Original article

Long-term cost-effectiveness analysis of endovascular *versus* open repair for abdominal aortic aneurysm based on four randomized clinical trials

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Background: **A number of published economic evaluations of elective endovascular aneurysm repair (EVAR) *versus* open repair for abdominal aortic aneurysm (AAA) have come to differing conclusions about whether EVAR is cost-effective. This paper reviews the current evidence base and presents up-to-date cost-effectiveness analyses in the light of results of four randomized clinical trials: EVAR-1, DREAM, OVER and ACE.**

Methods: **Markov models were used to estimate lifetime costs from a UK perspective and quality-adjusted life-years (QALYs) based on the results of each of the four trials. The outcomes included in the model were: procedure costs, surveillance costs, reintervention costs, health-related quality of life, aneurysm-related mortality and other-cause mortality. Alternative scenarios about complications, reinterventions and deaths beyond the trial were explored.**

Results: **Models based on the results of the EVAR-1, DREAM or ACE trials did not find EVAR to be cost-effective at thresholds used in the UK (up to £30 000 per QALY). EVAR seemed cost-effective according to models based on the OVER trial. These results seemed robust to alternative model scenarios about events beyond the trial intervals.**

Conclusion: **These analyses did not find that EVAR is cost-effective compared with open repair in the long term in trials conducted in European centres. EVAR did appear to be cost-effective based on the OVER trial, conducted in the USA. Caution must be exercised when transferring the results of economic evaluations from one country to another.**

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Introduction

Abdominal aortic aneurysm (AAA) is a condition where the aorta becomes dilated in the segment below the diaphragm and in extreme cases can rupture, usually with fatal consequences (approximately 80 per cent mortality)[1]. The prevalence of AAA (aortic diameter 3·0 cm or greater) is currently about 2 per cent in men aged 65 years[2,3]. The condition is less common in women[1].

Currently, there are two main methods of elective intervention – open repair and endovascular aneurysm repair (EVAR) – typically undertaken when the AAA diameter exceeds 5·5 cm. Open surgical repair requires a large abdominal incision and incurs a lengthy convalescence of about 2–3 months. It has been associated with a fairly high operative mortality rate of 4–10 per cent, although the operative risks appear to have diminished in recent years[4]. The repair is very durable and is likely to protect from AAA rupture for the rest of the patient's lifetime. EVAR was developed in the early 1990s. This method is less invasive than open repair and can be performed through small groin incisions under local anaesthesia. The procedure has a lower operative mortality risk, faster recovery time, fewer requirements for high-dependency care and a shorter hospital stay; however, not all patients have aortic anatomy that permits EVAR. The durability of EVAR does not appear to be as good as that for open repair, with a need for postrepair

surveillance and sometimes further, usually smaller, re-interventions to correct graft-related complications.

This paper estimates the cost-effectiveness of EVAR *versus* open repair for AAA over the patient's lifetime. There have been a number of published economic evaluations of these treatments, including a review by the UK National Institute for Health and Care Excellence (NICE), which have come to differing conclusions[5–8]. Consequently, there is considerable confusion about whether EVAR is cost-effective or not over the long term. In general, the results of cost-effectiveness analyses differ for two reasons: because of differences in the evidence (inputs or parameters), or because of differences in the methods or structure of the model (the variables and outcomes included in the analysis, and assumptions made about relationships between them). This paper reviews the current evidence base and adapts a previously published decision model[5] in the light of the recently available mid- and long-term results of all the relevant randomized clinical trials (RCTs): EVAR-1 (UK)[9], Dutch Randomized Endovascular Aneurysm Management (DREAM; The Netherlands)[10], Open *Versus* Endovascular Repair (OVER; USA)[11] and Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese (ACE; France)[12]. The chosen perspective for this study is the UK National Health Service (NHS).

There are important differences in population and settings between the four trials, which mean that a formal meta-analysis is not appropriate for all the outcomes. For example, it is very likely that there are substantial differences in the cost profile of different procedures in the UK and USA. It is also plausible that the absolute levels of early and late mortality and reintervention vary between the different patient populations and settings. However, it seems less likely that structural assumptions, such as the convergence of survival curves, are inconsistent between settings. Consequently, four separate models have been constructed based on the aggregate data reported by each trial. Each model represents outcomes and costs that might plausibly occur in a UK setting. In each model two sensitivity analyses (or scenarios) have been constructed to simulate the impact of AAA deaths and reinterventions that might occur after the trial interval. In scenario 1, EVAR is associated with a higher underlying rate of complications that require ongoing surveillance and reintervention, and cause more AAA-related deaths, than open repair. In scenario 2, there is no difference in complications, reinterventions or AAA deaths between EVAR and open repair in the interval beyond the trials, and no need for long-term surveillance. Obviously, there are as yet no randomized data that can inform which, if either, of these scenarios is correct, although EVAR-1 trial follow-up is ongoing. These scenarios represent two extremes and many others are possible; however, these scenarios illustrate suitable conditions for investigating whether EVAR may be cost-effective.

Methods

The model compares EVAR with open repair in patients considered fit for open repair and anatomically suitable for EVAR. For comparability of costs across the trials, the cost perspective is that of the UK NHS and the price year is 2008–2009 (the end of the follow-up of EVAR-1)[9]. Health effects are quantified in terms of quality-adjusted life-years (QALYs), and the annual discount rate for costs and QALYs is 3·5 per cent[13].

Model structure

QALYs and costs are estimated using a state-transition (Markov) model. The model structure represents the key events that can occur in a cohort of patients for 25 years following aneurysm repair, which in these patients is taken to be a lifetime. There are three 'states': alive, death from AAA-related causes, or death from other causes. Aneurysm repair (EVAR or open repair) takes place during the first interval or model cycle (6 months), incurring costs and reduced health-related quality of life (HRQL) compared with that in the general population[9]. Patients may die during the first 6 months from an AAA-related cause (mainly operative deaths) or other causes. Following aneurysm repair, patients require surveillance (see below) and may require surgical reintervention. After the first 6 months, patients without reintervention are assumed to have average HRQL for someone of that age[9]. Other possible systemic complications (such as renal failure, myocardial infarction) were included in some earlier modelling studies[14–17], but are not included in the present model as no evidence for any difference between endovascular and open repair exists[1].

Model parameters

The population in each model represents the distribution of patients observed in the corresponding trial (*Table 1*). The mean age at entry was 74 years in EVAR-1[9] and 70 years in the other trials[10–12]. About 90 per cent of patients were men in EVAR-1 and DREAM, and more than 99 per cent in OVER and ACE.

The models predict QALYs, overall survival and aneurysm-related deaths (if this is reported in the corresponding trial). Overall survival in each model is calibrated to the proportion alive at the end of the trial

Table 1 Baseline characteristics of the patients in the trials and assumptions made in each of the modelling scenarios

	EVAR-1[9]	DREAM[10]	OVER[11]	ACE[12]
Characteristics of trial patients				
Mean age (years)	74	70	70	70
Men (%)	90	90	99	99
Mean aneurysm size (cm)	6·1	6·5	5·7	5·5
Recruitment interval	1999–2004	2000–2003	2002–2007	2003–2008
Graft	Zenith®, Talent®, Gore®	Zenith®, Talent®, Gore®	Zenith®, Gore®, AneuRx®	Zenith®, Talent®, Gore®
Aspirin use (%)	53	40	59	n.r.
Final recruitment	1252	351	881	306
Follow-up (years)				
Maximum	10	8·2	9	4·8
Median	6	6·4	5·2*	3
Main assumptions made in each modelling scenario				
Health outcomes measured in the model	AAA-related mortality, overall survival, QALYs			
Convergence of survival curves	At 2 years	At 2 years	At 8 years	No difference at any time
Initial procedure cost	Greater for EVAR	Greater for EVAR	Less for EVAR	No difference (detailed resource use not reported)
Health-related quality of life	Small advantage for EVAR in first 3 months, thereafter no difference			
Reinterventions	Rate of reintervention after open repair estimated from EVAR-1[9]. Relative risks after EVAR estimated from respective trial			

*Mean value. EVAR, Endovascular Aneurysm Repair; DREAM, Dutch Randomized Endovascular Aneurysm Management; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese; n.r. not reported; AAA, abdominal aortic aneurysm; QALY, quality-adjusted life-year. Zenith®, Cook Medical (Bloomington, Indiana, USA); Talent® and AneuRx®, Medtronic (Minneapolis, Minnesota, USA); Gore®, W. L. Gore and Associates (Flagstaff, Arizona, USA).

reporting interval (3 years in ACE, 6 years in DREAM, and 8 years in EVAR-1 and OVER). The timing of deaths (shape of the survival curve) is also important because this will influence estimates of mean survival time (area under the survival curve), and these are estimated from data given in the trial and UK national life-tables. Estimates of rates of events and treatment effects beyond the trial interval are based on expert opinion and extrapolation from the trial results. *Table 1* lists the main assumptions made. Given that more than half of patients survive at least 8 years after AAA repair[9], these very long-term estimates may influence the predicted cost-effectiveness.

Aneurysm-related and other-cause mortality during the first 6 months

During the first 6 months, the model based on EVAR-1 uses the rates of all-cause and aneurysm-cause mortality reported by the trial during this interval: 15 deaths (10 aneurysm-related) per 100 patient-years with open repair and 8·5 (4·6 aneurysm-related) per 100 patient-years with EVAR.

The other trials (DREAM, OVER and ACE) reported 30-day mortality in those undergoing AAA repair. The models based on these trials estimate all-cause mortality during the first 6 months as the rate of 30-day hospital mortality observed in the RCT (*Fig. 1*) plus the rate of other-cause death that would be expected in a population with the baseline characteristics of that trial (see below).

Aneurysm-related mortality and probability of overall survival between 6 months and the end of the trial

All the RCTs found that the survival curves converged during follow-up. Despite the initial benefit of EVAR, there was no observed difference between endovascular and open repair in overall survival after 2 years in EVAR-1 or DREAM, or after 8 years in OVER (*Table 2*). This trend is also seen in observational data; for example, after 3 years in the USA Medicare registry matched by propensity score[18] and in a recent systematic review[19] of late outcomes. This is explained only partly by the higher rate of aneurysm-related deaths after hospital discharge (*Table 3*)[20]. There appear to be other mid-term deaths, classified as having cardiovascular causes in EVAR-1[21] and 'miscellaneous' causes in DREAM[10]. The reasons for this catch-up are not well understood, but may arise from misclassification of causes of death, or because open repair is most risky in frail patients who are at higher risk of dying early anyway from co-morbid conditions. In any event, given that it is observed in all the studies, it is unlikely to be due to chance. Therefore, it is necessary to incorporate this apparent catch-up in survival in the model in order to estimate life expectancy accurately.

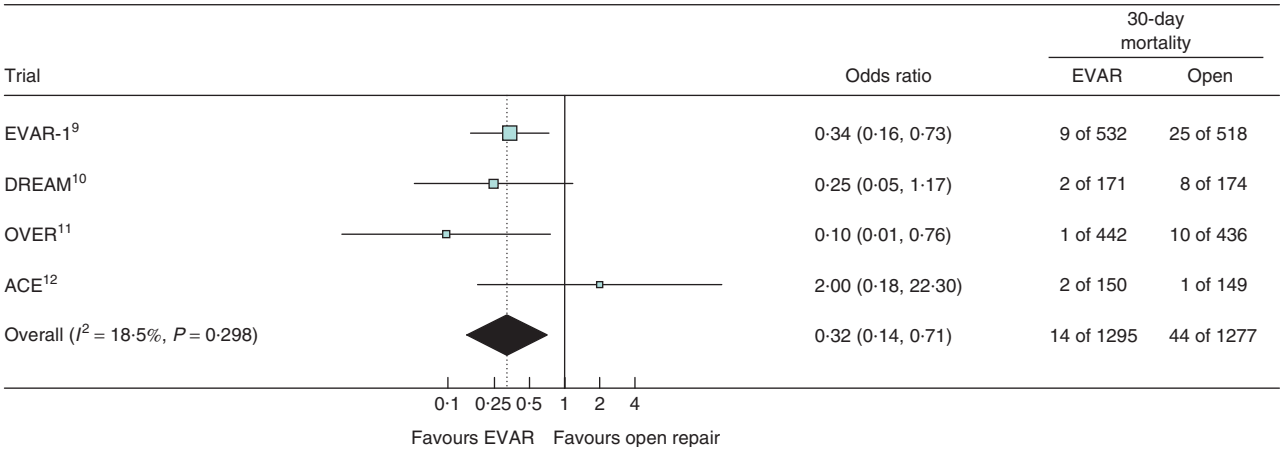

Fig. 1 Random-effects meta-analysis of 30-day mortality in the randomized trials. Odds ratios are shown with 95 per cent confidence intervals. Each model uses the trial-specific odds ratio. The pooled odds ratio is shown here for comparative purposes only. EVAR, endovascular aneurysm repair; DREAM, Dutch Randomized Endovascular Aneurysm Management; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese

Table 2 Overall survival reported in the randomized trials

	Mean age at baseline (years)	% alive			*P*	Hazard ratio for death from any cause (EVAR *versus* open repair)*
		EVAR	Open repair	Difference (EVAR – open)*		
EVAR-1[9]	74	54 (at 8 years)	54 (at 8 years)	0	–	1·03 (0·86, 1·23)
DREAM[10]	70	68·9 (at 6 years)	69·9 (at 6 years)	−1·0 (−10·8, 8·8)	–	1·04 (0·70, 1·52)†
OVER[11]	70	58 (at 8 years)‡	60 (at 8 years)‡	−2·0	0·81	0·97 (0·77, 1·22)
ACE[12]	70	86·3 (at 3 years)	86·7 (at 3 years)	−0·4	0·24	1·03 (0·98, 1·09)†

*Values in parentheses are 95 per cent confidence intervals (c.i.). †Not reported in the original paper; estimated based on the reported risk difference and *P* value or c.i. ‡Approximate Kaplan–Meier probability read from graph. EVAR, endovascular aneurysm repair; DREAM, Dutch Randomized Endovascular Aneurysm Management; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese.

The catch-up in mortality is implemented in the models by increasing the rate of other-cause mortality in the EVAR group (relative to the open repair group) so that the all-cause survival curves meet at 2 years after randomization (EVAR-1 and DREAM) or 8 years (OVER). The ACE trial found no difference in survival at any time (*Table 2*).

All-cause mortality risk after open repair in the model is based on UK life-tables[22], adjusted for the higher risks found in this population. Rates of all-cause mortality are higher in patients who have had successful AAA repair than would be expected in the general population[23,24]. In the EVAR-1 trial, 54 per cent of patients survived 8 years[9] (*Table 2*). This can be compared with the probability of survival in people of similar age (mean 74 years) in the general population[22]. After taking account of operative deaths, this implies a standardized mortality ratio (SMR) in these patients of about 1·1, which represents the relative increase in other-cause mortality rates in the general population that would be required so that the proportion alive after 8 years would be the same as in the open repair group of EVAR-1. Similar calculations based on overall survival in the open repair group in the other trials suggest that the SMR was about 1·5 in DREAM, OVER and ACE. These SMRs are used in the respective models. This method ensured that the probability of survival estimated by the model is calibrated to survival observed in the respective RCT.

AAA-related mortality has no effect on the results of the model during this interval (6 months to the end of the trial) because the probability of survival in the model is calibrated to overall survival reported in the trial. However, assumptions about the trend in AAA-related mortality become important when extrapolated beyond the trial follow-up.

Aneurysm-related mortality and probability of overall survival beyond trial follow-up

An important source of uncertainty is the rate of AAA-related deaths in each group after the trial follow-up, for which there are no randomized data. The EVAR-1 trial estimated that the rate of AAA death between 4 and 8 years

Table 3 Aneurysm-related mortality after hospital discharge reported in the randomized trials

	Proportion of patients at risk who died		Hazard ratio (EVAR *versus* open repair)
	EVAR	Open repair	
EVAR-1[9]			
AAA deaths			
6 months to 4 years	12 of 599	8 of 581	1·46 (0·56, 3·82)
4–8 years	10 of 472	2 of 461	4·85 (1·04, 22·72)
DREAM[10]			
AAA deaths after discharge	1 of 166	0 of 169	3·04 (0·12, 74·00)*
OVER[11]			
AAA deaths after discharge or > 30 days after AAA repair	8 of 444	3 of 437	2·60 (0·69, 9·72)*
ACE[12]	n.r.	n.r.	n.r.
Pooled relative risk†			3·39 (1·31, 8·78)

Values in parentheses are 95 per cent confidence intervals. *Relative risk not reported in original paper; calculated based on proportion of patients at risk who experienced event[20]. EVAR, endovascular aneurysm repair; AAA, abdominal aortic aneurysm; DREAM, Dutch Randomized Endovascular Aneurysm Management; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese; n.r. not reported. †Random-effects meta-analysis of relative risks of AAA death at 4–8 years from EVAR-1, and AAA death after discharge from DREAM and OVER. The DREAM model for scenario 1 uses the pooled relative risk rather than the trial results, as there were too few events in DREAM to give reliable and stable model predictions.

after repair was 0·2 per 100 patient-years after open AAA repair and 0·8 per 100 patient-years after EVAR (hazard ratio 4·85) (*Table 3*). DREAM and OVER recorded few AAA-related deaths after discharge and the relative risk is not statistically significant, although it appears similar in magnitude to that for EVAR-1.

For each RCT, two sensitivity analyses are considered. In the first scenario, the relative risks of late AAA deaths observed in the trial continue over the lifetime of the patient. Given that the survival curves meet during the trials, and if there is no difference in non-AAA-related deaths, this scenario implies that the survival curves diverge after the end of trial follow-up. In the second scenario, there is no difference in AAA deaths or deaths from other causes between EVAR and open repair after the latest published trial follow-up.

Reinterventions

All trials reported higher rates of reintervention following EVAR (*Table S1*, supporting information), although the difference was not statistically significant in the OVER trial. EVAR-1 has been criticized for failing to record all the complications of open repair, such as incisional hernias[6]. However, DREAM[10] and ACE[12] did include reinterventions for these complications. The models use the relative risks estimated by each trial during follow-up. In scenario 1, the relative risks of late reintervention observed in the trial continue over the lifetime of the patient. In scenario 2 there is no difference in reinterventions after the trial follow-up. The unit cost of a reintervention was taken to be £7536, based on estimates of hospital resource use reported in EVAR-1[5].

Hospital procedure costs

All trials that published hospital resource use for the initial procedure (days in ward, intensive care unit, blood products, operation room) found these were significantly lower after EVAR. EVAR reduces hospital stay by about 5 days (*Table 4*). Costs of open repair are taken from the EVAR-1 trial, to represent the UK perspective. The average differences in the costs of the procedures between EVAR and open repair are taken from the respective trials if these estimates were reported (EVAR-1, DREAM and OVER). These represent a plausible range of relative costs that might occur in the UK. Costs might vary between centres and over time for many reasons including type of centre, type of device and procedural technique. Currencies are converted to UK pounds at 2009 purchasing power parities[25]. The ACE trial found a similar reduction in length of stay but did not publish costs, and it is assumed in the ACE model that there is no difference in procedure cost.

Surveillance after aneurysm repair

Surveillance policy after aneurysm repair differed across the trials. Follow-up visits were scheduled at equal intervals in both groups in the EVAR-1 and OVER trials, with several visits in the first year and yearly follow-up thereafter. However, this protocol may not reflect standard clinical practice, particularly after open repair. The DREAM trial did not actively follow patients after 2 years following open repair. In the first scenario, patients are assumed to require one outpatient visit and computed tomography (CT) in the first year after open repair, with no further routine surveillance, whereas annual surveillance continues after

Table 4 Hospital length of stay and procedure costs reported in the randomized trials

	Hospital stay (days)			Costs		
	EVAR	Open repair	Difference (EVAR – open)	EVAR	Open repair	Difference (EVAR – open)
EVAR-1[9]	10·3	15·7	−5·4 (−11·6, −7·5)	£13 019	£11 842	+£1177 (−374, 2728)
DREAM[10]	n.r.	n.r.	n.r.	€14 915	€11 975	+€2940 (1493, 4386)
OVER[11]	5·0	10·5	−5·5 (−6·9, −4·1)	US $37 068	US $42 970	−US $5901 (−12 135, −821)
ACE[12]	5·8	10·4	−4·6*	n.r.	n.r.	n.r.

Values in parentheses are 95 per cent confidence intervals. EVAR, endovascular aneurysm repair; DREAM, Dutch Randomized Endovascular Aneurysm Management; n.r., not reported; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese.
*$P < 0·001$.

EVAR for the rest of their life. These data were based on the results of a survey of UK hospitals in 2004[26]. In clinical practice, the frequency of surveillance depends on many variables; for example, patients with diagnosed, untreated complications may have more frequent surveillance and more costly scans, and the guidelines of the European Society for Vascular Surgery[27] recommend duplex imaging at 5, 10 and 15 years after open repair. The cost of an outpatient visit and CT was taken to be £196, based on UK national unit costs[28]. In the second scenario, there is no difference in surveillance costs between EVAR and open repair after trial follow-up.

Health-related quality of life

The EVAR-1 trial found that patients incur a greater loss of HRQL following open repair than EVAR for the first 3 months (mean(s.e.m.) 0·05(0·02) difference in EQ-5D™ (EuroQol Group, Rotterdam, The Netherlands) index score), but there are no significant differences in HRQL after this time[9,26]. DREAM also found a small difference in favour of EVAR during the first 2 months, although this was offset later in the study and was non-significant throughout[7] (*Table S2*, supporting information). In this study, a small advantage for EVAR was assumed in the first 3 months (as in EVAR-1) and no subsequent difference.

Cost-effectiveness analysis

The model calculates mean costs and QALYs associated with each treatment in each trial. The incremental cost-effectiveness ratio (ICER) is calculated as the ratio of mean incremental costs divided by mean incremental QALYs. Conventionally, a treatment is usually considered cost-effective in the UK if the ICER is less than £20 000 or £30 000 per QALY[13]. Probabilistic sensitivity analysis (1000 Monte Carlo simulations, considering inputs as stochastic random variables based on each trial's data) was used to estimate mean costs and QALYs and confidence intervals for each model[29]. Differences in mean procedure costs and HRQL were considered normally distributed. Treatment effects (odds ratios and hazard ratios) relating to operative deaths, AAA-related deaths and reinterventions were assigned log-normal distributions.

The trials found unanimously that the survival curves converged even though the odds ratio for hospital mortality varied between trials. Therefore, in the probabilistic model, the survival curves should also converge on average across all the Monte Carlo simulations. This is implemented in the probabilistic model by assuming an inverse (negative) correlation between the initial treatment effect on hospital mortality and the rate of convergence of the survival curves. Thus, if the odds ratio for hospital mortality is higher or lower than average in a particular Monte Carlo simulation, the rate of convergence is adjusted proportionately to be slower or faster than average.

Results

The results for each of the four models over a 25-year follow-up are shown in *Table 5*. Each trial considered two scenarios after trial follow-up. The first scenario was more favourable to open repair, the second more favourable to EVAR.

In the model based on EVAR-1 under the first scenario, on average EVAR is more costly and less effective than open repair. In the second scenario, the ICER is £73 035 per QALY. Even under the most favourable assumptions regarding the post-trial interval, the 2-year advantage for EVAR in terms of overall survival is too short to offset the greater costs and reinterventions observed in the trial.

In the first scenario of the model based on DREAM, EVAR is only slightly more effective and the ICER exceeds £2 800 000 per QALY (the denominator of the ICER is close to zero). In the second scenario, the ICER is £61 462 per QALY, with a probability of being cost-effective at a threshold of £30 000 per QALY of 0·07.

In either scenario based on the OVER trial, EVAR is less costly and more effective than open repair, and the probability of being cost-effective exceeds 0·90. In the model based on ACE, in either scenario EVAR is

Table 5 Results of the model based on randomized trials showing two scenarios after trial follow-up

	Mean difference in cost (EVAR – open) (£)	Mean difference in QALYs (EVAR – open)	ICER (£/QALY)	Probability EVAR is cost-effective at thresholds of £20 000 per QALY	£30 000 per QALY
Scenario 1: EVAR associated with higher rates of AAA mortality, reintervention and surveillance than open repair after trial follow-up					
EVAR-1[9]	4014 (2167, 5942)	−0·02 (−0·19, 0·05)	D−	0·00	0·00
DREAM[10]	3181 (1557, 4986)	0·00 (−0·07, 0·05)	2 845 315	0·00	0·00
OVER[11]	−1852 (−5581, 2097)	0·05 (−0·06, 0·13)	D+	0·91	0·92
ACE[12]	2086 (1526, 2869)	−0·01 (−0·07, 0·00)	D−	0·00	0·00
Scenario 2: EVAR associated with the same rates of AAA mortality, reintervention and surveillance as open repair after trial follow-up					
EVAR-1[9]	3017 (1458, 4611)	0·04 (0·02, 0·07)	73 035	0·01	0·03
DREAM[10]	2608 (1036, 4131)	0·04 (0·01, 0·07)	61 462	0·03	0·07
OVER[11]	−2362 (−5984, 1017)	0·08 (0·02, 0·15)	D+	0·99	0·99
ACE[12]	1485 (1016, 2112)	−0·01 (−0·05, 0·00)	D−	0·00	0·00

Values in parentheses are 95 per cent confidence intervals. The incremental cost-effectiveness ratio (ICER) was not calculable for all trials: D+, endovascular aneurysm repair (EVAR) is less costly and more effective; D−, EVAR is more costly and less effective. QALY, quality-adjusted life-year; AAA, abdominal aortic aneurysm; DREAM, Dutch Randomized Endovascular Aneurysm Management; OVER, Open *Versus* Endovascular Repair; ACE, Anevrysme de l'aorte abdominale, Chirurgie *versus* Endoprothese.

more costly owing to continuing need for surveillance and reintervention, with no advantage in survival or HRQL.

Discussion

This study estimated the lifetime cost-effectiveness of EVAR *versus* open repair of AAA based on evidence from four randomized trials. The trials are heterogeneous in terms of patient population and settings, and hence an analysis that pooled all cost and outcome data across the trials would not be appropriate, in the sense that it would not answer whether EVAR was cost-effective for any particular decision-maker. Instead, separate analyses have been conducted based on the data from each trial and scenarios about what might occur beyond the trial interval. Other economic evaluations have already been published based on earlier results of some of these trials: EVAR-1[5], DREAM[7] and OVER[8]. However, it is difficult to compare the results of these studies because each was conducted according to a distinct methodology, differing in the perspective adopted (UK NHS, Dutch social insurer, US private health insurer), the time horizon (lifetime, 1 year, 2 years), the currency units (pounds, euros and dollars) and the implementation (Markov model, within-trial analysis). In this paper, common methods have been used for each analysis. Hence the variation in the results can be attributed to the different rates of events and resource use reported in each trial, and to the assumptions about how these rates might evolve beyond the trial follow-up.

The present model based on the EVAR-1 trial indicates that EVAR would be less effective than open repair over the long term if aneurysm-related deaths continued at the rate observed in the last 4 years of the trial. Even under an optimistic scenario that there were no differences in mortality, further reinterventions and surveillance beyond the trial, the cost would be approximately £73 000 per QALY gained and therefore not considered cost-effective. At UK prices, the acquisition cost of the endovascular device appears to be greater than potential savings from fewer days in hospital and shorter duration of surgery. The conclusions from this model are similar to those of a modelling study by the present authors based on 4-year EVAR-1 trial data[5].

The clinical results of the DREAM trial were similar to those of EVAR-1 at 8 years. An economic evaluation by the DREAM authors[7] based on patient-level data concluded that EVAR was not effective or cost-effective even at 1 year, because HRQL was slightly (but non-significantly) worse on average after EVAR. This was not confirmed by other trials, and the present study assumes that HRQL is the same in both groups after the first 3 months. However, a 1-year time horizon may be insufficient. Under an optimistic scenario, EVAR has a lifetime cost-per-QALY ratio of approximately £61 000. This is greater than would normally be considered cost-effective in the UK, although other countries have different thresholds.

An economic evaluation by the OVER authors[8] based on patient-level data at 2 years found that EVAR was cost-effective. The initial EVAR procedure is cost-saving in the OVER trial because the cost of hospital resources, and hence the savings arising from fewer hospital days and theatre time, are considerably greater in the USA and offset the acquisition price of the endovascular device. Caution must be exercised when transferring the results of economic evaluations to other countries. Prices of healthcare resources, clinical protocols and even the accounting system influence the estimated costs of procedures to some extent. Nevertheless. EVAR may be cost-saving in at least some centres in the UK, particularly where there is a shortage of intensive care facilities and hence a greater opportunity cost. The improved clinical results in OVER

may be due in part to its recruiting later and hence using clinicians with greater EVAR experience (and perhaps less experience of open repair). The learning curve for EVAR-1 was set at 20 procedures. Current evidence suggests that 50 or more procedures are needed before the learning curve plateaus[30]. A 2-year time interval is too short to draw meaningful conclusions about whether EVAR offers value-for-money compared with other technologies. In the present model based on the OVER trial, EVAR is effective over the long term because the observed gain in life-years during the first 8 years is greater than the life-years that potentially could be lost from AAA-related deaths after the trial, even under a pessimistic scenario.

The ACE trial authors did not conduct an economic evaluation. The clinical trial found no benefit from EVAR at any time, but greater need for reintervention. The lifetime model based on these initial trial data indicates that EVAR is not cost-effective. The ACE trial was conducted in a population with low operative risk and hence may not be comparable to the other trials.

It is acknowledged that these results are based on RCT data and thus may not be representative of all EVAR and open repair procedures. Registries and observational cohorts may yield different outcomes as they include patients of varying fitness, co-morbidity and anatomical suitability for EVAR[31]. However, not all patients in EVAR registries would be suitable for open repair, and so the restriction to RCT data seems appropriate.

This economic analysis does not find that EVAR is cost-effective compared with open repair over the long term based on the EVAR-1, DREAM or ACE trials. EVAR does appear to be cost-effective over the long term based on the OVER trial. These conclusions appear to be broadly robust to assumptions about what might occur beyond the trial intervals. The NICE[6] appraisal of endovascular repair conducted in 2008 recommended EVAR, and this conclusion was influenced to a large extent by the concerns of experts that the RCTs available at the time of the appraisal (EVAR-1 and DREAM) did not represent outcomes with modern devices[6]. Since then, OVER and ACE have published results. Given the widespread acceptance of EVAR in current practice, it is unlikely that another randomized trial will be conducted, and so modelling studies such as this one seem an appropriate way to summarize and present the current available evidence to decision-makers. EVAR devices and procedures have continued to develop, which may give EVAR an advantage in the future. EVAR devices used in these four trials were of an earlier technological generation, preoperative imaging was rudimentary, rehearsal and simulation not standard, and hybrid suites not available. Instructions for use were not always observed[32]. Clinical investigation is under way to determine whether the long-term performance of EVAR can be improved by targeting surveillance and reintervention at patients at highest risk of complications or secondary rupture[33].

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 Reinterventions reported in the randomized trials (Word document)

Table S2 Health-related quality of life reported in the randomized trials (Word document)