Endometriosis: diagnosis and management

Consultation on draft guideline - Stakeholder comments table
09/03/2017 to 20/04/2017

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ID	Stakeholder	Document	Page No	Line No	**Comments** Please insert each new comment in a new row	**Developer's response** Please respond to each comment
1	Bayer plc	Full	181	20	This use of the wording *'first-line management'* in recommendation 34, but not in recommendation 39 could be interpreted to suggest that analgesics are recommended *before* hormonal treatment, whereas the algorithm on page 13 is clear that both analgesics and hormonal treatment should be offered for initial management. The wording of the recommendations should reflect that both analgesics and hormonal treatments are options for initial/first-line management.	Thank you for your comment. Even though the wording is different we agree that both of them can be given initially. However, the difference in wording is intentional since hormonal treatments depend more on the women's preference or priorities and for some women cannot be the first line treatment (those women trying to conceive). This is less so the case for paracetamol or an NSAID.
2	Bayer plc	Short	9	9	This wording of recommendation 1.7.2 could be interpreted to suggest that analgesics should be offered *before* hormonal treatment, as they are described as *"first-line management"* under the heading 'pharmacological pain relief'. However, the algorithm in the full version of the draft guideline is clear that both analgesics and hormonal treatment should be offered for initial management. The wording of the recommendations should reflect that both analgesics and hormonal treatments are options for initial/first-line management.	Thank you for your comment. Even though the wording is different we agree that both of them can be given initially. However, the difference in wording is intentional since hormonal treatments depend more on the women's preference or priorities and for some women cannot be the first line treatment (those women trying to conceive). This is less so the case for paracetamol or an NSAID.
3	Betsi Cadwaldr	Full	11.1.3.4.68	41-43	Refer to a gynaecologist to discuss hormonal contraceptives or laparoscopy?? GnRH agonist treatment is not included?	Thank you for your comment. Even though effective, use of GnRH-a requires guidance from a specialist as (1) the Network Meta-Analysis showed that they had higher risk of withdrawal due to adverse events (2) their more serious adverse events (e.g. bone density changes) (3) are only licensed for a 6 month period and therefore require special considerations to ensure that women do not stay on this treatment indefinitely and (4) to negate their adverse effects add-back therapy using oestrogens, progestogens or both would usually be prescribed, too. Furthermore they are also more costly than other options. The Committee therefore decided not to be prescriptive about which treatment path to follow when first line treatment is not effective, not tolerated or is contraindicated and leave it to clinical judgement to weigh up the benefits and harms of options that could be used. A discussion of these issues has now been added to the rationale section for this recommendation in the full guideline.
4	Betsi Cadwaldr	General	General	General	1) Implementation of the referral pathway –as number of women with suspected endometriosis can be large and variable 2) Having the services of a gynae nurse practitioner and pain team specialist for EM at all secondary care sites--challenging 3) Recommending laparoscopic hysterectomy while ideal is not achievable and inability to do it laparoscopically should not be simply deemed as non-compliant. Suggest stating "Consider laparoscopic route"	Thank you for your comment. We believe that there should be access to these professionals and services and that this would improve quality of life for women with suspected or confirmed endometriosis. This was found to be a cost-effective service in our health economic analysis related to the organisation of services (please see section 5.1 in the full guideline). The Committee agreed that hysterectomy should be performed laparoscopically because it enables excisional surgery to be carried out at the same time. We have

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					Ease of access to EM centres for every primary/secondary care provider can be a challenge as NHS is struggling to sustain the elective services currently on offer--Improved access to EM centres would be helpful	reworded the heading of this section as well as the recommendation to indicate that it is the excision of the lesions rather than the hysterectomy that is the treatment of endometriosis in this context.
5	Betsi Cadwaldr	Short	1.3.4	24-26	……..offer an abdominal examination to exclude any masses. Suggest adding--- ultrasound scan of pelvis : which is much better than a simple abdominal examination in picking p any masses.	Thank you for your comment. This recommendation is related to the examination only. This is already recommended later in the document: 'If a transvaginal ultrasound is not appropriate (for example in women who have never had sexual intercourse), consider transabdominal ultrasound.'
6	Betsi Cadwaldr	Short	1.4.1 1.4.2 1.4.3	General	1.4.1 and 1.4.3 are recs stating: Consider and 1.4.2 states-Refer. Suggest avoiding variation and using **Consider** for all recs including 1.4.2	Thank you for your comment. The use of the word 'consider' in these recommendations reflects the strength of the evidence (please see for further information on the wording of NICE recommendations). In the recommendation that starts with 'refer' the Committee agreed that a stronger instruction could be used.
7	Betsi Cadwaldr	Short	1.4.5	General	Explain to women that EM is associated with a small increased risk of ovarian cancer—If this to be explained to all women with EM, it is a bit scary considering the absolute risk is very small as it states in the guidance. Qualifying the statement better with absolute risks will help practitioners in counselling.	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman).. That is to say; the absolute risk increase was considered to be so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. However, we revisited the evidence and it now became clear that due to various statistical and other limitations of the data it was impossible to calculate a clear absolute risk. After discussion, the Committee decided that if they were therefore unable to quantify the risk. We agree that the intention to reassure the women with a numerical estimation of the probability could therefore not be met. The recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) this information if they have further questions about the increased risk of cancer.
8	Betsi Cadwaldr	Short	1.4.6	General	No surveillance is advised for gynae cancers. This is true and the rec above doesn't quite help in counselling when stated with this rec.!! If	Thank you for your comment. The Committee discussed this issue at length. The purpose

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					one is told that there is a small increased risk, then it's natural to think of some form of surveillance. ?? risk is for those with ovarian endometriomas/severe/recurrent??	of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it if they have further questions about the increased risk of cancer.
9	Betsi Cadwaldr	Short	1.5.13	General	……does not have endometriosis, and offer alternative management! ……exclude other causes for symptoms ---sounds better than the current statement	Thank you for your comment. After a careful consideration the Committee decided not to change the recommendation. In this recommendation it is not the exclusion of other causes for symptoms that would lead to the conclusion that women do not have endometriosis but the laparoscopic inspection of the pelvis.
10	Betsi Cadwaldr	Short	1.5.2	General	Role of transperineal Ultrasound scan for those who have not been sexually active?	Thank you for your comment. The Committee discussed how a transperineal scan might also be unsuitable for a woman who has not had penetrative intercourse, and agreed that it would also be unsuitable for them. They concluded that it would not be appropriate to change the recommendation, although they did change the accompanying text in the full guideline (see section 9.2.7.5 of the full guideline).
11	Betsi Cadwaldr	Short	1.7.7	General	Offer hormonal treatment (for example, oral COC or long acting……..)—suggest adding---GnRH agonists in this list of hormonal treatment Consider adding—Hormonal treatment maynot/is not particularly effective for ovarian endometriomas	Thank you for your comment. After a careful consideration the Committee rephrased the recommendation by removing 'long acting reversible contraception' and adding 'oral combined contraceptive pill or progestogens'. A footnote has been added to emphasise that at the time of the guideline publication (September 2017), not all combined oral contraceptive pills or progestogens have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and

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						documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.
12	Betsi Cadwaldr	Short	1.9.8	General	Combine hysterectomy with excision of all visible EM—suggest adding……which may involve removal of ovaries if affected by endometriosis	Thank you for your comment. After a careful consideration the Committee rephrased the recommendations regarding hysterectomy and removed the recommendation you are referring to.
13	Betsi Cadwaldr	Short	1.9.9	General	Perform hysterectomy laparoscopically…. Sounds very directive! As a consultant in DGHundertaking lap hysterectomy for benign diseases like EM, can confirm that the number of individuals trained to do so are limited.This is too directive and not all hospitals/surgeons in the UK perform lap hysterectomy and such rec. would cause unnecessary delay and suffering for some women. Suggest: Consider laparoscopic hysterectomy rather than perform.	Thank you for your comment. After a careful consideration the Committee rephrased the recommendations regarding hysterectomy. The recommendation you are referring to was replaced by the recommendation '1.9.9 Perform hysterectomy (with or without oophorectomy) laparoscopically when combined with surgical treatment for endometriosis unless there are contraindications'.
14	British and Irish Association of Robotic Gynaecological Surgeons	Full	10	22	The fact that deep infiltrating endometriosis is diagnosable by imaging (TVS/MRI) as well as endometriomas should be made clear early on.	Thank you for your comment. Referral to a specialist endometriosis service has been recommended where there is a suspicion of deep endometriosis involving the bowel, bladder or ureter. We recommended that this service should have access to 'a healthcare professional with specialist expertise in gynaecological imaging of endometriosis'. Decisions about imaging would then be left to this professional's clinical judgement based on women's symptoms, priorities and preferences and other factors.
15	British and Irish Association of Robotic Gynaecological Surgeons	Full	130	13	Virgo Intacta women should be offered trans rectal scanning for pelvic endometriosis if not suitable for TV scan	Thank you for your comment. The Committee discussed how a transrectal scan might also be unsuitable for a woman who has not had penetrative intercourse, and agreed that it would also be unsuitable for them. They concluded that it would not be appropriate to change the recommendation, although they did change the accompanying text in the full guideline.
16	British and Irish Association of Robotic Gynaecological Surgeons	Full	265	7	We welcome the recognition of robotic surgery as a valid laparoscopic approach for endometriosis surgery. We believe that current prospective date is showing decreased major complication rates particularly in terms of bowel and ureteric leaks and fistulas.	Thank you for your comment.
17	British and Irish Association of Robotic Gynaecological Surgeons	Full	282	23	A new full meta-analysis of the excision vs ablation question for endometriosis has just been accepted by JMIG on 19/4/17 authored by jyotsna Pundir showing excision as the better option for the first time and making the Cochrane review out of date. A new Cochrane review is currently underway also including new evidence that is likely to show advantage of excision. You may wish to hold off your opinion on this until it appears shortly online in JMIG as it would have a significant effect on your guidance as the current guidance that excision = ablation is out of date. Am happy to discuss this if anyone wants.	Thank you for your comment. Thank you for highlighting this reference. Whilst outside our search dates (December, 2016), we have considered this paper and noted that 2/3 of the included studies were included in the guideline. The review findings are also consistent with those of the guideline.

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18	British and Irish Association of Robotic Gynaecological Surgeons	Full	39	10	Typo? "the" should read "there"?	Thank you for your comment. We have now corrected the error.
19	British and Irish Association of Robotic Gynaecological Surgeons	Full	50	9	Grammatical error	Thank you for your comment. We have now corrected the error.
20	British and Irish Association of Robotic Gynaecological Surgeons	Full	62	35	What about Neuropathy?	Thank you for your comment. We assume that your comment refers to neuropathic pain. We did not identify any evidence specific to neuropathic pain as a specific symptom of endometriosis. However, we (1) cross-referred to the NICE guideline on neuropathic pain and also (2) recommended that women could be referred if they have severe, persistent or recurrent symptoms. We believe that neuropathic pain could fall in the latter category.
21	British and Irish Association of Robotic Gynaecological Surgeons	Full	General	General	I am concerned that there is not enough weight given in this guideline overall to patients with significant neurological symptoms suggestive of sciatic or pudendal endometriosis. They may have scans showing no evidence of DIE but are definitely cases that should be seen in a specialist centre in conjunction with a specialist pain clinic as standard pain clinic protocols with neuromodulators don't tend to work as you've pointed out. There needs to be some provision for the specialist referral of these women especially as these lesions are potentially diagnosable on MR Neurography and potentially operable in very specialist hands and there are likely more of these cases than we think. There is a risk that they will be denied access to specialist centres if scans don't show DIE and they may be erroneously sent down a psychology pathway.	Thank you for your comment. The intention of this recommendation was that women with deep endometriosis involving the bowel, bladder or ureter would be treated in the services that best meets their needs. We agree that there are other women that may need referral to specialist services but it would be difficult to describe these women because there are other possible indications apart from neurological symptoms suggestive of sciatic or pudendal endometriosis that may require special considerations. These particular cases of referral would be left to clinical judgement. We have added further detail to the discussion section for this recommendation (section 6.6.5).
22	British and Irish Association of Robotic Gynaecological Surgeons	Full	General	General	Overall we would like to thank the committee for the obvious hard work that has gone into this guideline.	Thank you for your comment.
23	British Society for Gynaecological (BSGE)	full	13	Bottom of algorythm	What is meant by "pelvic signs of endometriosis". For example a fixed uterus or a visible vaginal nodule would be unsuitable for a gynaecology service	Thank you for your comment. Signs suggestive of endometriosis are highlighted in the short guideline section "Endometriosis symptoms and signs" such as reduced organ mobility and enlargement, tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions.
24	British Society for Gynaecological (BSGE)	Full	14	Within algorythm	"uncomplicated endometrioma" is unclear. An endometrioma that is adherent to its surrounding structures, for example would be more appropriately treated in a centre.	Thank you for your comment. The term 'uncomplicated' was intentionally used to allow for a surgeons' clinical judgment based on their experience and skill. We have added your example of a type of endometriosis that would require referral to the section that provides the rationale for this recommendation.

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25	British Society for Gynaecological (BSGE)	Full	14	Within alrogythm	Perform hysterectomy where possible is not a strong enough recommendation to make it clear open surgery is in most cases not appropriate, not because it is more invasive, but because without the advantages of laparoscopy, excision of endometriosis is often incomplete (or even not practical because of access)	Thank you for your comment. This recommendation has now been reworded to clarify that the combination of hysterectomy and surgical treatment would require it to be performed laparoscopically.
26	British Society for Gynaecological (BSGE)	Full	171	17	"a gynaecologist with training and skills in laparoscopic surgery" could mean any level of training. It needs to be mapped to a competence level from RCOG training.	Thank you for your comment. We agree that 'training and skills in laparoscopic surgery' is not very specific, but this is because being more specific in this instance would be outside the scope of this guideline. It is assumed that training and expertise to manage women with endometriosis could change over time, and the risk of being specific in the Guideline is that it might become obsolete in a few years. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training constituted, and update this in accordance with changes to training and their understanding of the disease.
27	British Society for Gynaecological (BSGE)	Full	303	10	"(with, for example, the oral contraceptive pill)"……add LNG-IUS, as shown by evidence (page 300, line 5).	Thank you for your comment. As the comment in parenthesis is only supposed to be an example, the Committee considered that adding any more treatments to the list might make it appear more like an exhaustive list than a signpost to the sorts of treatment to consider. Consequently the Committee did not alter the wording of the recommendation.
28	British Society for Gynaecological (BSGE)	Full	304	19	Mention should be made of the high frequency of adenomyosis with endometriosis, and that hysterectomy is a very effective treatment for adenomyosis. There is a risk that after endometriosis is excised, the symptom of dysmenorrhoea may remain if there is adenomyosis. Therefore, care givers should have a discussion about hysterectomy with women who have either decided not to have children, or whose family is complete and are considering surgery.	Thank you for your comment. We have now included some examples of indications for hysterectomy including adenomyosis in a new recommendation. We have also added text to the full guideline to explain the reason for this.
29	British Society for Gynaecological (BSGE)	Full	320	14	Endometrioma – the committee have not considered the treatment of endometrioma > 5cm. The approach to these may involve a 3 stage procedure (Tsolakidis D, Pados G, Vavilis D, Athanatos D, Tsalikis T, Giannakou A,Tarlatzis BC. The impact on ovarian reserve after laparoscopic ovarian cystectomy versus three-stage management in patients with endometriomas: a prospective randomized study. Fertil Steril 2010; 94:71–77).	Thank you for your comment. The Committee has considered your comment and altered the full guideline to discuss issues in the management of endometriomas >5cm and why no particular recommendation was made. We did not identify any clinical evidence particularly related to endometriomas >5cm and the reference that you mention was a comparison not included in the protocol for this review. Three-stage management was not an approach prioritised by the Committee for consideration in the review..
30	British Society for Gynaecological (BSGE)	Full	38	7	"The symptoms do not always correlate well with the severity of endometriosis"……need to add that there is considerable overlap between the symptoms of endometriosis and those from IBS, painful bladder syndrome and pain of unknown cause.	Thank you for your comment. The Committee discussed that some of the symptoms of endometriosis overlap to some degree with IBS and painful bladder syndrome. The hormone dependent pattern and

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						cyclical nature of symptoms would make it likely that symptoms of endometriosis would differ in the pattern to those of IBS and painful bladder syndrome. One of the central aims of this guideline is to reduce the time it takes to diagnose endometriosis. We therefore intentionally did not want to highlight this point in the introduction to this chapter and in the recommendations. Findings from our qualitative review also highlighted that many women with endometriosis receive the wrong diagnosis in the first instance and that endometriosis was not even suspected on first presentation. We have now explained this (particularly the cyclical nature of symptoms) more explicitly in the 'evidence to recommendations' section of this topic (see section 5.1.7.2).
31	British Society for Gynaecological (BSGE)	full	50	27	We believe that "expertise" should perhaps be further defined somewhere. One way of doing that is to mention they should have sufficient case load to maintain their skills	Thank you for your comment. We agree that 'expertise' is not very specific, but this is because being more specific in this instance would be outside the scope of a NICE Guideline; appropriate training and expertise to manage women with endometriosis will change over time, and the risk of being specific in the Guideline is that it might become obsolete in a few years. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training / skill constituted, and update this in accordance with changes to training and their understanding of the disease.
32	British Society for Gynaecological (BSGE)	Full	62	16	Cyclical change in bowel habits perhaps warrants a mention here	Thank you for your comment. The focus of this bullet is on the cyclical nature of these gastrointestinal symptoms. Painful bowel movements were highlighted here as a particular example. However, we did not want to provide an exhaustive list of possible cyclical gastrointestinal symptoms and believe that your example is captured as it is a 'cyclical gastrointestinal symptom'.
33	British Society for Gynaecological (BSGE)	Full	62	35	See comment above on short version page 6 lines 7-9, same applies here	Thank you for your comment. We have intentionally described this as 'suspected or confirmed deep endometriosis involving bowel, bladder or ureter' to ensure that women are referred to the service that best meets their needs. Adding 'cyclical changes in bowel habits' at this point would not be helpful because it is only one possible example of what may raise suspicions about deep endometriosis.
34	British Society for Gynaecological (BSGE)	Full	91 - 108	General	Evidence of increased risk of ovarian cancer is based on studies of low or very low quality and risk estimates range widely. This is insufficient evidence base for the committee to make such a potentially harmful statement (page 113, 8.1.7). The potential risks of young women anxious about an uncertain association between ovarian cancer and endometriosis probably outweigh the benefits of	Thank you for your comment. The Committee reflected on the evidence and the comments related to this. The two recommendations related to this have now been deleted. The purpose of the original wording which you have commented on was to try and balance the need of the woman to be fully informed about her condition with the

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					making the recommendation to inform women. It may simply frighten patients without the data to rationalise the concern.	need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; that the risk increase was considered to be so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that due to various limitations in the data they were unable to quantify the absolute risk and therefore would not be able to reassure the women with a numerical estimation of this probability. They therefore decided that recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Furthermore national screening is related to cervical not ovarian cancer and therefore the issue of surveillance may be misconstrued to indicate that women should not be invited to the regular screening tests. The discussion of these issues and why recommendations have not been made has now been moved to the full guideline.
35	British Society for Gynaecological (BSGE)	Full	General	General	Having read the very impressive and comprehensive full guideline we would suggest inclusion or at least mention of less common presentations of endometriosis in the interest of thoroughness. For example endometriosis affecting pelvic nerves is thought to be underdiagnosed and neuropelveology is shedding light on many previously ignored forms of endometriosis of the pelvic nerves, including sacral nerve roots, pudendal nerves and the sciatic and femoral nerves. Vegetative symptoms of endometriosis (generally thought to be the result of autonomic nervous system involvement) such as lack of energy, tiredness, clammy and sweaty palms etc warrants at least a mention.	Thank you for your comment. These less common presentations were not excluded from this guideline, but we did not identify any specific evidence base addressing the management of these subgroups. We therefore could not make any particular statements or recommendations related to these types of presentations.
36	British Society for Gynaecological (BSGE)	Full	General	General	This guideline will improve the care of women with endometriosis.	Thank you for your comment.
37	British Society for Gynaecological (BSGE)	Full & Short	General	General	We would like to congratulate the team for producing this excellent work, which was desperately needed and well overdue. We support the recommendation of the service provision network (which is similar to the cancer network) but believe there is room for important improvements and discussions should continue to formulate the best possible system. For example, we believe, there should be a clearer guide provided to the referrers to aid them in recognising those who are likely to benefit from specialist endometriosis centres to reduce the risk of multiple surgeries (which will be harmful to the patient and costly to the NHS).	Thank you for your comment. While we agree that clearer guides to referrers to help them recognise endometriosis are likely to benefit from specialist centre expertise would be beneficial, such recommendations would be outside the scope of the Guideline. As surgical techniques change the kinds of women who would be especially likely to benefit may change, and we do not want the Guideline to become obsolete if this should happen. Consequently the Committee concluded it would be up to professional and membership bodies to make it clear what the most important referral criteria would be.
38	British Society for	Full & Short	General	General	The BSGE has gone a long way to facilitate and encourage the provision of a high quality care within endometriosis centres. We believe, however, that there is a need for a serious conversation	Thank you for your comment. This comment clearly addresses an important issue which is

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	Gynaecological (BSGE)				about the national provision of this service to maintain the high quality of care. We should consider whether the current criteria for becoming an endometriosis centre goes far enough to ensure sufficient case load for centres for example (in our opinion the bar for the minimum number of cases should be higher than it currently is but we recognise the challenges that changing the criterial would bring about).	nevertheless outside the scope of the Guideline. The Committee - for example - said that surgeons in specialist centres should have "advanced laparoscopic surgical skills", but discussed how if they listed specific skills which are currently regarded as 'advanced' the Guideline would rapidly get out of date; surgical skill advances year-on-year and the principle behind the recommendation is that only the most skilful / experienced endometriosis surgeons should be working in specialist centres (regardless of the skill of an average surgeon in absolute terms). Consequently the Committee concluded it would be up to professional and membership bodies to make it clear what the standards for such accreditation would be.
39	British Society for Gynaecological (BSGE)	Full & Short	General	General	We feel strongly that the guidelines should make it clear that referral should be made for all patients diagnosed or suspected of having gastrointestinal or urinary tract endometriosis not only those that the referring gynaecologist thinks need surgery. It is conceivable that some gynaecology units that do not offer the full range of surgical treatment for severe endometriosis, may not be equipped with the expertise to counsel patient appropriately. We believe that in this group of patients, the counselling to formulate a plan for management should be undertaken by an endometriosis expert within an endometriosis centre. The patient should have the opportunity to discuss her options in a centre that offers the full range of treatments. If, after careful consideration of all options, conservative management is decided upon, it may be appropriate to continue the management locally within the gynaecology centre. In other words, when a patient is diagnosed with severe endometriosis, in particular endometriosis involving the gastrointestinal or urinary tract endometriosis, they should have the benefit of being seen and counselled in an endometriosis centre, even if the gynaecologist in the "gynaecology unit" feels surgery is not indicated.	Thank you for your comment. We believe that we have addressed this comment with the recommendation "Refer women to a specialist endometriosis service (endometriosis centre; see recommendation 1.1.4) if they have suspected or confirmed deep endometriosis involving the bowel, bladder or ureter." and related discussion in the full guideline.
40	British Society for Gynaecological (BSGE)	Full & Short	General	General	The importance of assessing the urinary tract to rule out hydronephrosis or hydroureter should be stressed.	Thank you for your comment. The intention of this guideline is to raise awareness and decrease the time to diagnosis of the condition. We therefore highlighted those signs and symptoms that would raise suspicion or rule in endometriosis rather than all other symptoms and signs that could rule out other conditions. This would then be left to clinical judgement depending on the particular symptoms and signs that are reported by the women.
41	British Society for	Short	10	22	The word "contraindication" may be open to interpretation here. Some would still maintain that obesity, previous surgery or more	Thank you for your comment.

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	Gynaecological (BSGE)				interestingly surgeons inability to perform laparoscopic excision are "contraindication" to laparoscopic surgery. These are still mentioned in some textbooks. Perhaps the wording can change to clarify. Planned Laparotomy to treat endometriosis is almost never the correct route.	We did not want to be too prescriptive about the details of all possible 'contraindications'. However, we believe that this recommendation sufficiently promotes the laparoscopic route of surgery.
42	British Society for Gynaecological (BSGE)	Short	11	1	Although this practice is common amongst endometriosis surgeons (including us), the evidence for this recommendation is poor. If included, this should be made clear.	Thank you for your comment. The Committee agree that the evidence for this practice is poor, but nevertheless - in their best judgement - argued that it was likely to improve patient outcomes in a cost-effective manner. The fact that the evidence base is poor is highlighted by the use of the word 'consider' and again in the discussion of the evidence in the full guideline.
43	British Society for Gynaecological (BSGE)	Short	11	10	Does this recommendation group endometriomas and deep disease under the same umbrella? There is high level evidence for use of Combine oral contraceptives after excision of endometriomas but the evidence of deep infiltrative endometriosis in general is less convincing. It is perhaps best to separate the two and recommend according to the level of evidence available for each. Our practice is to use adjunct hormonal treatment for both groups.	Thank you for your comment. The Committee made this decision based on evidence as well as their experience and expertise. It was therefore decided to combine both in one recommendation.
44	British Society for Gynaecological (BSGE)	Short	11	14	The wording can be improved as the recommendation can be interpreted as advocating hysterectomy for endometriosis. For example it can say: If hysterectomy is indicated (for example in presence of adenomyosis or heavy menstrual bleeding not responding to other treatments) all visible endometriotic lesions should be excised at the time of hysterectomy.	Thank you for your comment. The Committee discussed this at length, as the purpose of the recommendations was to give guidance on how to perform coincidental hysterectomies in women who have endometriosis, not to imply that hysterectomy was a positive treatment option for women with endometriosis. The wording of the recommendations have therefore been significantly changed to make this clearer, and the wording of the section heading changed to 'Hysterectomy in combination with surgical treatment for endometriosis' to further emphasise this.
45	British Society for Gynaecological (BSGE)	Short	6	24	The evidence for clear explanation of the risk of ovarian cancer is insufficient to include this advice in the recommendation. If published studies were consistent so an evidence based risk figure could be quoted the statement may be acceptable, but this is not the case. Rather than providing full information for patients this statement may result in patient anxiety and an increase in unnecessary removal of the ovaries at surgery. Ultimately this statement could result in patient harm (from unnecessary oophorectomy) as an unintended consequence. Advise await more robust evidence on this aspect.	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations

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						as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it, if they have further questions about the increased risk of cancer.
46	British Society for Gynaecological (BSGE)	Short	6	7-9	GPs would find it helpful to have guidance to assist them in recognition of "deep" endometriosis and refer to appropriate specialist services. We suggest including a list of most common features of this subtype of disease and specifying when a referral should be made to a centre as opposed to a gynaecology centre. Examples are: presence of bilateral endometriomas on ultrasound scan, presence of dyschezia, particularly cyclical dyschezia, urinary symptoms, presence of palpable or visible lesions in the posterior cul de sac, a fixed uterus etc. There is reasonable evidence to guide this list. This is particularly important as the first surgery is the best surgery and getting the referral criteria right is the key to ensure the patient will no go through multiple laparoscopies/laparotomies before referral to appropriate services. Equally, such guidance would hopefully reduce the number of unnecessary referral of those with low risk of having deep infiltrative endometriosis to centres.	Thank you for your comment. The intention of this recommendation was to improve diagnosis and decrease the time to diagnosis of the condition. We believe that signs of deep endometriosis involving the bowel, bladder or ureter could be variable and we did not want to be too prescriptive about the signs leading to referral. We have added further points to the discussion section in the full guideline to signpost these to the clinicians as possible reasons to raise suspicion and therefore lead to referral to a specialist endometriosis service.
47	British Society for Gynaecological (BSGE)	Short	8	12	We would suggest adding that a full pelvic survey and examination under anaesthetics must include visualisation of posterior cul de sac vaginally, a rectal examination, visualisation of ovarian fossa, vesicouterine fold, etc and should also include insertion of a rectal probe to ensure obliteration of pouch of douglas is not missed. This survey can not be done without insertion of a secondary port (we have come across this practice, not infrequently) also to guide general gynaecologists what to do if they come across deep infiltrative endometriosis that they don't feel confortable excising there and then (taking pictures and ideally videos for referral purposes)	Thank you for your comment. We recommended that 'during a diagnostic laparoscopy, a gynaecologist with training and skills in laparoscopic surgery should perform a systematic inspection of the pelvis'. The Committee did not want to be too prescriptive about the details of the examination. It is assumed that a 'gynaecologist with training and skills' would conduct this surgery appropriately. NICE guidelines are not text books for training purposes.
48	Centre for Reproduction Research	Full	65	16	Culley et al 2013 was conducted in the UK, not Australia	Thank you for your comment. A corresponding amendment was made.
49	Centre for Reproduction Research	Full	66	General	Regarding Culley et al 2013, it might be clearer to state 'N=44 comprising 22 women with endometriosis and their partners'	Thank you for your comment. We have now added your suggestion to the guideline text.
50	Centre for Reproduction Research	Full	72	General	In subtheme 2 psychosocial: dyspareunia, Culley et al 2013 reports on this issue and should be included	Thank you for your comment. We have now added a reference to the Culley et al. 2013 report to the psychosexual subtheme.
51	Centre for Reproduction Research	Full	72-3	General	Related to the above point, the 'psychosexual' subtheme could be amended to make clear that the impact of endometriosis on sex and intimacy may not be limited to dyspareunia. Culley et al 2013 reports	Thank you for your comment. We have amended the recommendations to make it clear

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					that 'women reported a range of other factors which impacted on intimacy: bleeding during and/or after sex, general fatigue and feeling unwell, reduced sexual desire as a result of medication, having a low mood, the stress of trying to get pregnant and feeling generally unattractive and unfeminine' (p12). It is essential healthcare practitioners are aware that sex and intimacy can be affected even if dyspareunia is not present.	that there should be information and support provided to women tailored to their individual needs (including psychosexual and sexual needs where relevant).
52	Centre for Reproduction Research	Full	78	General	While we are pleased to see the following in the draft guideline, they are best described as *recommendations* from Culley et al 2013, rather than findings: '1 study conducted in the UK among women with endometriosis and their partners found that consultations should be inclusive of the impact of endometriosis on quality of life, and on women, partners and the couple relationship. Healthcare practitioners can improve women's and couples' experiences by referring them to specialist services (e.g. pain clinics, psychosexual counselling, etc.). Following diagnosis of endometriosis, healthcare practitioners should raise the topic of planning for and having children, and open up a discussion that allows women and couples to explore this important issue and to receive evidence-based information (also balancing the potential risks of infertility created by the treatments).'	Thank you for your comment. We have now added more information to the Sub-theme 2: Consultations (facilitator) from Culley et al. 2013.
53	Centre for Reproduction Research	Full	81	General	We are pleased to see the guideline address concerns about fertility (sub theme 4). However, Culley et al 2013 illuminates just how concerning and anxiety inducing this can be, and the fact that women experience considerable worry about *anticipated* infertility (even if subsequently they do not experience fertility difficulties). We feel this could perhaps be emphasised more in the guideline – see p15-17 of Culley et al 2013 for further exploration of this.	Thank you for your comment. We have now provided additional information from Culley et al. 2013 to the Sub-theme 4: Worries about fertility (barrier).
54	Centre for Reproduction Research	Full	89	15-16	We are very pleased to see a consideration of the impact of the condition on relationships and partners throughout. The impact on partners is of importance not only for partners themselves, but also because how it impacts on partners will inevitably then further affect women with the condition. With regard to the recommendation on line 15-16, page 89, we would suggest referring specifically to consultations as one type of discussion in which partners should be included.	Thank you for your comment. We agree that consideration of the impact of the condition on women's partners is important, and are pleased you believe the Guideline is valuable in this respect. However we feel that existing NICE Guidance on patient experience is more comprehensive on this topic than we are able to be, and so hope that by clearly signposting this Guidance it will make it clearer how and when to involve partners in discussions.
55	Centre for Reproduction Research	Full	89	20-36	We welcome the research recommendations, in particular 'What information and support interventions are effective to help women with endometriosis deal with their symptoms and improve their quality of lives?' However, the text on 'why is this important' (page 89, line 23-36) appears to be there in error– this text is identical to that for 'Are specialist lifestyle interventions (diet and exercise) effective, compared with no specialist lifestyle interventions, for women with endometriosis?' (page 263, line 4-17). When the new text is inserted we would suggest that it would benefit from a focus on support, not merely information (see comment 8) and should include specific reference to psychosocial interventions – which are desperately needed.	Thank you for your comment. We have now corrected the error.

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56	Centre for Reproduction Research	Full	89	2-18	While we welcome these recommendations, it would be helpful to include an indication of which individuals and stakeholders should be taking responsibility for such action.	Thank you for your comment. NICE guidelines assume that the recommendations would be carried out by an appropriately trained healthcare professional. The particular section is related to information and support needs. We could not be too prescriptive about who would be providing this information or support since it ought to be provided throughout the pathway by all healthcare professionals caring for women with endometriosis.
57	Centre for Reproduction Research	Full	89	2-18	Again, while we welcome these recommendations, we feel the focus on information might be overemphasised at the expense of considering other types of support. In particular lines 8-14 suggest a very 'information heavy' approach. While we recognise that research recommendations are proposed to address which support is most effective, in the meantime increased support (not just information) is desperately needed and making more use of Clinical Nurse Specialists, increasing opportunities for referrals to psychosexual support and to counselling, etc. can all be recommended. Much information about endometriosis exists already – more crucial is to put into place support services. Clinicians could be advised to signpost patients to existing online and other resources.	Thank you for your comment. The Committee are constrained by a need to only make recommendations which are evidence based, of which health economics is one type of evidence. This means the Committee can only make recommendations on support interventions which might have resource implications to the NHS where there is a robust evidence base. As you correctly identify, there is a need for research in this area before more robust recommendations could be made.
58	Centre for Reproduction Research	Full	89	2-18	In addition, these recommendations appear to neglect the psychosocial impact of the condition: information and support which addresses this, as opposed to just the clinical elements, is desperately needed. At a minimum, information on how endometriosis can affect women and those around them emotionally, and advice on coping strategies, could be included in this list.	Thank you for your comment. The Committee discussed the recommendations and agree it could be made clearer that there is a significant psychosocial impact of the condition. Consequently a new recommendation has been added reading: "1.2.1 Be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support"
59	Centre for Reproduction Research	Full	General	General	While the guideline does make reference to the impact of endometriosis on emotional wellbeing, e.g. pages 10, 88, 89, we feel this point could be further expanded upon – and it could be made clear that a negative impact on emotional wellbeing is not limited to pre-diagnosis. Culley et al 2013 reported that women experience frustration, inadequacy, loss, guilt, powerlessness as well as low mood, depression, tearfulness and/or anger and irritability – as a result of living with condition as well as hormonal fluctuations associated with the condition and side effects of treatment. Male partners experienced considerable worry, helplessness, frustration and anger. In some cases the emotional effects and all-encompassing impact on life are profound and devastating. It is imperative that healthcare practitioners take into the account the potential psychosocial impact of the condition (especially given the findings on 'lack of knowledge', page 78-9) and that they appreciate the ways in which this condition can have considerable detrimental effects on the emotional wellbeing and quality of life of both women and those around them (partners, family, etc.); this guideline is an	Thank you for your comment. The Committee discussed the recommendations and agree it could be made clearer that there is a significant psychosocial impact of the condition. Consequently a new recommendation has been added reading: "1.2.1 Be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support"

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					excellent opportunity to raise awareness about the psychosocial impact of the condition.	
60	Centre for Reproduction Research	Full	General	General	Endometriosis can have a tremendous impact on sex and intimacy, for women and for couples. This can cause considerable distress, and women report little in the way of support in order to address this (see Culley et al 2013). We feel the guideline would benefit from highlighting this and providing a more detailed discussion and consideration. In particular, the recommendations appear to neglect advising healthcare practitioners to address this with women/couples and to refer on to psychosexual support services if needed.	Thank you for your comment. The Committee discussed the recommendations and agree it could be made clearer that there is a significant psychosexual impact of the condition. Consequently a new recommendation has been added reading: "1.2.1 Be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support" The original recommendation numbered 1.2.1 has also been amended to highlight the need for psychosexual information and support.
61	Centre for Reproduction Research	Full	General	General	While we recognise that the guideline does not cover 'investigation and assisted reproductive management of fertility problems related to endometriosis' we do recommend that future work be undertaken to provide guidance on fertility and endometriosis. Culley et al 2013 makes the following recommendation: 'Whilst there are separate guidelines on endometriosis and infertility there is no single combined guideline that addresses when these two problems co-exist. As such there is no clear guidance on how to treat infertile women or couples with endometriosis which can range from mild disease to severe and be associated with minimal symptoms or have a significant impact on everyday life. This is further complicated by the fact these extremes do not always correlate and women with severe endometriosis may have minimal symptoms but still be infertile. The approaches to the assessment and treatment of endometriosis are complex therefore and not necessarily consistent. Recent data regarding the response to ovarian stimulation and the outcome of IVF as well as the effect of endometriosis on pregnancy outcome are timely and would support the development of a new guideline focusing specifically on this which would help patients and healthcare providers make informed decisions about their care. The British Fertility Society and Infertility Network UK would be well placed to develop and disseminate these guidelines for healthcare providers and patients respectively.'	Thank you for your comment. Investigation and assisted reproductive management of fertility problems related to endometriosis was outside the scope of this guideline, therefore we cannot recommend research to be undertaken in this area.
62	Centre for Reproduction Research	Full	General	General	We welcome that the guideline addresses the need for preferences with regard to fertility to be taken into account in treatment decision making in several places. We would welcome an inclusion of the research evidence about how difficult this decision making process can be, in order to put this in context and to enable healthcare practitioners to recognise the complexities of this for women/couples. Culley et al 2013 reports: 'Endometriosis treatments often act as a contraceptive or may create risks to fertility. Some couples, therefore, were faced with a difficult choice. Accepting treatment would bring much needed relief from debilitating pain but would mean delaying any attempt to conceive or	Thank you for your comment. The Committee agrees on the importance of considering patient preferences and priorities in directing treatment options, for this reason decided to include recommendation 1.6.1 Offer endometriosis treatment according to the woman's symptoms, preferences and priorities, rather than the stage of the endometriosis.

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					in the case of hysterectomy, foregoing a pregnancy. However, rejecting treatment because of a desire for children meant sometimes having to live with extreme pain. The decision-making process surrounding this issue was further complicated when partners had different priorities in this regard. For example, in the case of one couple, the male partner was desperate for his wife to have a hysterectomy, due to the severe impact of endometriosis on her wellbeing and their life together. He felt that this was the way for her to live a more normal, pain free life. However, the female partner refused to do this as she felt that whilst she could just about cope with the physical pain of endometriosis, she would be unable to cope with the emotional pain of not having a child. This had caused significant tension between the partners.'	
63	Centre for Reproduction Research	Full	General	General	In addition, we feel research should be recommended for the following areas: - Further research into the psychosocial impact of endometriosis on adolescents and young women; this is a particularly under researched group and research with adult women reflecting on this period suggest that endometriosis may have particular impacts at this time of life transitions relating to education and work, relationship formation, sex and transition to adulthood. This may also provide insight into 'delayed diagnosis'. - Further research into the impact of endometriosis on partners and relationships (including female partners and same-sex relationships); the body of knowledge in this topic is still limited, but the limited evidence suggests the impact can be profound. Research which involves evaluation of psychosocial interventions to support women living with endometriosis (see comment 15).	Thank you for your comment. Even though we agree that little evidence was identified for this particular subgroup, we identified much qualitative evidence on information and support needs. These included the psychological and psychosexual impact of the condition on women. We have also addressed the issue of psychological impact in a new recommendation highlighting that endometriosis can be a long-term condition and can have a significant physical, sexual, psychological and social impact. This will raise awareness of these issues regardless of age. The Committee therefore felt that this was sufficiently addressed in the guideline and did not prioritise the topic above others for further research.
64	Centre for Reproduction Research	Full	General	General	The publication 'Endometriosis and cultural diversity: improving services for minority ethnic women' (Denny et al, 2010, Birmingham City University: Birmingham) is not included in the guideline and may make a valuable contribution, if it meets inclusion criteria. This publication is an output from the ENDOCUL study (funded by the National Institute for Health Research, Research for Patient Benefit programme) into the ways in which minority ethnic women experience endometriosis and its treatment (http://www.bcu.ac.uk/research/-centres-of-excellence/centre-for-health-and-social-care-research/research-clusters/health-understanding-for-all/endocul). As attachments cannot be included with this response (as per the checklist below) a pdf of this publication can be located by emailing claw@dmu.ac.uk. The report suggests that: - healthcare practitioners and support groups should ensure that the support and advice offered to minority ethnic patients is culturally and linguistically appropriate. - it is essential that endometriosis care and management is appropriate for and inclusive of Black and Minority Ethnic groups. Although the experiences and concerns of women in the ENDOCUL study arise for many women regardless of	Thank you for your comment. The report you cite is not published as a peer reviewed article and we have therefore not included it in our guideline. However, we recognised that the cultural background had not been sufficiently considered and have added it to one of our recommendations related to what to take into account when assessing the woman's information and support needs (i.e. their circumstances, symptoms, priorities, desire for fertility, aspects of daily living, work and study, cultural background, and their physical, psychosexual and emotional needs). We agree that these are important findings and have now added a reference to this study to the rationale for this recommendation (see section 7.7.5). We agree that there can be cultural barrier to access services and we have therefore also added this issue to our Equalities Impact Assessment form.

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					ethnicity, differences of culture, language and religion are often important to women in gaining a diagnosis and in the experience of living with endometriosis. For all women therefore, it is important that health professionals and those supporting women have a good understanding of the socio-cultural context of people living with endometriosis. Healthcare providers should access training specifically on the way in which ethnicity might impact on endometriosis. Healthcare providers should be encouraged to analyse data by ethnic group and establish any patterns of differential diagnosis, treatment or indeed access to treatment. There is a clear need for interpreting services to be available in NHS Trusts, alongside measures to increase the confidence of users in the effectiveness and confidentiality of services. - there is a lack of information available in alternative languages and tailored to different ethnic and cultural groups. Most of the women in this study were competent English speakers, but several expressed concern at the lack of adequate communication support for those with lower proficiency in English, and many commented on the failure of consultants to fully explain procedures in easy to understand terminology. The ENDOCUL study produced DVDs and leaflets in 5 languages, as well as a resource for healthcare professionals. - with regard to seeking diagnosis, willingness to discuss topics such as menstruation and dyspareunia, and attitudes towards privacy, confidentiality and being examined by male health professionals, varies across different ethnic groups; for example Greek women were more open to discussing such topics, whereas Chinese women valued privacy and confidentiality more highly and were more circumspect about discussing such topics. In addition, within ethnic minority communities there is a limited awareness of endometriosis. - it would be misguided to advance care taking an 'ethnocentric' approach, based on the assumption that all groups experience similar barriers and that the experiences of White British communities apply to all groups. For example, in the study, Pakistani women expressed concern about the potential impact of extensive internal examinations on proof of virginity (essential to marriage) and concern that if a woman had treatment with oral contraception (a common treatment for endometriosis) this might be interpreted as her being sexually active, which would also compromise marriage prospects. Chinese women valued privacy very highly, were more circumspect about discussing any personal issues with health professionals and placed great importance on confidentiality. Some women reported that negative interactions with individual healthcare providers were related to cultural insensitivity or misunderstandings. interviews with health professionals indicated varying degrees of knowledge and concern about the impact of ethnic identity on	

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					endometriosis. All expressed the view that it was important to treat patients as individuals, rather than focus on ethnicity. Nurses were more likely to acknowledge the potential impact of culture on access to care and experience of care, though this was often done in somewhat stereotypical ways. Consultants explicitly argued that women's concerns were primarily around getting a diagnosis and appropriate treatment to relieve their pain and address any fertility concerns. Healthcare practitioners thought ethnicity was not of major importance, though some ethnic differences were identified, and poor communication with people whose English is not good was seen as a problem.	
65	Department of Health	Full	General	General	Thank you for the opportunity to comment on the draft for the above clinical guideline.I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
66	Endometriosis UK	Full	171	17	"a gynaecologist with training and skills in laparoscopic surgery" could mean any level of training. It needs to be mapped to a competence level from RCOG training.	Thank you for your comment. We agree that 'training and skills in laparoscopic surgery' is not very specific, but this is because being more specific in this instance would be outside the scope of this guideline. It is assumed that training and expertise to manage women with endometriosis could change over time, and the risk of being specific in the guideline is that it might become obsolete in a few years. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training constituted, and update this in accordance with changes to training and their understanding of the disease.
67	Endometriosis UK	Full	303	10	"(with, for example, the oral contraceptive pill)"……add LNG-IUS, as shown by evidence (page 300, line 5).	Thank you for your comment. As the comment in parenthesis is only supposed to be an example, the Committee considered that adding any more treatments to the list might make it appear more like an exhaustive list than a signpost to the sorts of treatment to consider. Consequently the Committee did not alter the wording of the recommendation.
68	Endometriosis UK	Full	304	19	Mention should be made of the high frequency of adenomyosis with endometriosis, and that hysterectomy is a very effective treatment for adenomyosis. There is a risk that after endometriosis is excised, the symptom of dysmenorrhoea may remain if there is adenomyosis. Therefore, care givers should have a discussion about hysterectomy with women who have either decided not to have children, or whose family is complete and are considering surgery.	Thank you for your comment. We have now included some examples of indications for hysterectomy including adenomyosis in a new recommendation. We have also added text to the full guideline to explain the reason for this.
69	Endometriosis UK	Full	320	14	Endometrioma – the committee have not considered the treatment of endometrioma > 5cm. The approach to these may involve a 3 stage procedure (Tsolakidis D, Pados G, Vavilis D, Athanatos D, Tsalikis T, Giannakou A,Tarlatzis BC. The impact on ovarian reserve after laparoscopic ovarian cystectomy versus three-stage management in patients with endometriomas: a prospective randomized study. Fertil Steril 2010; 94:71–77).	Thank you for your comment. The Committee has considered your comment and altered the full guideline to discuss issues in the management of endometriomas >5cm and why no particular recommendation was made. We did not identify any clinical evidence particularly related to endometriomas >5cm and the

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						reference that you mention was a comparison not included in the protocol for this review. The paper you suggest was excluded by the Committee as it did not meet our standards for inclusion; three-stage management was not specified in the protocol.
70	Endometriosis UK	Full	38	7	"The symptoms do not always correlate well with the severity of endometriosis"……need to add that there is considerable overlap between the symptoms of endometriosis and those from IBS, painful bladder syndrome and pain of unknown cause.	Thank you for your comment. The Committee discussed that some of the symptoms of endometriosis overlap to some degree with IBS and painful bladder syndrome. The hormone dependent pattern and cyclical nature of symptoms would make it likely that symptoms of endometriosis would differ in the pattern to those of IBS and painful bladder syndrome. One of the central aims of this guideline is to reduce the time it takes to diagnose endometriosis. We therefore intentionally did not want to highlight this point in the introduction to this chapter and in the recommendations. Findings from our qualitative review also highlighted that many women with endometriosis receive the wrong diagnosis in the first instance and that endometriosis was not even suspected on first presentation. We have now explained this (particularly the cyclical nature of symptoms) more explicitly in the 'evidence to recommendations' section of this topic (see section 5.1.7.2).
71	Endometriosis UK	Full	59	14	There is no comment about an irregular cycle and stages 1/11 of endometriosis. This guidance is titled 'endometriosis: diagnosis and management' so should be for all stages of endometriosis. Of course, there may not be any research on this.	Thank you for your comment. The comment you are referring to is related to the guideline chapter "Signs and symptoms of endometriosis". The review was not restricted to a particular stage of endometriosis.
72	Endometriosis UK	Full	General	General	This guideline will improve the care of women with endometriosis.	Thank you for your comment.
73	Endometriosis UK	Long	18	8	This guideline does not cover women with endometriosis outside the pelvis: how are these women to be treated? A recommendation could be that they should be seen in the first instance by a specialist centre.	Thank you for your comment. Unfortunately women with endometriosis outside the pelvis are explicitly excluded from the scope of this Guideline in order to ensure that the work can be delivered in a timely fashion. While we accept the management of women with endometriosis outside the pelvis could benefit from NICE recommendations, we have not reviewed the evidence on how they should be managed and consequently cannot make recommendations on this topic.
74	Endometriosis UK	Short	10	15	Add to this sentence that it should include why surgical treatment may not be undertaken even if endometriosis is found and why. Add to this sentence explaining and discussing the different methods of laparoscopic surgery eg ablation and excision	Thank you for your comment. We believe that the different methods of laparoscopic surgery would be covered in the discussion that 'laparoscopy may include surgery'. We believe that this also implies that it may not include this and that this would be covered at the same time. However, the list of discussion points is not exhaustive and further topics could be discussed depending on individual circumstances and priorities.

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75	Endometriosis UK	Short	10	22	This will require a certain level of skill, training and expertise, which should be specified. For clarity, the main contraindications should be listed if possible.	Thank you for your comment. We did not want to be too prescriptive about the details of all possible 'contraindications'. However, we believe that this recommendation sufficiently promotes the laparoscopic route of surgery.
76	Endometriosis UK	Short	11	1-3	The long guidelines (p285, line 36-42) states that there is insufficient evidence to recommend hormonal therapy as standard prior treatment to surgery, and the decision should be made on an individual basis based on surgeon and patient preference. However, the summary to this takes out a lot of that detail and there is the risk that it could be interpreted as recommending GnRH agonists before surgery. Suggest adding to this paragraph more detail to make it clear that this decision should be make on an individual level based on surgeon and patient preference, and ensuring that the patient understands the possible benefits, risks and complications of the treatment.	Thank you for your comment. We have added the discussion about benefits, risks and complications related to GnRH agonists to the relevant section of the full guideline.
77	Endometriosis UK	Short	11	17	Additional areas for discussion should include explaining the need to remove all endometriosis at the same as the hysterectomy.	Thank you for your comment. The Committed agreed to include additional information in the full guideline text by highlighting some indications for hysterectomy (for instance in presence of adenomyosis or heavy menstrual bleeding not responding to other treatments) and that it would then be important that the endometriotic lesions would be removed at the same time as the hysterectomy.
78	Endometriosis UK	Short	11	4-8	This paragraph could be interpreted as the only time to consider excision surgery rather than ablation is to treat endometrioma's. Recommend either the title is changed to be clear it is just about endometrioma's, and/or the section is added to, to provide more details about ablation vs excision in all aspects of surgery.	Thank you for your comment. As you correctly point out, it was not the intention to imply that endometriomas are the only kind of condition that should be treated with excision rather than ablation. The section break has been removed to ensure that this recommendation is read as an adjunct to other recommendations on the surgical management of endometriosis.
79	Endometriosis UK	Short	12	19	To consider amending this to 'Defined as cyclical or non-cyclical pain lasting 6 months or more'.	Thank you for your comment. We believe that this definition would be understood to mean both cyclical and non-cyclical pain.
80	Endometriosis UK	Short	14	6	Could NICE recommend at what level (or minimum level) of experience/position/expertise that the lead should be, to ensure this role can be fulfilled effectively.	Thank you for your comment. We have recommended that the gynaecologist should have expertise in diagnosing and managing endometriosis including training and skills in laparoscopic surgery. In the relevant discussion section we have described that this should happen according to a recognised standard. However, levels may change over time and we therefore did not want to make a specific recommendation about any particular level.
81	Endometriosis UK	Short	15	11	The phrase 'delaying childbearing' is a culturally loaded phrase, and can be interpreted as implying that a woman's role is to bear children – and an implication that if she has not done so she is at fault; another implication is that she has brought the endometriosis on	Thank you for your comment. We have now deleted this sentence.

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					herself by this choice. This harks back to the 'career woman's disease' as endometriosis was labelled in 1950's America. It is still a current issue that some young women and girls (sometimes under 16) are told by doctors they will be OK once they have a baby; and that pregnancy is a cure for endometriosis. We request NICE include this only if there is evidence to this effect, and reword this sentence considering the wider social implications. Is it 'delaying childbirth' or is it that girls/women are starting puberty earlier and having more periods before they have children? It may be that, if the sentence has to stand, it could be turned around eg having children at a younger age may reduce the risk of endometriosis – if there is evidence for this.	
82	Endometriosis UK	Short	15	24	We have regular reports of delays of over 10 years between first reporting symptoms and diagnosis, and do not believe giving a 10 year maximum is accurate.	Thank you for your comment. The economic modelling gives a much more robust indication of the lengths and frequency of delays experienced by women with endometriosis, so we believe saying that delays of 4-10 years 'can' occur is not inaccurate given the context of the economic model confirming that these delays can occur and describing the probabilities of delays longer than this.
83	Endometriosis UK	Short	15	28	Implies that ultrasound can be used equally as laparoscopy for diagnosis, which is not the case..	Thank you for your comment. This sentence briefly alludes to the fact that there are more or less invasive tests available in the diagnosis of endometriosis. We have made it clear in the guideline that the less invasive tests may also be less definitive and that if symptoms persist women ought to be referred for further investigations or treatment.
84	Endometriosis UK	Short	3	11	Coordinated care is very important to women with suspected or confirmed endometriosis, who often report being 'passed around' and it is good to see this recognised in the guideline.	Thank you for your comment.
85	Endometriosis UK	Short	3	13	With an average length to diagnosis of 7.5 years, we support that the guidance recognises there should be processes in place for prompt diagnosis.	Thank you for your comment.
86	Endometriosis UK	Short	3	18 19	The expertise level, training and skill required should be defined to a specific competence level. Otherwise would mean any level of expertise or training.	Thank you for your comment. We agree that 'expertise' is not very specific, but this is because being more specific in this instance would be outside the scope of a NICE Guideline; appropriate training and expertise to manage women with endometriosis will change over time, and the risk of being specific in the Guideline is that it might become obsolete in a few years. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training / skill constituted, and update this in accordance with changes to training and their understanding of the disease.

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87	Endometriosis UK	Short	3	19	"a gynaecology nurse with an interest in endometriosis' could mean any level of knowledge or training. The training and knowledge required for to constitute 'an interest' should be defined to a specific competence level.	Thank you for your comment. We agree that this recommendation is not very specific, but this is because being more specific in this instance would be outside the scope of a NICE Guideline; appropriate training and expertise to manage women with endometriosis will change over time, and the risk of being specific in the Guideline is that it might become obsolete in a few years. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training / skill constituted, and update this in accordance with changes to training and their understanding of the disease. However the Committee did agree that the recommendation as written implied a lower level of knowledge and training than they intended, and to that end changed the point to read "a gynaecology nurse specialist with an expertise in endometriosis"
88	Endometriosis UK	Short	3	21	We support the recommendation for a multidisciplinary pain management service is included in the services that women with suspected or confirmed endometriosis should have access to. This is an important aspect of managing endometriosis, well valued where it is available but reported by women as not being offered in all areas.	Thank you for your comment.
89	Endometriosis UK	Short	3	4-5	We are pleased to see that the recommendations covers suspected as well as confirmed endometriosis.	Thank you for your comment.
90	Endometriosis UK	Short	4	1	The level of expertise, training and skills should be specified in terms of a healthcare with 'an interest in' gynaecological imaging	Thank you for your comment. The details related to the content or definition of training and expertise required for specialist healthcare professionals is outside the remit of the guideline developers. Training curricula and assessment and standards of practice are set by medical professional bodies.
91	Endometriosis UK	Short	4	10	We support the inclusion of access to multidisciplinary pain management service with experience in pelvic pain is included. Women with endometriosis often give managing pain as one of their biggest challenges, yet report limited access to pain management services.	Thank you for your comment.
92	Endometriosis UK	Short	4	28	We support the provision of information for women with suspected or confirmed endometriosis. The phrase 'potential long term effects' could refer to long term effects of having endometriosis or long term effects of treatment options, and both should be included.	Thank you for your comment. We agree that the phrase 'potential long-term effects' is ambiguous, and have removed it - the Committee discussed how the concept is adequately covered by a new recommendation which reads: "1.2.1 Be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support."

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93	Endometriosis UK	Short	4	6	The level of expertise, training and skills should be specified in terms of a healthcare with 'advanced' laparoscopic surgical skills, and mapped to a competence level.	Thank you for your comment. The details related to the content or definition of training and expertise required for specialist healthcare professionals is outside the remit of the guideline developers. Training curricula and assessment and standards of practice are set by medical professional bodies.
94	Endometriosis UK	Short	4	9	We are pleased to see that access to an endometriosis specialist nurse is included. Feedback from patients is that these roles are greatly valued in supporting management of the condition.	Thank you for your comment.
95	Endometriosis UK	Short	5	17	Given that a women with endometriosis may not present with symptoms and signs, and yet endometriosis is understood to double the risk of infertility, to ask NICE to consider if it could ever be appropriate to consider infertility alone as a sign of endometriosis.	Thank you for your comment. The preamble to this recommendation states '1 or more' of the list of symptoms and signs which means that infertility alone could be a sign of endometriosis and should be considered as such.
96	Endometriosis UK	Short	5	23	To add in that a normal abdominal or pelvic examination does not exclude the possibility of endometriosis.	Thank you for your comment. We agree that this was not adequately signposted in the short guideline, and have therefore added a new overarching recommendation at the beginning of the diagnostic section reading: "1.6.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, the ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation."
97	Endometriosis UK	Short	5	7	It is good to see guidance to suspect endometriosis presenting with 1 or more of the symptoms/signs listed. Far too many women report not even hearing the word 'endometriosis until diagnosis, sometimes after many years of presenting with symptoms.	Thank you for your comment.
98	Endometriosis UK	Short	5	7	We support this including young women aged 17 and under, as we receive reports that women under 18 can still be told that they are 'too young' to have endometriosis.	Thank you for your comment.
99	Endometriosis UK	Short	6	10	To delete the word 'consider'.	Thank you for your comment. The use of the word 'consider' in this recommendation reflects the strength of the evidence (please see for further information on the wording of NICE recommendations).
100	Endometriosis UK	Short	6	12	To delete 'gynaecological service'. The level of expertise supporting a young women with confirmed or suspected endometriosis should not be based on the postcode in which they live.	Thank you for your comment. We believe that this recommendation, rather than limiting services, will encourage referral of young women to shorten the delay in diagnosis. The Committee believed that, apart from women of any age with deep endometriosis involving the bowel, bladder or ureter, the majority of women would be referred or treated in gynaecological services. It would therefore not be appropriate to remove this service from this recommendation.

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101	Endometriosis UK	Short	6	16	'Consider outpatient follow-up' could be open to significant interpretation, for example at what frequency or on what basis would an outpatient follow-up occur.	Thank you for your comment. The Committee did not want to be too prescriptive about the frequency or indications. This would be left to clinical judgement since it is based on individual circumstances and priorities.
102	Endometriosis UK	Short	6	5	To ask NICE to consider if this statement should be amended to severe, persistence of *recurrence of 1 or more of the* symptoms ….' to avoid misinterpretation that all or a majority of the symptoms would be required for referral.	Thank you for your comment. Even though it is written in plural we believe that it would be understood that severe, persistent and recurrent could refer to one or more of the symptoms or signs.
103	Endometriosis UK	Short	7	13	We would ask the word 'consider' is removed from this line.	Thank you for your comment. The use of the word 'consider' in this recommendation reflects the strength of the evidence (please see for further information on the wording of NICE recommendations).
104	Endometriosis UK	Short	7	13	We would ask the word 'consider' is removed from this line.	Thank you for your comment. The use of the word 'consider' in this recommendation reflects the strength of the evidence (please see for further information on the wording of NICE recommendations).
105	Endometriosis UK	Short	8	11	"a gynaecologist with training and skills in laparoscopic surgery" could mean any level of training. It needs to be mapped to a competence level from RCOG training.	Thank you for your comment. The details related to the content or definition of training and expertise required for specialist healthcare professionals is outside the remit of the guideline developers. Training curricula and assessment and standards of practice are set by medical professional bodies. Therefore we cannot be specific here, but we would expect professional and membership bodies to make it clear to clinicians what appropriate training constituted, and update this in accordance with changes to training and their understanding of the disease.
106	Endometriosis UK	Short	8	13	NICE are asked to review why it isn't recommended that a biopsy is taken as standard, rather than 'considered, in order to support the diagnosis of endometriosis.	Thank you for your comment. As you may be aware, NICE use the word 'consider' as technical terms to indicate the strength of the evidence. The word 'consider' highlights that the evidence is poor.
107	Endometriosis UK	Short	8	2	Whilst we note that it is stated in an earlier paragraph that pelvic MRI should not be used as the primary investigation for diagnosis, to avoid any doubt we recommend that the following sentence is added: "Do not rule out the possibility of endometriosis if the MRI scan is normal."	Thank you for your comment. The Committee discussed this comment and agreed that this should be highlighted. Consequently a new recommendation was added, reading: "1.6.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, the ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation."
108	Endometriosis UK	Short	8	2	Whilst we note that it is stated in an earlier paragraph that pelvic MRI should not be used as the primary investigation for diagnosis, to	Thank you for your comment.

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					avoid any doubt we recommend that the following sentence is added: "Do not rule out the possibility of endometriosis if the MRI scan is normal."	The Committee discussed this comment and agreed that this should be highlighted. Consequently a new recommendation was added, reading: "1.6.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, the ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation."
109	Endometriosis UK	Short	8	6	At present the only sure way of diagnosing endometriosis is through a laparoscopy by an experienced and trained gynaecologist.	Thank you for your comment. Providing laparoscopic diagnosis to all women after first suspicions arise would be neither cost effective nor advisable because first line treatment can be effective and a pelvic examination or transvaginal ultrasound does identify some cases of endometriosis. If suspicion remains and symptoms remain despite treatment a referral for a laparoscopy is recommended in the guideline.
110	Endometriosis UK	Short	8	6	At present the only sure way of diagnosing endometriosis is through a laparoscopy by an experienced and trained gynaecologist.	Thank you for your comment. Providing laparoscopic diagnosis to all women after first suspicions arise would be neither cost effective nor advisable because first line treatment can be effective and a pelvic examination or transvaginal ultrasound does identify some cases of endometriosis. If suspicion remains and symptoms remain despite treatment a referral for a laparoscopy is recommended in the guideline.
111	Endometriosis UK	Short	8	7	To consider if this should this also include if the MRI scan was normal.	Thank you for your comment. The Committee discussed and decided to add an overarching recommendation regarding the normal diagnostic findings: 1.5.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, the ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.
112	Endometriosis UK	Short	8	7	To consider if this should this also include if the MRI scan was normal.	Thank you for your comment. The Committee discussed and decided to add an overarching recommendation regarding the normal diagnostic findings: 1.5.1 Do not exclude the possibility of endometriosis if the abdominal or pelvic examination, the ultrasound or MRI is normal. If clinical suspicion remains or symptoms persist, consider referral for further assessment and investigation.
113	Faculty of Sexual and	Short	11	1.9.7	As above, suggest change to: "for example, the combined oral contraceptive pill"	Thank you for your comment. We have made the change you suggest here to the recommendation.
114	Faculty of Sexual and	Short	9	1.7.7	For accuracy suggest reword as follows : "Offer hormonal treatment (for example, the combined oral contraceptive pill or long acting reversible contraception such as	Thank you for your comment. The committee decided to re-phrase the recommendation to "Offer hormonal treatment (for example, the oral combined contraceptive pill or progestogens) to women with suspected,

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					Depo-Provera, or the levonorgestrel intra-uterine system) to women with suspected, confirmed or recurrent endometriosis." Reason for this clarification: Progestogen only pills would not be effective and in terms of LARC methods, a copper IUD or a subdermal implant would not be effective treatments.	confirmed or recurrent endometriosis" as they felt that long acting reversible contraception might include e.g. copper coil, but this would not treat endometriosis and is therefore clinically incorrect.
115	Fair Treatment for the Women of Wales	Short	10	23	If DIE and / or sizable ovarian endometrioma are anticipated ahead of surgery, we believe it would be better to simply refer these patients immediately for specialised care (planned surgery for bowel/bladder/ureter/endometrioma) from the outset rather than having patients first endure a diagnostic lap, delaying surgical treatment until later. Such an approach would seem to be more cost effective and less disruptive to the patient. Internationally, many specialist centres are able to successfully combine diagnosis and treatment of complex cases during a single procedure provided adequate pre-operative preparation is performed (record review, imaging, involvement of multidisciplinary specialists - colorectal/urology etc.).	Thank you for your comment. Throughout the guideline we have recommended that women with suspected or confirmed endometriosis involving the bowel, bladder or ureter should be referred to a specialist endometriosis service (endometriosis centre). It is then anticipated that surgery would most likely be performed in this service. However, it is not always possible to know whether endometriosis is involving the bowel, bladder or ureter and if this is discovered during a diagnostic laparoscopy further surgery may nonetheless be required.
116	Fair Treatment for the Women of Wales	Short	11	1	We would like to be apprised of the evidence for pre-operative hormone suppression. As far as we are aware there are no data available supporting the benefit of GnRH-a therapy prior to complex surgery. The rationale is that the suppression will reduce inflammation secondary to the disease and therefore allow the surgeon to resect invasive areas with narrower margins. However, another school of thought is that as pre-operative suppression works to reduce visible inflammation, its use may hamper efforts at detection and removal of all areas of disease, increasing the risk of missed disease and a subsequent need for further surgery. Patients with deep disease often also have superficial disease and it is the latter we are concerned may be missed should such an approach be adopted. Further, we should like to know what evidence is available in terms of safety / recurrence rates / reoperation rates in patients undergoing surgery for DIE with and without pre-operative ovarian suppressive therapy with GnRH-a. Given the cost of GnRH-a therapy and its harsh side-effect profile, including long-term side-effects in some patients (as well as the published data of several endometriosis treatment centres that are successfully removing deep disease without this pre-operative suppressive protocol while maintaining low recurrence rates and low complication rates), it is hard to find any real reason to support this recommendation. Patient informed consent is potentially an issue here.	Thank you for your comment. We did not identify evidence for the use of pre-operative GnRH-a therapy. However, it was consensus in the Committee based on expertise and experience that in cases of endometriosis involving the bowel, bladder or ureter this practice would help reduce bleeding prior to the procedure and therefore facilitate surgery and improve outcome. Informed consent is important for any treatment or procedure including this one. We have raised the points related to the risk of missing superficial disease and informed consent to the 'considerations of clinical benefits and harms' section related to this recommendation (see section 11.3.4.2 of the full guideline.

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117	Fair Treatment for the Women of Wales	Short	11	10	We would like to know the rationale for recommending post-operative hormone treatment. If disease is fully excised, why would this be necessary? Does the evidence support this approach in terms of long-term outcomes? From our understanding, the evidence is limited in terms of re-operation / recurrence rates.	Thank you for your comment. The results from the network meta-analysis supported this recommendation. However, we agree that this was not based on long-term outcomes such as recurrence rates. The recommendation was based both on evidence and on the consensus in the Committee. If future research provides long-term outcomes that contradicts this recommendation it could be considered in an update of the guideline.
118	Fair Treatment for the Women of Wales	Short	11	14	No explanation is given as to indications for hysterectomy. The implication in the guideline is that endometriosis alone is an indication for hysterectomy. This is concerning given the rationale for this seems to be more based in theory (ie retrograde menstruation, a theory which is increasingly being debunked) than in terms of actually treating the disease. We know that endometriosis persists despite hysterectomy in most patients (who don't have the disease removed at the same time). What is the "added value" of hysterectomy in a patient with endometriosis? The problem is that this version of the guideline only focuses on endometriosis yet ignores the fact that many women with endometriosis have complex pain due to more than one underlying pathology. There is a high degree of comorbidity between endometriosis and uterine disorders, such as adenomyosis. Hysterectomy may be indicated in cases where adenomyosis is present but this really needs to be discussed in much more detail, given the tendency for women (even those who want children) to be offered hysterectomy (invariably without adequate treatment of their endometriosis) as a "definitive treatment".	Thank you for your comment. The Committee discussed this at length, as the purpose of the recommendations was to give guidance on how to perform coincidental hysterectomies in women who have endometriosis, not to imply that hysterectomy was a positive treatment option for women with endometriosis. The wording of the recommendations have therefore been significantly changed to make this clearer, and the wording of the section heading changed to 'Hysterectomy in combination with surgical treatment for endometriosis' to further emphasise this.
119	Fair Treatment for the Women of Wales	Short	11	16	What would the indication for removal of the ovaries be if a hysterectomy is indicated? If hysterectomy is being performed for uterine pathology then presumably the ovaries are irrelevant. If the hysterectomy is being performed alongside oophorectomy in order to achieve surgical menopause to suppress the woman's endometriosis and hopefully resolve her symptoms, this is another situation and should be clearly described, along with the circumstances under which this would be an appropriate option. It is vital that women being advised to consider this option are apprised of the long-term risks to health after oophorectomy. Again, we are concerned that there is no mention of the potential for endometriosis to persist post-menopause.	Thank you for your comment. On reflection the Committee rephrased the recommendations regarding hysterectomy as follows: 1.9.8 If hysterectomy is indicated (for example in presence of adenomyosis or heavy menstrual bleeding not responding to other treatments) excise all visible endometriotic lesions at the time of hysterectomy. 1.9.9 Perform hysterectomy (with or without oophorectomy) laparoscopically when combined with surgical treatment for endometriosis unless there are contraindications. 1.9.10 For women thinking about having a hysterectomy, discuss the possibility of having oophorectomy at the same time. Discussions should include: • what a hysterectomy involves and when it may be needed • the benefits and risks of hysterectomy • that hysterectomy will be combined with excision of all

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					Women also should be made aware that if they have on-going symptoms after surgical menopause they may no longer be eligible to the same care for their symptoms as they were before menopause owing to the arbitrary exclusion of menopausal patients from the NICE guidelines.	visible endometriotic lesions • endometriosis recurrence and the possible need for further surgery • the benefits and risks of having oophorectomy at the same time
120	Fair Treatment for the Women of Wales	Short	11	5	We believe it is essential to elaborate on why excision is favourable, and to describe the circumstances under which a more conservative approach (involving ablation) would be preferable (such as low ovarian reserve for a patient wishing to preserve fertility – although, again, discussion of options in order to provide informed choice is obligatory). Recurrence rates are significantly lower following cystectomy rather than ablation. Furthermore, for those fertility patients taking Clomid or similar, excision of all disease (including endometrioma) prior to commencing fertility treatment is desirable if patients are not to experience an intolerable level of pain / symptom recurrence.	Thank you for your comment. The reason for this was stated in the related discussion section of the full guideline. The evidence showed that there was lower risk of recurrence of endometriomas with excision rather than ablation. The Committee also agreed that ablative surgery had a greater negative impact on ovarian reserve. Fertility treatments were outside the scope of the guideline and we could therefore not comment on the role of excision related to this.
121	Fair Treatment for the Women of Wales	Short	12	11	No mention is made of excision of deep disease. We would like to know if the guideline supports the resection of deep endometriosis, bearing in mind that deep excision is the only treatment that has been shown in studies to improve fertility, quality of life outcomes, and reduce symptoms in patients with DIE? While these are observational follow-up studies, this really needs to be emphasised and referral pathways to centres providing such a service clarified.	Thank you for your comment. Opinions were divided in the Committee whether surgery would be the most effective treatment for women with endometriosis involving the bowel, bladder or ureter and who are trying to conceive. We have now reworded this recommendation to ensure that all options are discussed with the woman rather than recommending surgery.
122	Fair Treatment for the Women of Wales	Short	12	15	In some cases, suppressive therapy may be of benefit to women with adenomyosis / persistent endometriosis undergoing fertility treatments.	Thank you for your comment. Assisted reproductive methods and factors affecting outcomes from assisted reproductive techniques were outside the scope of the guideline.
123	Fair Treatment for the Women of Wales	Short	12	3	We would urge the committee to recommend excision over ablation in this instance. If deep disease is present in a patient with unexplained infertility, it would make sense for her to receive specialist care to remove (excise) invasive disease, given research findings which show the benefit of deep excision in improving fertility outcomes for patients. Not only does full excision reduce inflammation (a highly toxic and unfavourable atmosphere for pregnancy) it also reduces the likelihood of adhesion formation, thereby potentially restoring normal pelvic anatomy, making conception more likely.	Thank you for your comment. The evidence showed that surgery improved the chances of spontaneous pregnancy. These studies described surgery as excision or ablation. The Committee did not want to be too prescriptive about excision rather than ablation because there are some types of lesions that would necessitate one approach over the other. It was therefore agreed that either could be recommended.
124	Fair Treatment for the Women of Wales	Short	13	General	We would urge the committee to offer definitions of the terms, 'Excision' and 'Ablation'. The latter is actually a very non-specific term and therefore rather unscientific: it refers to a group of surgical techniques with varying effects on the tissue and so a full description of these would be required.	Thank you for your comment. After discussion with the Committee, it was decided that the terms - excision and ablation - are so well understood in clinical practice that the Guideline should not be changed; while we accept the risk of encouraging further use of imprecise language, the Guideline is primarily intended to be read by practicing clinicians and patients and their families /

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					We would also urge the committee to include definitions of 'DIE (deep infiltrating endometriosis)', and 'peritoneal', 'extra-peritoneal endometriosis'.	carers, who may therefore be confused if we deviate from commonly accepted terminology. We have now added definitions for deep infiltrating endometriosis and peritoneal endometriosis to the glossary of the full guideline. However, the Committee agreed that deep infiltrating endometriosis is not a very clear description and therefore referred to 'deep endometriosis involving the bowel, bladder or ureter' in the recommendations. DIE was now only used in the context of the evidence where studies frequently used this terminology.
125	Fair Treatment for the Women of Wales	Short	14	9-10	As a Wales-based organisation, we are concerned about lack of access to gynaecologists (and specialist multi-disciplinary teams) with the appropriate level of expertise so that patients can choose between ablation and excision. Currently, the system in Wales obviates patient choice, resulting in patients continuing to have repeated, ineffective (and often inappropriate) surgeries. The Equality Impact Assessment might also make mention of health inequalities incurred by way of geography. We are concerned that, currently, there appears to be no data being collected on patients returning for repeat surgeries within routine gynaecology departments, nor is there any protocol in place for patient evaluation. For a disease such as endometriosis, where success (or failure) of interventions can often only be measured in personal, qualitative terms, this seems like a glaring omission.	Thank you for your comment. We have added geographical inequalities to the Equality Impact Assessment form. We have now also recommended that all gynaecological services for women with suspected or confirmed endometriosis should have at least access to a gynaecology specialist nurse with expertise in endometriosis. We therefore believe that this guideline will promote greater access to services and addresses geographical variation. We agree that recurrence and repeat surgeries are not often well reported in research studies which is why the draft research recommendation related to surgery is proposing a 2 year follow-up period to report such outcomes (see section 11.2.8).
126	Fair Treatment for the Women of Wales	Short	15	10	We would ask the committee to clarify what is meant by "associated with menstruation" - does this imply an etiological association or simply that symptoms often present around menstruation / that it's a "menstrual disorder"? Perhaps a better statement would simply be that it is "hormone mediated". To state an etiological association seems somewhat presumptuous given the diversity of data on the etiology of endometriosis / likelihood of several mechanisms and the presence of disease in some cases in non-menstruating patients, such as infants, post-menopausal women, and men undergoing prostate cancer treatment, for example.	Thank you for your comment. We have now used 'hormone mediated' instead as suggested.
127	Fair Treatment for the Women of Wales	Short	15	11	This seems a moot point / old data. The studies that established this are very old and limited by the diagnostic modalities in use at the time. Many women have their onset of symptoms from an age when the average woman is not thinking about having children. Many women continue to have symptoms despite pregnancy. The average age of diagnosis is the mid-20s and the average age of first pregnancy in the UK is also in the mid-to-late 20s. The statement	Thank you for your comment. We have now deleted this sentence.

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					is dated and feeds into the belief that "pregnancy cures endometriosis", which is a potentially harmful, and erroneous, belief to propagate among those caring for women with the condition. We have considerable evidence of very young women being told to get pregnant as soon as possible either to 'cure' the condition, or before they 'inevitably become infertile'. Both of these statements are patently false and cause for considerable alarm.	
128	Fair Treatment for the Women of Wales	Short	15	13-17	We would urge the committee to add further detail re the severity of pain and extent of fatigue in some patients. It is important to emphasise just how debilitating this disease can be for many sufferers.	Thank you for your comment. We have now included further detail on pain (can be chronic and severe) and the level of impact the condition can have. We have also added a new recommendation to highlight this impact.
129	Fair Treatment for the Women of Wales	Short	15	18-20	Whilst this may be true, most accept an estimate of the disease affecting around 10% of women. It may be helpful if the guideline were to outline some statistics which could give a better idea of the magnitude of the problem, such as: What percentage of women have symptoms suggestive of endometriosis? What percentage of women with symptoms suggestive of endometriosis are found to have disease at laparoscopy? What percentage of fertility patients are found to have endometriosis at laparoscopy?	Thank you for your comment. This section is a brief description of the context to outline why guidance is needed. It is not meant to be a comprehensive review of all relevant information and we agree that much more could be said on the topic.
130	Fair Treatment for the Women of Wales	Short	15	21-26	We think it is also important to describe another key factor in sufferers delaying seeking help, which is the normalisation of pelvic pain in girls / women. This indicates, as a starting point, the necessity for education in schools of normal versus abnormal menstrual health.	Thank you for your comment. We have added in that there could be a delay in women seeking help.
131	Fair Treatment for the Women of Wales	Short	15	27-28	We would advise the committee to emphasise that whilst certain diagnostic techniques may be less invasive, they are generally also less definitive. Too many women continue to be told that they can't possibly have endometriosis (or adenomyosis) because the ultrasound scan didn't show anything.	Thank you for your comment. This sentence briefly alludes to the fact that there are more or less invasive tests available in the diagnosis of endometriosis. We have made it clear in the guideline that the less invasive tests may also be less definitive and that if symptoms persist women ought to be referred for further investigations or treatment.
132	Fair Treatment for the Women of Wales	Short	15	8-9	Whilst the guideline does state 'endometrial-like tissue', in the same sentence it mentions 'womb lining outside the womb'. We do not consider this making the distinction clear. The guideline does not explain that there are pathological differences between the tissue comprising endometriosis lesions and that constituting endometrium. It seems that the guideline is leaning towards reflux menstruation as the cause of endometriosis when research shows a whole range of possible factors implicated.	Thank you for your comment. This section is a brief description of the context to briefly outline why guidance is needed. It is not meant to be a comprehensive review of all relevant information and we agree that much more could be said on the topic.
133	Fair Treatment for the Women of Wales	Short	16	22-23	This is extremely worrisome to us because all too often, these patients slip through the net.	Thank you for your comment. Extra pelvic endometriosis and endometriosis post

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					We would like to know if separate guidelines will be written for both patients with extra-pelvic disease and menopausal patients so that their specific needs are met? If not, how can we ensure their issues are explicitly covered? At this point these patients are under-served by the services in place. It makes sense that specialist centres cater to the needs of all patients with endometriosis, including these sub-groups. Indeed, to the best of our belief, at one point, the BSGE guidelines incorporated diaphragmatic excision, and specified the need for a thoracic surgeon as part of their multi-disciplinary team – we wonder what has become of those criteria? The danger of excluding menopausal patients is that those with symptoms persisting into menopause may then be excluded from accessing care because "it falls outside the treatment guidelines". This is far from ideal and could be considered in breach of any equality impact assessment which should have age as a protected characteristic. Further, in the scoping document, the reason given for excluding these sub-groups was that instances of persistent and / or extra-pelvic endometriosis were rare. This seems to smack of confirmation bias: are such cases *really* rare, or is that they are *perceived* to be rare (as evidenced by its being excluded from the guideline) and so investigation, diagnosis, and treatment do not take place? Certainly, where our own research is concerned, there seem to be significant numbers of women who are in menopause with persistent endometriosis symptoms, never having had disease properly / fully removed. Where disease outside of the pelvis is concerned, patients find it impossible to have their symptoms properly investigated for potential endometriosis. If imaging doesn't reveal anything (as is often the case) they are dismissed. We believe it is incumbent upon NICE to make provisions for these women.	menopause were discussed with stakeholders and within NICE at the beginning of guideline development when the scope was finalised. In guideline development and particularly with a new topic it is inevitable that we have to be selective and focus on improving the care of the majority of women with the condition. It was felt that the guideline already covers a lot and will improve patient care and that in future updates such issues may be considered again.
134	Fair Treatment for the Women of Wales	Short	16	4-5	We would urge the committee to once again take the opportunity to distinguish between 'remove' and 'destroy' (excision and ablation), particularly as regards the potential superiority of the former technique.	Thank you for your comment. This section of the guideline is a brief description of the context to briefly outline why guidance is needed. On reflection we would prefer to keep it as it is as we think that it is reasonable to state that these two treatment options exist. This section is not meant to be comprehensive and be biased toward a particular treatment (such as excision).
135	Fair Treatment for the Women of Wales	Short	16	5	The description, 'deposits of endometrial tissue' harkens back to the notion of retrograde menstruation and implantation. It would be better to use a less theoretically laden term to describe the disease, given that multiple mechanisms are likely at play in the onset of the disease. 'Endometriotic-like tissue' would be more encompassing.	Thank you for your comment. We have revised the wording to 'endometriotic-like tissue' as suggested.

Endometriosis: diagnosis and management

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136	Fair Treatment for the Women of Wales	Short	16	7	'…affecting women throughout their reproductive lives (and sometimes beyond)'.	Thank you for your comment. We have added '(and sometimes beyond)' to this sentence as suggested.
137	Fair Treatment for the Women of Wales	Short	18	7-10	We would advise that just because some patients with peritoneal disease don't present with pain does not mean per se that peritoneal disease does not cause pain. The same could be said of slipped cervical discs. It's not unheard of for patients with severe endometriosis (including endometrioma) to present without pain yet no-one disputes the relationship between severe endometriosis and pain. There has been at least one RCT demonstrating significant improvement in patients undergoing surgery for stage 1 (peritoneal) endometriosis versus diagnostic laparoscopy only. It is hard to establish a clear relationship in part due to the difficulties in conducting RCTs involving surgical treatments.	Thank you for your comment. We have removed the sentence referring to the possibility that peritoneal disease may not cause pain and revised the first sentence to include 'may or may not experience pain or other symptoms'.
138	Fair Treatment for the Women of Wales	Short	18	General	It is vital that NICE (along with other similar guidelines) appreciate the problems with evidence-based medicine RCT requirements - certain treatment modalities lend themselves better to this paradigm than others. Pharmaceutical studies, for example, are traditionally conducted as RCTs yet it is far harder to conduct surgical RCTs. A lack of RCTs should not in itself be a reason not to recommend a treatment. Take the example of the parachute - there is no evidence that parachutes protect against gravitational-related injury (no RCT has ever been conducted on this nor will it ever be) yet few would jump out of a plane without one! To that end, it's important that EBM idealism does not stand in the way of common sense. Another important point to consider when developing guidelines is the simple fact that selection bias is involved in the publication of studies. Drug studies are typically funded by drug manufacturers and therefore findings are unlikely to be submitted for publication unless they place the product in a favourable light. Scientific journals introduce a further layer of bias - studies on treatments demonstrating significant findings are arguably more likely to be accepted for publication than ones that fail to show significant effects even though both are equally valuable from an EBM perspective. If enough potential effect sizes are studied, the chance of type 1 errors increases. Bias in publication decision-making augments what would otherwise be a small risk of these errors occurring by encouraging researchers to cast their nets wide in the hope of gleaning something significant from their data. These points should be borne in mind by guideline committees so as not to lose sight of	Thank you for your comment. In line with the methods and processes outlined in the NICE Manual, the Committee guides the identification of the most appropriate study design to address the question being asked in the guideline. All studies that meet pre-specified inclusion criteria are then rigorously assessed for likelihood of risk of bias (including selection bias and publication bias) before results of these studies are further assessed and synthesised according to the GRADE approach.

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					common sense and reason in their plight for evidence based idealism.	
139	Fair Treatment for the Women of Wales	Short	19	General	We wonder if there is scope for exploring the impact of environmental toxins on the prevalence / experience of endometriosis.	Thank you for your comment. This guideline has terms of reference set out in the scope meaning that it can only look at the diagnosis and management of pelvic endometriosis. Consequently exploring the impact of environmental toxins on endometriosis - while fascinating - would unfortunately be out of scope.
140	Fair Treatment for the Women of Wales	Short	3	13-15	We would urge the committee to add the fact that delayed diagnosis and (ineffective) treatment can lead to further complications, such as pelvic floor dysfunction, neuropathic pain, and issues caused by the impact of extensive adhesions on organ function.	Thank you for your comment. We believe that either of these is captured by 'delays can affect quality of life and result in disease progression'. The intention of this recommendation is to highlight the need to decrease the time to diagnosis rather than listing all adverse effects as a result of a delay in diagnosis (which would be impossible).
141	Fair Treatment for the Women of Wales	Short	4	24	It is important to ensure that the information being given to the patient by her healthcare provider is accurate and up-to-date. If, for example, the information overly focuses upon one theory at the expense of others (eg Sampson's Theory of Retrograde Menstruation) this may lead the patient to make erroneous assumptions and choices about treatment options, such as a hysterectomy being the best strategy for resolving endometriosis.	Thank you for your comment. It is always assumed that clinicians will interpret NICE guidelines in light of the best available evidence and their best clinical judgement. Consequently while we cannot specify what information to give to women (as you describe, this can become out of date quite quickly), we welcome professional and membership organisations keeping their membership informed on the latest developments pertinent to the information women want to receive.
142	Fair Treatment for the Women of Wales	Short	5	13	Gastrointestinal symptoms can be month long, not necessarily just cyclical / period-related	Thank you for your comment. Our aim was to achieve an earlier diagnosis and to distinguish general gastrointestinal symptoms from endometriosis related symptoms which usually are hormonally mediated, even if they persist all month.
143	Fair Treatment for the Women of Wales	Short	5	15	Urinary symptoms can be month long, not necessarily just cyclical / period-related	Thank you for your comment. Our aim was to achieve an earlier diagnosis and to distinguish general urinary symptoms from endometriosis related symptoms which usually are hormonally mediated, even if they persist all month.
144	Fair Treatment for the Women of Wales	Short	5	20	This assumes that the primary care / first line gynaecological care providers are familiar with the examination needed to assess for endometriosis and have the expertise to perform an accurate exam. There is no mention of tenderness without nodularity. While nodularity is a more specific marker of endometriosis than tenderness alone, most women with endometriosis will not present with detectable nodularity. Most women will, however, have tenderness on exam and their symptoms may well be reproducible on exam.	Thank you for your comment. Our aim was to achieve an earlier diagnosis and to distinguish general gastrointestinal symptoms from endometriosis related symptoms which usually are hormonally mediated, even if they persist all month.

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					Furthermore, it is important to differentiate between uterine and non-uterine tenderness (i.e. not performing just a bi-manual exam but also a digital exam and/or a rectovaginal exam to detect nodularity of the rectovaginal septum). Another important point for consideration is the timing of the exam. Previous studies have noted that the likelihood of nodularity being detected depends on when the exam is timed - examination around menstruation is more likely to detect a mass than at other times even if invasive disease is present. An absence of obvious mass/nodularity should not rule out a suspicion of endometriosis if suggestive symptoms and tenderness are present.	
145	Fair Treatment for the Women of Wales	Short	5	7	No mention of symptoms presenting in women post-menopause	Thank you for your comment. Endometriosis post menopause was excluded from the scope of this guideline.
146	Fair Treatment for the Women of Wales	Short	5	General	We would urge the committee to devise a far more extensive list of symptoms, to include back-pain, fatigue, nausea, even fainting episodes (as a result of extreme pain) as common symptoms of endometriosis. We would also like to see mention of heavy / prolonged periods as being possibly suggestive of a uterine condition rather than 'simply' endometriosis.	Thank you for your comment. The evidence for any of the symptoms including those that are listed, was very limited. The list therefore represents those symptoms and signs that were supported by the evidence or where clear consensus could be reached in the Committee.
147	Fair Treatment for the Women of Wales	Short	6	10	We are not convinced that paediatric / adolescent gynaecology services are sufficiently experienced to deal with the multifarious presentations of endometriosis in younger patients. It would be better to refer such patients to a specialist centre for the condition, which can provide services for complex gynopathology.	Thank you for your comment. We agree that such services may not be most specialised in the treatment of endometriosis. However, they are specialised in caring for young women and their specific needs and would therefore be appropriate in this sense. If such services are unable to deal with complex cases of endometriosis or suspect deep endometriosis involving the bowel, bladder or ureter they would still be able to refer to a specialist endometriosis centre.
148	Fair Treatment for the Women of Wales	Short	6	19	We would ask for more clarity on specific follow-up for patients at risk of hydronephrosis (ie secondary to utereral involvement), such as renal ultrasound / IVPs.	Thank you for your comment. Specific follow-up for this condition was outside the scope of the guideline. However, women with deep endometriosis involving the bowel, bladder or ureter would be referred to a specialist endometriosis service and it is assumed that they would be able to assess related risks such as hydronephrosis and use clinical judgement to decide whether or not follow-up is needed.
149	Fair Treatment for the Women of Wales	Short	6	23	The wording here is both ambiguous and unfortunate. Presumably it means that having a (suspected) diagnosis of endometriosis does not warrant additional / special screening for gynaecological cancers despite the slight increased risk of rare ovarian cancer and not that women with endometriosis should be precluded from all surveillance	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything

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					for gyn cancers !!! It might seem obvious but, if taken literally, it could present a problem!	relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it, if they have further questions about the increased risk of cancer.
150	Fair Treatment for the Women of Wales	Short	6	7	We wonder how reliable is this tentative diagnosis in the primary care / general gynae setting, and what can be done to improve the process of referring more complex cases for specialised care. Currently, this is very hit-and-miss and results in many, repeated, operations by non-specialists with cumulatively negative outcomes.	Thank you for your comment. We recommend that the gynaecologist (in both the gynaecology as well as the specialist service for women with endometriosis) should have expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery. It is therefore assumed that this would lead to fewer negative outcomes.
151	Fair Treatment for the Women of Wales	Short	7	12	We would also wish patients to be advised of the possibility of adenomyosis, particularly if heavy / prolonged periods are of significant concern.	Thank you for your comment. We have now included some examples of indications for hysterectomy including adenomyosis in a new recommendation. We have also added text to the full guideline to explain the reason for this.
152	Fair Treatment for the Women of Wales	Short	7	16	Serum CA125 is also sometimes elevated in women with severe adenomyosis. Where endometriosis is concerned, elevated CA125 is usually more of a marker for deep disease and / or ovarian endometrioma.	Thank you for your comment. The Committee, guided by the evidence, came to the conclusion that a negative CA125 test does not exclude endometriosis and that there would be many false negative results. These would have the consequence that women would be falsely reassured and would not get the correct treatment. We therefore concluded that this would not be a recommended test for endometriosis.
153	Fair Treatment for the Women of Wales	Short	8	1	We would urge the committee to make it plain that the healthcare professional most suited to using MRI scans to visualise endometriosis should be a radiologist with specialist expertise in interpreting images of deep infiltrating endometriosis. Too often members report disease being missed as a result of scans being examined by someone unfamiliar with the condition.	Thank you for your comment. We have recommended that women with suspected deep endometriosis involving the bowel, bladder or ureter should be referred to specialist endometriosis services. In these services we have recommended that there should be access to a healthcare professional with specialist expertise in

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						gynaecological imaging of endometriosis. We therefore assume that these professionals would have training in the interpretation of images.
154	Fair Treatment for the Women of Wales	Short	8	11	It is of vital importance that the gynaecologist performing the surgery is familiar with the wide array of visual presentations of the disease, and is accustomed to conducting near-contact laparoscopy in order to detect subtle disease. Patient and uterine positioning to provide full visualization of the posterior cul-de-sac are important basic skills that are not always employed, judging by some of the surgical images seen afterwards. In addition, for those patients presenting with diaphragmatic symptoms, we wonder how often an additional port is placed in order to examine the diaphragm fully.	Thank you for your comment. We recommend that the gynaecologist in both the gynaecology as well as the specialist service for women with endometriosis should have expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery. We have added to the discussion section that this should involve training in accordance with recognised standards. We therefore believe that the guideline will raise standards of care. Endometriosis outside the pelvis is not included in the scope of this guideline and we could therefore not make any direct statements about this, such as in relation to diaphragmatic symptoms.
155	Fair Treatment for the Women of Wales	Short	8	13	We would like to see data on the reliability of a small biopsy in precluding borderline changes in endometrioma. The cyst capsule is typically lined with focal areas of endometriosis. How accurate is a small biopsy in detecting malignant changes versus complete section analysis of an excised cyst capsule? We believe the latter would provide a more reliable indication of potential malignancy.	Thank you for your comment. Assessing the reliability of a small biopsy in precluding borderline changes in endometrioma was outside the scope of this guideline.
156	Fair Treatment for the Women of Wales	Short	8	24	No mention is made of photo-documentation / video-documentation of findings during surgery. A standard for documentation should be in place to ensure that patients referred on for specialist care have adequate documentation of their disease and can avoid a need for yet another diagnostic laparoscopy prior to surgical treatment, given that each and every surgery has risks attached and can cause post-surgical scarring (thereby making subsequent access and visualisation more difficult). A lack of detailed documentation is a lost opportunity and could result in the patient having unnecessarily undergone surgery. Better written documentation of operative findings is also needed. Many patients have simply a page of short-hand notes from their surgeon (often illegible and ambiguous). It's not uncommon for discrepancies to arise between the surgeon's notes, the covering letter to the GP, and the information relayed back to the patient at her post-operative consult (which often is not with the original surgeon who performed the case). This can cause confusion and again is a missed opportunity to accurately document the disease. Perhaps a model similar to that in place in the US would be of benefit i.e. typed transcripts in a structured format in full sentences covering each aspect of the procedure - what was done and what was found, ideally accompanied by close-up photos of any evidence of disease (or demonstrating lack of disease in the areas commonly affected).	Thank you for your comment. The Committee recommended that 'the gynaecologist should document a detailed description of the appearance and site of endometriosis'. The focus of this recommendation is on what should be done rather than how. However, we have extended the discussion section in the full guideline to highlight the importance of good documentation and how this could be done (e.g. through photo-documentation / video-documentation of findings during surgery).

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					This will help avoid missed diagnosis and reduce the need for patients to undergo multiple diagnostic laparoscopies over time. Ultimately, time spent in effective transcription and documentation can save time and money further down the line, as well as offer a potentially superior experience for the patient.	
157	Fair Treatment for the Women of Wales	Short	9	21	It is important to distinguish here between the oral contraceptive pill, the coil, and Leuprolide Acetate (GnRH analogues). There are no long-term published data showing the return of normal ovarian function following Leuprolide Acetate and there have been concerns (based on the proprietary studies) as to whether patients return to a normal range of ovarian function after cessation of the drug. In the original studies, patients were followed for a year following treatment discontinuation, and around 60% of these patients failed to return to a pre-defined "normal range" of estradiol. Further follow-up was not undertaken but, obviously, this could have a bearing on fertility. In the absence of long-term follow-up, the true impact of GnRH-a therapy on fertility may be unclear. We believe it is important to make patients aware of this lack of data, so they can make an informed choice.	Thank you for your comment. The evidence showed that hormonal treatment was effective in treating endometriosis related pain. We reflected on the wording of the recommendation and have added 'permanent' to now read 'has no permanent negative effect on subsequent fertility'. Leuprolide Acetate would not usually be used as first line treatment and there are other adverse effects that would need to be discussed with women considering this treatment. We have now added to the discussion section for this recommendation that 'although there can be a delay in return to fertility after stopping treatment with hormones (which might be a particular consideration for perimenopausal women), spontaneous pregnancy rates are not affected' which is what the evidence suggested.
158	Fair Treatment for the Women of Wales	Short	9	24-26	It is essential patients are made aware that hormone therapies are palliative at best; they do not eradicate disease. Further, in order for patients to make an informed choice about treatment options, they should be apprised of the fact that research has yet to show one hormone therapy as more effective than another, and that some of them have potentially worse / longer-lasting side-effects. In addition, given the considerable data demonstrating the magnitude of some side-effects and long-term implications of GnRH-analogues, we would wish for the guidelines to make clear that add-back HRT should be offered alongside these medications. Monitoring of bone density should also be considered if patients are having GnRH-a for extended periods and / or at a young age.	Thank you for your comment. The evidence showed that hormonal treatments were very effective in treating pain for women with endometriosis (whether palliative or not). We have discussed issues around choice of hormonal treatment and the specific considerations relate to GnRH-a treatments in the discussion section for these recommendations in the full guideline.
159	Fair Treatment for the Women of Wales	Short	9	9	It is worth remembering that the majority of patients seeking medical care for symptoms will have already tried to self-manage their issues by using over-the-counter medications, including paracetamol and NSAIDs (such as ibuprofen, or naproxen, contained within such brands as Feminax Ultra).	Thank you for your comment. We believe that this would be covered by clinical history taking. In the case where analgesics (this could be over-the-counter or prescribed) have not provide adequate pain relief, we recommended to 'consider other forms of pain management and referral for further assessment.'
160	Fibroid Network UK Patient Advocacy Group	General	11	General	Impact of Medical and Surgical Treatment of **Endometriosis** on the Cure of **Endometriosis** and Pain Liselotte Mettler, R. Ruprai, Ibrahim Alkatout	Thank you for your comment. We did include the articles by Mettler et al. 2014 "Impact of Medical and Surgical Treatment of Endometriosis on the Cure of Endometriosis and Pain" and Brown et al. 2012

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					Biomed Res Int. 2014; 2014: 264653. Published online 2014 Dec 15. doi: 10.1155/2014/264653 PMCID: PMC4279262 ArticlePubReaderPDF–1.4MCitation Select item 522370269. Protocol for developing, disseminating and implementing a core outcome set for **endometriosis** There is only limited evidence to support the use of progestagens and anti-progestagens for pain associated with endometriosis. **Progestagens and anti-progestagens for pain associated with endometriosis** Julie Brown[1,*], Sari Kives[2], Muhammad Akhtar[3] Editorial Group: Cochrane Gynaecology and Fertility Group DOI: 10.1002/14651858.CD002122.pub2 http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002122.pub2/full	"Progestogens and anti-progestogens for pain associated with endometriosis" in the review of hormonal treatments. The article by Hirsch et al. 2016 "Protocol for developing, disseminating and implementing a core outcome set for endometriosis" focuses on the development, dissemination and implementation of a core outcome set for endometriosis engaging with key stakeholders, including healthcare professionals, researchers and women with endometriosis which was outside the scope of this guideline. It was therefore not included in the guideline. Even though outside the scope, there are processes in NICE guideline development which allow the utilisation of papers specifying 'core outcomes', for instance to inform strategies (protocols) for our systematic reviews. However since this paper was published at the end of our guideline development it was impossible to use this because all review protocols were agreed a long time before this (and post hoc changes were not possible at this stage).
161	Fibroid Network UK Patient Advocacy Group	General	11.1.3.4.1	General	Guidance is needed on which contraception is the best for women with endometriosis & /or fibroids. And what endometriosis medication is safe to be use with each contraceptive method ie coil or oc. Please see my 1st comment above re contraception & medications for co morbidity. Also do coils cause side effects for women with endometriosis ie scar tissue, expulsion rates,perforation of the uterus, with or without large fibroids present? As we've heard from a lot of women who experienced more pain with copper coils or Mirena. Some statistics of outcomes would be beneficial & stats on removal rates with Primary or secondary diagnosis Endometriosis. Also what are the ICD/prom codes for Medications for Endometriosis as a therapy rather than a contraceptive? In addition guidance is needed re how effective progesterone/ SPRM is for endometriosis, as they are increasingly used for multiple menstrual disorders	Thank you for your comment. With regard to contraception, we recommended hormonal treatments which would have the dual function of treating endometriosis related pain as well as acting as a contraceptive (e.g. the combined oral contraceptive pill or a progestogen). Complications related to coils were outside the scope of this guideline. Some hormonal medications are currently not licensed in the UK for endometriosis and we have added footnotes in the short guideline where relevant. We did not identify any specific evidence related to the effectiveness of progesterone/SPRM for the treatment of endometriosis and could therefore not make specific recommendations about this.
162	Fibroid Network UK Patient Advocacy Group	General	11.3	General	**Is morcellation a risk factor for the spread of endometriosis?** **Morcellation of uterus & myoma can lead to iatrogenic endometriosis,parasitic myoma & peritoneal leiomyomatosis** **Long-term sequelae of unconfined morcellation during laparoscopic gynecological surgeryAviad CohenTogas Tulandi** http://www.maturitas.org/article/S0378-5122%2816%2930322-X/fulltext#.WNYqPYOf_Qw.twitter	Thank you for your comment. The assessment of morcellation as a risk factor for the spread of endometriosis was outside the scope of this guideline and therefor this paper was not included in the guideline.

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163	Fibroid Network UK Patient Advocacy Group	General	12	General	**Endometriosis fertility** index score maybe more accurate for predicting the outcomes of in vitro fertilisation than r-AFS classification in women with **endometriosis** Wenjun Wang, Ruiqi Li, Tingfeng Fang, Lili Huang, Nengyong Ouyang, Liangan Wang, Qingxue Zhang, Dongzi Yang Reprod Biol Endocrinol. 2013; 11: 112. Published online 2013 Dec 11. doi: 10.1186/1477-7827-11-112 PMCID: PMC3866946 ArticlePubReaderPDF–721KCitation	Thank you for your comment. The article by Wang et al. 2013 was excluded as it did not match the review protocol criteria, i.e. the effectiveness of staging system has not been evaluated. The study assessed the predictive value of the staging system in IVF outcome after surgery which was not part of the scope.
164	Fibroid Network UK Patient Advocacy Group	General	12.3	General	doi: 10.4103/0366-6999.199840 PMCID: PMC5324379 **Effects of Previous Laparoscopic Surgical Diagnosis of Endometriosis on Pregnancy Outcomes** Hui Li,1 Hong-Lan Zhu,2 Xiao-Hong Chang,1 Yi Li,2 Yue Wang,2 Jing Guan,3 and Heng Cui1	Thank you for your comment. The study by Li et al. 2017 was included in the guideline as it examines the effects of previous laparoscopic surgical diagnosis of endometriosis on pregnancy outcomes which is outside the scope of this guideline.
165	Fibroid Network UK Patient Advocacy Group	General	12.4.3.2	29	On reviewing patient online groups feedback for women with fibroids & endometriosis, there was a clear difference in miscarriage rates for women post treatment. For those who had medical/ contraceptive devices &/or or had endometrial ablation, recurrent miscarriage was more prevalent, than in women who had surgical alternatives to hysterectomy . The surgical group had more live births. This needs more study. Indicating the need to follow up patient outcomes for at least 2-4 yrs post treatment. This also underlines the need to monitor live birth rates rather than conception rates. There is a tendency for this to be better reported post surgery. Medical trials do not always report these outcomes at all or in a satisfactory detailed way which would allow a proper comparison of post medical treatment Live Birth Rates vs post surgery Live birth rates, as the birth rates are frequently & concerningly missing these crucial patient outcomes. Treatment of **Endometriosis** in Women Desiring **Fertility** D. Mavrelos, E. Saridogan J Obstet Gynaecol India. 2015 Feb; 65(1): 11–16. Published online 2015 Jan 22. doi: 10.1007/s13224-014-0652-y PMCID: PMC4342385 ArticlePubReaderPDF–411KCitation	Thank you for your comment. The paper by Mavrelos et al. 2015 was excluded in the early stages of the reviewing process as it did not match the inclusion criteria defined in the review protocol.
166	Fibroid Network UK Patient Advocacy Group	General	2	General	Algorithm issues Endometriosis is commonly found with other co-morbidities ie fibroids, Menorrhagia &/ or Adenomyosis. The algorithm should take into account the different patient categories & their treatment pathways This algorithm assumes that Endometriosis is present with no other comorbidities (which is not common).	Thank you for your comment. The assessment and treatment of co-morbidities are outside the scope of this guideline. However, the diagnosis and treatment of adenomyosis will be covered in the update of the Heavy Menstrual Bleeding guideline that is currently in development. We have now added 'consider ultrasound' to page one of the

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					It suggest 1st line treatment of medication , with an ultrasound only "considered" by the non specialist before medical treatment is started. Endometriosis may not be indentified with just a pelvic exam. The algorithm doesn't suggest that any diagnostic tests/ ultrasounds are done to identify Endometriosis prior to hormonal /NSAID's /paracetamol being given for 3 months Persistent severe Pain with or without palpable comorbidities should have an ultrasound to rule out other issues , i.e. PCOS, gyne Cancers, ectopic pregnancy, fibroids. If the patient has already used med treatments prior to seeing the dr, & they're unsuccessful then they should deal with diagnosis & referral. Also if the patient has pelvic masses over 3cm at initial pelvic exam, they should have the option of direct referral to a Gynaecologists. Blood in urine may be a sign of something else & an assumption of endometriosis shouldn't be dismissed & treated with med treatments before a proper diagnosis to confirm endometriosis & rule out other issues. The 1st line med treatments could just mask symptoms, delaying more effective treatments following a proper diagnosis. Medications for menstrual disorders can often mask symptoms, of cancer, & it's essential, particularly with new experimental drugs that Drs do additional diagnostics tests to rule out cancer,breather than assuming that a new pain issue may be endometriosis & continuing medication. https://www.ncbi.nlm.nih.gov/pubmed/27539216 Unexpected Uterine **Leiomyosarcoma** During Laparoscopic Hysterectomy Treated 6 Months With **Ulipristal** Acetate and Contained Power Morcellation. Istre O. J Minim Invasive Gynecol. 2017 Feb;24(2):198. doi: 10.1016/j.jmig.2016.08.004. Epub 2016 Aug 15. PMID:27539216 Primary care is where there are more problems with endometriosis being diagnosed. The algorithm would support the current practice Also a woman shouldn't be expected to be forced to take 3 months of the new med treatment, if they've spent years on failed med treatments & they want to have access to other treatments. The algorithm needs to be evidence based	algorithm and cross-referred to the second page for the details of this to indicate that this could be done at an earlier stage rather than after referral only. Apart from the examination we do not recommend any other diagnostic tests as a first line approach and we therefore have placed them on page two of the algorithm (after referral). Persistent or severe pain or other severe symptoms or if initial management is not effective, not tolerated or is contraindicated, were all highlighted indicators that can lead to referral in recommendation 1.4.1. The reviewed evidence that assessed the risk of cancer of the reproductive organs (chapter 8) did not identify an association between uterine cancer and endometriosis. Therefore masking of symptoms was not highlighted in the guideline.

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					Coexistence of Endometriosis in Women With Symptomatic Leiomyomas-A Reappraisal of the Current Literature [8J]. Nezhat, Camran MD; Balassiano, Erika MD; Abed, Sozdar MD; Nezhat, Ceana H. MD; Soliemannjad, Rose BS; Nezhat, Farr R. MD Obstetrics & Gynecology: May 2016 doi: 10.1097/01.AOG.0000483742.58479.4f INTRODUCTION: To re-assess the coexistence of histology-proven endometriosis in women with symptomatic leiomyomas. Reappraisal of our previous study performed in 2010. METHODS: Retrospective review of a prospective data-based collection of 244 medical records from patients who were treated for symptomatic leiomyoma from March 2011 to November 2014. 208 patients underwent laparoscopic, laparoscopic-assisted myomectomy (with and without robot assistance) or hysterectomy. All patients were consented for possible concomitant diagnosis and treatment of endometriosis. The remaining 36 patients underwent medical therapy and were excluded from the study. Patients who had myomectomy or supracervical hysterectomy, underwent mini-laparotomy for extracorporeal morcellation and specimen removal starting in April 2012. RESULTS: Of the 208 patients who underwent surgical therapy, 181 were diagnosed with concomitant leiomyomas and endometriosis, while 27 were diagnosed only with leiomyomas. Of those 27 patients, 9 of them also had adenomyosis. Patients with only fibroids were on average 4.0 years older than those with endometriosis and fibroids (Mean age 44 vs 40). Patients with both diagnoses were also more likely to present with pelvic pain and nulliparity than those with fibroids alone.	
167	Fibroid Network UK Patient Advocacy Group	General	5.1.7	General	The International **Endometriosis** Evaluation Program (IEEP Study) – A Systematic Study for Physicians, Researchers and Patients S. Burghaus, T. Fehm, P. A. Fasching, S. Blum, S. K. Renner, F. Baier, T. Brodkorb, C. Fahlbusch, S. Findeklee, L. Häberle, K. Heusinger, T. Hildebrandt, J. Lermann, O. Strahl, G. Tchartchian, B. Bojahr, A. Porn, M. Fleisch, S. Reicke, T. Füger, C.-P. Hartung, J. Hackl, M. W. Beckmann, S. P. Renner Geburtshilfe Frauenheilkd. 2016 Aug; 76(8): 875–881. doi: 10.1055/s-0042-106895 PMCID: PMC5000814 ArticlePubReaderCitation	Thank you for your comment. Assessing the effectiveness of an online multicentre documentation system for women with endometriosis was outside the scope of this guideline.
168	Fibroid Network UK Patient Advocacy Group	General	5.1.8	General	Is there a need for a UK Endometriosis or Menstrual Disorders Registry like the one created in the USA by PCORI & AHRQ for Fibroids Patients with multiple long-term conditions are likely to face an	Thank you for your comment. In NICE guidelines research recommendations can only be drafted where gaps in the evidence have been directly

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					increased risk of safety failures in primary care. Should a qualitatative, applied ethnographic approach which explores issues, incidents and trajectories be useful to identify strengths & deficiencies or failures in treatment management or care. Could the existing Uterine Fibroid Embolisation registry be used as an example to adopt a highly focused approach based on the existing literature concerning patient safety in primary care. To follow a cohort of cases over time. Given the need for tailored approaches in the clinical management of multimorbidity (in contrast to the guidelines-based approach ie, usual in single conditions), an individualised case approach is likely to be most fruitful for exploring the mechanisms by which multimorbidity leads to safety failures. An Endometriosis or Menstrual disorder registry, could monitor outcomes for endometriosis, comorbidities & fertility/infertility outcomes so recommendations, can be based on best treatments for the specific patient categories. As trials have shown that some treatments are less effective. This could provide better monitoring & diagnosis reviews of new symptoms which may identify & rule out cancer as a co-morbidity. Other Patients concerns have also highlighted a need for: • Evidence based guidance on whether medical contraceptive treatments are safe pre, & post surgery for women trying to conceive. • Better comparison of medical & surgical treatments with evidence based patient information of the treatment goals that patients want to achieve with uniform baselines & outcomes that can be compared. • Comparison of post treatment medical endometriosis treatments with post treatment surgery, instead of the current during , medical treatment comparison with post treatment surgeries which leads to overstated trial outcomes, for medical treatments that often lead to higher retreatment/ surgical outcomes. • Ie in Providing better monitoring of patient safety in trials ie repeat Mri scans of pregnant women post & during Ulipristal . Monitoring of patients who have become pregnant whilst taking ulipristal • Monitoring of informed consent & patient info • Women are not aware they were in a trial of a drug with a temporary menopause effect, whilst trying to conceive , with no data , on whether it affects ovarian reserve, or so much missing data in the trial, that it's difficult to access how frequently miscarriages occur compared to no treatment or alternative conservative surgery • There is a lack of clarity of what side effects there may be & effects on long term fertility. • They are worried that, although they may kept their wombs & ovaries, in an effort to "preserve their fertility" by medications not surgery, their wombs & ovaries, may be deteriorating or impaired following long term use of the drugs. It is unclear whether pregnancies are more possible after only short term use of hormonal iud / pills or injections. Endometriosis patient groups should be consulted during trial designs so that the outcomes they want measured are reflected in the results, rather than results being cherry picked & not reflecting patient concerns.	identified in the systematic reviews of the topics in the scope. It is possible that a registry could be informative. However, the assessment of this was outside the scope of this guideline and we could therefore not write a research recommendation to promote this. The same applies to qualitative studies exploring strengths & deficiencies in treatment management or care. The issue of multimorbidity is not directly addressed in this guideline. However, women with endometriosis who have other co-existing conditions were not excluded from the scope (such as women with endometriosis as well as adenomyosis). However, the guideline is focused on endometriosis and therefore the management of the comorbidities are not part of the scope of this. We recommended that women trying to conceive should not be prescribed hormonal treatments post-surgery. We agree that some of the other topics you highlight are important. However, we are unclear which part of the short or full guideline these points are referring to and are therefore unable to comment on these in detail. Some of the topics were not in the scope and others were not prioritised by the Committee as possible research recommendations.

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169	Fibroid Network UK Patient Advocacy Group	General	6.1	General	Diagnosis of Endometriosis & classifying pain This article suggests a new framework for classification of pain This Endometriosis study shows need for a pain classification system to predict pelvic pain before & after med/surgical treatment https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4573450/ Published online 2015 Aug 11. doi: 10.1093/humrep/dev147 PMCID: PMC4573450 **Pain typology and incident endometriosis** K.C. Schliep,1,2,* S.L. Mumford,1 C.M. Peterson,3 Z. Chen,1 E.B. Johnstone,3 H.T. Sharp,3 J.B. Stanford,2 A.O. Hammoud,3 L. Sun,1 and G.M. Buck Louis1	Thank you for your comment. The paper by Schliep et al. 2015 was excluded in the early stages of the reviewing process as it did not match the inclusion criteria defined in the review protocol.
170	Fibroid Network UK Patient Advocacy Group	General	6.3	General	Diagnosis & Co morbidities Adenomyosis and **endometriosis**. Re-visiting their association and further insights into the mechanisms of auto-traumatisation. An MRI study G. Leyendecker, A. Bilgicyildirim, M. Inacker, T. Stalf, P. Huppert, G. Mall, B. Böttcher, L. Wildt Arch Gynecol Obstet. 2015; 291(4): 917–932. Published online 2014 Sep 21. doi: 10.1007/s00404-014-3437-8 PMCID: PMC4355446 ArticlePubReaderPDF–1.6MCitation Developing symptom-based predictive models of **endometriosis** as a clinical screening tool: results from a multicenter study Kelechi E. Nnoaham, Lone Hummelshoj, Stephen H. Kennedy, Crispin Jenkinson, Krina T. Zondervan, World **Endometriosis** Research Foundation Women's Health Symptom Survey Consortium Fertil Steril. 2012 Sep; 98(3): 692– 701.e5. doi: 10.1016/j.fertnstert.2012.04.022 PMCID: PMC3679490 ArticlePubReaderPDF–725KCitation Extrapelvic **endometriosis**: a rare entity or an under diagnosed condition? Nikolaos Machairiotis, Aikaterini Stylianaki, Georgios Dryllis, Paul Zarogoulidis, Paraskevi Kouroutou, Nikolaos Tsiamis, Nikolaos Katsikogiannis, Eirini Sarika, Nikolaos Courcoutsakis, Theodora Tsiouda, Andreas Gschwendtner, Konstantinos Zarogoulidis, Leonidas Sakkas, Aggeliki Baliaka, Christodoulos Machairiotis Diagn Pathol. 2013; 8: 194. Published online 2013 Dec 2. doi: 10.1186/1746-1596-8-194	Thank you for your comment. Adenomyosis, genetics factors associated with endometriosis, pathogenesis of endometriosis and development of symptom-based predicative models of endometriosis were outside the scope of this guideline and therefore this paper is not included. Symptom based screening tools were not prioritised as part of the symptoms and signs of endometriosis review because the validity of screening tools would be a separate question with a different protocol and the intention was to identify those signs that would individually raise suspicion that the condition may be endometriosis. Unless a suspicion is raised in the first instance a screen tool would not be used in the first instance. Therefore this citation was not included in the guideline. Endometriosis outside the pelvis is not included in the scope of this guideline and therefore this paper is not included. Genetic factors related to endometriosis was not included as a topic in the scope and therefore this paper is not included. We had a look at this review and have included one of the papers from this citation (Emmert et al. 1998) in our surgical diagnosis section (see chapter 9.5) of the full guideline. Other studies in this review did not match any of the review protocols.

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					PMCID: PMC3942279 ArticlePubReaderPDF–3.1MCitation Article Genetic burden associated with varying degrees of disease severity in **endometriosis** Yadav Sapkota, John Attia, Scott D. Gordon, Anjali K. Henders, Elizabeth G. Holliday, Nilufer Rahmioglu, Stuart MacGregor, Nicholas G. Martin, Mark McEvoy, Andrew P. Morris, Rodney J. Scott, Krina T. Zondervan, Grant W. Montgomery, Dale R. Nyholt Mol Hum Reprod. 2015 Jul; 21(7): 594–602. Published online 2015 Apr 16. doi: 10.1093/molehr/gav021 PMCID: PMC4487449 ArticlePubReaderPDF–346KCitation Select item 371266224. **Endometriosis** in adolescents is a hidden, progressive and severe disease that deserves attention, not just compassion I. Brosens, S. Gordts, G. Benagiano Hum Reprod. 2013 Aug; 28(8): 2026–2031. Published online 2013 Jun 5. doi: 10.1093/humrep/det243 PMCID: PMC3712662 32. Medical Management of **Endometriosis**: Emerging Evidence Linking Inflammation to Disease Pathophysiology Kaylon L. Bruner-Tran, Jennifer L. Herington, Antoni J. Duleba, Hugh S. Taylor, Kevin G. Osteen Minerva Ginecol. Author manuscript; available in PMC 2014 Apr 1. Published in final edited form as: Minerva Ginecol. 2013 Apr; 65(2): 199–213. PMCID: PMC3718308 ArticlePubReaderPDF–452KCitation	The pathophysiology of endometriosis was outside the scope of the guideline and therefore this paper is not included.
171	Fibroid Network UK Patient Advocacy Group	General	6.6.5	8	Pharmaceutical treatments to prevent recurrence of **endometriosis** following surgery: a model-based economic evaluation Sabina Sanghera, Pelham Barton, Siladitya Bhattacharya, Andrew W Horne, Tracy Elizabeth Roberts BMJ Open. 2016; 6(4): e010580. Published online 2016 Apr 15. doi: 10.1136/bmjopen-2015-010580 PMCID: PMC4838778 ArticlePubReaderPDF–1.7MCitation	Thank you for your comment. This paper is described in section 11.3.8. It was decided that the de novo model developed by the Health Economist on this guideline was of more relevance to Committee decision-making as the process for estimate elicitation described in Sanghera was less transparent than that used in a NICE Guideline, and many parameters which are estimated in Sanghera were underpinned by robust evidence in this guideline.

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172	Fibroid Network UK Patient Advocacy Group	General	7	General	There needs to be more clarity on patient outcomes for each treatment to assist women with decisional conflict over treatments. Merely making general statements like women with Endometriosis are more likely to be infertile without giving statistics, is extremely distressing for women. Also saying that treatments are uterine conserving or "preserve fertility" is also unhelpful . The statistics are needed for live birth rates for each treatment for different patient categories & co morbidities . The guideline should make research recommendations in this area. Merely restating uncertainty which could be clarified by retrospective studies &/or requesting missing trial data from product manufacturers before products are made available on the NHS should be routine to ensure patient safety Patients should also be informed online & in leaflets about where to report side effects to particularly if they are taking part in trials as they state they don't know where to give this info to, & when they tell their Drs the Dr dismisses symptoms which may be debilitating for them. They also say they withdraw from medications because of side effects, but don't report it as they have lost faith in their Dr. We are concerned that patient engagement & feedback is encouraged as short & long term follow up data is often not reported in trials. Trials report patients being "lost to follow up" however their feedback may be valuable ie they may have had a positive outcome in terms of a live birth or they may have a negative outcome re iatrogenic side effects &/or cancer diagnosis. This would not show on NHS records as a result of the previous intervention as NHS coding would allow a subsequent issue to be recorded as a new episode ie primary diagnosis, uterine cancer, secondary diagnosis pain, or Menorrhagia , & the patient is then sent to oncology. Primary care Drs & patients are not often surveyed for endometriosis. This should be encouraged in subsequent audits of this guideline. There is a lack of information of information on best treatments for the patients specific personal needs . Treatment goals are not properly elicited or addressed in the current guidelines & rare endometriosis leaflets providing the full range of treatment options: Treatment priorities for women with endometriosis who contact us or discussion groups are various & Best treatments are ones that: • Have a a low failure rate • Have a permanent effect • Minimize the amount of time spent recuperating from a treatment • Does something right away to relieve symptoms (usually people with severe menorrhagia &/or pain) • Will Avoid taking indefinite medication • Improve sexual functioning & pain • Keep the ability to have a Live Healthy Birth There is evidence that Hysterectomy is more likely where women are dissatisfied with existing treatment: https://www.ncbi.nlm.nih.gov/pubmed/18590884 Womens Health	Thank you for your comment. Decisional conflict is something that we highlighted throughout the guideline to promote an individualised approach taking into account a woman's circumstances, symptoms, priorities, desire for fertility, aspects of daily living, work and study, cultural background, and their physical, psychosexual and emotional needs (see recommendation 1.2.2). Assisted reproductive management for women trying to conceive were outside the scope of this guideline. However, we have stated that these women's care should have multidisciplinary team involvement with input from a fertility specialist and that they should also receive all diagnostic fertility tests or preoperative tests, as well as other recommended fertility treatments such as assisted reproduction that are included in the NICE guideline on fertility problems. We have highlighted limitations of our approach related to fertility in the full guideline. We believe that this guidance will promote better care for women with endometriosis and hence reduce cases where women's symptoms are dismissed. We agree that studies often do not report the necessary information, such as loss to follow-up or live births. However, guidance on trial design as well as NHS coding is outside the remit of this guideline. Implementation tools, including tools relevant to auditing, are going to be published alongside the guideline. Qualitative data on information provision was reviewed (please see chapter 7) and the Committee recommended that there should be an assessment of a women's need for information based on their individual needs (see recommendation 1.2.2). Predictors of hysterectomy as a treatment choice was not in the scope of this guideline and we could therefore not make

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					Issues. 2008 Jul-Aug;18(4):319-27. doi: 10.1016/j.whi.2008.04.001. Predictors of hysterectomy as a treatment for menstrual symptoms. Factors that increased the likelihood of hysterectomy as a treatment for menstrual problems were varied. They included the number of menstrual symptoms experienced (odds ratio [OR], 1.63; p < .005) or conditions diagnosed (such as fibroids or excessive menstrual bleeding; OR, 2.5; p < .0005), a perception that information was available about menstrual problems (OR, 1.16; p < .001), being influenced in the decision making process to elect a treatment option (OR, 1.25; p < .025), and dissatisfaction with the other treatments tried before hysterectomy (OR, 0.63; p < .0005). There needs to be better coding of proms & ICD codes to monitor outcomes so probabilities can be provided for best treatment for different patient categories. Currently NHS websites say a treatment may preserve fertility but don't say for how long? The NHS also doesn't clarify whether the treatment impairs fertility for certain patient categories . One of the reasons, we believe that the information, isn't provided is because the NHS doesn't have the statistics, because of poor coding & long term follow up of patients,, particularly in primary care and in patients receiving medical treatment. Most Medical Trials end under 1 year, before post treatment effects are available.Medication Trials should be asked to provide 4 yr + follow up , so direct comparisons with post treatment surgery outcomes, can be made. The 2007 HMB (Heavy Menstrual Bleeding) NICE Guideline , requested audits of medical & surgical treatments. Many women with endometriosis also suffer from heavy bleeding and they were identified in the HMB CG44 audit. Patients were commonly found to also have fibroids. Patient outcomes were supposed to be monitored & competencies of Drs performing surgery. In subsequent audits , there was poor recording of the patient experience:: 1. No consultation with Patient groups . 2. Poor concordance with Patients recall of medical & surgical treatments & NHS case notes which the audit suggests was because "perhaps they did not receive full information about their treatments". Informed consent & choice seems to be lacking 3. Patient survey, largely not provided in the primary care setting. The poorly responded survey was mostly administered & followed up only when the patient had reached secondary care . This means that patients experience in primary Cary was not surveyed, which is significant amount of women with fibroids. Primary care is also where medical treatment is largely administered. 4. No figures are provided for medications provided to women with fibroids i.e. Oral medication , oral contraception, IUD's i.e. Mirena, NSAID's. So it is unclear how cost-effectiveness could be measured if the NHS cannot quantify what medications are given. 5. It's unclear if all outpatient surgeries are included in the audit i.e. Hysteroscopic treatments, vaginal myomectomy, laser myomectomy. None of these are broken down & outcomes provided.	any direct statements about what leads women to choose this. There is currently an update of the Heavy Menstrual bleeding guideline in progress and we can therefore not comment on the findings of audits in relation to this. The two suggested articles, measuring the impact of endometriosis on the quality of life, did not match any of our review protocols and were therefore not included in the guideline. However, in recommendation 1.1.2 we refer to the impact of a delay in diagnosis on quality of life and we have also added a recommendation about the impact that a long-term condition can have on physical, sexual, psychological and social wellbeing.

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					6. No fertility outcomes for all medical & surgical treatments. In particular live birth outcomes & miscarriage rates, which should be ascertainable from NHS coding statistics . 7. Only outcomes are provided for some Endometrial Ablation, Hysterectomy & Myomectomy (although it's unclear if this includes out patient surgeries , i.e. Polyp /fibroids done hysteroscopically). 8. Evidence of some patients having worse quality of life, or co morbidities arising post treatment such as pain & Endometriosis . No attempt is made in subsequent audits to address these issues or look at why this may be occuring 9. The audit suggests that over 70% of trusts were providing written information to patients. Women were complaining to us that no written information or just info on the 1 treatment that the Dr told them they could have, was provided in secondary care, across the UK health trusts. No patient describes being provided with the full range of medical & surgical endometriosis or fibroid treatment choices available whilst in primary care. Endometriosis is more common than diabetes & yet written info is not available. In rare case where leaflets are provided, there is often no info on best treatments long term . The information is poorest in relation to medical treatments. We are dismayed by the amount of women experiencing recurrent miscarriage, during & post medical treatment. There is no clear monitoring of outcomes post short medical trials & patient safety issues are being ignored , particularly as some drugs i.e. Ulipristal Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries Kelechi E. Nnoaham, Lone Hummelshoj, Premila Webster, Thomas d'Hooghe, Fiorenzo de Cicco Nardone, Carlo de Cicco Nardone, Crispin Jenkinson, Stephen H. Kennedy, Krina T. Zondervan Fertil Steril. Author manuscript; available in PMC 2013 Jun 12. Published in final edited form as: Fertil Steril. 2011 Aug; 96(2): 366–373.e8. Published online 2011 Jun 30. doi: 10.1016/j.fertnstert.2011.05.090 PMCID: PMC3679489 ArticlePubReaderPDF–808KCitation Impact of endometriosis on women's lives: a qualitative study Maryam Moradi, Melissa Parker, Anne Sneddon, Violeta Lopez, David Ellwood BMC Womens Health. 2014; 14: 123. Published online 2014 Oct 4. doi: 10.1186/1472-6874-14-123 PMCID: PMC4287196 ArticlePubReaderPDF–333KCitation	

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173	Fibroid Network UK Patient Advocacy Group	General	7.6	General	Patients decisional conflict. Lack of evidence based long term patient outcomes post medical or surgical treatment and fertility outcomes. Lack of qualitative information. Primary care patients not being surveyed re treatment outcomes & fertility outcomes pre & post treatments. Management of women with endometriosis and infertility or who are nulliparous, is poor, particularly in primary care. Maximizing their chances of pregnancy by minimizing risks to fertility is essential. Early Diagnosis of the disease, rather than just the symptoms, before treatment is started, would assist in the treatment of endometriosis, particularly in the presence of comorbidities, helping to eliminate unnecessary or ineffective interventions, which would also decrease costs to the NHS. Current issues Current medical therapy for fibroids is associated with suppression of ovulation, reduction of estrogen production, or disruption of the target action of estrogen or progesterone at the receptor level, and it has the potential to interfere in endometrial development and implantation, there appears to be no role for medical therapy as a stand- alone treatment for endometriosis in the infertile population. It appears to only , reversibly , treat the symptoms, in some cases, and only temporarily, It may have no significant long term effect on the endometrios disease itself When medications are withdrawn, symptoms & endometriosis remains. Post treatment outcomes on the endometriosis disease itself is poor. With a potential further issue re fertility. We have seen on patient forums , a strong base of women having children pre & post removal of endometriosis sites. However, in women who have a history of current or recent past use of medical treatments or older coils or Ulipristal /hormonal medications, for comorbidities like fibroids, there is a high rate of miscarriages, including recurrent miscarriages. There are also arising co-morbidities PCOS & endometrial hydraplasia . Therefore current treatments need to be monitored for iatrogenic issues which may be creating additional benign diseases.	Thank you for your comment. Healthcare professionals should provide information about the condition to women with suspected or confirmed endometriosis. This could mitigate some decisional conflict. However, we acknowledge that women's circumstances and priorities change and treatment choices then have to change, too (for example related to hormonal treatments). As well as provide guidance to healthcare professional the guideline is also intended to raise awareness to promote earlier identification and diagnosis of endometriosis. This may lead to better outcomes both in way of treating pain and subfertility. The treatment of fibroids or other comorbidities is outside the scope of this guideline. However, there is an update of the Heavy Menstrual Bleeding guideline in progress. We are therefore unable to comment on this.
174	Fibroid Network UK Patient Advocacy Group	General	7.7	General	1) Improving Trial/Study design – Incorporating Missing Data on Patient Baselines / Outcomes & Iatrogenic effects of treatments & Informed Consent 2) Better monitoring of Reasons Patients withdraw from treatments 3) Better Targeting of Treatments to specific Patient Categories with /without Comorbidies 4) Retrospective Studies of Treatments for Endometriosis on the NHS & producing recommendations & better literature on benefits & risks of treatments from that information. 5) Better patient history taking, & review if previous medical/surgical treatment is associated with poorer outcomes for subsequent treatment. And which Patient Categories respond best or worse to	Thank you for your comment. The Committee made recommendations for topics that were prioritised in the scope which set out the remit of the guideline. These recommendations were based on the best available evidence. The guideline provides recommendations on information provision, referral, monitoring and treatments for women with women who have different types of endometriosis (i.e. peritoneal endometriosis, deep endometriosis or endometriomas) with the aim to improve

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					each treatment, to better target effective treatment, improving cost effectiveness of treatments & reducing costly retreatments 6) Better monitoring of Primary & Out Patient care 7) Review of whether Long term, 1st Line Medical treatment is cost effective for specific Patient categories, ie 10 yr retrospective data should be available from 2007 . Does medical treatment reduce the necessity of surgery long term. 8) Monitoring which Patient categories receiving Medical or Surgical care are more likely to have a hysterectomy & which specific treatments are more likely to result in this? 9) Monitoring outcomes & Iatrogenic effects of Medical & Surgical Treatments 10) Diagnosis Audits , Better conversions of Diagnosis of Symptom to Diagnosis of the actual Disease condition 11) More Patient information on self management, diet & lifestyle 12) Including Patient groups views in Audit Reports 13) A change to Patient Coding & episodes, & Follow up of Diagnosis 14) NHS Fertility outcomes coding review & statistics re Pregnancy/Live Births/ Abortions & Miscarriages pre & post treatments 15) Patient Surveys in both Primary & Secondary Care & acting on that information 16) Audit monitoring & follow up of Patient concerns 17) Uniform Patient Information improvements, incorporating the info above 18) Improvements in Drs discussing Fertility wishes with clients 19) Stopping discrimination of women who may not want children, from having access to alternatives to hysterectomy. 20) Better Patient Safety monitoring 21) Reviewing the definition of safe treatment as just referring to mortality rather than morbidity 22) Clearly defining what is meant by "Preserving fertility" 23) Need for guidance on timing of when women should attempt to Try to conceive following Medical or Surgical Treatment 24) Updated guidance on which medical or surgical treatments are recommended & not recommended to preserve the ability to have a live healthy birth 25) Review of the Safe periods of time that Medical or Surgical Treatments can be administered before serious adverse effects on menopause or Live Birth 26) Review of Diagnosis of various types of Uterine/endometrial /leiomyosarcoma/ ovarian cancer are better techniques available? Should tests be carried out in primary or secondary care before any treatment is started? Whose responsibility is it to eliminate the diagnosis of cancer prior to treatment? 27) Monitoring Endometriosis & Co-morbidity development in women receiving NHS Treatments 28) Better monitoring of Re-treatment rates for Medical & Surgical Treatments to ascertain, best treatments 29) Monitoring of multiple medications &/or contraception & Guidance on best practice.	services (we believe that this would address your points 3, 17, 18, 24, 32 ,35 and 39). With regard to points 1, 4, 10, 12, 13, 14, 15, 16, 33 and 34 we would like to highlight that recommendations about how trials are conducted or recommendations on surveys and audits or other studies related to implementation, as well as patient coding, is outside the remit of this guideline. Topics related to co assessment and management of co-morbidities was outside the remit of this guideline (related to the points, 3, 26, 27, 29 and 33). NICE guidelines aim to improve standards in care including improving inequalities and an Equalities Impact Assessment form is provided which addresses the protected characteristics such as disabilities. We have now also added discrimination related to women who do not want to have children to this form (related to your topics 19 and 37). For other topics highlighted by you we have looked for evidence but none was identified (related to points 7, 36, and 38) and therefore recommendations were not drafted. Timing of treatment was reviewed but no evidence was identified. However, the Committee agreed that this was an important issue and recommended that processes should be in place to provide prompt diagnosis and treatment (see section 5.2.8 in the full guideline). This related to your points 25 and 31). Related to your question about the evidence (points 39 and 40) we identified evidence that hormonal treatments are effective in improving women's pain and therefore recommended for these treatments to be offered. We did not find data that these treatments would permanently remove endometriosis or remove the need for surgery. However, the Committee agreed that effective decrease of pain would improve women's quality of life. Issues that your raise that relate to outcomes and how they were measured (related to withdrawal from treatment (2) events and life births (24 and 25) we included outcomes 'withdrawal due to adverse events' and 'spontaneous pregnancy. The former to indicate that women discontinue treatments that have many side effects and the latter as a proxy for life births which was only rarely reported.

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					30) Better monitoring of Competency of Drs performing surgery/ Diagnosis of Endometriosis appropriate Medical Treatments & geographic variations in treatments. 31) Review of when First Line Medical treatment is appropriate 32) Review of qualitative studies on the Psychosocial effects of Endometriosis on women & the effects of failed treatments on their quality of life. 33) Review of whether Drs are referring Patients to treatment recommendations for other guidelines ie fertility or menorrhagia or if it would be better to encompass all in 1 guideline due to issues with multiple treatments for associated issues 34) Review of current Quality of life measures used in UK Trials, incorporating Patient & Patient org views & the previously mentioned Fertility QALYs as this disease & it's treatment may affect the organ that creates life. 35 Better evidencing of recommendations in current guidelines 36 Plugging the Black Hole in Cost effectiveness of treatments by removing guesstimates & linking symptoms to disease & subsequent treatments & outcomes 37) Review of how patients are dealt with learning difficulties or disabilities. 38) Question whether the wait & see approach for asymptomatic endometriosis is better than starting treatment ie where no pain is present & periods are manageable. 39) Where is the evidence based patient research, supporting that women want to go from having periods to the other extreme of Amenorrhea , particularly in women without Menorrhagia, which is the current focus of medical endometriosis & fibroid trials ie replacing Hysterectomy (Permanent sterilisation by removing the womb) with Temporary medical sterilisation (creating a Menopausal state, reducing blood supply to the womb, or Mirena 5 yr medical sterilisation). 40. Where is the evidence base that medical treatments permanently remove/shrink endometriosis or fibroids long term ie over 4yrs post treatment. Guidance is needed to confirm whether the medical treatment effects on endometriosis & symptoms, reverse, post treatment. Patients also ask how long do medical treatments have to be used, to permanently remove endometriosis &/or fibroids, without the need for surgery (which can be reviewed retrospectively between 2007-2017. If there is no data, post treatment can the data be provided & if not, how can cost – effectiveness be reviewed? If there is insufficient data, then why is it currently the 1st treatment offered.	
175	Fibroid Network UK Patient Advocacy Group	General	General	General	1. This guideline affects women who contact us with endometriosis & /or IBS & a Fibroids. Fertility and medical & surgical treatments for women with fibroids & endometriosis is a large issue. In this study "87.1% of patients with a chief concern of symptomatic fibroids also had a diagnosis of histology-proven endometriosis, which affirms the need for concomitant diagnosis and intraoperative treatment of both conditions. Overlooking the coexistence of	Thank you for your comment. (1) The coexistence of endometriosis in women with symptomatic leiomyoma was outside the scope of this guideline. (2) Heavy menstrual bleeding or fibroids do not always co-exist with endometriosis. Where these signs and symptoms

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					endometriosis in women with symptomatic leiomyoma may lead to suboptimal treatment of fertility and persistent pelvic pain. It is important for physicians to be aware of the possibility of this association and to thoroughly evaluate the abdomen and pelvis for endometriosis at the time of myomectomy or hysterectomy in an effort to avoid the need for reoperation." Strong Association Between **Endometriosis** and Symptomatic Leiomyomas. Nezhat C, Li A, Abed S, Balassiano E, Soliemannjad R, Nezhat A, Nezhat CH, Nezhat F. JSLS. 2016 Jul-Sep;20(3). pii: e2016.00053. doi: 10.4293/JSLS.2016.00053. PMID:27647977 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5019190/ 2. There would be costs implications for the NHS if treatments for endometriosis are used together with treatments for fibroids and Drs are unclear whether to follow the HMB guideline or the Endometriosis guideline. Clarity would be needed on which guideline to be followed and which treatments can be used in combination or separately. 3. This guideline should be updated regularly in conjunction with the Fibroid Cks & the HMB Guideline, which does not address Endometriosis or multi morbidity. We have observed in patient feedback that women with diagnosed fibroids & endometriosis or fibroids , endometriosis & PCOS & are being given drugs for each condition ie Esmya Ulipristal & Mirena coil or zoladex & Esmya with a Mirena coil in place to help with Menorrhagia and having debilitating side effects. This guideline doesn't explain what is safe to be prescribed in these instances & gps don't appear to be following the drug information, or are unclear which condition guideline they should be following, so they're giving treatments at the same time. PCOS is also quite common because of long anovolutary periods on some of the drugs in this guideline. This can also be a source of pain for endometriosis sufferers. The guideline information should set out the benefits & risks of each drug & how long they should be used for safely, particularly as this is often a chronic long term condition.	do co-exist treatment for both or all these conditions should be considered in line with the relevant guideline. The NICE pathway will highlight which other guidance may be related which will make it easier to navigate from one to the other. (3) Guidelines are updated regularly particularly when new evidence is identified. The HMB guideline is currently being updated.
176	Fibroid Network UK Patient Advocacy Group	General	General	General	Diet & lifestyle clinical studies should be included in the guideline to enable women to self manage symptoms. There are a no of studies ongoing at the moment . At the moment when women speak to their gps about lifestyle interventions, their request for info is dismissed & they are told that nothing would work, except drugs or medication. Some women have had no or limited resolution of their symptoms with medical or surgical interventions & would like access to evidence based lifestyle interventions to self manage, which have an overall positive effect on their health without side effects.	Thank you for your comment. Diet and lifestyle interventions were prioritised as interventions that we were trying to find evidence for. However, the Committee, when planning this strategy for the review of this topic, agreed to focus on evidence from randomised controlled trials only. For diet and other lifestyle measures (for example exercise) no such evidence was identified. The evidence for acupuncture and other non-

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					It seems a somewhat blinkered in menstrual disorders to dismiss healthy interventions, particularly as there is a clear cost effective benefit to women becoming more healthy and not having to resort to costly medication or surgery. The approach taken to type II diabetes , re diet & exercise advice to avoid severe symptoms of diabetes , should be adopted & research encouraged in this area. NHS lifestyle advice for diabetes & other conditions has saved the NHS millions , avoiding a large proportion of acute disease deterioration. Over countries healthcare organisations ie USA, Italy, China etc have taken this approach & started lifestyle & disease progression research, the UK lags behind. Dairy-Food, Calcium, Magnesium, and Vitamin D Intake and **Endometriosis**: A Prospective Cohort Study Holly R. Harris, Jorge E. Chavarro, Susan Malspeis, Walter C. Willett, Stacey A. Missmer Am J Epidemiol. 2013 Mar 1; 177(5): 420–430. Published online 2013 Feb 3. doi: 10.1093/aje/kws247 PMCID: PMC3626048 ArticlePubReaderPDF–131KCitation	pharmacological treatments in reducing pain, fatigue and other symptoms was very limited and of low quality. The Committee recognised this as an important gap in the evidence base of this guideline and therefore the included a research recommendation on this topic (see section 11.2.9 of the full guideline). Such research would then inform future updates of this guideline.
177	Fibroid Network UK Patient Advocacy Group	General	General	General	Is abnormal eutopic endometrium the cause of **endometriosis**? The role of eutopic endometrium in pathogenesis of **endometriosis** Haiyuan Liu, Jing He Lang Med Sci Monit. 2011; 17(4): RA92–RA99. Published online 2011 Apr 1. doi: 10.12659/MSM.881707 PMCID: PMC3539524 ArticlePubReaderPDF–253KCitation	Thank you for your comment. Aetiology of endometriosis was outside the scope of this guideline and therefore this paper was not included in the guideline.
178	Fibroid Network UK Patient Advocacy Group	Short	12.2.1	29	Outcomes. Spontaneous Pregnancy. The Panel correctly raised the issue of the importance for patients of measuring Live Birth Rates rather than just pregnancy rates. Measuring live birth rates is better for QALY measures as for women desiring children, the treatment goal is healthy children. Current Quality of life measures for Endometriosis don't fully incorporate these issues. We recommend that in this section of the guideline, clear guidance is given. This report outlines the issue & provides cost effectiveness calculations for women with a treatment goal of children "Evaluating Cost-Effectiveness of Interventions that Affect Fertility and Childbearing: How Health Effects are Measured Matters " PMC4418217 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4418217/ Spontaneous Or Ivf induced pregnancies measures the ability to conceive but that figure routinely doesn't translate into live healthy births due to miscarriages & planned or unexpected abortions, or iatrogenic affects of medical or surgical treatments ie for some	Thank you for your comment. Spontaneous pregnancy was used as an outcome because assisted reproduction was outside the scope of this guideline. We agree that live birth rates would have been the most important outcome, the Committee was aware that this would very rarely be reported in the trials (as stated in section 12.2.2 of the full guideline). Spontaneous pregnancy rates were frequently reported which enabled us to conduct a network meta-analysis to ascertain which treatment would be the most effective to improve this outcome. We did conduct a health economic analysis based the results of this network meta-analysis. However, we agree that measuring quality of life based on spontaneous pregnancy rates has obvious limitations which are discussed in the health economic appendix (see Appendix K).

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					women the issue is not the ability to conceive , but the ability to carry the pregnancy to full term & have a live healthy birth. "Preserving fertility" by "organ conserving" treatments are also limited terms often used in trials for alternatives to hysterectomy. It is too often assumed that if there is a uterus & ovaries , left after treatment, then it will automatically going to fully fully function to create a live healthy birth. Evidence shows, that this is not always the case & many women have recurrent miscarriages despite having their organs conserved & it is important that patients are followed up post treatment to see if the treatment goal of a live healthy birth, was achieved or whether the "fertility" or pregnancy was unsuccessful. Fertility is also a limited term. In the HMB CG44 Guideline it was defined as the ability to achieve pregnancy within a year of regular unprotected sex. This again doesn't measure live birth rates , only conception rates. This is a limitation of current trials & can lead to interventions , being overstated in their benefits to patients "fertility". The guideline should encourage & make recommendations for clinicians & Trials to report live birth outcomes otherwise the poor state of trial reports on patient outcomes will continue to not feel obliged to report the final outcomes ie birth, & just report the early stages of conception NHS ICD & prom outcomes also fail to follow follow up on patient outcomes . This should be encouraged as it will be difficult or impossible to measure cost effectiveness of treatments if an analysis is not done of rate of miscarriage/. Abortion, need for Ivf & need for further interventions ie Caesarian sections & other complication interventions. Also costs of consultations for miscarriage. Poor NHS ICD coding & Proms also doesn't clearly distinguish whether when a woman who has a termination of pregnancy, ie evacuating the contents of the uterus, post pregnancy on codes, is either as a result of miscarriage or planned abortion or it has an iatrogenic cause ie unplanned pregnancy whilst using Mirena or other oral medication resulting in pregnancy loss. Therefore clear reference to live birth rates post intervention is essential to address patient treatment goals & to address cost effectiveness. It is more likely that best treatments can be identified if it meets the patients ultimate treatment goal. Current medical trials end trials too early , often under a year, which gives insufficient time for a patient to recover hormonally from treatment & complete a full term pregnancy. Lack of longer full time follow up should be discouraged by the guideline, as it leads to patient uncertainty about long terms outcomes. It is not the treatment goal of patients to just try out pregnancy, it is to have children, & become a mother.	In the analysis of evidence the aim was to make our findings as robust as possible and use the maximum number of studies to base our conclusions on. This unfortunately meant that 'live births' could not feature in the analysis because the trials did not report this. We therefore concluded that spontaneous pregnancy was a reasonable proxy related to subfertility. The Committee agreed that it was important to consider women's ovarian reserve when planning treatment. This was not intended to mean that if there was a sufficient ovarian reserve conception would necessarily happen, but the Committee agreed that it would be more likely to be possible in these cases. There currently is an update of the HMB guideline in progress. Therefore we cannot comment on the details of this guideline since it is subject to change. Investigation of fertility problems related to endometriosis as well as care during pregnancy for women with endometriosis were areas that we explicitly highlighted in that scope as those that would not be covered in this guideline. It would therefore have been difficult to focus on longer term outcomes of pregnancies without considering the care during pregnancy. In our section related to surgical treatment when fertility is the priority we focused on studies where women had been unsuccessful in trying to conceive at the outset of the study. Therefore none of the spontaneous pregnancies would have been unplanned. Abortion was therefore not an outcome that was considered for inclusion in this chapter. As stated above we do agree that 'live birth rates' would have been a good outcome. However, this was not reported and we could therefore not assess the evidence.

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					Patient baseline characteristics are often also poorly reported in trials ie if nulliparous, multiparous, pre treatment It may assist to refer in the guideline to: -conception rates (post intervention) -Pregnancy Loss Costs ie abortion, - Fetal Death /Abnormalities -Live Birth Rates (Post intervention) To clearly draw a distinction.	We agree that trial reporting is not ideal. We would like to mention the COMET initiative which is working to encourage identification of 'core outcomes' for particular conditions and reference to which would have informed development of the review protocols for this guideline.
					There are terms used in NHS Hospitals ie ***Definitions*** In the UK, gravidity is defined as the number of times that a woman has been pregnant and parity is defined as the number of times that she has given birth to a fetus with a gestational age of 24 weeks or more, regardless of whether the child was born alive or was stillborn.	We do agree that this is the ultimate goal but also think that spontaneous pregnancy rate is a good starting point to achieve this. Please see our response above about the COMET initiative.
					For example, a woman who is described as 'gravida 2, para 2 (sometimes abbreviated to G2 P2) has had two pregnancies and two deliveries after 24 weeks, and a woman who is described as 'gravida 2, para 0' (G2 P0) has had two pregnancies, neither of which survived to a gestational age of 24 weeks. If they are both currently pregnant again, these women would have the obstetric résumé of G3 P2 and G3 P0 respectively. Sometimes a suffix is added to indicate the number of miscarriages or terminations a woman has had. So if the second woman had had two miscarriages, it could be annotated G3 P0+2.	Please see our response above about trial design being outside the remit of this guideline.
					A nulliparous woman (nullip) has not given birth previously (regardless of outcome). A primagravida is in her first pregnancy. A primiparous woman has given birth once. The term 'primip' is often used interchangeably with primagravida, although technically incorrect, as a woman does not become primiparous until she has delivered her baby. A multigravida has been pregnant more than once. A multiparous woman (multip) has given birth more than once. A grand multipara is a woman who has already delivered five or more infants who have achieved a gestational age of 24 weeks or more, and such women are traditionally considered to be at higher risk than the average in subsequent pregnancies.	Thank you for the definitions. We are unsure to which part of the guideline this is referring to. We agree that parity would be a useful baseline issue. However, most of the trials focussed on women who had so far not given birth and were unsuccessfully trying to conceive. We did describe the limitations of our approach and that live birth rates were not reported in the full guideline (please refer to section 12.2.2).

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					A grand multigravida has been pregnant five times or more. A great grand multipara has delivered seven or more infants beyond 24 weeks of gestation. It would be helpful to use some of these terms in baseline & outcome figures as it would assist women to know possible outcomes in order to determine the best treatment. Poor descriptions lead to patient uncertainty & decisional conflict. Where it is not reported in trials, the guideline can make a clear statement that there is no evidence provided re births after conception. This will encourage better reporting of patient outcomes & address overstated benefits & understated risks of treatments for patients. It is unfair to compare conception only rates with live birth rates as there is a known pregnancy loss rate difference which can be as high as 20%-50% loss for some treatments **Endometriosis** doubles odds for miscarriage in patients undergoing IVF or ICSI. Pallacks C, Hirchenhain J, Krüssel JS, Fehm TN, Fehr D. Eur J Obstet Gynecol Reprod Biol. 2017 Apr 5;213:33-38. doi: 10.1016/j.ejogrb.2017.04.008. [Epub ahead of print] PMID:28419910 This study demonstrates the issues re looking solely at conception rates rather than live birth rates & how live birth rates are better for monitoring cost effectiveness: **First series of 18 pregnancies after ulipristal acetate treatment for uterine fibroids** **Mathieu Luyckx, M.D Jean-Luc Squifflet** **, M.D., Ph.D.Pascale Jadoul** **, Rafaella VotinoJacques Donnez** DOI: http://dx.doi.org/10.1016/j.fertnstert.2014.07.1253 http://www.fertstert.org/article/S0015-0282(14)02024-X/pdf This studies abstract gives the impression that Ulipristal resulted in 18 out 21 getting pregnant with 13 live births . However, On reading the full report it confirms that only 1 pregnancy occurred with Ulipristal without any other intervention. In the woman who had complete shrinkage of fibroids post Ulipristal , she conceived, but had a miscarriage. 19 of the 21 women (90.5%) needed further interventions . This was myomectomy within a few months after Ulipristal.	The references that were cited did not match any of our review protocols because assisted reproduction or risk rates for pregnancy complications were not in the scope of this guideline. The papers were therefore not included in the guideline. When to try and conceive after an intervention was not a review question that was prioritised either in the scope or by the Committee. The reason being that this would depend on many aspects that are due to individual treatments, presentations and the type of endometriosis that was treated. Patient information is obligatory and has to be tailored to the individual woman's needs and priorities. We highlighted this in section 1.2 of the short guideline. The treatment of comorbid conditions were outside the scope of this guideline. However, fibroids are covered in the HMB guideline which is currently being updated. Please see our comment above for the reason why this citation has not been included.

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					66% of these women had 5 or more fibroids after Ulipristal, (which showed the drug was ineffective in shrinking them completely & they were large enough to still require surgery after surgery). Therefore: costs of pre op Meds Costs of pre surgical assessment Further ultrasound Costs of in patient myomectomy Time off work for patient recovery However many Trust ccg's made cost effectiveness projections based on surgery not being required as the drug managed the symptoms No comparisons made with myomectomy with no pre op. Myomectomy has a higher rate of pregnancies with live births with or without pre op drugs. In the one pregnancy that resulted in a live birth, with Ulipristal as a standalone therapy, there was unfortunately a fetal abnormality, but the baby survived. This pregnancy occurred during the ulipristal drug treatment. (Which also raises questions re patient info) Therefore, live birth rates better predicts cost effectiveness & may help identify the most cost effective treatment to achieve motherhood. Guidance should also be clear on when women are safe to attempt to Try to conceive (TTC) after having specific medical or surgical interventions ie 4 weeks, 3 months etc to avoid pregnancy loss while intervention drugs or healing process is still active post treatment, to improve fertility outcomes The Guideline should also be clear in patient info on what interventions can be safely used with other treatments, or unconnected treatments for other conditions. This is essential particularly where other frequent morbidities are present like Menorrhagia symptoms &/or fibroids or PCOS. Currently 1st line medical treatments for fibroids & Menorrhagia are Ulipristal , Mirena or NSAIDS. These co morbidities have recommended treatments which may assist , exacerbate &/or mask endometriosis symptoms. Or endometriosis may arise as an iatrogenic treatment side effect of treatments for these conditions. **Pregnancy outcomes in women with endometriosis: a national record linkage study** L Saraswat[1,*], DT Ayansina[2], KG Cooper[1], S Bhattacharya[3], D Miligkos[4], AW Horne[5]and	

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					S Bhattacharya[6]6 DOI: 10.1111/1471-0528.13920	
179	Guy's and St. Thomas's Hospitals Foundation Trust	Full	13	Fig 1	Pelvic exam should mean speculum as well as bimanual examination otherwise vaginal endometriosis will be missed	Thank you for your comment. The Committee discussed this and decided to recommend 'pelvic examination' which can encompass both bimanual and speculum examinations.
180	Guy's and St. Thomas's Hospitals Foundation Trust	Full	14	Fig 1	After excision or ablation to women not wishing to conceive I would suggest replace "consider" with "recommend" post operative hormonal treatment and examples should be IUS or COCP. The point being it is ideal management to insert an IUS at time of surgery	Thank you for your comment. The use of the word 'consider' in this recommendation reflects the strength of the evidence (please see for further information on the wording of NICE recommendations).
181	Guy's and St. Thomas's Hospitals Foundation Trust	Full	171	11-25	Excellent recommendations!	Thank you for your comment.
182	Guy's and St. Thomas's Hospitals Foundation Trust	Full	174	3-5	Totally agree. Staging has only confused the issue to date	Thank you for your comment.
183	Guy's and St. Thomas's Hospitals Foundation Trust	Full	283	5	Important point but need to emphasise potential effect on destruction of follicles thereby impairing ovarian reserve	Thank you for your comment. In this section the report is summarised using 'evidence statements'. These statements describe the evidence quality type of study and total numbers of participants as well as the reported outcomes. Discussion of this evidence is then provided in the section entitled 'Evidence to recommendation' where the potential effects on ovarian reserve were highlighted.
184	Guy's and St. Thomas's Hospitals Foundation Trust	Full	285	36 37	Very important finding to guide management	Thank you for your comment.
185	Guy's and St. Thomas's Hospitals Foundation Trust	Full	286	40	Typo. Laparoscopy	Thank you for your comment. We have now corrected the error.

Endometriosis: diagnosis and management

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186	Guy's and St. Thomas's Hospitals Foundation Trust	Full	302	25 26	Even 3 months can produce significant bone loss but addback can allow long term use. These women are often young women who have not reached peck bone mass hence 3 month rather than 6 without addback	Thank you for your comment. The text has been expanded to explain that add-back therapy can be concurrently prescribed to negate the adverse effects of GnRH-a treatment.
187	Guy's and St. Thomas's Hospitals Foundation Trust	Full	304	29	Eg. More importantly increase in heart disease	Thank you for your comment. We have now expanded the sentence by adding "cardiovascular disease".
188	Guy's and St. Thomas's Hospitals Foundation Trust	Full	309	27	I think the issue of HRT needs to be expanded as it should be encouraged rather than "discussed" and it is important to recommend continuous combined HRT or tibolone rather than oestrogen alone so that non-visible endometriosis is not stimulated	Thank you for your comment. HRT as a treatment related to hysterectomy plus oophorectomy was outside the scope of this guideline. However, we have revised this bullet point to read 'the possible benefits and risks of hormone replacement therapy after hysterectomy with oophorectomy (also see the NICE guideline on menopause)'.
189	Guy's and St. Thomas's Hospitals Foundation Trust	Full	310	28	Oophorectomy for benign disease is associated with increased morbidity and mortality (mainly due to heart disease) so this needs to be taken into account	Thank you for your comment. We did not find evidence for this particular long term outcome in the evidence review. The Committee considered this and we have now added this to the discussion section for this recommendation in the full guideline (by mentioning 'cardiovascular conditions' as potential risks of oophorectomy).
190	Guy's and St. Thomas's Hospitals Foundation Trust	Full	39	10	Typo – there is a belief not the is a belief	Thank you for your comment. We have now corrected the error.
191	Guy's and St. Thomas's Hospitals Foundation Trust	Full	50	9	Typo- delete be	Thank you for your comment. We have now corrected the error.
192	Guy's and St. Thomas's Hospitals Foundation Trust	Full	61	11.12	As mentioned above completely agree that speculum examination must be done otherwise vaginal nodules may be missed	Thank you for your comment. The Committee discussed this and decided to recommend 'pelvic examination' which can encompass both bimanual and speculum examinations.

Endometriosis: diagnosis and management

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193	Guy's and St. Thomas's Hospitals Foundation Trust	Full	General	General	The authors are to be congratulated. These guidelines are very sensible and will aid management. The areas that I have slight issue with are: 1. oophorectomy and HRT guidance – more guidance could be given. Patients are often wrongly given unopposed oestrogen post op and years later may run into problems eg ureteric obstruction laparoscopic hysterectomy for severe endometriosis. This is usually not possible with the cases that we have in our unit as the bowel involvement is so severe that laparoscopic approach is not the safest option	Thank you for your comment. HRT treatment post oophorectomy was outside the scope of this guideline and we were therefore only able to cross-refer to the NICE menopause guideline for this. We have reworded the heading and the recommendations related to hysterectomy to indicate that it is the excisional surgery rather than the hysterectomy that constitutes the treatment of endometriosis in this context. The laparoscopic route is therefore recommended because it best allows the excision of endometriotic lesions at the same time as the hysterectomy.
194	Guy's and St. Thomas's Hospitals Foundation Trust	Short	10	13-21	With the obesity crisis many women will need to discuss weight reduction at this point if laparoscopy is the next stage	Thank you for your comment. These are examples of what should be discussed with a women related to surgery. The list is not exhaustive and allows clinical judgement for any other matters, including weight reduction, to be discussed. However, the impact of obesity on laparoscopic surgery were outside the scope of this guideline.
195	Guy's and St. Thomas's Hospitals Foundation Trust	Short	11	20-23	This discussion needs to cover the fact that woman's morbidity and mortality is increased if ovaries are removed as their risk of heart disease is increased	Thank you for your comment. We have now added to the full guideline text that the implications of oophorectomy may include risks related to cardiovascular conditions.
196	Guy's and St. Thomas's Hospitals Foundation Trust	Short	5	20	Pelvic examination should include speculum and bimanual examinations	Thank you for your comment. The Committee discussed this and decided to recommend 'pelvic examination' which can encompass both bimanual and speculum examinations.
197	Guy's and St. Thomas's Hospitals Foundation Trust	Short	6	10	I would suggest changing this to 15 and under. 16 and 17 year olds may not want to be under a paediatric clinic	Thank you for your comment. We would like this to remain age 17 and under and leave it to individual healthcare professionals and the young women to decide whether this would be the most appropriate referral option.
198	Guy's and St. Thomas's Hospitals Foundation Trust	Short	6	21	I would recommend that "small" risk needs to be quantified	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were

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						unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it, if they have further questions about the increased risk of cancer.
199	Guy's and St. Thomas's Hospitals Foundation Trust	Short	9	18	I was surprised to see this here! I don't think it is worth mentioning as some people may start trying it and it has not been used here in the UK and may cause harm	Thank you for your comment. On reflection, the Committee decided to remove this recommendation on the basis that this intervention is not being used in clinical practice.
200	HQT Diagnostics	Full	General	General	We are very concerned that no guidance is being given about an anti-inflammatory diet. There is very good evidence that diet contributes to the Inflammation that presents as Endometriosis GP to refer patient at first presentation to a Dietitian or Nutritional Therapist who can review the current diet of the patient and suggest changes to one that is more anti-inflammatory Dietitians https://www.bda.uk.com/ Nutritional Therapists http://bant.org.uk/	Thank you for your comment. Specialist diets were included in our protocol, and therefore would have been included if any high-quality evidence was found supporting their use. Unfortunately no such evidence was found, and so the Committee felt unable to make recommendations.
201	HQT Diagnostics	Full	General	General	There is very good evidence that increasing Vitamin D levels of 25(OH)D to 100-150 nmol/L helps to prevent and treat the Inflammation that presents as Endometriosis GP to advise suitable amounts of Vitamin D to adjust the level and review after 3 months Source: https://is.gd/endo21 https://www.vitamindwiki.com/Inflammation https://www.ncbi.nlm.nih.gov/pubmed/23380045	Thank you for your comment. The Committee prioritised randomised controlled trials as study design in the protocol for the review question that included diet (see Appendix D). Therefore the publications that you highlight were not included.
202	HQT Diagnostics	Full	General	General	There is very good evidence that adjusting Omega-3 and Omega-6 levels helps to prevent and treat the inflammation that presents as Endometriosis **Key Indicators**….**Target**…**Comments** **Omega-3 Index**…>8%.....Is the Omega-3 level high enough ? **Omega-6/3 Ratio** <3:1……Is the Inflammation low enough ? Increasing Omega-3 may need 2-5 grams of Omega-3 per day. Reducing Omega-6 needs advice about diet and lifestyle from a Dietitian or Nutritional Therapist	Thank you for your comment. The Committee prioritised randomised controlled trials as study design in the protocol for the review question that included diet (see Appendix D). Therefore the publications that you highlight were not included.

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					Source: http://www.expertomega3.com/omega-3-studies/inflammatory-diseases https://www.ncbi.nlm.nih.gov/pubmed/25539770 https://is.gd/endo22	
203	NHS England	Full	181	l. 1	The decision to be cautious about the use of opioids and the decision to refer for diagnosis is sensible. This is also a point where good pain management services should be involved as they assess the biological as well as psychological and social impact of pain and can provide intervention at all levels balanced on the individual case. Drug options may be part of that plan but will be balanced according to the individual presentation.	Thank you for your comment. We have increased discussion of the pain management service in the full guideline to make it clearer when and how this service should get involved with the woman's management.
204	NHS England	Full	181	l. 4	NICE Neuropathic pain guidance (CG173) is mentioned but could be clearer within the guidance. Despite them being generic for neuropathic pain and specific research is lacking for endometriosis the underlying mechanisms are in part neuropathic. The best evidence available is contained within that guidance and as such should be emphasised more clearly. The review question is entirely appropriate and further work is required to evaluate the effectiveness of these agents for endometriosis.	Thank you for your comment. The Committee decided to cross-reference to CG173 rather than use the evidence within the CG173 to draft recommendations. The current guideline did not identify any relevant evidence and the Committee decided not to use the evidence from CG173. They felt that the evidence would be indirect and it would therefore be classified as very low quality. They felt it would be more appropriate for healthcare professionals to refer to CG173 rather than for the Committee to draw conclusion from evidence that may not always be applicable in the context of Endometriosis.
205	NHS England	Full	40	l. 40	The involvement of a multidisciplinary pain service with an expertise in pelvic pain is strongly supported within the specialist endometriosis services (endometriosis centers) model.	Thank you for your comment. We are pleased you support the recommendations on the involvement of a multidisciplinary pain service with an expertise in pelvic pain. Owing to significant stakeholder desire to reinforce this message some additional economic analysis around this point has been added to the full guideline.
206	NHS England	Full	49	l. 23	The inclusion of a multidisciplinary pelvic pain management service (namely a pain management service with pelvic pain expertise) is supported for the added benefits it will bring to this smaller but important patient population. The impact of this will be to optimise management and improve patients quality of life. Although more costly with this service the benefits will be seen in other areas such as medication use, hospital visits, GP visits, functional ability, potential to work, reduced carer requirement and general self worth. Difficult to put a financial value on but clearly of significance to both the individual and society.	Thank you for your comment. We are pleased you support the recommendations on the involvement of a multidisciplinary pain service with an expertise in pelvic pain. Owing to significant stakeholder desire to reinforce this message some additional economic analysis around this point has been added to the full guideline.
207	NHS England	Full	50	l. 23	The inclusion of a pain management service within gynaecological services is welcomed and there should be formal lines for referral and discussion about management decisions. Thus the link should be more formal than having access to but the physical input can be adjusted according to local demand.	Thank you for your comment. The Committee did not review any evidence relating to the optimal configuration of pain management services and so were unable to make a recommendation any stronger than that the woman should have 'access' to them.
208	NHS England	Full	50	l. 32	Pain management services with pelvic pain expertise should be part of the team rather than only having access available. In the short	Thank you for your comment.

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					term this may be difficult as there are not many such services about. In that case there should be a pain management service as part of the team rather than only having access to such a team. The reason is that early pain management involvement will allow a broader biopsychosocial understanding form earlier in the patients journey and aid optimal management. This is also highlighted in the health economic statement on p.51 l.34.	The Committee did not review any evidence relating to the optimal configuration of pain management services and so were unable to make a recommendation any stronger than that the woman should have 'access' to them.
209	NHS England	Full & Short	General	General	Overall we feel this is a well balanced document with genuine potential to improve patient care and management. The inclusion of pain management at local, specialist and specialised levels are welcomed. This should be integrated as part of the pathway.	Thank you for your comment.
210	NHS England	Full & Short	General	General	The inclusion of pain management in the multidisciplinary teams is welcomed and should be essential at the gynaecological service and endometriosis centre level.	Thank you for your comment.
211	NHS England	Full & Short	General	General	That this NICE guidance when finalised is proactively forwarded and used to update the NHS Choices website on endometriosis and pelvic pain. This should include the pain management recommendations. Also that this is more clearly linked to the neuropathic pain guidance on the site.	Thank you for your response. Your comments will be considered by NICE where relevant support activity is being planned.
212	NHS England	Full & Short	General	General	That this guidance is also used to inform both patients and carers and made available in a form to allow them to engage with the guidance.	Thank you for your comment. Guideline recommendations are available to all (including patients) and the key messages for patients will be highlighted in the information for the public table.
213	Pelvic Pain Support Network	Full	157	10 11	Could it be mentioned here that where there is severe CPP, dysmenorrhoea, endometriomas, deep nodules that an MRI should be considered as the latter can be obscured by adhesions and fibrosis during laparoscopy ?	Thank you for your comment. We have added these as examples of symptoms and signs that may be considered as indications for an MRI into this discussion section.
214	Pelvic Pain Support Network	Full	General	General	Reference to Culley in the qualitative section as from Australia is incorrect. This should be under UK	Thank you for your comment. A corresponding amendment was made.
215	Pelvic Pain Support Network	Full and Short	General	General	There are several references to TVS, MRI but expertise is very limited nationally. Health professionals and patients need to know where this expertise is.	Thank you for your comment. We have recommended that MRI should not be used as the primary investigation for endometriosis. However, it should be considered to assess the extent of deep endometriosis and should be carried out by a healthcare professional with specialist expertise in gynaecological imaging. There would be access to such healthcare professionals in specialist endometriosis services. We therefore believe that the guideline would address equalities in access to these professionals.
216	Pelvic Pain Support Network	Full and Short	General	General	Many specialist centres do not have access to a multi-disciplinary pelvic pain team/service as these are few and far between.	Thank you for your comment. The Committee accepts that many areas do not have access to a specialist pain management service, but in view of the economic and clinical evidence supporting the effectiveness of such a service believe it is important to ensure that these services are made available. The recommendation was made

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						precisely to ensure all women would have access to the service.
217	Pelvic Pain Support Network	Full and Short	General	General	The word "consider" is frequently used in many cases where the word "should" would greatly enhance patient care. What is the reason for this ?	Thank you for your comment. The use of the word 'consider' in these recommendations reflects the strength of the evidence (please see for further information on the wording of NICE recommendations).
218	Pelvic Pain Support Network	Short	15	Lines 11-12	Was this meant to say " associated with endometriosis" rather than "a risk factor for endometriosis" ?	Thank you for your comment. On reflection we have now deleted this sentence altogether.
219	Pelvic Pain Support Network	Short	General	General	There seems to be hardly any mention of the importance of Diagnosis in the short version. What is the reason for this ?	Thank you for your comment. We believe that this is covered by the recommendation that services should 'have processes in place for prompt diagnosis and treatment of endometriosis, because delays can affect quality of life and result in disease progression'.
220	Primary Care Women's Health Forum	Full	General	General	It is important to raise awareness and reduce the length of time to management of endometriosis to improve quality of life and reduce the complications associated with the condition. However this guidance does not give clear recommendations about who should be referred for laparoscopy and who should be managed in primary care. If all women are referred for laparoscopy the costs of referral, waiting times and risks of surgery will be increased. Without clearer guidance patient expectation will be to follow an unachievable pathway of care.	Thank you for your comment. We indicated that analgesics and hormonal treatments would be initial treatments. It is also recommended referring women to other services for investigations and treatment options if these initial treatments are 'not effective, not tolerated or contraindicated. After referral, treatment decisions would then be based on women's priorities and symptoms or signs and could involve another hormonal treatment (GnRH-a) or surgical options. We have now provided further detail to the relevant discussion section to explain what is meant by 'investigation and treatment options'.
221	Primary Care Women's Health Forum	Full	General	General	The guidance recommends that some women are referred to the gynaecology service and some to specialist centres. Most primary care clinicians (referrers) will be unable to make the distinction between the referral options without extra training with the risk being reduced availability of specialist clinicians because of an increase in referrals. Clearer recommendations are required or advice to refer following routine pathways with the gynaecology units making the tertiary referrals.	Thank you for your comment. The Committee discussed referral in detail and the algorithm provides a graphical guide to this. We agree that deep endometriosis involving the bowel, bladder or ureter may be difficult to diagnose for a primary care physician. However, the Committee believed that the combination of recommendations 1.3.1 and 1.4.1 would clarify when to suspect endometriosis (including cyclical bowel and ureter symptoms) and also the situations when to refer to other services. Deep endometriosis involving the bowel, bladder or ureter is present in the minority of cases. If the steps would result in referral of a women with deep endometriosis involving the bowel bladder or ureter to a gynaecology rather than the specialist endometriosis service it is most likely that deep endometriosis involving the bowel, bladder or ureter would be identified at this point and women would then be referred to a specialist service. We believe that the graphical presentation (the algorithm – see Figure 1) shows this process more clearly.
222	PRIME HEALTH LONDON	short	4	1.2	**Question 1**	Thank you for your comment.

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					Information & Support We are concerned that this recommendation is assuming that all possible Equality Impact were assessed. In addition to the areas identified, Prime Health London's research showed that there are other areas of equality that the recommendation do not highlight and as a consequence could marginalise BAME women. For example, some of the factors that prevent some cultural groups seeking gynaecological help maybe due to close family connections at primary care level. Also, in some cases where women may need an interpreter, until cultural awareness is effectively promoted, extreme care should be taken so as not to endanger but protect women from cultural stigma of being diagnosed with endometriosis.	We have altered the wording of the recommendations in the 'information and support' section to include a discussion of the information and support needs arising from a woman's cultural background. While we accept that there may be issues arising from the fact that different groups of women seek treatment at differential rates, the decision to seek initial diagnosis is outside the scope of this guideline; however we welcome efforts from support groups in raising awareness of the condition amongst BAME communities.
223	PRIME HEALTH LONDON	short	4	1.2	**Question 2** 1.2 **Endometriosis information and support** We are concerned that this recommendation may imply that there are currently available culturally sensitive support and information available for BAME women group. The Endocul research and Prime Health London's further research into the cultural impact of endometriosis have showed that currently, there are not sufficient information and support available either in the community, primary or to some degree at secondary care level for these marginalised group. Therefore, we feel this recommendation will be challenging in practice because research are showing that BAME women in particular, are finding it difficult to get the best care and patient experience due to: • High level lack of awareness of endometriosis • Initial lack of culturally sensitive information on Endometriosis • Cultural interpretation of signs and symptoms of Endometriosis. • Cultural stigma of being diagnosed with endometriosis We agree that there is an urgent need to educate young girls, but again, unless the cultural aspect of reproductive health is addressed with the parents, we could be flogging a "dead horse". This is because in some of the BAME groups, mothers and grandmothers are the gate keepers. For any reproductive health education to be effective among young girls from diverse cultural background, Gate Keepers need to understand the benefits, impact of endometriosis education on future aspirations and quality of family life before we can expect to achieve a measure of success of education of endometriosis in certain cultural young girls.	Thank you for your comment. We have altered the wording of the recommendations in the 'information and support' section to include a discussion of the information and support needs arising from a woman's cultural background. While we accept that there may be issues arising from the fact that certain BAME communities have 'gatekeepers' in a way that others do not. We welcome efforts from support groups in raising awareness of the condition amongst BAME communities.
224	PRIME HEALTH LONDON	short	6	1.4	1.4 Referral and monitoring Our evidence showed that currently there are a number of factors influencing certain cultural groups accessing primary and secondary healthcare pathways. These factors are causing extra delay in BAME women getting firm diagnosis of endometriosis. We feel therefore that unless some of these factors are addressed, navigating the referral and monitoring systems could be challenging for some cultural groups.	Thank you for your comment. We have altered the wording of the recommendations in the 'information and support' section to include a discussion of the information and support needs arising from a woman's cultural background.

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225	PRIME HEALTH LONDON	short	7	1.5	1.5 Diagnosing endometriosis 1.5.2 If a transvaginal scan is not appropriate (for example, in women who have 10 never had sexual intercourse), consider a transabdominal ultrasound scan 11 of the pelvis……. Although this is stated, evidence are coming back to our office of girls not sexually active being pressurized to submit to transvaginal ultrasound examination. For example - **In fact, only 4 weeks ago, we had a call from a girl who is not sexually active crying stating that the ultrasound person had insisted that she carried out transvaginal scan, but not agreeing to it, the person carried it out anyway**. I feel therefore that further clear guidelines to protect girls who are not sexually active but may require some form of ultrasound procedure is required.	Thank you for your comment. Young women aged 17 years and younger were part of our specific Equalities Impact Assessment groups and we therefore considered their treatment carefully throughout the guideline. We believe that this recommendation as well as the recommendation regarding referral to paediatric and adolescent gynaecology services will promote better practice in this area.
226	PRIME HEALTH LONDON	Short	General	General	**Questions 3** There is currently no structured BAME • Grass-root systematic Health promotion educational awareness campaign • Culturally sensitive support community Organisation • Culturally sensitive information & literature for the diverse cultural groups in England – where possible in various ethnic languages We feel therefore that there is an urgent need for a systematic community support for BAME women. Therefore setting taking up some of the above recommendations will help BAME women overcome many challenges in obtaining a firm diagnosis and support for endometriosis for themselves and family members. Our organisation, Prime Health London, has had experience of implementing grass-root systematic health promotion awareness campaign approaches and research into the level of lack of awareness and impact with various BAME & University women and we would be willing to submit our research findings and experiences to the NICE shared learning database	Thank you for your comment. We have altered the wording of the recommendations in the 'information and support' section to include a discussion of the information and support needs arising from a woman's cultural background. While we accept that there may be issues arising from the fact that different groups of women seek treatment at differential rates, the decision to seek initial diagnosis is outside the scope of this guideline; however we welcome efforts from support groups in raising awareness of the condition amongst BAME communities.
227	RCGP	Full	13	2.2.1	The algorithm is much clearer about what should happen in non-specialist services than the text in the short guideline. In particular that non-specialist should initiate trial of treatment with analgesics and hormonal treatments for a 3 month period before referral. Could it be included in the short guideline?	Thank you for your comment. The algorithm is meant to present the recommendations graphically and we have therefore changed the wording in the algorithm to be consistent with this.
228	RCGP	Full	52	5.2.7	• To illustrate the comment above about GPs, here are the relevant statements from the full version: *'The Committee*	Thank you for your comments.

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				6.6.2	• *discussed the obvious fact that no individual healthcare professional intentionally delays the diagnosis of endometriosis, but that this is currently not foremost on their minds when a woman presents with pelvic pain'* Is there any evidence to support it? • Similarly: *'…The Committee agreed that GPs do not always suspect endometriosis …'* What is the basis for this statement? The committee might argue that the inclusion of the word *'always'* almost certainly makes the statement correct; but I would maintain that it has the effect of denigrating GPs. I doubt the need for specialist nurses in every centre. What will they do? A discussion among work colleagues (none of whom has ever had a special interest in endometriosis) revealed a clear consensus that GPs need help with diagnosis, and specialist help with complicated cases where surgery is required, but we all feel confident at our ability to manage less complicated cases.	We agree that this wording was confusing and we have removed the word 'obvious' and have rephrased the sentence to clarify that these delays cause women concerns and that endometriosis should be suspected, i.e. at the first presentation of symptoms. With regard to your second point, the nurse acts as a vital link between the patient and their management pathway, being available to communicate with and support them when required. As most endometriosis nurses recruited to this role have other roles within gynaecology (as part of their working week) it's crucial to emphasise that nurses receive a robust training preferably with an accredited course which is supported by the RCN working in conjunction with BSGE to meet all expected criteria. This should equip the nurse to provide knowledge and expertise skills enabling them to meet patients psychological/psychosexual needs and expectations and by supporting them and their families through their pathway. We agree that they would not be required in every location treating endometriosis (where the role could be fulfilled by a gynaecology nurse specialist with an expertise in endometriosis), but the Committee believed the evidence of specialist support needs of women with endometriosis severe enough to be treated in specialist centres was so compelling that it necessitated a more highly specialist qualification.
229	RCGP	Full	7	1.5.4-5	• Again this is confusing with contradictory advice from NICE Ovarian Cancer CG122: ○ "1.1.2.1 Measure serum CA125 in primary care in women with symptoms that suggest ovarian cancer (see section 1.1.1). ○ 1.1.2.2 If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis. ○ 1.1.2.3 If the ultrasound suggests ovarian cancer, refer the woman urgently for further investigation. ○ 1.1.2.4 For any woman who has normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound: ○ assess her carefully for other clinical causes of her symptoms and investigate if appropriate if no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent."	Thank you for your comment. We do not believe that the recommendations are inconsistent with each other. The population described in CG122 1.1.2.1 are women in primary care with symptoms consistent with ovarian cancer, whereas the population in this guideline recommendation 1.5.4 are women in primary care with symptoms consistent with endometriosis and a coincidentally available report of serum CA-125 levels. It would be possible for a woman to have signs suggestive of both endometriosis and ovarian cancer, in which case she would have her serum CA-125 measured in keeping with CG122 1.1.2.1 and then this result not used to diagnose endometriosis in keeping with our recommendation 1.5.5. In all other cases the women form different populations.
230	RCGP	Full & Short		1.4.5 & 1.4.6 (Short) 8.6 (Full)	Risk of ovarian cancer. The recommendation is made that women should be advised they have a small (not quantified) risk of ovarian cancer, but that they should not be offered any additional surveillance. This can only be a harmful intervention.	Thank you for your comment. The Committee reflected on the evidence and the comments related to this. The two recommendations related to this have now been deleted. The purpose of the original wording which you have commented on was to try and balance the need of the woman to be fully informed about her condition with the need to avoid overinvestigating women with possible cancer

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						(not least because of the anxiety it would cause the woman). That is to say; that the risk increase was considered to be so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. However, since the evidence did not allow us to quantify this risk it was decided to remove this altogether. We have now explained in the full guideline why no recommendation was made. After discussion, the Committee decided that due to various limitations in the data they were unable to quantify the absolute risk and therefore would not be able to reassure the women with a numerical estimation of this probability. They therefore decided that recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Furthermore national screening is related to cervical not ovarian cancer and therefore the issue of surveillance may be misconstrued to indicate that women should not be invited to the regular screening tests. The discussion of these issues and why recommendations have not been made has now been moved to the full guideline.
231	RCGP	Full & Short	Algorithm	1.4.1 2.2	Referral. In both versions it is implied that patients should be referred to a specialist centre, and only after that be investigated. Given that both ultrasound and MRI are available to at least some GPs, why is there no option allowed for such investigation to take place by direct access from primary care?	Thank you for your comment. In the ultrasound section of the short guideline we state 'consider transvaginal ultrasound….' and we intentionally did not specify which service or healthcare professional should consider this. We did not exclude the possibility that this would be done in a primary care setting where available and appropriate. We agree that this was less clear in the algorithm figure where we tried to separate initial investigations from diagnosis and treatment. To address your comment we have now placed ultrasound in two different sections of the figure and cross referred.
232	RCGP	Full & short	General	General	• I have consulted both long & short versions, and it has been fascinating to contrast the careful, qualified statements in the full version with occasionally simpler, apparently less tentative statements in the short one. One general comment is the striking way in which primary care is virtually written out of the guidelines, The implication appears to be that primary care is responsible for the long delays in diagnosis without, apparently, any cited evidence. At one point self-help groups are quoted as laying the blame at GPs doors, but the guideline itself thinks such statements are likely to be subject to extensive recall bias. I wondered why there is the casual, but repetitive denigration of GPs, and then saw that the committee predominantly 7 specialists HCP's and 1 GP.	Thank you for your comment. We are sorry you felt the guideline does not appreciate GPs. The Committee included both a GP and a Commissioner, both of whom were aware of the pressures GPs are under. Furthermore the specialist HCPs on the Committee regularly expressed their support for the valuable work their GP colleagues performed for women with endometriosis. However, such comments are unlikely to be reflected in the Guideline as they do not relate to the diagnosis and management of women with pelvic endometriosis. We do not agree that primary care is written out of the guideline. In organisation of care we have now specifically referred to 'community services'. However, we did not want to specifically name the physician and service that should carry out the action in each recommendation because this could

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						depend on many different factors. We have made specific recommendations related to referral of women with suspected endometriosis which we believe apply mainly to primary care. In the review of qualitative evidence related to information and support that women need, there are some comments about GPs. These relate to what was reported in the studies rather than what was believed by the Committee. The quality of these comments was also appraised as only low to moderate quality. The Committee did, however, want to highlight the significant and well-evidenced delays experienced by women between the onset of symptoms and their first diagnosis. While this can be attributed to a variety of causes (lack of patient awareness of the condition, cultural expectations of painful periods etc.) the only factor over which NICE is directly able to make recommendations is the behaviour and training of GPs. This should not be taken to indicate that the Committee think that the behaviour and training of GPs is the largest (or even a substantial) contributor to the delay experienced by women, only that it is likely to be the most substantial contributor over which NICE is able to make recommendations, based on the experience of the Committee and Health Economic modelling.
233	RCGP	Full & Short	General	General	• The guidance given is clear and step by step with this complicated and disabling condition. The specialist endometriosis centres are welcome even though it means a lot of travelling for many patients. • Ideally I would like a little more recognition and guidance for those with chronic severe or even "burnt out" endometriosis which seems to give chronic bowel symptoms, and chronic pain and disability. The end of the road use of morphine derivatives results in even more disabling psychological and physical side effects. it's hard to sort out what are complications of surgery and what are the effects of the disease. GPs often have several such complex patients on their lists and even have to involve social care to help. Somehow the guidance seems light on this (understandably) although anxious to prevent the disease progression.	Thank you for your comment. One of our recommendations now describes that women with deep endometriosis involving the bowel, bladder or ureter can be referred to a specialist endometriosis service (endometriosis centre). These centres have access to the relevant specialists and decisions about whether or not opiates are an appropriate treatment option could be made by them rather than GPs.
234	RCGP	Short	4	1.1.3	• Should a psychologist or other mental health service be involved in the MDT for a specialist endometriosis team, given that so many women also have mental health symptoms associated with endometriosis. **Access to fertility services: There is a huge postcode lottery about access to fertility services across the country. Fertility problems: assessment and treatment. Clinical guideline NICE [CG156] Published date: February 2013 Last updated: August 2016. This makes recommendations about treatment of endometriosis in women with fertility problems. A tertiary service may be providing services to many areas all of which**	Thank you for your comment. There was insufficient evidence to recommend psychological or other mental health services in the guideline but we have added a recommendation that healthcare professionals should 'be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support.' In the guideline's 'Organisation of Care' section we have recommended that both gynaecological and specialist

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					have different policies re NHS funding, which is inequitable and complicated.	endometriosis services should have, at least, access to fertility services. It is the intention that the implementation of these recommendations will address the postcode lottery that you are referring to.
235	RCGP	Short	6	1.4.5	• This is very confusing. What does a small increased risk of ovarian cancer mean? There need to be some figures here for women and GPs to read. In the full guideline this recommendation appears to be based on studies that all have a high or very high risk of bias and very variable risk estimates. In addition the presenting signs and symptoms of ovarian cancer are similar to ovarian cancer, although the age group may be slightly different. • NICE Ovarian cancer: recognition and initial management Clinical guideline [CG122] Published date: April 2011. Quote: "1.1.1.2 Carry out tests in primary care (see section 1.1.2) if a woman (especially if 50 or over) reports having any of the following symptoms on a persistent or frequent basis – particularly more than 12 times per month: ○ persistent abdominal distension (women often refer to this as 'bloating') ○ feeling full (early satiety) and/or loss of appetite ○ pelvic or abdominal pain ○ increased urinary urgency and/or frequency." These symptoms are very like endometriosis and would lead to the woman having a CA-125 test	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the various with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it if they have further questions about the increased risk of cancer.
236	RCGP	Short	General	General	Non specialist services are mentioned as part of a managed clinical network but there is no clear pathway on it regarding referral. I think it would be useful to have clear guidance regarding primary care management (GP or GPWSI) with empirical hormone treatment either with the combined pill or Mirena IUS where the symptoms are not severe, pelvic scan is negative and pelvic exam is negative. Thereafter if the patient does not respond to this therapy referral can be made to specialist gynaecology services. This of course does not include women who require specialist fertility services	Thank you for your comment. We did not want to be too prescriptive about where each action would be performed and by whom. However, the recommendations on analgesics and hormonal treatments are relatively strong, i.e. they should be 'offered' and it is therefore assumed that this would happen when first suspicions about endometriosis emerge. We have now also stated more clearly that women can be referred if 'initial management is not effective, not tolerated or is contraindicated'. We have also renamed 'non specialist services' to 'community services'.
237	RCOG	Full	310	21–3	The recommendations on hysterectomy seem to lean heavily on hysterectomy alone which is supported by poor quality evidence but bilateral salpingo-oophorectomy alone is not discussed. The option of bilateral salpingo-oophorectomy alone after a successful trial of Gonadotrophin-releasing hormone analogues with or without add back HRT, should be discussed.	Thank you for your comment. We did not identify any evidence related to bilateral salpingo-oophorectomy and as you highlighted the evidence that was identified was of poor quality. We have now added examples of possible indications for hysterectomy to the recommendation. We also changed the heading of this section to indicate that hysterectomy alone would not be a treatment for endometriosis and should only be performed if

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						the lesions are excised at the same time. We believe that this provides greater clarity to this section. Bilateral salpingo-oophorectomy is less commonly used and would therefore require an evidence base to support a recommendation.
238	RCOG	Short	6	1–25	The Committee members expressed some concerns about section 1.4 on referral and monitoring- Is this section directed at primary care or secondary care? The Guideline implies that GPs should refer patients directly to a tertiary specialist endometriosis centre if they suspect deep endometriosis in the first instance without seeing their local gynaecologist. We are concerned that specialist centres may be overwhelmed by inappropriate referrals.	Thank you for your comment. We have now clarified that the section on referral relates to women with suspected or confirmed endometriosis whereas the section on monitoring is related to women with confirmed endometriosis. Women with deep endometriosis involving the bowel, bladder or ureter are only a smaller percentage of all women with endometriosis and referral to specialist endometriosis services of these women was found to be cost-effective. This would then improve the care of these women who are currently not consistently referred.
239	RCOG	Short	6	21	The committee are unclear as to the purpose of informing women that endometriosis is associated with a small increased risk of ovarian cancer. This is likely to create unnecessary anxiety and may increase the requests for ovarian screening (which the guideline does not recommended – 1.4.6) or the proportion of women requesting prophylactic salpingo-oophorectomy.	Thank you for your comment. The Committee discussed this issue at length. The purpose of the original wording which you have commented on was to try and balance the need of the woman to know everything relevant about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; the absolute risk increase was so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that if they were unable to quantify the risk and so reassure the women with a numerical estimation of the probability, the recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Consequently the two recommendations on monitoring for cancer have been deleted, and discussion of this issue moved into the full guideline, where women can still access (along with a detailed discussion of the benefits and harms of intervention) it if they have further questions about the increased risk of cancer.
240	RCOG	Short	7	1–14	The quality of the evidence for transvaginal ultrasound in the diagnosis of deep endometriosis involving bowel, bladder or ureters, is low or very low. Transvaginal ultrasound is highly operator dependent; and identification of deep endometriosis is not part of routine ultrasound training in the UK. Therefore, the committee's opinion is that the recommendation for transvaginal ultrasound as a diagnostic tool for deep endometriosis is unsupported.	Thank you for your comment. We have recommended that women with suspected deep endometriosis involving the bowel, bladder or ureter should be referred to specialist endometriosis services. In these services we have recommended that there should be access to a healthcare professional with specialist expertise in gynaecological imaging of endometriosis. We believe that this individual would have the experience to identify signs of deep endometriosis.

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241	RCOG	Short	7	9	Malignancy should be excluded if an endometrioma is excised. It follows that if treated but not excised, malignancy should also be excluded. The committee therefore suggest that "a biopsy of suspected endometriosis is recommended…" (rather than "should be considered" (recommendation 1.5.12)	Thank you for your comment. As you may be aware, NICE use the word 'consider' as technical terms to indicate the strength of the evidence. The word 'consider' highlights that the evidence is poor.
242	RCOG	Short	9	21–28	It would be very useful for clinicians if the information regarding the effectiveness and safety of hormonal treatments could be summarised and conveyed in the recommendations.	Thank you for your comment. The 'short guideline' lists the recommendations, context and recommendations for research in a concise format. Whereas the full guideline contains details of the methods, the evidence and discussions of the evidence that provide the rationale for recommendations. This information is therefore provided in the full rather than the short version.
243	Royal College of Nursing	All	General	General	The Royal College of Nursing welcomes the draft guidelines for diagnosis and management of endometriosis as it is very much needed. The RCN invited members who work in women's health to review the document on our behalf. The comments reflect the views of our members.	Thank you for your comment.
244	Royal College of Nursing	Short	10	8	There is no mention of referral or consultation with colorectal professionals on the risks of surgery or discussing joint surgery with urologists.	Thank you for your comment. In the section on 'organisation of care' it is recommended that a specialist endometriosis service has access to a colorectal surgeon or urologist. We believe that this would mean that such consultation would take place where applicable.
245	Royal College of Nursing	Short	11	23	There is no specific mention of HRT and endometriosis in the NICE Menopause Guideline, in this regard, we consider that HRT should be specifically included within this guideline.	Thank you for your comment. HRT is discussed in the NICE Menopause guideline (even if not in the particular context of endometriosis) and it was the consensus in the Committee that the guidance provided would be generalisable to women with endometriosis who have a hysterectomy with oophorectomy. Hysterectomy with oophorectomy would lead to menopause with possible symptoms that could be treated with HRT.
246	Royal College of Nursing	Short	18	22	*"Specialist lifestyle intervention"*: We agree, as this is a frequent question asked by women, especially diet.	Thank you for your comment.
247	Royal College of Nursing	Short	5	20	We are concerned at the level of skill needed for identifying tender nodularity in the posterior vaginal fornix, and visible vaginal endometriotic lesions within primary care and feel that this would be difficult to implement in practice.	Thank you for your comment. We agree that this can be difficult to identify, but the recommendations make it clear that women with suspected endometriosis can be investigated and referred even if examination does not detect abnormalities.
248	Royal College of Nursing	Short	6	10	There are very limited number of paediatric gynaecologist.	Thank you for your comment. We agree and this is why the clause 'depending on local service provision' was included.
249	Royal College of Nursing	Short	7	3	*"To identify endometriomas and deep endometriosis involving the bowel, 7 bladder or ureter."* Is this a more specialist scan, we do not think that many ultrasonographers have the same skills that a gynaecologist would have when scanning.	Thank you for your comment. This would not be a more specialist scan. The evidence suggested that an ultrasound was quite accurate when

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						diagnosing deep endometriosis involving the bowel, bladder or ureter.
250	Royal College of Nursing	Short	General	General	We welcome the guideline and the acknowledgement that this condition can affect women under 17.	Thank you for your comment.
251	Royal College of Nursing	Short	General	General	There is no reference to the use of gonadotrophin-releasing hormone agonists or IUS within the medical treatments?	Thank you for your comment. Even though highly effective, GnRH-a treatment needs specific consideration for adverse events and longer-term treatment. Rather than mentioning it as a direct treatment option the Committee decided to leave this to clinical judgement after referral if initial hormone treatment has not been effective ('for investigation and treatment options'). We have provided additional explanations to the discussion in the full guideline (see section 11.1.3.4).
252	Royal College of Nursing	Short	General	General	We would like to see more about education of young girls in relation to what a normal period is so that they present earlier.	Thank you for your comment. Education of young girls regarding their understanding of a period is outside the scope of this guideline, therefore the Committee cannot make a recommendation on that.
253	Royal College of Nursing	Short	General	General	In general, little is know about younger women and the time from presentation to diagnosis and the difficulties of getting a referral based on symptoms and we feel that they should be a group with special considerations and for further research.	Thank you for your comment. Younger women are a group that we have given special consideration to (see our Equalities Impact Assessment form). We specifically recommended that healthcare professionals should consider referring young women to services if they have suspected or confirmed endometriosis. We therefore aimed to promote greater equality in care for this particular group of women.
254	Royal Cornwall Hospital	Full	115	4-5	"is associated with cancer" seems a stronger statement than the evidence supports. Given that such a statement is highly emotive and may influence patients (and their doctors) to non-ovarian sparing surgery when conservative surgery would be more appropriate, suggest re-wording this as "may be associated with cancer, but any risk is low and unlikely to be clinically significant". It may be worth being more explicit in the text about how statistical significance does not necessarily mean a finding is clinically significant (and also how additional surveillance in this group may be an alternative explanation to the higher observed incidence)	Thank you for your comment. The Committee reflected on the evidence and the comments related to this. The two recommendations related to this have now been deleted. The purpose of the original wording which you have commented on was to try and balance the need of the woman to be fully informed about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; that the risk increase was considered to be so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that due to various limitations in the data they were unable to quantify the absolute risk and therefore would not be able to reassure the women with a numerical estimation of this probability. They therefore decided that recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Furthermore national screening is

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						related to cervical not ovarian cancer and therefore the issue of surveillance may be misconstrued to indicate that women should not be invited to the regular screening tests. The discussion of these issues and why recommendations have not been made has now been moved to the full guideline.
255	Royal Cornwall Hospital	Full	14	Box 3rd row	We have found general gynaecologists can miss significant endometriosis (especially nodules in the deep pelvis). We'd suggest being more explicit than just "Carry out detailed inspection of the pelvis" and adding to the flowchart "including draining fluid to enable visualisation of hidden deposits".	Thank you for your comment. This Figure is meant to present the recommendations visually in a pathway format.
256	Royal Cornwall Hospital	Full	170-171	Section 9.5.7 – 9.5.8	Suggest being more explicit that a negative laparoscopy is only highly specific if it is done in a methodical way and by a suitably trained and experienced surgeon. Here it may be useful to include that free fluid must be drained to enable adequate visualisation, a systematic approach used to inspect all areas of the pelvis, and that adequate images must be obtained. In the detailed text, it may be worth commenting on the significance of peritoneal pockets which are often overlooked. Finally, there is no reference to what a "suitably experienced" surgeon is – "training and skills in laparoscopic surgery" could infer a Y3 registrar.	Thank you for your comment. We have added to the full guideline some of the details provided in your comment to highlight that an experienced and skilled laparoscopic surgeon should carry out the inspection (as was recommended) to ensure that endometriosis is not missed.
257	Royal Surrey County Hospital NHS Trust	Full	271-273	General	More consideration needs to be given to energy modalities actually used. For example, Healey 2014 used a combination of monopolar and bipolar diathermy in the ablation arm and monopolar in the excision arm. Presume latter was monopolar cutting but in the ablation arm bipolar diathermy does not remove endo it just coagulates it and unipolar "ablation" will depend on waveform used ie pure cut or cut with coagulation (damped segment).	Thank you for your comment. Energy modality was included in the protocol, meaning that if there was high-quality evidence comparing one to another it could have been included. However, no such evidence was found. Committee opinion was that in the absence of evidence strongly indicating one modality over another, issues of surgical preference and necessity should dominate consideration of energy modality. Consequently they chose not to make a recommendation on this topic.
258	Royal Surrey County Hospital NHS Trust	Short	11	14	Suggest 'excision of all visible and palpable endometriosis'	Thank you for your comment. After a careful consideration the Committee rephrased the recommendations regarding hysterectomy. The recommendation you are referring to was replaced by the recommendation '1.9.9 Perform hysterectomy (with or without oophorectomy) laparoscopically when combined with surgical treatment for endometriosis unless there are contraindications'.
259	Royal Surrey County Hospital NHS Trust	Short	11	4	Ablation and excision are the same. It is a common misnomer. Ablation definition late Middle English (in the general sense 'taking away, removal'): from late Latin *ablatio(n-*), from Latin *ablat-* 'taken away', from *ab-* 'away' + *lat-* 'carried' (from the verb *ferre*). Suggest be more specific ie bipolar coagulation, laser vaporisation as elsewhere in the full version page 272. Usually the misnomer comes from the original articles. Some authors are accurate and clearly understand the energy used others not so. It would be helpful if this	Thank you for your comment. To our understanding, ablation and excision are not the same. Excision means to cut out (etymologically), which is not the same as taking away and ablation means to destroy, usually by coagulation. After careful consideration, the Committee decided that the terms are so well understood in clinical practice that the Guideline should not be changed.

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					was made clearer or we will encourage more studies comparing excision and ablation.	
260	Royal Surrey County Hospital NHS Trust	Short	15	27	Suggest 'visualisation and palpation of the pelvis', can be done laparoscopically	Thank you for your comment. This section is meant to be brief and we agree that it can be palpated. However, the aim is to highlight that there are more and less invasive methods of diagnosis available each of which is covered in the guideline. The recommendations then provide more detail on this.
261	Royal Surrey County Hospital NHS Trust	Short	18	3-6	As above excision and ablation mean the same thing and therefore not much logic in comparing them in general terms. Need to be more specific in comparing energy modalities.	Thank you for your comment. To our understanding, ablation and excision are not the same. Excision means to cut out (etymologically), which is not the same as taking away and ablation means to destroy, usually by coagulation. After careful consideration, the Committee decided that the terms are so well understood in clinical practice that the Guideline should not be changed.
262	The Gynaecology Group	Short	General	General	Re statement "Diagnosis is mainly by laparoscopic visualisation of the pelvis, but other, less invasive methods may be used, including ultrasound". We consider this inaccurate as at present definitive diagnosis can only be made by laparoscopy and histological diagnosis. The statement could have significant negative repercussions in that when a pelvic ultrasound is recorded as normal an inexperienced clinician may consider endometriosis to have been excluded. We would suggest "Diagnosis can only be made definitively by laparoscopic visualisation of the pelvis, but other, less invasive methods may be useful in assisting diagnosis, including ultrasound". It also needs to be considered the wide range of experience in pelvic ultrasound throughout the country.	Thank you for your comment. We have revised this sentence as suggested. We believe that the recommended 'expertise in diagnosing and managing endometriosis, including training and skills in laparoscopic surgery' will raise standards in the diagnosis of endometriosis throughout the country.
263	University College London Hospitals	Appendix A	General	General	**Appendix A. The guideline is linked to the HMB guideline** In the scope (documented in Appendix A) it states that treatment specific to adenomyosis in isolation will not be considered in this guideline. As this is the relationship between HMB and the endometriosis guideline, the linkage should never have been made. The HMB guideline states in the introduction: "The effectiveness of the various treatments as well as their risks and benefits are discussed in relation to their use in the treatment of HMB but the discussion cannot be extrapolated to the use of particular treatments to relieve other symptoms, such as hysterectomy for cancer or endometriosis." Thus, the HMB guideline states that it does not relate to endometriosis so the linkage needs to be removed.	Thank you for your comment. Appendix A refers to the scope of the guideline which has already been published. We believe that a cross-reference to the Heavy Menstrual Bleeding guideline is reasonable because women suspected of having Endometriosis are included in our guideline. Heavy menstrual bleeding can coexist with Endometriosis and a healthcare professional, before the diagnosis is confirmed, may well want to consult the Heavy Menstrual Bleeding guideline to rule in or out this condition.
264	University College London Hospitals	Appendix A	General	General	**Appendix A. The guideline is linked to the laparoscopic techniques for hysterectomy guideline (IPG239)** This guidance is not on the NICE static list and is ten years old, hence	Thank you for your comment. Appendix A refers to the scope of the guideline which has already been published. Interventional Procedures Guidance (IPG) is providing recommendations on whether or not a

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					referring to it is against NICE guidance (Social value judgements: Principles for the development of NICE guidance). In addition, this guidance does not cover hysterectomy when it is carried out as part of the treatment for endometriosis. This guidance includes the various options for hysterectomy including vaginal approach; which would be contraindicated when treating endometriosis as it will not enable excision of endometriosis as recommended in the guideline. In addition, Nice appraisal advice limits length of time that an appraisal is valid: When NICE publishes a Technology Appraisal a suggested review date is given. The length of time between guidance publication and the review date will vary between 1 and 5 years and varies depending on the available evidence for the technology, and knowledge of when ongoing research will be reported. The table below shows how the review date may be chosen:	particular intervention is safe and effective, but does not make any recommendations about the intervention's use. IPG239 is related to laparoscopic techniques for hysterectomy and this topic is covered in the guideline which is why there was a cross-reference to it in the scope. IPG239 is still extant guidance (it has not been stood down) and can therefore be referred to.

Evidence base	**Review date**
Rapid change anticipated	Around 1 year after publication
Change anticipated	Around 3 years after publication
Known pivotal research	Will vary according to the expected reporting dates of the studies

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					<table><tr><td>Slow change anticipated</td><td>Around 5 years after publication</td></tr></table> Guidance may be considered for review before the suggested review date if NICE is made aware of significant new evidence that is likely to change the existing recommendations. The exact timing of any such ad-hoc review proposal is dependent on the available capacity in the Technology Appraisals work programme. *N.B. The review date is when 'the consideration of a review' will take place, rather than an actual review or update of the guidance.* If you have a query about a specific topic please let me know and I will try to find out more information for you. Many thanks and I hope this information answers your query. Thus, the linkage to this guidance in the endometriosis guideline is incorrect.	
265	University College London Hospitals	Full Short	112 115 6	31-37 4 (8.6) 21 (1.4.5)	Page 112 Refers to studies on ovarian cancer (line 31 to 37) as having a high risk of bias Level of increased risk not given. Recommendation on page 115 line 4 (8.6). Explain to women that there is a small increased risk. Also, short guideline page 6 line 21 (1.4.5) This will result in increased anxiety especially as the increase is not quantified. Some women will demand removal of normal ovaries which will have other risks due to surgery and menopause. This will also result increased cost to the NHS. There may be demands for all women with an endometrioma to be screened in a cancer unit and have an MRI. This will overload resources. Thus, this comment is unhelpful and will put great demands on resources and cause undue anxiety to women. Recommendation 1.4.6. states 1.4.6 "Do not offer surveillance for gynaecological cancers to women with endometriosis" The anxiety caused by the previous recommendation cannot be offset by the second one or by providing screening since there is no proven screening/surveillance strategy for ovarian cancer detection in this population. Patients must be made aware of both of these points	Thank you for your comment. The Committee reflected on the evidence and the comments related to this. The two recommendations related to this have now been deleted. The purpose of the original wording which you have commented on was to try and balance the need of the woman to be fully informed about her condition with the need to avoid overinvestigating women with possible cancer (not least because of the anxiety it would cause the woman). That is to say; that the risk increase was considered to be so small that it did not necessitate any change to any cancer surveillance being offered to the woman for reasons unrelated to her endometriosis. After discussion, the Committee decided that due to various limitations in the data they were unable to quantify the absolute risk and therefore would not be able to reassure the women with a numerical estimation of this probability. They therefore decided that recommendations as phrased would likely be unhelpful; there are no good treatment options available to clinicians to reduce the risk and so a recommendation overemphasises the risk in relation to its management options. Furthermore national screening is related to cervical not ovarian cancer and therefore the issue of surveillance may be misconstrued to indicate that women should not be invited to the regular screening tests. The discussion of these issues and why recommendations have not been made has now been moved to the full guideline.

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					and any discussion with patients should keep the risks carefully in context.	
266	University College London Hospitals	Full	6.7	Line 21	Inform women with suspected or confirmed endometriosis that keeping a pain and symptom diary can aid discussions. The evidence is limited and if this is applied to care once referred to a gynaecologist or a centre then it contradicts the guidance for a focused history and examination and relevant investigations. Thus, is may detract from a diagnosis in these situations and be disheartening to a patient when her record keeping is not relevant to the consultation. Thus, it should have added at the end of the sentence……..in primary care, which is in keeping with the flow chart. Same for short guideline page 5 line 18 (1.3.2).	Thank you for your comment. The Committee agreed that a record of symptoms can aid discussions. This was based on a review of qualitative evidence suggesting that women with suspected endometriosis found this to be helpful.
267	University College London Hospitals	Full	Flowchart	Symptom diary	Flow chart suggests that this is used in primary care. See below	Thank you for your comment. Significant amendments have been made to the algorithm which now specifies discussion of keeping a pain diary following suspicion of endometriosis at first presentation. This presentation could be in community or gynaecology services. The Committee noted that all women with endometriosis should have access to appropriate support from specialist nurses who are available to communicate with and support the woman's physical, psychological/psychosexual and social needs and expectations and provide support to them and their families through their pathway
268	University College London Hospitals	Full	General	General	The terminology used in the full guideline for 'reproductive organ cancer' is variable. The term reproductive cancer is misleading and could be construed as relating to the behaviour of the tumour. The whole section on gynaecological cancer risk is entitled "Risk of cancer of reproductive organs" but in other areas "reproductive cancers" are referred to. We would suggest consistency using either "reproductive organ cancer" or "cancer of reproductive organs" rather than "reproductive cancers" for clarity.	Thank you for your comment. The Committee agreed that the term 'reproductive cancer' is potentially misleading, and 'cancer of reproductive organs' has been substituted throughout the full and short guideline
269	University College London Hospitals	Full	General	General	The full guideline does not indicate the source article(s) when evidence is analysed, hence it is difficult and mostly impossible to pass a judgement as to whether one agrees with the committee assessment. This is a major problem throughout the guideline and limits its transparency. The reference list at the end of the full guideline seems to be inadequate and does not include a large number of relevant articles which should have been included to support some of the recommendations included in the guideline. For example, the recommendation 54 in section 12.4.4 suggests surgical treatment of deep endometriosis of bowel, bladder and ureters to improve spontaneous pregnancy rates, but the reference list includes only 3 articles related to deep endometriosis none of which is related to fertility outcome.	Thank you for your comment. In the full guideline the sections entitled 'descriptions of clinical evidence' provide details of the included studies and GRADE profiles outline number of studies included for each comparison/outcome and citations are also provided in the Forest plots (see Appendix I). For the NMAs all included studies are listed in Tables 63 and 111). The full citations can then be found in the references section (section 13) of the full

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					Network metaanalyses are not possible to link to the source references either. Overall, the way the guideline is presented does not allow one to see what reference is included and what is excluded.	guideline. All excluded studies and reasons for their exclusion are provided in Appendix H. The rationale for each recommendation is provided in the sections entitled 'evidence to recommendations' and these rationales are not only related to study results but also based on discussions of other factors and consensus based on the expertise of Committee members. We would also like to highlight that recommendations on the surgical treatment of women with deep endometriosis involving bowel, bladder or ureter have been revised based on stakeholder comments (please see section 12.3.4).
270	University College London Hospitals	Full	Section 11.4.7	310	**Recommendation 51 states:** **51. For women thinking about having a hysterectomy, discuss the possibility of having oophorectomy at the same time. Discussions should include:** □ what a hysterectomy involves and when it may be needed □ how hysterectomy with and without oophorectomy could affect the woman's endometriosis symptoms □ the risks and benefits □ recurrence and the possible need for further surgery □ hormone replacement therapy (also see the NICE guideline on menopause). These recommendations seem to be based on the discussion in the previous pages about hysterectomy with or without oophorectomy and risk of re-operation and symptom recurrence. However, there doesn't seem to be any consideration of risk of cancer, which is reported to be increased in the guideline. Ovarian cancer risk is an important factor when counselling women considering ovarian conservation and our own experience in women with endometriosis would support a recommendation of removal of the tubes and ovaries (BSO) in those not requiring their fertility. We would suggest that the guidelines should state that ovarian cancer risk should form a specific part of the risk/benefit discussion in women considering endometriosis surgery and BSO should be strongly considered in women not requiring their fertility. There is, however, no evidence confirming the protective effect of salpingo-oophorectomy or oophorectomy in this situation and it is likely that many ovaries would need to be removed to prevent one cancer, so an absolute recommendation to perform BSO in this situation would be hard to support. We have also seen rare cases of endometriosis-related cancer despite prior oophorectomy, presumably in sites of peritoneal	Thank you for your comment. We have reconsidered our recommendations on the risk of ovarian cancer and revised the guideline. The two draft recommendations were removed because data limitations did not allow us to quantify this 'small' risk and even if quantifiable it would be difficult to recommend an action to take from this information. The Committee's intention was to reassure women about the 'small' risk which would not warrant procedures such as oophorectomy on this basis. Further details about the reasons for not making recommendations regarding the risk of cancer of reproductive organs is now provided in the discussion section of the full guideline.

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					endometriosis. This should also be included in the discussion with the woman.	
271	University College London Hospitals	Full	Section 12.4.3.5,	21-26	This section states: 'If a woman was asymptomatic then she would be unlikely to be offered surgical laparoscopy to improve fertility because of the surgical risks of reducing ovarian reserve. The Committee considered that, dependent on other tests (for example, chlamydia antibodies), an asymptomatic woman would be more likely to be offered an ultrasound scan, tubal patency testing and expectant management before assisted conception techniques were offered.' This statement is not correct, whether an asymptomatic infertile woman is offered surgery is not only dependent on impact of surgery on ovarian reserve, it is more dependent on how likely she is to become pregnant spontaneously after surgery. She would be very likely to be offered surgery if this expectation is high but less likely if it is low. Women with low expectation would be more likely to be offered ART, hence ovarian reserve would be an important factor to take into account.	Thank you for your comment. We believe that unless other tests are carried out it would be unclear how likely she is to become pregnant after surgery. We would therefore think that ovarian reserve is an important factor and ought to be considered from the outset.
272	University College London Hospitals	Full	Section 12.4.4.	Recommendation 54	This recommendatiosn states: **54. Consider laparoscopic surgery for women with deep endometriosis involving the bowel, bladder or ureter and who are trying to conceive (working in conjunction with a fertility specialist), because it may improve the chance of spontaneous pregnancy.** It is not clear what evidence was used for this recommendation. The recommendation does not provide any indication how beneficial this approach is, and does not give any indication whether the risks associated with this type of surgery can be justified for the level of benefit (benefit for infertility and benefit for pain).	Thank you for your comment. We agree that this recommendation is weak for the reasons you outline, and have replaced it with the wording below which we believe better reflects the uncertainty in the evidence: 1.11.3 Discuss the benefits and risks of laparoscopic surgery as a treatment option for women with deep endometriosis involving the bowel, bladder or ureter and who are trying to conceive (working with a fertility specialist). Topics to discuss may include: • whether it may alter the chance of future pregnancy • the possible impact on ovarian reserve • the effect of complications on fertility • alternatives to surgery • other fertility factors
273	University College London Hospitals	Full & appendices	General	General	We would like to congratulate the NICE for choosing this topic for guideline development and the Guideline Committee for putting this guideline together.	Thank you for your comment. To clarify, it was the Department of Health that referred the topic to NICE rather than NICE choosing it.
274	University of Birmingham	Full	195	Table 64	Unclear why Cheewadhanaraks 2012 excluded when compares DMPA vs COCP	Thank you for your comment. The study by Cheewadhanaraks et al. 2012 "Postoperative Depot Medroxyprogesterone Acetate versus Continuous Oral Contraceptive Pills in the Treatment of Endometriosis-Associated Pain: A Randomized Comparative Trial" was excluded as it compares continuous hormonal treatment to pharmacological treatments after surgery which is not in line with the review protocol. Our protocol specifies combinations of treatments (surgery plus hormonal treatments) only when they compare use after surgery to no use or use before

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						surgery. Two types of hormonal treatments after surgery would therefore not be included. We have therefore removed it from Table 64 in which it was erroneously included.
275	University of Birmingham	Full	195	Table 64	Typo in fourth row author	Thank you for your comment. We have now corrected the error.
276	University of Birmingham	Full	286	6	We are grateful to the GDG for mentioning the ongoing trial , which is the PRE-EMPT trial (ISRCTN97865475). It would be helpful to highlight the hormonal interventions compared, the outcomes collected, the size and quality and the parallel economic evaluation.	Thank you for your comment. Usually study details such as population, intervention and comparison, outcomes etc. are given for published studies included in the review. Therefore, no amendment was made to the full guideline. However, the details of the study will be passed to NICE surveillance team for consideration at the next review for update.
277	World Endometriosis Research Foundation	Appendix D	10	Bottom	In the "outcomes" section, the data regarding "number of women requiring" future additional treatment is only validly measured in studies that applied formal follow-up methods (i.e. knew the outcome of patients who in the future sought care from a clinic other than that at which they were enrolled into the study or who did not seek future care despite return of their symptoms). Accounting for that important impact on the accuracy of these numbers seems absent from the literature review.	Thank you for your comment. The review protocol was agreed with and signed off by the Committee and quality assured, post hoc changes are not possible at this stage. All outcomes were assessed using GRADE methodology to evaluate the quality of evidence (e.g. risk of bias). This includes a risk of bias assessment for the body of the evidence for each outcome including assessment of how well studies reporting outcomes accounted for possible confounding factors. The Committee was informed about the quality of the evidence base when drawing conclusions and drafting recommendations.
278	World Endometriosis Research Foundation	Appendix D	10	Top	In the "important confounders" comment at the top of page 10, it is noted that these are to be considered when comparative observational studies are included. However, most of the RCTs cited / summarised are too small to ensure randomisation. Therefore, large, well-designed observational studies that apply multivariable analyses will be more robust with respect to confounding control than several of the RCTs included.	Thank you for your comment. The review protocol was agreed with and signed off by the Committee and quality assured, post hoc changes are not possible at this stage. This includes signing off study design. The Committee considered RCTs would be the most appropriate design to address intervention reviews. All studies were assessed using GRADE methodology to evaluate the quality of evidence (e.g. risk of bias). This includes a risk of bias assessment for the body of the evidence for each outcome including assessment of how well studies reporting outcomes accounted for possible confounding factors. This particularly relates to observational studies where they were considered for inclusion (for instance using multivariable techniques). The Committee was informed about the quality of the evidence base when drawing conclusions and drafting recommendations. Also, observational studies were considered where appropriate as per the review protocol.
279	World Endometriosis Research Foundation	Appendix D	10	Top	In the "important confounders" comment at the top of page 10, it is unclear if "severity" is a measurement of pain with respect to impact on QoL or with respect to resistance to empirical treatment or if this is based on rAFS disease staging (which is not well correlated with patient outcomes and therefore is a measurement of surgical severity and not patient experience severity).	Thank you for your comment. The wording was intentionally ambiguous and we were referring to either severity of pain or severity of the condition each of which could potentially be a confounding factor in the analysis and could contribute to heterogeneity. As no

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						heterogeneity was found, correction for confounding factors was not deemed to be necessary.
280	World Endometriosis Research Foundation	Appendix D	10 (and again on page 12, and further repeats)	Bottom	In the "outcomes" section, there is no time metameter stated for any of these outcomes. In pain studies, including pain associated with endometriosis, there is a strong, short-term placebo effect. If pain relief is significant as measured by the VAS, for example, that is only indicative of improvement weeks (and more likely months) following initial initiation of the treatment being evaluated.	Thank you for your comment. As the review protocol was agreed with and signed off by the Committee and quality assured, post hoc changes are not possible at this stage. The Committee did not define particular time points to be included in the review, therefore pain outcomes were taken as they were reported in the studies.
281	World Endometriosis Research Foundation	Appendix D	General	General	While it is frequently noted in the "Equalities" texts that adolescents will be noted as a specific subgroup, it is not noted how that definition will be applied. There will be a lot of conflation between study of outcomes among adolescents and the reality that a large portion of adult women in endometriosis studies were in fact symptomatic during adolescents but due to diagnostic delays are only now the subjects of study in adulthood.	Thank you for your comment. We agree that there could be conflation. We have noted that we would look for subgroups of young women, but agree that this strategy might provide a result which would be difficult to interpret. None such evidence was identified.
282	World Endometriosis Research Foundation	Appendix D	H.5	General	It is unclear why case:control studies have been excluded for the review of literature on reproductive cancers. The study of most reproductive cancers, particularly ovarian cancer, requires a case:control design, which is valid and statistically asymptotically equivalent for relative risk calculations when the outcome is rare (<10%) – criterial absolutely met by these cancer outcomes.	Thank you for your comment. We agree that for particularly rare conditions, selecting a sample based on outcome is often necessary to get a sufficiently large number of people with the outcome of interest. However, a large cohort study would still be preferable, since it avoids the temporal issue that represents a problem in case-control studies, i.e. the temporal relationship between the supposed cause and effect cannot be determined. We included quite a few large cohort studies with a large sample of women, therefore we think that there is no need for the addition of case-control studies. Moreover, we also included registry studies, which will capture rare conditions and do not suffer from selection bias as much as case-control or cohort studies.
283	World Endometriosis Research Foundation	Appendix D	Page 11 (and again on Page 12, and further repeats)	Top	In the "review strategy" section, for the comment that begins, "If studies only report p-values," there is no statement regarding how the impact of sample size (which drives the calculation of p-values more strongly than the magnitude of effect) and the importance of avoiding solely dichotomizing at p-value<0.05 will be handled in the interpretation of individual and meta-analysed results.	Thank you for your comment. We agree that the protocol could be made clearer without it affecting or biasing prior analysis, therefore we have now amended it by stating that "if studies only report p-values, this information (including the sample size) will be provided in GRADE tables with a note that imprecision could not be assessed."
284	World Endometriosis Research Foundation	Full	116	General chapter 9	The chapter on diagnosis has missed out a substantial evidence base on the lower invasive diagnostic tests for endometriosis. There have been 5 recent publications of diagnostic test accuracy systematic reviews on the Cochrane Library relating to endometriosis, but this guideline only refers to the evidence from three of them (Nisenblat et al, 2016, reviewing blood biomarkers; Nisenblat et al, 2016a, reviewing imaging tests; Gupta et al, 2016	Thank you for your comment. The list of potential biomarkers is too long for all of them to be included in the guideline. The Committee had to narrow this down and prioritised those where there was currently most variation in practice or uncertainty around its effectiveness or cost-effectiveness. Diagnosis of endometriosis using urinary biomarkers was therefore not

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					reviewing endometrial biomarkers). Hence this guideline fails to be comprehensive in reviewing the evidence. Missing is any mention of: 1. Urinary biomarkers (reference: Liu E, Nisenblat V, Farquhar C, Fraser I, Bossuyt PM, Johnson N, Hull ML. Urinary biomarkers for the non-invasive diagnosis of endometriosis. Cochrane Database Syst Rev 2015;12:CD012019.) Combinations of low invasive tests (reference: Nisenblat V, Prentice L, Bossuyt PMM, Farquhar C, Hull ML, Johnson N. Combination of the non-invasive tests for the diagnosis of endometriosis. Cochrane Database Syst Rev 2016;7:CD012281.)	prioritised in the review protocol by the Committee because it is not established in current practice and there are other biomarkers that are in use with uncertain effectiveness. The systematic review on combinations of non-invasive tests was checked for studies matching the protocol. The majority of those related to combinations of tests that were not included in the protocol. The remaining combinations were tests that the Committee had already agreed not to recommend (CA-125) or a combination of two tests that the Committee already recommended individually for the majority of women with suspected endometriosis (pelvic examination combined with ultrasound) based on the evidence of the individual accuracy. The review was therefore not included. We have now added to the discussion section that the Committee were aware of these reviews but that they had to prioritise a number of non-invasive tests that are currently available in use.
285	World Endometriosis Research Foundation	Full	172	15	The sentences states that the ASRM system predicts pregnancy rates. This is widely believed not to be true.	Thank you for your comment. Based on your comment we have deleted 'This is useful in the prediction of natural conception' from this section.
286	World Endometriosis Research Foundation	Full	172	18	The Endometriosis Fertility Index does predict pregnancy rates following laparoscopic surgery, so therefore this statement is not entirely accurate.	Thank you for your comment. The Committee considered your comment but did not believe that there was a particular endometriosis classification system that would allow assessment of superficial versus deep endometriosis to guide treatment choices. Since investigation of fertility problems as well as assisted reproduction was outside the scope of the guideline, evidence of predictive value of fertility staging systems in improving pregnancy rates after a particular treatment was not reviewed. We have now also emphasised this more in the discussion section for this set of recommendations and have referred readers to the NICE guideline on fertility (CG156) for fertility assessment and testing.
287	World Endometriosis Research Foundation	Full	172	27	A number of studies have compared the Endometriosis Fertility Index with the ASRM staging system.	Thank you for your comment. The Committee has considered your comment and felt that there was no particular endometriosis classification system that would allow assessment of superficial versus deeply endometriosis to guide treatment choices. Since the investigation of fertility problems as well as assisted reproduction was outside the scope of the guideline we could not review the evidence predictive value of staging systems for fertility in improving pregnancy rates after a particular treatment. We have now also emphasised this more in the discussion section for this set of recommendations and have referred readers to the NICE guideline on fertility (CG156) for fertility assessment and testing.

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288	World Endometriosis Research Foundation	Full	172	General chapter 10	The missing information from this chapter is a publication that is admittedly recent, but it systematically reviews all staging systems in a published consensus process (reference: Johnson NP, Hummelshoj L, Adamson GD, Keckstein J, Taylor HS, Abrao MS, Bush D, Kiesel L, Tamimi R, Sharpe-Timms KL, Rombauts L, Giudice LC, for the World Endometriosis Society Sao Paulo Consortium. World Endometriosis Society consensus on the classification of endometriosis. Hum Reprod 2017;32:315-324.). A key overarching consensus statement from this document, should at least appear in the narrative of the full version is: "Until better classification systems are validated, all women with endometriosis undergoing surgery should have a r-ASRM score and stage completed, women with deep endometriosis should have an Enzian classification completed, and women for whom fertility is a future concern should have an EFI score completed, and documented in the medical/surgical records".	Thank you for your comment. This paper was not included for two reasons: (1) this is a consensus paper that does not present findings of systematic reviews but describes the decision making process by which the panel reached consensus (which does not meet the protocol of study design); and (2) the paper does not address the specific question that we were asking (the effectiveness of staging systems to guide treatment strategies). The Committee agreed that visualisation during laparoscopy and recording of findings were more appropriate than staging to guide treatment choices. This is explained in section 10.6.2 which provides the rationale for this decision.
289	World Endometriosis Research Foundation	Full	173	24	If infertility is considered a symptom, the Endometriosis Fertility Index is an indication of the severity of the symptom and therefore is clinically useful for making treatment decisions.	Thank you for your comment. The Committee has considered your comment and felt that there was no particular endometriosis classification system that would allow assessment of superficial versus deeply endometriosis to guide treatment choices which is what the protocol was designed to address. Since the investigation of fertility problems as well as assisted reproduction was outside the scope of the guideline we could not review the evidence predictive value of staging systems for fertility in improving pregnancy rates after a particular treatment. We have now also emphasised this more in the discussion section for this set of recommendations and have referred readers to the NICE guideline on fertility (CG156) for fertility assessment and testing.
290	World Endometriosis Research Foundation	Full	174	21-25	It is not correct that there are no effective staging systems. This is true for pain but it is not true for infertility.	Thank you for your comment. The Committee has considered your comment and felt that there was no particular endometriosis classification system that would allow assessment of superficial versus deeply endometriosis to guide treatment choices which is what the protocol was designed to address. Since the investigation of fertility problems as well as assisted reproduction was outside the scope of the guideline we could not review the evidence predictive value of staging systems for fertility in improving pregnancy rates after a particular treatment. We have now also emphasised this more in the discussion section for this set of recommendations and have referred readers to the NICE guideline on fertility (CG156) for fertility assessment and testing.
291	World Endometriosis Research Foundation	Full	311	General chapter 12	The section on treatments for women with a fertility concern has glaring omissions and hence is an inadequate part of this guideline. For reference regarding obtaining a more comprehensive fertility guideline, a useful document would be the World Endometriosis Society consensus on the current management of endometriosis (reference: Johnson NP, **Hummelshoj L**; World Endometriosis	Thank you for your comment. The Committee have considered your comment but decided not to include the references suggested by you in the review. With regards to the World Endometriosis Society consensus

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					Society Montpellier Consortium. Consensus on current management of endometriosis. Hum Reprod 2013 Jun;28(6):1552-68). This section only deals with surgery as it relates to women for whom fertility is a concern and medical treatments for endometriosis (widely accepted to not have any fertility benefit). The section alludes to the NICE guideline on managing infertility, but this is wholly inadequate, as there are specific aspects of managing fertility delay for women with endometriosis. Consequently there is no mention of lipiodol treatment, IUI, or IVF specifically as it relates to women with endometriosis (and no useful reference from which this information can be accessed). The publication mentioned above nicely summarises the fertility treatments available for women with endometriosis (both current management in 2013 and 'innovative treatments' at that time) and consideration should be given to adopting a similar approach in this guideline. For example, key evidence on treating endometriosis related infertility are omitted, for example the marked fertility benefit from use of >/= 3 months of GnRHa suppression in the lead in to an IVF cycle (the so-called 'ultra-long IVF proptocol), with an estimated Peto odds ratio for clinicsl pregnancy of 4.28, 95% CI 2.00 to 9.15 (Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev 2006;1:CD004635.). It also fails to mention the marked fertility benefit from a lipiodol hysterosalpingogram for women with endometriosis-related infertility attempting natural conception – Peto OR 3.70, 95%CI 1.30 to 10.50 (Ref 1: Johnson NP, Farquhar CM, Hadden WE, Suckling J, Yu Y, Sadler L. The FLUSH Trial – Flushing with Lipiodol for Unexplained (and endometriosis-related) Subfertility by Hysterosalpingography: a randomised trial. Hum Reprod 2004; 19: 2043-51. Ref 2: Mohiyiddeen L, Hardiman A, Fitzgerald C, Hughes E, Mol BWJ, Johnson N, Watson A. Tubal flushing for subfertility. Cochrane Database of Systematic Reviews 2015, Issue 5. Art. No.: CD003718. DOI: 10.1002/14651858.CD003718.pub4).	on the current management of endometriosis paper: according to the review protocol, a consensus paper is not the type of study to be included in the review. With regards to the Sallam et al. 2006, Johnson et al. 2004 and Mohiyiddeen et al. 2015 papers: they were excluded in the early stages of the reviewing process as they did not match the inclusion criteria defined in the review protocol.
292	World Endometriosis Research Foundation	Full	334	41	This reference is an abstract presented at FIGO in 2009 – wouldn't it be more appropriate to reference the resulting paper? Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, Jenkinson C, Kennedy SH, Zondervan KT; World Endometriosis Research Foundation Global Study of Women's Health consortium. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril 2011 Aug;96(2):366-373	Thank you for your comment. In line with your suggestion, the reference has been updated.
293	World Endometriosis Research Foundation	Full	42	Table 10	The amount of time for the surgeries seems low for the surgeon. While at times noted may be accurate or actually performing that aspect of the procedure, the amount of time preoperatively, getting to the hospital in preparing for the surgery, performing the opening and closing aspects of the surgery, documenting findings in our group reports and medical records postoperatively, discussing results with the family, and possibly follow-up in the hospital postoperatively, as well as postoperative visit in the office will dramatically increase the duration of time reported in these tables for the surgeon.	Thank you for your comment. The time for surgeries was based on Committee consensus and on values given in Lalchandani, S., Baxter, A., Phillips, K. (2005). The issue of operating times (meaning the time for performing the relevant aspect of the procedure) being distinct from the total time (meaning the other aspects you raise) was discussed by the Committee and the Health Economist's approach agreed to be the best possible given

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						the constraints of the evidence. This assumption is validated in Table 12, where approximations from the NHS Reference Costs are overlaid onto the model and the agreement indicated.
294	World Endometriosis Research Foundation	Short	10	5-7	Revise "…available evidence does not currently support the use of traditional Chinese medicine…"	Thank you for your comment. To our understanding, the evidence that is available will be all the evidence that has been published currently. Therefore, on reflection, the Committee decided not to include your suggested phrasing.
295	World Endometriosis Research Foundation	Short	15	11 14	The term "subfertility" has been replaced by the term "infertility". Reference is the international glossary on infertility and fertility care by ICMART et al.	Thank you for your comment. The term 'subfertility' is commonly found in the evidence that was used for this guideline and we believe it is understood by clinicians. We have now added a definition of this to the glossary.
296	World Endometriosis Research Foundation	Short	3	16-21	Women should also have mental health access when presenting.	Thank you for your comment. We have revised the recommendations to promote greater awareness of the psychological impact that endometriosis can have.
297	World Endometriosis Research Foundation	Short	4	3-16	Specialist endometriosis centres should also have access to mental health services.	Thank you for your comment. There was insufficient evidence to recommend psychological or other mental health services in the guideline but we have added a recommendation that healthcare professionals should 'be aware that endometriosis can be a long term condition and can have a significant physical, sexual, psychological and social impact. Women may have complex needs and may require long term support.'
298	World Endometriosis Research Foundation	Short	5	24-26	A rectal exam can also be performed.	Thank you for your comment. The Committee considered this to be the exception rather than the norm and therefore did not want to specifically highlight this as an alternative to a pelvic examination for women who have never had sexual intercourse. Clinical judgement can then be used for women where this may be deemed to be appropriate based on the symptoms or signs that are reported.
299	World Endometriosis Research Foundation	Short	6	15-25	Add another sub-section: Patients with more than three years of infertility should be referred to a fertility specialist.	Thank you for your comment. The assessment and management of infertility was not part of the scope of this guideline. We included fertility only as an outcome in our management reviews. This meant that women in these sections were women actively trying to conceive. This is a limitation of this guideline and we have outlined this in the relevant 'evidence to recommendation' section.
300	World Endometriosis	Short	7	Section	Not all endometriosis is in the pelvis. Suggest evaluation also based on review of symptoms and history of present illness (e.g. catamenial pneumothorax) – it doesn't help to only focus on the pelvis.	Thank you for your comment. We are aware that not all endometriosis occurs in the pelvis,

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	Research Foundation					however this is less common than pelvic endometriosis and it was therefore not prioritised in the scope of this guideline which is intended to apply to the majority of all women with endometriosis.
301	World Endometriosis Research Foundation	Short	8	13-17	Add: and send biopsy to pathologist for review and diagnosis	Thank you for your comment. We believe that this action is commonly understood to be needed when recommending 'taking a biopsy' and does not need specifying.
302	World Endometriosis Research Foundation	Short	8	Section	Add: detailed documentation should be standardised on reporting utilising validated forms such as those provided by the World Endometriosis Research Foundation EPHect system, the American Society for Reproductive Medicine staging system, the Enzian system, and/or the Endometriosis Fertility Index. Otherwise it is impossible to compare staging and outcomes.	Thank you for your comment. The Committee recommended that 'the gynaecologist should document a detailed description of the appearance and site of endometriosis'. The focus of this recommendation is on what should be done rather than how. However, we have extended the discussion section in the full guideline to highlight the importance of good documentation and how this could be done (e.g. through photo-documentation / video-documentation of findings during surgery).
303	World Endometriosis Research Foundation	Short	9	21-23	Revise: "Explain to women with suspected or confirmed…" <u>that hormonal treatment for endometriosis pain is unlikely to have long-term effects on future fertility, but these therapies preclude concomitant conception and can postpone fertility until age-related decline further compromises fertility status</u>.	Thank you for your comment. On reflection, the Committee decided to amend this recommendation by adding "no permanent negative effect" as they agreed that there is a delay to return to fertility, but, unless a woman is premenopausal, this delay is not permanent.
304	World Endometriosis Research Foundation	Short	Recommendations for research	General	**It is critical to investigate and understand the basic mechanisms underlying pain**	Thank you for your comment. While we accept research in this area may help women, it would be outside the scope of this guideline to consider, as this guideline relates only to the diagnosis and management of pelvic endometriosis.
305	World Endometriosis Research Foundation	Short	Recommendations for research	General	**Determine the cause(s) of endometriosis** It is only possible to improve treatment of endometriosis if the causes of endometriosis are understood, be they genetic markers, environmental, or behavioural.	Thank you for your comment. While we accept research in further research in this area is important, it is outside the scope of this guideline. This guideline relates only to guidance on specific diagnostic tests and management strategies related to pelvic endometriosis and research. Research can only be recommended on the topics that were covered.
306	World Endometriosis Research Foundation	Short	Recommendations for research	General	**Determine long-term consequences of endometriosis** This knowledge will help us understand effectiveness of early intervention – including long-term effects of treatments.	Thank you for your comment. While we accept research in further research in this area is important, it is outside the scope of this guideline. This guideline relates only to guidance on specific diagnostic tests and management strategies related to pelvic endometriosis and research. Research can only be recommended on the topics that were covered.
307	World Endometriosis	Short	Recommendations for research	General	**Establish a histology-based classification system** With the new understanding that endometriotic lesions undergo various cellular and molecular changes that ultimately lead to fibrosis,	Thank you for your comment. While we accept research in further research in this area is

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	Research Foundation				the natural history is clear, that is: gradual progression of fibrogenesis. With this, it is possible to classify endometriosis based on histology and pathology.	important, it is outside the scope of this guideline. This guideline relates only to guidance on specific diagnostic tests and management strategies related to pelvic endometriosis and research. Research can only be recommended on the topics that were covered.
308	World Endometriosis Research Foundation	Short	Recommendations for research	General	**Invest in biomarker research** Biomarkers can be used to monitor treatment effect.	Thank you for your comment. Our protocol was restricted to only a limited number of biomarkers that were prioritised by the Committee. Even though some of the research recommendations are taken up by research bodies, it is outside the scope of NICE guidelines to directly support investment in any particular research programme.

Registered stakeholders