National Institute for Health and Care Excellence

Draft for consultation

Abdominal aortic aneurysm: diagnosis and management

Evidence review L: Anaesthesia and analgesia for people having surgical repair of an abdominal aortic aneurysm

NICE guideline <number>

Evidence reviews

May 2018

Draft for Consultation

Commissioned by the National Institute for Health and Care Excellence

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Anaesthesia and analgesia for people having surgical repair of unruptured and ruptured abdominal aortic aneurysm

Review questions

What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) endovascular repair (EVAR) and ii) open repair of an unruptured abdominal aortic aneurysm?

What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) EVAR and ii) open repair of a ruptured abdominal aortic aneurysm?

Introduction

Repair of abdominal aortic aneurysms (AAAs) is associated with a variety of risks, including bleeding, infection, nerve or spinal damage, as well as cardiovascular, respiratory, gastrointestinal, and renal complications. People undergoing AAA repair often have cardiovascular and respiratory comorbidities, which can increase the incidence and severity of the aforementioned risks. Optimising how anaesthesia and analgesia are used is an important part of minimising the incidence of complications. This review aims to assess the use of local, regional or general anaesthesia and different analgesic regimens in 'optimising' surgical outcome amongst people undergoing surgery for unruptured and ruptured AAA.

PICO table

Table 1: Inclusion criteria

Parameter	Inclusion criteria
Population	People undergoing surgery for a confirmed ruptured or unruptured AAA
Interventions	Regional or local anaesthesia and/or analgesia in the surgical repair of a ruptured or unruptured AAA
Comparators	General anaesthesia and/or analgesia in the surgical repair of a ruptured or unruptured AAA
Outcomes	Mortality Adverse events Complications of surgery, including pain, blood loss, wound complications, gut motility, and respiratory complications Need for additional intervention Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth Quality of life Resource use and costs

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

A focused search strategy was used to pull in all studies that assessed the effectiveness of perioperatively administered local or regional anaesthesia and/or analgesia compared to general anaesthesia and/or analgesia in 'optimising' surgical outcome amongst people undergoing surgery for an AAA. Randomised, quasi-randomised and non-randomised controlled trials were considered for inclusion. Studies were excluded if they:

- were not in English;
- were not full reports of the study (for example, published only as an abstract);
- were not peer-reviewed;
- focused on postoperative anaesthesia and/or analgesia.

Prospective cohort studies were to be considered for inclusion if insufficient trial evidence was identified and if they had sample sizes larger than 500 and were conducted across multiple centres. Full details of the inclusion criteria are available in the review protocol in Appendix A.

Clinical evidence

Included studies

From an initial database of 2,201 abstracts, 116 full-text articles were ordered. Of these 7 studies conducted in people with unruptured AAA met inclusion criteria for this review, whereas no studies were identified relating to ruptured AAA.

An update search was conducted in December 2017, to identify any relevant studies published during guideline development. The search found 222 abstracts; all of which were not considered relevant to this review question. As a result no additional studies were included.

Excluded studies

The list of papers excluded at full-text review, with reasons, is given in Appendix H.

Summary of clinical studies included in the evidence review

Table 2: Summary of included studies

Study	Details
Baron J-F, Bertrand M, Barré E, et al. (1991) Combined epidural and general anesthesia versus general anesthesia for abdominal aortic	Study design: quasi-randomised controlled trial Location: France Population: high-risk surgical patients scheduled for elective abdominal aortic reconstruction

Study	Details
surgery. Anesthesiology, 75: 611-8	Sample size: 167 Follow-up: not reported Intervention: epidural anaesthesia plus general anaesthesia Comparator: balanced general anaesthesia Outcomes: mortality, cardiovascular morbidity, respiratory morbidity, renal failure, gastrointestinal bleeding, sepsis, major surgical complication & postoperative hospital stay
Broekema AAA, Kuizenga K, Hennis PJ (1996). Does epidural sufentanil provide effective analgesia per- and postoperatively for abdominal aortic surgery? Acta Anaesthesiol Scandinavica 40: 20-5	Study design: double-blind randomised controlled trial Location: Netherlands Population: people undergoing open surgical repair of unruptured AAA Sample size: 40 Follow-up: not reported Intervention: opioid epidural plus general anaesthesia Comparator: general anaesthesia plus placebo Outcomes: complications, adverse events, blood loss, & need for additional analgesia
Davies MJ, Silbert BS, Mooney PJ et al. (1993) Combined epidural and general anaesthesia versus general anaesthesia for abdominal aortic surgery: A prospective randomised trial. Anaesthesia and Intensive Care 21: 790-4	Study design: randomised controlled trial Location: Australia Population: people undergoing open surgical repair of unruptured AAA Sample size: 50 Follow-up: not reported Intervention: epidural combined with general anaesthesia Comparator: general anaesthesia-alone: Outcomes: mortality, cardiovascular complications, respiratory complications, hepatic complications, renal complications, Length of hospital stay, length of ICU stay, intraoperative blood loss & infections
Davis. (1987) Intrathecal morphine in aortic aneurysm surgery. Anaesthesia 42: 491-7	Study design: randomised controlled trial Location: UK Population: men undergoing open surgical repair of unruptured AAA Sample size: 30 Follow-up: not reported Intervention: intrathecal opioid plus general anaesthesia: Comparator: general anaesthesia-alone Outcomes: pain & clinical respiratory depression
Dodds TM, Burns K, DeRoo DB et al. (1997) Effects of anesthetic technique on myocardial wall motion abnormalities during abdominal aortic surgery. Journal	Study design: double blind, randomised controlled trial Location: Lebanon Population: people undergoing open surgical repair of unruptured AAA Sample size: 73 Follow-up: not reported

Study	Details
of Cardiothoracic and Vascular Anesthesia 11: 129-36	Intervention: epidural plus general anaesthesia: Comparator: general anaesthesia-alone Outcomes: in-hospital mortality, cardiac morbidity, respiratory morbidity, renal insufficiency & blood loss
Fleron M-H, Weiskopf RB, Bertrand M et al. (2003) A comparison of intrathecal opioid and intravenous analgesia for the incidence of cardiovascular, respiratory, and renal complications after abdominal aortic surgery. Anesth Analg 97: 2-12	Study design: randomised controlled trial Location: France Population: people undergoing open surgical repair of unruptured AAA or aortoiliac occlusive disease Sample size: 217 Follow-up: not reported Intervention: Intrathecal opioid plus general anaesthesia Comparator: general anaesthesia-alone: Outcomes: major complications, cardiovascular complications, respiratory complications, renal complications & length of hospital stay
Norris EJ, Beattie C, Perler BA et al. (2001) Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology 95: 1054-67	Study design: double-blind, randomised controlled trial Location: USA Population: patients undergoing open surgery to repair unruptured AAA or surgery for aortoiliac occlusive disease, and visceral and renal arterial reconstruction Sample size: 168 Follow-up: not reported Intervention: epidural anaesthesia combined with a light general anaesthesia Comparator: general anaesthesia plus placebo Outcomes: mortality, cardiac complications, respiratory complications, renal complications, intraoperative blood loss, reoperation & readmission to ICU

See Appendix D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

See Appendix F for full GRADE tables.

Economic evidence

Included studies

A literature search was conducted jointly for all review questions by applying standard health economic filters to a clinical search for AAA. This search returned a total of 5,173 citations. Following review of all titles and abstracts, no studies were identified as being potentially relevant to review question 13 or review question 24.

An update search was conducted in December 2017, to identify any relevant health economic analyses published during guideline development. The search found 814

abstracts; all of which were not considered relevant to this review question. As a result no additional studies were included.

Excluded studies

No studies were retrieved for full-text review.

Evidence statements

Use of anaesthesia and analgesia during repair of unruptured AAAGeneral anaesthesia combined with an epidural compared with general anaesthesia alone during elective open repair

Mortality

- Very low-quality evidence from up to 3 RCTs, including up to 400 people undergoing elective open repair of an AAA, could not differentiate levels of in-hospital mortality or 12-month mortality between people who received general anaesthesia combined with an epidural and those who received general anaesthesia alone.

Adverse events

- Very low-quality evidence from up to 4 RCTs, including up to 450 people undergoing elective open repair of an AAA, could not differentiate the postoperative incidence of myocardial infarction, congestive heart failure or general cardiovascular morbidity between people who received general anaesthesia combined with an epidural and those who received general anaesthesia-alone.
- Very low-quality evidence from up to 4 RCTs, including up to 450 people undergoing elective open repair of an AAA, could not differentiate the postoperative incidence of acute respiratory failure or pneumonia between people who received general anaesthesia combined with an epidural and those who received general anaesthesia alone.
- Very low-quality evidence from up to 4 RCTs, including up to 327 people undergoing elective open repair of an AAA, could not differentiate the postoperative incidence of renal failure or renal insufficiency between people who received general anaesthesia combined with an epidural and those who received general anaesthesia alone.

Surgical complications

- Very low-quality evidence from up to 5 RCTs, including up to 327 people undergoing elective open repair of an AAA, could not differentiate the levels of surgical complications between people who received general anaesthesia combined with an epidural and those who received general anaesthesia alone. Moderate quality evidence from 1 RCT, including 40 people undergoing elective open repair of an AAA, reported less need for additional analgesia in people who received general anaesthesia combined with an epidural compared with those who received general anaesthesia alone.

Need for reoperation

- Very low-quality evidence from 1 RCT, including 160 people undergoing elective open repair of an AAA, could not differentiate reoperation rates between people who received general anaesthesia combined with an epidural and those who received general anaesthesia alone.

Resource use

- Very low-quality evidence from up to 2 RCTs, including up to 217 people undergoing elective open repair of an AAA, could not differentiate the duration of postoperative hospital stay or postoperative stay in the intensive care unit between people who received general anaesthesia combined with an epidural and those who received general anaesthesia-alone.

General anaesthesia combined with intrathecal opioid compared with general anaesthesia alone during elective open repair

Mortality

- Very low-quality evidence from 1 RCT of 217 people undergoing elective open repair of an AAA could not differentiate levels of in-hospital mortality between people who received general anaesthesia combined with intrathecal opioid injection and those who received general anaesthesia alone.

Adverse events

- Very low quality evidence from 1 RCT of 217 people undergoing elective open repair of an AAA could not differentiate the postoperative incidence of myocardial infarction or congestive heart failure between people who received general anaesthesia combined with intrathecal opioid injection and those who received general anaesthesia alone.
- Very low quality evidence from up to 2 RCTs, including up to 242 people undergoing elective open repair of an AAA, could not differentiate the postoperative incidence of respiratory depression, acute respiratory failure or pneumonia between people who received general anaesthesia combined with intrathecal opioid injection and those who received general anaesthesia alone.

Anaesthesia and analgesia during elective EVAR

No evidence was identified relating to anaesthesia and/or analgesia during elective EVAR.

Use of anaesthesia and analgesia during repair of ruptured AAA

No evidence was identified relating to ruptured AAA.

Recommendations

L1. Consider using epidural analgesia in addition to general anaesthesia for people having open repair of an unruptured AAA.

L2. Consider using local infiltrative anaesthesia alone for people having EVAR of a ruptured AAA.

Rationale and impact

Why the committee made the recommendations

The committee noted that there was some evidence that adding an epidural to general anaesthesia reduced the need for further analgesia for people having open repair of an unruptured AAA. This was consistent with their own clinical experience of better pain control with an epidural. Adding an epidural is fairly widespread in current practice, and the committee agreed that it should be recommended as an option.

No evidence was found on anaesthesia and analgesia for people undergoing EVAR for unruptured AAA. The committee agreed that no recommendations were needed in this area because they had recommended that EVAR should not be used to treat unruptured infrarenal aneurysms, elsewhere in the guideline.

No evidence was identified on the optimal use of anaesthesia and analgesia in people having open surgical repair or EVAR of a ruptured AAA. The committee agreed, based on their knowledge and experience, that general anaesthesia alone is widely accepted as best practice for open repair. With this in mind, it did not make a recommendation on this. It made a recommendation on the use of local infiltrative anaesthesia alone in people having EVAR for ruptured AAA because some anaesthetists are not aware that it is a valid option in this patient group.

Impact of the recommendations on practice

The use of an epidural in addition to general anaesthesia for people having open repair of an unruptured AAA is already fairly widespread in current practice. Therefore the overall impact of the recommendation is likely to be small, although it may reduce existing variation.

The committee agreed that the potential impact of this recommendation on practice is unclear, because it is difficult to predict the proportion of people for whom EVAR under local infiltrative anaesthesia might be an option. The main aim of this recommendation is to raise awareness of this option among anaesthetists.

The committee agreed that it is not clear what impact the recommendation on local infiltrative anaesthesia alone for people having EVAR of a ruptured AAA will have on practice, because it is difficult to predict the proportion of people for whom surgery under local infiltrative anaesthesia might be an option. The main aim of this recommendation is to raise awareness of this option among anaesthetists.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The guideline committee discussed the relative importance of a variety of outcomes and agreed that the following would be useful to their decision-making:

- Mortality
- The adverse events of anaesthesia or analgesia

- Additional surgical interventions or changes to the approach to anaesthesia and/or analgesia

The quality of the evidence

Use of anaesthesia and analgesia during repair of unruptured AAA

The committee noted that the evidence was limited to the comparison of general anaesthesia alone with general anaesthesia with an epidural or an intrathecal opioid. No evidence was found for other combinations of anaesthesia and analgesia. It was considered that some of the evidence may not have been generalisable to the UK context, primarily because of the formulations and doses of the interventions used. This affected the applicability of the evidence. This applicability was further affected by the populations in a number of the studies, which included people other than those undergoing open repair of an AAA, such as those undergoing surgery for aortoiliac occlusive disease, and those undergoing visceral or renal arterial reconstruction requiring abdominal aortic cross-clamping.

The committee noted that only 1 outcome in 1 comparison reached significance (the need for additional analgesia in the comparison of epidural plus general anaesthesia and general anaesthesia-alone), though this was likely a result of low event rates and small sample sizes. For this reason, the committee noted that there is an absence of evidence, not evidence of absence with regard to differences in the effects of the interventions and comparators studied.

No evidence was identified for anaesthesia and/or analgesia in people undergoing EVAR for unruptured AAA. The committee agreed that it was not necessary to draft consensus recommendations as they had recommended that EVAR should not be used to treat unruptured infrarenal aneurysms elsewhere in the guideline.

Use of anaesthesia and analgesia during repair of ruptured AAA

Since no evidence was identified for anaesthesia and/or analgesia in people undergoing any type of repair of ruptured AAA, the committee agreed that it was appropriate to draft consensus recommendations based on their collective skills, knowledge and experiences (discussed in the benefits and harms section below).

Benefits and harms

Use of anaesthesia and analgesia during repair of unruptured AAA

On the whole, the identified evidence relating to elective open repair did not allow the committee to draw many distinctions between the use of general anaesthesia alone, general anaesthesia with an epidural, and general anaesthesia with an intrathecal injection of opioid. However, the committee noted that the addition of an epidural to general anaesthesia was associated with a lower need for additional analgesia compared with the use of general anaesthesia alone. This preference for the addition of an epidural to general anaesthesia was also supported by the committee's own clinical experience. The superior analgesic effect of adding an epidural has also been demonstrated and accepted in more general terms, such as in abdominal surgery more broadly, and the committee noted that there was no biological reason to expect that this result would be different in this population.

The committee subsequently discussed the possible populations in which the addition of an epidural to general anaesthesia would be contraindicated, but concluded that there were no such populations that could be specified. In the absence of explicit contraindications, possible reasons not to undertake an epidural might include possible side effects (including cardiac, respiratory, or gastrointestinal complications), the failure rate of epidurals, and the need for relatively intensive postoperative management to maximise benefits of an epidural. However, the committee did not feel that these concerns, when properly accounted for in the management of the patient, outweighed the possible benefits of using an epidural in conjunction with general anaesthesia in people undergoing open repair of an unruptured AAA.

The potential complications of epidural mean that some are now trying alternative methods, including the use of wound catheters to apply local anaesthesia, a technique that is being used more and more in abdominal surgery and which some are starting to use in the open repair of unruptured AAAs. However, the group did not feel that they had sufficient evidence or cause to explicitly recommend the use of wound catheters at this point.

No evidence was identified for optimal use of anaesthesia or analgesia in people undergoing elective EVAR. The committee noted that they recommended the procedure should not be performed in elective cases but acknowledged that in some circumstances, such as a hostile abdomen, EVAR may be warranted. In such situations no approach to anaesthesia and/or analgesia is considered superior to another. The committee agreed that it was important to tailor the approach to the individual patient, particularly in the case of people undergoing complex EVAR. They agreed that some important factors that should be considered include the ‘ease’ of the planned surgery, based upon the size, morphology and position of the aneurysm as well as the estimated duration of surgery, the patient’s preference and concerns (for example, general anaesthesia may be preferable to patients who are anxious about being in the operating theatre). The committee agreed any recommendations on the use of anaesthesia or analgesia in people undergoing elective EVAR would be misleading as they had recommended that the procedure should not be performed in elective cases, elsewhere in the guideline.

Use of anaesthesia and analgesia during repair of ruptured AAA

No evidence was identified for the optimal management of anaesthesia and/or analgesia in people having open repair or EVAR of a ruptured AAA.

The committee agreed that the use of general anaesthesia alone is widely accepted as best practice when performing open surgical repair of a ruptured AAA. Furthermore, the committee agreed that the use of epidurals in addition to general anaesthesia is not considered safe or appropriate in the context of ruptured aneurysm. This is for a number of reasons; including a lack of sufficient time to administer an epidural when a patient is losing blood quickly, as well as the fact that people with ruptured AAA are generally not in a condition to tolerate administration of an epidural. The committee agreed that no recommendation was necessary as it is common practice to use anaesthesia alone during open surgery for ruptured AAA.

In the context of EVAR, the committee concluded that the approach of using anaesthesia and/or analgesia should be based primarily on the stability of the

patient's condition. The committee felt that there was a lack of awareness among anaesthetists of the potential for effectively using local infiltrative anaesthesia alone in people undergoing EVAR for an AAA, at least at the start of the procedure. General anaesthesia can lead to loss of sympathetic control and muscle tone, which in patients with a ruptured aneurysm can lead to profound hypotension; for this reason, the use of local anaesthesia alone (at least initially) may be preferable.

Support for the use of local infiltrative anaesthesia alone in people undergoing EVAR for a ruptured AAA also came from a supplementary piece of evidence identified by the committee. A subgroup analysis of an included RCT for the question on EVAR versus open repair in ruptured AAA (IMPROVE) found that people who underwent EVAR for a ruptured AAA under local anaesthesia had a lower mortality (13%) than those who underwent the procedure under general anaesthesia (34%). This translated to a meaningful benefit for local anaesthesia (OR 0.25 (95% CI 0.10 to 0.70)), which the committee agreed may indicate a survival advantage associated with the use of local anaesthesia. However, the committee also acknowledged that this was a non-randomised comparison and there is no further evidence to support this. They also acknowledged that local infiltration alone may be distressing for the patient, or that it may not be feasible in all circumstances.

Cost effectiveness and resource use

No cost-effectiveness evidence was identified for this review area, and it was not prioritised for economic modelling.

Use of anaesthesia and analgesia during repair of unruptured AAA

The committee considered that the use of an epidural in addition to general anaesthesia during open surgical repair is already widespread practice, so recommending their use would have a limited impact on resource use.

Use of anaesthesia and analgesia during repair of ruptured AAA

The committee considered that the use of general anaesthesia alone in people undergoing open repair of a ruptured AAA is already widespread practice, so recommending its use will have a limited impact on resource use. The committee also agreed that the recommendation to consider local infiltrative anaesthesia alone for people having EVAR for ruptured AAA is unlikely to lead to any substantial change in resource use.

Other factors the committee took into account

No other factors were discussed by the committee.

Appendices

Appendix A – Review protocols

Review protocol for review question 13: Anaesthesia and analgesia for people having surgical repair of an unruptured abdominal aortic aneurysm

Review question 13	What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) EVAR and ii) open repair of an unruptured abdominal aortic aneurysm?
Objectives	To assess the use of local, regional or general analgesia and anaesthesia in 'optimising' surgical outcome amongst people undergoing surgery for an unruptured abdominal aortic aneurysm
Type of review	Intervention
Language	English only
Study design	Systematic reviews of study designs listed below: Randomised controlled trials Quasi-randomised controlled trials Non-randomised controlled trials If insufficient evidence identified, prospective cohort studies presenting comparative evidence will be considered (n >500; multicentre)
Status	Published papers only (full text) No date restrictions
Population	People undergoing surgery for a confirmed unruptured abdominal aortic aneurysm Subgroups: age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity); fitness/risk for surgery
Intervention	Regional or local anaesthesia and/or analgesia in the elective surgical repair of an unruptured abdominal aortic aneurysm
Comparator	General anaesthesia and/or analgesia in the elective surgical repair of an unruptured abdominal aortic aneurysm
Outcomes	Mortality Adverse events of anaesthesia or analgesia, including renal, pulmonary and cardiac Complications of surgery, including pain, blood loss, wound complications, gut motility, and respiratory complications Need for additional intervention: surgical, conversion from local/regional to general Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth Quality of life Resource use, including length of hospital or intensive care stay and readmissions, and costs

Review question 13	What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) EVAR and ii) open repair of an unruptured abdominal aortic aneurysm?
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published Pharmacological interventions not available in the UK Postoperative anaesthesia and/or analgesia
Baseline characteristics to be extracted in evidence tables	Age, Sex Size of aneurysm Position of aneurysm Comorbidities
Search strategies	See Appendix B
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.

Review protocol for review question 24: Anaesthesia and analgesia for people having surgical repair of a ruptured abdominal aortic aneurysm

Review question 24	What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) EVAR and ii) open repair of a ruptured abdominal aortic aneurysm?
Objectives	To assess the use of local, regional or general analgesia and anaesthesia in 'optimising' surgical outcome amongst people undergoing surgery for a ruptured abdominal aortic aneurysm
Type of review	Intervention
Language	English only
Study design	Systematic reviews of study designs listed below: Randomised controlled trials Quasi-randomised controlled trials Non-randomised controlled trials If insufficient evidence identified, prospective cohort studies presenting comparative evidence will be considered (n >500; multicentre)
Status	Published papers only (full text) No date restrictions
Population	People undergoing surgery for a ruptured abdominal aortic aneurysm Subgroups: age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity)

Review question 24	What is the most effective approach to anaesthesia and/or analgesia in improving surgical outcome in people undergoing i) EVAR and ii) open repair of a ruptured abdominal aortic aneurysm?
Intervention	Regional or local anaesthesia and/or analgesia in the surgical repair of a ruptured abdominal aortic aneurysm
Comparator	General anaesthesia and analgesia in the surgical repair of a ruptured abdominal aortic aneurysm
Outcomes	Mortality Adverse events of anaesthesia or analgesia, including renal, pulmonary and cardiac Complications of surgery, including pain, blood loss, wound complications, gut motility, and respiratory complications Need for additional intervention: surgical, conversion from local/regional to general Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth Quality of life Resource use, including length of hospital or intensive care stay and readmissions, and costs
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published Pharmacological interventions not available in the UK Postoperative anaesthesia and/or analgesia
Baseline characteristics to be extracted in evidence tables	Age Sex Size of aneurysm Comorbidities
Search strategies	See Appendix B
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.

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Appendix B – Literature search strategies

Clinical search literature search strategy

Main searches

Bibliographic databases searched for the guideline

- Cumulative Index to Nursing and Allied Health Literature - CINAHL (EBSCO)
- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (Wiley)
- Health Technology Assessment Database – HTA (Wiley)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE Epub Ahead of Print (Ovid)
- MEDLINE In-Process (Ovid)

Identification of evidence for review questions

The searches were conducted between November 2015 and October 2017 for 31 review questions (RQ). In collaboration with Cochrane, the evidence for several review questions was identified by an update of an existing Cochrane review. Review questions in this category are indicated below. Where review questions had a broader scope, supplement searches were undertaken by NICE.

Searches were re-run in December 2017.

Where appropriate, study design filters (either designed in-house or by McMaster) were used to limit the retrieval to, for example, randomised controlled trials. Details of the study design filters used can be found in section 4.

Search strategy review questions 13 and 24

Medline Strategy, searched 11th February 2016 **Database: Ovid MEDLINE(R) <1946 to January week 1 2016** **Search Strategy:**
1 Aortic Aneurysm, Abdominal/
2 Aortic Rupture/
3 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort* or spontan* or juxtarenal* or juxta-renal* or juxta renal* or paraerenal* or para-renal* or para renal* or suprarenal* or supra renal* or supra-renal* or short neck* or short-neck* or shortneck* or visceral aortic segment*)).tw.
4 (AAA or RAAA).tw.
5 or/1-4
6 exp Anesthesia/
7 (anaesthe* or anesthe*).tw.
8 exp Anesthetics/
9 Anesthesiology/
10 Nurse Anesthetists/
11 exp Analgesia/
12 Analgesi*.tw.
13 Pain Management/

Medline Strategy, searched 11th February 2016 Database: Ovid MEDLINE(R) <1946 to January week 1 2016 Search Strategy:
14 (Pain* adj4 (manag* or relie*)).tw.
15 or/6-14
16 5 and 15
17 Animals/ not humans/
18 16 not 17
19 limit 18 to english language

Health Economics literature search strategy

Sources searched to identify economic evaluations

- NHS Economic Evaluation Database – NHS EED (Wiley) last updated Dec 2014
- Health Technology Assessment Database – HTA (Wiley) last updated Oct 2016
- Embase (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

Search filters to retrieve economic evaluations and quality of life papers were appended to the population and intervention terms to identify relevant evidence. Searches were not undertaken for qualitative RQs. For social care topic questions additional terms were added. Searches were re-run in September 2017 where the filters were added to the population terms.

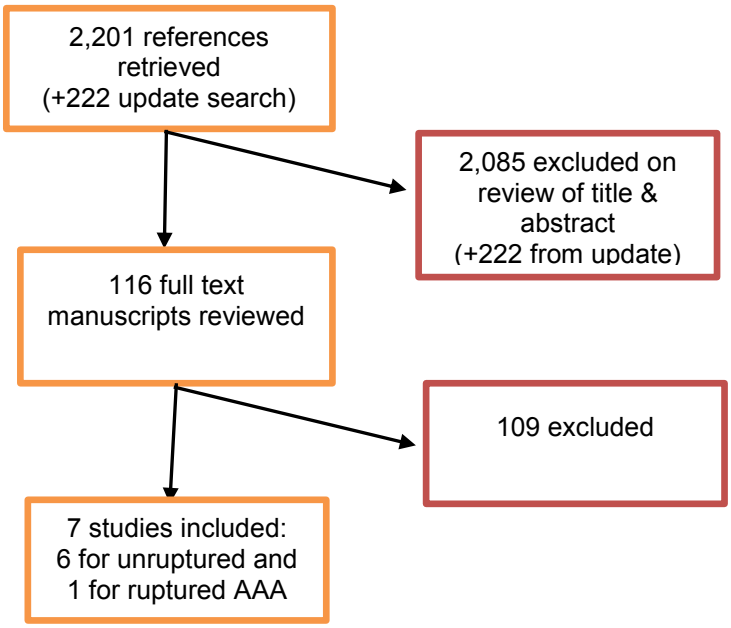
Health economics search strategy

Medline Strategy
Economic evaluations
1 Economics/
2 exp "Costs and Cost Analysis"/
3 Economics, Dental/
4 exp Economics, Hospital/
5 exp Economics, Medical/
6 Economics, Nursing/
7 Economics, Pharmaceutical/
8 Budgets/
9 exp Models, Economic/
10 Markov Chains/
11 Monte Carlo Method/
12 Decision Trees/
13 econom*.tw.
14 cba.tw.
15 cea.tw.
16 cua.tw.
17 markov*.tw.
18 (monte adj carlo).tw.
19 (decision adj3 (tree* or analys*)).tw.
20 (cost or costs or costing* or costly or costed).tw.
21 (price* or pricing*).tw.

Medline Strategy
22 budget*.tw. 23 expenditure*.tw. 24 (value adj3 (money or monetary)).tw. 25 (pharmacoeconomic* or (pharmaco adj economic*)).tw. 26 or/1-25 Quality of life 1 "Quality of Life"/ 2 quality of life.tw. 3 "Value of Life"/ 4 Quality-Adjusted Life Years/ 5 quality adjusted life.tw. 6 (qaly* or qald* or qale* or qtime*).tw. 7 disability adjusted life.tw. 8 daly*.tw. 9 Health Status Indicators/ 10 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. 11 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. 12 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. 13 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. 14 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. 15 (euroqol or euro qol or eq5d or eq 5d).tw. 16 (qol or hql or hqol or hrqol).tw. 17 (hye or hyes).tw. 18 health* year* equivalent*.tw. 19 utilit*.tw. 20 (hui or hui1 or hui2 or hui3).tw. 21 disutili*.tw. 22 rosser.tw. 23 quality of wellbeing.tw. 24 quality of well-being.tw. 25 qwb.tw. 26 willingness to pay.tw. 27 standard gamble*.tw. 28 time trade off.tw. 29 time tradeoff.tw. 30 tto.tw. 31 or/1-30

Appendix C – Clinical evidence study selection

Review question 13 and 24 study selection



Appendix D – Clinical evidence tables

Full citation	**Baron J-F, Bertrand M, Barré E, et al. (1991) Combined epidural and general anesthesia versus general anesthesia for abdominal aortic surgery. Anesthesiology 75: 611-8**
Study details	Study type: Quasi-randomised controlled trial Location(s): France Aim(s): To determine whether intraoperative thoracic epidural anaesthesia in combination with light general anaesthesia alters postoperative morbidity compared to a standard technique of balanced general anaesthesia Study dates: not reported Follow-up: not reported Sources of funding: not reported
Participants	Population: High-risk surgical patients scheduled for elective abdominal aortic reconstruction Sample size: 167 Inclusion criteria: patients undergoing elective open repair of AAA or aortoiliac occlusive disease were included. All participants had no contraindications for epidural anaesthesia (preoperative coagulopathy, localised infection or septicaemia and graft sepsis), a left ventricular ejection fraction greater than 35%; and an aortic surgical procedure performed via a midline xiphopubic skin incision. Exclusion criteria: not reported Baseline characteristics: • Mean age: epidural plus general anaesthesia group, 62 years; general anaesthesia-alone group, 61 years • Sex: epidural plus general anaesthesia group, 94.2% male; general anaesthesia-alone group, 86.4% male • Mean aneurysm size: not reported • Previous myocardial infarction: epidural plus general anaesthesia group, 15.1%; general anaesthesia-alone group, 18.5% • History of angina: epidural plus general anaesthesia group, 19.7%; general anaesthesia-alone group, 17.3% • ST-T abnormalities: epidural plus general anaesthesia group, 15.1%; general anaesthesia-alone group, 18.5% • Rhythm other than sinus: epidural plus general anaesthesia group, 2.3%; general anaesthesia-alone group, 7.4% • Hypertension: epidural plus general anaesthesia group, 44.2%; general anaesthesia-alone group, 43.4%
Intervention	Epidural anaesthesia plus general anaesthesia Intraoperative thoracic epidural anaesthesia in combination with light general anaesthesia: • An epidural catheter was inserted via the T8-T9 interspace, and thoracic epidural anaesthesia was induced using an initial 10ml dose of a mixture of plain bupivacaine 0.5% and lidocaine 2%; if necessary, additional incremental doses to a total of up to 16ml were given until a thoracoabdomina sensitive blockade was induced • General anaesthesia was induced using fentanyl (6 micrograms/kg), flunitrazepam (0.02 mg/kg) and pancuronium bromide (0.1 mg/kg);

Full citation	**Baron J-F, Bertrand M, Barré E, et al. (1991) Combined epidural and general anesthesia versus general anesthesia for abdominal aortic surgery. Anesthesiology 75: 611-8**
	• Anaesthesia was maintained under controlled ventilation (50% nitrous oxide in oxygen) by continuous epidural infusion (6-8ml/h) of the bupivacaine-lidocaine mixture described above; • When required, a low concentration of isoflurane was administered to maintain anaesthesia; this was increased to control arterial blood pressure during aortic cross clamping.
Comparison	Balanced general anaesthesia: • Induced using fentanyl (6 micrograms/kg), flunitrazepam (0.02 mg/kg) and pancuronium bromide (0.1 mg/kg); • Maintained under controlled ventilation (50% nitrous oxide in oxygen) by increments of fentanyl (approximately 1.5 micrograms/kg every 20 minutes) and pancuronium bromide; • When required, a low concentration of isoflurane was administered to maintain anaesthesia; this was increased to control arterial blood pressure during aortic cross clamping.
Outcomes measures	Mortality, cardiovascular morbidity, respiratory morbidity, renal failure, gastrointestinal bleeding, sepsis, major surgical complication, postoperative hospital stay
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Randomisation performed using table of random numbers. 2. Allocation concealment (selection bias): Unclear risk – it was not clear whether appropriate allocation concealment was performed 3. Blinding of participants and personnel (performance bias): Low risk – Authors did not state whether blinding was performed; however this is unlikely to have affected study results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Unclear risk – Authors did not state whether blinding was performed. 5. Incomplete outcome data (attrition bias): Low risk – Although 6 patients from the epidural plus general anaesthesia group were excluded due to non-functioning epidural catheter and subsequent use of general anaesthesia, this was unlikely to have bias study results. 6. Selective reporting (reporting bias): Low risk - All outcomes clearly defined. 7. Other bias: High risk – Postoperative analgesia was not the same in each group (possible performance bias). Furthermore, the study population included some patients who were undergoing surgery for aortoiliac occlusive disease (44%), rather than AAA. Overall risk of bias: High Directness: partially applicable

Full citation	Broekema AAA, Kuizenga K, Hennis PJ (1996). Does epidural sufentanil provide effective analgesia per- and postoperatively for abdominal aortic surgery? Acta Anaesthesiol Scandinavica, 40: 20-5
Study details	Study type: Double-blind randomised controlled trial Location(s): Netherlands Aim(s): To assess the efficacy of epidural sufentanil in providing peri- and postoperative analgesia Study dates: Not reported Follow-up: Not reported Sources of funding: Not reported
Participants	Population: people undergoing open surgical repair of unruptured AAA Sample size: 40 Inclusion criteria: people aged 20 to 80 years undergoing open surgical repair of unruptured AAA were included. All participants were categorised as ASA class I, II, or III Exclusion criteria: not reported Baseline characteristics: • Mean age: opioid epidural plus general anaesthesia group, 63 years; general anaesthesia-alone group, 67 years • Sex: opioid epidural plus general anaesthesia group, 90% male; general anaesthesia-alone group, 70% male • Mean aneurysm size: not reported • Comorbidities: not reported
Intervention	Opioid epidural plus general anaesthesia: Intraoperative thoracic epidural of 50 micrograms sufentanil in 10 ml normal saline solution in combination with general anaesthesia • Epidural injection of 50 micrograms sufentanil in 10 ml NaCl 0.9% • General anaesthesia induced using intravenous midazolam 0.1-0.2 mg * kg-1, sufentanil 0.5 micrograms * kg-1 and vecuronium 0.1 mg * kg-1;
Comparison	General anaesthesia-alone (Epidural placebo plus general anaesthesia): Intraoperative thoracic epidural of 10 ml normal saline solution in combination with general anaesthesia • Epidural injection of 10 ml NaCl 0.9% • General anaesthesia induced using intravenous midazolam, sufentanil and vecuronium; • Maintained under controlled ventilation (60% nitrous oxide in oxygen and halothane at a 1% inspiratory concentration)
Outcomes measures	Complications, adverse events, blood loss, & need for additional analgesia
Risk of bias assessment (using	1. Random sequence generation (selection bias): Unclear risk – Authors stated that randomisation was performed but the method was not reported. 8. Allocation concealment (selection bias): Unclear risk – The approach to allocation concealment not described.

Full citation	**Broekema AAA, Kuizenga K, Hennis PJ (1996). Does epidural sufentanil provide effective analgesia per- and postoperatively for abdominal aortic surgery? Acta Anaesthesiol Scandinavica, 40: 20-5**
Cochrane risk of bias tool)	2. Blinding of participants and personnel (performance bias): Low risk – Authors stated that the trial was double blind, No further details were provided. 3. Blinding of outcome assessment (detection bias): Low risk – Authors stated that the trial was double blind, No further details were provided. 4. Incomplete outcome data (attrition bias): Low risk – Few losses to follow-up were reported across treatment arms; reasons for follow-up were adequately reported. 5. Selective reporting (reporting bias): Unclear risk 6. Other bias: Low risk – none identified Overall risk of bias: Moderate Directness: directly applicable

Full citation	**Davies MJ, Silbert BS, Mooney PJ, et al. (1993) Combined epidural and general anaesthesia versus general anaesthesia for abdominal aortic surgery: A prospective randomised trial. Anaesthesia and Intensive Care, 1993, 21: 790-4**
Study details	Study type: Randomised controlled trial Location(s): Australia Aim(s): To examine the potential for combined epidural and general anaesthesia to reduce the incidence of respiratory and cardiovascular complications, decrease the duration of postoperative intensive care stay, and reduce the incidence of postoperative infections and complications. Study dates: not reported Follow-up: not reported Sources of funding: not reported
Participants	Population: people undergoing open surgical repair of unruptured AAA Sample size: 50 Inclusion criteria: Patients undergoing open repair of unruptured AAA Exclusion criteria: contraindications to epidural anaesthesia (septicaemia, abnormal coagulation status, infection at the proposed puncture site, neurological disease) Baseline characteristics: • Mean age: epidural plus general anaesthesia group, 65 years; general anaesthesia-alone group, 67 years • Sex: epidural plus general anaesthesia group, 84% male; general anaesthesia-alone group, 92% male • Mean aneurysm size: not reported • Angina: epidural plus general anaesthesia group, 12%; general anaesthesia-alone group, 20% • Left ventricular failure: epidural plus general anaesthesia group, 4%; general anaesthesia-alone group, 4% • Hypertension: epidural plus general anaesthesia group, 44%; general anaesthesia-alone group, 52%

Full citation	**Davies MJ, Silbert BS, Mooney PJ, et al. (1993) Combined epidural and general anaesthesia versus general anaesthesia for abdominal aortic surgery: A prospective randomised trial. Anaesthesia and Intensive Care, 1993, 21: 790-4**
	• Myocardial infarction: epidural plus general anaesthesia group, 20%; general anaesthesia-alone group, 24% • COPD: epidural plus general anaesthesia group, 20%; general anaesthesia-alone group, 64%
Intervention	Thoracic epidural combined with general anaesthesia: • On arrival in the operating theatre, a 16-guage Tuohy needle was inserted into the epidural space of the lower thoracic spine (usually T9-10); an 18-guage epidural catheter was then inserted • Following a 2ml test dose of lidocaine 1.5% with 1 in 200,000 adrenaline, a further 5ml was injected preoperatively into the epidural catheter; after this, 5ml was injected each hour intraoperatively • General anaesthesia was induced by administering fentanyl 1-3 micrograms/kg and thiopental sodium 2-4mg/kg, and the trachea was intubated following pancuronium bromide 0.1mg/kg; the patients lungs were ventilated with 66% N20 in oxygen and eflurane
Comparison	General anaesthesia-alone: • General anaesthesia was induced by administering fentanyl 1-3 micrograms/kg and thiopental sodium 2-4mg/kg, and the trachea was intubated following pancuronium bromide 0.1mg/kg; the patients lungs were ventilated with 66% N20 in oxygen and eflurane
Outcomes measures	Mortality, cardiovascular complications, respiratory complications, hepatic complications, renal complications, Length of hospital stay, length of ICU stay, intraoperative blood loss, infections,
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Authors stated that randomisation was performed; however the method of randomisation was not reported. 2. Allocation concealment (selection bias): Unclear risk – The approach to and use of allocation concealment was unclear 3. Blinding of participants and personnel (performance bias): Low risk – Authors did not state whether blinding was performed; however this is unlikely to have affected study results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Unclear risk – Authors did not state whether blinding was performed 5. Incomplete outcome data (attrition bias): Low risk – Losses to follow-up were small and relatively balanced across treatment arms. 6. Selective reporting (reporting bias): Low risk – Low risk - All relevant outcomes were reported. 7. Other bias: High risk – Postoperative analgesia was not the same in each group (possible performance bias). Overall risk of bias: High Directness: directly applicable

Full citation	Davis. (1987) Intrathecal morphine in aortic aneurysm surgery. Anaesthesia, 42: 491-7
Study details	Study type: Randomised controlled trial Location(s): UK Aim(s): The present study compares low-dose intrathecal morphine with balanced anaesthesia in aortic aneurysm surgery. Study dates: not reported Follow-up: not reported Sources of funding: not reported
Participants	Population: men undergoing open surgical repair of unruptured AAA Sample size: 30 Inclusion criteria: Male patients who presented for aortic aneurysm surgery (open repair), who were in sinus rhythm, were not taking beta-adrenoceptor blocking drugs or calcium antagonists and had not sustained a recognised myocardial infarction in the preceding 6 months were included Exclusion criteria: not reported Baseline characteristics: • Mean age: epidural plus general anaesthesia group, 65.6 years; general anaesthesia-alone group, 53.8 years • Sex: 100% male • Mean aneurysm size: not reported • Comorbidities: not reported
Intervention	Intrathecal opioid plus general anaesthesia: • Intrathecal injection of 0.8 mg preservative-free morphine in 4ml of 0.9% saline, without barbotage, at the L2-3 level through a 25-G needle immediately before pre-oxygenation. They received no further analgesia in theatre.
Comparison	General anaesthesia-alone: • Papaveretum 0.1 mg/kg by slow intravenous injection during preoxygenation and additional doses of the same drug during surgery to a total dose of 0.25-0.5 mg/kg depending upon body weight and pre-operative condition: the mean dose (standard deviation) was 30±10 mg with a range of 10-40 mg.
Outcomes measures	Pain & clinical respiratory depression
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Authors stated that randomisation was performed; however the method of randomisation was not reported. 2. Allocation concealment (selection bias): Unclear risk – The approach to and use of allocation concealment was not reported 3. Blinding of participants and personnel (performance bias): Low risk – It is unclear whether participants were blinded to treatment allocations; however this is unlikely to have affected study results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Low risk – Assessors blinded to intervention allocation. 5. Incomplete outcome data (attrition bias): Low risk – There were low rates of losses to follow-up across treatment arms 6. Selective reporting (reporting bias): Low-risk All relevant outcomes were reported

Full citation	Davis. (1987) Intrathecal morphine in aortic aneurysm surgery. Anaesthesia, 42: 491-7
	7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	Dodds TM, Burns K, DeRoo DB, ET AL. (1997). Effects of anesthetic technique on myocardial wall motion abnormalities during abdominal aortic surgery. Journal of Cardiothoracic and Vascular Anesthesia, 11: 129-36
Study details	Study type: Double blind, randomised controlled trial Location(s): Lebanon Aim(s): to assess whether supplementation of general anaesthesia with epidural anaesthesia would decrease the incidence of new left ventricular segmental wall motion abnormalities during abdominal aortic surgery Study dates: not reported Follow-up: not reported Sources of funding: not reported
Participants	Population: people undergoing open surgical repair of unruptured AAA Sample size: 73 Inclusion criteria: patients scheduled for open repair of unruptured infrarenal AAA via an anterior, transperitoneal approach were included Exclusion criteria: a primary diagnosis of aortic occlusive disease, previous coronary artery bypass surgery, and contraindications to placement of an epidural catheter (coagulopathy, localized infection at site of insertion) or a pre-existing neurological deficit Baseline characteristics: • Mean age: epidural plus general anaesthesia group, 71 years; general anaesthesia-alone group, 71 years • Sex: epidural plus general anaesthesia group, 80% male; general anaesthesia-alone group, 80.7% male • Mean aneurysm size: not reported • Myocardial infarction: epidural plus general anaesthesia group, 27%; general anaesthesia-alone group, 38% • Hypertension: epidural plus general anaesthesia group, 67%; general anaesthesia-alone group, 54%
Intervention	Epidural plus general anaesthesia: • All patients were sedated with intravenous midazolam, as needed, while in a holding area outside the operating room, during placement of invasive catheters and the epidural; • Before induction of general anaesthesia, an epidural catheter was placed between the tenth thoracic and second lumbar interspace, using a loss-of-resistance technique, in all patients; • Induction of anaesthesia was similar in both study groups and was accomplished, after preoxygenation, with fentanyl, 2 to 5 micrograms, followed by thiopental sodium, 2 to 4mg/kg, endotracheal intubation followed administration of vecuronium, 0.1mg/kg, or suxamethonium, 1mg/kg

Full citation	**Dodds TM, Burns K, DeRoo DB, ET AL. (1997). Effects of anesthetic technique on myocardial wall motion abnormalities during abdominal aortic surgery. Journal of Cardiothoracic and Vascular Anesthesia, 11: 129-36**
	• Anaesthesia was maintained with a nitrous oxide/oxygen ratio of 1:1 and enflurane, 0.5 to 1.0 MAC (end-tidal concentration); vecuronium was used to maintain surgical relaxation • After the induction of general anaesthesia, patients were administered (in divided doses) 6 to 9 mL of 1.5% lidocaine with 1:200,000 adrenaline which served as a test dose and to establish initial epidural blockade; subsequently, a further 5 to 8 mL of 0.5% bupivacaine was administered followed by an infusion at 6 to 8 mL/h.
Comparison	General anaesthesia-alone • All patients were sedated with intravenous midazolam, as needed, while in a holding area outside the operating room, during placement of invasive catheters and the epidural; • Before induction of general anaesthesia, an epidural catheter was placed between the tenth thoracic and second lumbar interspace, using a loss-of-resistance technique, in all patients; • Induction of anaesthesia was similar in both study groups and was accomplished, after preoxygenation, with fentanyl, 2 to 5 micrograms, followed by thiopental sodium, 2 to 4mg/kg, endotracheal intubation followed administration of vecuronium, 0.1mg/kg, or suxamethonium, 1mg/kg • Anaesthesia was maintained with a nitrous oxide/oxygen ratio of 1:1 and enflurane, 0.5 to 1.0 MAC (end-tidal concentration); supplemental doses of fentanyl, 1 to 2 micrograms/kg/h, were administered as needed, and vecuronium was used to maintain surgical relaxation
Outcomes measures	In-hospital mortality, cardiac morbidity, respiratory morbidity, renal insufficiency & blood loss
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Authors reported that randomisation was performed; however no information was provided as to how it was performed. 2. Allocation concealment (selection bias): Unclear risk – The approach to and use of allocation concealment was not reported. 3. Blinding of participants and personnel (performance bias): Low risk –The anaesthetist caring for the patient was aware of group assignment, but patients were blinded to treatment group. This is unlikely to have affected study results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Low risk – Assessors were blinded to treatment allocations. 5. Incomplete outcome data (attrition bias): Low risk – There were low rates of losses to follow-up across treatment arms. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported. 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**Fleron M-H, Weiskopf RB, Bertrand M, Mouren S et al. (2003) A comparison of intrathecal opioid and intravenous analgesia for the incidence of cardiovascular, respiratory, and renal complications after abdominal aortic surgery. Anesth Analg, 97: 2-12**
Study details	Study type: Randomised controlled trial Location(s): France Aim(s): to evaluate whether the administration of neuraxial opioids, in the intraoperative and immediate postoperative periods, would reduce the combined incidence of major cardiac, respiratory, and renal complications after major abdominal aortic surgery Study dates: not reported Follow-up: not reported Sources of funding: not reported
Participants	Population: people undergoing open surgical repair of unruptured AAA or aortoiliac occlusive disease Sample size: 217 Inclusion criteria: patients undergoing elective open repair of AAA or aortoiliac occlusive disease were included. Exclusion criteria: contraindications to dural puncture (clinical signs of coagulopathy, localized infection, septicaemia, graft infection, previous lumbar spinal surgery). Baseline characteristics: • Mean age: epidural plus general anaesthesia group, 67 years; general anaesthesia-alone group, 66 years • Sex: epidural plus general anaesthesia group, 89% male; general anaesthesia-alone group, 88% male • Mean aneurysm size: not reported • Aortic disease: epidural plus general anaesthesia group, 68%; general anaesthesia-alone group, 62% • Coronary artery disease: epidural plus general anaesthesia group, 39%; general anaesthesia-alone group, 35% • Hypertension: epidural plus general anaesthesia group, 51%; general anaesthesia-alone group, 58% • Congestive heart failure: epidural plus general anaesthesia group, 3%; general anaesthesia-alone group, 8% • COPD: epidural plus general anaesthesia group, 34%; general anaesthesia-alone group, 30% • Diabetes: epidural plus general anaesthesia group, 11%; general anaesthesia-alone group, 16%
Intervention	Intrathecal opioid plus general anaesthesia: • Balanced general anaesthesia with intravenous sufentanil, isoflurane, and 50% nitrous oxide combined with intrathecal opioid (1 micrograms/kg sufentanil with 8 micrograms/kg preservative-free morphine injected at the L4-5 interspace)
Comparison	General anaesthesia-alone: • Balanced general anaesthesia with intravenous sufentanil, isoflurane and 50% nitrous oxide. Anaesthesia was induced with intravenous 0.5 micrograms/kg IV sufentanil, and 1–2 mg/kg IV propofol
Outcomes measures	Major complications, cardiovascular complications, respiratory complications, renal complications & length of hospital stay
Risk of bias assessment	1. Random sequence generation (selection bias): Low risk – randomisation was performed using computer-generated random sequences

Full citation	**Fleron M-H, Weiskopf RB, Bertrand M, Mouren S et al. (2003) A comparison of intrathecal opioid and intravenous analgesia for the incidence of cardiovascular, respiratory, and renal complications after abdominal aortic surgery. Anesth Analg, 97: 2-12**
(using Cochrane risk of bias tool)	2. Allocation concealment (selection bias): Unclear risk – The approach to and use of allocation concealment was not reported. 3. Blinding of participants and personnel (performance bias): Low risk – patients and those taking care of them were not blinded; however this is unlikely to have affected study results because objective outcomes were assessed. 4. Blinding of outcome assessment (detection bias): Unclear risk – Authors did not report whether outcome assessors were blinded to treatment allocations. 5. Incomplete outcome data (attrition bias): Low risk – There were low rates of losses to follow-up across treatment arms. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported. 7. Other bias: High risk – Study population included some patients who were undergoing surgery for aortoiliac occlusive disease (35%), rather than AAA. Overall risk of bias: Moderate Directness: partially applicable

Full citation	**Norris EJ, Beattie C, Perler BA et al. (2001) Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology, 95: 1054-67**
Study details	Study type: Double-blind, randomised controlled trial Location(s): USA Aim(s): To compare alternate combinations of intraoperative anaesthesia and postoperative analgesia with respect to postoperative outcomes in patients undergoing surgery of the abdominal aorta Study dates: August 1993 to July 1997 Follow-up: not reported Sources of funding: not reported
Participants	Population: patients undergoing open surgery to repair unruptured AAA or surgery for aortoiliac occlusive disease, and visceral and renal arterial reconstruction Sample size: 168 Inclusion criteria: patients undergoing elective abdominal aortic reconstructive surgery were included. Procedures included open abdominal aortic surgery for unruptured AAA or aortoiliac occlusive disease, as well as visceral and renal arterial reconstruction requiring abdominal aortic cross-clamping. Exclusion criteria: patients whose procedure required clamping of the thoracic aorta, contraindication to any feature of the proposed clinical management (including epidural anaesthesia, previous surgery or severe deformity of the thoraco-lumbar spine, previous or current neurologic disease affecting the lower hemithorax or below) opioid dependence and major surgery in the previous 14 days Baseline characteristics:

Full citation	**Norris EJ, Beattie C, Perler BA et al. (2001) Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. Anesthesiology, 95: 1054-67**
	• Mean age: epidural plus general anaesthesia group, 68 years; general anaesthesia-alone group, 69 years • Sex: unclear as se • Mean aneurysm size: not reported • Comorbidities: not adequately reported
Intervention	Thoracic epidural anaesthesia combined with a light general anaesthesia: • Thoracic epidural catheter placement was performed via the midline approach using a standard loss-of-resistance technique at the T8–T9 interspace for patients requiring a left flank incision, and at the T10–T11 interspace for patients requiring a midline incision. Epidural bolus: 6ml (left flank incision) or 8ml (midline incision) of 0.5% bupivacaine with 50 micrograms fentanyl • General anaesthesia was achieved as follows: each subject received 10–15ml/kg of lactated Ringer's solution before induction, followed by incremental doses of sodium thiopental (up to 500mg) and fentanyl (up to 250 micrograms, including sedation fentanyl) until unconsciousness was achieved; general anaesthesia was maintained using 50% nitrous oxide in oxygen and enflurane (0.2–0.8% end tidal)
Comparison	General anaesthesia plus placebo: • General anaesthesia was achieved as follows: each subject received 10–15ml/kg of lactated Ringer's solution before induction, followed by incremental doses of sodium thiopental (up to 500mg) and fentanyl (up to 250 micrograms, including sedation fentanyl) until unconsciousness was achieved; general anaesthesia was maintained using 50% nitrous oxide in oxygen and enflurane (0.2–0.8% end tidal)
Outcomes measures	Mortality, cardiac complications, respiratory complications, renal complications, intraoperative blood loss, reoperation, readmission to ICU
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Authors reported that randomisation was performed but the methods were not specified 2. Allocation concealment (selection bias): Unclear risk – The approach to and use of allocation concealment was not reported. 3. Blinding of participants and personnel (performance bias): Low risk – it is unclear whether patients were blinded to treatment allocations; however, this is unlikely to have affected study results. 4. Blinding of outcome assessment (detection bias): Unclear risk – Authors did not report whether outcome assessors were blinded to treatment allocations. 5. Incomplete outcome data (attrition bias): Low risk – There were low rates of losses to follow-up across treatment arms. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported. 7. Other bias: patients undergoing elective abdominal aortic reconstructive surgery were included. Procedures included open abdominal aortic surgery for unruptured AAA or aortoiliac occlusive disease, as well as visceral and renal arterial reconstruction. Overall risk of bias: Moderate Directness: partially applicable

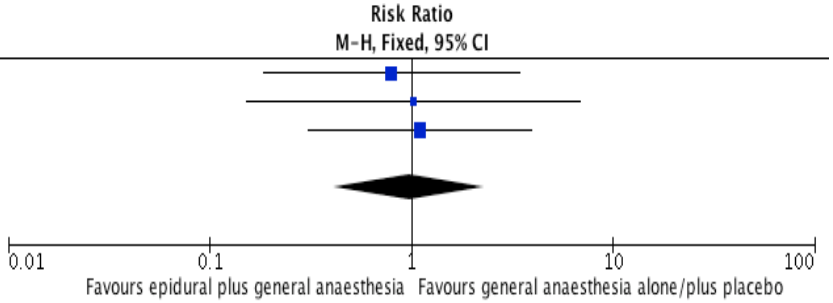
Appendix E – Forest plots

Epidural plus general anaesthesia versus general anaesthesia-alone/plus placebo during open repair of unruptured AAA

Mortality

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	3	81	4	86	38.4%	0.80 [0.18, 3.45]
Dodds	2	36	2	37	19.5%	1.03 [0.15, 6.91]
Norris	5	85	4	75	42.1%	1.10 [0.31, 3.96]
Total (95% CI)		**202**		**198**	**100.0%**	**0.97 [0.41, 2.29]**
Total events	10		10			

Heterogeneity: $Chi^2 = 0.11$, df = 2 (P = 0.95); $I^2 = 0\%$
Test for overall effect: Z = 0.07 (P = 0.95)

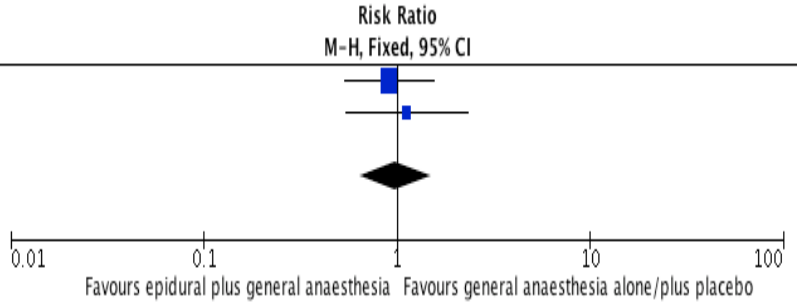


Cardiovascular adverse events

Any cardiovascular adverse event

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	19	81	22	86	68.4%	0.92 [0.54, 1.56]
Dodds	11	36	10	37	31.6%	1.13 [0.55, 2.33]
Total (95% CI)		**117**		**123**	**100.0%**	**0.98 [0.64, 1.51]**
Total events	30		32			

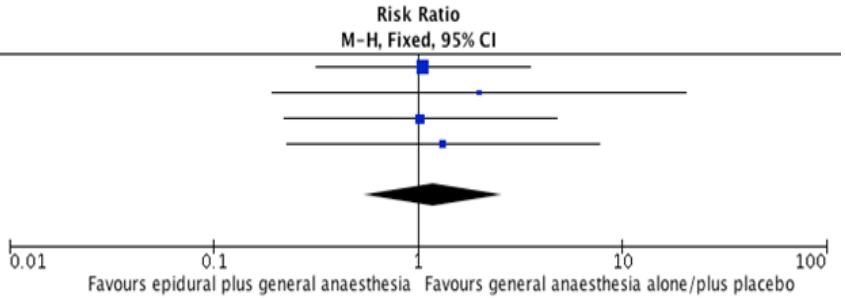
Heterogeneity: $Chi^2 = 0.21$, df = 1 (P = 0.65); $I^2 = 0\%$
Test for overall effect: Z = 0.07 (P = 0.94)



Myocardial infarction

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	5	81	5	86	44.4%	1.06 [0.32, 3.53]
Davies	2	25	1	25	9.1%	2.00 [0.19, 20.67]
Dodds	3	36	3	37	27.1%	1.03 [0.22, 4.76]
Norris	3	85	2	75	19.4%	1.32 [0.23, 7.71]
Total (95% CI)		**227**		**223**	**100.0%**	**1.19 [0.54, 2.60]**
Total events	13		11			

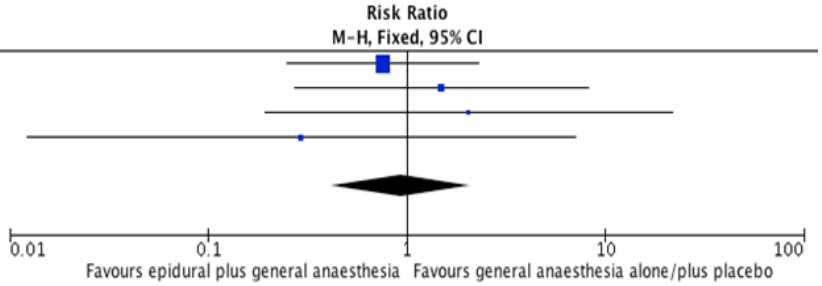
Heterogeneity: Chi² = 0.27, df = 3 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.43 (P = 0.66)



Congestive heart failure

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	5	81	7	86	59.7%	0.76 [0.25, 2.29]
Davies	3	25	2	25	17.6%	1.50 [0.27, 8.22]
Dodds	2	36	1	37	8.7%	2.06 [0.19, 21.69]
Norris	0	85	1	75	14.0%	0.29 [0.01, 7.12]
Total (95% CI)		**227**		**223**	**100.0%**	**0.94 [0.42, 2.10]**
Total events	10		11			

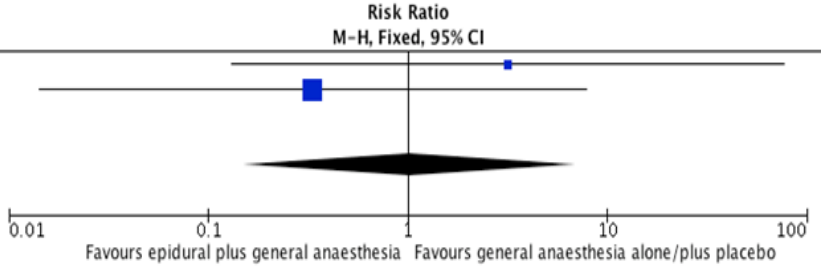
Heterogeneity: Chi² = 1.37, df = 3 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.16 (P = 0.87)



Ventricular tachyarrhythmia

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	1	81	0	86	24.4%	3.18 [0.13, 77.03]
Davies	0	25	1	25	75.6%	0.33 [0.01, 7.81]
Norris	0	85	0	75		Not estimable
Total (95% CI)		**191**		**186**	**100.0%**	**1.03 [0.15, 7.07]**
Total events	1		1			

Heterogeneity: Chi² = 0.97, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.98)

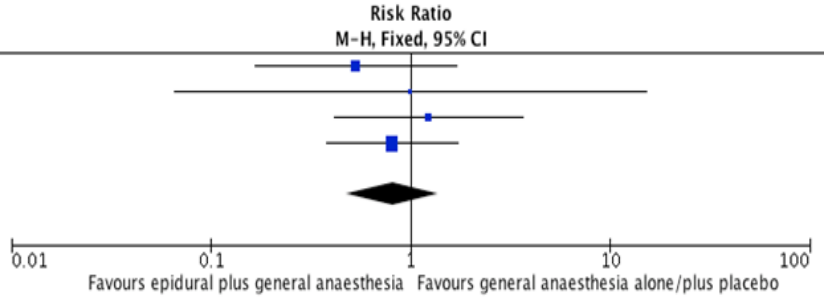


Respiratory adverse events

Acute respiratory failure (prolonged ventilation)

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	4	81	8	86	29.3%	0.53 [0.17, 1.70]
Davies	1	25	1	25	3.8%	1.00 [0.07, 15.12]
Dodds	6	36	5	37	18.7%	1.23 [0.41, 3.68]
Norris	11	85	12	75	48.2%	0.81 [0.38, 1.72]
Total (95% CI)		**227**		**223**	**100.0%**	**0.81 [0.48, 1.39]**
Total events	22		26			

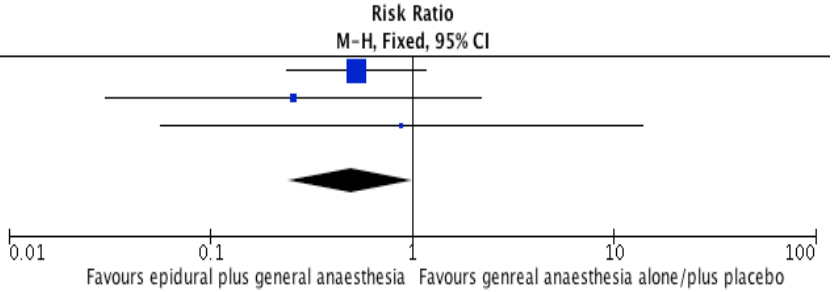
Heterogeneity: $Chi^2 = 1.10$, $df = 3$ ($P = 0.78$); $I^2 = 0\%$
Test for overall effect: $Z = 0.76$ ($P = 0.45$)



Pneumonia

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	8	81	16	86	75.6%	0.53 [0.24, 1.17]
Dodds	1	36	4	37	19.2%	0.26 [0.03, 2.19]
Norris	1	85	1	75	5.2%	0.88 [0.06, 13.86]
Total (95% CI)		**202**		**198**	**100.0%**	**0.50 [0.24, 1.01]**
Total events	10		21			

Heterogeneity: $Chi^2 = 0.56$, $df = 2$ ($P = 0.76$); $I^2 = 0\%$
Test for overall effect: $Z = 1.93$ ($P = 0.05$)

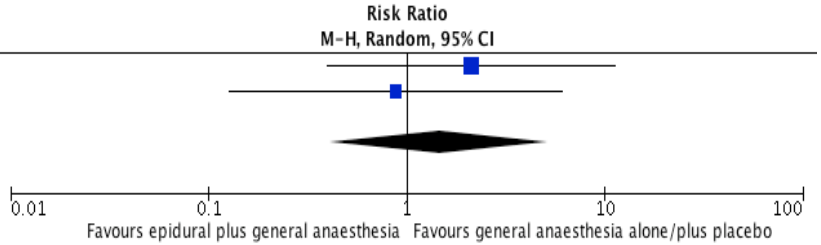


Renal adverse events

Renal failure

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Baron	4	81	2	86	57.3%	2.12 [0.40, 11.28]
Norris	2	85	2	75	42.7%	0.88 [0.13, 6.11]
Total (95% CI)		**166**		**161**	**100.0%**	**1.46 [0.41, 5.17]**
Total events	6		4			

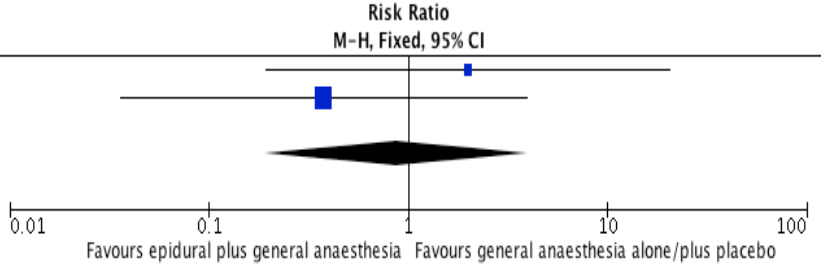
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.45$, df = 1 (P = 0.50); $I^2 = 0\%$
Test for overall effect: Z = 0.59 (P = 0.56)



Renal insufficiency

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davies	2	25	1	25	30.4%	2.00 [0.19, 20.67]
Dodds	1	36	2	27	69.6%	0.38 [0.04, 3.92]
Total (95% CI)		**61**		**52**	**100.0%**	**0.87 [0.19, 3.98]**
Total events	3		3			

Heterogeneity: $Chi^2 = 0.98$, df = 1 (P = 0.32); $I^2 = 0\%$
Test for overall effect: Z = 0.18 (P = 0.86)

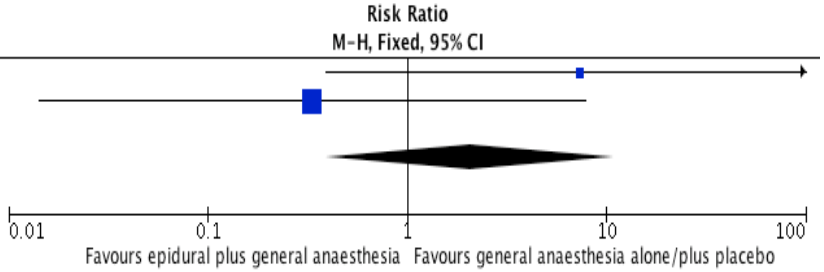


Gastrointestinal adverse events

Gastrointestinal bleeding

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	3	81	0	86	24.4%	7.43 [0.39, 141.58]
Davies	0	25	1	25	75.6%	0.33 [0.01, 7.81]
Total (95% CI)		**106**		**111**	**100.0%**	**2.07 [0.39, 10.95]**
Total events	3		1			

Heterogeneity: $Chi^2 = 2.01$, df = 1 (P = 0.16); $I^2 = 50\%$
Test for overall effect: Z = 0.85 (P = 0.39)

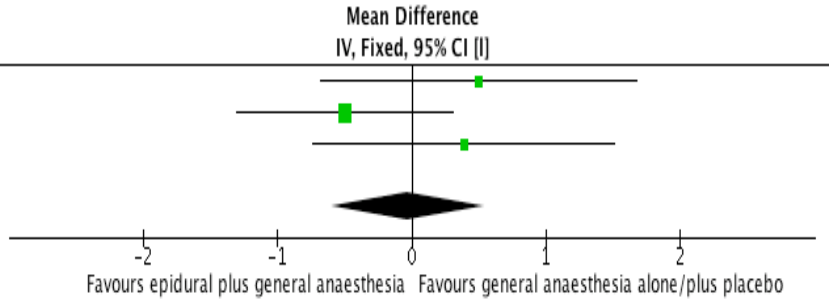


Surgical complications

Blood loss

Study or Subgroup	Epidural plus general anaesthesia Mean [l]	SD [l]	Total	General anaesthesia alone/plus placebo Mean [l]	SD [l]	Total	Weight	Mean Difference IV, Fixed, 95% CI [l]
Broekma	2.4	2.4	20	1.9	1.2	20	23.7%	0.50 [-0.68, 1.68]
Davies	2.3	1.3	25	2.8	1.6	25	50.3%	-0.50 [-1.31, 0.31]
Dodds	2.97	2.67	36	2.58	2.2	37	26.0%	0.39 [-0.73, 1.51]
Total (95% CI)			**81**			**82**	**100.0%**	**-0.03 [-0.60, 0.54]**

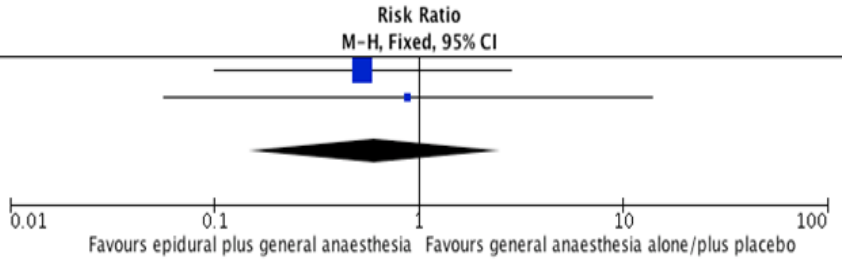
Heterogeneity: $Chi^2 = 2.62$, df = 2 (P = 0.27); $I^2 = 24\%$
Test for overall effect: Z = 0.11 (P = 0.91)



Sepsis

Study or Subgroup	Epidural plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baron	2	81	4	86	78.5%	0.53 [0.10, 2.82]
Norris	1	85	1	75	21.5%	0.88 [0.06, 13.86]
Total (95% CI)		**166**		**161**	**100.0%**	**0.61 [0.15, 2.51]**
Total events	3		5			

Heterogeneity: $Chi^2 = 0.10$, df = 1 (P = 0.76); $I^2 = 0\%$
Test for overall effect: Z = 0.69 (P = 0.49)

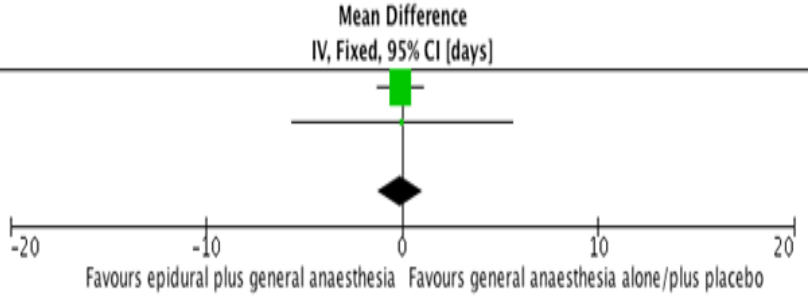


Resource use

Length of stay

Study or Subgroup	Epidural plus general anaesthesia Mean [days]	SD [days]	Total	General anaesthesia alone/plus placebo Mean [days]	SD [days]	Total	Weight	Mean Difference IV, Fixed, 95% CI [days]
Baron	15.6	3.8	81	15.7	3.9	86	95.9%	-0.10 [-1.27, 1.07]
Davies	16	8	25	16	12	25	4.1%	0.00 [-5.65, 5.65]
Total (95% CI)			106			111	100.0%	-0.10 [-1.24, 1.05]

Heterogeneity: $Chi^2 = 0.00$, df = 1 (P = 0.97); $I^2 = 0\%$
Test for overall effect: Z = 0.16 (P = 0.87)

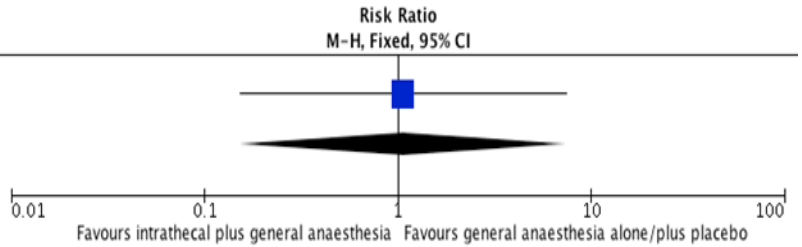


Intrathecal opioid plus general anaesthesia versus general anaesthesia-alone during open repair of unruptured AAA

Respiratory adverse events: respiratory depression

Study or Subgroup	Intrathecal plus general anaesthesia Events	Total	General anaesthesia alone/plus placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Davis	0	13	0	12		Not estimable
Fleron	2	105	2	112	100.0%	1.07 [0.15, 7.44]
Total (95% CI)		118		124	100.0%	1.07 [0.15, 7.44]
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.07 (P = 0.95)



Appendix F – GRADE tables

Epidural plus general anaesthesia versus general anaesthesia-alone/plus placebo during open repair of unruptured AAA

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Epidural plus general anaesthesia**	**General anaesthesia-alone**	**Summary of results**	
In-hospital mortality; effect sizes below 1 favour epidural plus general anaesthesia group									
3 (Baron 1991, Dodds 1997, Norris 2001)	RCTs	Serious[1]	Very Serious[2,3]	Not serious	Very serious[4]	202	198	RR 0.97 (0.41, 2.29)	Very low
Cardiovascular mortality; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[5]	N/A	Very serious[4]	25	25	RR 2.00 (0.19, 20.7)	Very low
12-month mortality; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Norris	RCT	Not serious	Serious[2]	N/A	Very serious[4]	85	75	RR 0.88 (0.30, 2.62)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention (in Baron 1991) includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
5. Lidocaine-adrenaline formulation & dosing (in Davies 1993 and Dodds 1997) varies significantly from that used in UK practice, downgrade 1 level.

Any adverse event

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Adverse events (myocardial infarction, congestive heart failure, ventricular tachyarrhythmias, supraventricular tachyarrhythmias, respiratory failure, renal insufficiency, gastrointestinal haemorrhage, hepatic failure, sepsis); effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[2]	N/A	Very serious[3]	25	25	RR 1.27 (0.73, 2.23)	Very low

1. Different postoperative analgesia were used in each treatment arm, downgrade 1 level
2. Lidocaine-adrenaline formulation & dosing used varies significantly from that used in UK practice, downgrade 1 level.
3. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Cardiovascular adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Any postoperative cardiovascular adverse event; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Baron 1991, Dodds 1997)	RCTs	Serious[1]	Very Serious[2,3]	Not serious	Very serious[4]	117	123	RR 0.98 (0.64, 1.51)	Very low
Cardiac death; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Norris 2001	RCT	Not serious	Serious[2]	N/A	Very serious[4]	85	25	RR 0.30 (0.01, 7.22)	Very low
Myocardial infarction; effect sizes below 1 favour epidural plus general anaesthesia group									
4 (Baron 1991, Davies 1993 Dodds 1997, Norris 2001)	RCTs	Serious[1]	Very Serious[2,3]	Not serious	Very serious[4]	227	223	RR 1.19 (0.54, 2.60)	Very low
Congestive heart failure; effect sizes below 1 favour epidural plus general anaesthesia group									
4 (Baron 1991, Davies 1993 Dodds 1997, Norris 2001)	RCTs	Serious[1]	Very Serious[2,3]	Not serious	Very serious[4]	227	223	RR 0.94 (0.42, 2.10)	Very low
Prolonged myocardial ischaemia; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Very Serious[2,3]	N/A	Very serious[4]	81	86	RR 1.06 (0.57, 1.98)	Very low

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Epidural plus general anaesthesia**	**General anaesthesia-alone**	**Summary of results**	
Ventricular tachyarrhythmia; effect sizes below 1 favour epidural plus general anaesthesia group									
3 (Baron 1991, Dodds 1997, Norris 2001)	RCTs	Serious[1]	Very Serious[2,3]	Not serious	Very serious[4]	191	186	RR 1.03 (0.15, 7.07)	Very low
Supraventricular tachyarrhythmia; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[5]	N/A	Very serious[4]	25	25	RR 1.00 (0.22, 4.49)	Very low
Unstable angina; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Norris 2001	RCT	Not serious	Serious[2]	N/A	Very serious[4]	85	75	RR 0.88 (0.02, 44.0)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention in Baron 1991 includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
5. Lidocaine-adrenaline formulation & dosing used (in Davies 1993 and Dodds 1997) varies significantly from that used in UK practice, downgrade 1 level.

Respiratory adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Any respiratory adverse event; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Serious[2,3]	N/A	Serious[4]	81	86	RR 0.92 (0.71, 1.19)	Very low
Acute respiratory failure (prolonged ventilation); effect sizes below 1 favour epidural plus general anaesthesia group									
4 (Baron 1991, Davies 1993 Dodds 1997, Norris 2001)	RCT	Serious[1]	Serious[2,3]	Not serious	Very serious[5]	227	223	RR 0.81 (0.48, 1.39)	Very low
Duration of ventilation (hours); effect sizes below 0 favour epidural plus general anaesthesia group									
1 Broekema 1996	RCT	Not serious	Not serious	N/A	Serious[6]	20	20	MD 2.20 (-2.79, 7.19)	Moderate
Minor atelectasis; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Serious[2,3]	N/A	Very serious[5]	81	86	RR 1.06 (0.74, 1.52)	Very low
Major atelectasis; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Serious[2,3]	N/A	Very serious[5]	81	86	RR 2.65 (0.53, 13.3)	Very low
Pneumonia; effect sizes below 1 favour epidural plus general anaesthesia group									
3 (Baron 1991, Dodds 1997, Norris 2001)	RCTs	Serious[1]	Serious[2,3]	Not serious	Serious[4]	202	198	RR 0.50 (0.24, 1.01)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention (in Baron 1991) includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.
5. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
6. Non-significant result, downgrade 1 level.

Renal adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Epidural plus general anaesthesia**	**General anaesthesia-alone**	**Summary of results**	
Renal failure; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Baron 1991, Norris 2001)	RCTs	Serious[1]	Serious[2,3]	Not serious	Very serious[4]	166	161	RR 1.46 (0.41, 10.95)	Very low
Renal insufficiency; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Dodds 1997, Davies 1993)	RCTs	Serious[1]	Serious[5]	Not serious	Very serious[4]	61	52	RR 0.87 (0.19, 3.98)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention in Baron 1991 includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
5. Lidocaine-adrenaline formulation & dosing used (in Davies 1993 and Dodds 1997) varies significantly from that used in UK practice, downgrade 1 level.

Gastrointestinal adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Epidural plus general anaesthesia**	**General anaesthesia-alone**	**Summary of results**	
Gastrointestinal bleeding; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Baron 1991, Davies 1993)	RCTs	Serious[1]	Very serious[2,3]	Serious[4]	Very serious[5]	106	111	RR 2.07 (0.39, 10.95)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention in Baron 1991 includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. I^2 value between 33.3% and 66.7%, downgrade 1 level.
5. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Surgical complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Any major surgical complication; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Very serious[2,3]	N/A	Very serious[4]	81	86	RR 0.69 (0.26, 1.85)	Very low
Blood loss; effect sizes below 0 favour epidural plus general anaesthesia group									
3 (Broekema 1996, Davies 1993, Dodds 1997)	RCTs	Serious[1]	Serious[5]	Not serious	Serious[6]	81	82	MD -0.03 (-0.60, 0.54)	Very low
1 Norris 2001	RCT	Not serious	Serious[2]	N/A	Very serious[7]	85	75	Median difference = 0	Very low
Need for additional analgesia; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Broekema 1996	RCT	Not serious	Not serious	N/A	Serious[8]	20	20	RR 0.38 (0.17, 0.88)	Moderate
Sepsis; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Baron 1991, Norris 2001)	RCTs	Serious[1]	Very serious[2,3]	Not serious	Very serious[4]	166	161	RR 0.61 (0.15, 2.51)	Very low
Wound infection; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[5]	N/A	Very serious[4]	25	25	RR 1.50 (0.27, 8.22)	Very low
Urinary tract infection; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[5]	N/A	Very serious[4]	25	25	RR 3.00 (0.13, 70.3)	Very low
Pulmonary infection; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Davies 1993	RCT	Serious[1]	Serious[5]	N/A	Very serious[4]	25	25	RR 2.00 (0.19, 20.7)	Very low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention in Baron 1991 includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
5. Lidocaine-adrenaline formulation & dosing used (in Davies 1993 and Dodds 1997) varies significantly from that used in UK practice, downgrade 1 level.
6. Non-significant result, downgrade 1 level.
7. Median reported with level of statistical significance not reported, downgrade 2 levels.
8. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.

Need for reoperation

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Reoperation; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Norris 2001	RCT	Not serious	Serious[1]	N/A	Very serious[2]	85	75	RR 1.06 (0.34, 3.33)	Very low

1. Study samples included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Resource use

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Duration of postoperative hospital stay (days); effect sizes below 0 favour epidural plus general anaesthesia group									
2 (Baron 1991, Davies 1993)	RCTs	Serious[1]	Very serious[2,3]	Not serious	Serious[4]	106	111	MD -0.10 (-1.24,1.05)	Very low
Duration of postoperative stay in intensive care unit (hours); effect sizes below 0 favour epidural plus general anaesthesia group									
1 Baron 1991	RCT	Serious[1]	Very serious[2,3]	N/A	Serious[4]	25	25	MD 3.00 (-14.6, 20.6)	Very low
Readmission to intensive care unit; effect sizes below 0 favour epidural plus general anaesthesia group									
1 Broekema 1996	RCT	Not serious	Not serious	N/A	Very serious[5]	85	75	RR 1.76 (0.33, 9.36)	Low

1. Different postoperative analgesia were used in each treatment arm (Baron 1991 and Davies 1993), downgrade 1 level
2. Study samples (in Baron 1991 and Norris 2001) included patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
3. Intervention in Baron 1991 includes flunitrazepam, which is not available in the UK, downgrade 1 level.
4. Non-significant result, downgrade 1 level.
5. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels

Intrathecal opioid plus general anaesthesia versus general anaesthesia-alone during elective open repair

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
30-day mortality; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	RR 0.30 (0.06, 1.43)	Very low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Any adverse event

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Adverse events (myocardial damage or infarction, congestive heart failure, new cardiac arrhythmia, new segmental or lobar atelectasis, confirmed pneumonia, severe respiratory depression, acute respiratory failure, or renal insufficiency); effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Serious[2]	105	112	RR 0.74 (0.48, 1.14)	Low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.

Cardiovascular adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Myocardial infarction; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	RR 0.53 (0.17, 1.72)	Very low
Congestive heart failure; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	RR 1.07 (0.22, 5.17)	Very low

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
New cardiac arrhythmia; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	RR 0.53 (0.14, 2.08)	Very low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Respiratory adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Respiratory depression; effect sizes below 1 favour epidural plus general anaesthesia group									
2 (Fleron 2003, Davis 1997)	RCTs	Not serious	Serious[1]	Not serious	Serious[2]	118	124	RR 0.92 (0.71, 1.19)	Low
Acute respiratory failure (prolonged ventilation); effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[3]	105	112	RR 0.81 (0.48, 1.39)	Very low
Major atelectasis; effect sizes below 0 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Serious[4]	105	112	MD 2.20 (-2.79, 7.19)	Low
Pneumonia; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[3]	105	112	RR 1.06 (0.74, 1.52)	Very low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.
3. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
4. Non-significant result, downgrade 1 level.

Renal adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Renal failure; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	RR 0.83 (0.32, 2.15)	Very low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Resource use

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Epidural plus general anaesthesia	General anaesthesia-alone	Summary of results	
Renal failure; effect sizes below 1 favour epidural plus general anaesthesia group									
1 Fleron 2003	RCT	Not serious	Serious[1]	N/A	Very serious[2]	105	112	median difference = 0	Very low

1. Study sample included a proportion patients who are undergoing surgery for aortoiliac occlusive disease as well as some undergoing AAA repair, downgrade 1 level.
2. Median reported with level of statistical significance not reported, downgrade 2 levels

Appendix G – Economic evidence study selection

Appendix H – Excluded studies

Clinical studies

Short Title		Reason for exclusion
Abdallah (2013)	Analgesic benefits of preincisional transversus abdominis plane block for abdominal aortic aneurysm repair	Not a controlled trial or systematic review of controlled trials
Aivatidi (2011)	Oxidative stress during abdominal aortic aneurysm repair - Biomarkers and antioxidant's protective effect: A review	Study does not contain a relevant intervention
Ansley (2006)	Is anesthesia good for you? Timing is everything!	Not a controlled trial or systematic review of controlled trials
Arar (2015)	Combined spinal-epidural anesthesia or local anesthesia + Sedoanalgesia in abdominal aortic Aneurism Repair?	Not a controlled trial or systematic review of controlled trials (retrospective study)
Asakura (2010)	In reply: The anesthetic technique of choice for better outcomes in high-risk elderly patients undergoing endovascular repair of aortic aneurysm	Not a controlled trial or systematic review of controlled trials
Ballantyne (2004)	Does epidural analgesia improve surgical outcome?	Not a controlled trial or systematic review of controlled trials
Barbieri (2011)	Analgesia and endocrine surgical stress: effect of two analgesia protocols on cortisol and prolactin levels during abdominal aortic aneurysm endovascular repair	Study does not contain a relevant intervention
Baril (2007)	Endovascular Abdominal Aortic Aneurysm Repair: Emerging Developments and Anesthetic Considerations	Not a controlled trial or systematic review of controlled trials
Baril (2009)	The management of ruptured infrarenal abdominal aortic aneurysms	Not a controlled trial or systematic review of controlled trials
Barker (2005)	High thoracic epidural with general anesthesia for combined simultaneous on-pump coronary artery bypass grafts and abdominal aortic aneurysm repair	Not a peer-reviewed publication
Bayly (2001)	In-hospital mortality from abdominal aortic surgery in Great Britain and Ireland: Vascular Anaesthesia Society audit	Study does not contain a relevant intervention
Berggren (1989)	Eleven years of aortic aneurysm surgery: changes in techniques and results	Not a controlled trial or systematic review of controlled trials
Blake (1998)	Patient-controlled epidural versus intravenous pethidine to supplement epidural bupivacaine after abdominal aortic surgery	Study does not contain a relevant intervention (postoperative pain management)
Blay (2006)	Efficacy of low-dose intrathecal morphine for postoperative analgesia after abdominal aortic surgery: A double-blind randomized study	Study does not contain a relevant intervention (postoperative pain management)

Short Title		Reason for exclusion
Bookallil (1968)	Anaesthetic management of aortic aneurysms	Not a controlled trial or systematic review of controlled trials
Botney (1998)	Comparison of lumbar and thoracic epidural narcotics for postoperative analgesia in patients undergoing abdominal aortic aneurysm repair	Study does not contain a relevant intervention
Boylan (1998)	Epidural bupivacaine-morphine analgesia versus patient-controlled analgesia following abdominal aortic surgery. Analgesic, respiratory, and myocardial effects	Study does not contain a relevant intervention
Brady (2005)	Perioperative beta-blockade (POBBLE) for patients undergoing infrarenal vascular surgery: results of a randomized double-blind controlled trial	Study does not contain a relevant intervention
Brimacombe (1993)	A review of anaesthesia for ruptured abdominal aortic aneurysm with special emphasis on preclamping fluid resuscitation	Not a controlled trial or systematic review of controlled trials
Bull (1964)	Anaesthetic Problems in Resection of Abdominal Aortic Aneurysms	Not a controlled trial or systematic review of controlled trials
Carli (1997)	Combined epidural/general anaesthesia	Not a controlled trial or systematic review of controlled trials
Chiesa (2013)	Open repair of juxtarenal aortic aneurysms	Not a controlled trial or systematic review of controlled trials
Chlebowski (1999)	Anesthesia for abdominal aortic aneurysm surgery part I: Preoperative evaluation	Not a controlled trial or systematic review of controlled trials
Chlebowski (1999)	Anesthesia for abdominal aortic surgery part II: Intraoperative and postoperative management	Not a controlled trial or systematic review of controlled trials
Chuter (1999)	Abdominal aortic aneurysm in high-risk patients: Short- to intermediate- term results of endovascular repair	Not a controlled trial or systematic review of controlled trials
Crawford (1982)	A comparison of intercostal block with general anesthesia for abdominal aortic aneurysm resection	Not a controlled trial or systematic review of controlled trials
Crosby (1990)	A randomized double-blind comparison of fentanyl- and sufentanil-oxygen anesthesia for abdominal aortic surgery	Study does not contain a relevant intervention
Cunningham (1989)	Anaesthesia for abdominal aortic surgery: A review (Part I)	Not a controlled trial or systematic review of controlled trials
Cunningham (1989)	Anaesthesia for abdominal aortic surgery--a review (Part II)	Not a controlled trial or systematic review of controlled trials

Short Title		Reason for exclusion
Cunningham (1991)	Abdominal aortic surgery: Anesthetic implications	Not a controlled trial or systematic review of controlled trials
Curley (1996)	Rectus sheath bupivacaine analgesia after aortic surgery	Not a controlled trial or systematic review of controlled trials
Elisha (2014)	Anesthesia case management for endovascular aortic aneurysm repair	Not a controlled trial or systematic review of controlled trials
Ellard (2013)	Anaesthesia for vascular emergencies	Not a controlled trial or systematic review of controlled trials
Ellis (2005)	Pro: vascular stents in the radiology suite-an anesthesiologist is needed	Not a controlled trial or systematic review of controlled trials
Faggioli (2011)	Preferences of patients, their family caregivers and vascular surgeons in the choice of abdominal aortic aneurysms treatment options: The PREFER study	Not a controlled trial or systematic review of controlled trials
Fitzgerald (2003)	Perioperative Anaesthesiological Management and Outcome of the Ruptured Abdominal Aortic Aneurysm	Not a controlled trial or systematic review of controlled trials
Flaherty (2014)	Regional anesthesia for vascular surgery	Not a controlled trial or systematic review of controlled trials
Florence (1978)	Neuroleptanaesthesia for surgery of the abdominal aorta	Not a controlled trial or systematic review of controlled trials
Galt (1991)	The effect of ibuprofen on cardiac performance during abdominal aortic cross-clamping	Study does not contain a relevant intervention
Gamulin (1991)	Renal consequences of infrarenal aortic cross-clamping in humans: Influence of different anesthetic techniques	Not in English
Gold (1994)	The effect of lumbar epidural and general anesthesia on plasma catecholamines and hemodynamics during abdominal aortic aneurysm repair	No relevant outcomes reported
Gold (1997)	Comparison of lumbar and thoracic epidural narcotics for postoperative analgesia in patients undergoing abdominal aortic aneurysm repair	Study does not contain a relevant intervention
Gottlieb (2014)	Anesthesia for major vascular surgery	Not a controlled trial or systematic review of controlled trials
Haljamae (1999)	Anaesthesia in non-cardiac vascular surgery	Not a controlled trial or systematic review of controlled trials
Hartman (1997)	Anesthesia for abdominal aortic reconstruction	Not a controlled trial or systematic review of controlled trials

Short Title		Reason for exclusion
Her (1990)	Combined epidural and general anesthesia for abdominal aortic surgery	Not a controlled trial or systematic review of controlled trials
Herring (2013)	Anaesthesia for abdominal vascular surgery	Not a controlled trial or systematic review of controlled trials
Houweling (1992)	A haemodynamic comparison of epidural versus intrathecal sufentanil to supplement general anaesthesia for abdominal aortic surgery	Not a population of people undergoing surgery for an abdominal aortic aneurysm
Houweling (1993)	A haemodynamic comparison of intrathecal morphine and sufentanil supplemented with general anaesthesia for abdominal aortic surgery	Not a population of people undergoing surgery for an abdominal aortic aneurysm
Javid (2007)	Should all patients with a ruptured AAA be anaesthetised by a vascular specialist?	Study does not contain a relevant intervention
Joseph (1973)	Bloood loss and acid-base balance during elective abdominal aortic aneurysmectomy	Not a controlled trial or systematic review of controlled trials
Joshi (1997)	Ruptured aortic aneurysm and cardiac arrest associated with spinal anesthesia	Not a controlled trial or systematic review of controlled trials
Karkos (2011)	A meta-analysis and metaregression analysis of factors influencing mortality after endovascular repair of ruptured abdominal aortic aneurysms	Not a controlled trial or systematic review of controlled trials
Karlsen (1999)	Anaesthesia for abdominal aortic surgery	Not a controlled trial or systematic review of controlled trials
Karnwal (2009)	Endovascular abdominal aneurysm repair in nonagenarians: never beyond the limits	Not a peer-reviewed publication
Karthikesalingam (2012)	Locoregional anesthesia for endovascular aneurysm repair (Structured abstract)	Not a controlled trial or systematic review of controlled trials
Kilickan (2002)	Abdominal aortic aneurism operation in a high risk patient under combined spinal epidural anesthesia	Not a controlled trial or systematic review of controlled trials
Knight (1963)	Anaesthesia for the leaking abdominal aortic aneurysm	Not a controlled trial or systematic review of controlled trials
Kothandan (2016)	Anesthetic considerations for endovascular abdominal aortic aneurysm repair	Not a controlled trial or systematic review of controlled trials
Koyama (2012)	Efficacy of oral clonidine premedication on postoperative management for open abdominal aortic surgery	Not a peer-reviewed publication
Krajcer (2012)	Single-center experience of percutaneous abdominal aortic aneurysm repair with local anesthesia and conscious sedation: technique and results	Not a controlled trial or systematic review of controlled trials
Kunisawa (2014)	The dexmedetomidine concentration required after remifentanil anesthesia is three-fold	Not a controlled trial or systematic review of

Short Title		Reason for exclusion
	higher than that after fentanyl anesthesia or that for general sedation in the ICU	controlled trials
Lachat (2000)	Regarding "Feasibility of endovascular repair of abdominal aortic aneurysms with local anesthesia with intravenous sedation"	Not a peer-reviewed publication
Lachat (2000)	Regarding 'Feasibility of endovascular repair of abdominal aortic aneurysms with local anesthesia with intravenous sedation'	Not a peer-reviewed publication
Lichtor (2005)	Depth of anesthesia monitors and shock	Not a controlled trial or systematic review of controlled trials
Lindahl (2011)	Should I choose open surgery or EVAR for my aortic aneurysm repair? reflections on the PREFER study on patients' preferences	Not a controlled trial or systematic review of controlled trials
Lippman (2003)	Anesthesia for endovascular repair of abdominal and thoracic aortic aneurysms: A review article	Not a controlled trial or systematic review of controlled trials
Lippmann (2010)	The anesthetic technique of choice for better outcomes in high-risk elderly patients undergoing endovascular repair of aortic aneurysms	Not a peer-reviewed publication
Lippmann (2015)	An alternative anaesthetic technique on nonagenerians undergoing endovascular aortic surgery and long term outcomes	Not a peer-reviewed publication
Lombardo (2009)	Epidural plus general anesthesia vs general anesthesia alone for elective aortic surgery: effects on gastric electrical activity and serum gastrin secretion	No relevant outcomes reported
Lorentz (2008)	Anesthesia for endovascular surgery of the abdominal aorta	Not a controlled trial or systematic review of controlled trials
Lubarsky (1998)	The impact of choice of muscle relaxant on postoperative recovery time (multiple letters)	Not a controlled trial or systematic review of controlled trials
Mathes (2000)	Continuous spinal anesthetic technique for endovascular aortic stent graft surgery	Not a controlled trial or systematic review of controlled trials
Mehta (2010)	Endovascular aneurysm repair of ruptured abdominal aortic aneurysm: the Albany Vascular Group approach	Not a controlled trial or systematic review of controlled trials
Mehta (2010)	Ruptured Abdominal Aortic Aneurysm: Endovascular Program Development and Results	Not a controlled trial or systematic review of controlled trials
Miller (1989)	Continuous alfentanil infusion for abdominal aortic surgery	Not a controlled trial or systematic review of controlled trials
Muehling (2008)	Prospective randomized controlled trial to evaluate "fast-track" elective open infrarenal aneurysm repair	Study does not contain a relevant intervention
Muehling (2009)	A prospective randomized trial comparing traditional and fast-track patient care in elective open infrarenal aneurysm repair	Study does not contain a relevant intervention

Short Title		Reason for exclusion
Panaretou (2009)	Combined anaesthesia and postoperative epidural analgesia in patients with chronic obstructive pulmonary disease undergoing abdominal aortic aneurysm repair	Not a peer-reviewed publication
Panaretou (2009)	The effect of combined anaesthesia with epidural postoperative analgesia on splanchnic perfusion in patients undergoing abdominal aortic aneurysm repair	Not a peer-reviewed publication
Panaretou (2009)	Ropivacaine 0.2% vs. Levobupivacaine 0.125% combined with fentanyl for epidural analgesia after abdominal aortic aneurysm repair	Not a peer-reviewed publication
Panaretou (2012)	Combined general-epidural anesthesia with continuous postoperative epidural analgesia preserves sigmoid colon perfusion in elective infrarenal aortic aneurysm repair	No relevant outcomes reported
Paries (2002)	A multicenter experience with the Talent endovascular graft for the treatment of abdominal aortic aneurysms	Not a controlled trial or systematic review of controlled trials
Park (2002)	Anesthesia for endovascular repair of abdominal aortic aneurysm	Not a controlled trial or systematic review of controlled trials
Pichel (2008)	Focus on: Vascular anaesthesia	Not a controlled trial or systematic review of controlled trials
Pol (2014)	Frailty should determine type of anesthesia in reducing postoperative delirium after vascular surgery and not vice versa	Not a controlled trial or systematic review of controlled trials
Primieri (1991)	[A comparison of the hemodynamic effects of midazolam and propofol during anesthetic induction in patients at vascular risk]	Not in English
Rasmussen (1946)	Paravertebral injection of procaine for pain produced by aortic aneurysm	Not a controlled trial or systematic review of controlled trials
Riddell (2005)	Endovascular abdominal aortic aneurysm repair	Not a controlled trial or systematic review of controlled trials
Robertson (2011)	Anaesthesia for endovascular surgery	Not a controlled trial or systematic review of controlled trials
Saleh (1980)	Anesthesia and monitoring for aortic aneurysm surgery	Not a controlled trial or systematic review of controlled trials
Salman (2013)	Comparison of effects of epidural bupivacaine and intravenous meperidine analgesia on patient recovery following elective abdominal aortic surgery	Study does not contain a relevant intervention
Saratzis (2013)	Acute kidney injury after endovascular repair of abdominal aortic aneurysm	Not a controlled trial or systematic review of controlled trials

Short Title		Reason for exclusion
Schurmann (2012)	Tips and tricks: Patient selection, when to carry on and when to stop	Not a controlled trial or systematic review of controlled trials
Seeling (1985)	Infrarenal aortic bypass operations - influence of neuroleptanaesthesia and continuous epidural anaesthesia on cardiovascular responses during surgery	Not in English
Shigematsu (1985)	Evaluation of anesthetic management for the surgery of the aortic aneurysm	Not a controlled trial or systematic review of controlled trials
Sitzman (2000)	Combined general and epidural anesthesia for abdominal aortic aneurysm surgery	Not a controlled trial or systematic review of controlled trials
Smaka (2011)	Perioperative management of endovascular abdominal aortic aneurysm repair: update 2010	Not a controlled trial or systematic review of controlled trials
Smeets (1993)	Endocrine-metabolic response to abdominal aortic surgery: A randomized trial of general anesthesia versus general plus epidural anesthesia	No relevant outcomes reported
Stoneham (2014)	IR relevant locoregional techniques	Not a controlled trial or systematic review of controlled trials
Svensson (1992)	Aortic dissection and aortic aneurysm surgery: clinical observations, experimental investigations, and statistical analyses. Part I	Not a controlled trial or systematic review of controlled trials
Telford (2010)	Anaesthesia for abdominal vascular surgery	Not a controlled trial or systematic review of controlled trials
Tham (1997)	Back pain following postoperative epidural analgesia: an indicator of possible spinal infection	Not a controlled trial or systematic review of controlled trials
Tsakiliotis (2011)	Evaluation of hemodynamic parameters in endovascular treatment of ruptured abdominal aortic aneurysms (RAAAs) using different anaesthetic techniques. Preliminary study	Not a peer-reviewed publication
Varty (2011)	Comments regarding 'Local anaesthesia for endovascular repair of infra-renal aortic aneurysms'	Not a controlled trial or systematic review of controlled trials
Wozniak (2005)	Anesthesia for open abdominal aortic surgery	Not a controlled trial or systematic review of controlled trials
Xue (2014)	Comparing cardioprotective effects of anesthesia methods in patients undergoing elective abdominal aortic surgery	Not a controlled trial or systematic review of controlled trials
Young (1988)	Anaesthesia for elective abdominal aortic surgery	controlled trial or systematic review of controlled trials
Zaugg (2014)	Sevoflurane-Compared with propofol-based anesthesia reduces the need for inotropic support in patients undergoing abdominal aortic aneurysm repair: Evidence of	Not a controlled trial or systematic review of controlled trials

Short Title		Reason for exclusion
	cardioprotection by volatile anesthetics in noncardiac surgery	

Economic studies

No full text papers were retrieved. All studies were excluded at review of titles and abstracts.

Appendix I – Glossary

Abdominal Aortic Aneurysm (AAA)

A localised bulge in the abdominal aorta (the major blood vessel that supplies blood to the lower half of the body including the abdomen, pelvis and lower limbs) caused by weakening of the aortic wall. It is defined as an aortic diameter greater than 3 cm or a diameter more than 50% larger than the normal width of a healthy aorta. The clinical relevance of AAA is that the condition may lead to a life threatening rupture of the affected artery. Abdominal aortic aneurysms are generally characterised by their shape, size and cause:

- Infrarenal AAA: an aneurysm located in the lower segment of the abdominal aorta below the kidneys.
- Juxtarenal AAA: a type of infrarenal aneurysm that extends to, and sometimes, includes the lower margin of renal artery origins.
- Suprarenal AAA: an aneurysm involving the aorta below the diaphragm and above the renal arteries involving some or all of the visceral aortic segment and hence the origins of the renal, superior mesenteric, and celiac arteries, it may extend down to the aortic bifurcation.

Abdominal compartment syndrome

Abdominal compartment syndrome occurs when the pressure within the abdominal cavity increases above 20 mm Hg (intra-abdominal hypertension). In the context of a ruptured AAA this is due to the mass effect of a volume of blood within or behind the abdominal cavity. The increased abdominal pressure reduces blood flow to abdominal organs and impairs pulmonary, cardiovascular, renal, and gastro-intestinal function. This can cause multiple organ dysfunction and eventually lead to death.

Cardiopulmonary exercise testing

Cardiopulmonary Exercise Testing (CPET, sometimes also called CPX testing) is a non-invasive approach used to assess how the body performs before and during exercise. During CPET, the patient performs exercise on a stationary bicycle while breathing through a mouthpiece. Each breath is measured to assess the performance of the lungs and cardiovascular system. A heart tracing device (Electrocardiogram) will also record the hearts electrical activity before, during and after exercise.

Device migration

Migration can occur after device implantation when there is any movement or displacement of a stent-graft from its original position relative to the aorta or renal arteries. The risk of migration increases with time and can result in the loss of device fixation. Device migration may not need further treatment but should be monitored as it can lead to complications such as aneurysm rupture or endoleak.

Endoleak

An endoleak is the persistence of blood flow outside an endovascular stent - graft but within the aneurysm sac in which the graft is placed.

- Type I – Perigraft (at the proximal or distal seal zones): This form of endoleak is caused by blood flowing into the aneurysm because of an incomplete or ineffective seal at either end of an endograft. The blood flow creates pressure within the sac and significantly increases the risk of sac enlargement and rupture. As a result, Type I endoleaks typically require urgent attention.

- Type II – Retrograde or collateral (mesenteric, lumbar, renal accessory): These endoleaks are the most common type of endoleak. They occur when blood bleeds into the sac from small side branches of the aorta. They are generally considered benign because they are usually at low pressure and tend to resolve spontaneously over time without any need for intervention. Treatment of the endoleak is indicated if the aneurysm sac continues to expand.

- Type III – Midgraft (fabric tear, graft dislocation, graft disintegration): These endoleaks occur when blood flows into the aneurysm sac through defects in the endograft (such as graft fractures, misaligned graft joints and holes in the graft fabric). Similarly to Type I endoleak, a Type III endoleak results in systemic blood pressure within the aneurysm sac that increases the risk of rupture. Therefore, Type III endoleaks typically require urgent attention.

- Type IV– Graft porosity: These endoleaks often occur soon after AAA repair and are associated with the porosity of certain graft materials. They are caused by blood flowing through the graft fabric into the aneurysm sac. They do not usually require treatment and tend to resolve within a few days of graft placement.

- Type V – Endotension: A Type V endoleak is a phenomenon in which there is continued sac expansion without radiographic evidence of a leak site. It is a poorly understood abnormality. One theory that it is caused by pulsation of the graft wall, with transmission of the pulse wave through the aneurysm sac to the native aneurysm wall. Alternatively it may be due to intermittent leaks which are not apparent at imaging. It can be difficult to identify and treat any cause.

Endovascular aneurysm repair

Endovascular aneurysm repair (EVAR) is a technique that involves placing a stent –graft prosthesis within an aneurysm. The stent-graft is inserted through a small incision in the femoral artery in the groin, then delivered to the site of the aneurysm using catheters and guidewires and placed in position under X-ray guidance.

- Conventional EVAR refers to placement of an endovascular stent graft in an AAA where the anatomy of the aneurysm is such that the ‘instructions for use’ of that particular device are adhered to. Instructions for use define tolerances for AAA anatomy that the device manufacturer considers appropriate for that device. Common limitations on AAA anatomy are infrarenal neck length (usually >10mm), diameter (usually ≤30mm) and neck angle relative to the main body of the AAA

- Complex EVAR refers to a number of endovascular strategies that have been developed to address the challenges of aortic proximal neck fixation associated with complicated aneurysm anatomies like those seen in juxtarenal and suprarenal AAAs. These strategies include using conventional infrarenal aortic stent grafts outside their ‘instructions for use’, using physician-modified endografts, utilisation of

customised fenestrated endografts, and employing snorkel or chimney approaches with parallel covered stents.

Goal directed therapy

Goal directed therapy refers to a method of fluid administration that relies on minimally invasive cardiac output monitoring to tailor fluid administration to a maximal cardiac output or other reliable markers of cardiac function such as stroke volume variation or pulse pressure variation.

Post processing technique

For the purpose of this review, a post-processing technique refers to a software package that is used to augment imaging obtained from CT scans, (which are conventionally presented as axial images), to provide additional 2- or 3-dimensional imaging and data relating to an aneurysm's, size, position and anatomy.

Permissive hypotension

Permissive hypotension (also known as hypotensive resuscitation and restrictive volume resuscitation) is a method of fluid administration commonly used in people with haemorrhage after trauma. The basic principle of the technique is to maintain haemostasis (the stopping of blood flow) by keeping a person's blood pressure within a lower than normal range. In theory, a lower blood pressure means that blood loss will be slower, and more easily controlled by the pressure of internal self-tamponade and clot formation.

Remote ischemic preconditioning

Remote ischemic preconditioning is a procedure that aims to reduce damage (ischaemic injury) that may occur from a restriction in the blood supply to tissues during surgery. The technique aims to trigger the body's natural protective functions. It is sometimes performed before surgery and involves repeated, temporary cessation of blood flow to a limb to create ischemia (lack of oxygen and glucose) in the tissue. In theory, this "conditioning" activates physiological pathways that render the heart muscle resistant to subsequent prolonged periods of ischaemia.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent (medication that promotes blood clotting) that can be used to prevent, stop or reduce unwanted bleeding. It is often used to reduce the need for blood transfusion in adults having surgery, in trauma and in massive obstetric haemorrhage.