Endovascular vs. Open Repair for Abdominal Aortic Aneurysm: Systematic Review and Meta-analysis of Updated Peri-operative and Long Term Data of Randomised Controlled Trials

Objectives

The objective was to investigate whether endovascular aneurysm repair (EVAR) has better peri-operative and late clinical outcomes than open repair for non-ruptured abdominal aortic aneurysm.

Methods

Electronic bibliographic sources (MEDLINE, EMBASE, and CENTRAL) were searched up to July 2019 using a combination of thesaurus and free text terms to identify randomised controlled trials (RCTs) comparing the outcomes of EVAR and open repair. The systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Pooled estimates of dichotomous outcomes were calculated using odds ratio (OR) or risk difference (RD) and 95% confidence interval (CI). A time to event data meta-analysis was performed using the inverse variance method and the results were reported as summary hazard ratio (HR) and 95% CI.

Results

Seven RCTs reporting a total of 2 983 patients were included in quantitative synthesis. Three of the trials reported long term follow up that extended to 15.8 years, 14.2 years, and 12.5 years. Meta-analysis found significantly lower odds of 30 day (OR, 0.36; 95% CI 0.20–0.66) and in hospital mortality with EVAR (RD –0.03; 95% CI –0.04 to −0.02). Meta-analysis of the three trials reporting long term follow up found no significant difference in all cause mortality at any time between EVAR and open repair (HR 1.02; 95% CI 0.93–1.13; p = .62). The hazard of all cause (HR 0.62; 95% CI 0.42–0.91) and aneurysm related death within six months (HR 0.42; 95% CI 0.24–0.75) was significantly lower in patients who underwent EVAR, but with further follow up, the pooled hazard estimate moved in favour of open surgery; in the long term (>8 years) the hazard of aneurysm related mortality was significantly higher after EVAR (HR 5.12; 95% CI 1.59–16.44). The risk of secondary intervention (HR 2.13; 95% CI 1.69–2.68), aneurysm rupture (OR, 5.08; 95% CI 1.11–23.31), and death due to rupture (OR, 3.57; 95% CI 1.87–6.80) was significantly higher after EVAR, but the risk of death due to cancer was not significantly different between EVAR and open repair (OR, 1.03; 95% CI 0.84–1.25).

Conclusions

Compared with open surgery, EVAR results in a better outcome during the first six months but carries an increased risk of aneurysm related mortality after eight years.

What this paper adds

Following the recent National Institute for Health and Care Excellence draft guidance proposing that patients should not be offered endovascular aneurysm repair (EVAR) if open surgical repair is suitable, long term data of randomised controlled trials, with follow up of up to 15 years, have been published. This review is the first to include the most updated data and use time to event meta-analytical methods. Significantly lower odds of peri-operative mortality were confirmed with EVAR. The hazard of all cause and aneurysm related death within six months of surgery was significantly lower after EVAR, but with further follow up the pooled hazard estimate moved in favour of open surgery; in the long term (>8 years), the hazard of aneurysm related mortality was significantly higher in patients who underwent EVAR. The risk of secondary intervention, aneurysm rupture, and death due to rupture was significantly higher after EVAR, but there was no significant difference in the risk of death due to cancer.

Introduction

Abdominal aortic aneurysm (AAA) repair is a major component of vascular service provision. The prevalence of AAA in men 65 years of age attending the Swedish nationwide AAA screening programme in a contemporary setting was 1.5%.1 After a mean of 4.5 years, 29% of patients had surgery for AAA, with a 30 day mortality of 0.9%.1 Despite the application of national screening programmes in several countries, AAA remains a significant healthcare burden across the world with a considerable associated mortality. In a large Swedish registry based cohort study, the AAA mortality was 36 deaths per 100 000 men aged 65–74 years in the early 2000s dropping to 10 deaths per 100 000 men of the same age in 2015.2

The past couple of decades have witnessed the advent and evolution of endovascular aneurysm repair (EVAR), which has become an established less invasive treatment with a marked improvement in peri-operative morbidity, mortality, and recovery compared with traditional surgery. From 2009 to 2013, an increase was observed in the proportion of repairs being performed as endovascular procedures in the UK (54% in 2009 rising to 66% in 2013), and this trend has stabilised over the last few years, with EVAR procedures accounting for 68% of the elective infrarenal AAA repairs in 2017.3 However, recent studies have shown that the early survival benefit of EVAR decreases or is even lost over time, with EVAR carrying a higher risk of rupture and secondary intervention than open surgical repair in the long term.4,5 As a result, the UK's National Institute for Health and Care Excellence (NICE) issued a draft guidance on AAA diagnosis and management with the notable recommendation that patients should not be offered EVAR if open surgical repair is suitable.6 This recommendation has led to much debate around the optimal treatment of unruptured AAA and has cast a shadow over the potential benefits of EVAR.

Long term results of randomised controlled trials (RCTs) with follow up of up to 15 years have been published recently.5,7,8 In view of the absence of a systematic review and meta-analysis of the most updated long term outcome data and the global ongoing controversy over the potential benefits of

EVAR, a meta-analysis was undertaken of published high quality long term data of EVAR vs. open surgical repair for unruptured AAA. Such analysis will produce more precise and powerful outcome estimates than the individual RCTs and help inform decision making.

Objectives

The objective was to investigate whether EVAR has better peri-operative and late clinical outcomes than open repair for unruptured AAA.

Methods

Review design

The objectives and methodology of the review were pre-specified in a protocol. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.9

Criteria for considering studies for this review

Types of studies

RCTs comparing outcomes of EVAR vs. open repair in patients with unruptured infrarenal AAA.

Types of participants

Male or female patients of any age who were diagnosed with AAA and underwent elective standard EVAR or open repair. Patients with symptomatic or ruptured AAA and those who required complex endovascular procedures for the treatment of AAA were not included.

Types of interventions

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Intervention of interest: EVAR

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Control intervention: open aneurysm repair

Types of outcome measures

Primary outcomes

- 30 day and in hospital mortality
- All cause mortality
- Aneurysm related mortality

Secondary outcomes

- Re-intervention

After interrogation of included studies, additional secondary outcomes were defined:

- aneurysm rupture
- death due to aneurysm rupture
- death due to malignancy

Search methods for identification of studies

The literature search strategy was developed by the review author team in collaboration with a clinical information specialist. Studies related to the subject were identified by searching electronic information sources and bibliographic reference lists of relevant articles.

Electronic searches

The Healthcare Databases Advanced Search (HDAS) interface developed by the NICE was used to interrogate the following electronic bibliographic databases: the National Library of Medicine's database (MEDLINE), Excerpta Medica Database (EMBASE), and the Cochrane Register of Studies (CRS) (CENTRAL). A combination of controlled vocabulary (thesaurus) and free text terms was used to search the databases. No language constraints were applied. The literature search was last run in July 2019. The search strategy is presented in Appendix 1.

Searching other resources

The bibliographic lists of the selected trials were screened for additional studies.

Study selection and data collection

Selection of studies

Two review authors (G.A., S.A.) conducted the pre-specified literature searches and evaluated the eligibility of studies for inclusion independently. When disagreement arose, a third review author (F.T.) acted as arbitrator.

Data extraction and management

One review author (G.A.) extracted data from selected studies. The collected data were then cross checked by a second review author (S.A.). Retrieved data were entered into a spreadsheet. Only published material was considered. The following types of data were extracted from the selected studies:

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study related data

- data related to risk of bias assessment
- demographics and clinical characteristics of the study populations
- aneurysm morphometric data
- outcome data

Assessment of risk of bias in included studies

The risk of bias tool developed by the Cochrane Collaboration was used to assess the risk of bias of selected RCTs.10 The risk of bias assessment was performed independently by two review authors (G.A., S.A.). A third review author acted as adjudicator in the event of disagreement (F.T.). Furthermore, a summary of findings table was generated and the quality of evidence was graded using the system developed by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) working group applying an online platform (https://gdt.gradepro.org/app/).11

Data analysis

Measures of treatment effect

Pooled estimates of dichotomous outcome data were calculated using the odds ratio (OR) and 95% confidence interval (CI). If one or more studies reported zero events in both groups, the risk difference (RD) and 95% CI were calculated instead. A meta-analysis of time to event data was conducted using the inverse variance method and the result was reported as summary hazard ratio (HR) and 95% CI. A mixture of direct (e.g. from reported HRs with CI) and indirect methods was applied (e.g. from survival curves with or without numbers at risk) to calculate the individual study HR and standard error (SE) for specific outcome measures.12 Data extracted from published Kaplan–Meier curves were digitised using the open source software Plot Digitizer (http://plotdigitizer.sourceforge.net). If the incidence rate ratio, calculated by (events/person time) group 1/(events/person time) group 2 was reported by the studies, it was used as an approximation

to HR. For the additional outcomes (aneurysm rupture, death due to aneurysm rupture and death due to malignancy), the studies provided no sufficient data for time to event meta-analysis; therefore, those variables were analysed as dichotomous data and the summary OR and 95% CI was calculated.

Unit of analysis issues

The individual patient.

Dealing with missing data

No attempt was made to contact the primary authors enquiring about missing data.

Assessment of heterogeneity

Between study heterogeneity was examined with the Cochrane's Q ($\chi 2$) test. Inconsistency was quantified by calculating I2 and was interpreted it using the following guide: 0%–40% might not be important; 30%–60% may represent moderate heterogeneity; 50%–90% may represent substantial heterogeneity; and 75%–100% may represent considerable heterogeneity.10

Assessment of reporting biases

It was planned to visually assess the symmetry of funnel plots and perform the Egger's test if more than 10 studies were identified.

Data synthesis

Fixed effect models were applied, unless significant statistical heterogeneity was present ($p < .050$ and $I2 \geq 75\%$), in which case random effects meta-analysis was conducted. A forest plot was created for each treatment effect.

Subgroup analysis and investigation of heterogeneity

No subgroup analysis was undertaken.

Sensitivity analysis

One trial at a time was excluded and analysis for each of the primary and secondary outcomes was repeated. Trials that were judged to be of high risk of bias in two or more domains were excluded and the analyses were repeated. Studies with short or medium term follow up (<8 years) were also excluded from time to event data meta-analyses.

Results

Results of the search

After discarding irrelevant reports and excluding articles with reasons, the literature search identified seven RCTs in 18 publications that fulfilled the inclusion criteria (Fig. 1).5,7,8,13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 Reports on cost effectiveness, quality of life and post hoc analysis, and those published as a conference abstract were not considered. A protocol in a peer reviewed journal was found for three of these trials.25, 26, 27 One of the trials was published in Chinese.21

Figure 1

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Figure 1. Study flow diagram using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) template for randomised controlled trials comparing endovascular vs. open repair for abdominal aortic aneurysm. *Duplicates were not removed using the Healthcare Databases Advanced Search (HDAS) interface since database specific thesaurus terms were used. EVAR = endovascular aneurysm repair; RCT = randomised controlled trial.

Description of studies

The trials reported a total of 2983 patients, 1518 of whom underwent EVAR and the remaining 1465 open repair. Four of these trials were large multicentre studies that were conducted in five different countries: the UK (EVAR-1, 37 centres), The Netherlands (DREAM, 26 centres), Belgium (DREAM, four centres), France (ACE, 25 centres), and the USA (OVER, 42 centres). The remaining three trials were smaller trials conducted in China,21 Canada,22 and The Netherlands.23,24 The recruitment period spanned from 1999 to 2011, and the follow up ranged from 30 days to a median of 12.4 years. Three of the trials (EVAR-1, OVER, and DREAM) reported long term follow up that extended up to 15.8 years, 14.2 years, and 12.5 years, respectively. These trials conducted an additional analysis of extended follow up that ended in June 2015 in the EVAR-1 trial,5 December 2016 in the OVER trial,7 and January 2016 in the DREAM trial.8 The study characteristics are presented in Table 1, the inclusion and exclusion criteria for patient enrolment in Table S1, and the baseline demographics and clinical characteristics of the study populations in Table S2. Notably, EVAR-1 randomised older patients with larger AAA than the other trials.

Risk of bias in included studies

In general, the study quality was high. One or more outcomes of interest in the review (aneurysm related mortality and secondary interventions) were not reported or reported incompletely in four of the trials (ACE, OVER, Chen et al.,21 Soulez et al.22), so they could not be entered in a meta-analysis, thus these trials were judged to be high risk of bias in the selective reporting domain of the Cochrane tool. For the rest of the domains, the risk of bias was judged to be low or unclear. The risk of bias graph and summary are presented in Fig. 2, and the supports for judgement are presented in Appendix 2.

Effects of interventions

Primary outcomes

Thirty day mortality was reported by four studies (EVAR-1, OVER, ACE, Lottman et al.;23,24 total of 1265 patients in the EVAR group and 1207 patients in the open repair group). It was 1.2% after EVAR and 3.1% after open repair, thus significantly lower in patients who underwent EVAR (OR, 0.36; 95% CI 0.20–0.66; p = .001). The statistical heterogeneity was not significant (p = .31, I2 = 17%). Similarly, in hospital mortality, reported by five studies (EVAR-1, OVER, DREAM, Chen et al.,21 Soulez et al.;22 total of 1297 patients in the EVAR group and 1269 patients in the open repair group), was 1.4% after EVAR and 4.5% after open repair, thus significantly lower in patients that underwent EVAR (RD –0.03; 95% CI –0.04 to −0.02; p < .001). The statistical heterogeneity was negligible (p = .58, I2 = 0%) (Fig. 3).

Meta-analysis of the three trials reporting long term follow up (EVAR-1, OVER, DREAM) with a total of 2484 patients found no significant difference in all cause mortality at any time between EVAR and open repair (HR 1.02; 95% CI 0.93–1.13; p = .62), with negligible statistical heterogeneity (p = .56, I2 = 0%). All cause mortality within six months from surgery was significantly lower after EVAR than after open repair (HR 0.62; 95% CI 0.42–0.91; p = .010), whereas the difference became non-significant at longer intervals post-AAA treatment (Fig. 4).

Meta-analysis of two trials (EVAR-1, DREAM) with a total of 1603 patients found no significant difference in aneurysm related mortality at any time between EVAR and open repair (HR 1.11; 95% CI 0.78–1.59; p = .55), and the statistical between study heterogeneity was moderate (p = .19; I2 = 43%). Interestingly, meta-analysis of aneurysm related mortality at different time intervals following treatment showed that the pooled estimate within six months was in favour of EVAR (HR 0.42; 95% CI 0.24–0.75; p = .003), whereas as the interval from the treatment lengthened, the pooled HR moved in favour of open repair reaching statistical significance at the 4–8 and > 8 year intervals (Fig. 5).

Secondary outcomes

Two studies (EVAR-1, DREAM) with a total of 1603 patients reported data on re-intervention in long term follow up. Meta-analysis of these trials found a significantly higher hazard of re-intervention with EVAR than with open surgical repair (HR 2.13; 95% CI 1.69–2.68; $p < .001$), and the statistical heterogeneity was moderate ($p = .15$; $I2 = 51\%$) (Fig. 6).

Additional outcomes

Two trials (OVER, DREAM) with a total of 1232 patients reported data on aneurysm rupture in long term follow up. Meta-analysis showed that the odds of rupture was significantly higher in EVAR (OR, 5.08; 95% CI 1.11–23.31; $p = .040$) with an insignificant statistical heterogeneity ($p = .61$, $I2 = 0\%$) (Fig. S1).

Deaths secondary to aneurysm rupture or cancer were reported in all three trials reporting long term follow up (EVAR-1, OVER, DREAM) with a total of 2484 patients. Meta-analysis found that the odds of death due to rupture was significantly higher after EVAR than after open repair (OR, 3.57; 95% CI 1.87–6.80; $p < .001$), and the statistical heterogeneity was moderate ($p = .11$, $I2 = 55\%$). The odds of death due to cancer was not significantly different between EVAR and open repair (OR, 1.03; 95% CI 0.84–1.25; $p = .80$) with low statistical heterogeneity ($p = .45$; $I2 = 0\%$) (Fig. S1).

Sensitivity analysis

The differences in all cause mortality at six months (HR 0.70; 95% CI 0.38–1.31; $p = .27$) and the aneurysm related mortality at > 8 years (HR 2.78; 95% CI 0.08–100.01; $p = .58$) became insignificant when the EVAR-1 trial was excluded from the analysis. Furthermore, the difference in the odds of death due to rupture became insignificant when the EVAR-1 trial was removed (OR, 1.57; 95% CI 0.60–4.07; $p = .36$). The difference in the odds of rupture became insignificant when the DREAM trial was removed (OR, 6.98; 95% CI 0.86–57.00; $p = .070$).

Discussion

Summary of main results

Meta-analysis of RCT data found significantly lower odds of peri-operative (in hospital and 30 day) mortality with EVAR than with open repair. Meta-analysis of long term follow up data showed that the hazard of all cause and aneurysm related death at any time following intervention was not significantly different between EVAR and open repair. An interesting finding was that the hazard of all cause and aneurysm related death within six months from surgery was significantly lower in patients who underwent EVAR, but with longer follow up, the pooled hazard estimate moved in favour of open surgery and, in the long term (>8 years), the difference in hazard of aneurysm related mortality was significantly lower in patients who underwent open repair. Notably, these differences were driven by the results of the EVAR-1 trial, which recruited older patients with larger AAAs. The hazard of secondary intervention, aneurysm rupture, and death due to rupture was significantly higher after EVAR, but the risk of death due to cancer was not significantly different between EVAR and open surgical repair.

Overall completeness and applicability of evidence

All seven RCTs directly investigated the review question, i.e. whether EVAR has better clinical outcomes than open surgery for unruptured AAA. One trial provided 30 day data only and focused the analysis on health related quality of life after EVAR and open repair.23 Aneurysm related mortality, which is the most important outcome to assess the comparative efficacy of EVAR and open repair, was reported by two trials only (EVAR-1 and DREAM). The selected trials applied broad inclusion criteria for patient enrolment and were conducted in four European countries, the USA, Canada, and China, representing practices across the developed world. Eligible patients had aneurysm morphology suitable for standard EVAR and were considered physiologically fit for open surgical repair. In the OVER trial, the authors explicitly stated that patients had to meet the manufacturer's indications for the endovascular system that would be used if so assigned. One would argue that anatomical suitability for EVAR spreads across a wide spectrum of morphological parameters, thus outcomes of patients lying at the border of anatomical suitability are unknown. Furthermore, the trials were conducted more than a decade ago, when newer generation aortic devices, sophisticated EVAR planning software, and modern radiology equipment were not available, which would limit the applicability of the review findings in current practices. Furthermore, the accumulated experience of surgery, radiology, and operating theatre staff as well as the efficient coordination between team members might confer different outcomes in contemporary practice. Very few women were recruited in the trials hence the results may not be generalisable to female patients.

Quality of the evidence

A small number of RCTs reporting a total of a few thousand patients have been conducted to investigate comparative clinical outcomes of EVAR and open repair for unruptured AAA. Three of the trials (EVAR-1, OVER, DREAM) reported long follow up of a median of 12.7, 10.2, and 9.4 years, respectively. Another two studies (ACE and Soulez et al.22) reported medium term follow up of a mean of around two and a half years, whereas Chen et al.21 reported short term follow up and Lottman et al.23,24 presented 30 day data only. Because there was evidence that the HR for the primary outcomes (all cause and aneurysm related mortality) did not remain constant over the full 10 years, the ACE and Soulez et al.22 trials were not included in the meta-analysis of time to event data.

The largest study, which dominated the meta-analysis outcomes, was the EVAR-1 with 1252 patients. This is evident in sensitivity analyses, which showed that the pooled estimate for all cause mortality at six months, aneurysm related mortality >8 years, and death due to rupture changed when the EVAR-1 trial was excluded from the meta-analysis. This finding may be explained by the fact that EVAR-1 enrolled older patients with larger aneurysms, which have been shown to be poor prognostic indicators following EVAR.28 One could argue that in the presence of such a small

number of trials, the lack of statistical significance in sensitivity analyses is probably due to lack of precision.

The key methodological constrain was selective reporting in four trials (OVER, ACE, Soulez et al.22 and Chen et al.21), which did not report data for the key outcome of interest in this review (aneurysm related mortality). Consistency of the results across the trials was noted, which is reflected in the low or moderate heterogeneity for all outcomes. The overall quality of the body of evidence contributing to the results of the review was high. The certainty in the meta-analysis findings was judged to be high or moderate for all primary and secondary outcomes (Table 2).

Potential biases in the review process

The review was conducted in accordance with the PRISMA guidelines and every effort was made to mitigate bias. The review is strengthened by a vigorous search of the literature to identify all relevant studies and obtain all relevant data. However, no attempt was made to contact the authors for missing data.

Agreements and disagreements with other studies or reviews

A few systematic reviews on long term outcomes of EVAR vs. open repair have been published recently, none of which have included the most updated data of the OVER trial.29, 30, 31 Notably, previous reviews failed to identify three randomised clinical trials investigating comparative outcomes of EVAR and open aneurysm repair. Furthermore, none of the previously published reviews conducted meta-analysis of aneurysm related mortality at different time intervals from the index procedure and meta-analysis of deaths due to rupture or cancer in the long term. Those reviews are also flawed by mixing randomised clinical trials and observational studies in meta-analysis models, a practice that is not recommended,10 and are dominated by observational rather high quality randomised data. They are also limited by the fact that they performed analysis of time to event outcome data (e.g. all cause mortality or re-intervention) as a binary response variable, which is not an optimal meta-analytical strategy because ignoring censored observations is inefficient.32

An individual patient data meta-analysis of the four RCTs with a median follow up of 5.5 years found that within three years, the survival curves of patients who underwent EVAR and open repair converged and beyond three years, aneurysm related mortality was significantly higher in the EVAR group.33 This review was conducted three years ago, when long term follow up data up to 15 years were not available.

The results of the analysis are corroborated by findings of large administrative registries investigating comparative outcomes of endovascular vs. open repair for intact AAA. A large study of health insurance claims data in Germany found that in hospital mortality was lower following EVAR than after open repair and a trend toward lower long term survival after EVAR.34 Similarly, in propensity score matched cohorts of Medicare beneficiaries, EVAR compared with open repair was associated with a substantial early survival advantage that gradually decreased over time, with the rate of late rupture being significantly higher after endovascular repair than after open repair.35 It should be noted that none of those registries provided data on very long follow up extending up to 15 years.

The review findings are reflected in the quality of life following surgery for AAA. The DREAM study group found less severe disruption to health related quality of life and health status in the short term in patients who underwent EVAR. However, during longer term follow up, patients who were treated by open repair appeared to have improved quality of life and health status.36

There have been concerns previously expressed about the increased cancer risk related to exposure to external radiation from the procedure and/or surveillance with computed tomography.37 Such concerns that patients undergoing EVAR are at increased risk of developing abdominal cancer compared with those undergoing open repair are not reflected in the results of the quantitative synthesis, which found similar risks of death from any cause or cancer after EVAR and open repair.

Conclusions

Implications for practice

The meta-analysis demonstrated that EVAR carries a lower peri-operative and early (within six months) mortality risk than open surgical repair for unruptured infrarenal AAA. The long term aneurysm related mortality, re-intervention and rupture rates are higher after EVAR than after open repair, and patients who develop rupture following EVAR are more likely to die than those whose aneurysm ruptures after open repair. Interpreted in the context of an ever increasing life expectancy, the findings reinforce the European Society for Vascular Surgery guidelines, which recommend open repair for patients with reasonable prospects of long term survival.38 In contrast, those with shorter life expectancy are likely to benefit from EVAR rather than open repair, particularly if their surgical risk is higher than average. In individual patients, clinicians should thus base their recommendations on the perceived risk of AAA rupture, life expectancy, and surgical risk. However, the differences in outcome between open repair and EVAR appear more qualitative than quantitative, with patients who undergo open surgery taking the bulk of the AAA and intervention related risk upfront (in the peri-operative period), and those undergoing EVAR distributing this risk over their lifetimes. Individual patients' culture, prejudices, personality, and personal circumstances may thus lead them to view the prospect of undergoing either treatment from different perspectives to that of the clinician (or healthcare provider) during the shared decision making process. Some

patients, for example, may value early survival more than freedom from late complications, and may thus legitimately choose EVAR over open repair, even if appropriately counselled.

Implications for research

It remains uncertain which individual patients would benefit from EVAR and which from open repair based on their physiological status. Personalised or precision medicine applying medical models where interventions for AAA treatment are tailored to the individual patient based on their predicted response or risk is an unexplored field in AAA disease.

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Figure 1. Study flow diagram using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) template for randomised controlled trials comparing endovascular vs. open repair for abdominal aortic aneurysm. *Duplicates were not removed using the Healthcare Databases Advanced Search (HDAS) interface since database specific thesaurus terms were used. EVAR = endovascular aneurysm repair; RCT = randomised controlled trial.

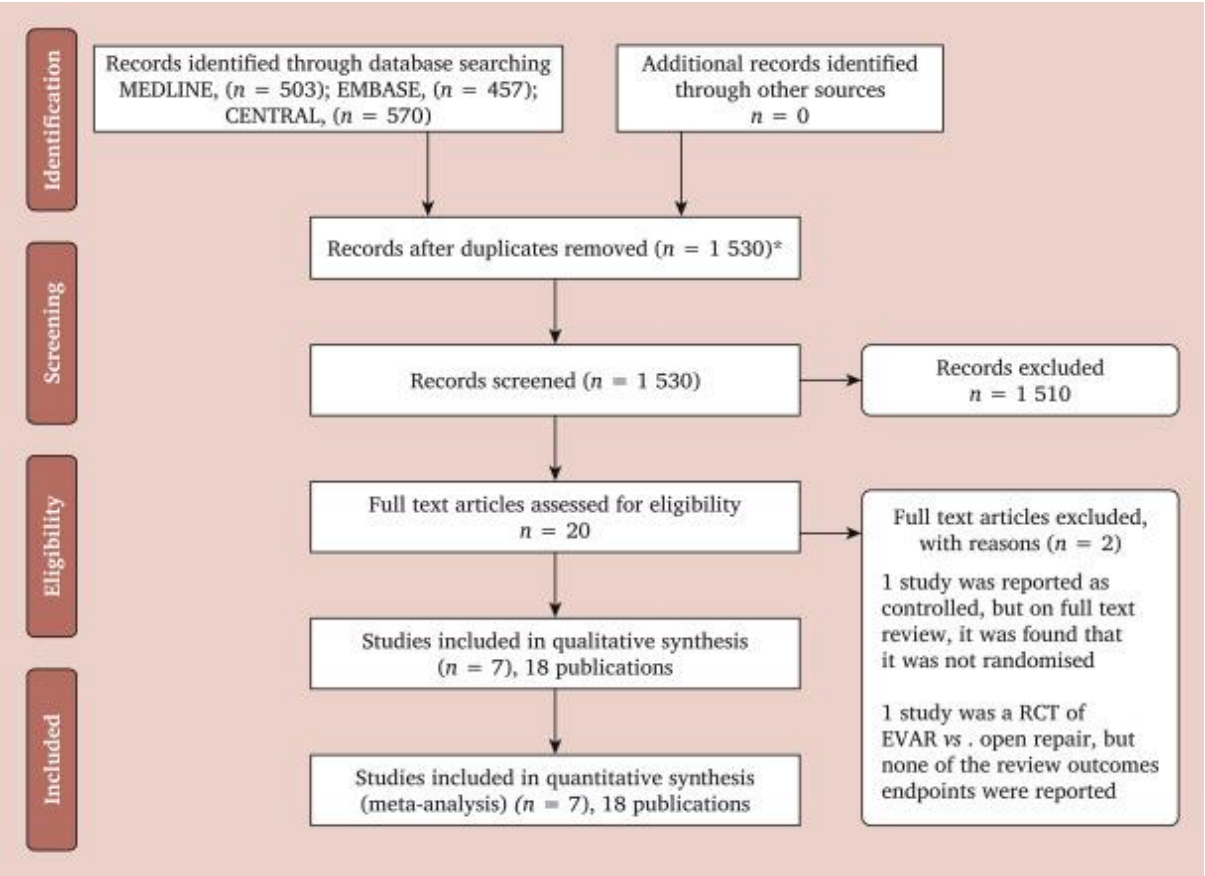
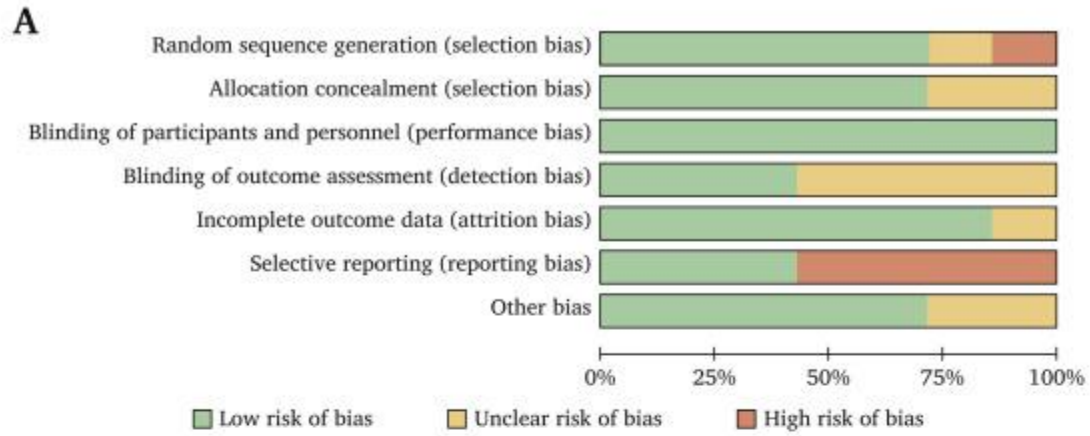


Figure 2. (A) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies combining endovascular vs. open repair for abdominal aortic aneurysm (B) Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



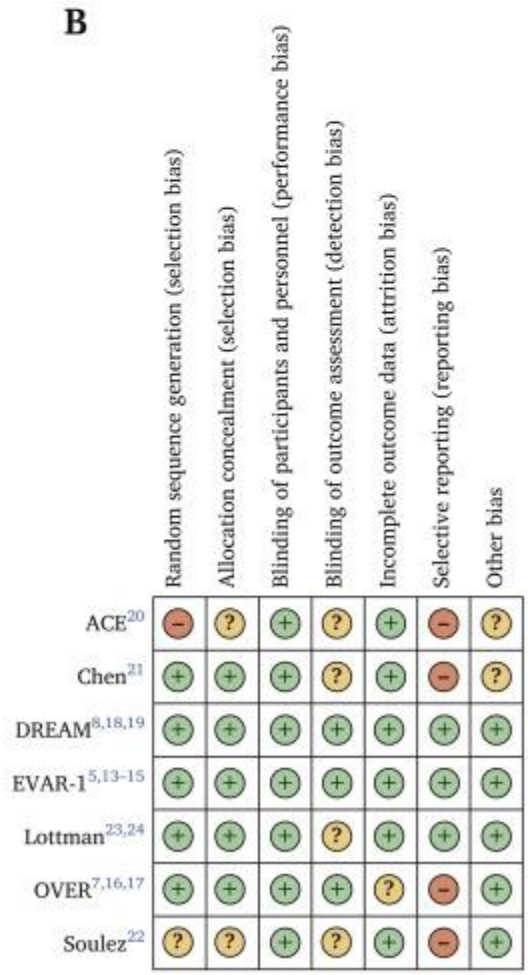
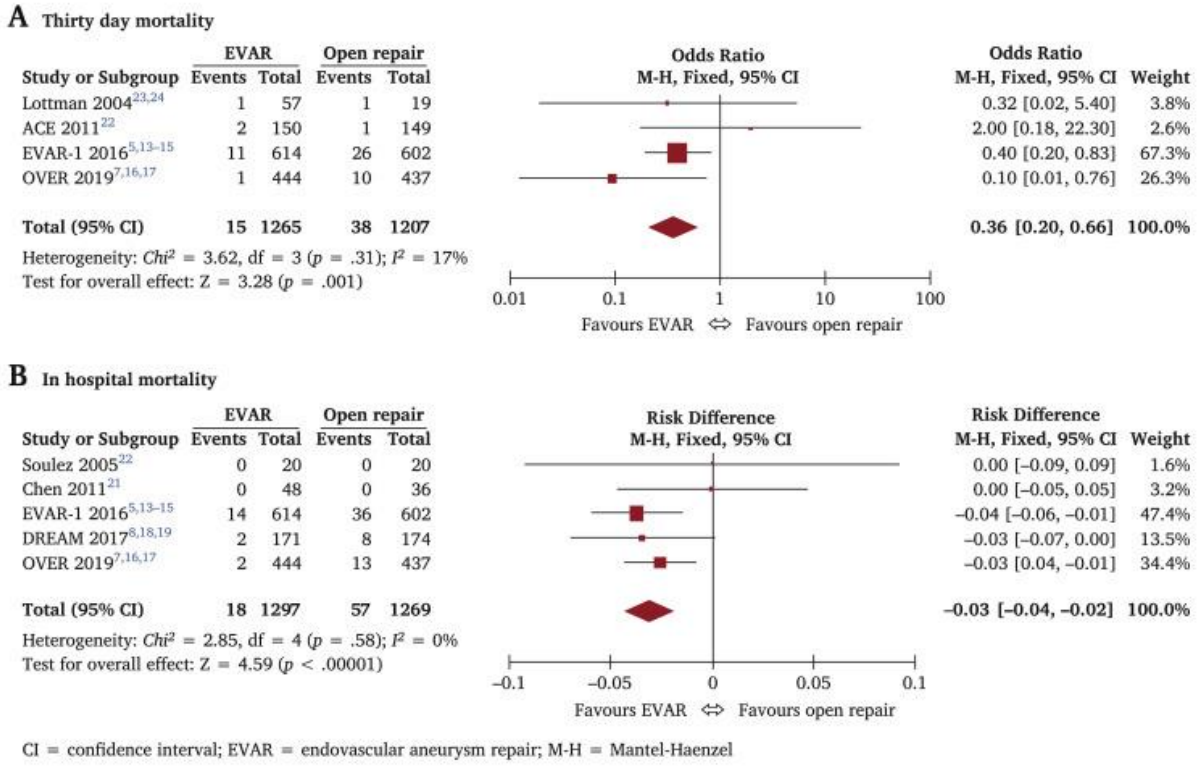
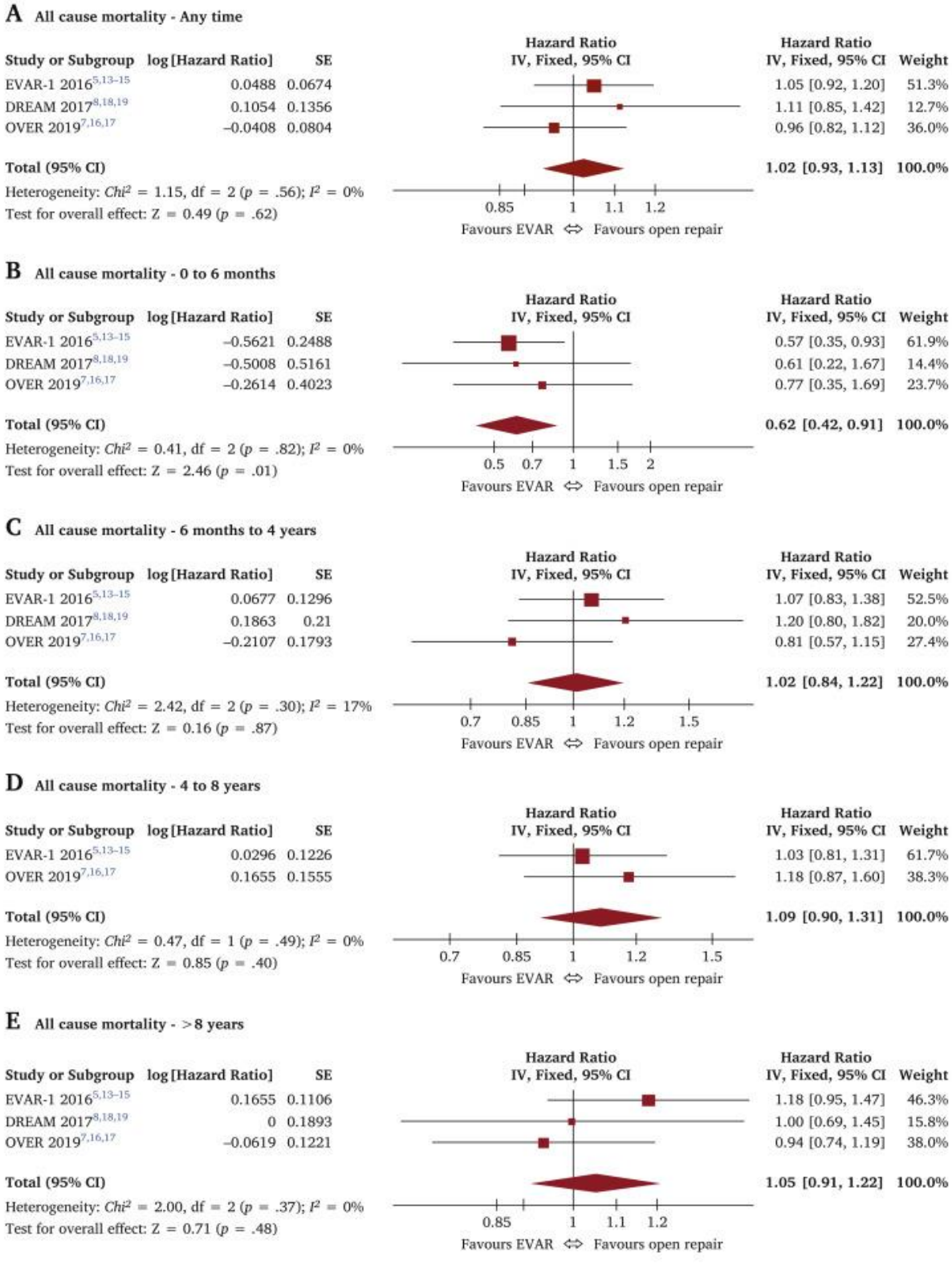


Figure 3. Forest plots of 30 day and in hospital mortality in patients treated by endovascular vs. open repair for abdominal aortic aneurysm. The solid squares denote the odds ratios (ORs) or risk differences (RDs), the horizontal lines represent the 95% confidence intervals, and the diamonds denote the pooled ORs or RDs. CI = confidence interval; EVAR = endovascular aneurysm repair; M–H = Mantel–Haenszel.



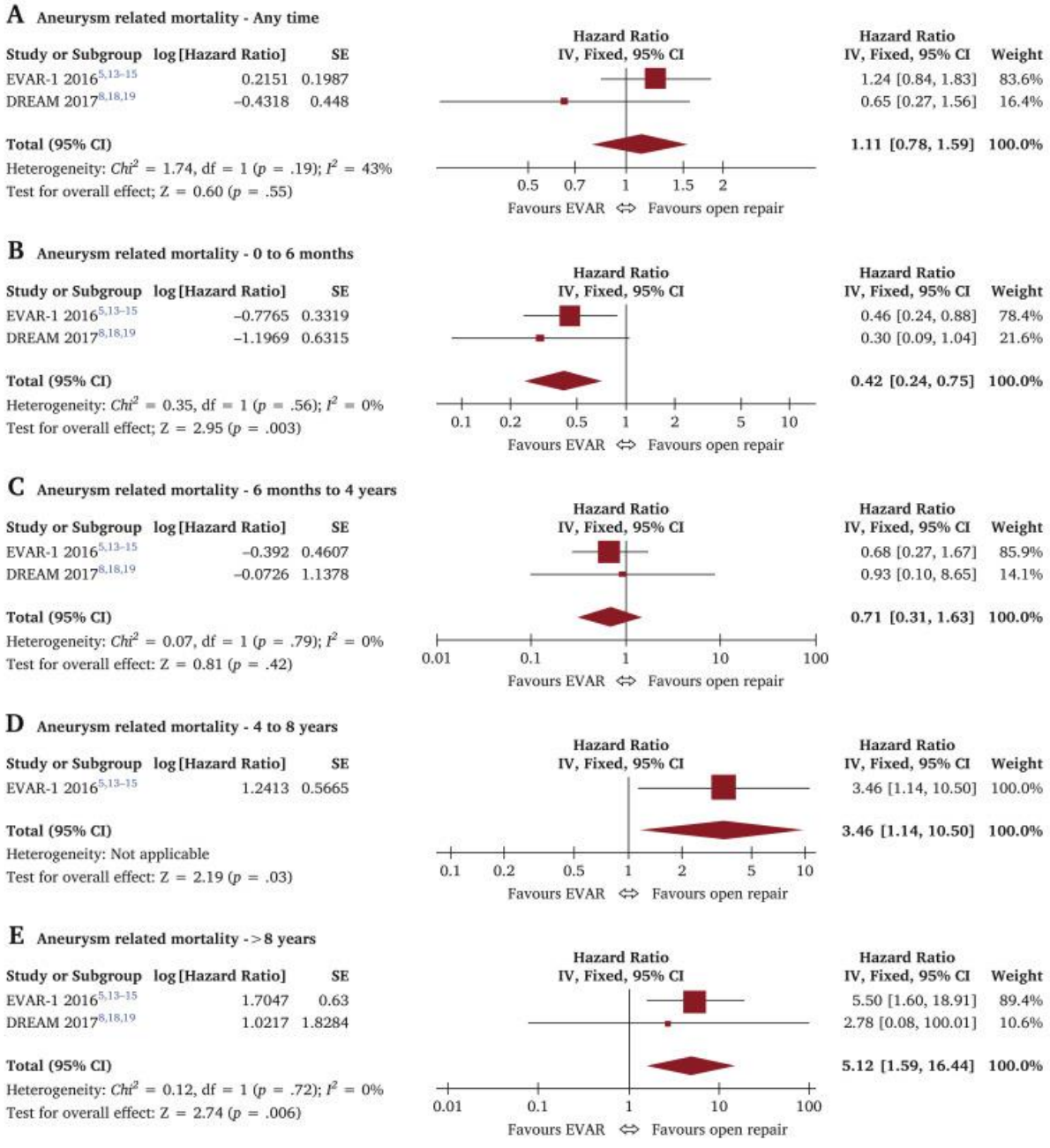
CI = confidence interval; EVAR = endovascular aneurysm repair; M-H = Mantel-Haenzel

Figure 4. Forest plots of all cause mortality in patients treated by endovascular vs. open repair of abdominal aortic aneurysm. The solid squares denote the hazard ratios (HRs), the horizontal lines represent the 95% confidence intervals, and the diamonds denote the pooled HRs. CI = confidence interval; EVAR = endovascular aneurysm repair; IV = inverse variance; SE = standard error.



CI = confidence interval; EVAR = endovascular aneurysm repair; IV = inverse variance; SE = standard error

Figure 5. Forest plots of aneurysm related mortality in patients treated by endovascular vs. open repair of abdominal aortic aneurysm. The solid squares denote the hazard ratios (HRs), the horizontal lines represent the 95% confidence intervals, and the diamonds denote the pooled HRs. CI = confidence interval; EVAR = endovascular aneurysm repair; IV = inverse variance; SE = standard error.



CI = confidence interval; EVAR = endovascular aneurysm repair; IV = inverse variance; SE = standard error

Table 1. Characteristics of randomised controlled trials comparing endovascular *vs.* open repair for abdominal aortic aneurysm

Trial, year, country, journal	Recruitment period	No of centres	Extended follow up	Length of follow up	EVAR	Open	Total	Intention to treat
OVER,[7,16,17] 2019, USA, *N Engl J Med*	Oct 2002–Apr 2008	42	Up to Dec 2016	Mean, 8.4 years; median, 9.4 years (range 0.02–14.2) (IQR 5.7–11.2)	444	437	881	Yes
DREAM,[8,18,19] 2017, Netherlands, *J Vasc Surg*	Nov 2000–Dec 2003	30	Up to Jan 2016	Median, 10.2 years (IQR 5.0–12.5)	173	178	351	Yes
EVAR-1,[5,13–15] 2016, UK, *Lancet*	Sep 1999–Aug 2004	37	Up to Jun 2015[a]	Mean, 12.7 years; median, 12.4 years (range, 1.8–15.8)	626	626	1252	Yes
ACE,[20] 2011, France, *J Vasc Surg*	Mar 2003–Mar 2008	25	None	Mean, 2.5 years (SD, 1.2); median, 3 years (range 0–4.8)	150	149	299	Yes
Chen *et al.*,[21] 2011, China, Zhonghua Wai Ke Za Zhi	Jan 2009–Jan 2011	1	None	12 months	48	36	84	Yes
Soulez *et al.*,[22] 2005, Canada, *J Vasc Interv Radiol*	Sep 1998–Jul 2002	1	None	Mean, 29 months (SD 13) (range 9–48) for the EVAR group and 27 months (SD 11) (range 12–48) for the open repair group	20	20	40	NR
Lottman *et al.*,[23,24] 2004, Netherlands, *J Endovasc Ther*	Sep 1996–Oct 1999	2	None	30 days	57	19	76	Yes

EVAR = endovascular aneurysm repair; IQR = interquartile range; NR = not reported; SD = standard deviation.
[a] For the primary mortality outcome; up to March 2015 for graft related complications and re-interventions.

Table 2. A summary of findings table of randomised controlled trials comparing endovascular *vs.* open repair for abdominal aortic aneurysm. The quality of evidence was graded using the system developed by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) working group

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consi-derations	EVAR	Open aneurysm repair	Relative (95% CI)	Absolute (95% CI)		
In hospital mortality												
5	Randomised trials	Not serious	Not serious	Not serious	Not serious	None	18/1297 (1.4%)	57/1269 (4.5%)	RD −0.03 (−0.04 to −0.02)	30 more per 1,000 (from 20 more to 40 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
30 day mortality												
3	Randomised trials	Serious[a]	Not serious	Not serious	Not serious	None	15/1265 (1.2%)	38/1207 (3.1%)	OR 0.36 (0.20 to 0.66)	20 fewer per 1,000 (from 25 fewer to 10 fewer)	⊕⊕⊕○ MODERATE	IMPORTANT
All cause mortality (follow up: range 9.4 years to 12.4 years)												
3	Randomised trials	Not serious	Not serious	Not serious	Not serious	None	1243 participants	1241 participants	HR 1.02 (0.93 to 1.13) (all cause mortality)	NA	⊕⊕⊕⊕ HIGH	IMPORTANT
Aneurysm related mortality (follow up: range 10.2 years to 12.4 years)												
2	Randomised trials	Serious[†]	Not serious	Not serious	Not serious	None	799 participants	804 participants	HR 1.11 (0.78 to 1.59) (aneurysm related mortality)	NA	⊕⊕⊕○ MODERATE	CRITICAL
Re intervention (follow up: range 10.2 years to 12.4 years)												
2	Randomised trials	Serious[†]	Not serious	Not serious	Not serious	None	799 participants	804 participants	HR 2.13 (1.69 to 2.68) (re-intervention)	NA	⊕⊕⊕○ MODERATE	IMPORTANT

CI = confidence interval; EVAR = endovascular aneurysm repair; HR = hazard ratio; NA = not applicable; OR = odds ratio; RD = risk difference.
[a] The ACE trial was judged to be high risk of selection bias.
[†] The second largest trial (OVER) reported no data on this outcome.