better than older patients with open repair, but this should not be used to ignore the benefit they gain from EVAR. This is supported by observational studies of young patients. Lee et al J Vasc Surg. 2015 Mar;61(3):636-41 in examining 169 patients under the age of 60 years old followed for a mean of 12 years found that "*after elective aneurysm repair, younger patients have a moderate life expectancy related to malignant disease and cardiovascular health. EVAR offers durability and long-term survival similar to those with open repair in these younger patients as long as aneurysm anatomy and IFU are adhered to.*" The reintervention rates were 12% in the EVAR and 16% in the open repair cohorts, and no late aneurysm ruptures or aneurysm related deaths were seen. This is supported by UK data from the National Vascular Registry / HQIP / RCS CEU.	Lee et al. (2015) was considered for our supplementary review of observational data, but was not eligible as no attempt is made to adjust for confounding characteristics. In passing, we note that the authors provide an unusually clear demonstration of the kinds of selection biases the committee strongly suspect are at play in all unadjusted observational data regarding the anatomical characteristics of the AAAs. While we accept that the long-term survival differences between the 2 groups do not meet the investigators' standard of statistical significance, it certainly could not be argued that the EVAR cohort had better survival. We are not aware that any of the datasources you list provide long-term outcome data.
				Failing to set the NICE guidance in light of these known flaws in the data within the trials underpinning the guidance is not	The committee's critical appraisal of the RCTs was that they are at low risk of bias in terms of their internal validity.We have

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				placing patients at the centre of the guidance, and leads to significant questions regarding patient-facing nature of the NICE process, and suggests that the process is all about costs, not what is best for patients. We are unclear whether the panel were made aware of the scale and nature of these deficiencies in the trials underpinning the guidelines.	taken steps to ensure that our analyses account for any potential bias. The committee found the suggestion that the RCTs have poor external validity – that is, that they provide a poor estimate of treatment effect for the present decision context, primarily because they report care that was delivered a relatively long time ago – potentially more persuasive. However, supplementary work undertaken to explore this issue, by examining casemix-adjusted observational data, has not tended to support the hypothesis that things have changed for the better for EVAR to a greater degree than they have for OSR. Of most note, it appears that the RCTs provide a valid estimate of the relative 30-day mortality benefit with which EVAR has been associated throughout the past 20 years (see **Theme 2**) and the trials' suggestion of late excess mortality for EVAR is strongly validated by the observational data (see **Theme 9**).
				We are certain that not all relevant evidence has been used in assessing EVAR, and that the 'NICE process' dominated by reliance on RCTs, which do not reflect real-world practice, has failed patients in this case. It is unclear how patients are to be assessed for 'fitness for open repair.' All scoring methods have been excluded in this draft guideline, and there is no evidence for CPEX. Consequently, clinicians are likely to err on the side of risk aversion, and the population will be undertreated on the basis of these guidelines. This is effectively limiting access to care, and the population rate of aneurysm-related death will consequently elevate very significantly. It is not tenable that	We trust that your concerns have been allayed by the additional work that has been undertaken to validate the use of RCT data, and revise the HE modelling using additional 'real-world' data. The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-

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				patients fall into two categories (fit for open, and unfit for open), and is an extraordinary oversimplification of vascular surgical patients, most of whom sit in a grey area between fit and unfit, and are better served by EVAR than open repair.	set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
St George's University Hospital NHS Foundation Trust	Draft guideline	9	181-182	**Point 1.5.3** – We do not agree with this point. Patients should be presented with a choice of surgical and non-surgical options. Some patients may choose not to have surgery at all and must be counselled about the risk of aneurysm rupture, and others might hold a preference for either open or endovascular repair. Evidence exists that patients prefer EVAR and are also prepared to travel to access services that deliver EVAR routinely and have low peri-operative mortality rates (Reise et al. EJVES 2010; 39:55-61, Holt et al BJS 2010;97:504-510, Winterborn et al J Vasc Surg. 2009;49(3):576-581). We are concerned that in constructing these guidelines that patient choice has not been taken into consideration. This is against the NHS Constitution *"Key Principle 4: NHS services must reflect, and should be coordinated around and tailored to, the needs and preferences of patients."*	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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St George's University Hospital NHS Foundation Trust	Draft guideline	10	183-185	**Point 1.5.4** – We do not agree with this point. There is evidence using population statistics that the UK remains an outlier in terms of the rate of AAA surgery that is offered, and the subsequent rate of aortic related death in the UK exceeds other countries many fold. In a recent NEJM paper (Karthikesalingam et al. NEJM 2016;375:2051-9) it was shown that the UK had a rate of AAA repair of 30/100,000 population, whereas it was 62/100,000 in the USA giving an odds ratio of 2.06 [95%ci 2.03-2.08]. Conversely, the aneurysm-related mortality rate in the UK population was between 34-53/100,000 in the UK vs. 9-16/100,000 in the USA (OR 3.60 [95%ci 3.55-3.64]). Simply put, in the UK we operate on half as many AAA as in the USA, and patients suffer triple the rate of aneurysm-related deaths. Similarly, in a large population-based study (Br J Surg. 2018 Apr;105(5):520-528) ninety-day mortality rates were worse in England than in Sweden (5·0 versus 3·9 per cent respectively; P < 0·001). Five-year survival was worse in England. Mortality for elective AAA repair was initially poorer in England than Sweden, but improved over time alongside greater uptake of EVAR. Centres performing a greater proportion of EVAR procedures achieved better results in England. A further population based UK-USA study (J Vasc Surg. 2016 Aug;64(2):321-327) demonstrated that the operative mortality was greater in England (4.09% vs 1.96 %; P < .01) and EVAR less common (37.33% vs 64.36%; P < .01). These observations persisted in age- and gender-matched comparison. Therefore, to adopt an 'EVAR 2' stance, based on what is widely regarded amongst the vascular surgery community as being a seriously flawed trial due to the long delays to intervention and the number of crossovers between groups,	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Increased rupture rates can only be considered unacceptable if it is clear that treatment would have provided better survival prospects. In this case, the existing evidence – EVAR-2 RCT – shows that managing people for whom OSR is an unsuitable option conservatively does, indeed, lead to a higher rate of rupture; however, the short- and long-term risks associated with EVAR in people with this degree of comorbidity are enough to counterbalance this benefit, with the result that intervention confers no net survival benefit for people in this group. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made aresearch recommendation noting that such a study would be helpful.

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				would be to withhold treatment to patients in the NHS for a treatable pathology. This is ethically difficult. Further, to not treat these cases electively will increase the number of ruptures presenting within the NHS, which will increase the population mortality from AAA in the UK, heavily burden in and out of hospital emergency services and vascular surgical services, and far outstrip any potential benefit derived from the NAAASP. Such a policy would require the NAAASP to be stopped as two diametrically opposed policies cannot co-exist in a publicly-funded system, and to screen for a condition that you cannot then treat is not ethical. There is already evidence published from the NAAASP that shows that there is a wide variation in the proportion of patients not offered surgery for AAA. This is between 2 and 25%, with the centres with the highest rates of turndown having the lowest ratee of EVAR. For clarification, this is in screened patients. To remove EVAR from treatment algorithms will mean that it will not be ethical to continue the NAAASP as many patients would be diagnosed with a screen-detected condition for which no treatment would be offered. This is against the most basic ethics of screening. When screening is terminated, the population AAA-mortality rate and AAA rupture rate will increase to historic rates. Further, we know that in the UK patients are less likely to be offered repair of ruptured AAA than in other countries. A recent paper in the Lancet (Karthikesalingam et al. Lancet 2014;383:963-969) demonstrated that only 58% of patients with ruptured AAA are offered repair, whereas in the USA 80% are offered repair. There was no overall difference in operative mortality between the USA and UK for the procedures performed, but due to the non-treatment of an additional 22% of cases in the UK, the overall mortality was considerably	

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				higher in the UK than the USA for all patients (OR 1.473 [1.376-1.576; p<0.0001]) and rates of palliation (ie not offering surgery) were much higher in the UK than in the USA (OR 3.193 [2.951-3.455; p<0.0001]). Under these proposed guidelines, patients not treated electively with EVAR would be offered treatment with EVAR when they rupture. The draft guidance around this point is at best inconsistent, and at worst disadvantages patients, and is incompatible with the NHS Constitution. *"Key Principle 1: The NHS provides a comprehensive service, available to all … and has a wider social duty to promote equality through the services it provides."*	
St George's University Hospital NHS Foundation Trust	Draft guideline	10	186-191	**Point 1.5.5 & 6** – The definition of complex AAA used in this guideline does not fit with clinical practice. For any AAA that is outside the IFU for a standard graft to be defined as complex is not correct. The reintervention rate of EVAR is higher outside IFU, and this does need to be taken into account in the guidelines. Off IFU surgery should be considered more carefully than in the past, and alternative treatment strategies considered. These may include conservative management, open repair, or complex endovascular techniques for non-standard aneurysms. Complex EVAR has a clear place in the management of more extensive aneurysmal pathologies, and the vascular community is not in equipoise about the role of these treatments in the correct pathologies, when delivered by relevant experts. The direction of the guideline that patients should receive either open repair or no treatment is to withhold treatment to patients who are otherwise treatable, which is not consistent with the NHS Constitution, nor international best practice guidelines.	The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. An exploratory analysis from the HE model focusing on fEVAR alone was deemed possible as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details. The committee were mindful of the finding, from casemix-adjusted observational evidence, that there is no difference in perioperative mortality between complex EVAR and OSR. Moreover, they noted that such evidence as is available on the long-term effects of complex EVAR is sufficiently concerning that, even if it could be shown that it is associated with a large reduction in perioperative mortality, there should be real

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				We support the use of research to derive further evidence regarding the longer-term clinical and cost-effectiveness of fenestrated endografting, and iliac branch grafts. This is more likely to be through registries than RCTs, which have already been shown not to be feasible to run due to a lack of equipoise in the clinical community on this matter for complex aneurysms. The clearest opportunity for this is the NIHR-funded UK COMPASS registry with 5-year follow-up. Thoraco-abdominal branched endografts and TEVAR are correctly not considered within the terms of reference of this draft guidance. There is no equipoise for these pathologies where endovascular techniques are now performed almost exclusively. Costs will increase dramatically as, within the advice of this guidance, every single patient off IFU for standard EVAR will simply be offered FEVAR. This is an unintended consequence of this guidance, which has not been appropriately considered.	equipoise about whether any such effect translates into net health gain over a patient's lifetime. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
St George's University Hospital NHS Foundation Trust	Draft guideline	11	204-206	**Point 1.6.3** – It will be a very difficult to run an RCT for FEVAR vs open thoracoabdominal aneurysm repair in the emergency setting. To place this in the guidance suggests a misunderstanding about the nature of fenestrated endografts, which are custom made for individuals, and cannot be made in a ruptured setting. There would be a role to collect further evidence in this space for parallel graft techniques through registry data, such as the NIHR-funded UK COMPASS. A trial set-up has been attempted in the UK and abroad, but there is a lack of clinical equipoise on the matter of endovascular techniques vs open repair in the repair of complex aneurysm morphologies such as supra-renal aneurysms and thoraco-abdominal aneurysms. Physician-modified grafts are very rarely performed in the UK, and in general are not supported by the community outside dire emergency.	The committee recognised that some AAA anatomy appears to present absolute contraindication to emergency EVAR. However, the committee were also aware that some units will go to great lengths to find an endovascular solution to as many ruptured AAAs as possible. Another stakeholder has drawn our attention to a publication describing the adoption of an EVAR-only approach to ruptured aneurysms (excluding suprarenal AAAs and TAAAs) (Mayer et al., 2012).

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St George's University Hospital NHS Foundation Trust	Draft guideline	11	217-220	**Point 1.7.1 & 2** – We agree that EVAR needs surveillance and that the optimal surveillance frequencies are currently not established. There is a large body of work that suggests that most patients have a low risk of endograft-related reinterventions (below), and that for them a more limited surveillance programme can be adopted. As much of the excess cost of EVAR lies in post-procedural surveillance (up to half), then rationalising surveillance in those for whom this is safe would reduce overall costs and patient burden post EVAR. It is estimated that 75% of patients fall within this low-risk cohort. Conversely, to ensure the safety and efficacy of EVAR, patients at a higher risk of reintervention should be placed on to surveillance programmes as currently. Br J Surg. 2015 Apr;102(5):509-15 PLoS One. 2015 Jul 15;10(7):e0129024 Br J Surg. 2013 Sep;100(10):1302-11 Ann Vasc Surg. 2015 Feb;29(2):197-205 J Vasc Surg. 2016 Jun;63(6):1428-1433 Vasc Endovascular Surg. 2017 Aug;51(6):417-428 Proc Inst Mech Eng H. 2017 Nov;231(11):1048-1063 BMC Med Inform Decis Mak. 2017 Aug 3;17(1):115	Thank you for your comment. NICE guidelines are only able to make recommendations in areas included within the scope of the guideline. Unfortunately, risk factors for endograft-related complications was not part of the scope developed for this guideline, and therefore it is not possible to make any recommendations in this area. For this reason the proffered studies could not be considered in this iteration of the guideline but have been noted as potential evidence for future updates of the guideline and we will highlight this to the NICE Guideline Surveillance Team.
St George's University Hospital NHS Foundation Trust	Draft guideline	12	231	**Point 1.8.2** – What evidence is there to suggest that '*healthcare professionals are not all aware that type II endoleaks without sac expansion can be managed conservatively'?* This is elementary practice, and it seems to be a comment and major assumption with no evidence to back it up. We are not aware of any current clinicians with an aortic practice to whom this comment would apply.	Thank you for your comment. No RCTs, quasi-randomised controlled trials or cohort studies with sample sizes of 500 or more were found. The committee discussed the potential usefulness of gathering evidence from small retrospective cohort studies and case series but agreed that none of these types of studies would have sufficient quality, or statistical power, to be useful for their decision making. As a result, the committee drafted informal consensus recommendations based on their clinical experience. They agreed that type II endoleak, the most common form of post-

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					EVAR endoleak, may be considered benign if found in the absence of signs of sac expansion. As such, a recommendation to consider intervention for type II endoleaks only in people who have sac expansion following EVAR discourages interventions that, in the absence of sac expansion, may be more harmful than beneficial.
St George's University Hospital NHS Foundation Trust	Draft guideline	13 16	259 336-341	**Research proposals** have been poorly posed in the context that with these guidelines fewer AAA will be treated, despite being treatable. No prior clinical trials into medications to reduce aneurysm growth rate have provided neither positive outcomes, nor value for money, so to continue down this line seems unlikely to yield significant gains. Research in to surveillance: There is a large body of literature on this topic as above. It is concerning that the Committee are not aware of this and have not used this in the development of this guideline. This suggests that the committee have not been advised by those current in the breadth of aortic research.	Thank you for your comment. The committee noted that there are currently no established non-surgical interventions available to prevent AAAs from growing, and subsequently rupturing. They believed that clinical research in this area would be useful for developing a secondary prevention strategy to prevent aneurysms rupturing. Identified trials suggested that the macrolide roxithromycin may have a role in reducing aneurysm growth; however, it is currently not licensed for use in the UK. The committee considered that it was inappropriate to extrapolate the potential benefits of roxithromycin to other macrolides, and agreed that more evidence is needed to ascertain the clinical utility of the drug class. As a result, a research recommendation was drafted. The committee also noted data from observational studies highlighting an association between diabetes and lower rates of aneurysm growth, and were aware that researchers had previously suggested that this association was likely to be due to the protective effect of metformin. As a result, the committee believed that randomised controlled trials were needed to categorically determine whether metformin reduces the rate of aneurysm growth.
St George's University Hospital NHS	Evidence review K & Health	17	302	It is not clear why the NICE committee has adopted a QALY level of £20,000 for ICER. We believe that this is not consistent with current methodology.	As per NICE's Social Value Judgements (2012):

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Foundation Trust	economic appendix				*NICE has never identified an ICER above which interventions should not be recommended and below which they should. However, in general, interventions with an ICER of less than £20,000 per QALY gained are considered to be cost effective.*
Medtronic UK	Evidence review K And Economic Appendix and Model	24	582 - 586	**Economic model and subsequent recommendations are not sensitive to improvements in surgical technique and in-hospital efficiencies since EVAR-1.** In addition to these device changes, the economic model and subsequent recommendations are not sensitive to improvements in surgical technique and in-hospital efficiencies since EVAR-1. Figure 1 shows that efficiencies of the EVAR admissions are continually improving with length of stay and critical care time decreasing significantly since 2012/13. Medtronic recommend that NICE also use databases such as HES and NVR to further inform the resource utilization of EVAR and OSR in current practice. Other benefits of endovascular repair include use of local anesthesia (LA) which is an option for EVAR instead of general anesthesia (GA). A meta-analysis (Hajibandeh et al. 2018) of EVAR outcomes with either regional anesthesia or general anesthesia showed that perioperative mortality, morbidity, and length of stay were significantly shorter with regional anesthesia (RA) compared to GA. Those authors suggested because of these advantages, LA or RA should be considered in selected patients. Similarly, in a subset analysis of the ENGAGE registry by Broos et al. 2015, patients were divided into those that had local anesthesia (groin +/- sedation), regional anesthesia (spinal and epidurals), and general anesthesia (multiple or more invasive techniques).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 3 on secular trends in the evidence and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. We have reviewed evidence on length of stay following AAA repair, and provide comments below. We note, however, that your comments relate exclusively to resource use associated with EVAR, and how that appears to have changed since the EVAR-1 trial. Of course, from a health economic perspective, the cost implications of a given technology can only be assessed in comparison with an alternative approach. In this case, this means that it is very important to consider how resource use with OSR may also have changed over time, in order to arrive at the best estimate possible of the incremental costs associated with EVAR.

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				They found procedure duration, hospital time were shorter for LA and RA compared to GA with no differences in systemic and surgical complications. They did note that LA could influence imaging quality and more contrast was used in LA group. Based on these findings, the authors recommended a "preferential use of local regional anesthesia for EVAR, restricting GA only to those with predefined contraindications". It is also noted that the use of LA does not prevent a conversion to GA if necessary and so these authors felt the potential benefits were coming at little to no risk.	We have obtained means and SDs for NVR data for EVAR and OSR from the NVR. These show that resource use with EVAR and OSR have reduced by a very similar amount since the EVAR-1 trial, with the result that the difference between the 2 is essentially unchanged. Details are provided in **Theme 6a**. Procedure duration, which is not captured in the NVR or other potentially relevant sources, is harder to estimate. As detailed in **Theme 5**, we conclude that there are no relevant, contemporary, casemix-adjusted data for this parameter. In our base case, we retain our reliance on randomised evidence, as these data at least reflect reliably matched cohorts in a UK setting, and there are no more current data with these advantages. However, we explore the impact of more contemporary, albeit methodologically less reliable, data in sensitivity analysis and find that it has no impact on model outcomes – see **Theme 5**.
Association of British HealthTech Industries (ABHI)	Evidence review K And Economic Appendix and Model	24	582-586	**Evidence review, model and recommendations do not account for changes in devices over time.** The model assumptions on outcomes and cost are based largely on results from the EVAR-1 study, which enrolled patients from 1999 to 2004. In EVAR-1 the devices used were Cook Zenith (56% of cases), Medtronic Talent (30%), and smaller numbers of Gore Excluder and Medtronic AneuRX. EVAR device technology has continued to evolve since then, with significant device advances and improved clinical outcomes. Both the Cook Zenith and Gore Excluder devices have been updated, and the Medtronic Talent and AneuRX	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**.

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				graft have been replaced by devices with significantly improved outcomes. These improvements in device design and outcomes are well documented have not been recognised in the model or guideline recommendations, for example:	Plesae see Theme 3 on secular trends in the evidence and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
				Patel et al 2018 "Devices used were implanted between 1999 and 2004 and newer devices may be expected to have better results…" "EVAR devices improve constantly, and sizing and imaging for deployment is better than between 1999 and 2004…"	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Epstein 2014 "EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future. EVAR	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.

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				devices used in these four trials were of an earlier technological generation..." "Endovascular technologies and their clinical applications are evolving rapidly. This indicates that EVAR should continue to be considered a research technology."	
				England and McWilliams 2018 "What started as a series of devices constructed in the operating theatre has evolved into mass produced 'off-the-shelf' systems which can treat a range of patients. Not only has anatomical eligibility increased but other vascular diseases are now being treated using a stent-graft." "…we have seen huge developments in EVAR technologies and their applicability. Devices… are repositionable within the aorta and can conform to more challenging anatomy."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Liang 2018 "The current generation of endografts have been in use only for the past decade; long-term durability of these devices remains unknown but has a clear dependence on adherence to the device instructions for use"	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Patel 2016 "EVAR devices are constantly being improved and sizing and imaging methods available for deployment are better now than they were between 1999 and 2004…"	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.
				Picel and Kansal 2014 "Stent-graft design continues to rapidly evolve as new devices are under development to address the shortcomings of the early stent-grafts."	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making.

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				Chambers 2009 The previous health technology assessment from the National Institute for Health Research (NIHR) acknowledged improvement in devices and practice over time and accounted for this improvement. "This apparent increase in the risk of death with time from EVAR may be confounded by evolution of devices and surgical technique, as those patients with the longest follow-up underwent EVAR with the oldest devices. We tried adjust for this by estimating parametric survival models, including a variable representing the year that the device was fitted..." Parameters for this HTA were included as a sensitivity analysis in NIHR 2018 health technology assessment (Patel), and found EVAR to be cost effective. Schermerhorn 2015 "The outcomes of endovascular repair have been improving over time." Across the Medicare population, the rate of total reinterventions at 2 years after endovascular repair decreased over time, from 10.4 in 2001 to 9.1 percent in 2007. These results were statistically significant due to the large sample size. "In a comparison of the results of repairs performed from 2005 through 2008 with those performed from 2001 through 2004, the overall survival rates were higher in the later period...." "The decline in perioperative mortality probably represents operators' increased familiarity with the procedure and improvements in endografts over time." While this is a U.S. study, the NICE guidance references other evidence from Medicare.	This study is included in our supplementary review of casemix-adjusted observational evidence. See **Theme 2** and **Theme 9** for comments.

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				Verhoeven 2014 "From 1998 to July 2004, the stent-graft was constructed with the original permeability (OP) e-PTFE fabric (n = 55; 45%); from July 2004 until the end of the study the stent-grafts incorporate a low-permeability (LP) e-PTFE fabric (n = 67; 55%)." "Technical success was achieved in 396/400 (99%) patients. Two patients needed intraoperative open conversion" "No patients required conversion to open repair during follow-up" "No stent-graft migration was noticed in any patient during follow-up" "Recently, the early results of the ENGAGE registry were published, showing promising real-world performance of the Endurant stent-graft (Medtronic Endovascular, Santa Rosa, CA, USA) in the short term. Early results of the C3 Excluder are comparable to the results of the ENGAGE registry in terms of initial technical success (both 99.0%)…" "Real-world performance as reflected by the European C3 module of GREAT indicates that the new C3 Excluder stentgraft offers excellent early and short-term outcome."	Uncontrolled case series – no quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts
				Hogg 2011 The low porosity Excluder endograft (Excluder low-permeability endoprosthesis [ELPE]; W. L. Gore & Associates Inc, Flagstaff, Ariz) introduced in 2004…" "A sustained sac regression after AAA exclusion with ELPE is noted up to 5-year follow-up."	No quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts
				Budtz-Lilly et al. (Eur J Vasc Endovasc Surg (2017) 54, 13e20)	Unadjusted registry data. See **Theme 3b**.

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				Analysis of Vascunet registry with 34,000 patients from 2005-2009 and 49,000 patients from 2010-2013. Peri-operative mortality for EVAR decreased (odds ratio 0.59, P<0.0001) whilst peri-operative mortality for OSR increased between the two time points. Verzini 2014 Newer stent grafts performed substantially better than those used before 2004, with significantly fewer complications and re-interventions Stokmans 2012 Mortality, complication rates and reinterventions with Medtronic devices used 2009-2011 significantly lower than those in EVAR-1 trial Lilja 2017 The Swedish Vascular Registry was analysed across four time periods between 1994 and 2014: short and long-term outcomes improved with time for both elective and ruptured aneurysm endovascular repair.	The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Uncontrolled case series – no quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts Unadjusted data. Shows similar reduction in EVAR and OSR 30-day mortality. Does not provide any long-term outcomes that are specific to repair approach.

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Association of British HealthTech Industries (ABHI)	Evidence review K And Economic Appendix and Model	24	582-586	**Modern stent grafts are designed to avoid issues and failures that were experienced in EVAR-1** It is important that the committee understand that a substantial number of stent grafts used in the EVAR 1 trial had attributes that are known to be associated with particular failure modes. Modern devices are designed to avoid these attributes and can reasonably be expected to reduce the rate of failures (requiring secondary intervention). During recruitment of the EVAR 1 study, it was not universally established that 'active fixation' i.e. the provision of hooks or barbs intended to engage with the aortic wall was desirable. After experience gained particularly with the Talent and Aneurx stent grafts, current stent-grafts are all provided with active fixation. In the EVAR 1 study, 206 (40%) of implanted stent grafts lacked active fixation and therefore stent migration was an issue. During recruitment of the EVAR 1 study, delivery system profiles were larger than current devices and ranged between 20Fr and 25Fr. This equates to diameters of 6.7mm to 8.3mm. The significance of this dimension is that the diameter of the access vessels, particularly the external iliac artery lie in a similar range and it was common for delivery systems to dilate the access vessels during introduction of the stent graft. In the presence of disease, dilation can often lead to stenosis or occlusion, requiring surgical revision after the EVAR index procedure. Some early generation devices, including some used in EVAR-1, had issues with the permeability of the stent fabric which consequently led to sac expansion. These fabrics are no longer in use in current generation EVAR devices.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee agreed that the only patient-relevant outcome for which there is any evidence that newer grafts may have superior performance is reintervention rates. They accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. Evidence from Verzini et al. (2014) was used, as you and other stakeholders recommend. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. Thank you for summarising for us the technical developments that may have led to lower reintervention rates.

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				Large delivery systems also increase the risk of leg ischemia during the procedure. The pain of leg ischemia would have discouraged the use of local anaesthesia, giving rise to higher rates of complication in the post-operative recovery period. Modern stent grafts universally now employ active fixation and have delivery systems ranging in diameter from 4.7mm to 7.7mm. Additional design details have also helped to reduce device failures associated with many of the implants implanted in EVAR 1: • Avoidance of oxide-coated Nitinol wire • Improvements in stent fabric permeability • Equal radial force across the stent and bifurcations • Increased sizing options available • Greater conformability • Improved deliverability and greater control during deployment **MEDTRONIC EVAR DEVICES, date of CE Mark and EVAR-1 usage:** AnueRx, 1997 (no longer commercialised), 3% of EVAR-1 devices Talent,2000 (no longer commercialised), 32% of EVAR-1 devices Endurant, 2008 Endurant II, 2011 Endurant IIs, 2014 **GORE EVAR DEVICES, date of CE Mark and EVAR-1 usage:** Excluder, 1997, 6% of EVAR-1 devices	

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				Excluder low permeability, 2004 **COOK EVAR DEVICES, date of CE Mark and EVAR-1 usage:** Zenith Abdominal Endovascular Graft, 1999, 54% of EVAR-1 devices Zenith Flex Abdominal, 2007 Zenith LP Abdominal, 2010 Zenith Alpha Abdominal, 2014 **TERUMO EVAR DEVICES, date and EVAR-1 usage:** Anaconda, Generation 3, 2005 Fenestrated Anaconda, 2010 – customised device, no CE Mark Anaconda ONE-LOK, 2011 Treovance, 2013 Treovance, 2014 TREO, 2015	
Association of British HealthTech Industries (ABHI)	Evidence review K And Economic Appendix and Model	24	582-586	**Evidence review, model and recommendations do not account for improvement in surgical and** anaesthetic **technique over time.** EVAR surgical technique has evolved since EVAR-1 enrolled patients, and outcomes have improved as a result. The improvements in technique and corresponding improvement in outcomes should be taken into account in the model. Chambers 2009	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 3 on secular trends in the evidence and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence.

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				The previous NIHR HTA acknowledged improvement in practice over time and accounted for this improvement: "This apparent increase in the risk of death with time from EVAR may be confounded by evolution of devices and surgical technique…. We tried to adjust for this by estimating parametric survival models, including a variable representing the year that the device was fitted..." Parameters for this HTA were included as a sensitivity analysis in NIHR 2018 HTA (Patel), and found EVAR to be cost effective. Epstein 2014 (EVAR-1) "EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future… preoperative imaging was rudimentary, rehearsal and simulation not standard, and hybrid suites not observed. Instructions for use were not always available." Schermerhorn 2015 (US Medicare study) "The outcomes of endovascular repair have been improving over time." "The decline in perioperative mortality probably represents operators' increased familiarity with the procedure…" Hajibandeh 2018 EVAR allows the use of local anaesthetic techniques to reduce the risks of surgery: In a meta-analysis of 15,472 EVAR cases, patients treated with loco-regional anaesthetic techniques had significantly lower mortality and morbidity. Broos 2015	The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making. See **Theme 2** and **Theme 9** for comments. This analysis collects observational evidence that makes no attempt to adjust effects for casemix. The authors also found – but made no attempt to adjust for – evidence of publication bias. We will capture these effects, to the extent that such techniques have been adopted in practice, in our use of contemporary resource-use data. Note that the authors

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				In the ENGAGE registry use of local or regional anaesthesia was associated with shorter procedure time and reduced ITU and hospital length of stay.	conclude that the 'type of anesthesia used during EVAR has no influence on perioperative mortality and morbidity'.
Association of British HealthTech Industries (ABHI)	Evidence review K And Economic Appendix and Model	24	582-586	**Evidence review, model and recommendations do not account for changes in device deployment over time.** EVAR deployment systems have also evolved since EVAR-1 enrolled patients, and outcomes have improved as a result. We recommend that this is taken into account within the model and guidance: England and McWilliams 2018 "…we have seen huge developments in EVAR technologies and their applicability. Devices are now deployable on smaller delivery systems, are repositionable within the aorta and can conform to more challenging anatomy." Verhoeven 2014 "The C3 Gore Excluder stent-graft is a third-generation modern device featuring an original design with a flexible, catheter-mounted introduction, and active infrarenal attachment with barbs. The deployment mechanism has been modified into a three-step sequence, which enables positioning of the stent-graft up to three times prior to final release from the delivery catheter."	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 3 on secular ternds in the evidence and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence. The cited text represents the authors' opinion with no clinical results that are relevant to the committee's decision-making. Uncontrolled case series – no quantitative comparison of patient-relevant outcomes with OSR or with earlier endografts

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				"Early real-world experience shows that the new C3 delivery system offers advantages in terms of device repositioning resulting in high deployment accuracy." "This resulted in a high rate (96.2%) of accurate proximal deployment of the stent-graft and low use (4.8%) of unplanned proximal cuff-extenders, which was lower than older EVAR series."	
Association of British HealthTech Industries (ABHI)	Evidence review K	26	704-712	**Guidance does not account for patient preference**. Recommendation 1.5.2-4 and 1.5.6 remove patient choice in the treatment of their AAA. Patient choice is now central to the consent and the support decision process. Studies suggest that the majority of patients would choose EVAR when presented with the risks and outcomes from EVAR versus open surgery (see below evidence). However, the guidance effectively removes the option for letting patients assess their own risks and make an informed choice regarding their care. This is not in keeping with NICE's goals for patient shared decision making; "We've updated all of our guidelines to highlight the importance of balancing professional judgment and expertise with the needs and wishes of people receiving care." Winterborn 2009 84 percent of patients preferred EVAR when presented with the risks and outcomes from EVAR versus open surgery. Most important concerns of patient preference for patients that need AAA repair include 4 of 5 areas where EVAR consistently outperforms open repair: pain, time to recovery of physical functioning, length of hospital stay, and body appearance. Chaikof 2018	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual.

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				"Several prediction models developed to estimate operative risk for open AAA repair and EVAR hold the promise of better informing patients of their individual risk of perioperative mortality and provide surgeons a useful tool to ensure an informed discussion with patients and their families." Reise 2010 Performed a survey in 2008 of patients' preference for EVAR vs OSR and concluded that 18% preferred OSR and 46% preferred EVAR. Notably, 40% said they would follow the advice of their physician. Respondents in this study prioritized having a shorter recovery time (50%), minimising ICU time (42%) with the least concern for scar size (10%) and impotence (27%). Faggioli 2011 Looked at specific elements of each procedure by presenting patients with hypothetical scenarios relating to type of anaesthesia, time to return to normal activities, reintervention risk, risk of severe procedural complications etc. As expected risk of major complications, reinterventions, or mortality were the most important components in choosing EVAR or OSR. Return to daily activities was also important. Given the evidence now available to the committee we recommend that patient choice is considered within the guideline.	
Jotec-a fully owned subsidiary of CryoLife Inc	Evidence review D	General	General	We are concerned that this recommendation may imply that Is this not a comparison of the EVAR 1 trial open cohort versus the EVAR 2 EVAR cohort? We also wonder what the experience and volume of these centres were? Non randomised data used to support either side of this current debate could be very misleading. Perhaps the NICE	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate

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				committee should accept the limitations of the current randomised data available and lobby the NIHR to fund a proper contemporary Randomised Controlled Trial led by a centre with a history of academic excellence and a balance between open and endovascular repair:	
Jotec-a fully owned subsidiary of CryoLife Inc	Evidence review D	General	General	The NICE document seems to conflict with current GMC guidance on consent: "You must give patients the information they want or need about… options for treating or managing the condition, including the option not to treat…". When the GMC uses "you must", it does so to underline an over-riding duty of a doctor. We are concerned that the proposed NICE guidance suggests that clinicians should not offer EVAR or complex EVAR to certain groups of patients, yet the option to treat them endovascularly must be discussed	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate
Jotec-a fully owned subsidiary of CryoLife Inc	Evidence review D	General	General	There have also been many EVAR registries both led by National Vascular Societies like the UK NVR and Industry e.g. ENGAGE that have demonstrated impressive safe medium term outcomes for contemporary EVAR practice. With superior EVAR technology which is constantly evolving, as a specialty we are on the cusp of delivering PEVAR and 23 hour AAA care in carefully selected patients. We are concerned that these facts have not been fully considered.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate
Jotec-a fully owned subsidiary of CryoLife Inc	Evidence review D	General	General	A contemporary rerun of the EVAR 1 trial looking at the performance of so called "superior EVAR technology" vs OSR funded by the National Research Institutes to ensure current real word data can be reviewed rather than relying on outdated previous EVAR trials that do not reflect current practice and outcomes.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.

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Royal Free London Foundation Trust - Department of Vascular Surgery	Draft guideline	General	General	The Department of Vascular Surgery at the Royal Free London is comprised of 14 vascular surgeons who practice a mixture of conventional surgery and endovascular interventions with the aim to deliver the highest quality vascular care to the population of North Central London. The ability to choose the correct modality for the patients we treat based on available evidence and local experience is the reason why our vascular unit achieves good outcomes. In 2016, we performed 59 infrarenal aneurysm repairs, and 76 emergency, complex or thoracic aneurysm repairs. The average length of stay was 8 days for open repairs and 3 days for endovascular repair. The risk adjusted survival for both was 98.1%. Our compliance for data entry on the NVR has been 100% since 2014. As a quaternary referral centre with a robust and active multidisciplinary team [MDT], and a referral base comprised of district vascular units as well as general practitioners, we see our role as leaders of practice as well as excellent practitioners. Thus, we read the NICE proposed guidelines for the care of aneurysms with some concern, as they fundamentally contradict what we believe to be standard of practice, and if adopted, will threaten the wellbeing of patients in the United Kingdom. In the main, we are concerned that the evidence included in the guidelines has been unnecessarily restrictive and does not reflect the values, achievements and the global clinically accepted standard of practice. Although we appreciate it is the mandate of NICE to review only what is considered 'gold level evidence', the quality of the randomized controlled trial data in the field of EVAR is poor, and the economic data is not	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate

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				in keeping with current practice. **We feel greater emphasis should be given to more modern data published in the peer reviewed literature, even if it falls outside of randomized controlled trials.**	
Royal College of Nursing	Draft guideline		192	We are also using Rectus Sheath Catheters to deliver the infusion of local anaesthetics for pain relief effectively. I wonder why this technique is not discussed.	Thank you for your comment. No evidence was identified relating to the use of rectus sheath catheters to deliver analgesia in people undergoing repair of unruptured or ruptured AAA. Furthermore, the committee were not aware of this technique routinely being used during AAA surgery. As a result, the committee did not deem it appropriate to recommend their use as standard practice. This does not mean that they cannot be used at the discretion of the treating clinicians.
The British Society of Interventional Radiology	Draft guideline		1.7.4/5	If contrast enhanced CT is contraindicated, and ultrasound (by implication) is unreliable, why is there no mention of the use of unenhanced CT (with or without ultrasound)? A combination of unenhanced CT (to measure sac size, assess the integrity of the framework of the device and position) with ultrasound to assess for sac perfusion would seem to be more appropriate (particularly as there is limited data to tell us one way or another).	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The

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					evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
EVAR trial post-operative	General	General	General	**"Predicting risk of rupture and rupture-preventing re-interventions utilising repeated measures on aneurysm**	Thank you for providing early sight of this paper, which has now been published:

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surveillance group				**sac diameter following endovascular abdominal aortic aneurysm repair" NIHR 11/36/46** Dear Project Manager for the AAA guidelines, On behalf of the EVAR trials post-operative surveillance group I enclose the manuscript under consideration of publication at the British Journal of Surgery fast track. This is funded by award 11/36/46 of the NIHR HTA intended for consideration of this new evidence in the post-consultation period. A technical document of clinical and HE modelling is being assembled. On 29 June, that manuscript was accepted for publication fast track by the British Journal of Surgery.	Grootes I, Barrett JK, Ulug P, Rohlffs F, Laukontaus SJ, Tulamo R, Venermo M, Greenhalgh RM, Sweeting MJ. Predicting risk of rupture and rupture-preventing reinterventions following endovascular abdominal aortic aneurysm repair. British Journal of Surgery. 2018 Sep;105(10):1294-304.
EVAR trial post-operative surveillance group				This is to confirm that, following the first (methodology) manuscript which we have made available to NICE for consideration during the consultation period, HE modelling is underway towards the second publication on clinical and HE implications. This is aimed for submission in July to a high impact journal for consideration of fast track publication. It is based on our recent findings of trajectories of growth based on EVAR 1 trial data validated on the Helsinki more recent series. This could impact on future optimal surveillance methodology. We find that the EVAR 1 trial follow- up protocol was sub- optimal in retrospect (world first RCT on EVAR versus open repair).	Thank you for providing early sight of the risk modelling paper. The HE modelling work that builds on it seems, on the face of it, well placed to fill an evidence gap that the committee identified as important. We will pass this information to our surveillance team to help inform subsequent updates of this guideline.

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				We remain prepared to send a technical document on this at the earliest moment but we regret that it is not ready by the deadline today. Yours, [This text was identified as confidential so has been removed.]	
The British Society of Interventional Radiology	Draft guideline		1.5.5	The comment above goes too for so called complex EVAR. All of these patients have an open surgical option. Up until now many of those have been regarded as high risk for surgery, but if the co-morbidity and anaesthetic reasons are removed, the cohort is very limited. That will have knock on effects on the skills to deliver those that are remaining indicated. At the moment NHSE recommends complex EVAR centres covering 2.5 million population, on the expectation that this will generate around 25 complex EVARs per year. The draft guidelines will mean that this will need to be revised to a very few centres.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate
Royal College of General Practitioners	Draft guideline	3	30	Whilst 1/3 of UK deaths from ruptured abdominal aortic aneurysm (AAA) are in women a paper in press for the Lancet is concerned about the estimated incremental cost effectiveness ratio in screening women and an over-diagnosis rate of 33%. The authors suggest an AAA screening programme for women, mimicking that in men, is unlikely to be cost-effective. They call for further research on the aortic diameter distribution in women and potential quality of life decrements associated with screening are needed to assess the full benefits and harms of modified options. http://hdl.handle.net/2381/42322	The committee were in agreement that their recommendation on identifying women with AAA relates to opportunistic case finding, as opposed to population-based screening. The distinction between the two is that with case finding, healthcare-seeking individuals are offered imaging rather than a screening programme actively inviting people who are at risk for imaging. The committee considered that opportunistic case finding could lead to downstream cost savings due to early identification of AAA in women, who are known to have an increased risk of rupture compared to men. With this in mind the committee agreed that the recommendation should not be changed. Our preliminary view of Sweeting et al.'s study (which has now published) is that it is not inconsistent with the committee's view of the evidence and recommendations. Although this

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					study cannot be seen as supporting population-level screening, it does demonstrate that identifying AAA in women is likely to lead to net health gains. Moreover, if an indiscriminate population-level approach yields net health gains at a cost of between £20–30,000/QALY, it is very likely that the opportunistic approach the committee recommends will be somewhat more cost effective (because it does not incur the costs of screening women who are relatively unlikely to have AAA, and focuses on those who are at highest risk).
Bedford Hospital NHS Trust	Draft guideline	4	54-57	The guidelines do not acknowledge a lower treatment threshold in women (5cm) despite acknowledging a higher risk of rupture elsewhere in the guidelines (page 4, line 69) and the fact that aneurysm in women rupture at a smaller diameter.	Thank you for your comment. Evidence review F provides a detailed account of the committee's discussions about thresholds for surgery. Evidence review C also highlights that women were more likely to experience aneurysm rupture than men, however it was also noted that there is currently no published evidence indicating that women with AAA should be treated differently to men with AAA. Upon review of the identified evidence it was noted that women were underrepresented in the included studies and no evidence of differences between genders were explored. Since there was no robust evidence to confirm the optimum threshold for considering surgery in women, the committee were reluctant to recommend a different threshold from the widely accepted 5.5 cm threshold used for men. The committee also discussed whether the size threshold may vary according to age but acknowledged that there was no available evidence indicating that the size and resultant risk of rupture was dependent on age.
Bedford Hospital NHS Trust	Draft guideline	5	77.78,79	AAA Screening Program recommends two ITI AP measurements one, with probe in transverse direction and one	Thank you for your comment. The guideline recommends that aneurysm sizes should be

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				in longitudinal direction. This has not been made clear in the guidelines.	determined by taking maximum anterior-posterior inner-to-inner aortic measurements using ultrasound, in accordance with the NHS AAA screening programme. This means that both transverse and longitudinal measurements should be recorded as specified by the screening programme.
The British Society of Interventional Radiology	Draft guideline	7	124	1.3.3 Scanning patients with USS every 2 years rather than every year represents a change of practice. There are a subset of aneurysms which progress more rapidly within that time frame and therefore could be at greater risk of rupture. (see ref1.5.1)	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Bedford Hospital NHS Trust	Draft guideline	7	126	Our current practice is a six monthly scan for an aneurysm 4 to 5cm and 3 monthly when it is more than 5cm in diameter.	Thank you for your comment. Evidence review D provides a detailed description of the

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					committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Calderdale and Huddersfield Foundation Trust	Draft guideline	7	127	The interval for screening moves from 2 years to 3 months. It makes more sense to have a graduated approach with surveillance over 3cm-4cm at 2 years. 4-4.5cm 1 year and 4.5-5.5cm 3 monthly.	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals

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					because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Bedford Hospital NHS Trust	Draft guideline	8	137	We use risk scoring systems to inform rather than dictate the decision making. Rationale for the use of various risk assessment tools must be left at the discretion of the clinicians.	Thank you for your comment. The committee had little confidence about the clinical utility of risk assessment tools because they could not see how using tools with c-statistics of around 0.70 would inform appropriate decisions about patient management and prognostic outcomes. The committee considered that use of risk assessment tools with insufficient discriminatory power could have potentially harmful effects on patient care. This is because such tools could result in the decision to operate on a patient who shouldn't be operated on, or vice versa. The committee discussed decision-making without the use of risk assessment tools. They noted that most of the clinical data used to derive risk assessment tools are commonly collected and are already available before surgery. They agreed that individual variables (as opposed to risk models) can be still useful for making judgments of an individual's risk of postoperative morbidity and mortality.

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Bedford Hospital NHS Trust	Draft guideline	9	167	We believe in cumulative effect of marginal gains; Remote Ischaemic Reperfusion is one such manoeuvre. It will be impossible to demonstrate its benefits in randomised controlled trial, but it does make theoretical sense. We believe that the fear of dysrhythmias is unfounded.	Thank you for your comment. The committee noted that the body of evidence on RIPC (identified in evidence review J) strongly indicated no benefit to postoperative outcomes, and some potential for harm. Meta-analysis of 2 RCTs revealed higher rates of arrythmia in patients who received RIPC during AAA repair compared with those who did not. Unlike beta-blockers, the committee felt that there was no particular circumstance where routine use of RIPC should be considered.
The British Society of Interventional Radiology	Draft guideline	9	172	1.5.1 It will be impossible to determine the growth of an aneurysm of more than 1cm / year in some cases and offer treatment if the frequency of assessment with USS is reduced to every two years (See ref 1.3.3)	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an

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					asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
Bedford Hospital NHS Trust	Draft guideline	9	176	Women are at a higher risk of rupture at a smaller size.	Thank you for your comment. Evidence review F provides a detailed account of the committee's discussions about thresholds for surgery. Evidence review C also highlights that women were more likely to experience aneurysm rupture than men, however it was also noted that there is currently no published evidence indicating that women with AAA should be treated differently to men with AAA. Upon review of the identified evidence it was noted that women were underrepresented in the included studies and no evidence of differences between genders were explored. Since there was no robust evidence to confirm the optimum threshold for considering surgery in women, the committee were reluctant to recommend a different threshold from the widely accepted 5.5 cm threshold used for men. The committee also discussed whether the size threshold may vary according to age but acknowledged that there was no available evidence indicating that the size and resultant risk of rupture was dependent on age.
Calderdale and Huddersfield Foundation Trust	Draft guideline	9	177	Contradicts recommendation for screening two yearly	Thank you for your comment. Evidence review D provides a detailed description of the committee's discussions about identified evidence relating to monitoring intervals. The identified health economic evidence demonstrated that a biennial imaging interval was a cost effective strategy for monitoring aneurysms between 3.0 cm and 4.4 cm in diameter (small aneurysms). This evidence was further supported by expert testimony from the NHS AAA screening programme indicating imaging intervals for small

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					aneurysms are likely to be extended from annual intervals because small aneurysms have a considerably lower risk of rupture than initially though. In light of your comment, coupled-with the fact that the screening programme have not specified when they will be changing their imaging intervals, the committee agreed that it would be more useful to recommend that imaging surveillance intervals are amended in line with those used by national screening programme, rather than specify specific intervals in the guideline. As a result, the recommendation has been changed to the following: "Offer surveillance with aortic ultrasound to people with an asymptomatic AAA in accordance with intervals used by the NHS AAA Screening programme"
The British Society of Interventional Radiology	Draft guideline	9	179	1.5.2 Mortality argument: - We accept there may be increased rates of re intervention for EVAR vs open repair and therefore an increased mortality beyond 10 years. However, EVAR has a lower mortality compared with surgery (1.7% EVAR vs 4.2%OSR :-EVAR 1). Accepting a higher mortality rate by not offering EVAR would be contrary to VASQIP guidance (3.5%mortality accepted per unit). Performing open repair only therefore, may lead to unacceptably high AAA related early mortality rates.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. The committee gave very careful consideration to the balance between the short-term advantages of EVAR and its long-term disadvantages.

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				In our unit, we looked at mortality for patients having an elective EVAR who were over 80 years old between 2009 and 2018. There were **173** cases with **2** deaths (**1.15% mortality**). This suggests that mortality rates are, in fact, lower even in this more co morbid group of patients from endovascular repair at 30days in hospital. We speculate that this difference in observed real world practice in the elderly co morbid patients compared with EVAR 1 trial data, may be due to the fact that earlier generation devices were used in these older trials and the subsequent increased expertise in performing EVAR. Whilst we recognise that the only randomised control data that is available are from the EVAR and DREAM trials we would question the relevance of this data in today's modern endovascular practice.	Thank you for giving us details of your experience; please see **Theme 3c**. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. There are, in fact, 4 RCTs included in our systematic review (OVER and ACE as well as EVAR-1 and DREAM).
				It may be helpful to include real world registry data in this analysis from the National vascular and Eurostar Registries. We acknowledge the limitations from registry data which include, voluntary submission and lack of long term outcomes.	For discussion of the use of NVR and other registries to estimate perioperative mortality, please see **Theme 3a** and **Theme 3b**.
				In our practice, confirmed by the data submitted to the NVR database, the mortality for elective open repair in the last 7 years is higher than elective EVAR (**OSR 5.7% vs EVAR 0.5%**). This is real world, honest data from a balanced open / endovascular large vascular network performing more than 100 elective aneurysm procedures per year. This is contrary to the published data.	Thank you for giving us details of your experience; please see **Theme 3c**.
				These draft guidelines, if implemented, would potentially increase the number of open repairs which would increase the	

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				short term AAA related mortality in patients with aneurysmal disease. GIRFT and NAAASP recommend detection to treatment targets of eight weeks for patients with aneurysmal disease. A sea change in practice of this magnitude, in preference to open repair, would have huge implications on the delivery of AAA services nationwide. With increased open surgery we foresee increased delays to treatment timelines, more cancellations due to the general lack of critical care capacity in the UK, increased length of hospital stay and an increased risk of rupture and death whilst waiting. There is also the issue of de skilling of surgical and Interventional Radiology teams committed to a balanced endovascular practice. Moral argument There would be a cohort of patients who are deemed not fit for open surgery who are known to have an AAA from the screening program or from in hospital surveillance. These patients, using the draft guidance as it currently stands, would be denied an elective EVAR and turned down for open surgery but then potentially present in an emergency situation as a rupture. We are then morally obliged offer them emergency EVAR which seems perverse as they have been declined this option in an elective setting. A proportion of these patients would die before ever reaching care and the mortality from emergency endovascular repair remains disproportionally higher than in an elective setting even in these more co morbid patients.	The committee agreed that it is of value to diagnose AAA, even in people for whom repair is not suitable. The guideline emphasises the importance of providing treatment for risk factors for rupture (smoking, hypertension) and for secondary prevention of cardiovascular disease. Obviously, steps such as these will provide benefit for the patient that would not have been possible if the AAA had remained undiagnosed. Additionally, in some cases, they may lessen the impact of comorbidities in a way that makes repair viable in future. The evidence from EVAR-2 suggests that people with medical comorbidities of sufficient seriousness to contraindicate OSR face a substantially greater force of mortality from those factors than they do from AAA rupture. In other words, most participants who were randomised to no intervention died with – rather than from – their AAA. In the context of a treatment with known short-term risks and costs, and no evidence of

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					extension of life expectancy, the committee agreed that the balance of benefits and harms favours conservative management. In the setting of ruptured AAA, there is obviously a different balance of benefits and harms associated with the decision between intervening or not. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made aresearch recommendation noting that such a study would be helpful.
				Economic argument Our economic review of the supplied data appears sound although somewhat confusing. The difference appears to be roughly the cost of the device with similar QUALY. It may be worth looking at whether the device cost could be reduced. We appreciate that re interventions were higher in the trial setting with EVAR and this undoubtedly increases the overall cost in the EVAR group. However, as before, these were older generation devices with greater device related complications.	NICE has no role in setting the price of medical devices. However, we do provide sensitivity analyses showing cost-effectiveness results at different graft prices in the HE report (see figure HE47, figure HE59, figure HE70, figure HE78, figure HE93 and figure HE94). In response to stakeholder comments such as this, the HE model was revised to take account of evidence on the reduced rate of reinterventions following EVAR in modern practice. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**.
				We also recognise that secondary re interventions are higher when devices are used outside the manufacturer's instructions for use (IFU) and as such, this cavalier practice to endovascular repair for AAA disease should be discouraged	The guidance contains a recommendation explicitly discouraging the use of off-IFU EVAR (although we believe there is enough uncertainty in this area that it would be reasonable to pursue randomised research in the area):

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				and it is regrettable that NICE have not mentioned this a draft recommendation. There is no long term data on re interventions in patients undergoing open repair compared to EVAR and as such, long term cost comparisons cannot be made.	*Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.* There is high-quality randomised evidence and additional casemix-adjusted observational evidence on re-interventions in patients undergoing OSR compared with EVAR. These data informed the committee's considerations and were used as inputs to the HE model.
The British Society of Interventional Radiology	Draft guideline	9	181	1.5.3 There are a subset of patients that are not suitable for open surgical repair for reasons other than co morbidity that may be suitable for EVAR e.g. patients with hostile abdomens, radiotherapy etc. decreasing the number of overall EVARs would reduce expertise and make treating these patients more challenging with similar arguments as mentioned above .	On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual abdominal copathologies or other considerations provde a relative contraindication to OSR See **Theme 14**.
Bedford Hospital NHS Trust	Draft guideline	9	181	This guideline is ethically unacceptable and against several articles of NHS constitution on patient choice, patient involvement and shared decision making.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 15 for NICE's view on the importance of joint decision making between the clinician and individual. .
Bedford Hospital NHS Trust	Draft guideline	10	183	Between the cohort of patients at very low risk and very high risk for open surgery, there is a larger group of patients with a "higher" risk for open repair but considerably low risk for EVAR	It seems likely that the people to whom you are referring would not have been considered clearly contraindicated for OSR when the trials recruited. Therefore, their outcomes are

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				(endovascular aneurysm repair). It will be ethically and morally unacceptable to not offer them lifesaving treatment.	included in the cohorts that have been used to assess the relative benefits and harms of EVAR and OSR. This evidence shows that OSR provides better net outcomes for the average person with AAA who was considered eligible for randomisation. Clearly, it is possible that a different pattern of benefits, risks and costs might obtain in subgroups of patients within this overall cohort. However, the committee looked carefully for such subgroups, and concluded that none could be identified on the basis of current best evidence. See **Theme 12**.
Bedford Hospital NHS Trust	Draft guideline	10	183	We are concerned that the committee might have compared incorrect groups. We believe that instead of comparing EVAR versus OR the committee should have considered the outcomes of EVAR versus "no treatment" in this middle group of patients.	This comment suggests that there is a group of patients that were considered suitable for randomisation to OSR who would not now be considered for that treatment, despite the fact that a careful analysis of those trials shows that long-term results are superior for people receiving OSR. It is also worth noting that any subgroup effects the trials did suggest tended to indicate that EVAR has most benefit in younger and/or fitter people (see Brown et al., 2007; Lederle et al., 2012). These results challenge the orthodoxy that EVAR is most vital for people with higher baseline risks.
Bedford Hospital NHS Trust	Draft guideline	10	183	We believe that EVAR is now an established and accepted form of treatment; its clinical value having been established with several multi-centre randomised controlled trials with low perioperative risks. The current risk–benefit profile for EVAR is likely to be even better due to improvements in devices, expertise and use of modern imaging equipment and safer contrast agents (CO2). In view of this, it is ethically and morally unacceptable not to offer such treatment to patients at risk of dying from ruptured aneurysm.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. Please see Theme 3 for secular trends in the evidence and the review of observational evidence (K2) that was carried out after consultation which includes more recent evidence.

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					However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
Calderdale and Huddersfield Foundation Trust	Draft guideline	10	183, 189	There are patients with a reasonable life expectancy and large AAA (8cm) that are a high rupture risk where the benefit of EVAR would outweigh the risk of rupture. There are technical reasons behind not doing open repairs on patients who have, for example, hostile abdomen, chronic pancreatitis, or a large hernia.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. However, the committee recognised that there are challenges to the generalisability of EVAR-2 to contemporary practice, in large measure because of its deliberately non-prescriptive eligibility criteria. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful. On discussing stakeholder comments, NICE concluded that it would be helpful to make an explicit recommendation that it is reasonable to consider EVAR in circumstances where unusual

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					abdominal copathologies or other considerations provde a relative contraindication to OSR. See **Theme 14**.
				There needs to be more guidance on medical and anaesthetic fitness for intervention.	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice.
				Current low mortality for AAA repair in NVR, if adopt a policy for open operations for all repairs, would increase the mortality rate. The AAA QIP data has shown a reduction of mortality from 7.9% to less than 2% in recent years, a large part of this reduction is due to the more wide scale use of EVAR.	For discussion of the Vascular Society's AAA Quality Improvement Programme, please see **Theme 2a**.
				An increase in open repairs would have a direct impact on critical care bed requirements as EVARs are currently sent to the wards	For discussion of the resource implications of in-hospital care with EVAR and OSR, please see **Theme 6a**.

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				If units are judged by outcomes then a large percentage of the patients would be denied beneficial treatment due to the implicit need to reach favourable target driven outcomes. It is felt that this recommendation is based on lack of evidence of the benefit of EVAR but our clinical experience would suggest that EVAR is a useful method of repairing AAA in appropriately selected patients. The recommendation removes the right of patient choice. We acknowledge that we may have pushed the boundaries in the use of EVARS but feel that the recommendation to exclude them all together in the elective setting seems extreme. We are concerned about the opposing views re the use of EVARS in AAA treatment between these guidelines and the recommendations/messages emanating from scientific meetings, which brings into question the independence/value of such meetings. The recommendations has placed to much emphasis on cost/ benefit of EVAR and to little on clinical/QOL benefit to the patient.	The committee acknowledged that, at least for infrarenal AAAs, EVAR is undoubtedly associated with a lower rate of perioperative mortality than OSR. However, they were confident that OSR can be provided with a low absolute level of risk. For details, please see **Theme 2**. The committee considered carefully whether subgroups are likely to exist with combinations of risk factors – age, sex, AAA diameter – that represent a different balance of benefits, harms and costs from the average member of the cohort. They were unable to find plausible evidence that any such subgroups can be reliably identified – see **Theme 12**. It is NICE's statutory responsibility to consider the balance between the benefits and costs of competing approaches to healthcare. The evidence shows that HRQoL is adversely affected by OSR, compared with EVAR, only in the short term. Two RCTs

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					found that there is a significant advantage for EVAR at 3 weeks postoperatively (DREAM) and 4 weeks postoperatively (EVAR-1). However, both trials found that the benefit had disappeared by the 3rd postoperative month. One of these trials (DREAM) showed that, thereafter, OSR is associated with significant **gain** in HRQoL, compared with EVAR, in the medium term; however, this finding was not replicated by EVAR-1 and OVER, both of which found there to be no difference in HRQoL beyond the short term. Therefore, the worst that can be said for OSR is that is is neutral for HRQoL in the medium term.
Bedford Hospital NHS Trust	Draft guideline	10	186	We think it is reasonable argument provided a randomised controlled trial could be set up and ethically justified. Until then it will be unacceptable to decline lifesaving treatment to these individuals.	In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
The British Society of Interventional Radiology	Draft guideline	10	196	1.6.1 This guidance suggests offering EVAR for ruptured aneurysms as opposed to open surgery. The implication would be that the numbers of elective EVARS reduce and expertise in performing EVAR for rupture would be lower and therefore likely to increase the mortality from ruptured aneurysms. From a governance and training perspective, we struggle to understand how NICE could justify performing a procedure only in an emergency setting and not in an elective situation. There is a fundamental flaw in the argument that ruptured aneurysms should be treated with EVAR in an emergency setting. The IMPROVE trial failed to demonstrate superiority of EVAR vs OR in ruptured AAA, nor was the trial powered for the subsequent subgroup analyses (women and local anaesthetic).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. IMPROVE shows meaningful benefits for people randomised to an EVAR-if-possible strategy in short-term HRQoL and

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					midterm survival. These are both important drivers of overall patient benefit.
Bedford Hospital NHS Trust	Draft guideline	10	196	If these guidelines were imposed, some patients will have open elective repair of their aneurysms; majority will have not treatment at all as we are not to offer EVAR in elective settings. We are concerned that expertise and infrastructure to offer an endovascular repair in an emergent situation will simply not exist in most vascular centres.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate.
Calderdale and Huddersfield Foundation Trust	Draft guideline	10	196	This point contradicts recommendations not to offer EVAR to any patients in the elective setting. Some of the vascular surgeons have a view that patients turned down for elective AAA intervention should not be offered intervention in the context of ruptures. There may be a subset of patients where this view may be challenged in the acute setting where EVAR may be offered	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. In economic analyses, we found that offering emergency EVAR to people for whom OSR has previously been considered unsuitable is likely to be associated with a reasonable balance of benefits and costs (although it may be less easy to justify in older people, as they are less likely to survive the surgery and less likely to achieve meaningful subsequent llife expectancy). See HE.9.4.
The British Society of Interventional Radiology	Draft guideline	11	208	1.6.4 This is not a clear evidence based recommendation	Thank you for your comment. Evidence review L provides a detailed description of the committee's discussions about anaesthesia and analgesia during repair of ruptured or unruptured AAA. Since no evidence was identified for anaesthesia and/or analgesia in

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					people undergoing any type of repair of ruptured AAA, the committee agreed that it was appropriate to draft consensus recommendations based on their collective skills, knowledge and experiences (discussed in the benefits and harms section of the evidence review). To reflect their consensus recommendations, the committee agreed it was only appropriate to make this recommendation at the 'consider' level to ensure sufficient flexibility in decision making.
The British Society of Interventional Radiology	Draft guideline	11	219	1.7.2 To our knowledge there is no validated risk assessment tool to detect complications following EVAR and from this draft guidance neither are these recommended for open repair. .	Thank you for your comment. Studies identified in evidence review H indicated that risk assessment tools had insufficient discriminatory power at predicting postoperative outcomes. For this reason recommendations were drafted to highlight that the risk assessment tools considered in the review should not be used decision making for AAA repair; be it EVAR or open repair.
Bedford Hospital NHS Trust	Draft guideline	11	221	Use of Duplex Ultra Sound scan and plain X-rays as post-EVAR surveillance modalities has evolved over time and with experience of several hundred vascular and endovascular specialists throughout the world. We believe that simple non-invasive modalities provide enough information to guide the use of selective contrast enhanced CT scan when required.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging,

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					with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.

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The British Society of Interventional Radiology	Draft guideline	12		There appears to be a difficulty with the definition of a complex EVAR. There are devices and device combinations which have an IFU and CE mark, such as short angulated necks with the use of endoanchors, and chimney/parallel grafts. Are those with CE mark acceptable? Similarly should an off the shelf fEVAR gain CE mark, would this still be recommended against (I would presume so given the assessment of the present data)?	The committee acknowledged the difficulty you raise, and revised its definition of complex EVAR The committee agreed that 'complex' AAA is a heterogeneous category and that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. See **Theme 10** for details. An exploratory analysis from the HE model focusing on fEVAR alone was deemed possible as part of post-consultation discussion. This analysis concluded that fEVAR has a very low probability of providing reasonable value for money, compared with OSR. See **Theme 10a** for details.
Royal College of General Practitioners	Draft guideline	16 Research		These guidelines suggested additional areas for research to include https://doi.org/10.1016/j.jvs.2017.10.044. . What is the most cost-effective and clinically effective surveillance protocol for the patient with a small aneurysm? •Should the aortic size index replace aortic diameter as a determinant for recommending aneurysm repair? •Do female patients benefit from a refined metric, such as the aortic size index, or size threshold for recommending repair? •Which quality and volume metrics best identify centres that should engage in either EVAR or OSR of an aortic aneurysm? •Does use of a perioperative mortality risk scoring scheme provide benefit in patient and family communication and mutual decision-making? •Does a perioperative mortality risk scoring scheme provide utility to surgeons, patients, and families in guiding recommendations for repair in the high-risk patient?	Thank you for your comment. The committee were aware of a number of different areas for research proposed in other guidelines and noted that there was some overlap with the research recommendations made in the NICE AAA guideline. The committee agreed that, where possible, their research recommendations should remain independent of those specified in other guidelines as duplicating research recommendations would preclude a thriving research environment in various areas that would improve the diagnosis and management of AAA.

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				•Can perioperative mortality risk scoring schemes be further refined to enhance their predictive ability? •Does a frailty assessment enhance our ability to identify those patients who will not benefit from aneurysm repair? •Can a single risk-benefit scoring scheme be developed that incorporates risk of repair, risk of aneurysm rupture, and anticipated life expectancy? •Would a risk-benefit scoring scheme that incorporates risk of repair, risk of aneurysm rupture, and anticipated life expectancy assist in mutual decision-making between the surgeon, the patient, and the patient's family? •Will a defined system of care and associated time benchmark from first medical contact to intervention improve outcomes for the patient with a ruptured aneurysm? •Which factors are most important in optimizing patient outcomes within a system of care for the treatment of a ruptured aneurysm? •Is prophylaxis for deep venous thrombosis needed for the patient undergoing EVAR? Does the patient undergoing OSR and at low or moderate risk for deep venous thrombosis benefit from heparin prophylaxis? •What is the optimal haemoglobin level that necessitates transfusion in the stable postoperative patient without ongoing blood loss? •What is the optimal interval, imaging modality, and duration for postoperative surveillance after aneurysm repair? •What is the most cost-effective and clinically effective surveillance protocol for the patient after EVAR?	
The British Society of Interventional Radiology	Draft guideline	26	623	The argument that is made against EVAR relates to the worse long term survival. This seems to be predominantly from the EVARI and EVARII Trials. These were inevitably performed many years ago and the devices in contemporary use have	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been

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				been significantly developed, with this knowledge, the intention being to counter those problems. It seems likely (and it is considered to be so around the rest of the world)that these longer term problems are likely to be less and continue in that way). The proposed guidance will mean that very few patients will be offered EVAR for unruptured AAA in the UK, which will be out of step with the remainder of the world. It is possible that this will turn out to be appropriate, but it seems unlikely given the advances in technology and materials.	amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. The finding that EVAR is associated with excess post-perioperative mortality is strongly supported by the review of casemix-adjusted observational evidence that we have conducted in response to stakeholders' criticism that the consultation draft placed too much weight on RCTs alone – see **Theme 9**. In fact, this evidence suggests that the trials may represent an underestimate of the true effect in real-world practice.
Bedford Hospital NHS Trust	Draft guideline	26	626	This argument relies on historical data on older devices and relative inexperience of operators. It also compares reported data on endovascular procedures against presumptions on open repair complications as they mostly go unreported.	For discussion of the argument that RCTs of EVAR -v- OSR in elective infrarenal AAA reflect an obsolescent standard of care, please see **Theme 1**. It is true that the EVAR-1 trial did not initially collect data on hernia. However, the investigators were mindful of this criticism, and retrospectively obtained data on hernia interventions required following EVAR and OSR for all trial participants. These were reported in the long-term follow-up reports (Patel et al., 2016; Patel et al., 2018); these rates are incorporated in the HE model that was developed for this guideline. We also incorporated other laparotomy-related complications recorded in US registry data (Schermerhorn et al., 2015) that had not been retrospectively included in the

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					EVAR-1 reintervention data. Therefore, we are confident that the HE model developed to support decision-making for this guideline does not underestimate the late complications of OSR.
Bedford Hospital NHS Trust	Draft guideline	26	629	This argument is an unfortunate interpretation of data and ignores the fact that this cohort has more comorbidities and in general older than the open repair group. Their long term survival is inevitably poorer compared to healthier individuals regardless of aneurysm or EVAR.	All evidence considered for this guideline adjusted for the selection biases you mention (either by randomisation or by a statistical method to reduce confounding in observational data).
Bedford Hospital NHS Trust	Draft guideline	26	629-639	We are concerned that this conclusion relies on two unproven arguments (no long term benefits and poor cost effectiveness) and it is difficult to be confident that a different committee with a different skill mix would not have come to a different conclusion. After all it is only the plausibility that we are considering rather than evidence. This argument will never be put forward by a clinician for a cancer treatment for example.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. We do not agree that similar judgements do not apply in cancer treatment or elsewhere in NICE's decision-making.
Bedford Hospital NHS Trust	Draft guideline	26	629-639	We are concerned that guideline relies on historical cost analysis data. The practice has changed since then for example more and more centres are adopting single team operating (endovascular surgeons) rather than relying on a team of vascular surgeons and interventional radiologists, length of stay has reduced to 24 hours rather than 9 days in the studies considered by the committee and the post EVAR surveillance is infrequent and by cheaper modalities. On the other hand we believe that cost of open repair has been underestimated by not taking into account that more and more patients are being operated by two consultants and length of stay has remained relatively unchanged.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. On considering stakeholder comments such as this one, the committee agreed – on a balance of considerations – that we should revise the resource-use inputs to our economic analyses reflect contemporary evidence, even though they

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					had misgivings about the presence of clear selection biases in those data. See **Theme 6** for details. We are unaware of any recommendation that dual consultant operating is required for AAA repair. We do not believe it was used in the evidence-base that informed the committee's recommendations. Presumably, if this practice is being adopted, it is expected to lead to patient benefits that justify the additional resource, though we have not seen any evidence on this topic. We do not agree that length of stay has 'remained relatively unchanged' for people undergoing OSR. The difference between resource-use reported in EVAR-1 and the 2017 NVR is essentially identical for EVAR and OSR.
City Hospitals Sunderland NHS Foundation Trust (CHS)	Draft guideline	27	632 - 639	This recommendation is nonsensical. There is no "average patient" and to make a recommendation based on this, disregards all the patients within the wide interval of risk due to their medical fitness level and the risk attached to their aneurysm size, is not acceptable practice. Since the authors have never defined the term "costs" stating "large" costs is meaningless.	The average patient has average fitness and an AAA of average size, and their outcomes are defined by the mean outcomes of the cohort. Clearly, it is possible that a different pattern of benefits, risks and costs might obtain in subgroups of patients within this overall cohort. However, the committee looked carefully for such subgroups, and concluded that none could be identified on the basis of current best evidence. See **Theme 12**.
Bedford Hospital NHS Trust	Draft guideline	28	683-684	We are concerned that committee are comparing unequal groups (OR versus EVAR); harm will not be minimised in patients who receive "no treatment" as they will not be likely to survive long term. Comparison should have been between "EVAR" versus "no treatment" in a cohort with relatively higher risk for open repair but low risk for EVAR.	This comment suggests that there is a group of patients that were considered suitable for randomisation to OSR who would not now be considered for that treatment, despite the fact that a careful analysis of those trials shows that long-term results are superior for people receiving OSR. It is also worth noting that any subgroup effects the trials did suggest tended to indicate that EVAR has most benefit in younger and/or fitter

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					people (see Brown et al., 2007; Lederle et al., 2012). These results challenge the orthodoxy that EVAR is most vital for people with higher baseline risks.
The British Society of Interventional Radiology	Draft guideline	33	810	The follow up recommendations are unclear. Many centres use Ultrasound or ultrasound and plain radiography to monitor the integrity of the graft. Following an initial CTscan at 30 days, I would suggest that CT should be utilised if there is concern on ultrasound+/- plain film.I in my experience, the development of type 1 and type 3 endoleaks is extremely rare. The current guideline will have a significant negative impact on radiology departments and patients as well as increasing the radiation burden to patients. The cost of surveillance will increase and the patient will be exposed the potential risks of contrast injection.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced

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					ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		54-55	Slow growing aneurysm rupture rate is approx. 3% - local belief is that these patients need to be seen within 4 weeks. 2 weeks is too short a time frame for logistical reasons.	Thank you for your comment. The committee drafted recommendations to reflect current expectations in the NHS AAA screening programme. In the screening programme, aneurysms 5.5 cm or larger are referred to be seen by a vascular specialist within 2 weeks of diagnosis.
Royal Bournemouth and Christchurch Hospitals NHS	Draft guideline		56-57	These patients are currently not seen – they are sent postal information and placed on a surveillance pathway. They are given an option for an appointment but most patients do not wish to come to hospital and will liaise with their GP. This pathway works well. Our experience is that these patients do	Thank you for your comment. The committee drafted recommendations to reflect current expectations in the NHS AAA screening programme. In the screening programme, aneurysms 5.5 cm or larger are referred to be seen by a vascular specialist within 2 weeks of

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Foundation Trust				not necessarily need to be seen but do need adequate information.	diagnosis. Aneurysms less than 5.5 cm in diameter are not referred to a regional vascular service but are seen by a vascular nurse in the screening programme (who is also member of a regional vascular service) to obtain some clinical input/advice. This clinical input is usually obtained within 12 weeks of diagnosis. The committee were mindful that women with smaller aneurysms are not seen by the screening programme or referred to the regional vascular service. Therefore, there is some need for clinical input. This logic underpinned their recommendations.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		81-82	CE arterial phase CT needs to include the chest.	Thank you for your comment. The committee agreed that clinicians performing CT scans would take appropriate images of the operating field and adjacent areas when planning for surgery. As a result, they did not think that it was necessary to add this wording to the recommendation.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		126	Current practice at RBCH is 6 monthly and this is believed to be sufficient and have a local database of patient follow up to prove it.	Thank you for your comment. The committee initially specified a 3-monthly surveillance interval for AAAs larger than 4.5 cm in diameter to comply with surveillance intervals specified by the NHS AAA screening programme. Upon further discussion, the committee were mindful that surveillance intervals may change in the future. As a result the recommendation (renumbered from 1.3.3 to 1.2.3) was changed to the following: "1.2.3 Offer surveillance with aortic ultrasound to people with an asymptomatic AAA. Base the frequency of surveillance on the intervals used by the NHS AAA screening programme"

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Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		179-185	EVAR 1 was designed to evaluate whether EVAR was a suitable alternative to open surgery. EVAR 2 was designed to evaluate whether EVAR was suitable for patients with aneurysms who were not fit for open surgery and each study was powered for that purpose only and not designed to assess the health economics of each EVAR procedure. Most people would view that modern day practice of AAA care in particular EVAR interventions is very different from that during the time of these studies – examples would include timing and indications of secondary intervention for EVAR and follow up strategies.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. The detailed collection of economic data was a key part of the EVAR trials' design. For specific comments on the statistical power of the elective RCTs, please see **Theme 9b**. The committee accepted that more effort could have been made to explore reintervention rates that are relevant to modern-day practice. They agreed that this is especially pertinent because – unlike the purported evolution of perioperative and long-term survival over time – reintervention rates are not merely a function of any developments of operative technique and technology, but also reflect evolving attitudes to which complications it is necessary to address. Therefore, the committee advised that the HE model should be revised to address this issue. However, these modifications did not have a substantive impact on model outputs. Full details are provided in **Theme 7**. The follow-up regimen mandated in the RCTs was relatively intensive – the committee agreed that current NHS practice often relies on less frequent use of less sensitive tests (and other stakeholders have supported this view in criticising our recommendation of CT-based follow-up). Therefore, the committee concluded that RCT results reflect an optimistic

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					view of rates of late complication-related mortality and morbidity associated with EVAR – a conculsion that is apparently supported by observational data (see **Theme 11)**.
				It is felt that further consideration would be useful in relation to clinical selection criteria for AAA intervention for the functionally more viable aging population, who may not get any additional prophylactic benefit for their elective AAA repair (i.e. there is a feeling that because we can treat aneurysms, we may be treating them in this older population which may not infer any additional prophylactic/longevity benefit).	The committee agreed that, in the absence of risk models with adequate predictive validity (see Evidence review H), the decision as to the suitability of OSR or EVAR for any individual has to be judged by vascular MDTs in the light of their comorbidities. The committee noted that the judgements involved in this kind of decision-making are a critical part of a vascular MDT's skill-set, and analogous decisions are made in current practice, albeit at different implied thresholds of fitness (e.g. whether to offer any repair, or whether to offer OSR in preference to EVAR). However, on discussing stakeholder feedback on this issue, the committee agreed that, while the EVAR-2 RCT has a fair degree of internal validity, its deliberately non-prescriptive eligibility criteria can make it challenging to apply to current practice. Therefore, the committee agreed that it would be valuable to generate new high-quality research in this area. They made a research recommendation noting that such a study would be helpful.
				We would also be the only modern health care service in the world who would not be offering EVAR as a treatment option in this setting.	

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				The costings again reflect practices that are now altered and are not aligned to modern day practice (e.g. ultrasound follow up/day case EVAR). Would NVR outcome data not be more useful to assess clinical outcomes for both techniques? We have concerns that if only considering EVAR in a rupture setting then the teams will be deskilled and will not maintain competency unless they are doing these regularly in the elective setting.	On considering stakeholder comments such as this one, the committee agreed – on a balance of considerations – that we should revise the resource-use inputs to our economic analyses reflect contemporary evidence, even though they had misgivings about the presence of clear selection biases in those data. See **Theme 6** for details. The follow-up regimen mandated in the RCTs was relatively intensive – the committee agreed that current NHS practice often relies on less frequent use of less sensitive tests (and other stakeholders have supported this view in criticising our recommendation of CT-based follow-up). Therefore, the committee concluded that RCT results reflect an optimistic view of rates of late complication-related mortality and morbidity associated with EVAR – a conculsion that is apparently supported by observational data (see **Theme 11)**. The committee reached the firm conclusion that it would not be appropriate to rely on unadjusted NVR data to support decision-making – see **Theme 3a**.
Royal Bournemouth and Christchurch Hospitals NHS	Draft guideline		195-202	These are reasonable statements but are dependent upon individual units IR capacity/out of hours cover (this may be variable in different units).	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact

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Foundation Trust					section in the guideline for information on implementation issues.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		203	Unstable patients who have complex AAA should not be considered for any intervention. However, stable contained ruptures with complexity should be considered for transfer to a quaternary complex aneurysm centre for treatment.	It is not clear on what basis you make this statement. Clearly, if there is insufficient experience in a given unit to attempt a repair, then the possibility of transfer should always be considered.
Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust	Draft guideline		221-222	The use of ultrasound and contrast ultrasound, in addition to plain film radiography as a surveillance tool will make the use of CT angiography more selective and reduce radiation exposure in the longer term, as is the practice within our unit.	Thank you for your comment. Upon consideration of your comments, along with other similar comments received, the committee has changed the recommendations as follows: 1.7.3 Consider contrast-enhanced CT angiography or colour duplex ultrasound for assessing sac size and limb kinking. 1.7.4 Use contrast-enhanced CT angiography if an endoleak is suspected. If contrast-enhanced CT angiography is contraindicated, use contrast-enhanced ultrasound. 1.7.5 Do not exclude endoleaks based on a negative colour duplex ultrasound alone, in people who have had EVAR. The committee recognised that, in practice, identifying complications after EVAR usually involves sequential imaging, with ultrasound frequently used as the first-line test and other imaging modalities used to detect specific complications. The evidence demonstrated that colour duplex ultrasound was highly accurate at identifying changes in sac size when

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					compared with contrast-enhanced CT angiography. Increases in sac size are often believed to indicate an endoleak even if no leak can be seen on the ultrasound. There was little evidence on graft kinking, but the committee agreed based on their experience that colour duplex ultrasound and CT angiography were equally as effective at detecting this type of complication. The evidence reviewed demonstrated that contrast-enhanced ultrasound was the only imaging technique that had acceptable accuracy for directly identifying endoleaks when compared with contrast-enhanced CT angiography. Importantly, other imaging techniques had unacceptably high rates of false-negative results. In particular, colour duplex ultrasound is highly accurate at identifying changes in sac size, but has suboptimal sensitivity for directly detecting type I and III endoleaks. For this reason, the committee agreed that in situations where the definitive exclusion of endoleak is important, either contrast enhanced CT angiography or contrast-enhanced ultrasound should be used. As CT angiography is no longer being recommended as the first-line imaging modality for identifying complications after EVAR, the committee believes that previous concerns about costs and exposure to ionising radiation have now been addressed/minimised. Please refer to evidence review W for further details.
Royal Bournemouth and Christchurch Hospitals	Draft guideline	General	General	Other point to consider include: Moving a standard of care from EVAR to open in the elective setting will require an increase in ITU beds that are currently not required.	Thank you for your comment. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice

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NHS Foundation Trust				Decision of mortality of open versus EVAR at 15 years in the EVAR1 accounts for the remaining just over 100 patients. Therefore this is grossly underpowered as a study and therefore any conclusions are misleading. Also as so many are dead from all cause mortality, have any of the AAA repairs done their job? EVAR1 was only powered for mortality up to 3 years – again therefore this cannot be used as supporting evidence to guide recommendations.	whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. The committee's conclusions on the long-term risks associated with EVAR were not solely based on EVAR-1; rather they reflect a range of randomised and observational data. It was the committee's confident interpretation of this evidence that EVAR is associated with unignorable excess mortality in the long term – see **Theme 9**. For specific comments on the statistical power of the elective RCTs to identify differences in long-term survival, please see **Theme 9b**. It is in the nature of long-term survival effects that they become most evident in the proportion of the cohort that lives the longest.
Health Education England	Draft guideline	General	General	1. Health Education England (HEE) exists to support the delivery of excellent healthcare and health improvement to the patients and public of England. We do this by ensuring that the present and future workforce has the right numbers, skills, values and behaviours, at the right time and in the right place. We welcome the opportunity to respond to the National Institute for Health and Care Excellence's (NICE) consultation. While we have no remit to comment on the clinical management changes proposed to the management of AAA in the UK, we are aware that the Vascular Surgery community has concerns about the proposals and they will be responding separately. 2. HEE has a responsibility to ensure that the NHS has a current and future workforce which is both fit for the future and	Thank you for setting out the context of your comments. In light of stakeholders' feedback, NICE has reflected on the clinical evidence and appropriateness and implementability of the recommendations related to aneurysm repair. The recommendations have been amended to reflect the need for a rebalancing of practice whilst supporting individualised care around which interventions are appropriate. See rationale and impact section in the guideline for information on implementation issues. We endorse this comment.

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				sufficiently flexible to accommodate major changes in clinical practice. These proposals suggest that the evidence base for EVAR is insufficient to justify routine use in elective aneurysm repair but that there is a role in the management of ruptured AAA. Two major groups of medical professionals are directly involved in the direct management of AAA - Vascular Surgeons (VS) and Interventional Radiologists (IR) but recognition should be given to the other members of the clinical workforce who are also involved (critical care clinicians, nurses and therapists). 3. This response only focuses on the medical workforce whose training might be directly impacted by these proposals - bearing in mind that the needs of training must be secondary to implementation of best care for patients. We will need to work with their educator community to find a way to support training which will enable changes to management which is in the best interest of patients. 4. An immediate concern is that any reduction in elective EVAR usage will reduce opportunities for trainees in VS and IR to gain experience for the deployment of EVAR in the acute setting. This could potentially mean fewer clinicians with the necessary EVAR skills being trained in the future as well as more patients requiring conventional open repair (with a subsequent impact on the critical care workforce). However, a successful screening and public health based approach might mitigate this with fewer patients requiring AAA rupture management in future years. It should be borne in mind though that this might mean a smaller specialist workforce with the necessary expertise and with potentially fewer centres of expertise to manage these patients. Consideration should also	Noted

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				be given to the potential role of novel surgical interventions such as robotics in the management of these cases - which too will impact on education and training requirements. 5. HEE will continue to work with colleagues in VS and IR should NICE recommendations significantly change practice - with education and training adapting to meet best practice for patients.	Thank you for this commitment. We hope that it goes some way to allaying the anxieties some other stakeholders have expressed.

Responses to common themes

Arising in stakeholder comments regarding the use of endovascular and opens surgical repair for unruptured AAA

Contents

Theme 1. Alleged obsolescence of randomised data

The most common theme of stakeholders' objections to the draft guidance on which consultation comments were sought is that the analyses that informed the committee's decision-making placed too much emphasis on randomised trials that, because they began recruitment up to 20 years ago, reflect a historical standard of care.

In the first instance, we respond to this contention with a robust defence of NICE's stated position that RCTs invariably provide the most reliable estimate of the benefits and harms of competing courses of action:

> *The Institute has a preference for RCTs directly comparing the intervention with 1 or more relevant comparators and these should be presented in the reference-case analysis if available.*
>
> (Guide to the methods of technology appraisal, 2013, ¶5.2.1, as referred to in Developing NICE guidelines, 2018, ¶7.3)

We need not rehearse, here, the reasons for which, all other things being equal, randomised evidence is most likely to provide an unbiased estimate of treatment effect.

Nevertheless, the committee were sensitive to stakeholders' assertion that all other things are not equal, in this case – that, while the results of OSR are unlikely to have improved over this period, EVAR may have done: operators have mastered techniques they were still learning when the trials took place, and devices have become ever-more reliable over the same time.

Therefore, in response to stakeholders' suggestions that it may not be appropriate to rely on randomised evidence alone to estimate the short- and long-term relative effects of EVAR and OSR, we conducted a new review of casemix-adjusted comparative observational studies presenting results for both techniques (See Evidence review K2). We considered studies that used any of the methods of adjustment enumerated in NICE DSU Technical Support Document 17 (Faria et al., 2015). In addition, although simple multivariable regression is generally considered insufficient to isolate the independent effect of treatment in the presence of selection bias, we identified studies that used such techniques and included them in stratified analyses.

The committee agreed that the results of this review substantiated the conclusions they had drawn from randomised evidence; if anything, it appears that the trials somewhat overestimate the benefits of EVAR. Details are provided in **Theme 2** (perioperative mortality for infrarenal AAA), **Theme 4b** (perioperative mortality for complex AAA), **Theme 8** (reintervention rates) and **Theme 9** (long-term survival).

Theme 2. Perioperative mortality

Multiple stakeholders highlight the fact that EVAR is associated with lower perioperative mortality than OSR as prima facie evidence that it is imperative that people with AAA have access to EVAR.

The committee were fully aware of the perioperative mortality risks associated with EVAR and OSR: it is inarguable that the latter has significantly greater odds of death, probably around a threefold increase (see **Theme 3**).

However, the committee felt certain that, in ways such as those detailed below (see also Theme 3b), it should be possible to optimise systems so that OSR, as well as EVAR, is associated with a low absolute risk of mortality. They firmly disagreed with stakeholders who suggest that returning to an OSR-led approach to AAA repair will inevitably lead to perioperative mortality levels that were seen before EVAR became the predominant mode of repair.

The 2008 Vascunet audit is cited by many to draw attention to historically high perioperative mortality rates, with the associated worry that we will see similarly disappointing results if the past decade's trend of increasing reliance on EVAR is reversed. The committee did not share this view. They noted that the major finding of the Vascunet audit was that the UK's mortality rate for OSR was significantly higher than that observed elsewhere. However, this was at a time when all participating countries used OSR for the majority of intact AAAs. Therefore, it is difficult to argue that a shift to a more EVAR-based strategy has been responsible for minimising this problem – only an improvement in OSR outcomes would do that. A reduction in OSR perioperative mortality is observed in successive NVRs (even though, in the view of the committee, there has been a trend over time for OSR to be reserved for increasingly high-risk anatomy).

In this respect, the committee noted the impact of the Vascular Society's AAA Quality Improvement Programme, the provisions of which raised standards in EVAR and OSR alike (see **Theme 2a**). The introduction of the National AAA Screening Programme, starting in 2008, has also led to many AAAs being diagnosed at a smaller diameter and at a younger age than would be the case if they had been left to present symptomatically or incidentally; this will also have contributed to lower perioperative risk for both procedures. The committee also argued that many general improvements in patient care have had beneficial impacts for the perioperative survival of people undergoing both EVAR and OSR. Factors such as improvements in imaging technology, better cardiovascular risk management (including increasingly widespread use of statins), improved prevention and treatment of nosocomial infections would all contribute to reducing perioperative mortality across the board.

In this context, it is not surprising that, across studies that have adjusted for the selection biases according to which people receive EVAR or OSR, there has been no change in relative mortality over time (see **Theme 3)**. Both approaches appear to have benefited proportionately from rising standards.

The committee noted that the 2 most recent datapoints in the supplementary review of casemix-adjusted observational evidence report perioperative mortality rates of 0.6% and 0.5% for OSR (Sugimoto et al., 2017 and Symonides et al., 2018). The latter figure is an especially attractive target, as it comes from a recent, countrywide database of publicly funded practice in Europe (Poland). In view of these features, the committee saw no reason why the NHS should not aspire to a similarly low level of perioperative mortality.

Theme 2a. Vascular Society AAA Quality Improvement Programme

Many stakeholders draw our attention to the Vascular Society's AAA Quality Improvement Programme, which was designed to address the high perioperative mortality in the UK, relative to other countries, that was revealed in the 2008 Vascunet report. This initiative is credited as being the key driver behind a substantial reduction in perioperative mortality over the following years. Some stakeholders contend that the primary reason for this was a shift towards increasing use of EVAR.

The committee noted that the Quality Improvement Programme's remit was broad. The central principles of the improvement framework clearly provided benefits for all types of AAA repair, including: standards regarding preoperative risk modification, multidisciplinary working, minimum staffing provision, minimum volume requirements, audit recommendations, as well as technical standards for both OSR and EVAR. All of these factors are likely to have been important in the observed reduction in perioperative mortality, which occurred for both EVAR and OSR over the period. It was noted that, if system improvement were as simple as just encouraging people to do more EVAR, the substantial efforts behind the VSQIP would have been unnecessary.

The committee agreed that the Quality Improvement Programme should be seen as a success when judged against its stated aim of reducing perioperative mortality. However, when it comes to the choice between EVAR and OSR, the evidence shows clearly that, now that the necessary correction in short-term outcomes has been achieved, continuing to focus on perioperative risk alone will lead to net harm across the cohort. Accordingly, when the short-term benefits of EVAR are balanced against its costs and its long-term harms, the committee concluded that OSR should be seen as the preferred approach.

Theme 3. Perioperative mortality – unruptured infrarenal AAA

During development of the guideline, the committee gave very careful consideration to the most appropriate estimate of perioperative mortality associated with EVAR and OSR.

The method used in the base-case economic model – that is, using current registry data to inform baseline rates and RCT data to inform relative effects – is well established as best practice in HE modelling. For instance, NICE DSU Technical Support Document 13 (Kaltenhalter et al., 2013) provides a hierarchy of evidence sources that, all else equal, are likely to be preferred for various inputs to a HE model. This hierarchy explicitly identifies the optimal source of evidence for clinical effect sizes as ‘Meta-analysis of RCTs with direct comparison between comparator therapies, measuring final outcomes’ and the preferred type of evidence for baseline clinical data as 'Case series or analysis of reliable administrative databases specifically conducted for the study covering patients solely from the jurisdiction of interest'.

The review of casemix-adjusted observational evidence, which we undertook in response to stakeholders’ common contention that the consultation draft placed too much reliance on the RCTs, produced findings that strongly validate this position. The pooled OR is 0.32 (0.28 to 0.37). These estimates are extremely similar to the pooled effect of OR=0.33 (0.20 to 0.55) estimated in RCTs. When the dataset is restricted to the 8 casemix-adjusted observational studies that explicitly limit their datasets to infrarenal cases, the pooled OR is 0.37 (0.24, 0.55) – marginally less favourable for EVAR.

Perhaps more importantly, these analyses reveal no secular trend suggesting an increasing advantage associated with EVAR, compared with OSR, over time. While stakeholders are correct in their assertion that perioperative mortality with infrarenal EVAR has generally fallen since the RCTs were undertaken, the same is also true of OSR, when it is measured in cohorts that are matched for prognostic factors with EVAR candidates. The net result is that the relative effect has remained stable over time. This finding provides strong validation for the base-case parameterisation of our HE model – using current registry data to inform baseline rates and RCT data to inform relative effects.

Multiple stakeholders cite Schermerhorn et al.’s (2015) year-by-year analysis of US Medicare data from 2001–2008 as evidence of a decreasing trend in perioperative mortality with EVAR. Again,

however, this study also shows a significant decrease in OSR perioperative mortality over the same period, and the authors' test for interaction shows that there is no significant difference in the pace at which the respective rates decreased (p=0.129).

Theme 3a. Alternative sources for perioperative mortality (unruptured infrarenal AAA): National Vascular Registry

In detailed discussion during development of the guideline, the committee firmly rejected crude perioperative results from registries such as the NVR as a suitable basis for estimating true differences in effectiveness between EVAR and OSR. The committee noted that there are clear selection biases defining the people who tend to be offered each procedure in current practice, and that there is also a very high risk of reporting bias in the data that gets submitted to the registry. For example, which AAAs get classified as 'infrarenal' is very likely to vary depending on the type of repair attempted.

The committee's view that unadjusted registry data provide a critically biased estimate of effect is validated by our review of casemix-adjusted observational evidence (see Evidence review K2). Among the 25 studies reporting perioperative mortality that attempt to provide balanced cohorts (either by randomisation or by risk-adjustment), only 1 small study has ever found that EVAR is associated with a perioperative mortality benefit of the magnitude implied by unadjusted NVR data.

For all these reasons, the committee are convinced that the NVR does not provide a valid estimate of relative perioperative mortality.

Nevertheless, if we set aside these principled objections, and use NVR data as the HE model's estimate of relative effect for unruptured infrarenal AAA, EVAR remains associated with a net QALY loss, compared with OSR, over the average patient's lifetime. Because this alteration has relatively little effect on costs, OSR remains the dominant option, with an 87% probability of providing best value for money if QALYs are valued at £20,000 each and a 79% chance of optimality at £30,000/QALY (see HE.9.1.1.5).

Theme 3b. Alternative sources for perioperative mortality (unruptured infrarenal AAA): Vascunet (Budtz-Lilly et al., 2017)

Several stakeholders cite the recent publication by Budtz-Lilly et al. (2017) as evidence that we have underestimated the perioperative benefit conferred by EVAR, in comparison with OSR. We question the relevance of this study. Firstly, it appears to include AAAs of all anatomical complexity – not just the infrarenal cases in relation to which its results are cited. Secondly, it does not present a casemix-adjusted estimate of EVAR compared with OSR (in any case, the authors appear to have collected data on age, sex and AAA diameter alone, which would be inadequate to assess the comparability of cohorts and adjust for any imbalances, especially given the known heterogeneity of anatomical complexity and the high incidence of comorbidity in this population).

The finding on which stakeholders place most weight is that, in a stratified comparison of repairs from 2005–2009 and 2010–2013, EVAR perioperative mortality rates became significantly lower, whereas OSR perioperative mortality rates significantly increased. While the improvement in EVAR results is hypothetically explicable as a result of better patient care, it is less easy to explain a deterioration in outcomes for OSR. The authors note that this is a surprising finding, and suggest that

> *A higher rate of anatomically demanding cases which are selected for open repair in the endovascular era may contribute to this development.…*

The committee were very mindful of this danger (e.g. see discussion of NVR data for complex repair, below), which was a major reason why they concluded that unadjusted observational data do not provide a valid estimate of true differences in effectiveness between EVAR and OSR.

Budtz-Lilly et al. also speculate that

> *The dramatic reduction in the percentage of open repair cases is another important factor. The volume–outcome relationship in complex vascular surgical procedures is well established. The decreasing number of open repairs per centre may have resulted in reduced technical competence.*

Their findings provide circumstantial support for this hypothesis – there was no evidence that OSR mortality had risen in high-volume centres. However, whether this is a true phenomenon or not, it should have relatively little impact on the NICE committee's decision-making. NICE guidance should be based on an evidence-based view of the benefits, harms and costs that would be achieved with alternative approaches to patient care. In this case, recommendations encouraging a higher volume of OSR practice could be expected to undo any deterioration in results that has arisen owing to reduced workload, so it would not be appropriate to base recommendations on data that suffer from this effect. Moreover, while service models addressing volume–outcome dynamics were explicitly beyond the scope of this guideline, it remains possible for the NHS to optimise results by giving consideration to an appropriate level of centralisation, if that is deemed necessary to obviate any low-volume effects that can be seen in historical data.

Finally, despite our substantial misgivings about the relevance of an unaddressed bias in evidence from Budtz-Lilly et al. (2017), we note that the crude odds ratios implied by their data – 0.37 (0.32 to 0.43) for 2005–2009 and 0.24 (0.21 to 0.28) for 2010–2013 – are entirely consistent with the RCT-based estimate on which we place primary reliance – 0.33 (0.20 to 0.55). Of particular note is that the range used for deterministic and probabilistic analyses in the HE model encompasses the full range of Budtz-Lilly et al.'s estimates; the fact that model conclusions are robust to these analyses demonstrates that conclusions would not be different if the questionable data were preferred.

Theme 3c. Alternative sources for perioperative mortality (unruptured infrarenal AAA): stakeholders' reported experience

Multiple stakeholder provide their own results in their consultation comments. While we are grateful for the attempt to contextualise the proposed guidance, such estimates cannot be a substitute for rigorously identified, appraised and synthesised evidence from published literature. Just as units will seldom publish case series detailing mediocre experience, we consider it unlikely that we would receive analogous information from stakeholders whose results do not meet the standards to which they aspire.

Theme 4. Perioperative mortality with EVAR and OSR – unruptured complex AAA

In the consultation draft, the committee acknowledged that the paucity of credible empirical data made results for complex AAA much more uncertain than those for infrarenal cases. To estimate perioperative mortality, in the absence of complex-AAA-specific data meeting the protocol of the systematic review, the committee agreed that a reasonable approximation could be achieved by

taking the baseline risk for complex AAA from the NVR and assuming that the relative effect observed in the infrarenal RCTs applies.

Theme 4a. Alternative sources for perioperative mortality (unruptured complex AAA): National Vascular Registry

As in the case of infrarenal AAAs, some stakeholders cite the NVR as a source of evidence on relative perioperative mortality for complex AAA. In particular, attention is drawn to the apparently high mortality for OSR (19.6% in 2014–15; 18.4% in 2014–16). The committee concluded that it was in these data that the biases inherent in the NVR had most seriously distorted outcomes that could be expected from a system in which either EVAR or OSR were used as the primary mode of repair. They discussed the cases of complex AAA that are selected for open repair (and subsequently get reported to the NVR), and agreed that these tend to be inherently more complex than those for which EVAR is often preferred, at present.

We note that the authors of the NVR report are mindful of these dangers: in presenting these figures, the 2017 report comments that

> *Direct comparison of these figures is difficult and the open procedures may represent a more complex anatomical AAA to repair.*

One evident shortcoming of the NVR's complex AAA data, from the perspective of the current guideline, is that they include some thoraco-abdominal aneurysms, which are mostly excluded from the scope of this guideline. The committee agreed that these cases carry inherently more risk, and the most complex of them are disproportionately likely to be repaired with OSR. The committee agreed that this was a good example of a more general trend towards reserving OSR for the most anatomically challenging cases. This will inevitably result in the NVR reporting perioperative mortality rates for complex OSR that are misleadingly high, for the purpose of estimating the true balance of risks between OSR and EVAR in cases of similar complexity.

Moreover, the committee expressed the view that, even where EVAR and OSR were used for similarly complex AAAs, the EVAR cases are more likely to be reported to the NVR as complex. The processes underlying this issue are well summarised by the Liverpool Clinical Trials Unit, in their stakeholder comments (#481):

> *Vascular anatomies suitable for similar FEVAR configurations (with similar technical complexity of implantation) may require open surgical strategies of varying complexity, with cross clamp level ranging from infrarenal to supracoeliac, and therefore different operative risks. Similarly, juxtarenal AAAs that can be treated by open repair with the same level of aortic cross clamp may require FEVARs of varying complexity.*

The committee acknowledged this kind of heterogeneity. However, they noted that all types of FEVAR in these scenarios would be considered 'complex' and reported to the NVR as such, whereas a case that could be repaired using OSR with an infrarenal cross-clamp would almost certainly be reported as infrarenal. Data recording in this circumstance – and others like it – would have the effect of artificially reducing both the complex and the infrarenal mortality rates for EVAR, compared with identical cases undergoing OSR (this is a variant of the Will Rogers phenomenon).

For all these reasons, the committee emphasised that it would be extremely misleading to compare the reported NVR mortality rates directly. As noted in the consultation draft,

The committee advised that the Registry data, particularly for complex AAA repairs, are likely to be subject to substantial selection and reporting biases, with EVAR repairs reported to the Registry as complex cases likely to be inherently less complex than open repairs reported as complex.… The committee agreed that… a cost-effectiveness analysis using the reported [NVR] complex repair perioperative mortality rates directly would not provide a meaningful comparison of EVAR and open surgical repair.

Theme 4b. Perioperative mortality (unruptured complex AAA): review of casemix-adjusted observational evidence

Our review of casemix-adjusted observational data suggests that the committee's distrust of the unadjusted NVR data is appropriate. There is substantial heterogeneity in reported outcomes, but none of the 9 included studies suggests that complex EVAR is associated with a perioperative mortality benefit as large as that implied by a comparison of unadjusted NVR data. The pooled odds ratio in the primary analysis does suggest that EVAR has a lower risk of death than OSR, although this is subject to substantial uncertainty (0.877 [0.367 to 2.096]); if this value is used in the HE model, complex EVAR becomes dominated by OSR.

This evidence suggests that the value borrowed from infrarenal RCTs, as used in the base-case HE model reported in the consultation draft (0.33 [0.20 to 0.55]), is more likely to be an overestimate of the perioperative benefits of complex EVAR, compared with OSR, than an underestimate.

Theme 5. Intraoperative resource use

The base-case HE model reported in the consultation draft relied on detailed data from EVAR-1 to estimate intraoperative resource use.

In EVAR-1, mean theatre time was 191 minutes for EVAR and 215 minutes for OSR. Stakeholders suggest that these data have limited relevance to the present-day context, because EVAR procedures are now accomplished in less time, owing to increased operator skill and more efficient technology.

While the committee agreed that this hypothesis is plausible, there are very few alternative sources of intraoperative data that are credible and relevant. In considering stakeholders' feedback, we reviewed the following:

- Multiple stakeholders cite Burgers et al. (2016), a Dutch cost–utility model for which the authors assumed 146 minutes of theatre time for EVAR and 228 minutes for OSR, referenced to unpublished data from the Dutch Surgical Aneurysm Audit and 'expert opinion'. Therefore, it is unclear what the empirical basis for these estimates is; they may simply represent the authors' best guesses. Even if the numbers come directly from the unpublished audit, there is no suggestion that those data adjusted for the significant selection biases that will inevitably be present in observationally collected data of this type. This is likely to be particularly relevant for theatre time, as the committee's expectation is that the cases that are selected for OSR are disproportionately likely to have anatomical complexities that are likely to prolong procedures. We note that Burgers et al.'s estimate of OSR procedure time is somewhat higher than was recorded in the RCTs; while it is plausible that EVAR times have gone down, it is less easy to explain rising OSR times, except in consequence of the kind of selection biases the committee hypothesise.

- Stakeholders also place weight on Verhoeven et al. (2014), which presents non-comparative data from European centres enrolled in a global registry for a single EVAR device. A median procedure time of 120 minutes (range 50–667 minutes) is reported. It would be inappropriate to adopt an estimate of median theatre time in an HE model, especially given the predictable skewness of this variable, as evident in the very high upper bound to the reported range. The absence of comparator data for OSR for comparable procedures further compromises the applicability of this datasource.
- We also looked for theatre time data in the casemix-adjusted observational evidence that was assembled in response to stakeholders' criticism that the consultation draft placed too much emphasis on RCTs alone. Only 1 study reported duration of infrarenal AAA repair in matched cohorts (Sugimoto et al., 2017); this reports mean theatre times of 163 minutes for EVAR and 250 minutes for OSR. The fact that this study represents a Japanese setting diminishes its applicability, arguably critically so. Again, OSR duration appears long, compared with the trials, and 1 fairly likely explanation is substantial selection bias relating to AAA characteristics (none of which were included in the authors' matching algorithm).

The view of the committee is that none of these data are sufficiently reliable to adopt as a superior estimate of theatre time; therefore, the HE model retains its reliance on randomised evidence, in the base case. However, we explored the impact of adopting the estimates from Burgers et al. and Sugimoto et al. in sensitivity analyses. Whereas, in the base case, theatre time is associated with an additional £464 with OSR, compared with EVAR, that number rises to £1,430 using Burgers et al.'s estimates and £1,371 using Sugimoto et al.'s data. While these are obvious increases in EVAR's favour, neither is sufficient to amount to net cost saving with EVAR, so OSR remains dominant.

For complex AAA, the base-case HE model reported in the consultation draft assumed identical theatre time as in infrarenal operations, in the absence of any data, and we retain this approach in our updated model. However, in our review of casemix-adjusted observational data, we identified 2 studies that report mean procedure duration in propensity-matched cohorts undergoing endovascular versus open repair for juxtarenal and pararenal aortic aneurysms (Orr et al., 2017; Tinelli et al., 2018). In this dataset, the mean theatre time was 108 minutes shorter with EVAR than with OSR. The fact that these studies are based on Italian and US practice may diminish their direct relevance to our model (to a greater degree than would be expected with effectiveness data, as theatre time may reflect structural and/or cultural factors that go beyond the requirements imposed by the repair itself). However, we used these data in sensitivity analysis, to see whether they have an impact on results. When we use these data (and these data alone, from the casemix-adjusted dataset), the additional theatre costs for OSR, compared with EVAR, rises from £502 to £1,709, with the result that total incremental costs associated with complex EVAR fall from £9,695 to £8,488. However, the ICER remains above £44,000 / QALY.

Theme 6. Postoperative resource use

Theme 6a. Length of hospital stay (including critical care)

The base-case HE model reported in the consultation draft relied on data from EVAR-1 to estimate perioperative resource use.

Many stakeholders point out that, compared with when the RCTs were undertaken, people undergoing EVAR now spend much less time in hospital in general and in critical care in particular.

The committee agreed that this corresponds with their experience, too. They acknowledged that the HE modelling supporting their decision-making should ideally reflect the resource use that would be expected if the decision being simulated were adopted in present-day NHS practice.

Stakeholders have directed us to a number of sources of observational evidence on length of hospital stay derived from research, registries and routine datasets; however, the strong consensus is that we should rely on the most recent data from the National Vascular Registry.

The committee discussed this issue at length. The attraction of a current datasource with good coverage of UK NHS activity is obvious. However, the committee were mindful that current selection practices pose a high risk of generating biased results. They recalled that they had been extremely reluctant to take perioperative mortality data from the NVR on face value, and had found that their scepticism was supported by published casemix-adjusted observational evidence (see **Theme 3a**). The committee considered that the direction and impact of the selection bias inherent in NVR data is uncertain: while recent history suggests that people who have undergone OSR in the UK are somewhat younger and fitter than those selected for EVAR, more of them have large AAAs, and the committee believed that, even within the 'infrarenal' category, OSR cases are more likely to feature anatomical complexities. The impact of these types of characteristics on perioperative resource use is difficult to predict.

We obtained means and SDs of these parameters from the NVR (as stakeholders note, hospital stay data in the published report are only available as medians and interquartile ranges, which are inappropriate for HE analysis). We also reviewed the casemix-adjusted observational studies identified for post-consultation review and found a small number (all North American) reported some details of perioperative resource use.

The data from these 2 sources are shown in the table below, which compares them with the EVAR-1 numbers used in the HE model reported in the consultation draft.

Table Con01: Perioperative length of stay, unruptured infrarenal AAA

	EVAR-1			NVR 2017 (Jan–Dec 2016)			Casemix-adjusted observational data[a]		
	EVAR (n=614)	OSR (n=602)	Diff.	EVAR (n=2,907)	OSR (n=1,246)	Diff.	EVAR	OSR	Diff.
Critical care days	1.42	4.35	−2.93	0.42	3.37	−2.95	(n=1,446)	(n=6,131)	−1.61[b]
Ward days	8.34[c]	11.41[c]	−3.07[c]	3.89	7.13	−3.24	–	–	−4.06[d]
Total days	**9.76**	**15.76**	**−6.00**	**4.31**	**10.50**	**−6.19**	**(n=41,520)**	**(n=46,205)**	**−5.67[e]**

[a] *Primary analysis, based on studies using a recommended method to adjust for potential confounders*
[b] *ITU; Huang et al. (2015) and Jetty et al. (2012)*
[c] *Includes preoperative stay; if these are omitted, the difference becomes −2.72 days.*
[d] *Inferred as difference between total LoS and ITU*
[e] *Huang et al. (2015), Jetty et al. (2012) and Schermerhorn (2015)*

Comparing perioperative resource-use data from EVAR-1 (as used in the consultation model) with analogous estimates from the 2017 NVR report shows that, for people undergoing EVAR, the mean number of ward days has reduced by 4.45 days, and critical care days have also reduced by 1.00 days. This supports stakeholders' contention that stays for primary EVAR procedures have become shorter over the last 15 years. However, it is also apparent that perioperative resource use for people undergoing OSR has fallen by a similar amount: 4.28 ward days and 0.98 critical care days. The net result is that, when it comes to the difference between EVAR and OSR (that is, the

incremental cost against which any incremental benefit of EVAR must be assessed), there is essentially no difference between the randomised data and the NVR. The casemix-adjusted observational data are also broadly comparable (though somewhat less favourable for EVAR).

For complex AAA, data are – as usual – sparser and much more uncertain. Data from the NVR suggest that present-day total LoS with both EVAR and OSR is fairly similar to the historical infrarenal figures from EVAR-1. However, there is a conspicuous difference in the composition of that time, with mean critical care time reported as over 7 days for OSR compared with less than 2 for EVAR.

Parameterising the HE model with these data instead of the EVAR-1 numbers has the effect of increasing cost savings associated with EVAR, in this area, from £4,029 to £6,428, with a commensurate reduction in ICER, from £66,154 to £50,410/QALY compared with OSR.

However, the committee's concern with relying on unadjusted NVR data – especially in respect of AAAs that have been reported as complex – was very relevant, here. The committee had no confidence that the 217 OSR cases that had been reported to the NVR as complex (including an unknown proportion of thoraco-abdominal aneurysms) over a 3-year period were indicative of typical cases of infradiaphragmatic complex AAA. They noted that these cases were subject to a much higher mortality rate than is seen in any casemix-adjusted data (see **Theme 4b**, above), and were equally concerned that the perioperative resource use for these cases provides a poor estimate of the true values to be expected in the population of interest.

None of the observational studies we identified provide a casemix-adjusted estimate of mean length of stay with complex EVAR and OSR (either critical care or overall). However, 2 studies report medians and IQRs from propensity-score-matched cohorts (Orr et al., 2017 and Tinelli et al., 2018). Therefore, as an exploratory analysis, we used published methods to estimate the mean from these quantiles (Wan et al., 2014; Luo et al., 2018). The results must be viewed as approximate, but provide no support for the NVR data. Indeed, they suggest that the mean differences between complex EVAR and OSR are relatively similar to the analogous mean differences observed in infrarenal cases.

Table Con02: Perioperative length of stay, unruptured complex AAA

	EVAR-1 (infrarenal AAA)			NVR 2017 (Jan 2014–Dec 2016)			Casemix-adjusted observational data		
	EVAR (n=614)	OSR (n=602)	Diff.	EVAR (n=1,838)	OSR (n=217)	Diff.	EVAR	OSR	Diff.
Critical care days	1.42	4.35	−2.93	1.82	7.46	−5.64	(n=365)	(n=365)	−1.32[a,b]
Ward days	8.34	11.41	−3.07	6.96	8.38	−1.42	–	–	−4.33[c]
Total days	**9.76**	**15.76**	**−6.00**	**8.78**	**15.84**	**−7.06**	**(n=263)**	**(n=263)**	**−5.65[a,d]**

[a] *Approximated from median and IQR using the methods of Wan et al. (2014) and Luo et al. (2018)*
[b] *ITU; Orr et al. (2017) and Tinelli et al. (2018)*
[c] *Inferred as difference between total LoS and ITU*
[d] *Orr et al. (2017)*

We also note that, in their recent cost–utility analysis of fEVAR compared with OSR for complex AAAs, Ciani et al. (2018) calculated a mean difference in overall LoS of −4.83 days, including ITU time of −0.88 days. These estimates were derived from pooled analyses of observational comparative studies; however, none of the included studies made any attempt to adjust for

selection biases in their cohorts. Therefore, for the reasons stated above, we would treat these findings with as much caution as any other unadjusted estimates.

Theme 6b. Rehabilitation

Multiple stakeholders suggest that one benefit of EVAR, compared with OSR, is that patients are more likely to be discharged home, and less likely to require rehabilitation, following repair. Because this outcome was not included in the HE model reported in the consultation draft, stakeholders suggest that we have underestimated NHS/PSS costs associated with OSR.

We included this outcome in our model of emergency repair, as the IMPROVE trial has empirical findings in this area. However, none of the elective RCTs provide analogous figures, so no such outcome appeared in the HE model reported in the consultation draft.

The committee broadly agreed with stakeholders that a longer recuperation is to be expected following OSR than EVAR and that, in some cases, this may increase resource use following the initial hospital admission. Although the impact of rupture followed by repair will invariably be greater than an elective procedure, the fact that fewer people were discharged home following OSR than EVAR in IMPROVE provides indirect support for this hypothesis.

In our supplementary review of casemix-adjusted observational data, we identified 4 studies that reported the proportion of patients discharged to a location other than home following AAA repair. None of these studies are explicitly limited to infrarenal cases, though they are likely to comprise the majority of participants. These data all come from North American settings, where discharge patterns are very unlikely to be comparable to the UK NHS. Therefore, it would be inappropriate to apply the rates directly in our HE model. Instead, we took the relative effect from these studies (an odds ratio of 0.31 [0.25 to 0.38] in favour of EVAR), and applied this to data from a UK study that does not distinguish between EVAR and OSR (91.94% discharged home; Karthikesalingam et al., 2016). In this way, we estimated expected rates of discharge home of 95.3% (EVAR) and 85.9% (OSR). Karthikesalingam et al. also report the proportion of patients discharged to another hospital (49.9% of those not discharged home); we assumed that the remainder entered nursing/residential care.

We assumed that the costs associated with rehabilitation were as reported in the IMPROVE trial, which are equivalent to an additional 36 days in hospital or 55 days in nursing/residential care for people who require such care. These assumptions were considered to be pessimistic, as it is very likely that people requiring rehabilitation following AAA rupture and subsequent surgery will be frailer and require more extensive care than those who have undergone an elective procedure. Therefore, model results with this adjustment applied should be interpreted as providing a best-case scenario for the cost-savings that might be achieved with EVAR, in this area.

The total costs calculated in this way were relatively substantial: £435 for people undergoing infrarenal EVAR compared with £1,238 for those receiving infrarenal OSR – a difference of £803 per case, on average. Applying these costs in the model reduces the incremental costs with which EVAR is associated from £3,854 to £2,927. OSR remains the dominant option.

We followed the same process in complex AAA, with the exception that we substituted an odds ratio for discharge home from a source that specifically considered complex AAA (0.23 [0.14, 0.39]; Orr et al. 2017). This led to costs of £300 for complex EVAR, compared with £1,063 for complex OSR – a difference of £763. Applying these costs in the model reduces the incremental costs with which complex EVAR is associated from £10,587 to £9,695. The ICER for complex EVAR reduces

from £56,324 to £50,410/QALY, compared with OSR (9% / 27% probability of being associated with an ICER better than £20,000/QALY / £30,000/QALY). As such, complex EVAR is unlikely to be considered a reasonable use of NHS resources.

Theme 7. Perioperative quality of life

Some stakeholders point out that, in our HE model, the quality of life decrements associated with AAA repair appear relatively insubstantial. We accept this criticism, and have taken steps to revise the analysis. In doing so, it became apparent that we had somewhat misused HRQoL data from the RCTs, assuming that the differential impact on HRQoL between EVAR and OSR lasts for longer than the evidence suggests. We have also corrected this.

Full details of the revised inputs are provided in HE.8.1.11. In brief:

- We have revised our calculations better to reflect the experience reported in the EVAR-1 RCT: (a) the biggest measured difference in HRQoL occurs 1 month after repair, and (b) there is no difference in HRQoL between people undergoing EVAR and those undergoing OSR once 3 months have elapsed (see Brown et al., 2012). This is validated by other randomised evidence (in fact, 1 other RCT reporting EQ-5D measurements – DREAM, de Bruin et al., 2016 – found that, although OSR is associated with significantly worse HRQoL than EVAR 3 weeks after surgery, it is significantly better than EVAR by month 3).
- It is unlikely that a value measured some time after surgery is adequate to reflect the experience of surgery itself, and the committee accepted that the physiological insult of an OSR procedure is much greater than that associated with EVAR. Therefore, we should attempt to capture the impact on HRQoL of the procedure itself. Because it is notoriously difficult to measure HRQoL following major surgery, we used data regarding the amount of time people spend in critical care and in hospital to estimate how swiftly they recover, and used simple linear interpolation to estimate quality of life for the period until the 3-month point at which convergence is known to occur (see above).

The net result of these calculations is that, in the 30 days following repair, people receiving EVAR lose 20% of their HRQoL, whereas people having OSR lose 41% of theirs. Over the full 3 postoperative months, the average decrements are 8% and 19%, respectively. This is compared with an approach used in the consultation version of the model that amounted to a loss of 3.6% with EVAR and 10.3% with OSR, for the first 3 months including the perioperative period. For the perioperative month in complex AAAs, people receiving EVAR lose 24% of their HRQoL, whereas people having OSR lose 53% of theirs. Over the full 3 postoperative months, the average decrements are 9% and 23%, respectively. In the consultation version of the model, we assumed identical HRQoL as for infrarenal repair. The committee confirmed that these estimates enhanced the model's face-validity.

Although no stakeholder explicitly contends that the difference in HRQoL between EVAR and OSR may be greater in current-day practice than it was when measured in the EVAR-1 trial, this would be in keeping with the arguments raised elsewhere in responses. However, even if we assume that EVAR is associated with no loss of HRQoL at all (and OSR remains associated with the same impact as outlined above), the long-term benefits of OSR are more than enough to outweigh this level of immediate gain – EVAR remains dominated in infrarenal cases, and its ICER falls only to £47,302/QALY, for complex AAA.

Theme 8. Reintervention rates

In response to some helpful suggestions from stakeholders, we have substantially revised the way in which the original HE model estimates reintervention rates.

As a first step, we have revised the HE model's calculation of reintervention rates to better reflect the EVAR-1 data. We have realised that it was incorrect to treat trial participants experiencing their first 'life-threatening' and 'other serious' reinterventions as representing mutually exclusive categories, when the sum of the 2 categories is greater than the number of all reinterventions. This shows that some people will appear in both groups. However, because we apply a multiplier for number of events to reflect evidence from EVAR-1 showing that a proportion of people who undergo 1 reintervention undergo subsequent procedures as well (see HE.2.2.9.1), the model was effectively double-counting some reinterventions. We have solved this problem by making the 'life-threatening' and 'other serious' reintervention categories mutually exclusive: instead of calculating each individually, we now calculate 'life-threatening' reinterventions, and then calculate 'other serious' reinterventions as the difference between 'any' reinterventions and this amount. This has the result that modelled reintervention counts can replicate the EVAR-1 evidence very well: 8-year life-threatening event-rates with EVAR and OSR are 10% and 6% in the model, compared with 10% and 5% in the trial, and 8-year any event-rates are 25% and 11%, compared with 23% and 10% (rates do not match perfectly because (a) we use the covariate-adjusted HRs from EVAR-1 to make use of the most accurate treatment effect possible, and (b) the competing hazard of mortality is lower in the model than in the trial, for reasons discussed in elsewhere).

Secondly, we have explored stakeholders' suggestion that EVAR reintervention rates can be assumed to be lower, in current practice, than was observed in the trials. The committee discussed this issue at the post-consultation meeting. They agreed that, in their experience, there are fewer EVAR reinterventions in the current era. They noted that, in part or in whole, this is because of increased awareness about which late complications need to be addressed, and not necessarily a direct result of increased operator expertise and/or technological standards. However, it was agreed that, if reinterventions have reduced without – as much as is known – patient outcomes suffering, the precise reason is immaterial.

To acknowledge this issue, the HE model was configured to apply a reduced rate of reinterventions in its EVAR arm (but not its OSR arm).

Several stakeholders cited an Italian paper comparing results with different generations of stent-grafts (Verzini et al., 2014). This study reports that new grafts are subject to lower reintervention rates than old ones, with a HR (adjusted for confounders) of 0.67 (0.49 to 0.93). The committee agreed that this was a relatively optimistic estimate, and other evidence supports their caution. Schermerhorn et al.'s (2015) year-by-year analysis of US Medicare data – which is also cited by some stakeholders as evidence of reducing reintervention rates – shows that, from 2001–2007, 2-year all reintervention rates fell from 10.4% to 9.1%, equivalent to a HR of 0.87. Of note, the rate of 'major' reinterventions did not decline at all over this period; the authors comment that the reduction in all reinterventions 'seemed to be driven by a decrease in the number of minor reinterventions…, which probably represents a more conservative attitude toward the management of type 2 (side branch) endoleak'. A recent meta-analysis by Kent et al. (2018) gives 2-year reintervention rates for 6 different grafts. Comparing mean rates for 'old' and 'new' grafts (using Verzini et al.'s schema, but excluding grafts that appear in both lists in different iterations, for which Kent et al. do not provide data) gives a HR of 0.76.

Nevertheless, in order to provide a best-case exploration of this issue, the model was configured to modify all EVAR reintervention rates using the HR of 0.67 from Verzini et al. (2014). Coupled with

the correction noted above, we found that the model was able to replicate Verzini et al.'s findings very well: without the multiplier, the model predicts that, after 8 years' follow-up, 25.3% of people will have required at least 1 reintervention, where Verzini et al. report a 25.8% reintervention rate with older-generation stent-grafts; when we apply the HR, the 8-year figure in the model falls to 17.3%, compared with a figure of 16.4% for newer-generation devices in the study.

This adjustment resulted in a conspicuous reduction in expected incremental reintervention costs – from £2,750 in the base-case model reported in the consultation draft to £1,036. However, the effect on QALYs was much less pronounced, and EVAR remains dominated by OSR.

It is even less clear whether any reduction in EVAR reinterventions applies in the case of complex AAAs. We are aware that some authors have found that off-IFU EVAR is associated with higher rates of reintervention (Igari et al., 2014; Herman et al., 2018), whereas others have not (Beckerman et al., 2016; Walker et al., 2015). When the HE model is configured to assume that reintervention rates have reduced in the same way as in the infrarenal case, the ICER for EVAR reduces from £64,164 to £50,410 (9% / 27% probability of being associated with an ICER better than £20,000/QALY / £30,000/QALY).

Theme 8a. Costs and disutilities associated with reinterventions

Some stakeholders express concern about how the original HE model estimates the cost and/or quality of life impact of reinterventions. We have reviewed these parameters in the light of this feedback and the made the revisions described below.

In the base-case model on which consultation comments were sought, we assumed the following:

- All 'life-threatening' reinterventions (as defined in the EVAR RCTs; see table 1 in Patel et al., 2018) incur
  - the total cost of emergency OSR, reflecting a high cost associated with an urgent full graft reintervention (see HE.2.2.11.3)
  - the HRQoL impact of primary elective OSR to repair an AAA (see HE.2.2.12.3).
- All 'serious' graft-related reinterventions repair incur
  - the cost associated with single vessel angioplasty (from the NHS reference costs; see HE.2.2.11.3)
  - the HRQoL impact of primary elective EVAR to repair an AAA (see HE.2.2.12.3).
- Hernia repairs incur evidence-based costs and disutilities (see HE.2.2.11.3 and HE.2.2.12.3).
- Other laparotomy-related reinterventions (bowel resection, lysis of adhesions, hospitalisation without intervention) also have costs and disutilities that are specific to the type of reintervention (see HE.2.2.11.3 and HE.2.2.12.4).

We note that, in their most recent publication, the EVAR investigators have adopted a single HRQoL impact and a single cost to apply to all life-threatening and serious reinterventions, reflecting the mean estimated cost across all episodes on which they collected data (Patel et al., 2018). These are an absolute utility decrement of 0.0604 (SE 0.0258), which is assumed to apply for 6 months, and a mean cost of £8,670 (SE £831). These figures appear to be in-line with stakeholders' expectation (the predominant concern is that the cost we had used for life-threatening reintervention – £17,089 – was unrealistically high).

Therefore, in our revised base-case, we replicate Patel et al.'s approach (2018), and use the single average HRQoL impact and cost for all graft-related reinterventions they report. This approach has

the advantage of using estimates that are directly based on evidence collected in the relevant population. It has the disadvantage of lacking granularity, to enable us to explore any possible differences in cost and HRQoL impact between life-threatening and other serious interventions, or between post-EVAR and post-OSR graft-related interventions. To address this, we configured the model to explore 3 sensitivity analyses:

- assuming all life-threatening reinterventions attract the cost of emergency OSR and the HRQoL impact of elective OSR (similar to the approach in the consultation draft);
- assuming all life-threatening reinterventions attract the cost of emergency EVAR and the HRQoL impact of elective EVAR;
- assuming post-EVAR life-threatening reinterventions attract the cost of emergency EVAR and the HRQoL impact of elective EVAR, while post-OSR life-threatening reinterventions attract the cost of emergency OSR and the HRQoL impact of elective OSR

In all 3 of these scenarios, we assume that other serious reinterventions have the cost of angioplasty and the HRQoL impact of elective EVAR without the adjustment for critical care disutility (similar to the approach in the consultation draft).

We did not revise any inputs relating to hernia repairs and other laparotomy-related reinterventions (other than to update NHS reference costs to 2016/17), as these are well evidenced, rely on standard sources, and did not appear to meet with any stakeholder concern.

Neither the revised base case nor the sensitivity analyses cause a material change in cost–utility results. In the elective infrarenal setting, EVAR remains dominated in all cases (though assuming differential costs for EVAR and OSR reinterventions reduces the incremental cost with which EVAR is associated by around £500 to a little over £2,300 per case). In the elective complex setting, the ICER for EVAR compared with OSR ranges between approximately £44,000/QALY and £50,500/QALY.

Theme 9. Long-term survival with EVAR and OSR – unruptured infrarenal AAA

Stakeholders have suggested that it is inappropriate for our HE analyses to model long-term excess mortality with EVAR, compared with OSR.

Our analysis of casemix-adjusted observational evidence validates the reasonableness of simulating a long-term survival advantage for OSR. In nonrandomised studies, the pooled HR is 1.29 (1.17 to 1.43), suggesting that, once people have survived the period of perioperative risk, those who have undergone EVAR face a rate of death that is 29% higher than those who received OSR. This is significantly higher than the HR calculated from the trials (p=0.031); one possible explanation for this finding – other than residual selection bias – is that the more intensive follow-up of trials was able to minimise the worst effects of late endograft failure (annual CTs were mandated in all 3 RCTs for which long-term results are available).

In this dataset, there is no evidence that long-term results for EVAR have improved, relative to OSR, over time; this is in contrast to stakeholders' contention that any long-term excess mortality that may historically have been associated with EVAR will have been eradicated by developing expertise and technology.

If the HR from the observational data is applied in the HE model, the dominance of OSR over EVAR becomes even more pronounced, such that the average person undergoing infrarenal EVAR loses as much as 0.6 discounted QALYs, compared with what they could have expected

with OSR. The same adjustment renders OSR dominant for complex AAA, as well (that is, the long-term benefits are more than enough to offset the increased perioperative risk we simulate in that setting).

For our base case, we retain our preference for randomised data over these estimates, as – despite the efforts the authors of observational studies have made to provide balanced cohorts – randomisation remains by far the best defence against confounding. However, we do take these observational data as providing validation that (a) EVAR is very likely to be associated with excess long-term mortality, compared with OSR, and (b) this effect does not seem to have diminished over time.

Some stakeholders cite Verzini et al.'s finding (2014) that reintervention rates are lower with more modern grafts than they were with earlier ones (see **Theme 8**, above), and suggest that this should be taken as evidence that long-term survival is also likely to be more favourable. However, this is something the study explicitly looks at, finding no evidence of longer overall survival with newer grafts (p=0.537 over 8 years' follow-up).

Theme 9a. Proportional hazards in post-perioperative phase of HE model

It is very important to note that we only apply the proportional hazards approach in the post-perioperative phase of our HE model. In this context, the crossing of overall survival functions is irrelevant, so long as it can be shown to be a result of perioperative excess mortality with OSR, followed by a long-term survival benefit.

All evidence – both from randomised and observational designs – suggests this is a strongly supportable assumption, and that a proportional hazards model of survival conditional on perioperative survival provides an excellent description of observed data.

Our primary justification for this approach is the demonstrably excellent fit it achieves to empirical data. Figure HE08A shows how well the model fits the post-perioperative data from EVAR-1 by adopting this approach (and configuring other parameters in our model to match the EVAR-1 population). Similarly, Figure HE16 demonstrates a very good fit to the observed overall survival in EVAR-1.

This appearance can be formally verified: Grambsch and Therneau's test for would not reject the null hypothesis of proportional hazards for any of the 3 RCTs (p>0.05, in all cases).

Stakeholders have noted that the most recent EVAR-1 publications have only shown a statistically significant benefit for OSR over EVAR in the post-8-year period, which is advanced as evidence that we should have taken a piecewise approach to modelling long-term survival. Although we configured our model to explore this kind of approach in scenario analysis (assuming no difference in post-perioperative survival until 8 years; see below), we believe that this is an inferior method for several reasons:

- In the EVAR-1 post-perioperative dataset, formal hypothesis testing shows that data are consistent with proportional hazards (p=0.269 by Grambsch–Therneau test). Similarly, comparing a piecewise Cox model with breaks at 0.5, 4 and 8 years with a constant-HR model provides no support for the piecewise approach (p=0.390 when difference in the two −2-log-likelihoods is compared to a chi-squared distribution with 3 degrees of freedom [see Collett 2015]). This finding provides a strong validation of the proportional hazards assumption.

- The 3 post-perioperative HRs in the EVAR-1 dataset – 1.13 (0.87 to 1.47) 6 months–4 years, 1.07 (0.83 to 1.37) 4–8 years, 1.25 (1.00 to 1.56) >8 years – are statistically indistinguishable (p=0.65) and it would be fallacious to assume this is an effect that develops over time just because the last of the 3 meets an arbitrary definition of significance.
- Relatedly, the fact that the model is probabilistically parameterised means that uncertainty attaching to the base-case HR is propagated throughout the model and reflected in our estimates of decision uncertainty. This approach reflects uncertainty better than believing all significant effects and assuming all insignificant effects are 0.
- Adopting a single post-perioperative HR allows us to make use of all available RCTs, not just EVAR-1, which increases the precision of our estimate.

For all these reasons, the committee were convinced that the best approach for the base case was to adopt the most parsimonious model, assuming a (relatively small) constant excess hazard with EVAR, rather than no difference followed by a larger HR.

However, it should be understood that the committee's preferred approach is also a conservative one. Because we anticipated that some people would prefer only to reflect 'significant' effects, the model was configured, as a scenario analysis, to adopt the assumption that differences in post-perioperative survival only emerge after 8 years. This scenario results in greater benefit for OSR (in infrarenal elective cases, QALYs gained rise from 0.152 to 0.232; in complex elective cases, QALYs gained by EVAR fall from 0.192 to 0.125 and the ICER goes up from £50,410 to £77,081).

Furthermore, we undertook scenario analyses in which we configured the model to use parametric fits to the EVAR-1 data, including options in which curves were fitted separately to each arm. This approach makes no assumption about the proportionality (or even functional form) of hazards. We do not prefer this approach for our base case, because the proportional hazards model enables us to make use of more RCT data, bring survival expectation up to date, and investigate subgroup effects with a much greater degree of flexibility. However, if the proportional hazards assumption is for some reason deemed unreliable, these analyses can be used instead. They all result in worse cost effectiveness for EVAR compared with OSR than our base case (see HE.3.1.1.4, HE.3.1.2.4, HE.3.2.1.4, HE.3.3.1.4, HE.3.3.2.4 and HE3.4.1.4 [pre-consultation results], and HE.9.1.1.4, HE.9.1.2.4, HE.9.3.1.4 [post-consultation results]).

Theme 9b. Statistical power of EVAR-1 trial

In discussing the available data on long-term survival, and the use made of it in the HE model, several stakeholders consider it important that power calculations for the EVAR-1 trial were based on expected survival outcomes at around 3 years. This criticism can be refuted in 3 ways: firstly, stakeholders use this argument to imply that any long-term differences observed in the trial are not reliable; however, the pre-hoc power of an experiment has no bearing on its type I error-rate – lack of power will influence the precision, not the accuracy, of results. Secondly, we do not rely on EVAR-1 alone. Instead, we meta-analyse 3 RCTs with long-term follow-up (see HE.2.2.6.1). The explicit purpose of meta-analysis to increase power ('Many individual studies are too small to detect small effects, but when several are combined there is a higher chance of detecting an effect') and to improve precision (Cochrane Handbook v5.1.0). Thirdly, it should be noted that the HE model is probabilistic, meaning that the degree of imprecision that is present in the parameters is propagated throughout the model, in order to enable robust exploration of its implications for decision uncertainty. In this context, there is a direct relationship between the power of studies as inputs and the certainty of cost–utility results as outputs.

Theme 10. Heterogeneity of complex AAA

The committee agreed with the contention put forward by several stakeholders that 'complex' AAA is a heterogeneous category, comprising several types of anatomy and demanding a variety of approaches in both the endovascular and open paradigms. They agreed that optimal decision-making for this population would be based on detailed analysis of reliable data subdividing people according to types of complex aneurysm and repair. However, with the possible exception of fenestrated EVAR (fEVAR; see **Theme 10a**, below), there is a critical dearth of specific evidence in this area.

In the absence of data enabling focused analysis on different types of complex AAA, the committee agreed that it would be of value to explore more general evidence which combines experience with various types of complex AAA repair.

NICE's methods are clear that uncertainty about the true balance of costs, benefits and harms associated with a treatment should make committees more cautious about recommending technologies (see Developing NICE guidelines, chapters 7 and 9). In this case, the committee has been provided with no credible evidence that complex EVAR – either as an overarching category or in one of its subtypes – provides net health gains over a patient's lifetime and does so at a cost that can be considered a reasonable use of NHS resources.

However, the committee recognised that the very poor evidence associated with this area made the optimal decision uncertain, and noted that the HE modelling undertaken to explore it suggested that complex EVAR (in at least some of its forms) might provide reasonable value for money if multiple model parameters were at the beneficial end of plausible ranges. Therefore, the committee agreed that it would be valuable to conduct randomised research that can inform future decision-making. Mindful of the heterogeneity of the 'complex' AAA category, they added the stipulation that this research should be stratified in a way that will help to reveal any differences in the balance of benefits, harms and costs between EVAR and OSR according to AAA anatomy (at least distinguishing between juxtarenal, pararenal and suprarenal AAAs).

Theme 10a. Estimated HE model results for fEVAR

Having assembled a small dataset of casemix-adjusted observational evidence in response to stakeholder feedback that the review protocol on which the consultation draft had been based was too restrictive, it appeared feasible to undertake an exploratory analysis that focused on fEVAR in particular.

This analysis was largely based on our base-case model for complex AAA, but adopted 3 fEVAR-specific parameters:

- Baseline perioperative mortality risk from NVR (3.9% with fEVAR)
- Relative mortality effect from review of casemix-adjusted observational data (OR for fEVAR -v- OSR: 1.079 [0.362 to 3.215])
- Cost of fEVAR graft (£16,502 as cited by Ciani et al., 2018)

We did not identify any credible evidence for intraoperative or postoperative resource-use. Ciani et al. (2018) use mean differences in overall LoS and ITU days derived from unadjusted observational comparative studies of fEVAR -v- OSR. However, if we are to use unadjusted data, there is little reason not to use the NVR – even though the committee felt certain that results were particularly biased in the area of perioperative resource use for complex AAA (see **Theme 6a**,

above), these reservations would apply equally to published cohort studies with no adjustment for casemix.

The analysis suggested that fEVAR is dominated by OSR, with substantially worse net health effects (0.27 QALYs worse than OSR), but substantially higher costs (slightly more than £10,000), even though fEVAR benefits from the likely biased estimate of perioperative resource use for complex AAA from the NVR. The probability of fEVAR being considered cost effective is 1.2%, if QALYs are valued at £20,000 each, or 2%, at £30,000.

We note that other authors who have attempted to estimate the cost effectiveness of fEVAR have also reached negative conclusions. Ciani et al. (2018) estimated a base-case ICER of £74,580/QALY, and Michel et al.'s analysis (2015) concludes that fenestrated and branched EVAR 'is not a cost-effective option for para/juxtarenal AAA'. A recent update from the same authors reached similar conclusions (Michel et al., 2018).

Theme 11. CT-led post-EVAR surveillance

Multiple stakeholders argue that, by assuming that people who have undergone EVAR will be followed up with regular CTs, the HE model undertaken to support decision-making for this guideline is at odds with current practice (which tends to favour ultrasound-led surveillance) and consequently overestimates costs associated with EVAR. We do not agree with this argument for 2 reasons: firstly, recommendations made elsewhere in the guideline stipulate that ultrasound should not be used as the primary screening modality for post-EVAR surveillance, and CT should be preferred. This was based on an evidence review in which the sensitivity of ultrasound, for detecting potentially life-threatening complications, was found to be suboptimal when compared with a reference standard of CT. Secondly, the RCTs on which the HE model's estimate of long-term effect are based all mandated regular CT follow-up. On reviewing casemix-adjusted 'real-world' evidence of long-term survival following EVAR and OSR, we found a pooled estimate of the excess mortality associated with EVAR that was significantly greater than observed in the RCTs. One possible explanation for this finding – other than residual selection bias – is that the more intensive follow-up of trials was able to minimise the worst effects of late endograft failure. Therefore, if we were to reduce the assumed intensity – and, consequently, cost – of post-EVAR follow-up in the HE model, we should arguably increase the hazard associated with undiagnosed complications at the same time. This would make EVAR look less, not more, cost effective.

Theme 12. Subgroups of people for whom EVAR for unruptured AAA is the optimal choice

It is a common theme of stakeholders' feedback that there are identifiable subgroups of people whose characteristics – e.g., age, gender, smoking status, comorbidities, and anatomic complexity – make EVAR or OSR a more suitable option.

Above all, stakeholders suggest that decision-making should account for the risk of perioperative mortality associated with characteristics such as these. The guideline includes a review question on tools for predicting surgical outcomes (evidence review H). On reviewing the assembled evidence, the committee concluded that none of the available risk-assessment tools has sufficient discriminatory power to be safely used in decision-making for patients.

Throughout developing the guideline, the committee were keen to review evidence on subgroups. As noted in Evidence review K:

For each of these recommendations, the committee considered whether there were any specific groups that would benefit from standard or complex EVAR for unruptured AAAs. They explored groups defined by age, sex, AAA diameter and life expectancy, but there were no groups in which the benefits would outweigh the harm and costs.

The original economic model was configured to explore the possibility of such subgroups. We undertook extensive analyses according to age, sex and aneurysm diameter, attempting to identify a population in which EVAR represents an effective use of NHS resources -- HE.3.1.1.3, HE.3.1.2.3, HE.3.2.1.3, HE.3.3.1.3, HE.3.3.2.3 and HE.3.4.1.3. None of these analyses revealed a population that could be expected to derive enough benefit to justify the costs of the procedure.

We also simulated cohorts of people with lower-than-average life expectancy, to see whether reduced capacity to benefit from long-term survival would remove the advantage OSR has in our base case, and make EVAR a preferable option -- see HE.3.1.1.4 & HE.3.1.2.4. Although these analyses identified some populations who could expect a small QALY gain from EVAR, compared with OSR, none of these came at a cost that would be considered a reasonable use of NHS resources (that is, the money could be used to produce substantially more QALYs elsewhere in the NHS).

The committee also noted that, in contrast to the widespread view asserted by stakeholders that access to EVAR is most vital for people with higher baseline risk of perioperative mortality, most evidence suggests that the approach has most short-term value in people with the most favourable characteristics. In a subgroup analysis of the EVAR-1 cohort, Brown et al. (2007) found that EVAR only confers a perioperative survival benefit, compared with OSR, in people judged to benefit from 'good' fitness. In OVER, Lederle et al. (2012) found that younger participants had a significant benefit from EVAR whereas older people did not (indeed, the results were very nearly reversed). Regression analyses based on the Vascunet dataset suggest that female sex and increasing aneurysm diameter are greater risk factors for people undergoing EVAR than they are for people having OSR (Mani et al., 2015; Budtz-Lilly et al., 2017; note no formal test for interaction reported, though coefficients give the appearance of representing meaningful differences between the 2 models).

Despite these findings, the committee acknowledged that it is inevitable that, if clinicians had access to much better predictive information about candidates for AAA repair, it would be possible to identify some who would derive more benefit from EVAR than OSR. Consequently, it is plausible that offering EVAR to such people would become cost effective if they could be identified a priori with a high degree of reliability. With this in mind, the committee's research recommendations regarding elective and emergency AAA repair stipulated that trials should be stratified according to potentially prognostic factors, including age, sex, comorbidities and ethnicity.

Theme 13. Quality of life impact of living with an untreated AAA

Multiple stakeholders contend that the committee's recommendation that people for whom OSR is not a suitable option should not receive EVAR will cause anxiety and psychological morbidity for people who are not offered any repair of their AAA.

The committee discussed this issue, and emphasised the importance of the initial consultation, to ensure the patient understands the balance of hazards they face. The committee agreed that it would be good practice to advise people in this situation that, among people who were randomised to no intervention in the EVAR-2 trial, the majority died with, rather than from, their AAA, and that the trial showed no overall survival benefit for people receiving EVAR. The committee concluded

that, as the people for whom surgical repair is inappropriate are subject to comorbidities that are inevitably life-limiting, it is important to move away from the 'ticking time-bomb' model of AAA to a more realistic appraisal of the competing hazards faced by such people and the risks inherent in treating them.

A number of stakeholders have cited a recent study in the British Journal of Surgery (Bath et al., 2018) as contemporaneous evidence for a negative impact on the quality of life of people living with an AAA. However, this study actually identified

> *a transient reduction in mental quality of life [QoL] scores... following the diagnosis of AAA, returning to baseline levels after 12 months.... Participants thought about their AAA and the AAA growth progressively less 12 months after the initial screening diagnosis. AAA growth rate had no influence over HRQoL parameters.*

The same authors found that comorbidities (e.g. angina and stroke) were a more important determinant of a person's mental quality of life than their AAA. If a person's comorbidities have made OSR unsuitable, then the fact that those other health concerns play a bigger role in their quality of life than the aneurysm is an important finding. We also note that this study focuses on men who have been diagnosed with small AAAs in the NAAASP. It may be argued that the population of interest, here (people with larger AAAs that may be assumed to be more likely to rupture), experience different psychological morbidity. However, the cited evidence does not support any such conclusion.

Notably, however, the EVAR-2 RCT found no significant differences in EQ-5D between people receiving EVAR and those randomised to no intervention; nor was there a detectable effect on the SF-36 mental component summary score (although there was a significant disutility associated with EVAR on the physical component score over the first 3 months of the trial).

For all these reasons, a negative impact of living with an untreated AAA has not been explicitly included in the economic model for this guideline. Nevertheless, it can be demonstrated that the results of the analysis are not critically dependent on this factor. In their recently published model analysing screening women for AAA, the SWAN collaborators explored this issue in a sensitivity analysis in which they assumed a lifetime utility decrement of 0.1 to reflect psychological morbidity for people who are aware of their AAA but for whom surgery is contraindicated (Sweeting et al., 2018). This is a very large disutility – approximately equivalent to a diagnosis of congestive heart failure, osteoarthritis or schizophrenia – which has no basis in evidence, but is used as an extreme value to test model sensitivity. If we do the same, the ICER for EVAR compared with no intervention only falls to £31,144/QALY. This demonstrates that no plausible level of disutility could be enough to counterbalance the harms and costs associated with EVAR.

Theme 14. Hostile abdomen and other abdominal pathology contraindicating OSR

Throughout development of the guideline, the committee noted that there is a small group of people with unruptured AAA in whom there may be relative contraindications to OSR for reasons other than medical comorbidity – for example, hostile abdomen or horseshoe kidney. When agreeing the draft guidance on which stakeholder feedback was sought, the committee took the view that these patients are sufficiently uncommon that they would be handled on a case-by-case basis, and vascular MDTs would not need specific guidance on when to consider EVAR rather than OSR for these reasons.

However, on reviewing stakeholder feedback, the committee noted that their draft guidance had commonly been interpreted as implying that they did not recommend EVAR in these cases, as well as those where OSR is either possible or contraindicated because of medical comorbidity. Therefore, they agreed that they should make their position explicit in a new recommendation.

The committee emphasised that this recommendation should not be used as a means of extending EVAR to people who could reasonably have OSR, or those whose medical unsuitability for OSR provides a good indication that they cannot expect net health gain from any intervention. In particular, the committee had seen no evidence that there are any aortic morphological characteristics that should be used as a reason for preferring EVAR over OSR, and emphasised that the abdominal copathologies envisaged in the recommendation are those that complicate repair of the vascular defect, not those that comprise the defect itself.

Theme 15. Clinician judgement

In common with all NICE guidelines, our AAA guidance contains the important contextualising statement that

> *The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.*

This is a clear statement of NICE's position that individual treatment decisions should be guided but not exclusively defined by our guidance. This recognition complements NICE's fundamental responsibility to provide evidence-based guidance on the best ways to prevent, diagnose and treat disease and ill health.

Theme 16. Evidence considered by TA167 claimed to be able to distinguish between subgroups of people with different balances of benefits and harms

Stakeholders note that, although the modelling evidence available to the committee for TA167 suggested that EVAR is very unlikely to represent an effective use of NHS resources across the cohort of people with AAA, it is possible to identify subgroups of people in whom the balance of benefits, harms and costs is different (Chambers et al., 2009). In particular, this study suggests that EVAR may be a cost-effective alternative to OSR in people with 'poor' fitness, especially those who are older and/or have larger aneurysms.

Three important assumptions of Chambers et al.'s analysis are

(a) that absolute perioperative risk is predictable on the basis of a person's perceived fitness (the analysis imagines that we can identify people who have twice, 4 times and 8 times the odds of death)

(b) that fitness has an impact that is totally independent of age and AAA diameter (which are handled separately in their analyses)

(c) that the relative effectiveness of EVAR and OSR is not affected by fitness or other risk factors (i.e. there is no interaction between risk factors and treatment allocation)

All of these are difficult to support based on current evidence. In the case of (a), the committee concluded that none of the available risk-assessment tools has sufficient discriminatory power to be safely used in decision-making for patients (see evidence review H). This does not rule out the possibility that clinical acumen alone is able to distinguish between people with categorically different prospects of perioperative mortality; however, we are unaware of any evidence on this. For (b), it is clear that fitness will be strongly correlated with age and probably AAA diameter, as well. This factor makes it even harder to rely on clinician judgement alone: a risk model could theoretically estimate the independent effects of fitness as distinct from age and anatomy; it would be extremely challenging for a person to perform the same adjustment mentally. As regards (c), there is evidence that there are interactions between risk factors and treatment effect. In a subgroup analysis of the EVAR-1 cohort, Brown et al. (2007) found that EVAR only confers a perioperative survival benefit, compared with OSR, in people judged to benefit from 'good' fitness; in people with 'moderate' and 'poor' fitness, there was no significant benefit. Similarly, regression analyses based on the Vascunet dataset suggest that female sex and increasing aneurysm diameter are greater risk factors for people undergoing EVAR than they are for people having OSR (Mani et al., 2015; Budtz-Lilly et al., 2017; note no formal test for interaction reported, though coefficients give the appearance of representing meaningful differences between the 2 models).

For these reasons, we cannot interpret Chambers et al.'s analysis as providing a reliable estimate of the balance of costs and effects in people with specified characteristics. Rather, it demonstrates that, if we **could** reliably predict perioperative risk in a way that is not counfounded by other factors and appropriately accounts for interactions with treatment, it might be possible to identify people who would stand to have greater or lesser benefits from EVAR, given the other assumptions of the analysis.

However, our concerns about the other assumptions of the analysis mean that, even if one was to accept the validity of their risk-stratification, the implications for decision-making are not straightforward. In fact, the major difference between Chambers et al.’s subgroup analysis and ours is not that their model is more sensitive to effect modification than ours; it is that their model has a more optimistic base case for EVAR than ours (0.041 QALYs gained at an ICER of £48,990, compared with our estimate of 0.152 fewer QALYs leading OSR to dominate EVAR). Accordingly, when effect modifiers are applied in the 2 models, they have the potential to produce an ICER that reflects an effective use of NHS resources in Chambers et al.’s case, but this is very much less likely in our model. Assuming fixed costs, in order for EVAR to be associated with an ICER of £20,000/QALY or better compared with OSR, a subgroup in Chambers et al.’s model would have to benefit from a net QALY gain in that population that is 0.059 QALYs greater than the estimate at the mean of their cohort (that is, an advantage for EVAR of 0.100 QALYs compared with a base case of 0.041). In our model, the equivalent figure is 0.298 QALYs (a gain of 0.146 QALYs compared with a base case of 0.152 QALYs lost).

Subsequent analyses building on the Chambers et al. model by members of that team share our conclusion that the 2009 base case was inappropriately optimistic for EVAR (see Brown et al., 2012, Epstein et al., 2014, and Patel et al., 2018). The later publications do not repeat the attempt to provide risk-stratified results; however, it is extremely likely that, if they did, they would find less ability to discriminate between populations with better or worse cost effectiveness, certainly at a threshold of £20,000/QALY.

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