



Cochrane
Library

Cochrane Database of Systematic Reviews

Surgery for small asymptomatic abdominal aortic aneurysms (Review)

Ulug P, Powell JT, Martinez MAM, Ballard DJ, Filardo G

Ulug P, Powell JT, Martinez M-MA, Ballard DJ, Filardo G.
Surgery for small asymptomatic abdominal aortic aneurysms.
Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD001835.
DOI: [10.1002/14651858.CD001835.pub5](https://doi.org/10.1002/14651858.CD001835.pub5).

www.cochranelibrary.com

TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	4
BACKGROUND	8
OBJECTIVES	9
METHODS	9
Figure 1.	10
RESULTS	11
Figure 2.	12
Figure 3.	13
DISCUSSION	16
AUTHORS' CONCLUSIONS	18
ACKNOWLEDGEMENTS	18
REFERENCES	19
CHARACTERISTICS OF STUDIES	23
DATA AND ANALYSES	29
Analysis 1.1. Comparison 1: Early repair compared to ultrasound surveillance for small asymptomatic AAA, Outcome 1: Health service costs	29
APPENDICES	29
WHAT'S NEW	37
HISTORY	37
CONTRIBUTIONS OF AUTHORS	38
DECLARATIONS OF INTEREST	38
SOURCES OF SUPPORT	38
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	38
INDEX TERMS	39

[Intervention Review]

Surgery for small asymptomatic abdominal aortic aneurysms

Pinar Ulug¹, Janet T Powell¹, Melissa Ashley-Marie Martinez², David J Ballard³, Giovanni Filardo^{4,5}

¹Vascular Surgery Research Group, Imperial College London, London, UK. ²Department of Neurology, University of Arizona, Phoenix, AZ, USA. ³Department of Health Policy and Management, UNC Gillings School of Global Public Health, North Carolina, USA. ⁴Robbins Institute for Health Policy and Leadership, Baylor University, Waco, USA. ⁵Department of Statistical Science, Southern Methodist University, Dallas, USA

Contact: Janet T Powell, j.powell@imperial.ac.uk.**Editorial group:** Cochrane Vascular Group.**Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 7, 2020.**Citation:** Ulug P, Powell JT, Martinez M-MA, Ballard DJ, Filardo G. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database of Systematic Reviews* 2020, Issue 7. Art. No.: CD001835. DOI: [10.1002/14651858.CD001835.pub5](https://doi.org/10.1002/14651858.CD001835.pub5).

Copyright © 2020 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

An abdominal aortic aneurysm (AAA) is an abnormal ballooning of the major abdominal artery. Some AAAs present as emergencies and require surgery; others remain asymptomatic. Treatment of asymptomatic AAAs depends on many factors, but the size of the aneurysm is important, as risk of rupture increases with aneurysm size. Large asymptomatic AAAs (greater than 5.5 cm in diameter) are usually repaired surgically; very small AAAs (less than 4.0 cm diameter) are monitored with ultrasonography. Debate continues over the roles of early repair versus surveillance with repair on subsequent enlargement in people with asymptomatic AAAs of 4.0 cm to 5.5 cm diameter. This is the fourth update of the review first published in 1999.

Objectives

To compare mortality and costs, as well as quality of life and aneurysm rupture as secondary outcomes, following early surgical repair versus routine ultrasound surveillance in people with asymptomatic AAAs between 4.0 cm and 5.5 cm in diameter.

Search methods

The Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register, CENTRAL, MEDLINE, two other databases, and two trials registers to 10 July 2019. We handsearched conference proceedings and checked reference lists of relevant studies.

Selection criteria

We included randomised controlled trials where people with asymptomatic AAAs of 4.0 cm to 5.5 cm were randomly allocated to early repair or imaging-based surveillance at least every six months. Outcomes had to include mortality or survival.

Data collection and analysis

Three review authors independently extracted data, which were cross-checked by other team members. Outcomes were mortality, costs, quality of life, and aneurysm rupture. For mortality, we estimated risk ratios (RR) (endovascular aneurysm repair only), hazard ratios (HR) (open repair only), and 95% confidence intervals (CI) based on Mantel-Haenszel Chi² statistics at one and six years (open repair only) following randomisation.

Main results

We found no new studies for this update. Four trials with 3314 participants fulfilled the inclusion criteria. Two trials compared early open repair with surveillance and two trials compared early endovascular repair (EVAR) with surveillance. We used GRADE to assess the certainty

of the evidence for mortality and cost, which ranged from high to low. We downgraded the certainty in the evidence from high to moderate and low due to risk of bias concerns and imprecision (some outcomes were only reported by one study).

All four trials showed an early survival benefit in the surveillance group (due to 30-day operative mortality with repair) but no evidence of differences in long-term survival. One study compared early open repair with surveillance with an adjusted HR of 0.88 (95% CI 0.75 to 1.02, mean follow-up 10 years; HR 1.21, 95% CI 0.95 to 1.54, mean follow-up 4.9 years). Pooled analysis of participant-level data from the two trials comparing early open repair with surveillance (maximum follow-up seven to eight years) showed no evidence of a difference in survival (propensity score-adjusted HR 0.99, 95% CI 0.83 to 1.18; 2226 participants; high-certainty evidence). This lack of treatment effect did not vary to three years by AAA diameter ($P = 0.39$), participant age ($P = 0.61$), or for women (HR 0.84, 95% CI 0.62 to 1.11). Two studies compared EVAR with surveillance and there was no evidence of a survival benefit for early EVAR at 12 months (RR 1.92, 95% CI 0.73 to 5.06; 846 participants; low-certainty evidence).

Two trials reported costs. The mean UK health service costs per participant over the first 18 months after randomisation were higher in the open repair surgery than the surveillance group (GBP 4978 in the repair group versus GBP 3914 in the surveillance group; mean difference (MD) GBP 1064, 95% CI 796 to 1332; 1090 participants; moderate-certainty evidence). There was a similar difference after 12 years. The mean USA hospital costs for participants at six months after randomisation were higher in the EVAR group than in the surveillance group (USD 33,471 with repair versus USD 5520 with surveillance; MD USD 27,951, 95% CI 25,156 to 30,746; 614 participants; low-certainty evidence). After four years, there was no evidence of a difference in total medical costs between groups (USD 48,669 with repair versus USD 46,112 with surveillance; MD USD 2557, 95% CI -8043 to 13,156; 614 participants; low-certainty evidence).

All studies reported quality of life but used different assessment measurements and results were conflicting.

All four studies reported aneurysm rupture. There were very few ruptures reported in the trials of EVAR versus surveillance up to three years. In the trials of open surgery versus surveillance, there were ruptures to at least six years and there were more ruptures in the surveillance group, but most of these ruptures occurred in aneurysms that had exceeded the threshold for surgical repair.

Authors' conclusions

There was no evidence of an advantage to early repair for small AAA (4.0 cm to 5.5 cm), regardless of whether open repair or EVAR is used and, at least for open repair, regardless of patient age and AAA diameter. Thus, neither early open nor early EVAR of small AAAs is supported by currently available evidence. Long-term data from the two trials investigating EVAR are not available, so, we can only draw firm conclusions regarding outcomes after the first few years for open repair. Research regarding the risks related to and management of small AAAs in ethnic minorities and women is urgently needed, as data regarding these populations are lacking.

PLAIN LANGUAGE SUMMARY

Surgery for small abdominal aortic aneurysms that do not cause symptoms

Background

An aneurysm is a ballooning of an artery (blood vessel), which, in the case of an abdominal aortic aneurysm (AAA), occurs in the major artery in the abdomen (aorta). Ruptured AAAs cause death unless surgical repair is rapid, which is difficult to achieve. Surgery is recommended for people with aneurysms bigger than 5.5 cm in diameter or who have associated pain, to relieve symptoms and reduce the risk of rupture and death. However, there are risks with surgery. Surgical repair consists of re-lining the aorta with strong synthetic material, either by open surgery or endovascular repair (a minimally invasive keyhole procedure). Small asymptomatic (no symptoms) AAAs are at low risk of rupture and are monitored through regular imaging so they can be surgically repaired if they grow.

Key results

We found four well-conducted trials that randomised 3314 participants with small (diameter 4.0 cm to 5.5 cm) asymptomatic AAAs to early repair or regular, routine ultrasounds to check for aneurysm growth (surveillance) (search current to 10 July 2019). In the surveillance group, the aneurysm was repaired if it was enlarging, reached 5.5 cm in diameter, or became symptomatic. The trials showed an early survival benefit in the surveillance group because of the number of deaths within 30 days of surgery (operative mortality). The trials found no difference in long-term survival between early repair (open or endovascular) and surveillance over three to eight years of follow-up. After three years, about 31% of the participants randomised to surveillance eventually had the aneurysm repaired, rising to 75% after 12 years.

Two trials reported costs. For the first 18 months, costs were lower with surveillance than either open repair or endovascular repair. After four years, one trial found similar total medical costs for early endovascular repair and surveillance groups. After 12 years, another trial found lower hospital costs with surveillance than with open repair.

The four studies used different ways to measure quality of life and results were conflicting. The percentage of aneurysm ruptures in the surveillance group appeared higher in the trials using open repair but these have not restricted participants to those with aortic anatomy suitable for endovascular repair. Most ruptures were in people whose previous aneurysm diameter exceeded the threshold for surgical repair.

Reliability of the evidence

The methods within the studies using open repair were good and the reliability of the evidence was high to moderate for the two trials comparing open repair with surveillance. For the two trials comparing endovascular repair with surveillance, the risk of bias was unclear to high and the reliability of the evidence was low. The four trials suggest no overall advantage with early surgery for small AAAs (4.0 cm to 5.5 cm). The two trials comparing early open surgical repair to surveillance found this result holds true regardless of patient age or aneurysm size (within the range of 4.0 cm to 5.5 cm diameter). Furthermore, the two trials that focused on endovascular repair, also found no benefit over surveillance. Neither early open nor early endovascular repair of small AAAs is supported by the current evidence.

SUMMARY OF FINDINGS

Summary of findings 1. Early open repair compared to ultrasound surveillance for small asymptomatic abdominal aortic aneurysms

Early open repair compared to ultrasound surveillance for small asymptomatic AAA

Patient or population: small asymptomatic AAA

Setting: hospital

Intervention: early open repair (open surgery)

Comparison: ultrasound surveillance

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (RCTs)	Certainty of the evidence (GRADE)	Comments
	Risk with ultrasound surveillance	Risk with early repair				
Mortality (follow-up to 6 years)	Study population 0.28 (0.25 to 0.31)		HR 0.99 (CI 0.83 to 1.18) ^a	2226 (2 RCTs)	⊕⊕⊕⊕ High	No clear evidence to support a difference in survival between early open repair and surveillance.
Costs (per participant) (follow-up to 18 months)	GBP 3914	GBP 4978	MD GBP 1064 higher (796.32 higher to 1331.68 higher)	1090 (1 RCT)	⊕⊕⊕○ Moderate ^b	In UKSAT , the mean health service costs per participant were higher in the surgery than the surveillance group, and remained higher at 12-years of follow-up. This estimate accounted for semi-annual surveillance visits, aneurysm repair, and any associated follow-up.
QoL ^c (follow-up to 24 months)	See comment			2226 (2 RCTs)	—	In UKSAT , early-surgery survivors reported minor improvements in MOS-20 based current health perceptions and less negative changes in bodily pain (after 1 year). In ADAM , early-surgery and surveillance groups did not differ for most SF-36 scales, but the study authors reported that the early-surgery group had better scores for general health and lower scores for vitality (during the first 2 years); more participants became impotent after early repair compared with surveillance (after 1 year); maximum activity level declined more rapidly over time in the early-repair group.

<p>Aneurysm rupture (follow-up 6 years)</p>	<p>See comment</p>	<p>2226 (2 RCTs)</p>	<p>—</p>	<p>In UKSAT, there were 25 ruptures – at least 17 in the surveillance group vs ≥ 6 in the early-repair group (2 with emergency repairs, group unknown). 15/25 had an aneurysm diameter < 5.5 cm at previous follow-up.</p> <p>In ADAM, there were 13 ruptures – 11 in the surveillance group and 2 in the early-repair group (last diameter preceding rupture was not reported).</p>
---	--------------------	----------------------	----------	--

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AAA: abdominal aortic aneurysm; **CI:** confidence interval; **EVAR:** endovascular aneurysm repair; **GBP:** Great British pounds; **HR:** hazard ratio; **MD:** mean difference; **MOS-20:** 20-item Medical Outcomes Study; **QoL:** quality of life; **RCT:** randomised controlled trial; **SF-36:** 36-item Short Form.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

^aFrom pooled individual participant analysis (estimated from Figure 1 in [Filardo 2013](#)).

^bDowngraded one level for imprecision due to evidence from one trial only.

^cUKSAT measured QoL with the MOS-20 short-form, ADAM used the SF-36 form.

Summary of findings 2. Early endovascular repair compared to ultrasound surveillance for small asymptomatic abdominal aortic aneurysms

Early endovascular repair compared to ultrasound surveillance for small asymptomatic AAA

Patient or population: small asymptomatic AAA

Setting: hospital

Intervention: early endovascular repair (EVAR)

Comparison: ultrasound surveillance

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with ultrasound surveillance	Risk with early repair				

Mortality (follow-up at 1 year)	See comment		RR 1.92 (0.73 to 5.06) ^a	846 (2 RCTs)	⊕⊕○○ Low ^b	Surveillance group: 6 deaths, 408 alive, 126 lost to follow-up; EVAR: 12 deaths, 420 live, 116 lost to follow-up. Neither trial reached target sample size.
Costs (follow-up at 6 months)	USD 5520	USD 33,471	MD 27,951 USD higher (25,156 higher to 30,746 higher)	614 (1 RCT)	⊕⊕○○ Low ^c	Hospital costs were higher in the EVAR group at 6 months.
Costs (follow-up to 48 months)	USD 46,112	USD 48,669	MD 2557 USD higher (8043 lower to 13,156 higher)	614 (1 study)	⊕⊕○○ Low ^d	No clear evidence to support a difference in total medical costs between groups by 48 months.
QoL (follow-up to 24 months)	See comment			605 (2 RCTs)	—	CAESAR reported similar SF-36 scores between the groups in all domains (after 1 year). PIVOTAL reported no treatment-related differences in EQ-5D scores (24 months).
Aneurysm rupture (overall follow-up)	See comment			1088 (2 RCTs)	—	In CAESAR no ruptures observed for aneurysms < 5.5 cm diameter (2 ruptures in the surveillance group that exceeded repair threshold). PIVOTAL reported 1 rupture in the EVAR group and 2 ruptures in the surveillance group.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AAA: abdominal aortic aneurysm; **CI:** confidence interval; **EVAR:** endovascular aneurysm repair; **MD:** mean difference; **QoL:** quality of life; **RCT:** randomised controlled trial; **RR:** risk ratio; **USD:** United States dollars.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

^aAs no deaths occurred in the **CAESAR** surveillance group, summary data from Kaplan-Meier plots was used to pool data for deaths at one year (**CAESAR** and **PIVOTAL**).

- ^bDowngraded two levels because of risk of bias concerns (attrition bias as considerable participant loss to follow-up in both trials and neither trial reached target sample size). Loss to follow-up was 13% in [CAESAR](#) and 27% in [PIVOTAL](#) (balanced between randomised groups in each case).
- ^cDowngraded two levels because of risk of bias concerns (only 84% of participants were included, a proportion of costs were taken from Medicare fee schedules rather than direct costing, unclear attrition bias for cost outcome) and imprecision as data from [PIVOTAL](#) trial only.
- ^dDowngraded two levels because of risk of bias concerns (only 84% of participants were included, a proportion of costs were taken from Medicare fee schedules rather than direct costing, unclear attrition bias for cost outcome) and imprecision as data from [PIVOTAL](#) trial only.

BACKGROUND

Description of the condition

An aneurysm is an abnormal dilatation of an artery, the name coming from the Ancient Greek word 'ανεύρυσμα' meaning dilation. The most common arterial aneurysm is found in the infrarenal abdominal aorta of the older population, and known as an abdominal aortic aneurysm (AAA). The most common definition of an AAA is based on the diameter of the abdominal aorta: an abdominal aortic diameter of 3.0 cm or more (usually is more than two standard deviations above the mean diameter for men), is considered to be aneurysmal (Lederle 1988; Lindholt 1999). An alternative definition is that the maximum infrarenal aortic diameter is at least 1.5 times larger than the expected normal infrarenal aortic diameter or suprarenal aortic diameter (Kent 2014). This 1.5-fold diameter increase also provides a useful basis for the definition of AAA in women in whom the mean aortic diameter is smaller than in men (Rogers 2013).

The prevalence and incidence rates of AAA have decreased since the late 1990s, attributed partially to the decline in smoking (Sampson 2014; Sidloff 2014). Prevalence is negligible before the age of 55 to 60 years, and after this increases steadily with age (Sampson 2014). In 1990, the global prevalence in 75- to 79-year olds was 2423 per 100,000 population versus 2275 per 100,000 population in 2010; there also was a decline in incidence in both high- to low-middle income countries (Sampson 2014). At both times, the prevalence was highest in high-income countries and lowest in Latin America and Central Asia. Population screening studies offer the best evidence regarding the contemporary prevalence of AAA. Data from the Swedish Screening Programme showed the prevalence in 65-year old men is 1.7% with an additional 0.5% with an already known AAA (Svensjö 2011); 1.3% in the UK National Screening Programme (Jacomelli 2016); and 3.3% in a Danish screening programme (Grøndal 2015). AAAs are approximately four times less common in women versus men, with the pooled prevalence of AAA in women over 60 years of age at 0.7% (Ulug 2016).

The natural history of small AAA is progressive growth for most patients and the majority of cases have no symptoms (asymptomatic). For people with AAA of 3.0 to 5.5 cm in diameter 1. there is no difference in aneurysm growth rates between men and women (both on average 2.2 mm per year but increasing exponentially with AAA diameter); 2. smoking increases aneurysm growth rates by 0.35 mm per year (about 16%); and 3. diabetes is associated with decreased aneurysm growth rates by 0.51 mm per year (approximately 25% reduction) (Sweeting 2012). Randomised trials have not yet identified an effective treatment to limit AAA growth. The risk of AAA rupture is low for people with AAA less than 5.5 cm in diameter (Sweeting 2012); but, following rupture, mortality is very high at 40% to 50% if repaired (Bown 2002). However, about half do not even reach hospital alive giving an overall mortality of about 80%. In recent years, the use of endovascular repair (EVAR) (in suitable patients), rather than open surgical repair of ruptured AAAs, has been associated with lower mortality (Kontopodis 2020).

Smoking is the strongest risk factor for AAA, with an odds ratio greater than 3 for the association (Lederle 2000; Svensjö 2011), and higher in women (Stackelberg 2014). At a pathobiological level, the cause of AAA is multifactorial, with atherosclerosis and inflammation involved (Sakalihasan 2018).

Description of the intervention

For asymptomatic AAAs, management depends on the size of the aneurysm. Intervention should be considered at the point where the risk of AAA rupture outweighs the risk of AAA repair. Clinical guidelines now recommend repair in men after the diameter reaches 5.5 cm, although a lower threshold (5.0 cm) is recommended for women (Wanhainen 2019). For smaller aneurysms, regular surveillance using ultrasonography is recommended (Wanhainen 2019). There are two established forms of AAA repair. The first to be established was open surgical repair, with the AAA being exposed through either a transabdominal or a retroperitoneal incision. The aorta is clamped above and below the aneurysm, the aneurysm sac opened, and a synthetic inlay graft sewn into place proximally and distally, replacing the diseased aorta. The clamps are removed and the aneurysm sac is then wrapped around the graft before closure of the incision layers. The next to be established was endovascular aneurysm repair, where the compressed synthetic graft is delivered into place by catheter, usually from an artery in the groin, and is then placed into position above and below the AAA, expanded *in situ* and held in place using expandable stents and other methods. Other methods of AAA repair remain experimental.

How the intervention might work

The aim of both forms of intervention is to avoid the risk of AAA rupture and probable death, by relining the dilated segment of the aorta with a synthetic graft. There are several different reasons why this type of intervention might work. First, the thinned and weakened AAA wall is no longer directly subject to arterial pressures, with increased blood pressure being associated with increased risk of AAA rupture (Sweeting 2012). Second, the synthetic graft is stronger than the thinned and aneurysmal aortic wall and can resist the repetitive rise and fall of blood pressure as the pulse is conducted to the lower limbs. Third, the synthetic graft acts as a barrier between the blood and the diseased aorta, so that the biological interactions between blood and tissue which promote aortic degeneration are avoided. Nevertheless, interventions are associated with a risk of operative mortality and morbidity and these risks appear higher for open repair than EVAR (Powell 2017), and are higher in women than men (Ulug 2017). The risk of AAA rupture is not completely eradicated after repair, especially in the case of EVAR (Patel 2016).

Why it is important to do this review

The unclear area of care for small AAAs, resulting from the uncertainty surrounding the risk of rupture versus the risk of intervention and expansion rates identified by the RAND panel (Ballard 1992), highlighted the need for randomised controlled trials (RCT) comparing early surgery and selective surveillance as treatment options. This led to the design of the Aneurysm Detection And Management (ADAM) trial (ADAM), the United Kingdom Small Aneurysm Trial (UKSAT) (UKSAT), and the Canadian trial [pers comm], which used open surgery to perform the repairs. Later, when EVAR became available, the Comparison of surveillance versus Aortic Endografting for Small Aneurysm Repair (CAESAR), and the Positive Impact of endoVascular Options for Treating Aneurysms early (PIVOTAL) trials were conducted using EVAR as the surgical option. Most recently, pooling the participant-level data from the ADAM and UKSAT trials has enabled investigation of the possibility that age or AAA diameter might affect survival

differences between early repair and surveillance (Filardo 2013; Filardo 2014). As the current guidelines for management of AAA state, "[d]ebate remains for patients presenting with AAAs between 4.0 cm and 5.4 cm regarding the most appropriate role for either early treatment or surveillance and selective repair for those aneurysms that subsequently enlarge beyond 5.4 cm" (Chaikof 2018). It is now several years since these trials have reported and there have been advances in anaesthesia, intensive care and surgery that might reduce perioperative risks. The epidemiology of AAA is changing, with their onset being delayed and the mean age at AAA repair rising steadily. This update will assess whether there is any new evidence available to help guide management of small AAA.

OBJECTIVES

To compare mortality and costs, as well as quality of life and aneurysm rupture as secondary outcomes, following early surgical repair versus routine ultrasound surveillance in people with asymptomatic AAAs between 4.0 cm and 5.5 cm in diameter.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs in which participants were randomly allocated to early surgery versus ultrasound surveillance.

Types of participants

We included men or women of any age with an asymptomatic AAA. The aneurysm was restricted to the abdominal aorta distal to the renal arteries. The maximum antero-posterior diameter, measured using ultrasound or computed tomography (CT) scanning, must have been at least 4.0 cm and less than 5.5 cm. The aneurysm should have been non-tender on examination and the participant assessed as generally fit for surgery.

Types of interventions

We included studies involving repair of the aneurysm consisting of insertion of a prosthetic inlay graft either by open surgery (abdominal or retroperitoneal route) or by EVAR. Surveillance of the maximum antero-posterior diameter was to be performed regularly, with a maximum interval of six months. The timing of early surgery will vary with healthcare system, but should have been within three months of randomisation.

Types of outcome measures

Primary outcomes

The key outcome measures had to include at least one of the following.

- Mortality: death rate during a specified period of time following randomisation.
- Direct hospital costs from trial data: all hospital costs using specific survey or standard costing manuals which included inpatient stays, surgery, and outpatient attendances including ultrasound surveillance.

Secondary outcomes

- Quality of life (QoL): a standard generic measure using a validated instrument encompassing typical domains such as pain, health perceptions, mental health, and physical and social functioning.
- Rupture: rate of aneurysm rupture diagnosed at postmortem, operation, or certified as the underlying cause of death.
- Cause of death: mortality by underlying cause of death according to the International Classification of Diseases.
- Operative mortality: measured as 30-day or 'in hospital' mortality, or both.

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist conducted systematic searches of the following databases for RCTs and controlled clinical trials without language, publication year, or publication status restrictions:

- Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web; searched 10 July 2019);
- Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Register of Studies Online (CRSO; 2019, Issue 6);
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily, and Ovid MEDLINE) (searched from 1 January 2017 to 10 July 2019);
- Embase Ovid (searched from 1 January 2017 to 10 July 2019);
- CINAHL EBSCO (searched from 1 January 2017 to 10 July 2019);
- AMED Ovid (searched from 1 January 2017 to 10 July 2019).

The Information Specialist modelled search strategies for other databases on the search strategy designed for CENTRAL. Where appropriate, they were combined with adaptations of the highly sensitive search strategy designed by Cochrane for identifying RCTs and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6; Lefebvre 2011). Search strategies for major databases are provided in [Appendix 1](#).

The Information Specialist searched the following trials registries on 10 July 2019:

- World Health Organization International Clinical Trials Registry Platform (who.int/trialsearch);
- ClinicalTrials.gov (clinicaltrials.gov).

Searching other resources

We checked the reference lists of relevant studies. We supplemented the searches with information from experts in the field and from handsearches of the following conference proceedings:

- Society for Vascular Surgery Annual Meeting (through to 15 November 2019);
- European Society for Vascular Surgery Annual Meeting (through to 15 November 2019).

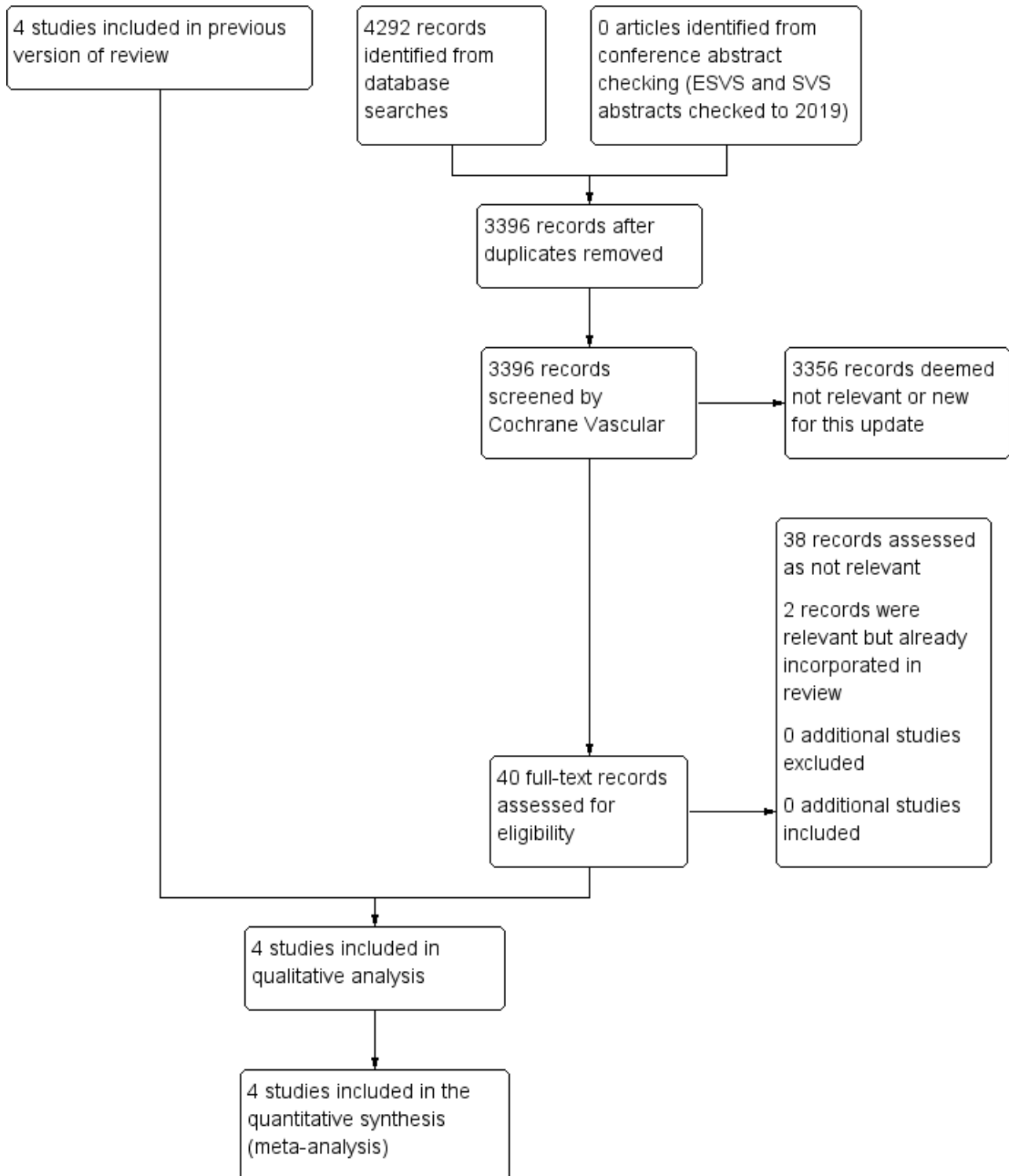
Data collection and analysis

Selection of studies

We assessed the articles identified by the searches using Covidence software (covidence.org). Initial screening was carried out to remove obviously non-relevant articles. Remaining articles were

then assessed independently in duplicate (JTP and PU) according to the [Criteria for considering studies for this review](#). We listed all studies excluded after full-text assessment and their reasons for exclusion in the [Characteristics of excluded studies](#) table. We constructed a PRISMA diagram to illustrate the study selection process ([Figure 1](#)). Any disagreements were resolved by discussion.

Figure 1. Study flow diagram.



Data extraction and management

For this update, two review authors (JTP and PU) cross-checked the previous data extractions and re-extracted data from the two trials comparing EVAR with surveillance. Previously, two review authors (GF and MAMM) abstracted the data, which another team member (DJB) cross-checked. The data collected on each trial included information on the participants (age and sex distribution, aneurysm size), the interventions (graft type, frequency of ultrasound surveillance), and the outcomes (as specified in [Criteria for considering studies for this review](#)).

Assessment of risk of bias in included studies

We discussed each of the trials and agreed on their inclusion or exclusion based on the adequacy of the random allocation, attainment of adequate sample size, and completeness of follow-up. The nature of the interventions did not permit participants or observers to be blinded, and so this lack did not disqualify trials from inclusion. In addition, we assessed the risk of bias of the included studies using the 'Risk of bias' tool described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The following domains were assessed and judged to be at low risk of bias, high risk of bias, or unclear risk of bias: selection bias, performance and detection bias, attrition bias, reporting bias, and other sources of bias.

Measures of treatment effect

We estimated risk ratios (RR) (EVAR only), hazard ratios (HR) (open repair only), and 95% confidence intervals (CIs) based on the Mantel-Haenszel Chi² statistic to assess the efficacy of the intervention at one year (endovascular and open repair) and six years (open repair only) following randomisation. We estimated the HRs reported for open repair from a participant-level meta-analysis that was executed to summarise evidence from the UKSAT and ADAM trials (Filardo 2013; Filardo 2014).

Unit of analysis issues

We used each participant with an AAA of diameter 4.0 cm to 5.5 cm who received early surgical repair versus routine ultrasound surveillance as the unit of analysis.

Dealing with missing data

None of the included studies used single or multiple imputation procedures to deal with missing data. Although the incidence of missing data in the trials comparing open repair with surveillance was very low, the incidence of missing data in the trials comparing EVAR with surveillance was moderate, with 24% of participants lost to follow-up for mortality and clinical events by 12 months of randomisation.

Assessment of heterogeneity

We assessed heterogeneity using the I² statistic. We considered I² values of 50% or greater to indicate substantial heterogeneity. Moreover, we used a Chi² test to assess heterogeneity in the participant-level meta-analysis we executed to summarise evidence from the UKSAT and ADAM trials. If we identified heterogeneity, we explored reasons for it.

Assessment of reporting biases

We intended to use funnel plots for publication bias. However, we did not test for funnel plot asymmetry as the power of the test is low when fewer than 10 trials are included in the analysis (Page 2019). All included studies were assessed for selective reporting bias and published findings on the main study outcome of this review.

Data synthesis

We estimated RRs (EVAR only), HRs (open repair only), and 95% CIs based on Mantel-Haenszel Chi² statistic. We calculated the RR summary estimates by employing a fixed-effect model meta-analyses approach. We estimated HRs from a participant-level meta-analysis that we executed to summarise evidence from the UKSAT and ADAM trials (Filardo 2013; Filardo 2014).

Subgroup analysis and investigation of heterogeneity

We analysed and presented separately studies comparing early EVAR to surveillance and studies comparing early open repair to surveillance. Given the differences in surgical techniques, we did not estimate the overall effect associated with early repair irrespective of the type of surgery compared to surveillance. Accordingly, we executed tests for heterogeneity for each meta-analysis, one reporting on early EVAR versus surveillance and one reporting on early open repair versus surveillance.

Sensitivity analysis

We included all relevant published studies in this review. We did not carry out a sensitivity analysis due to the small number of included studies in each outcome.

Summary of findings and assessment of the certainty of the evidence

We prepared a 'Summary of findings' table for each of the comparisons 'Early open repair compared to ultrasound surveillance for small asymptomatic AAA' and 'Early endovascular repair compared to ultrasound surveillance for small asymptomatic AAA' to present the main findings from the review. We included the outcomes of mortality, costs, QoL, and aneurysm rupture. See [Summary of findings 1](#) and [Summary of findings 2](#). We used GRADEprofiler software to create the tables (GRADEpro GDT). The GRADE criteria were used to rank the certainty of the evidence for each outcome based on risk of bias, inconsistency, indirectness, imprecision, and publication bias (Guyatt 2008). We have provided a description for each step to downgrade the certainty of the evidence.

RESULTS

Description of studies

See [Figure 1](#).

Results of the search

We identified four RCTs from the electronic searches (ADAM; CAESAR; PIVOTAL; UKSAT), and one from personal communication (Canadian trial [pers comm]).

Included studies

See [Characteristics of included studies](#) table. We included four RCTs involving 3314 participants, which fulfilled the criteria for

consideration in the present review (ADAM; CAESAR; PIVOTAL; UKSAT). We used results from analyses of pooled participant-level data from the UKSAT and ADAM trials in the comparison of early open repair to selective surveillance (Filardo 2013; Filardo 2014).

All four trials enrolled participants with small (4.0 cm to 5.5 cm) non-tender, asymptomatic AAAs who were considered fit for surgery. The trials excluded participants who were considered unfit for surgery, had symptoms associated with the aneurysm, were unable to attend the follow-up visit, or were unable to give informed consent. The ADAM study further excluded people who had received a revascularisation procedure within three months of enrolment, had a myocardial infarction within six months of enrolment, or were expected to survive less than five years because of invasive cancer or another life-threatening disease. The CAESAR trial, besides excluding people not anatomically suitable for EVAR, further excluded people who had severe comorbidities or a suprarenal or thoracic aorta of 4.0 cm or greater in diameter, or that needed urgent repair. The PIVOTAL study further excluded people who had had an abdominal or thoracic repair, an aneurysm originating 1.0 cm or less from the most distal main renal artery, life expectancy of less than three years, Society for Vascular Surgery score greater than two with the exception of age and controlled hypertension, baseline serum creatinine level greater than 2.5 mg/dL, or when the participant did not meet the indications for use of the endograft device. Costs were investigated for PIVOTAL in a study within a study (PIVOTAL Economic Study), involving the same participants, in parallel with the PIVOTAL trial.

Age inclusion criteria were 50 to 79 years (ADAM), 50 to 79 years (CAESAR), 40 to 90 years (PIVOTAL), and 60 to 76 years (UKSAT). Despite the relatively wider age range eligible for inclusion in the ADAM, CAESAR, and PIVOTAL trials, the majority of the participants fell within the same age range as the UKSAT trial: 88% (ADAM), approximately 70% (CAESAR), and approximately 70% (PIVOTAL). This is perhaps unsurprising given that AAA prevalence is much higher in older age groups.

Study designs were similar, with participants randomly allocated to either early surgery or selective surveillance. All trials except UKSAT recommended surgery within one month of randomisation; UKSAT recommended surgery within three months of randomisation. In the four trials, most participants assigned to the early-surgery group received endovascular or standard open repair within six weeks of randomisation. Likewise, in all four trials, participants

assigned to selective surveillance were followed, without repair, at regular intervals (at minimum once every six months), and surgery was performed within six weeks if 1. the aneurysm reached 5.5 cm in diameter; or 2. the aneurysm enlarged by a minimum of 0.7 cm in six months (ADAM), 1.0 cm in one year (UKSAT), greater than 1.0 cm in one year (CAESAR), or a minimum of 0.5 cm between two six-month assessments (PIVOTAL); or 3. the aneurysm became symptomatic. The primary outcomes of all trials was mortality. Only PIVOTAL and UKSAT measure cost, and all trials assess QoL using a variety of validated questionnaires.

Adherence to assigned treatment was very high across the four trials (UKSAT had the lowest adherence rate at 92.6%), and at the end of the trials, mortality status was ascertained in 100% (ADAM; UKSAT) and in 50% of participants (CAESAR; PIVOTAL). Approximately 62% (ADAM), 48% (CAESAR), 31% (PIVOTAL), and 75% (UKSAT) of the participants in the selective-surveillance group eventually underwent aneurysm repair.

In total, 3314 participants with asymptomatic AAAs of antero-posterior diameter 4.0 cm to 5.5 cm were randomised to early repair (1680 participants: 569 in ADAM, 182 in CAESAR, 366 in PIVOTAL, and 563 in UKSAT; 50.7%) or routine ultrasound or CT surveillance every six months (three months if diameter 5.0 cm to 5.5 cm in ADAM and UKSAT) (1634 participants: 567 in ADAM, 178 in CAESAR, 362 in PIVOTAL, and 527 in UKSAT; 49.3%). The primary outcome of the included studies was all-cause mortality and secondary outcomes were AAA-related death, morbidity, and QoL. Follow-up for vital status ranged from 3.5 to 8.0 years (mean 4.9 years) in the ADAM trial; median 32.4 months (interquartile range (IQR) 21.0 to 44.1) in the early EVAR group and 30.9 (IQR 18.3 to 45.3) in the surveillance group in the CAESAR trial; 20 (standard deviation (SD) 12 months; range 0 to 41 months) in the PIVOTAL trial; and up to 12 years (range 8 to 12 years; mean 10 years) in the UKSAT trial.

Excluded studies

We excluded one trial that did not fulfil the criteria for consideration (Canadian trial [pers comm]). This study ended early because of inadequate recruitment and was not sufficiently complete for inclusion in this review. See Characteristics of excluded studies table.

Risk of bias in included studies

See Figure 2 and Figure 3 for the 'Risk of bias' summary.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item for the outcomes of mortality and cost presented as percentages across all included studies.

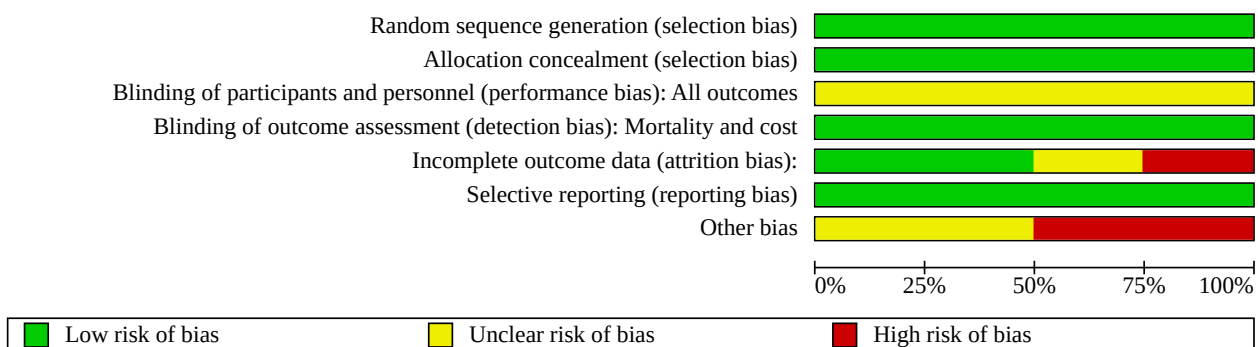


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): Mortality and cost	Incomplete outcome data (attrition bias):	Selective reporting (reporting bias)	Other bias
ADAM	+	+	?	+	+	+	?
CAESAR	+	+	?	+	?	+	-
PIVOTAL	+	+	?	+	-	+	-
UKSAT	+	+	?	+	+	+	?

Allocation

The methods of randomisation of the included studies ensured good balance across study groups as they all used independent

automated computer randomisation, either by telephone or the Internet (ADAM; CAESAR; PIVOTAL; UKSAT). Adherence to assigned treatment was high, with the lowest adherence rate across the four

trials at 92.6% ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)). Therefore, risk of selection bias was low.

Blinding

The nature of the interventions did not permit the blinding of participants or observers to which treatment group they were in, so we judged all studies at unclear risk of performance bias. For the outcome of mortality, vital status was assessed using the same methodology for both participants in the early-repair group and participants in the routine ultrasound surveillance group in each trial and near complete results were available as a result of low lost-to-follow-up rate. Therefore, any misclassification which might have occurred would have been non-differential and its impact on the trial results would be limited. So, for the main outcome of mortality, the risk of detection bias was low in all studies ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)). The risk of bias was low for costs ([PIVOTAL](#); [UKSAT](#)). However, as QoL was patient reported; not complete in any of the studies; and reported using a variety of validated questionnaires, the risk for detection bias was unclear for this outcome ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)).

Incomplete outcome data

We ascertained mortality status to six years in 100% of participants in [ADAM](#) and [UKSAT](#). The loss to clinical follow-up was low; so we judged the risk of attrition bias in these trials as low. The attrition bias for [CAESAR](#) and [PIVOTAL](#) was notable for both mortality and clinical follow-up. In [CAESAR](#), within 12 months of randomisation, 13% of participants overall were lost to follow-up for both mortality and clinical follow-up (21/182 participants in the endovascular group and 24/178 participants in the surveillance group), so we judged the risk of attrition bias as unclear. In [PIVOTAL](#), within 12 months of randomisation 27% of participants overall were lost to follow-up (similar in both randomised groups, 95/366 participants in the endovascular group and 102/362 participants in the surveillance group), so we judged the risk of attrition bias as high for mortality.

The health economic analysis of the [PIVOTAL](#) trial that was undertaken separately by the Duke Clinical Research Institute only included 614/728 participants randomised ([Characteristics of included studies](#) table). The reason for this was due to not all patients being treated at hospitals that generated detailed patient bills. Missing information was balanced between groups, so this was judged to represent an unclear risk of bias for the outcome of cost.

Selective reporting

All included studies published findings on the primary outcome of mortality and reported on the outcomes preplanned in their protocols ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)). Risk of selective reporting bias was low ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)).

Other potential sources of bias

The [CAESAR](#) trial was originally funded by Cook Medical. In December 2006, during the enrolment phase of the trial, Cook Medical withdrew sponsorship, and the trial continued as full spontaneous research. According to the [CAESAR](#) study team, the design, data collection, data analysis, data interpretation, and writing of reports regarding the trial were at all times conducted independently from the sponsor. However, we could not exclude a possible conflict of interest in the [CAESAR](#) trial given that the

sponsor of the study, Cook Medical, withdrew and so this was judged at high risk of bias. The [PIVOTAL](#) trial was sponsored by Medtronic Vascular, who hold the [PIVOTAL](#) trial study database. Two members of the [PIVOTAL](#) research team who received funding from, and were consultants for, Medtronic declared conflicts of interest; a third member of the [PIVOTAL](#) research team had previously been a consultant for Medtronic and so this was judged at high risk of bias. The Vascular Surgery Academic Coordinating Center of the Cleveland Clinic was independently responsible for the conduct of the [PIVOTAL](#) trial and its analysis. Also, neither [CAESAR](#) or [PIVOTAL](#) reached their recruitment target. Other potential sources of bias for the outcomes of mortality and cost for remaining trials included in this review were low ([ADAM](#); [UKSAT](#)). In all of the trials potential other sources of bias for QoL outcomes were unclear ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)).

Effects of interventions

See: [Summary of findings 1](#) Early open repair compared to ultrasound surveillance for small asymptomatic abdominal aortic aneurysms; [Summary of findings 2](#) Early endovascular repair compared to ultrasound surveillance for small asymptomatic abdominal aortic aneurysms

Open repair compared to surveillance

Mortality

Two studies compared early open repair with surveillance ([ADAM](#); [UKSAT](#)). In both studies, the 30-day elective operative mortality in the early-surgery group ([UKSAT](#): 5.5%; [ADAM](#): 2.1%) led to an early mortality disadvantage in this study group. However, in both studies after a mean follow-up of three years, there was no difference in mortality between groups.

In the [UKSAT](#) study, the long-term mortality (follow-up range: 8 to 12 years, mean 10 years) was 63.9% in the early-surgery group and 67.3% in the surveillance group. The [UKSAT](#) investigators found no clear evidence to support a difference in long-term survival between the early-surgery and surveillance groups (adjusted HR 0.88, 95% CI 0.75 to 1.02). However, the HRs were non-proportional among study groups, as revealed by the survival curves crossing approximately at the three-year mark; the risk associated with operative mortality in the early-repair group showed an initial survival disadvantage for this group compared to the selective-surveillance group. The estimated adjusted HRs were in the direction of greater benefit of early surgery for younger participants and those with larger aneurysms, but none of the tests for interaction showed a clear effect.

At the end of the [ADAM](#) trial follow-up (range 3.5 to 8.0 years, mean 4.9 years), the observed mortality in the early-repair group was 25.1% and in the selective-surveillance group was 21.5%. However, as in the [UKSAT](#) study, there was no clear evidence of a difference in long-term survival between study groups (adjusted HR 1.21, 95% CI 0.95 to 1.54). The study authors did not report violation of the proportional hazard assumption. Study results showed a possible modification of effect with age and AAA size but none of the tests for interaction were reported as significant. Moreover, the analysis of the pooled participant-level data from the [ADAM](#) and [UKSAT](#) trials demonstrated no clear difference in survival between early open repair and surveillance, regardless of participant age or aneurysm diameter ([Filardo 2013](#); [Filardo 2014](#)). In women only, combined results for survival to three years showed no clear

difference between study groups (HR 0.84, 95% CI 0.62 to 1.11). There were too few women enrolled for any longer-term analyses (Filardo 2014 and unpublished data).

We performed meta-analyses of mortality up to six years to assess the effect of open repair versus surveillance (ADAM; UKSAT). The analysis of pooled participant-level data from the UKSAT and ADAM trials conducted to assess mortality up to six years found no clear evidence to support a difference in survival between early open repair and surveillance (HR 0.99, 95% CI 0.83 to 1.18; 2 trials, 2226 participants; high-certainty evidence; Summary of findings 1). This analysis is reported in Filardo 2013 and Filardo 2014. Additional analyses conducted using this pooled data set showed this lack of a clear difference in survival persisted regardless of participant age or AAA diameter within the range of 4.0 cm to 5.5 cm (Filardo 2013; Filardo 2014).

Costs

For open repair compared to surveillance, only UKSAT provided information on costs. There were no cost data for ADAM.

In UKSAT, the mean health service costs per participant over the four to six years' follow-up period postrandomisation were higher in the surgery than the surveillance group (GBP 4978 with surgery versus GBP 3914 with surveillance; mean difference (MD) GBP 1064, 95% CI 796 to 1332; 1090 participants; moderate-certainty evidence; Analysis 1.1). This estimate accounted for semi-annual surveillance visits, aneurysm repair, and any associated follow-up. For example, if surveillance was conducted only once per annum, the mean cost difference in favour of surveillance widened to GBP 1256 (95% CI 990 to 1522). A 25% increase in cost of aneurysm repair further increased the difference to GBP 1636 (95% CI 1340 to 1932). After 12 years, the resource consequences of early surgery had increased costs by GBP 1326 (95% CI 960 to 1692).

Quality of life

Both studies comparing open repair with surveillance reported QoL using different validated questionnaires (ADAM; UKSAT).

UKSAT assessed QoL using the 20-item Medical Outcomes Study short-form. At the time of randomisation, QoL was similar in the two groups, but early-surgery participants reported minor improvements in current health perceptions and less negative changes in bodily pain at one year after randomisation.

ADAM assessed QoL using the 36-item Short Form (SF-36) form. The early-surgery and surveillance groups did not differ for most SF-36 scales at most of the time points measured, but the study authors reported that the early-surgery group had better scores for general health, particularly during the first two years following randomisation, but had lower scores for vitality. ADAM reported that more participants became impotent after randomisation to early repair compared with surveillance, a difference that only became apparent more than one year after randomisation. In ADAM, maximum activity level declined more rapidly over time in the early-repair group.

Aneurysm rupture

In UKSAT, during six years of follow-up there were 25 ruptures, of which two participants survived. It is not clear how the ruptures were distributed between the randomised groups, though at least 17 ruptures occurred in the surveillance group and at least six

ruptures occurred in the early-surgery group. Of these 25 aneurysm ruptures, only 15 ruptures had occurred in participants with aneurysms of less than 5.5 cm in diameter. In UKSAT, as in other studies, the rupture rate was almost four times higher in women compared with men (Sweeting 2012).

In ADAM, over a period of similar follow-up, there were 13 ruptures, of whom 11 were in the surveillance group and two in the early-surgery group. Of the 11 participants in the surveillance group, there were seven deaths, and in the early-surgery group there was one death. The last diameter before rupture was not recorded, therefore, we were unable to assimilate the data from two studies.

Other outcomes

30-day operative mortality is reported under 'Mortality'.

Endovascular repair compared to surveillance

Mortality

Two studies compared early EVAR with surveillance (CAESAR; PIVOTAL). In both trials, the 30-day operative mortality in the early-repair group (CAESAR: 0.6%; PIVOTAL: 0.3%) led to an early disadvantage in terms of survival in this study group. The lower 30-day mortality rate observed in the CAESAR and PIVOTAL studies, compared to the UKSAT and ADAM trials, was expected due to the use of EVAR.

In CAESAR, one year after randomisation, there were no deaths in the surveillance group, and four deaths in the endovascular group. At the end of the CAESAR trial follow-up (maximum: 54 months, median: 32.4 months), the estimated all-cause mortality for the early-repair group was 14.5% and for the selective-surveillance group was 10.1%. However, there was no clear evidence of a difference between the two groups for long-term survival (HR 0.76, 95% CI 0.30 to 1.93). The authors did not report a violation of the proportional hazard assumption.

In PIVOTAL, one year after randomisation, there were six deaths in the surveillance group, and eight deaths in the endovascular group. At the end of the PIVOTAL trial follow-up (range 0 to 41 months, mean 20 (SD 12 months)), the estimated all-cause mortality for both groups was 4.1%, and long-term survival showed no clear difference between groups (HR 1.01, 95% CI 0.49 to 2.07). The authors reported no evidence of non-proportional hazards between groups over time.

In both CAESAR and PIVOTAL trials, there was increasing loss to follow-up over time. Since at 12 months after randomisation there were no deaths in the surveillance group of CAESAR, the number of deaths at later time points were unclear and no formal meta-analysis was possible. As no participant-level data were available, we have used summary data from Kaplan-Meier plots to pool data for deaths at 12 months (early EVAR: 12 deaths among 432 participants; surveillance group: 6 deaths among 414 participants), which showed no clear evidence of a difference in survival (RR 1.92, 95% CI 0.73 to 5.06; 2 trials, 846 participants; low-certainty evidence).

Costs

For the EVAR versus surveillance comparison, the PIVOTAL Economic Study investigated costs (Eisenstein 2013), which is a

study within [PIVOTAL](#) using the same participants. No cost data were available for [CAESAR](#).

The [PIVOTAL](#) Economic Study reported higher total medical costs (including AAA-related clinic visits and imaging studies, AAA repair (endovascular device or open surgery), and other inpatient care (including secondary procedures, emergency department visits, other hospitalisations, and rehabilitation and skilled nursing facility care) in the early EVAR group at six months (USD 33,471 in the EVAR group versus USD 5520 in the surveillance group; MD USD 27,951, 95% CI 25,156 to 30,746; 1 trial, 614 participants; low-certainty evidence). However, there were greater total medical costs in the surveillance group in months 7 to 48 (USD 40,592 versus USD 15,197 in the EVAR group; MD USD 25,395, 95% CI 15,184 to 35,605). These differences balanced out across the full 48 months studied such that there was no clear evidence to support a difference in total medical costs between the two interventions (USD 48,669 in the EVAR group versus USD 46,112 in the surveillance group; MD USD 2557, 95% CI -8043 to 13,156; 1 trial, 614 participants; low-certainty evidence).

Quality of life

Both studies that compared EVAR with surveillance reported QoL using different measurements ([CAESAR](#); [PIVOTAL](#)).

[CAESAR](#) assessed QoL using the SF-36 form and reported comparable scores in the early EVAR and surveillance groups at randomisation. At six months, the total SF-36 and the physical and mental domain scores had all increased with respect to baseline in the early-repair group, while participants in the surveillance group scored lower. However, by one year after randomisation, the two groups had similar SF-36 scores in all domains.

The [PIVOTAL](#) Economic Study assessed QoL between the early EVAR and surveillance groups using the EQ-5D instrument, and reported results from 710 participants who completed the EQ-5D instrument at baseline, 12, and 24 months. There were no clear differences between the intervention groups at baseline on any of the EQ-5D domains, and no treatment-related differences in either the QoL domains or the utility score at 12 or 24 months' follow-up. Participants in the EVAR group reported lower visual analogue scale scores at 12 months, but this difference did not persist at 24 months.

Aneurysm rupture

Both [CAESAR](#) and [PIVOTAL](#) trials selected participants according to aneurysm morphology criteria, which may have influenced the rupture rates ([Powell 2008](#)). In addition, the selection criteria in the [PIVOTAL](#) trial included only people with 4 cm to 4.9 cm diameter aneurysms. Both trials provided three years of participant follow-up data.

Aneurysm ruptures were not different between the groups in either trial. There were two aneurysm ruptures in the surveillance arm of the [CAESAR](#) trial, both in participants in whom the aneurysm exceeded the repair threshold. In the [PIVOTAL](#) trial, there was one rupture in the EVAR group and two in the surveillance group.

Other outcomes

Aneurysm-related mortality (elective mortality and rupture-related mortality) was low and not different between the groups in both the [CAESAR](#) and [PIVOTAL](#) trials. The [CAESAR](#) trial also reported

that 4/182 participants had conversion to open repair, 16.4% participants in the surveillance group had lost suitability for EVAR by three years, re-interventions occurred in 10 participants in the EVAR group but no participant in the surveillance group, and that the mean aneurysm growth rate was less than 2 mm/year.

DISCUSSION

The results from the four included trials suggest no overall advantage to early repair for small AAA ([ADAM](#); [CAESAR](#); [PIVOTAL](#); [UKSAT](#)). Furthermore, the more recent trials focused on the efficacy of EVAR and found no benefit ([CAESAR](#); [PIVOTAL](#)), and analysis of the pooled participant-level data from the earlier open-repair trials showed that the lack of any treatment-related survival benefit was consistent across all participant ages and aneurysm diameters within the small AAA range ([Filardo 2013](#); [Filardo 2014](#)). Thus, the currently available evidence supports neither early open nor early EVAR of small AAAs. Our results affirm the Society for Vascular Surgery and the European Society for Vascular Surgery's strong recommendation in favour of surveillance for people with a fusiform AAA of 4.0 cm to 5.4 cm ([Chaikof 2018](#)). While the development of endovascular technology offers an improvement in operative mortality compared to open surgery and better short-term survival in general ([Lederle 2009](#); [Prinssen 2004](#); [United Kingdom EVAR Trial Investigators 2010](#)), its efficacy is limited by high rates of re-operation for complications unique to EVAR over longer follow-up, including stent migration, stent wire fracture, metal fatigue, graft insertion site problems, and endoleak ([Becquemin 2011](#); [De Bruin 2010](#); [EVAR Trial Participants 2005](#); [Wilt 2006](#)). For small AAA in particular, early EVAR does not appear to offer advantages compared to surveillance (see [Analysis 1.1](#)), and its use could expose patients to unnecessary risk and ultimately higher healthcare costs ([Ballard 2012](#)). Likewise, [Analysis 1.1](#) shows that early open repair offers no better outcomes compared to surveillance for people with small AAAs.

However, it should be kept in mind that the results presented are derived from RCT settings which, particularly for the surveillance group, may not reflect current practice in terms of either the resources available for care or the patient compliance with follow-up schedules that can be expected. Thus, while we can conclude that there is no clear evidence to support a difference in *efficacy* between early repair and surveillance in small AAAs, the question regarding *effectiveness* requires further investigation, particularly for small AAAs approaching the 5.5 cm cut-off, where one meta-analysis suggested an eight-month surveillance interval is needed to adequately manage the risk of expansion past 5.5 cm ([Bown 2013](#)), and poor compliance with surveillance could move patients' risks towards greater benefit with early repair. As there is currently no registry containing surveillance data for small AAAs, a large, prospective, population-based comparative effectiveness study is needed ([Ballard 2012](#)).

Future research should include investigating the possible differences in QoL between the various management strategies available for small AAA, taking into account that these might differ by age, and the evidence that moderate exercise (rather than the strict limitation on physical activity previously advised for people with unrepaired small AAA) benefits patients under surveillance ([Myers 2010](#); [Tew 2012](#)).

The apparently lower risks of rupture associated with aneurysms morphologically suitable for EVAR and the apparently higher rates

of rupture in women need to be elucidated. There is some evidence that these risks differ in men and women with AAA (Abedi 2009; Lo 2013; McPhee 2007; Mehta 2012; UKSAT), but studies to date have generally included very few women, and, in the absence of sufficient data to rigorously examine the competing risks and the timing of intervention in women (Rudaranchana 2013), recommendations for management in women remain a 'best guess' guided largely by the evidence available for men.

Establishing optimal treatment guidelines for people with small AAAs becomes even more relevant to improving public health and patient outcomes when the likelihood of increased AAA screening in the future is taken into account. The evidence from three randomised population screening trials, summarised in one Cochrane Review, shows the benefits of screening older men for AAA (Cosford 2007). A national screening programme for all men aged 65 years and older runs in the UK (Jacomelli 2016; Oliver-Williams 2019), and the U.S. Preventive Services Task Force (USPSTF) recommends AAA screening for men aged 65 to 75 years who have ever smoked (US Preventive Task Force). The Society for Vascular Surgery has also recommended screening of all men aged 60 to 85 years for AAA; women aged 60 to 85 years with cardiovascular risk factors; and men and women aged 50 years and older with a family history of AAA (Kent 2004). These recommendations are based on evidence that screening for AAA and repair of large AAAs (5.5 cm or more in diameter) leads to decreased AAA-specific mortality. However, the USPSTF also indicates that there is possible evidence of harms of screening and early treatment, including an increased number of surgeries with associated clinically significant morbidity and mortality, and short-term psychological harms (US Preventive Task Force). These harms are of most concern for people with aneurysms in the 4.0 cm to 5.5 cm range, for whom current treatment guidelines are ambiguous.

Summary of main results

See [Summary of findings 1](#) and [Summary of findings 2](#). Findings from this review indicate that there was no survival advantage with early repair compared to selective surveillance in people with asymptomatic aneurysms sized 4.0 cm to 5.5 cm in diameter. Results from the UKSAT, ADAM, CAESAR, and PIVOTAL trials showed no clear evidence to support a difference in survival between the study treatment groups; the analysis of the pooled participant-level data from the ADAM and UKSAT studies showed that this held true regardless of participant age or AAA diameter for open repair (Filardo 2013; Filardo 2014). In the absence of long-term, participant-level data for the PIVOTAL and CAESAR trials, we cannot draw firm conclusions about the long-term effects of early EVAR. However, findings to date suggest no advantage to early surgery for small AAA, and the currently available evidence supports neither early open nor early EVAR of small AAAs. The Society for Vascular Surgery and the European Society for Vascular Surgery guidelines strongly recommend surveillance for men with a fusiform AAA of less than 5.5 cm diameter but suggest a reduced diameter threshold for elective repair in women (Chaikof 2018; Wanhainen 2019). The UK National Institute for Health and Care Excellence (NICE) recommends a diameter threshold for elective repair of 5.5 cm in both men and women (NICE 2020).

Overall completeness and applicability of evidence

This review was based on all trials to date that were suitable for inclusion. However, one limitation of the present review is the low

proportion of women and non-white races in the trials. The gender imbalance is exacerbated by the late onset of the disease in women and by the approximately three times higher prevalence of AAA in men than in women, and that black race has a strong negative association with AAA (Lederle 1997; Lederle 2000). Thus, while it is indisputable that the study results might be difficult to generalise to women and non-white men, this review provides critical data that can benefit the population with the highest prevalence of AAA and, therefore, the vast majority of people with AAA. Future research regarding the management of small AAA should focus on ethnic minorities and women, as data regarding these populations are lacking. In particular, future research should assess whether the AAA-management recommendations, which are based on studies in which women are under-represented, are applicable to women given their smaller body frames and, therefore, smaller abdominal aortas. This is critical given the evidence that risk of rupture, risks associated with repair, and progression of disease may differ between men and women (Abedi 2009; Brown 2003; Lo 2013; McPhee 2007; Mehta 2012; RESCAN Collaborators 2013; UKSAT). Another limitation of the evidence is that, although cost data can be summarised, there are no summary data for cost-effectiveness.

Quality of the evidence

The UKSAT, ADAM, CAESAR, and PIVOTAL trials were very similar in design and, more importantly, were all well-conducted studies. All relevant studies were identified and included in this review. Moreover, all relevant data were obtained. In summary, bias was a concern for the CAESAR and PIVOTAL trials due to considerable loss to follow-up of participants within 12 months, the inability of either trial to reach the planned recruitment numbers and potential bias concerning conflicts of interest. There were no such concerns for the ADAM and UKSAT trials. Therefore the certainty of evidence for mortality summarised in this review is high for early open repair compared to surveillance (ADAM; UKSAT), but low for early EVAR compared to surveillance (CAESAR; PIVOTAL). For costs, we downgraded the certainty of the evidence from high to moderate for early open repair compared to surveillance for imprecision as only UKSAT provided data for this outcome. Our certainty in the evidence for costs in early EVAR compared to surveillance was downgraded from high to low due to risk of bias concerns and imprecision as only PIVOTAL provided cost data.

Potential biases in the review process

Two members of the review authors (GF, MAMM) independently abstracted the data, which were cross-checked by other team members (DJB). To further reduce bias, the role of JTP and DB (trialists in the UKSAT (JTP) and ADAM (DB) studies and authors in the present review) in abstracting the data was limited to cross-checking the information abstracted. Strengths of the present review regarding potential biases are: 1. all relevant studies were identified and included in the review; 2. all the studies included in the review had similar designs and methods; 3. relevant data for all studies were obtained; and 4. all the studies included in the review shared the same main primary outcome, and this outcome is the outcome of interest for this review.

Agreements and disagreements with other studies or reviews

To our knowledge, this is the only systematic review published to date on this topic. Our findings are consistent with contemporary

data regarding the safety of surveillance in more recent evidence from nationwide screening programmes for AAA in men in England and Sweden (Oliver-Williams 2019; Wanhainen 2016).

AUTHORS' CONCLUSIONS

Implications for practice

The results from the four included trials demonstrate no advantage to early repair for small abdominal aortic aneurysm (AAA) (4.0 cm to 5.5 cm), regardless of whether open or endovascular repair (EVAR) is used and, at least for open repair, regardless of patient age and AAA diameter. Thus, neither early open nor early EVAR of small AAAs is supported by currently available evidence. The current evidence supports contemporary clinical guideline recommendations to delay the timing of AAA repair until the aneurysm reaches 5.5 cm in diameter. Long-term data from the two trials investigating EVAR are not available, so we can only draw firm conclusions regarding outcomes after the first few years for open repair.

Implications for research

Future research needs to move away from the 'procedure as a solution' focus that has dominated AAA research and management

to date and focus on what remains unknown about the disease itself. Large, prospective, population-based studies are needed to investigate disease progression in relation to AAA morphology (including shape, size, location, volume, and ratio of healthy aorta to the aneurysm). An early focus of this work should be to determine whether AAA volume is superior to diameter as a measure of disease progression. Another important question is whether efficacy or effectiveness of the various treatment options (open repair, EVAR, and the emerging medical management options) differs based on AAA morphology. Finally, research regarding the risks related to and management of small AAAs in ethnic minorities and women is urgently needed, as data regarding these populations are lacking. In particular, future research should assess whether the AAA management recommendations, which are based on studies in which women are under-represented, are applicable to women given their smaller body frames and, therefore, smaller abdominal aortas.

ACKNOWLEDGEMENTS

The review authors wish to thank Cochrane Vascular for assistance during this update.

REFERENCES

References to studies included in this review

ADAM {published data only}

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Effect of age on survival between open repair and surveillance for small abdominal aortic aneurysms. *American Journal of Cardiology* 2014;**114**(8):1281-6.

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. *Mayo Clinic Proceedings* 2013;**88**(9):910-9.

Lederle FA, Johnson GR, Wilson SE, Acher CW, Ballard DJ, Littooy FN, et al. Quality of life, impotence, and activity level in a randomized trial of immediate repair versus surveillance of small abdominal aortic aneurysm. *Journal of Vascular Surgery* 2003;**38**(4):745-52.

Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, et al, Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. The aneurysm detection and management study screening programme: validation cohort and final results. *Archives of Internal Medicine* 2000;**160**(10):1425-30.

Lederle FA, Johnson GR, Wilson SE, Chute EP, Littooy FN, Bandyk D, et al, Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. Prevalence and associations of abdominal aortic aneurysm detected through screening. *Annals of Internal Medicine* 1997;**126**(6):441-9.

Lederle FA, Johnson GR, Wilson SE, Gordon IL, Chute EP, Littooy FN, et al, The Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Investigators. Relationship of age, gender, race, and body size to infrarenal aortic diameter. *Journal of Vascular Surgery* 1997;**26**(4):595-601.

Lederle FA, Wilson SE, Johnson GR, Littooy FN, Acher C, Messina LM, et al. Design of the abdominal aortic Aneurysm Detection and Management Study. *Journal of Vascular Surgery* 1994;**20**(2):296-303.

Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *New England Journal of Medicine* 2002;**346**(19):1437-44.

CAESAR {published data only}

Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E, for the CAESAR Trial Group. Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair (CAESAR): results from a randomised trial. *European Journal of Vascular and Endovascular Surgery* 2011;**41**(1):13-25.

Cao P, CAESAR Trial Collaborators. Comparison of Surveillance vs Aortic Endografting for Small Aneurysm Repair (CAESAR) trial: study design and progress. *European Journal of Vascular and Endovascular Surgery* 2005;**30**(3):245-51.

De Rango P, Verzini F, Parlani G, Cieri E, Romano L, Loschi D, et al. Quality of life in patients with small abdominal aortic

aneurysm: the effect of early endovascular repair versus surveillance in the CAESAR trial. *European Journal of Vascular and Endovascular Surgery* 2011;**41**(3):324-31.

NCT00118573. Comparison of surveillance versus aortic endografting for small aneurysm repair. clinicaltrials.gov/ct/show/NCT00118573 (accessed 14 November 2011).

PIVOTAL {published data only}

Eisenstein EL, Davidson-Ray L, Edwards R, Anstrom KJ, Ouriel K. Economic analysis of endovascular repair versus surveillance for patients with small abdominal aortic aneurysms. *Journal of Vascular Surgery* 2013;**58**(2):302-10.

NCT00444821. The (PIVOTAL) study. clinicaltrials.gov/ct/show/NCT00444821 (accessed 8 April 2014).

Ouriel K, Clair DG, Kent CK, Zarins CK, PIVOTAL investigators. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *Journal of Vascular Surgery* 2009;**50**(2):449.

Ouriel K, Clair DG, Kent KC, Zarins CK, for the Positive Impact of Endovascular Options for treating Aneurysms Early (PIVOTAL) Investigators. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *Journal of Vascular Surgery* 2010;**51**(5):1081-7.

Ouriel K. The PIVOTAL study: a randomized comparison of endovascular repair versus surveillance in patients with smaller abdominal aortic aneurysms. *Journal of Vascular Surgery* 2009;**49**(1):266-9.

UKSAT {published data only}

Brown LC, Thompson SG, Greenhalgh RM, Powell JT, UK Small Aneurysm Trial Participants. Fit patients with small abdominal aortic aneurysms (AAAs) do not benefit from early intervention. *Journal of Vascular Surgery* 2008;**48**(6):1375-81.

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Effect of age on survival between open repair and surveillance for small abdominal aortic aneurysms. *American Journal of Cardiology* 2014;**1148**(8):1281-6.

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. *Mayo Clinic Proceedings* 2013;**88**(9):910-19.

The UK Small Aneurysm Trial Participants. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *British Journal of Surgery* 2007;**94**(6):702-8.

The UK Small Aneurysm Trial Participants. Health service costs and quality of life for early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet* 1998;**352**(9141):1656-60.

The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet* 1998;**352**(9141):1649-55.

The UK Small Aneurysm Trial Participants. The UK Small Aneurysm Trial: design, methods and progress. *European Journal of Vascular and Endovascular Surgery* 1995;**9**(1):42-8.

The United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *New England Journal of Medicine* 2002;**346**(19):1445-52.

References to studies excluded from this review

Canadian trial [pers comm] {unpublished data only}

Cole CW. [personal communication]. Conversation with review authors Dr Ballard and Prof Powell 1998.

Additional references

Abedi 2009

Abedi NN, Davenport DL, Xenos E, Sorial E, Minion DJ, Edean ED. Gender and 30-day outcome in patients undergoing endovascular aneurysm repair (EVAR): an analysis using the ACS NSQIP dataset. *Journal of Vascular Surgery* 2009;**50**(3):486-91.

Ballard 1992

Ballard DJ, Etchason JA, Hilborne LH, Campion ME, Kamberg CJ, Solomon DH, et al. Abdominal Aortic Aneurysm Surgery. A Literature Review and Ratings of Appropriateness and Necessity. Santa Monica (CA): RAND, 1992. [file://icnas3.cc.ic.ac.uk/pulug/downloads/JRA04.pdf]

Ballard 2012

Ballard DJ, Filardo G, da Graca B, Powell JT. Clinical practice change requires more than comparative effectiveness evidence: abdominal aortic aneurysm management in the USA. *Journal of Comparative Effectiveness Research* 2012;**1**(1):31-44.

Becquemini 2011

Becquemini JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *Journal of Vascular Surgery* 2011;**53**(5):1167-73.

Bown 2002

Bown MJ, Sutton AJ, Bell PR, Sayers RD. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *British Journal of Surgery* 2002;**89**(6):714-30. [DOI: doi.org/10.1046/j.1365-2168.2002.02122.x]

Bown 2013

Bown MJ, Sweeting MJ, Brown LC, Powell JT, Thompson SG. Surveillance intervals for small abdominal aortic aneurysms: a meta-analysis. *JAMA* 2013;**309**(8):806-13.

Brown 2003

Brown PM, Zelt DT, Sobolev B. The risk of rupture in untreated aneurysms: the impact of size, gender, and expansion rate. *Journal of Vascular Surgery* 2003;**37**(2):280-4.

Chaikof 2018

Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *Journal of Vascular Surgery* 2018;**67**(1):2-77. [DOI: doi.org/10.1016/j.jvs.2017.10.044] [PMID: 29268916]

Cosford 2007

Cosford PA, Leng GC, Thomas J. Screening for abdominal aortic aneurysm. *Cochrane Database of Systematic Reviews* 2007, Issue 2. [DOI: [10.1002/14651858.CD002945.pub2](https://doi.org/10.1002/14651858.CD002945.pub2)]

De Bruin 2010

De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *New England Journal of Medicine* 2010;**362**(20):1881-9.

Eisenstein 2013

Eisenstein EL, Davidson-Ray L, Edwards R, Anstrom KJ, Ouriel K. Economic analysis of endovascular repair versus surveillance for patients with small abdominal aortic aneurysms. *Journal of Vascular Surgery* 2013;**58**(2):302-10.

EVAR Trial Participants 2005

EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;**365**(9478):2179-86.

Filardo 2013

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. *Mayo Clinic Proceedings* 2013;**88**(9):910-19.

Filardo 2014

Filardo G, Lederle FA, Ballard DJ, Hamilton C, da Graca B, Herrin J, et al. Effect of age on survival between open repair and surveillance for small abdominal aortic aneurysms. *American Journal of Cardiology* 2014;**114**(8):1281-6.

GRADEpro GDT [Computer program]

McMaster University (developed by Evidence Prime) GRADEpro GDT. Hamilton (ON): McMaster University (developed by Evidence Prime), (accessed prior to 7 June 2020). Available at gradepr.org.

Grøndal 2015

Grøndal N, Søgaard R, Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65-74 years from a population screening study (VIVA trial). *British Journal of Surgery* 2015;**102**(8):902-6. [DOI: doi.org/10.1002/bjs.9825] [PMID: 25923784]

Guyatt 2008

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**:924.

Higgins 2011

Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Jacomelli 2016

Jacomelli J, Summers L, Stevenson A, Lees T, Earnshaw JJ. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery* 2016;**103**(9):1125-31. [DOI: doi.org/10.1002/bjs.10173] [PMID: 27270466]

Kent 2004

Kent KC, Zwolak RM, Jaff MR, Hollenbeck ST, Thompson RW, Schermerhorn ML, et al. Screening for abdominal aortic aneurysm: a consensus statement. *Journal of Vascular Surgery* 2004;**39**(1):267-9.

Kent 2014

Kent KC. Clinical practice. Abdominal aortic aneurysms. *New England Journal of Medicine* 2014;**371**(22):2101-8. [DOI: doi.org/10.1056/NEJMc1401430] [PMID: 25427112]

Kontopodis 2020

Kontopodis N, Galanakis N, Antoniou SA, Tsetis D, Ioannou CV, Veith FJ, et al. Meta-analysis and meta-regression analysis of outcomes of endovascular and open repair for ruptured abdominal aortic aneurysm. *European Journal of Vascular and Endovascular Surgery* 2020;**59**(3):399-410. [DOI: doi.org/10.1016/j.ejvs.2019.12.023] [PMID: 31932143]

Lederle 1988

Lederle FA, Walker JM, Reinke DB. Selective screening for abdominal aortic aneurysms with physical examination and ultrasound. *Archives of Internal Medicine* 1988;**148**(8):1753-6. [PMID: 3041938]

Lederle 1997

Lederle FA, Johnson GR, Wilson SE, Chute EP, Littooy FN, Bandyk D, et al. Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. Prevalence and associations of abdominal aortic aneurysm detected through screening. *Annals of Internal Medicine* 1997;**126**(6):441-9.

Lederle 2000

Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, et al. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. The aneurysm detection and management study screening program: validation cohort and final results. *Archives of Internal Medicine* 2000;**160**(10):1425-30.

Lederle 2009

Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT Jr, Matsumura JS, Kohler TR. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA* 2009;**302**(14):1535-42.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JP, Green S editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Lindholt 1999

Lindholt JS, Vammen S, Juul S, Henneberg EW, Fasting H. The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm. *European Journal of Vascular and Endovascular Surgery* 1999;**17**(6):472-5. [DOI: doi.org/10.1053/ejvs.1999.0835] [PMID: 10375481]

Lo 2013

Lo RC, Bensley RP, Hamdan AD, Wyers M, Adams JE, Schermerhorn ML. Gender differences in abdominal aortic aneurysm presentation, repair, and mortality in the Vascular Study Group of New England. *Journal of Vascular Surgery* 2013;**57**(5):1261-8.

McPhee 2007

McPhee JT, Hill JS, Eslami MH. The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001-2004. *Journal of Vascular Surgery* 2007;**45**(5):891-9.

Mehta 2012

Mehta M, Byrne WJ, Robinson H, Roddy SP, Paty PS, Kreienberg PB, et al. Women derive less benefit from elective endovascular aneurysm repair than men. *Journal of Vascular Surgery* 2012;**55**(4):906-13.

Myers 2010

Myers JN, White JJ, Narasimhan B, Dalman RL. Effects of exercise training in patients with abdominal aortic aneurysm: preliminary results from a randomized trial. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2010;**30**(6):374-83.

NICE 2020

National Institute for Health and Care Excellence. NICE Guideline. Abdominal aortic aneurysm: diagnosis and management (NG156), 2020. www.nice.org.uk/guidance/ng156 (accessed 6 May 2020).

Oliver-Williams 2019

Oliver-Williams C, Sweeting MJ, Jacomelli J, Summers L, Stevenson A, Lees T, et al. Safety of men with small and medium abdominal aortic aneurysms under surveillance in the NAAASP. *Circulation* 2019;**139**(11):1371-80. [DOI: doi.org/10.1161/CIRCULATIONAHA.118.036966] [PMID: 30636430]

Page 2019

Page MJ, Higgins JP, Sterne JA. Chapter 13: Assessing risk of bias due to missing results in a synthesis. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook.

Patel 2016

Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *Lancet* 2016;**388**(10058):2366-74. [DOI: [doi.org/10.1016/S0140-6736\(16\)31135-7](https://doi.org/10.1016/S0140-6736(16)31135-7)] [PMID: 27743617]

Powell 2008

Powell JT, Brown LC, Greenhalgh RM, Thompson SG. The rupture rate of large abdominal aortic aneurysms: Is this modified by anatomical suitability for endovascular repair? *Annals of Surgery* 2008;**247**(1):173-9. [DOI: doi.org/10.1097/SLA.0b013e3181557d2a] [PMID: 18156938]

Powell 2017

Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemini JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery* 2017;**104**(3):166-78. [DOI: doi.org/10.1002/bjs.10430] [PMID: 28160528]

Prinssen 2004

Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *New England Journal of Medicine* 2004;**351**(16):1607-18.

RESCAN Collaborators 2013

RESCAN Collaborators, Bown MJ, Sweeting MJ, Brown LC, Powell JT, Thompson SG. Surveillance intervals for small abdominal aortic aneurysms: a meta-analysis. *JAMA* 2013;**309**(8):806-13.

Rogers 2013

Rogers IS, Massaro JM, Truong QA, Mahabadi AA, Kriegel MF, Fox CS, et al. Distribution, determinants, and normal reference values of thoracic and abdominal aortic diameters by computed tomography (from the Framingham Heart Study). *American Journal of Cardiology* 2013;**111**(10):1510-6. [DOI: doi.org/10.1016/j.amjcard.2013.01.306] [PMID: 23497775]

Rudarakanchana 2013

Rudarakanchana N, Powell JT. Advances in imaging and surveillance of AAA: when, how, how often? *Progress in Cardiovascular Diseases* 2013;**56**(1):7-12.

Sakalihasan 2018

Sakalihasan N, Michel JB, Katsargyris A, Kuivaniemi H, Defraigne JO, Nchimi A, et al. Abdominal aortic aneurysms. *Nature reviews. Disease Primers* 2018;**4**(1):34. [DOI: doi.org/10.1038/s41572-018-0030-7] [PMID: 30337540]

Sampson 2014

Sampson UK, Norman PE, Fowkes FG, Aboyans V, Song Y, Harrell FE Jr, et al. Global and regional burden of aortic dissection and aneurysms: mortality trends in 21 world regions, 1990 to 2010. *Global Heart* 2014;**9**(1):171-80. [DOI: doi.org/10.1016/j.gheart.2013.12.010] [PMID: 25432126]

Sidloff 2014

Sidloff D, Stather P, Dattani N, Bown M, Thompson J, Sayers R, et al. Aneurysm global epidemiology study: public health measures can further reduce abdominal aortic aneurysm mortality. *Circulation* 2014;**129**(7):747-53. [DOI: doi.org/10.1161/CIRCULATIONAHA.113.005457] [PMID: 24249717]

Stackelberg 2014

Stackelberg O, Björck M, Larsson SC, Orsini N, Wolke A. Sex differences in the association between smoking and abdominal aortic aneurysm. *British Journal of Surgery* 2014;**101**(10):1230-7. [DOI: doi.org/10.1002/bjs.9526] [PMID: 24916023]

Svensjö 2011

Svensjö S, Björck M, Gürtelschmid M, Djavani Gidlund K, Hellberg A, Wanhainen A. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. *Circulation* 2011;**124**(10):1118-23. [DOI: doi.org/10.1161/CIRCULATIONAHA.111.030379] [PMID: 21844079]

Sweeting 2012

Sweeting MJ, Thompson SG, Brown LC, Powell JT, RESCAN collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *British Journal of Surgery* 2012;**99**(5):655-65. [DOI: doi.org/10.1002/bjs.8707] [PMID: 22389113]

Tew 2012

Tew GA, Moss J, Crank H, Mitchell PA, Nawaz S. Endurance exercise training in patients with small abdominal aortic aneurysm: a randomized controlled pilot study. *Archives of Physical Medicine and Rehabilitation* 2012;**93**(12):2148-53.

Ulug 2016

Ulug P, Powell JT, Sweeting MJ, Bown MJ, Thompson SG, SWAN Collaborative Group. Meta-analysis of the current prevalence of screen-detected abdominal aortic aneurysm in women. *British Journal of Surgery* 2016;**103**(9):1097-104. [DOI: doi.org/10.1002/bjs.10225] [PMID: 27346306]

Ulug 2017

Ulug P, Sweeting MJ, von Allmen RS, Thompson SG, Powell JT, SWAN collaborators. Morphological suitability for endovascular repair, non-intervention rates, and operative mortality in women and men assessed for intact abdominal aortic aneurysm repair: systematic reviews with meta-analysis. *Lancet* 2017;**389**(10088):2482-91. [DOI: [doi.org/10.1016/S0140-6736\(17\)30639-6](https://doi.org/10.1016/S0140-6736(17)30639-6)] [PMID: 28455148]

United Kingdom EVAR Trial Investigators 2010

United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *New England Journal of Medicine* 2010;**362**(20):1872-80.

US Preventive Task Force

US Preventive Services Task Force. Screening for abdominal aortic aneurysm: US Preventive Services Task Force

Recommendation Statement. *JAMA* 2019;**322**(22):2211-18. [DOI: [10.1001/jama.2019.18928](https://doi.org/10.1001/jama.2019.18928)]

Wanhainen 2016

Wanhainen A, Hultgren R, Linné A, Holst J, Gottsäter A, Langenskiöld M, et al. Outcome of the Swedish Nationwide Abdominal Aortic Aneurysm Screening Program. *Circulation* 2016;**134**(16):1141-8. [DOI: doi.org/10.1161/CIRCULATIONAHA.116.022305] [PMID: 27630132]

Wanhainen 2019

Wanhainen A, Verzini F, van Herzele I, Allaire E, Bown M, Cohnert T, et al. European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *European Journal of Vascular and Endovascular Surgery* 2019;**57**(1):8-93. [DOI: doi.org/10.1016/j.ejvs.2018.09.020] [PMID: 30528142]

Wilt 2006

Wilt TJ, Lederle FA, MacDonald R, Jonk YC, Rector TS, Kane RL. Comparison of endovascular and open surgical repairs for abdominal aortic aneurysm. Evidence Report/Technology Assessment 2006;**144**:1-113.

References to other published versions of this review

Ballard 1999

Ballard DJ, Filardo G, Fowkes FG, Powell JT. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database of Systematic Reviews* 1999, Issue 3. [DOI: [10.1002/14651858.CD001835](https://doi.org/10.1002/14651858.CD001835)]

Ballard 2008

Ballard DJ, Filardo G, Fowkes G, Powell JT. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: [10.1002/14651858.CD001835.pub2](https://doi.org/10.1002/14651858.CD001835.pub2)]

Filardo 2012

Filardo G, Powell JT, Martinez MAM, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database of Systematic Reviews* 2012, Issue 3. [DOI: [10.1002/14651858.CD001835.pub3](https://doi.org/10.1002/14651858.CD001835.pub3)]

Filardo 2015

Filardo G, Powell JT, Martinez MAM, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database of Systematic Reviews* 2015, Issue 2. [DOI: [10.1002/14651858.CD001835.pub4](https://doi.org/10.1002/14651858.CD001835.pub4)]

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

ADAM

Study characteristics

Methods	Study design: intention to treat Method of randomisation: equal probability of assignment to each of the 2 study groups using automated telephone/computer Concealment of allocation sequence: full
Participants	Country: US Number: 1136 Age: 50–79 years Sex: 1126 men and 10 women Inclusion criteria: small (4.0–5.5 cm) non-tender asymptomatic AAAs considered fit for immediate surgery. People who were considered unfit for early surgery, had symptoms associated the aneurysm, were unable to attend the follow-up visit, or were unable to give informed consent were excluded. People who received a revascularisation procedure within 3 months of enrolment, who had a myocardial infarction within 6 months of enrolment, or who were expected to survive < 5 years because of invasive cancer or other life-threatening disease were also excluded.
Interventions	Treatment: surgery, 569 participants, of whom 527 had early aneurysm repair; 42 had no elective operation due to death, refusal, etc.

ADAM (Continued)

Surveillance: 567 participants, of whom 349 had aneurysm repair when they met the criteria listed below (in 9%, the procedures were performed despite an AAA that did not meet the repair criteria listed below).

Participants assigned to the early-surgery group received standard open repair within 6 weeks after randomisation, while participants assigned to selective surveillance were followed without repair at similar regular intervals (at minimum once every 6 months), and surgery was performed within 6 weeks if: 1. the aneurysm reached 5.5 cm; or 2. the aneurysm enlarged by a minimum of 0.7 cm in 6 months or 1.0 cm in 1 year; or 3. the aneurysm became symptomatic.

Outcomes	Primary: survival during mean follow-up (range 3.5–8.0 years; mean 4.9 years); 30-day surgical mortality Secondary: quality of life
Notes	Supported by the Cooperative Studies Program of the Department of Veterans Affairs Office of Research and Development, Washington, DC, USA.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The method of randomisation was of equal probability of assignment to each of the 2 study groups using automated telephone/computer.
Allocation concealment (selection bias)	Low risk	Full concealment of sequence allocation.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Could not blind participants due to nature of intervention.
Blinding of outcome assessment (detection bias) Mortality and cost	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate. Vital status was assessed using the same methodology for both participants in the early-repair group and participants in the routine ultrasound surveillance group. In case misclassification occurred, this would have been non-differential and its impact on the study results would be limited.
Incomplete outcome data (attrition bias)	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate.
Selective reporting (reporting bias)	Low risk	Authors published findings on all the study outcomes including the study outcome of this review.
Other bias	Unclear risk	We did not identify other possible risk of bias for mortality outcomes. Other sources of bias for quality of life outcomes and assessment of aneurysm rupture were unclear.

CAESAR
Study characteristics

Methods	Study design: intention to treat Method of randomisation: designed with equal probability (1:1 ratio) of assignment to either immediate endovascular repair or surveillance using a computer-generated random number list, stratified by centre using a permuted block design, and carried out online through the Internet.
---------	--

CAESAR (Continued)

Concealment of allocation sequence: full

Participants	<p>Country: Italy</p> <p>Number: 360</p> <p>Sex: 345 men and 15 women</p> <p>Age: 50–79 years</p> <p>Inclusion criteria: people with small (4.1–5.4 cm) asymptomatic AAAs, without high surgical risk, and who would have benefited from early repair.</p> <p>Patients were excluded if they had severe comorbidities or a suprarenal/thoracic aorta \geq 4.0 cm, needed urgent repair, or were unable or unwilling to give informed consent or follow the protocol.</p>
Interventions	<p>Treatment: surgery, 182 participants, of whom 175 had early endovascular surgery; 6 declined treatment and 1 underwent open repair according to person's choice</p> <p>Surveillance: 178 participants, of whom 172 had aneurysm repair when they met the criteria below (6 patients had endovascular repair against protocol: 5 per patient choice and 1 with a surgeon not participating in the study)</p> <p>Participants assigned to early endovascular repair underwent aneurysm repair a median of 22 days after randomisation, while participants assigned to surveillance were seen every 6 months and repair allowed if the aneurysm grew to 5.5 cm diameter, rapidly increased in diameter ($>$ 1 cm/year), or became symptomatic.</p>
Outcomes	<p>Primary: mortality from any cause</p> <p>Secondary: quality of life; aneurysm-related deaths (defined as death caused directly or indirectly by aneurysm rupture or aneurysm repair), aneurysm rupture, perioperative (30 days or inpatient) or late adverse events (defined according to SVS/AAVS reporting standards), conversion to open repair, loss of treatment options (anatomical suitability for endovascular repair), and aneurysm growth rate</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation designed with equal probability (1:1 ratio) of assignment to either immediate endovascular repair or surveillance by means of a computer-generated random number list, stratified by centre using a permuted block design and carried out online through the Internet.
Allocation concealment (selection bias)	Low risk	Full concealment of sequence allocation.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Could not blind participants due to nature of intervention.
Blinding of outcome assessment (detection bias) Mortality and cost	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate. Vital status was assessed using the same methodology for both participants in the early-repair group and participants in the routine ultrasound surveillance group. In case misclassification occurred, this would have been non-differential and its impact on the study results would be limited.

CAESAR (Continued)

Incomplete outcome data (attrition bias)	Unclear risk	13% of participants overall were lost to follow-up within 12 months of randomisation for both mortality and clinical follow-up (missing participants were similar in both randomised groups).
Selective reporting (reporting bias)	Low risk	Authors published findings on the main study outcome of this review.
Other bias	High risk	Conflicts of interest: Cook Medical withdrew sponsorship. We did not identify other possible risk of bias for mortality outcomes. Other sources of bias for quality of life and assessment of aneurysm rupture were unclear.

PIVOTAL
Study characteristics

Methods	<p>Study design: intention to treat</p> <p>Method of randomisation: created with equal probability of assignment to each of the treatment groups by means of a computer-generated random-number code</p> <p>Concealment of allocation sequence: full</p>
Participants	<p>Country: US</p> <p>Number: 728</p> <p>Sex: 631 men and 97 women</p> <p>Age: 40–90 years</p> <p>Inclusion criteria: people with small (4.0–5.0 cm) AAAs</p> <p>Patients were excluded from the study if they had evidence of symptoms referable to the aneurysm, an abdominal or thoracic repair, an aneurysm originating ≤ 1.0 cm from the most distal main renal artery, life expectancy < 3 years, inability to provide informed consent, predicted non-compliance with the protocol, SVS score > 2 with the exception of age and controlled hypertension, baseline serum creatinine level > 2.5 mg/dL, or when the patient did not meet the indications for use of the endograft device.</p>
Interventions	<p>Treatment: surgery, 366 participants, of whom 322 had early endovascular surgery; 4 underwent open surgery, 6 underwent repair outside of the 30-day window of randomisation, 9 were withdrawn per patient request, 10 were withdrawn per physician request for deteriorating health status between randomisation and scheduled repair, 2 were treated with an endograft device that was not in the protocol, and 13 received no repair for reasons not specified</p> <p>Surveillance, 362 participants, of whom 100 had aneurysm repair when they met the criteria listed below</p> <p>Participants assigned to early endovascular repair underwent aneurysm repair ≤ 30 days of randomisation, while participants assigned to surveillance were seen at 1 month, 6 months, and every 6 months thereafter for a minimum of 36 months and a maximum of 60 months after operation. Participants were offered aneurysm repair when symptoms thought referable to the aneurysm developed, when the diameter of the aneurysm reached 5.5 cm, or when the aneurysm enlarged ≥ 0.5 cm between any 2 6-month assessments</p>
Outcomes	<p>Primary: frequency of rupture or aneurysm-related death</p> <p>Secondary: healthcare costs</p>

PIVOTAL (Continued)

Notes

The PIVOTAL Economic Study involved the same participants and ran in parallel with the PIVOTAL trial. The main trial was co-ordinated from the Cleveland Clinic, OH, USA. The Economic Study was co-ordinated by the Duke Clinical Research Institute, Raleigh NC, USA. These studies were funded by 2 separate grants from Medtronic and each had separate institutional review board (ethical) approval. These both used the same participants but investigated different outcomes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation procedure was designed to provide equal probability of assignment to each of the treatment groups by means of a computer-generated random-number code.
Allocation concealment (selection bias)	Low risk	Full concealment of allocation sequence.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Could not blind participants due to nature of intervention.
Blinding of outcome assessment (detection bias) Mortality and cost	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate. Vital status was assessed using the same methodology for both participants in the immediate-repair group and participants in the routine ultrasound surveillance group. In case misclassification occurred, this would have been non-differential and its impact on the study results would be limited. Similarly, there was a low risk of bias for the assessment of the secondary outcome of cost.
Incomplete outcome data (attrition bias)	High risk	27% of participants overall were lost to clinical and mortality follow-up within 12 months of randomisation (similar in both randomised groups). Cost data were only available for 84% of participants but balanced across groups.
Selective reporting (reporting bias)	Low risk	Authors published findings on the main study outcome of this review.
Other bias	High risk	Conflicts of interest: the study was funded by Medtronic Vascular, which now holds the trial database. The funding source was not specified in the report of trial results, but was specified in the 2009 paper describing the rationale and protocol for the study (PIVOTAL). In addition, 2 members of the research team were acknowledged as paid consultants of Medtronic.

UKSAT
Study characteristics

Methods	Study design: intention to treat Method of randomisation: concealed randomisation using automated telephone/computer Concealment of allocation sequence: full
Participants	Country: UK Number: 1090

UKSAT (Continued)

Sex: 902 men and 188 women

Age: 60–76 years

Inclusion criteria: asymptomatic (non-tender) infrarenal aneurysm. Maximum anteroposterior diameter 4.0–5.5 cm. Fit for elective surgery

Interventions	<p>Treatment: surgery, 563 participants, of whom 528 had early open aneurysm repair; 35 had no elective operation due to death, refusal, etc.</p> <p>Control: surveillance, 527 participants, of whom 401 had aneurysm repair when they met the criteria listed below</p> <p>Participants assigned to the early-surgery group received standard open repair within 6 weeks after randomisation, while participants assigned to selective surveillance were followed without repair at similar regular intervals (at minimum once every 6 months), and surgery was performed within 6 weeks if: 1. the aneurysm reached 5.5 cm; or 2. the aneurysm enlarged by a minimum 1.0 cm in 1 year; or 3. the aneurysm became tender or symptomatic</p>
Outcomes	<p>Primary: survival during mean follow-up (range 8–12 years, mean 10 years); 30-day surgical mortality</p> <p>Secondary: healthcare costs</p>
Notes	The Medical Research Council and the British Heart Foundation supported this trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Concealed randomisation using automated telephone/computer.
Allocation concealment (selection bias)	Low risk	Full concealment of allocation sequence.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Could not blind participants due to nature of intervention.
Blinding of outcome assessment (detection bias) Mortality and cost	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate. Vital status was assessed using the same methodology for participants in the immediate-repair group and routine ultrasound surveillance group. In case misclassification occurred, this would have been non-differential and its impact on the study results would be limited. Similarly, there was a low risk of bias for the assessment of the secondary outcome of cost.
Incomplete outcome data (attrition bias)	Low risk	Unlikely given the primary outcome of mortality and low lost-to-follow-up rate. Also applies to secondary outcome of cost.
Selective reporting (reporting bias)	Low risk	Authors published findings on all the study outcomes including the study outcome of this review.
Other bias	Unclear risk	We did not identify other possible risk of bias for mortality and cost outcomes. Other sources of bias for quality of life and assessment of aneurysm rupture were unclear.

AAA: abdominal aortic aneurysm; AAVS: American Association for Vascular Surgery; SVS: The Society for Vascular Surgery.

Characteristics of excluded studies [ordered by study ID]

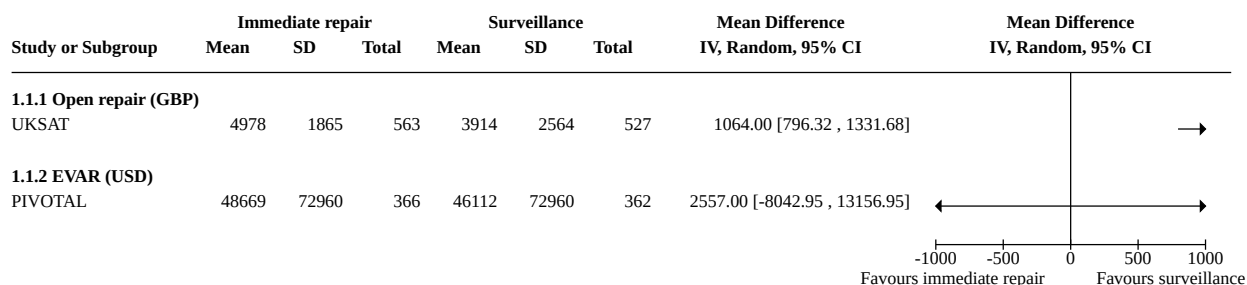
Study	Reason for exclusion
Canadian trial [pers comm]	Trial stopped early because of an inadequate rate of recruitment after 104 participants had been enrolled (Cole CW, personal communication, 1998).

DATA AND ANALYSES

Comparison 1. Early repair compared to ultrasound surveillance for small asymptomatic AAA

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Health service costs	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1.1 Open repair (GBP)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.1.2 EVAR (USD)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Early repair compared to ultrasound surveillance for small asymptomatic AAA, Outcome 1: Health service costs



APPENDICES

Appendix 1. Database searches

Source	Search strategy	Hits retrieved
CENTRAL via CRSO	#1 MESH DESCRIPTOR Aorta, Abdominal EXPLODE ALL TREES WITH QUALIFIERS SU 182 #2 MESH DESCRIPTOR Aortic Aneurysm 180 #3 MESH DESCRIPTOR Aortic Aneurysm, Abdominal 536 #4 aort*:TI,AB,KY 10764	941

(Continued)

- #5 (juxta renal):TI,AB,KY 1
- #6 juxtarenal:TI,AB,KY 10
- #7 (juxta renal or juxtarenal):TI,AB,KY 11
- #8 (pararenal or para renal):TI,AB,KY 11
- #9 (suprarenal or supra renal):TI,AB,KY 43
- #10 (short neck* or shortneck*):TI,AB,KY 15
- #11 (visceral aortic segment):TI,AB,KY 1
- #12 abdominal:TI,AB,KY 34733
- #13 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 43563
- #14 aneur?sm*:TI,AB,KY 4331
- #15 #13 AND #14 1859
- #16 (aort* adj3 (dilat* or bulg* or expan*)):TI,AB,KY 135
- #17 #1 OR #2 OR #3 OR #15 OR #16 2062
- #18 MESH DESCRIPTOR Endovascular Procedures EXPLODE ALL TREES 7805
- #19 MESH DESCRIPTOR Stents EXPLODE ALL TREES 3895
- #20 MESH DESCRIPTOR Vascular Surgical Procedures 617
- #21 MESH DESCRIPTOR Blood Vessel Prosthesis EXPLODE ALL TREES 438
- #22 MESH DESCRIPTOR Blood Vessel Prosthesis Implantation EXPLODE ALL TREES 438
- #23 endovasc*:TI,AB,KY 3104
- #24 endostent*:TI,AB,KY 1
- #25 endoluminal:TI,AB,KY 203
- #26 endoprosthe*:TI,AB,KY 356
- #27 (graft or endograft*):TI,AB,KY 22835
- #28 percutaneous*:TI,AB,KY 17242
- #29 stent*:TI,AB,KY 13732
- #30 (Palmaz or Zenith or Dynalink or Hemobahn or Luminex* or Memotherm or Wallstent):TI,AB,KY 642
- #31 (Viabahn or Nitinol or Intracoil or Tantalum):TI,AB,KY 475
- #32 EVAR:TI,AB,KY 242
- #33 (surger* or surgic* or repair):TI,AB,KY 214399
- #34 MESH DESCRIPTOR Ultrasonography, Doppler EXPLODE ALL TREES 2861
- #35 MESH DESCRIPTOR Tomography EXPLODE ALL TREES 15188
- #36 (screen* or ultrasound or scan* or surveillance):TI,AB,KY 104111
- #37 #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 339263

(Continued)

#38 #17 AND #37 1814

MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-In- dexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) 1946 to 2017, 2018, and 2019 only	1 exp Aorta, Abdominal/su [Surgery] 2 Aortic Aneurysm/ 3 Aortic Aneurysm, Abdominal/ 4 aort*.ti,ab. 5 "juxta renal".ti,ab. 6 juxtarenal.ti,ab. 7 (juxta renal or juxtarenal).ti,ab. 8 (pararenal or para renal).ti,ab. 9 (suprarenal or supra renal).ti,ab. 10 (short neck* or shortneck*).ti,ab. 11 visceral aortic segment.ti,ab. 12 abdominal.ti,ab. 13 or/4-12 14 aneur?sm*.ti,ab. 15 13 and 14 16 (aort* adj3 (dilat* or bulg* or expan*)).ti,ab. 17 1 or 2 or 3 or 15 or 16 18 exp Endovascular Procedures/ 19 exp Stents/ 20 Vascular Surgical Procedures/ 21 exp Blood Vessel Prosthesis/ 22 exp Blood Vessel Prosthesis Implantation/ 23 endovasc*.ti,ab. 24 endostent*.ti,ab. 25 endoluminal.ti,ab. 26 endoprosthe*.ti,ab. 27 (graft or endograft*).ti,ab. 28 percutaneous*.ti,ab. 29 stent*.ti,ab. 30 (Palmaz or Zenith or Dynalink or Hemobahn or Luminex* or Memotherm or Wallstent).ti,ab. 31 (Viabahn or Nitinol or Intracoil or Tantalum).ti,ab. 32 EVAR.ti,ab.	848
--	---	-----

(Continued)

- 33 (surger* or surgic* or repair).ti,ab.
 34 exp Ultrasonography, Doppler/
 35 exp Tomography/
 36 (screen* or ultrasound or scan* or surveillance).ti,ab.
 37 or/18-36
 38 17 and 37
 39 randomized controlled trial.pt.
 40 controlled clinical trial.pt.
 41 randomized.ab.
 42 placebo.ab.
 43 drug therapy.fs.
 44 randomly.ab.
 45 trial.ab.
 46 groups.ab.
 47 or/39-46
 48 exp animals/ not humans.sh.
 49 47 not 48
 50 38 and 49
 51 (2017* or 2018* or 2019*).ed.
 52 50 and 51

 Embase 2017, 2018, and
 2019 only

- 1 exp abdominal aorta/su [Surgery]
 2 Aortic Aneurysm/
 3 abdominal aortic aneurysm/
 4 aort*.ti,ab.
 5 "juxta renal".ti,ab.
 6 juxtarenal.ti,ab.
 7 (juxta renal or juxtarenal).ti,ab.
 8 (pararenal or para renal).ti,ab.
 9 (suprarenal or supra renal).ti,ab.
 10 (short neck* or shortneck*).ti,ab.
 11 visceral aortic segment.ti,ab.
 12 abdominal.ti,ab.
 13 or/4-12
 14 aneur?sm*.ti,ab.

2067

(Continued)

- 15 13 and 14
- 16 (aort* adj3 (dilat* or bulg* or expan*)).ti,ab.
- 17 1 or 2 or 3 or 15 or 16
- 18 exp endovascular surgery/
- 19 exp stent/
- 20 exp vascular surgery/
- 21 exp blood vessel prosthesis/
- 22 endovasc*.ti,ab.
- 23 endostent*.ti,ab.
- 24 endoluminal.ti,ab.
- 25 endoprosthe*.ti,ab.
- 26 (graft or endograft*).ti,ab.
- 27 percutaneous*.ti,ab.
- 28 stent*.ti,ab.
- 29 (Palmaz or Zenith or Dynalink or Hemobahn or Luminex* or Memotherm or Wallstent).ti,ab.
- 30 (Viabahn or Nitinol or Intracoil or Tantalum).ti,ab.
- 31 EVAR.ti,ab.
- 32 (surger* or surgic* or repair).ti,ab.
- 33 exp Doppler ultrasonography/
- 34 exp tomography/
- 35 (screen* or ultrasound or scan* or surveillance).ti,ab.
- 36 or/18-35
- 37 17 and 36
- 38 randomized controlled trial/
- 39 controlled clinical trial/
- 40 random\$.ti,ab.
- 41 randomization/
- 42 intermethod comparison/
- 43 placebo.ti,ab.
- 44 (compare or compared or comparison).ti.
- 45 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
- 46 (open adj label).ti,ab.
- 47 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.

(Continued)

48 double blind procedure/
 49 parallel group\$1.ti,ab.
 50 (crossover or cross over).ti,ab.
 51 ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or
 intervention\$1 or patient\$1 or subject\$1 or participant\$1)).ti,ab.
 52 (assigned or allocated).ti,ab.
 53 (controlled adj7 (study or design or trial)).ti,ab.
 54 (volunteer or volunteers).ti,ab.
 55 trial.ti.
 56 or/38-55
 57 37 and 56
 58 (2017* or 2018* or 2019*).em.
 59 57 and 58
 60 from 59 keep 2001-2067

 CINAHL 2017, 2018, and
 2019 only

S50 S48 AND S49
 S49 EM 2017 OR EM 2018 OR EM 2019
 S48 S34 AND S47
 S47 S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44
 OR S45 OR S46
 S46 MH "Random Assignment"
 S45 MH "Single-Blind Studies" or MH "Double-Blind Studies" or MH "Triple-
 Blind Studies"
 S44 MH "Crossover Design"
 S43 MH "Factorial Design"
 S42 MH "Placebos"
 S41 MH "Clinical Trials"
 S40 TX "multi-centre study" OR "multi-center study" OR "multicentre study"
 OR "multicenter study" OR "multi-site study"
 S39 TX crossover OR "cross-over"
 S38 AB placebo*
 S37 TX random*
 S36 TX trial*
 S35 TX "latin square"
 S34 S17 AND S33
 S33 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27
 OR S28 OR S29 OR S30 OR S31 OR S32

108

(Continued)

S32 TX screen* or ultrasound or scan* or surveillance

S31 (MH "Tomography+")

S30 (MH "Ultrasonography, Doppler+")

S29 TX surger* or surgic* or repair

S28 TX EVAR

S27 TX Viabahn or Nitinol or Intracoil or Tantalum

S26 TX Palmaz or Zenith or Dynalink or Hemobahn or Luminex* or Memotherm or Wallstent

S25 TX stent*

S24 TX endoprothe*

S23 TX endoluminal

S22 TX endostent*

S21 TX endovasc*

S20 (MH "Blood Vessel Prosthesis")

S19 (MH "Stents+")

S18 (MH "Endovascular Procedures+")

S17 S1 OR S2 OR S3 OR S15 OR S16

S16 TX aort* N3 (dilat* or bulg* or expan*)

S15 S13 AND S14

S14 TX aneur?sm*

S13 S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12

S12 TX abdominal

S11 TX visceral aortic segment

S10 TX short neck* or shortneck*

S9 TX suprarenal or supra renal

S8 TX pararenal or para renal

S7 TX juxta renal or juxtarenal

S6 TX juxtarenal

S5 TX juxta renal

S4 TX aort*

S3 (MH "Aortic Aneurysm, Abdominal")

S2 (MH "Aortic Aneurysm")

S1 (MH "Aorta, Abdominal/SU")

AMED 2017, 2018, and
2019 only

1 Aortic Aneurysm/

0

(Continued)

- 2 aort*.ti,ab.
- 3 "juxta renal".ti,ab.
- 4 juxtarenal.ti,ab.
- 5 (juxta renal or juxtarenal).ti,ab.
- 6 (pararenal or para renal).ti,ab.
- 7 (suprarenal or supra renal).ti,ab.
- 8 (short neck* or shortneck*).ti,ab.
- 9 visceral aortic segment.ti,ab.
- 10 abdominal.ti,ab.
- 11 or/2-10
- 12 aneur?sm*.ti,ab.
- 13 11 and 12
- 14 (aort* adj3 (dilat* or bulg* or expan*)).ti,ab.
- 15 1 or 13 or 14
- 16 exp Stents/
- 17 exp Vascular surgery/
- 18 endovasc*.ti,ab.
- 19 endostent*.ti,ab.
- 20 endoluminal.ti,ab.
- 21 endoprosthe*.ti,ab.
- 22 (graft or endograft*).ti,ab.
- 23 percutaneous*.ti,ab.
- 24 stent*.ti,ab.
- 25 (Palmaz or Zenith or Dynalink or Hemobahn or Luminex* or Memotherm or Wallstent).ti,ab.
- 26 (Viabahn or Nitinol or Intracoil or Tantalum).ti,ab.
- 27 EVAR.ti,ab.
- 28 (surger* or surgic* or repair).ti,ab.
- 29 (screen* or ultrasound or scan* or surveillance).ti,ab.
- 30 or/16-29
- 31 15 and 30
- 32 exp CLINICAL TRIALS/
- 33 RANDOM ALLOCATION/
- 34 DOUBLE BLIND METHOD/
- 35 Clinical trial.pt.

(Continued)

36 (clinic* adj trial*).tw.
 37 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw.
 38 PLACEBOS/
 39 placebo*.tw.
 40 random*.tw.
 41 PROSPECTIVE STUDIES/
 42 or/32-41
 43 31 and 42
 44 ("2017" or "2018" or "2019").yr.
 45 43 and 44

ICTRP Search Portal	abdominal aortic aneurysm OR Aortic Aneurysm OR juxtarenal OR pararenal AND surgery OR surgical OR Stents OR Endovascular Procedures OR Blood Vessel Prosthesis OR Tomography OR Doppler Ultrasonography	69
Clinicaltrials.gov	abdominal aortic aneurysm OR Aortic Aneurysm OR juxtarenal OR pararenal surgery OR surgical OR Stents OR Endovascular Procedures OR Blood Vessel Prosthesis OR Tomography OR Doppler Ultrasonography INTERVENTIONAL STUDIES	99

WHAT'S NEW

Date	Event	Description
6 May 2020	New search has been performed	Searches rerun. No new studies included or excluded.
6 May 2020	New citation required but conclusions have not changed	Searches rerun. No new studies included or excluded. New author joined the review team. Relevant review sections checked and updated according to current Cochrane standards. 'Summary of findings' tables added. Conclusions not changed.

HISTORY

Protocol first published: Issue 3, 1999

Review first published: Issue 4, 1999

Date	Event	Description
26 June 2014	New search has been performed	Searches re-run. No new studies included.
26 June 2014	New citation required but conclusions have not changed	Searches re-run. No new studies included. Relevant review sections updated according to current Cochrane standards. Conclusions not changed.
17 October 2011	New search has been performed	New author added

Date	Event	Description
17 October 2011	New citation required but conclusions have not changed	CAESAR and PIVOTAL results included in the analysis
20 May 2008	New search has been performed	ADAM trial results incorporated in analysis. CAESAR and PIVOTAL trials added to ongoing studies.
8 April 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

PU: study assessment, updated the 'Background', incorporated recent supporting evidence, applied GRADE recommendations.

JP: study assessment, updated the 'Background', incorporated recent supporting evidence, applied GRADE recommendations.

MAM: study assessment, data extraction, risk of bias assessment in previous version, reviewed update.

DB: study assessment, data extraction, risk of bias assessment in previous version, reviewed update.

GF: study assessment, data extraction, risk of bias assessment in previous version, reviewed update.

DECLARATIONS OF INTEREST

PU: none.

JTP: was a co-principal investigator in the UKSAT study and as such has declared that her institution received grants from British Heart Foundation (Chief Investigator) and the Medical Research Council (co-applicant). As recommended, steps were taken to ensure no involvement in data extraction for the UKSAT trial. JTP also declares that her institution has received grants/support from National Institute for Health Research Health Technology Assessment (NIHR HTA) for involvement in studies on endovascular repair in aneurysm rupture, angiotensin-converting enzyme (ACE) inhibitors to slow AAA growth; and NIHR HTA support for individual patient meta-analysis of small AAA growth rates and screening women for AAA (a modelling study).

MAMM: none.

DJB: was a co-investigator of the [ADAM](#) trial and appropriate steps were taken to ensure no involvement in data extraction for this study.

GF: declared that pooled analysis reported in this review ([Filardo 2013](#)) was funded by the Agency for Healthcare Research and Quality (AHRQ), grant number R01HS018576.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- The Chief Scientist Office, Scottish Government Health Directorates, the Scottish Government, UK

The Cochrane Vascular editorial base is supported by the Chief Scientist Office.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

2020 review version

For this update, the term 'immediate' has been replaced by 'early' throughout the text, to be consistent with the definition used in the trials. The definition of early was less than one month after randomisation for all trials except [UKSAT](#); for [UKSAT](#) it was less than three months.

For this update, we reconsidered the current clinical relevance of the outcomes. Following discussion, we took the decision to remove the outcomes of life expectancy, long-term cost-effectiveness, non-hospital health service costs, and societal costs. We also reordered direct hospital costs to become a primary outcome and quality of life to a secondary outcome. We re-extracted and re-analysed data from [CAESAR](#) and [PIVOTAL](#) trials to check an issue with participant numbers. Since we only had Kaplan-Meier data for the [CAESAR](#) and [PIVOTAL](#) trials,

we could not conduct a one-year survival comparison between early endovascular repair and surveillance, because there were no deaths in the surveillance group of the [CAESAR](#) trial.

In addition, for the source of cost data routine statistics have been replaced with standard costing manuals.

Previous versions

We did not report the overall effect for the 30-day mortality in this review. Inherent within the comparison between early repair and surveillance with selective repair is the fact that early mortality is always lower in the surveillance group; participants in the early-repair group underwent a procedure that carries at least some risk of operative mortality (the extent of the risk depending on whether open or endovascular surgery was used) almost immediately after enrolment, while patients in the surveillance group were simply monitored. As such, 30-day mortality is not a measure of interest. However, since the 30-day mortality effects differed between the included studies, we did report these effects for each individual study in the descriptions of the included studies.

A second difference between this update of the review and the protocol was the use of hazard ratios to describe one- and six-year survival for the [ADAM](#) and [UKSAT](#) trials. We based this decision on the fact that, when we conducted this review, we had the participant-level data for these two studies and were able to pool these data to estimate the hazard ratios. Since we only had tabular data for the [CAESAR](#) and [PIVOTAL](#) trials, we could not estimate a hazard ratio for the one-year survival comparison between early endovascular repair and surveillance. The term 'immediate' has replaced 'early' throughout the text, to be consistent with the trials' definitions.

INDEX TERMS

Medical Subject Headings (MeSH)

Aortic Aneurysm, Abdominal [diagnostic imaging] [mortality] [*surgery]; Aortic Rupture [epidemiology]; Asymptomatic Diseases [mortality] [*therapy]; Cost-Benefit Analysis; Endovascular Procedures; Organ Size; Quality of Life; Randomized Controlled Trials as Topic; Survival Analysis; Time Factors; Ultrasonography; Watchful Waiting

MeSH check words

Female; Humans; Male