Abdominal aortic aneurysm: diagnosis and management

NICE guideline

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This guideline covers diagnosing and managing abdominal aortic aneurysms. It aims to improve care by helping people who are at risk to get tested, specifying how often to monitor asymptomatic aneurysms, and identifying when aneurysm repair is needed and which procedure will work best.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- People with an abdominal aortic aneurysm, their families and carers

This version of the guideline contains:

- the draft recommendations
- rationale and impact sections that explain why the committee made the recommendations and how they might affect practice
- the guideline context
- recommendations for research.

This guideline will update NICE technology appraisal guidance 167 (published February 2009).

Information about how the guideline was developed is on the guideline's page on the NICE website. This includes the evidence reviews, the scope, and details of the committee and any declarations of interest.

Contents

Recommendations

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 *Diagnosis*

Identifying people at risk of abdominal aortic aneurysms

1.1.1 Tell all men aged 66 and over who have not already been screened about the NHS AAA screening programme, and advise them that they can self-refer.

1.1.2 Encourage men aged 66 or over to self-refer to the NHS abdominal aortic aneurysm (AAA) screening programme if they have not already been screened and they have any of the following risk factors:

- chronic obstructive pulmonary disease (COPD)
- coronary, cerebrovascular or peripheral arterial disease
- European family origin
- family history of AAA
- hyperlipidaemia
- hypertension
- they smoke or used to smoke.

1.1.3 Consider an aortic ultrasound for women aged 70 and over if AAA has not already been excluded on abdominal imaging and they have any of the following risk factors:

- COPD
- coronary, cerebrovascular or peripheral arterial disease
- European family origin
- family history of AAA

- hyperlipidaemia
- hypertension
- they smoke or used to smoke.

Identifying asymptomatic abdominal aortic aneurysms

1.1.4 Offer an aortic ultrasound to people in whom a diagnosis of asymptomatic AAA is being considered if they are not already in the NHS screening programme.

- Refer people with an abdominal aorta diameter of 5.5 cm or larger to a regional vascular service, to be seen within 2 weeks of diagnosis.
- Refer people with an abdominal aorta diameter of 3–5.4 cm to a regional vascular service, to be seen within 12 weeks of diagnosis.

1.1.5 Offer an aortic ultrasound to people with a suspected AAA on abdominal palpation.

> To find out why the committee made the recommendations on identifying people at risk of AAAs and identifying asymptomatic AAAs and how they might affect practice, see rationale and impact.

Identifying symptomatic or ruptured abdominal aortic aneurysms

1.1.6 Think about the possibility of ruptured AAA in people with new abdominal and/or back pain, cardiovascular collapse, or loss of consciousness. Be aware that ruptured AAA is particularly likely if they also have any of the following risk factors:

- an existing diagnosis of AAA
- age over 60
- they smoke or used to smoke
- history of hypertension.

1.1.7 Be aware that AAAs are more likely to rupture in women than men.

1.1.8 Offer an immediate bedside aortic ultrasound to people in whom a diagnosis of symptomatic and/or ruptured AAA is being considered. Discuss immediately with a regional vascular service if:

- the ultrasound shows an AAA **or**
- the ultrasound is not immediately available or it is non-diagnostic, and an AAA is still suspected.

To find out why the committee made the recommendations on identifying symptomatic or ruptured AAAs and how they might affect practice, see rationale and impact.

Imaging technique

1.1.9 When measuring aortic size with ultrasound, report anterior-posterior inner-to-inner diameter as a minimum, in accordance with the NHS AAA screening programme. Clearly document any additional measurements taken.

1.1.10 For people with an abdominal aorta diameter of 5.5 cm or larger who are being evaluated for elective surgery, offer thin-slice contrast-enhanced arterial-phase CT angiography.

1.1.11 For people with a suspected ruptured AAA who are being evaluated for surgery, consider thin-slice contrast-enhanced arterial-phase CT angiography.

To find out why the committee made the recommendations on imaging technique and how they might affect practice, see rationale and impact.

1.2 *Emergency transfer to regional vascular services*

1.2.1 Be aware that there is no single symptom, sign or prognostic risk assessment tool that determines whether people with a suspected or confirmed ruptured abdominal aortic aneurysm (AAA) should be transferred.

1.2.2 When making transfer decisions, be aware that people with a confirmed ruptured AAA who have a cardiac arrest and/or have a persistent loss of consciousness (in the emergency department or during transfer) have a negligible chance of surviving AAA repair.

1.2.3 For guidance on care of people with a ruptured AAA for whom repair is considered inappropriate, see the NICE guideline on care of dying adults in the last days of life.

1.2.4 When people with a suspected ruptured or symptomatic unruptured AAA have been accepted by a regional vascular service for emergency assessment, ensure that they leave the referring unit within 30 minutes of the decision to transfer.

1.2.5 Emergency departments, ambulance services and regional vascular services should collaborate to:

- provide a protocol for the safe and rapid transfer of people with a suspected ruptured or symptomatic unruptured AAA who need emergency assessment at a regional vascular service
- train clinical staff involved in the care of people with a suspected ruptured or symptomatic unruptured AAA in the transfer protocol
- review the transfer protocol at least every 3 years.

To find out why the committee made the recommendations on emergency transfer to regional vascular services and how they might affect practice, see rationale and impact.

Supporting people during transfer

1.2.6 Consider a restrictive approach to volume resuscitation (permissive hypotension) for people with a suspected ruptured or symptomatic AAA during emergency transfer to a regional vascular service.

To find out why the committee made the recommendation on supporting people during transfer and how it might affect practice, see rationale and impact.

1.3 *Monitoring and reducing the risk of rupture*

Reducing the risk of rupture

1.3.1 Offer a referral to a stop smoking service to people with an abdominal aortic aneurysm (AAA) who smoke. For more guidance, see the NICE guideline on stop smoking interventions and services.

1.3.2 Ensure that people with an AAA who have hypertension receive care in line with the NICE guideline on hypertension in adults.

> To find out why the committee made the recommendations on reducing the risk of rupture and how they might affect practice, see rationale and impact.

Monitoring the risk of rupture

1.3.3 Offer surveillance with aortic ultrasound to people with an asymptomatic AAA:

- every 3 months if the AAA is 4.5–5.4 cm
- every 2 years if the AAA is 3.0–4.4 cm.

1.3.4 See recommendation 1.1.4 on when to refer people to a regional vascular unit.

> To find out why the committee made the recommendations on monitoring the risk of rupture and how they might affect practice, see rationale and impact.

1.4 *Predicting and improving surgical outcomes*

Predicting surgical outcomes for unruptured aneurysms

1.4.1 Consider cardiopulmonary exercise testing when assessing people for elective repair of an asymptomatic abdominal aortic aneurysm (AAA), if it will assist in shared decision-making.

1.4.2 For guidance on other preoperative tests, see the NICE guideline on routine preoperative tests for elective surgery.

1.4.3 Do not use the following risk assessment tools in shared decision-making for elective repair of an asymptomatic unruptured AAA:

- Comorbidity Severity Score
- Glasgow Aneurysm Scale
- Medicare risk prediction tool
- Modified Leiden score
- Physiological and Operative Severity Score for enUmeration of Mortality (POSSUM)
- Vascular-POSSUM
- Vascular Biochemical and Haematological Outcome Model (VBHOM)
- Vascular Governance North West (VGNW) risk model.

See Vascular Quality Initiative (VQI) score in Society of Vascular Surgery 2018 guidelines

To find out why the committee made the recommendations on predicting surgical outcomes for unruptured aneurysms and how they might affect practice, see rationale and impact.

Predicting surgical outcomes for ruptured aneurysms

1.4.4 Do not use any single symptom, sign or patient-related risk factor to determine whether aneurysm repair is suitable for a person with a ruptured AAA.

1.4.5 Do not use patient risk assessment tools (scoring systems) to determine whether aneurysm repair is suitable for a person with a ruptured AAA.

To find out why the committee made the recommendations on predicting surgical outcomes for ruptured aneurysms and how they might affect practice, see rationale and impact.

Improving surgical outcomes

1.4.6 Offer people with an AAA information, support and interventions for secondary prevention of cardiovascular disease. For more information refer to the NICE guidance on:

- stop smoking interventions and services

- diet, weight management and exercise
- medicines optimisation
- lipid modification and statin therapy
- diabetes management
- hypertension diagnosis and management
- antiplatelet therapy.

1.4.7 Do not routinely start beta blockers immediately before surgery for people having aneurysm repair.

1.4.8 Do not offer remote ischaemic preconditioning to people having aneurysm repair.

1.4.9 For guidance on preventing and treating surgical site infections and on preventing venous thromboembolism, see the NICE guidelines on surgical site infections and reducing the risk of venous thromboembolism.

To find out why the committee made the recommendations on improving surgical outcomes and how they might affect practice, see rationale and impact.

1.5 *Repairing unruptured aneurysms*

1.5.1 Consider aneurysm repair for people with an unruptured abdominal aortic aneurysm (AAA), if it is:

- symptomatic
- asymptomatic and 5.5 cm or larger
- asymptomatic, larger than 4.0 cm and has grown by more than 1 cm in 1 year.

1.5.2 For people with unruptured AAAs meeting the criteria in 1.5.1, offer open surgical repair unless there are anaesthetic or medical contraindications.

1.5.3 Do not offer endovascular repair (EVAR) to people with an unruptured infrarenal AAA if open surgical repair is suitable.

1.5.4 Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.

1.5.5 Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.

1.5.6 Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition.

To find out why the committee made the recommendations on repairing unruptured aneurysms and how they might affect practice, see rationale and impact.

Anaesthesia and analgesia

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

To find out why the committee made the recommendations on anaesthesia and analgesia for repair of unruptured aneurysms and how they might affect practice, see rationale and impact.

1.6 *Repairing ruptured aneurysms*

1.6.1 Consider endovascular repair (EVAR) or open surgical repair for people with a ruptured infrarenal abdominal aortic aneurysm (AAA). Be aware that:

- EVAR provides more benefit than open surgical repair for most people, especially for women and for men over the age of 70
- open surgical repair is likely to provide a better balance of benefits and harms in men under the age of 70.

1.6.2 Consider open surgical repair for people with a ruptured complex AAA.

1.6.3 Do not offer complex EVAR to people with a ruptured AAA if open surgical repair is suitable, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.

> To find out why the committee made the recommendations on repairing ruptured aneurysms and how it might affect practice, see rationale and impact.

Anaesthesia and analgesia

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

> To find out why the committee made the recommendation on anaesthesia and analgesia and how it might affect practice, see rationale and impact.

Abdominal compartment syndrome

1.6.5 Be aware that people can develop abdominal compartment syndrome after EVAR or open surgical repair of a ruptured AAA.

1.6.6 Assess people for abdominal compartment syndrome if their condition does not improve after EVAR or open surgical repair of a ruptured AAA.

> To find out why the committee made the recommendations on abdominal compartment syndrome and how they might affect practice, see rationale and impact.

1.7 *Monitoring for complications after endovascular aneurysm repair*

1.7.1 Enrol people who have had endovascular aneurysm repair (EVAR) into a surveillance imaging programme.

1.7.2 Base the frequency of surveillance imaging on the person's risk of graft-related complications.

1.7.3 Use contrast-enhanced CT angiography to detect postoperative complications and further aneurysm expansion.

1.7.4 If contrast-enhanced CT angiography is contraindicated, consider contrast-enhanced ultrasound to detect endoleaks and further aneurysm expansion.

1.7.5 Do not use colour duplex ultrasound as the main imaging technique to detect endoleaks in people who have had an EVAR.

To find out why the committee made the recommendations on monitoring for complications after endovascular aneurysm repair and how they might affect practice, see rationale and impact.

1.8 *Managing endoleaks after endovascular aneurysm repair*

1.8.1 Consider open, endovascular or percutaneous intervention for type I and type III endoleaks following endovascular aneurysm repair (EVAR).

1.8.2 Consider intervention for type II endoleaks in people who have sac expansion following EVAR.

1.8.3 Consider further investigation of type V endoleaks following EVAR.

To find out why the committee made the recommendations on managing endoleaks after endovascular repair and how they might affect practice, see rationale and impact.

Terms used in this guideline

This section defines terms that have been used in a specific way for this guideline. For general definitions, please see the glossary.

Complex EVAR

Any endovascular strategy that is outside the 'instructions for use' of aortic stent–grafts, typically adopted because of an AAA's anatomical complexity. This includes using unmodified endografts outside their 'instructions for use', physician-modified endografts, customised fenestrated endografts, and 'snorkel' or 'chimney' approaches with parallel covered stents.

Endoleak

The persistence of blood flow outside an endovascular stent-graft but within the aneurysm sac in which the graft is placed. There are 5 types of endoleak:

- Type I – blood flowing into the aneurysm because of an incomplete or ineffective seal at either end of an endograft.
- Type II – blood flowing into the sac from small side branches of the aorta.
- Type III – blood flowing into the aneurysm sac through defects in the endograft.
- Type IV – blood flowing through the graft fabric into the aneurysm sac.
- Type V – continued sac expansion without radiographic evidence of a leak site.

Infrarenal AAA

An aneurysm located in the lower segment of the abdominal aorta, below the arteries that supply the kidneys.

Permissive hypotension

A method of fluid administration that aims to reduce bleeding by keeping a person's blood pressure within a lower-than-normal range.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Monitoring frequencies and repair thresholds

What are the most effective and cost effective frequencies for monitoring people with unruptured abdominal aortic aneurysms (AAA) of different diameters, and what is the optimal threshold for repair?

Why this is important

More frequent monitoring increases the chances of identifying aneurysms that have grown large enough to need repair. However, monitoring requires resources and the absolute risk of AAA rupture is relatively low, so there are opportunity costs to consider. Effective planning is important to maximise surgical outcomes and to ensure that the greatest benefit is obtained for the person with an AAA whilst posing the least potential harm. It is important to establish how often aneurysms should be monitored to keep the risk of rupture as low as possible while making the best use of NHS resources.

2 Effectiveness of endovascular aneurysm repair and open surgical repair of unruptured and ruptured abdominal aortic aneurysms

What is the effectiveness and cost effectiveness of complex endovascular aneurysm repair (EVAR) versus open surgical repair in people for whom open surgical repair is suitable for:

- elective repair of an unruptured AAA **or**
- emergency repair of a ruptured AAA?

Why this is important

EVAR is a widely performed non-invasive alternative to open surgical repair. However, it is more expensive. Although EVAR has been shown to produce no long-term benefit over open surgical repair in people with unruptured infrarenal aneurysms, it is less clear whether this is the same in people with unruptured or ruptured juxtarenal, suprarenal type IV, and short-necked infrarenal aneurysms. As a result, research is needed to identify how effective complex EVAR is in these populations.

3 Macrolides for slowing aneurysm growth and reducing the risk of rupture

What are the benefits and harms of macrolides (such as azithromycin) for reducing AAA growth rates and the risk of rupture?

Why this is important

Small AAAs are currently managed by monitoring, until the aneurysm reaches a diameter at which surgical repair is needed. There are currently no non-surgical interventions available to prevent AAAs from growing, and subsequently rupturing. Clinical research in this area would be useful for developing a secondary prevention strategy to prevent rupture.

4 Metformin for slowing aneurysm growth and reducing the risk of rupture

What are the benefits and harms of metformin for reducing AAA growth rates and the risk of rupture?

Why this is important

Observational study data suggests an association between diabetes and slower aneurysm growth, and it has been proposed that this is caused by taking metformin. Randomised controlled trials are needed to determine whether metformin reduces the rate of aneurysm growth.

5 Tranexamic acid for preventing and treating excessive blood loss during EVAR or open surgical repair

Does tranexamic acid improve survival in people who are having repair (EVAR or open surgical repair) of a ruptured AAA?

Why this is important

Tranexamic acid is used to reduce blood loss in major trauma, postpartum bleeding and surgery. As a result, it could benefit people with a ruptured AAA. By slowing down blood loss from a ruptured aneurysm, the use of tranexamic acid could give emergency services more time to transfer a patient to regional vascular services, and regional vascular services more time to repair the ruptured aneurysm.

6 Preoperative exercise programmes for improving the outcome of aneurysm repair

What is the clinical effectiveness and cost effectiveness of preoperative exercise programmes for improving outcomes of people who are having repair of an AAA?

Why this is important

NHS providers have started devoting resources to exercise programmes, based on a relatively small body of evidence. Further research on the effectiveness of these programmes is needed to inform funding decisions.

Other recommendations for research

Direct oral anticoagulants after AAA repair

What are the benefits of postoperative use of Direct Oral Anticoagulants (DOACS) for improving outcomes after repair of AAA?

Transfer to specialist vascular units

Within what time period should people with suspected ruptured or symptomatic unruptured abdominal aortic aneurysms be transferred from a non-specialist setting to a specialist vascular unit?

Permissive hypotension

Does permissive hypotension improve survival or improve the stability of patients undergoing repair of ruptured AAA?

Surveillance after endovascular aneurysm repair

What are the risks, benefits and cost implications of different surveillance protocols in people who have undergone EVAR?

Which device and patient related variables can be used in a risk model to inform amendments to surveillance frequencies and modalities in patients who have undergone EVAR?

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

Identifying asymptomatic abdominal aortic aneurysms

Recommendations 1.1.1–1.1.5

Why the committee made the recommendations

The committee were mindful that some men and all women who are at risk of AAA are not seen by the NHS AAA screening programme. The recommendations highlight these groups and specify risk factors significantly associated with AAA that could be used to facilitate opportunistic screening.

Aortic ultrasound is recommended because it is the standard technique used in clinical practice. It has high diagnostic accuracy, and is associated with lower costs and fewer side effects than CT. People with an AAA diameter of 5.5 cm or larger need to be seen by a regional vascular service within 2 weeks because their aneurysm is at high risk of rupture. The risk is lower in people with smaller AAAs, so they do not need to be seen as urgently.

How the recommendations might affect practice

The recommendations outlining key risk factors will increase the number of people being screened and improve the chances of diagnosing the condition early, before complications develop. This, in turn, may reduce associated costs and minimise the risk of AAA-related mortality. The recommendations should also promote equal access to healthcare, as they provide guidance on when a diagnosis of AAA should be investigated in women, who are not covered by the NHS AAA screening programme.

Using aortic ultrasound to detect AAAs is good practice. The recommendations ensure that the time within which people with newly-identified aneurysms are seen by regional vascular services is proportional to the risk of rupture. These timings reflect current expectations within the NHS AAA screening programme.

Full details of the evidence and the committee's discussion are in evidence review A: Risk factors for predicting presence of an abdominal aortic aneurysm and evidence review B: Imaging techniques to diagnose abdominal aortic aneurysms.

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Identifying symptomatic or ruptured abdominal aortic aneurysms

Recommendations 1.1.6–1.1.8

Why the committee made the recommendations

Based on their own experience, the committee highlighted the most important signs and symptoms of ruptured AAAs, because:

- non-specialists commonly misdiagnose them
- reducing misdiagnosis should increase the chance of survival
- urgent discussion of a suspected ruptured AAA with a regional vascular service will improve the chances of appropriate treatment and survival.

Aortic ultrasound is the standard technique for detecting ruptured AAA. A ruptured AAA is a medical emergency, and bedside ultrasound is the quickest reliable method to confirm the presence of an AAA. An immediate discussion with the regional vascular unit ensures appropriate treatment is started as soon as possible. The committee recognised that the sensitivity of aortic ultrasound is not 100% and several factors can make it difficult to visualise the aorta. Since AAA rupture is a life-threatening medical emergency, they agreed that it would be safest to discuss any non-diagnostic ultrasound findings with the regional vascular unit.

How the recommendations might affect practice

There is variation in awareness of AAAs among non-specialists. Implementing the recommendations should reduce this variation and increase the chance of ruptured AAAs being diagnosed earlier.

Using bedside aortic ultrasound to detect AAAs is common practice. Preventing delays in treatment through immediate discussions with a regional vascular unit should improve outcomes for people with ruptured AAAs.

Full details of the evidence and the committee's discussion are in evidence review B: Imaging techniques to diagnose abdominal aortic aneurysms and evidence review N: Signs, symptoms and risk factors predicting ruptured or symptomatic unruptured aneurysms before arrival at the hospital, and in non-specialist hospital settings.

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Imaging technique

Recommendations 1.1.9–1.1.11:

Why the committee made the recommendations

There was no clear evidence on which approach to AAA sizing is the best. The Committee agreed that it was important to take consistent measurements for aneurysm sizing, so that the results of different tests are comparable. The NHS AAA screening programme specifies a preferred measurement, and the committee agreed this would be the most appropriate one to use in practice.

The committee recommended thin-slice contrast-enhanced arterial-phase CT angiography for imaging in people being evaluated for elective surgery, as it is widely recognised as the gold standard technique for measuring aneurysm size and anatomy before repair. For suspected ruptured AAAs, CT angiography should also be considered; however, the committee recognised that in certain patients, the clinical presentation may mean vascular specialists consider that immediate transfer for open repair is necessary without first obtaining a CT scan.

No evidence was found demonstrating whether or not post-processing techniques affected postoperative outcomes of people having elective or emergency AAA repair surgery. As post-processing techniques are an established part of clinical practice, the committee agreed not to make recommendations in this area.

How the recommendations might affect practice

Implementing a consistent minimum measurement to be used across the NHS will improve the reproducibility of results, improving surveillance for individuals people with AAA and the ability to analyse data at the population level.

Thin-slice contrast-enhanced arterial-phase CT angiography is widely used for imaging in people being evaluated for AAA repair, so this recommendation is unlikely to make a major difference to current practice. The recommended timings reflect current expectations within the NHS AAA screening programme.

As post-processing techniques are established in practice, a lack of recommendations on these will not have an impact.

Full details of the evidence and the committee's discussion are in evidence review B: Imaging techniques to diagnose abdominal aortic aneurysms.

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Emergency transfer to regional vascular services

Recommendations 1.2.1–1.2.5

Why the committee made the recommendations

There was no evidence on symptoms, signs or risk assessment tools for deciding whether people with ruptured aneurysms are likely to survive transfer to regional vascular services. Based on their own experience, the committee highlighted specific circumstances in which people are unlikely to survive transfer and subsequent aortic repair. This will help reduce the number of people being given ineffective and invasive treatment at the end of life.

The committee referred to the NICE guideline on care of dying adults in the last days of life to ensure that appropriate and compassionate care is given to people with ruptured AAA when the decision has been made not to operate.

There was also no evidence on how quickly people should be transferred to regional vascular units. In the absence of evidence, the committee adapted recommendations from the NICE guideline on service delivery for major trauma. They agreed, based on their experience of emergency transfer, that the timing specified for people with major trauma was appropriate for people with AAA and manageable for referring units.

How the recommendations might affect practice

The recommendations on assessing people for transfer will raise awareness among emergency staff, but will have little impact on clinical practice.

The NICE guidelines on care of dying adults cover current practice, so organisations are unlikely to need to change practice.

The recommendations on transfer speed will minimise variations in transfer times across the NHS. The timeframe recommended is the same as for major trauma, and the committee agreed that this is a reasonably similar situation.

Full details of the evidence and the committee's discussion are in evidence review O: Signs, symptoms and risk factors indicating suitability for transfer to a regional vascular service and evidence review P: Time period for transfer to regional vascular services.

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Supporting people during transfer

Recommendation 1.2.6:

Why the committee made the recommendations

As there was no evidence specific to the use of permissive hypotension during transfer of people with ruptured or symptomatic AAA, the committee agreed that a consensus recommendation was needed in this important clinical area. As a result it adapted recommendations from the NICE guideline on assessment and initial management for major trauma.

How the recommendations might affect practice

The recommendation will reduce the likelihood of inappropriate fluid administration during transfer of people with ruptured AAA between hospitals. This, in turn, will improve the outcomes of endovascular aneurysm repair and open surgical repair procedures. The recommendation is in line with NICE recommendations on fluid administration for other major trauma, and the committee agreed that this is a reasonably similar situation.

Full details of the evidence and the committee's discussion are in evidence review Q: Permissive hypotension during transfer of people with ruptured AAA to regional vascular services.

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Reducing the risk of rupture

Recommendations 1.3.1 and 1.3.2

Why the committee made the recommendations

Based on the evidence, the committee agreed that none of the risk factors associated with AAA growth or rupture would affect monitoring frequency or help surgeons decide when to operate. As a result, the committee focused on modifiable risk factors that could influence the management of people with known AAAs. There was some evidence that high blood pressure increases the chance of AAA growth and rupture, and the committee knew from their own experience that people with an AAA do not always receive appropriate management for high blood pressure. There is also evidence that smoking increases the risk of AAA rupture. As a result, the committee referred to the NICE guidelines on these topics.

The committee agreed that there was not enough high-quality evidence to make clinical recommendations on non-surgical interventions for slowing aneurysm growth and reducing the risk of rupture. In light of this, they made research recommendations on 2 promising non-surgical interventions that they believed would have a positive impact on reducing aneurysm growth.

How the recommendations might affect practice

The NICE guidelines on hypertension and stop smoking services cover current practice, so organisations are unlikely to need to change practice.

Non-surgical interventions for small AAAs are not usually used outside of clinical trials, so a lack of recommendations will have little impact on practice.

Full details of the evidence and the committee's discussion are in evidence review C: Risk factors associated with abdominal aortic aneurysm growth or rupture.

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Monitoring the risk of rupture

Recommendations 1.3.3 and 1.3.4

Why the committee made the recommendations

The committee recommended ultrasound surveillance every 3 months for people with asymptomatic AAAs of 4.5–5.4 cm in diameter because:

- ultrasound is current practice and no evidence was found for other imaging techniques (CT, MRI or wall stress analysis)

- monitoring every 3 months is current practice for people with aneurysms of this size, and there was evidence that this frequency of monitoring offers the best balance between benefits and costs.

The committee recommended ultrasound surveillance every 2 years for people with asymptomatic AAAs of 3–4.4 cm in diameter because:

- ultrasound is current practice and no evidence was found for other imaging techniques (CT, MRI or wall stress analysis)
- the absolute risk of aneurysm rupture is low and so monitoring yearly (which is current practice) offers few benefits over monitoring every 2 years
- monitoring every 2 years offers the best balance between benefits and costs.

How the recommendations might affect practice

People with small AAAs (3.0–4.4 cm) currently have an aortic ultrasound every year. Changing this to every 2 years should reduce costs to the NHS.

Full details of the evidence and the committee's discussion are in evidence review D: Monitoring for abdominal aortic aneurysm expansion and risk of rupture.

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Predicting surgical outcomes in unruptured aneurysms

Recommendations 1.4.1–1.4.3

Why the committee made the recommendations

There was limited evidence that cardiopulmonary exercise testing can help identify people who are at risk of dying within 30 days and within 90 days of aneurysm repair. While the evidence was limited, the committee agreed that cardiopulmonary exercise testing can help with shared decision-making between healthcare professionals and patients when the benefits and harms of surgery are uncertain. For example, it can identify people who are at high risk during surgery, and encourage discussions about the precautions needed to reduce these risks.

There are other tests for assessing people before surgery, but there was no evidence available for them. One study found that higher estimated glomerular filtration rate (eGFR) was associated with improved outcomes after elective EVAR, but it did not give clear eGFR thresholds that could be used in decision-making. In the absence of evidence, the committee referred to the NICE guideline on routine preoperative tests for elective surgery. Some of the studies reviewed for that guideline focused on people having elective AAA repair.

The evidence highlighted that none of the risk assessment tools had a high enough predictive accuracy at predicting postoperative outcomes. This led the committee to conclude that these tools would not improve decision-making and could potentially lead to inappropriate decisions about patient management. They agreed that this could lead to harm, and therefore advised that risk assessment tools should not be used.

How the recommendations might affect practice

Cardiopulmonary exercise testing is likely to have an impact on the decision to undertake elective AAA repair, as it indicates that perioperative risks need to be taken into consideration. The use of cardiopulmonary exercise testing will have limited impact on practice as it is only recommended in situations where it will help in shared decision-making.

Risk assessment tools are not widely used outside the context of research. Therefore, the recommendations will have little impact on practice.

Full details of the evidence and the committee's discussion are in evidence review G: Tests for predicting outcomes after repair of unruptured abdominal aortic aneurysms and evidence review H: Risk assessment tools for predicting surgical outcomes of patients who undergo elective abdominal aortic aneurysm repair.

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Predicting surgical outcomes in ruptured aneurysms

Recommendations 1.4.4 and 1.4.5

Why the committee made the recommendations

There is evidence that some risk factors and risk assessment tools are associated with poor postoperative outcomes. However, it is not clear how any particular factor or combination of factors could be used to decide if aneurysm repair is suitable for a person with a ruptured AAA.

How the recommendations might affect practice

The recommendations will have a beneficial impact, by ensuring decisions about care are not made based on inappropriate factors or tools. This, in turn, should prevent inappropriate decisions being made about patient care.

Full details of the evidence and the committee's discussion are in evidence review S: Risk factors for predicting survival after AAA rupture.

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Improving surgical outcomes

Recommendations 1.4.6–1.4.9

Why the committee made the recommendations

The committee made a recommendation on cardiovascular disease because it is common in people with AAA and it is best practice to reduce the risk of problems in people who have it.

The evidence showed that giving beta blockers just before surgery does not help, and that they cause problems such as low blood pressure and a slow heartbeat. The committee noted that some people with AAA may need to take beta blockers for other conditions (such as atrial fibrillation). As a result, they recommended against routine acute use before AAA repair, rather than recommending against beta blockers altogether.

Remote ischaemic preconditioning was not recommended because there was evidence that it does not improve outcomes and that it can cause problems such as an irregular heartbeat.

The committee recommended further research because there was not enough evidence to make recommendations on exercise programmes before surgery, or on any interventions after AAA repair.

How the recommendations might affect practice

Providing support to reduce the risk of problems from cardiovascular disease is already current practice. In addition, beta blockers and routine ischaemic preconditioning are not currently in routine use before AAA repair, so these recommendations should have a minimal impact on practice.

Full details of the evidence and the committee's discussion are in evidence review J: Pre- and postoperative interventions to optimise outcomes after abdominal aortic aneurysm repair.

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Repairing unruptured aneurysms

Recommendations 1.5.1–1.5.6

Why the committee made the recommendations

When to repair

The committee noted that a number of factors are considered before treating asymptomatic aneurysms; one of which is size. It is good practice to repair large aneurysms (over 5.5 cm in diameter), and to monitor smaller aneurysms (less than 4 cm in diameter) until they become larger. There is some debate as to whether aneurysms between 4 cm and 5.5 cm should be repaired immediately or whether they should be monitored and only repaired when they become larger. Based on the available evidence, the committee highlighted factors that would help healthcare professionals decide when to repair aneurysms.

Which technique to use

There is no evidence that EVAR for people with an unruptured infrarenal AAA provides long-term benefit compared with open surgical repair. While EVAR is associated with fewer perioperative deaths, it has more long-term complications, and these complications mean that people will need further procedures. There is some evidence that EVAR is associated with worse long-term survival than open surgical repair. EVAR also has higher net costs than open surgical repair. The evidence shows that, even if long-term benefits were achievable, they could not plausibly be sufficient to outweigh these costs.

Open surgical repair is unsuitable for some people with an unruptured AAA because of their anaesthetic risk and/or medical comorbidities. For these people, the risks of their AAA rupturing, if no repair is attempted, have to be balanced against the perioperative risks and long-term complications associated with EVAR. The evidence shows that the average person receiving EVAR has an uncertain chance of a small net benefit, compared with the large and certain increase in costs. Therefore, the committee agreed that elective EVAR cannot be considered an effective use of NHS resources in this population.

The evidence for complex EVAR was limited in quantity and quality. However, complex EVAR grafts are much more expensive than standard devices, so the difference in cost between EVAR and open surgical repair is even greater than in infrarenal AAAs. The committee also noted that the instructions for use of the grafts that are currently available do not cover complex AAAs. Although there is currently no evidence that complex EVAR has better outcomes than open surgical repair, people with complex AAAs have higher perioperative mortality rates. Because of this, a perioperative survival benefit equivalent to that seen with EVAR for infrarenal AAAs could potentially be more influential in complex AAAs. Therefore, the committee agreed that more information would be helpful, so it recommended that the use of complex EVAR should be restricted to randomised trials.

The committee also discussed complex EVAR for people for whom open surgical repair is not a suitable option because of their anaesthetic risk and/or medical co-morbidities. They agreed that, in this population, people who need complex EVAR could not plausibly have better outcomes than those who need standard infrarenal EVAR. As they had not recommended standard EVAR in this population, the committee agreed that they could not recommend complex EVAR either. The committee did not recommend using complex EVAR in randomised trials in these circumstances, because it would be unethical to randomise people to a treatment with a high risk of perioperative death when there is no prospect of long-term benefits at reasonable cost.

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

Goal-directed therapy

The evidence did not show any benefit from goal-directed therapy for people having repair of an unruptured AAA. Goal-directed therapy covers a broad range of different haemodynamic monitoring and management practices, some of which are routinely performed during major surgery. The committee recognised that it was not possible to specify which practices should not be performed and agreed that drafting recommendations would be too prescriptive.

How the recommendations might affect practice

The committee considered that the recommendation on when to repair unruptured aneurysms is unlikely to impact on current clinical practice because it reflects what is already being done within the NHS.

The recommendations on EVAR will have a large impact on practice, as EVAR is a widely performed procedure. EVAR is currently used more frequently than open surgical repair in some areas, so a diverse group of people both within and outside the national screening programme will need to update their knowledge. The recommendations will also affect the timing and type of information about treatment options given to patients who are diagnosed with small-to-medium AAAs and are being monitored for signs of growth. The recommendations will minimise harm by reducing long-term mortality and the need for reintervention as a result of problems with EVAR. Reductions in EVAR use and subsequent EVAR-related reinterventions will lead to cost savings within the NHS.

A lack of recommendations on goal-directed therapy will not impact on practice. Basic haemodynamic management is routinely performed during most surgical procedures, but goal-directed therapy is rarely performed during AAA surgery.

Full details of the evidence and the committee's discussion are in evidence review F: Thresholds for abdominal aortic aneurysm repair and evidence review K: Effectiveness of endovascular aneurysm repair, open surgical repair and non-surgical management of unruptured abdominal aortic aneurysms.

Return to recommendations

Anaesthesia and analgesia during unruptured aneurysm repair

Recommendation 1.5.7

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.

How the recommendations might affect 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.

Full details of the evidence and the committee's discussion are in evidence review L: Anaesthesia and analgesia for people having surgical repair of an abdominal aortic aneurysm.

Return to recommendations

Repairing ruptured aneurysms

Recommendations 1.6.1–1.6.3

Why the committee made the recommendations

Which technique to use

The evidence showed that, compared with open surgical repair, a strategy that uses EVAR (where anatomically possible) to repair ruptured infrarenal AAAs provides a reasonable balance of benefits and costs.

As the average cost-effectiveness results for EVAR were favourable, the committee discussed whether they should recommend EVAR whenever it is possible. They decided not to, for 2 reasons.

Firstly, there is uncertainty in the evidence for EVAR. People who had EVAR for a ruptured AAA were followed up for at most 7 years. People who had EVAR for an unruptured AAA were followed up for 15 years, and the committee noted that these data suggested that EVAR may be worse than open surgical repair in the long run (see why the committee made the recommendations on repairing unruptured aneurysms). There are some signs that a similar long-term pattern may develop in trials of ruptured AAA, so it is possible that longer-term data would show EVAR to be worse than open surgical repair for people with ruptured AAA as well.

Secondly, there was evidence that the balance of benefits and costs of EVAR varies between different groups of people with ruptured AAA. In particular, women clearly have better short-term survival after EVAR, whereas the evidence favours open surgical repair for younger men. Therefore, the committee recommended that either EVAR or open repair can be considered, and provided detail on the groups for which each approach is likely to be best.

Complex EVAR is only recommended within the context of an RCT because there is currently no evidence to support it as an option for people with ruptured complex AAA.

Tranexamic acid

No evidence on the use of tranexamic acid in people with a ruptured AAA was identified. The committee was aware that tranexamic acid is included in some major haemorrhage protocols and some patients, without major trauma, may receive it before undergoing surgery. In the committee's experience, tranexamic acid is not routinely used in people with a ruptured AAA, so it agreed to recommend research in this area.

Goal-directed therapy

There was no evidence on goal-directed therapy for people having repair of a ruptured aneurysm. Goal-directed therapy covers a broad range of different haemodynamic monitoring and management practices; some of which are routinely performed during major surgery. The committee recognised that it was not possible to specify which practices should not be performed and agreed that drafting recommendations would be too prescriptive.

How the recommendations might affect practice

The recommendations will have little impact on current practice, as both standard EVAR and open surgery are currently offered to people with ruptured infrarenal AAA. In relation to complex EVAR, the recommendation not to use it outside of randomised trials will limit the use of a technically complex and expensive procedure in people for whom open surgery is a safe and suitable option.

A lack of recommendations on goal-directed therapy will not impact on practice. Basic haemodynamic management is routinely performed during most surgical procedures, but goal-directed therapy is rarely performed during AAA surgery.

A lack of recommendations on tranexamic acid will have little impact on practice. Tranexamic acid is used in varying degrees across the NHS, but it is not standard practice for people with ruptured or symptomatic AAAs who are being transferred prior to surgery.

Full details of the evidence and the committee's discussion are in evidence review T: Effectiveness of endovascular aneurysm repair compared with open surgical repair of ruptured abdominal aortic aneurysms.

Return to recommendations

Anaesthesia and analgesia during ruptured aneurysm repair

Recommendation 1.6.4

Why the committee made the recommendations

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.

How the recommendations might affect practice

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.

Full details of the evidence and the committee's discussion are in evidence review L: Anaesthesia and analgesia for people having surgical repair of an abdominal aortic aneurysm.

Return to recommendations

Abdominal compartment syndrome

Recommendations 1.6.5 and 1.6.6

Why the committee made the recommendations

There was no evidence relating to preventing or managing abdominal compartment syndrome in people who are having surgery to repair a ruptured AAA. The committee agreed it was important to raise awareness of this potentially life-threatening condition, and made recommendations to highlight that it can occur after both endovascular aneurysm repair and open surgical repair.

How the recommendations might affect practice

The recommendations will ensure that clinicians are aware of abdominal compartment syndrome in people who have undergone repair of ruptured AAA. This may result in better postoperative assessment and management.

Full details of the evidence and the committee's discussion are in evidence review U: Preventing abdominal compartment syndrome following repair of ruptured abdominal aortic aneurysm.

Return to recommendations

Monitoring for complications after endovascular aneurysm repair

Recommendations 1.7.1–1.7.5

Why the committee made the recommendations

Imaging surveillance after endovascular repair (EVAR) is good practice, because there is a risk that people will develop complications from the procedure or need another operation. These risks are lower after open surgery, so surveillance is not standard practice and in this case the committee did not recommend it.

The committee noted the frequency of EVAR surveillance is highly variable in practice. In the absence of evidence on how often imaging should be done, the committee agreed a recommendation to tailor surveillance to the perceived risk of complication. This should maximise attention for those patients at greatest risk, and help to identify complications earlier.

Since there is a lack of evidence on surveillance programmes for people who have had EVAR, the committee recommended further research in this area.

Contrast-enhanced CT angiography is the gold standard test for imaging surveillance after EVAR. The identified evidence demonstrated that no other imaging technique had acceptable accuracy at identifying endoleaks in comparison with contrast-enhanced CT angiography. Importantly, other imaging techniques had higher rates of false-negative results. Although there was little or no evidence on graft kinking, occlusion, or migration, the committee agreed that contrast-enhanced CT angiography was the best imaging technique for detecting these types of complications, based on their clinical experience. Overall, they agreed that contrast-enhanced CT angiography should be the preferred test for imaging surveillance after EVAR but noted that it may be unsuitable for some people, for example people who are allergic to the contrast agent or have renal failure. In this case, contrast-enhanced ultrasound is more likely than other suitable tests to identify endoleaks. Contrast-enhanced ultrasound was not recommended for assessing for other complications because the evidence only covered endoleaks.

The committee agreed that it is particularly important not to miss these complications, so the sensitivity of a test is more important than its specificity. Colour duplex ultrasound does not adequately rule out endoleaks, and in particular has poor sensitivity for type I and III endoleaks, so the committee agreed that it cannot be recommended as a first-line surveillance test. In addition, the evidence showed that the accuracy of the test was dependent on the ultrasound operator, so the accuracy will be highly variable in practice. The high variability in diagnostic accuracy, and resultant potential for harm, led the committee to recommend that the test should not be used as the main imaging technique to detect endoleaks. However, the committee agreed based on their experience that it can be a useful follow-up test for evaluating abnormalities identified on surveillance imaging.

How the recommendations might affect practice

The recommendations on surveillance programmes and frequency of surveillance reflect current practice, so organisations are unlikely to need to change practice.

There is variation in which imaging techniques are used for surveillance. Some centres use ultrasound only, and some use contrast-enhanced CT angiography and ultrasound. Colour duplex ultrasound is widely used, but contrast-enhanced ultrasound is not. Therefore, there will be infrastructure and training costs for centres that are not using the imaging techniques recommended here. In particular, sonographers will need training on cannulation and administering contrast agents.

Full details of the evidence and the committee's discussion are in evidence review V: Postoperative surveillance after surgical repair of abdominal aortic aneurysms and evidence review W: Accuracy of imaging techniques in identifying complications after surgery.

Return to recommendations

Managing endoleaks after endovascular repair

Recommendations 1.8.1–1.8.3

Why the committee made the recommendations

Endoleak following EVAR is common, and can have a negative impact on patient prognosis and long-term quality of life. In the absence of evidence, the committee made recommendations based on their experience because:

- it is good practice to repair type I and III endoleaks and some type II endoleaks
- healthcare professionals are not all aware that type II endoleaks without sac expansion can be managed conservatively
- there are circumstances when sac expansion occurs without imaging evidence of a leak site (called type V endoleak), and these situations need further investigation.

How the recommendations might affect practice

The recommendations will have minimal impact on current practice as it is common practice to intervene for type I and type III endoleaks, and type II endoleaks if there is evidence of aneurysm sac expansion.

Full details of the evidence and the committee's discussion are in evidence review X: Managing complications after abdominal aortic aneurysm repair.

Return to recommendations

Context

Aortic aneurysms develop when the wall of the aorta weakens, causing it to bulge and form a balloon-like expansion. When this occurs in the abdomen and the aorta reaches a diameter at least 1.5 times the normal, or greater than 3 cm in total, it is called an abdominal aortic aneurysm (AAA).

The stretching and increased wall tension may eventually cause the aneurysm to rupture. The subsequent internal bleeding is fatal before emergency repair can be attempted in 80% of people. Even when people have emergency repair, only about half of them survive beyond 30 days.

There is a long period of growth before an AAA reaches this life-threatening state. The rate of growth may depend on a number of factors, including increasing age, smoking, blood pressure and a family history of aneurysm.

Because most AAAs are asymptomatic, it is difficult to establish their prevalence. Screening studies in the UK have estimated a prevalence of between 1.3 and 12.7%, depending on the age group studied and the definition of AAA. AAAs are most frequent in men over 65. In this group, AAA rupture causes 3,000 deaths, or 1.7% of deaths, each year in England and Wales.

Most AAAs are diagnosed opportunistically during clinical examination or investigation for another condition, although there is a national screening programme for AAA which enrols men at age 65.

Although the incidence of abdominal aortic aneurysms is approximately 6 times lower in women, the rate of aneurysm rupture is significantly higher. The guideline committee carefully considered the impact of their recommendations on women during guideline development.

Finding more information and resources

To find out what NICE has said on topics related to this guideline, see our web page on aortic aneurysms.

National Institute for Health and Care Excellence

Draft for consultation

Abdominal aortic aneurysm: diagnosis and management

Evidence review K: Effectiveness of endovascular aneurysm repair, open surgical repair and non-surgical management of unruptured abdominal aortic aneurysms

NICE guideline <number>

Evidence reviews

May 2018

Draft for Consultation

Commissioned by the National Institute for Health and Care Excellence

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Disclaimer

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

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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ISBN:

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Effectiveness of endovascular aneurysm repair, open surgical repair and non-surgical management of unruptured abdominal aortic aneurysms

Review question

What are the relative benefits and harms of EVAR, open surgical repair and non-surgical management in people with unruptured abdominal aortic aneurysms?

Introduction

This review question aims to assess the advantages and disadvantages of elective endovascular aneurysm repair (EVAR) in comparison with conventional open surgical repair for the treatment of unruptured abdominal aortic aneurysms (AAAs). Furthermore, this question aims to explore advantages and disadvantages of elective EVAR in comparison with non-surgical management when open surgical repair is not possible.

PICO table

Table 1: Inclusion criteria

Parameter	Inclusion criteria
Population	People undergoing surgery for a confirmed unruptured AAA Subgroups: fitness for surgery, age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity), ethnicity
Interventions	Elective standard (on-instructions for use [IFU]) EVAR for infrarenal and juxtarenal AAA Elective complex EVAR for infrarenal, juxtarenal and suprarenal AAA, including: fenestrated EVAR EVAR with chimneys EVAR with snorkels branched grafts 'CHIMPS' (CHIMneys, Periscopes, Snorkels) infrarenal devices used for juxtarenal AAA – that is, off-IFU use of standard devices Open repair Non-surgical management
Comparators	Each other
Outcomes	Mortality/survival Peri- and post-operative complications Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth Need for reintervention Quality of life Resource use, including length of hospital or intensive care stay, and costs

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual (2014). 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 Cochrane systematic review (Paravastu et al. 2014) comparing EVAR and open surgical repair of unruptured AAAs was identified as a reliable source of randomised controlled trials (RCTs) relevant to this review question. Since the systematic review was published in 2014, the Cochrane Vascular Group worked in collaboration with the NICE Guideline Updates Team and performed update literature searches to facilitate identification of any RCTs published after publication of the systematic review by Paravastu et al. (2014). Data were extracted from the systematic review, individual RCTs within it, and RCTs identified from update literature searches to compare the efficacy of elective EVAR with that of open surgical repair of 'simple' unruptured infrarenal aneurysms. Since the Cochrane systematic review did not explicitly consider complex aneurysm anatomies (such as juxtarenal and suprarenal type IV aneurysms) a supplementary literature search was performed by NICE. Although RCTs were judged to be the optimal study design for this question, non-randomised comparative studies, and prospective cohort studies comparing EVAR and open surgical repair of unruptured complex AAAs were also included because the committee expected fewer RCTs evaluating complex EVAR to be published since it makes up a small subset of elective EVAR procedures.

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.

Clinical evidence

Included studies

Standard EVAR

The 2014 Cochrane systematic review (Paravastu et al, 2014) included 4 RCTs (reported across multiple publications) comparing EVAR with open surgical repair of infrarenal AAA. The update literature search performed by Cochrane Vascular Group yielded 354 abstracts, of which 4 full manuscripts were ordered. Of the 4 articles reviewed, an additional publication reporting an RCT (EVAR-1 trial) that was already included in the Cochrane review was identified. Thus, a total of 4 RCTs, published across multiple publications, was considered relevant for comparisons between standard EVAR and open surgical repair of unruptured AAAs. The 2014 Cochrane systematic review included 1 RCT (EVAR-2 trial) comparing EVAR with non-surgical management, in patients for whom open surgical repair was considered unsuitable. The update literature search performed by Cochrane Vascular Group yielded 1 publication reporting long-term follow-up of the EVAR-2 trial.

In December 2017, Cochrane performed another literature search to identify studies which were published during guideline development. The search yielded a total of 296 abstracts; of which, 4 full manuscripts were ordered. Upon review of these 4 articles, a publication of another RCT (DREAM trial) already included in the Cochrane review was identified.

Complex EVAR

With regard to complex aneurysm anatomies, searches conducted by NICE yielded 2,220 abstracts. Of these, 16 studies were identified as being potentially relevant. Following full-text review, 1 study was included. An update search was conducted by NICE in December 2017. The search yielded 191 abstracts; of which, 7 full manuscripts were ordered. Following full-text review, no new studies were identified.

Excluded studies

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

Summary of clinical studies included in the evidence review

A summary of the included studies is provided in the tables below.

Standard EVAR compared with open surgical repair of unruptured infrarenal AAA

Study	Details
Paravastu SC, Jayarajasingam R, Cottam R et al. (2014) Endovascular repair of abdominal aortic aneurysm. Cochrane Database Syst Rev;(1): CD004178. doi: 10.1002/14651858.CD004178.pub2.	Study design: systematic review Location: UK Population: patients with unruptured AAA Sample size: 4 RCTs including 2,745 participants Follow-up: 30 days, up to 4 years, up to 8 years Intervention: standard EVAR using any type of endovascular device Comparators: open surgical repair Outcomes: All-cause mortality, aneurysm-related mortality, endograft-related complications, major complications, minor complications, and quality of life. Assessed at the following time points: 30 days, up to 4 years up to 8 years. Note: details about included studies can be found in Appendix D
ACE trial (results reported in multiple publications outlined in the Cochrane systematic review)	Study design: multicentre, non-blinded, randomised controlled trial Location: France Population: patients with asymptomatic unruptured abdominal aortic or aorto-iliac aneurysm Sample size: 299; 99% male Follow-up: up to 4 years Intervention: standard EVAR Comparators: Open surgical repair Outcomes: All-cause mortality, major adverse events (myocardial infarction, permanent stroke, permanent haemodialysis, major amputation, paraplegia and bowel infarction), vascular reinterventions and minor complications
DREAM trial (results reported in multiple publications outlined in the Cochrane systematic review)	Study design: multicentre, non-blinded, randomised controlled trial Location: Netherlands Population: patients with unruptured AAA

Study	Details
NB: a new publication was identified from update searches van Schaik T G, Yeung KK, Verhagen HJ et al. (2017) Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. European Journal of Vascular and Endovascular Surgery 54 (5), 671	Sample size: 351; 91% male Follow-up: up to 15 years 3 Intervention: standard EVAR Comparators: Open surgical repair Outcomes: All-cause mortality, aneurysm-related mortality, complications and reintervention rates
EVAR1 trial (results reported in multiple publications outlined in the Cochrane systematic review) NB: a new publication was identified from update searches Patel R, Sweeting MJ, Powell JT et al. (2016) Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repairtrial 1 (EVAR trial 1): a randomised controlled trial. Lancet. 388(10058):2366-2374.	Study design: multicentre, non-blinded, randomised controlled trial Location: UK Population: patients with unruptured AAA Sample size: 1,252; 91% male Follow-up: up to 15 years Intervention: standard EVAR Comparators: Open surgical repair Outcomes: All-cause mortality, aneurysm-related mortality, complications and reintervention rates
OVER trial (results reported in multiple publications outlined in the Cochrane systematic review)	Study design: multicentre, non-blinded, randomised controlled trial Location: USA Population: patients with unruptured AAA Sample size: 881; 99% male Follow-up: 8 years Intervention: standard EVAR Comparators: Open surgical repair Outcomes: All-cause mortality, aneurysm-related mortality, complications and reintervention rates

70 **Complex EVAR compared with open surgical repair of juxtarenal (complex) aneurysms**

Study	Details
Donas Konstantinos P, Eisenack Markus, Panuccio Giuseppe, Austermann Martin, Osada Nani, and Torsello Giovanni (2012) The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 56, 285-90	Study design: non-randomised comparative study Location: Germany Population: patients with primary degenerative juxtarenal AAAs Sample size: 90; 92% (83/90) male Follow-up: 30-days Intervention: complex EVAR (chimney-EVAR or fenestrated-EVAR) Comparators: open surgical repair Outcomes: 30-day mortality, the need for re-intervention and length of stay,

EVAR vs no intervention for patients in whom open surgery is not considered appropriate

Study	Details
Sweeting M J, Patel R, Powell J T, and Greenhalgh R M (2017) Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair: Very Long-term Follow-up in the EVAR-2 Randomized Controlled Trial. Annals of Surgery. 24 Note: Other publications relating to this trial that reported data at different follow-up periods were considered	Study design: multicentre, non-blinded, randomised controlled trial Location: UK Population: patients with large aneurysms in whom open surgical repair was considered inappropriate Sample size: 404; sex-specific proportions were not reported Follow-up: 12 years Intervention: EVAR Comparators: open surgical repair Outcomes: All-cause mortality, aneurysm-related mortality, graft-related complications and graft-related re-interventions.

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 systematic review of economic literature was conducted jointly for all review questions in this guideline by applying standard health economic filters to a clinical search for AAA (see Appendix B). A total of 5,173 studies was identified. The studies were reviewed to identify cost–utility analyses exploring the costs and effects of elective surgical procedures to repair unruptured AAAs. Studies that met the eligibility criteria were assessed using the quality appraisal criteria as outlined in the Developing NICE guidelines: the manual (2014).

Following an initial review of titles and abstracts, the full texts of 46 studies were retrieved for detailed consideration. Following full-text review, 15 of the 46 studies were judged to be potentially applicable cost–utility analyses for elective repair. Of these, 5 were UK studies. It was decided to exclude the non-UK studies because of their lower applicability to UK practice.

An update search was conducted in December 2017, to identify any relevant cost–utility analyses that had been published during guideline development. This search returned 814 studies. Following review of titles and abstracts, the full texts of 8 studies were retrieved for detailed consideration. Three were determined to be potentially applicable for elective repair; however they were non-UK studies, and were selectively excluded. A total of 5 studies was therefore included as economic evidence for the elective repair of unruptured AAA.

Excluded studies

Studies that were excluded after full-text review, and reasons for exclusion, are provided in Appendix J – Excluded studies.

Summary of studies included in the economic evidence review

Michaels et al. (2005)

Michaels et al. (2005) published the first UK cost–utility analysis comparing EVAR with open surgical repair for the elective repair of infrarenal AAA, based on early (perioperative; 30-day) results of the EVAR-1 and DREAM trials. The analysis modelled a cohort of 70-year old men with an initial AAA diameter of 5.5cm. A decision tree was developed to model the surgical procedure followed by general population survival for 10 years. Other inputs, such as EVAR complications, were derived from a 2005 NICE review of non-RCT data. Costs and QALYs were both discounted by 3.5% per year. Model results (Table 3) suggest that EVAR is associated with a high ICER of over £100,000/QALY compared with open surgical repair, with a near 0% likelihood of the ICER falling under £20,000 per QALY gained.

A secondary analysis was also reported comparing EVAR with providing no intervention; however it was based on non-randomised evidence only, therefore these results have been excluded due to possessing very serious limitations.

Epstein et al. (2008)

Epstein et al. (2008) developed a lifetime Markov model comparing EVAR with open surgical repair in the UK, based on 4-year data from the EVAR-1 randomised study. Perioperative outcomes included mortality and conversion from EVAR to open surgical repair, followed by symptom-free survival subject to risks of major cardiovascular events, AAA-related readmission and death. All-cause mortality rates were assumed to converge after 2 years. Health-related quality of life effects (EQ-5D), resource use and costs were informed by data collected during EVAR-1. All outcomes were discounted by 3.5% per year.

The model found EVAR to incur higher total costs and accrue fewer QALYs per patient than open surgical repair (Table 3), and the difference in costs was statistically significant. EVAR had a 1% probability of having an ICER of £20,000 or less per QALY gained, which remained less than 10% in all but extreme scenario analyses.

Chambers et al. (2009)

Chambers et al. (2009) developed an NIHR-funded cost–utility model as part of their EVAR health technology assessment to support NICE Technology Appraisal 167. It evaluated EVAR in 2 populations: people who are fit enough to undergo open surgical repair and people who are not. For the primary analysis comparing EVAR with open surgical repair, a Markov model was developed using patient-level data from the EUROSTAR registry dataset, with a similar structure to the Epstein et al. (2008) model. The EUROSTAR data informed multivariable models predicting baseline risks of perioperative mortality, postoperative AAA-related mortality and other cause mortality, with relative risks informed by the DREAM and EVAR-1 studies or expert advice. The aneurysm-related mortality benefit associated with EVAR was assumed to persist for the lifetime horizon. Quality of life (EQ-5D) and resource use inputs were informed by the EVAR-1 trial. Outcomes were discounted by 3.5% per year.

EVAR was found to be associated with a QALY gain, and to incur a higher cost per patient, compared with open surgical repair, resulting in an ICER was £48,990 per QALY gained (Table 3). The probability of EVAR possessing an ICER below £20,000 was 26%.

The secondary analysis evaluated EVAR compared with continued monitoring or discharge without intervention. This analysis included the option of repairing AAA at diameters below

5.5 cm, such that the study is relevant to the question of early intervention for this guideline. Its methods and details are described fully in Evidence review F. Briefly, the authors concluded that EVAR may have an ICER below £20,000 compared with providing no intervention in somebody with a 5.5 cm aneurysm aged 73 or younger. In people with larger aneurysms, EVAR became increasingly cost effective, compared with no intervention (e.g. it was cost effective in people aged up to 79 years old if the AAA is 8.0 cm).

Brown et al. (2012)

Brown et al. (2012) conducted an economic evaluation with a Markov model broadly similar to the Epstein et al. (2008) and Chambers et al. (2009) models, with the inclusion of a waiting period via an 'intention to treat' analysis, with outcomes divided into more granular time periods: randomisation to 6 months, 6 months for 4 years, 4–8 years, and after 8 years. Data up to 8 years were informed by mid-term outcomes of EVAR-1. Quality of life (EQ-5D) and resource use inputs were obtained from the EVAR-1 data. Outcomes were discounted by 3.5% per year. Results (Table 3) suggest that EVAR is dominated by open surgical repair, with higher overall costs and fewer total QALYs per patient, with the EVAR ICER being £20,000 per QALY gained or better in 1% of model runs.

The authors also conducted a within-trial economic analysis based on the EVAR-2 trial, comparing EVAR with 'no intervention' for infrarenal AAA in people deemed unfit for open surgical repair. Quality of life (EQ-5D) and resource use were from the trial, captured in the same manner as the EVAR-1 study. The within-trial intention-to-treat analysis (8-year duration) found EVAR to have a mean ICER of £264,900 per QALY gained over 'no intervention', with 0% probability of the ICER being under £20,000. Results of a lifetime analysis, with survival extrapolated using parametric survival curves fitted to the EVAR-2 data, reduced the EVAR ICER to £30,274 per QALY gained. However, costs were not extrapolated beyond the trial.

Epstein et al. (2014)

Epstein et al. (2014) presented a further iteration of the Epstein et al. (2008) model, using outcomes data from the ACE, DREAM, EVAR-1 (8-year data) and OVER studies. Clinical and resource use inputs were obtained from each trial. The trial data were not synthesised. Instead, 4 sets of results were presented. The reintervention rate following open surgical repair was estimated using EVAR-1 trial data, with relative effects from each study used to estimate EVAR reintervention rates. Quality of life was informed by the EVAR-1 EQ-5D data. To normalise country-specific follow-up protocols, the authors applied a single postoperative outpatient CT scan for open surgical repair patients and continued annual monitoring following EVAR. Outcomes were discounted by 3.5% per year.

EVAR was dominated by open surgical repair in the EVAR-1 and ACE analyses, with an ICER of almost £3,000,000 per QALY gained in the DREAM analysis (Table 3). Each analysis predicted a 0% probability of EVAR having an ICER below £20,000 per QALY gained compared with open surgical repair. Conversely, the OVER analysis found a cost saving and QALY gain per patient for EVAR, with a 91% probability that its ICER is under £20,000. The authors attribute this to higher hospital costs in the US setting of the OVER trial, and the fact that the OVER trial predicts more favourable long-term survival for EVAR compared with the other trials.

Table 2: Cost–utility results of included economic studies – all infrarenal AAA repair

Study & comparison	Incremental (EVAR)		ICER	Probability ICER of £20k or better
	Costs (£)	QALYs		
Michaels et al. (2005)				
EVAR vs. OSR	11,449	0.10	£110,000	~0%
Epstein et al. (2008)				
EVAR vs. OSR	3,758	-0.02	Dominated	1.2%
Chambers et al. (2009)				
EVAR vs. OSR	2,002	0.041	£48,990	26.1%
Brown et al. (2012)				
EVAR vs. OSR	3,521	-0.042	Dominated	1%
EVAR vs. no intervention [a]				
Trial analysis	10,214	0.037	£264,900	0%
Lifetime analysis	10,214	0.350	£30,274	23%
Epstein et al. (2014)				
EVAR vs. OSR				
ACE	2,086	-0.01	Dominated	0%
DREAM	3,181	0.00	£2,845,315	0%
EVAR-1	4,014	-0.02	Dominated	0%
OVER	-1,852	0.05	Dominant	91%
Note: (a) The population in this analysis was not considered to be anaesthetically fit to undergo OSR (the EVAR-2 study population).				
Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical repair; QALYs, quality-adjusted life years.				

Further details of the included economic studies are available in Appendix H – Economic evidence tables and the separate economic analysis appendix.

Economic model

The effectiveness of EVAR compared with open surgical repair for the repair of unruptured AAAs was identified as a priority for new economic analysis. Clinical evidence has become available since the existing technology appraisal (TA 167) was published, including the ACE and OVER trials, as has longer-term data from the DREAM and EVAR trials. Furthermore, the TA guidance is focused on infrarenal AAA, whereas the scope of this guideline has a wider population containing other types of AAA. A new economic model was therefore developed to support decision-making in this area.

Methods

The model began at the point when the decision is made to conduct, or not to conduct, the elective repair of an AAA. Two distinct populations were modelled: (1) those for whom open surgical repair is a suitable intervention, comparing EVAR with open surgical repair; and (2) those for whom open surgical repair is not a suitable intervention, because of raised intraoperative risk, comparing EVAR with no intervention. Much of the input data for these 2 models was informed by anonymised patient-level survival data from the EVAR-1 and EVAR-2 trials, respectively, which the EVAR trial investigators provided to NICE. Within each population, the model also evaluated infrarenal AAAs and complex AAAs as separate groups. The perspective on costs was those incurred by the NHS and Personal Social Services (PSS), and the perspective on outcomes was the direct health effects for people using AAA services. The main outcomes were incremental costs and QALYs, and the resulting ICER. The model time horizon was the lifetime of the patient (to a maximum age of 100), composed of 1-month cycles, with all outcomes discounted by 3.5% per year (Developing NICE guidelines, 2014).

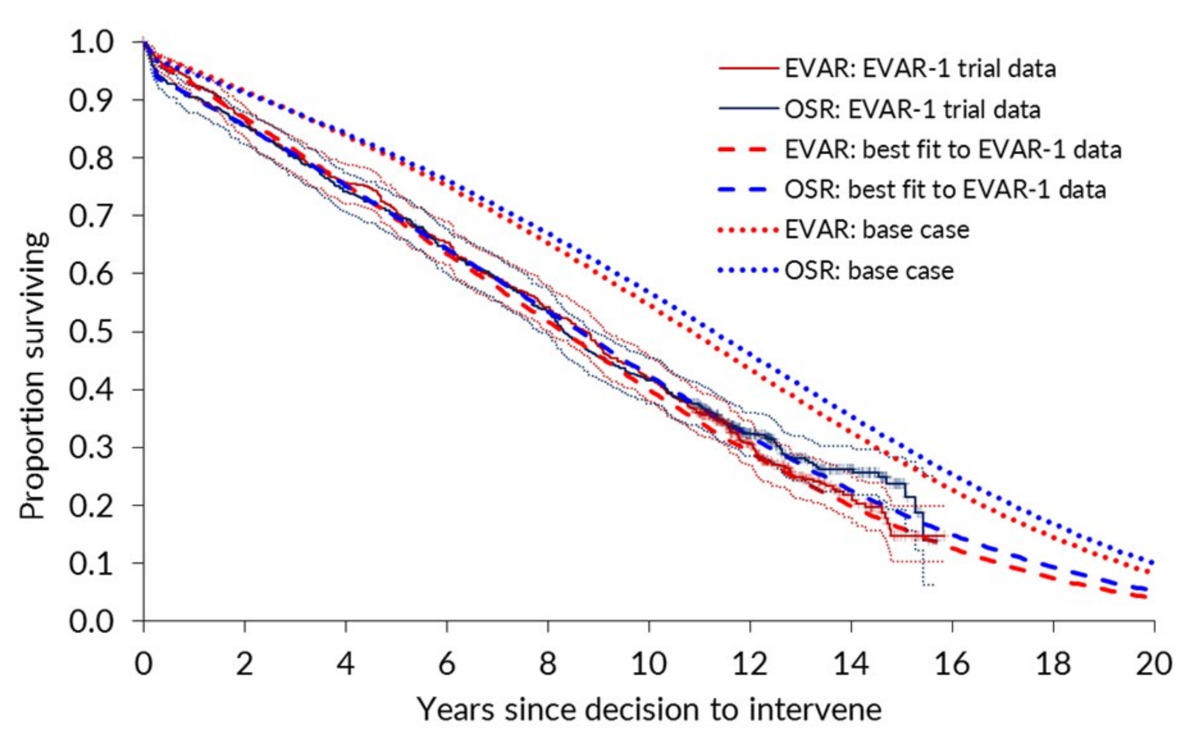
In the population for whom open surgical repair is a suitable intervention, modelled patients were first at risk of death while waiting for their elective intervention: 2 months for infrarenal EVAR and any open surgical repair; 4 months for complex EVAR. The extended waiting time for complex EVAR is due to the need for those EVAR devices to be custom-made to suit the patient's aortic anatomy, whereas standard EVAR devices suitable for infrarenal AAAs are readily available. This was followed by 1 perioperative cycle, in which the intervention occurs, with a risk of perioperative mortality. In the base-case model, this was informed by the UK National Vascular Registry (2016) data on EVAR (0.4%), representing a current snapshot of UK practice outcomes. To estimate the OSR perioperative mortality rate relative to EVAR, the model used the results of a Cochrane systematic review of elective AAA repair trials (odds ratio for EVAR versus open surgical repair: 0.33; Paravastu et al., 2014). This approach combined using an estimate of current UK practice outcomes (the registry) for baseline data and the best available randomised evidence for the relative effectiveness between EVAR and OSR from (the Cochrane review).

Surviving patients move into the post-perioperative survival (long-term) phase of the model, informed by general population mortality rates, calibrated to post-perioperative survival data from the EVAR-1 open surgical repair arm (though the EVAR arm would have been equally appropriate for this). The long-term relative effectiveness of EVAR was informed by hazard ratio from a meta-analysis of long-term elective repair data (EVAR-1, DREAM and OVER). Throughout the model, patients are at risk of complications requiring reintervention, informed by the EVAR-1 trial. Laparotomy-related reinterventions, such as bowel resection, were also captured based on US Medicare data.

In the population for whom open surgical repair is not a suitable intervention, EVAR waiting time, perioperative and long-term mortality data were informed by the only relevant RCT: the EVAR-2 trial. For this population, survival on the comparator strategy of 'no intervention' was modelled from the point of randomisation, with no waiting time or perioperative periods. The 'no intervention' survival data were adjusted for the effect of crossover, using the rank preserving structure failure-time (RPSFT) technique, as one-third of participants randomised to this arm instead received EVAR. The RPSFT method is a well established method for accounting for trial crossover, estimating what the survival of trial participants who switched arm would have looked like had they not switched (the counterfactual), and adjusting the observed treatment effect accordingly. The same technique to calibrate general population survival data as described above was then used. Postoperative EVAR complications were included using event rates reported in the EVAR-2 study. On the 'no intervention' arm, the model includes the complication of the unrepaired AAA rupturing. In the EVAR-2 trial, the rate of rupture was reported to be 12.4% per year. This rate is used to determine the proportion of patients in each cycle who require emergency repair (though 89% of EVAR-2 ruptures were fatal before emergency intervention could be commenced).

In order to explore subgroups effects, the model for both populations was configured so that perioperative and long-term survival estimates could be influenced by effect modifiers. For perioperative mortality, the effects of age, AAA diameter and sex were captured based on data from the European 'Vascunet' registry (Mani et al., 2015). AAA diameter was a significant predictor of death, more prominently for EVAR, and age was a predictor of perioperative death for open surgical repair. For post-perioperative mortality, multivariable Cox regressions using the EVAR-1 data found AAA size to be a significant determinant of long-term survival. Using the EVAR-2 data, being treated with EVAR was associated with improved survival for up to 4.5 years. The effect of age was implicitly captured in this by our use of calibrated general population survival data. Effect modifiers were used in specific subgroup analyses and in probabilistic sensitivity analysis, to fully explore the effect of uncertain patient characteristics on outcomes. Our base-case deterministic results are evaluated for the trial mean cohorts.

Base case overall survival curves are presented in Figure 1 and Figure 2.



Note: While base-case survival may seem to overpredict survival in the EVAR-1 trial, the apparent differences are explained by: (1) applying waiting time mortality rates for each arm of the trial as observed in the data; (2) the use of UK registry data to inform baseline estimate of perioperative mortality (lower than RCT estimates; (3) perioperative and long-term survival relative effects being informed by meta-analysed data from several RCTs, rather than just EVAR-1; and (4) uplifting survival data calibrated to the OSR arm of EVAR-1, which recruited in 1999–2003, to reflect 2015–16 values using UK life tables.

Figure 1: Base case (and true fit) overall survival profiles – infrarenal AAAs – population for whom open surgical repair is an option, compared with EVAR-1 trial data

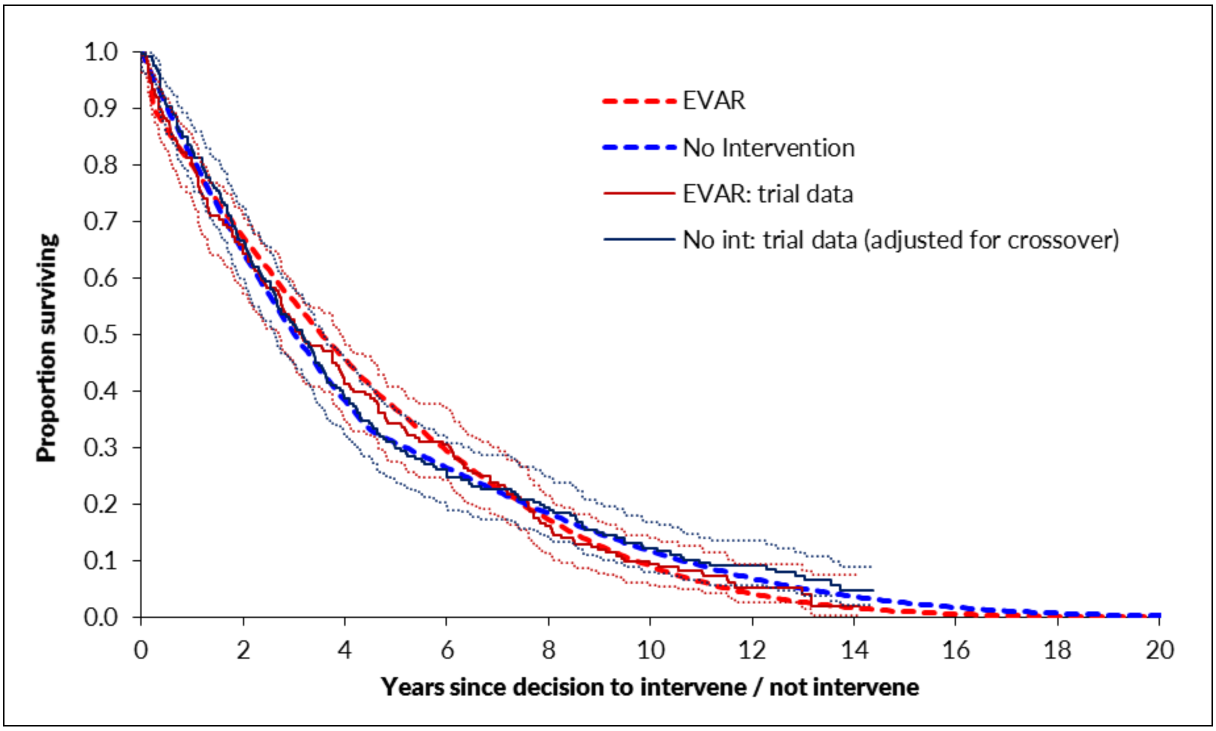


Figure 2: Base case overall survival profile – infrarenal AAAs – population for whom open surgical repair is not an option, versus EVAR-2 trial data

People with more complex aneurysms – that is, cases in which a standard EVAR graft cannot be used within the terms of its instructions for use – were also simulated in the model, as a separate subpopulation. There are no long-term, randomised data comparing EVAR and open surgical repair for the repair of complex AAAs. The model therefore used the UK National Vascular Registry (2016), which reports perioperative mortality rates in UK practice for complex repair. Taking the registry's EVAR mortality rate (3.6%) as the starting point, the model applies the relative effect from the Cochrane meta-analysis of elective infrarenal AAA repairs to this value to obtain an estimated complex repair perioperative mortality rate for open surgical repair (10.1%). The relevant effect modifiers may then be applied to the resulting baseline estimates. In the population for whom open surgical repair is not a suitable option, the Registry data were used to estimate a 'relative effect of complexity' on perioperative mortality following EVAR, relative to infrarenal EVAR (odds ratio = 8.8). This relative effect is used to increase the perioperative mortality rate from the EVAR-2 trial, to estimate the equivalent EVAR perioperative mortality rate in people with complex aneurysms. Owing to the absence of long-term evidence, post-perioperative survival and reintervention rates for people with repaired complex aneurysms were assumed to be equal to those for people with repaired infrarenal aneurysms; the guideline committee advised that this is a plausible assumption. The overall survival of people on the 'no intervention' strategy, based on EVAR-2 trial data, was assumed to be independent of aneurysm complexity, due to the absence of long-term survival data in people with untreated complex AAA. Again, the guideline committee advised that this was a reasonable approach to take.

Resource use was obtained from the detailed published EVAR-1 data (Brown et al. 2012), to which up-to-date national unit costs were applied. The cost of standard and complex EVAR devices were obtained from NHS Trusts by members of the guideline development committee. Following advice from the committee, a strategy of 'no intervention' is assumed to incur non-zero costs, associated with a further outpatient attendance and CT scan. Quality of life was primarily informed by the published 1-year EVAR-1 EQ-5D data, supplemented by decrements for complications identified by informal searches.

For complete details of model methods and parameters, please see the separate economic analysis appendix.

Results

In the base-case model, in a cohort for whom open surgical repair is a suitable option, elective EVAR was found to be dominated by open surgical repair, producing fewer QALYs at a higher total NHS and personal social service (PSS) cost (Table 3). Probabilistic sensitivity analysis showed that its ICER had <1% likelihood of being £20,000 per QALY gained or better, and no individual parameter reversed this result when varied between its upper and lower bounds. For the repair of complex AAAs in this population, the base-case ICER was £95,815 per QALY gained. Here, EVAR was associated with a QALY gain of 0.166 per patient, due to the wider gap between EVAR and open surgical repair in estimated perioperative mortality – that is, fewer individuals are predicted to survive open surgical repair to experience any improved long-term survival prospects. However, this benefit is offset by the substantially higher device cost associated with complex EVAR, such that it remains highly unlikely (1%) to have an ICER of £20,000 per QALY gained or better. This finding is not sensitive to variation in any individual parameter. No subgroup could be identified in which EVAR represented an effective use of NHS resources, when compared with open surgical repair.

In the population for whom open surgical repair is not a suitable option, an EVAR strategy was compared with offering no AAA repair. On the comparator arm, the individual does not undergo any surgical procedure, and therefore faces no waiting time or perioperative mortality risk. However, they continue living with an unrepaired AAA that is at risk of rupturing. The ICER for EVAR compared with this strategy was found to be £460,863 per QALY gained (Table 4), with a modest gain in QALYs (0.033) coming at a high additional cost (£15,438) per patient. No parameter had the capacity to change the conclusion about this ICER in one-way sensitivity analysis, and probabilistic sensitivity analysis showed a 0% probability that the ICER is £20,000/QALY or better. For the repair of complex AAAs in this population, the base-case cost–utility results showed that EVAR was clearly dominated by the 'no intervention' strategy. The relatively high perioperative mortality rate associated with complex EVAR, which is never offset by differences in long-term survival, causes a net loss of QALYs, while the high cost of the custom-built device leads to a high incremental cost. Here, too, EVAR has a 0% probability of having an ICER of £20,000 per QALY gained or better. No subgroup could be identified in which standard or complex EVAR represented an effective use of NHS resources, when compared with no intervention in people for whom open surgical repair is not a suitable option.

For detailed results, sensitivity analyses and discussion, including limitations and comparison with published analyses, please see the separate health economics appendix.

Table 3: NICE cost–utility model results, population for whom open surgical repair is an option

Treatment strategy	Total		Incremental		ICER
	Costs (£)	QALYs	Costs (£)	QALYs	
Infrarenal AAA repair					
OSR EVAR	£13,438 £19,770	6.640 6.480	£6,331	-0.160	EVAR dominated
Complex AAA repair					
OSR EVAR	£13,206 £29,139	6.033 6.199	£15,933	0.166	£95,815
Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.					

Table 4: NICE cost–utility model results, population for whom open surgical repair is not an option

Treatment strategy	Total		Incremental		ICER
	Costs (£)	QALYs	Costs (£)	QALYs	
Infrarenal AAA repair					
No intervention EVAR	£909 £16,363	2.313 2.347	£15,438	0.033	£460,863
Complex AAA repair					
No intervention EVAR	£942 £24,556	2.324 1.565	£23,632	-0.759	EVAR dominated
Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years.					

Evidence statements

EVAR compared with open repair for patients in whom surgery is considered appropriate

Clinical evidence

- Four RCTs provided moderate to high-quality evidence on all-cause mortality in people with unruptured AAAs in whom surgery was considered appropriate. The studies reported that:
  - Perioperative mortality (30-day or in-hospital) was lower with EVAR than with open surgical repair (high-quality evidence; from 4 RCTs, including 2,783 people).
  - 0–4-year mortality could not be differentiated between EVAR and open surgical repair (moderate-quality evidence from 4 RCTs, including 2,783 people).
  - There was no difference in 0–8-year mortality between EVAR and open surgical repair (high-quality evidence from 3 RCTs, including 2,484 people).
  - There was no difference in 0–15-year mortality between EVAR and open surgical repair (high-quality evidence from 2 RCTs, including 1,603 people).
  - 8–15-year mortality was higher with EVAR than with open surgical repair (high-quality evidence from 1 RCT, including 1,252 people).

- Four RCTs provided very low- to high-quality evidence on AAA-specific mortality in people with unruptured AAAs in whom surgery was considered appropriate. The studies reported that:
  - 0–4-year AAA-specific mortality could not be differentiated between EVAR and open surgical repair (very low-quality evidence from 4 RCTs, including 2,783 people).
  - 0–8- year AAA-specific mortality could not be differentiated between EVAR and open surgical repair (moderate-quality evidence from 3 RCTs, including 2,484 people).
  - 0–15-year AAA-specific mortality could not be differentiated between EVAR and open surgical repair (very low-quality evidence from 2 RCTs, including 1,603 people).
  - 8–15-year AAA-specific mortality was higher with EVAR than with open surgical repair (high-quality evidence from 1 RCT including 1,252 people).
- Low- to moderate-quality evidence from 4 RCTs, including 2,783 people with unruptured AAAs, could not differentiate cardiac-, and stroke-related mortality rates between patients treated by EVAR and those treated by open repair (follow-up not reported). Moderate-quality evidence from 4 RCTs, including 2,783 people, reported lower rates of pulmonary-related mortality in patients treated by EVAR than those treated by open surgery.
- High-quality evidence from 2 RCTs, including 2,432 people with unruptured AAAs, reported lower pulmonary complication rates in patients treated by EVAR compared with those treated by open repair (follow-up not reported). Low-quality evidence from 3 RCTs, including up to 2,432 people with unruptured AAAs, could not differentiate non-fatal stroke, sexual dysfunction and renal complication rates between patients treated by EVAR and those treated by open repair (follow-up not reported).
- Very low-quality evidence from 3 RCTs, including 2,484 people with unruptured AAAs, reported higher rates of any type of reintervention in patients treated by EVAR compared with those treated by open repair at 4-year and 8-year follow-up. Moderate-quality evidence from 1 RCT, including 546 people with unruptured AAA, could not differentiate rates of any type of reintervention between patients treated by EVAR and those treated by open repair between 8- and 15-year follow-up. When considering total follow-up periods, high-quality evidence from 2 RCTs including 1,603 people reported higher rates of any type of reintervention in patients treated by EVAR than those treated by open repair at follow-up of up to 15 years.
- High-quality evidence from 1 RCT, including 351 people with unruptured AAA reported higher rates of AAA-related reintervention in patients treated by EVAR compared with those treated by open repair at follow-up of up to 15 years. High-quality evidence from another RCT including up to 1,252 people with unruptured AAAs, reported higher rates of life-threatening reintervention in patients treated by EVAR compared with those treated by open repair at follow-up of up to 15 years.
- Moderate-quality evidence from 1 RCT, including 1,341 people with unruptured AAAs, could not differentiate quality of life measures (SF-36, and EQ-5D scores) between patients treated by EVAR and those treated by open repair at 2-year follow-up.
- High-quality evidence from 4 RCTs, including 2,747 people with unruptured AAAs, reported shorter length of hospital stay in patients treated by EVAR compared with those treated by open repair.

Economic evidence

Published evidence

- Five partially applicable cost–utility analyses with potentially serious limitations, based on data from the ACE, DREAM and EVAR-1 trials, found that EVAR was either dominated by open surgical repair, or associated with an ICER of £48,990 to £2.8 million per QALY gained. The EVAR ICER was associated with a 0% to 26% probability of being £20,000 per QALY gained or better. One of these studies, when using data from the OVER trial, found EVAR to have higher incremental QALYs and lower incremental costs than open surgical repair, with a 91% probability of its ICER being £20,000 per QALY gained or better.

NICE model

- One directly applicable cost–utility analysis with minor limitations found EVAR to produce fewer QALYs per patient at a higher cost per patient than open repair, for the elective repair of infrarenal AAAs in people for whom open repair may be an appropriate intervention. This result was robust to one-way sensitivity analyses. The ICER had <1% probability of being £20,000 or better.

Complex EVAR compared with open repair for patients with juxtarenal aneurysms

Clinical evidence

- Very-low quality evidence from 1 non-randomised controlled trial, including 90 people with unruptured juxtarenal aneurysms, could not differentiate 30-day mortality between patients treated by EVAR and those treated by open repair.
- Very-low quality evidence from 1 non-randomised controlled trial, including 90 people with unruptured juxtarenal aneurysms, could not differentiate haemodialysis, pneumonia, stroke and reintervention rates between patients treated by EVAR and those treated by open repair at mean follow-up of 15.2 months.
- Low-quality evidence 1 non-randomised controlled trial, including 90 people with unruptured juxtarenal aneurysms, reported shorter length of hospital stay in patients treated by EVAR compared with those treated by open repair.

Economic evidence

Published evidence

- No cost–utility analyses were identified in this population.

NICE model

- One directly applicable cost–utility analysis with potentially serious limitations found EVAR to have an ICER of £95,815 per QALY gained compared with open repair, for the elective repair of complex AAAs in people for whom open repair may be an appropriate intervention. The finding that EVAR is unlikely to be associated with an ICER of £20,000 per QALY or better was robust to one-way sensitivity analyses. The ICER had a 1% probability of being £20,000 or better.

EVAR vs no intervention for patients in whom open surgery is not considered appropriate

Clinical evidence

- Low- to moderate quality evidence from 1 RCT, including 404 people with unruptured AAAs that were considered unsuitable for open repair, could not differentiate all-cause mortality rates between patients treated by EVAR and those who received no intervention at 6-month, 4-year, 8-year and 12-year follow-up.

- Low-quality evidence from 1 RCT, including 404 people with unruptured AAAs that were considered unsuitable for open repair, could not differentiate AAA-related mortality rates between patients treated by EVAR and those who received no intervention at 6-month follow-up. Conversely, moderate-quality evidence from the same study reported lower AAA-related mortality rates in patients treated by EVAR compared with those who received no intervention at 4- and 8-year follow-up.
- Very low-quality evidence from 1 RCT, including 404 people with unruptured AAAs that were considered unsuitable for open repair, could not differentiate rates of fatal myocardial infarction and stroke-related mortality between patients treated by EVAR and those who received no intervention at 4-year follow-up.
- Low-quality evidence from 1 RCT, including 404 people with unruptured AAAs that were considered unsuitable for open repair, reported higher rates of non-fatal myocardial infarction in patients treated by EVAR than those who received no intervention at 4-year follow-up. Low-quality-evidence from the same trial could not differentiate rates of non-fatal stroke in patients treated by EVAR compared with those who received no intervention at 4-year follow-up.
- Very low-quality evidence from 1 RCT, including 404 people with unruptured AAAs that were considered unsuitable for open repair, could not differentiate quality of life measures (SF-36, and EQ-5D scores) between patients treated by EVAR and those who received no intervention at 2-year follow-up.

Economic evidence

Published evidence

- One partially applicable cost–utility analysis with potentially serious limitations, based on the EVAR-2 trial, found that EVAR had an ICER of £264,900 per QALY compared with no treatment over 8 years, with 0% probability of this being less than £20,000. A lifetime analysis with very serious limitations had an equivalent ICER of £30,274 and probability of 23%.

NICE model

- One directly applicable cost–utility analysis with minor limitations found EVAR to be associated with an ICER of £460,863 compared with no intervention, for the elective repair of infrarenal AAAs in people for whom open repair is not considered to be a suitable intervention. This result was robust to one-way sensitivity analyses. The ICER had 0% probability of being £20,000 or better.
- The equivalent result for the repair of complex AAAs, in an analysis with minor limitations, showed EVAR to be dominated by no intervention, with a 0% probability of its ICER being £20,000 or better.

Recommendations

K1. For people with unruptured AAAs meeting criteria in 1.5.1, offer open surgical repair unless there are anaesthetic or medical contraindications.

K2. Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is suitable.

K3. Do not offer EVAR to people with an unruptured infrarenal AAA if open surgical repair is unsuitable because of their anaesthetic and medical condition

K4. Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is a suitable option, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.

K5. Do not offer complex EVAR to people with an unruptured AAA if open surgical repair is not a suitable option because of their anaesthetic and medical condition.

Research recommendations

RR6. What is the effectiveness and cost-effectiveness of complex EVAR versus open surgical repair in people with an unruptured AAA for whom open surgical repair is a suitable option?

Rationale and impact

Why the committee made the recommendations

There is no evidence that elective EVAR for people with an unruptured infrarenal AAA provides long-term benefit compared with open surgical repair. While EVAR is associated with fewer perioperative deaths, it has more long-term complications, and these complications mean that people will need further procedures. There is some evidence that EVAR is associated with worse long-term survival than open surgical repair. EVAR also has higher net costs than open surgical repair. The evidence shows that, even if long-term benefits were achievable, they could not plausibly be sufficient to outweigh these costs.

Open surgical repair is unsuitable for some people with an unruptured AAA because of their anaesthetic risk and/or medical co-morbidity. For these people, the risks of their AAA rupturing, if no repair is attempted, have to be balanced against the perioperative risks and long-term complications associated with EVAR. The evidence shows that the average person receiving EVAR has an uncertain chance of a small net benefit, compared with the large and certain increase in costs. Therefore, the committee agreed that EVAR for unruptured AAA (elective repair) cannot be considered an effective use of NHS resources in this population.

The evidence for complex EVAR was limited in quantity and quality. However, complex EVAR grafts are much more expensive than standard devices, so the difference in cost between EVAR and open surgical repair is even greater than in infrarenal AAAs. The committee also noted that the instructions for use of the grafts that are currently available do not cover complex AAAs. Although there is currently no evidence that complex EVAR has better outcomes than open surgical repair, people with complex AAAs have higher perioperative mortality rates. Because of this, a perioperative survival benefit equivalent to that seen with EVAR for infrarenal AAAs could potentially be more influential in complex AAAs. Therefore, the committee agreed that more information would be helpful, so it recommended that the use of complex EVAR should be restricted to randomised trials.

The committee also discussed complex EVAR for people for whom open surgical repair is not a suitable option because of their anaesthetic risk and/or medical comorbidities. They agreed that, in this population, people who need complex EVAR could not plausibly have better outcomes than those who need standard infrarenal EVAR. As they had not recommended standard EVAR in this population, the committee agreed that they could not recommend complex EVAR either. The committee did not recommend using complex EVAR in randomised trials in these circumstances, because it would be unethical to randomise people to a treatment with a high risk of perioperative death when there is no prospect of long-term benefits at reasonable cost.

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

Impact of the recommendations on practice

The recommendations on EVAR will have a large impact on practice, as EVAR is a widely performed procedure. EVAR is currently used more frequently than open surgical repair in some areas, so a diverse group of people both within and outside the national screening programme will need to update their knowledge. The recommendations will also affect the timing and type of information about treatment options given to patients who are diagnosed with small-to-medium AAAs and are being monitored for signs of growth. The recommendations will minimise harm by reducing long-term mortality and the need for reintervention as a result of problems with EVAR. Reductions in EVAR use and subsequent EVAR-related reinterventions will lead to cost savings within the NHS.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee agreed that the outcomes that matter most are long-term survival, as well as a reduction in the need for reintervention. This is because committee members believed that, apart from the fundamental need to prevent aneurysm rupture, AAA repair should also ensure that people live as long as possible and have the best quality of life possible following intervention.

The quality of the evidence

The committee agreed that, in cases of infrarenal AAA, the evidence relating to all-cause mortality and AAA-related mortality was of sufficient quality to conclude that EVAR was superior to open surgery during the first 30 days after repair. However, the evidence that this benefit is not maintained in the long term is also of high quality. Furthermore, in the RCT that was the largest, the most directly applicable and had the longest follow-up (EVAR-1), EVAR was associated with worse all-cause mortality once follow-up extended beyond 8 years. Across all the RCTs, there was also high-quality evidence that EVAR is associated with approximately double the rate of reintervention seen after open surgical repair. The committee noted that large, observational data sources outside the UK (the Swedish vascular registry and the American Medicare registry) mirrored evidence from RCTs included in the review.

The committee considered that the single RCT (EVAR-2 trial) comparing EVAR with no intervention highlighted no differences in most outcome measures between groups; however, the study had some limitations. The committee noted that a considerable proportion (34%) of the no intervention group ultimately received EVAR; this was not taken into account by investigators in earlier publications of this study. However, the most recent publication (Sweeting et al., 2017) presented an analysis using an established statistical technique (rank-preserving structural failure time; RPSFT) to correct for any bias introduced in this way, and the committee were also aware that the original modelling undertaken for this guideline had used the same technique. Nevertheless, the committee recognised that, while plausible, the assumptions underpinning the RPSFT cannot be empirically validated.

The committee noted that the evidence comparing complex EVAR with open surgical repair was extremely limited in quantity and quality. No RCTs were identified and the single non-randomised comparative study that met this review's inclusion criteria was small in size and only assessed mortality rates at 30-day follow-up. The results of the study, coupled with results from a new health economic model developed for this population (discussed below), led the committee to conclude that there was no evidence that complex EVAR yields a net advantage over open surgery. However, the committee were mindful that longer-term evidence from large RCTs could clarify the clinical utility of complex EVAR, and inform future health economic modelling. Thus, they recommended that the procedure should not be performed outside the confines of an RCT.

The committee noted that the evidence on which they based their decision making was from patients randomised between 1999 and 2004 and that there have been several iterations of design amendments to EVAR devices since this time. However, the committee found no evidence that newer devices perform better than their earlier counterparts and did not consider this to be a reason to reject the evidence reviewed

Benefits and harms

The committee agreed that the clinical evidence demonstrated an advantage of EVAR over open surgery in the short-term (30-day and in-hospital mortality). Once people survived the perioperative period, there was no difference in survival between the treatments until 8-years post-surgery. After this point, open surgery yielded better survival than EVAR. The committee also noted clear evidence that reintervention rates are higher – approximately double – with EVAR than with open repair.

The committee noted that some clinicians and patients may prefer EVAR, because of the additional risk associated with open surgical repair in the perioperative period. However, they agreed that it would be to the benefit of the average candidate for elective AAA repair if the vascular community shifted its focus to intermediate- to long-term outcomes. The committee recognised that the recommendations represent a substantial change to practice and some resistance to change may be encountered.

As the committee were unconvinced by the data relating to complex EVAR, they discussed the potential for harm if patients who could receive open repair are offered complex EVAR. Committee members agreed that, in the absence of evidence of benefit, it would be inappropriate to recommend the use of complex EVAR as standard practice. However, the committee noted that the data relating to open surgical repair for complex AAA are also uncertain, and so the balance of benefits, harms and costs in this population is also uncertain. To reduce this uncertainty, the committee agreed that complex EVAR should only be performed in the well-controlled environment of an RCT. As a result, a research recommendation was made to ensure that data would be collected to inform future updates of the guideline.

In the absence of evidence relating to complex EVAR in patients with medical or anaesthetic contraindications to open surgical repair, the committee considered evidence from other AAA patient populations (alongside original health economic modelling; see below). Having seen convincing evidence that, when compared with no intervention, standard EVAR does not represent a reasonable balance of benefits, harms and costs for people with infrarenal AAA, the committee agreed that the most optimistic expectation possible is that EVAR outcomes would be no worse in people with complex AAAs. The more likely outcome is that they will be substantially worse, owing to higher perioperative mortality. Moreover, while it is inconceivable that there would be additional benefits for this population, compared with the infrarenal group, it is certain that complex EVAR grafts cost more than standard EVAR grafts (see below). Therefore, while the committee discussed whether research was warranted in this area, they decided that it would be unethical to randomise people to an expensive intervention that is known to have a high risk of perioperative mortality, when there is no realistic prospect of long-term benefits that would justify the costs.

Cost effectiveness and resource use

Unruptured infrarenal AAA

The committee discussed the cost-effectiveness evidence for the repair of unruptured infrarenal AAA. The committee were aware that this population, in people for whom open surgical repair is a suitable option, comprised the majority of both clinical and published economic evidence for this review question. The committee agreed that the published UK economic evidence could only reasonably be interpreted as evidence that EVAR was not likely to be an effective use of NHS resources, though it was noted that none of the studies included the longest-term follow-up that is currently available, namely 15 years of data from the EVAR-1 trial. The committee therefore considered evidence from the new economic model developed for this guideline.

The committee were satisfied with the modelling approach of: (1) using National Vascular Registry data to inform baseline perioperative mortality, and the results of a Cochrane meta-analysis to inform relative effects; (2) estimating long-term survival by calibrating general population mortality to the EVAR-1 open surgical repair data conditional on surviving for 30 days after the intervention, and; (3) estimating relative long-term survival using a hazard ratio from a meta-analysis of long-term data from 3 RCTs (DREAM, EVAR-1 and OVER). The committee agreed that the new economic model provided compelling evidence that EVAR is not a cost-effective option for infrarenal AAA compared with open surgical repair. The base-case model results indicate that EVAR produces fewer QALYs than open surgery at a higher total cost to the NHS and PSS, and this is reflected in the probabilistic results, with a low probability of its ICER being £20,000 per QALY gained or better. Results were also robust to scenario and one-way sensitivity analyses, including using only EVAR-1 study data.

The committee discussed the cost results from the new model, and agreed that the high acquisition cost of EVAR was likely to be the key cost difference between EVAR and open surgery in practice. It advised that the modelled cost of complications following EVAR appeared low compared with clinical experience. However, it was agreed that any increase in EVAR complication costs would strengthen the cost-effectiveness results in favour of open surgical repair, and would therefore not affect interpretation of the evidence. The committee also discussed the cost of routine monitoring following EVAR and advised that, in practice, adherence to scheduled monitoring following EVAR is less than 100%. The committee discussed the implications of this on the cost-effectiveness evidence. It agreed that, although the expected cost of ongoing monitoring per patient may be lower than the model predicts, this would be counteracted to some degree because people who fail to attend scheduled scans may be more likely to experience complications that require reintervention. The committee also saw that the model conclusion did not change when assumptions were applied that were favourable to EVAR, but highly implausible, such as assuming monitoring appointments following EVAR incur no cost, or that no post-EVAR complications occur. It was therefore agreed that, while the effect of non-adherence to follow-up appointments on EVAR cost-effectiveness results is unclear, it cannot plausibly be sufficient to change conclusions drawn from the new economic model.

The committee discussed the use of the EVAR-1 trial to inform much of the new model, noting that a potential criticism of the model is its use of the relatively old evidence. The committee were not aware of any evidence to suggest that newer EVAR devices are superior to the generation of devices used in the EVAR-1 trial, in terms of perioperative mortality, long-term mortality, complication rates and secondary interventions (Hammond et al., 2016). The committee highlighted that more recent patient registries, such as the Medicare and SwedVasc databases, include data on patients who received newer-generation EVAR devices, and that the mortality and complications rates used in the new model are consistent with these data sources. The committee therefore agreed that, on balance, the value of the long-term data provided by the EVAR-1 trial offsets the relatively long time since trial recruitment, and more recent registry data serve to validate the model. The committee were aware that the National Vascular Registry data was preferred to inform some baseline model inputs as it is a UK registry, and that randomised trials were preferred to provide estimates of relative effectiveness as they would be subject to less bias than equivalent data from registries.

The committee discussed the QALY outcomes of the model, recognising that incremental QALYs were small in absolute terms, and the point estimate was more uncertain than for incremental costs. However, the unequivocal high incremental cost associated with EVAR led the committee to agree that the ‘true’ QALY gain for EVAR would need to be implausibly high for EVAR to be cost effective compared with open surgery (via, for example, superior long-term survival in EVAR patients, counter to the available long-term evidence). To achieve an ICER of £20,000 per QALY gained, EVAR would need to generate 0.317 QALYs more than open surgery per patient, compared with a base-case estimate of 0.160 QALYs *less* than open surgery. The committee were aware that modelled and empirical survival curves crossed over, with a longer-term survival benefit associated with open surgical repair offsetting its worse perioperative outcomes. The committee saw that the model suggests open surgical repair is increasingly cost-effective in younger patients, and agreed that this was consistent with its expectations, as younger people will typically be more likely to survive the open surgery procedure and experience the long-term survival benefit.

The committee discussed whether the cost-effectiveness results for EVAR might be influenced by a person’s underlying life expectancy. In particular, if it were possible to identify individuals who were less likely to live to experience the long-term survival benefit associated with open surgical repair, might EVAR be a cost-effective intervention for those people. A threshold analysis was conducted in which the hazard ratio used to calibrate general population survival to ‘match’ the EVAR-1 population was varied between 1 and 15. These values indicated a relatively healthy population with a mortality hazard equal to the general population of the same age, and a relatively unhealthy population with mortality hazard of 15-times the general population, respectively. Across this range of underlying life expectancies, EVAR remained dominated by open surgical repair.

The committee advised that patients often express a preference for EVAR compared with open surgical repair, typically due to the increased short-term risks associated with open surgery. However, the committee were not aware of any evidence formally eliciting patient preference over EVAR and open surgery. The committee heard that this preference was implicitly captured in the model to some extent by applying a larger quality of life decrement following open surgery, compared with EVAR, and by discounting health outcomes over time. The committee noted that, while individual choice is important in all care provided by the NHS, this did not compel them to recommend care that is not cost effective, as per Principle 5 of NICE’s Social Value Judgements. Given this, and based on its assessment of the evidence from the new economic model (and other published economic evaluations), the committee made strong recommendations that people with an unruptured infrarenal AAA for whom open surgical repair is a suitable option should be offered open surgical repair, and that EVAR should not be offered in such cases

The committee then considered the cost-effectiveness evidence for infrarenal AAA repair in people for whom open surgical repair is not a suitable option due anaesthetic risk and/or medical comorbidity. This evidence comprised 1 published, UK cost–utility analysis, and modelling conducted for this guideline. The committee were aware of the extensive trial crossover that occurred in EVAR-2, from the ‘no intervention’ control arm to EVAR, and that its per-protocol analysis breaks trial randomisation in a way that is likely to bias in favour of EVAR (as it can be expected that participants who ‘crossed over’ to receive EVAR were the fittest members of the cohort, with the longest life expectancy). The committee therefore placed greater emphasis on the economic model, which adjusted for crossover using a well-established statistical method (RPSFT). These data did not show any long-term survival benefit for EVAR compared with no intervention. The committee explained that many people with AAAs die with – rather than from – their aneurysms, and this would be particularly true in a population which is defined by the presence of comorbidities that are invariably life-limiting.

The committee advised that, since the population for which open surgical repair is unsuitable is defined by substantial anaesthetic risk and/or medical comorbidity, the most appropriate analysis uses calibrated general population life tables at 1999–2001 levels; not inflating the analysis to 2015–16 lifetables, which would reflect a general increase in the health of the UK population. The committee then discussed its preferred base-case ICER for EVAR, which exceeded £460,000 per QALY gained compared with ‘no intervention’, and agreed that this indicates EVAR for this population is not an effective use of NHS resources. The committee also understood that variation of parameters to extreme values – for example, assuming no survival differences beyond 5 years, and assuming there are no EVAR graft complications at any time – do not cause the ICER to fall to a level that would be considered to represent good value for money. To achieve an ICER of £20,000 per QALY gained in this population, compared with providing no intervention, EVAR would need to generate 0.772 incremental QALYs per patient, compared with a base case estimate of 0.033 QALYs.

The committee discussed whether the cost-effectiveness evidence suggested that there may be differences in the balance of benefits and harms between men and women, both when open surgical repair is a suitable option and when it is not, for the elective repair of unruptured infrarenal AAA. None of the preferred ICERs were sensitive to the sex of the cohort; nor were they sensitive to differences in age or AAA size. The committee therefore determined that there was no identifiable subgroup for whom EVAR represents a reasonable use of NHS resources, so its recommendations were appropriate to the relevant population as a whole.

Unruptured complex AAA

The committee discussed the cost-effectiveness evidence for the repair of unruptured complex AAA. The committee agreed that here the term ‘complex’ has a broad meaning, generally referring to non-standard AAA repairs. Typically, a complex AAA is one for which a standard EVAR device cannot be used within the terms of its instructions for use (IFU), and a complex device is one that is custom made, requiring bespoke adaptations, such as fenestrations and branches. As no published economic evidence was identified for this population, the committee considered only the new economic model.

The committee were aware that there is no randomised comparative evidence evaluating complex AAA repair, and consequently the economic model relies on a degree of assumption, particularly regarding the transferability of data on infrarenal AAA. The committee advised that once a person has survived to 30 days after their intervention, survival thereafter is expected to be relatively similar to people with repaired infrarenal AAA. On this basis, the use of data for infrarenal AAA to model long-term survival was agreed to be a reasonable approach. The committee were also aware that the bespoke nature of complex EVAR devices had implications for obtaining reliable unit costs. However, they were satisfied that an average cost obtained from 3 NHS Trusts was likely to adequately reflect a typical UK cost, significantly in excess of the cost of a standard EVAR device.

The committee reviewed the ICERs predicted by the new economic model for the repair of unruptured, complex AAA. The committee noted that EVAR was associated with more net QALYs than open surgery in this population, as it is predicted to have a larger perioperative survival benefit than in the infrarenal population, which means fewer patients are expected to survive to experience any long-term survival benefits of open surgery. The committee agreed that these results were plausible, though less certain than in the unruptured infrarenal population, because of the lack of directly applicable clinical evidence. However, they agreed that the magnitude of these uncertain benefits were unlikely to be sufficient to outweigh the unambiguous additional costs associated with complex EVAR compared with open surgical repair, as reflected in a base-case ICER of over £95,000 per QALY gained and a very small probability of the true figure being £20,000 or better. To achieve an ICER of £20,000 per QALY gained, complex EVAR would need to generate 0.797 QALYs more than open surgery per patient, compared with a base case estimate of 0.166 QALYs.

The committee discussed other assumptions applied in the model, such as the complication rates used. They agreed that complex AAA repairs are likely to be more susceptible to subsequent complications and reintervention than infrarenal aneurysm repairs. The committee noted that a scenario analysis had been included in the model that applied a complication rate double that of infrarenal repair, and that this has no material impact on cost-effectiveness results.

The committee advised that the 30-day mortality rate reported in the National Vascular Registry for open repair in this population (19.6%) is high compared with clinical experience, and that the estimate for EVAR (3.6%) is more representative of current practice. They agreed that anatomical complexity is less problematic for open repair, during which a surgeon can tailor the graft to suit the anatomy during the procedure, and that this is not typically possible with EVAR, for which custom devices are built in advance of the procedure. As such, the difference between the Registry's infrarenal and complex open surgical repair mortality rates (3.0% and 19.6%) was agreed to be too large. The committee advised that the Registry data, particularly for complex AAA repairs, are likely to be subject to substantial selection and reporting biases, with EVAR repairs reported to the Registry as complex cases likely to be inherently less complex than open repairs reported as complex. For example, AAAs with a short infrarenal 'neck' would be considered routine if addressed with open surgery, whereas the same anatomy would render a case 'complex' for EVAR, as it would be outside the terms of the devices' IFUs. In this way, the committee concluded that the model may be biased in favour of EVAR by using the Registry to source its baseline perioperative mortality data for complex AAA. The committee agreed that, due to the likely selection and reporting biases underlying the Registry data, a cost-effectiveness analysis using the reported complex repair perioperative mortality rates directly would not provide a meaningful comparison of EVAR and open surgical repair. Rather, the preferred approach was to take the EVAR Registry data as the baseline mortality rate – as it more closely reflects clinical experience than the open surgical repair value – and then apply a measure of relative effect to this, derived from RCT evidence, to estimate the mortality rate for open surgical repair.

The committee also considered the transferability of resource-use data for infrarenal AAA repair to complex cases. Based on clinical experience, they advised that a longer hospital stay is typically observed for all complex AAA patients compared with infrarenal AAA patients, but proportionally more so in complex EVAR patients. The committee agreed that reflecting this in the new model would reduce the incremental cost of hospital resources for open repair compared with EVAR, thereby increasing the ICER associated with EVAR beyond the base-case value of £95,815.

The committee was satisfied that the new model provides a reasonable prediction of the likely cost-effectiveness of EVAR in people with a complex unruptured AAA for whom surgical repair is a suitable option. However, they were cautious about the lack of directly applicable, randomised comparative evidence underlying the model, as this increased uncertainty regarding the true ICER for EVAR in this population, and the committee were also mindful that the model had plausibly demonstrated that the benefits of complex EVAR may outweigh its harms, albeit at a cost that was very unlikely to be justified by any gains. The committee therefore made a recommendation that the use of EVAR in this population should be limited to the context of an RCT (that should include resource-use in its data collection), to ensure that any use of EVAR in this population provides direct, comparative clinical effectiveness and cost-effectiveness evidence.

The committee then discussed complex AAA repair in people for whom open surgical repair is not a suitable option, due to concerns regarding anaesthetic risk and/or medical comorbidity. The committee agreed that outcomes associated with complex EVAR would certainly be no better than infrarenal EVAR, and would probably be worse, whereas outcomes in complex AAA patients who receive no intervention are not likely to be different to infrarenal AAA patients who receive no intervention. The committee were also aware that bespoke EVAR devices for complex repair are more expensive than standard EVAR devices for infrarenal repair, and that the ICER for infrarenal AAA repair in this population was £460,000 per QALY gained. The committee therefore agreed that complex EVAR will be more expensive than standard EVAR and will provide health outcomes that are at best equivalent and at worst substantially less favourable, meaning there is no possibility that EVAR could be cost effective in this population compared with a strategy of 'no intervention'. This result is clearer than in people with complex AAA for whom open surgery is a suitable option, where the base-case ICER for EVAR compared with open surgery was £95,000 (described above). In this population, it is feasible that EVAR may be more likely to be cost-effective than in infrarenal cases, because AAA complexity also worsens the expected outcomes from open surgery.

The committee were aware that there is no published cost-effectiveness evidence in this population, and so the only evidence was from the economic model developed by NICE. The base-case model found EVAR to be dominated by a strategy of 'no intervention', though the committee recognised that the analysis had necessarily been informed by some assumptions, such as generalising long-term survival data from the EVAR-2 population, and low-quality data, namely estimating a 'complexity effect' from the National Vascular Registry. The estimated EVAR perioperative mortality rate of 41% was felt to be higher than observed in clinical practice; therefore this analysis was deemed to be more speculative than the infrarenal AAA repair analyses conducted for this guideline. However, the unequivocal result of EVAR being dominated was seen to be supportive of the committee's view that complex EVAR cannot be cost effective in this population. The committee therefore made a strong recommendation against the use of EVAR in people with a complex unruptured AAA for whom surgical repair is not a suitable option.

The committee considered whether the cost-effectiveness evidence suggests there may be differences in the balance of benefits and harms between men and women, for the elective repair of unruptured complex AAA. None of the preferred ICERs from the modelling were sensitive to the sex of the cohort; nor were they sensitive to differences in age or AAA size. The committee therefore determined that there was no identifiable subgroup for whom complex EVAR represents a reasonable use of NHS resources, so its recommendations were appropriate to the relevant population as a whole.

Other factors the committee took into account

The committee noted that complex EVAR is a procedure-related term which encompasses a variety of different AAA anatomies, stent designs and surgical difficulties which have been grouped together.

The committee agreed it was not necessary to specify AAA symptomatology in the recommendations because it was considered that the evidence relating to asymptomatic aneurysms was transferrable to symptomatic aneurysm.

The committee discussed any potential differences between postoperative outcomes of EVAR between men and women. They agreed that, although the majority of the evidence presented was in men, there was no reason to believe that outcomes would differ in women. Therefore no recommendations were made specific to women.

Appendices

Appendix A – Review protocols

Review protocol for assessing the effectiveness of endovascular aneurysm repair compared with open surgical repair of unruptured abdominal aortic aneurysms

Review question 12	**The original question was:** **What is the effectiveness of EVAR compared to open repair surgery in reducing morbidity and mortality in people with unruptured abdominal aortic aneurysms?** **The committee agreed to retrospectively change the question to:** **What are the relative benefits and harms of EVAR, open surgical repair and non-surgical management in people with unruptured abdominal aortic aneurysms?**
Objectives	To assess the advantages and disadvantages of elective endovascular aneurysm repair in comparison with conventional open surgical repair for the treatment of unruptured abdominal aortic aneurysms To explore the subgroup effects of various patient characteristics, leading to more tailored recommendations
Type of review	Intervention
Language	English only
Study design	i) Systematic reviews of study designs listed below Randomised controlled trials Quasi-randomised controlled trials Non-randomised controlled trials for comparisons in people eligible for complex EVAR only Prospective cohort studies for comparisons in people eligible for complex EVAR only ii) Analysis of UK registry data (National Vascular Registry)

	Interventions		
	Standard (on-IFU) EVAR	Complex EVAR	
		Off-IFU use of standard EVAR	Other complex EVAR
Infrarenal	Systematic reviews RCTs Quasi-RCTs	Systematic reviews RCTs Quasi-RCTs Non-randomised controlled trials Prospective cohort studies UK registry data (National Vascular Registry)	Systematic reviews RCTs Quasi-RCTs Non-randomised controlled trials Prospective cohort studies UK registry data (National Vascular Registry)
Juxtarenal	Systematic reviews RCTs Quasi-RCTs	Systematic reviews RCTs Quasi-RCTs Non-randomised controlled trials	Systematic reviews RCTs Quasi-RCTs Non-randomised controlled trials

<table>
<tr><td>Review question 12</td><td>The original question was:
What is the effectiveness of EVAR compared to open repair surgery in reducing morbidity and mortality in people with unruptured abdominal aortic aneurysms?
The committee agreed to retrospectively change the question to:
What are the relative benefits and harms of EVAR, open surgical repair and non-surgical management in people with unruptured abdominal aortic aneurysms?</td></tr>
<tr><td></td><td><table>
<tr><td></td><td></td><td>Prospective cohort studies
UK registry data (National Vascular Registry)</td><td>Prospective cohort studies
UK registry data (National Vascular Registry)</td></tr>
<tr><td>Suprarenal / ‘type IV’</td><td>-</td><td>-</td><td>Systematic reviews
RCTs
Quasi-RCTs
Non-randomised controlled trials
Prospective cohort studies
UK registry data (National Vascular Registry)</td></tr>
</table></td></tr>
<tr><td>Status</td><td>Published papers only (full text)
No date restrictions</td></tr>
<tr><td>Population</td><td>People undergoing surgery for a confirmed unruptured abdominal aortic aneurysm
Subgroups: fitness for surgery, age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity), ethnicity</td></tr>
<tr><td>Intervention</td><td>Elective standard (on-IFU) EVAR for infrarenal and juxtarenal abdominal aortic aneurysms
Elective complex EVAR for infrarenal, juxtarenal and suprarenal abdominal aortic aneurysms, including:
fenestrated EVAR
EVAR with chimneys
EVAR with snorkels
branched grafts
‘CHIMPS’ (CHIMneys, Periscopes, Snorkels)
infrarenal devices used for juxtarenal AAA – that is, off-IFU use of standard devices
Open repair
Non-surgical intervention
Summary:
<table>
<tr><td></td><td>No surgery</td><td>Open repair</td><td>Standard (on-IFU) EVAR</td><td>Off-IFU use of standard EVAR</td><td>Other complex EVAR</td></tr>
<tr><td>Infrarenal</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>Iliac-branched only</td></tr>
<tr><td>Juxtarenal</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>Suprarenal / ‘type IV’</td><td>✓</td><td>✓</td><td>-</td><td>-</td><td>✓</td></tr>
</table></td></tr>
<tr><td>Comparator</td><td>Each other</td></tr>
</table>

Review question 12	**The original question was:** **What is the effectiveness of EVAR compared to open repair surgery in reducing morbidity and mortality in people with unruptured abdominal aortic aneurysms?** **The committee agreed to retrospectively change the question to:** **What are the relative benefits and harms of EVAR, open surgical repair and non-surgical management in people with unruptured abdominal aortic aneurysms?**
Outcomes	Mortality/survival Peri- and post-operative complications Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth Need for reintervention Quality of life Resource use, including length of hospital or intensive care stay, and costs
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published
Baseline characteristics to be extracted in evidence tables	Age Sex Size of aneurysm Comorbidities
Search strategies	See Appendix B
Review strategies	i i) Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. The update of Paravastu et al's 2014 Cochrane review (ongoing at the time of protocol development) comparing endovascular and open surgical repair of unruptured AAAs will be used as the RCT evidence base for infrarenal AAAs in people who are considered 'fit for surgery' 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. ii) Expert witnesses will attend a Committee meeting to answer questions from members of the Committee. They will be invited to present their evidence at a Committee meeting in the form of expert testimony based on a written paper. The Developer will write up the expert testimony and agree this with the witness after the meeting. i and ii) All key findings will be summarised in evidence statements.
Key papers	Sharath Chandra Paravastu, V, Rubaraj Jayarajasingam, Rachel Cottam, Simon J. Palfreyman, Jonathan A. Michaels, and Steven M. Thomas. Endovascular repair of abdominal aortic aneurysm. Cochrane Database of Systematic Reviews (1), 2014 – SYSTEMATIC REVIEW; included papers: • ACE • DREAM • EVAR 1 • EVAR 2 • OVER

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 question 12

Paravastu SC, Jayarajasingam R, Cottam R et al. (2014) Endovascular repair of abdominal aortic aneurysm. Cochrane Database Syst Rev;(1): CD004178. doi: 10.1002/14651858.CD004178.pub2.

Medline Strategy, searched 15th August 2017 **Database: Ovid MEDLINE(R) 1946 to August Week 1 2017** **Search Strategy:**	
1	Aortic Aneurysm, Abdominal/
2	(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.
3	(AAA or cAAA).tw.
4	or/1-3
5	exp Stents/

Medline Strategy, searched 15th August 2017 Database: Ovid MEDLINE(R) 1946 to August Week 1 2017 Search Strategy:
6 Vascular Surgical Procedures/ or Blood Vessel Prosthesis/ or Blood Vessel Prosthesis Implantation/ 7 (blood adj4 vessel* adj4 (transplant* or graft* or implant*)).tw. 8 (endovasc* or endostent* or endograft* or EVAR* or Palmaz or stent* or graft*).tw. 9 (endovascular* adj4 aneurysm* adj4 repair*).tw. 10 (endovascular* adj4 aort* adj4 repair*).tw. 11 or/5-10 12 4 and 11 13 Aortic Aneurysm, Abdominal/su [Surgery] 14 12 or 13 15 (complex or fenestrat* or branched or chimney* or snorkel* or periscope* or sandwich* or CHIMPS).tw. 16 14 and 15 17 (FEVAR or F-EVAR or BEVAR or B-EVAR or BREVAR or BR-EVAR or CHEVAR or CH-EVAR or Co-EVAR or CoEVAR or Co-FEVAR or CoFEVAR).tw. 18 (complex adj4 EVAR*).tw. 19 17 or 18 20 16 or 19 21 animals/ not humans/ 22 20 not 21 23 limit 22 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

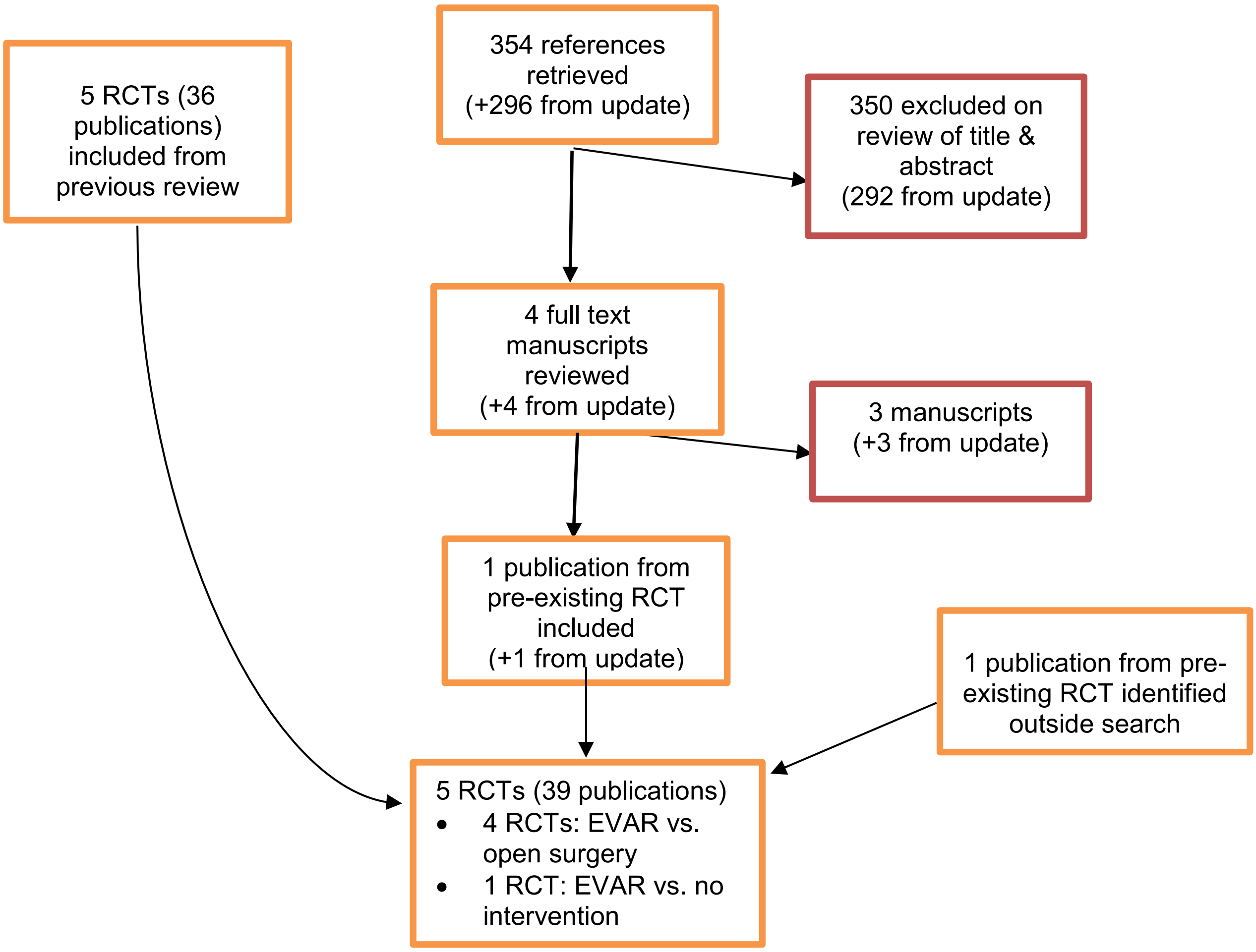
Medline Strategy
Economic evaluations 1 Economics/ 2 exp "Costs and Cost Analysis"/ 3 Economics, Dental/ 4 exp Economics, Hospital/ 5 exp Economics, Medical/

Medline Strategy
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. 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.

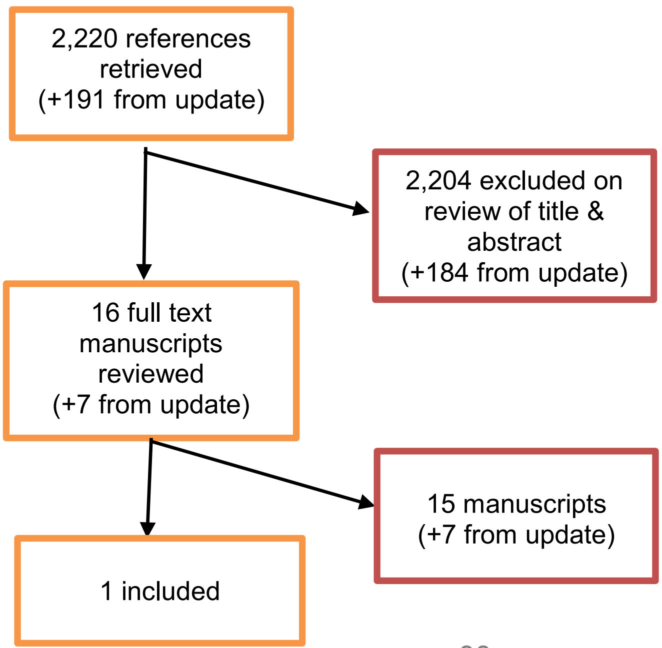
Medline Strategy	
23	quality of wellbeing.tw.
24	quality of well-being.tw.
25	qwb.tw.
26	willingness to pay.tw.
27	standard gamble*.tw.
28	time trade off.tw.
29	time tradeoff.tw.
30	tto.tw.
31	or/1-30

Appendix C – Clinical evidence study selection

Cochrane systematic review update search



Complex EVAR versus open surgery study selection



Appendix D – Clinical evidence tables

Standard EVAR compared with open surgical repair of simple AAA

Full citation	**Paravastu SC, Jayarajasingam R, Cottam R et al. (2014) Endovascular repair of abdominal aortic aneurysm. Cochrane Database Syst Rev;(1): CD004178. doi: 10.1002/14651858.CD004178.pub2.**
Study details	Study type: systematic review Location: UK Aim: to assess the effectiveness of EVAR versus conventional open surgical repair in individuals with AAA considered fit for surgery, and EVAR versus best medical care in those considered unfit for surgery, and EVAR versus best medical care for those considered unfit for surgery Study dates: literature searched for publications up to January 2013 Follow-up: 30 days, up to 4 years, and up to 8 years Sources of funding: this study was supported by funding from the UK National Institute of Health Research (NIHR)
Participants	Population: patients with unruptured AAA, diagnosed by ultrasound or computed tomography, in whom surgical treatment was indicated Sample size: 4 RCTs including 2,745 participants Inclusion criteria: RCTs comparing EVAR with open surgical repair in individuals with unruptured AAAs that were considered fit for surgery Exclusion criteria: studies with inadequate data or studies that used an inadequate randomisation technique (not specified). Additionally, studies assessing complex and hybrid endovascular techniques (including fenestrated EVAR) were excluded.
Methods	Literature searches were performed on the Cochrane Central Register of Controlled trials and the Cochrane Vascular Specialised Register (constructed from weekly electronic searches of MEDLINE, Embase, CINAHL, and AMED databases. Additional searches were also performed on the World Health Organisation International Clinical Trials Registry, ClinicalTrials.gov website and the ISRCTN register. Bibliographies of included studies were reviewed to identify any additional studies that were relevant to the review question. Two independent reviewers were involved in study selection, data extraction, and risk of bias assessments. Any disagreements were resolved through discussion.
Intervention	EVAR using any type of endovascular device

Full citation	Paravastu SC, Jayarajasingam R, Cottam R et al. (2014) Endovascular repair of abdominal aortic aneurysm. Cochrane Database Syst Rev;(1): CD004178. doi: 10.1002/14651858.CD004178.pub2.
Comparison	Open surgical repair (for people in whom surgery was considered suitable), or best medical care (for people in whom surgery was not considered suitable)
Outcomes measures	All-cause mortality, aneurysm-related mortality, endograft-related complications, major complications, minor complications, and quality of life. Assessed at the following time points: 30 days, up to 4 years up to 8 years.
Study Appraisal using AMSTAR (Assessing the Methodological Quality of Systematic Reviews)	1. Was an 'a priori' design provided? Yes 2. Was there duplicate study selection and data extraction? Yes 3. Was a comprehensive literature search performed? Yes 4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? Yes 5. Was a list of studies (included and excluded) provided? Yes 6. Were the characteristics of the included studies provided? Yes 7. Was the scientific quality of the included studies assessed and documented? Yes 8. Was the scientific quality of the included studies used appropriately in formulating conclusions? Yes 9. Were the methods used to combine the findings of studies appropriate? Yes 10. Was the likelihood of publication bias assessed? Yes 11. Was the conflict of interest included? Yes Overall risk of bias: Low Directness: directly applicable

Studies included in the systematic review by Paravastu et al.

Full citation	ACE trial (results reported in multiple publications outlined in the Cochrane systematic review)
Study details	Study type: multicentre, non-blinded, randomised controlled trial Location: France Aim: to assess the results of EVAR and of open surgery in relatively good-risk patients presenting with an asymptomatic abdominal aortic or aorto-iliac aneurysm Study dates: 2003 to 2008 Follow-up: up to 4 years Sources of funding: not reported
Participants	Population: patients with asymptomatic unruptured abdominal aortic or aorto-iliac aneurysm Sample size: 299; 99% male Inclusion criteria: men with AAA >5 cm in men and women with AAA >4.5 cm were included. Furthermore patients with common iliac artery aneurysms >3.0 cm, an aneurysm upper neck free of major thrombus or calcification, ≥1.5 cm length and angle between the neck, the axis of the aneurysm <60° and iliac arteries compatible with the introducer sheath were included Exclusion criteria: previous AAA surgery, a ruptured aneurysm, a mycotic aneurysm, severe iodine allergy and life expectancy <6 months, or patients graded as category 3 using the SVS/AAVS classification system Baseline characteristics: Mean age: EVAR group, 68.9 years; Open surgery group, 70.0 years Sex: EVAR group, 100% male; Open surgery group, 98% male Mean aneurysm diameter: EVAR group, 55.2 mm; Open surgery group, 55.6 mm Diabetes: EVAR group, 13.3%; Open surgery group, 19.5% Hypertension: EVAR group, 66.0%; Open surgery group, 63.8% Hyperlipidaemia: EVAR group, 68.7%; Open surgery group, 65.8% Carotid artery disease: EVAR group, 8.0%; Open surgery group, 8.1% Renal insufficiency: EVAR group, 14.0%; Open surgery group, 10.1% Pulmonary disease: EVAR group, 19.3%; Open surgery group, 28.2%
Intervention	EVAR
Comparison	Open surgical repair
Outcomes measures	All-cause mortality, major adverse events (myocardial infarction, permanent stroke, permanent haemodialysis, major amputation, paraplegia and bowel infarction), vascular reinterventions and minor complications

Full citation	ACE trial (results reported in multiple publications outlined in the Cochrane systematic review)
Risk of bias assessment (from the Cochrane review)	1. Random sequence generation (selection bias): Low risk – A clinical research unit performed randomisation by centre 2. Allocation concealment (selection bias): Low risk – Treatment allocation was notified less than 24 hours to the investigator 3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured 4. Blinding of outcome assessment (detection bias): Unclear – It is unclear whether assessors were blinded 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**DREAM trial (results reported in multiple publications outlined in the Cochrane systematic review)** **NB: a new publication was identified from update searches** **van Schaik T G, Yeung KK, Verhagen HJ et al. (2017) Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. European Journal of Vascular and Endovascular Surgery 54 (5), 671**
Study details	Study type: multicentre, non-blinded, randomised controlled trial Location: Netherlands Aim: to assess the differences in results of conservative EVAR and open surgical treatment of unruptured AAA Study dates: 2000 to 2003 Follow-up: up to 15 years Sources of funding: the trial was funded by a grant from the Netherlands National Health Insurance Council.
Participants	Population: patients with unruptured AAA Sample size: 351; 91% male Inclusion criteria: men with AAA >5 cm in men and women with AAA >4.5 cm were included. Furthermore patients with common iliac artery aneurysms >3.0 cm, an aneurysm upper neck free of major thrombus or calcification, ≥1.5 cm length and angle between the neck, the axis of the aneurysm <60° and iliac arteries compatible with the introducer sheath were included Exclusion criteria: a ruptured aneurysm, a mycotic aneurysm, presence of anatomical variations, connective tissue disease, history of organ transplant, or life expectancy <2 years Baseline characteristics: Mean age: EVAR group, 70.7 years; Open surgery group, 69.6 years Sex: EVAR group, 93% male; Open surgery group, 90% male Mean aneurysm diameter: not reported Comorbidities: not reported
Intervention	EVAR
Comparison	Open surgical repair
Outcomes measures	All-cause mortality, aneurysm-related mortality, complications and reintervention rates
Risk of bias assessment (from	1. Random sequence generation (selection bias): Low risk – Randomisation was performed centrally with the use of a computer-generated permuted block sequence and stratified according to study centre in blocks of 4 patients 2. Allocation concealment (selection bias): Low risk – Allocation concealment was performed appropriately

Full citation	**DREAM trial (results reported in multiple publications outlined in the Cochrane systematic review)** **NB: a new publication was identified from update searches** **van Schaik T G, Yeung KK, Verhagen HJ et al. (2017) Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. European Journal of Vascular and Endovascular Surgery 54 (5), 671**
the Cochrane review)	3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured 4. Blinding of outcome assessment (detection bias): Low risk – Outcome assessors were blinded to group allocations 5. Incomplete outcome data (attrition bias): Low risk – Analysis was performed using an intention-to-treat basis 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**EVAR1 trial (results reported in multiple publications outlined in the Cochrane systematic review)** **NB: a new publication was identified from update searches** **Patel R, Sweeting MJ, Powell JT et al. (2016) Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repairtrial 1 (EVAR trial 1): a randomised controlled trial. Lancet. 388(10058):2366-2374.**
Study details	Study type: multicentre, non-blinded, randomised controlled trial Location: UK Aim: to assess the efficacy of EVAR in the treatment of AAA in terms of mortality, quality of life, durability and cost-effectiveness Study dates: 1999 to 2004 Follow-up: up to 15 years Sources of funding: the trial was funded by the National Health Service Research and Development Health Technology Assessment Programme
Participants	Population: patients with unruptured AAA Sample size: 1,252; 91% male Inclusion criteria: patients ≥60 years with AAA ≥5.5 cm in diameter were included Exclusion criteria: contraindications for surgery Baseline characteristics: Mean age: EVAR group, 74.1 years; Open surgery group, 74.0 years Sex: EVAR group, 90.3% male; Open surgery group, 90.1% male Mean aneurysm diameter: EVAR group, 64.0 mm; Open surgery group, 65.0 mm Diabetes: EVAR group, 9.8%; Open surgery group, 11.0% Cardiac disease: EVAR group, 41.8%; Open surgery group, 43.0%
Intervention	EVAR
Comparison	Open surgical repair
Outcomes measures	All-cause mortality, aneurysm-related mortality, complications and reintervention rates
Risk of bias assessment	1. Random sequence generation (selection bias): Low risk – Participants were randomised to groups on a 1:1 basis using randomly permuted block sizes constructed using STATA. Randomisation is stratified by centre and was performed centrally. 2. Allocation concealment (selection bias): Low risk – Allocation was performed only after all baseline data were recorded

Full citation	EVAR1 trial (results reported in multiple publications outlined in the Cochrane systematic review) NB: a new publication was identified from update searches Patel R, Sweeting MJ, Powell JT et al. (2016) Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repairtrial 1 (EVAR trial 1): a randomised controlled trial. Lancet. 388(10058):2366-2374.
	3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured 4. Blinding of outcome assessment (detection bias): Unclear – It is unclear whether assessors were blinded 5. Incomplete outcome data (attrition bias): Low risk – Analysis was performed using an intention-to-treat basis and all participants were accounted for 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	OVER trial (results reported in multiple publications outlined in the Cochrane systematic review)
Study details	Study type: multicentre, non-blinded, randomised controlled trial Location: USA Aim: to compare postoperative outcomes after EVAR and open repair Study dates: 2002 to 2008 Follow-up: 8 years Sources of funding: this study was supported by the United States' Cooperative Studies Program of the Department of Veterans Affairs Office of Research and Development
Participants	Population: patients with unruptured AAA Sample size: 881; 99% male Inclusion criteria: patients with AAA ≥5 cm, an iliac aneurysm (associated with an AAA) ≥3 cm, an AAA ≥4.5 cm which had increased in size by ≥0.7 cm in 6 months, an AAA ≥4.5 cm which had increased in size by ≥1 cm in 12 months, an AAA ≥4.5 cm that was considered saccular (a portion of the circumference of the aorta at the level of the aneurysm is considered normal) or an AAA ≥4.5 cm that was associated with distal embolism were included Exclusion criteria: previous AAA repair, a ruptured aneurysm or likelihood of poor compliance to the study protocol Baseline characteristics: Mean age: EVAR group, 69.6 years; Open surgery group, 70.5 years Sex: EVAR group, 99.3% male; Open surgery group, 99.5% male Mean aneurysm diameter: EVAR group, 57.0mm; Open surgery group, 57.0 mm Coronary artery disease: EVAR group, 39.2%; Open surgery group, 42.3% Myocardial infarction: EVAR group, 23.6%; Open surgery group, 25.2% Coronary revascularization: EVAR group, 35.8%; Open surgery group, 35.0% Cerebrovascular disease: EVAR group, 15.1%; Open surgery group, 16.0% Hypertension: EVAR group, 78.2%; Open surgery group, 75.5% Claudication: EVAR group, 14.9%; Open surgery group, 18.5% Diabetes: EVAR group, 22.5%; Open surgery group, 22.9% COPD: EVAR group, 28.4%; Open surgery group, 30.4%
Intervention	EVAR
Comparison	Open surgical repair

Full citation	OVER trial (results reported in multiple publications outlined in the Cochrane systematic review)
Outcomes measures	All-cause mortality, aneurysm-related mortality, complications and reintervention rates
Risk of bias assessment	1. Random sequence generation (selection bias): Low risk – Randomisation was performed by 'permuted block design' 2. Allocation concealment (selection bias): Low risk – Allocation was performed only after all baseline data were recorded 3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured 4. Blinding of outcome assessment (detection bias): Low risk – Outcomes were adjudicated by a blinded outcomes assessment committee 5. Incomplete outcome data (attrition bias): Low risk – Analysis was performed using an intention-to-treat basis and all participants were accounted for 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Complex EVAR compared with open surgical repair of juxtarenal aneurysms

Full citation	**Donas Konstantinos P, Eisenack Markus, Panuccio Giuseppe, Austermann Martin, Osada Nani, and Torsello Giovanni (2012) The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 56, 285-90**
Study details	Study type: non-randomised comparative study Location: Germany Aim: to compare endovascular techniques (fenestrated and chimney approaches) for treating juxtarenal AAAs with open surgical repair Study dates: January 2008 to December 2010 Follow-up: mean of 15.2 months Sources of funding: self-funded study performed at a University hospital
Participants	Population: patients with primary degenerative juxtarenal AAAs defined as complex AAAs with a short infrarenal necks (<9 mm) or aneurysmal extension to the inter-renal aorta Sample size: 90; 92% male Inclusion criteria: patients less than 68 years who were considered physiologically fit were included in the open repair group. Another indication for open repair was the coexistence of accessory polar renal arteries with evidence of significant kidney perfusion. Patients considered high-risk for open repair due to the presence of more than 3 cardiovascular comorbidities were included in the fenestrated-EVAR (f-EVAR) or chimney-EVAR (c-EVAR) groups. Patients that met the following criteria were included in the c-EVAR group: symptomatic aneurysms, aneurysms that displayed rapid eccentric growth (greater than 0.5 cm per year), aneurysms that had at least a 15 mm distance between the target vessel for chimney grafts and the upper aortic branch, a patent left subclavian artery, absence of severe kinking of the descending aorta, extensive thrombus in the aortic arch and juxtarenal segment, aneurysms with involvement of less than 2 aortic side branches. Any patients that did not meet criteria for inclusion in the c-EVAR group were assigned to the f-EVAR group. Exclusion criteria: Patients with persistent type I endoleaks after conventional EVAR, proximal para-anastomotic pseudoaneurysms after open repair, or ruptured, mycotic, or inflammatory juxtarenal AAAs were excluded Baseline characteristics: Mean age: c-EVAR group, 74.5; f-EVAR group, 73.7 years; Open surgery group, 71.2 years Sex: c-EVAR group, 90% male; f-EVAR group, 100% male; Open surgery group, 87.1% male Mean aneurysm diameter: c-EVAR group, 62.0 mm; f-EVAR group, 65.0 mm; Open surgery group, 60.0 mm Cardiac comorbidities: c-EVAR group, 73.3%; f-EVAR group, 82.3%; Open surgery group, 29.0% Renal comorbidities: c-EVAR group, 23.3%; f-EVAR group, 17.2%; Open surgery group, 6.5%

Full citation	**Donas Konstantinos P, Eisenack Markus, Panuccio Giuseppe, Austermann Martin, Osada Nani, and Torsello Giovanni (2012) The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 56, 285-90**
	Respiratory comorbidities: c-EVAR group, 33.3%; f-EVAR group, 37.9%; Open surgery group, 19.3% Previous aortic intervention: c-EVAR group, 36.6%; f-EVAR group, 27.6%; Open surgery group, 6.5% Previous myocardial infarction: c-EVAR group, 30%; f-EVAR group, 24.1%; Open surgery group, 0%
Intervention	c-EVAR, f-EVAR
Comparison	Open surgical repair
Outcomes measures	30-day mortality, deterioration of renal function, blood loss, transfusion requirements, the need for re-intervention, length of stay,
Risk of bias assessment (using ROBINS-I tool)	1. Is there potential for confounding of the effect of intervention in this study? No 2. Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? Patients were selected for different surgical interventions according to characteristics indicative of operative difficulty or fitness for surgery. 3. Do start of follow-up and start of intervention coincide for most participants? Yes 4. Were intervention groups clearly defined? Yes 5. Was the information used to define intervention groups recorded at the start of the intervention? Yes 6. Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome? No 7. Were there deviations from the intended intervention beyond what would be expected in usual practice? No 8. Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome? 9. Were important co-interventions balanced across intervention groups? Unclear 10. Was the intervention implemented successfully for most participants? Yes 11. Did study participants adhere to the assigned intervention regimen? Yes 12. Were outcome data available for all, or nearly all, participants? Yes 13. Were participants excluded due to missing data on intervention status? No 14. Were participants excluded due to missing data on other variables needed for the analysis? No 15. Could the outcome measure have been influenced by knowledge of the intervention received? No – objective outcome measures were assessed

Full citation	Donas Konstantinos P, Eisenack Markus, Panuccio Giuseppe, Austermann Martin, Osada Nani, and Torsello Giovanni (2012) The role of open and endovascular treatment with fenestrated and chimney endografts for patients with juxtarenal aortic aneurysms. Journal of vascular surgery 56, 285-90
	16. Were outcome assessors aware of the intervention received by study participants? Yes – it was not possible to blind outcome assessors; however, this is unlikely to affect study results 17. Were the methods of outcome assessment comparable across intervention groups? Yes 18. Were any systematic errors in measurement of the outcome related to intervention received? No 19. Is the reported effect estimate likely to be selected, on the basis of the results, from multiple outcome measurements within multiple outcome measurements within the outcome domain? No Overall risk of bias: moderate Directness: directly applicable

EVAR vs no intervention for patients in whom open surgery is not considered appropriate

Full citation	**EVAR 2 trial (results reported in multiple publications outlined in the Cochrane systematic review)** **NB: a new publication was identified from update searches** **Sweeting M J, Patel R, Powell J T, and Greenhalgh R M (2017) Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair: Very Long-term Follow-up in the EVAR-2 Randomized Controlled Trial. Annals of Surgery. 24**
Study details	Study type: multicentre, non-blinded, randomised controlled trial Location: UK Aim: compare long-term total and aneurysm-related mortality in physically frail patients with AAA who were randomised to either early EVAR or no intervention Study dates: patients were recruited from September 1999 to August 2004 Follow-up: mean of 12 years Sources of funding: this study was funded by the National Institute for Health Research Health Technology Assessment programme
Participants	Population: patients with large aneurysms in whom open surgical repair was considered inappropriate Sample size: 404; sex-specific proportions were not reported

Full citation	EVAR 2 trial (results reported in multiple publications outlined in the Cochrane systematic review) NB: a new publication was identified from update searches Sweeting M J, Patel R, Powell J T, and Greenhalgh R M (2017) Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair: Very Long-term Follow-up in the EVAR-2 Randomized Controlled Trial. Annals of Surgery. 24
	Inclusion criteria: patients over 60 years old with AAAs at least 5.5 cm in diameter (confirmed by computed tomography) who were considered physically ineligible for open repair, and anatomically suitable for EVAR, were included. The appropriateness of surgery was determined locally by the treating surgeon, radiologist, anaesthetist and cardiologist. Exclusion criteria: not reported Baseline characteristics: Mean age: EVAR group, 77.2 years; No repair group, 76.4 years Sex: EVAR group, 85.3% male; No repair group, 86.5% male Mean aneurysm diameter: EVAR group, 68.0 mm; No repair group, 67.0 mm Diabetes: EVAR group, 15.4%; No repair group, 14.1% History of cardiac disease: EVAR group, 67.0%; No repair group, 73.9%
Intervention	EVAR
Comparison	No intervention
Outcomes measures	All-cause mortality, aneurysm-related mortality, graft-related complications and graft-related re-interventions.
Risk of bias assessment (using Cochrane)	1. Random sequence generation (selection bias): Low risk – Randomisation was performed appropriately, using randomly permuted block sizes. 2. Allocation concealment (selection bias): Low risk – Allocation was done only after all baseline data were recorded 3. Blinding of participants and personnel (performance bias): Unclear – Due to the nature of the interventions, it was not possible to blind participants and personnel 4. Blinding of outcome assessment (detection bias): Unclear risk – insufficient information was available 5. Incomplete outcome data (attrition bias): Low risk – reasonable rates of loss to follow-up, and reasons for losses were explained 6. Selective reporting (reporting bias): Low risk – Study reported on all predefined outcomes 7. Other bias: High risk – there was a considerably high rate of crossover between groups: 33.8% (70/207) patients in the no intervention were ended up being treated by EVAR during the trial. Authors analysed 4- and 8-year follow-up data using a intention-to-treat approach, which would not have taken crossover into account.

Full citation	**EVAR 2 trial (results reported in multiple publications outlined in the Cochrane systematic review)** **NB: a new publication was identified from update searches** **Sweeting M J, Patel R, Powell J T, and Greenhalgh R M (2017) Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair: Very Long-term Follow-up in the EVAR-2 Randomized Controlled Trial. Annals of Surgery. 24**
	Overall risk of bias: high risk for analyses performed at 4-and 8-year follow-up; low risk for analyses performed at 12-year follow-up because appropriate measures were taken to minimise bias due to crossover. Directness: directly applicable

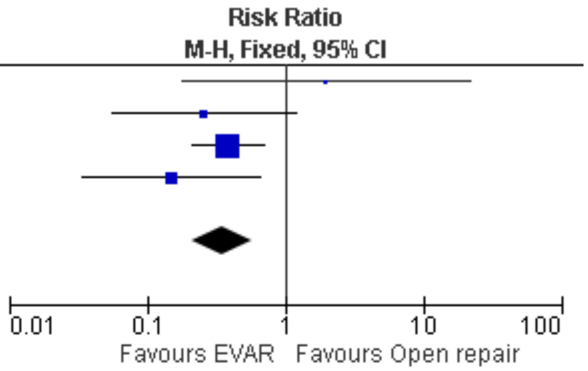
Appendix E – Forest plots

EVAR compared with open surgery for patients in whom open surgery is considered appropriate

Short-term all-cause mortality (30-day and in-hospital)

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ACE (1)	2	150	1	149	1.7%	1.99 [0.18, 21.68]
DREAM (2)	2	173	8	178	13.6%	0.26 [0.06, 1.19]
EVAR1 (3)	14	626	36	626	62.1%	0.39 [0.21, 0.71]
OVER	2	444	13	437	22.6%	0.15 [0.03, 0.67]
Total (95% CI)		**1393**		**1390**	**100.0%**	**0.34 [0.21, 0.57]**
Total events	20		58			

Heterogeneity: $Chi^2 = 3.54$, $df = 3$ ($P = 0.32$); $I^2 = 15\%$
Test for overall effect: $Z = 4.16$ ($P < 0.0001$)

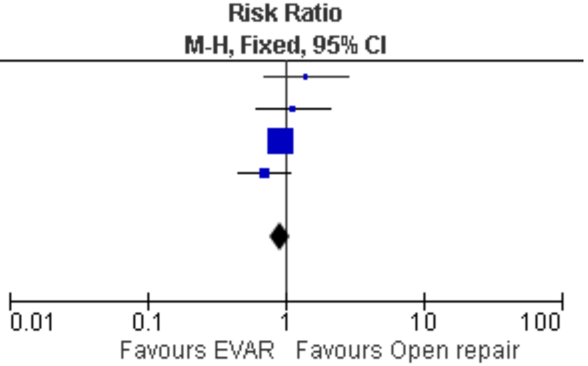


Footnotes
(1) One patient in OSR did not undergo surgery
(2) 2 in EVAR and 4 in OSR did not undergo surgery
(3) Of the 626 patients in each group, 12 in EVAR died prior to repair and 19 in OSR died before surgery and 5 refused surgery

All-cause mortality up to 4 years

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACE	17	150	12	149	5.1%	1.41 [0.70, 2.84]
DREAM	20	173	18	178	7.5%	1.14 [0.63, 2.09]
EVAR1 (1)	153	626	164	626	69.2%	0.93 [0.77, 1.13]
OVER	31	444	43	437	18.3%	0.71 [0.46, 1.10]
Total (95% CI)		**1393**		**1390**	**100.0%**	**0.93 [0.79, 1.10]**
Total events	221		237			

Heterogeneity: Chi² = 3.22, df = 3 (P = 0.36); I² = 7%
Test for overall effect: Z = 0.84 (P = 0.40)

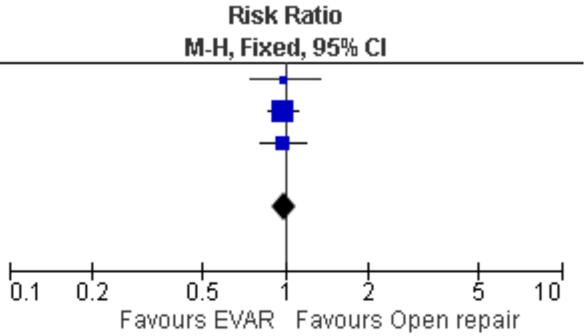


Footnotes
(1) Patients who died prior to intervention were included (Intention to treat analysis)

All-cause mortality up to 8 years

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI
DREAM	58	173	60	178	12.6%	0.99 [0.74, 1.33]
EVAR1	260	626	264	626	56.1%	0.98 [0.86, 1.12]
OVER	146	444	146	437	31.3%	0.98 [0.82, 1.19]
Total (95% CI)		**1243**		**1241**	**100.0%**	**0.99 [0.89, 1.09]**
Total events	464		470			

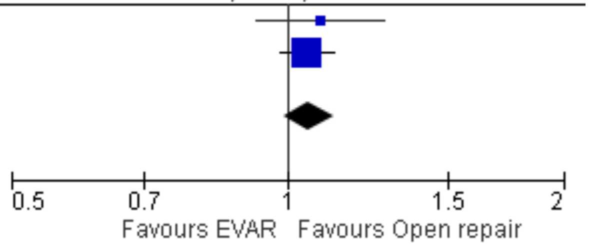
Heterogeneity: Chi² = 0.00, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.28 (P = 0.78)



All-cause mortality up to 15 years

	EVAR		Open repair			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**	**M-H, Fixed, 95% CI**
DREAM	113	173	107	178	19.2%	1.09 [0.92, 1.28]	
EVAR1 (1)	466	626	444	626	80.8%	1.05 [0.98, 1.12]	
Total (95% CI)		**799**		**804**	**100.0%**	**1.06 [0.99, 1.13]**	
Total events	579		551				

Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.71 (P = 0.09)

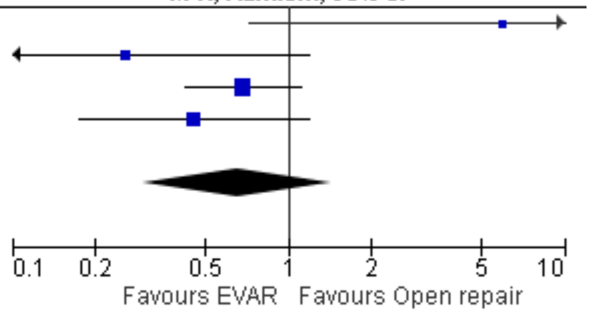


Footnotes
(1) Patients who died prior to intervention were included (Intention to treat analysis)

AAA-related mortality up to 4 years

	EVAR		Open repair			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**M-H, Random, 95% CI**
ACE	6	150	1	149	10.9%	5.96 [0.73, 48.91]	
DREAM	2	173	8	178	17.3%	0.26 [0.06, 1.19]	
EVAR1	26	626	38	626	42.8%	0.68 [0.42, 1.11]	
OVER	6	444	13	437	29.0%	0.45 [0.17, 1.18]	
Total (95% CI)		**1393**		**1390**	**100.0%**	**0.65 [0.30, 1.42]**	
Total events	40		60				

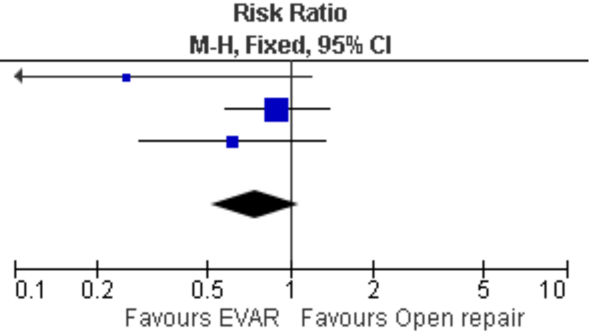
Heterogeneity: Tau² = 0.31; Chi² = 6.26, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 1.08 (P = 0.28)



AAA-related mortality up to 8 years

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
DREAM	2	173	8	178	12.3%	0.26 [0.06, 1.19]
EVAR1	36	626	40	626	62.5%	0.90 [0.58, 1.39]
OVER	10	444	16	437	25.2%	0.62 [0.28, 1.34]
Total (95% CI)		**1243**		**1241**	**100.0%**	**0.75 [0.52, 1.08]**
Total events	48		64			

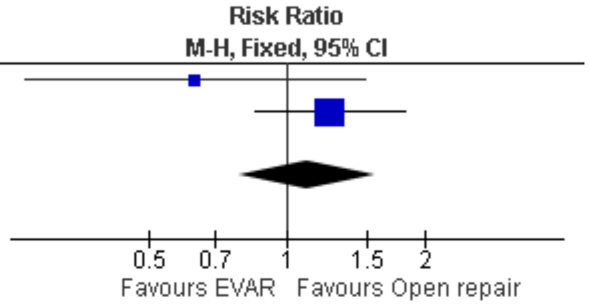
Heterogeneity: Chi² = 2.79, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 1.55 (P = 0.12)



AAA-related mortality up to 15 years

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
DREAM	8	173	13	178	22.2%	0.63 [0.27, 1.49]
EVAR1 (1)	56	626	45	626	77.8%	1.24 [0.85, 1.81]
Total (95% CI)		**799**		**804**	**100.0%**	**1.11 [0.79, 1.56]**
Total events	64		58			

Heterogeneity: Chi² = 2.01, df = 1 (P = 0.16); I² = 50%
Test for overall effect: Z = 0.59 (P = 0.55)

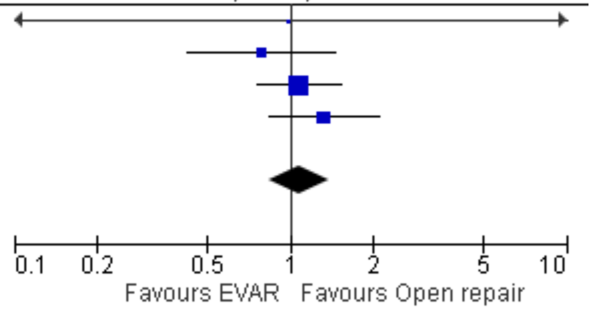


Footnotes
(1) Patients who died prior to intervention were included (Intention to treat analysis)

Cardiac-related mortality (follow-up not specified)

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACE	1	150	1	149	0.9%	0.99 [0.06, 15.73]
DREAM	16	173	21	178	19.5%	0.78 [0.42, 1.45]
EVAR1	59	626	55	626	51.9%	1.07 [0.76, 1.52]
OVER	39	444	29	437	27.6%	1.32 [0.83, 2.10]
Total (95% CI)		**1393**		**1390**	**100.0%**	**1.08 [0.84, 1.40]**
Total events	115		106			
Heterogeneity: Chi² = 1.79, df = 3 (P = 0.62); I² = 0%						
Test for overall effect: Z = 0.63 (P = 0.53)						

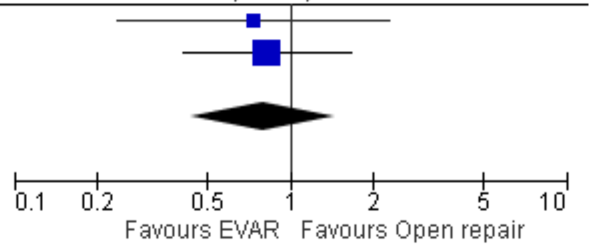
Risk Ratio
M-H, Fixed, 95% CI



Stroke-related mortality (follow-up not specified)

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI
DREAM	5	173	7	178	28.9%	0.73 [0.24, 2.27]
EVAR1	14	626	17	626	71.1%	0.82 [0.41, 1.66]
Total (95% CI)		**799**		**804**	**100.0%**	**0.80 [0.44, 1.44]**
Total events	19		24			
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						

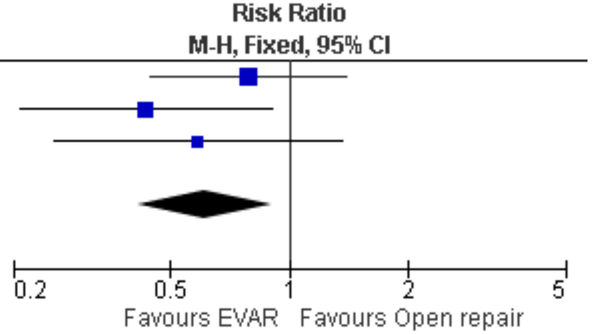
Risk Ratio
M-H, Fixed, 95% CI



Pulmonary-related mortality (follow-up not specified)

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
OVER	20	444	25	437	40.6%	0.79 [0.44, 1.40]	
EVAR1	10	626	23	626	37.1%	0.43 [0.21, 0.91]	
DREAM	8	173	14	178	22.3%	0.59 [0.25, 1.37]	
Total (95% CI)		**1243**		**1241**	**100.0%**	**0.61 [0.41, 0.91]**	
Total events	38		62				

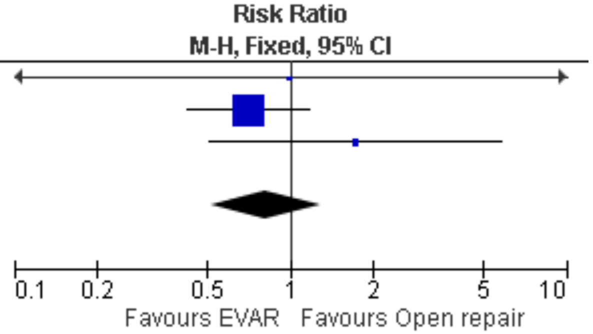
Heterogeneity: Chi² = 1.58, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 2.43 (P = 0.01)



Non-fatal stroke (follow-up not specified)

Study or Subgroup	EVAR Events	EVAR Total	Open repair Events	Open repair Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ACE	1	150	1	149	2.6%	0.99 [0.06, 15.73]
EVAR1	24	626	34	626	87.1%	0.71 [0.42, 1.18]
OVER	7	444	4	437	10.3%	1.72 [0.51, 5.84]
Total (95% CI)		**1220**		**1212**	**100.0%**	**0.82 [0.52, 1.29]**
Total events	32		39			

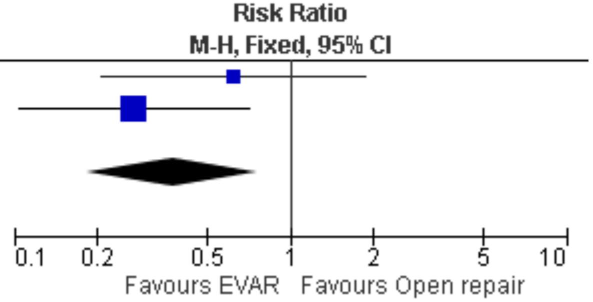
Heterogeneity: Chi² = 1.77, df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.86 (P = 0.39)



Pulmonary complications (follow-up not specified)

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ACE	5	150	8	149	30.0%	0.62 [0.21, 1.85]
DREAM	5	173	19	178	70.0%	0.27 [0.10, 0.71]
Total (95% CI)		**323**		**327**	**100.0%**	**0.38 [0.18, 0.76]**
Total events	10		27			

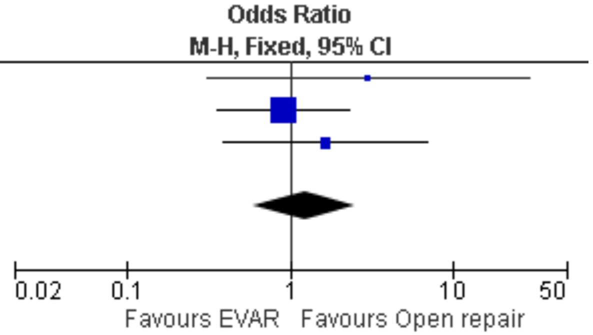
Heterogeneity: Chi² = 1.25, df = 1 (P = 0.26); I² = 20%
Test for overall effect: Z = 2.70 (P = 0.007)



Renal complications (follow-up not specified)

	EVAR		Open repair			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
ACE	3	150	1	149	7.4%	3.02 [0.31, 29.37]
EVAR1 (1)	9	509	9	463	70.0%	0.91 [0.36, 2.31]
OVER	5	444	3	437	22.6%	1.65 [0.39, 6.94]
Total (95% CI)		**1103**		**1049**	**100.0%**	**1.23 [0.60, 2.55]**
Total events	17		13			

Heterogeneity: Chi² = 1.17, df = 2 (P = 0.56); I² = 0%
Test for overall effect: Z = 0.56 (P = 0.57)



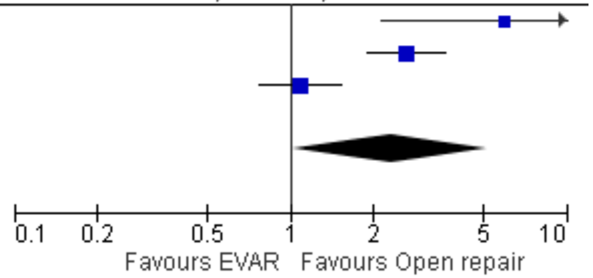
Footnotes
(1) Renal failure was assessed based on annual GFR, hence only patients with minimum of one-year follow up were included.

Need for reintervention up to 4 years

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
ACE	24	150	4	149	24.3%	5.96 [2.12, 16.76]
EVAR1	121	626	46	626	38.0%	2.63 [1.91, 3.63]
OVER	61	444	55	437	37.7%	1.09 [0.78, 1.53]
Total (95% CI)		**1220**		**1212**	**100.0%**	**2.30 [1.03, 5.18]**
Total events	206		105			

Heterogeneity: Tau² = 0.42; Chi² = 19.03, df = 2 (P < 0.0001); I² = 89%
Test for overall effect: Z = 2.02 (P = 0.04)

Risk Ratio
M-H, Random, 95% CI

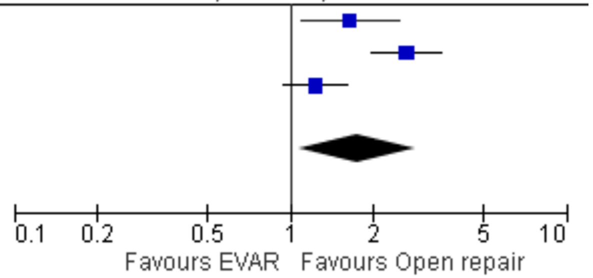


Need for reintervention up to 8 years

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
DREAM	48	173	30	178	30.7%	1.65 [1.10, 2.47]
EVAR1	145	626	55	626	34.3%	2.64 [1.97, 3.52]
OVER	98	444	78	437	35.0%	1.24 [0.95, 1.61]
Total (95% CI)		**1243**		**1241**	**100.0%**	**1.75 [1.07, 2.85]**
Total events	291		163			

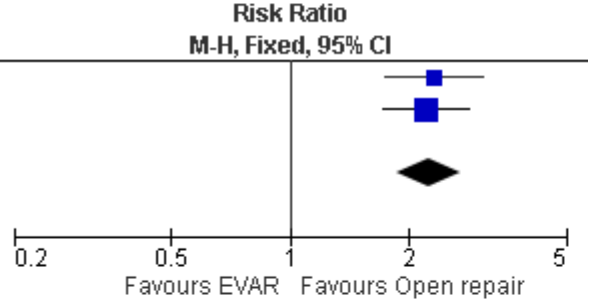
Heterogeneity: Tau² = 0.16; Chi² = 14.38, df = 2 (P = 0.0008); I² = 86%
Test for overall effect: Z = 2.25 (P = 0.02)

Risk Ratio
M-H, Random, 95% CI



Need for reintervention up to 15 years

	EVAR		Open repair			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
DREAM	99	173	44	178	37.0%	2.32 [1.74, 3.08]
EVAR1 (1)	164	626	74	626	63.0%	2.22 [1.72, 2.85]
Total (95% CI)		**799**		**804**	**100.0%**	**2.25 [1.86, 2.72]**
Total events	263		118			
Heterogeneity: Chi² = 0.05, df = 1 (P = 0.82); I² = 0%						
Test for overall effect: Z = 8.36 (P < 0.00001)						

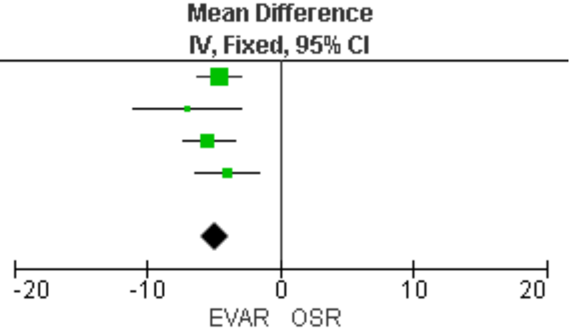


Footnotes
(1) Patients who died prior to intervention were included (Intention to treat analysis)

Length of stay

	EVAR			Open surgical repair				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
ACE	5.8	5.5	150	10.4	8.3	149	43.9%	-4.60 [-6.20, -3.00]
DREAM	6	19.7	173	13	19.7	178	6.6%	-7.00 [-11.12, -2.88]
EVAR1	10.3	17.8	614	15.7	16.9	602	29.4%	-5.40 [-7.35, -3.45]
OVER	3	17.9	444	7	17.9	437	20.0%	-4.00 [-6.36, -1.64]
Total (95% CI)			**1381**			**1366**	**100.0%**	**-4.87 [-5.93, -3.82]**

Heterogeneity: $Chi^2 = 1.94$, $df = 3$ ($P = 0.59$); $I^2 = 0\%$
Test for overall effect: $Z = 9.02$ ($P < 0.00001$)



Appendix F – GRADE tables

EVAR compared with open surgery for patients in whom open surgery is considered appropriate

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
All-cause mortality at 30 days or within hospital; effect sizes below 1 favour EVAR									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Not serious	1,362	1,361	RR 0.34 (0.21, 0.57)	High
All-cause mortality up to 4 years; effect sizes below 1 favour EVAR									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Serious[1]	1,393	1,390	RR 0.93 (0.79, 1.10)	Moderate
All-cause mortality up to 8 years; effect sizes below 1 favour EVAR									
3 (DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Not serious	1,243	1,241	RR 0.99 (0.89, 1.09)	High
All-cause mortality between 8 and 15 years; effect sizes below 1 favour EVAR									
1 EVAR1 trial	RCT	Not serious	Not serious	Not serious	Not serious	626	626	HR[a] 1.25 (1.00, 1.56) (Although 95% CI crosses 1 authors note this as a statistically significant result; p=0.048)	High
All-cause mortality up to 15 years; effect sizes below 1 favour EVAR									
2 (EVAR 1, DREAM trials)	RCTs	Not serious	Not serious	Not serious	Not serious	799	804	RR 1.06 (0.99, 1.13)	High
AAA-related mortality up to 4 years; effect sizes below 1 favour EVAR									

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Serious[2]	Very serious[3]	1,393	1,390	RR 0.65 (0.30, 1.42)	Very low
AAA-related mortality up to 8 years; effect sizes below 1 favour EVAR									
4 (DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Serious[1]	1,243	1,241	RR 0.75 (0.52, 1.08)	Moderate
AAA-related mortality between 8 and 15 years; effect sizes below 1 favour EVAR									
1 EVAR1	RCT	Not serious	Not serious	Not serious	Not serious	626	626	HR[a] 5.82 (1.64, 20.65)	High
AAA-related mortality up to 15 years; effect sizes below 1 favour EVAR									
2 (EVAR 1, DREAM trials)	RCTs	Not serious	Not serious	Serious[2]	Very serious[3]	799	804	RR 1.11 (0.79, 1.56)	Very low
Cardiac-related mortality (follow-up not specified) ; effect sizes below 1 favour EVAR									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Serious[1]	1,393	1,390	RR 1.08 (0.84, 1.40)	Moderate
Stroke-related mortality (follow-up not specified) ; effect sizes below 1 favour EVAR									
2 (DREAM & EVAR1 trials)	RCTs	Not serious	Not serious	Not serious	Very serious[3]	799	804	RR 0.80 (0.44, 1.44)	Low
Pulmonary-related mortality (follow-up not specified) ; effect sizes below 1 favour EVAR									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Serious[1]	1,243	1,241	RR 0.61 (0.41, 0.91)	Moderate

a. Hazard ratios were reported adjusting for age, sex, maximum aneurysm diameter, FEV1, log creatinine, statin use, BMI, smoking status, systolic blood pressure, and total cholesterol

1. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.
2. I^2 value between 33.3% and 66.7%, downgrade 1 level.

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
3. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Endograft-related complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Any endograft complication (not specified)									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Very serious[1]	Not serious	1,393	N/A	ACE: 27.3% (41/150) DREAM: 27.7% (48/173) EVAR1: 45.0% (282/626) OVER: 24.8% (110/444) Overall rate: 34.5%	Low
Endoleaks									
4 (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Very serious[1]	Not serious	1,296	N/A	ACE: 27.3% (41/150) DREAM: 11.7% (20/173) EVAR1: 22.3% (118/529) OVER: 24.8% (110/444) Overall rate: 22.3%	Low
Graft migration									
2 (DREAM & EVAR1 trials)	Systematic review (2 RCTs)	Not serious	Not serious	Not serious	Not serious	799	N/A	DREAM: 4.0% (7/173) EVAR1: 1.9% (12/444) Overall: 3.1% (15/617)	Low
1. Unexplained variation in complication rates reported across included studies, downgrade 2 levels.									

Other complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Non-fatal stroke (follow-up not reported); effect sizes below 1 favour EVAR									
3 (ACE, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Very serious[1]	1,220	1,212	RR 0.82 (0.52, 1.29)	Low
Pulmonary complications (follow-up not reported); effect sizes below 1 favour EVAR									
2 (ACE & DREAM trials)	RCTs	Not serious	Not serious	Not serious	Not serious	323	327	RR 0.38 (0.18, 0.76)	High
Renal complications (follow-up not reported); effect sizes below 1 favour EVAR									
3(ACE, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Very serious[1]	1,103	1,049	RR 1.23 (0.60, 2.55)	Low
Sexual dysfunction (follow-up not reported); effect sizes below 1 favour EVAR									
ACE trial	RCT	Not serious	Not serious	Not serious	Very serious[1]	150	148	RR 0.63 (0.25, 1.58)	Low
1. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Need for reintervention

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Any reintervention up to 4 years; effect sizes below 1 favour EVAR									
3 (ACE, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Very serious[1]	Serious[2]	1,220	1,212	RR 2.30 (1.03, 5.18)	Very low
Any reintervention up to 8 years; effect sizes below 1 favour EVAR									
3v(DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Very serious[1]	Serious[2]	1,243	1,241	RR 1.75 (1.07, 2.85)	Very low
Any reintervention between 8 and 15 years; effect sizes below 1 favour EVAR									
1 EVAR1	RCT	Not serious	Not serious	Not serious	Serious[3]	264	282	HR[a] 1.51 (0.71, 3.19)	Moderate
Any reintervention up to 15 years; effect sizes below 1 favour EVAR									
2 (EVAR 1, DREAM trial)	RCT	Not serious	Not serious	Not serious	Not serious	799	804	RR 2.25 (1.86, 2.72)	High
AAA-related reintervention up to 15 years; effect sizes below 1 favour EVAR									
1 DREAM trial	RCT	Not serious	Not serious	N/A	Not serious	178	173	RR 6.66 (3.70, 12.5,)	High
Life threatening reintervention up to 15 years; effect sizes below 1 favour EVAR									
1 EVAR1	RCT	Not serious	Not serious	N/A	Not serious	302	300	HR[a] 2.09 (1.42, 3.08)	High

a. Hazard ratios were reported adjusting for age, sex, maximum aneurysm diameter, FEV1, log creatinine, statin use, BMI, smoking status, systolic blood pressure, and total cholesterol
1. I^2 value >66.7%, downgrade 2 levels.
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. Non-significant result (95% CI crosses the line of no effect), downgrade 1 level.

Quality of life

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**Open repair**	**Summary of results**	
Mean changes in SF-36 Mental component scores at 2 years; effect sizes below 0 favour EVAR									
1 EVAR1 trial	RCT	Not serious	Not serious	N/A	Serious[1]	1,220	1,212	MD 0.92 (-0.39, 2.23)	Moderate
Mean changes in SF-36 physical component scores at 2 years; effect sizes below 0 favour EVAR									
1 EVAR1 trial	RCT	Not serious	Not serious	Not serious	Serious[1]	1,220	1,212	MD -0.20 (-1.59, 1.19)	Moderate
Mean changes in EQ-5D scores at 2 years; effect sizes below 0 favour EVAR									
1 EVAR1 trial	RCT	Not serious	Not serious	Not serious	Serious[1]	1,103	1,049	MD 0.01 (-0.01, 0.03)	Moderate
1. Non-significant result (95% CI crosses the line of no effect), downgrade 1 level.									

Length of stay

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**Open repair**	**Summary of results**	
Length of hospital stay; effect sizes below 0 favour EVAR									
4, (ACE, DREAM, EVAR1 & OVER trials)	RCTs	Not serious	Not serious	Not serious	Not serious	1,381	1,366	MD -4.87(-5.93, -3.82)	High

Complex EVAR compared with open surgical repair for patients with juxtarenal aneurysms

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
30-day mortality; effect sizes below 1 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Very serious[2]	59	31	RR 0.11 (0.01, 2.16)	Very low

1. Patients were selected for different surgical interventions according to characteristics indicative of aneurysm anatomy complexity and fitness for surgery, downgrade 2 levels.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Need for persistent haemodialysis at 30 days; effect sizes below 1 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Very serious[2]	59	31	RR 0.11 (0.01, 2.16)	Very low
Pneumonia at 30 days; effect sizes below 1 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Very serious[2]	59	31	RR 0.18 (0.01, 4.24)	Very low
Stroke at 30 days; effect sizes below 1 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Very serious[2]	59	31	RR 0.18 (0.01, 4.24)	Very low

1. Patients were selected for different surgical interventions according to characteristics indicative of aneurysm anatomy complexity and fitness for surgery, downgrade 2 levels.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Reintervention

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Need for reintervention; effect sizes below 1 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Very serious[2]	59	31	RR 2.10 (0.25, 18.00)	Very low

1. Patients were selected for different surgical interventions according to characteristics indicative of aneurysm anatomy complexity and fitness for surgery, downgrade 2 levels.
2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.

Length of stay

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
Length of hospital stay; effect sizes below 0 favour EVAR									
1 Donas (2012)	Non-randomised controlled trial	Very serious[1]	Not serious	Not serious	Not serious	59	31	MD -3.70 (-4.86, -2.54)	Low

1. Patients were selected for different surgical interventions according to characteristics indicative of aneurysm anatomy complexity and fitness for surgery, downgrade 2 levels.

EVAR vs no intervention for patients in whom open surgery is not considered appropriate

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**No intervention**	**Summary of results**	
All-cause mortality at 6 months; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	HR[a] 1.32 (0.68, 2.54)	Moderate
All-cause mortality at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	HR[a] 1.02 (0.75, 1.37)	Low
All-cause mortality at 8 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	HR[a] 0.96 (0.61, 1.51)	Low
All-cause mortality at 12 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Not serious	Not serious	Not serious	Serious[2]	197	207	HR[a] 0.83 (0.65, 1.07)	Moderate
AAA-related mortality at 6 months; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	HR[a] 1.78 (0.75, 4.21)	Low
AAA-related mortality at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Not serious	197	207	HR[a] 0.34 (0.16, 0.72)	Moderate
AAA-related mortality at 8 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Not serious	197	207	HR[a] 0.17 (0.04, 0.84)	Moderate
Fatal myocardial infarction at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Very serious[3]	197	207	RR 0.74 (0.38, 1.42)	Very low
Stroke-related mortality at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Very serious[3]	197	207	RR 1.75 (0.42, 7. 23)	Very low

a. Hazard ratios were reported adjusting for age, sex, maximum aneurysm diameter, FEV1, log creatinine, statin use, BMI, smoking status, systolic blood pressure, and total cholesterol
1. Investigators analyses did not take into account a considerably high rate of crossover (34%) from the no intervention group to the EVAR group, downgrade 1 level.
2. Non-significant result (95% CI crosses the line of no effect), 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.

Endograft-related complications and reintervention

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**Open repair**	**Summary of results**	
Any graft-related complication (including endoleak, infection, stenosis, migration, thrombosis rupture, and kinking)									
1 EVAR2 trial	RCT	Not serious	Not serious	Not serious	Not serious	197	N/A	49.2% (97/197)	High
Graft-related reinterventions									
1 EVAR2 trial	RCT	Not serious	Not serious	Not serious	Not serious	197	N/A	27.9% (55/197)	High

Major complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**Open repair**	**Summary of results**	
Cardiovascular events (not specified) at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	HR[a] 1.07 (0.60, 1.91)	Low
Non-fatal myocardial infarction at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Serious[2]	197	207	RR 5.25 (1.17, 23.68)	Low
Non-fatal stroke at 4 years; effect sizes below 1 favour EVAR									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Very serious[3]	197	207	RR 1.84 (0.55, 6.18)	Very low

a. Hazard ratios were reported adjusting for age, sex, maximum aneurysm diameter, FEV1, log creatinine, statin use, BMI, smoking status, systolic blood pressure, and total cholesterol
1. Investigators' analyses did not take into account a considerably high rate of crossover (34%) from the no intervention group to the EVAR group, downgrade 1 level.
2. Non-significant result (95% CI crosses the line of no effect), 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.

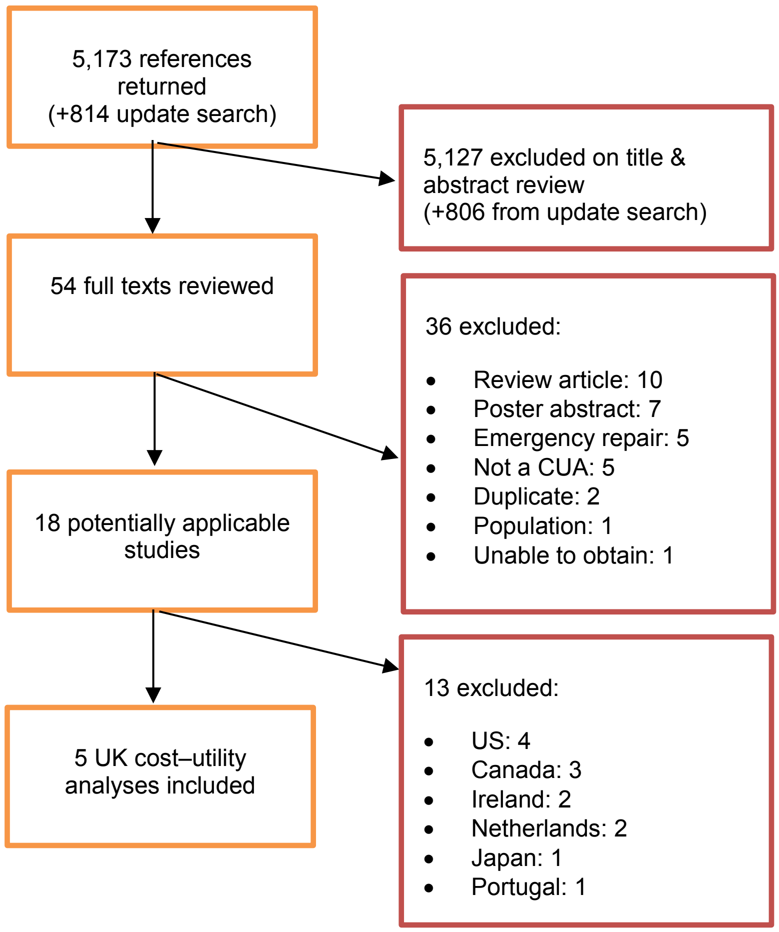
Quality of life

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**EVAR**	**Open repair**	**Summary of results**	
SF-36 scores at 2 years									

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	EVAR	Open repair	Summary of results	
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Very serious[2]	197	207	No difference between groups.	Very low
EQ-5D scores at 2 years									
1 EVAR2 trial	RCT	Serious[1]	Not serious	Not serious	Very serious[2]	197	207	No difference between groups.	Very low

1. Investigators' analyses did not take into account a considerably high rate of crossover (34%) from the no intervention group to the EVAR group, downgrade 1 level.
2. Effect sizes and measures of dispersion were not reported, downgrade 2 levels.

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Study, Population, Country and Quality	Data Sources	Other Comments	Incremental (EVAR vs. OSR / no repair)			Conclusions	Uncertainty
			Cost (£)	Effect (QALYs)	ICER (£)		
Michaels et al. (2005) Decision tree model comparing EVAR with OSR (and EVAR with no repair). UK. **Partially applicable** [a] **Potentially serious limitations** [b,c,d,e]	Effects: EVAR-1 and DREAM studies for operative outcomes. NICE review of non-RCTs for other EVAR outcomes. Costs: Intervention, monitoring and reintervention. Tariff costs for primary procedure plus £4500 for EVAR. Other resource use from EUROSTAR registry and assumptions. Utilities: Short term recovery decrements (NR), followed by general age-related utility after successful repair.	Cohort: male, 70 years old, 5.5cm AAA. 10-year time horizon. 3.5% discount rates. Price year 2003-04. No long-term CV events. General population life expectancy applied after successful repair.	EVAR vs. OSR 11,449	0.10	110,000	'The results of this analysis suggested that, in patients in whom conventional open repair would be an alternative, EVAR provided a slight additional benefit, but at a cost that would not normally be considered appropriate for funding by the NHS.'	EVAR ICER <£20,000 in ~0% of 1000 PSA model runs, compared with OSR. Base case result robust to scenario analyses (e.g. assuming £0 EVAR device cost: ICER >£50,000).

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; NR, not reported; OSR, open surgical repair; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year.

a. Only considers infrarenal aneurysms.
b. Relative effects only available for operative outcomes for EVAR vs. OSR comparison; no randomised data used for 'unfit for OSR' population.
c. Successful repair effectively considered a 'cure' as patients return to general population life expectancy (long-term data not available at the time of analysis).
d. Reintervention and complications (endoleak) only modelled for EVAR, and no long-term complications modelled.
e. 10-year time horizon (15 in scenario analysis); shorter than lifetime, and current long-term EVAR-1 data suggest long-term survival differences.

Study, Population, Country and Quality	Data Sources	Other Comments	Incremental (EVAR vs. OSR)			Conclusions	Uncertainty
			Cost (£) (95% CI)	Effect (QALYs) (95% CI)	ICER (£)		
Epstein et al. (2008) Markov model comparing EVAR with OSR based on EVAR-1 patients and data. UK. **Partially applicable** [a] **Potentially serious limitations** [b,c,d]	Effects: EVAR-1 study. Costs: EVAR-1 study, NHS reference costs and UK literature. Utilities: UK population norms (Kind et al. 1999), 1-month surgery morbidity (EVAR-1), cardiovascular conditions (UK literature).	2-year convergence of EVAR and OSR overall survival, despite 4-year aneurysm-related survival benefit for EVAR. 'Other cause' EVAR mortality catch-up factor applied in the model. Aneurysm-related readmissions modelled. Cardiovascular conditions were MI and stroke. Lifetime horizon, 3.5% discount rate applied to all outcomes.	3,758 (2,439; 5,183)	-0.02 (-0.189; 0.165)	EVAR dominated	'EVAR is unlikely to be cost-effective for all patients within collectively funded healthcare systems.' 'EVAR may be cost-effective in a subpopulation of elderly patients fit for open surgery … if patients maintain this early survival advantage over open surgery.'	EVAR ICER 1.2% likely to be ≤£20,000 per QALY gained. Various scenario analyses. Probability was 14.7% if OSR perioperative mortality was 8% (from 5%); and was 26.2% if the patient was aged 82 (from 74) and differences in cardiovascular event rates were omitted.

Key: CI, confidence interval; EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical repair QALY, quality-adjusted life year; VGNW, Vascular Governance North West; yo, years old.

a. Only considers infrarenal aneurysms.
b. Informed by early results from a single study.
c. Unclear whether difference in aneurysm-related mortality over 4 years is extrapolated to lifetime.
d. Potential conflict of interest.

Study, Population, Country and Quality	Data Sources	Other Comments	Incremental (EVAR vs. OSR)			Conclusions	Uncertainty
			Cost (£)	Effect (QALYs)	ICER (£)		
Chambers et al. (2009) Markov model comparing EVAR with OSR. UK. **Partially applicable** [a] **Potentially serious limitations** [b,c,d]	<u>Effects:</u> Baseline risk equations estimated using IPD from the EUROSTAR study. Relative effects from systematic review (EVAR-1 and DREAM). <u>Costs:</u> Intervention, monitoring and readmission. Resource use from EVAR-1. Costs from EVAR-1 and UK sources. <u>Utilities:</u> UK population norms (Kind et al. 1999), surgery-related decrements for 6 months (EVAR-1).	Lifetime horizon, 3.5% discount rates, Markov model. Price year 2007. Risk equations constructed to predict operative mortality, post-operative mortality, and readmission. Readmissions are AAA-related only. No long-term CV events. Non-AAA mortality converges after ~3 years. AAA-related mortality benefit of EVAR maintained. Rupture fatality rate assumed 100%.	2,002	0.041	48,990	'The base-case decision model found that EVAR is not cost-effective on average for patients who are fit for open surgery 'If patients can be classified into good, average and poor operative risk, then for patients of most ages and aneurysm sizes, EVAR is cost-effective compared with open repair in patients of poor risk but not cost-effective in patients of good risk.'	EVAR ICER 26.1% likely to be ≤£20,000 per QALY gained. ICER is <£30,000 in patients with subjectively poor operative fitness. ICER <£20,000 where (1) EVAR sustained an overall survival benefit over OSR for the patient's lifetime and (2) unit cost of EVAR equal to OSR, follow-up costs lower and reintervention rates lower. ICER £21-22,000 if EVAR operative mortality odds ratio improved (from 0.35 to 0.25), and if overall mortality rates converge at 8 years (vs. 3 years).

Key: CI, confidence interval; EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; IPD, individual patient data; OSR, open surgical repair; QALY, quality-adjusted life year.

a. Only considers infrarenal aneurysms.
b. Relative effects largely drawn from a single study (EVAR-1).
c. Impact of long-term non-aneurysm complications not captured by model.
d. Assumption of maintained AAA-related mortality difference not supported by 15-year EVAR-1 study data.

Study, Population, Country and Quality	Data Sources	Other Comments	Incremental (EVAR vs. OSR / no repair)			Conclusions	Uncertainty
			Cost (£)	Effect (QALYs)	ICER (£)		
Brown et al. (2012) Markov model comparing EVAR with OSR. Trial analysis comparing EVAR with no repair. UK. **Partially applicable** [a] **Potentially serious limitations** [b,c,d]	Effects: EVAR-1 and EVAR-2 studies, including ITT analyses. Costs: Intervention, monitoring and readmission. Resource use from EVAR trials. Costs from trials and UK sources. In EVAR-2 analysis, costs not extrapolated beyond observed 8-year data. Utilities: EVAR-1 analysis: surgery-related decrements for 3 months (EVAR-1 analysis). EVAR-2 analysis: EQ-5D data from trial.	EVAR-1 analysis: Lifetime horizon. EVAR-2 analysis: 8-year analysis and lifetime analysis. 3.5% discount rates. Price year 2008-09. EVAR-1 model: Follow-up divided into first 6 months, 6 months to 4 years, 4 to 8 years, and 8 years onwards. AAA mortality converges after 8 years. Ongoing non-AAA mortality SMR of 1.1 vs. general population (based on EVAR-1 and UKSAT). EVAR-2 analysis: 2 analyses presented, 1 ITT (by randomised group) and 1 per protocol (excludes subjects who crossed over from 'no surgery' to intervention). No long-term CV events.	EVAR-1 3,521 EVAR-2 *8-years* 10,214 *Lifetime* 10,214	 -0.042 0.037 0.350	 EVAR dominated 264,900 30,274	EVAR-1 'For patients with large AAA, who are deemed anatomically suitable for EVAR and anaesthetically fit for open repair, [EVAR] is a more costly treatment option [than OSR] and unlikely to be cost-effective in all patients.' EVAR-2 'For patients deemed anatomically suitable for EVAR but too unfit to for open repair, EVAR offers a long-term benefit in aneurysm mortality … no benefits in quality of life and high rates of adverse events, complications and reinterventions after EVAR contribute to poor cost-effectiveness.'	EVAR-1 EVAR ICER 1% likely to be ≤£20,000 per QALY gained compared with OSR. PSA mean costs: £3,519 (95% CI: 1,919 to 5,053). PSA mean QALYs: -0.032 (-0.117 to 0.096). Robust to univariate sensitivity analysis based on alternative clinical data (OVER) and modelling assumptions (Epstein 2008, NICE 2009). EVAR-2 0% and 3% of 1000 bootstrapped ICERs were ≤£20,000 (ITT analysis). Mean ICER of lifetime 'per protocol' analysis was £17,805 (61% ≤£20,000).

Key: CI, confidence interval; EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; ITT, intention to treat; OSR, open surgical repair; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; SMR, standardised mortality ratio; UKSAT, UK Small Aneurysm Trial.

a. Only considers infrarenal aneurysms.

b. Relative effects largely drawn from a single study for each analysis (EVAR-1 and EVAR-2), though these are the only studies to provide ITT data.

c. Impact of long-term non-aneurysm complications not captured by model.

d. Long-term costs not included in the EVAR-2 lifetime extrapolation.

Study, Population, Country and Quality	Data Sources	Other Comments	Incremental (EVAR vs. OSR)			Conclusions	Uncertainty
			Cost (£) (95% CI)	Effect (QALYs) (95% CI)	ICER (£)		
Epstein et al. (2014) Markov model comparing EVAR with OSR based on 4 RCTs. UK. **Partially applicable** [a] **Potentially serious limitations** [b,c]	Effects: EVAR-1, ACE, DREAM and OVER studies. Costs: EVAR-1 (UK), ACE (France), DREAM (Netherlands) and OVER (US). Converted to 2009 UK pounds using purchasing power parities. Utilities: 3-month surgery morbidity (EVAR-1).	Model based on Epstein el al. (2008) EVAR-1 model. EVAR-1 8-year data used. Cardiovascular complications not modelled. 4 individual models, no synthesis of RCT data. Each analysis applies the relative survival (including convergence of curves), reintervention data and resource us from the relevant RCT. Lifetime horizon, 3.5% discount rate applied to all outcomes.	EVAR-1 4,014 (2,167; 5,942) ACE 2,086 (1,526; 2,869) DREAM 3,181 (1,557; 4,986) OVER -1,852 (-5,581; 2,097)	 -0.02 (-0.19, 0.05) -0.01 (-0.07, 0) 0 (-0.07, 0.05) 0.05 (-0.06, 0.13)	 EVAR dominated EVAR dominated 2,845,315 Dominant	'This economic analysis does not find that EVAR is cost-effective compared with open repair over the long term based on the EVAR-1, DREAM or ACE trials. EVAR does appear to be cost-effective over the long term based on the OVER trial.'	EVAR ICER 0% likely to be <£20,000 in the base case EVAR-1, ACE and DREAM analyses, rising to 3% in a favourable scenario. EVAR ICER 91% likely to be <£20,000 in the base case OVER analysis, rising to 99% in a favourable scenario.

Key: CI, confidence interval; EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical repair QALY, quality-adjusted life year; RCT, randomised controlled trial.

a. Only considers infrarenal aneurysms.

b. Each analysis informed by a single study; no synthesis of data.

c. EVAR-1 analysis is very similar to previous models (Epstein et al. 2008; Chambers et al. 2009; Brown et al. 2012); other analyses use non-UK resource use data.

Appendix J – Excluded studies

Clinical studies

No.	Study	Reason for exclusion
1	Belczak Sergio Quilici, Lanziotti Luiz, Botelho Yuri et al. (2014) Open and endovascular repair of juxtarenal abdominal aortic aneurysms: a systematic review. Clinics (Sao Paulo, and Brazil) 69, 641-6	Systematic review including studies that prospective and retrospective cohort studies. Individual studies were assessed to determine if they met inclusion criteria for this review question.
2	Bruen Kevin J, Feezor Robert J, Daniels et al. (2011) Endovascular chimney technique versus open repair of juxtarenal and suprarenal aneurysms. Journal of vascular surgery 53, 895-5	Authors collected data from patients who underwent EVAR and compared their results with retrospectively collected data from historical controls.
3	de Bruin , J L, Vervloet M G, Buimer M et al. (2013) Renal function 5 years after open and endovascular aortic aneurysm repair from a randomized trial. : John Wiley and Sons Ltd (Southern Gate, Chichester, West Sussex PO19 8SQ, United Kingdom)	Conference abstract.
4	Deery SE, Lancaster RT, Gubala AM et al. (2017) Early experience with fenestrated endovascular compared to open repair of complex abdominal aortic aneurysms in a high-volume open aortic center. Annals of vascular surgery	Retrospective cohort study design.
5	Di Xiao, Ye Wei, Liu Chang-Wei et al. (2013) Fenestrated endovascular repair for pararenal abdominal aortic aneurysms: a systematic review and meta-analysis. Annals of vascular surgery 27, 1190-200	Systematic review that assessed data from retrospective case series (single arm, non-comparative studies). Case series are not listed for inclusion in the review protocol.
6	Donas Konstantinos P, Torsello Giovanni, Pitoulias Georgios A et al. (2011) Surgical versus endovascular repair by iliac branch device of aneurysms involving the iliac bifurcation. Journal of vascular surgery 53, 1223-9	Retrospective cohort study design.
7	Donas Konstantinos P, Torsello Giovanni et al. (2012) Early outcomes for fenestrated and chimney endografts in the treatment of pararenal aortic pathologies are not significantly different: a systematic review with pooled data analysis. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 19, 723-8	Systematic review that assessed data from retrospective and prospective case series (single arm, non-comparative studies). Case series are not listed for inclusion in the review protocol.
8	Fanelli F (2017) Do the long-term outcomes of EVAR justify its generalised use? Cardiovascular and interventional radiology. Conference: cardiovascular	Conference abstract

No.	Study	Reason for exclusion
	and interventional radiological society of europe, and CIRSE 2017. Denmark 40(2 Supplement 1), S58-s59	
9	Gallitto E, Gargiulo M, Freyrie A et al. (2015) The endovascular treatment of juxta-renal abdominal aortic aneurysm using fenestrated endograft: early and mid-term results. The Journal of cardiovascular surgery ,	Case series
10	Gupta P K, Brahmbhatt R, Kempe K et al. (2017) Thirty-day outcomes after fenestrated endovascular repair are superior to open repair of abdominal aortic aneurysms involving visceral vessels. Journal of Vascular Surgery ,	Retrospective cohort study involving retrospective analysis of data from an American surgical registry.
11	Han Y, Zhang S, Zhang J et al. (2017) Outcomes of Endovascular Abdominal Aortic Aneurysm Repair in Octogenarians: Meta-analysis and Systemic Review. European Journal of Vascular and Endovascular Surgery.	Systematic review which included studies that employed multiple study designs. Individual studies were assessed to establish if they met criteria for inclusion in this NICE review.
12	Health Quality, and Ontario (2009) Fenestrated endovascular grafts for the repair of juxtarenal aortic aneurysms: an evidence-based analysis. Ontario health technology assessment series 9, 1-51	Systematic review including studies that employed various study designs. Individual studies were assessed to determine if they met inclusion criteria for this review question.
13	Katsargyris Athanasios, Oikonomou Kyriakos, Klonaris Chris et al. (2013) Comparison of outcomes with open, fenestrated, and chimney graft repair of juxtarenal aneurysms: are we ready for a paradigm shift? Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 20, 159-69	Systematic review that assessed data from retrospective and prospective case series (single arm, non-comparative studies). Case series are not listed for inclusion in the review protocol.
14	Lederle F A, Stroupe K T, Kyriakides T C, Ge L, and Freischlag J A (2016) Long-term Cost-effectiveness in the Veterans Affairs Open vs Endovascular Repair Study of Aortic Abdominal Aneurysm: a Randomized Clinical Trial.	Investigators performed secondary data analysis using data from a study (OVER trial) that is included in a systematic review identified as relevant to this review question. No additional relevant data was reported in this new publication.
15	Li Yue, Zhang Tao, Guo Wei et al. (2015) Endovascular chimney technique for juxtarenal abdominal aortic aneurysm: a systematic review using pooled analysis and meta-analysis. Annals of vascular surgery 29, 1141-50	Systematic review including studies that employed various study designs. Individual studies were assessed to determine if they met inclusion criteria for this review question.
16	Locham S S, Nejim B, Aridi H et al. (2017) Perioperative outcomes of patients undergoing fenestrated endovascular repair vs open repair of intact abdominal aortic aneurysms involving the visceral vessels: 10-year national study. Journal of the American	Conference abstract

No.	Study	Reason for exclusion
	College of Surgeons 225 (4 Supplement 1), S220	
17	Nordon I M, Hinchliffe R J, Holt P J et al. (2009) Modern treatment of juxtarenal abdominal aortic aneurysms with fenestrated endografting and open repair--a systematic review. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 38, 35-41	Systematic review that assessed data from prospective and retrospective case series (single arm, non-comparative studies). Case series are not listed for inclusion in the review protocol.
18	Orr Nathan T, Davenport Daniel L, Minion David J, and Xenos Eleftherios S (2017) Comparison of perioperative outcomes in endovascular versus open repair for juxtarenal and pararenal aortic aneurysms: A propensity-matched analysis. Vascular 25, 339-345	Retrospective cohort study involving retrospective analysis of data from an American surgical registry.
19	Raux Maxime, Patel Virendra I, Cochennec Frederic et al. (2014) A propensity-matched comparison of outcomes for fenestrated endovascular aneurysm repair and open surgical repair of complex abdominal aortic aneurysms. Journal of vascular surgery 60, 858-4	Retrospective cohort study.
20	Sala-Almonacil VA, Zaragoza-Garcia JM, Ramirez-Montoya M et al. (2017) Fenestrated and chimney endovascular aneurysm repair versus open surgery for complex abdominal aortic aneurysms. The Journal of cardiovascular surgery 58(6), 801-813	Study employed a mixture of study designs: prospectively collected data of patients who underwent EVAR was compared against data from a historical cohort
21	Stather P W, Sidloff D, Dattani N et al. (2013) Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm.	Systematic review including studies that employed various study designs. Individual studies were assessed to determine if they met inclusion criteria for this review question.
22	Tsilimparis Nikolaos, Perez Sebastian, Dayama Anand et al. (2013) Endovascular repair with fenestrated-branched stent grafts improves 30-day outcomes for complex aortic aneurysms compared with open repair. Annals of vascular surgery 27, 267-73	Retrospective cohort study involving retrospective analysis of data from an American surgical registry.
23	Ultee Klaas H. J, Zettervall Sara L, Soden Peter A et al. (2017) Perioperative outcome of endovascular repair for complex abdominal aortic aneurysms. Journal of vascular surgery 65, 1567-1575	Retrospective cohort study involving retrospective analysis of data from an American surgical registry.
24	van Lammeren GW, Unlu C, Verschoor S et al. (2017) Results of open pararenal abdominal aortic aneurysm repair: single	Case series

No.	Study	Reason for exclusion
	centre series and pooled analysis of literature. Vascular 25(3), 234-241	
25	Yaoguo Yang, Zhong Chen, Lei Kou, and Yaowen Xiao (2017) Treatment of complex aortic aneurysms with fenestrated endografts and chimney stent repair: Systematic review and meta-analysis. Vascular 25, 92-100	Systematic review comparing 2 approaches of performing complex EVAR (fenestrated versus chimney endografts). The aim of this review question is to compare complex EVAR with open surgical repair or no intervention. Thus, comparisons between different types of complex EVAR are out of scope of this review question.

Economic studies

Study	***Primary reason for exclusion***
Selectively excluded	
Blackhouse et al. (2009). A cost-effectiveness model comparing endovascular repair to open surgical repair of abdominal aortic aneurysm in Canada. *Value in Health,* 12(2): 245-52.	Non-UK (Canada)
Bosch et al. (2002). Abdominal aortic aneurysms: cost-effectiveness of elective endovascular and open surgical repair. *Radiology,* 225(2): 337-44.	Non-UK (US)
Bowen et al. (2005). Systematic review and cost-effectiveness analysis of elective endovascular repair compared to open surgical repair of abdominal aortic aneurysms. Interim report. Ontario Ministry of Health & Long-term Care.	Interim results of Tarride et al. (2008)
Burgers et al. (2016). Cost-effectiveness of Elective Endovascular Aneurysm Repair Versus Open Surgical Repair of Abdominal Aortic Aneurysms. Eur J Vasc Endovasc Surg, 52: 29-40.	Non-UK (Netherlands)
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Lederle et al. (2016). Long-term cost-effectiveness in the vetereans Affairs Open vs Endovascular Repair Study of aortic abdominal aneurysm: a randomised clinical trial. *JAMA Surg,* 151(12): 1139-1144.	Non-UK (US)
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Prinssen et al. (2007). Cost-effectiveness of conventional and endovascular repair of abdominal aortic aneurysms: Results of a randomized trial. *J Vasc Surg,* 46: 883-90.	Non-UK (Netherlands)
Sousa et al. (2014). Cost-effectiveness of the endovascular repair of abdominal aortic aneurysm in Portugal. *Angiol Cir Vasc,* 10(2): 41-8.	Non-UK (Portugal)
Sultan & Hynes (2011a). Clinical efficacy and cost per quality-adjusted life years of pararenal endovascular aortic aneurysm repair compared with open surgical repair. *J Endovasc Ther,* 18: 181-96.	Non-UK (Republic of Ireland)
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Excluded based on study selection criteria	
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Badger et al. (2014). Endovascular treatment for ruptured abdominal aortic aneurysm (review). *Cochrane Database of Systematic Reviews,* 7.	Review article, no additional CUAs
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Hayes et al. (2010). Cost-effectiveness analysis of endovascular versus open surgical repair of acute abdominal aortic aneurysms based on worldwide experience. *J Endovasc Ther,* 17: 174-82.	Population (emergency repair)
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Kapma et al. (2007). Emergency abdominal aortic aneurysm repair with a preferential endovascular strategy: mortality and cost-effectiveness analysis. *J Endovasc Ther,* 14: 777-84.	Not a CUA
Kapma et al. (2014). Cost-effectiveness and cost–utility of endovascular versus open repair of ruptured abdominal aortic aneurysm in the Amsterdam Acute Aneurysm Trial. *Br J Surg,* 101(3): 208-15.	Population (emergency repair)
Lederle. (2009). Repair of nonruptured abdominal aortic aneurysm: a systematic review of randomized trials. *Vascular,* 17: S71.	Poster abstract
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Perras et al. (2009). Elective endovascular abdominal aortic aneurism repair versus open surgery: a review of the clinical and cost-effectiveness.	Review article, no additional CUAs
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Powell et al. (2017). Comparative clinical effectiveness and cost effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: three year results of the IMPROVE randomised trial. BMJ, 359.	Population (emergency repair)

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Sala-Almonicil et al. (2017). Fenestrated and chimney endovascular aneurysm repair versus open surgery for complex abdominal aortic aneurysms. *J Cardiovasc Surg,* 58(6): 801-13.	Not a CUA.
Stroupe et al. (2012). Cost-effectiveness of open versus endovascular repair of abdominal aortic aneurysm in the OVER trial. *J Vasc Surg,* 56: 901-10.	Duplicate of Lederle et al. (2012)
Silverstein et al. (2005). Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. *BUMC Proceedings,* 18: 345-67.	Review article, no additional CUAs
Sultan et al. (2009a). A prospective clinical and quality of life analysis of open repair (OR), endovascular repair (EVAR), and best medical treatment in high-risk patients: cost-effectiveness during global recession. *Vascular,* (17): S2.	Poster abstract
Sultan et al. (2009b). Five-year experience with EVAR without fenestration for juxtarenal AAA repair: clinical efficacy, reintervention rates, and cost-effectiveness. *Vascular,* 17: S74.	Not found
Sultan & Hynes (2010a). Five-year experience with pararenal endovascular aortic repair (PEVAR) without fenestration: clinical efficacy, reintervention rates & cost-effectiveness. *J Vasc Surg,* 51(6): S89.	Poster abstract
Sultan & Hynes (2010b). Five-year experience with pararenal endovascular aortic repair (PEVAR) without fenestration: clinical efficacy, reintervention rates & cost-effectiveness. *J Vasc Surg,* 51(4): 1068-9.	Poster abstract
Sultan & Hynes (2010c)	Poster abstract
Sultan & Hynes (2011b). A mid- to long-term experience of clinical efficacy and cost per quality-adjusted-life years with pararenal endovascular aortic repair (PEVAR) without fenestration for pararenal AAA compared with open surgical repair. *Cardiovasc Interv Radiol,* 3 (332/677).	Poster abstract
Sultan & Hynes (2012). Clinical efficacy and cost per quality-adjusted life years of para-renal endovascular aortic aneurysm repair compared with open surgical repair. *JACC,* 60(17): B38.	Poster abstract
Sweeting et al. (2015). Individual-patient meta-analysis of three randomized trials comparing endovascular versus open repair for ruptured abdominal aortic aneurysm. *Br J Surg,* 102: 1229-39.	Review article, no additional CUAs
Tarride et al. (2011). Should endovascular repair be reimbursed for low risk abdominal aortic aneurysm patients? Evidence from Ontario, Canada. *Int J Vasc Med,* 2011.	Not a CUA
Taylor et al. (2012). EVAR is now cost effective and should replace open surgery for all suitable patients: con. *Cardiovasc Interv Radiol,* 35: S48.	Review article, no additional CUAs
Tremont et al. (2016). Endovascular Repair for Ruptured Abdominal Aortic Aneurysms has Improved Outcomes Compared to Open Surgical Repair. Vasc Endovasc Surg, 50(3) 147-55.	Population (emergency repair)
Van Bochove et al. (2016). Cost-effectiveness of open versus endovascular repair of abdominal aortic aneurysm. *J Vasc Surg,* 63(3): 827-38.	Review article, no additional CUAs
Weinkauf et al. (2017). Open versus endovascular aneurysm repair trial review. *Surgery,* 162(5): 974-78.	Duplicate of Lederle et al. (2016)
Wilt et al. (2006). Comparison of endovascular and open surgical repairs for abdominal aortic aneurysm. *Evid Rep Technol Assess,* 144: 1-113.	Review article, no additional CUAs
Key: CUA, cost–utility analysis.	

Appendix K – Research recommendation

Research recommendation	**What is the effectiveness and cost-effectiveness of complex EVAR versus open surgical repair in people with an unruptured AAA for whom open surgical repair is a suitable option?**
Population	People undergoing elective surgery for unruptured abdominal aortic aneurysm Sub-grouped by: age, sex, comorbidities (including cardiovascular disease, renal disease, COPD, obesity) and ethnicity
Intervention(s)	• Complex EVAR for infrarenal, juxtarenal and suprarenal abdominal aortic aneurysms, including: • fenestrated EVAR • EVAR with chimneys • EVAR with snorkels • branched grafts • 'CHIMPS' (CHIMneys, Periscopes, Snorkels) • infrarenal devices used for juxtarenal AAA – that is, off-IFU use of standard devices
Comparator(s)	Open surgical repair
Outcomes	• Mortality/survival • Peri- and post-operative complications • Successful exclusion of the aneurysm, aneurysm rupture, or further aneurysm growth • Need for reintervention • Quality of life • Resource use, including length of hospital or intensive care stay, and costs
Study design	Randomised controlled trial

Potential criterion	**Explanation**
Importance to patients, service users or the population	EVAR is a widely performed non-invasive alternative to open surgical repair. However, it is more expensive. Although EVAR has been shown to produce no long-term benefit over open surgical repair in people with unruptured infrarenal aneurysms, it is less clear whether this is the same in people with unruptured or ruptured juxtarenal, suprarenal type IV, and short-necked infrarenal aneurysms. As a result, research is needed to identify how effective complex EVAR is in these populations.
Relevance to NICE guidance	High priority: it is currently unclear whether EVAR can improve long-term outcomes of people with complex aneurysm anatomies.
Current evidence base	A single non-randomised controlled trial assessing the efficacy of chimney- and fenestrated-EVAR in 90 people was identified from literature searches. The study reported no significant differences in 30-day mortality, complication, and reintervention rates between patients treated by complex EVAR and those who received open surgery. The results of this study, coupled with data from a new health economic model produced by NICE led the committee to conclude that complex EVAR yielded no benefit over open surgery in the short-term. The committee considered that longer-term evidence from large RCTs was needed to clarify the clinical utility of complex EVAR, and inform health economic modelling.
Equality	No specific equality concerns are relevant to this research recommendation.

Potential criterion	Explanation
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

Appendix L – 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.

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Membership of Abdominal Aortic Aneurysm guideline committee

NICE National Institute for Health and Care Excellence

The Committee will operate as an advisory Committee to NICE's Board, developing clinical guideline on Abdominal Aortic Aneurysm

The terms of reference and standing orders for the Committee can be found in appendix D of Developing NICE guidelines: the manual.

The Committee has 16 members, to include 12 core members

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Membership list

Agreed Constituency	Name	Job Title, Organisation	Comment
Chair			
Chair	Andrew Bradbury	Sampson Gamgee Professor of Vascular Surgery, University of Birmingham and Consultant Vascular and Endovascular Surgeon, Heart of England NHS Foundation Trust	
Core members / Members			
Vascular Surgeon	Alun Davies	Professor of Vascular Surgery & Honorary Consultant Surgeon, Imperial College School of Medicine	Joined September 2016
Radiologist	Chris Hammond	Consultant Vascular Radiologist, Leeds Teaching Hospitals NHS Trust	
Radiographer	Mark Hampshire	Superintendent IR radiographer at St. Thomas' Hospital	Joined October 2017
Theatre Nurse	Karen Jellett	Theatre Nurse, North Bristol NHS Trust	
Anaesthetist	Adam Pichel	Consultant in Anaesthesia with special interest in Vascular Surgery, Manchester Royal Infirmary	
A&E Consultant	Tamsin Ribbons	Consultant in Emergency Medicine, Dorset County Hospital	
Lay member	Leslie Ruffell	N/A	Joined July 2016

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Vascular Scientist	Matthew Slater	Vascular Scientist, Cambridge University Hospitals	
Lay member	Alan Huw Smith	N/A	
Vascular Nurse	Hazel Trender	Senior Vascular Nurse Specialist Sheffield Vascular Institute, Northern General Hospital, Sheffield	Joined October 2017
Vascular Surgeon	Noel Wilson	Consultant Vascular Surgeon, Kent & Canterbury Hospital	
Co-opted members			
GP	Ivan Bennett	GP, The Range Medical Practice Manchester	Joined April 2016
Geriatrician	Jugdeep Dhesi	Geriatrician, Guy's & St Thomas' NHS Foundation Trust	
Paramedic	Jacqualine Lindridge	Paramedic, London Ambulance Service NHS Trust	
Paramedic	Sammer Tang	Paramedic, South Western Ambulance Service NHS Foundation Trust	
Resigned members			
Lay member	Roger Good	N/A	Resigned November 2015
GP	Eshan Senanyake	GP, Grantham Practice, London	Resigned February 2016
Vascular Surgeon	Matt Thompson	Professor of Vascular Surgery, St George's, University of London and Consultant Vascular Surgeon, St George's Vascular Institute	Resigned June 2016
Radiographer	Gillian Kitching	Radiographer, Manchester Royal	Resigned

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

		Infirmary	June 2017
Vascular Nurse	Claire Martin	Vascular Nurse, Frimley Park Hospital	Resigned June 2017

Date last reviewed: 21/05/2018

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Declaration of Interests

The effective management of conflicts of interests is an essential element in the development of the guidance and advice that NICE publishes. Please refer to the NICE website for the Policy on Conflicts of Interest.

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
Ivan Bennett	GP, The Range Medical Practice Manchester	None declared March 2016	N/A	N/A
Andrew Bradbury	Sampson Gamgee Professor of Vascular Surgery, University of Birmingham and Consultant Vascular and Endovascular Surgeon, Heart of England NHS Foundation Trust	None declared April 2015	N/A	N/A
Alun Davies	Professor of Vascular Surgery & Honorary Consultant Surgeon, Imperial College School of Medicine	Private vascular practice, performs on average 2 AAA cases per year, one open surgery and one EVAR. Private practice matches NHS practice and approx. 2% of private practice relates to topics covered in this guideline. These are remunerated on a fee for service basis. July 2016	Specific, Personal, Financial	Declare and leave the meeting when making recommendations on relevant topics.

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Jugdeep Dhesi	Geriatrician, Guy's & St Thomas' NHS Foundation Trust	None declared September 2015	N/A	N/A
Chris Hammond	Consultant Vascular Radiologist, Leeds Teaching Hospitals NHS Trust	CardioVascular and Interventional Radiology paper June 2016 on Mortality and Rates of Secondary Intervention After EVAR June 2017	Specific, personal, non-financial	Declare and participate
Karen Jellett	Theatre Nurse, North Bristol NHS Trust	None declared October 2015	N/A	N/A
Jacqualine Lindridge	Paramedic, London Ambulance Service NHS Trust	None declared November 2015	N/A	N/A
Adam Pichel	Consultant in Anaesthesia with special interest in Vascular Surgery, Manchester Royal Infirmary	Chairman of the Vascular Anaesthesia Society of Great Britain and Ireland April 2015	Non-specific, personal non-financial	Declare and participate
Adam Pichel		Co-author of studies on CPET included in evidence review for Review Question 8: Grant S W, Hickey G L, Wisely N A, Carlson E D, Hartley R A, Pichel A C, Atkinson D, and Mccollum C N (2015) Cardiopulmonary Exercise Testing And Survival After Elective Abdominal Aortic Aneurysm Repair. British	Specific, personal, non-financial	Declare and participate at the discretion of the Chair

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

		Journal of Anaesthesia 114(3), 430-436 Hartley R A, Pichel A C, Grant S W,Hickey G L, Lancaster P S, Wisely N A, Mccollum C N, and Atkinson D (2012) Preoperative Cardiopulmonary Exercise Testing And Risk Of Early Mortality Following Abdominal Aortic Aneurysm Repair. The British Journal of Surgery 99(11), 1539-46 November 2017		
Tamsin Ribbons	Consultant in Emergency Medicine, Dorset County Hospital	None declared September 2015	N/A	N/A
Leslie Ruffell	N/A	None declared July 2017	N/A	N/A
Matthew Slater	Vascular Scientist, Cambridge University Hospitals	None declared October 2015	N/A	N/A
Alan Huw Smith	Lay member	Lay member on National Abdominal Aortic Aneurysm Screening Programme Research Committee (Unpaid) December 2015	Personal, specific, non-financial	Declare and participate

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Sammer Tang	Paramedic, South Western Ambulance Service NHS Foundation Trust	None declared November 2015	N/A	N/A
Hazel Trender	Senior Vascular Nurse Specialist Sheffield Vascular Institute, Northern General Hospital, Sheffield	None declared October 2017	N/A	N/A
Noel Wilson	Consultant Vascular Surgeon, Kent & Canterbury Hospital	Private vascular practice, performs on average less than 1 AAA case per year. Private practice matches NHS practice and no more than 1% of private practice relates to topics covered in this guideline. These are remunerated on a fee for service basis. September 2015	Specific, Personal, Financial	Declare and leave the meeting when making recommendations on relevant topics.
Resigned members				
Roger Good	Lay member	None declared October 2015	N/A	N/A
Eshan Senanyake	GP	None declared October 2015	N/A	N/A
Matt Thompson	Professor of Vascular Surgery, St George's Vascular Institute	Departmental research grant funding from Medtronic and Endologix for PhD students – AAA treatments and developing PROMs. No commercial funding supporting salary.	Specific, non-personal financial	Excluded from discussion of review questions which pertain to products manufactured by these companies.

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

		April 2015		
Matt Thompson		Member of a medical advisory board for Endologix. This is a regular paid commitment. Advisory boards occur twice yearly – in March and November. Topics discussed are confined to EVAS (Endovascular Aneurysm Sealing) and the use of the Nellix endograft. No other grafts are discussed. April 2015	Specific, personal financial	Excluded from discussion of review questions which pertain to products manufactured by these companies.
Matt Thompson		Principal Investigator of the Global Registry. This involves overseeing the clinical conduct of the research study and will involve writing the manuscript when appropriate. No financial payment for this role. April 2015	Personal, specific, non-financial	Declare and participate
Matt Thompson		Consultancy for Medtronic and Endologix.	Personal, specific, financial	Excluded from discussion of review questions which pertain to products manufactured by these companies

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

		December 2015		.
Matt Thompson		Speaker fees from Medtronic and Endologix: For Endologix, gave a lecture at a sponsored symposium on 29.1.15 (Leipzig Interventional Talk) and 29.4.15 (Charing Cross symposium). Both talks were on EVAS and the Nellix graft. For Medtronic, gave a lecture on thoracic endovascular evidence on 17.11.15. April 2015	Personal, specific, financial	Excluded from discussion of review questions which pertain to products manufactured by these companies.
Matt Thompson		Author/co-author on published departmental research papers on abdominal aortic aneurysm. April 2015	Specific, personal, non-financial	Declare And participate. Would have been excluded from discussion of review questions which include these papers.

2.0.3 DOC Cmte membership list

Committee membership list – AAA guideline Committee

Gillian Kitching	Radiographer, Manchester Royal Infirmary	None declared September 2015	N/A	N/A
Claire Martin	Vascular Nurse, Frimley Park Hospital	None declared September 2015	N/A	N/A

Date last reviewed: 21/05/2018