Health economics appendix

HE.1 General

The economic approach to provide evidence to support decision making around a clinical review question begins with a systematic search of the literature. The aim of this is to source any published economic evaluations of relevance to the topic of interest. At this stage it may become apparent that evidence exists in the literature which exactly meets the review question criteria and therefore there is no need for original economic analysis. If this proves not to be the case it may be decided that economic modelling can generate some useful analysis. The aim is to produce a cost-utility analysis is order to weigh up the benefits and harms of comparable interventions. The extent to which this is possible will be driven by the availability of evidence upon which to parameterise the clinical pathway and disease natural history.

HE.1.1 Decision problem

Table HE01: Review questions

RQ 12	What are the relative benefits and harms of EVAR, open surgical repair and non-surgical management in people with unruptured abdominal aortic aneurysms?
RQ 23	What is the effectiveness of EVAR compared to open repair surgery in repairing ruptured abdominal aortic aneurysms?

The effectiveness of EVAR compared with open surgical repair (OSR) was identified as an area of priority for new economic analysis. The use of EVAR has been evaluated in a previous NICE technology appraisal (TA167), which is updated in this guideline. Updating technology appraisal guidance must be informed by robust economic evidence. New clinical evidence has become available since the TA analyses were conducted, particularly longer term follow-up of 3 UK trials: EVAR-1 (15-year follow-up), EVAR-2 (14-year follow-up) and IMPROVE (7-year follow-up). Participants in the EVAR-2 trial were not suitable candidates for OSR, owing to anaesthetic risk and/or medical comorbidity, and IMPROVE trial participants had suspected ruptured abdominal aortic aneurysm (AAA). These populations were not fully captured by the analyses in TA167. Furthermore, the TA guidance is focused on infrarenal aneurysms, whereas the scope of this guideline has a wider population containing other types of abdominal aortic aneurysm. These other aneurysms may be suitable for more complex EVAR or open surgical repair.

Table HE02: PICO

Population	People for whom surgery is being considered to repair a confirmed abdominal aortic aneurysm (AAA), including: • Unruptured AAAs (elective) and ruptured AAAs (emergency); • Infrarenal AAAs and other ('complex') AAAs; • For whom open surgical repair (OSR) is considered to be a suitable intervention, and for whom OSR is not considered to be a suitable intervention (due to medical or anaesthetic contraindications).
Intervention	Endovascular aneurysm repair (EVAR), including standard (on-IFU) and complex (off-IFU).
Comparator	OSR (compared with EVAR in the population for whom OSR is considered to be a suitable intervention). No intervention (compared with EVAR in the population for whom OSR is not considered to be a suitable intervention).
Outcomes	A cost–utility analysis was developed based on the quality of life (in quality adjusted life years [QALYs]) and costs associated with: • The elective repair of unruptured AAAs or the emergency repair of ruptured AAAs; • The decision not to repair unruptured or ruptured AAAs (in the population for whom OSR is not considered to be a suitable intervention).
Key	*IFU, instructions for use.*

HE.1.2 Systematic review of published cost–utility analyses

HE.1.2.1 Methods

A systematic review of economic literature was conducted jointly for all review questions in this guideline. The search strategy was based on that used to identify clinical evidence for these intervention questions, with the RCT filter removed and a standard economic filter applied. The search terms are provided in Appendix B of every Evidence Review for this guideline.

Search strategy

A total of 5,173 studies was identified. The studies were reviewed to identify economic evaluations in the form of cost–utility analyses exploring the costs and effects of surgical procedures to repair abdominal aortic aneurysms, either unruptured (elective) or ruptured (emergency). Following an initial review of titles and abstracts, the full texts of 46 studies were retrieved for detailed consideration for the comparison of endovascular and open repair in either an elective or emergency setting.

An update search was conducted in December 2017, to identify any relevant cost–utility analyses that had been published during guideline development. This search return 814 studies. Following review of titles and abstracts, the full texts of 8 studies were retrieved for detailed consideration for the comparison of endovascular and open repair in either an elective or emergency setting.

<u>Elective repair of unruptured AAA</u>

Following full-text review, 15 of the 46 studies from the original search were judged to be potentially applicable cost–utility analyses for elective repair. Five studies, including those determined to be among the highest quality analyses of the 15, were UK analyses. As such, the remaining 10 (non-UK) studies were selectively excluded, as their applicability to the present guideline would be lower than the UK analyses. Three of the 8 studies reviewed from the update search were determined to be potentially applicable for elective repair, however

they were non-UK studies. A total of 5 studies was therefore included as economic evidence for elective repair.

Emergency repair of ruptured AAA

Following full-text review, 5 of the 46 studies from the original search were judged to be potentially applicable cost–utility analyses for emergency repair. Due to the smaller number of potentially applicable studies, we did not selectively exclude non-UK studies. Three studies were excluded due to possessing very serious limitations. Two of the 8 studies reviewed from the update search were determined to be potentially applicable for emergency repair. One of these (Powell et al., 2017) was an analysis of the IMPROVE trial, using more recent data than another IMPROVE analysis that was identified by the original search (Powell et al., 2015). The more recent study does not draw on any other data sources; the only additional information used comes from the longer-term IMPROVE follow-up. As such, we excluded the earlier study (Powell et al., 2015). The other potentially relevant study from the update search was excluded due to possessing very serious limitations (Takayama, 2017). A total of 2 studies was therefore included as economic evidence for emergency repair.

The methods and results of each included study, for unruptured and ruptured AAAs, are detailed in turn below. Studies that were excluded after full-text review, and reasons for exclusion, are provided in Evidence Review K and Evidence Review T.

Quality appraisal

Studies that met the eligibility criteria were assessed using the quality appraisal criteria as outlined in Developing NICE guidelines (NICE 2014).

HE.1.2.2 Results

HE.1.2.2.1 Elective repair of unruptured AAA

Michaels et al., (2005)

Michaels et al., (2005) published the first UK cost–utility analysis comparing EVAR with OSR for the elective repair of infrarenal aneurysms, based on early (perioperative) results of the EVAR-1 and DREAM trials. A decision tree was developed to model the surgical procedure. The EVAR arm included reintervention (potentially converting to OSR), endoleak, operative or aneurysm mortality, or successful surgery followed by general population survival for 10 years. The OSR arm was much simpler, consisting of operative or surgical mortality, and successful repair then ongoing general population survival. The primary analysis was designed to model a cohort of 70-year-old men with an initial AAA diameter of 5.5cm. A secondary analysis was also conducted comparing EVAR with providing no intervention, to reflect the EVAR-2 study population. The randomised EVAR-2 data were not available to inform this analysis, however; it was based on non-randomised evidence. These results have therefore been excluded due to very serious study limitations.

Model inputs were derived from a combination of early trial data (for the EVAR vs. OSR analysis) and a 2005 NICE review composed of non-RCT data. The NICE review found that 1.9% of primary EVAR procedures were converted to OSR during surgery, and 12.3% converted to OSR when a reintervention became necessary. EVAR was subject to a 17.6% probability of perioperative endoleak, with a 4.9% rate per month thereafter. Endoleak spontaneously healed in 6% of cases, and persisted despite reintervention in 19.7% of cases. Procedure costs were obtained from NHS reference costs (2003-04) for OSR, with an increment of £4500 applied to EVAR to reflect the higher mechanism cost. Reintervention was costed based on the EUROSTAR registry case mix, while post-EVAR follow-up was assumed to consist of 2 outpatient visits and CT scans per year. Quality of life was informed

by a general UK value for a 65-74 year old man (0.8), with temporary utility decrements during recovery for 2 and 4 weeks after EVAR and OSR respectively. Costs and QALYs were both discounted by 3.5% per year.

Model results (Table HE03) suggest that EVAR is not cost-effective compared with OSR, in an analysis based on perioperative differences in effectiveness only (no randomised long-term data were available). The CEAC presented shows that close to zero of 1000 probabilistic model runs produced an EVAR ICER under £20,000 per QALY gained. This result was consistent across scenario analyses, including applying an EVAR device cost of £0 (ICER: £53,773), reflecting its higher reintervention costs (though no OSR complications were modelled).

Table HE03: Michaels et al., (2005) cost–utility model results

Comparison	*Incremental (EVAR)*		*EVAR ICER (£/QALY)*	*Prob. <£20k*
	Costs (£)	*QALYs*		
EVAR vs. OSR	11,449	0.10	110,000	~0%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

Epstein et al., (2008)

Epstein et al., (2008) developed a lifetime Markov model comparing EVAR with OSR in the UK setting, based on data from the EVAR-1 randomised study. Only infrarenal aneurysms were therefore captured in the analysis, which is true of all 5 included studies. The model commenced at the point of intervention, with possible perioperative outcomes of mortality and conversion from an EVAR procedure to an open procedure. Surviving patients then moved to a 'symptom-free survival' health state, and could transition between this and the 'major cardiovascular event' and 'aneurysm-related readmission' states over time, or death (an absorbing state). Long-term mortality was informed by EVAR-1, in which all-cause mortality rates after EVAR and OSR converged after 2 years despite lower aneurysm-related mortality following EVAR for up to 4 years. A 'catch up' multiplier was applied to non-aneurysm mortality after EVAR in the model to ensure that all-cause survival in the 2 arms converged after 2 years.

Aneurysm-related quality of life effects were informed by EQ-5D data collected during EVAR-1. A decrement of 0.027 was applied after EVAR for 1 month, compared with 0.094 after OSR or a secondary procedure. These decrements were deducted from general age- and gender-related UK utility estimates (Kind et al., 1999). Decrements associated with myocardial infarction (0.075) and stroke (0.075 to 0.500) were derived from a UK study. Costs were derived either from the EVAR-1 trial itself or from other UK sources, with ongoing outpatient CT monitoring required following EVAR (2 in year 1, then 1 annually), but only once following OSR. All outcomes were subject to a discount rate of 3.5% per year.

Base-case results suggest that EVAR is associated with higher total costs and fewer QALYs per patient than OSR (Table HE04). Incremental costs were greater than zero to a statistically significant degree, while the 95% confidence interval around incremental QALYs crossed zero. Probabilistic sensitivity analysis was conducted to propagate parameter uncertainty through the model, finding that EVAR had a 1.2% probability of having an ICER of £20,000 or better per QALY gained. This probability remained less than 10% in most scenario analyses conducted. It increased to 14.7% if the perioperative mortality rate for OSR was increased to 8% (from 5%), and increased to 26.2% if the patient was aged 82 (from 74) and differences in cardiovascular event rates were omitted.

Table HE04: Epstein et al., (2008) base case cost–utility model results

Randomised group	*Total*		*Incremental (EVAR)*		*ICER (£/QALY)*	*Probability ICER <£20k*
	Costs (£)	*QALYs*	*Costs (£)*	*QALYs*		
OSR EVAR	12,065 15,823	5.07 5.05	3,758	-0.02	EVAR dominated	1.2%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

Chambers et al., (2009)

Chambers et al., (2009) developed an NIHR-funded cost–utility model as part of their EVAR health technology assessment to support NICE Technology Appraisal 167. Its objective was to determine the cost-effectiveness of EVAR for the elective repair of infrarenal AAAs, including in people who are fit enough to undergo OSR and those who are not. With a focus on infrarenal aneurysms and elective repair, it is narrower in scope that the present guideline. A systematic review of the literature was conducted to answer the clinical objective, and to provide inputs to an economic evaluation (the "York model"). The primary results of the York model compared the cost-effectiveness of EVAR with OSR for the repair of large (≥5.5 cm) aneurysms, when the decision to operate has already been taken. An exploratory analysis evaluated potentially repairing aneurysms at diameters below 5.5 cm, such that the study is also relevant to the question of early intervention for this guideline. Those methods and details are described in Evidence Review F.

For the primary analysis comparing EVAR with OSR, a Markov model was developed using individual patient-level data (IPD) from the EUROSTAR registry dataset (1994 to 2006). The model structure was based on the Epstein et al., (2008) model that preceded it, adapted to allow age, aneurysm size and fitness to affect baseline risks, and to allow variation in the timing of surgery. IPD informed baseline risks of perioperative mortality, and postoperative AAA-related mortality and other cause mortality. Multivariable models were fitted to the data to predict the event risks over time, with relative risks for EVAR and OSR informed predominantly by the EVAR-1 and DREAM studies, or expert advice. EVAR-1 was used to inform baseline AAA-related readmission, but other admissions (e.g. cardiovascular events) were not modelled. The 4-year aneurysm-related mortality benefit associated with EVAR that was observed in EVAR-1 was assumed to persist over the lifetime model horizon. Aneurysm ruptures were assumed to be fatal in 100% of cases.

Resource use associated with the aneurysm repair, postoperative monitoring, and readmission was informed by the EVAR-1 trial, and unit costs were from NHS reference costs, other UK national sources, the EVAR-1 trial or the stent manufacturers directly (product list prices were confidential). Like the Epstein (2008) model, post-EVAR monitoring was 2 outpatient CT scans in year 1 and annual scans thereafter, and post-OSR monitoring was 1 scan after 1 year only. The EVAR-1 trial was also used to inform quality of life inputs, but unlike the Epstein model utility decrements of 0.027 following EVAR and 0.077 following OSR or readmission were used, and both lasted for 6 months. Otherwise, general population values by age and gender were used (Kind et al., 1999). The model took a NHS perspective, with costs reported in 2007 UK pounds, and outcomes discounted at a rate of 3.5% per year.

The base case York model found EVAR to be associated with a QALY gain, where the Epstein model had found it to incur a net QALY loss. EVAR was again found to incur a higher cost per patient, though the additional cost was smaller than the previous model. Despite these more favourable results for EVAR, the ICER was £48,990 per QALY gained for the average patient. The probability of EVAR having an ICER better than £20,000 and £30,000 was 26.1% and 42.4%, respectively. The ICER for EVAR was better than £20,000 per QALY gained only in relatively extreme scenarios, where either (1) EVAR sustained an overall

survival benefit over OSR for the patient's lifetime, or (2) the unit cost of EVAR was equal to OSR, follow-up costs were lower and EVAR reintervention rates were lower. If the EVAR odds ratio associated with operative mortality improved (from 0.35 to 0.25), or if it took longer for overall mortality rates to converge (8 years instead of 3), then the ICER was £21-22,000.

Operative fitness (for open surgery) was included as a covariate in the authors' risk equations, from "good" (no pre-existing conditions) through "moderate" (subjectively considered to have 2x odds of operative mortality) and "poor" (4x odds) to "very poor" (8x odds). This categorisation, and its increase in mortality risk, was defined subjectively by the authors, rather than empirically, as there is no agreed standard definition of operative fitness. When a subgroup of patients with "poor" fitness is considered, the ICER was below £30,000 per QALY gained at all ages (70 to 85) and all aneurysm diameters (5.5 to 7.5 cm). EVAR ICERs were almost all above £30,000 in people with moderate or good operative fitness. However, the authors recognise that there is no formal or widely agreed criteria for defining operative fitness.

Table HE05: Chambers et al., (2009) primary cost–utility model results

Randomised group	*Incremental (EVAR)*		*ICER (£/QALY)*	*Probability ICER <£20k*
	Costs (£)	*QALYs*		
EVAR vs. OSR	2,002	0.041	48,990	26.1%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

Brown et al., (2012)

Brown et al., (2012) conducted an economic evaluation building on previous UK models with longer-term follow-up data. Its scope was the elective repair of infrarenal aneurysms. The Markov model was broadly similar to the Epstein (2008) and Chambers (2009) models before it, with 2 notable structural differences. The first was the inclusion of a waiting period between a patient being scheduled for surgery and the intervention taking place, captured in the "primary admission" health state. This is therefore an 'intention to treat' analysis, from the point of randomisation in the clinical evidence (EVAR-1), designed to capture deaths during waiting time and avoid biased postoperative relative effects (as the least fit patients are the most likely to die while waiting for aneurysm repair). In the EVAR-1 study, participants randomised to EVAR waited 1 extra week for their intervention, on average. The second structural difference was splitting the long-term outcomes into more granular periods; randomisation to 6 months, 6 months to 4 years, 4 to 8 years, and 8 years to lifetime. The authors reported that this was to capture the increased risk of reintervention in the first 6 months, which may not be representative of outcomes beyond 6 months. Data up to 8 years were informed by mid-term outcomes of EVAR-1, which had not been published at the time of the earlier UK models. Based on this longer-term data, aneurysm-related mortality converged after 8 years. Beyond 8 years, non-aneurysm mortality was estimated by a standardised mortality ratio of 1.1 relative to the general population, based on the EVAR-1 study and UK Small Aneurysm Trial (Powell et al., 2007).

Intervention costs were obtained from the EVAR-1 study micro-costing, which captured all aspects of the primary admission and had been used in previous cost–utility analyses. Unit costs were from national UK sources or from the trial survey to participating centres, inflated to 2008/09 prices where necessary. The total primary admission costs were £13,019 for EVAR and £11,842 for OSR, with device and related consumables costing £6,124 for EVAR and £782 for OSR. The reintervention cost (£7,536) was also obtained from EVAR-1. Outpatient follow-up with a CT scan was assumed to occur once after OSR and annually after EVAR. A quality of life decrement was applied for 3 months after repair or reintervention. The authors report that a bigger decrement is applied following OSR compared with EVAR, but the explicit utility values are not reported. They are likely to be

similar, if not the same as, the Chambers et al., (2009) inputs, as the same source data were used.

Base-case results suggest that EVAR is dominated by OSR, with higher overall costs and generating fewer total QALYs per patient. The QALY benefit caused by better operative survival with EVAR is eroded, over time, by its higher reintervention rate and by the 'catch up' effect applied to its non-aneurysm mortality rate. Probabilistic analysis showed that the cost difference was statistically significant, with the EVAR ICER better than £20,000 per QALY gained in only 1% of model runs. Comparing their results to those of the NICE appraisal of EVAR, the authors identified significant parameter differences but their results were robust to each one individually. Results were also robust to applying assumptions used in the original Epstein (2008) model, and clinical data from the OVER study (which did not report an ITT analysis).

Table HE06: Brown et al., (2012) primary cost–utility model results

Randomised group	*Total*		*Incremental (EVAR)*		*ICER (£/QALY)*	*Probability ICER <£20k*
	Costs (£)	*QALYs*	*Costs (£)*	*QALYs*		
OSR EVAR	12,263 15,784	5.433 5.391	3,521	-0.042	EVAR dominated	1%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

The authors also conducted a within-trial (non-model) analysis based on the EVAR-2 trial, comparing EVAR with 'no intervention' for infrarenal aneurysms in people deemed unfit for OSR. The primary analysis was an ITT analysis, comparing the outcomes of the 2 randomised groups. A secondary analysis presented a 'per protocol' analysis, which excluded patients on the 'no treatment' arm who did go on to receive an elective aneurysm repair procedure (30.9%). Quality of life (EQ-5D) and UK resource use were obtained from the EVAR-2 trial, captured in the same manner as the EVAR-1 study.

The primary analysis time horizon was 8 years, as per EVAR-2, though a secondary analysis was also conducted in which parametric survival curves were fitted to the 8-year data and used to extrapolate survival over a lifetime horizon. Separate parametric functions were fitted to each arm as observed Kaplan–Meier plots were observed to cross over. Based on a combination of statistical goodness of fit, validation using EUROSTAR registry data, and perceived clinical validity, the Weibull functions were selected for the lifetime analysis. Gamma functions were selected as second-best fits. In the long-term analysis, costs were not extrapolated beyond the 8-year data.

Base-case results from the 8-year ITT analysis found EVAR to have a mean ICER of £264,900 per QALY gained over 'no intervention', with 0% of 1,000 bootstrapped ICERs being better than £20,000 per QALY gained. Excluding 'no intervention' trial subjects who did go on to receive surgical aneurysm repair at some point during follow-up in a secondary, per protocol analysis, EVAR was associated with greater incremental costs per patient, but the EVAR QALY gain increased by a much larger magnitude. The mean ICER was £35,253 per QALY gained, though it was still found to be highly unlikely to be under £20,000. The within-trial, 8-year analysis potentially omits longer term survival differences, and this is reflected in the lifetime analysis results. The ITT analysis saw incremental QALYs increase from 0.037 to 0.350, with an ICER of £30,274 per QALY gained. This reflects the sensitivity of the model to long-term survival assumptions; in this case, extrapolating the observed benefit of EVAR over 'no intervention' across a lifetime. Omitting patients randomised to 'no intervention' who did receive aneurysm repair, the effect was more pronounced, with a mean ICER of £17,805 per QALY gained and 61% of bootstrapped ICERs being under £20,000. Interpretation of this set of results is difficult given the presence, and clear importance of, crossover from the 'no repair' trial arm to receiving surgical intervention.

Table HE07: Brown et al., (2012) secondary cost–utility model results: patients not fit for OSR

Comparison	Incremental (EVAR)		ICER (£/QALY)	Probability ICER <£20k
	Costs (£)	QALYs		
8-year analysis				
EVAR vs. No intervention				
ITT	10,214	0.037	264,900	0%
Per protocol	14,066	0.399	35,235	3%
Lifetime analysis				
EVAR vs. No intervention				
ITT	10,214	0.350	30,274	23%
Per protocol	14,066	0.790	17,805	61%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; ITT, intention-to-treat; QALYs, quality-adjusted life years.

Epstein et al., (2014)

Epstein et al., (2014) presented a further iteration of the original EVAR-1 model (Epstein et al., 2008), using data from additional RCTs that had been conducted since the initial model. Clinical and resource use inputs were obtained from each of the ACE, DREAM and OVER trials, as well as the EVAR-1 8-year follow-up data. Four sets of results were presented, with no synthesis of trial data into a single model. Of the 4 trials, the OVER study was the most favourable for EVAR relative to OSR; it was the only study to estimate a lower intervention cost with EVAR, and survival curves converged after 8 years, which is the longest duration of survival benefit observed. In the base-case analyses, the relative risks of postoperative aneurysm-related mortality persist over the lifetime of the patient. Scenario analyses assume that EVAR and OSR patients have the same long-term aneurysm and other-cause mortality risks beyond the duration of the relevant trial.

The reintervention rate following OSR was estimated using EVAR-1 trial data, with relative effects from each study used to estimate EVAR reintervention rates. These relative effects were applied for the duration of the lifetime models. Scenario analyses assumed that the higher reintervention rate for EVAR, present in all 4 trials, ceased after each trial duration.

Quality of life was informed by the EVAR-1 data showing a 3-month postoperative advantage (0.05 EQ-5D) for EVAR over OSR. Costs obtained from each trial were converted from their original currency to UK pounds using purchasing power parities (price year 2009), with the exception of the EVAR-1 analysis as EVAR-1 was itself a UK study. The different trials used different follow-up schedules, reflected in their estimates of resource use and costs. For the base-case analysis of this model, the authors applied a single postoperative outpatient CT scan for OSR patients and continued annual monitoring following EVAR, based on a clinical survey conducted during the EVAR-1 study. A second scenario applied no difference in follow-up requirement, which reflected the study protocols for EVAR-1 and OVER. Outcomes were discounted by 3.5% per year.

Base-case results showed that EVAR was dominated by OSR in the EVAR-1 and ACE analyses. EVAR was associated with an incremental cost of between £2,086 and £4,014 per patient across the EVAR-1, ACE and DREAM analyses. While not dominated in the DREAM analysis, EVAR had only a negligible QALY gain (zero at 2 decimal places), leading to an ICER of almost £3,000,000 per QALY gained. In all 3 of these analyses, probabilistic sensitivity analysis indicated a 0% probability of EVAR having an ICER of less than £20,000 per QALY gained compared with OSR. The OVER study represents an outlier in the model results; it was associated with an estimated cost saving of £1,852 per patient and a mean QALY gain of 0.05, meaning it dominates OSR. The probability that its ICER was better than

£20,000 was 91%. The authors attribute this to higher hospital costs in the US setting of the OVER trial, such that the lower length of stay associated with EVAR produces significant perioperative cost savings over OSR. The QALY gain from OVER is attributable to the 8-year period of survival benefit for EVAR, whereas the equivalent benefit for the other trials is modelled to last a maximum of 2 years. An analysis that combines all scenarios described above, each of which favours EVAR, did not change the overall cost-effectiveness conclusion. It remained very unlikely (0% to 3%) that the EVAR ICER would be better than £20,000 in the EVAR-1, ACE and DREAM analyses, while its cost-effectiveness case in the OVER analysis was strengthened further.

Table HE08: Epstein et al., (2014) primary cost–utility model results

Comparison & study	*Incremental (EVAR)*		*EVAR ICER (£/QALY)*	*Prob. <£20k*
	Costs (£) (95%CI)	*QALYs (95%CI)*		
EVAR vs. OSR				
ACE	2,086 (1,526, 2,869)	-0.01 (-0.07, 0.00)	Dominated	0%
DREAM	3,181 (1,557, 4,986)	0.00 (-0.07, 0.05)	2,845,315	0%
EVAR-1	4,014 (2,167, 5,942)	-0.02 (-0.19, 0.05)	Dominated	0%
OVER	-1,852 (-5,581, 2,097)	0.05 (-0.06, 0.13)	Dominant	91%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

HE.1.2.2.2 Emergency repair of ruptured AAA

Kapma et al., (2014)

Kapma et al., performed a cost–utility analysis alongside the AJAX trial, an RCT comparing EVAR with OSR for the repair of 116 ruptured AAAs conducted in 2 centres in the Netherlands. No modelling was conducted; instead, cost and QALY outcomes were derived from data collected during the study. No extrapolation beyond the 6-month data was conducted.

The AJAX study appeared to include subjects judged to be anatomically suitable to receive EVAR. A provider perspective was adopted, with hospital resource use data comprising surgery, blood products used, reintervention, use of intensive care and routine care, and diagnostics. Resource use data were collected at 30 days and 6 months post-intervention, and costed using national prices for the Netherlands, or study centre records (2010 prices). The EQ-5D-3L and SF-36 questionnaires were administered to elicit information on health-related quality of life, at 30 days, 3 months and 6 months after surgery. These could not be obtained at baseline, owing to the nature of an emergency procedure; therefore, the authors assumed patients experienced quality of life of the general population before the rupture. To obtain QALYs, EQ-5D valued were assumed to apply for the duration of the time interval since the previous questionnaire. Missing quality of life data were imputed backwards using the last available observation or, if only a 30-day record was obtained, imputed forwards. Bootstrapping was performed to characterise uncertainty in the estimates of incremental costs and QALYs, generating 25,000 samples of the same group with replacement.

Base-case results found that EVAR patients accrued an expected value of 0.324 QALYs, compared with 0.298 among OSR patients, though the difference was not statistically significant. EVAR had a marginally lower 30-day combined mortality and reintervention rate, and a lower 6-month mortality rate; however OSR patients were more likely to report severe problems in all 5 EQ-5D domains at 6 months. EVAR was €10,189 more expensive than OSR in terms of total costs (£9,111; conversion: 0.8942 [HMRC month exchange rate, November 2017]) largely attributable to the primary procedure cost and a higher use of subsequent hospital resources over the 6 month period. Overall total costs were noticeably higher than the IMPROVE analysis (see below), despite the shorter time horizon, driven by

much higher primary procedure costs, ward days required, and intensive care costs. The ICER for EVAR was €391,885 per QALY gained (£350,429), with a probability of less than 25% that the true ICER is better than €80,000 (£71,537) per QALY. A cost scenario analysis found the conclusions were robust until the cost of stents was reduced by 50%. Results were not sensitive to other cost scenarios or a subgroup analysis based on age.

Table HE09: Kapma et al., (2014) cost–utility model results

Randomised group	*Total*		*Incremental (EVAR)*		*ICER (€/QALY)*
	Costs (€)	*QALYs*	*Costs (€)*	*QALYs*	
OSR	31,616 (~£28,271)	0.298	10,189 (~£9,111)	0.026	391,885 (~£350,429)
EVAR	41,350 (~£36,976)	0.324			

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

The primary limitation of this analysis is its short time horizon. In using only data collected as part of the AJAX study, without any extrapolation, the authors were limited to the latest follow-up data of 6 months. This limitation is particularly important in the context of the short-term mortality benefit observed with EVAR. Additionally, the AJAX study is a relatively small trial, with its cost–utility results based on 57 EVAR patients and 59 OSR patients. Finally, resource use data were only obtained from 1 hospital.

Powell et al., (2017)

A within-trial cost–utility analysis was also undertaken for the IMPROVE study (Powell et al., 2017), a pragmatic RCT comparing a strategy of EVAR where anatomically possible, otherwise OSR, with a strategy of OSR only, for the repair of symptomatic or ruptured AAAs. This was a 3-year analysis, following an earlier 1-year analysis (Powell et al., 2015) that has been excluded from our review to avoid double-counting the same study. As such, this was the only UK economic evaluation identified that was informed by trial-based effectiveness evidence for ruptured aneurysm repair. No modelling was conducted; instead, cost and QALY outcomes were derived from resource use and EQ-5D data collected for IMPROVE. No extrapolation beyond the 3-year data was conducted, though clinical data from 6 years of follow up were presented by the authors.

Participants randomised to the EVAR strategy only received it if they were found to be anatomically suitable to do so, such that over one-third of those participants actually received open surgery. Resource use data collected included perioperative (30-day) inpatient resources, comprising stents, grafts and other device-related items (costed at list prices), time spent in the emergency room and theatre, and the subsequent use of critical, specialist or routine care, including staff time. Missing data were imputed, conditional on fully observable characteristics such as age and sex, using available observations from other participants who underwent repair. Standard UK sources were used to inform unit costs of resource items which, based on the sources listed, appear to be 2011-12 prices. The EQ-5D-3L questionnaire was administered to study subjects at 3, 12 and 36 months after surgery. The authors estimated QALYs using an area under the curve approach between EQ-5D data points. All outcomes were discounted by 3.5% annually.

Bootstrapping was performed to characterise uncertainty in the estimates of incremental costs and QALYs. The resulting set of paired cost and QALY outputs were used to estimate mean incremental costs and QALYs. The number of bootstrap simulations was not reported; however the earlier IMPROVE study by the same authors used 500 simulations (Powell et al., 2015).

Base-case results suggest that participants randomised to EVAR experienced 0.166 additional QALYs on average compared with OSR after 3 years. This gain was accrued through improved EQ-5D utility scores (0.76 vs. 0.66 at 3 months, 0.78 vs. 0.71 at 12 months, and 0.74 vs. 0.73 at 36 months), and superior survival after the perioperative period, though this benefit is not statistically significant. The mean total cost of EVAR study subjects was lower than OSR, attributable to its lower typical requirement for days spent in critical care and transfer to a different hospital. While EVAR patients were more likely to require more reintervention, fewer were classified as life-threatening. EVAR was therefore found to dominate OSR, with a probability of being cost effective in excess of 90% at all potential opportunity cost per QALY thresholds. This result was robust to the exclusion of symptomatic AAAs – therefore only including confirmed ruptures – and having adjusted for crossover between the 2 trial arms, in a 'complier average causal effect' analysis.

Table HE10: Powell et al., (2017) cost–utility model results

Randomised group	*Total*		*Incremental (EVAR)*		*ICER (£/QALY)*	*Probability ICER <£20k*
	Costs (£)	*QALYs*	*Costs (£)*	*QALYs*		
EVAR OSR	16,878 19,483	1.41 0.97	-2,605	0.166	EVAR dominates	>90%

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR: open surgical repair; QALYs, quality-adjusted life years.

Like the Kapma et al., analysis, the primary limitation of this analysis is its relatively short time horizon; it is based on 3-year data from the IMPROVE study with no extrapolation. There may be long-term differences in survival and reintervention rates in people treated with EVAR and OSR (Patel et al., 2016). The authors present Kaplan-Meier survival plots over 6 years, depicting a higher mortality rate for trial participants who were randomised to EVAR than those randomised to OSR beyond 3 years. By 6 years, the 2 survival curves almost cross over. This suggests there may be important long-term effects following emergency repair that have not been explored in the 3-year, within-trial analysis. The authors also state that the pragmatic nature of the trial, with extensive crossover from the EVAR arm to OSR, is a limitation of the study, complicating identification of the true relative effect of EVAR compared with OSR. However, it still provides a reasonable comparison of an 'EVAR if possible' world with an OSR-only world; in this respect, it is well suited to inform decision-making about whether a service in which EVAR is available should be commissioned.

HE.1.2.3 Discussion

HE.1.2.3.1 Elective repair of unruptured AAA

The systematic review of economic evaluations for this guideline identified 15 cost–utility analyses comparing EVAR with OSR and/or no repair that were potentially suitable for inclusion. No studies were found to be directly applicable to the UK or present decision problem; all exhibited potentially serious limitations, and all presented similar conclusions. As such, only the 5 UK studies were included. All 5 were modelling studies, and clinical data were predominantly informed by ongoing outputs from the EVAR-1 randomised trial. The earliest of these, Michaels et al., (2005), only had relative effects on perioperative outcomes, and found OSR to be cost-effective relative to EVAR. Studies using the increasing follow-up data to develop more complex models came to the same conclusion (Epstein et al., 2008; Chambers et al., 2009; Brown et al., 2012; Epstein et al., 2014). The most recent Epstein study included analyses using data from different trials, and only the OVER trial analysis – based on US resource use and a relatively fit patient cohort – suggested that EVAR was cost-effective over OSR. Michaels et al., (2005) and Brown et al., (2012) also presented comparisons of EVAR with no surgery in patients who were not considered to be fit enough to undergo OSR. The earlier analysis appears to predate the available trial evidence (EVAR-

2), whereas the second was hindered by trial crossover, with subjects randomised to 'no repair' going on to receive surgical intervention. The ITT analysis suggests that EVAR would not be cost-effective. The per-protocol analysis produces ICERs that are closer to conventional cost-per-QALY thresholds; however, even in this analysis, an ICER below £20,000 per QALY is only obtained by making assumptions that are extremely favourable to EVAR..

The latest, 15-year data from the EVAR-1 trial have recently been published, representing the longest follow up of EVAR and OSR patients. New health economic modelling was prioritised to capture these data, and potentially more recent non-UK trial data too (e.g. the OVER study). Furthermore, none of the published studies extended beyond the repair of infrarenal aneurysms; those which were considered to be anatomically ideal candidates for endovascular repair. Our scope is broader, including other types of AAA that may require more complex, custom-made EVAR devices. It was hoped that a new model would also provide cost–utility evidence for these types of complex aneurysm repair.

Emergency repair of ruptured AAA

The systematic review of economic evaluations for this guideline identified 6 cost–utility analyses comparing EVAR with OSR for the repair of ruptured AAAs that were potentially suitable for inclusion. Three were judged to have very serious methodological limitations, and 1 was excluded as an earlier iteration of a more recent study identified during the update search. A total of 2 studies was therefore included in the economic evidence. Of these, 1 was directly applicable to the decision problem, while the other was only partially applicable due to its non-UK setting.

The 1 UK analysis that was included was a within-trial economic evaluation undertaken alongside the IMPROVE study (Powell et al., 2017). This compared EVAR with OSR for the emergency repair of symptomatic or ruptures aneurysms (the majority were confirmed ruptures), and found EVAR to dominate OSR by providing improved health outcomes and incurring lower total costs. The analysis had potentially serious limitations, most notably its 3-year time horizon. Its results contrasted the other included study, a within-trial analysis of AJAX trial from the Netherlands, which found EVAR to be associated with a smaller QALY benefit and high incremental costs. This was a small trial, however, and was a particularly short-term analysis, with a 6-month time horizon. A short time horizon potentially omits important differences in longer term reintervention and mortality rates between EVAR and OSR, which have been observed in randomised elective repair data (Patel et al., 2016), and are suggested by 6-year survival data from the IMPROVE trial (Powell et al., 2017).

Health economic modelling of elective repair strategies was prioritised by the committee for this guideline. Economic modelling for the existing NICE TAs predates the AJAX and IMPROVE trial data; therefore incorporating emergency repair of ruptured AAAs into the new model structure was also prioritised

HE.1.2.4 Excluded studies

Studies excluded from the elective and emergency repair economic literature reviews following full-text review, and reasons for exclusion, are provided in Evidence Review K and Evidence Review T respectively.

HE.2 New cost–utility model – introduction

We built 2 cost–utility models to address the 2 review questions prioritised by the guideline committee, distinguished by the populations included in the model. A person will undergo a preoperative assessment before AAA repair in clinical practice, from which the clinician might determine that the mortality risk associated with OSR is too high, owing to the person's comorbidities and other risk factors. EVAR is a less invasive procedure, meaning it is typically left as the only repair intervention available for this population. The 2 model populations are therefore: (1) people for whom OSR is a viable intervention to consider, and (2) people for whom OSR is not considered to be an appropriate option. The 'fit for OSR' model captures economic and health outcomes following the point at which the decision has been made to attempt to repair an AAA, by either EVAR or open repair. The 'unfit for OSR' model estimates outcomes from the point at which a decision has been made either to repair the aneurysm using EVAR, or not to attempt repair, leaving the aneurysm in place. For both populations, we divided our analysis into subgroups defined by the urgency of AAA repair (elective [unruptured aneurysms] and emergency [ruptured aneurysms]), and again by aneurysm complexity (infrarenal and complex). The 8 resulting unique subpopulations included in the model are shown in Table HE11.

Table HE11: Populations included in the new cost–utility analysis

Total AAA population							
Population for whom OSR is suitable				Population for whom OSR is not suitable			
Elective repair (unruptured AAA)		Emergency repair (ruptured AAA)		Elective repair (unruptured AAA)		Emergency repair (ruptured AAA)	
Infrarenal	Complex	Infrarenal	Complex [a]	Infrarenal	Complex	Infrarenal	Complex [a]

Note: (a) Emergency repair of complex aneurysms using EVAR does not tend to occur in practice, due to the need for custom-made EVAR devices for complex aneurysms. In the model, all patients in these subgroups are assumed to receive the comparator (OSR or 'no intervention'), and no comparison with EVAR is presented.

The models use a patient perspective for outcomes and an NHS and PSS perspective for costs, in line with Developing NICE guidelines (NICE 2014). The key health economic outcomes, used to determine cost effectiveness, are incremental costs and QALYs, and the resulting ICER.

The state-transition models have a cycle length of 1 month and run until patients reach 100 years old. The UK trials evaluating AAA repair interventions had mean patient ages of 74-76, while the UK National Vascular Registry reports than 91% of AAA repairs occur in people within the range of 66 to 85 years old. As such, a maximum age of 100 is likely to capture the majority of important differences in outcomes between competing interventions for AAA repair patients. Patients entering the model pass through the series of discrete health states over time. This allows costs and QALYs to be accrued for each cycle spent in each particular health state, for the duration of the model.

As per Developing NICE guidelines (NICE 2014), all future cost and QALY outcomes are discounted at a rate of 3.5% per year. This reflects societal time preference; costs that are incurred today are more important than costs incurred next year, and health benefits accrued next year are less important than health benefits accrued today.

The model structure was developed in collaboration with the guideline committee, and was selected for the following reasons:

- For comparability. Existing, published cost–utility analyses evaluating surgical techniques have largely taken similar model structures (see Section HE.1.2.2), such that the similarities and differences with our model should be easily identifiable.
- For transparency. We recognise that a time-to-event model, such as a Discrete Event Simulation, may also have been suitable, but such models are often viewed as 'black boxes'. The inputs and calculations are typically less clear, requiring greater technical expertise to thoroughly review and critically appraise.
- For simplicity. The relevant clinical states lend themselves to being defined by discrete health states, primarily alive and dead.

HE.2.1.1 Identifying sources of parameters

The majority of model inputs have been derived from the key UK randomised trials in this area: EVAR-1, EVAR-2 and IMPROVE, supplemented by data from other, non-UK trials, and registry data (UK National Vascular Registry; European Vascunet Registry). Results of the EVAR and IMPROVE trials are published (Brown et al., 2012; Patel et al., 2016; Powell et al., 2014; Sweeting et al., 2017), though their respective trial investigators provided us with anonymised patient-level survival data, capturing up-to-date follow-up that is slightly longer than the most recent trial publications.

All trials were identified in the systematic literature review conducted for these review questions. Specifically, these trials inform the following model inputs, to varying degrees: pre-operative, perioperative and post-operative survival, reintervention and rupture rates, quality of life, resource use and costs. Where these sources did not provide data required by the model, parameters were identified through informal searches that aimed to satisfy the principle of 'saturation' (that is, to 'identify the breadth of information needs relevant to a model and sufficient information such that further efforts to identify more information would add nothing to the analysis' [Kaltenthaler et al., 2011]). This process identified the 2 registries mentioned above. We conducted searches in a variety of general databases, including Medline (via PubMed), the Cochrane Database of Systematic Reviews and GoogleScholar.

When searching for quality of life, resource use and cost parameters, searches were conducted in specific databases designed for this purpose: the CEA (Cost-Effectiveness Analysis) Registry and the NHS Economic Evaluation Database (NHS EED).

We also asked the expert guideline development committee to identify model parameters and data sources, where required. For example, the committee provided evidence regarding the unit costs of EVAR devices. We reviewed the sources of parameters used in the published CUAs identified in our systematic review (see Section HE.1.2.2, above); during the review, we also retrieved articles that did not meet the formal inclusion criteria, but appeared to be promising sources of evidence for our model. We studied the reference lists of articles retrieved through any of these approaches to identify any further publications of interest.

Selecting parameters

Our overriding selection criteria were as follows:

- The selected studies should report outcomes that correspond as closely as possible to the health states and events simulated in the model.
- The selected studies should report a population that closely matches the UK population (ideally, they should be drawn from the UK population).
- All other things being equal, more powerful studies (based on sample size and/or number of events) were preferred.

- Where there was no reason to discriminate between multiple possible sources for a given parameter, we gave consideration to quantitative synthesis (meta-analysis), to provide a single summary estimate.

HE.2.2 EVAR vs. OSR – people for whom OSR is a possible intervention

HE.2.2.1 Model structure

As described above, the model takes a state-transition structure. Patients enter the model once the decision has been made to intervene to repair an AAA, either by EVAR or OSR. Elective patients, who have been referred for non-emergency AAA repair, initially spend time on the waiting list, and are subject to a risk of death during this time. They then go on to receive their intervention, which lasts for 1 model cycle, in which the patient is at risk of the appropriate perioperative (30-day) mortality risk. Patients who survive the elective procedure transition to long-term 'postoperative survival', where they are subject to a risk of reintervention to resolve complications, but otherwise remain until death or the end of the model time horizon. Some previous analyses have explicitly modelled the distinction between AAA-related mortality and all-cause mortality, but this has typically required the author to implement a 'catch-up' effect to non-AAA mortality. We avoided this this potential confusion by simply modelling overall survival, which inherently comprises AAA-related and other-cause deaths. Emergency patients, presenting with ruptured aneurysms requiring immediate repair, follow the same model structure, except they spend no time on the waiting list. Figure HE01 provides a schematic depiction of the model structure.

Table HE12: Modelled health states – Intervention model 1: EVAR vs. OSR

Health States	
Waiting list	An elective patient joins the waiting list ahead of their repair procedure, and is subject to a risk of death during this time. Emergency patients do not use this health state.
Elective repair	An elective patient spends 1 cycle in the repair health state, undergoing either EVAR or OSR, experiencing the relevant hospital stay, and is subject to the associated risk of perioperative mortality.
Emergency repair	An emergency patient spends 1 cycle in the repair health state, undergoing either EVAR or OSR, experiencing the relevant hospital stay, and is subject to the associated risk of perioperative mortality.
Post-operative survival	A patient who survived the perioperative model cycle resides in this state for the rest of the model duration, subject to risks of reintervention and death.
Reintervention	A patient in the post-operative survival state is subject to an ongoing risk of complications that require reintervention.
Death	Patients can transition to the death health state from the waiting list state, the procedure states or the post-operative state, and remain there for the duration of the model.

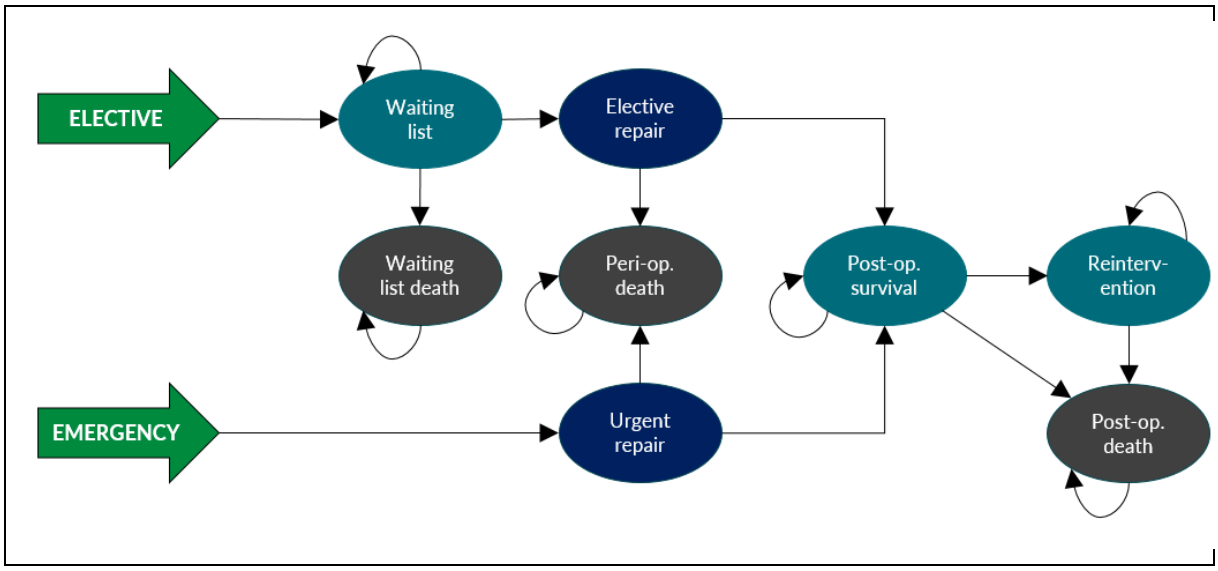


Figure HE01: Structure of new cost–utility model

HE.2.2.2 Cohort parameters

Relevant baseline cohort parameters included in the model are age, sex and aneurysm diameter. These are informed by the EVAR-1 and IMPROVE trials for elective and emergency cases respectively. Age and sex are effect modifiers that alter the probability of perioperative death (see Section HE.2.2.3), long-term post-perioperative survival prospects, and quality of life are also included, allowing us to conduct subgroup analyses and to fully characterise those factors in probabilistic sensitivity analysis.

The mean age of the elective repair population is 74 years, the mean aneurysm size is 6.5 cm, and 91% of the cohort is male (based on EVAR-1 trial data). The mean age of the emergency repair population is 76 years, the mean aneurysm size is 8.4 cm, and 78% of this cohort is male (based on IMPROVE trial data). That women make up a bigger proportion of emergency repairs than elective repairs may reflect that the UK NHS AAA Screening Programme invites men to have their aorta scanned; therefore, AAAs in men are more likely to be identified and referred for elective repair before they rupture.

HE.2.2.3 Treatment effects

The EVAR-1 long-term follow-up publication reported relative effects (piecewise hazard ratios [HRs]) from randomisation, in an intention-to-treat (ITT) analysis. The HRs therefore included deaths during the waiting period. More deaths were recorded during the waiting period on the OSR arm, which also had a notably skewed distribution, with more participants waiting extended periods for their intervention compared with those on the EVAR arm. We were advised by the guideline development committee that no difference in waiting time deaths would be expected, except when EVAR is used to repair a complex AAA, because these patients have wait for longer as their bespoke EVAR device is manufactured.

We were provided with anonymised survival data from the EVAR-1 trial, with which it was possible to disentangle waiting times from the overall survival records. Additionally, the risk of death is significantly higher during AAA repair, and in the immediate 30 days thereafter, than subsequently. To model these distinct components of overall survival separately we subtracted 30 days from overall survival records; we therefore had 3 separate phases of overall survival (preoperative, perioperative and post-perioperative):

- Survival during the lead-in time (time spent on the waiting list prior to elective intervention)

- Perioperative survival during the intervention procedure and up to 30 days after
- Survival conditional on surviving the waiting and perioperative periods (post-perioperative survival).

We also received anonymised patient-level survival data from the IMPROVE trial. IMPROVE was a pragmatic trial, such that individuals were randomised to either an OSR arm or an 'EVAR if possible' arm, on which participants were treated with EVAR if anatomically suitable, and OSR if not. Over 35% of those randomised to this arm received OSR as their intervention. As such, in our analysis of emergency cases, the 'EVAR' arm is in fact an 'EVAR if possible' arm – a world that permits the use of EVAR alongside OSR. For emergency cases, the risk of perioperative mortality is much higher, such that the difference between perioperative and post-perioperative risk of death is more pronounced. We therefore took the same approach to distinguish between perioperative and post-perioperative survival (emergency repair has no associated waiting period).

Our methods and assumptions for applying treatment effects to each of these components of overall survival are described in turn below.

HE.2.2.4 Waiting time mortality

Once the decision has been made to provide a surgical intervention to repair an AAA, an elective NHS patient can expect to have to wait for a period before the procedure. The guideline committee advised that the waiting time is typically around 2 months for the repair of infrarenal aneurysms, regardless of whether the procedure is EVAR or OSR. The EVAR-1 study reported a median waiting time of 44 and 35 days on the EVAR and OSR arms, respectively (Brown et al., 2012). However, the mean time from randomisation to intervention or death was 60 days on the EVAR arm and 93 days on the OSR arm, and the mortality rate while waiting was higher for OSR (3.0% vs. 1.9%). This implies that there is something different about preparing for OSR that increases the risk of death; or that participants randomised to OSR were systematically more likely to die in the first place than those randomised to EVAR; or that the result is a random occurrence, with no 'true' difference in mortality while waiting. The guideline committee advised that this last explanation is the most plausible; therefore, the model assumes that elective EVAR and OSR patients are subject to a common mortality rate while on the waiting list. Using pooled EVAR-1 trial data, the waiting time mortality probability is 2.4%, over a mean waiting time of 76 days, equating to a mortality rate of 1% per month spent on the waiting list.

Elective patients are assumed to wait for 2 months before their intervention, which the committee advised reflects standard practice in the NHS. Standard EVAR devices, which are suitable for infrarenal aneurysms, are readily available in specialist centres, such that the associated waiting time is the same as for open surgery. However, the committee advised that people with complex aneurysms typically have to wait an additional duration for EVAR, as custom-made endovascular stent-grafts require additional time to manufacture. In the model, these patients are subject to 2 additional months of waiting time, and the associated mortality risk. This is not the case for patients with complex aneurysms undergoing open repair, as the surgeon manually adapts a standard stent-graft during the open procedure for complex cases.

The model assumes that there is no waiting time for emergency repair cases.

HE.2.2.5 Perioperative mortality

HE.2.2.5.1 Elective repair

In the base-case model, we use UK National Vascular Registry (NVR) data (2016) to inform baseline perioperative mortality rates. For elective repairs, the NVR data on EVAR are used,

reported for both infrarenal (0.4%) and complex (3.6%) AAAs, as these data were consistent with the experience of the guideline development committee. We then apply a measure of relative effect to these baseline EVAR perioperative mortality rates, to estimate the equivalent mortality rates for OSR in infrarenal and complex cases.

In our primary analysis, this relative effect is informed by a meta-analysis of elective infrarenal AAA trials undertaken as part of a Cochrane systematic review (Paravastu et al., 2014). It pooled 30-day mortality rates from the EVAR-1, DREAM, ACE and OVER trials. The resulting odds ratio (OR) for EVAR compared with OSR was 0.33 (95% CI: 0.20 to 0.55), meaning the odds of perioperative death with EVAR are 3 times lower than with OSR. As the EVAR-1 trial is the most applicable to the UK NHS context, we apply the EVAR-1 OR in a sensitivity analysis (0.37). There are no randomised, comparative data on the effectiveness of different complex repair techniques. We therefore assume the same relative effect observed in infrarenal AAA repair applies to complex repair. The guideline committee advised that this was an acceptable assumption.

This approach, of using registry data to inform baseline rates and RCT data to inform relatively effects, combines the most accurate 'snapshot' of outcomes in current UK practice with a randomised estimate of the difference between the 2 treatment options. It produces an estimate of what the observed trial treatment effect might look like in a real-world setting.

After applying the RCT-based relative effect data to the baseline NVR data for EVAR repairs, we obtain the baseline perioperative mortality rates for OSR (Table HE13). As shown in the table, the choice of which intervention to use for baseline NVR perioperative mortality, onto which is the Cochrane OR is applied, is nontrivial. It has an important bearing on resulting perioperative mortality estimates. The guideline committee advised that the NVR perioperative mortality rate for elective OSR for complex AAAs (19.6%) was significantly higher than its own clinical experience. The mortality results obtained using the EVAR registry data for baseline mortality, then applying the Cochrane relative effect to determine the OSR mortality rates, were judged to more accurately represent current UK practice outcomes. Hence, the EVAR NVR data are used to inform baseline perioperative mortality in the base-case analysis. A sensitivity analysis is conducted that uses the OSR data instead, using the Cochrane OR to estimate the mortality rate for EVAR.

The guideline committee considered whether perioperative mortality rates from the NVR should be used directly to inform relative effectiveness in the model. Not only was the complex OSR mortality rate agreed to be higher than observed in practice, the committee also agreed that the observational NVR data will inherently be subject to substantial selection biases. Instead, the approach adopted utilises both the greatest strength of randomised evidence – informing the treatment effect OR while controlling for confounding factors – and the greatest strength of registry data – presenting an accurate baseline snapshot of real-world practice.

Table HE13: Perioperative mortality – infrarenal and complex AAAs – elective cases

EVAR	*Relative effect*	*OSR*
Baseline = EVAR (base case)		
Infrarenal EVAR (NVR): 0.4%	OR = 1/0.33 →	Infrarenal OSR: 1.3%
Complex EVAR (NVR): 3.6%		Complex OSR: 10.1%
Baseline = OSR (sensitivity analysis)		
Infrarenal EVAR: 1.0%	← OR = 0.33	Infrarenal OSR (NVR): 3.0%
Complex EVAR: 7.4%		Complex OSR (NVR): 19.6%
Key: OR, odds ratio; NVR, National Vascular Registry (2016)		

Effect modifiers for perioperative mortality – elective repair

To make the model capable of producing detailed subgroup analyses, we explored ways of applying effect modifiers that influence a person's risk of perioperative mortality. The baseline values in Table HE13 are applicable to individuals whose characteristics match the 'average' person recorded in the NVR, while the relative effect ORs are applicable to people whose characteristics match the pooled Cochrane meta-analysis cohort. These are used in our base-case deterministic analysis. However, the model may therefore give unrepresentative results if it uses these inputs for, say, a 100% female cohort.

The 3 key effect modifiers we explore are: age, aneurysm diameter and sex. Age and AAA size have been identified as important factors in previous analyses (Chambers et al., 2009). A person's age will affect their life expectancy, and therefore their likelihood of surviving to experience differences between interventions in long-term outcomes. AAA size may affect the technical difficulty of an intervention, and in people for whom 'no intervention' is being considered (see Section HE.2.3), it may affect the risk of subsequent AAA rupture. Clearly, they have the potential to influence the balance between the benefits, harms and costs of different interventions. Sex has also been included to determine whether this balance differs between men and women, as most of the existing evidence is in men. Recent results from the IMPROVE study suggest there may be important differences in clinical outcomes between men and women (Powell et al., 2017). To capture these 3 effect modifiers, we ran logistic regression analyses using the EVAR-1 data, to determine the extent to which these characteristics influence the probability of 30-day mortality. However, there were too few perioperative deaths in the EVAR-1 study to obtain meaningful results (10 following EVAR, 25 following OSR).

We identified a similar analysis using data from a multicentre European registry (Vascunet), containing 5,895 elective AAA repairs from 2005 to 2009, in which a multivariable logistic regression was conducted to determine predictors of 30-day mortality from EVAR and OSR (Mani et al., 2015). Though non-randomised, this was felt to be a stronger source of data for this epidemiological analysis. These regressions included age, sex and aneurysm diameter, among other variables that were not amenable to detailed analysis using the datasets available to us (e.g. the presence of cerebrovascular disease). The authors of the study provided us with the equivalent multivariable logistic regressions containing only age, sex and aneurysm size (Table HE14). We use the resulting ORs to adjust our EVAR and OSR perioperative mortality estimates in Table HE13, assuming that those values are appropriate for the mean NVR population (see equations eqHE01 to eqHE07). Obtaining the mean NVR values was less straightforward for age and AAA diameter, because the NVR Annual Report (2016) reported these data categorically, rather than their mean values. We estimate the mean values as shown in Table HE15. A limitation of this is that the NVR report does not provide data on the size of complex aneurysms, and so we assume they are equal in size to infrarenal aneurysms. We might expect complex aneurysms, affecting blood vessels secondary to aorta, are more likely to be larger in size; however, in the absence of data, we make this simplifying assumption.

As noted above, these effect modifiers are not applied in our base-case analysis, which is instead evaluated for the mean cohort of the EVAR-1 trial. We do, however, apply them for our probabilistic sensitivity analysis (PSA) results. This is because the PSA captures our uncertainty in baseline patient characteristics (age, sex and AAA diameter); it is therefore appropriate to capture the full uncertainty in the effect of these different characteristics. We also use the effect modifiers in extensive subgroup analysis, to evaluate the influence of the patient's age, sex and AAA size on cost–utility outcomes. In these probabilistic and scenario analyses, we apply the effect modifiers to both infrarenal and complex AAA elective repair patients, as the Vascunet data do not distinguish between the 2 levels of aneurysm complexity.

Table HE14: Perioperative mortality – effect modifiers – elective repair

Characteristic	*Odds ratios, EVAR (95% CI)*	*Odds ratios, OSR (95%CI)*
Age, per year	1.040 (0.989 – 1.094)	1.051 (1.024 – 1.079)
Aneurysm diameter, per cm	1.266 (1.052 – 1.523)	1.147 (1.033 – 1.275)
Sex = female	1.206 (0.454 – 3.208)	1.085 (0.669 – 1.761)

Table HE15: Baseline effect modifier characteristics – elective perioperative mortality – NVR (2016)

Characteristic	*EVAR data*		*OSR data*	
	Infrarenal	**Complex**	**Infrarenal**	**Complex**
Age (years)				
<66	8.6%	15.4%	24.4%	26.1%
66-75	35.8%	39.6%	50.5%	42.8%
76-85	47.4%	40.8%	24.0%	29.7%
85<	8.2%	4.3%	1.1%	1.4%
Mean [a]	**75.5**	**73.4**	**70.2**	**70.7**
AAA diameter, cm				
<4.5	4.0%	NR	2.2%	NR
4.5-5.4	5.5%	NR	4.4%	NR
5.5-6.4	62.1%	NR	60.9%	NR
6.5-7.4	17.7%	NR	18.5%	NR
7.4<	10.7%	NR	14.0%	NR
Mean [b]	**6.3**	Assume 6.3	**6.4**	Assume 6.4
Sex = female	11.0%	15.5%	12.0%	16.7%

Notes:
(a) All individuals within a category are assumed to be at the median age within that group as follows: 60, 70, 80 and 90 years, respectively.
(b) All individuals within a category are assumed to be at the median aneurysm size within that group as follows: 4cm, 5cm, 6cm, 7cm and 8cm, respectively.

to eqHE07 show the application of the perioperative mortality effect modifiers in the model. These show how the log-odds of perioperative mortality is calculated, for EVAR and OSR respectively, centring the cohort characteristics on the NVR data as this is the source of our baseline data.

In an applied example, we estimate the EVAR and OSR 30-day mortality rates for a person who is female, aged 70, with a 7.5 cm AAA. This individual is different to the mean characteristics of the NVR dataset, in which 11% of elective, infrarenal EVAR patients are female, the mean age is older (75.5 years) and the mean AAA size is smaller (6.3 cm). Accordingly, in order to fully explore the impact of these differences, baseline EVAR perioperative mortality is adjusted using the relevant effect-modifying odds ratios from Table HE14. The resulting probability of perioperative mortality with EVAR is 0.53%, meaning a 70-year old woman with a 7.5 cm AAA faces a higher operative risk with EVAR than our base-case EVAR-1 cohort (0.41%). The OSR perioperative mortality risk for this individual remains similar to the EVAR-1 cohort value (1.21% versus 1.20%).

In all, our estimation of perioperative mortality rates takes the following order:

1. Obtain baseline 30-day EVAR mortality rates, for infrarenal and complex aneurysms, from the NVR (2016);
2. Apply an odds ratio from the Cochrane review (Paravastu et al., 2014) to obtain the equivalent mortality rates for OSR;

3. **Scenario analysis & PSA only:** To these 'mean' EVAR and OSR mortality rates, apply effect modifiers for age, sex and aneurysm size obtained from the Vascnuet registry (Mani et al., 2015).

We recognise that an alternative approach would have been to apply the effect modifiers to the baseline mortality rates for EVAR – that is, to swap the order of (2) and (3) in the list above. We would then apply the RCT-based relative effect to this modified EVAR mortality rate, to determine the mortality rate for OSR. This approach would have meant assuming EVAR and OSR share common effect modifiers, because the effect modifying ORs would only be applied once (to the baseline EVAR mortality rates). This assumption was discussed with the committee, who agreed that, based on the results of the logistic regression (Table HE14), it would be inappropriate to have EVAR and OSR sharing common effect modifiers. The example was given that it is appropriate that aneurysm size has a bigger effect on perioperative survival with EVAR than with OSR, as size is less of a complicating factor with open surgery.

The relative influence of each effect modifier on the risk of perioperative mortality with an infrarenal AAA is shown in Figure HE02. The risk of death increases with age, most markedly for OSR, suggesting that the invasive nature of open repair is likely to make it significantly riskier in older patients. There is a clear difference in mortality rates by sex, too, with females facing a higher risk of death (red plots) than males (blue plots), all else equal. Bigger AAAs are also associated with higher mortality risks. Figure HE03 shows the same projections for elective complex AAA repair; the same effect modification data are used, but the baseline (base-case) mortality rates are higher. The figures therefore show similar shapes, but the scale on the y-axis shows the mortality risks in this population change dramatically, and the differences between groups are much starker.

$$lnOdds_{\text{NVR\_EVAR}} = \ln\left(\frac{Prob_{\text{NVR\_EVAR}}}{1 - Prob_{\text{NVR\_EVAR}}}\right) = \ln\left(\frac{0.42\%}{1 - 0.42\%}\right) = -5.477 \quad \textbf{(eqHE01)}$$

$$lnOdds_{\text{EVAR}} = lnOdds_{\text{NVR\_EVAR}} + (\%fem_{\text{cohort}} - \%fem_{\text{NVR}}) \times lnOR_{\text{fem[EVAR]}} + (age_{\text{cohort}} - age_{\text{NVR}}) \times lnOR_{\text{age\_per\_yr[EVAR]}} + (AAAsize_{\text{cohort}} - AAAsize_{\text{NVR}}) \times lnOR_{\text{AAA\_per\_cm[EVAR]}} \quad \textbf{(eqHE02)}$$

$$lnOdds_{\text{EVAR}} = -5.477 + (100\% - 11\%) \times 0.187 + (70 - 75.5) \times 0.039 + (7.5 - 6.3) \times 0.236 = -5.233 \quad \textbf{(eqHE03)}$$

$$Prob_{\text{EVAR}} = \frac{e^{-5.233}}{1 + e^{-5.233}} = 0.53\% \quad \textbf{(eqHE04)}$$

$$lnOdds_{\text{OSR}} = (lnOdds_{\text{NVR\_EVAR}} - lnOR_{\text{EVAR-v-OSR}}) + (\%fem_{\text{cohort}} - \%fem_{\text{NVR}}) \times lnOR_{\text{fem[OSR]}} + (age_{\text{cohort}} - age_{\text{NVR}}) \times lnOR_{\text{age\_per\_yr[OSR]}} + (AAAsize_{\text{cohort}} - AAAsize_{\text{NVR}}) \times lnOR_{\text{AAA\_per\_cm[OSR]}} \quad \textbf{(eqHE05)}$$

$$lnOdds_{\text{OSR}} = -5.477 + 1.11 + (100\% - 11\%) \times 0.082 + (70 - 75.5) \times 0.050 + (7.5 - 6.3) \times 0.137 = -4.400 \quad \textbf{(eqHE06)}$$

$$Prob_{\text{OSR}} = \frac{e^{-4.400}}{1 + e^{-4.400}} = 1.21\% \quad \textbf{(eqHE07)}$$

1

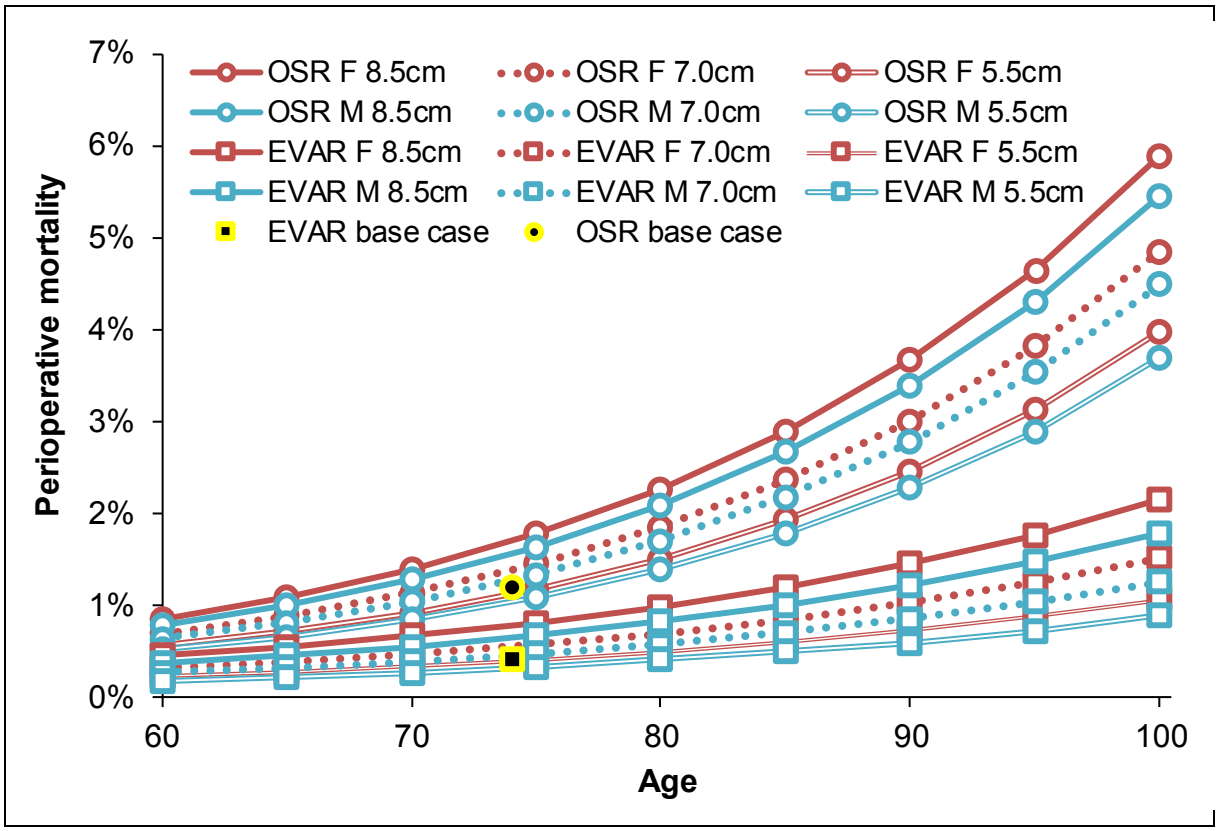


Figure HE02: Effect modification – perioperative mortality (elective, infrarenal)

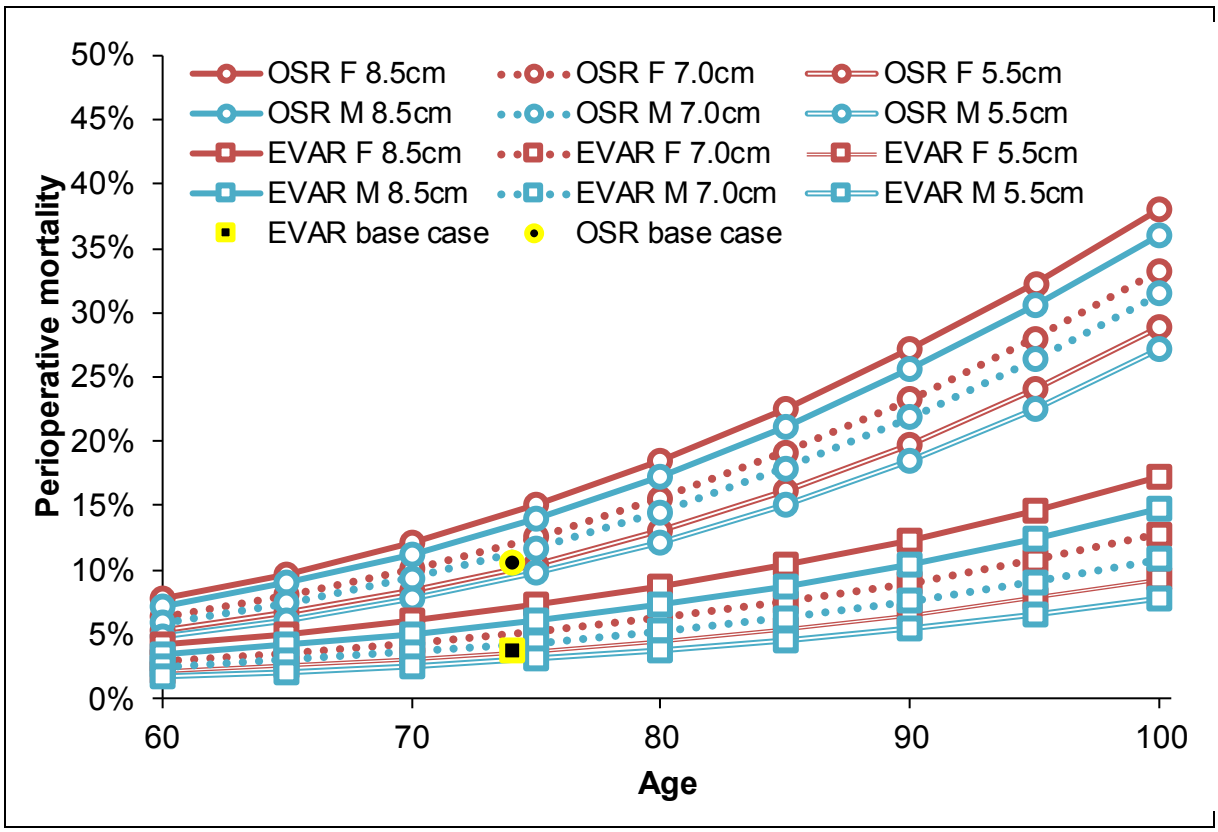


Figure HE03: Effect modification – perioperative mortality (elective, complex)

HE.2.2.5.2 Emergency repair

For emergency repair, the NVR data for OSR – not EVAR – are not used to inform baseline perioperative mortality. This is because the guideline committee advised that the EVAR registry data do not reflect its experience of emergency repair outcomes in NHS practice. The NVR data show that emergency EVAR has a 20.7% perioperative mortality rate (Table HE16), whereas the committee's experience is a value much closer to that shown in the IMPROVE trial (35.4%). The registry suggests that mortality following emergency OSR is 40.4%, which is much closer to the IMPROVE estimate of 38.6% for OSR. We therefore use the registry data for open surgery to inform our 'snapshot' of UK practice in this population. We then apply relative effects from a Cochrane meta-analysis (Badger et al., 2017) of emergency AAA repair studies (IMPROVE, AJAX, ECAR, Hinchcliffe et al., 2006) to estimate the mortality rate for EVAR. This pooled OR, for EVAR relative to OSR, is 0.88 (95%CI: 0.66 to 1.16), meaning that EVAR is associated with lower 30-day mortality at the point estimate.

The resulting emergency perioperative mortality rates are therefore: 40.4% for emergency OSR, based on the NVR data, and 37.4% for emergency EVAR, having applied the Cochrane OR. We conduct sensitivity analyses that use the EVAR registry figures as the baseline data rather than the OSR figures, and/or the relative effect OR from the UK-based IMPROVE trial (0.94) rather than the pooled Cochrane value.

Table HE16: Perioperative mortality – infrarenal and complex AAAs – emergency repair

EVAR periop. mortality	*Relative effect used*	*OSR periop. mortality*
Baseline = OSR (base case)		
Infrarenal EVAR: 37.4%	← OR = 1/0.88	Infrarenal OSR (NVR): 40.4%
Complex EVAR: N/A [a]		Complex OSR (NVR): 61.9%
Baseline = EVAR (sensitivity analysis)		
Infrarenal EVAR (NVR): 20.7%	OR = 0.88 →	Infrarenal OSR: 22.9%
Complex EVAR (NVR): N/A [a]		Complex OSR: 41.5% [b]

Notes:
(a) EVAR is not used to repair ruptured complex AAAs. Any patients in the model who require emergency repair of a complex AAA will receive open surgery.
(b) Given that emergency EVAR for complex AAAs does not occur in practice, it is not possible to use complex EVAR registry data as the baseline. To estimate the perioperative mortality of emergency OSR for complex AAAs, here we instead use the estimate for infrarenal OSR, and apply to it a complexity-related adjustment obtained from the NVR open surgery data: (70.5% vs. 40.4%; OR = 3.68).

Key: OR, odds ratio; NVR, National Vascular Registry (2016)

Effect modifiers for perioperative mortality – emergency repair

Like elective repair, we wanted to have the ability to perform meaningful subgroup analyses for the comparison of EVAR with OSR in emergency cases. Like before, we specifically wanted to evaluate age, sex and aneurysm size as determinants of perioperative mortality. There were significantly more perioperative deaths in the IMPROVE trial than in the EVAR-1 trial (234 within 60 days), such that for this analysis we were able to conduct a logistic regression analysis using the trial data, unlike for elective repair where we had to use analysis of the European Vascunet registry.

We tested various model forms, including polynomial age terms and all potentially relevant interactions between different variables. The best-fitting model, according to Akaike Information Criterion (AIC) statistics, omitted aneurysm size, which was not a significant predictor of perioperative mortality; included a treatment variable to distinguish between EVAR and OSR, rather than fitting a separate model for each intervention; and included an interaction between EVAR and female (Table HE17). The resulting ORs suggest the

perioperative mortality for emergency repair is more likely if the patient is older. Women have double the odds of mean of perioperative death with OSR, but are less likely than men to die as a result of EVAR.

The ORs below are used to change the baseline estimates of perioperative mortality in Table HE16 to reflect the characteristics of cohort being modelled. Like before, the effect modifying ORs are not used in our base-case deterministic analysis, which is instead evaluated at the mean characteristics of the IMPROVE study. The modifiers are used to explore scenario analyses (see Section HE.3); for example, we might want to model a 100% female cohort, to evaluate the cost-effectiveness results in women. They are also applied in our PSA results, in order to fully capture the effect of uncertain patient characteristics. Due to the presence of a treatment and sex interaction term, to apply the modifiers in these circumstances it was necessary to adjust the intercept term such that the model predicts perioperative mortality according to our baseline values from the National Vascular Registry.

The relative influence of age and sex on the risk of perioperative mortality with a ruptured infrarenal AAA is shown in Figure HE04. The most prominent feature of this figure is the higher mortality risk faced by females undergoing OSR; at its peak, the difference between men and women is close to 20%. Conversely, the EVAR perioperative mortality risk is consistently lower in women than it is in men. Age is a significant determinant of the risk of death; the EVAR risk is lower than 20% in 60-year old men, but exceeds 40% in 80-year old men, and is around 60% in 90-year old men.

Table HE17: Perioperative mortality – effect modifiers – emergency repair

Characteristic	*Odds ratio (95% CI)*
Age, per year	1.067 (1.041 – 1.093)
Sex = female	2.019 (1.125 – 3.622)
Treatment = EVAR	1.110 (0.756 – 1.629)
Interaction term Treatment = EVAR Sex = female	0.411 (0.184 – 0.919)
Intercept term	0.004 (0.001 – 0.026)

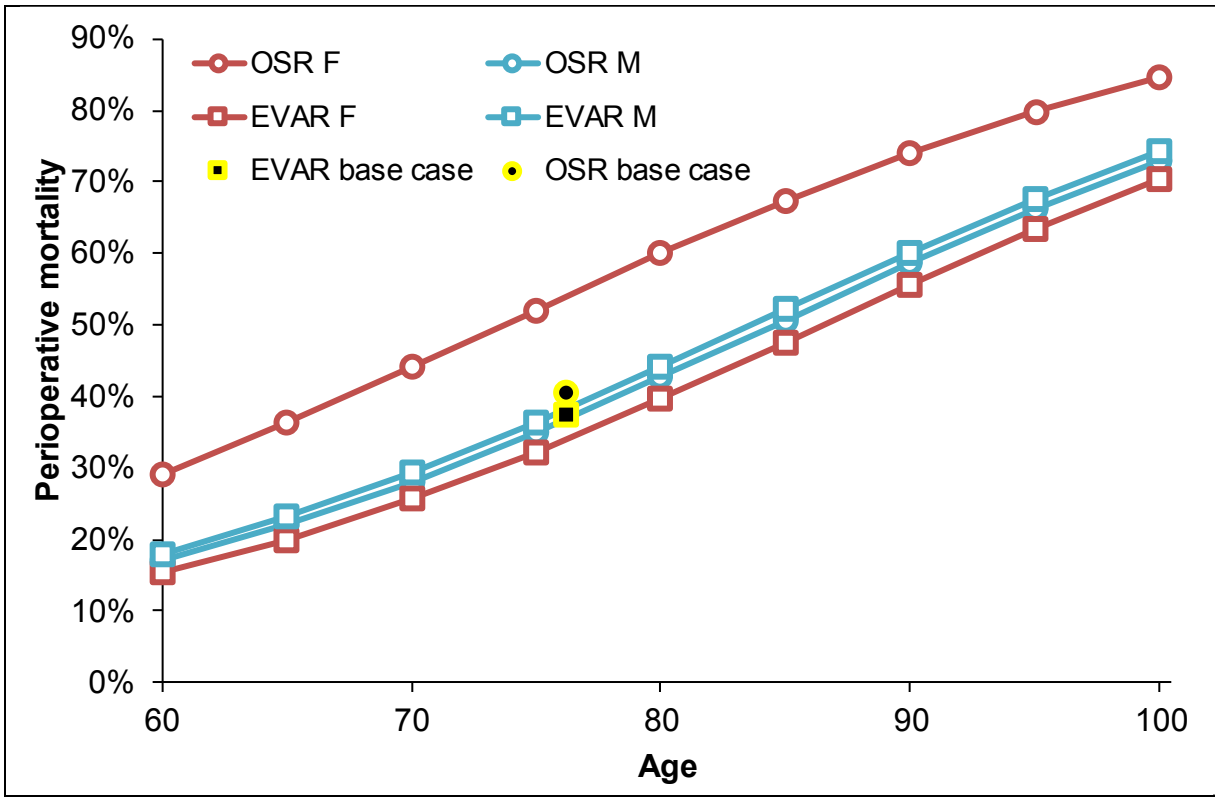


Figure HE04: Effect modification – perioperative mortality (elective, infrarenal)

HE.2.2.6 Post-perioperative survival (long term)

HE.2.2.6.1 Elective repair

The EVAR trial investigators provided us with anonymised long-term survival data from the EVAR-1 trial, which was deemed to be highly applicable, being the only UK trial in this population. The committee advised that there is no evidence to suggest newer-generation EVAR devices are associated with different long-term mortality than the devices that were used during EVAR-1; indeed, there is evidence to suggest they are equivalent (Hammond et al., 2016). As such, EVAR-1's long-term outcomes are likely to be transferable to current UK practice.

With the EVAR-1 survival data, we removed the waiting time (days from randomisation or preoperative death) and perioperative (intervention time plus 30 days) durations from each individual record. Trial participants who died during either of these periods were therefore omitted from the remaining data, such that we had a dataset containing only individuals who survived beyond 30 days post-intervention (i.e. reached the 'post-perioperative' phase of overall survival). These data are the basis for modelling long-term survival, conditional on surviving the waiting time and perioperative periods, which have been described in detail above.

We took 2 approaches to modelling the post-perioperative survival phase:

1. Drawing in external data, by calibrating UK general population survival curves to reflect the EVAR-1 population (OSR arm), then applying relative effects from a meta-analysis of 3 trials with long-term data to obtain a hazard ratio (HR) for EVAR.
2. Using the EVAR-1 data exclusively, by fitting parametric survival curves to the EVAR and OSR data directly.

The first of these approaches is our preferred base case. The parametric curves fitted to the EVAR-1 data begin to produce unrealistic results when the cohort age is set to extreme values relative to the EVAR-1 mean of 74 years. Being directly linked to age-related background mortality statistics, the second approach produces plausible survival estimates at all cohort ages. For example, it will prevent a population with inherently worse survival prospects than the general population from ever having a lower risk of death than the general population; this can occur at the tail-end of parametric survival curves informed by few observations. Secondly, as shown below, the long-term survival data for AAA patients do exhibit a shape that is similar to general all-cause mortality, such that this method can produce visually excellent fits to the EVAR-1 data. Furthermore, exploring different approaches in sensitivity analysis allowed the extent to which the choice of extrapolation method affects model outcomes (see HE.2.2.8). Both methods are described below.

Base-case approach: calibrated all-cause mortality data

We obtained UK general population survival curves from national life tables (ONS, 2017). The ratio of men to women in EVAR-1 was used to obtain a sex-weighted average general population survival curve. Comparing this with EVAR-1 post-perioperative survival, it became clear that people who have received an AAA elective repair with either EVAR or OSR have relatively similar survival prospects to the general UK population (Figure HE05). We sought to identify a HR to adjust the general population mortality rate, until it matched the OSR survival data from EVAR-1 as closely as possible (the choice of OSR as 'baseline' was aribitrary; the EVAR arm would have been equally appropriate for this calibration exercise). The EVAR trials recruited between 1999 and 2004. As such, we used ONS life tables from that time period (1999–2001) to perform this calibration; that is to say, we calibrated the general population survival of UK 74 year olds *at the time of trial recruitment* to match the trial population.

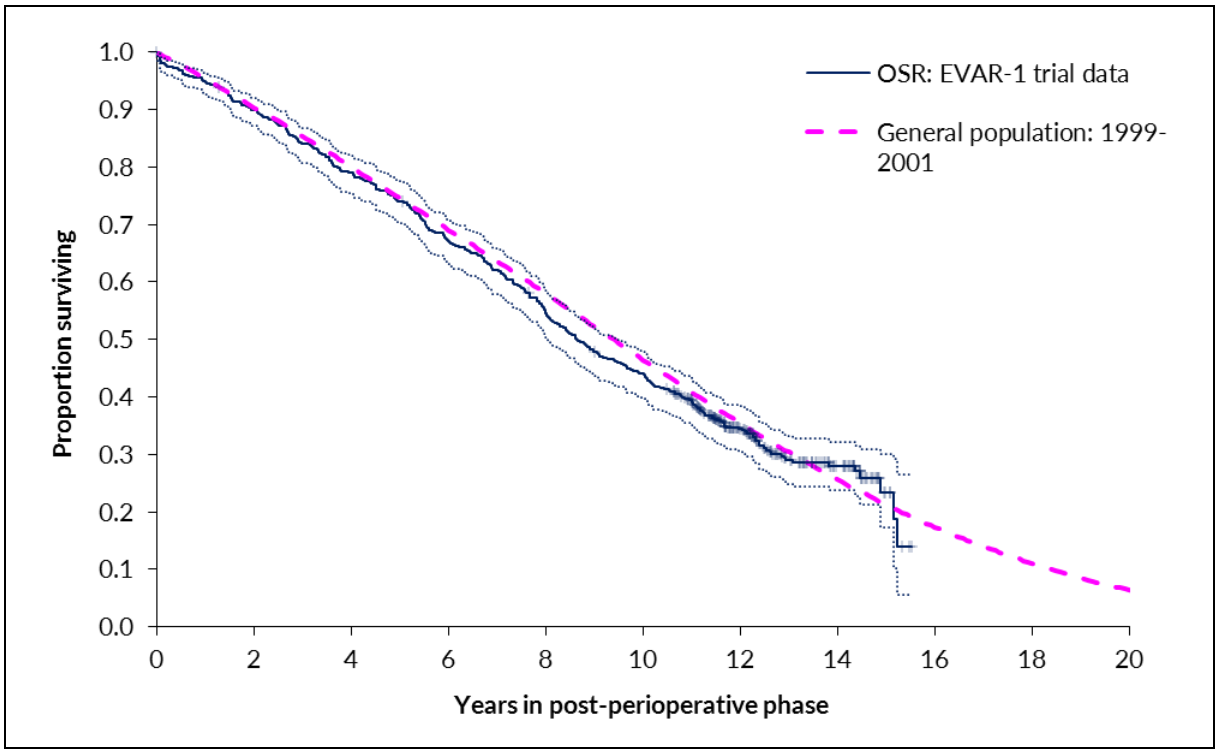


Figure HE05: EVAR-1 post-perioperative survival compared with 1999–2001 general population survival

We used numerical optimisation (Excel Solver's generalised reduced gradient [nonlinear] algorithm) to estimate the value of HR. The quantity that we sought to minimise was $wRMSE$,

a weighted measure of the root mean squared error (RMSE) of the adjusted lifetable compared with the survival function observed in the relevant RCT arm:

$$wRMSE = \sqrt{\sum_{j=1}^{j=n} w(t_j)\left[S(t_j)_{\text{RCT}} - S(t_j)_{\text{AAA}}\right]^2} \quad \textbf{(eqHE08)}$$

, where n is the number of discrete time-points at which deaths were observed in the trial, and $S(t)_{\text{RCT}}$ is the survival estimate for time j in the trial and $S(t)_{\text{AAA}}$ is the survival estimate derived from the adjusted lifetable. This is calculated as

$$S(t_i)_{AAA} = \prod_{j=1}^{j=i}\left[\frac{S(t_j)_{\text{GenPop}}}{S(t_{j-1})_{\text{GenPop}}}\right]^{HR} \quad \textbf{(eqHE09)}$$

, where $S(t)_{\text{GenPop}}$ is the estimate derived from the lifetable.

The weighting factor for the ith time-point is the inverse of the variance of the RCT survival estimate for that time-point expressed as a proportion of the summed inverse variance for all time-points (so that the weighting factors sum to 1 overall):

$$w(t_i) = \frac{1/\text{SE}(S[t_i])^2_{\text{RCT}}}{\sum_{j=1}^{j=n} 1/\text{SE}\left(S[t_j]\right)^2_{\text{RCT}}} \quad \textbf{(eqHE10)}$$

The purpose of weighting the RMSE estimate was to avoid excess leverage being exerted by the uncertain tails of the survival distributions from the RCTs.

To estimate uncertainty in HR, we performed 1,000 bootstrap replications from the RCT data, sampling with replacement to derive a new $S()_{\text{RCT}}$, on which we performed the optimisation procedure described above to estimate a series of values for HR. In each case, the resulting distribution of HR estimates formed an obvious lognormal distribution, so we defined the parameter in our model using the mean and standard deviation of the bootstrapped $\ln(HR)$s.

The resulting value of HR that minimised $wRMSE$ was **1.080**, with a bootstrapped mean and 95% confidence interval of of 1.081 (0.974 to 1.195). This indicates that, on average, an EVAR-1 trial participant who survived open repair for an AAA had a slightly higher hazard of death than the general population of the time. Given that the AAA had been repaired by this point, this finding is likely to reflect the presence of risk factors that are naturally associated with both development of an AAA and early mortality.

Applying this HR to general population survival data from 1999–2001, and ageing the cohort by 3 months – to reflect that, on average, they will have had to wait for 2 months for elective procedure and then have 1 perioperative month – shows that the approach achieves an excellent fit to observed post-perioperative survival of people receiving OSR in EVAR-1 (Figure HE06).

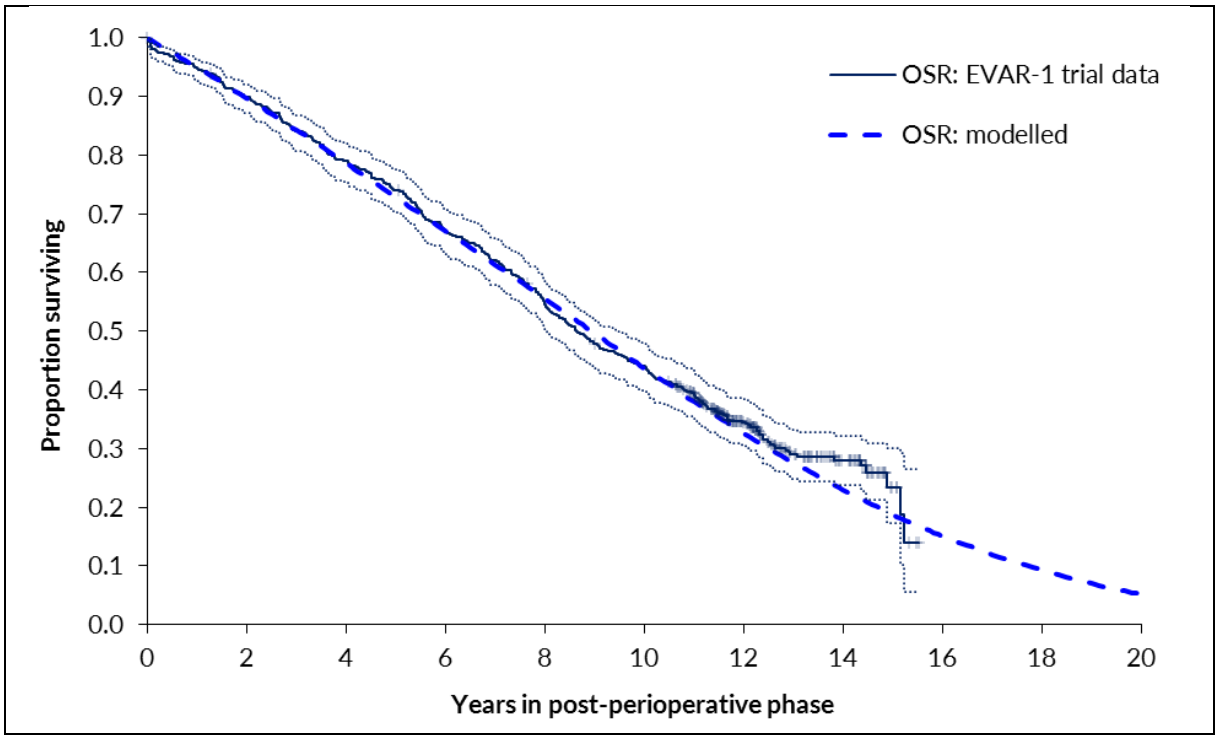


Figure HE06: General population survival (1999–2001) calibrated to EVAR-1 post-perioperative survival (OSR arm)

To ensure that our model cohort is relevant to the present day, we apply the HR of 1.080 to *current* life tables (2013–15) in the base-case analysis. This reflects a general increase in survival prospects in the UK since the EVAR trials recruited, though it implicitly assumes that people who entered EVAR-1 in 1999–2003 will have experienced the same relative gain in overall survival as the wider population. The expert guideline committee were satisfied that this is appropriate for the EVAR-1 study population.

Base-case approach: relative long-term survival effects

The methods described above provided us with a post-perioperative survival curve for OSR. We then applied a second HR to our calibrated OSR curve, to obtain the post-perioperative survival curve for people who received EVAR. The EVAR-1 data suggest OSR is associated with a long-term survival benefit over EVAR (beyond 8 years). This long-term benefit is reflected in the overall post-perioperative mortality HR from the EVAR-1 data, which we found to be 1.107 (95% confidence interval: 0.967 to 1.268). However, rather than applying this HR to the calibrated curve for OSR, we identified 2 RCTs that also report relatively long-term survival outcomes: the DREAM and OVER studies. These report 12- and 8-year survival data, respectively.

We did not have access to patient-level data from the DREAM and OVER trials. It was therefore impossible to observe post-perioperative survival, by extracting the waiting and perioperative periods from overall survival, the way we did with EVAR-1 data. However, DREAM and OVER still provide useful long-term survival evidence, from a total of 351 and 881 participants respectively. Rather than omit them and just use our EVAR-1 HR (1.107), we used the method described by Parmar et al., (1998), as implemented in a tool provided by Tierney et al., (2007), to estimate HRs from published Kaplan-Meier survival plots and number-at-risk data. We extracted these data from the DREAM and OVER publications (de Bruin et al., 2010; van Schaik et al., 2017; Lederle et al., 2012), starting at the 1-year data point rather than the baseline data point. By 1-year, it is likely that almost all surviving participants will have completed the waiting and 30-day perioperative phases. We recognise that this is a simplification, given that we would expect the majority of participants to have

completed the perioperative phase substantially earlier than at 1 year. However, the Tierney approach is more accurate if number-at-risk data are available for each data point extracted, and the trials only reported the number-at-risk on an annual basis.

Through this approach, Parmar et al.'s method predicts a post-1-year HR for EVAR compared with OSR of 1.116 (95% CI: 0.839 to 1.485) from the DREAM study, and 1.012 (95% CI: 0.788 to 1.300) from the OVER study (Figure HE07). Meta-analysing these with our EVAR-1 data (HR=1.107) using a fixed effects model, our estimated pooled HR for post-perioperative survival is **1.089** (95% CI: 0.976 to 1.216; I^2 = 0%) (Figure HE07).

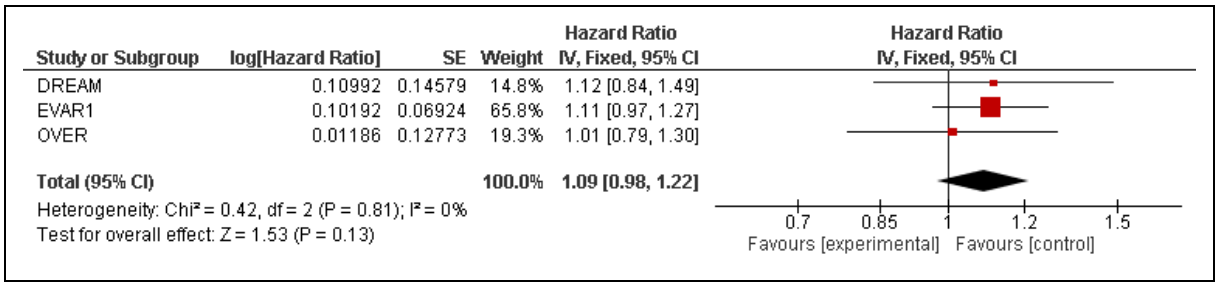
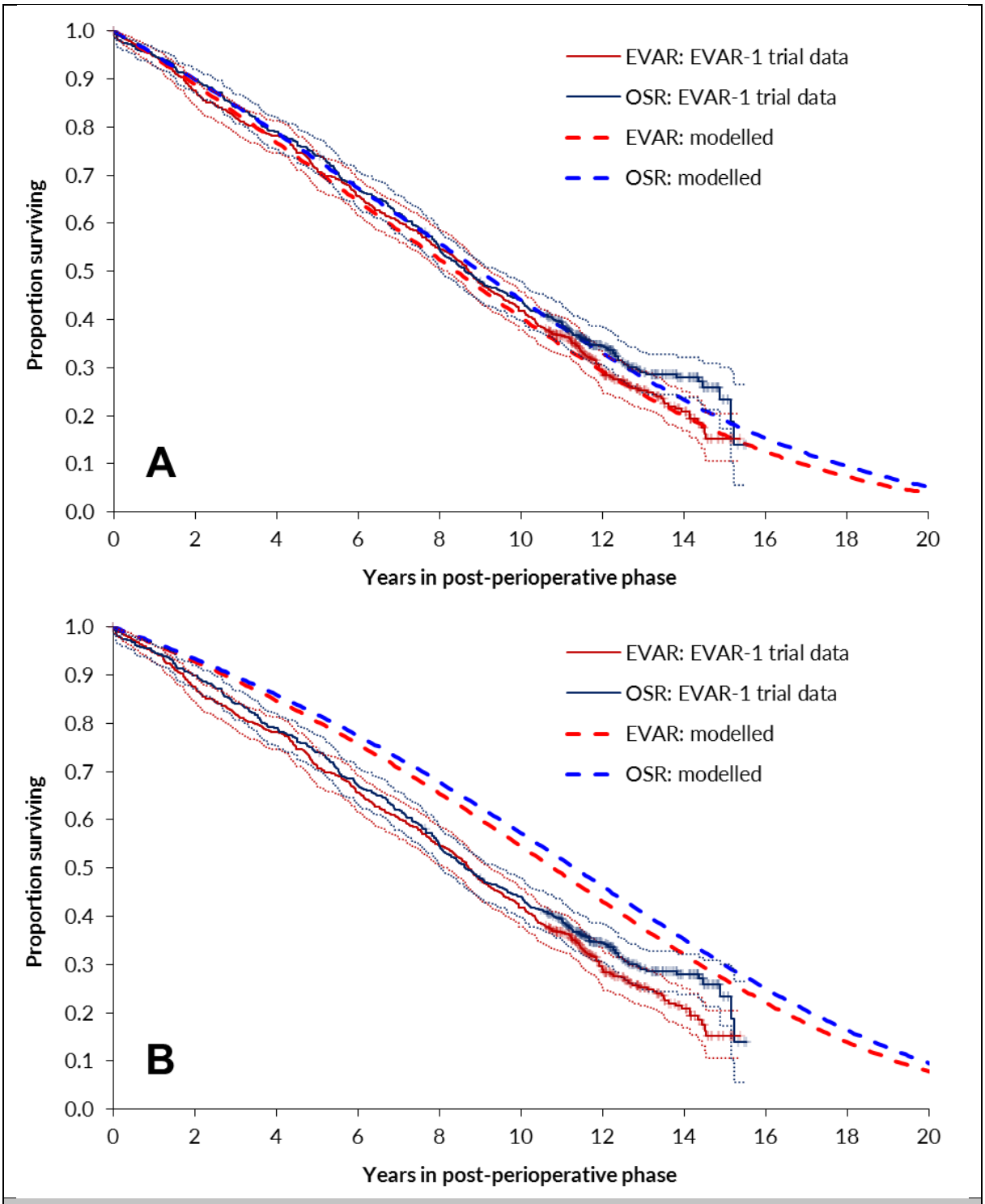


Figure HE07: DREAM and OVER survival meta-analysis results of post-1 year data and EVAR-1 post-perioperative data

The EVAR trials recruited in 1999 to 2004. As such, if we use 1999–2001 UK lifetables, again age the cohort by 3 months, and apply the EVAR-1 HR of 1.107, we obtain the post-perioperative survival estimates in Figure HE08(A). This indicates that the calibrated general population mortality approach is able to provide an excellent fit to the observed data. However, we do not use this curve in our base-case analysis. Firstly, we use 2013–15 general population life tables rather than 1999–2001, to reflect the general increase in life expectancy since the EVAR trials recruited. Our base-case survival curves are therefore superior to the EVAR-1 Kaplan-Meier plots. Secondly, we apply our pooled HR (1.089) to our estimated OSR post-perioperative survival curve, to model EVAR, to make use of as much randomised, long-term comparative data as possible. The resulting base-case survival plots are presented in Figure HE08 (B).

The EVAR-1 survival curves most notably begin to diverge after around 8 years, and the trial investigators' piecewise HR suggests this is the point at which survival differences become statistically significant. As such, we also analysed the EVAR-1 data for participants who survived for at least 8 years following the waiting and perioperative periods. For this population the mortality HR for EVAR relative to OSR is 1.297 (95% CI: 1.035 to 1.627). We use this HR in a sensitivity analysis, in which we assume that there is no difference in mortality rates between EVAR and OSR for the first 8 years after intervention (as the survival curves are close together for this period), then in patients who survival for 8 years, the HR of 1.297 in favour of OSR is applied.



Note: base case departs from optimal fit to empirical data because (a) general population lifetables from 2013–15 are used (rather than 1999–2001), (b) a meta-analysed hazard ratio is used for EVAR vs. OSR (rather than that observed in EVAR-1 alone) and (c) cohort age and sex are set to average of all participants in EVAR-1 (rather than just those randomised to OSR).

Figure HE08: Modelled post-perioperative survival compared with that observed in EVAR-1, showing (A) optimal fit and (B) base case

Effect modifiers for post-perioperative mortality – elective repair

For the purpose of subgroup analysis and PSA, we also estimated the effect of baseline age, sex and AAA diameter on post-perioperative survival outcomes, through a multivariable Cox regression obtained using the EVAR-1 trial data. Various combinations of covariates were

tested, including interactions and polynomial terms, but the coefficients in Table HE18 provided an adequate fit to the data. In our base-case analysis, we do not apply the post-perioperative survival effect modifiers shown in Table HE18; nor do we apply perioperative mortality effect modifiers. Instead, our base-case results are evaluated at the mean patient characteristics of the EVAR-1 study. When these long-term survival effect modifying HRs are applied, we substitute the HR for EVAR (1.116) for our meta-analysed 'best' estimate of **1.089**. In addition, we do not utilise the HR associated with age, because age is already accounted for by our use of UK life tables as the basis of our survival curves. Applying the age HR shown below would be double-counting the impact of age. However, both treatment and age were included in the Cox regression to provide appropriately adjusted estimates of the independent effects of sex and AAA diameter.

Table HE18: Post-perioperative survival effect modifiers – Cox regression – EVAR-1 (for scenario analysis and PSA only)

Variable	*HR*	*95% CI*
EVAR (vs. OSR) [a]	1.116	0.975 – 1.279
Baseline age, per year [b]	1.083	1.070 – 1.097
Sex = female (vs. male)	1.044	0.833 – 1.308
AAA diameter, cm	1.087	1.013 – 1.167

Note: (a) When post-perioperative survival effect modifiers are applied, the EVAR HR shown is replaced by the meta-analysed estimated of 1.089. (b) When post-perioperative survival effect modifiers are applied, the age HR shown is not used, as doing so would double-count the effect of age on mortality, which is already captured by our use of calibrated UK population life tables.

Key: CI, confidence interval; HR. hazard ratio.

There are no long-term, randomised comparative survival data in people following the repair of a complex (non-infrarenal) AAA. As a result, we assume that people who have a successfully repaired complex aneurysm, surviving the 30-day perioperative period, have the same survival prospects as people who have had an infrarenal aneurysm successfully repaired. This is modelled by applying the same EVAR and OSR post-perioperative survival curves shown above following complex EVAR and complex OSR respectively. The guideline development committee agreed that this is a reasonable modelling assumption – that generally, once a person has received successful aneurysm repair, there is little expectation that their survival prospects will be different if the aneurysm was complex, rather than infrarenal.

The guideline development committee agreed that assuming comparable post-perioperative outcomes between infrarenal AAA and complex AAA patients is a reasonable modelling assumption. It was explained that generally, once a person has received successful aneurysm repair, there is little expectation that their survival prospects will be different if the aneurysm was complex, rather than infrarenal.

Secondary approach: parametric curves based on EVAR-1 data

Our alternative approach was to use the EVAR-1 data exclusively, without drawing on information from general population survival or other, non-UK trials. For this, we fit parametric survival functions to the post-perioperative survival data for each trial arm (EVAR and OSR). Standard parametric functions were evaluated using Stata 13.0 (exponential, gamma, Gompertz, log-logistic, log-normal and Weibull). Model selection followed the principles set out in Latimer (2011), based on visual inspection of the fit to the data, including review of diagnostic plots and hazards, and statistical goodness of fit based on AIC and BIC. This identified that 2 functions were clearly superior to others, and were presented to the guideline committee for validation.

First, a simple regression analysis was done with no patient covariates included in the models. The resulting functions are used for deterministic analysis of the parametric

approach here. However, to ensure that this approach could provide meaningful subgroup analysis and PSA results, a baseline age variable was included, as were sex and AAA diameter variables.

The Gompertz function was found to provide the best statistical fit to the EVAR-1 post-perioperative survival data for both interventions, based on AIC and BIC. The gamma function consistently produced the next-best fit according to the AIC and BIC statistics (Table HE19). In terms of visual fit to the data, the Gompertz and gamma functions provided superior fits to the data than alternative functions (EVAR: Figure HE09; OSR: Figure HE10). Their long-term survival projections were also plausible compared with other functions which, to varying degrees, appear to underestimate the mortality hazard beyond the observed data, resulting in relatively high long-term survival. With little to choose between the Gompertz and gamma functions visually, the Gompertz is used in this scenario analysis based on its superior statistical fit. The gamma function is used in a sensitivity analysis for this approach. We also fit parametric survival functions using a treatment covariate to distinguish between EVAR and OSR, with shared age, sex and AAA diameter coefficients. However, the guideline development committee advised that it is more reasonable to expect that EVAR and OSR will exhibit long-term survival profiles with different shapes, due to differences in their complication rates. As such, this is used in a further sensitivity analysis. All parametric model parameters are provided in Section HE.6.

Generally, using the fitted parametric curves produces a bigger difference in life-expectancy – and therefore QALYs – in favour of OSR than our base-case approach, using calibrated general population survival data.

Table HE19: Statistical fit of parametric survival functions for post-perioperative EVAR-1 survival

Model	***EVAR data***		***OSR data***	
	AIC	**BIC**	**AIC**	**BIC**
Exponential	1630	1634	1568	1572
Gamma	1572	1585	1537	1550
Gompertz	1571 [a]	1580 [a]	1534 [a]	1543 [a]
Log-logistic	1640	1649	1585	1593
Log-normal	1699	1708	1672	1681
Weibull	1592	1601	1549	1558

Note: (a) The model that provides the best fit to the observed data is signified by the lowest AIC and BIC statistic.

Key: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion.

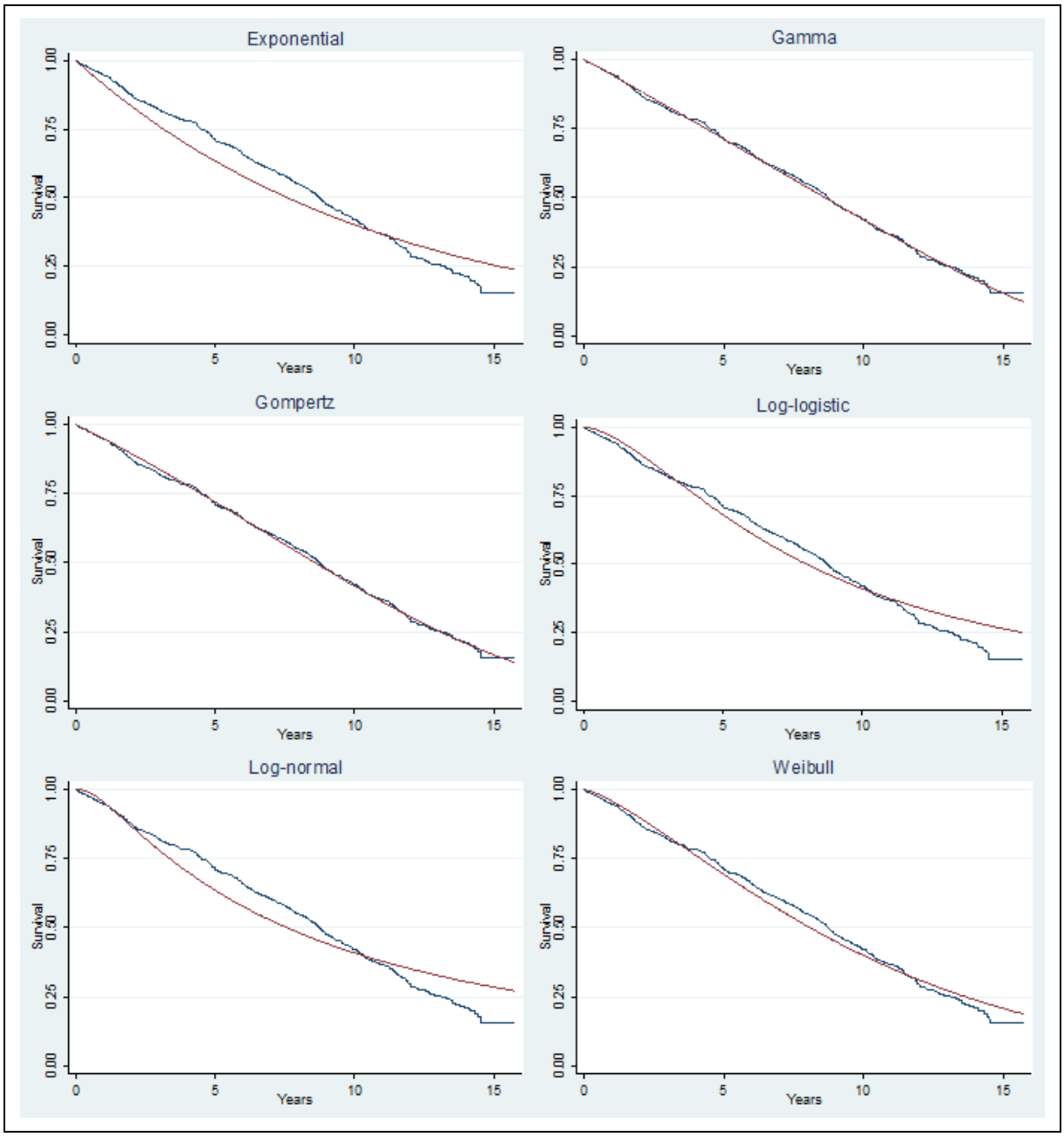


Figure HE09: Visual fit of parametric survival functions for post-perioperative EVAR-1 survival – EVAR arm

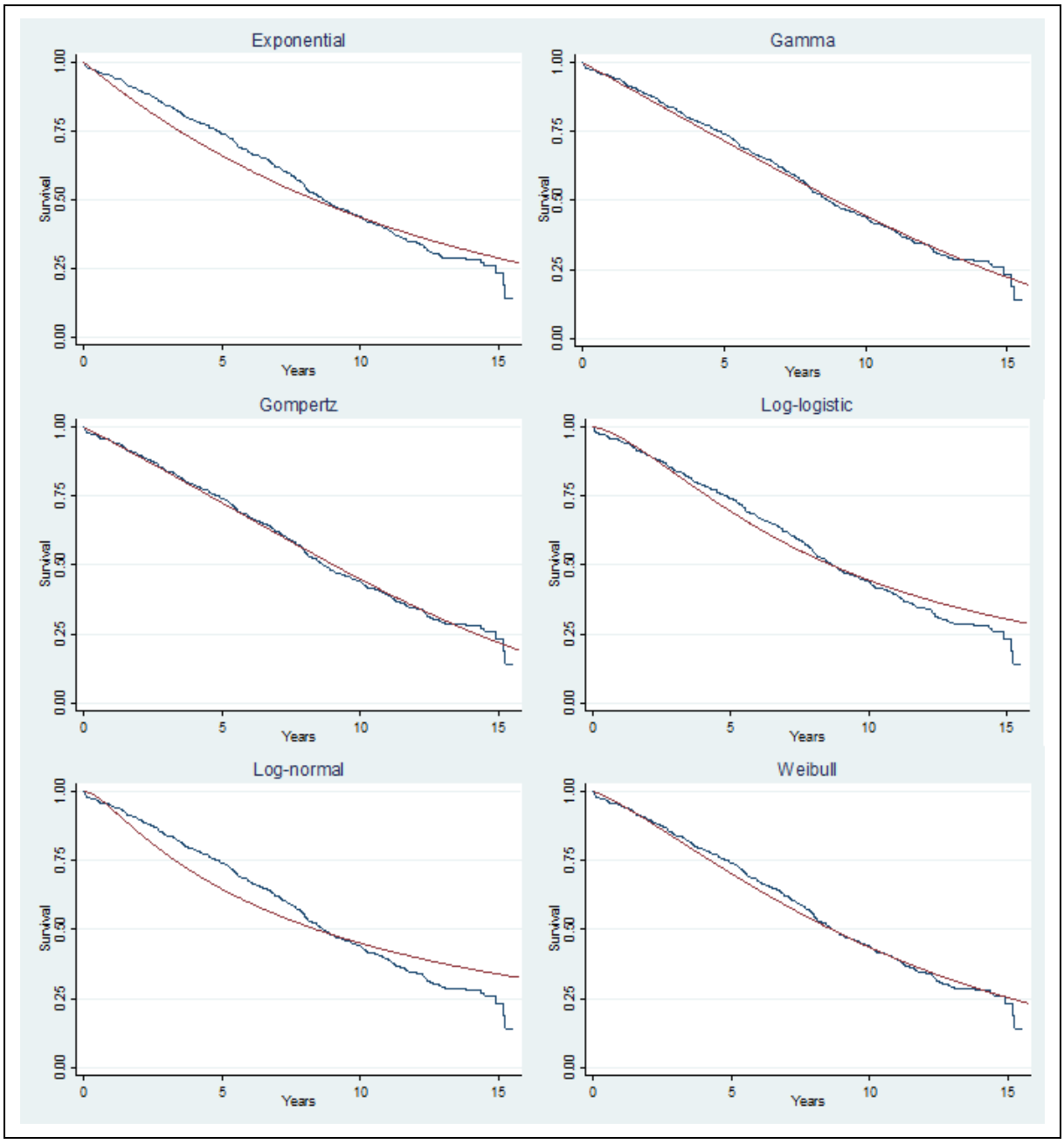


Figure HE10: Visual fit of parametric survival functions for post-perioperative EVAR-1 survival – OSR arm

HE.2.2.6.2 Emergency repair

Base-case approach: calibrated all-cause mortality data

We used the same approach of calibrating general population survival to match the population of interest to inform post-perioperative survival in emergency repair patients. Here, we calibrated general population survival data to match the IMPROVE trial control arm as closely as possible, rather than the EVAR-1 trial. IMPROVE is a newer study, having recruited between 2009 and 2012; therefore we used ONS lifetables for England and Wales from 2009-11. Like with the elective repair data, we sought to identify the HR that, when applied to the general population survival data, minimises the $wRMSE$ between the resulting curve and the trial OSR post-perioperative survival data (see eqHE08 to eqHE10).

It became clear that a single HR was unable to adjust general population survival to provide an acceptable fit to the IMPROVE post-perioperative survival data. This is because there is a relatively high mortality rate in the short-term, immediately after the 30-day perioperative period. Thereafter, the OSR survival profile exhibits a clear change in mortality hazard at around 3 years; before this time, the OSR survival curve diverges from the EVAR curve, and after this time, it flattens and converges with the EVAR curve. A single HR value could not reconcile these issues to provide a well-fitting calibration of general population survival. We took 2 steps to resolve this. First, for the purpose of this calibration only, we extended the perioperative period from 30 days to 60 days, as the mortality rate between day 30 and day 60 (post-OSR) was significantly higher than the mortality rate after day 60. Second, we took a piecewise approach, using 2 hazard ratios, $HR1$ and $HR2$, and a user-defined "cut-point". $HR1$ is applied to general population survival at all times before the cut-point; $HR2$ is applied after the cut-point. We used Excel Solver's generalised reduced gradient [nonlinear] algorithm to estimate the values of $HR1$ and $HR2$ that jointly minimised $wRMSE$ for a given cut-point. By methodically testing different cut-points at 0.5-year intervals, we determined that a 3-year cut-point produced the best fit to the post-60-day survival data. A 3.5-year cut-point also produced a reasonable fit to the data.

These decisions provide 2 limitations. Firstly, the model still uses 30-day mortality figures to inform perioperative mortality. The use of 60-day mortality was solely to increase the likelihood of producing a good-fitting post-perioperative survival function. We are therefore implicitly assuming that it is reasonable to apply our post-60-day, long-term survival function after day 30 following intervention. This would therefore omit important differences in mortality between day 30 and 60; however, it is not apparent that this causes substantive bias in the direction of either intervention, as relatively high 30-to-60-day mortality rates were present in *both* OSR and EVAR arms of IMPROVE. Using 30-day mortality rates, rather than 60-day mortality rates, also retains consistency with our use of National Vascular Registry data for baseline mortality rates (only 30-day rates are reported). The second limitation is that our base-case cut-point, at which the calibration HR switches from favouring EVAR to favouring OSR, was not identified by a quantitative method, as this proved numerically intractable when also estimating 2 hazard ratios. Despite this, the resulting survival profiles provide an excellent visual fit to the IMPROVE data (Figure HE11). While an analytically-determined optimal cut-point would almost certainly not be precisely 3 years, there is little scope to improve on our visual fit to the data. The effect of applying a 3.5-year cut-point was evaluated in sensitivity analysis.

As before, we performed 1,000 bootstrap replications from the RCT data to estimate uncertainty in HR, and we defined the parameter in our model using the mean and standard deviation of the bootstrapped $\ln(HR)$s. The resulting values of $HR1$ and $HR2$ that minimised $wRMSE$, separated at a cut-point of 3 years, were **3.187** (bootstrapped mean: 3.192; 95% CI: 2.381 to 4.120) and **1.364** (bootstrapped mean: 1.286; 95% CI: 0.646 to 2.212) respectively. This indicates that, on average, an IMPROVE trial participant who survived open repair for an AAA had a 3-times higher hazard of death than the general population of the time for 3 years. After 3 years, the hazard remains slightly higher than the general population, but the difference is no longer statistically significant. The values of $HR1$ and $HR2$ used in a sensitivity analysis with a 3.5-year cut-point are: **3.024** (bootstrapped mean: 3.016; 95% CI: 2.257 to 3.935) and **1.133** (bootstrapped mean: 1.041; 95% CI: 0.385 to 2.052).

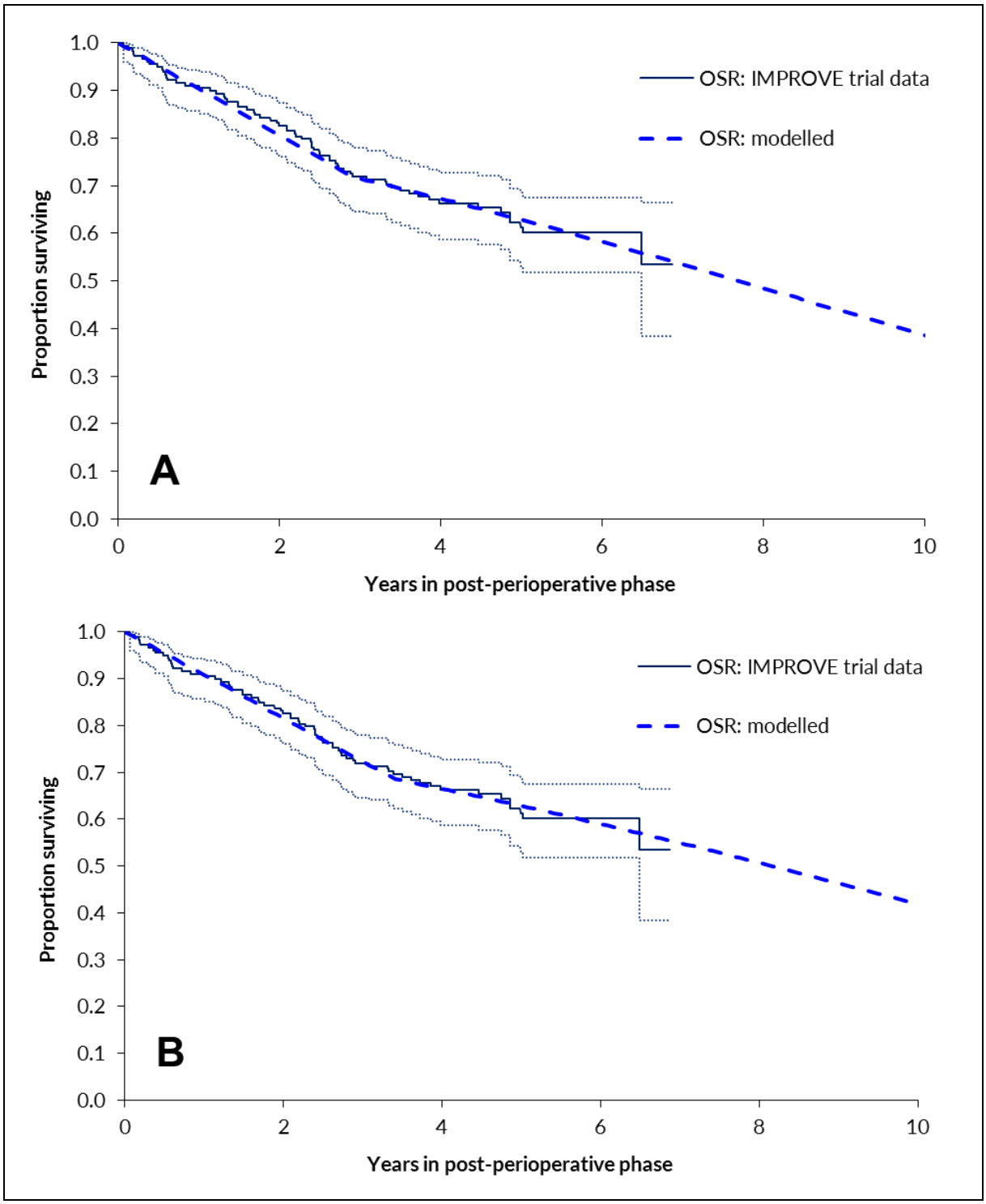


Figure HE11: General population survival (2009–11) calibrated to IMPROVE post-perioperative survival (OSR arm). Piecewise approach with cutpoint at (A) 3 years or (B) 3.5 years.

As before, to ensure that our model cohort is relevant to the present day, we apply $HR1$ and $HR2$ to *current* life tables (2013–15). This reflects a general increase in survival prospects in the UK since the IMPROVE trial recruited, though it implicitly assumes that people who entered IMPROVE in 2009–12 will have experienced the same relative gain in overall survival as the wider population. The expert guideline committee were satisfied that this is appropriate for the IMPROVE study population. We also increase the age of modelled patients by 1 month from baseline when determining their post-perioperative mortality

hazard, to reflect that they will be slightly older following the 30-day perioperative procedure (this is captured in Figure HE11).

Base-case approach: relative long-term survival effects

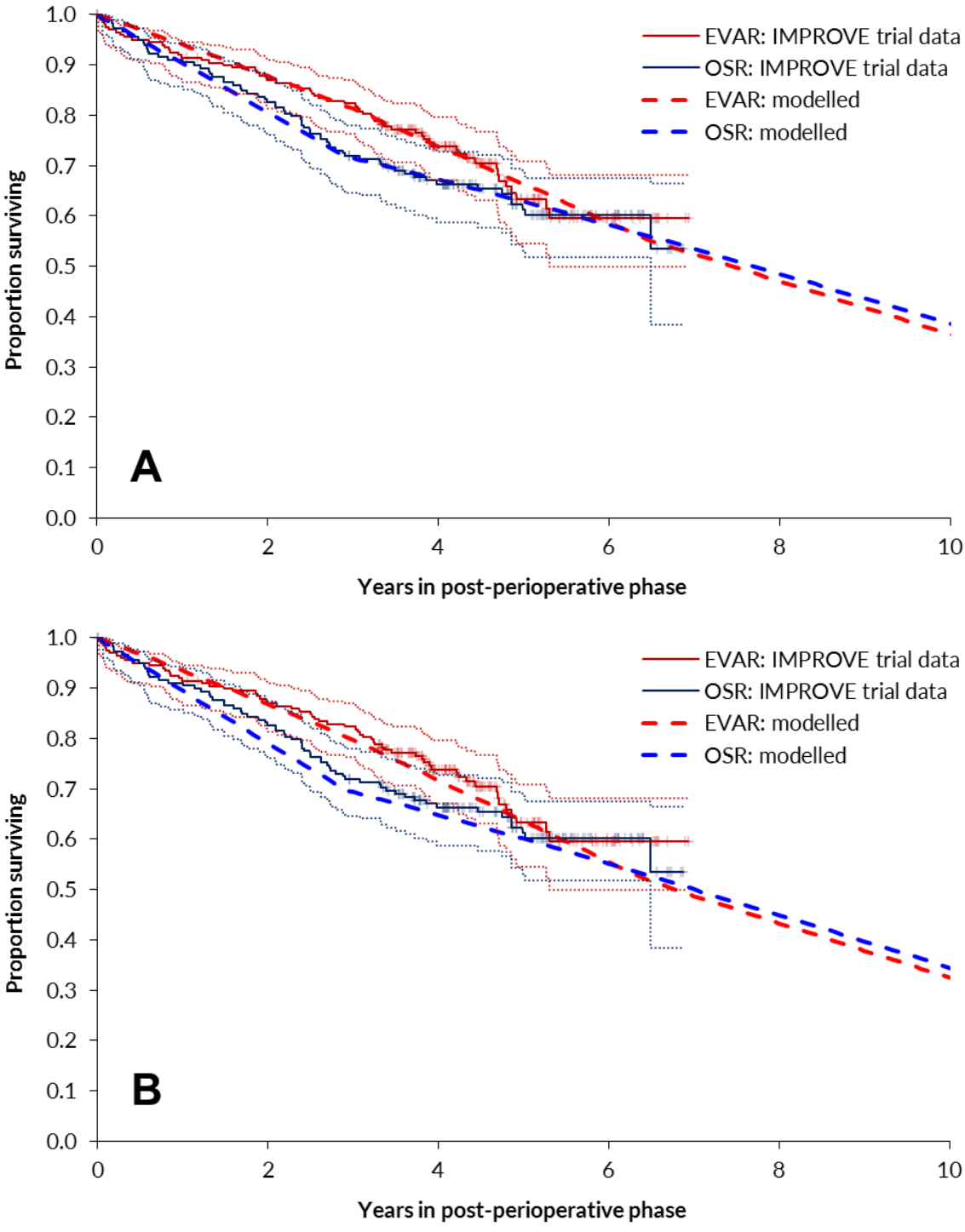
The methods described above provided us with a post-perioperative survival curve for OSR. We then applied a second HR to our calibrated OSR curve, to obtain the post-perioperative survival curve for people who received EVAR. The IMPROVE data suggest EVAR is associated with a notable survival benefit for up to 3 years after aneurysm repair, after which time people who received OSR have a lower mortality rate, shown by a near convergence of the 2 survival curves by around 6 years. To reflect this difference, we ran a piecewise Cox model with a cut-point matching the cut-point used to calibrate general population mortality to the IMPROVE data. In the base-case analysis, this is 3 years. The Cox model produces 2 HR values: $HR_{Cox}1$ for the relative mortality hazard for EVAR vs OSR in time period 1 (0–3 years), and $HR_{Cox}2$ for the relative hazard after 3 years. The values were: $HR_{Cox}1$ = **0.605** (95% CI: 0.393 to 0.932), and $HR_{Cox}2$ = **1.585** (95% CI: 0.852 to 2.948). These reflect the observed lower EVAR mortality rate in the first 3 years after aneurysm repair, and lower OSR mortality thereafter. The hazard ratios are applied to the baseline mortality hazard (i.e. general population calibrated to the IMPROVE OSR arm), after adding 1 month to the cohort's age to account for time spent in the 30-day perioperative period.

At the end of the observed 6.5-year data, the survival curves of OSR and EVAR are shown to almost converge. However, we have no information about what the relative survival of EVAR and OSR looks like after this point. This is problematic because the IMPROVE survival dataset is much less mature than the EVAR-1 (and EVAR-2) datasets, with around 40% of participants still alive the end of the available follow-up. As such, the method of extrapolating beyond the available data is important, affecting a large proportion of modelled patients who survive to that point. Assuming that $HR_{Cox}2$ carries on beyond the observed follow-up may inappropriately extrapolate a survival benefit for OSR into the future, as the OSR survival curve would continue to be flatter than the EVAR curve. However, assuming that there is no survival difference after this point may be equally inappropriate; the data that produced $HR_{Cox}2$ are the longest-term evidence available, and clearly do suggest a lower mid-term mortality rate than EVAR. An alternative approach is to adopt the HR for our elective repair model from the point at which the IMPROVE data runs out (6.5 years). This assumes that, in the long term, the relative effect in overall survival between EVAR and OSR is the same regardless of whether the intervention was elective or an emergency. After discussion with the guideline development committee, this approach was adopted in our base-case analysis. To obtain the EVAR survival curve, we therefore apply the following to our calibrated OSR curve:

- Years 0-3 after intervention: $HR_{Cox}1 = 0.605$
- Years 3-6.5 after intervention: $HR_{Cox}2 = 1.585$
- Years 6.5+ after intervention: $HR_{elective} = 1.089$

The resulting curves are shown in Figure HE12.

Due to the importance of survival extrapolation when such a high proportion of modelled patients are affected by it, we have tested the following sensitivity analyses: (1) allow the trend of lower OSR mortality after year 3 in IMPROVE to project forward for the model's lifetime horizon; (2) use the elective repair HR derived specifically in EVAR-1 participants who survived for at least 8 years (HR = 1.297); (3) assume no difference in mortality rates (HR = 1) beyond the available IMPROVE data; and (4) assume no difference in post-perioperative mortality rates at any time.



Note: base case departs from optimal fit to empirical data because (a) general population lifetables from 2013–15 are used (rather than 2009–11) and (b) cohort age and sex are set to average of all participants in EVAR-1 (rather than just those randomised to OSR).

Figure HE12: Modelled post-perioperative survival compared with that observed in IMPROVE, showing (A) optimal fit and (B) base case

Effect modifiers for post-perioperative mortality – emergency repair

For the purpose of subgroup analysis and PSA, we also estimated the effect of age and sex on post-perioperative survival outcomes, through a multivariable Cox regression obtained using the IMPROVE trial data (Table HE20). We also included AAA diameter as an

explanatory variable; however, this was dropped as its HR (0.987; 95% CI: 0.977 – 0.997) indicated that having a large aneurysm at the time of intervention was associated with superior long-term survival. This effect was determined to be improbable, and likely to be an artefact of the IMPROVE dataset, and the HR being close to 1 indicates that excluding it is unlikely to have a notable bearing on model results. In exploring various interaction terms and functional forms, we identified a clear interaction between sex and time (Figure HE13), such that a 3-year cut point for the sex HR significantly improved the visual fit of the model. As per the elective repair analysis, we do not apply these effect modifiers in our base-case analysis, nor do we apply perioperative mortality effect modifiers. Instead, our base-case results are evaluated at the mean patient characteristics of the IMPROVE study. When applying the effect modifiers for subgroup analyses and PSA, we do not use the HR associated with age, because age is already accounted for by our use of UK life tables as the basis of our survival curves. Applying the age HR shown below would double-count the effect of age. However, age was included in the Cox regression to provide more accurate estimates of the independent effects of treatment and sex.

In the sensitivity analysis where the 3.5-year cut-point is applied to the general population survival calibration, the 3.5-year cut-point Cox regression values in Table HE20 are used.

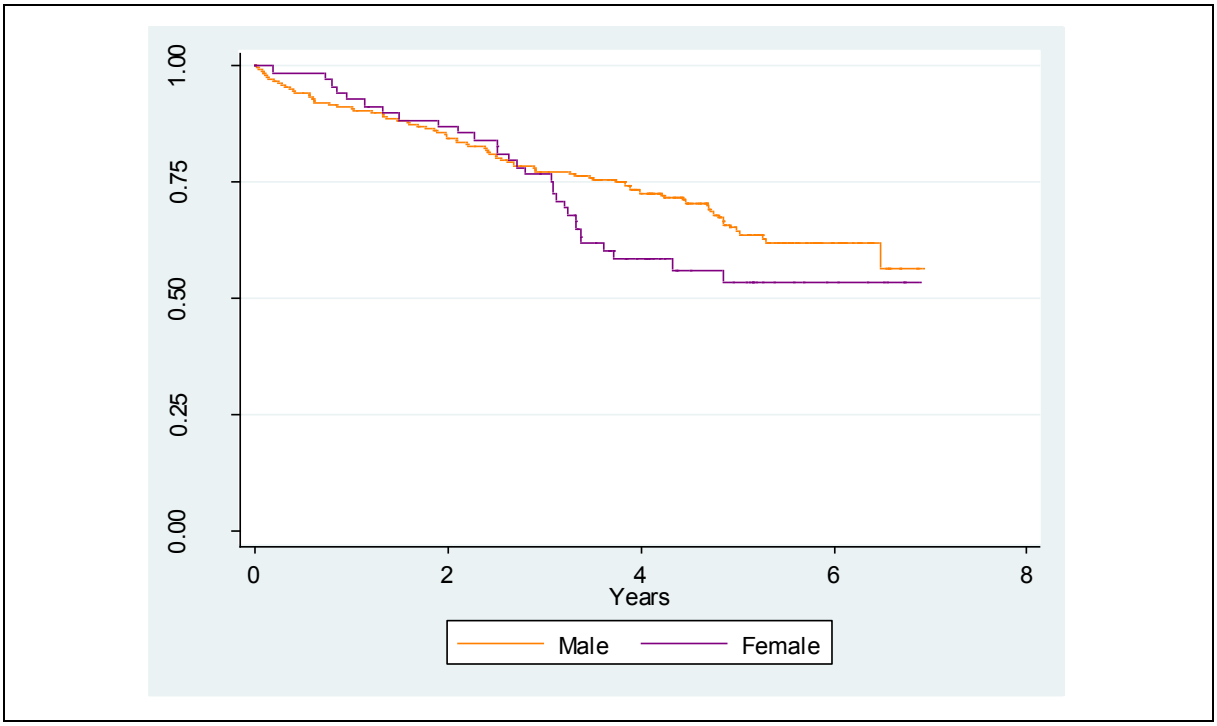


Figure HE13: IMPROVE post-perioperative survival data by sex

Table HE20: Post-perioperative survival effect modifiers – Cox regression – IMPROVE (for subgroup analyses and PSA only)

Variable	*3-year cut-point*		*3.5-year cut-point*	
	HR	*95% CI*	*HR*	*95% CI*
EVAR (vs. OSR): 0-cut years	0.601	0.390 – 0.928	0.683	0.458 – 1.016
EVAR (vs. OSR): >cut years [a]	1.438	0.769 – 2.688	1.451	0.668 – 3.061
Age, per year [b]	0.895	0.513 – 1.559	1.043	1.017 – 1.070
Sex = female (vs. male): 0–cut years	1.868	0.964 – 3.623	1.366	0.861 – 2.169
Sex = female (vs. male): >cut years	1.041	1.015 – 1.067	0.594	0.202 – 1.745

Note: (a) EVAR HR is replaced by elective repair value of 1.089 after 6.5 post-perioperative years. (b) When post-perioperative survival effect modifiers are applied, the age HR shown is not used, as doing so would double-count the effect of age on mortality, which is already captured by our use of calibrated UK population life tables.

Key: CI, confidence interval; HR. hazard ratio.

Emergency repair for complex AAAs with EVAR does not typically occur in UK practice, as the time required to manufacture a bespoke EVAR device to fit the patient's anatomy makes it impractical. As a result, it is assumed that all individuals in this group will receive open surgery, and no comparison is modelled.

Secondary approach: parametric curves based on IMPROVE data

Taking the same approach as elective repair, we explored the more traditional survival analysis method of fitting parametric functions to the post-perioperative survival data for emergency repairs. Standard parametric functions, fitted separately to the IMPROVE trial arms, were evaluated using Stata 13.0 (exponential, gamma, Gompertz, log-logistic, log-normal and Weibull). Like before, model selection was driven by visual fit, statistical goodness of fit, and guideline committee validation.

The exponential functions were found to provide the best statistical fit to the IMPROVE post-perioperative survival data, producing the lowest AIC and BIC values across the interventions. The Gompertz function was the second-best fit on this basis. In terms of visual fit to the data, the Gompertz function provided a superior fit to survival over time on the EVAR arm, while the Gompertz and gamma functions were the most suitable for the OSR data (see Figure HE14 and Figure HE15).

Based on its relatively strong results in terms of statistical fit, superior visual fit, and optimal fit to more mature data in the elective setting, the primary parametric curves analysis uses the Gompertz function curves to estimate both EVAR and OSR survival. The exponential function is used in a sensitivity analysis for the OSR data, but not for the EVAR data, as it produces implausibly optimistic long-term survival estimates. Like before, we also fit parametric survival functions using a treatment covariate to distinguish between EVAR and OSR, rather than separate functions. We also fit parametric models that include age, sex and AAA diameter coefficients, to facilitate subgroup analysis and PSA. All parametric model parameters are provided in Section HE.6.

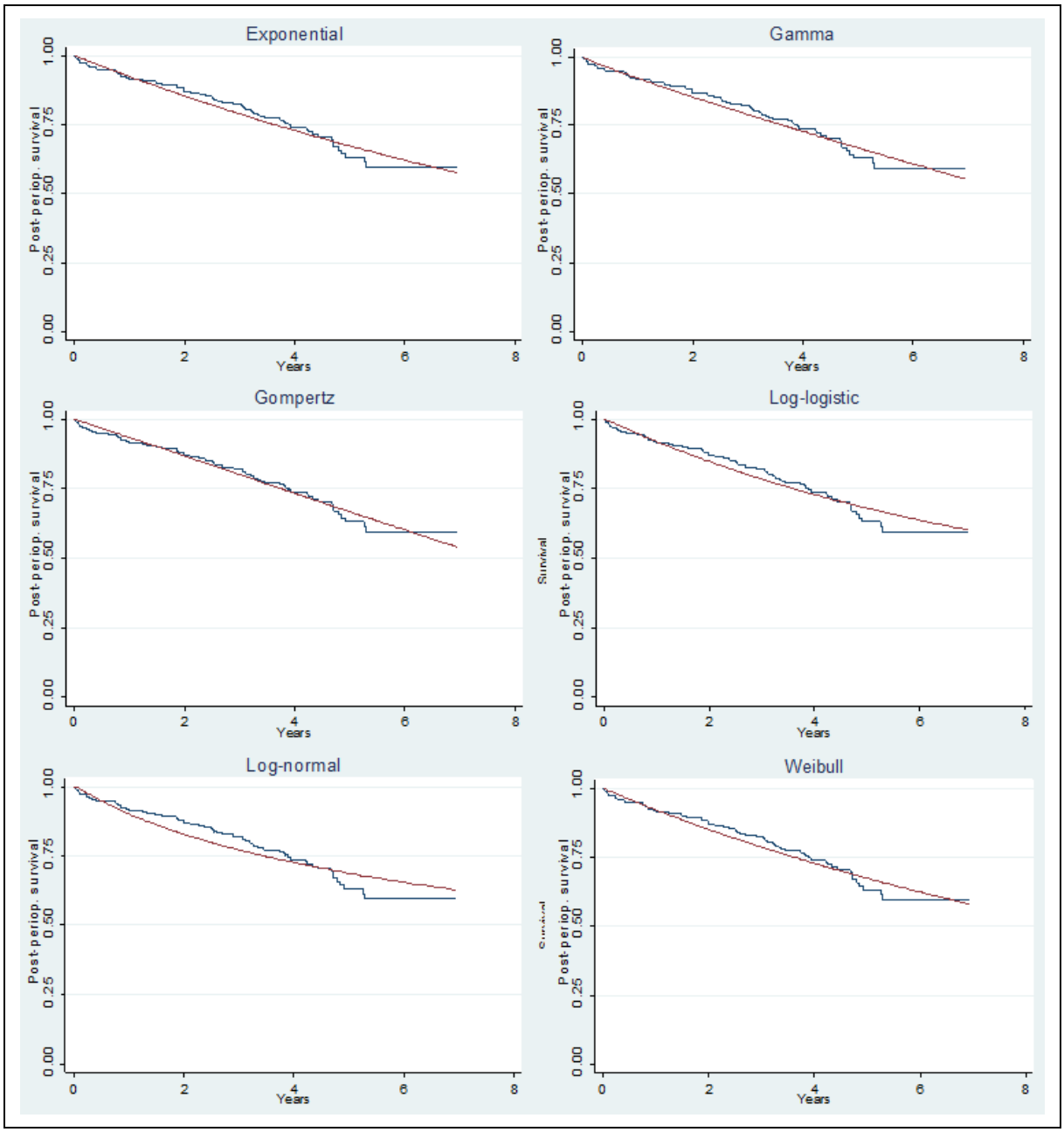


Figure HE14: Visual fit of parametric survival functions for post-perioperative survival – IMPROVE, EVAR arm

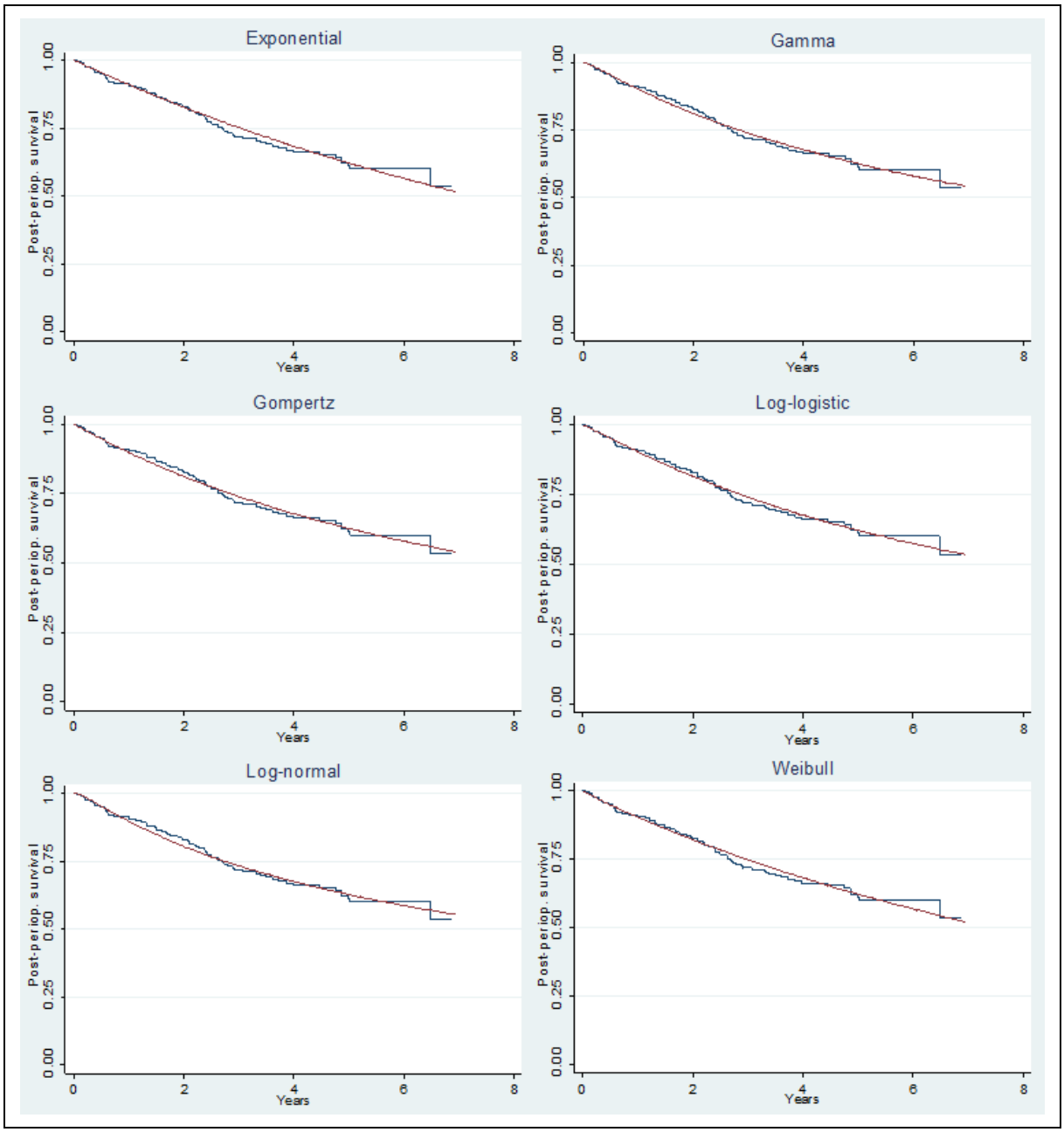


Figure HE15: Visual fit of parametric survival functions for post-perioperative survival – IMPROVE, OSR arm

Table HE21: Statistical fit of parametric survival functions for post-perioperative EVAR-1 survival

Model	*EVAR data*		*OSR data*	
	AIC	**BIC**	**AIC**	**BIC**
Exponential	386 [a]	389 [a]	335 [a]	347 [a]
Gamma	388	398	338	356
Gompertz	387	393	336	351
Log-logistic	390	397	336	352
Log-normal	397	404	337	352
Weibull	388	394	337	352

Note: (a) The model that provides the best fit to the observed data is signified by the lowest AIC and BIC statistic.

Key: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion.

HE.2.2.7 Overall survival

When the 3 components of survival – waiting time, perioperative time and post-perioperative time – are combined, as described above, we obtain estimates of overall survival.

HE.2.2.7.1 Elective repair

Figure HE16 provides a comparison of the EVAR-1 Kaplan-Meier survival data and our base-case projection of overall survival for a cohort with elective, infrarenal AAAs (dotted lines). At first appearance, our model appears to significantly overestimate survival observed in the trial. However, the EVAR-1 data are shown only as a benchmark for comparison. As described above, there are reasons why our base-case analysis intentionally differs from the EVAR-1 trial data, as follows:

1. We have not used the EVAR-1 data to inform baseline perioperative mortality. We have instead used National Vascular Registry data to provide a snapshot of 30-day mortality associated with EVAR in the UK, and to this baseline figure we apply the relative effect of OSR (obtained from the EVAR-1 trial in our base-case). The registry data show that 30-day mortality in the UK from elective, infrarenal EVAR procedures is 0.4%; much lower than the EVAR-1 trial value of 1.6%. This suggests that perioperative outcomes in NHS practice today may be superior to when the EVAR-1 study procedures were performed (it recruited between 1999 and 2003). When the OSR relative effect from EVAR-1 is applied to the lower baseline figure for EVAR, its perioperative mortality is estimated to be 1.3%, again much lower than is trial value of 4.2%. Use of the more recent UK registry data to inform baseline perioperative mortality therefore explains the higher early survival in our model compared with the observed EVAR-1 study data.

2. We use the results of a Cochrane meta-analysis to inform the relative effect of EVAR versus OSR in terms of perioperative mortality, rather than the EVAR-1 figure alone. The meta-analysed value is a stronger estimate, based on a significantly larger number of observations from a total of 4 RCTs.

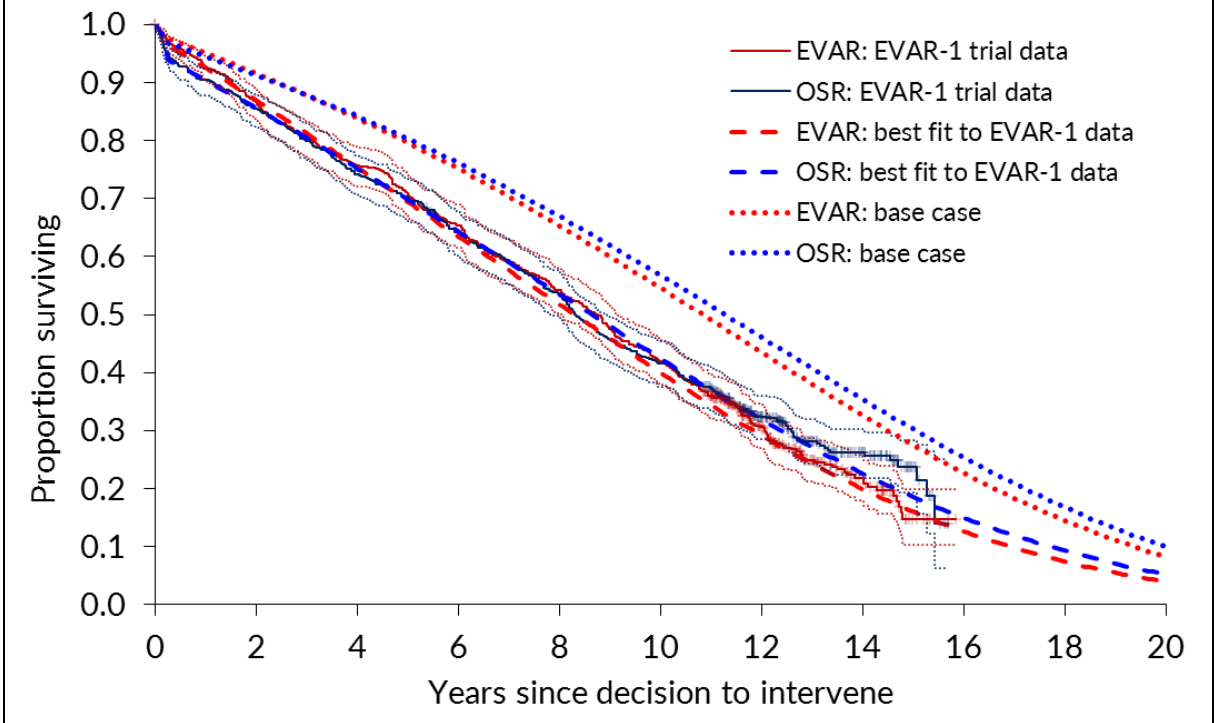
3. Post-perioperative survival is not informed by the EVAR-1 study data alone. Our base-case approach applies a HR to model EVAR post-perioperative survival relative to OSR. This HR was obtained from a meta-analysis of the EVAR-1, DREAM and OVER trials.

4. The EVAR-1 study recruited participants between 1999 and 2003. Our base-case approach involved calibrating 1999–2001 general population survival to match the post-perioperative OSR data from the trial as closely as possible. We apply the HR

to achieve this calibration to 2013–15 general population survival, to reflect the improved survival prospects of the population today compared with at the time of EVAR trial recruitment.

However, our model can be configured to adopt assumptions that optimise fit to the EVAR-1 data. This means: (1) using the EVAR-1 trial to inform baseline perioperative mortality rates; (2) using the perioperative survival odds ratio from EVAR-1, rather than a meta-analysed value; (3) using the long-term survival EVAR HR from the EVAR-1 trial, rather than our meta-analysis; and (3) using 1999–2001 background mortality data in the model. The resulting excellent 'true' fit of the model to EVAR-1 overall survival is depicted by dashed lines in Figure HE16.

The overall survival profiles using our secondary, parametric curve approach – separate Gompertz functions for EVAR and OSR – are shown in Figure HE17(A). Here, perioperative mortality is informed only by the EVAR-1 trial, to show the excellent fit of the model to the data. In part B of the figure we show our base-case overall survival profiles in this secondary approach. These diverge from the EVAR-1 data slightly, as baseline and relative perioperative mortality rates are instead informed by UK registry data and a Cochrane meta-analysis of RCTs respectively. Survival profiles obtained using different post-perioperative parametric functions are shown in Section HE.2.2.8.



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

Figure HE16: Overall survival profiles in base-case model – elective & infrarenal – compared with EVAR-1 survival data

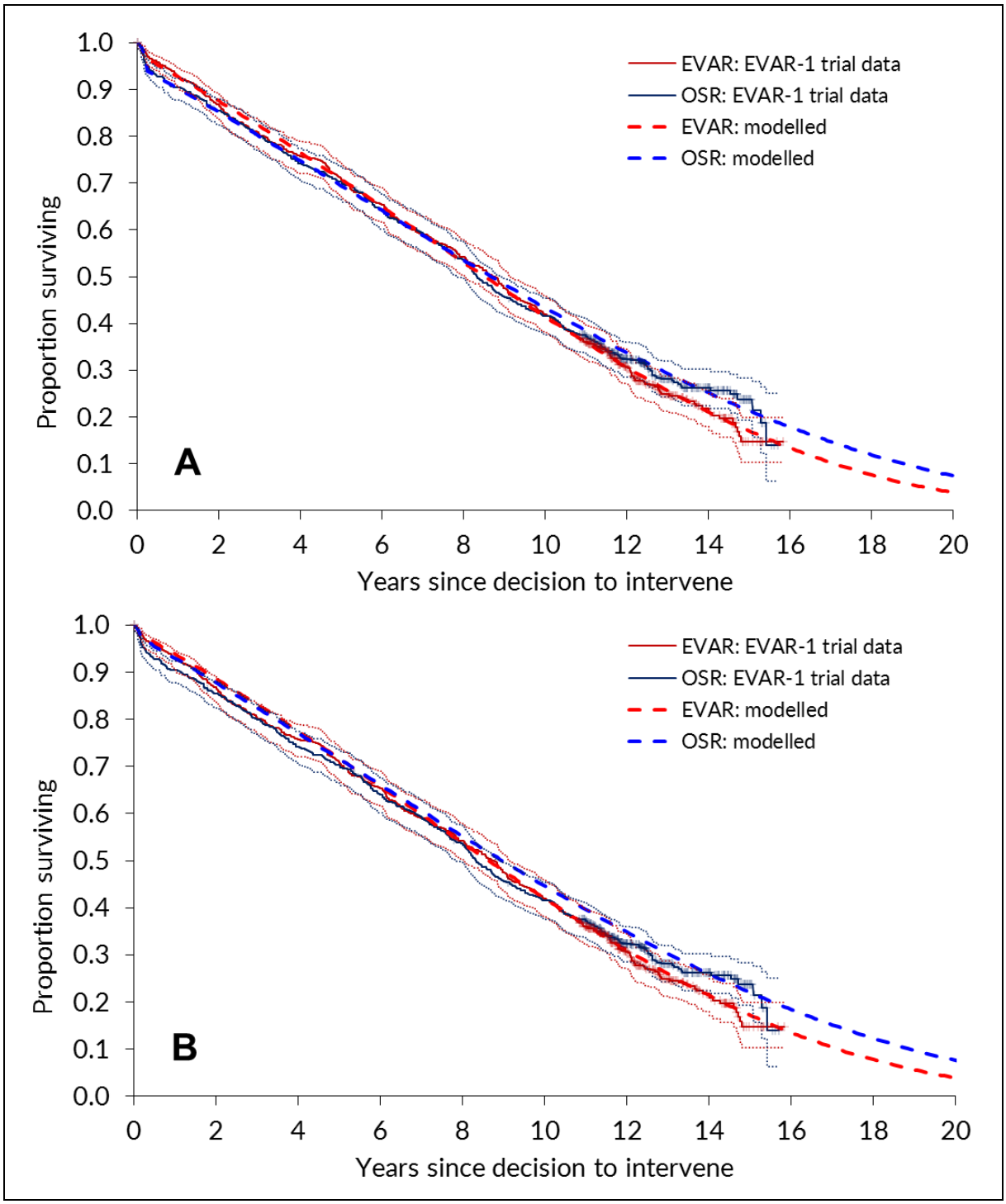


Figure HE17: Overall survival profiles using parametric survival curves for EVAR-1 post-perioperative survival: (A) with EVAR-1 perioperative mortality; (B) with base-case registry and pooled perioperative mortality data.

For complex repair, there is no directly applicable survival data from an RCT against which to compare our simulated estimates. Instead, Figure HE18 shows the base-case projections of survival for people with complex AAAs next to the base-case curves for infrarenal AAAs (from Figure HE16), for comparison. The observed differences in the curves are largely due to the higher perioperative mortality rate estimated for the repair of complex AAAs and, to a lesser extent, 2 months of additional waiting time for a custom-made EVAR device to repair complex aneurysms. There are no differences in post-perioperative mortality rates between infrarenal and complex aneurysm patients in the model. The EVAR curves almost converge

at approximately 14 years, whereas it takes the OSR curves 20 years to converge to the same degree, due to the large predicted increase in perioperative mortality associated with complex OSR.

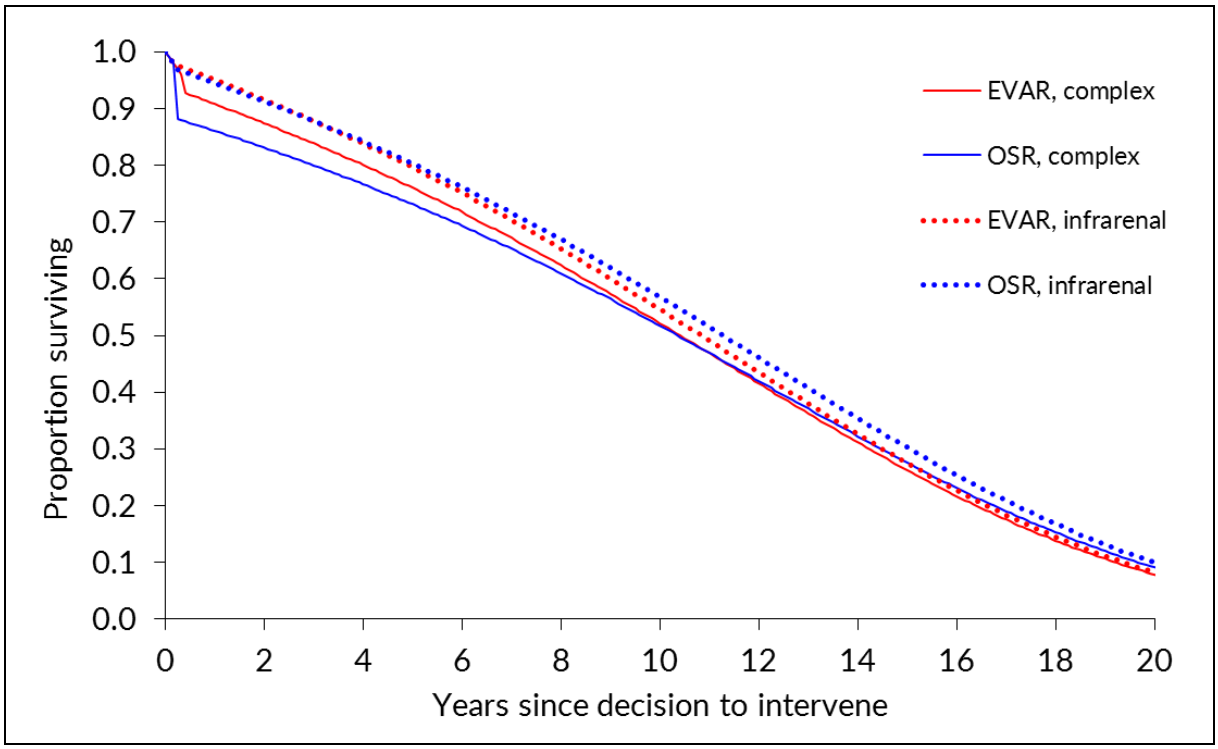
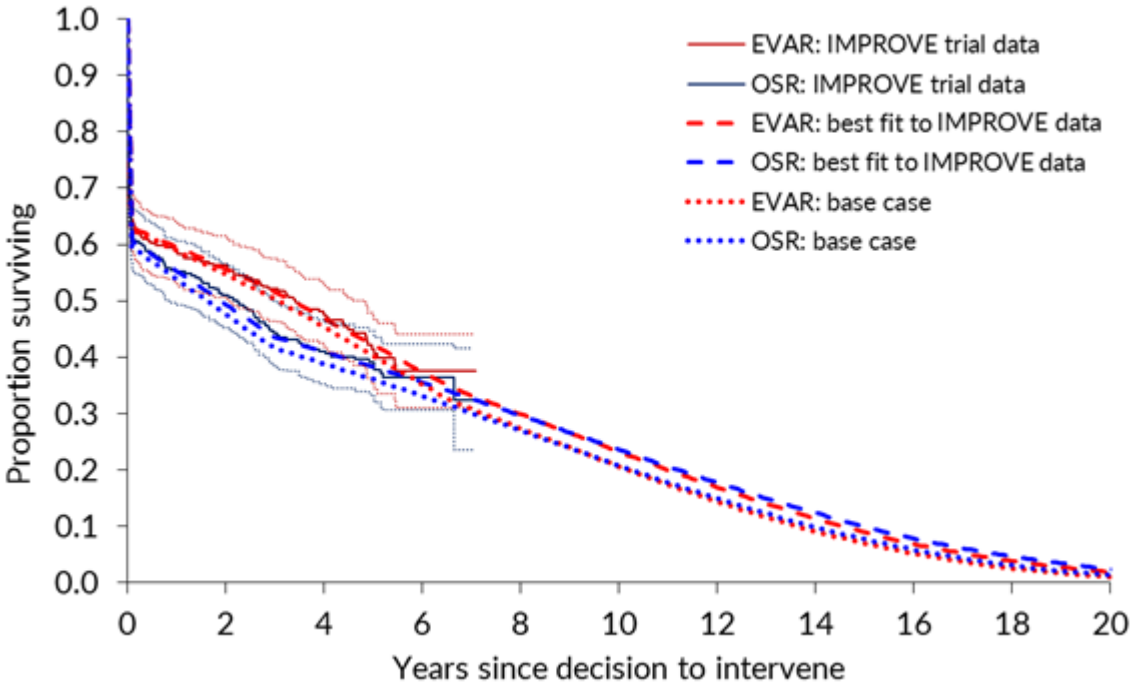


Figure HE18: Overall survival profiles in base-case model – elective & complex compared with elective & infrarenal

HE.2.2.7.2 Emergency repair

Figure HE19 provides a comparison of the IMPROVE Kaplan–Meier survival data and our base-case projection of overall survival for a cohort with infrarenal AAAs requiring emergency repair (dotted lines). Here, our base-case model appears to underestimate survival relative to the trial. Again, the differences can be explained by our selection of a more appropriate base-case for our analysis: using perioperative survival data from the NVR for our baseline mortality rates; using a Cochrane meta-analysis to inform perioperative mortality relative effects; and implementing 2013-15 UK life tables rather than the 2009-11 data used in our survival calibration. Additionally, as our calibration of general population survival to match the IMPROVE study used the OSR arm of the trial, the mean age of that post-perioperative group is younger than the overall baseline age of the trial by more than 1 year. When all of these adjustments are reversed, the excellent 'true' fits to the data achieved by the calibrated life tables approach are shown by the dashed lines.

Note that, as described earlier, extrapolation of survival beyond the incomplete IMPROVE data is potentially important due to the large proportion of patients still alive the end of follow-up. In our base-case model, we apply the EVAR HR from the elective repair model after 6.5 post-perioperative years. This is identifiable below in the small difference in mortality after this time, instead of projecting the superior OSR survival after 3 years into the unknown, long-term period.



Note: While base-case survival may seem to underpredict survival in the IMPROVE trial, the apparent differences are explained by: (1) the use of UK registry data to inform baseline estimate of perioperative mortality (lower than RCT estimates; (2) perioperative survival relative effects being informed by meta-analysed data from several RCTs, rather than just IMPROVE; (3) uplifting survival data calibrated to the OSR arm of IMPOVE, which recruited in 2009–2012, to reflect 2015–16 values using UK life tables; and (4) differences in the age of IMPROVE participants who survived surgery and the overall trial cohort.

Figure HE19: Overall survival profiles in base-case model – emergency & infrarenal – compared with IMPROVE survival data

The overall survival profiles using our secondary, parametric curve approach – again, separate Gompertz functions for EVAR and OSR – are shown in Figure HE20(A). Here, perioperative mortality is informed only by the IMPROVE trial, to show the excellent fit of the model to the data. For these curves, the highest mortality rate from the elective and emergency repair functions is always used. This prevents the implausible situation whereby a person whose AAA ruptured has a lower mortality risk than a person whose AAA was repaired before it ruptured, which could occur because the IMPROVE data are less mature than the long-term data used for unruptured AAA, making its long-term mortality projection more uncertain. In part B of the figure we show our base-case overall survival profiles in this secondary approach. These diverge from the IMPROVE data slightly, as baseline and relative perioperative mortality rates are instead informed by UK registry data and a Cochrane meta-analysis of RCTs respectively. Survival profiles obtained using different post-perioperative parametric functions are shown in Section HE.2.2.8.

Emergency repair for complex AAAs with EVAR does not typically occur in UK practice, as the time required to manufacture a bespoke EVAR device to fit the patient's anatomy makes it impractical. As a result, it is assumed that all individuals in this group will receive open surgery, and no comparison is modelled.

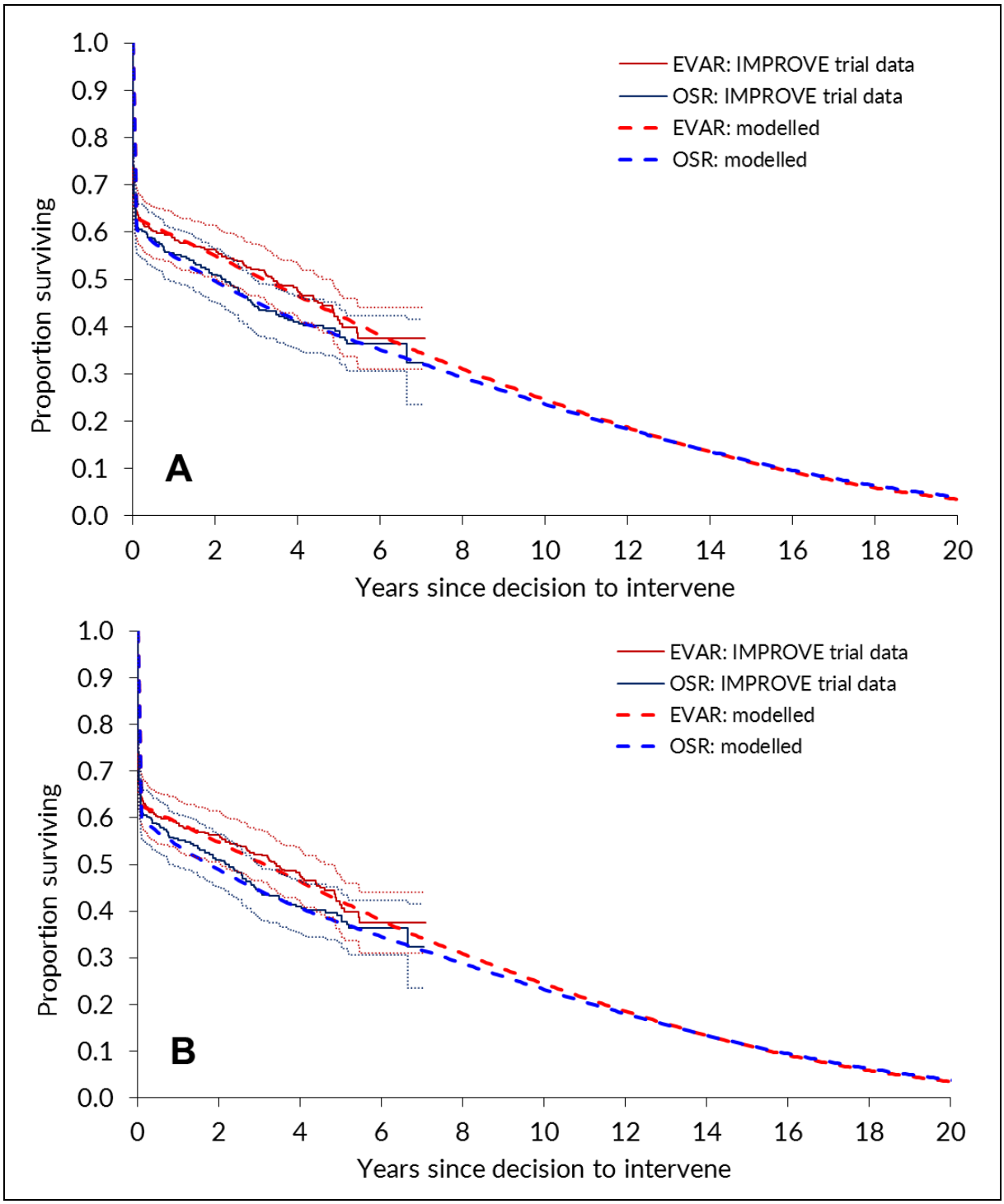


Figure HE20: Overall survival profiles using parametric survival curves for IMPROVE post-perioperative survival: (A) with IMPROVE perioperative mortality; (B) with base-case registry and pooled perioperative mortality data.

HE.2.2.8 Survival sensitivity analyses

The following alternative approaches to modelling survival have been included as sensitivity analyses for the 'fit for OSR' population:

1. Perioperative mortality
    a. Informing baseline mortality rates by alternative NVR data or data from the UK trials, EVAR-1 and IMPROVE

b. Using the UK trials, EVAR-1 and IMPROVE, to inform relative mortality effects, rather than the Cochrane meta-analyses (Paravastu et al., 2014; Sweeting et al., 2017)

c. Applying age, sex and AAA diameter effect modifiers

2. Post-perioperative mortality

a. Using parametric curves fitted to the EVAR-1 and IMPROVE trial data, including specifying models for each trial arm separately, with and without effect-modifying covariates, and including them in the same model with a treatment variable. The resulting overall survival profiles are provided in Figure HE21 to Figure HE23.

b. For elective repair: applying the post-perioperative mortality HR derived from the EVAR-1 data (1.107), from which we were able to remove waiting and perioperative deaths from the data. Our base-case HR (1.089) is a pooled estimate incorporating summary survival data from the DREAM and OVER trials, with the first year of their survival data removed to estimate post-perioperative survival.

c. For elective repair: assuming that EVAR and OSR post-operative mortality rates are equal for 8 years, followed by an EVAR HR of 1.297. An alternative long-term survival scenario applies no difference in post-perioperative mortality rates at any time.

d. For emergency repair, long-term survival extrapolation scenarios are: (1) allowing the observed trend in the IMPROVE survival data after 3 years to project forward over the model's lifetime horizon (EVAR HR = 1.585); (2) applying the EVAR-1 post-8 years HR (1.297) after 6.5 years; (3) assuming EVAR and OSR have equal post-perioperative mortality rates after 6.5 years; (3) and (4) applying no difference in post-perioperative mortality rates at any time.

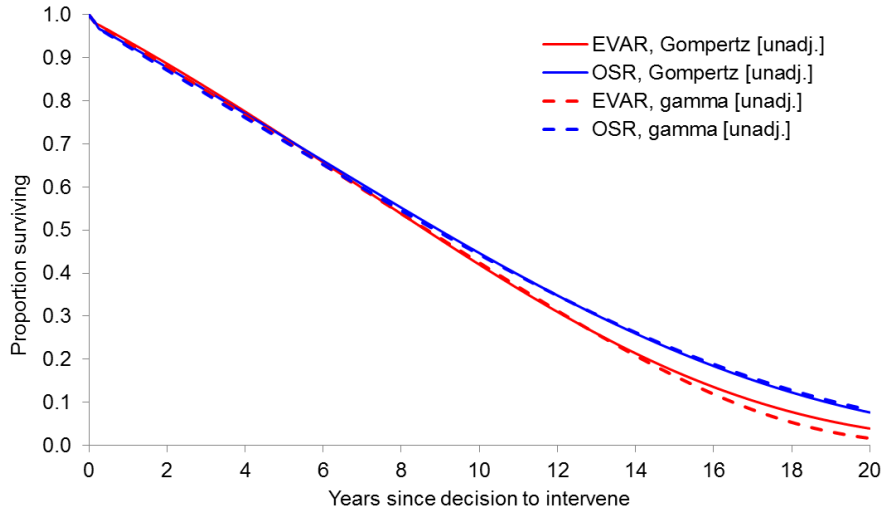
e. For emergency repair: applying a 3.5-year cut-point for the piecewise calibration of general UK population mortality to the IMPROVE trial, and the relative effects Cox model, rather than the base-case cut-point of 3 years.

f. Applying age, sex and AAA diameter effect modifiers.

g. Using 1999–2001 (elective) and 2009–11 (emergency) UK general population survival data in the model, which was calibrated to match the EVAR-1 and IMPROVE trials, rather than scaling up our survival estimates by using 2013-15 life tables.

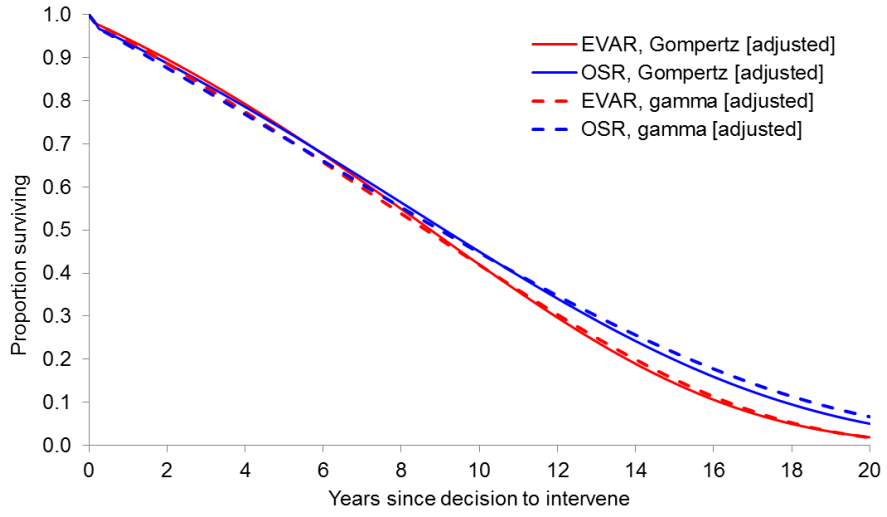
No covariate adjustment

Separate models for EVAR and OSR



Adjusted for age, sex and AAA size

Separate models for EVAR and OSR



No covariate adjustment

Common model with treatment variable

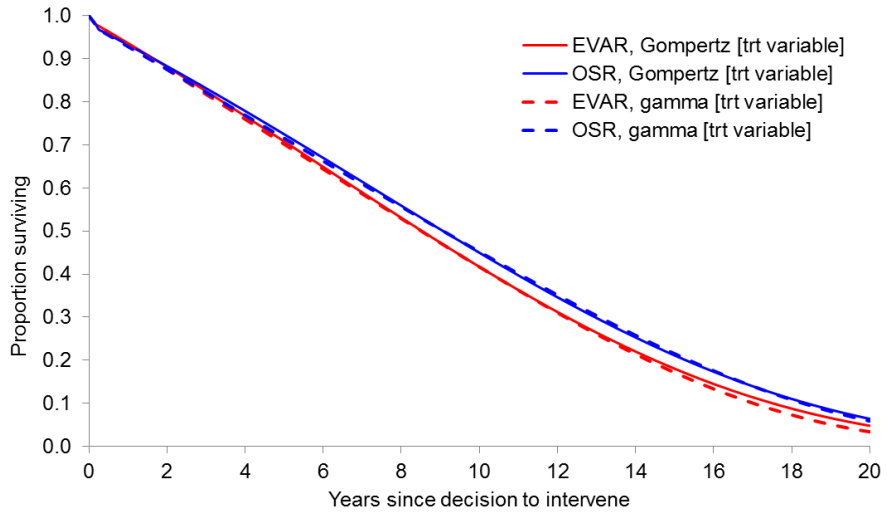
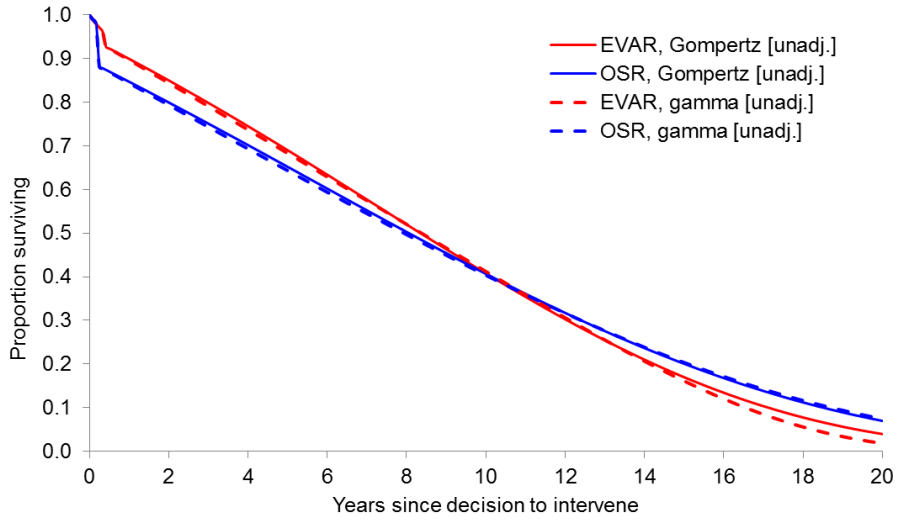


Figure HE21: Comparison of alternative overall survival profiles from parametric curves – elective & infrarenal repair

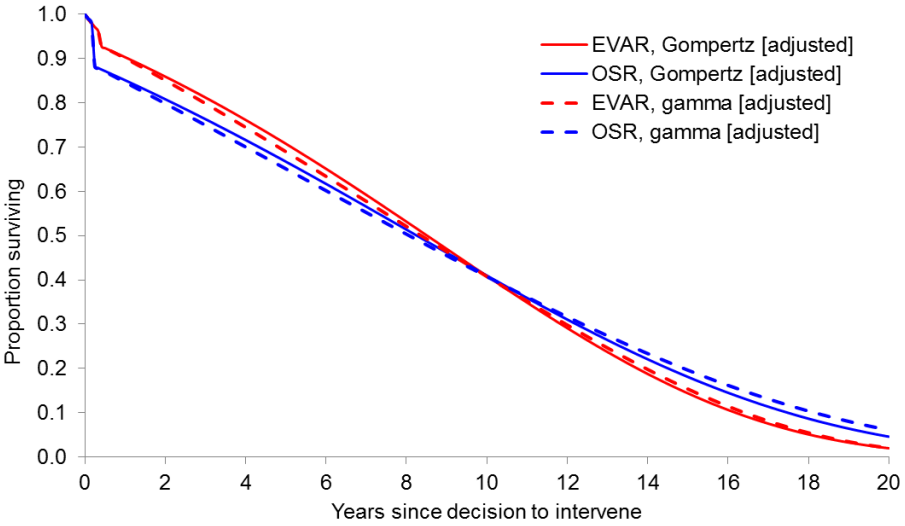
No covariate adjustment

Separate models for EVAR and OSR



Adjusted for age, sex and AAA size

Separate models for EVAR and OSR



No covariate adjustment

Common model with treatment variable

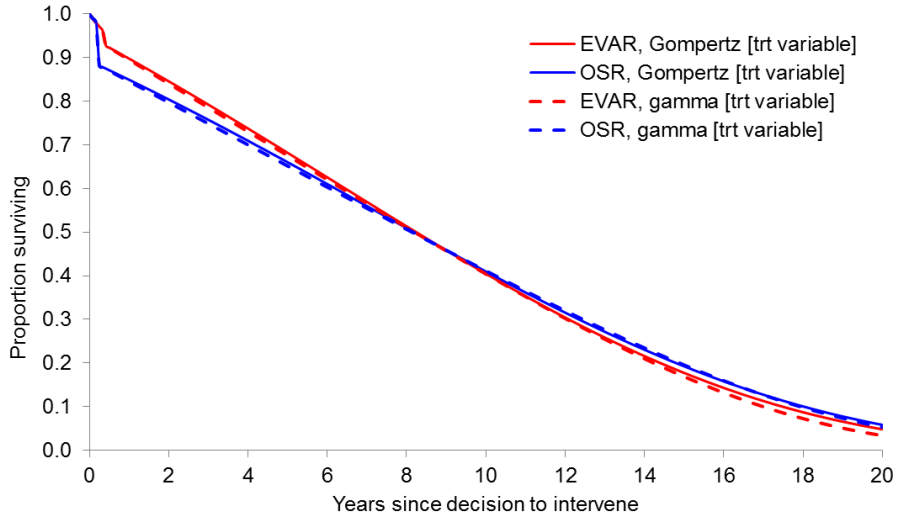


Figure HE22: Comparison of alternative overall survival profiles from parametric curves – elective & complex repair

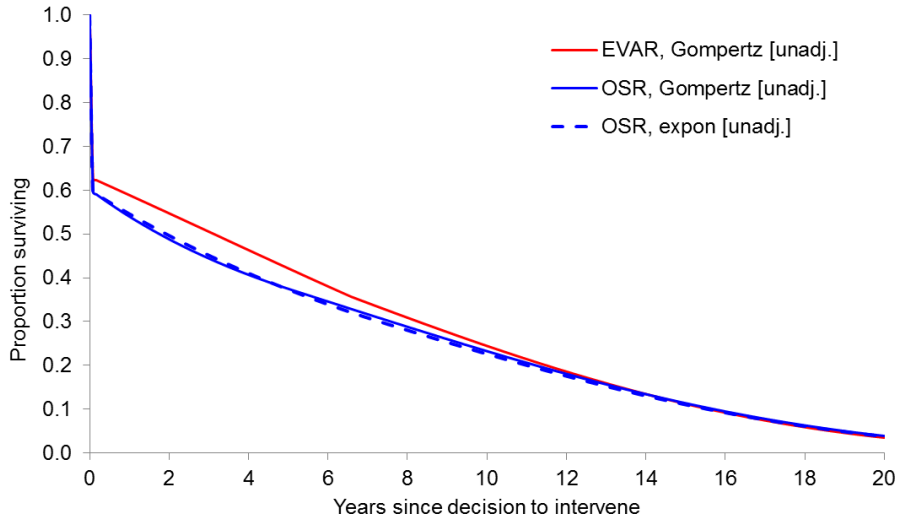
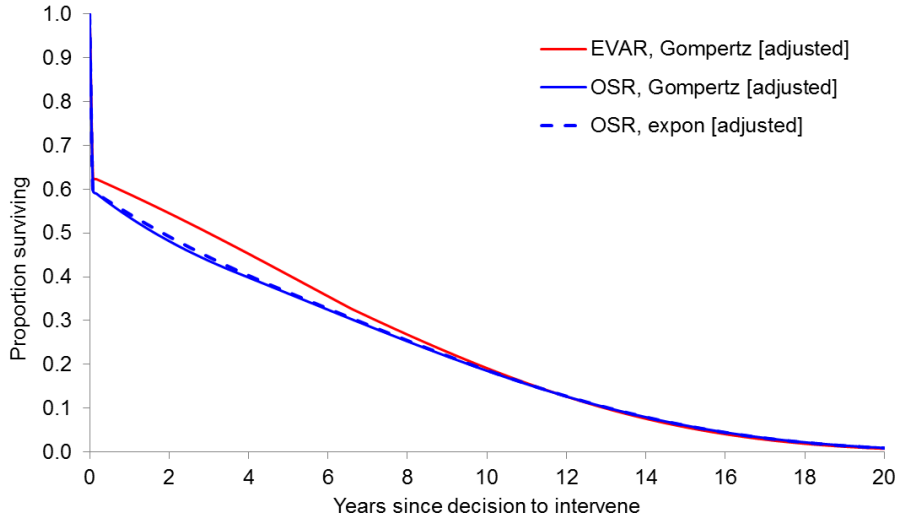
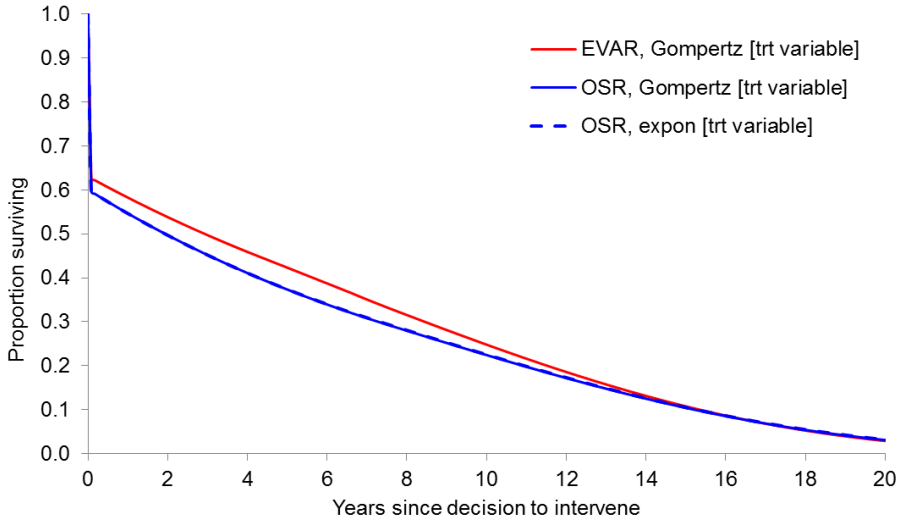
No covariate adjustment ***Separate models for EVAR and OSR***	
Adjusted for age, sex and AAA size ***Separate models for EVAR and OSR***	
No covariate adjustment ***Common model with treatment variable***	

Figure HE23: Comparison of alternative overall survival profiles from parametric curves – emergency & infrarenal repair

HE.2.2.9 Reintervention

HE.2.2.9.1 Elective repair

A key aspect of the intervention decision is the risk of complication, and ultimately reintervention, in the years after the procedure. The RCT evidence typically suggests that graft-related complications are more common following elective aneurysm repair with EVAR than with OSR. This is reflected in the EVAR-1 data, which are used to inform reintervention rates in the elective repair model. The committee were satisfied that this was an appropriate data source for reintervention rates, as although the EVAR trials recruited in 1999 to 2004, no difference in the safety and durability of newer EVAR devices has been identified (Hammond et al., 2016).

The trial investigators categorised graft-related reintervention procedures as either 'life-threatening' or 'serious' severity levels. Life-threatening procedures included the most invasive complications, such as a graft infection and graft replacement. Procedures categorised as 'serious', were important but not considered to be life-threatening, such as endoleaks and hernias. The probability of an event within each category occurring was reported for the first 6 months after AAA repair, 6 months to 4 years, 4 to 8 years, and >8 years. We convert these results to monthly probabilities in order to apply them as probabilities per cycle in our model (Table HE22). Because the ">8 years" data have no fixed end point in time, it was not possible to convert those results to monthly probabilities. We therefore assume the monthly probabilities associated with the 4-8 year time period can be applied for the model duration beyond 8 years.

Table HE22: Graft-related reintervention rates, elective repair

Reintervention	***EVAR***		***OSR***	
Life-threatening	Event prob.	Prob/month	Event prob.	Prob/month
0 to 6 months	3.27%	0.55%	3.04%	0.51%
6 months to 4 years	4.39%	0.11%	0.35%	0.01%
Years 4-8 [a]	3.43%	0.07%	2.44%	0.05%
Serious	Event prob.	Prob/month	Event prob.	Prob/month
0 to 6 months	7.30%	1.26%	3.04%	0.51%
6 months to 4 years	8.71%	0.22%	1.40%	0.03%
Years 4-8 [a]	5.18%	0.11%	3.60%	0.08%

Note: a) Event probabilities derived from data for years 4 to 8 applied for the duration of the model beyond 8 years, in the absence of longer-term data.

The EVAR-1 data on graft-related reintervention rates were based on the time to *first* reintervention. It is possible that an individual could experience more than 1 reintervention. In the EVAR-1 trial, the mean number of graft-related reinterventions conditional on having at least 1 was 1.63 among EVAR patients, and 1.42 among OSR patients. To reflect this, once a patient experiences a reintervention in the model, we apply the relevant figure as a multiplier. For example, an elective EVAR patient who required a reintervention could, on average, expect to require 0.63 more reinterventions on average over the course of their lifetime. A limitation of this is that it will slightly overestimate the impact of the additional 0.63 reinterventions, as in reality they would occur at some point in the future and so would be subject to discounting. To explore how influential this assumption is, we conduct extreme value sensitivity analysis around reintervention rates (see Section HE.3.1).

A criticism of the EVAR trials is that they did not capture other types of reintervention, particularly laparotomy-related procedures that are likely to be more prevalent following open surgery (Schermerhorn et al., 2015). As a response to this, the EVAR-1 investigators retrospectively obtained data on hernia interventions required following EVAR and OSR, which were included among the total graft-related reintervention figures in the long-term

follow up report (Patel et al., 2016). We obtained specific quality of life data and NHS unit costs for hernia repair, and therefore wanted to separate hernia events from the total graft-related reintervention figures. We did so using the US registry data of 39,966 match individuals (Schermerhorn et al., 2015). In these data, there were 610 hernia procedures following EVAR, and 6,391 graft-related procedures, such that hernia operations made up 9.5% of the total figure. The equivalent figure in people whose aneurysm had been repaired by OSR was 80.2% (3070/3828), showing that a reintervention following OSR is much more likely to be a hernia repair than a reintervention following EVAR. In the EVAR-1 trial, hernias were retrospectively captured within the 'serious' graft-related reintervention data. We therefore assume that hernia repairs made up 9.5% of EVAR-1 serious graft-related reinterventions following EVAR, and 80.2% following OSR.

We also incorporated other laparotomy-related complications recorded by the US registry into our model. Unlike hernia repairs, these had not been retrospectively included in the EVAR-1 reintervention data. We obtained the rates of lysis of adhesion interventions, bowel resection interventions, and laparotomy-related hospitalisations without intervention, for the following 4 time periods after AAA repair: year 0 to 1, year 1 to 2, year 2 to 5 and year 5 to 8. These were converted to probabilities per month for used in our model. The resulting monthly probabilities indicate that laparotomy-related interventions are more likely to occur following OSR than EVAR (Table HE23). The monthly probabilities derived from the data in the last time period – years 5 to 8 – are applied for the duration of the model thereafter.

Neither myocardial infarction nor stroke events were included, as the incidence of these events is not statistically significantly different between the interventions.

Table HE23: Laparotomy-related reintervention procedures, elective repair

Reintervention	***EVAR***		***OSR***	
Lysis of adhesions	Events / N at risk	Prob/month	Events / N at risk	Prob/month
Year 0-1	55 / 39,966	0.01%	232 / 39,966	0.05%
Year 1-2	46 / 36,234	0.01%	134 / 33,532	0.03%
Years 2-5	97 / 32,184	0.01%	220 / 33,372	0.02%
Years 5-8 [a]	40 / 14,427	0.01%	68 / 13,355	0.01%
Bowel resection	Events / N at risk	Prob/month	Events / N at risk	Prob/month
Year 0-1	304 / 39,966	0.06%	371 / 39,966	0.08%
Year 1-2	220 / 36,234	0.05%	235 / 33,532	0.06%
Years 2-5	377 / 32,184	0.03%	442 / 33,372	0.04%
Years 5-8 [a]	134 / 14,427	0.03%	151 / 13,355	0.03%
Hospitalisation	Events / N at risk	Prob/month	Events / N at risk	Prob/month
Year 0-1	1026 / 39,966	0.22%	1723 / 39,966	0.37%
Year 1-2	732 / 36,234	0.17%	1005 / 33,532	0.25%
Years 2-5	1325 / 32,184	0.12%	1575 / 33,372	0.13%
Years 5-8 [a]	427 / 14,427	0.08%	502 / 13,355	0.11%

Note: a) Event probabilities derived from data for years 5 to 8 applied for the duration of the model beyond 8 years, in the absence of longer-term data.

There are no randomised, comparative evidence in a population with complex, rather than infrarenal, aneurysms. As such, and in agreement with the guideline committee, we assume that the graft and laparotomy-related reintervention rates described above are transferable to people undergoing complex AAA repair. A sensitivity analysis is included that doubles the

risk of graft-related reintervention in people undergoing complex repair, owing to the complex nature of their aneurysm.

A further one-way sensitivity analysis is included in the elective model that captures the incidence of pulmonary complications which occur during the perioperative period. This was included based on the Cochrane systematic review by Paravastu et al., (2014), which found 30-day pulmonary complications to be more common during OSR. This result was driven entirely by the DREAM trial; therefore the scenario analysis includes these data: 10.7% complication rate during OSR, 2.9% during EVAR (Prinssen et al., 2004). Any impact of pulmonary complications on mortality will implicitly contribute to the 30-day perioperative mortality rates associated with OSR and EVAR; however, this scenario explicitly captures additional costs and QALY effects of pulmonary complications.

HE.2.2.9.2 Emergency repair

Reintervention data from the IMPROVE trial are used to inform reintervention rates in the emergency repair model. The study reported an event rate on the OSR arm of 0.208 reintervention procedures per year (65 procedures in 313.1 person-years), and a covariate-adjusted HR for people on the EVAR arm of 1.12 (95%CI: 0.80 – 1.56). The equivalent reintervention rate per year on the EVAR arm is therefore 0.233. The equivalent probabilities per model cycle (month) are: 1.4% for OSR and 1.6% for EVAR.

The trial investigators categorised graft-related reintervention procedures as either 'life-threatening' or 'serious' severity levels. They also categorised events as either 'arterial-related', 'laparotomy-related' or 'other', by epoch: 0-3 months and 3-36 months. We used the number of events in each category to apportion the overall reintervention probabilities per cycle (1.4% and 1.6%) between the severity levels and type of procedure (excluding the small number of procedures categorised as 'other'), for the 2 time periods. For example, in the time period of 0–3 months, 50 reintervention procedures on the OSR arm were arterial-related. The total number of reintervention procedures, excluding those categorised as 'other', was 77, meaning 65% were arterial, or graft, related. Of these, 33 (66%) were life-threatening. The remaining 35% of procedures were laparotomy-related, of which 3 (11%) were life-threatening. After apportioning the overall reintervention probabilities according to these data, the resulting probabilities of arterial-related reintervention are shown in Table HE24. We assume the monthly probabilities associated with the 3–36 month time period can be applied for the model duration beyond 3 years.

Table HE24: Arterial (graft)-related reintervention rates, emergency repair

Reintervention	*EVAR*	*OSR*
Life-threatening	Prob/month	Prob/month
0 to 3 months	0.70%	0.74%
3 months to 3 years [a]	0.56%	0.60%
Serious	Prob/month	Prob/month
0 to 3 months	0.92%	0.38%
3 months to 3 years [a]	1.11%	0.51%

Note: a) Event probabilities derived from data for this time period are applied for the duration of the model beyond 3 years, in the absence of longer-term data.

Like the EVAR-1 data, the IMPROVE data on graft-related reintervention rates were based on the time to *first* reintervention. It is possible that an individual could experience more than 1 reintervention. In the IMPROVE trial, the mean number of graft-related reinterventions conditional on having at least 1 was 1.36 among EVAR patients, and 1.41 among OSR patients. Like in the elective model, once a patient experiences a reintervention in the model, we apply the relevant figure as a multiplier. Again, to explore how influential this assumption

is, we conduct extreme value sensitivity analysis around reintervention rates (see Section HE.3.2).

For laparotomy-related reintervention procedures, the IMPROVE data report the number of events that were bowel resections and the number that were lysis of adhesions, in the period from 3 months to 3 years. 60% of such events were bowel resections. We therefore apportion the proportion of events that were laparotomy-related, derived as described above, between bowel resection and lysis of adhesion procedures, resulting in the per-cycle probabilities shown in Table HE25.

Table HE25: Laparotomy-related reintervention rates, emergency repair

Reintervention	*EVAR*	*OSR*
Life-threatening	Prob/month	Prob/month
0 to 3 months	0.12%	0.24%
3 months to 3 years [a]	0.10%	0.24%
Serious	Prob/month	Prob/month
0 to 3 months	0.18%	0.36%
3 months to 3 years [a]	0.15%	0.36%

Note: a) Event probabilities derived from data for this time period are applied for the duration of the model beyond 3 years, in the absence of longer-term data.

HE.2.2.10 Resource use

The information used to allocate appropriate resource use to the treatment elements of the model is sourced from the primary evidence base, where available. The following areas of resource use are captured within the intervention model:

- The primary procedure, including repair devices, other consumables, theatre time, and ambulance conveyance
- Perioperative hospital care after the primary procedure, including intensive care
- Ongoing monitoring of a successfully repaired aneurysm
- Reintervention, including hospitalisations without reintervention

HE.2.2.10.1 Primary procedure and perioperative care

To inform resource use associated with the primary repair procedure, NHS Reference Costs (2015–16) for entire hospital spells for a given procedure were considered in the first instance. However, they were identified as being potentially unreliable, with a lack of clarity regarding the extent to which both repair devices and procedure complexity are captured. The 2 key UK trials of EVAR and OSR both conducted resource utilisation questionnaires of their centres and, being UK trials, these data were used instead of the simple, overarching NHS spell costs. For elective cases, EVAR-1 data were used (Brown et al., 2012), and for emergency cases, IMPROVE data were used (Powell et al., 2015; 2017).

Table HE26: Resource use – primary intervention procedure

Resource per patient	*EVAR*	*OSR*
Elective repair – Brown et al., (2012)		
Theatre time (mins)	191	215
Fluoroscopy duration (mins)	25	2
Blood products (ml)	141	863
Preoperative stay (days)	1.81	2.16
Postoperative stay (days)	6.53	9.25
ITU stay (days)	0.59	2.47
HDU stay (days)	0.83	1.88
Emergency repair – Powell et al., (2015; 2017)		
Emergency room attendance	1 [a]	1 [a]
CT scan with contrast	1 [a]	1 [a]
Theatre time (mins)	157	180
Fluoroscopy duration (mins)	[b]	[b]
Blood products (ml)	[b]	[b]
Routine ward stay (days)	7.0	7.8
Critical care (days)	5.3 [c]	7.4 [c]
Transfer to second hospital	3.2%	12.1%
Time in second hospital (days)	0.7	4.8
Outpatient attendances	3.2 [d]	2.9 [d]
Nursing home (days)	0	1.8
Family doctor home visits	2.8	2.5
Community nurse home visits	2.2	2.1

Notes:

(a) Study reports minutes spent in emergency room and assumes a CT scan occurred in that time. NHS reference costs available for CT, and is therefore applied directly, assuming 1 attendance and scan per patient.

(b) Some resource use items could not be costed based on the resource use data reported by Powell et al., (2015), therefore the resource use estimate for elective repair has been assumed.

(c) Study collected critical care (ITU and HDU) costs at a much more granular level in their own micro-costing approach, which would be lost by applying a single per-day cost to the values shown here. Critical care resource use is therefore costed directly from the IMPROVE study, adjusted for inflation (see Section HE.2.2.11).

(d) Follow up outpatient attendances not costed, to avoid double-counting routine monitoring costs (see next sub-section).

Key: CT, computed tomography; HDU, high-dependency unit; ITU, intensive therapy unit.

Based on feedback from the guideline committee, and in the absence of comparative evidence, we assume that the resource requirements to repair a complex AAA (non-infrarenal) are the same the EVAR-1 and IMPROVE data, above, with the following exceptions:

- Complex EVAR does not typically exist in clinical practice as a treatment option for ruptured aneurysms, due to the time required to manufacture a bespoke device. In the model, all emergency complex cases receive OSR, and no comparison of interventions is presented in this setting.

- A scenario analysis is conducted where OSR for a complex aneurysm requires an additional 2 hours of theatre time compared with an infrarenal aneurysm. This is to reflect the additional work required of the surgeon in manually adapting an off-the-shelf stent-graft during surgery to repair a complex AAA.

An appropriate unit cost for each resource use item was identified, and was multiplied by the resource requirement to 'micro-cost' each procedure. These costs are detailed in Section HE.2.2.11.

HE.2.2.10.2 Ongoing monitoring

The model assumes that patients require some level of ongoing postoperative monitoring, for clinicians to identify the need for reintervention. Based on expert advice from the guideline committee, follow-up is more intensive following EVAR compared with OSR. Specifically, there is an outpatient consultation at 1 month after EVAR, followed by an outpatient CT scan 1 month later. Thereafter, patients attend 1 outpatient imaging appointment per year, for 5 years. To reflect recommendations made by the committee elsewhere in the guideline, our base case assumes that CT scans are used for continued follow up. Those who received OSR attend an outpatient consultation after 2 months, without the need for imaging, and no follow-up monitoring thereafter.

Two monitoring sensitivity analyses are included: one in which the 5 years of continued monitoring is conducted by ultrasound scan rather than CT, and one in which patients who underwent OSR require the same level of subsequent monitoring as those who received EVAR.

HE.2.2.10.3 Reintervention

Resource use was not directly elicited for reintervention procedures in EVAR-1 or IMPROVE. Instead, we assume the resources used are reflected by the NHS reference cost assigned to each procedure (see Section HE.2.2.11). Reintervention procedures are assumed to require 2 follow-up outpatient CT scans.

HE.2.2.11 Costs

HE.2.2.11.1 Primary procedure and perioperative care

The cost of each resource use item within the model was obtained from a number of standard sources. NHS Reference Costs are typically used as the source of unit costs for inpatient and outpatient procedures as well as hospital stay information. These are used to obtain the unit cost of components of the primary procedure, as described in Section HE.2.2.10, and reintervention procedures. The NHS reference costs that specifically cover aneurysm repair were not used directly, because it was unclear whether they included the cost of devices such as EVAR, and some unit costs appeared to be inconsistent (for example, "complex" repairs costing less than procedures that were not labelled as complex). However, note that costs for some components of the primary procedure (consumables; critical care for emergency repair) were obtained directly from the source trial and inflated to 2015–16 prices using the PSSRU health service inflation indices (Curtis, 2016).

The EVAR-1 study micro-costing approach will also have captured the resources associated with emergency repair of AAAs that ruptured while the patient is on the waiting list (that is, time between the decision to intervene and surgery). As such, we do not apply any additional unit cost to the proportion of aneurysms that rupture while on the waiting list for elective repair, as this resource use (as well as clinical outcomes) will have been captured implicitly in the intention-to-treat analysis.

The unit cost of AAA repair devices is included in the EVAR-1 and IMPROVE resource use and costing data. However, these values are likely to reflect costs in a select number of trial centres, and may not reflect the prices faced by the NHS on average. The extent to which the cost of a device is capture in NHS Reference Costs is unclear, such that extracting the device cost from the total spell cost is not possible. Instead, the following device costs are included in the model:

1. Costs obtained from the NHS Trusts of members of the guideline committee (for EVAR devices only).
2. Costs reported in the IMPROVE trial (Powell et al., 2015), being the more recent of the 2 main UK studies, inflated to 2015/16 prices.
3. Costs reported on NHS Supply Chain (as at 13/10/2017).

For the endovascular repair of complex aneurysms, custom-made EVAR devices are required and these can cost significantly more than off-the-shelf EVAR stent-grafts. It was only possible to obtain a unit cost for these devices from the guideline committee, as they are not listed in standard cost sources. The cost of an OSR stent-graft is assumed to remain the same regardless of whether the aneurysm is infrarenal or complex, given that it is manually adapted by the surgeon during the procedure. In our base case analysis, we use prices elicited from the guideline committee for EVAR devices, and costs from the IMPROVE study for open repair devices. Scenario analyses applying the IMPROVE costs for standard EVAR devices, and devices costs obtained from NHS Supply Chain, are also explored, though the committee-derived cost for complex EVAR is still used in these scenarios.

Table HE27: AAA repair device unit costs (bold denotes base case)

Source	*EVAR*	*OSR*
Guideline committee	**Infrarenal: £6,500** **Complex: £15,686**	NR
IMPROVE trial	Infrarenal: £5,993 [a] Complex: NR	**£655** [b]
NHS Supply Chain (13/10/2017)	Infrarenal: £6,186 (Cook) Complex: NR	£659 (mean from various listings: £473 to £833)

Note:
(a) Inflated from £5,700 using HCHS inflation indices 297.0/282.5 (Curtis, 2016).
(b) Inflated from £623 using HCHS inflation indices 297.0/282.5 (Curtis, 2016).

Table HE28: Primary procedure unit costs, excluding main devices

Resource item and unit	*Unit cost*	*Source*
Elective repair resource items		
Device consumables	EVAR: £512 OSR: £99	Brown et al., (2012); PSSRU (2016)
Theatre time, hour	£831	NHS Scotland (2016) [R142X Vascular Surgery]
Fluoroscopy	Up to 20 mins: £141 20-40 mins: £139 Over 40 mins: £279	NHS (2015-16) [IMAGDA RD30Z to RD32Z])
Blood products, 450ml (unit)	£124	NHS Blood & Transplant Price list (2017-18)
Vascular surgery ward, day	EVAR: £292 Complex EVAR: £410 OSR: £257	NHS (2015-16) [EL_XS YR03Z; YR04Z; YQ03A, YQ03B]
ITU stay, day	£1017	NHS (2015-16) [CC, Surgical adult, XC06Z]
HDU stay, day	£718	NHS (2015-16) [CC, Surgical adult, XC07Z]
Emergency repair resource items		
Consumables [a]	EVAR: £775 [a]	Same as elective repair estimates.

Resource item and unit	*Unit cost*	*Source*
	OSR: £489 [a]	
Emergency call and ambulance	£243	NHS (2015-16) [AMB ASC01 & ASS02]
Emergency room attendance and scan	£408	NHS Reference Costs (2015-16) [EM T01A VB01Z & T02A VB01Z]
Theatre time, hour	£831	NHS Scotland (2016) [R142X Vascular Surgery]
Vascular surgery ward, day	EVAR: £292 Complex EVAR: £410 OSR: £257	NHS (2015-16) [EL_XS YR03Z; YR04Z; YQ03A, YQ03B]
Critical care, per patient [b]	EVAR: £7,014 [b] OSR: £10,171 [b]	Powell et al., (2017) ; PSSRU (2016)
Transfer to second hospital [c]	£236 [c]	NHS (2015-16) [AMB ASS02]
Second hospital stay, day [d]	£336 [d]	NHS (2015-16) [EL_XS YR03Z, YR04Z, YQ03A, YQ03B]
Nursing home stay, per day	£152	PSSRU (2016) [1.3]
Family doctor, visit (15 mins)	£59	PSSRU (2016) [10.3]
Community nurse, visit (15 mins)	£11	PSSRU (2016) [10.1]

Notes:

(a) Device consumables could not be costed based on the resource use data reported by Powell et al., (2015; 2017), therefore the sum of blood products, fluoroscopy and other consumables for elective repair has been assumed.

(b) Study reports micro-costing based on the number of organs supported in critical care and by location (ITU or HDU), but does not report the resource use at this level of granularity, which would be lost by applying a single critical care unit cost to the total number of days. We therefore use the authors' own UK micro-costed estimates per patient, inflated from 2011–12 to 2015–16 prices using the PSSRU HCHS inflation indices (297.0 / 282.5).

(c) Assumed to be equal to 1 ambulance journey.

(d) Stay at second hospital assumed to be equal to cost of a stay on a vascular surgery ward.

Key: HDU, high-dependency unit; ITU, intensive therapy unit.

In the emergency repair setting, applying the device cost derived from the committee to all EVAR patients would cause the model to overestimate the cost of this strategy, because EVAR was only offered where the person was anatomically suitable. The impact of this on other resource use items was implicitly captured by the intention-to-treat analysis. To avoid overestimating the cost of the EVAR device, by applying it to too many patients, we apply it only to the proportion of IMPROVE participants who were randomised to EVAR and actually received EVAR: 64%. The remaining 36% of patients on the EVAR arm of the model instead incur the lower cost of an open repair device. Patients do not incur the cost of both devices, because the decision on device type is made before repair is commenced. In a sensitivity analysis, all unit costs are derived from the IMPROVE study data, meaning this adjustment is not required.

There was also a small degree of crossover from OSR to EVAR in the elective repair data (EVAR-1); 0.8% of participants randomised to EVAR had this procedure converted to open repair. In the model, this proportion of patients incurs an additional cost of the open surgery graft device, because the decision to convert is made while a planned EVAR procedure is in progress, such that the cost of the EVAR device is still incurred.

The resulting total perioperative costs are shown below.

Table HE29: Total primary procedure perioperative costs

Primary procedure	*Total cost*			
	Elective, infrarenal	**Elective, complex**	**Emergency, infrarenal**	**Emergency, complex**
EVAR	£13,561 [a]	£23,728 [a]	£17,258 [b]	N/A
OSR	£10,921	£10,921	£17,089	£17,089

Note:
(a) Includes 0.8% of patients who convert to OSR and incur additional device cost.
(b) Includes 36% of patients who receive OSR due to anatomical unsuitability for EVAR. The 64% of patients who actually receive EVAR incur the full EVAR procedure cost: £19,366.

HE2.2.2.11.2 Ongoing monitoring

The cost of an outpatient vascular surgery consultation is informed by NHS Reference Costs (2015–16). The vast majority of activity records suggest these consultations occur face-to-face (£140), with a small proportion being telephone consultations (£73), such that the average cost is £140. The cost of imaging was also informed by NHS Reference Costs, with an ultrasound scan costing £58 and a CT with contrast £104.

Table HE30: Outpatient monitoring unit costs

Resource	*Activity-weighted average cost*	*NHS reference cost source & derivation*
Consultation	£140	Face to face (WF01A): £140 Telephone (WF01C): £73
CT scan	£104	1 area, post contrast (RD21A): £102 1 area, pre & post contrast (RD22Z): £119
US scan	£58	Vascular ultrasound (RD47Z)

Key: CT, computed tomography; US, ultrasound.

HE2.2.2.11.3 Reintervention

The cost of reintervention procedures were also obtained from NHS Reference Costs (2015–16), as detailed in Table HE31. The exception is life-threatening graft-related procedures, which are assumed to incur the total cost of emergency OSR, reflecting a high cost associated with an urgent full graft reintervention.

Table HE31: Reintervention procedure unit costs

Reintervention	*Activity-weighted average cost*	*NHS reference cost source & derivation*
Graft-related		
Life-threatening	£17,089	Equal to emergency OSR cost.
Serious (non-hernia)	£4,628	Inpatient procedures: percutaneous transluminal angioplasty of single blood vessel (YR11A–D; range: £1,492 to £12,763)
Hernia	£4,030	Inpatient procedures: abdominal hernia procedures (FZ17E–G; range: £1,891 to £6,941)
Laparotomy-related		
Bowel resection	£6,294	Inpatient procedures: major small intestine procedures (FZ67C–FZ77E; range: £1,121 to £15,224)
Lysis of adhesions	£3,955	Inpatient procedures: non-malignant gastrointestinal tract disorders, single intervention (FZ91E–H; range: £1,586 to £8,305)
Hospitalisation	£1,304	Inpatient procedures: non-malignant gastrointestinal tract disorders, no intervention (FZ91J–M; range: £328 to £18,387)
Perioperative pulmonary complication (scenario analysis only)		
Pulmonary complication	£2,129	Inpatient procedures: pulmonary oedema (DZ20D–F); unspecified acute lower respiratory tract infection (DZ22K–Q); bronchopneumonia (DZ23H–N). Range: £508 to £7,743).

As described in Section HE.2.2.9, we apply the total number of graft-related reintervention procedures at the time of the first reintervention, therefore the relevant unit cost (above) is subject to a multiplier to reflect that people who experience a graft reintervention will, on average, experience more than 1 during their lifetime.

HE.2.2.12 Quality of life

Patient health-related quality of life (HRQL) is captured in the model in 3 components:

1. General population HRQL, prevailing when a modelled patient is not recovering from AAA repair or experiencing a reintervention
2. Reduced HRQL while recovering from AAA repair
3. Reduced HRQL while living with a complication and recovering from the subsequent reintervention

Time spent in a particular health state, or with a particular condition, is multiplied by the HRQL experienced in that state or with that that condition (utility value), to produce a health outcome measure that jointly captures quality and length of life: QALYs.

HE.2.2.12.1 General population HRQL

The guideline development committee advised that a person with an AAA leads a broadly normal life, other than the requirement for monitoring the size of the aneurysm and the risk of rupture. Based on this, we follow the approach used in previous UK cost–utility analyses of assuming that a patient will experience the average HRQL (utility value) of the general population for his or her age (Chambers et al., 2009; Brown et al 2012). This also applies to people whose AAA has been successfully repaired, as long as the person is out of the immediate post-surgery recovery period and is not experiencing a complication. The general

UK age-related utility weights used, obtained from a UK study that administered the EQ-5D-3L questionnaire to 3,392 individuals, are shown in Table HE32.

Table HE32: General UK population utility weights used in the model

Age (years) [a]	*Utility weight – Men (n; 95%CI* [b]*)*	*Utility weight – Women (n; 95%CI* [b]*)*	*Source*
55 to 64	0.78 (196; 0.74 to 0.82)	0.81 (288; 0.78 to 0.84)	Kind et al., (1999)
65 to 74	0.78 (228; 0.74 to 0.82)	0.78 (260; 0.75 to 0.81)	
75 and older	0.75 (108; 0.70 to 0.80)	0.71 (206; 0.67 to 0.75)	

Note:
(a) UK population norm EQ-5D data are also available for younger age groups than those shown here, however AAA is not typically observed in younger individuals, therefore only utility weights in the age range likely to be relevant to decision-making are shown.
(b) 95% confidence interval estimated using published standard deviation and assuming utility values follow a beta distribution.

HE.2.2.12.2 HRQL during recovery

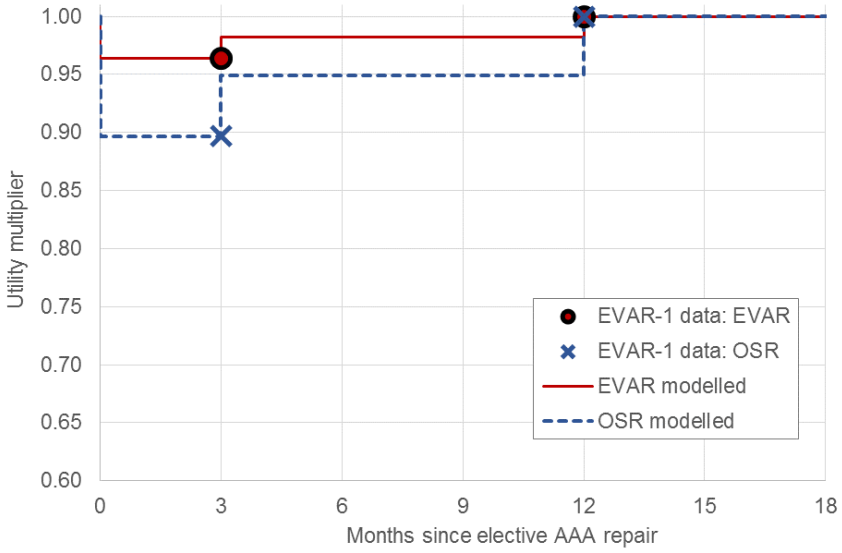
Consistent with previous UK cost–utility analyses, we apply a loss in HRQL for a period following intervention to repair an AAA.

Elective repair

The EQ-5D-3L questionnaire was administered to participants in the EVAR-1 trial, which showed that participants who received EVAR had better quality of life than participants who received OSR after 3 months. The difference was not statistically significant after 1 year.

We capture this HRQL benefit for EVAR in the model by applying it as a multiplier, to reduce the person's prevailing utility from the general population value to reflect that they are recovering from either EVAR or OSR. For EVAR, the utility multiplier is 0.964, as the utility loss at 3 months reported in the EVAR-1 trial (0.027; Epstein et al., 2008) is 3.6% of the baseline utility value (0.75). This means that a patient's HRQL, derived from general population values, will be multiplied by 0.964 following intervention with EVAR. The additional utility loss at 3 months in participants who received OSR was 0.05 (Greenhalgh et al., 2005). The utility multiplier for OSR patients is therefore 0.897, as the total utility loss at 3 months (0.027+0.05) is 10.3% of the baseline utility value (0.75). Given that the AAA repair procedure is completed in 1 day, we assume that the recovery period begins immediately and the patient experiences the relevant utility multiplier for 3 months.

The benefit in HRQL for EVAR has been shown to be eradicated by month 12 after the primary procedure (Greenhalgh et al., 2005). As there are only 2 longitudinal data points, we assume that quality of life recovers in a linear fashion between month 3 and month 12. This implies that the average utility multiplier during the 9-month period will be halfway between the multiplier at 3 months and a value of 1, assuming that HRQL fully recovers after 1 year. For EVAR, the average utility multiplier during this period is 0.982; for OSR, it is 0.949.



Note: A utility multiplier of 0.90 means the quality of life value (utility weight) is reduced by 10%. The recovery period is assumed to begin immediately, such that the 3-month utility loss is applied in full for 3 months. After this point, the average utility weight between 2 observations is applied for the duration between those data points. A utility multiplier of 1 means the person's quality of life is not reduced at all. The faster a person's utility multiplier returns to a value of 1, the shorter is their recovery from the intervention.

Figure HE24: Utility multipliers for recovery period following elective AAA repair

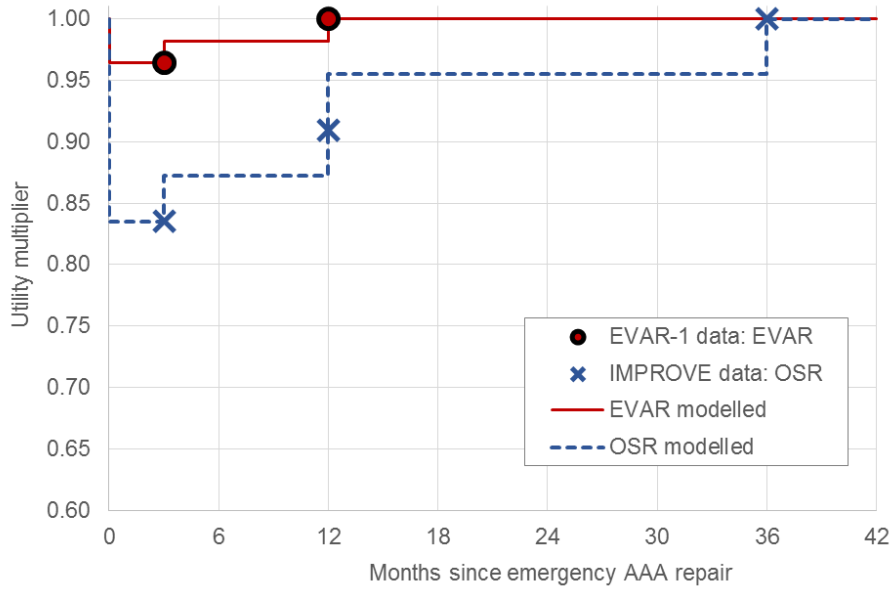
Emergency repair

The EQ-5D-3L questionnaire was also administered to participants in the IMPROVE trial. Results showed that participants who received EVAR had better quality of life than participants who received OSR after 3 months and 12 months (Powell et al., 2017). The difference was not statistically significant after 3 years.

Similar to elective repairs, we capture this HRQL benefit for EVAR in the model by applying it as a series of multipliers. However, given the nature of emergency AAA repair, it was not possible for the IMPROVE investigators to collect EQ-5D data at baseline. We therefore assume that the baseline utility value from the EVAR-1 study (0.75) applies to patients prior to their AAA rupturing, which appears to have been the approach taken in within-trial IMPROVE cost–utility analyses (Powell et al., 2014, 2017). We therefore assume that the HRQL loss at 3 months after repair with EVAR is the same as for patients who receive elective EVAR: 0.027, or a utility multiplier of 0.964. Again, we assume that the recovery period begins immediately and the patient experiences this utility reduction for 3 months. Between 3 months and 1 year, HRQL is shown to improve by 0.02. We assume that this indicates a return to pre-intervention baseline after 1 year, therefore the midpoint between utility multipliers of 0.964 and 1 (i.e. no utility loss) is applied from month 3 to month 12 (0.982).

For participants randomised to OSR, the additional utility loss at 3 months was 0.097 (Powell et al., 2017). The OSR utility multiplier at 3 months is therefore 0.835, based on the total utility loss at 3 months of 0.124 (0.027+0.097). The trial found that participants randomised to OSR still had lower mean EQ-5D utility than those randomised to EVAR at 12 months, with a difference of 0.068. As before, we assume that the average utility multiplier between month 3 and month 12 is experienced during this 9-month period. This is the midpoint of the 3-month value, 0.835, and the 12-month value, which is 0.909 (as EVAR patients are back the baseline value of 0.75, and 0.068 is 9.1% of this value). The utility multiplier applied for this duration is therefore 0.872. The next IMPROVE data point was collected at 3 years, and by this time the HRQL benefit associated with EVAR had been eradicated. We assume that the

quality of life experienced by people who received OSR improves back to its baseline level in a linear fashion, by applying the midpoint of the utility multiplier at 1 year (0.909) and 3 years (1) for this 2-year period. The utility multiplier applied for this duration is therefore 0.955.



Note: EVAR-1 data are used to model the emergency EVAR arm, because no baseline EQ-5D data could be collected as part of the IMPROVE study, and the utility loss associated with EVAR is not explicitly reported. A utility multiplier of 0.90 means the quality of life value (utility weight) is reduced by 10%. The recovery period is assumed to begin immediately, such that the 3-month utility loss is applied in full for 3 months. After this point, the average utility weight between 2 observations is applied for the duration between those data points. A utility multiplier of 1 means the person's quality of life is not reduced at all. The faster a person's utility multiplier returns to a value of 1, the shorter is their recovery from the intervention.

Figure HE25: Utility multipliers for recovery period following emergency AAA repair

HE.2.2.12.3 HRQL during graft-related reintervention

When a reintervention is required, a reduction in HRQL is applied to reflect the complication itself and the reintervention recovery period. For a life-threatening graft-related reintervention, we assume that the impact on HRQL can be estimated by the HRQL impact of elective OSR to repair an AAA, which is consistent with the approaches taken by Chambers et al., (2009) and Brown et al., (2012). It would be computationally burdensome to track patients who experience a reintervention over time to ensure the appropriate time-varying utility multiplier is used in each cycle, requiring a series of 'tunnel states' for little anticipated impact on cost–utility results. Instead, when a patient requires a life-threatening graft-related reintervention, we apply the average OSR utility multiplier for a duration of 1 year. This value is 0.936 (from 3 months at 0.897 and 9 months at 0.949). In each model cycle the baseline utility of the cohort is known, based on UK general population data which, with the utility multiplier, allows the model to compute a one-off QALY loss associated with each life-threatening reintervention.

Similarly, a one-off QALY loss is calculated for other serious graft-related reintervention procedures (e.g. endoleak), by assuming their impact on HRQL can be approximated by the recovery period associated with elective EVAR, reflecting a less invasive procedure. The average utility multiplier applied for 1 year for these events is therefore 0.978 (from 3 months at 0.964 and 9 months at 0.982). A limitation of this approach is that estimating a one-off QALY will very slightly overestimate the overall impact on quality of life of each reintervention, for 2 reasons. Firstly, some of the utility loss would be reduced by discounting

if the recovery spanned 2 different model years. Secondly, a small proportion of patients will die of other causes during the recovery period, and will therefore not experience the full year of reduced HRQL.

The only graft-related reintervention that is modelled differently, in terms of its impact on HRQL, is a hernia. Quality of life data are more readily available from people with hernias, compared with the broader collection of other graft-related complications. An economic evaluation for NICE Technology Appraisal 83 (Laparoscopic surgery for inguinal hernia repair; 2004) reported EQ-5D utility weights for a baseline 'healthy' population (0.952), very shortly after surgery (0.74), and at 1 month and 3 months after surgery (0.82 and 0.85) (McCormack et al., 2003). We converted the latter 3 values to utility multipliers relative to the baseline 'healthy' value: 0.777, 0.861 and 0.893, respectively. As before, we use linear interpolation between the 3 time points to obtain 2 average utility values: 0.819 for the first month after surgery, and 0.877 for the next 2 months. We use McCormack's utility value for persistent hernia pain to reflect the HRQL of living with a hernia that requires intervention: 0.836 (utility multiplier: 0.878). This value suggests that living with a hernia is detrimental to HRQL, rather than just the intervention and recovery. Based on the TA83 analysis, we assume a person typically has to wait for 6 months for their hernia surgery, experiencing the pre-intervention utility reduction during this period (McCormack et al., 2003). In the absence of a final observation at which the EQ-5D returned to the healthy population level, we assume that after 3 months HRQL returns to its pre-hernia baseline level. With these data and assumptions, the model calculates a one-off QALY loss associated with each hernia reintervention.

As an example, if a person lives for 9 months (0.75 years) with a utility weight of 0.75, they will experience a total of 0.563 QALYs. If the person instead developed a hernia that was repaired 6 months later, over the same 9 month period they would accrue the number of QALYs shown in Table HE33.

Table HE33: Example QALY loss incurred by hernia and hernia surgery

Description	*Duration*	*Utility weight*	*QALYs*
Living with hernia	6 months (0.5 years)	0.75 * 0.878 = 0.659	0.329
Immediate recovery from surgery	1 month (0.08 years)	0.75 * 0.819 [a] = 0.615	0.051
Ongoing recovery from surgery	2 months (0.17 years)	0.75 * 0.877 [b] = 0.658	0.110
Total (0.75 years)			0.490

Notes:
(a) Where 0.819 is the average of utility multipliers immediately after surgery (0.777) and at 1 month (0.861)
(b) Where 0.877 is the average of utility multipliers at 1 month (0.861) and 3 months (0.893).

The total undiscounted QALY loss associated with the hernia in this example is 0.072 (0.563 hernia-free QALYs minus 0.490).

HE.2.2.12.4 HRQL during other reintervention

The other laparotomy-related reintervention procedures included in the model (bowel resection and lysis of adhesions) also incur losses to the patient's quality of life, in the same way that the impact of a hernia was calculated, described above. For these procedures, we identified an EQ-5D-derived utility before laparoscopic surgery of 0.795, in a UK study of 80 patients undergoing laparoscopic colorectal surgery (Dowson et al., 2013). The EQ-5D utility immediately after surgery was 0.331, rising to 0.891 after 42 days. We assume that 0.891 reflects the person's true HRQL, such that the pre-surgery baseline of 0.795 indicates the disorder that required laparoscopic reintervention was detrimental to quality of life. This can be quantified by the utility multiplier: 0.795 / 0.891 = **0.892**. We apply this for the 6 months

before surgery, the typical waiting time for laparoscopic intervention, obtained from NICE TA83. Similarly, the utility multiplier immediately after surgery is 0.331 / 0.891 = **0.371**. We assume that utility recovers linearly from this level over 42 days.

In the scenario in which we model a higher incidence of pulmonary complications during elective OSR relative to EVAR, an additional utility multiplier of 0.95 during the perioperative model cycle is applied. This approximates the approach taken in NICE NG78 (Cystic fibrosis: diagnosis and management; 2017), where a 0.05 utility decrement was applied for pulmonary infections.

HE.2.2.13 Key assumptions

Key assumptions built into the 'EVAR vs. OSR' model are summarised in Table HE34. Model parameters are presented in full in Section HE.6.

Table HE34: Key assumptions of the 'EVAR vs. OSR' ('fit for OSR' population) cost–utility model

- *For the elective repair of unruptured AAAs, the decision is to attempt aneurysm repair with either EVAR or OSR, in people for whom OSR is deemed to be a potentially appropriate intervention.*
- *For the emergency repair of ruptured AAAs, the comparison presented is between a system in which the aneurysm is repaired by EVAR if the aorta is anatomically suitable for it, otherwise OSR, and a system in which EVAR is never used.*
- *Overall survival can be modelled as 3 distinct parts: waiting time survival (for elective cases), perioperative (30-day) survival, and post-perioperative (long-term) survival.*
- *There is no difference in the mortality rate of people waiting for an elective EVAR or elective OSR procedure while on the waiting list. All elective patients wait for 2 months for their intervention, with the exception of people waiting for EVAR to repair a complex AAA, because the EVAR devices for this population are custom-made to order. This group waits for a further 2 months.*
- *Patients with a ruptured AAA receive emergency care and therefore have no waiting time.*
- *EVAR is not typically used for people with a ruptured complex AAA. EVAR devices for complex aneurysms are custom-made to order, which makes them impractical for emergency repair.*
- *The UK National Vascular Registry provides a representative source of baseline perioperative (30-day) mortality data: EVAR data for the elective repair of unruptured aneurysms (infrarenal and complex), and OSR data for the emergency repair of ruptured aneurysms (infrarenal).*
- *Age, sex and aneurysm size are important effect modifiers for perioperative EVAR mortality. For elective repairs, the influence of each is informed by a European registry (Vascunet; Mani et al., 2015), and is applied to both infrarenal and complex AAA repair. For emergency repairs, they are characterised by a logistic regression analysis conducted using the IMPROVE study data.*
- *It is acceptable to calibrate UK general population survival data to match post-perioperative survival in the EVAR-1 and IMPROVE trials, as closely as possible.*
  - *For emergency repairs, we used survival data from 60 days post-intervention, to which general population survival was calibrated. This provided a much better fit than using data from 30 days. We therefore assume that the resulting, long-term survival curves can be applied after the 1-month perioperative model cycle.*
  - *It is appropriate to scale the resulting survival estimates up using present day life tables. Our calibration method identified the hazard ratio(s) that characterise the difference between post-perioperative survival in the RCT and the general population at that time. To reflect a general improvement in survival since then, we scale survival up using 2013-15 UK life tables.*
  - *The long-term survival estimates, based largely on data from infrarenal aneurysms, can be transferred to complex aneurysms, such that if a person survives the perioperative (30-day) period their long-term survival is independent of aneurysm complexity.*
- *It is appropriate to meta-analyse long-term survival data comparing elective EVAR and elective OSR to determine their relative effectiveness in terms of post-perioperative mortality. We used published summary data from the DREAM and OVER trials for this purpose, to supplement EVAR-1 study data.*

- *It was necessary to omit the first year of the DREAM and OVER summary data. In doing so, we assume that relative survival beyond 1-year in these studies approximates post-perioperative (i.e. post-30-day) relative survival.*

- *The relative effectiveness of EVAR compared with OSR in both perioperative and post-perioperative survival, derived largely from infrarenal AAA trials, is transferable to other types of AAA ('complex' cases).*
- *Age, sex and aneurysm size are important effect modifiers for post-perioperative (long-term) survival. The influence of each is informed by Cox regression models using EVAR-1 study data (for elective repairs) and IMPROVE study data (for emergency repairs). These are applied to infrarenal and complex AAAs.*
- *The difference between emergency EVAR and emergency OSR in long-term mortality rates (beyond 6.5 years) is equal to the long-term hazard ratio for those interventions in elective cases. This assumption has been made to utilise more mature elective repair data in the emergency repair model, which would otherwise rely heavily on uncertain extrapolation.*
- *New-generation EVAR devices and surgical techniques have not affected the relative safety and effectiveness of EVAR and OSR. Existing trials, with historic enrolment periods (e.g. 1999 to 2003 for the EVAR-1 study) are applicable for the present comparison.*
- *There is no difference in the procedure cost between complex and infrarenal AAA repairs, such that the resource use data used in the model, largely informed by infrarenal aneurysms, can be transferred to complex cases.*
  - *The cost of a complex EVAR device is significantly more than a standard EVAR device.*
- *There is no difference in the rate of reintervention procedures between complex and infrarenal AAA repairs, such that the complication data used in the model, largely informed by infrarenal aneurysms, can be transferred to complex cases.*
- *Reintervention procedures are categorised as either 'graft-related' or 'laparotomy-related', and then either 'life-threatening' or 'serious (not life-threatening)'. People who experience 1 graft-related reintervention will, on average, experience more than 1 during their lifetime. The cost and health implications of the extra reintervention procedures are incurred at once, at the time of the first reintervention. Laparotomy-related complications are assumed to occur only once.*
- *After EVAR, patients are followed up by an outpatient consultation and CT scan within 2 months of the intervention, followed by annual outpatient consultations and ultrasound scans for 5 years. After OSR, patients are followed up at 1 outpatient attendance only.*
- *The impact of aneurysm repair and reintervention procedures on the patient's quality of life can be characterised by one-off 'QALY loss' decrements.*

HE.2.3 EVAR vs. No Intervention – people for whom OSR is not a suitable intervention

HE.2.3.1 Model structure

Like the 'EVAR vs. OSR' analysis, the 'EVAR vs. no intervention' model – looking at a population for whom open surgery is not a suitable option, because of medical or anaesthetic contraindications – adopts a state-transition structure. The structure is very similar to that in Figure HE01; however here, not all elective patients receive an intervention. Since open surgery is not an option in this population, the relevant comparison is EVAR compared with no EVAR (i.e. no attempt to repair the aneurysm). Patients therefore enter the model once the decision has been made that EVAR would be an appropriate intervention for them but OSR would not. Simulated elective patients who receive EVAR spend time on the waiting list like before, whereas those who receive no intervention spend their remaining time in the 'post-operative' health state (the terminology implying that 'no intervention' is itself the chosen intervention). These patients face a risk of their unrepaired AAA rupturing, requiring an emergency EVAR procedure, though a proportion of these ruptures will be fatal before the emergency procedure could be started.

Table HE35: Modelled health states – Intervention model 2: EVAR vs. No Intervention

Health States	
Waiting list	An elective EVAR patient joins the waiting list ahead of their repair procedure, and is subject to a risk of death during this time. Emergency patients do not use this health state.
Elective repair	An elective EVAR patient spends 1 cycle in the repair health state, undergoing either EVAR or OSR, experiencing the relevant hospital stay, and is subject to the associated risk of perioperative mortality.
Emergency repair	An emergency EVAR patient spends 1 cycle in the repair health state, undergoing EVAR, experiencing the associated hospital stay, and is subject to the associated risk of perioperative mortality. Patients on the 'no intervention' arm are assumed to experience 100% mortality due to a ruptured AAA.
Post-operative survival	An EVAR patient who survived the perioperative model cycle resides in this state for the rest of the model duration, subject to risks of reintervention and death. Non-emergency patients who receive no intervention start the model in this health state. Patients on this arm are assumed to experience 100% mortality in the emergency setting.
Reintervention	A patient in the post-operative survival state is subject to an ongoing risk of complications that require reintervention. For EVAR patients, the possible reinterventions are based on the EVAR-2 trial. For 'no intervention' patients, the possible reintervention is a rupture of their untreated AAA.
Death	Patients can transition to the death health state from the waiting list state, the procedure states or the post-operative state, and remain there for the duration of the model.

Figure HE26 provides a schematic depiction of the model structure for this population. Unlike the population for whom OSR is a possible option, here there is a 'no intervention' decision faced by the surgeon. In elective cases, this leads the patient straight to the long-term, "post-operative" survival state. In emergency cases, this leads to death due to the ruptured, unrepaired aneurysm. In either setting, if the decision is made to repair, the only available technique is EVAR. Apart from this, the clinical pathway for repair is the same as the 'fit for OSR' model.

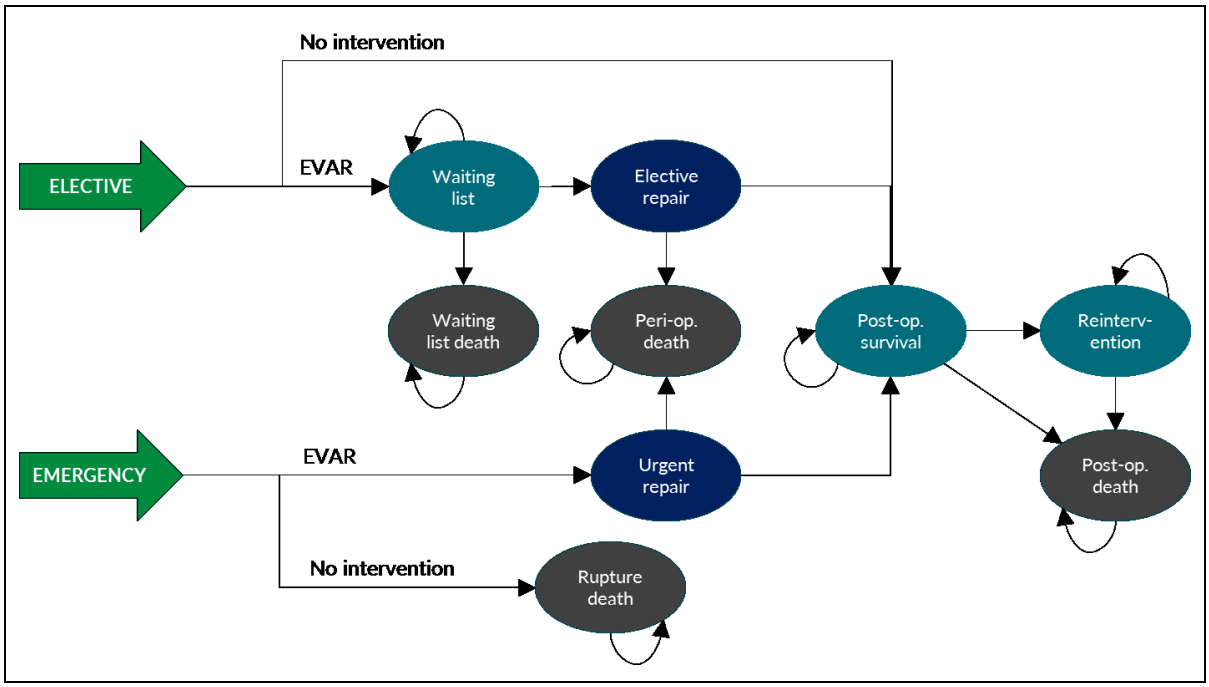


Figure HE26: Structure of original cost–utility model – EVAR vs. No Intervention

HE.2.3.2 Cohort parameters

Relevant baseline cohort parameters included in the model are age, sex and aneurysm diameter. The EVAR-2 trial is the only source of randomised comparative evidence with which to evaluate the options available to people for whom OSR is not suitable. It compared elective EVAR with no intervention, in people with unruptured, infrarenal AAAs, and is therefore used to inform baseline cohort inputs for elective cases. In the absence of alternative data in this population in people with ruptured aneurysms, we use the IMPROVE trial data to inform baseline age and sex when we compared emergency EVAR with no intervention.

The mean age of the elective repair population is 76 years, the mean aneurysm size is 6.7 cm, and 86% of the cohort is male (based on EVAR-2 trial data). The mean age of the emergency repair population is 76 years, the mean aneurysm size is 8.4 cm, and 78% of this cohort is male (based on IMPROVE trial data).

HE.2.3.3 Treatment effects

The EVAR-2 trial was the only source of randomised comparative evidence with which to evaluate the available options in people for whom OSR is not a suitable option. Typically, a person is part of this population if clinicians determine that their risk of death during an open surgical procedure is too high. In this situation, the available options for management are EVAR or choosing to leave the AAA unrepaired.

In our primary analysis, we use the relative effects reported by the EVAR-2 trial comparing EVAR with no intervention, for elective (unruptured) AAAs. The EVAR-2 trial is directly applicable to the UK context, with over 14 years of follow up data. We were provided with anonymised survival data from the EVAR-2 trial, with which it was possible to disentangle waiting times from the overall survival records. Additionally, the risk of death is significantly higher during AAA repair, and in the immediate 30 days thereafter, than subsequently. Like with the 'fit for OSR' model, we sought to model these distinct phases of EVAR survival separately by subtracting 30 days from overall survival records; we therefore had 3 separate components of overall EVAR survival (preoperative, perioperative and post-perioperative):

- Survival during the lead-in time (time spent on the waiting list prior to elective EVAR)

- Perioperative survival during the EVAR procedure and up to 30 days after
- Survival conditional on surviving the waiting and perioperative periods (post-perioperative survival).

A limitation of the EVAR-2 trial is its extensive crossover, with participants who were randomised to the no intervention arm instead receiving EVAR. This occurred in 71 out of 207 participants randomised to no intervention (34.2%), which limits the validity of survival data for the no intervention arm, as crossover is typically non-random. People who switched to EVAR are likely to have been those who were deemed likely to benefit from doing so, meaning the remaining population on the no intervention arm is systematically different to the population originally randomised to EVAR. Indeed, participants who switched have been identified to have been fitter, at baseline, than participants randomised to EVAR (Sweeting et al., 2017). The trial investigators conducted an analysis to adjust for this crossover effect (Sweeting et al., 2017), however, the reported HR is from the point of randomisation. Using this HR would not allow us to dissect overall survival on the EVAR arm into its 3 distinct components. Instead, we conducted the crossover analysis ourselves, obtaining a crossover-adjusted (or 'counterfactual') set of survival times for participants randomised to 'no intervention'. We could then use the crossover-adjusted survival dataset to model survival on the 'no intervention' arm separately from the EVAR arm, which instead could be analysed in terms of waiting, perioperative and post-perioperative survival.

HE.2.3.3.1 Adjusting for EVAR-2 crossover

To adjust for the impact on survival data of EVAR-2 participants who were randomised to no intervention going on to receive EVAR, we used a Rank-Preserving Structure Failure-Time (RPSFT) model (Robins & Tsiatis, 1991). This was performed using the *strbee* function in Stata 13.0. This approach splits the survival time of a person who 'switched' treatment into 2 components: the pre-switch, 'untreated' survival time, and the post-switch, 'treated' survival time. For the EVAR-2 study, the switching time was the time at which a person randomised to intervention received EVAR; until that time they had received no intervention, and had therefore stuck to their randomised study arm. The RPSFT approach does not affect this 'untreated' survival time. Instead, it identifies a parameter (Ψ) with which the post-switch, 'treated' survival time can be adjusted, in order to estimate the counterfactual survival that *would have* been observed if the participant had not switched (i.e. had remained on their randomised no intervention arm). This adjustment is performed in the form of an 'accelerated failure time' model, as follows:

$$Adjusted_T = Untreated_T + Treated_T \times e^{\Psi} \quad \textbf{(eqHE11)}$$

The survival times for participants randomised to EVAR, and participants randomised to no intervention who did not break randomisation by receiving EVAR, remain unchanged. With these data, and the counterfactual survival times for participants who switched, we are able to conduct survival analysis of the 2 randomised groups, with the RPSFT parameter Ψ decontaminating the no intervention arm of its switching selection bias (Figure HE27). The EVAR-2 study data that were made available to us did not contain the date of randomisation, therefore we were unable to incorporate re-censoring into the *strbee* function.

Before adjusting the no intervention arm for crossover, the hazard ratio (HR) for survival between no intervention and EVAR was 1.03 (95%CI: 0.84–1.26), in favour of no intervention. Following adjustment for crossover using the RPSFT model, the HR was 1.06 (95%CI: 0.87–1.30). This implies that participants who were randomised to the no intervention, but switched to EVAR, experienced lower expected survival than if they had remained on the no intervention arm. This is consistent with the EVAR-2 investigators' crossover adjustment, which reported a HR of 1.08 (95%CI: 0.80–1.47) in favour of 'no intervention', compared with an unadjusted, intention-to-treat HR of 1.06 (95%CI: 0.68–1.30).

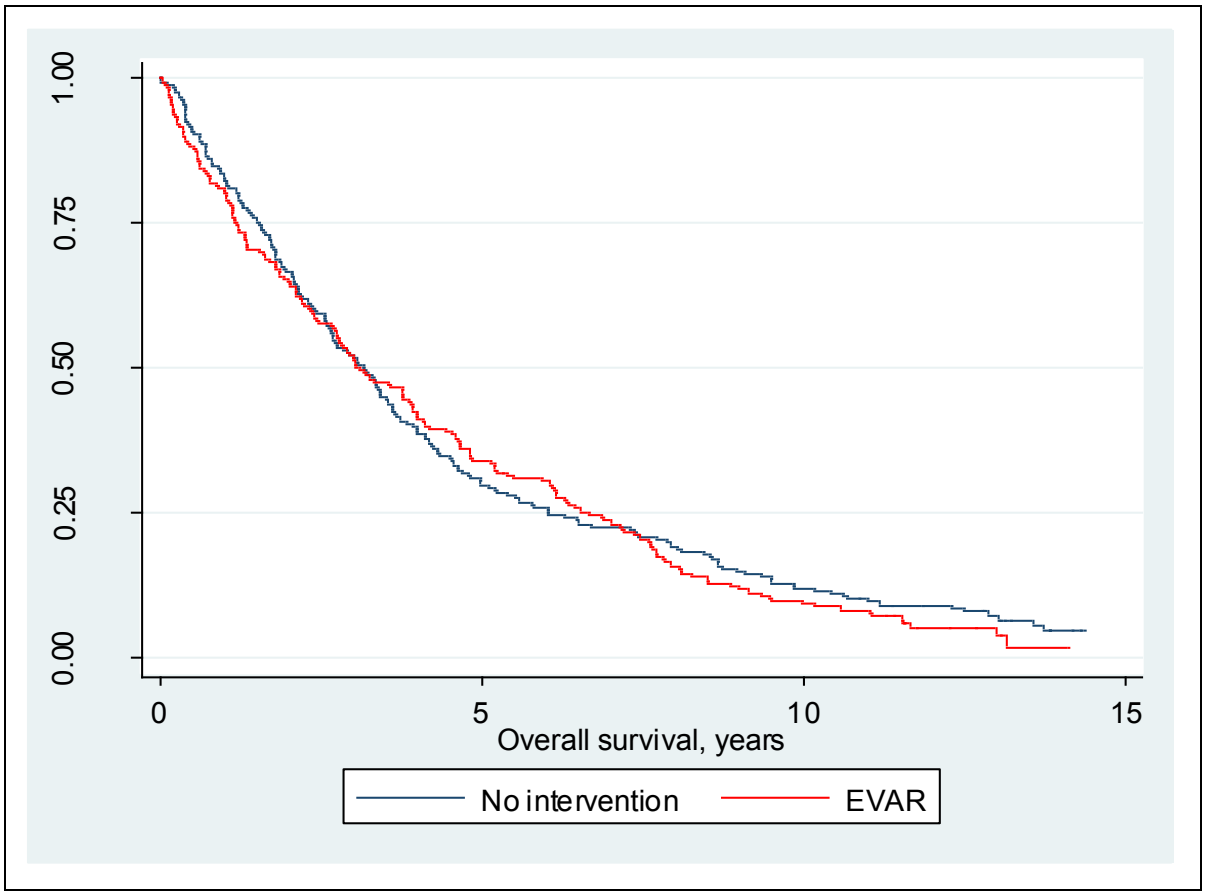


Figure HE27: Comparison of EVAR-2 Kaplan-Meier survival plots following RPSFT adjustment to correct for crossover from no intervention to EVAR

Using the EVAR-2 trial data, we extracted waiting times and 30-day perioperative periods from the survival data of participants on the EVAR arm. For the no intervention arm, there is no distinction between these 3 components of survival, as there is no operation (therefore no waiting time and no perioperative period). We therefore use the full, crossover-adjusted survival dataset to model survival on the no intervention arm. Below, we describe EVAR waiting time and perioperative mortality inputs, followed by long-term survival, which includes overall survival on the 'no intervention' arm.

HE.2.3.4 EVAR waiting time mortality

The rationale for incorporating waiting time mortality has been described for the EVAR vs. OSR model (Section HE.2.2.3). In EVAR-2, the mean time spent waiting for elective EVAR, including death if the participant died without intervention, was 93 days, during which time 9.1% of participants died. The resulting waiting time mortality per month (cycle) is 3.0% per month. However, this mortality rate was found to be significantly higher than mortality among participants on the 'no intervention' arm over the same period. Applying a higher pre-intervention mortality rate to the EVAR arm would bias the analysis against EVAR. As such, our model assumes that patients waiting for elective EVAR are subject to the same monthly mortality probability as patients on the 'no intervention' arm (which is described in detail below). Like before, elective EVAR patients with infrarenal aneurysms are on the waiting list for 2 months, while simulated patients with complex aneurysms are required to wait for an additional 2 months for their custom-made EVAR device.

The model assumes that there is no waiting time for emergency repair cases.

HE.2.3.5 EVAR perioperative mortality

HE.2.3.5.1 Elective repair

Perioperative mortality is only captured in the model on the EVAR arm. In the base-case model, we use the EVAR-2 data to inform perioperative outcomes for elective repair. This differs from the approach taken in the EVAR vs. OSR model, which used registry data to inform baseline perioperative survival rates. The UK National Vascular Registry does not explicitly record EVAR outcomes in people for whom OSR was not considered appropriate, and it was deemed inappropriate to use the overall registry data for baseline perioperative mortality (i.e. 0.4% of EVAR procedures). Instead, the EVAR-2 30-day mortality rate of 7.3% is used.

There are no randomised, comparative data evaluating treatment strategies for people with complex aneurysms in this population. To model EVAR perioperative mortality in this group, we used the UK National Vascular Registry data on perioperative EVAR mortality, to estimate a log-odds ratio associated with aneurysm complexity (relative to infrarenal cases). The reported 30-day mortality rates were 0.4% for infrarenal aneurysms and 3.6% for complex aneurysms, resulting in a complexity log-odds ratio of 2.18 (odds ratio: 8.83). We apply this to the EVAR-2 perioperative mortality rate (on the log-scale), resulting in an estimate of the 30-day elective, complex EVAR mortality in people for whom OSR is unsuitable: 40.9%. This reflects a higher expected operative failure rate from EVAR in people requiring complex repair. The guideline development committee advised that this figure is somewhat higher than their experience of clinical practice, but recognised the limited data in this population. Accordingly, we subject the figure to extreme value sensitivity analysis.

HE.2.3.5.2 Emergency repair

For emergency EVAR, we use the IMPROVE 30-day mortality rate (35.4%) as the baseline rate, which is then increased to reflect that the population of interest is less 'fit' than IMPROVE study participants (for whom OSR was a suitable option) on average. To obtain this relative 'fitness factor', we took the 30-day EVAR mortality rates from the EVAR-1 (1.6%) and EVAR-2 (7.3%) studies, and estimated the log-odds ratio between them (1.55; odds ratio: 4.70). This was applied to the IMPROVE perioperative mortality rate (on the log-scale), resulting in an estimate of the 30-day emergency EVAR mortality rate in people for whom OSR is unsuitable: 72.1%. The mortality rate among ruptures on the no intervention arm was set to 100%, meaning all untreated emergency cases end in fatality during the first cycle of the model.

Emergency EVAR for complex aneurysms does not typically occur in practice, due to the need to custom-build EVAR devices for such patients. No comparison between EVAR and no intervention in this population has been conducted.

Table HE36: Perioperative mortality – people for whom OSR is unsuitable

Population	*Data used*	*Calculation required*	*Perioperative mortality*
Elective repair			
Infrarenal EVAR	EVAR-2	None	7.3%
Complex EVAR	EVAR-2 (baseline) NVR (complexity effect)	EVAR-2 baseline: 7.3% NVR (0.4% vs. 3.6%): complexity OR = 4.70	42.1%
Emergency repair			
Infrarenal EVAR	IMPROVE (baseline) EVAR trials (fitness effect)	IMPROVE baseline: 35.4% EVAR trials (1.6% vs. 7.3%): fitness OR = 8.83	72.1%

Population	Data used	Calculation required	Perioperative mortality
Complex EVAR	N/A	N/A	N/A
Key: OR, odds ratio; NVR, National Vascular Registry (2016)			

Effective modifiers – elective EVAR

To make the model capable of producing detailed subgroup analyses, we explored ways of applying effect modifiers that influence a person's risk of perioperative mortality. The baseline and treatment effect values in Table HE36 are applicable to individuals whose characteristics match the 'average' EVAR-2 participant. These are used in our base-case deterministic analysis, but may provide unrepresentative results if a cohort with different characteristics is modelled.

Like before, the 3 key effect modifiers we explore are: age, sex, and aneurysm diameter. There were insufficient perioperative deaths on the EVAR arm of the EVAR-2 study to inform a logistic regression model. In the absence of alternative evidence, we made use of the same European registry (Vascunet) data that we used for the 'fit for OSR' model (Table HE14; Mani et al., 2015). Doing so makes the assumption that, although they apply to a very different baseline likelihood of death, the **relative** effects of age, sex and aneurysm size on EVAR perioperative mortality are common in people who are fit for OSR and people who are not fit for OSR. These effect modifiers are applied in probabilistic and subgroup analyses, for both infrarenal and complex AAA elective EVAR patients.

HE.2.3.6 Post-perioperative survival (long term)

HE.2.3.6.1 Elective repair

For the 'no intervention' arm, elective patients move immediately to the "post-perioperative" survival health state, reflecting their long-term, overall survival profile. We use the crossover-adjusted EVAR-2 survival data as the basis for this in the model. For EVAR patients, having accounted for waiting and perioperative mortality above, we explicitly model post-perioperative survival. This is broadly the same approach that was taken for the 'EVAR vs. OSR' model, which used EVAR-1 data. Like before, we took 2 approaches to modelling the post-perioperative survival phase:

1. Calibrating UK general population survival curves to reflect the EVAR-2 population (control arm), then applying relative effects from the EVAR-2 trial to obtain a survival curve for EVAR.
2. Using the EVAR-2 data exclusively, by fitting parametric survival curves to the EVAR and 'no intervention' data directly.

For consistency with the 'fit for OSR' model, the first of these approaches is our preferred base-case. Like the EVAR-1 data, the long-term survival data for EVAR-2 participants does exhibit a shape that is similar to general all-cause mortality, such that this method can produce visually excellent fits to the trial data. Furthermore, being directly linked to age-related background mortality statistics, it will ensure that plausible mortality hazards are applied across all cohort ages. The committee was satisfied with the approach, the alternative approach of using the parametric survival curves was tested in sensitivity analysis (see Section HE.3.3). Both methods are described below.

Base-case approach: calibrated all-cause mortality data

The methods we employed have largely been described in Section HE.2.2.3. Briefly, we used UK general population survival curves (ONS, 2017), sex-weighted by the ratio of men to women in EVAR-2. Comparing this with EVAR-2 survival on the no intervention arm, it is

clear that people who entered the EVAR-2 have worse survival prospects than the general UK population (Figure HE28). We sought to identify a HR to adjust the general population mortality rate, until it matched the control arm survival data from EVAR-2 as closely as possible. Like before, we used UK life tables from 1999–2001 to reflect the population at the time of EVAR-2 recruitment. We used numerical optimisation (Excel Solver's generalised reduced gradient [nonlinear] algorithm) to estimate the value of HR that minimised $wRMSE$. We performed 1,000 bootstrap replications from the RCT data, sampling with replacement, to characterised our uncertainty in the estimated $\ln(HR)$s.

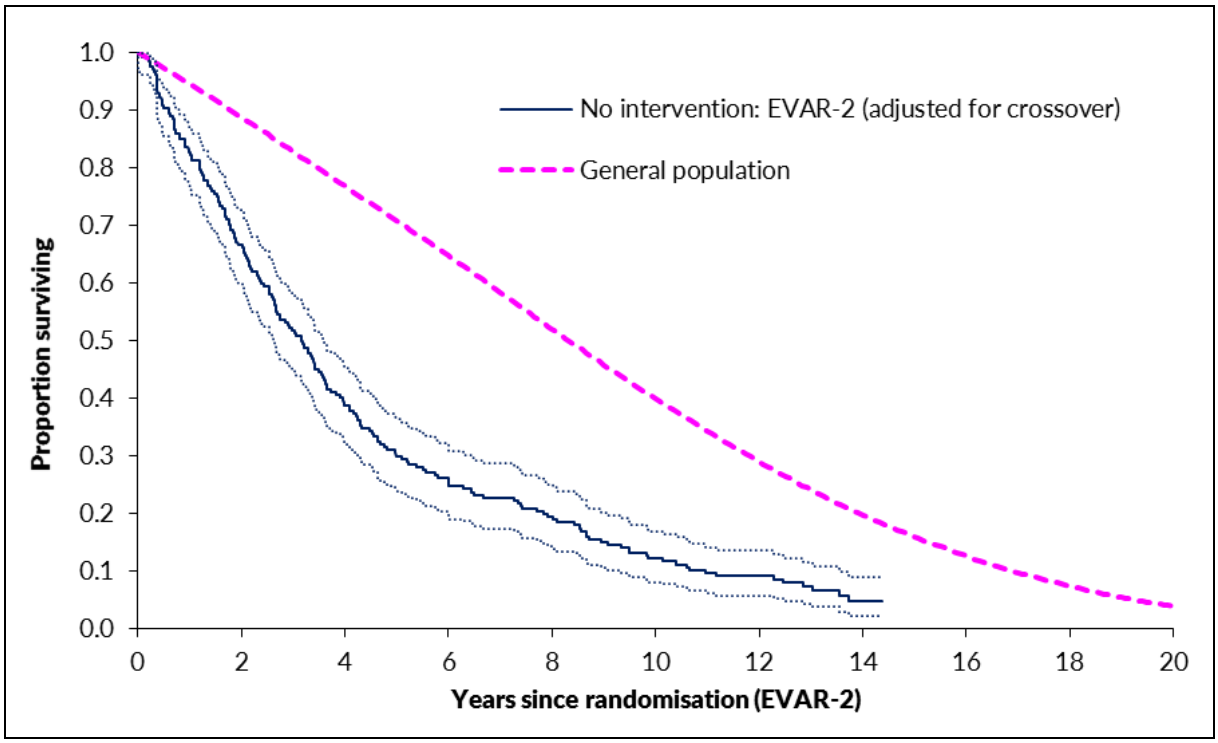


Figure HE28: EVAR-2 survival compared with 1999–2001 general population survival

Like with the calibration of UK general population survival to the IMPROVE study data, it became clear that a single HR was unable to produce an acceptable fit to the EVAR-2 long-term survival data. This is due to a visible reduction in the mortality rate, occurring at some point between year 4 and 5. We therefore took a piecewise approach, using 2 hazard ratios, $HR1$ and $HR2$, and a user-defined "cut-point". Excel Solver algorithm identified $HR1$ and $HR2$ that jointly minimised $wRMSE$ for a given cut-point. We determined that a 4.5-year cut-point produced the best fit to the EVAR-2 no intervention survival data. A 5-year cut-point produced a reasonable fit to the data. Again, a limitation of this approach is that our base-case cut-point (4.5 years) was not identified by systematic, quantitative method, but a comparison of cut-points at 0.5-year intervals. Despite this, the resulting survival profiles provide an excellent visual fit to the EVAR-2 'no intervention' data (Figure HE32).

The resulting best-fit values of $HR1$ and $HR2$ that minimised $wRMSE$, separated at a cut-point of 4.5 years, were **3.539** (bootstrapped mean: 3.570; 95% CI: 3.002 to 4.189) and **1.625** (bootstrapped mean: 1.677; 95% CI: 1.215 to 2.379) respectively (Figure HE29 (A)). This indicates that, on average, an EVAR-2 trial participant had a 3.5-times higher hazard of death than the general population of the time for 4.5 years. For those alive after 4.5 years, the hazard is 1.6 times higher than the general population. The values of $HR1$ and $HR2$ used in a sensitivity analysis with a 5-year cut-point are: **3.500** (bootstrapped mean: 3.509 [95% CI: 2.976 to 4.144]) and **1.484** (bootstrapped mean: 1.528 [95% CI: 1.082 to 2.172]) (Figure HE29 (B)). It was not necessary to age these patients to account for any months spent on the waiting list or undergoing the primary procedure, as it is the 'no intervention' arm.

In the analysis in the population for whom OSR is a suitable intervention, we applied our calibration HR values to *current* life tables (2013–15), to capture the general increase in survival prospects in the UK since the trials recruited. The guideline committee advised that doing so would not be appropriate in an analysis of people for whom OSR is not a suitable option (i.e. the EVAR-2 trial population). This is because the reasons an individual would have been excluded from the EVAR-1 study in 1999–2003 – instead being offered enrolment into EVAR-2 – are the same, largely medical reasons that would apply today. The committee agreed that although the UK population has become healthier, on average, since 1999–2003, this has had the effect of shrinking the population that meets the EVAR-2 trial criteria, as those medical criteria remain unchanged. It is therefore appropriate to use the 1999–2001 general population survival data for this analysis.

There are no randomised data comparing treatment strategies in people with complex AAAs; and no data at all were identified looking at outcomes associated with not treating such aneurysms. We therefore apply the same overall survival curves for people with complex AAAs who receive no intervention in the model. This means clinical outcomes for people on this arm are not affected at all by aneurysm complexity. The guideline development committee were satisfied that this was a reasonable approach to take.

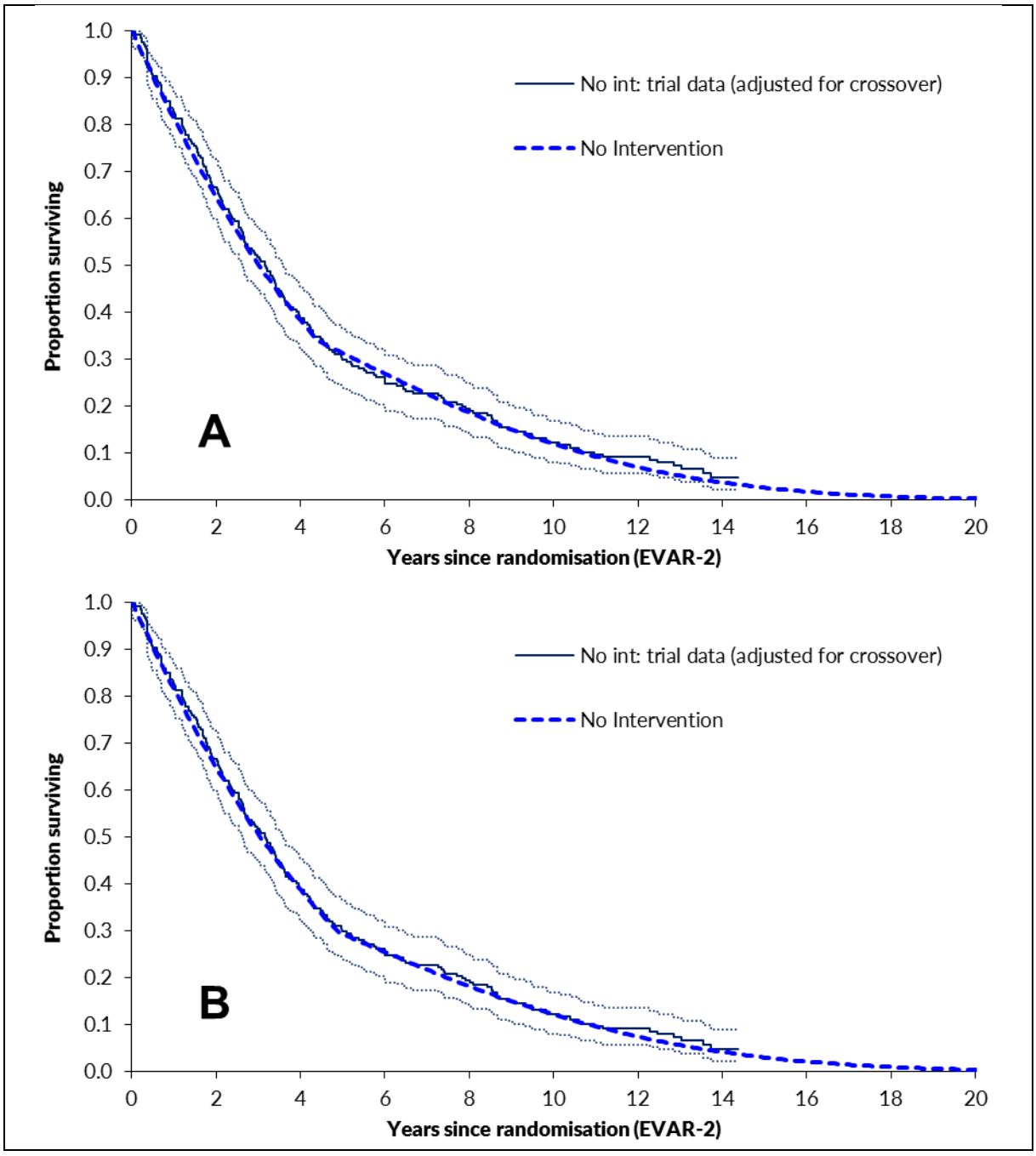


Figure HE29: General population survival (1999–2001) calibrated to EVAR-2 survival (no intervention arm). Piecewise approach with cut-point at (A) 4.5 years or (B) 5 years.

Base-case approach: relative long-term survival effects

The methods described above provided us with an overall survival curve for the 'no intervention' arm. We then applied a second set of HRs to model the survival of people on the EVAR arm. This was informed by the EVAR-2 trial data only, as there are no other RCTs in the relevant population. Given that there is clearly a change in the expected mortality hazard for 'no intervention' patients after around 4.5 years, we also took a piecewise approach to the Cox model here, with the same cut-point of 4.5 years.

Using overall survival data without intervention and post-perioperative EVAR data to obtain these relative effect HR values would have biased against EVAR. This is because people on the EVAR arm are a few months older at the point of post-perioperative survival, having been

through a period of waiting and intervention, and will have a slightly raised mortality hazard by virtue of being older. To account for this in our estimation of relative long-term survival effects, we reduced crossover-adjusted overall survival times on the EVAR-2 'no intervention' arm by 30 days plus the mean EVAR waiting time of 93 days. This had the effect of ageing the no intervention arm by a notional 30-day perioperative period and typical waiting time. Any participants on the 'no intervention' arm whose overall survival time was less than 123 days – meaning they did within this notional waiting and perioperative duration – were removed from the data.

The Cox model therefore used post-perioperative EVAR survival data and adjusted 'no intervention' survival data. The resulting HR for 0 to 4.5 years, for EVAR versus 'no intervention', is **0.742** (95%CI: 0.571–0.964). After 4.5 years, the HR is **1.454** (95%CI: 0.997–2.199). In the economic model, post-perioperative EVAR survival is estimated by applying these HRs to the overall survival curve for 'no intervention' patients, after ageing the cohort by 3 months from its baseline age, to reflect that people who receive EVAR will be slightly older than baseline when they enter the post-perioperative phase.

The HRs suggest that EVAR is associated with a lower mortality hazard in the first few years after AAA repair, compared with people who received no intervention. However, after 4.5 years, people who received no intervention experience better survival prospects. The guideline committee agreed that this is a reasonable characterisation of outcomes observed in practice, advising that it is not uncommon to be presented with aneurysms that they would have expected to rupture long before reaching their present size.

In the absence of evidence on long-term survival outcomes following the repair of complex aneurysms, we assume that the post-perioperative mortality rates shown above are transferable to complex repairs. The guideline committee were satisfied that this provides a reasonable estimation of long-term survival for complex cases, advising that once individuals survive the high-risk perioperative period, their survival prospects are expected to be similar, regardless of aneurysm type. The only difference, like before, is that people who require complex EVAR will spend more time on the waiting list, and will consequently be slightly older than infrarenal AAA patients when they enter the post-perioperative phase. To account for this, we age the complex EVAR cohort by a further 2 months.

Effect modifiers for post-perioperative mortality – elective repair

For the purpose of subgroup analysis and PSA, we also estimated the effects of age, sex and AAA diameter on long-term survival outcomes, through a multivariable Cox regression obtained using the post-perioperative EVAR-2 survival data (Table HE37). Again, we tested various combinations of covariates, including interactions and polynomial terms. We found that including sex in a piecewise manner about the cut-point provided a model with best fit to the data. In our base-case analysis, we do not apply these long-term survival effect modifiers; nor do we apply perioperative mortality effect modifiers. Instead, our base-case results are evaluated at the mean patient characteristics of the EVAR-2 study. When these long-term survival effect-modifying HRs are applied, we do not use the HR associated with age, because age is already accounted for by our use of UK life tables as the basis of our survival curves. However, age was included in the Cox regression to provide appropriately adjusted estimates of the independent effects of the other variables.

Table HE37: Post-perioperative survival effect modifiers – Cox regression – EVAR-2 (for subgroup analysis and PSA only)

Variable	*4.5-year cut-point*		*5-year cut-point*	
	HR	*95% CI*	*HR*	*95% CI*
EVAR (vs. none): 0-cut years	0.724	0.557 – 0.941	0.759	0.589 – 0.978
EVAR (vs. none): >cut years	1.422	0.972 – 2.081	1.393	0.928 – 2.090

Variable	*4.5-year cut-point*		*5-year cut-point*	
	HR	*95% CI*	*HR*	*95% CI*
Age, per year [a]	1.027	1.010 – 1.045	1.027	1.010 – 1.045
Sex = female (vs. male)	1.024	0.752 – 1.394	1.023	0.752 – 1.393
AAA diameter, per cm	1.060	0.963 – 1.166	1.058	0.961 – 1.164

Note:
(a) When post-perioperative survival effect modifiers are applied, the age HR shown is not used, as doing so would double-count the effect of age on mortality, which is already captured by our use of calibrated UK population life tables.

Key: CI, confidence interval; HR. hazard ratio.

The same post-perioperative survival outcomes and effect modifiers are applied in the model for patients with complex AAAs, requiring a custom-made EVAR device. The only way that the presence of complex aneurysm affects clinical outcomes, compared with infrarenal aneurysms, is through its impact on perioperative mortality, increasing from 7.3% to 42.1% (described above). The expert guideline development committee advised that this is reasonable, as the survival expectations of these groups are similar conditional on surviving the 30-day perioperative period.

Secondary approach: parametric curves based on EVAR-1 data

Like before, we also explored using the alternative approach of fitting parametric survival functions to the trial data. For this population, we used the EVAR-2 survival data. We tested standard parametric functions using Stata 13.0 (exponential, gamma, Gompertz, log-logistic, log-normal and Weibull), with model selection determined by visual fit and statistical goodness of fit to the data, and guideline committee validation. For the EVAR arm, we used the post-perioperative survival data from EVAR-2 (modelling waiting time and perioperative mortality separately). For the 'no intervention' arm, we used the overall survival data.

Based on its strong results in terms of statistical and visual fit, the primary parametric curves analysis uses the Gompertz function to characterise post-perioperative survival of EVAR patients (Table HE38; Figure HE30). The gamma model, which provides an equally good visual fit to the data, is included in the model for sensitivity analysis, as is the Weibull function, which performs with in terms of AIC and BIC. For 'no intervention' overall survival, the statistical goodness of fit results are inconclusive (Table HE38). The gamma function has the lowest AIC, closely followed by the exponential, Weibull and Gompertz functions, whereas the exponential model has the lowest BIC, followed by the Weibull and Gompertz functions. All 4 of these curves provide acceptable fits to the 'no intervention' overall survival data (Figure HE31), and so to maximise comparability with the EVAR data, the Gompertz model is used in the base case analysis. The gamma, exponential and Weibull functions are included as sensitivity analyses.

We also fit parametric models that include age, sex and AAA diameter coefficients, to facilitate subgroup analysis and PSA. For the 'EVAR vs OSR' models, we also fit parametric survival functions using a treatment covariate to distinguish between EVAR and OSR as a sensitivity analysis. For the present analysis this was not possible, as we use different survival data for the 2 model arms: post-perioperative survival for EVAR, and overall survival for 'no intervention'. They are only modelled as separate, distinct functions. All model parameters are provided in Section HE.6.

Table HE38: Statistical fit of parametric survival functions for post-perioperative EVAR-2 survival

Model	*EVAR Post-perioperative survival*		*No intervention Overall survival*	
	AIC	**BIC**	**AIC**	**BIC**
Exponential	494	497	639	642 [a]
Gamma	492	502	639 [a]	649
Gompertz	490 [a]	496 [a]	641	647
Log-logistic	511	517	642	648
Log-normal	525	531	648	655
Weibull	491	497	640	647

Note: (a) The model that provides the best fit to the observed data is signified by the lowest AIC and BIC statistic. The absolute values do not hold any context to the models. AIC and BIC statistics should only be compared within an analysis (e.g. comparing all AIC statistics for EVAR). Statistics for different datasets, for example the Gompertz AIC for EVAR and the Gompertz AIC for 'no intervention' should not be compared with each other.

Key: AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion.

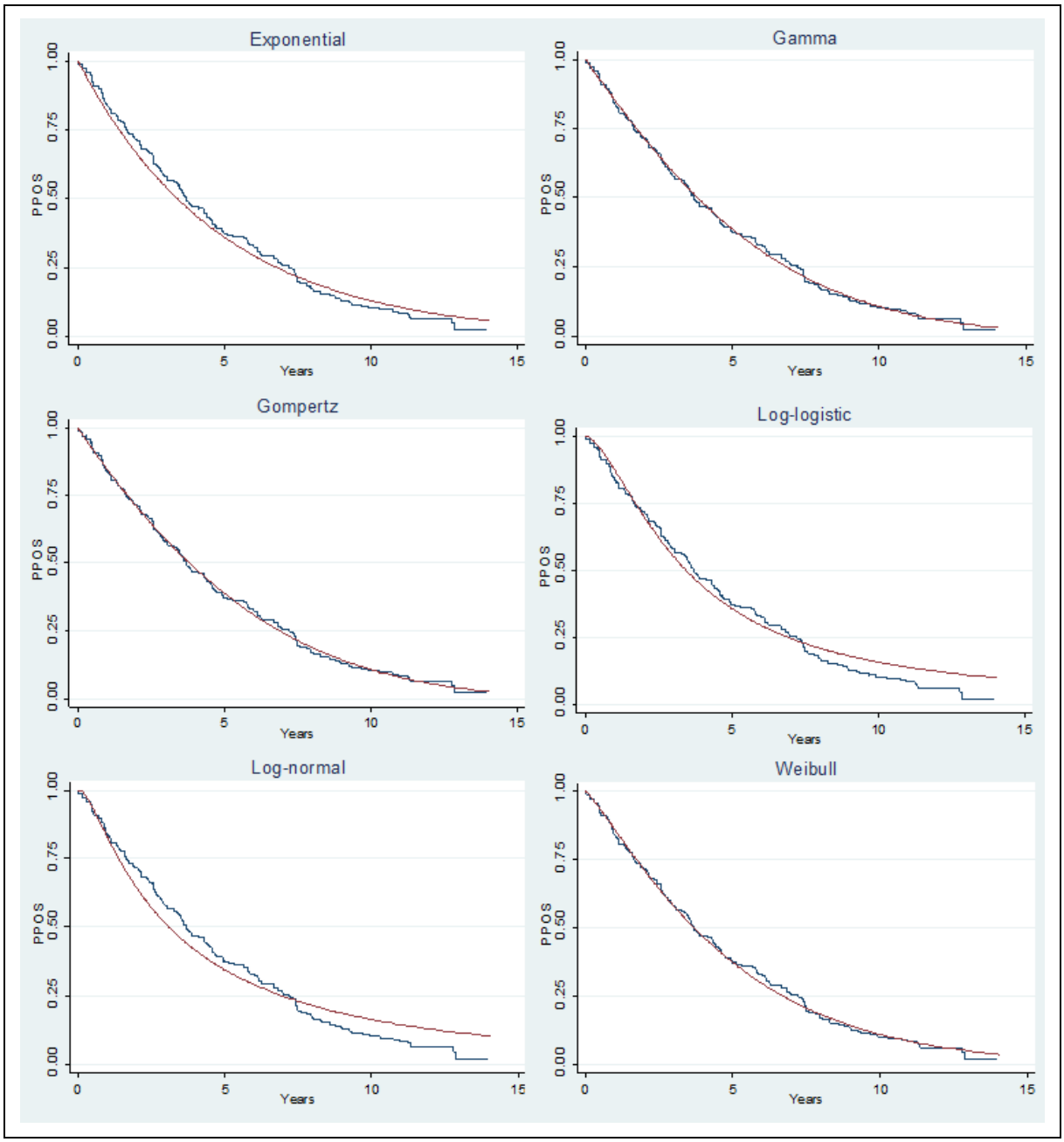


Figure HE30: Visual fit of parametric survival functions for post-perioperative survival – EVAR-2, EVAR arm

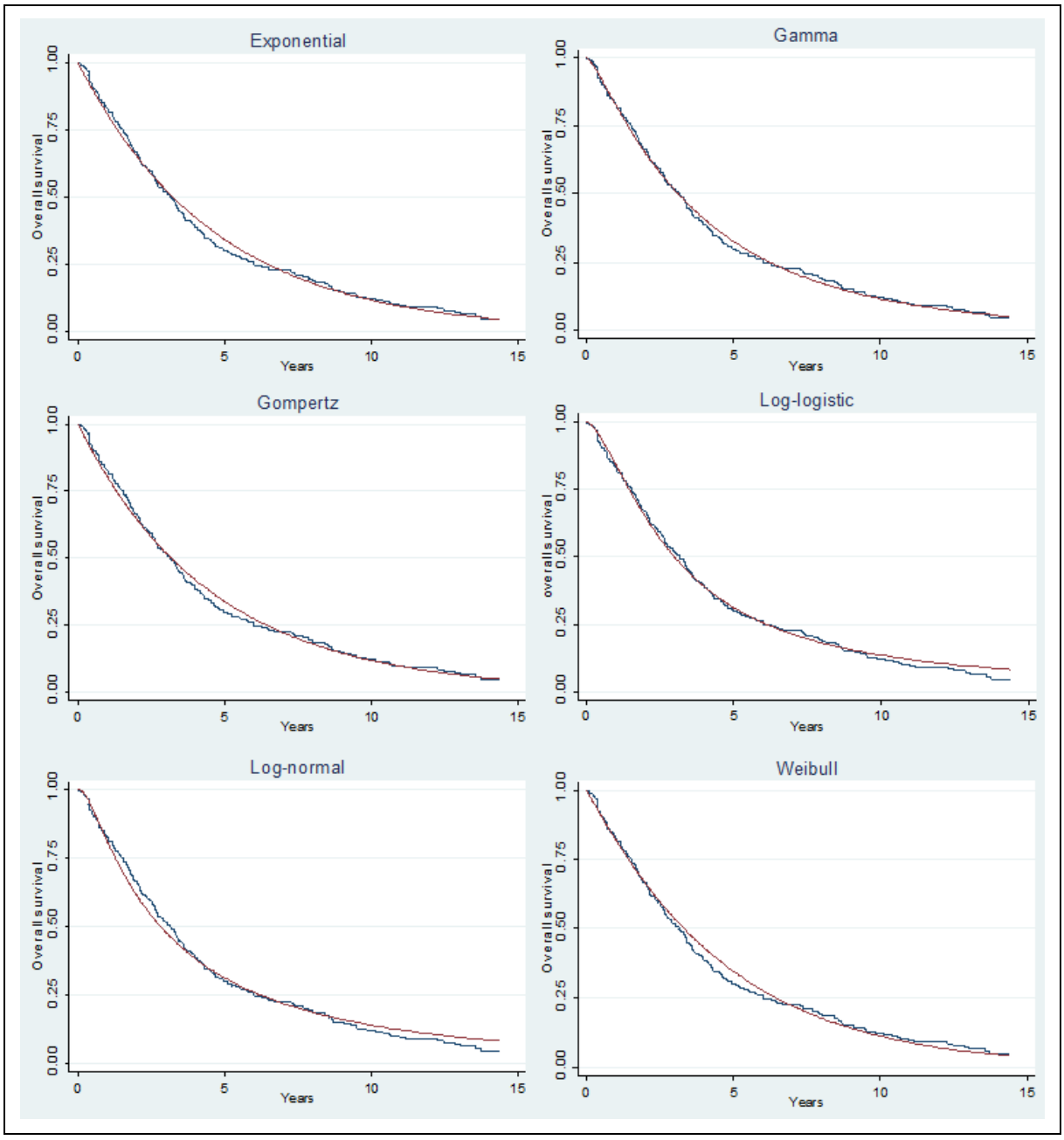


Figure HE31: Visual fit of parametric survival functions for overall survival – EVAR-2 'no intervention' arm

HE.2.3.6.2 Emergency repair

For emergency EVAR in this population, modelled patients who survive the perioperative period are assumed to have the same long-term survival prospects as elective EVAR patients. The estimated survival curves derived from the calibration of general UK survival, described above, are used to model post-perioperative survival following emergency EVAR. Similarly, in sensitivity analyses using parametric curves to characterise survival, the curves presented above for EVAR are used. Differences in overall survival between elective and emergency EVAR patients occur by emergency patients having no waiting time but a much higher risk of perioperative mortality. On the 'no intervention' arm for emergency cases, the patient's ruptured aneurysm is assumed to have a 100% mortality rate.

HE.2.3.7 Overall survival

When the 3 components of survival – waiting time, perioperative time and post-perioperative time – are combined, as described above, we obtain estimates of overall survival.

HE.2.3.7.1 Elective repair

Figure HE32 presents a comparison of the EVAR-2 Kaplan-Meier survival data and our base-case projection of overall survival for a cohort with unruptured infrarenal AAAs (dotted lines). Unlike for the 'fit for OSR' population, the modelled base-case curves immediately provide a closer fit to the trial data. This is because there is much less data for the 'unfit for OSR' population, meaning we relied more heavily on the single UK trial (EVAR-2), whereas previously we drew in perioperative and long-term mortality data from other trials. Further, for this population we have not scaled up our calibrated general population survival estimates using more recent life tables. As described above, this is because the guideline committee advised that the reasons a person would meet the criteria for EVAR-2 – and therefore be deemed unfit for OSR – will still apply today, such that the general health of this subgroup has not increased in line with the UK population.

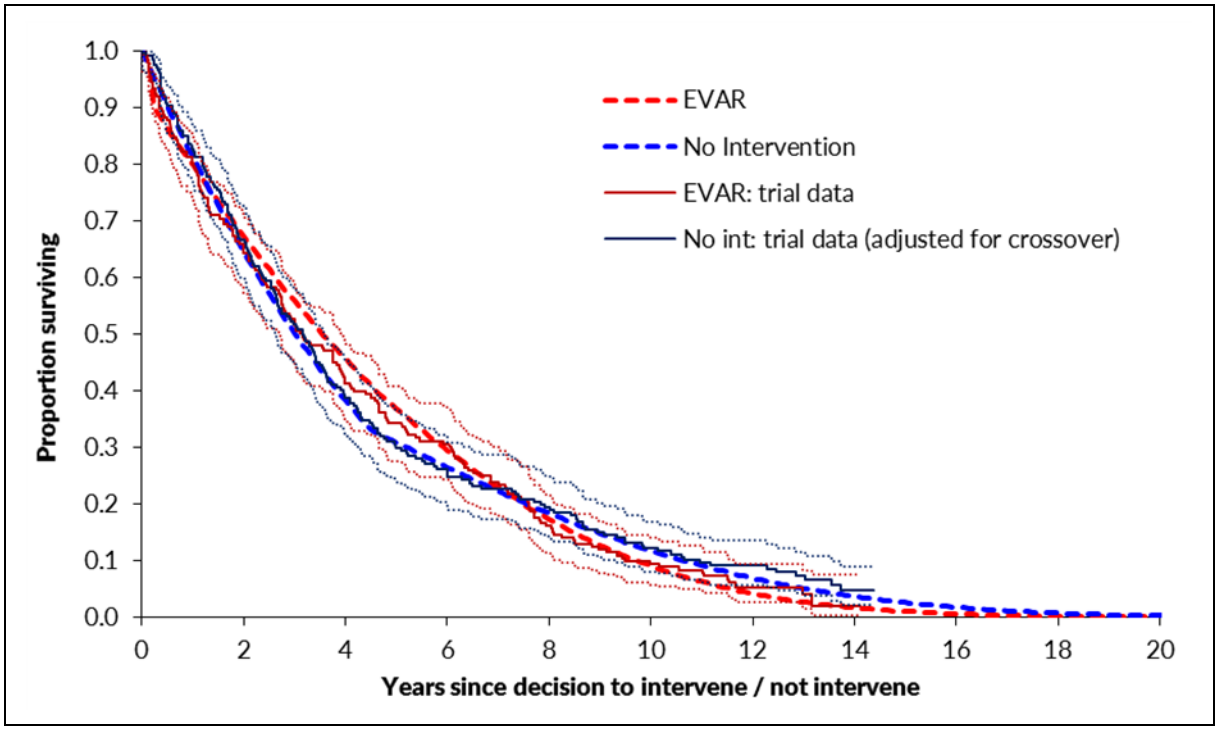


Figure HE32: Overall survival profiles in base-case model – elective & infrarenal – compared with EVAR-2 survival data

The model fits the 'no intervention' arm particularly well, and the EVAR arm reasonably well, perhaps slightly overestimating EVAR survival between years 2 to 6. This slightly poorer fit to the EVAR data is, to some extent, a result of our model applying a fixed 2-month duration waiting for elective repair; whereas in the trial, the mean time before intervention (or death) was 93 days, and a number of participants waited for significantly longer. This led to a relatively high pre-operative mortality rate on the EVAR arm, which we have omitted. Instead, our model applies a mortality rate equal to that of the 'no intervention' arm for EVAR patients on the waiting list, and all patients spend exactly 2 cycles (months) on the waiting list, as this was the guideline committee's best estimate of current NHS practice.

The overall survival profiles using our secondary, parametric curve approach – separate Gompertz functions for post-perioperative survival following EVAR and overall survival

following 'no intervention' – are shown in Figure HE33. The parametric models appear to have some difficulty capturing the 'kink' observed in survival on the 'no intervention' arm, meaning that 2 curves are closer together using this approach than when our base-case, general population mortality calibration approach is used. Survival profiles obtained using different post-perioperative parametric functions are shown in Section HE.2.3.8.

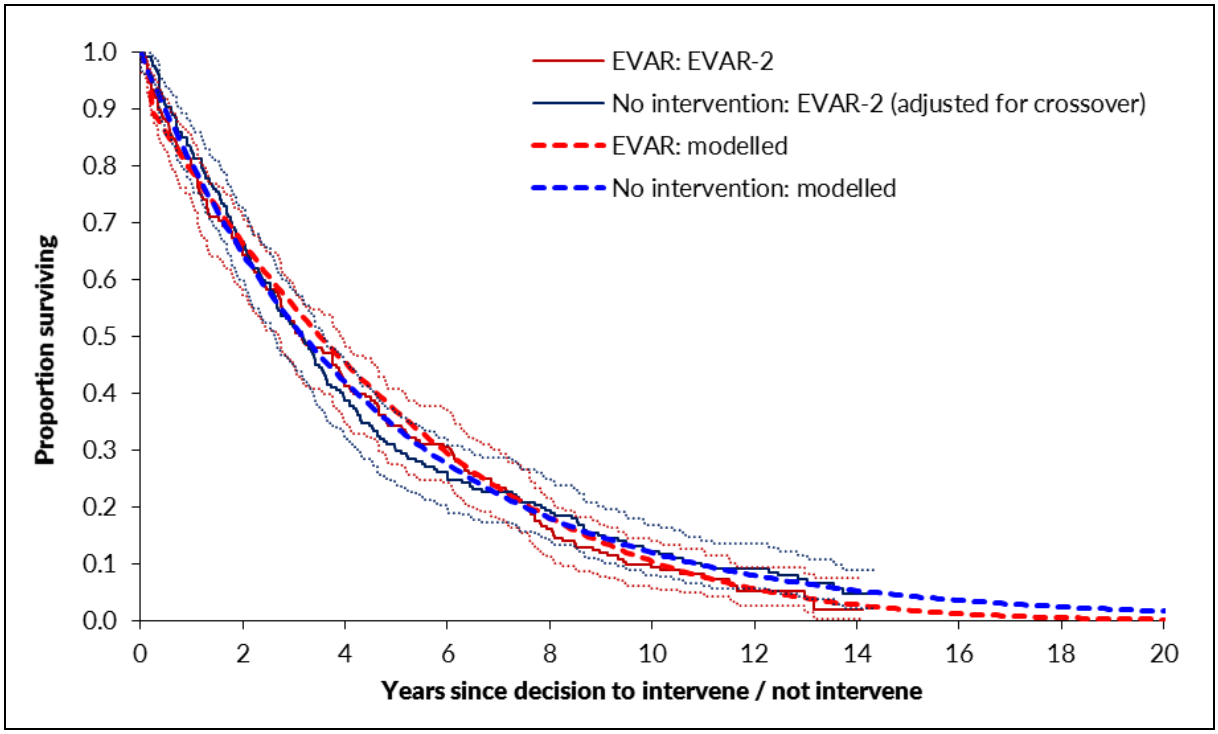


Figure HE33: Overall survival profiles using parametric survival curves for EVAR-2 post-perioperative EVAR survival and overall 'no intervention' survival.

For complex repair, there is no directly applicable data from an RCT against which to compare simulated survival. Instead, Figure HE34 shows the base-case projections of survival for people with complex AAAs next to the base-case curves for infrarenal AAAs (from Figure HE32), for comparison. The observed differences in the curves are due to the higher perioperative mortality rate estimated for the repair of complex AAAs and, to a lesser extent, 2 weeks of additional waiting time for a custom-made EVAR device to repair complex aneurysms. There are no differences in post-perioperative mortality rates between infrarenal and complex EVAR patients in the model, and there is no difference in overall survival among 'no intervention' patients.

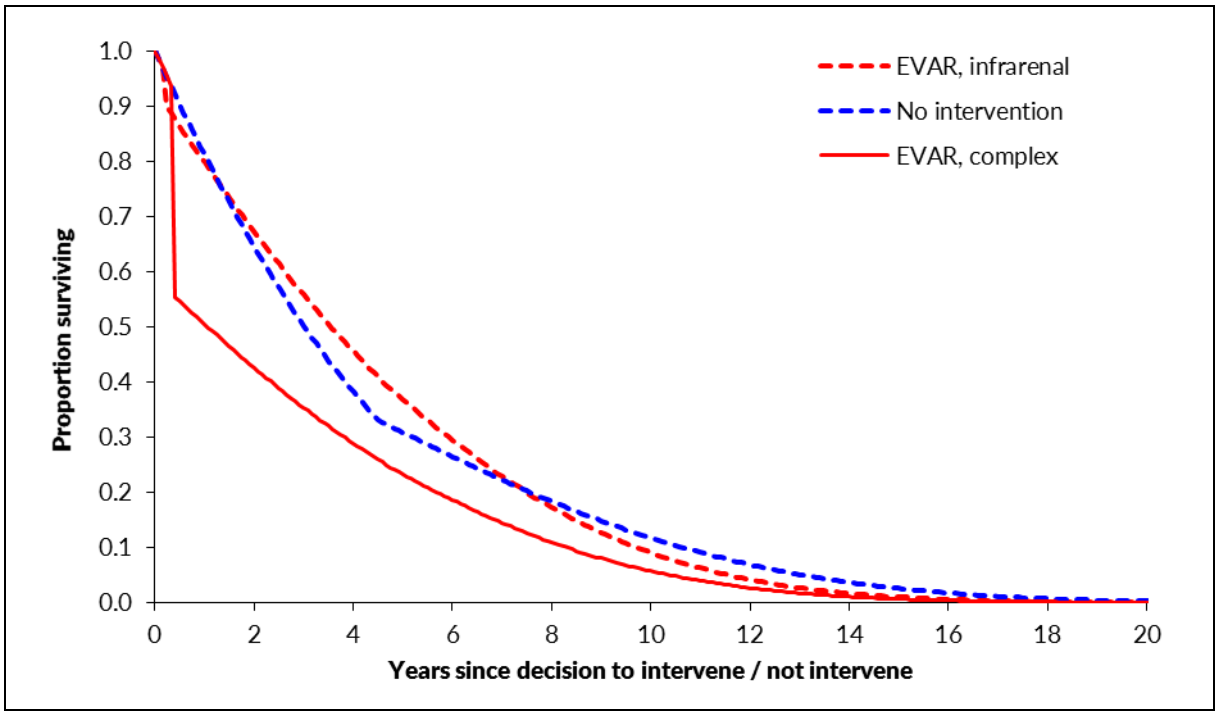


Figure HE34: Overall survival profiles in base-case model – elective & complex compared with elective & infrarenal

HE.2.3.7.2 Emergency repair

Figure HE35 presents a comparison of the modelled overall survival curves for a cohort of this 'unfit for OSR' population with ruptured infrarenal AAAs requiring emergency repair. We have not presented these curves alongside the EVAR-2 or IMPROVE data, because the EVAR-2 data are elective cases, and the IMPROVE data are in a 'fit for OSR' population and recruited several years later than the EVAR trials. In this population, opting to provide no intervention results in 100% mortality, due to the ruptured aneurysm. If EVAR is attempted, patients surviving the high perioperative mortality rate (72.1%) are subject to the same long-term survival profile as elective patients.

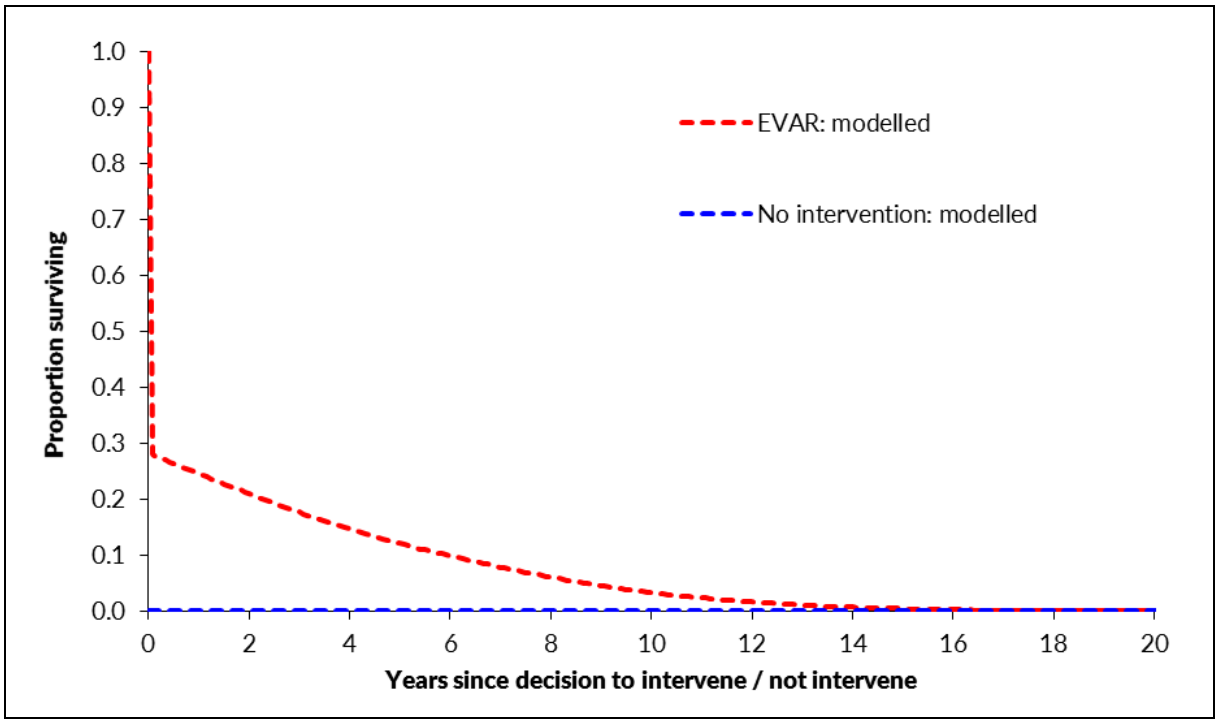


Figure HE35: Overall survival profile in base-case model – emergency & infrarenal, EVAR

Emergency repair for complex AAAs with EVAR does not typically occur in UK practice, as the time required to manufacture a bespoke EVAR device to fit the patient's anatomy makes it impractical. As a result, it is assumed that all individuals in this group will receive open surgery, and no comparison is modelled.

HE.2.3.8 Survival sensitivity analyses

The following alternative approaches to modelling survival have been included as sensitivity analyses for the 'unfit for OSR' population:

1. Using parametric curves fitted to the EVAR-2 trial data, including the use of different functions for each trial arm. The resulting overall survival profiles are presented in Figure HE36.

2. Assuming that EVAR patients who survive for 4.5 years have the same mortality risk as people who received no intervention beyond this point. This is based on our piecewise Cox model that determined the EVAR HRs for 0 to 4.5 years ($HR1$ = 0.742 [95%CI: 0.571–0.964]) and after 4.5 years ($HR2$ = 1.454 [95%CI: 0.997–2.119]). The HR after 4.5 years is not statistically significant at the 95% confidence level, therefore this scenario sets $HR2$ to a value of 1. This scenario therefore favours EVAR. In reality, the EVAR-2 Kaplan-Meier curves clearly converge, such that a catch-up effect of improved long-term survival after 'no intervention' must exist (see Figure HE28).

3. Assuming there is no difference in post-perioperative mortality rates following EVAR and 'no intervention' mortality rates (i.e. $HR1$ = $HR2$ = 1), such that the only difference in survival is caused by the risk involved with undergoing an EVAR procedure.

4. Scaling up our survival estimates by using survival data from 2013-15 UK life tables rather than the base-case 1999–2001 values.

5. Applying age, sex and AAA diameter effect modifiers.

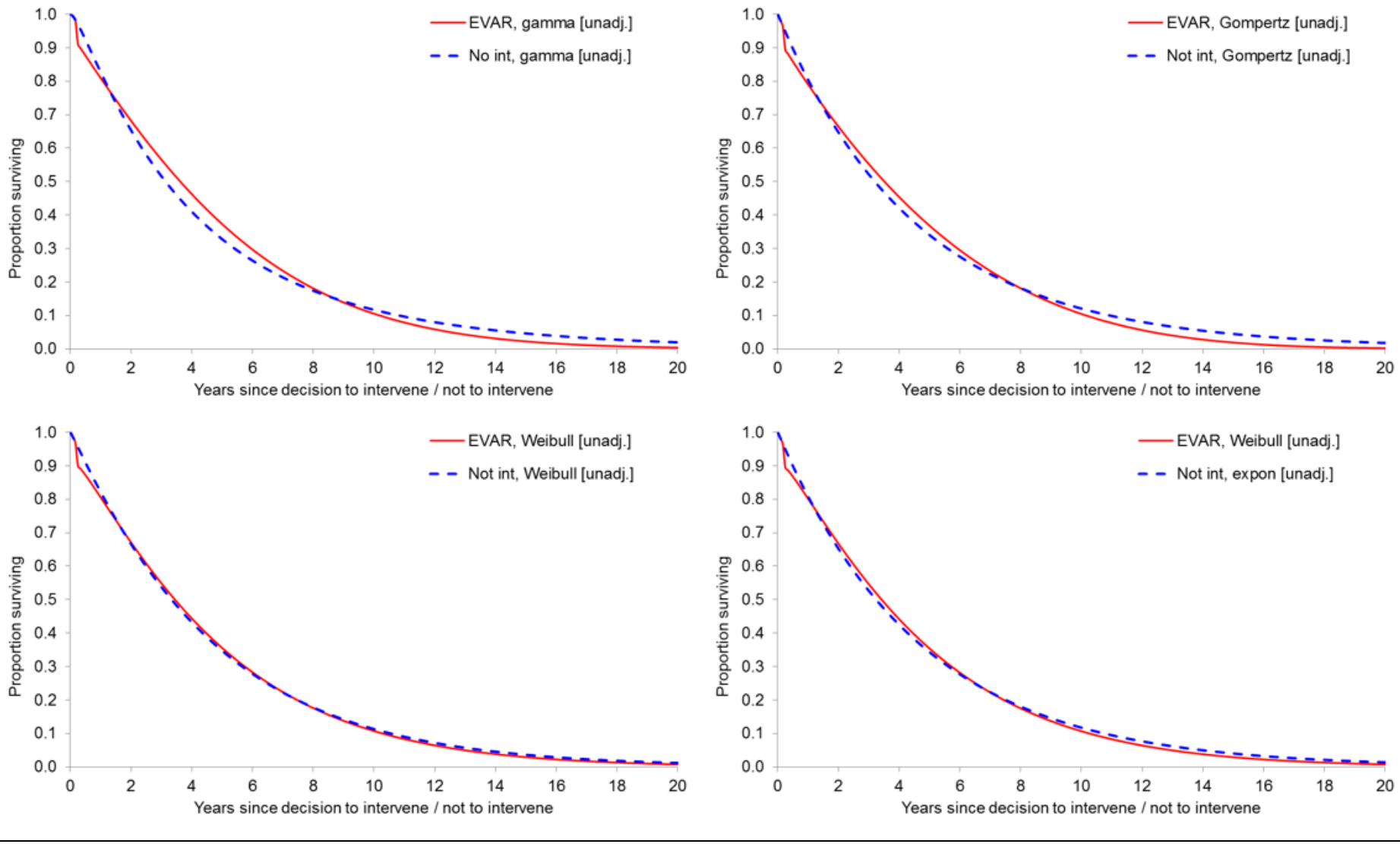
6. Applying a 5-year cut-point for the calibration of general UK population mortality to the EVAR-2 trial, and the relative effects Cox model, rather than the base-case cut-point of 4.5 years.

The model's overall survival curves using parametric curves for EVAR post-perioperative survival and 'no intervention' overall survival are shown in Figure HE36, for elective (unruptured) infrarenal AAA repair, in people for whom OSR is not suitable.

The equivalent overall survival curves are not presented for the elective repair of complex AAAs in this population, as the only difference is in the perioperative mortality rate in EVAR patients. In the base-case analysis this is 40.9% in people with complex AAAs, compared with 7.3% in people with infrarenal AAAs in the figures above. The survival profile of 'no intervention' patients remains the same. As a result, the overall survival curve with complex EVAR is noticeably worse than the 'no intervention' arm following EVAR's perioperative phase, and the survival profile remains worse than that of unrepaired patients for the duration of the model. This remains true of all available EVAR parametric curves for post-perioperative survival.

Similarly, we do not present the equivalent overall survival curves for the emergency repair of infrarenal AAAs in this population. Again, the only difference in EVAR survival profiles is caused by the increase in perioperative mortality in the emergency setting (72.1%), such that only a relatively small proportion of patients is expected to survive intervention. Because of this, choosing different parametric functions to model subsequent survival has negligible effect on the overall survival profile for EVAR. There is no overall survival curve for 'no intervention' patients in the emergency setting, as an untreated ruptured AAA is assumed to have a 100% mortality rate.

No covariate adjustment, separate models for EVAR and 'no intervention'



Adjusted for age, sex and AAA size, separate models for EVAR and 'no intervention'

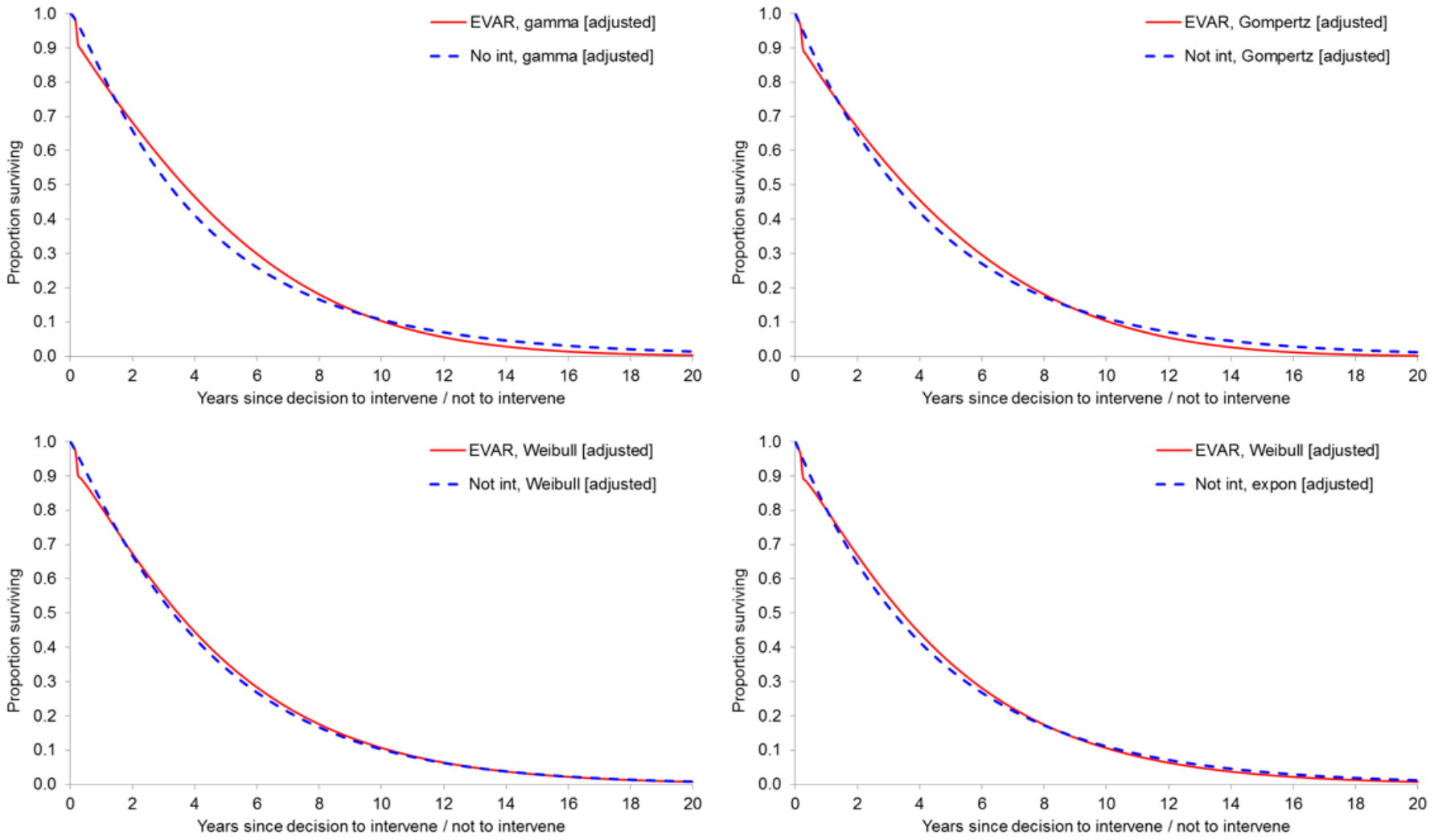


Figure HE36: Comparison of alternative overall survival profiles from parametric curves – elective & infrarenal repair – population for whom OSR is not a suitable intervention

HE.2.3.9 Reintervention

In the 'unfit for OSR' model, patients treated using EVAR are subject to a long-term reintervention risk. Patients on the 'no intervention' arm are subject to a long-term risk of their untreated aneurysm rupturing. Both of these risks are informed by the EVAR-2 trial.

For EVAR patients, we use the overall graft-related reintervention rates, which were reported for 3 time periods: the first 6 months after AAA repair; 6 months to 4 years; and >4 years (Sweeting et al., 2017). Unlike for the EVAR-1 and IMPROVE trials, the EVAR-2 publication did not distinguish between 'life-threatening' and 'serious' events. To estimate this distinction ourselves, we compared the different events that occurred in EVAR-2 with how those events were categorised as either 'life-threatening' or 'serious' by the EVAR-1 investigators (Patel et al., 2016), after removing the small number of "other" procedures. By doing this, we estimate that 50% of graft reintervention procedures in EVAR-2 patients were life-threatening, and 50% were serious but not life-threatening. Accordingly, we split the occurrence of graft-related procedures 50/50 between the 2 severity categories. We then converted the resulting event rates to monthly probabilities in order to apply them as probabilities per cycle in our model (Table HE39). We have only included graft-related complications in this model, as laparotomy-related and pulmonary complications – which were included in the 'EVAR vs. OSR' model – are primarily considerations when undergoing open surgery, which is not appropriate for this population.

Table HE39: Graft-related EVAR reintervention procedures

		Probability per month	
Reintervention	***Event rate/year***	Life-threatening	Serious
0 to 6 months	0.253	1.04%	1.04%
6 months to 4 years	0.038	0.16%	0.16%
Years 4+	0.038	0.16%	0.16%

For 'no intervention' patients, the EVAR-2 investigators report a rupture rate of 12.4% per year. We convert this to a 1.03% rupture probability per month (cycle). Non-emergency patients whose AAA is not repaired are subject to this rupture probability. We assume that a patient can experience a maximum of 1 rupture. The effect of ruptures on mortality is captured implicitly within the EVAR-2 'no intervention' arm data, however ruptures also incur cost and quality of life implications. We capture these outcomes in the model when a rupture occurs (see Sections HE.2.3.10 and HE.2.3.12, respectively).

As there is no analogous RCT for the repair of ruptured aneurysms in this population, we assume that the same EVAR reintervention rates apply to people who underwent emergency repair. On the 'no intervention' arm, 100% of modelled patients experience a fatal rupture at the start of the model.

HE.2.3.10 Resource use

The model for this population includes the same resource use items as those captured by the 'fit for OSR' model (see Section HE.2.2.10).

HE.2.3.10.1 Primary procedure and perioperative care

Perioperative resource use data collected in the EVAR-2 trial (Brown et al., 2012) were not reported to the same level of detail as the EVAR-1 and IMPROVE trials (Brown et al., 2012; Powell et al., 2015 & 2017). As such, we assume that the EVAR-1 and IMPROVE resource use data associated with EVAR (Table HE26) are directly transferable to people who are unfit for OSR, in the elective and emergency settings respectively. The resulting procedure costs are detailed in Section HE.2.3.11. This assumption was endorsed by the expert

guideline committee. However, we have included a sensitivity analysis in which all perioperative hospital costs associated with EVAR are increased by 20% relative to the EVAR-1 estimates. This is to reflect that, because we know that the 'EVAR vs. no intervention' (EVAR-2) population is less fit than the EVAR-1 population on average, an increase in hospital resource use may be expected.

On the 'no intervention' arm of the model, deciding not to intervene incurs much lower costs than attempting to repair the aneurysm with EVAR. For non-emergency (unruptured) patients, based on the advice of the guideline committee, this decision is associated with 1 outpatient attendance and, in some patients, an additional CT scan. We assume that the extra CT scan is required in 50% of patients. Otherwise, the patient is discharged to the care of their general practitioner, and incurs no further AAA-related resource use unless their aneurysm ruptures in the future. We assume that no resource use is associated with not attempting to repair a ruptured AAA.

HE.2.3.10.2 Ongoing monitoring

Like the 'EVAR vs. OSR' decision problem, here we assume that there is an outpatient consultation at 1 month after EVAR, followed by an outpatient CT scan 1 month later. Thereafter, patients attend 1 outpatient ultrasound appointment per year, for 5 years. A scenario analysis assumes that monitoring is conducted using a CT scan rather than ultrasound. Patients on the 'no intervention' arm are assumed to have been discharged, and therefore require no ongoing hospital imaging, other than the extra, initial CT scan in 50% of cases.

HE.2.3.10.3 Reintervention

Resource use was not directly elicited for reintervention procedures in EVAR-1 or EVAR-2. Instead, we assume the resources used are reflected by the NHS reference cost assigned to each procedure (see Section HE.2.3.11). Reintervention procedures are assumed to require 2 follow-up outpatient CT scans.

HE.2.3.11 Costs

The cost of EVAR devices and almost all primary procedure resource items are identical to the 'EVAR vs. OSR' model (shown in Table HE27). For elective repair, the only difference is that there can be no conversion to OSR in this population, which occurred in 0.8% of EVAR patients in EVAR-1.

In IMPROVE, 36% of participants randomised to EVAR actually received OSR. In the 'fit for OSR' model, these switching patients are accounted for in our EVAR devices costs; however, it is not appropriate use this cost in people for whom OSR is not an option. We therefore adjusted the IMPROVE primary procedure cost to reflect that 36% of its total were obtained from people who actually received OSR, whereas here, 100% of patients on the emergency EVAR arm will receive EVAR. To do this, we used the ratio of primary admission EVAR to OSR costs from the EVAR-1 trial (1.241) which, alongside the known proportion of participants who contributed to the IMPROVE average cost but received OSR (36%), allowed us to estimate the emergency EVAR cost in people who actually received EVAR. The resulting total perioperative costs are shown below.

Table HE40: Total perioperative costs – EVAR where OSR is not a suitable option

Procedure	*Total cost*			
	Elective, infrarenal	**Elective, complex**	**Emergency, infrarenal**	**Emergency, complex**
EVAR	£13,556	£23,722	£18,559	N/A

The one-off cost associated with deciding not to intervene for non-emergency patients, of 1 outpatient attendance and an extra CT scan in 50% of cases, is £188 (unit costs provided in Table HE30). For emergency cases, the base-case model applies no cost to the decision not to intervene. While the guideline committee agreed that this was a reasonable assumption to make, an extreme value sensitivity analysis applying a very high unit cost of deciding not to intervene in the emergency setting is also explored.

HE.2.3.11.1 Ongoing monitoring

The cost of an outpatient vascular surgery consultation is the same as the 'EVAR vs. OSR' model, informed by NHS reference costs (2015-16): £140 (see Table HE30). Similarly, there is no change to the unit cost of imaging: £58 per ultrasound scan and £94 per CT scan.

HE.2.3.11.2 Reintervention procedures and AAA rupture

The source of unit costs for EVAR reintervention procedures depends on the severity of the procedure, as detailed in Table HE41. Life-threatening graft-related complications are assumed to incur the cost of an emergency EVAR procedure, reflecting a high cost associated with an urgent full graft reintervention. In the 'EVAR vs. OSR' model, the cost of an emergency OSR procedure was used, but that may be inappropriate in a patient population for whom an open surgical procedure has already been deemed to be inappropriate. The unit cost of a serious (non-life-threatening) reintervention is informed by NHS reference costs (2015-16), and is identical to the cost used in the 'EVAR vs. OSR' model.

Table HE41: EVAR reintervention unit costs where OSR is not a suitable option

Reintervention	*Activity-weighted average cost*	*NHS reference cost source & derivation*
Graft-related		
Life-threatening	£12,866	Equal to emergency EVAR procedure cost.
Serious	£4,628	Inpatient procedures: percutaneous transluminal angioplasty of single blood vessel (YR11A–D; range: £1,492 to £12,763)

Patients on the 'no intervention' arm do not undergo a repair procedure, and are therefore at a continued risk of aneurysm rupture. This is the main determinant of costs incurred by patients on this model arm. We assume that emergency EVAR is the only procedure available to attempt to repair a ruptured AAA in this population, which has a unit cost of £19,366 (see Table HE40). However, not all people with a ruptured AAA will undergo a repair attempt. In the EVAR-2 trial, a repair attempt was made in 6 of the 55 ruptures on the 'no intervention arm' (10.9%). The expert guideline committee confirmed that this figure is consistent with its current NHS experience, advising that approximately 10% of ruptures in this patient population will reach the point of an emergency repair attempt. To reflect this, the rupture unit cost of £19,366 is incurred only by the proportion of patients who reach the point of intervention (10.9%), to give a weighted average rupture unit cost of £2,025.

For the 10.9% of ruptures that undergo a repair attempt, we also apply a one-off cost to account for subsequent follow-up assessments. This is the same as the EVAR monitoring requirement: 1 outpatient consultation, 1 CT scan, and 5 outpatient consultations and ultrasound scans. It is applied as a one-off cost at the time of the repair procedure to avoid the computational burden of tracking ruptured patients over time. Doing this is slightly favourable to EVAR, in terms of comparing EVAR with 'no intervention', because it front-loads the monitoring cost associated with ruptures among 'no intervention' patients. In reality, some patients will die before completing their 5 years of follow up. The cost of imaging in future years would also be reduced by the effect of discounting. However, it does not have a noticeable bearing on cost-effectiveness results.

Table HE42: Rupture unit cost

Item	*Cost / Value*	*Source*
Rupture repair	£19,366	Equal to emergency EVAR total cost.
Rupture follow up	£1,224	1 consultation, 1 CT scan, 5 consultations with US (all outpatient attendances)
Proportion of ruptures in whom repair is attempted	10.9%	EVAR-2: 6 repair attempts were made in 55 ruptures among participants who received no intervention.
Unit cost per rupture	£2,025	£19,366 * 10.9%
Key: CT, computed tomography; US, ultrasound.		

HE.2.3.12 Quality of life

Like the 'fit for OSR' model, patient HRQL is captured in the model as 3 components: general age-related HRQL, reduced HRQL while recovering from AAA repair, and reduced HRQL while living with a complication and recovering from the subsequent reintervention or rupture.

HE.2.3.12.1 General age-related HRQL

The baseline EQ-5D utility among EVAR-2 patients is 0.61, compared with the general, UK age-related mean of 0.75 for people of the same age (76 years). While the EVAR-1 trial population, in people for whom both EVAR and OSR were suitable interventions, had a baseline utility close to the general population value, the EVAR-2 mean of 0.61 indicates that its participants have, on average, significantly lower quality of life than the general population. This is plausible, given that the main entry criterion for EVAR-2 was that invasive, open surgery is not considered to be a viable option for these patients, indicative of medical conditions and patient characteristics that may affect a person's quality of life. We therefore assume baseline utility equals 0.61 in this model. This baseline utility increases if the starting cohort is younger than the base case value of 76, with the scale of the increase informed by UK age-related utility norms (Table HE32; Kind et al., 1999).

HE.2.3.12.2 HRQL during recovery

EQ-5D data were collected directly during the EVAR-2 trial, and identified no difference in HRQL in participants randomised to EVAR and 'no intervention' over 12 months. However, to be consistent with previous UK cost–utility analyses and our 'EVAR vs. OSR' model, we apply a loss in HRQL for a period following the use of EVAR to repair.

Elective repair

Based on the EVAR-1 study, we assume that EVAR recipients experience a loss of utility at 3 months quantifiable by a utility multiplier of 0.964 (i.e. quality of life is reduced by 3.6%). By 12 months, this loss is eradicated and the person's HRQL returns to the person's baseline level, with a mean utility multiplier of 0.982 (i.e. a 1.8% reduction) applied between month 3 and month 12 to reflect this (see Figure HE24).

Emergency repair

Consistent with the 'EVAR vs. OSR' model, emergency EVAR patients experience the same utility loss over 12 months as elective EVAR patients.

In a scenario analysis, we assume that recovery from EVAR is associated with no loss of HRQL, which implies that the patient makes an immediate recovery and return to their baseline HRQL.

HE.2.3.12.3 HRQL during graft-related reintervention

When a reintervention is required, a reduction in HRQL is applied to reflect the complication itself and the reintervention recovery period. For a life-threatening graft-related reintervention, we assume that the impact on HRQL can be estimated by the HRQL impact of elective OSR to repair an AAA, based on the EVAR-1 EQ-5D data. This is consistent with the approaches taken by Chambers et al., (2009), Brown et al., (2012) and our 'EVAR to OSR' model. While we recognise that the population of interest here cannot receive OSR, we apply this level of utility decrement (-6.4% over 12 months) to reflect that a life-threatening reintervention may require a substantial recovery period relative to serious but non-life-threatening procedures.

Similarly, again matching our 'fit for OSR' model, a one-off QALY loss is calculated for other serious graft-related complications (e.g. endoleak), by assuming their impact on HRQL can be approximated by the recovery period associated with elective EVAR (-2.2% over 12 months). This reflect a less invasive procedure and easier recovery.

HE.2.3.12.4 HRQL during AAA rupture

No laparotomy-related complications are included in this model, as they are more important in patients who receive OSR. Instead, a HRQL loss is modelled for patients on the 'no intervention' arm who experience a rupture of their aneurysm. We assume that this is reflected by the HRQL of a life-threatening graft-reintervention (i.e. -6.4% over 12 months), captured as a one-off QALY loss in the same way that utility decrements for other reintervention procedures have been modelled. The utility loss of -6.4%, or a multiplier of 0.936, is itself based on recovery from elective OSR, from the EVAR-1 trial. This is experienced by the 10.9% of ruptures that lead to a repair attempt; the rest will be fatal, and are reflected in the EVAR-2 survival data.

Applying this OSR decrement is potentially slightly biased in favour of the EVAR arm, given that patients who rupture in this model will only be eligible to receive emergency EVAR, which is less invasive than OSR and therefore less harmful to a person's HRQL. We test this assumption in extreme value sensitivity analysis around the QALY loss associated with these ruptures (see Section HE.3.3).

Recovery from rupture is the only direct loss of quality of life among 'no intervention' patients in the model, who otherwise live with the baseline utility value for their age (0.61 in the base case analysis).

HE.2.3.13 Key assumptions

Key assumptions built into the 'EVAR vs. no intervention' economic model are summarised in Table HE43. Model parameters are present in full in Section HE.6.

Table HE43: Key assumptions of the 'EVAR vs. No Intervention' ('unfit for OSR' population) cost–utility model

- *For both elective repair of unruptured AAAs and emergency repair of ruptured AAAs, the decision is to attempt aneurysm repair with EVAR or not to attempt aneurysm repair, because OSR is not considered to be a viable option in this patient population.*
- *Overall survival for EVAR patients can be modelled as 3 distinct parts: waiting time survival, perioperative (30-day) survival, and post-perioperative (long-term) survival. Overall survival for patients who receive 'no intervention' does not have to be separated this way.*
- *There is no difference in the mortality rate of people waiting for an elective EVAR and of people who receive no intervention. All elective EVAR patients wait for 2 months for their intervention, with the exception of people waiting for EVAR to repair a complex AAA, because the EVAR devices for this population are custom-made to order. This group waits for a further 2 months.*

- *Patients with a ruptured AAA receive emergency care and therefore have no waiting time.*
- *EVAR is not typically used for people with a ruptured complex AAA. EVAR devices for complex aneurysms are custom-made to order, which makes them impractical for emergency repair.*
- *The EVAR-2 study is the most appropriate source of baseline perioperative (30-day) EVAR mortality data, for elective cases. The National Vascular Registry is not used, because we use it to model outcomes for people for whom both EVAR and OSR are suitable interventions. In the present population, for whom OSR is not a suitable option, 30-day mortality rates will be higher.*
- *For emergency repairs, the most appropriate source of baseline perioperative (30-day) EVAR mortality is the UK-based IMPROVE trial.*
  - *To adjust these figures to be more applicable to a population for whom OSR is not a viable option, we increase the baseline (IMPROVE) mortality rates using an odds ratio derived from a comparison of the EVAR-2 and EVAR-1 trials. This odds ratio (4.70) represents a "fitness effect", quantifying the increase in odds of 30-day EVAR mortality in people who were deemed not to be candidates for OSR, compared with those who are deemed fit for OSR (i.e. those who entered EVAR-2 instead of EVAR-1).*
  - *Using this odds ratio implicitly assumes that the 'fitness of OSR' effect observed in elective repairs is transferable to emergency repairs.*
  - *It also implicitly assumes that the 119 potential participants who decline to enter the EVAR-2 study are not systematically different to the 404 participants who were randomised.*
- *The mortality rate associated with an untreated ruptured (emergency) AAA is 100%, such that if a decision is taken not to attempt to repair the aneurysm using EVAR, the patient will die.*
- *Age, sex and aneurysm size are important effect modifiers for perioperative EVAR mortality. For elective repairs, the relative influence of each is informed by a European registry (Vascunet; Mani et al., 2015), and is applied to both infrarenal and complex AAA repair. Emergency repairs are characterised by a logistic regression analysis conducted using the IMPROVE study data.*
- *It is acceptable to calibrate UK general population survival data to match post-perioperative survival in the EVAR-2 trial as closely as possible.*
  - *It is not appropriate to scale the resulting survival estimates up using present day life tables. This is because the characteristics and risk factors that meant OSR was not a suitable option when the EVAR trials recruited are the same characteristics and risk factors today, such that this subgroup will not have experienced the same increase in life expectancy experienced by the general population in that time. Instead, the general increase in population health will have lifted people out of the EVAR-2 subgroup, meaning this patient population is smaller today.*
  - *The long-term survival estimates, based largely on data from infrarenal aneurysms, can be transferred to complex aneurysms, such that once a person has survived the perioperative (30-day) period their long-term survival is independent of aneurysm complexity.*
  - *For emergency repairs, in the absence of randomised comparative data in people for whom OSR is not a viable intervention, post-perioperative survival for EVAR patients can be informed by our estimates for elective cases.*
- *Aneurysm complexity has no impact on overall survival in people who receive 'no intervention'. The presence of a complex (non-infrarenal) AAA only affects the risk of perioperative mortality associated with EVAR.*
- *Age, sex and aneurysm size are important effect modifiers for post-perioperative (long-term) survival. The influence of each is informed by Cox regression models using EVAR-2 study data. These are applied to infrarenal and complex AAAs.*
- *New-generation EVAR devices and surgical techniques are neither significantly safer nor more effective than those used in the EVAR-2 trial.*
- *Resource use associated with the primary AAA repair procedure (for EVAR) can be characterised by EVAR-1 trial data in elective cases, rather the EVAR-2. The former is preferred because it reports its resource use data in much greater detail. For emergency EVAR, resource use data from the IMPROVE study are used, in the absence of an alternative source of data.*
- *There is no difference in the procedure cost between complex and infrarenal AAA repair using EVAR, such that the resource use data used in the model, informed by infrarenal aneurysms (EVAR-1 and IMPROVE), can be transferred to complex cases.*
  - *A complex EVAR device costs significantly more than a standard EVAR device.*

- *The decision to provide no intervention is associated with 1 additional outpatient attendance and, in 50% of patients, 1 additional CT scan. In emergency cases, offering no intervention is associated with no cost.*
- *After EVAR, patients are followed up by an outpatient consultation and CT scan within 2 months of the intervention, followed by annual outpatient consultations and ultrasound scans for 5 years. Patients whose aneurysm was not repaired are not followed up, unless their AAA ruptures.*
- *There is no difference in the long-term rate of reintervention procedures between elective and emergency cases. Once an emergency EVAR patient has survived the perioperative (30-day) period, their expected reintervention rate is the same as a person who had received elective EVAR.*
- *Similarly, there is no difference in the reintervention rates of complex and infrarenal AAA repairs with EVAR, owing to the lack of data regarding complex AAA repair.*
- *Graft-related reintervention procedures are captured by the model, and are categorised as either 'life-threatening' or 'serious (not life-threatening)'. People who experience 1 graft-related reintervention will, on average, experience more than 1 during their lifetime. The cost and health implications of the extra reintervention procedures are incurred at once, at the time of the first reintervention.*
- *Laparotomy-related procedures are not captured for this population, as they are more prevalent following OSR, which is not a suitable intervention for this subgroup.*
- *Patients with unruptured AAAs who receive no intervention are subject to an ongoing risk of their untreated aneurysm rupturing.*
- *A ruptured AAA requires emergency EVAR. The proportion of ruptures that reach a hospital to receive emergency EVAR is informed by the EVAR-2 trial data (the number of ruptures among untreated participants who received an intervention [11%]). This proportion of ruptures incur the cost and quality-of-life implications of a ruptured AAA repaired by EVAR. The remainder are assumed to die before emergency EVAR could be attempted.*
- *The impact of aneurysm repair and reintervention procedures on the patient's quality of life can be characterised by one-off 'QALY loss' decrements.*

HE.3 Original cost–utility model – results

HE.3.1 EVAR vs. OSR – 'fit for OSR' population – elective repair (unruptured)

HE.3.1.1 Infrarenal AAA

HE.3.1.1.1 Deterministic base case

The base-case, deterministic analysis found that OSR dominates EVAR for the repair of unruptured infrarenal aneurysms; that is, the total cost per patient associated with EVAR is higher, and it is expected to generate fewer QALYs per patient (Table HE44). At this level of incremental cost (£6,331 per patient), EVAR would need to generate 0.317 additional QALYs per patient to have an ICER of £20,000 per QALY gained. For both interventions, the primary procedure is the main contributor to total costs (Table HE45). This cost is higher for EVAR, which also has higher monitoring and graft-related reintervention costs, partly offset by fewer laparotomy-related complications. The accrual of undiscounted QALYs in each arm (Figure HE37) shows the small health gain associated with EVAR in the first 4 years of the model, with its superior perioperative survival and smaller impact on HRQL. Over time the superior post-perioperative survival of OSR patients causes a visible difference in cumulative QALYs.

Table HE44: Base case cost–utility model results – elective repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	*(£/QALY)*
OSR	£13,438	6.640			
EVAR	£19,770	6.480	£6,331	-0.160	Dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Table HE45: Components of total discounted costs – elective repair, infrarenal AAA

	Total discounted cost	
Cost component	**EVAR**	**OSR**
Primary procedure & stay	£13,239	£10,662
Post-repair monitoring	£1,317	£133
Graft-related complications	£4,719	£1,786
Other complications	£494	£857
Total	£19,770	£13,438

Key: EVAR, endovascular aneurysm repair; OSR, open surgical aneurysm repair.

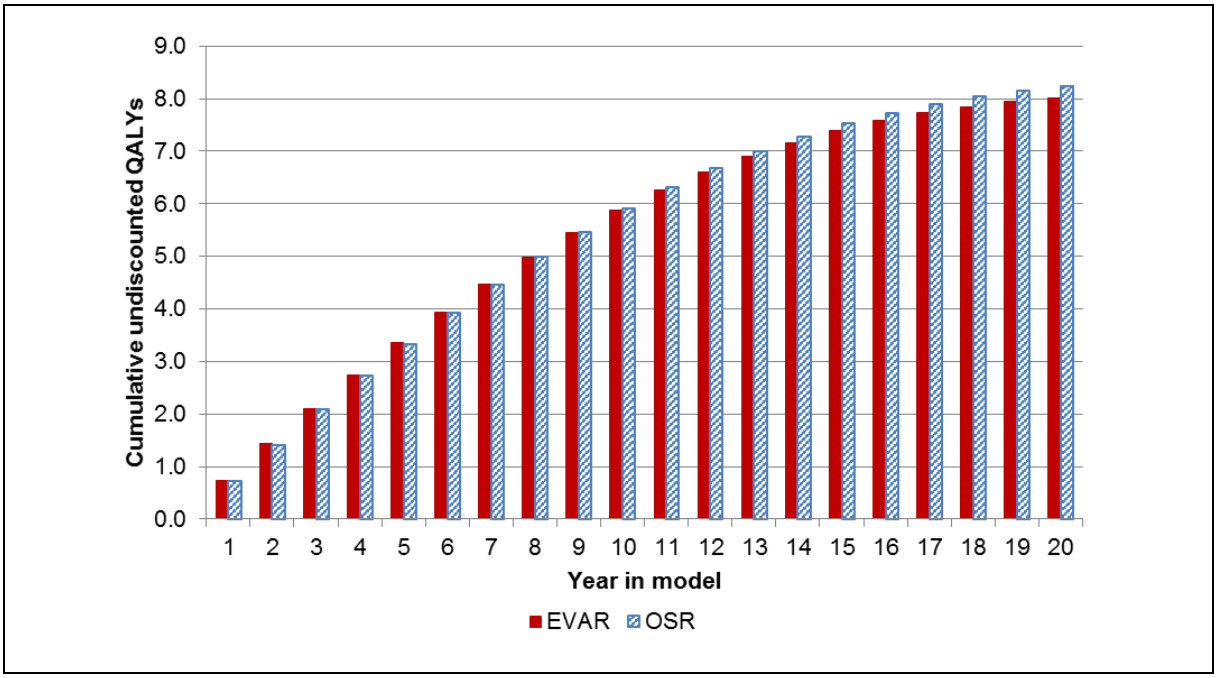


Figure HE37: Accrual of undiscounted QALYs over time – elective repair, infrarenal AAA

HE.3.1.1.2 Sensitivity analysis

The PSA results, simultaneously capturing parameter uncertainty, also find EVAR to be dominated. EVAR had an ICER of £20,000 or better in 0.1% of 5,000 probabilistic simulations (Figure HE38, Figure HE39). The total cost associated with EVAR was higher than that of OSR in 100% of model runs, and OSR dominated EVAR 86.4% of the time.

In one-way sensitivity analysis (Figure HE40), no individual model parameter, when varied between its plausible bounds, nor model scenario (e.g. including pulmonary complications), caused the cost-effectiveness conclusion to change; that is, the incremental net monetary benefit (INMB) with QALYs valued at £20,000 each favoured OSR in all cases. The base-case result was the most sensitive to variation in long-term survival differences. Even when the post-perioperative HR favours EVAR (0.976), instead of the base-case estimate in favour of OSR (1.089), the ICER for EVAR still exceeds £20,000 per QALY gained.

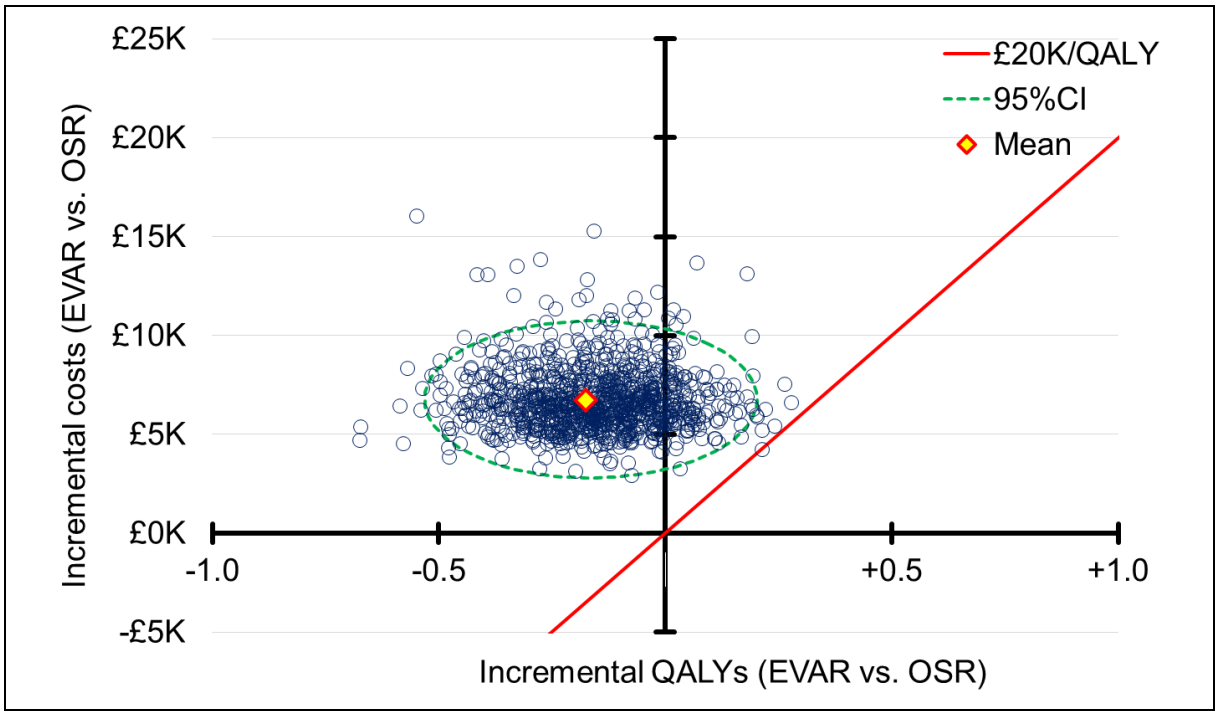


Figure HE38: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

The mean probabilistic results are £6,765 in incremental costs for EVAR, and -0.164 incremental QALYs for EVAR, such that OSR dominates EVAR.

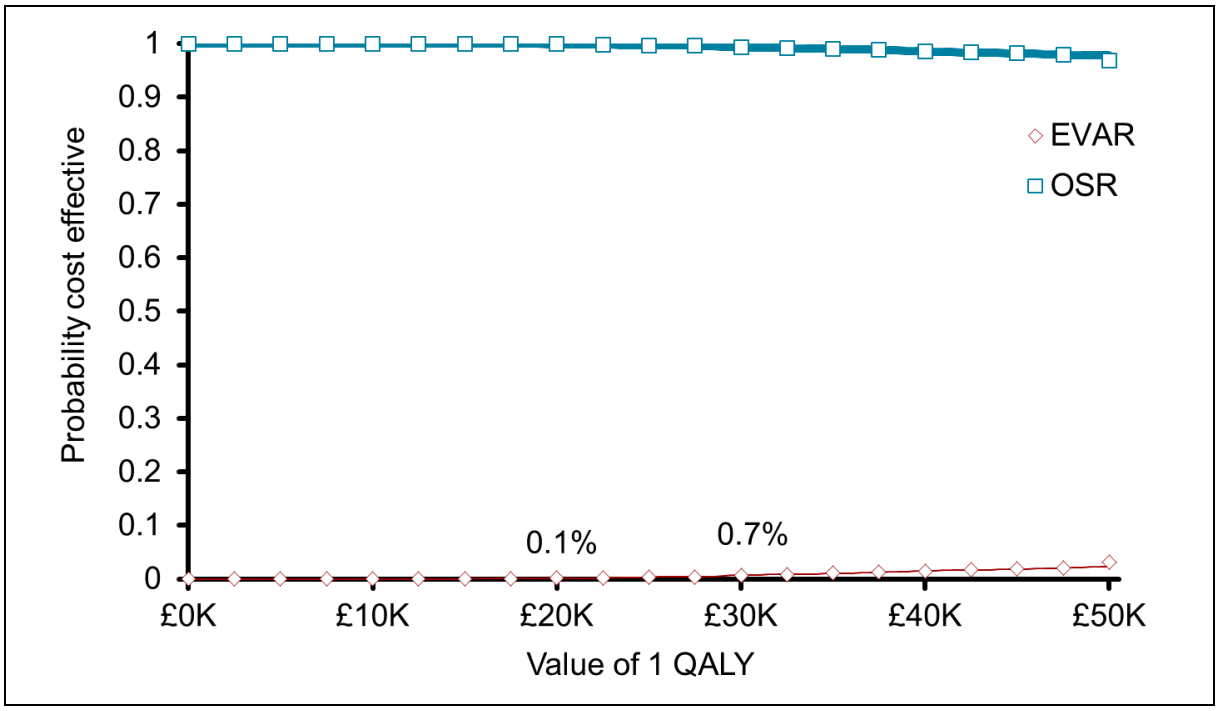
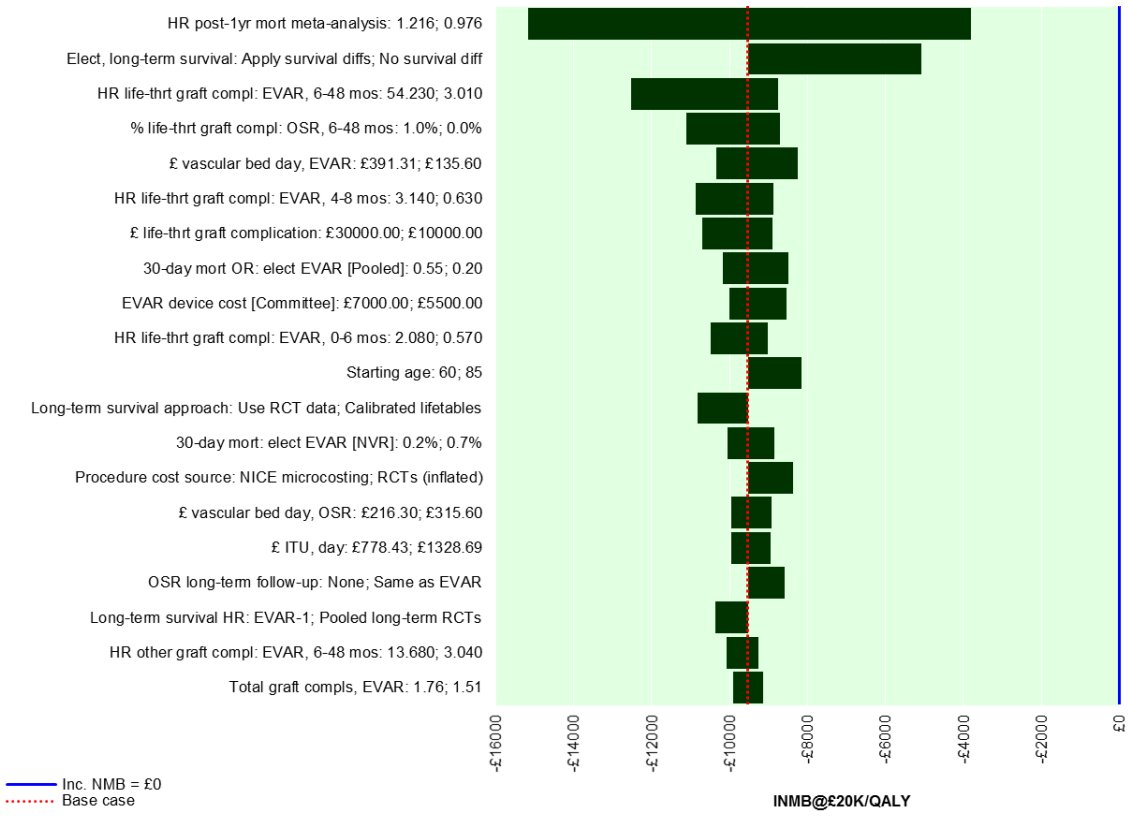


Figure HE39: Probabilistic sensitivity analysis (5,000 runs) – CEAC



Key: INMB, incremental net monetary benefit (at a value of £20,000 per QALY).

Figure HE40: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.1.1.3 Subgroup analyses

The majority of scenario analyses described in the methods section of this appendix have been captured in the univariate sensitivity analysis above. These can be identified where the INMB value only varies in one direction from the base-case value, reflecting that 1 scenario setting is used in the base-case analysis itself. Here, we present the results of some key scenarios in more detail, including different patient age, sex and aneurysm size profiles, which are perioperative and long-term survival effect modifiers.

Baseline age

In a cohort with the sex split and mean AAA diameter of the EVAR-1 trial (91% male, 9% female; 6.5 cm), age was not found to significantly influence cost-effectiveness conclusions (Figure HE41). At no baseline patient age, from 50 to 100 years, did the INMB for EVAR compared with OSR exceed £0; meaning the EVAR ICER was always worse than £20,000 per QALY gained.

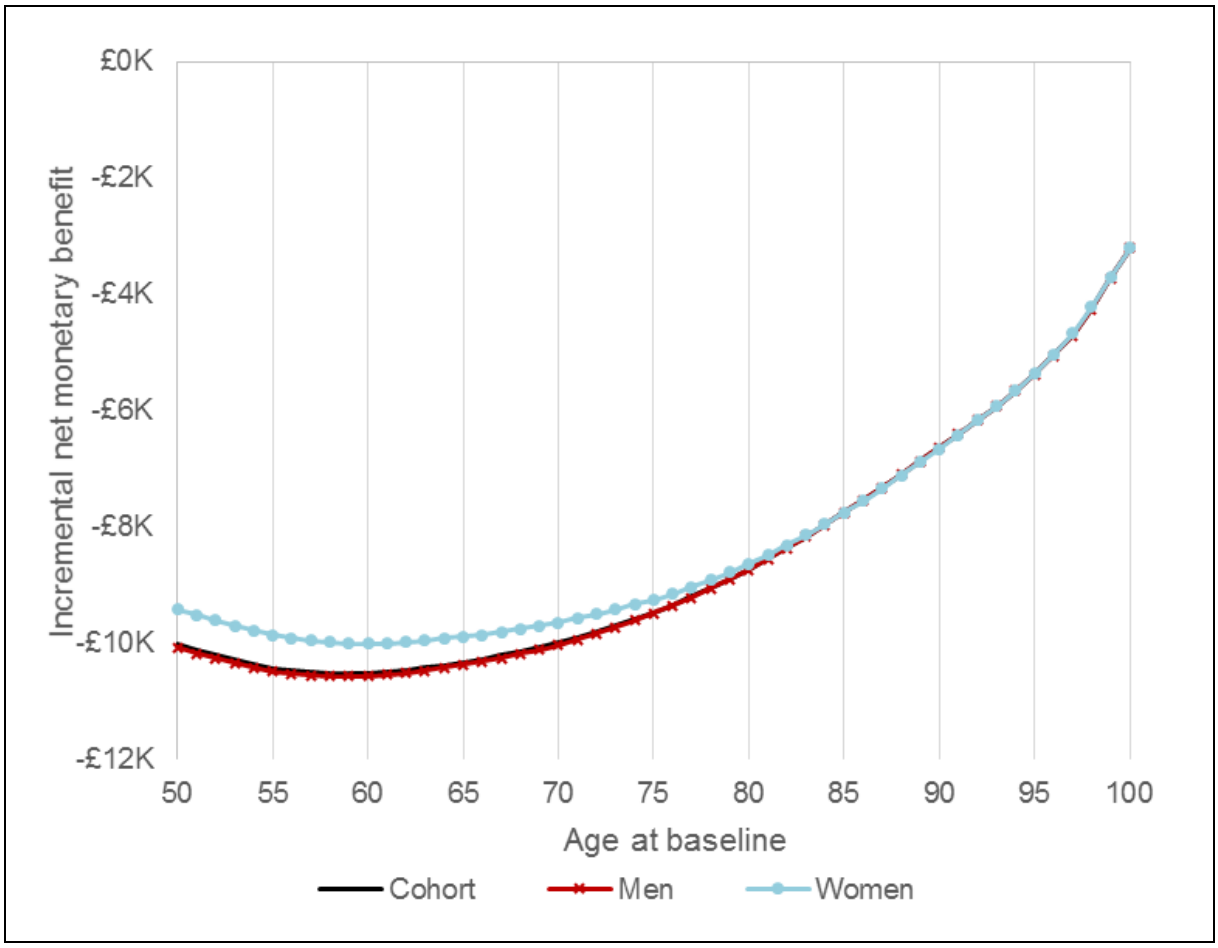


Figure HE41: INMB by age and sex – EVAR vs. OSR – elective repair, infrarenal AAA

Sex

The result above is not sensitive to the sex of the person with an AAA. In both men and women, EVAR is dominated by OSR at the mean EVAR-1 cohort age and aneurysm size. For both sexes, the ICER remains worse than £20,000 per QALY gained at all ages from 50 to 100, shown by the negative INMB of EVAR.

Aneurysm diameter

The base-case result is not sensitive to baseline AAA diameter (Figure HE42). At all pre-operative aneurysm sizes between 4 cm and 12 cm, elective repair using EVAR had an ICER worse than £20,000 per QALY gained compared with OSR.

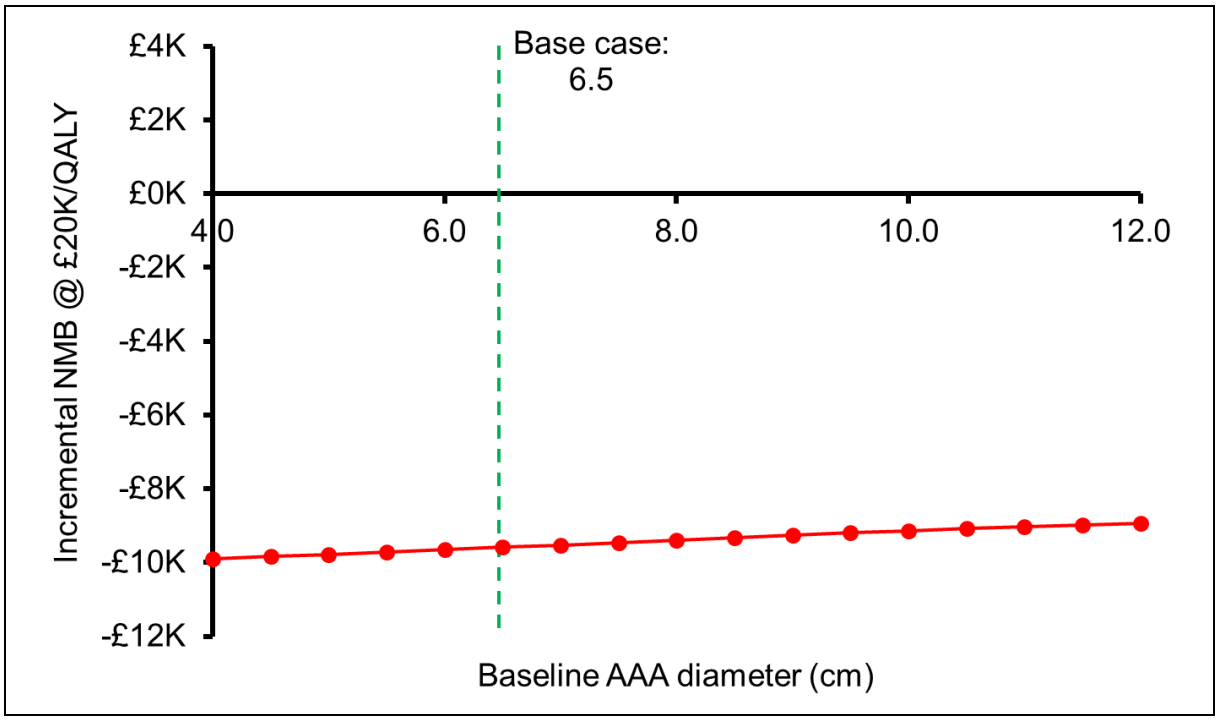


Figure HE42: INMB by aneurysm size – EVAR vs. OSR – elective repair, infrarenal AAA

HE.3.1.1.4 Scenario analyses

Perioperative mortality – alternative baseline values

As described in Section HE.2.2.3, our base-case analysis uses 30-day EVAR mortality rates from the UK National Vascular Registry to characterise baseline mortality rates. This provides a snapshot of outcomes associated with current UK practice of EVAR. We then applied the odds ratio from a Cochrane meta-analysis (Paravastu et al., 2014) to inform the relative perioperative mortality rate associated with OSR. Using the EVAR registry value was preferred by the guideline development committee, as the mortality rate (0.4%) was deemed to reflect its experience more closely than the OSR figure (3.0%). However, in these scenario analyses, we use the OSR registry figure (and apply the trial-based relative effects in reverse to obtain the EVAR mortality rate); and we use the EVAR-1 trial 30-day mortality rates (1.6% and 4.2%). Using these values from EVAR-1 means the analysis makes no use of the registry data.

In all scenarios, the difference in QALYs gets closer to zero, but incremental costs for EVAR remain at around £6,000 per patient, such that OSR continues to dominate EVAR (Table HE46).

Table HE46: Sensitivity analysis: baseline perioperative mortality – elective repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	Costs	QALYs	Costs	QALYs	*(£/QALY)*
Baseline perioperative mortality: OSR, UK registry (3.0%)					
OSR	£13,398	6.528			
EVAR	£19,747	6.443	£6,349	-0.084	dominated
Baseline perioperative mortality: EVAR, EVAR-1 study (1.6%)					
OSR	£13,355	6.407			
EVAR	£19,711	6.403	£6,356	-0.004	dominated
Baseline perioperative mortality: OSR, EVAR-1 study (4.2%)					
OSR	£13,370	6.448			
EVAR	£19,724	6.417	£6,354	-0.031	dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Perioperative mortality – threshold analysis

Varying the base-case perioperative mortality odds ratio (0.33 in favour of EVAR) from 0.05 (more favourable for EVAR) to 1.00 (no difference between EVAR and OSR) does not cause the ICER for EVAR to be better than £20,000 per QALY gained. In elective cases perioperative mortality rates are generally low, such that enough patients survive an OSR procedure to benefit from its superior long-term survival prospects to offset the perioperative gains for EVAR.

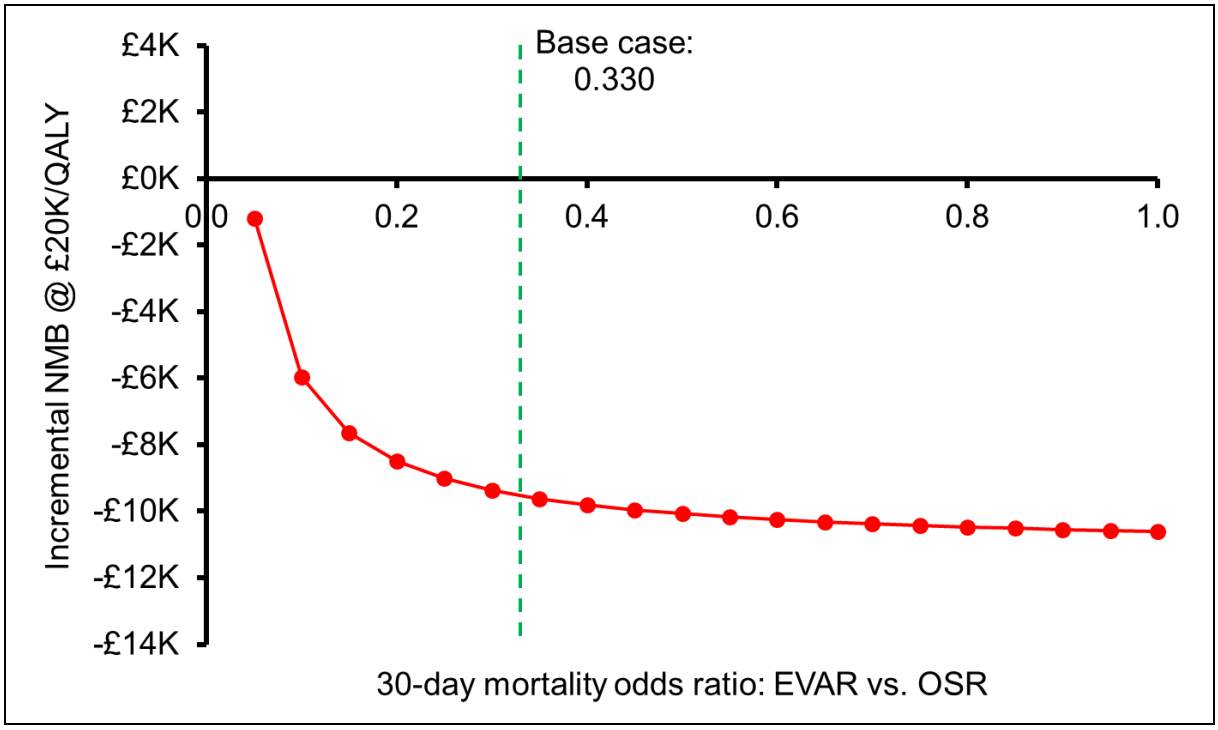


Figure HE43: INMB by perioperative EVAR mortality odds ratio – EVAR vs. OSR – elective repair, infrarenal AAA

Post-perioperative mortality – parametric survival curves

The use of parametric curves, fitted to the EVAR-1 study data, was not found to be among the most influential model inputs in univariate sensitivity analysis (see Figure HE53). However, in that analysis, only the preferred set of parametric curves was tested; namely the Gompertz models for both treatment arms. The cost–utility results using alternative curves, and using a common function with a treatment variable to distinguish between EVAR and OSR, are provided in Table HE47. None of these parametric model settings change the cost-effectiveness conclusion. The main effect of using them is to reduce the total number of discounted QALYs, largely due to the parametric curves being fitted to the EVAR-1 trial data directly, which enrolled in 1999 to 2003. In our base-case approach, calibrating general population mortality, we scale up the survival estimates using more recent UK life tables (2013-15).

Table HE47: Sensitivity analysis: parametric curves to model post-perioperative survival – elective repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
Separate models: both Gompertz					
OSR	£13,180	5.791			
EVAR	£19,276	5.555	£6,095	-0.236	dominated
Separate models: both gamma					
OSR	£13,165	5.771			
EVAR	£19,228	5.472	£6,064	-0.298	dominated
Common model with treatment variable: Gompertz					
OSR	£13,181	5.780			
EVAR	£19,262	5.555	£6,081	-0.225	dominated
Common model with treatment variable: gamma					
OSR	£13,164	5.746			
EVAR	£19,216	5.474	£6,052	-0.272	dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Post-perioperative mortality – threshold analysis

In our base-case analysis, the difference in post-perioperative mortality between EVAR and OSR is informed by the meta-analysis of long-term survival from 3 RCTs (EVAR-1, DREAM and OVER; HR = 1.089 in favour of OSR; see HE.2.2.6.1). Figure HE44 shows the impact of varying this parameter over its 95% confidence interval. It shows that the ICER for EVAR remains worse than £20,000 per QALY gained even at values of HR that are less than 1, denoting a lower long-term mortality hazard after EVAR. The EVAR ICER is better than £20,000 when the post-perioperative mortality HR takes a value of 0.906 (in favour of EVAR).

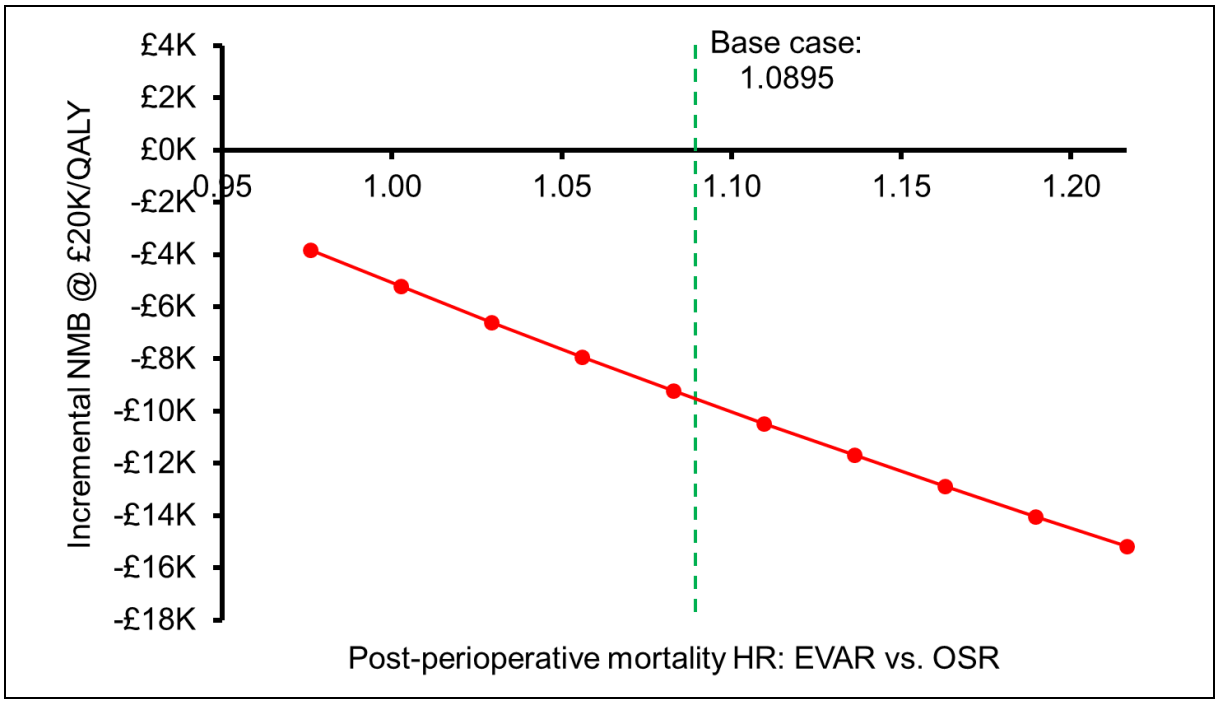


Figure HE44: INMB by post-perioperative EVAR mortality hazard ratio – EVAR vs. OSR – elective repair, infrarenal AAA

Post-perioperative mortality – identifying a less healthy population

We conducted a further sensitivity analysis, in which there was no difference in post-perioperative mortality rates between EVAR and OSR for 8 years. After this point, the HR for EVAR derived from the EVAR-1 study data was applied (1.297), meaning EVAR patients who survive for 8 years have a higher mortality hazard than OSR patients thereafter. Under this scenario, we ran a threshold analysis on the HR used to calibrate general UK population mortality rates to match the EVAR-1 study population. In the base-case analysis this HR is 1.080, indicating that after AAA repair, EVAR-1 study participants have a slightly higher mortality hazard than the age-matched general public. The purpose of varying this HR was to explore a circumstance where the patient is only *just* considered to be fit enough for open surgery to be considered. This subpopulation would be at the less-fit end of the spectrum of EVAR-1 study participants. Specifically, we wanted to identify whether EVAR may be cost-effective for patients who are unlikely to live for 8 years, and would therefore be unlikely to experience any long-term survival benefit from OSR. Here, you would expect the lower perioperative mortality of EVAR to make it the most effective option.

Figure HE45 shows the INMB results for EVAR compared with OSR, at a value of £20,000 per QALY, for all calibration HRs from 1 to 15. As the value of HR increases, the patient being treated becomes less healthy relative to the general population, and so less likely to live for 8 or more post-perioperative years. EVAR produces a negative INMB at all values of HR, meaning its ICER is always worse than £20,000 per QALY gained. The cost-utility results when HR = 15, where the patient has a mortality hazard 15-times that of the general population even after successful AAA repair, are presented in Table HE48. Here, less than 1% of OSR patients survive for long enough to experience its superior long-term HR beyond 8 years. As a result, the perioperative survival benefit of EVAR does lead to a discounted QALY gain overall (+0.022 per patient). Total costs for EVAR are lower than before, as the higher underlying mortality rate means more patients die before completing their follow-up schedule or requiring reintervention. However it still incurs a higher total cost than OSR, producing an ICER of over £200,000 per QALY gained.

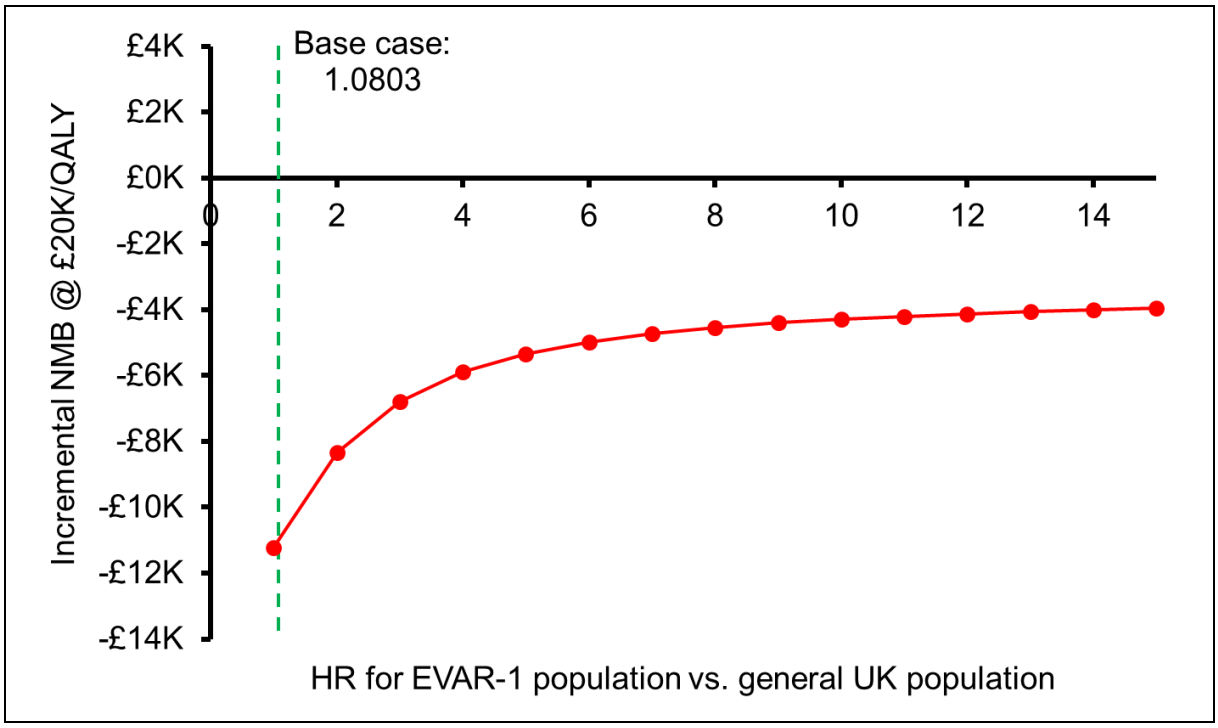


Figure HE45: INMB by post-perioperative general mortality calibration hazard ratio – EVAR vs. OSR – elective repair, infrarenal AAA

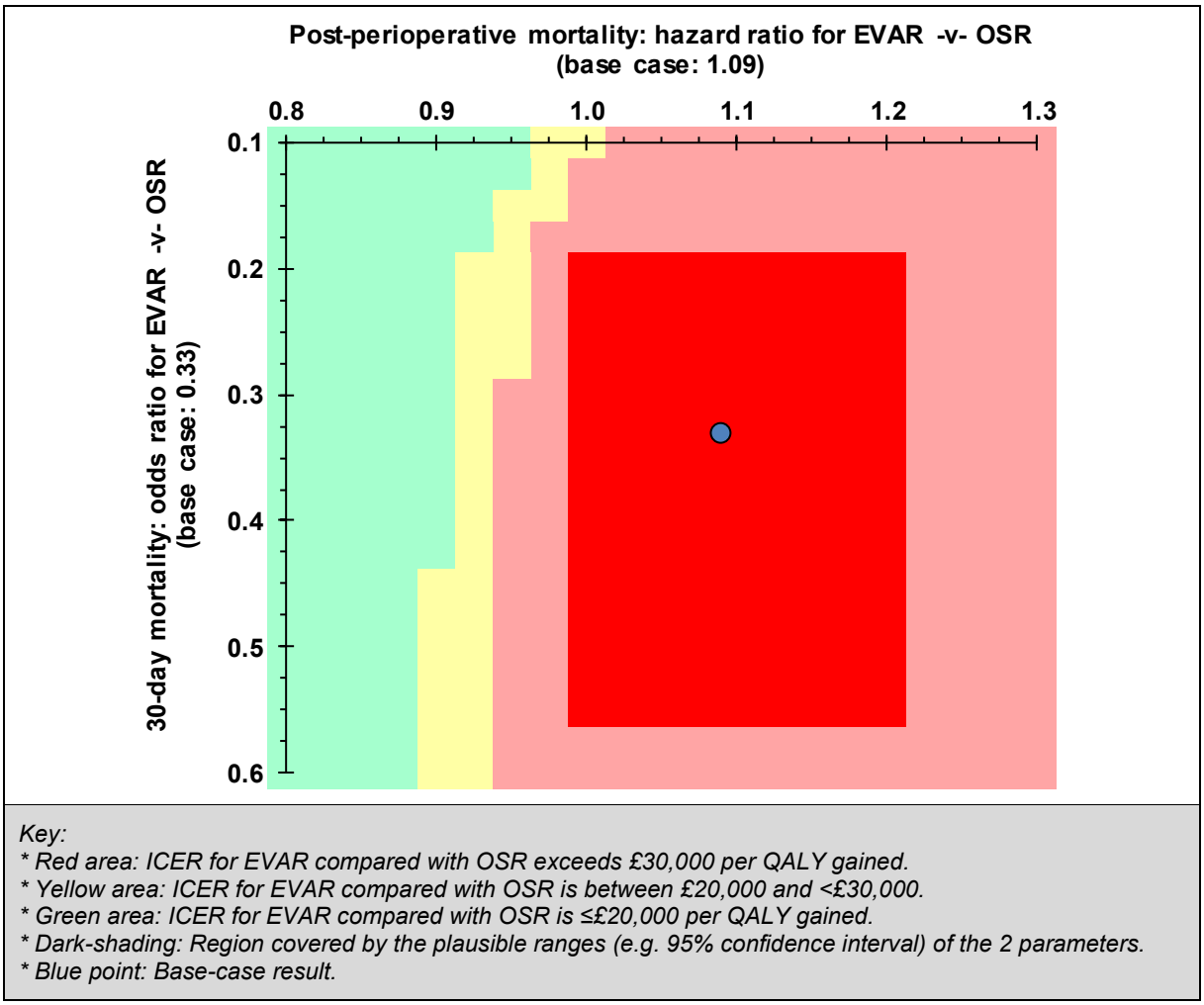
Table HE48: Sensitivity analysis: general mortality calibration HR = 15; no difference in post-perioperative survival for 8 years (EVAR HR = 1.297 thereafter) – elective repair, infrarenal AAA

	Total (discounted)		*Incremental*		
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***ICER***
OSR	£12,062	1.505			
EVAR	£16,453	1.526	£4,390	0.022	£201,005

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Two-way analysis: Relative effectiveness in 30-day and post-perioperative mortality

In a two-way analysis, we explored the cost effectiveness of EVAR when both its 30-day mortality relative effectiveness (OR) and post-perioperative mortality relative effectiveness (HR) were varied. The results of this two-way analysis (Figure HE46) indicate that we can be highly certain that no plausible level of simultaneous variation in these parameters will cause the EVAR ICER to be £20,000 or better. All ICERs in the region defined by their 95% confidence intervals has an ICER in excess of £30,000 per QALY gained. Reducing this ICER is highly dependent on the post-perioperative mortality HR; though to be £20,000 or better, this HR needs to take a value of less than 1, indicating superior long-term survival after EVAR. This is unlikely on the basis of the available long-term evidence.



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE46: Two-way sensitivity analysis – 30-day mortality vs. post-perioperative mortality – elective repair, infrarenal AAA

EVAR device cost

Our base-case unit cost per EVAR device was sourced from members of the guideline development committee. We explored variation in the cost of EVAR in a threshold analysis, and found that its ICER compared with OSR remains worse than £20,000 per QALY gained even if the cost is £0 (Figure HE47). With an EVAR device cost of £0, EVAR is no longer dominated by OSR because it now has a lower total cost per patient (Table HE49). However, the additional 0.160 additional QALYs associated with OSR can be achieved at an ICER of £90 per QALY gained over EVAR, which is significantly below a threshold ICER of £20,000. Hence, OSR remains strongly favoured in this scenario.

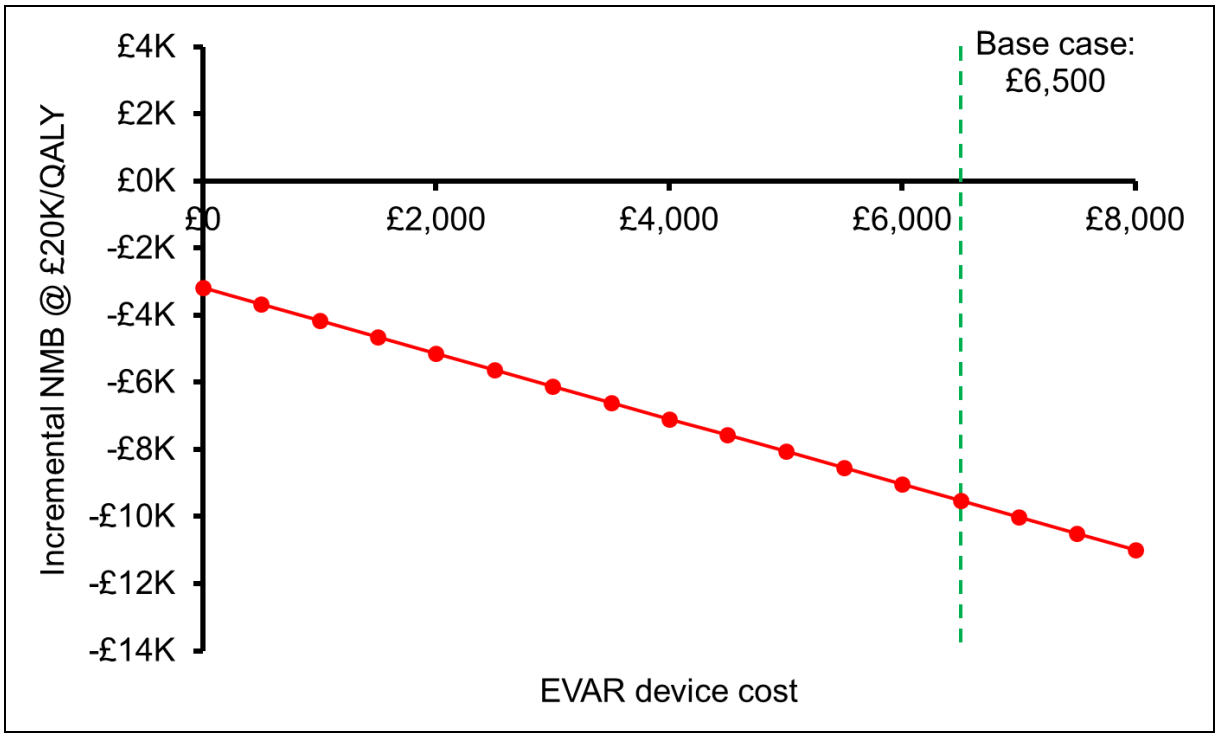


Figure HE47: INMB by EVAR device cost – EVAR vs. OSR – elective repair, infrarenal AAA

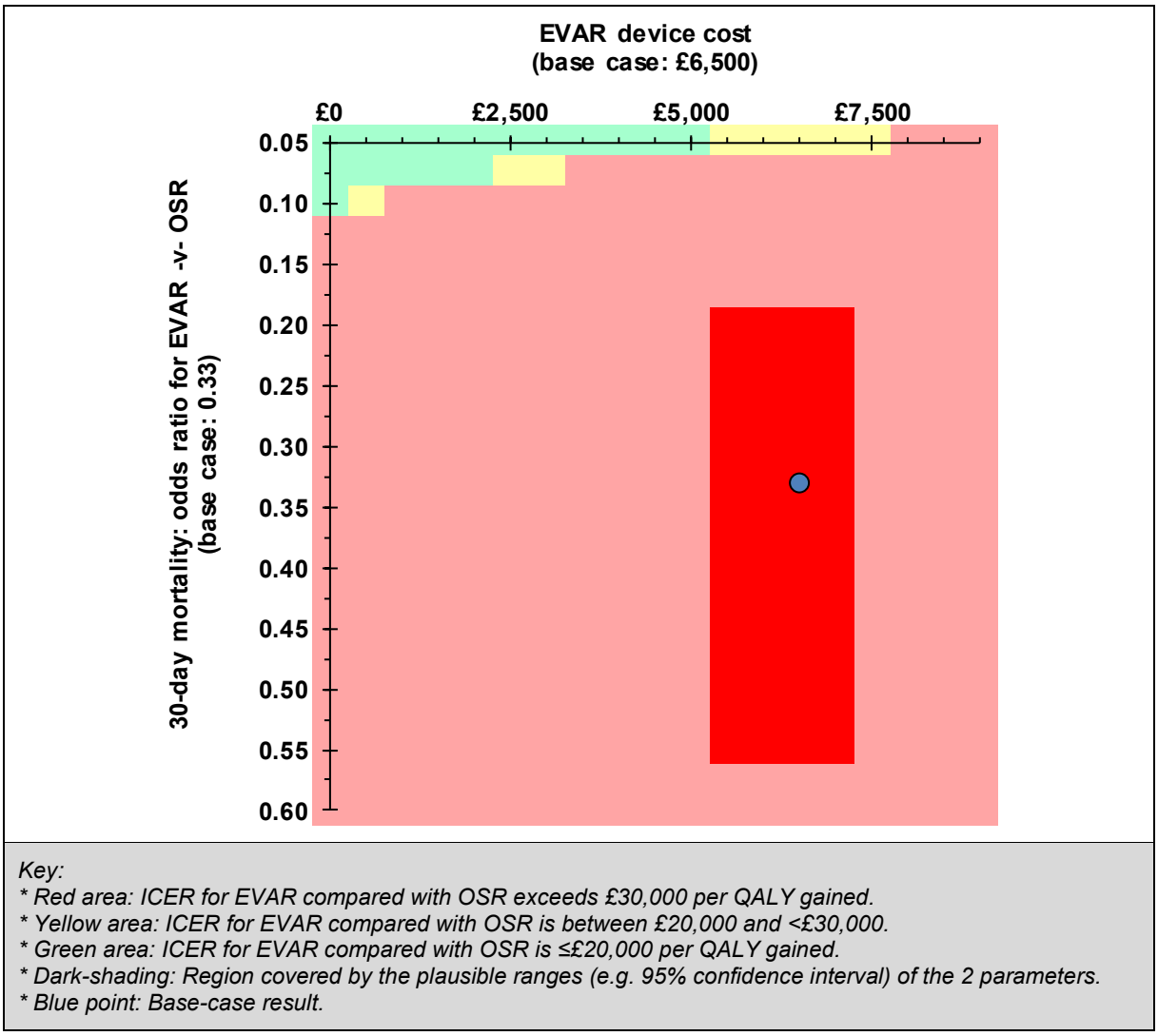
Table HE49: Sensitivity analysis: EVAR device cost = £0 – elective repair, infrarenal AAA

	Total (discounted)		*Incremental*		
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***ICER***
EVAR	£13,424	6.480			
OSR	£13,438	6.640	£14	0.160	£90

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Two-way analysis: EVAR device cost and perioperative mortality

In a two-way sensitivity analysis, we varied both the cost per EVAR device and the 30-day mortality odds ratio to extreme values. The results (Figure HE48) show that the EVAR exceeds £30,000 per QALY gained at almost all combinations of these parameters. The ICER is between £20,000 and £30,000 when the odds ratio is very low (that is, much better for EVAR), though the EVAR device costs also needs to be lower for the ICER to be better than £20,000 per QALY gained (to a cost of £5,250 or less). The location of the plausible range for these inputs, denoted by the dark-shaded region, indicates we can be relatively certain that no combination of these 2 inputs is likely to achieve an ICER that is better than £20,000 per QALY gained.

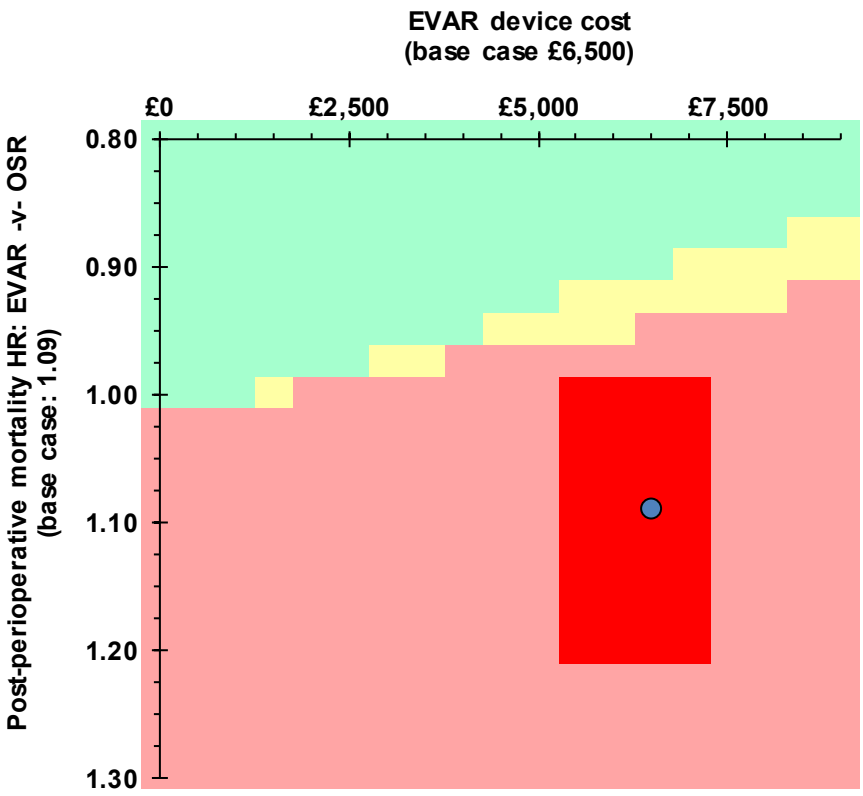


Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE48: Two-way sensitivity analysis – EVAR cost vs. 30-day mortality odds ratio – elective repair, infrarenal AAA

Two-way analysis: EVAR device cost and long-term mortality

In another two-way analysis, we explored the costeffectiveness of EVAR when its post-perioperative mortality relative effectiveness was varied alongside the device cost. Here, like before, all ICERs within the region of plausible values exceed £30,000 per QALY gained (Figure HE49). For the ICER to be better than £20,000 per QALY gained, the long-term mortality HR needs to be 1 or less (unless the device cost is effectively £0). However, even at some HRs less than 1 (that is, better survival following EVAR), the ICER exceeds £20,000 unless device cost is also lower than its base-case value.



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE49: Two-way sensitivity analysis – EVAR cost vs. post-perioperative mortality hazard ratio – elective repair, infrarenal AAA

Reintervention rates

A potential limitation of our analysis is its use of data from the EVAR trials for key model inputs, given that they recruited between 1999 and 2004. The expert guideline development committee advised that they do not believe more modern EVAR devices are significantly safer or more effective than the generation of EVAR devices used in the trials (Hammond et al., 2016). However, to simulate a model scenario for this, we conducted an extreme value sensitivity analysis in which all graft-related complications were omitted from the model. A second level of this scenario set the post-perioperative mortality HR between EVAR and OSR to a value of 1, denoting no difference in long-term survival prospects. In the first scenario, OSR still dominates EVAR (Table HE50). In the second, more extreme scenario, with no graft-related complications and no long-term OSR survival benefit, EVAR generates 0.072 incremental QALYs per patient; however the ICER remains far in excess of £20,000.

Table HE50: Sensitivity analysis: newer EVAR devices – elective repair, infrarenal AAA

Strategy	Total (discounted)		Incremental		ICER (£/QALY)
	Costs	QALYs	Costs	QALYs	
No graft-related reintervention procedures					
OSR	£11,352	6.650			
EVAR	£14,962	6.496	£3,610	-0.154	dominated
No graft-related reintervention procedures, equal post-perioperative mortality rates					
OSR	£11,352	6.650			
EVAR	£14,982	6.722	£3,630	0.072	£50,762

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

HE.3.1.2 Complex AAA

HE.3.1.2.1 Deterministic base case

The base-case, deterministic analysis found that EVAR is associated with an expected QALY gain (+0.166) over OSR. The absolute difference in perioperative survival between EVAR and OSR is larger here than in infrarenal AAAs, such that the lower post-perioperative mortality rate among OSR patients is never enough to offset the initial loss compared with EVAR (see Figure HE18), and this is evident in terms of total undiscounted QALYs (Figure HE50). However, in this population, the total cost of EVAR (£29,139) is substantially higher than for infrarenal AAAs (£19,770), mainly due to the increased cost of bespoke EVAR devices required for complex aneurysms. This leads to an incremental (discounted) cost of £15,933 per patient compared with OSR. The resulting ICER is £95,815 per QALY gained. At this level of incremental cost, complex EVAR would need to generate 0.797 additional QALYs per patient to have an ICER of £20,000 per QALY gained.

Table HE51: Base case cost–utility model results – elective repair, complex AAA

Strategy	Total (discounted)		Incremental		ICER (£/QALY)
	Costs	QALYs	Costs	QALYs	
OSR	£13,206	6.033			
EVAR	£29,139	6.199	£15,933	0.166	£95,815

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Table HE52: Components of total discounted costs – elective repair, complex AAA

Cost component	Total discounted cost	
	EVAR	OSR
Primary procedure & stay	£22,583	£10,662
Post-repair monitoring	£1,242	£121
Graft-related complications	£4,834	£1,679
Other complications	£481	£745
Total	**£29,139**	**£13,206**

Key: EVAR, endovascular aneurysm repair; OSR, open surgical aneurysm repair.

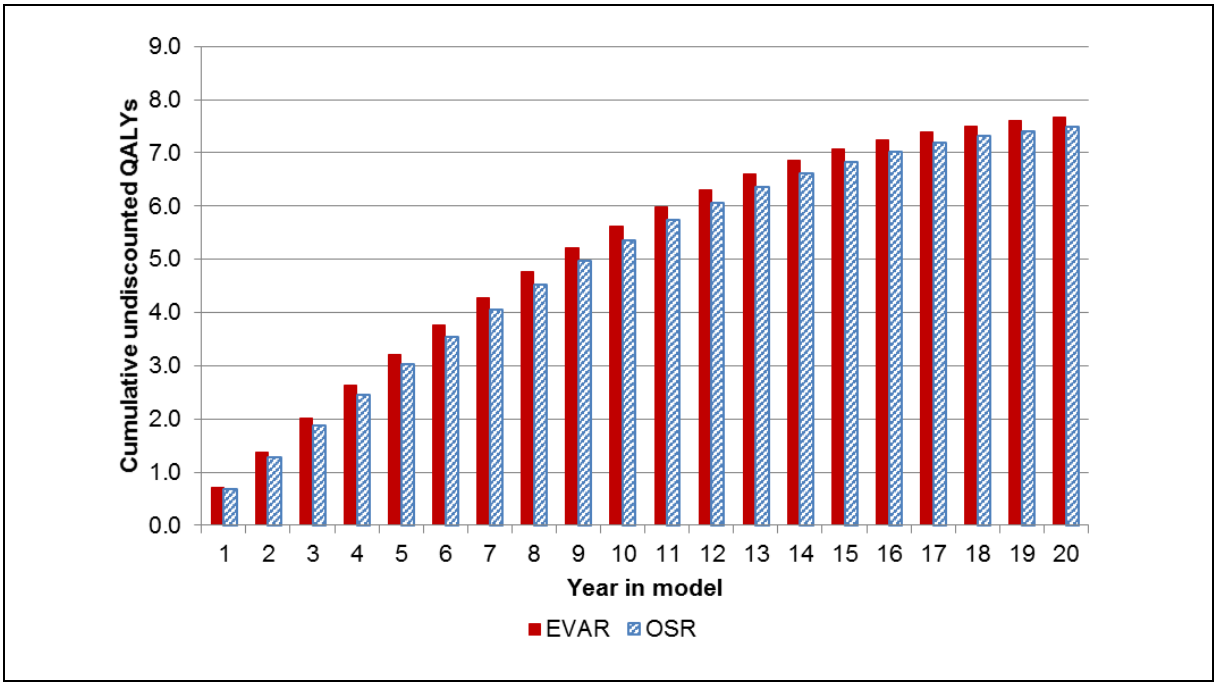


Figure HE50: Accrual of undiscounted QALYs over time – elective repair, complex AAA

HE.3.1.2.2 Sensitivity analysis

The probabilistic ICER for EVAR is £85,693, with 0.9% of 5,000 simulations predicting the ICER to be £20,000 or better (Figure HE51, Figure HE52).

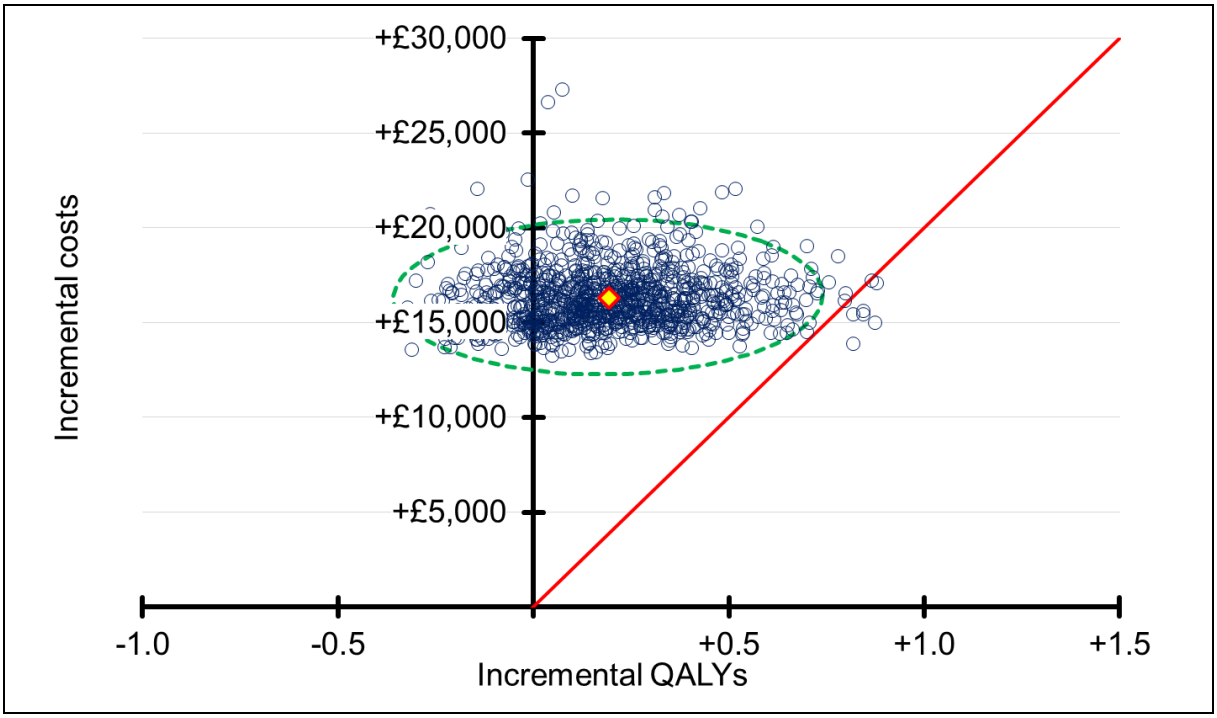


Figure HE51: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

The mean probabilistic results are £16,354 in incremental costs for EVAR, and 0.191 incremental QALYs for EVAR, with an ICER of £85,693 per QALY gained.

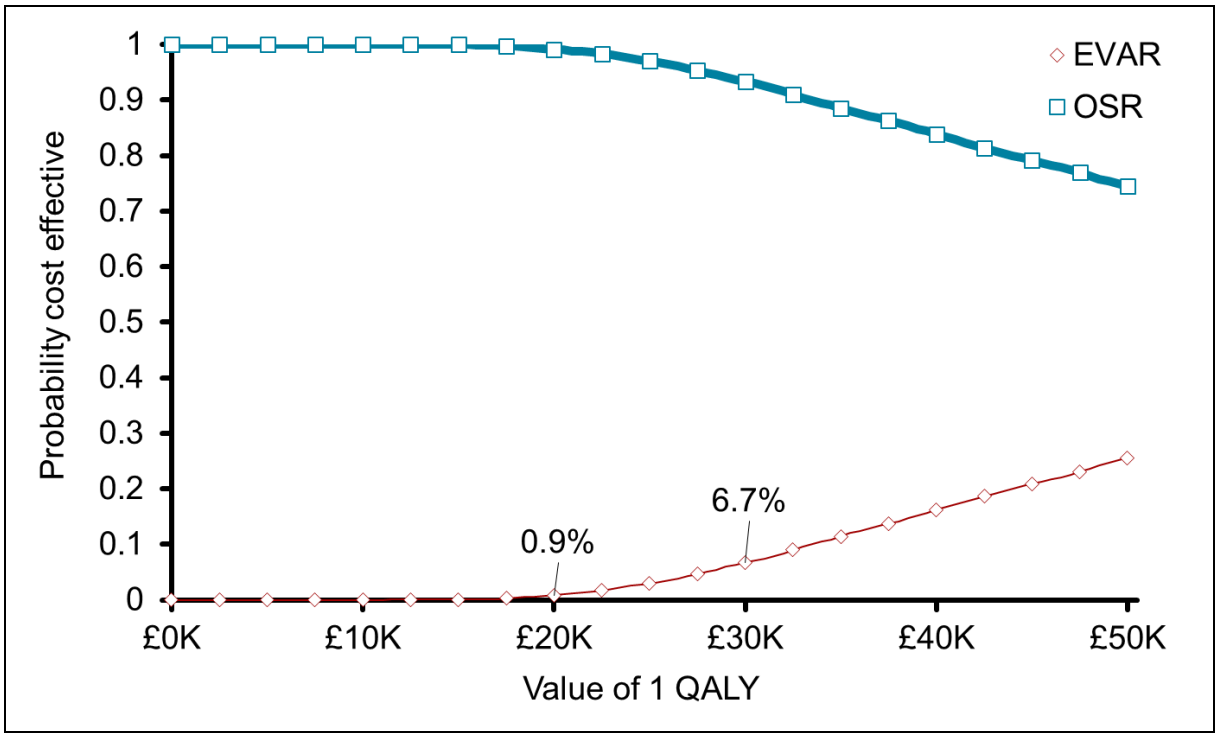
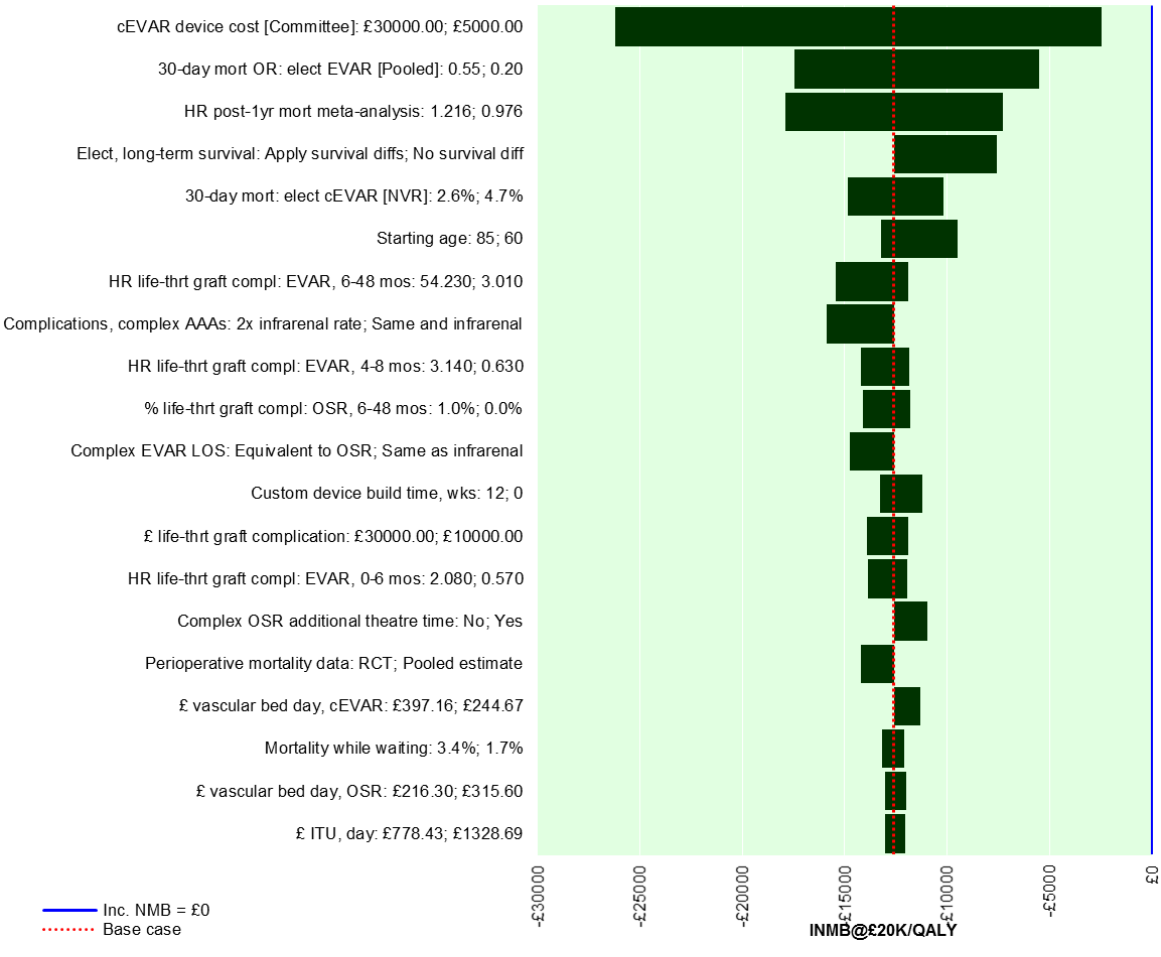


Figure HE52: Probabilistic sensitivity analysis (5,000 runs) – CEAC

In deterministic sensitivity analysis, no individual model parameter, when varied between its plausible bounds, nor model scenario, caused the cost-effectiveness conclusion to change. The base-case result was the most sensitive to extreme variation in the uncertain cost of complex EVAR devices, and to differences in perioperative and long-term survival rates, but none of these caused the EVAR ICER to be better than £20,000 per QALY gained.



Key: INMB, incremental net monetary benefit (at a value of £20,000 per QALY).

Figure HE53: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.1.2.3 Subgroup analysis

Baseline age

In a cohort with the sex split and mean AAA diameter of the EVAR-1 trial (91% male, 9% female; 6.5 cm), age was not found to significantly influence cost-effectiveness conclusions (Figure HE54). At no baseline patient age, from 50 to 100 years, did the INMB for EVAR compared with OSR exceed £0; meaning the EVAR ICER was always worse than £20,000 per QALY gained.

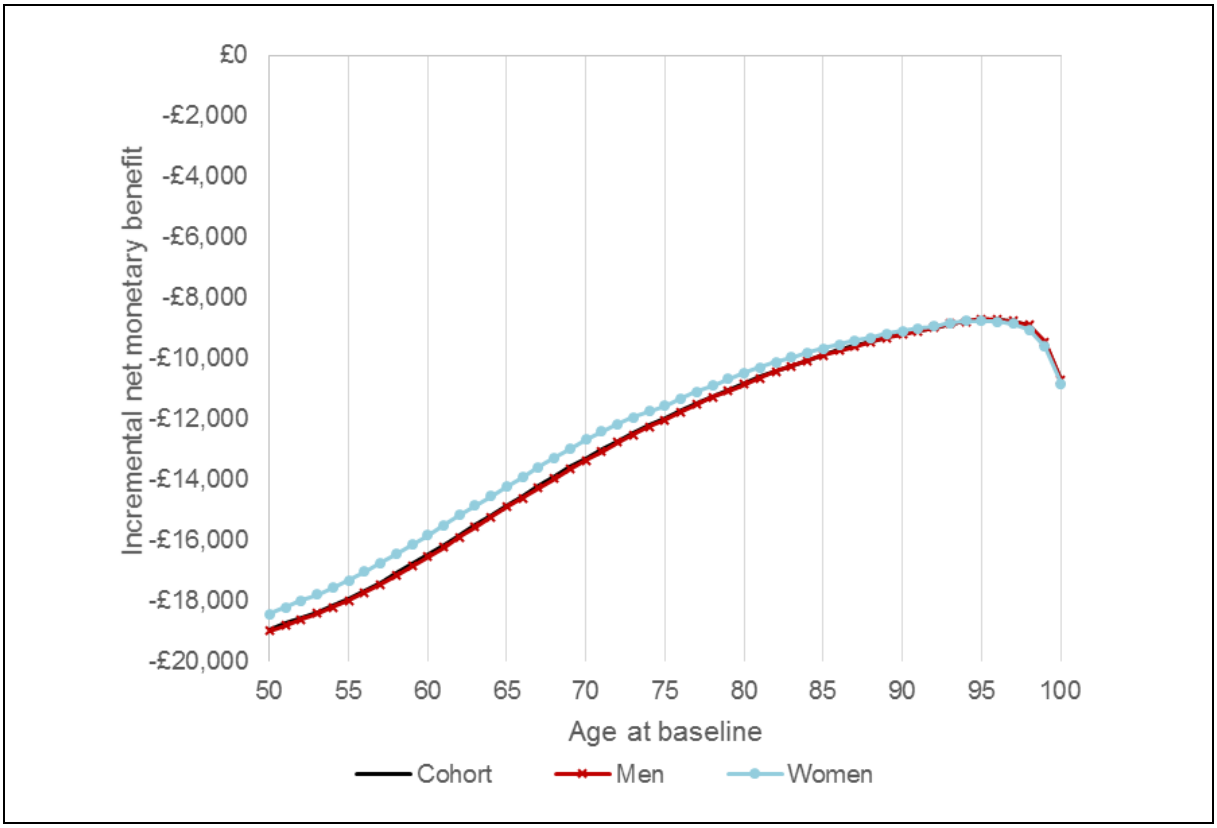


Figure HE54: INMB by age and sex – complex EVAR vs. OSR – elective repair, complex AAA

Sex

The result above is not sensitive to the sex of the person with an AAA. In men, at the mean EVAR-1 cohort age and aneurysm size, complex EVAR has an ICER of £86,664 per QALY gained compared with OSR. In women, the equivalent ICER is £74,401. Note that these are both lower than the mean deterministic ICER due to the use of perioperative and post-perioperative survival modifiers (with these, the overall cohort ICER becomes £85,486). For both sexes, the ICER remains worse than £20,000 per QALY gained at all ages from 50 to 100, shown by the negative INMB of EVAR.

Aneurysm diameter

Like in the case of infrarenal AAAs, the base-case result elective complex AAA repair is not sensitive to baseline AAA diameter. The ICER for complex EVAR, compared with OSR, varied from £135,736 per QALY gained in 4 cm aneurysms to £70,976 in 12 cm aneurysms. The ICER improves in larger aneurysms because they have a higher long-term, post-perioperative mortality hazard (HR = 1.087 per cm), meaning fewer patients survive for long enough to experience the survival benefit associated with OSR. Despite this, the high cost of complex EVAR means it still does not represent value for money compared with OSR in the elective setting.

HE.3.1.2.4 Scenario analysis

Perioperative mortality – alternative baseline values

As described in Section HE.2.2.3, our base-case analysis uses 30-day EVAR mortality rates from the UK National Vascular Registry to characterised baseline mortality rates. We apply the odds ratio from a Cochrane meta-analysis (Paravastu et al., 2014) to inform the relative

perioperative mortality rate associated with OSR, implicitly assuming these relative effect data are transferable to complex aneurysm repair. Using the EVAR registry value was preferred by the guideline development committee, as the mortality rate (3.6%) was deemed to reflect is experience more closely than the OSR figure (19.6%). The committee suggested that NVR data are likely to be subject to substantial selection and reporting biases, with EVAR repairs reported as complex cases likely to be inherently less complex than open repairs reported as complex. For example, AAAs with a short infrarenal 'neck' would be considered routine if addressed with open surgery, whereas the same anatomy would render a case 'complex' for EVAR, as it would be outside the terms of the devices' IFUs.

Despite the committee's misgivings about its accuracy, we examined the impact of using the OSR registry figure for our baseline mortality estimate, applying the trial-based relative effects in reverse to obtain a mortality rate for EVAR (7.4%). The resulting 30-day mortality estimates are significantly higher than when the EVAR registry data are used as baseline data. The committee advised that this may be due to the non-randomised nature of the registry data, with OSR cases recorded as "complex" being inherently *more complex* than EVAR cases recorded as "complex" (because open surgery is not made significantly more complicated by the presence of a complex aneurysm).

In this scenario, the deterministic ICER falls from a base-case value of £95,815 per QALY gained to £28,988 (for EVAR compared with OSR). This is a large improvement in EVAR cost-effectiveness, driven by +0.550 incremental QALYs, compared with +0.166 in the base-case analysis. Even so, the ICER remains higher than £20,000 per QALY gained. To reach this level, complex EVAR would need to generate +0.797 incremental QALYs per patient.

Table HE53: Sensitivity analysis: baseline perioperative mortality – elective repair, complex AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	*(£/QALY)*
Baseline perioperative mortality: complex OSR, UK registry (19.6%)					
OSR	£12,988	5.412			
EVAR	£28,926	5.962	£15,939	0.550	£28,988

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Perioperative mortality – threshold analysis

Varying the base-case perioperative mortality odds ratio (0.33 in favour of EVAR, derived from trials in infrarenal AAAs) from 0.05 to 1.00 shows that the base-case ICER, using EVAR registry data for baseline mortality estimates, is sensitive to extreme values of this input (Figure HE55). If the odds ratio takes a value of 0.14, the 30-day mortality rate for OSR becomes 20.9%, while the EVAR rate remains 3.6%. Here, the ICER for EVAR falls to £18,554 per QALY gained over OSR. However, this odds ratio represents an extreme value because: (1) it lies outside the bounds of the point estimate's 95% confidence interval (0.20 and 0.55); and (2) it was derived from trials looking at infrarenal aneurysms, whereas the committee advised that the procedure complexity of EVAR is likely to be influenced more than OSR by the presence of a complex aneurysm. As such, it is likely that an equivalent odds ratio from RCTs in complex aneurysms would be higher than the base-case figure of 0.33, rather than lower.

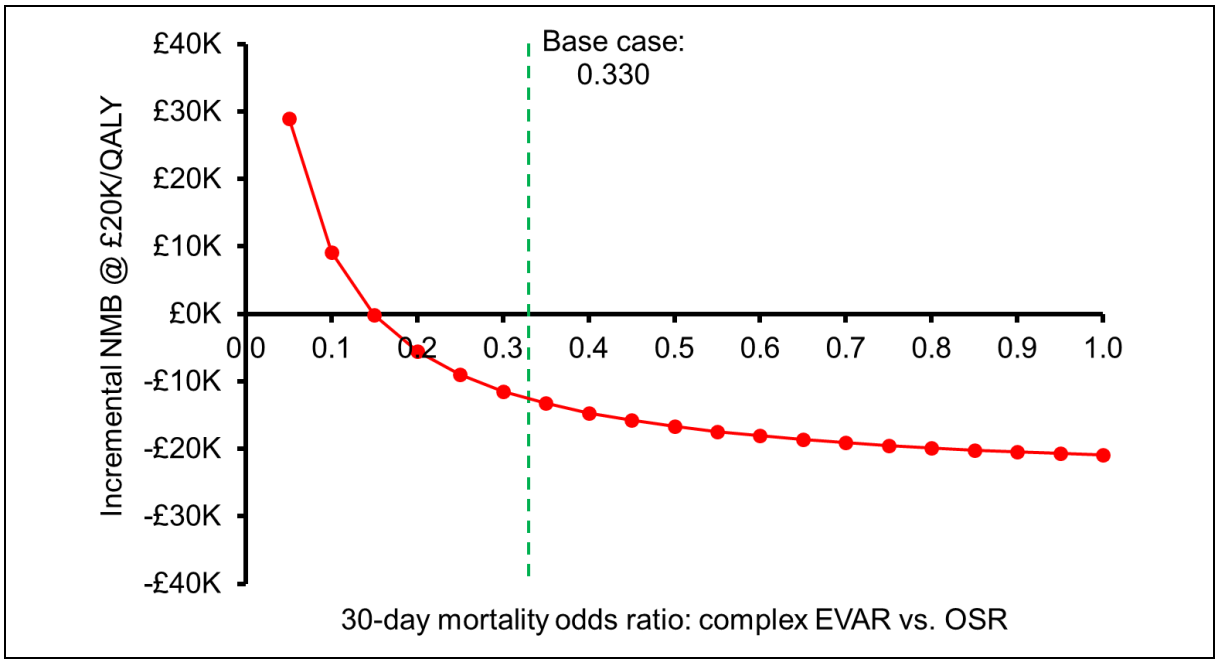


Figure HE55: INMB by perioperative EVAR mortality odds ratio – complex EVAR vs. OSR – elective repair, complex AAA

Post-perioperative mortality – parametric survival curves

We explored the use of parametric survival functions to characterise post-perioperative survival in people following the elective repair of an unruptured complex AAA, using the curves fitted to EVAR-1 survival data (Figure HE09 & Figure HE10). None of these parametric model specifications cause a change in the base-case cost-effectiveness result for this population, worsening the cost-effectiveness of complex EVAR (Table HE54). As before, the only notable effect is to reduce the total number of discounted QALYs, owing to the recruitment period of the EVAR-1 trial (1999 to 2004).

Table HE54: Sensitivity analysis: parametric curves to model post-perioperative survival – complex repair, complex AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
Separate models: both Gompertz					
OSR	£12,996	5.261			
EVAR	£28,721	5.371	£15,725	0.111	£142,274
Separate models: both gamma					
OSR	£12,992	5.242			
EVAR	£28,678	5.294	£15,686	0.051	£306,052
Common model with treatment variable: Gompertz					
OSR	£12,993	5.251			
EVAR	£28,708	5.371	£15,715	0.121	£130,043
Common model with treatment variable: gamma					
OSR	£12,986	5.220			
EVAR	£28,667	5.295	£15,681	0.075	£208,592

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Post-perioperative mortality – threshold analysis

In our base-case analysis, the difference in post-perioperative mortality between complex EVAR and OSR is informed by the same meta-analysis of long-term survival used for the infrarenal AAA population: HR = 1.089 in favour of OSR. The ICER for EVAR remains worse than £20,000 per QALY gained if this difference is eradicated (HR = 1), and even at values of HR that are less than 1, denoting a better long-term survival after EVAR. The EVAR ICER is better than £20,000 when the post-perioperative mortality HR takes a value of 0.841 (favouring EVAR).

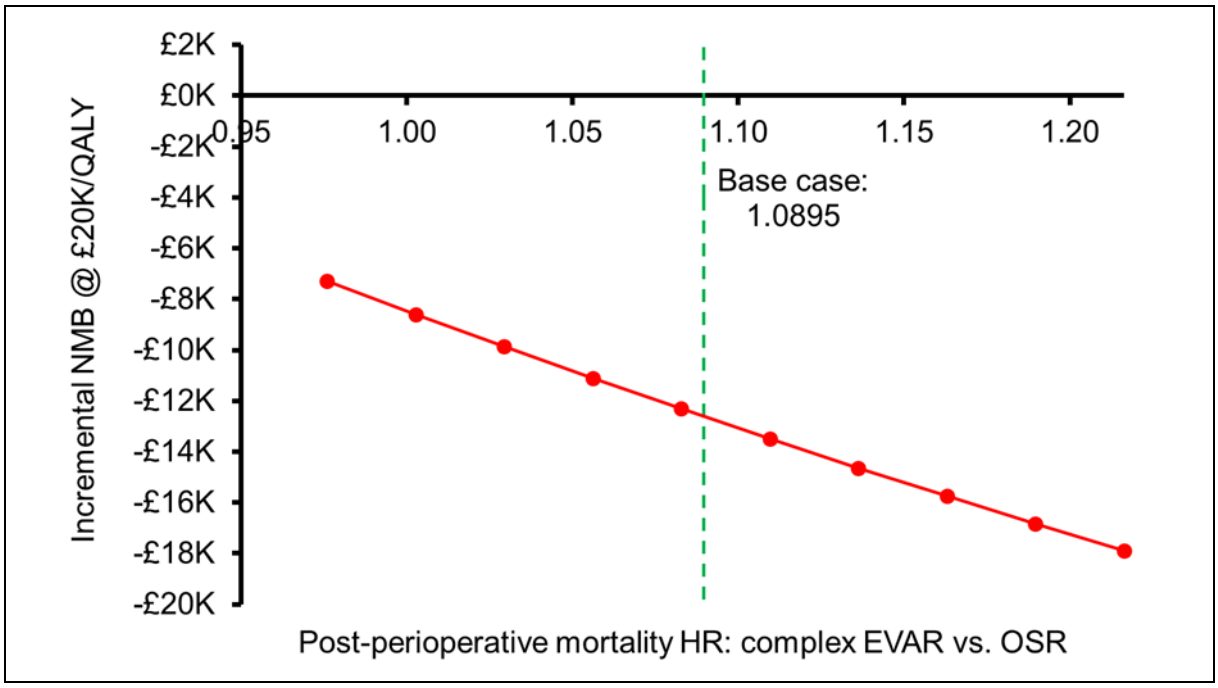


Figure HE56: INMB by post-perioperative EVAR mortality hazard ratio – complex EVAR vs. OSR – elective repair, complex AAA

Post-perioperative mortality – identifying a less healthy population

Like for the infrarenal AAA population, we conducted a threshold analysis under the assumption that no difference in post-perioperative mortality rates between EVAR and OSR exists for 8 years, followed by an EVAR HR of 1.297. We varied the HR used to calibrate general UK population mortality rates to match the EVAR-1 study population (1.080), to explore the cost-effectiveness of EVAR in a less-fit subgroup of complex AAA patients. A higher calibration HR means the patient is less likely to live for 8 years, and is therefore less likely to experience the long-term survival benefit from OSR.

Like the results for the infrarenal AAA population, EVAR produces a negative INMB at all values of calibration HR between 1 and 15, when compared with OSR (Figure HE57). Even in very unfit patients, with a post-perioperative mortality hazard 15-times that of the age-matched general population, meaning less than 1% are expected to survive for 8 years, the superior perioperative survival benefit of EVAR does not offset its higher overall cost sufficiently to produce a cost-effective ICER (Table HE55). Here, its ICER remains above £20,000 per QALY gained (£27,458) even if we assume that the complex EVAR device costs the same as a standard EVAR device.

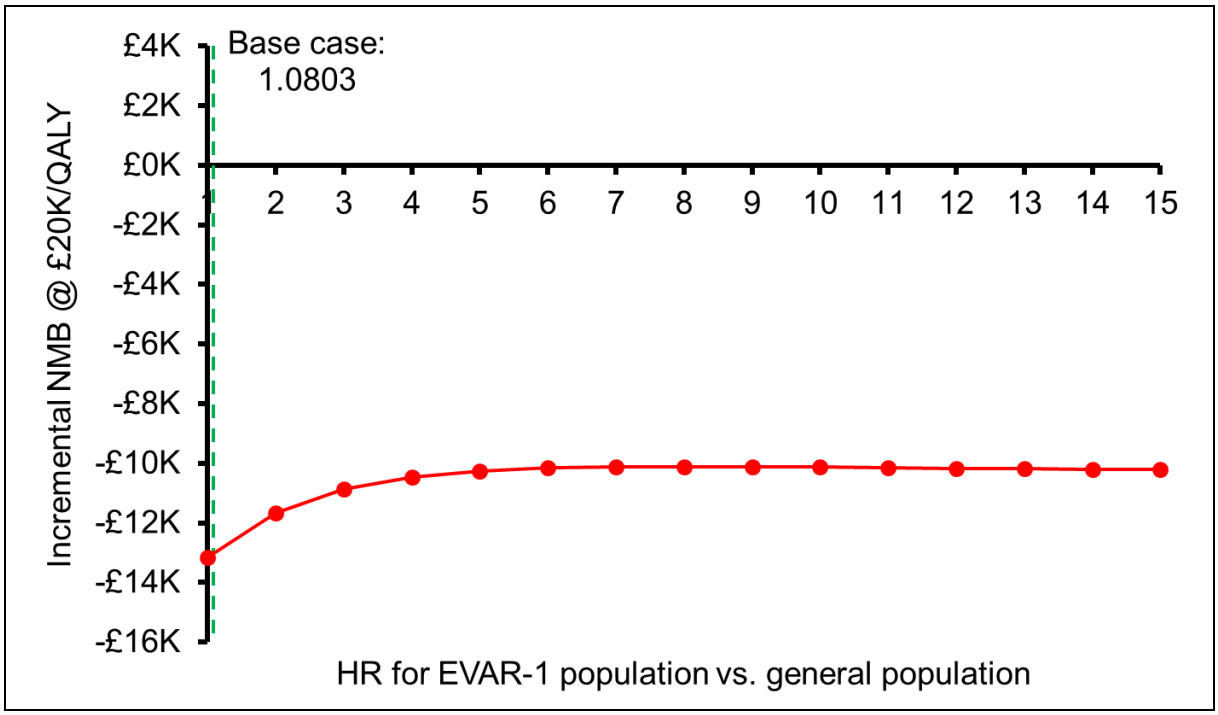


Figure HE57: INMB by post-perioperative general mortality calibration hazard ratio – EVAR vs. OSR – elective repair, complex AAA

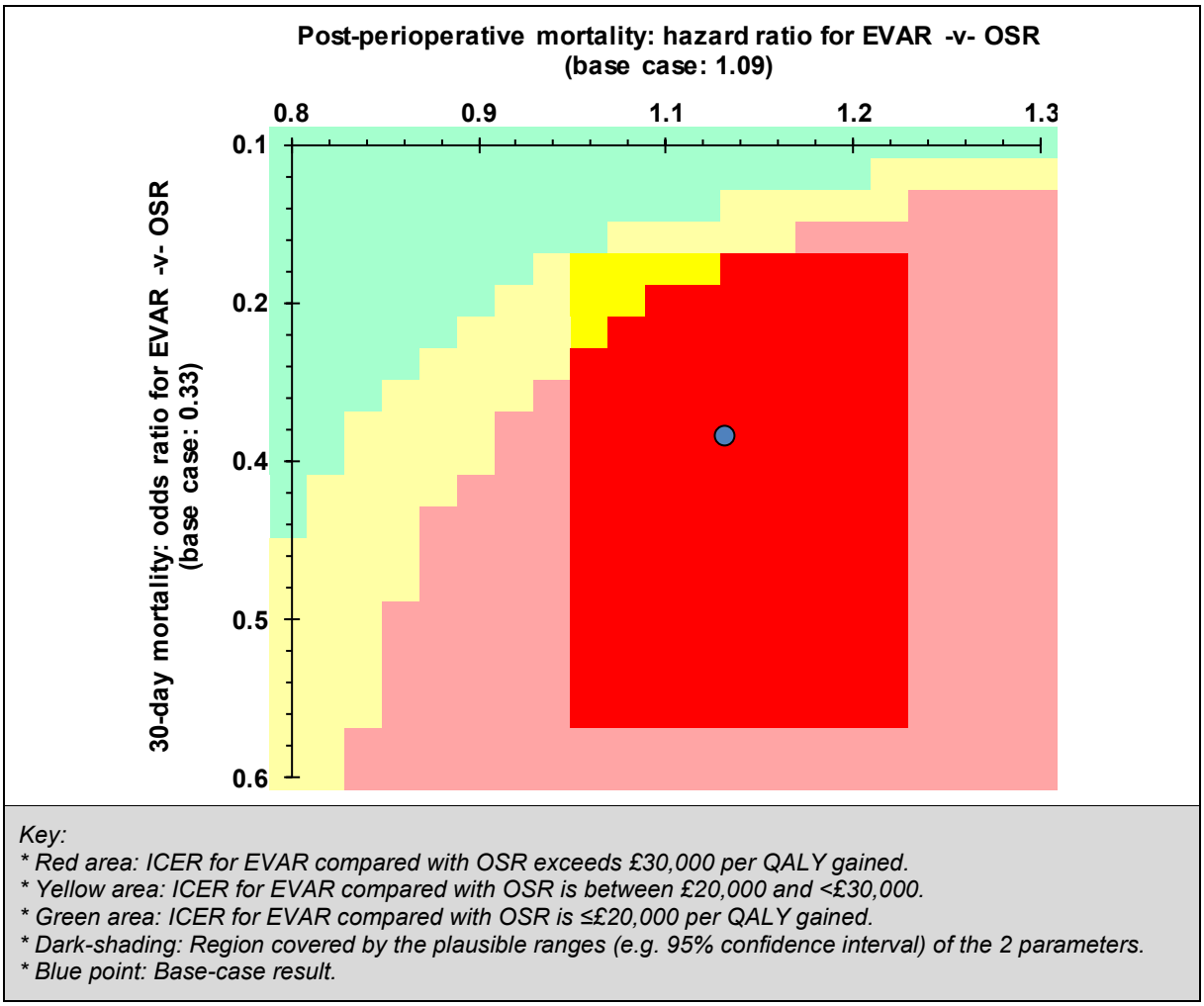
Table HE55: Sensitivity analysis: general mortality calibration HR = 15; no difference in post-perioperative relative survival for 8 years (EVAR HR = 1.297 thereafter) – elective repair, complex AAA

	Total (discounted)		*Incremental*		
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***ICER***
Base case unit cost of complex EVAR device (£15,686)					
OSR	£11,978	1.371			
EVAR	£26,153	1.569	£14,175	0.198	£71,642
Assume unit cost of complex EVAR device is no higher than standard EVAR device (£6,500)					
OSR	£11,978	1.371			
EVAR	£17,411	1.569	£5,433	0.198	£27,458

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Two-way analysis: Relative effectiveness in 30-day and post-perioperative mortality

In a two-way analysis, we explored the cost-effectiveness of EVAR when both its 30-day mortality relative effectiveness (OR) and post-perioperative mortality relative effectiveness (HR) were varied. Both of these parameters featured prominently in one-way sensitivity analysis (see Figure HE53). The results of this two-way analysis (Figure HE58) indicate that, even when both parameters are at the most favourable bound of their 95%CIs for EVAR, EVAR is not associated with an ICER of £20,000 or better. However, in contrast to the analogous analysis in the infrarenal setting (see Figure HE46), there is a small chance of the EVAR ICER being between £20,000 and £30,000 per QALY gained within the 95% confidence intervals of both parameters; for example, with a 30-day OR of 0.25, and a post-perioperative HR of 1. However, the plausible range region is dominated by red, indicating an EVAR ICER in excess of £30,000. For the ICER to be better than £20,000 per QALY gained, both parameters must take extreme values in favour of EVAR. This finding is consistent with our probabilistic analysis, in which we found that there is a small chance that EVAR is associated with an ICER better than £30,000/QALY (6.7%; see Figure HE52).



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE58: Two-way sensitivity analysis –30-day mortality vs. post-perioperative – elective repair, complex AAA

Complex EVAR device cost

Our base-case unit cost per complex EVAR device was sourced from members of the guideline development committee. Like in the infrarenal AAA analysis, we explored variation in the cost of EVAR in a threshold analysis, using £1,000 intervals. This analysis found that complex EVAR would be cost effective, at a value of £20,000 per QALY, if its unit cost were less than £2,000. Its INMB versus OSR becomes positive just below this value (Figure HE59). In reality, a complex EVAR unit cost of £2,000 is implausible; it is 87% lower than our base-case estimate, and is even substantially lower than our base-case cost of *standard* EVAR devices. The custom-made nature of complex EVAR means its unit cost is much higher than that of a standard device.

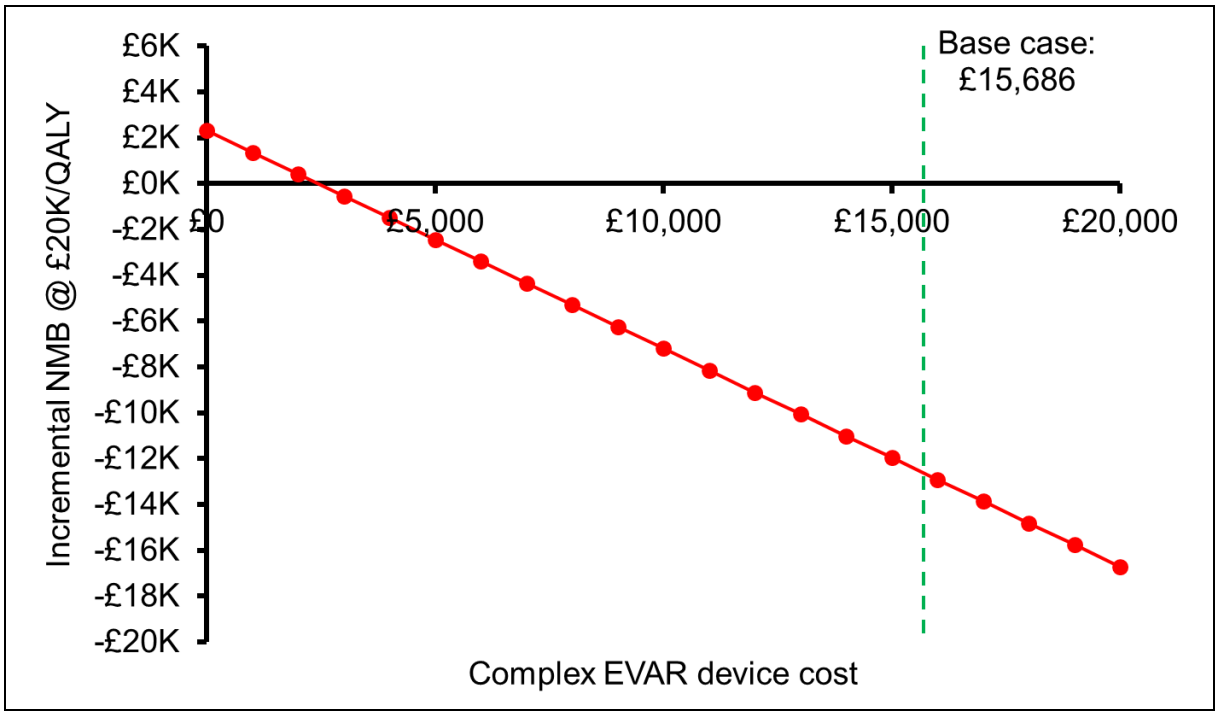


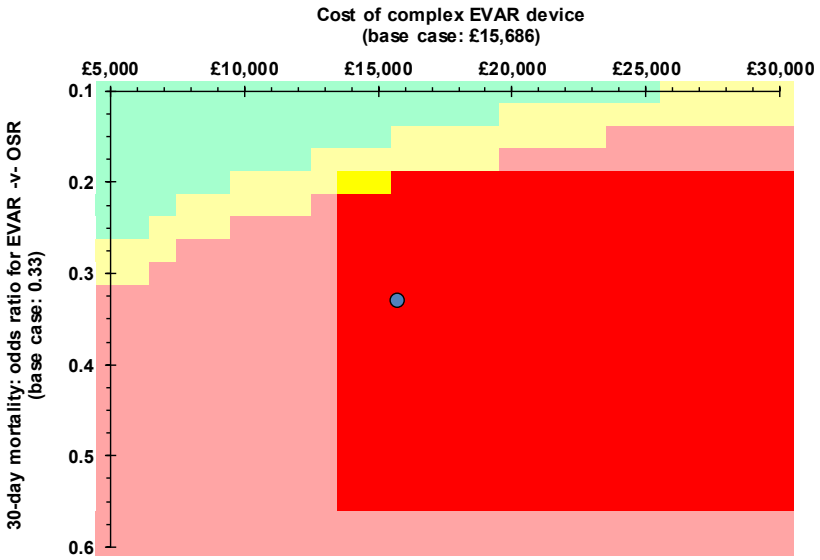
Figure HE59: INMB by EVAR device cost – EVAR vs. OSR – elective repair, complex AAA

Two-way analysis: complex EVAR device cost and perioperative mortality

In a two-way sensitivity analysis, we varied both the cost per custom-made, complex EVAR device and the 30-day mortality odds ratio to extreme values. The results (Figure HE60) indicate that the EVAR exceeds £20,000 per QALY gained at all plausible values of these 2 parameters – namely the 95% confidence interval of the mortality OR, and the plausible minimum and maximum cost values (£13,500 to £30,000, the range of values specified by the committee). The ICER is only in the £20–30,000/QALY range if the OR is set to 0.2 and the complex EVAR device cost is assumed to be £15,000 or less. For the ICER to be better than £20,000 at this level of relative effectiveness, the cost of EVAR would need to be lower than £10,000.

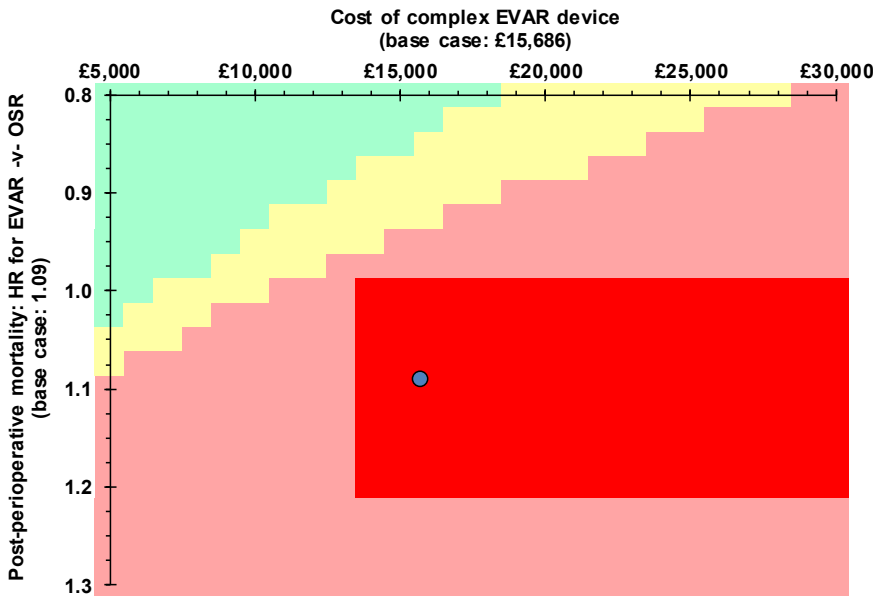
Two-way analysis: Complex EVAR device cost and long-term mortality

We also explored the cost-effectiveness of EVAR when its post-perioperative mortality relative effectiveness was varied alongside the cost per bespoke device. Here, all ICERs within the region of plausible values exceed £30,000 per QALY gained (Figure HE61). For the ICER to be better than £20,000 per QALY gained, the long-term mortality HR needs to be 1 or less; that is, a person must face a mortality hazard no higher than people who received OSR, despite the long-term complication risk associated with EVAR. Even at some HRs less than 1, however, the ICER exceeds £20,000 unless device cost is also lower than its base-case value. For example, if the EVAR post-perioperative mortality hazard was 10% lower than OSR (HR = 0.9), its ICER would only be better than £20,000 if the cost of an EVAR device is £12,000 or less (substantively lower than our base-case point estimate of £15,686).



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE60: Two-way sensitivity analysis – EVAR cost vs. 30-day mortality odds ratio – elective repair, complex AAA



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE61: Two-way sensitivity analysis – EVAR cost vs. post-perioperative mortality hazard ratio – elective repair, complex AAA

Reintervention rates

To explore the possibility that EVAR devices have become safer and more robust since the EVAR-1 trial was conducted, we ran a sensitivity analysis in which all graft-related complications were omitted from the model (whereas in the base-case they occur more frequently on the EVAR arm). In a further extreme analysis, we set the post-perioperative mortality HR between complex EVAR and OSR to a value of 1, denoting no difference in long-term mortality rates.

In the first scenario, a modest reduction in incremental costs and increase in incremental QALYs sees the EVAR ICER fall to £74,480 per QALY gained over OSR. When the long-term survival benefit for OSR is also omitted, EVAR is predicted to generate +0.386 incremental QALYs for people with unruptured complex AAAs; however, its ICER remains worse than £20,000/QALY, even in this favourable and extreme scenario.

Table HE56: Sensitivity analysis: newer EVAR devices – elective repair, complex AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
No graft-related reintervention procedures					
OSR	£11,294	6.042			
EVAR	£24,221	6.216	£12,927	0.174	£74,480
No graft-related reinterventions, equal post-perioperative mortality rates					
OSR	£11,294	6.042			
EVAR	£24,240	6.428	£12,946	0.386	£33,514

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

HE.3.2 EVAR vs. OSR – 'fit for OSR' population – emergency repair (ruptured)

HE.3.2.1 Infrarenal AAA

HE.3.2.1.1 Deterministic base case

The base-case, deterministic analysis found that a strategy that allows EVAR, where anatomically appropriate, generates 0.288 expected QALYs per person more than a strategy that relies on OSR for all cases. This benefit is composed of superior perioperative survival, and lower mortality rate for the first 3 post-perioperative years. After this point, our model has a lower mortality rate among OSR patients; however, this is never sufficient to catch up with the EVAR, in terms of total undiscounted QALYs (Figure HE62).

As shown in Table HE57, the EVAR strategy also has a higher expected cost per patient (+£1,641) than the OSR-alone approach. In contrast to the elective setting (see HE.3.1.1.1), the costs of the primary procedure and perioperative care are similar between the 2 strategies. This is because the additional cost of EVAR devices is almost totally offset by savings in postoperative care (including critical and nursing home stays; see HE.2.2.10.1). However, people receiving EVAR remain subject to higher monitoring and reintervention costs for the remainder of their lives, so total costs remain higher for the strategy that allows EVAR than for the OSR-alone approach.

The resulting ICER is around £5,700 per QALY gained, suggesting that (assuming conventional thresholds apply) the extra costs associated with a strategy that allows EVAR for the emergency repair of rupture infrarenal AAAs are easily justified by the expected benefits, so the approach provides good value for money compared with OSR in all cases (Table HE57). For the ICER to be as high as a £20,000, the EVAR strategy would need to be significantly worse than our base-case result, generating only 0.082 extra QALYs over OSR.

Table HE57: Base case cost–utility model results – emergency repair, infrarenal AAA

Strategy	Total (discounted)		Incremental		ICER (£/QALY)
	Costs	QALYs	Costs	QALYs	
OSR only	£25,422	2.734			
EVAR where possible	£27,063	3.022	£1,641	0.288	£5,699

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Table HE58: Components of total discounted costs – emergency repair, infrarenal AAA

Cost component	Total discounted cost	
	EVAR where possible	OSR only
Primary procedure & stay	£17,258	£17,089
Post-repair monitoring	£783	£82
Graft-related complications	£8,194	£6,409
Other complications	£828	£1,842
Total	**£27,063**	**£25,422**

Key: EVAR, endovascular aneurysm repair; OSR, open surgical aneurysm repair.

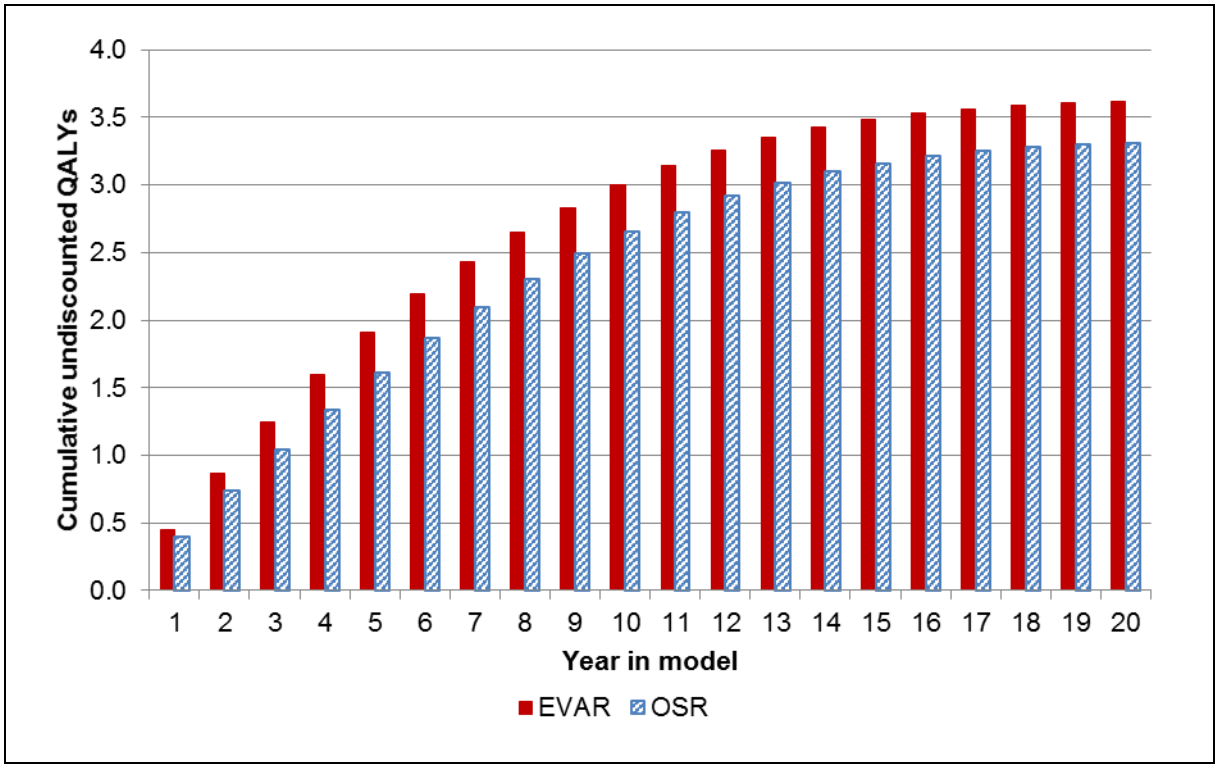


Figure HE62: Accrual of undiscounted QALYs over time – emergency repair, infrarenal AAA

HE.3.2.1.2 Sensitivity analysis

The mean probabilistic ICER for EVAR is £5,220, and there is a reasonable degree of confidence that it is better than £20,000 (80.3% of 5,000 simulations; Figure HE63 and Figure HE64). However, 3 model parameters had the potential to cause the EVAR ICER to be worse than £20,000, when varied within their 95% confidence limits, which would change the cost-effectiveness conclusion. Specifically, if the post-perioperative survival HRs took

values at their upper confidence limits – suggesting survival with the EVAR strategy is worse than our base-case point estimate – its ICER would exceed £20,000. A similar finding would result if the 'true' odds ratio for perioperative mortality is at the upper confidence limit of current evidence – which would imply superior 30-day survival with OSR. However, our base-case value (0.88), findings in the elective setting and the fact that OSR is a more invasive procedure all suggest that a true perioperative benefit for OSR is unlikely. We explore simultaneous variation in perioperative and post-perioperative mortality effectiveness in two-way sensitivity analysis, in a later section.

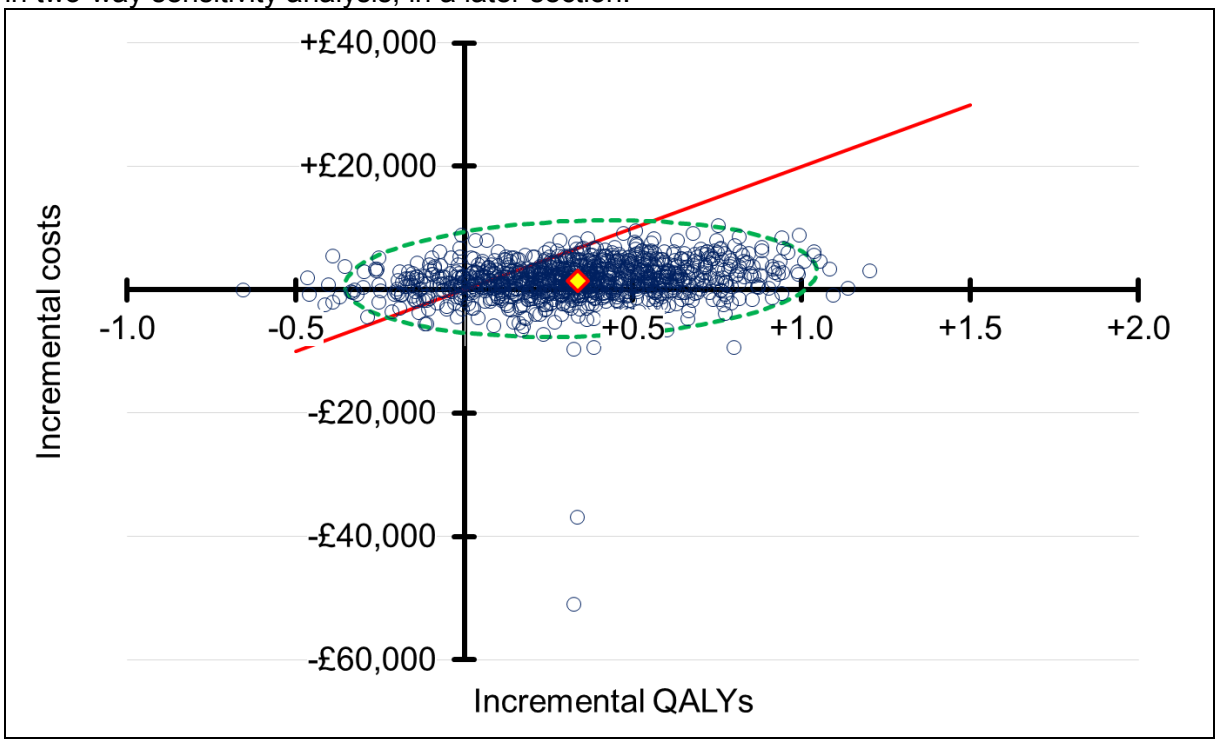


Figure HE63: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

The mean probabilistic results are £1,802 in incremental costs for EVAR, and 0.345 incremental QALYs for EVAR, with an ICER of £5,022 per QALY gained.

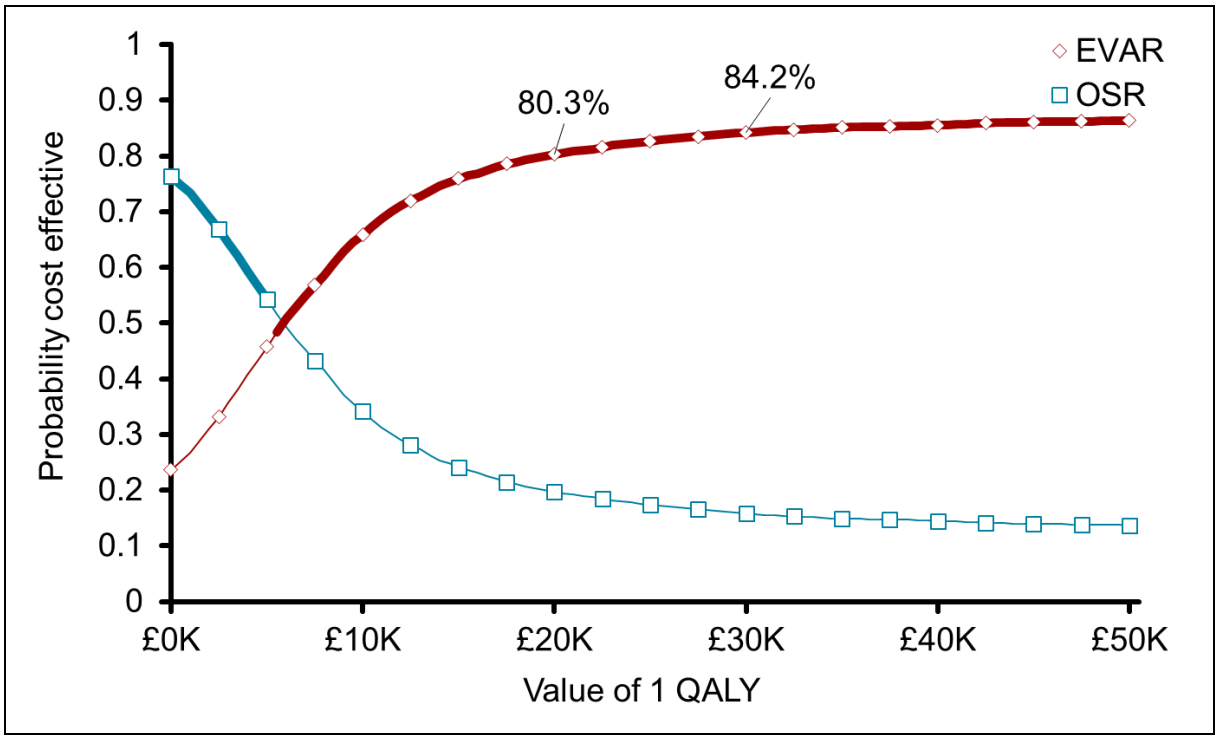
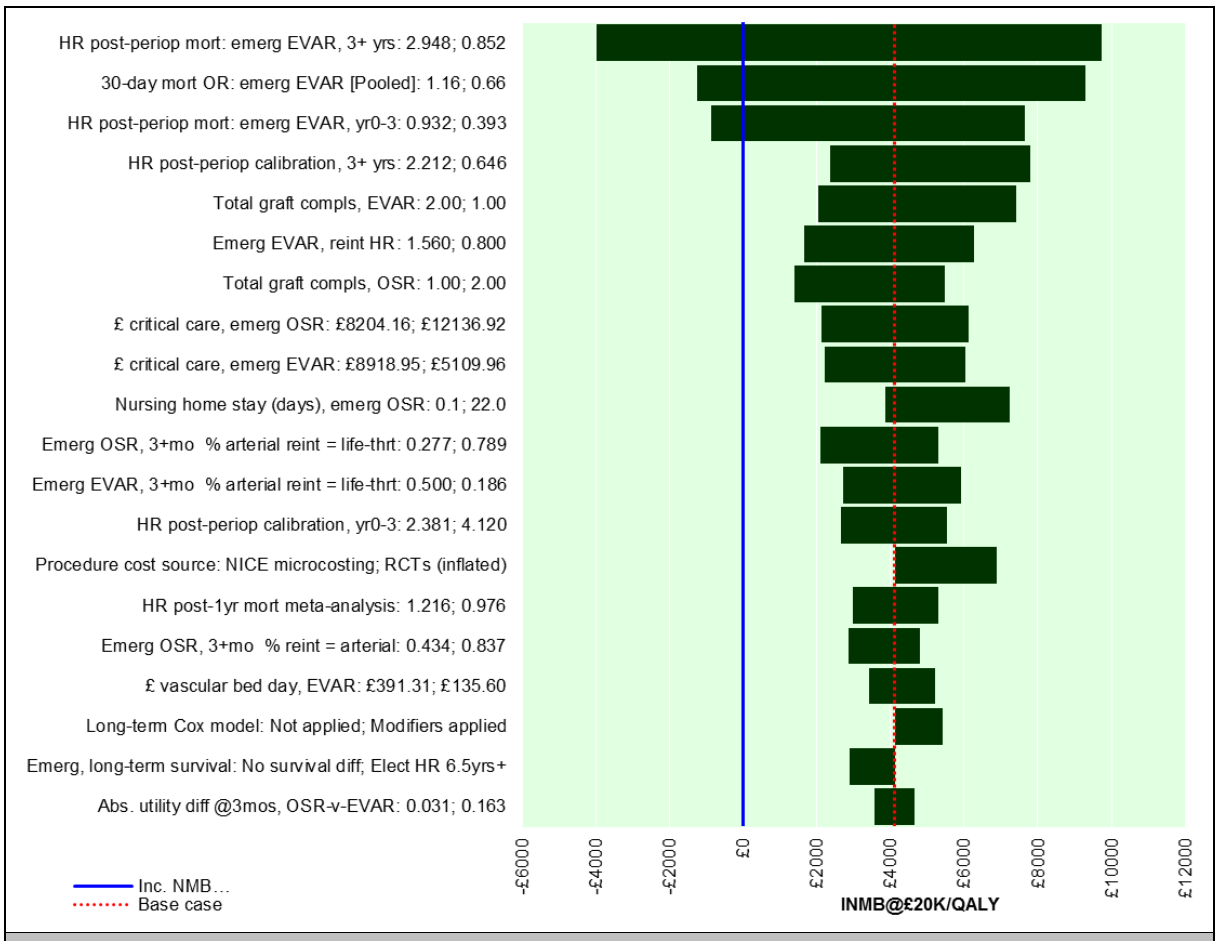


Figure HE64: Probabilistic sensitivity analysis (5,000 runs) – CEAC



Key: INMB, incremental net monetary benefit (at a value of £20,000 per QALY).

Figure HE65: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.2.1.3 Subgroup analysis

Baseline age

In a cohort with the sex split and mean AAA diameter of the IMPROVE trial (78% male, 9% female; 8.4 cm), age was not found to be a significant predictor of cost-effectiveness conclusions (see solid line in Figure HE66). At all ages from 50 to 100 years, EVAR had an ICER that was better than £20,000 per QALY gained compared with OSR. The INMB for EVAR remained close to £5,000 at all ages up to 90, representing net gain to the NHS despite its higher cost. In people aged over 90, the INMB moved towards £0 as the model time horizon ends when a patient reaches 100 years old.

Figure HE66: INMB by age and sex – EVAR vs. OSR – emergency repair, infrarenal AAA

Sex

While Figure HE66 shows the 'average' cost effectiveness of emergency EVAR, at the IMPROVE cohort characteristics, is insensitive to age, it also displays a marked difference by the patient's sex. The INMB for EVAR is above £0 at all patient age levels in women, reaching a peak n women aged 61. This represents a large net benefit for the NHS; the EVAR ICER for a 61-year old woman is just £2,718 per QALY gained. This high degree of EVAR cost-effectiveness in women is because being female is a major predictor of perioperative mortality with OSR, based on our logistic regression analysis (see Table HE17). EVAR is therefore relatively much more effective in women.

By contrast, EVAR has an ICER worse than £20,000 compared with OSR in men at all ages up to 70, depicted by INMB values below £0 (Figure HE66). This is because the result that being female significantly increases the 30-day mortality risk associated with OSR clearly

implies that being *male* does not increase this risk. OSR is therefore closer to EVAR in terms of perioperative survival. As a result, in men aged 70 or younger in this population, with ruptured infrarenal AAAs, the cost-effective repair technique is OSR. These men are sufficiently young to: (1) have a relatively good chance of surviving the OSR procedure, and (2): be more likely to survive for long enough to experience the lower long-term OSR mortality rates.

Despite this, the positive INMB in women is so large that it offsets the negative INMB in men, such that EVAR is cost-effective at all ages for the 'average' member of the IMPROVE cohort (22% of whom were female).

Aneurysm diameter

The base-case result is not sensitive to baseline AAA diameter (Figure HE67). At all pre-operative aneurysm sizes between 4 cm and 12 cm, emergency repair using EVAR had an ICER better than £20,000 per QALY gained compared with OSR. This was the case in both all-male and all-female cohorts (not shown).

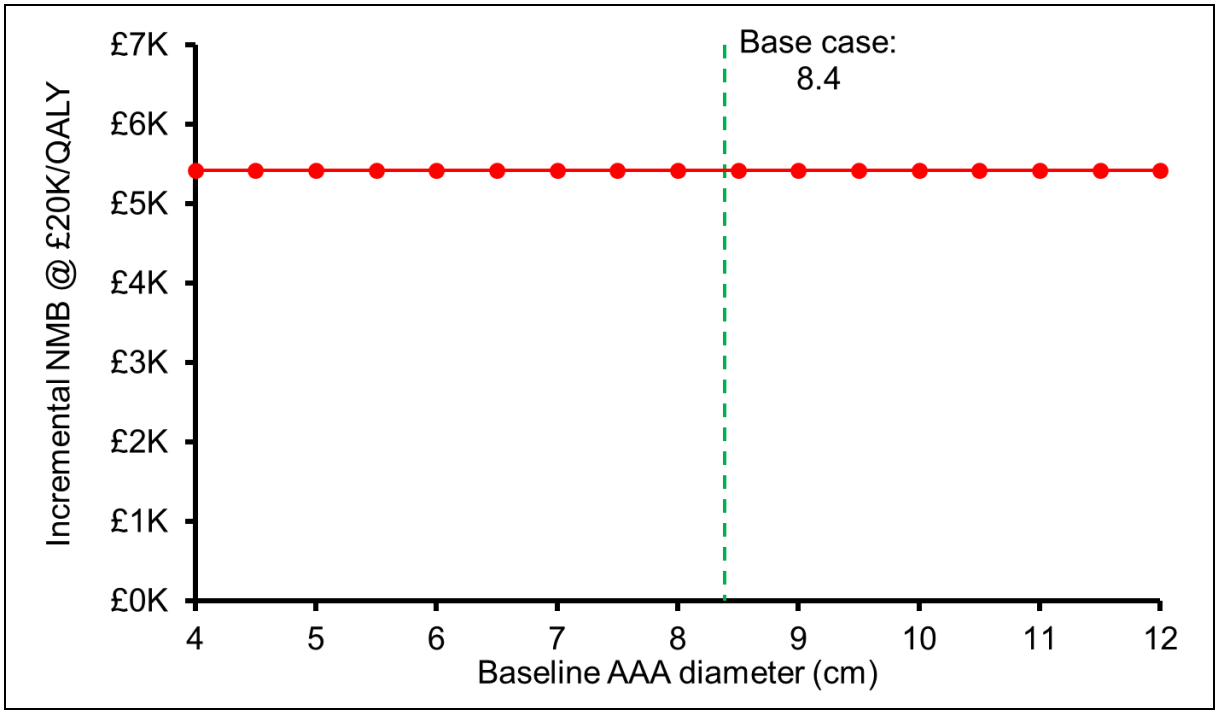


Figure HE67: INMB by aneurysm size – EVAR vs. OSR – emergency repair, infrarenal AAA

HE.3.2.1.4 Scenario analysis

Perioperative mortality – alternative baseline values

As described in Section HE.2.2.3, our base-case analysis uses 30-day EVAR mortality rates from the UK National Vascular Registry to characterise baseline mortality rates. To these baseline values, we applied the odds ratio from a Cochrane meta-analysis (Badger et al., 2017) to inform the relative perioperative mortality rate associated with emergency EVAR. The guideline committee advised that the registry mortality rate for OSR (40.4%) was more representative of their expectations of emergency AAA repair than the EVAR mortality rate (20.7%). We therefore use the OSR figure as our base-case baseline data in emergency repair analyses, unlike the elective repair analyses, which used the registry's EVAR mortality rates. In the scenario analyses shown in Table HE59, we instead use the EVAR registry

figure (and apply the trial-based relative effects in reverse to obtain the OSR mortality rate); and we use the IMPROVE trial 60-day mortality rates (37.0% and 39.4%) in separate analyses. Using these values from IMPROVE means the analysis makes no use of the registry data.

In all scenarios, the ICER for EVAR remains around £5,700 to £6,200 per QALY gained compared with OSR; significantly better than £20,000 (Table HE59).

Table HE59: Sensitivity analysis: baseline perioperative mortality – emergency repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
Baseline perioperative mortality: EVAR, UK registry (20.7%)					
OSR only	£27,795	3.530			
EVAR where possible	£29,596	3.819	£1,802	0.288	£6,252
Baseline perioperative mortality: EVAR, IMPROVE study (37.0%)					
OSR only	£25,469	2.750			
EVAR where possible	£27,114	3.039	£1,645	0.288	£5,707
Baseline perioperative mortality: OSR, IMPROVE study (39.4%)					
OSR only	£25,558	2.780			
EVAR where possible	£27,211	3.069	£1,653	0.289	£5,722

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Perioperative mortality – threshold analysis

Varying the base-case perioperative mortality odds ratio (0.88 in favour of emergency EVAR) from 0.50 to 1.50 causes the INMB for EVAR to change as displayed in Figure HE68. At the base-case odds ratio, and all odds ratios lower than it, EVAR is cost-effective over OSR (assuming QALYs are valued at £20,000 each). This remains the case until the odds ratio becomes 1.09, a value at which OSR is associated with a lower perioperative mortality rate than EVAR. At this point, the ICER for EVAR exceeds £20,000 per QALY gained, and its INMB turns negative. This does not necessarily represent an extreme value analysis, as the threshold odds ratio of 1.074 is well within the 95% confidence interval of the meta-analysis (0.66 to 1.16); however, it is still relatively far from the point estimate of 0.88, a figure that favours EVAR and is consistent with the experience of the expert guideline committee.

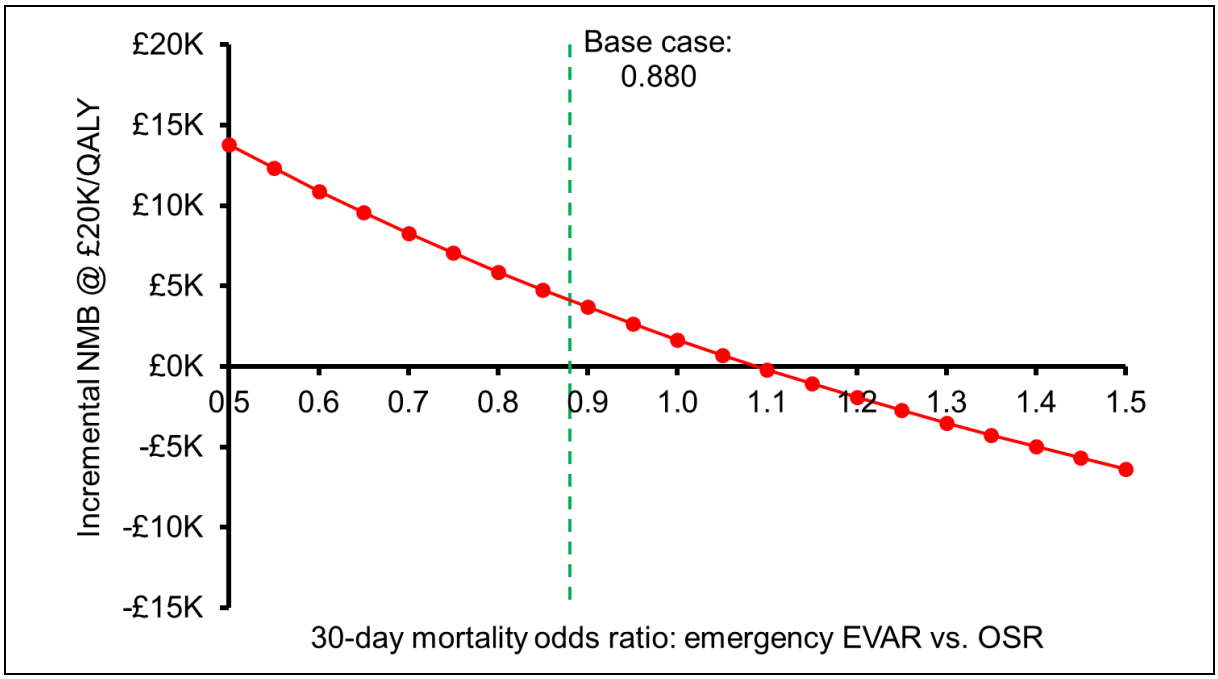


Figure HE68: INMB by perioperative EVAR mortality odds ratio – EVAR vs. OSR – emergency repair, infrarenal AAA

Post-perioperative mortality – parametric survival curves

The use of parametric curves to characterise post-perioperative survival, fitted to the IMPROVE study data, including modelling EVAR and OSR in a common function, was not found to substantively influence cost-effectiveness results (Table HE60).

Table HE60: Sensitivity analysis: parametric curves to model post-perioperative survival – emergency repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
Separate models: both Gompertz					
OSR only	£25,921	2.990			
EVAR where possible	£27,583	3.318	£1,662	0.329	£5,057
Separate models: Gompertz for EVAR, exponential for OSR					
OSR only	£25,910	2.973			
EVAR where possible	£27,576	3.315	£1,666	0.342	£4,876
Common model with treatment variable: Gompertz					
OSR only	£25,868	2.938			
EVAR where possible	£27,531	3.296	£1,663	0.358	£4,648

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Post-perioperative mortality – duration and magnitude of OSR benefit

In our base-case analysis, the difference in post-perioperative mortality between EVAR and OSR is informed by the IMPROVE Cox model up to 6.5 years after the perioperative period. After this point, the model takes on the post-perioperative HR from the elective repair model (1.089), to make use of the long-term data available in that setting. Due to the uncertainty inherent in extrapolating beyond limited direct follow-up data, we explored the following scenario analyses: (1) assuming that the post 3-year HR from IMPROVE continues

indefinitely ($HR2 = 1.585$); (2) using the elective repair HR derived specifically from EVAR-1 participants who survived for at least 8 years (HR = 1.297) after 6.5 years; (3) assuming no difference in mortality rates (HR = 1) beyond the available IMPROVE data; and (4) assuming there is no difference in post-perioperative mortality rates at any time. Of these, analyses (1), (2) and (4) are favourable to OSR. The first projects the observed trend for higher EVAR mortality after 3 years over a lifetime, the second enhances long-term survival prospects following OSR, and the latter removes the significant early post-perioperative survival benefit of EVAR. Despite this, the ICER for EVAR remains better than £20,000 per QALY gained in all analyses.

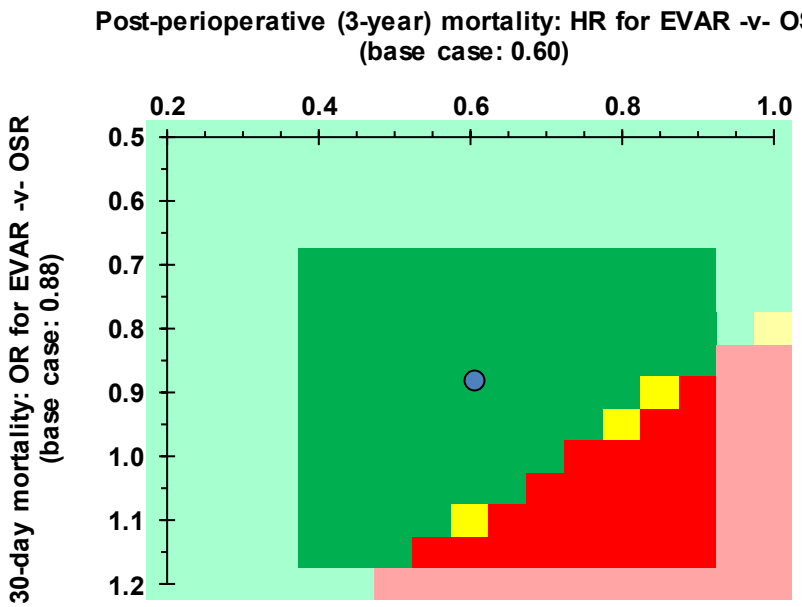
Two-way analysis: Relative effectiveness in 30-day and post-perioperative mortality

In a two-way analysis, we explored the cost effectiveness of EVAR when both its 30-day mortality relative effectiveness (OR) and post-perioperative mortality relative effectiveness (HR up to 3 years) were varied. At their base-case values both parameters favour EVAR. The results of this two-way analysis (Figure HE46) indicate that we can be reasonably confident that the EVAR strategy for ruptured AAA has an ICER that is better than £20,000 per QALY gained compared with only using OSR. The region covered by the OR and HR 95% confidence intervals is predominantly green. The EVAR strategy's ICER only exceeds £20,000 when both parameters are at the pessimistic ends of their confidence intervals; for example, a 30-day OR of 1.0 and a post-perioperative 3-year HR of 0.8.

Table HE61: Sensitivity analysis: OSR post-perioperative survival benefit – emergency repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
Extrapolating IMPROVE HR (years 3 to 6.5) over the model time horizon (year 3+)					
OSR only	£25,217	2.735			
EVAR where possible	£26,758	2.833	£1,540	0.098	£15,653
Increased survival benefit associated with OSR after 6.5 years (HR = 1.297)					
OSR only	£25,325	2.735			
EVAR where possible	£26,918	2.931	£1,593	0.196	£8,119
No difference in mortality rates after 6.5 years (HR = 1 after this point)					
OSR only	£25,470	2.734			
EVAR where possible	£27,135	3.069	£1,665	0.335	£4,970
No difference in post-perioperative mortality rates (HR = 1 at all times)					
OSR only	£25,198	2.735			
EVAR where possible	£26,679	2.954	£1,482	0.219	£6,764

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.



Key:
** Red area: ICER for EVAR compared with OSR exceeds £30,000 per QALY gained.*
** Yellow area: ICER for EVAR compared with OSR is between £20,000 and <£30,000.*
** Green area: ICER for EVAR compared with OSR is ≤£20,000 per QALY gained.*
** Dark-shading: Region covered by the plausible ranges (e.g. 95% confidence interval) of the 2 parameters.*
** Blue point: Base-case result.*

Figure HE69: Two-way sensitivity analysis – 30-day mortality vs. post-perioperative mortality – emergency repair, infrarenal AAA

EVAR device cost

We again explored the effect of changing the unit cost of EVAR in a threshold analysis. At the base-case estimate (£6,500 per EVAR device), the ICER for the EVAR strategy was around £5,700 per QALY gained over OSR, for ruptured infrarenal AAA. As such, this threshold analysis focused primarily on the effect of increasing the base-case unit cost, rather than decreasing it; we used £500 increments from £5,000 to £15,000 per device. The EVAR strategy was no longer cost effective once the EVAR price reached £13,000, as this is the point at which its INMB versus OSR becomes negative (Figure HE70). This is double the base-case cost and is close to our cost estimate for custom-made, complex EVAR devices, making it an unlikely unit cost for a standard EVAR device.

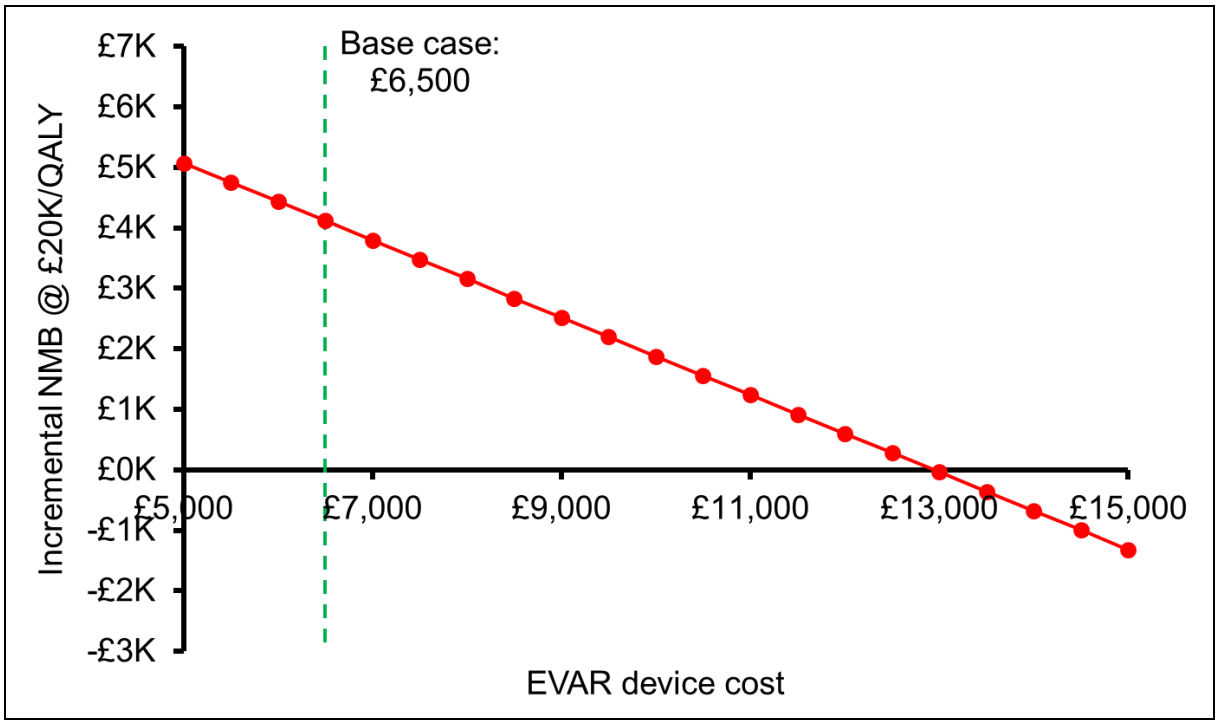


Figure HE70: INMB by EVAR device cost – EVAR vs. OSR – emergency repair, infrarenal AAA

Reintervention rates

In the elective repair analyses, we explored 2 extreme scenarios to characterise a setting in which modern EVAR devices are significantly safer and more effective than those used in the RCTs. These involved omitting all graft-related complications from the model, and setting the post-perioperative mortality HR between EVAR and OSR to a value of 1 (as per the third scenario in Table HE61 above). Given the base-case ICER in the emergency setting is £5,699, here EVAR would invariably be cost-effective under these scenarios.

HE.3.2.2 Complex AAA

EVAR is not typically possible for the repair of a ruptured complex AAA. Such aneurysms require custom-built EVAR devices, which are made to order, and are therefore not readily available to surgeons for emergency cases. Accordingly, no results are presented for this population.

HE.3.3 EVAR vs. No intervention – 'unfit for OSR' population – elective repair (unruptured)

HE.3.3.1 Infrarenal AAA

HE.3.3.1.1 Deterministic base case

In the population for whom OSR is not a suitable intervention, in our base-case, offering EVAR leads to substantially more cost than 'no intervention' (Table HE63). Mostly, these costs are associated with the procedure itself, but some continue to be evident in subsequent phases of the analysis. The cost of treating ruptures in the 'no intervention' arm provides only a minimal counterbalance to this expenditure.

The profile of cumulative undiscounted QALYs (Figure HE71) shows the early EVAR loss due to perioperative mortality, but by the third year of the model EVAR patients have accrued

more QALYs than 'no intervention' patients (Figure HE71). This benefit is slowly attenuated as time progresses, reflecting our modelling of post-perioperative survival, which suggests a benefit for EVAR over the first 4.5 years, followed by a benefit for 'no intervention' after this point (see 'relative long-term survival effects' in HE.2.3.6.1, above). By the end of the lifetime model, an expected QALY benefit remains for EVAR (+0.033 per patient), but this is modest compared with the additional cost of £15,438 per patient, leading to a high base-case, deterministic ICER of £460,000 per QALY gained for EVAR, compared with not attempting to repair the infrarenal aneurysm (Table HE62). With this incremental cost, EVAR would need to generate 0.772 additional QALYs per patient to attain an ICER of £20,000.

Table HE62: Base case cost–utility model results – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER (£/QALY)*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	
No repair	£924	2.313			
EVAR	£16,363	2.347	£15,438	0.033	£460,863

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Table HE63: Components of total discounted costs – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

	Total discounted cost	
Cost component	**EVAR**	**No repair**
Primary procedure & stay	£13,072	£0
Post-repair monitoring	£932	£192
Graft-related complications and ruptures	£2,359	£732
Total	**£16,363**	**£924**

Key: EVAR, endovascular aneurysm repair.

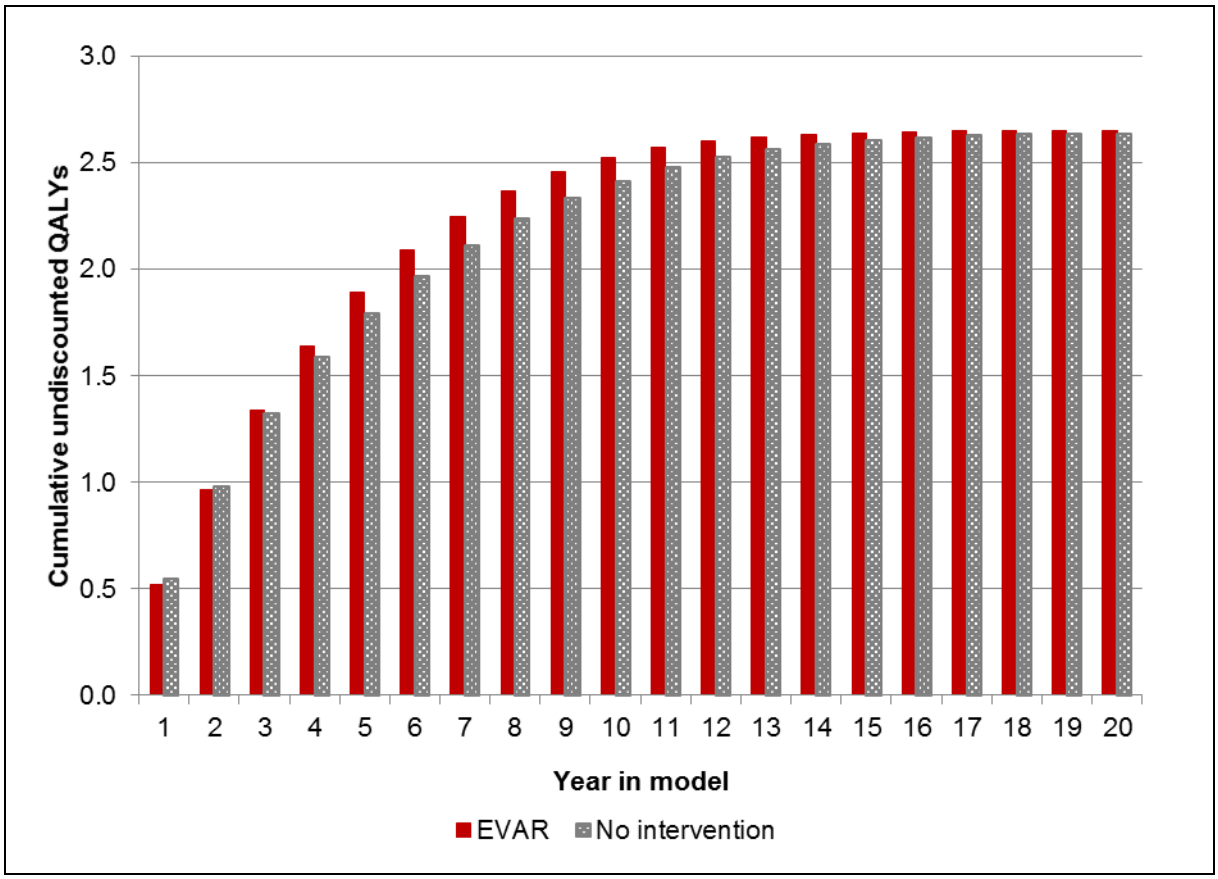


Figure HE71: Accrual of undiscounted QALYs over time – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

HE.3.3.1.2 Sensitivity analysis

The mean probabilistic ICER for EVAR (£398,077) is consistent with the deterministic result, and 0% of 5,000 simulations predicted it to be £20,000 or better (Figure HE72 and Figure HE73). No individual model parameter, when varied between its plausible bounds, nor model scenario, caused the cost-effectiveness conclusion to change (Figure HE74). The incremental NMB value still varies considerably at different cohort baseline age values, however, this analysis did not apply perioperative and long-term survival effect modifiers. These are explored in more detail in subgroup analyses.

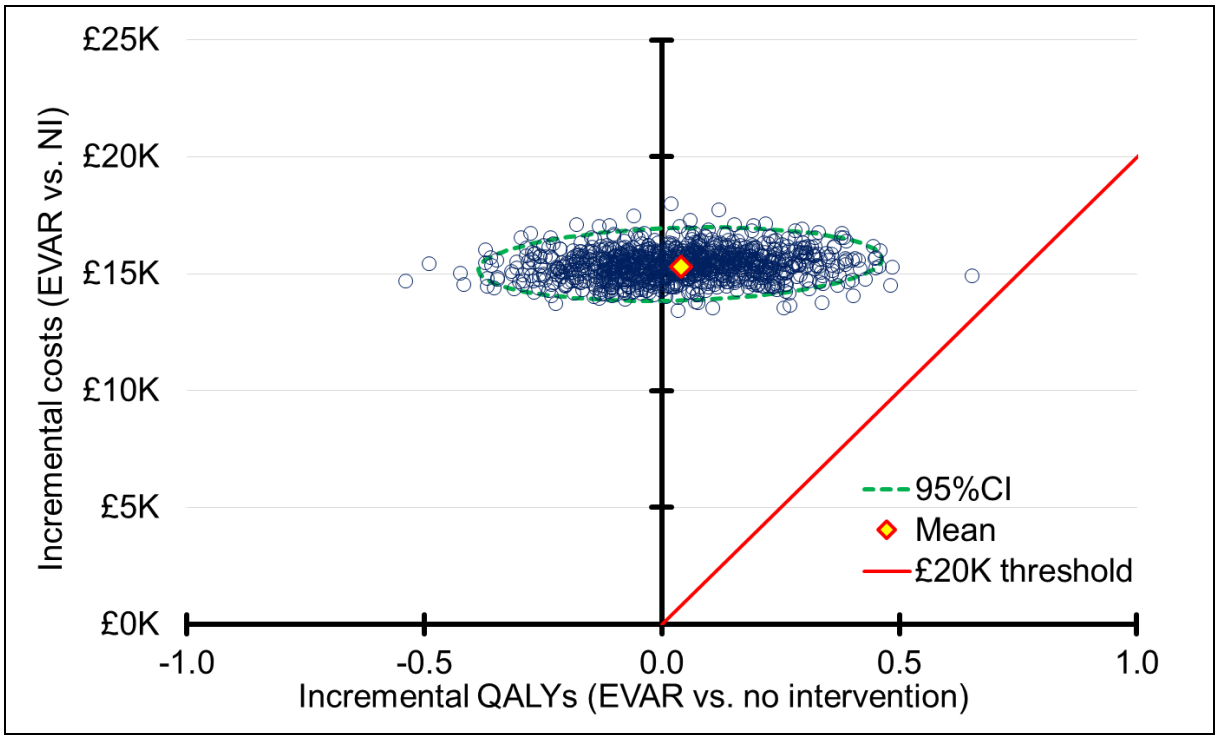


Figure HE72: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

The mean probabilistic results are £15,408 in incremental costs for EVAR, and 0.039 incremental QALYs for EVAR, with an ICER of £398,077 per QALY gained.

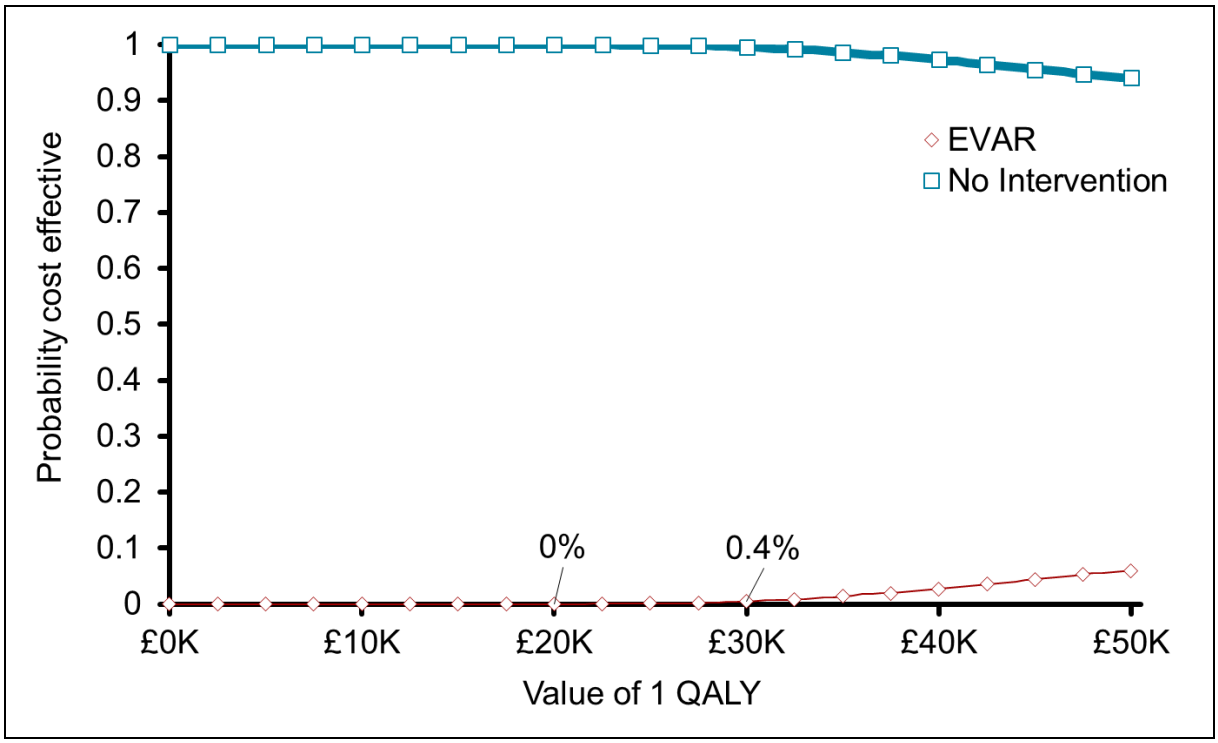
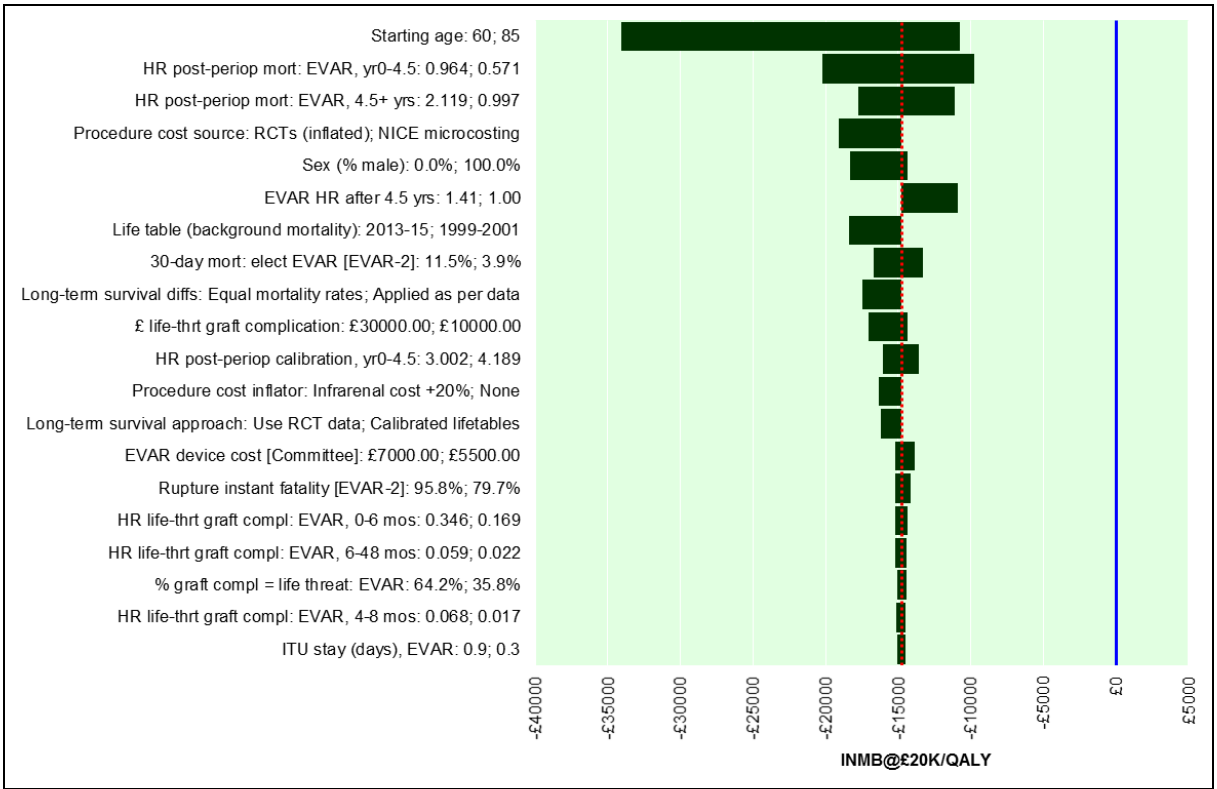


Figure HE73: Probabilistic sensitivity analysis (5,000 runs) – CEAC



Key: INMB, incremental net monetary benefit (at a value of £20,000 per QALY).

Figure HE74: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.3.1.3 Subgroup analysis

Baseline age

In a cohort with the sex split and mean AAA diameter of the EVAR-2 trial (86% male, 14% female; 6.7 cm), age was not found to significantly influence cost-effectiveness conclusions (Figure HE75). At no baseline patient age, from 50 to 100 years, did the INMB for EVAR compared with providing no repair exceed £0; meaning the EVAR ICER was always worse than £20,000 per QALY gained. This is unsurprising given the deterministic base-case ICER value of over £460,000 per QALY gained.

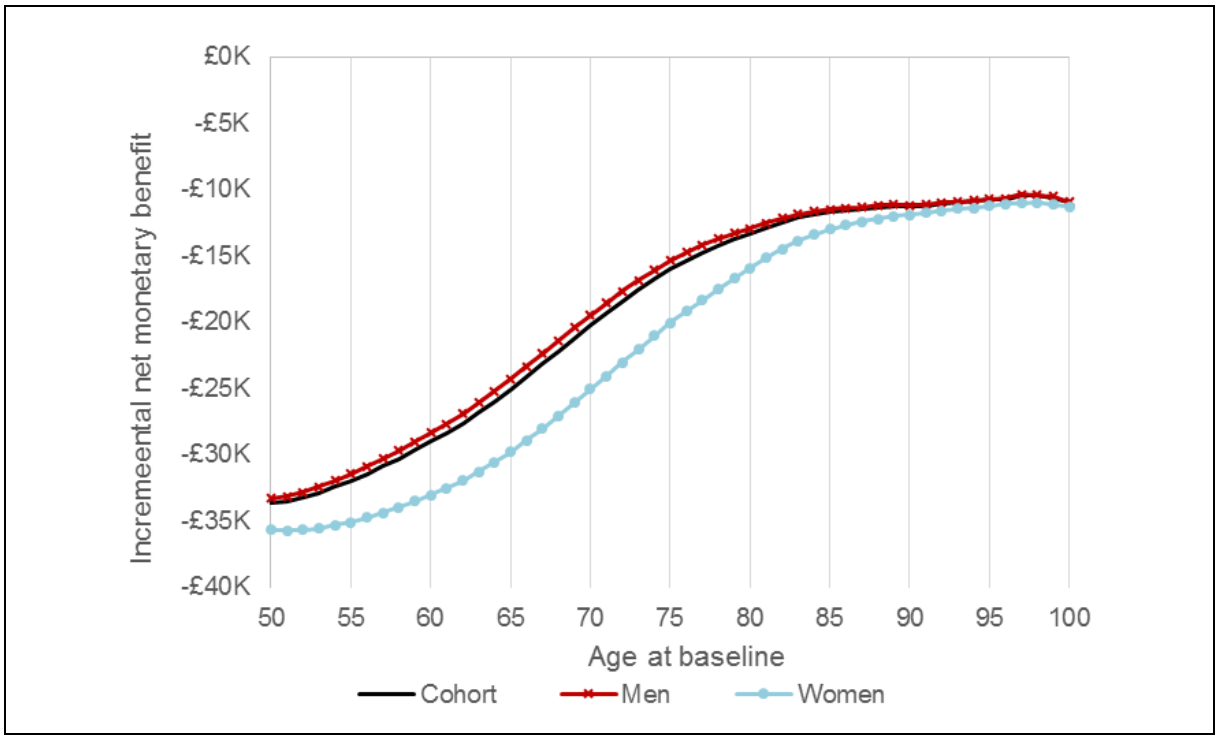


Figure HE75: INMB by age and sex – EVAR vs. no intervention – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Sex

The result above is not sensitive to the sex of the person with an AAA. In both men and women, the EVAR ICER remains worse than £20,000 per QALY gained at all ages from 50 to 100, shown by its negative INMB.

Aneurysm diameter

The base-case result is not sensitive to baseline AAA diameter (Figure HE76). At all pre-operative aneurysm sizes between 4 cm and 12 cm, elective repair using EVAR had an ICER worse than £20,000 per QALY gained compared with providing no intervention. The net loss of health caused by intervention actually increases (gets worse) as AAA size increases, because it is a significant predictor of perioperative EVAR mortality, whereas there is no difference in its effect on long-term survival between EVAR and ‘no intervention’.

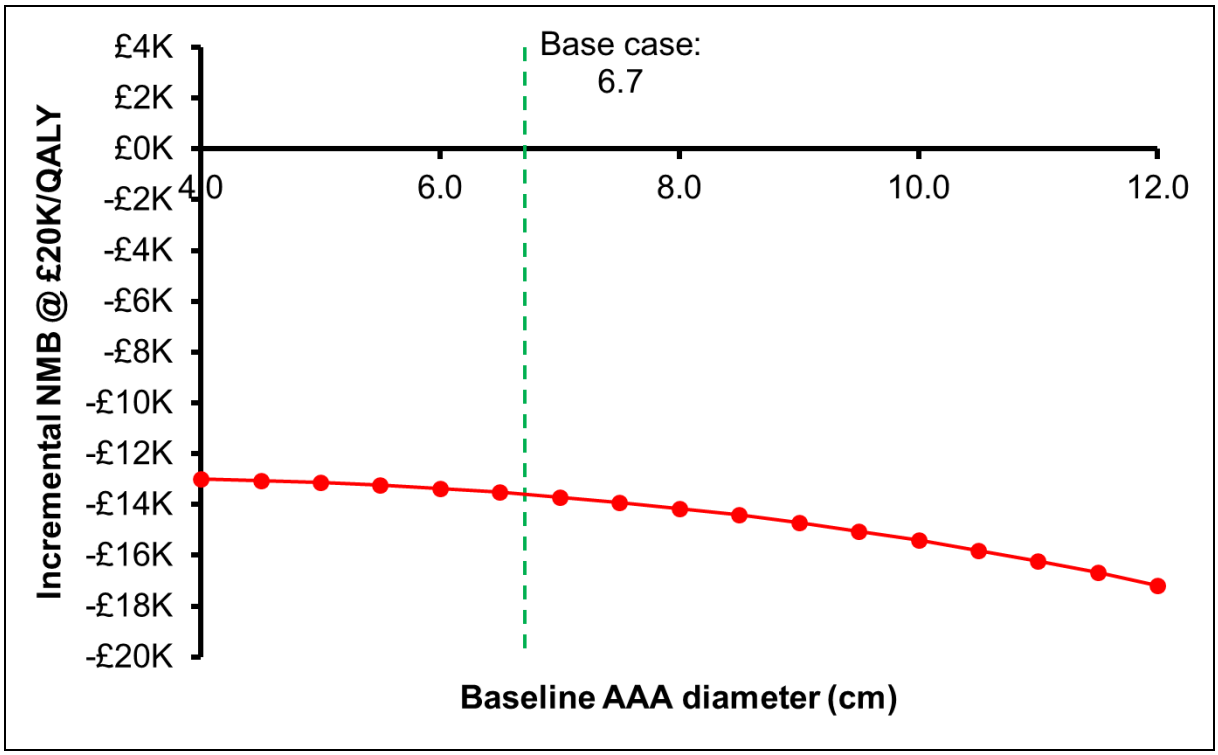


Figure HE76: INMB by aneurysm size – EVAR vs. no intervention – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

HE.3.3.1.4 Scenario analysis

Perioperative mortality – threshold analysis

For the population in whom OSR is not a suitable intervention, the only source of baseline perioperative mortality data included in the model is from the EVAR-2 trial. The National Vascular Registry mortality rates were agreed to be more representative of a healthier population, for whom OSR would be considered. As such, we do not present alternative baseline data for EVAR 30-day mortality in this population. Instead, we conduct a threshold analysis around the base-case EVAR mortality rate of 7.3% (Figure HE77). Varying this rate from 1% to 20% does not cause the ICER for EVAR to be better than £20,000 per QALY gained, compared with providing no intervention. Even at extreme low 30-day mortality rates – for example, 1% is outside EVAR's 95% confidence interval (3.9% to 11.5%) – the high incremental cost associated with EVAR means any QALY gains in this population do not represent good value for money.

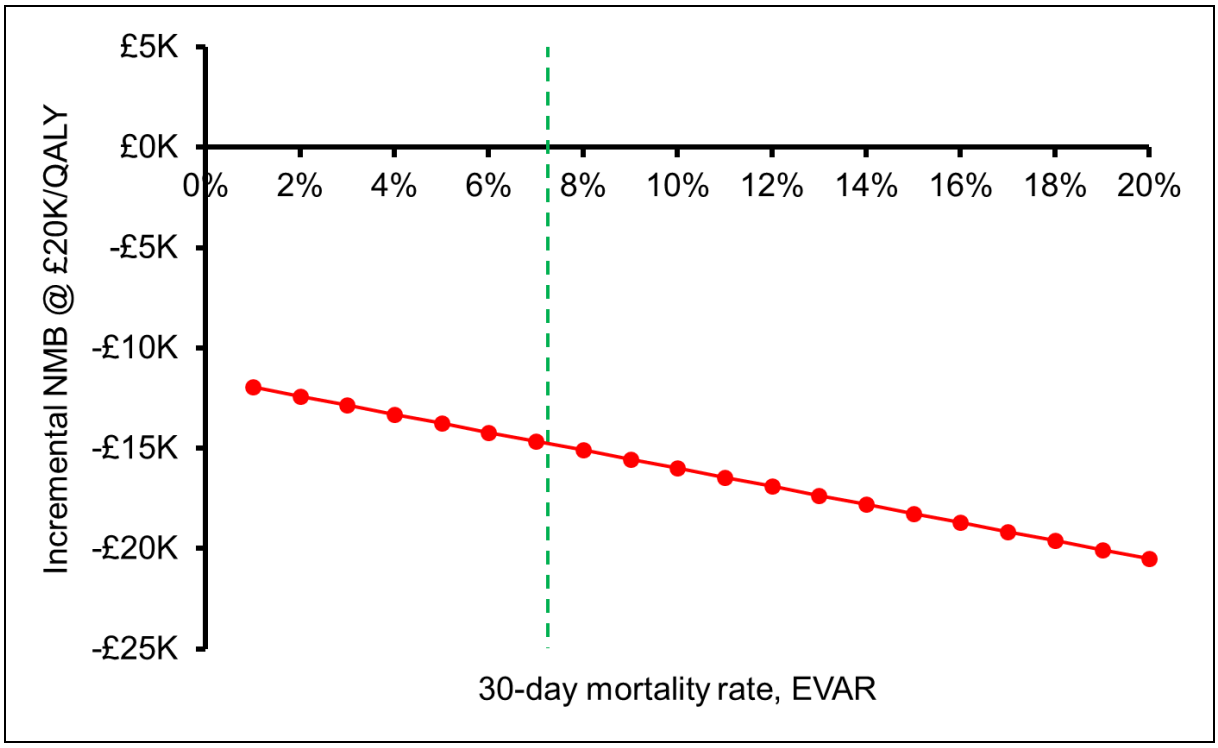


Figure HE77: INMB by perioperative EVAR mortality rate – EVAR vs. no intervention – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Post-perioperative mortality – parametric survival curves

The use of parametric curves, fitted to the EVAR-2 study data, tends to cause EVAR to produce a smaller number of incremental QALYs, and potentially QALY losses, compared with 'no intervention'. In Table HE64, this is observable in the negative incremental QALYs associated with EVAR relative to no intervention, whereas in our base-case analysis, based on UK life tables calibrated to match the EVAR-2 population, EVAR is predicted to generate +0.033 incremental QALYs Using all potentially suitable parametric functions, elective EVAR is typically dominated by 'no intervention', or its ICER is exceptionally high, in people for whom OSR in not an option. This reflects the somewhat optimistic estimate of long-term survival with EVAR in our base-case modelling (see HE.2.3.7.1).

Table HE64: Sensitivity analysis: parametric curves to model post-perioperative survival – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

		EVAR function		
		Gamma	**Gompertz**	**Weibull**
'No intervention' function	**Exponential**	Inc. costs: £15,289 Inc. QALYs: -0.040 ICER: Dominated	Inc. costs: £15,383 Inc. QALYs: -0.037 ICER: Dominated	Inc. costs: £15,387 Inc. QALYs: -0.028 ICER: Dominated
	Gamma	Inc. costs: £15,676 Inc. QALYs: 0.004 ICER: £4.27m	Inc. costs: £15,669 Inc. QALYs: -0.004 ICER: Dominated	Inc. costs: £15,673 Inc. QALYs: 0.005 ICER: £3.12m
	Gompertz	Inc. costs: £15,465 Inc. QALYs: -0.023 ICER: Dominated	Inc. costs: £15,371 Inc. QALYs: -0.040 ICER: Dominated	Inc. costs: £153756 Inc. QALYs: -0.031 ICER: Dominated
	Weibull	Inc. costs: £15,390 Inc. QALYs: -0.030 ICER: Dominated	Inc. costs: £15,458 Inc. QALYs: -0.030 ICER: Dominated	Inc. costs: £15,462 Inc. QALYs: -0.022 ICER: Dominated

Key: ICER, incremental cost-effectiveness ratio; Inc., incremental; QALY, quality-adjusted life-year.

Note that, in all of the analyses above, the 2 arms were modelled separately. Here, it was not possible to include EVAR and 'no intervention' in a common parametric function, distinguished by a treatment variable, because the EVAR functions are used to model post-perioperative survival, whereas the 'no intervention' functions model overall survival.

Post-perioperative mortality – duration and magnitude of relative effects

In our base-case analysis, the difference in post-perioperative mortality between EVAR and the 'no intervention' arm is informed by a Cox model developed using the EVAR-2 study data. This was split into 2 parts, in a piecewise analysis, with different EVAR HRs before and after 4.5 post-perioperative years; EVAR patients have a lower mortality hazard than people with unrepaired aneurysms for the first period, but a higher mortality hazard thereafter. However, the HR after 4.5 years (1.454) is not statistically significant at the 95% confidence level (95%CI: 0.997–2.119). We therefore present a scenario analysis in which this HR is set to a value of 1, meaning there is no difference in mortality rates after 4.5 years. This favours EVAR, by removing the long-term survival benefit associated with 'no intervention'. However the ICER for EVAR remains far in excess of £20,000 per QALY gained (Table HE65). We also present an extreme scenario in which there is no difference in post-perioperative mortality rates at all, such that the only difference in survival is caused by the risk during an EVAR procedure. This scenario favours 'no intervention' by removing the significant survival benefit observed in EVAR patients during the first 4.5 years after intervention. As a result, the survival loss incurred as a result of the risk of perioperative mortality is never recovered, and EVAR is dominated.

Table HE65: Sensitivity analysis: long-term survival effects – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	*(£/QALY)*
No difference in mortality rates after 4.5 post-perioperative years (HR = 1 after this point)					
No repair	£924	2.313			
EVAR	£16,477	2.546	£15,553	0.233	£66,801
No difference in post-perioperative mortality rates (HR = 1 at all times)					
No repair	£924	2.313			
EVAR	£16,203	2.204	£15,279	-0.109	dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

EVAR device cost

We explored varying the unit cost of an EVAR device from our base-case estimate of £6,500, testing values from £0 to £8,000. EVAR produced a negative INMB across this range of device costs, compared with 'no intervention' at a value of £20,000 per QALY (Figure HE78). With an EVAR device cost of £0, the total cost of the EVAR strategy falls but remains significantly higher than providing no intervention. The cost of the 'no intervention' strategy itself falls slightly, because £0 per EVAR device reduces the cost of emergency repair for unrepaired AAAs that go on to rupture. The resulting ICER is around £280,000 per QALY gained (Table HE66).

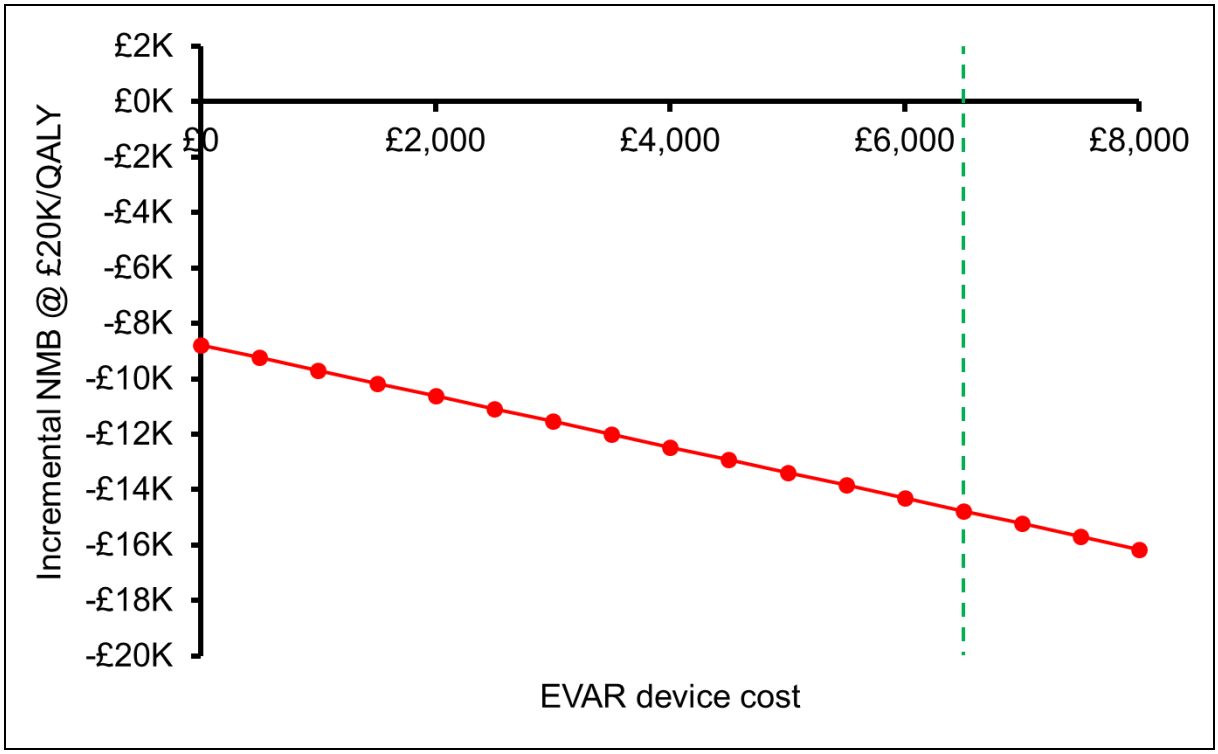


Figure HE78: INMB by EVAR device cost – EVAR vs. no intervention – elective repair, infrarenal AAA – population for whom OSR is not a suitable intervention

Table HE66: Sensitivity analysis: EVAR device cost = £0 – elective repair, infrarenal AAA – population for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***ICER***
No repair	£646	2.313			
EVAR	£10,095	2.347	£9,449	0.033	£282,074

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Reintervention rates

Like for previous analyses, to explore the possible impact if it could be shown that modern EVAR devices are any safer and/or more effective than older generation devices, we conducted an extreme value sensitivity analysis in which all graft-related complications were omitted from the model. In this population, this means all reintervention procedures are omitted and, as EVAR is the only intervention, this analysis favours EVAR. The second, more extreme scenario also applies a mortality HR of 1 after 4.5 years, eradicating the base-case long-term survival benefit of 'no intervention'; this is effectively the most optimistic scenario that could be advanced for EVAR. However, in both of these scenarios, the ICER for EVAR remains well above £20,000 per QALY (£320,000 and £57,833 per QALY gained, respectively).

Table HE67: Sensitivity analysis: newer EVAR devices – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
No graft-related reintervention procedures					
No repair	£924	2.313			
EVAR	£14,004	2.353	£13,079	0.040	£323,650
No graft-related reinterventions, equal mortality rates after 4.5 post-perioperative years					
No repair	£924	2.313			
EVAR	£14,006	2.539	£13,082	0.226	£57,833

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Rupture of untreated aneurysms

As explained in Section HE.2.3.12, our base-case model applies a HRQL decrement associated with aneurysm repair by OSR, for patients on the 'no intervention' arm whose untreated AAA ruptures and is repaired (base-case value = 0.936, or a 6.4% reduction in utility for 1 year). To explore the influence of this assumption, we conducted a threshold analysis around the utility multiplier. It has no influence on cost-effectiveness conclusions, even if people on the 'no intervention' arm are susceptible to particularly devastating ruptures, reducing their quality of life by 50% for a year (Figure HE79).

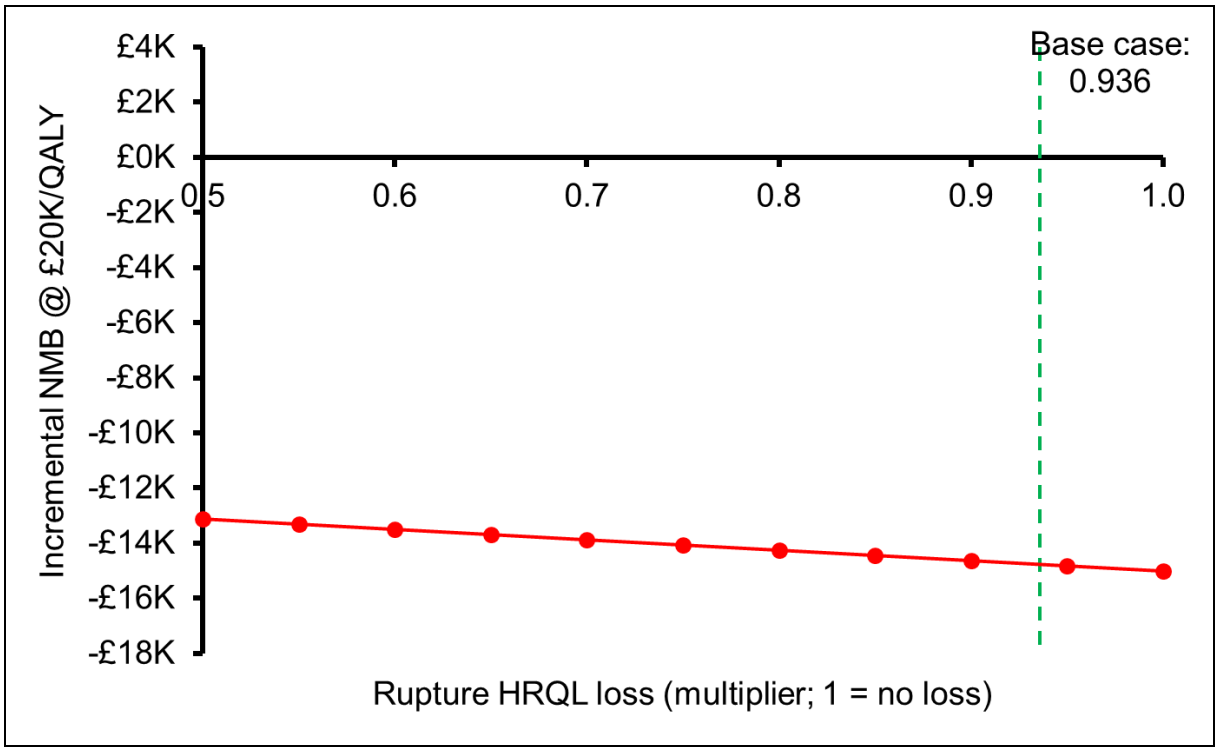


Figure HE79: INMB by HRQL multiplier associated with rupture – EVAR vs. no intervention – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

To further explore the impact of ruptures in untreated patients, we varied the proportion of ruptures that reach the point of emergency intervention. In our base-case analysis, 11% of ruptures undergo an emergency EVAR repair attempt. As such, only 11% of ruptures incur costs and HRQL effects; in the remaining 89% of people, the ruptured AAA is assumed to be fatal before repair could be attempted. Even if this value was set to 100%, such that all ruptures received an attempted repair with EVAR, the balance of costs and benefits still favours 'no intervention' at the point of deciding whether or not to attempt elective EVAR (Figure HE80). Here, the EVAR ICER is around £280,000 per QALY gained compared with 'no intervention'.

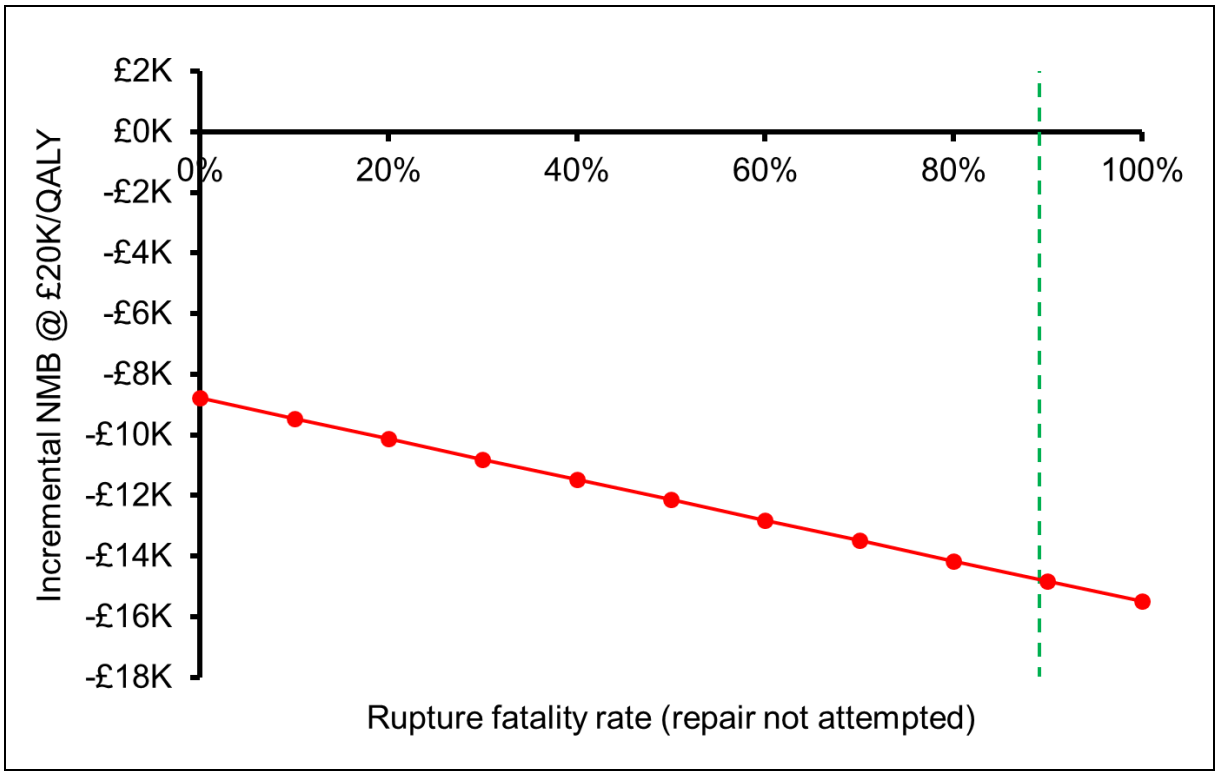


Figure HE80: INMB by rupture fatality rate in untreated AAAs – EVAR vs. no intervention – elective repair, infrarenal AAA – people for whom OSR is not a suitable intervention

The rupture rate in untreated AAAs (12.4% per year in the base-case analysis) did not feature among the top-20 variables to which model results are the most sensitive (see Figure HE74). However, this is likely to be heavily influenced by only 11% of ruptures incurring the cost of emergency EVAR, with 89% proving fatal and incurring no cost. If this figure is set to 100%, such that all ruptured AAAs do undergo an emergency repair attempt, then the rupture rate in untreated AAAs would still need to be an implausibly high 57% per year for the balance of costs, risks and benefits to favour elective EVAR over 'no intervention' (this is the point at which its ICER is £20,000 per QALY gained).

HE.3.3.2 Complex AAA

HE.3.3.2.1 Deterministic base case

In this population, for people with complex AAAs, EVAR was found to be dominated by 'no intervention' (Table HE68). The additional cost associated with the custom-made EVAR device increases the incremental cost of attempting to repair, but the high predicted perioperative mortality rate suggests that doing so causes fewer expected QALYs than not attempting to repair (-0.759). The perioperative mortality risk associated with EVAR in this population and inferior overall survival prospects lead to a large difference in cumulative incremental QALYs over the duration of the model (Figure HE81).

Table HE68: Base case cost–utility model results – elective repair, complex AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER (£/QALY)*
Strategy	Costs	QALYs	Costs	QALYs	
No repair	£924	2.324			
EVAR	£24,556	1.565	£23,632	-0.759	dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Table HE69: Components of total discounted costs – elective repair, complex AAA – people for whom OSR is not a suitable intervention

	Total discounted cost	
Cost component	EVAR	No repair
Primary procedure & stay	£21,988	£0
Post-repair monitoring	£569	£192
Graft-related complications & ruptures	£2,000	£732
Total	**£24,556**	**£924**

Key: EVAR, endovascular aneurysm repair.

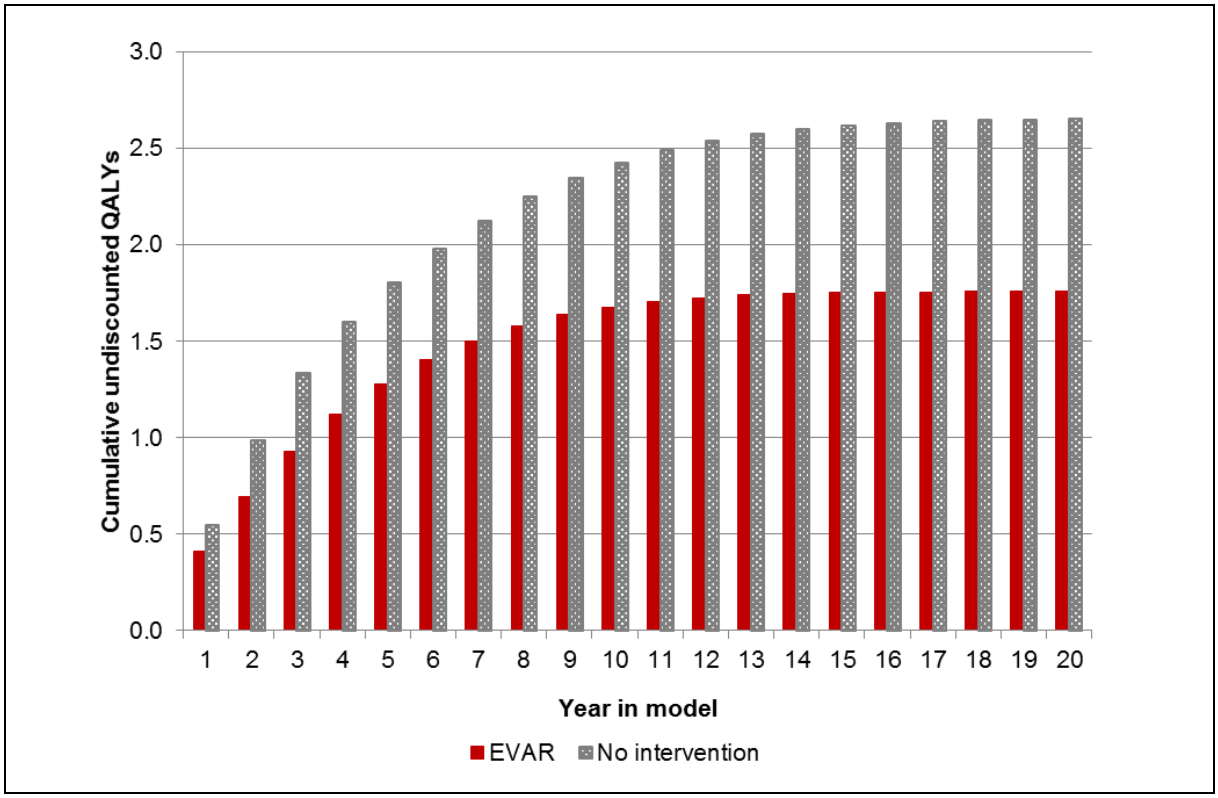


Figure HE81: Accrual of undiscounted QALYs over time – elective repair, complex AAA – people for whom OSR is not a suitable intervention

HE.3.3.2.2 Sensitivity analysis

None of 5,000 simulations predicted the EVAR ICER to be £20,000 or better, and no individual model parameter, when varied between its plausible bounds, nor model scenario, came close to changing the cost-effectiveness conclusion. The mean probabilistic results are

£23,520 in incremental costs for EVAR, and -0.751 incremental QALYs for EVAR, consistent with the deterministic base-case results.

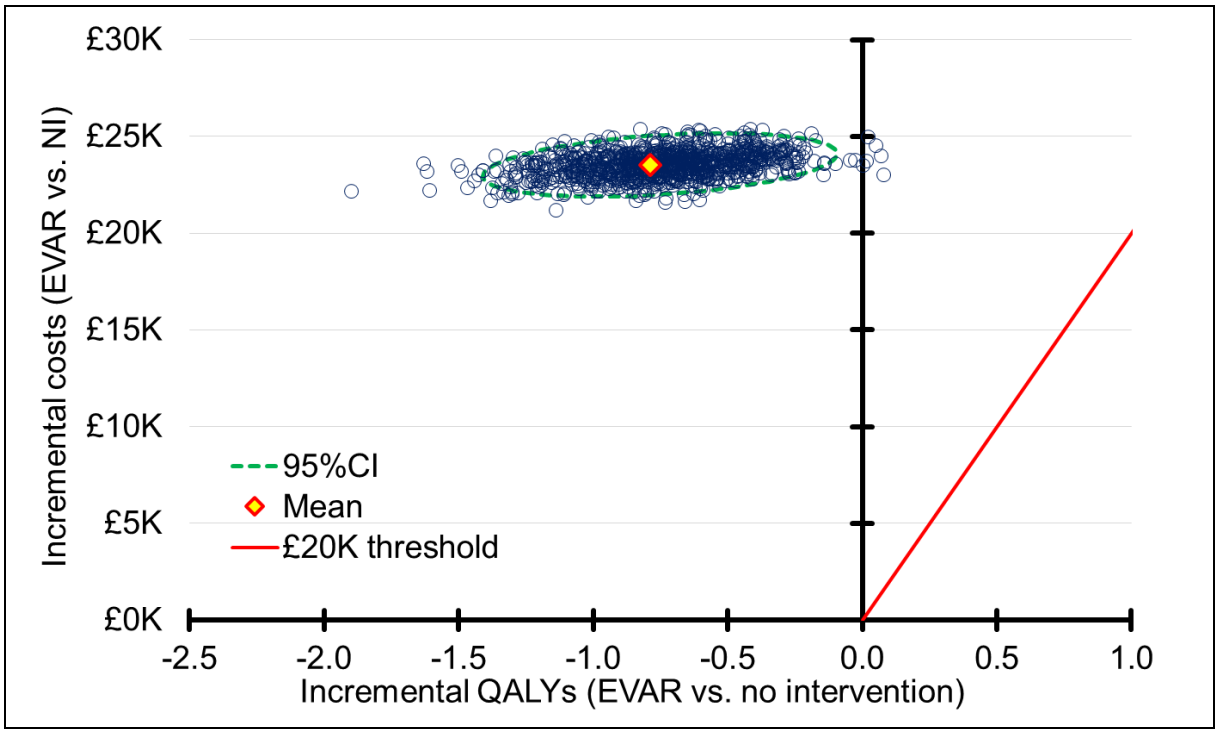


Figure HE82: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

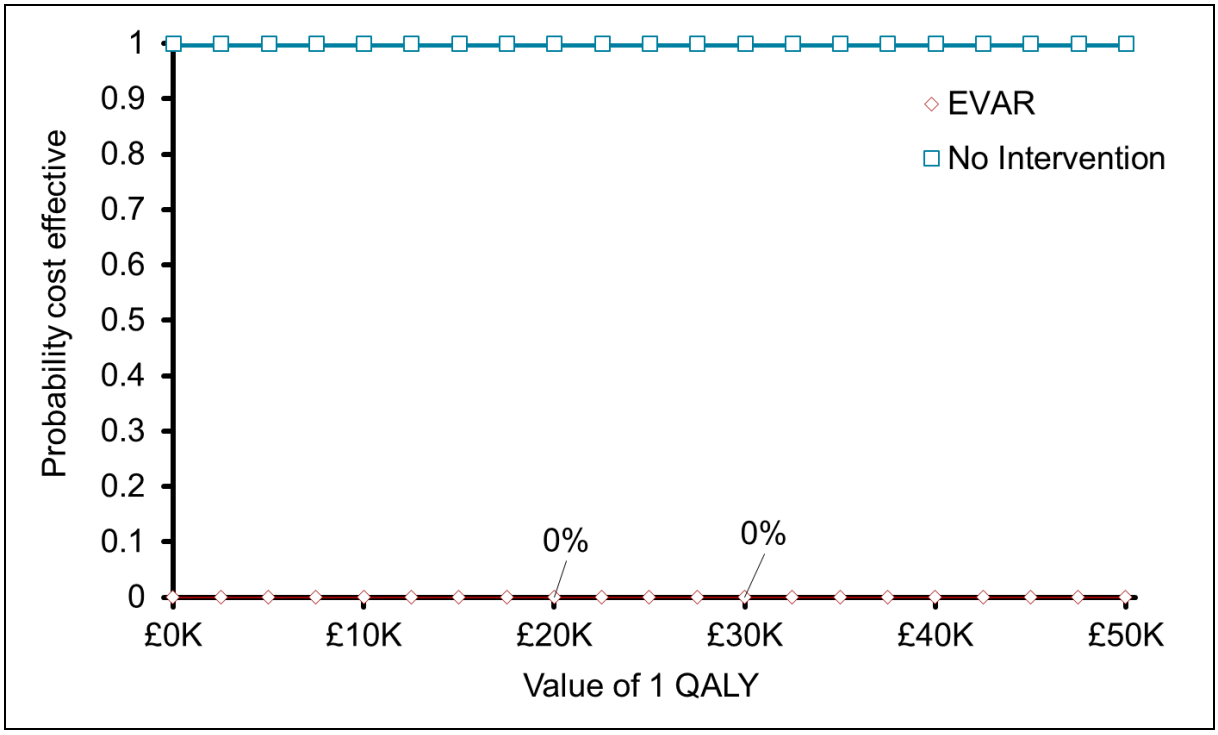
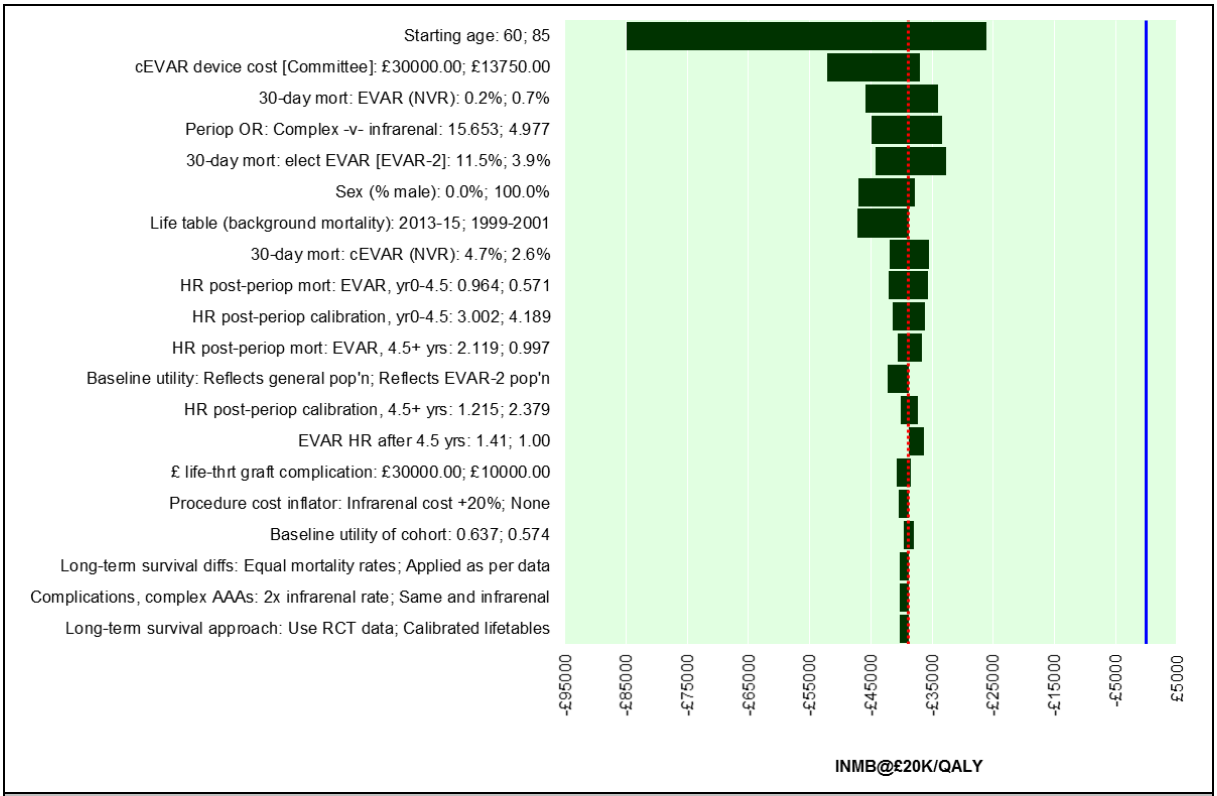


Figure HE83: Probabilistic sensitivity analysis (5,000 runs) – CEAC



Key: INMB, incremental net monetary benefit (at a value of £20,000 per QALY).

Figure HE84: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.3.2.3 Subgroup analysis

Baseline age, sex and aneurysm diameter

The result above is not sensitive to the age, sex or aneurysm diameter of the person with an AAA. In both men and women, at all ages from 50 to 100 years and at all AAA diameters from 4 cm to 12 cm, elective EVAR is dominated by 'no intervention, and therefore causes a net loss of health to the person with AAA and the NHS.

HE.3.3.2.4 Scenario analysis

Perioperative mortality – threshold analysis

For the population in whom OSR is not considered to be a suitable intervention, the only source of baseline perioperative mortality data included in the model is from the EVAR-2 trial. The National Vascular Registry mortality rates were agreed to be more representative of a healthier population, for whom OSR would be considered. As such, we do not present alternative baseline data for EVAR 30-day mortality in this population. However, the guideline development committee advised that our base-case EVAR mortality rate in this population (40.9%) may be relatively high. We therefore present a threshold analysis around this model input, varying it between 5% and 50% (Figure HE85). Across this range of perioperative mortality values, EVAR remains associated with a substantial negative INMB, indicating that, when QALYs are valued at £20,000 each, it is not cost-effective compared with 'no intervention'.

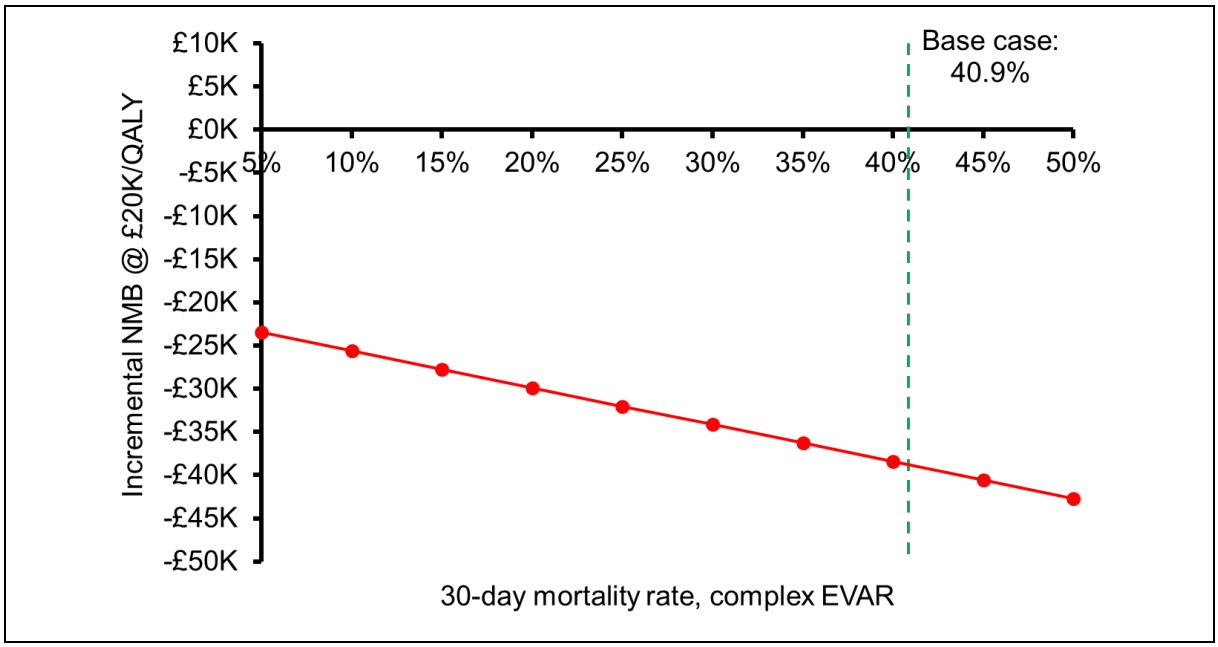


Figure HE85: INMB by perioperative EVAR mortality rate – EVAR vs. no intervention – elective repair, complex AAA – people for whom OSR is not a suitable intervention

Post-perioperative mortality

In the base-case model, the overall survival profile of patients whose complex AAA is repaired with EVAR is worse than patients who received no intervention at all times (Figure HE34). Its post-perioperative survival prospects do not offset the initial loss caused by perioperative mortality, and under these circumstances, EVAR can only be dominated by 'no intervention'. This result is not altered if parametric survival curves based on EVAR-2 data are used to characterise post-perioperative mortality, rather than the base-case use of calibrated life-tables; in fact, using the parametric curves increases the overall QALY loss associated with EVAR.

Cost-effectiveness conclusions in this population also remain the same when post-perioperative HRs between EVAR and 'no intervention' are set to 1 (analogous to the results presented in Table HE65). We conducted a threshold analysis around the mortality HR used after 4.5 years which, in the base-case analysis, favours 'no intervention' ($HR2$ = 1.454), to identify what this HR would need to be for the cost-effectiveness conclusions to favour EVAR. The HR for years 0 to 4.5 already favours EVAR ($HR1$ = 0.742). EVAR continues to produce a negative INMB at all $HR2$ values as low as 0.01. At this extreme value ($HR2$ = 0.01) EVAR is predicted to produce +0.519 incremental QALYs but, owing to its substantially higher costs, it remains associated with a high ICER of £46,878 per QALY gained.

Complex EVAR device cost

In this population, EVAR remains dominated at all levels of EVAR device cost, varied from the base-case estimate of £15,686 to as low as £0.

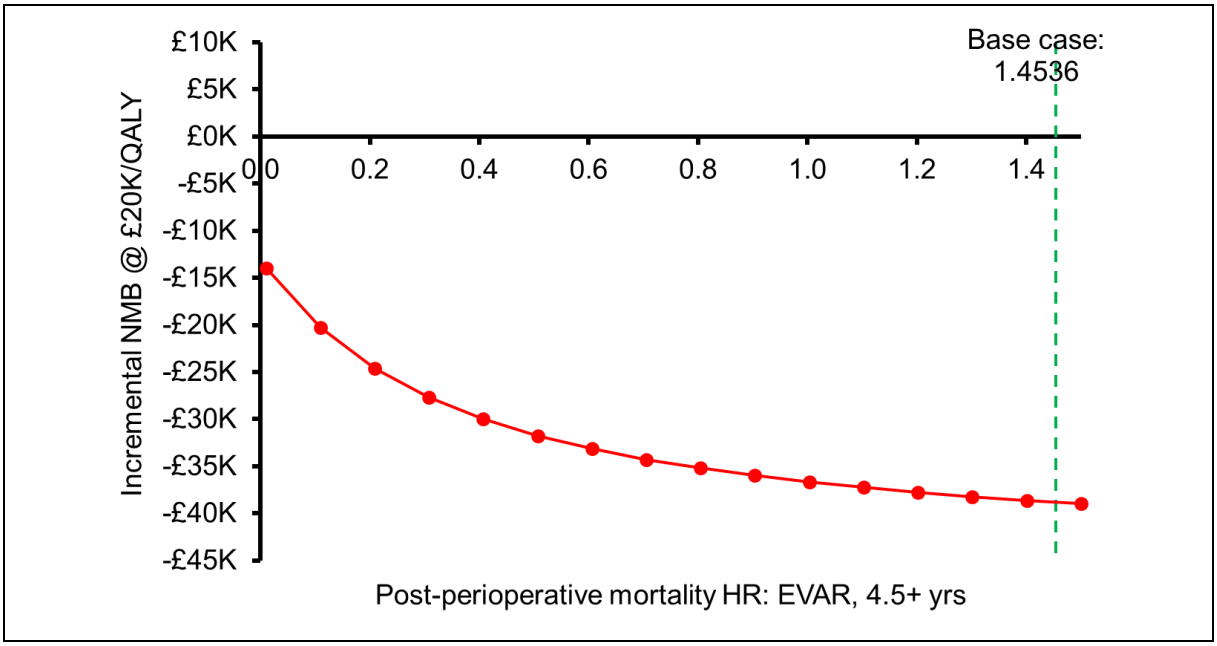


Figure HE86: INMB by mortality HR after 4.5 years – EVAR vs. no intervention – elective repair, complex AAA – people for whom OSR is not a suitable intervention

Reintervention rates

We used the same analyses as before to explore the possible impact if it could be shown that modern EVAR devices are safer and/or more effective than older generation devices, first omitting all graft-complications, and then also applying a mortality HR of 1 after 4.5 years, eradicating the base-case long-term survival benefit of 'no intervention'. In both of these scenarios, providing no aneurysm repair to people with unruptured, complex AAAs continued to dominate EVAR.

Table HE70: Sensitivity analysis: newer EVAR devices – elective repair, complex AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
No graft-related reintervention procedures					
No repair	£924	2.308			
EVAR	£22,557	1.614	£21,566	-0.694	Dominated
No graft-related reinterventions, equal mortality rates after 4.5 post-perioperative years					
No repair	£924	2.308			
EVAR	£22,558	1.721	£21,567	-0.587	Dominated

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; OSR, open surgical aneurysm repair; QALY, quality-adjusted life year.

Rupture of untreated aneurysms

We also explored the 2 sensitivity analyses around ruptures in untreated AAAs that were considered for infrarenal AAA patients. These were: (1) increasing the rupture HRQL loss to 50% for 1 year, and (2) assuming that no ruptures are fatal, such that 100% receive the full cost of emergency EVAR. Neither of these extreme value analyses was sufficient to prevent EVAR being dominated by 'no intervention' for the elective repair of complex AAAs in this population. In scenario (2), EVAR remained dominated even at implausibly high rupture rates in untreated aneurysms (e.g. 10% per month).

HE.3.4 EVAR vs. No intervention – 'unfit for OSR' population – emergency repair (ruptured)

HE.3.4.1 Infrarenal AAA

HE.3.4.1.1 Deterministic base case

In people presenting with a ruptured infrarenal AAA for whom OSR is not a suitable intervention, the base-case analysis found that EVAR had an ICER of £25,514 per QALY gained, compared with not attempting to repair the aneurysm (Table HE71). The average total discounted QALYs for a patient undergoing a repair attempt is 0.770, compared with certain death if no repair is attempted, at a cost of £19,640 per patient. We do not present the difference in total undiscounted QALYs over time here, as there are 0 QALYs on the 'no intervention' arm.

For these patients, the NICE 'end of life' criteria are likely to be applicable: (1) life expectancy without intervention is likely to be less than 2 years; (2) the intervention is expected to generate at least 0.25 additional years of life; and (3) the overall patient population in this group is likely to be small (NICE guide to the methods of technology appraisal, 2013). It is therefore appropriate to consider ICERs that exceed the usual benchmark of £20,000 per QALY gained, instead comparing them to higher thresholds, such as £30,000 or £50,000.

Table HE71: Base case cost–utility model results – emergency repair, infrarenal AAA

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	***(£/QALY)***
No repair	£0	0.000			
EVAR	£19,640	0.770	£19,640	0.770	£25,514

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Table HE72: Components of total discounted costs – emergency repair, infrarenal AAA

	Total discounted cost	
Cost component	**EVAR**	**No repair**
Primary procedure & stay	£18,559	£0
Post-repair monitoring	£300	£0
Graft-related complications	£781	£0
Total	**£19,640**	**£0**

Key: EVAR, endovascular aneurysm repair.

HE.3.4.1.2 Sensitivity analysis

The mean probabilistic ICER for EVAR (£24,846) is consistent with the deterministic result. In terms of cost-effectiveness acceptability, 23.4% of 5,000 simulations predicted the EVAR ICER to be £20,000 or better. However, the equivalent values for £30,000 and £50,000 were 66.0% and 94.7% respectively (Figure HE87 and Figure HE88). No individual model parameter, when varied between its plausible bounds, nor model scenario, caused the EVAR ICER to exceed £50,000 per QALY gained, though a cohort baseline age of 85 years gets close to doing so (Figure HE89). However, this analysis did not apply perioperative and long-term survival effect modifiers. These are explored in more detail in subgroup analyses.

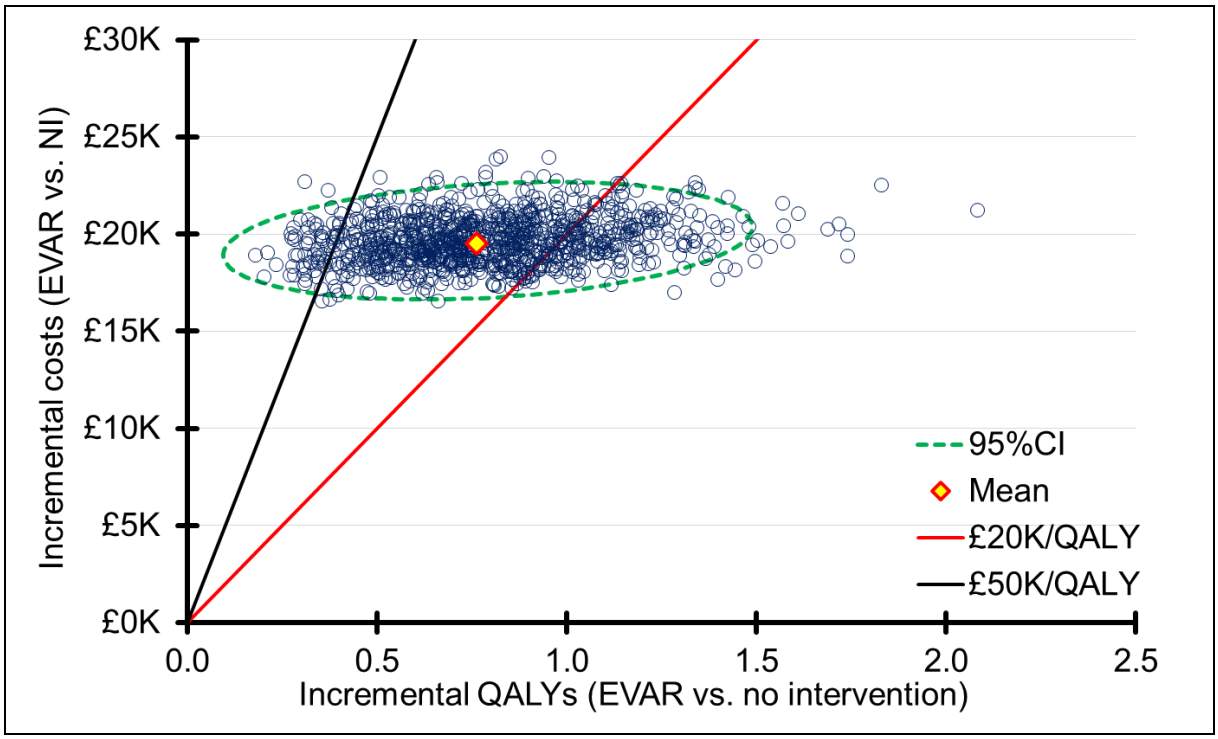


Figure HE87: Probabilistic sensitivity analysis (5,000 runs) – cost-effectiveness plane

The mean probabilistic results are £19,658 in incremental costs for EVAR, and 0.791 incremental QALYs for EVAR, with an ICER of £24,846 per QALY gained.

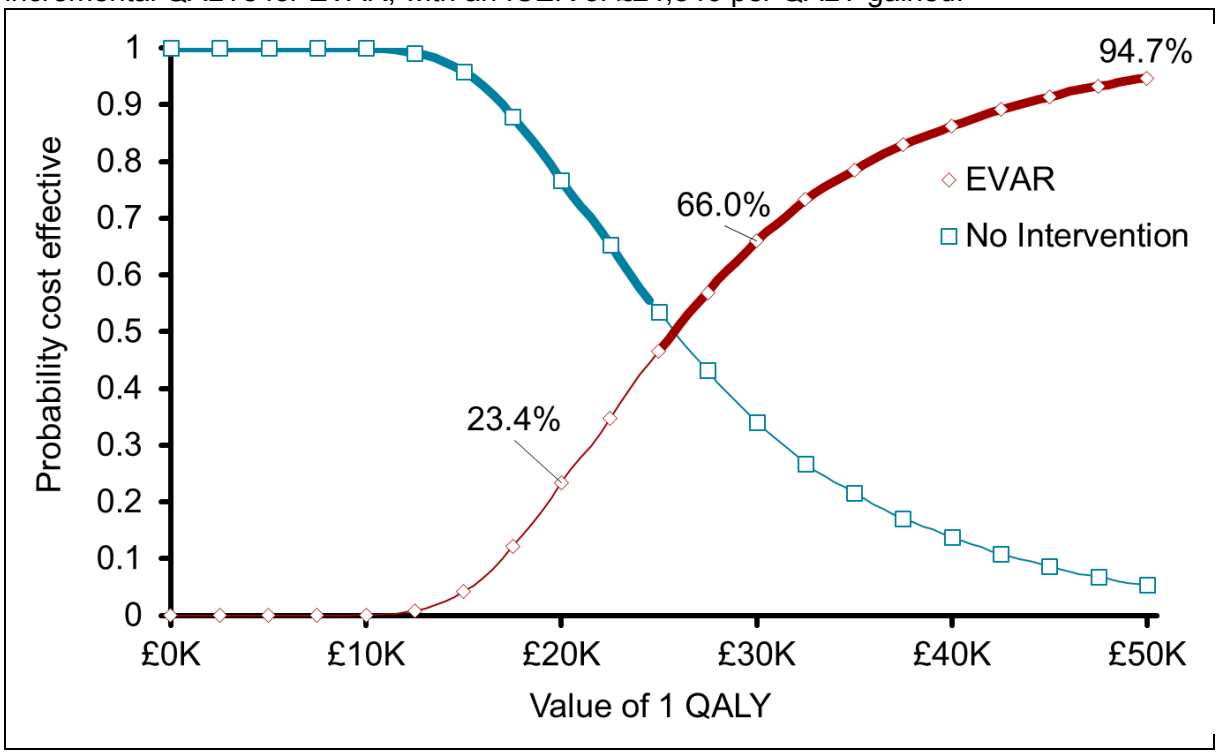
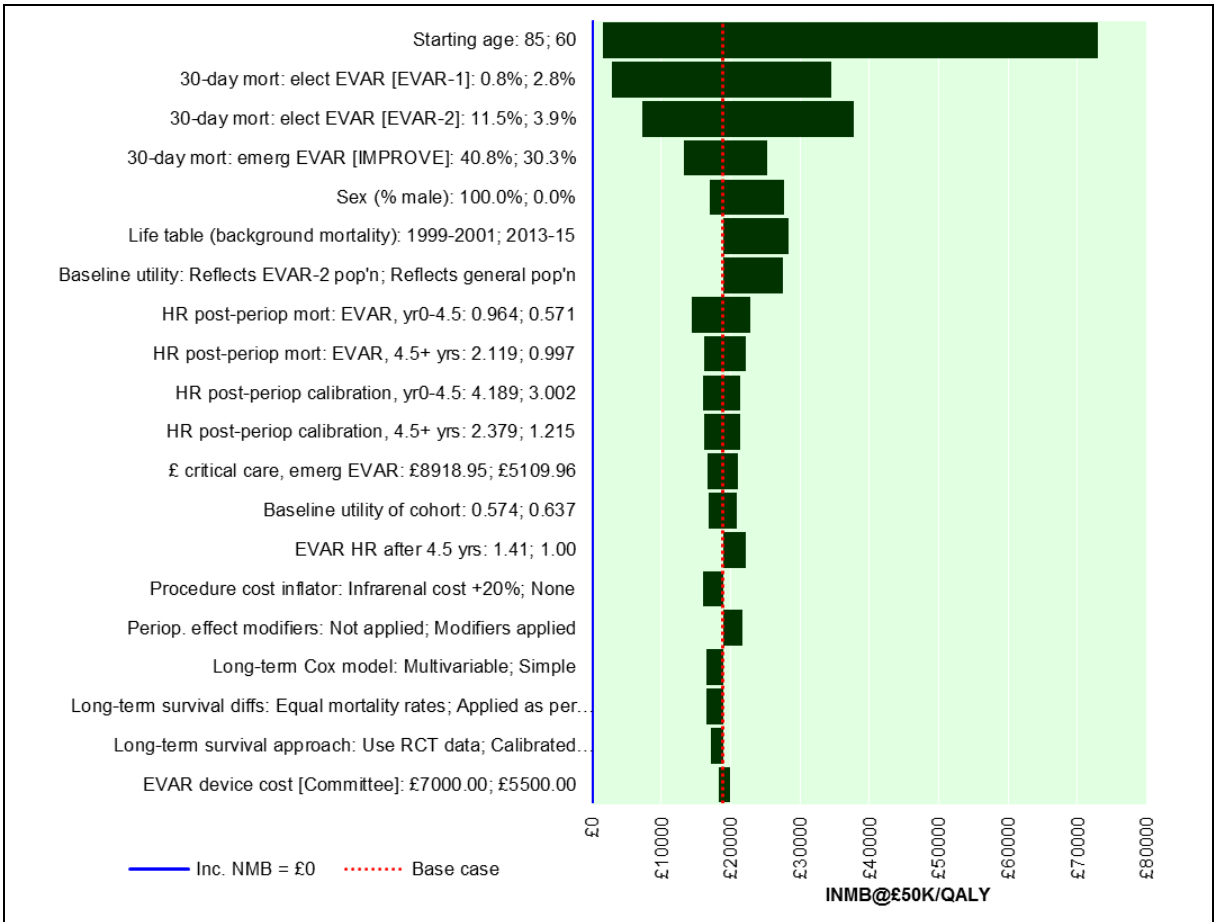


Figure HE88: Probabilistic sensitivity analysis (5,000 runs) – CEAC



*Key: INMB, incremental net monetary benefit (at a value of **£50,000** per QALY).*

Figure HE89: Univariate sensitivity analysis – 20 most influential parameters & scenarios

HE.3.4.1.3 Subgroup analysis

Baseline age

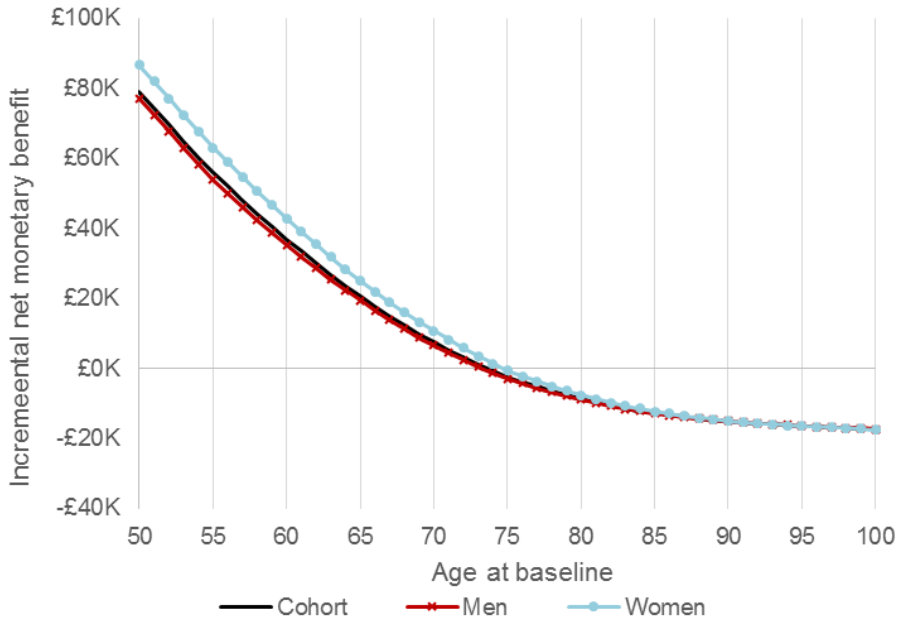
In a cohort with the sex split and mean AAA diameter of the IMPROVE trial (78% male, 9% female; 8.4 cm), age was found to be an important predictor of cost-effectiveness conclusions regarding whether to attempt emergency EVAR, in people for whom OSR is not an option. EVAR had an ICER that was better than £20,000 per QALY gained compared with 'no intervention' at all ages up to and including 73 years (Figure HE90). In people aged 74 and older, the perioperative mortality risk associated with emergency EVAR, and the life expectancy of patients who do survive the initial procedure, are not high enough, such that the ICER exceeds £20,000. Given that the end of life criteria are applicable to this patient group, the equivalent figure with INMB evaluated at £50,000 per QALY is also presented below. At this QALY value, EVAR produces a positive INMB at all ages up to and including 83 years.

Sex

The results in Figure HE90 show that cost-effectiveness conclusions are not dramatically influenced by the sex of the person with an AAA. EVAR has an ICER that is better than £50,000 in men aged up to 83, and women aged up to 84. The ICERs are better than £20,000 at ages up to 73 and 74, respectively. This relative lack of sensitivity to sex is unlike the population with ruptured AAAs for whom OSR is a possible option. In that group, being

female is strongly associated with OSR 30-day mortality, such that EVAR is much more likely to be cost-effective in women. In the present comparison, OSR is not an option, and so this effect does not apply and sex is less influential.

£20,000 per QALY



£50,000 per QALY

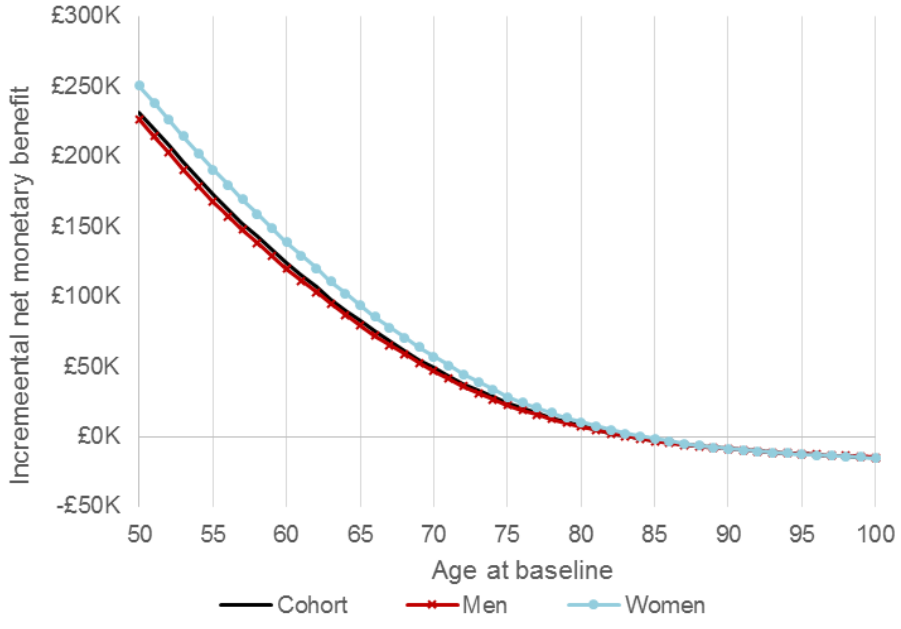


Figure HE90: INMB by age and sex – EVAR vs. no intervention – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

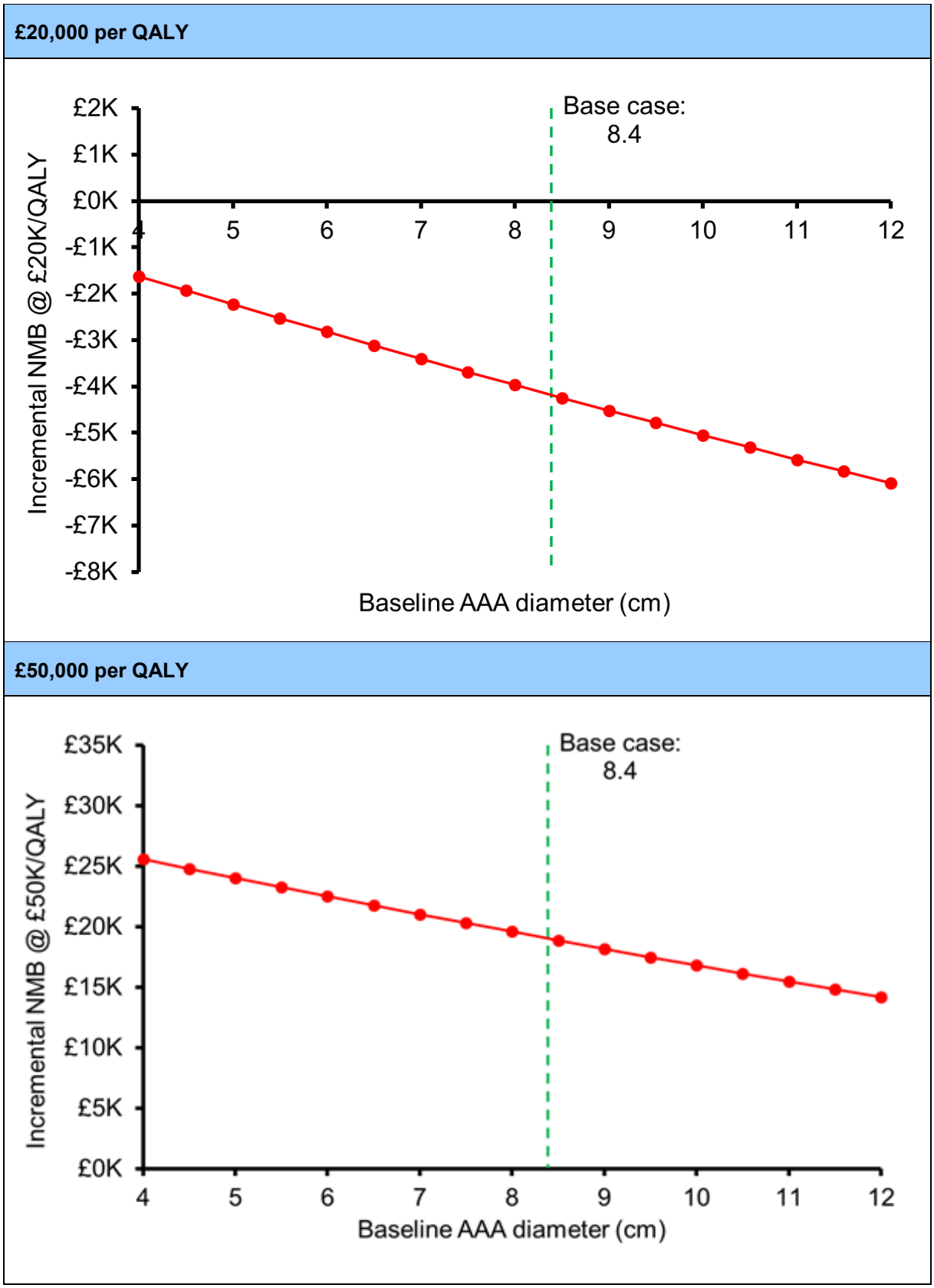


Figure HE91: INMB by aneurysm size – EVAR vs. no intervention – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Aneurysm diameter

The base-case result is not sensitive to baseline AAA diameter (Figure HE91). At all pre-operative aneurysm sizes between 4 cm and 12 cm, emergency repair using EVAR had an ICER worse than £20,000 per QALY gained compared with no intervention. However, the ICER was better than £50,000 across this range of AAA sizes.

HE.3.4.1.4 Scenario analysis

Perioperative mortality – alternative baseline values

As described in Section HE.2.3.3, for emergency EVAR in this population, we use the IMPROVE 30-day mortality rate (35.4%) as our baseline rate, which is then increased to reflect that the population of interest is less 'fit' than IMPROVE study participants, using an odds ratio (4.70) derived by comparing EVAR-1 and EVAR-2 perioperative mortality rates. The resulting mortality rate is 72.1%. This is the only source of perioperative mortality data that was obtained for this analysis; therefore we do not present alternative sources of baseline data in this population. Instead, we conduct a threshold analysis around the base-case EVAR mortality rate (Figure HE92). Varying this rate between extreme values of 5% and 95%, at 5% increments, suggests that the perioperative mortality rate of emergency EVAR must be lower than 65% in this population for its ICER to be £20,000 or better, relative to 'no intervention'. The EVAR ICER remains under £50,000 per QALY gained at all perioperative mortality rates up to and including 85%.

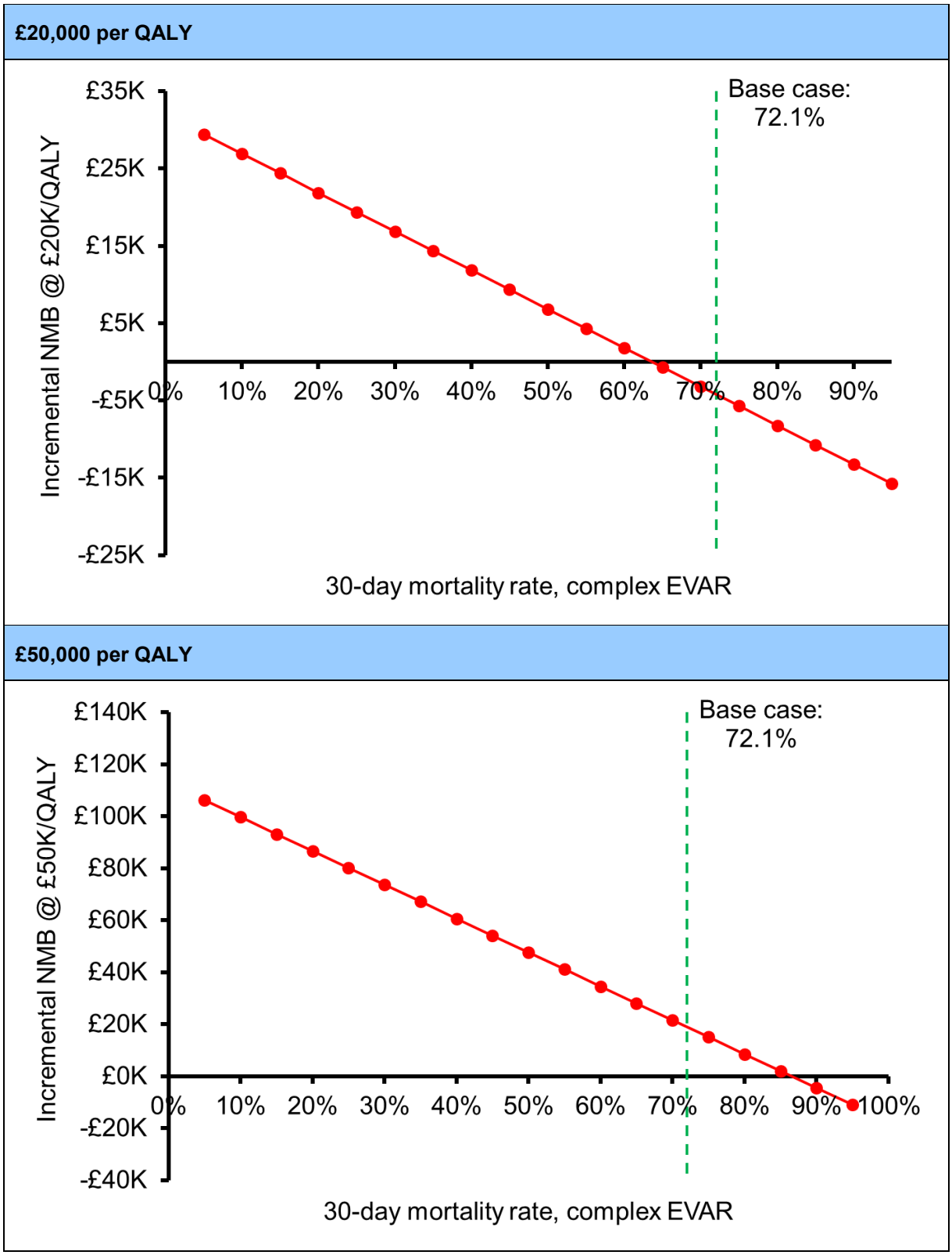


Figure HE92: INMB by perioperative EVAR mortality rate – EVAR vs. no intervention – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Post-perioperative mortality – parametric survival curves

The use of parametric curves to characterise post-perioperative survival, fitted to the EVAR-2 study data, was not found to substantively influence cost-effectiveness results (Table HE73).

These inputs only affect the EVAR arm, given that an unrepaired rupture is assumed to have a 100% mortality rate. The ICER for emergency EVAR, compared with doing nothing, remains just under £27,000 per QALY gained, close to the deterministic ICER from the base-case analysis (£25,236). This lack of sensitivity is due to the high perioperative mortality rate, which means relatively few patients survive the emergency EVAR procedure to experience the different post-perioperative survival profiles. Additionally, all of these survival curves provide similar, reasonable fits to the data, such that there is little variation between them.

Table HE73: Sensitivity analysis: parametric curves to model post-perioperative survival – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Incremental result shown (EVAR vs NI)	*EVAR function*		
	Gamma	**Gompertz**	**Weibull**
Costs	£19,612	£19,610	£19,611
QALYs	0.737	0.734	0.737
EVAR ICER	£26,627	£26,709	£26,608

Key: ICER, incremental cost-effectiveness ratio; NI, no intervention; QALY, quality-adjusted life-year.

Post-perioperative mortality (EVAR)

In our base-case analysis, EVAR post-perioperative mortality is informed by our survival analysis of elective patients in the EVAR-2 dataset (see Section HE.2.3.3). It is not appropriate to test a scenario in which the survival estimates for the 2 emergency arms are equal, due to the 100% mortality associated with an untreated ruptured AAA. As such, the same long-term survival scenarios that were tested in Table HE65 are included here, but are applied only to the EVAR arm. In both scenarios – the first favouring EVAR, the second favouring 'no intervention' – the EVAR ICER remains between £20,000 and £30,000 per QALY gained (Table HE74).

Table HE74: Sensitivity analysis: long-term EVAR survival effects – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Strategy	*Total (discounted)*		*Incremental*		*ICER (£/QALY)*
	Costs	**QALYs**	**Costs**	**QALYs**	
EVAR post-perioperative mortality equal to elective 'no intervention' after 4.5 years (HR = 1)					
No repair	£0	0.000			
EVAR	£19,678	0.835	£19,678	0.835	£23,559
EVAR post-perioperative mortality equal to elective 'no intervention' (HR = 1 at all times)					
No repair	£0	0.000			
EVAR	£19,584	0.717	£19,584	0.717	£27,304

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

EVAR device cost

We varied the cost per EVAR device from £5,000 to £15,000 in a threshold analysis, and evaluated the INMB of emergency EVAR compared with 'no intervention', at values of £30,000 and £50,000 per QALY. These were chosen due to the appropriateness of the 'end of life' criteria in this patient group. The unit cost would need to approach £10,000 for EVAR to have an ICER worse than £30,000 per QALY gained, compared with providing no emergency repair attempt (Figure HE93). Its ICER was never worse than £50,000 per QALY gained at any unit cost per device up to £15,000 (Figure HE94). Given that our base-case

estimate is £6,500 per EVAR device, the cost required for EVAR to no longer be cost effective, factoring in end of life considerations, is implausibly high.

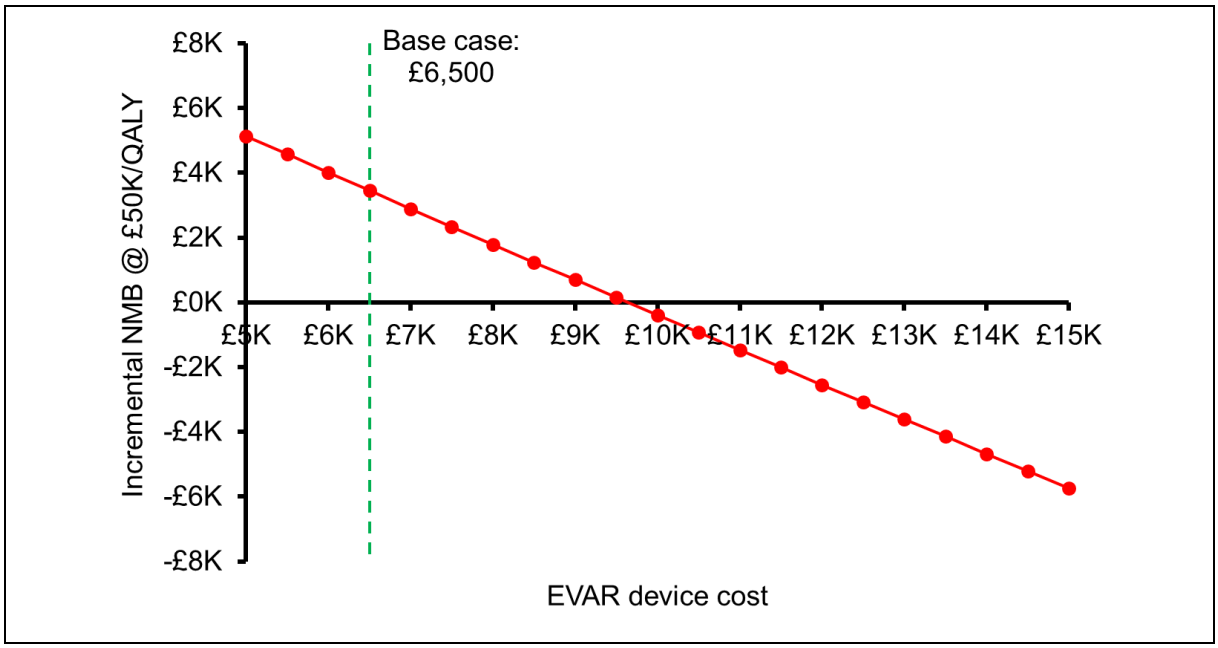


Figure HE93: INMB at £30,000 per QALY, by EVAR device cost – EVAR vs. no intervention – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

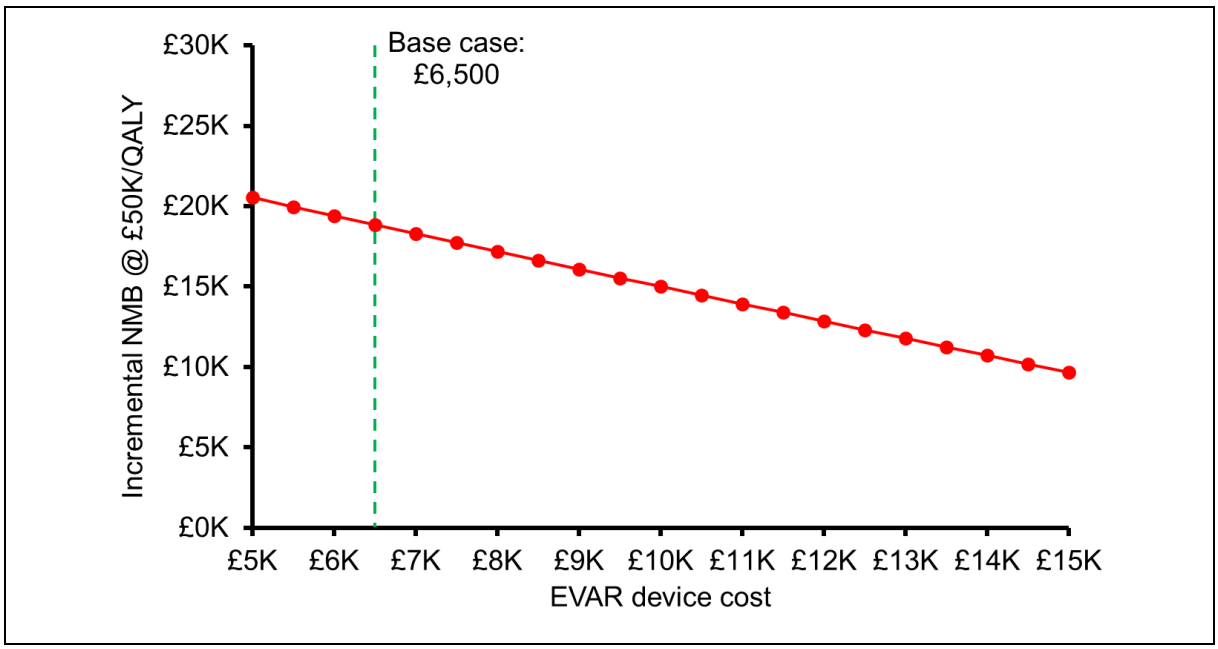


Figure HE94: INMB at £50,000 per QALY, by EVAR device cost – EVAR vs. no intervention – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

Reintervention rates

To explore hypothetical improvements in modern EVAR devices compared with the generation of devices used in the RCTs, we omit all graft-related complications from the model. This causes a modest improvement in the ICER for EVAR (Table HE75), though it remains above £20,000 per QALY gained. The relatively small effect is because of the high

perioperative mortality with emergency EVAR in this population (72.1%), meaning only a relative small proportion of patients survive the procedure to benefit from the 0% reintervention rate thereafter. In previous populations, a further, more extreme scenario was also explored, in which post-perioperative mortality rates were set to a value of 1. However, this is not appropriate in the present patient group, due to the 100% mortality rate in people with an untreated ruptured AAA.

Table HE75: Sensitivity analysis: newer EVAR devices – emergency repair, infrarenal AAA – people for whom OSR is not a suitable intervention

	Total (discounted)		*Incremental*		*ICER*
Strategy	**Costs**	**QALYs**	**Costs**	**QALYs**	*(£/QALY)*
No repair	£0	0.000			
EVAR	£18,859	0.772	£18,859	0.772	£24,426

Key: EVAR, endovascular aneurysm repair; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Cost of 'no treatment'

Lastly, as described in Section HE.2.3.11, the base-case model applies no cost to the decision not to intervene. The guideline committee agreed that this was likely to be the most appropriate assumption for this analysis. However, we undertook a threshold analysis around the cost incurred by not intervening on a ruptured AAA, for example, any palliative care costs. Specifically, we sought to identify the cost at which the EVAR ICER was £20,000 per QALY. The cost of 'no intervention' that achieves this ICER is £4,245 per patient. This is one-third of the estimated cost of an EVAR procedure (minus the device), and therefore appears to be very high for a 'no intervention' strategy.

HE.3.4.2 Complex AAA

EVAR is not typically possible for the repair of a ruptured complex AAA. Such aneurysms require custom-built EVAR devices, which are made to order, and are therefore not readily available to surgeons for emergency cases. Accordingly, no results are presented for this population.

HE.4 Discussion

HE.4.1.1 Principal findings

The new modelling analyses presented here covered the following comparisons and patient populations:

- EVAR compared with OSR, in people for whom OSR is a possible option
    - Elective repair (unruptured AAAs) & emergency repair (ruptured AAAs)
    - Infrarenal AAAs and complex (non-infrarenal) AAAs
- EVAR compared with 'no intervention', in people for whom OSR is not a possible option
    - Elective repair (unruptured AAAs) & emergency repair (ruptured AAAs)
    - Infrarenal AAAs and complex (non-infrarenal) AAAs

In people for whom OSR may be a suitable intervention, our principal finding is that EVAR is highly unlikely to be considered cost effective for the elective repair of unruptured aneurysms, compared with OSR. For infrarenal aneurysms, EVAR is associated with higher total costs and lower QALYs than OSR, such that it is a dominated strategy. In this population, the difference in perioperative mortality rates between the 2 options is small. As a result, a large proportion of OSR patients survive the procedure to experience the long-term survival benefits associated with OSR. For people with complex AAAs, EVAR is not dominated; it produces more QALYs than OSR. The general increase in perioperative mortality rates associated with complex AAAs causes a bigger absolute change in OSR mortality, such that a smaller proportion of OSR patients survive to experience its long-term survival benefits. However, custom-made EVAR devices to repair complex AAAs are more expensive, to the extent that EVAR is unlikely to be cost-effective in this group too. These results were not sensitive to the person's age, sex or aneurysm size.

The cost–utility conclusions were not the same in people who require emergency repair for a ruptured AAA. For this population, it is more accurate to say that our comparison was between: (1) a system in which EVAR was used in people whose aorta is anatomically suitable, otherwise OSR, and (2) a system in which OSR is used in all patients. Here, we found that the EVAR strategy is very likely to have an ICER that is better than £20,000 per QALY compared with OSR, with a deterministic ICER of around £5,700, and is therefore likely to be considered to represent an effective use of NHS resources. The relatively large difference in perioperative mortality between the 2 interventions, driven entirely by its relative effectiveness in women, dominates the analysis, leading to the favourable ICER for the EVAR strategy. However, our subgroup analyses identified some important details behind these 'average' cohort results. We found emergency EVAR to be much more likely to be cost-effective in women rather than men, because being female was found to significantly increase the risk of perioperative mortality associated with OSR (but not EVAR). The ICER for EVAR is better than £20,000 per QALY gained in women of all ages from 50 to 100. There is no difference in perioperative mortality rates in men, such that the EVAR ICER is worse than £20,000 per QALY gained in younger men (aged 70 or less). In these people, perioperative survival after OSR is sufficiently high that the additional costs associated with EVAR do not represent reasonable value for money. Results were not sensitive to aneurysm size.

No comparison of emergency EVAR with OSR was performed explicitly for ruptured complex AAAs, because it is not typically possible to repair complex aneurysms with EVAR in this setting, as the device needs to be custom-made to order.

In people for whom OSR is not considered to be a suitable intervention, because their likelihood of surviving the invasive procedure is perceived to be too low, our main finding is that EVAR is again highly unlikely to be cost-effective for the elective repair of unruptured aneurysms, here compared with not attempting aneurysm repair. For infrarenal AAAs, providing EVAR may, depending on model assumptions, produce a modest benefit in expected QALYs, but its high cost relative to a strategy of 'no intervention' produces an ICER that exceeds £460,000 per QALY gained (where EVAR is not dominated). For complex AAAs in this relatively unfit population, the perioperative mortality risk involved with EVAR means that EVAR provides fewer QALYs than not intervening. Neither of these results is sensitive to the patient's age, sex or AAA diameter, and so leaving the aneurysm untreated is the cost-effective strategy in all cases, assuming QALYs are value at conventional levels.

In the emergency setting for this population, we assumed that deciding not to attempt AAA repair was associated with a 100% mortality rate. Compared with this strategy, providing emergency EVAR for infrarenal AAAs was associated with an ICER of around £25,500 per QALY gained. The estimated QALY gain (+0.770), and certain death without attempting EVAR, mean the NICE 'end of life criteria' are likely to be applicable here. Accordingly, higher QALY valuations were evaluated. EVAR was likely to have an ICER of £30,000 or better, and almost certain to have an ICER of £50,000 or better. However, these results were found to be sensitive to the patient's age. The EVAR ICER, compared with 'no intervention', is better than £20,000 per QALY gained in younger patients (aged up to 73 years). In people aged 74 and older, the perioperative mortality risk associated with emergency EVAR increases to a level at which the ICER exceeds £20,000. The ICER exceeds £50,000 in patients aged 84 and older. Results were not sensitive to sex or aneurysm size.

No comparison of emergency EVAR with 'no intervention' was performed explicitly for ruptured complex AAAs in this population. Again, this is because it is not typically possible to repair complex aneurysms with EVAR as the device needs to be custom-made to order.

In summary, our analyses suggest that elective EVAR is unlikely to be a cost-effective option for the repair of any unruptured AAA, compared with OSR in people for whom OSR may be suitable, and compared with leaving the aneurysm untreated in people for whom OSR is not suitable. However, a strategy that permits emergency EVAR where an aneurysm is anatomically suitable is likely to be considered cost effective for the repair of ruptured AAAs, compared with OSR, in people for whom OSR may be suitable. This is more likely to be true in women and in older men. In people for whom OSR is not a suitable option, treating ruptured AAAs with emergency EVAR has an ICER that is likely to be better than £30,000 per QALY gained, compared with providing no attempt at aneurysm repair.

HE.4.1.2 Strengths of the analysis

The cost–utility analyses conducted for this guideline have a number of strengths, advancing much of the modelling that precedes it. Firstly, we were provided with access to the most up-to-date, long-term survival data for the 3 UK trials in this area: EVAR-1, EVAR-2 and IMPROVE. These data allowed us to model overall survival in a detailed way, including modelling its 3 distinct component parts: waiting time, perioperative (30-day), and post-perioperative (long-term) survival. No previous analyses were able to use survival data as mature as these sources and, for elective repair comparing EVAR with OSR, we were also able to draw on published long-term data from non-UK trials (DREAM and OVER). For the EVAR-2 trial, we also attempted to account for extensive crossover from the 'no intervention' arm to the EVAR arm, using a validated method. Ultimately, our base-case approach to implementing the survival data into the model – by calibrating general population survival data to match the relevant trials – was able to provide excellent fits to the data (see Sections HE.2.2.3 and HE.2.3.3). We feel this provides a near-complete characterisation of survival in elective repair patients with infrarenal AAAs. Although the survival data in emergency repair patients were less mature, they are still relatively long-term (7 years), and supplementing our

model beyond this with the mature data on elective cases was seen as a reasonable approach to extrapolation.

The relative effectiveness of EVAR and OSR in terms of perioperative survival in both the elective and emergency settings was obtained from recent Cochrane meta-analyses of the relevant RCTs. No additional data were identified through the evidence review to supplement these Cochrane values, meaning they are the most up-to-date estimate of relative effects from the largest number of randomised observations. This is clearly superior to relying on an individual trial to inform differences in clinical outcomes. While our inputs for relative 30-day survival are drawn from these pooled RCT estimates, we use UK registry data to inform baseline perioperative mortality rates (National Vascular Registry, 2016). Using these data ensures that our baseline estimates are from the best current 'snapshot' of outcomes in the NHS, to which the RCT-derived best estimates of relative effectiveness are applied.

One of the main objectives of this analysis, and ultimately another of its strengths, is that we have attempted to model beyond the population with infrarenal aneurysms. In particular, our models provide cost–utility results for EVAR, OSR and 'no intervention' in people with 'complex' AAAs, that is, aneurysms that are not covered by the instructions for use of EVAR devices. The custom-made nature of EVAR devices to repair complex AAAs means their prices are not easily available, therefore we sourced up-to-date, accurate costs directly from NHS Trusts. To inform clinical outcomes associated with the repair of complex aneurysms, we also use the National Vascular Registry to make baseline perioperative outcomes as representative of UK practice as possible. While various assumptions were made to model complex AAAs, particularly regarding the transferability of data in infrarenal AAAs – making these results necessarily more exploratory – such assumptions were validated by the expert guideline development committee.

The existence of a technology appraisal (TA167) preceding this guideline has allowed our modelling to address some of the critical comments levelled at the TA analyses. Areas that we feel have been explicitly addressed in the present model are described in Table HE76.

Table HE76: Areas in which the model attempts to address concerns regarding TA167 analyses

Item	*Concern*	*Addressed in the new model*
Over-reliance on the EVAR trials	That existing models rely too heavily on the EVAR trials to inform their clinical and economic inputs.	For both elective and emergency repair analyses, our model utilises relative effects on perioperative mortality from published Cochrane meta-analyses of the relevant RCTs. For elective repair, we have also meta-analysed differences in long-term survival from 3 trials: DREAM and OVER, as well as EVAR-1. However, in the population for whom OSR is not a suitable option for AAA repair, the EVAR-2 trial remains the only source of randomised, comparative evidence. Being UK trials, EVAR-1, EVAR-2 and IMPROVE are the most appropriate to inform resource use and quality of life data.

Item	*Concern*	*Addressed in the new model*
Inclusion of reinterventions	That laparotomy-related procedures had not been adequately captured.	Since TA167, the EVAR trial investigators have retrospectively incorporated hernia procedures to their reporting. They are also included in the IMPROVE trial reporting and, accordingly, are captured in the present model. We have also captured additional laparotomy-related procedures (lysis of adhesions and bowel resection), which are more prevalent following open surgery, based on a matched comparison of US Medicare data. The particular resource use and quality of life implications of these complications are captured.
Survival extrapolation	That overall survival had been assumed to converge after 4 years, based on EVAR-1 data, despite a perceived clinical rationale for lower late AAA-related mortality following EVAR.	The present analyses have used longer-term survival (and reintervention) data than were available at the time of TA167. In the case of elective repair, this includes 15-year follow-up of EVAR-1, as well as several years of DREAM and OVER survival data. These data are consistent with the previous approach of having overall survival converge after around 4 years, and in fact suggest that OSR is associated with superior long-term survival.
Intermediate care	That resource use associated with intermediate care, such as home visits, had not been captured.	Home visits by family doctors and nurses, and days spent in a nursing home, were captured and reported in the primary procedure resource data of the IMPROVE study, and are therefore included in our emergency repair analyses.
Conversion to OSR	That the unit cost of an EVAR procedure being converted to OSR was too high (£42,000).	The cost of an EVAR procedure being converted to an open procedure is assumed to have been captured in the intention-to-treat primary procedure resource use data from EVAR-1 and IMPROVE. As a result, we do not apply any additional procedure cost for the proportion of patients who required a conversion; only the relatively low cost of an additional open repair graft is incurred.
Subgroup analysis	That analysing subgroups of patients may be inappropriate due to the already small population size.	Our primary analyses remain ‘average cohort’ analyses, evaluated at the mean patient characteristics of the relevant UK trials (EVAR-1, EVAR-2 and IMPROVE). We explore the impact of sex, baseline age and AAA size only in explicit sensitivity analyses, and to fully characterise our uncertainty in the evidence base for probabilistic sensitivity analysis.

The analyses presented here also benefit from extensive one-way and scenario analyses. All parameters and key scenarios were included in univariate analyses; these largely suggest that the base-case deterministic results across the different modelled populations are relatively robust. However, we have also explored key inputs in greater detail, from patient characteristics such as age, sex and aneurysm size, to structural modelling assumptions, such as the use of parametric survival curves and alternative baseline 30-day mortality data. These were subject to different scenarios, extreme value analyses (using a value far from the base-case point-estimate), and threshold analyses. In particular, our modelling of age and sex subgroups showed important distinctions in cost–utility outcomes between men and women, and where the balance between costs and benefits changes at different ages. The

extent to which these inputs affect perioperative and long-term mortality outcomes was informed by analyses of European registry data or the UK trials.

Lastly, that these models were developed in close collaboration with the expert guideline committee is an asset to the analyses. Model conceptualisation and development began at a relatively early stage during guideline development, and the committee had several opportunities to review and discuss its evolution over time, advising on inputs, validating outputs, and requesting additional analyses. This invariably increases the degree to which the analysis results are robust and applicable to UK practice.

HE.4.1.3 Limitations of the analysis

The modelling presented here is subject to some limitations of note, which should be kept in mind while interpreting the cost–utility results (although it should also be emphasised that the guideline committee was aware of these limitations in making their recommendations).

A primary limitation is the limited evidence to inform our analyses in some patient populations. The largest amount of evidence exists for the elective repair of unruptured AAAs, including 3 trials with long-term follow-up data, in people for whom OSR is a possible intervention. All of these trials excluded people with complex aneurysms. Because of this, our analyses in people with complex aneurysms necessarily rely on assumptions about the transferability of data from people with infrarenal aneurysms. For example, we have assumed that the measures of relative effectiveness in perioperative (30-day) mortality between EVAR and OSR, derived from infrarenal AAA trials, can be used in people with complex AAAs. We use baseline mortality estimates from people with complex aneurysms, but apply the randomised measures of relative effectiveness in infrarenal AAAs to these baseline values. Cost–utility results are somewhat sensitive to whether complex EVAR data or complex OSR data are used for the baseline figure, to which the odds ratio should be applied. However, the committee was clear that the base-case choice (EVAR data as the baseline figure) gave a more accurate representation of outcomes in current UK practice. For long-term survival, we assumed that once a person with a complex AAA has survived the perioperative period, their survival prospects are the same as a person whose aneurysm was infrarenal. We also assumed that reintervention, resource use and HRQL inputs were transferable to complex AAAs, though complex EVAR devices had their own unit cost and additional waiting time requirement, as they must be custom-made to order. It is unclear whether these assumptions over- or underestimate the cost-effectiveness of EVAR compared with OSR in complex AAAs, but the guideline committee advised that it was reasonable in the absence of alternative data.

Only 1 trial has been identified in people for whom OSR in not a suitable intervention, though it has long-term follow-up data. However, the trial (EVAR-2) was subject to extensive crossover of participants from the ‘no intervention’ arm to EVAR. This causes bias in the resulting survival estimates, breaking trial randomisation if the people who switch differ systematically compared with those who do not. We adjusted the survival data for crossover using a well-established method (RPSFT), though this inevitably adds a degree of uncertainty to the resulting survival estimates. This trial (EVAR-2) did not report resource use or cost data as extensively as the EVAR-1 trial; as such, we use the more complete data by assuming the EVAR-1 resource use are transferable to the EVAR-2 population. If anything, this will underestimate the total cost in patients who receive EVAR, as one may expect a less-fit patient group to incur higher resource use. For people in this population with complex AAAs, we again assume that the majority of inputs are transferable from data on people with infrarenal AAAs, with the exception of the baseline perioperative mortality rate of EVAR, and the cost of a bespoke complex EVAR device. It was agreed that aneurysm complexity is unlikely to affect survival prospects in people who do not undergo an elective repair attempt, therefore the EVAR-2 control arm survival data are applied here.

Several RCTs evaluate this comparison in the emergency setting, though only 1 has relatively long-term survival data. Since the IMPROVE survival data are less mature than EVAR-1 and EVAR-2, it was necessary to rely on more extensive extrapolation to conduct a lifetime analysis. In people for whom OSR is a possible intervention, we have assumed that the measure of relative effectiveness from the mature long-term data in elective patients can be transferred to emergency patients. This occurs once the IMPROVE survival data are exhausted, after 6.5 post-perioperative years. At this point, it is perhaps reasonable to assume that 2 individuals, identical in all aspects other than 1 had elective AAA repair 6.5 years ago, the other an emergency procedure, will have similar survival prospects. For people in whom OSR is not a suitable intervention, there are no randomised, comparative data. The most appropriate approach was agreed to be to adjust the EVAR perioperative mortality rate in IMPROVE, using a 'fitness' effect derived from a comparison of the elective EVAR-1 and EVAR-2 trials, and then assuming the EVAR-2 survival data apply thereafter. The IMPROVE resource use and HRQL were also transferred to this group.

The limitations described above can be broadly grouped as limitations associated with a lack of randomised, comparative evidence. There are also a number of more specific and, generally, more minor issues, spanning various model inputs. In terms of our approach to survival analysis, the hazard ratios used to calibrate general population survival to match the trial populations required a piecewise approach for the EVAR-2 and IMPROVE trials. The 'cut-point' for these analyses was identified in an iterative way; we tested different cut-points at 0.5 year intervals, and selected the most suitable from those (by minimising an objective goodness-of-fit criterion and checking visual fit to the data). An excellent fit to the empirical data was achieved in this way. However, it is possible that marginally superior results could be obtained by testing approaches comprising more than 2 cut-points and/or cut-points occurring at less round numbers. Further, this calibration was based on the average cohort of the relevant RCT; we did not run it separately for men and women, or different baseline ages, which may have had a minor influence on our subgroup analysis results.

In capturing reintervention procedures in our models, we supplemented RCT data with some lower quality evidence, from a matched comparison of US Medicare data. While we would not typically do this, here it served the purpose of ensuring we capture a known difference in the prevalence of laparotomy-related complications between EVAR and OSR; these procedures have not typically been reported in RCTs. For other reinterventions, we utilised time-to-first event data from the UK trials. However, people who required 1 graft-related reintervention were typically likely to experience more than 1 in total. We took a simple approach of applying the cost and QALY effects of all future reintervention procedures at the time at which a person experiences their first reintervention. This "front-loads" the impact of reinterventions that would have occurred in the future, though the impact of cost–utility results is likely to be minor, attributable to those outcomes not being subject to the strictly correct amount of discounting. Our use of one-off QALY losses to characterise the total HRQL impact of all reintervention procedures, and some costs associated with reintervention procedures (e.g. future monitoring), is also subject to this "front-loading" limitation; though, again, the impact on cost–utility results has been shown to be negligible.

We identified a limitation with NHS reference costs, which would usually be our primary source of UK cost data for procedures (such as EVAR and OSR). They appeared to be subject to some inconsistencies, for example with complex repair procedures appearing to cost less than non-complex procedures. We were not satisfied that the "complex" label used in the reference costs was consistent with our own interpretation of complexity. Further, the extent to which the cost of EVAR devices is captured in NHS reference costs was unclear. We resolved this by obtaining costs from the NHS Trusts of guideline committee members.

All assumptions that were required during this modelling are detailed throughout the methods sections above, and are summarised in Sections HE.2.2.13 and HE.2.3.13. We attempted to mitigate limitations by conducting sensitivity analyses, including the use of extreme values and different data sources, particularly where an important assumption was employed; for

example, the extrapolation of relative effectiveness in terms of long-term mortality. These analyses found our base-case results to be largely robust to different assumptions, and highlighted some subgroups in whom the balance of cost and benefits may differ to the base-case, 'average cohort' results.

HE.4.1.4 Comparison with other CUAs

The results of our analyses are broadly consistent with those of previous CUAs, where the populations are comparable. No published analyses were identified that evaluated AAA repair strategies explicitly in people with complex aneurysms.

HE.4.1.4.1 Elective repair

EVAR vs. OSR

The largest body of published economic evidence is in the elective repair of infrarenal AAAs, noting that we selectively excluded studies that did not report a UK-based analysis (see Section HE.1.2). Our cost–utility conclusion, that EVAR is unlikely to be cost effective in this population, is shared by all UK-based analyses (Michaels et al., 2005; Epstein et al., 2008; Chambers et al., 2009; Brown et al., 2012; Epstein et al., 2014). The Michaels, Epstein and Brown analyses were largely based on data from the EVAR-1 study and, to a lesser extent, the DREAM study. Our primary analysis uses data from both of these trials, but has the advantage of much more mature survival data. The published studies relied more heavily on uncertain extrapolation beyond the data that were available at the time. The long-term data that were made available to us also allowed us to partition survival into 3 distinct components (waiting time, perioperative and post-perioperative), whereas other studies were based on ITT analysis from the point of randomisation into the trials. Despite these advantages of our analysis, the consistent results suggest that assumptions and extrapolations made in previous studies may still have led to accurate conclusions about the cost-effectiveness of EVAR.

The most notable areas of divergent conclusions are provided by the Chambers study. Its Markov model was developed using patient-level European registry data (EUROSTAR) to develop a series of risk equations, supplemented by relative effectiveness data from RCTs. In their base-case analysis, EVAR was found to produce +0.04 incremental QALYs per patient, with an ICER of £48,990 per QALY gained, compared with OSR. Although this still far exceeds £20,000, it is more equivocal than our base-case result, in which EVAR is dominated by OSR, and results of the other published UK analyses. Results of the Chambers study are highly sensitive to assumptions around long-term, aneurysm-related mortality; however, at the time of the study, the possible overall survival benefits of OSR in the long-term were not known (Patel et al., 2016). These results have been captured in the present model, without distinguishing between aneurysm-related and other-cause mortality. The authors also found that EVAR was more likely to be cost-effective in older people, particularly with larger AAAs, with ICERs approaching £20,000 per QALY gained in less-fit individuals. Our analysis did not find age or AAA size to make EVAR at all likely to be cost-effective in this population, though we did not attempt to disentangle age from other factors that may make an individual subjectively more or less fit. Instead, we kept the 'fit for OSR' and 'unfit for OSR' populations separate in distinct analyses, defined by the EVAR-1 and EVAR-2 selection criteria. It should be noted that analysis of 'fitness' in Chambers et al.'s study was not based on any empirical data; rather, cohorts were simulated who were subject to arbitrarily higher risks of perioperative mortality. It is unclear whether real-life cohorts with analogous risks can be identified in practice.

To a lesser extent, our conclusions diverge from the Epstein et al., (2014) study. This is only in its US-based analysis, exclusively using data from the OVER study, which finds elective EVAR to be dominant over OSR. This places EVAR in the entirely opposite quadrant of a cost–utility plane to our findings, and the findings of most other analyses. This result is

primarily driven by 2 reasons. Firstly, the OVER trial reports the best overall survival results for EVAR compared with all other elective repair trials. Our analysis incorporates the OVER trial results, by using meta-analyses of 30-day and long-term survival that included the study to obtain pooled estimates. Second, resource use and cost data from the US are significantly different, and less applicable, to the UK setting. For example, the cost of a post-operative hospital stay is much higher in the US. It would not be appropriate for our analysis to use non-UK data to inform resource use and cost inputs.

EVAR vs. no intervention in people for whom OSR is unsuitable

The only published study we identified in people for whom OSR is not a suitable intervention was based on the EVAR-2 study (Brown et al., 2012). This produced within-trial analyses and lifetime analyses, based on extrapolation beyond the available 8-year data. The lifetime ITT analysis suggested that EVAR had an ICER of £30,274 per QALY gained compared with 'no intervention'. A lifetime per-protocol analysis, which looked only at participants who stuck to their randomised arm, had an equivalent ICER of £17,805. In both cases, the result is much better for EVAR than our base-case ICER of £460,000 per QALY gained. We had access to longer term survival data that required much less extrapolation, and allowed us to separate out EVAR waiting, perioperative and post-perioperative survival periods. The authors fitted parametric curves to their less-mature overall survival data, which crossed over at around 3 years and substantially favoured EVAR thereafter. This survival benefit was accentuated when the analysis was extrapolated beyond the 8-year data. However, the most recent follow-up data show the survival curves cross back over after around 7 years, such that there is better survival on the control arm after this point (Sweeting et al., 2017). This suggests the Brown extrapolation is unlikely to represent the true long-term survival profile following EVAR. Further, the authors did not extrapolate costs beyond 8 years, biasing the analysis in favour of EVAR which is associated with long-term complications. We also adjusted our survival estimates for participants switching from 'no intervention' to EVAR (see Figure HE27), which is more appropriate than both an ITT analysis, with such extensive crossover, and a per-protocol analysis, which breaks randomisation.

Table HE77**: Comparison with published UK cost–utility analyses comparing EVAR with OSR for unruptured infrarenal AAA**

	Current analysis	Brown et al., 2012	Chambers et al., 2009	Epstein et al., 2008	Epstein et al., 2014	Michaels et al., 2005
Analysis type	Model (state-transition)	Model (Markov)	Model (Markov)	Model (Markov)	Model (Markov)	Model (decision tree)
Time horizon	Lifetime	Lifetime	Lifetime	Lifetime	Lifetime	10 years
Discount rate (costs / QALYs):	3.5% / 3.5%	3.5% / 3.5%	3.5% / 3.5%	3.5% / 3.5%	3.5% / 3.5%	3.5% / 3.5%
Short-term treatment effects	Perioperative mortality OR = 0.33 (Cochrane review)	0 to 6 months: EVAR AAA-related mortality HR = 0.47 (EVAR-1). Non-AAA survival curves converge at 2 years (EVAR-1).	EVAR operative mortality OR = 0.35 (EVAR-1, DREAM). Baseline survival adjusted for patient characteristics (EUROSTAR data).	EVAR mortality rate = 1.6% OSR mortality rate = 5.0% (EVAR-1)	0 to 6 months: EVAR mortality rate = 8.5 per 100 patient years; OSR = 15 per 100 patient years (EVAR-1)	EVAR 30-day mortality rate = 1.85% OSR 30-day mortality rate = 5.80% (EVAR-1, DREAM)
Long-term treatment effects	EVAR mortality HR = 1.09 (DREAM, EVAR-1, OVER)	EVAR AAA-related mortality HR = 1.46, 6 mos to 4 yrs; 4.85, 4 yrs to 8 yrs; (EVAR-1); 1.00 after 8 yrs (based on EUROSTAR data).	EVAR non-AAA mortality HR = 1.072 (EVAR-1). EVAR AAA-related mortality HR = 1.5 (clinical opinion). Baseline survival adjusted for patient characteristics (EUROSTAR data).	General population survival after successful AAA repair, plus 2x rate of CV-related mortality.	EVAR AAA-related mortality HR = same as Brown et al., (2012). OSR: general population survival adjusted by SMR = 1.1 (required to match population survival to EVAR-1 cohort at 8 years).	General population survival after successful AAA repair, adjusted for excess aneurysm-related mortality (values NR).
Complications included	Graft-related (EVAR-1); laparotomy-related (Medicare data)	Graft-related (EVAR-1)	Graft-related; EVAR HR = 6.75 (EVAR-1)	Graft-related; cardiovascular events (EVAR-1).	Graft-related (EVAR-1)	Graft-related (NICE review of non-RCT studies).
Main source of resource use data	EVAR-1	EVAR-1	EVAR-1	EVAR-1	EVAR-1	NHS reference costs; EUROSTAR

	Current analysis	Brown et al., 2012	Chambers et al., 2009	Epstein et al., 2008	Epstein et al., 2014	Michaels et al., 2005
Cost of EVAR device	£6,500	£5,219	~£5,000	NR	NR	£4,500
Price year	2015-16	2008-09	2007	2004	2009	2003-04
Main source of HRQL data	EVAR-1	EVAR-1	EVAR-1	EVAR-1	EVAR-1	General population
Total costs:						
EVAR	£19,770	£15,784	NR	£15,823	NR	NR
OSR	£13,438	£12,263	NR	£12,065	NR	NR
Total QALYs:						
EVAR	6.480	5.391	NR	5.05	NR	NR
OSR	6.640	5.433	NR	5.07	NR	NR
Incremental (E vs O):						
Costs	£6,331	£3,521	£2,002	£3,758	£4,014	£11,449
QALYs	-0.160	-0.042	0.041	-0.02	-0.02	0.10
ICER	Dominated	Dominated	£48,990 a	Dominated	Dominated	£110,000
Probabilistic sensitivity analysis	<1% of 5,000 ICERs under £20k	1% of 1,000 ICERs under £20k	26% of PSA b ICERs under £20k	1% of PSA b ICERs under £20k	<1% of 1,000 ICERs under £20k	<1% of 1,000 ICERs under £20k

Notes:
Chambers et al., (2009) analysis was used in NICE Technology Appraisal 167. The appraisal committee's preferred ICER was £12,000 (see Section HE.4.1.5).
Number of probabilistic model runs not reported.

Key: HR, hazard ratio; HRQL, health-related quality of life; ICER, incremental cost-effectiveness ratio; NR, item not reported; OR, odds ratio; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life-year; SMR, standardised mortality ratio

HE.4.1.4.2 Emergency repair

Our systematic literature review of studies comparing strategies to repair ruptured AAAs was not restricted to studies that contained a UK-based analysis, as there is less cost–utility evidence in this population. Of the 2 studies that were identified, our model results are somewhat consistent with the UK analysis (Powell et al., 2017), but are inconsistent with the non-UK analysis (Kapma et al., 2014). The former, an economic evaluation conducted alongside the IMPROVE trial, found the strategy that allows emergency EVAR where anatomically suitable dominates a strategy that allows only OSR. This result is consistent with ours, in that EVAR is likely to be considered to provide good value for money, but it is notably stronger. Our analysis does not find the EVAR strategy to be dominant; rather, it has an ICER of around £5,700 per QALY gained. The differences are in part due to different time horizons; the published study took a 3-year time horizon, whereas our model made use of the most up-to-date IMPROVE data (7 years), extrapolated to a lifetime horizon. A 3-year time horizon will not capture all differences in health and cost outcomes between the 2 arms, particularly as the EVAR and OSR strategies' survival curves visibly converge after approximately 3 years (see Figure HE19). It is important to explore different extrapolations in survival beyond this point, which we have captured in sensitivity analysis. Furthermore, there were some differences in the costs used in the 2 analyses, increasing the incremental cost associated with EVAR. Our unit cost of a patient being transferred to a different hospital, based on more recent NHS reference costs, appears to be lower than the cost used in the IMPROVE study, while the unit cost per EVAR device used in our analysis is higher (£6,500 compared with £5,700).

The Dutch analysis by Kapma et al., found that EVAR for the repair of ruptured AAAs had an ICER in excess of £350,000 per QALY gained over OSR. The study was based on the AJAX trial of 57 EVAR patients and 59 OSR patients. Importantly, the analysis had only a 6-month time horizon, compared with the lifetime horizon of our model. A 6-month horizon will omit differences in health and cost outcomes, including a survival benefit over approximately 7 years observed in the IMPROVE trial. Our analysis captures perioperative outcomes from the relatively small AJAX study, in its use of a pooled measure of relative effectiveness from a Cochrane review. Further, resource use and cost data used in the Kapma model are applicable to the Dutch setting. It would not be appropriate for our analysis to use non-UK data to inform resource use and cost inputs.

Table HE78: Comparison with published UK cost–utility analyses comparing EVAR with OSR for ruptured infrarenal AAA

	Current analysis	Kapma et al., 2014	Powell et al., 2017
Analysis type	Model (state-transition)	Within-trial economic evaluation (AJAX)	Within-trial economic evaluation (IMPROVE)
Country	UK	Netherlands	UK
Time horizon	Lifetime	6 months	3 years
Discount rate (costs / QALYs)	3.5% / 3.5%	NA / NA (<1 year)	3.5% / 3.5%
Short-term treatment effects	Perioperative mortality OR = 0.88 (Cochrane review)	30-day mortality rate (AJAX): EVAR = 21% OSR = 25%	0 to 3 months: EVAR mortality HR = 0.92 (IMPROVE).
Long-term treatment effects	EVAR mortality HR = 0.60, 0 to 3 years; 1.58, 3 to 6.5 years (IMPROVE); 1.09 after 6.5 years (DREAM, EVAR-1, OVER).	6-month mortality rate: EVAR = 28% OSR = 31% (AJAX)	3 months to 3 years: EVAR mortality HR = 0.57 (IMPROVE).
Complications included	Graft-related (IMPROVE); laparotomy-related (Medicare data)	Reoperations and readmissions (AJAX)	Aneurysm-related; EVAR HR = 1.02 (IMPROVE)
Main source of resource use data	IMPROVE	AJAX	IMPROVE
Cost of EVAR device	£6,500	£3,800 to £6,600 a	£5,700
Price year	2015-16	2010	2011-12
Main source of HRQL data	IMPROVE	AJAX	IMPROVE
Total costs:			
EVAR	£27,063	£37,000 a	£16,878
OSR	£25,422	£28,000 a	£19,483
Total QALYs:			
EVAR	3.022	0.324	1.41

	Current analysis	Kapma et al., 2014	Powell et al., 2017
OSR	2.734	0.298	0.97
Incremental (E vs O):			
Costs	£1,641	£9,000 a	-£2,605
QALYs	0.288	0.026	0.166
ICER	£5,699	£350,000 a	Dominant
Probabilistic sensitivity analysis	80% of 5,000 ICERs under £20k	~10% of 25,000 bootstrapped ICERs under £20k a, b	>90% of bootstrapped ICERs under £20k b, c

Notes:
Kapma et al., (2014) costs reported in euros. Approximate value in pounds presented following conversion using HMRC exchange rate (November 2017).
Bootstrap resampling is a method of generating a number of hypothetical samples of the same dataset (typically by selecting 1 data point, recording the data and replacing it, then selecting a second data point, and so on until a desired number of data points have been recorded).
Powell et al., (2017) does not report the number of bootstrap selections made, however an earlier iteration of the study by the same authors (Powell et al., 2015) reported 500.

Key: HR, hazard ratio; HRQL, health-related quality of life; ICER, incremental cost-effectiveness ratio; NA, not applicable; R, item not reported; OR, odds ratio; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life-year; SMR, standardised mortality ratio

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HE.4.1.5 Comparison with TA167

The committee for TA167 concluded that EVAR was likely to be cost effective compared with OSR, identifying £12,000 per QALY gained to be the most plausible ICER (NICE, 2009). This ICER was derived from a model by the Assessment Group for the Appraisal, based largely on the EVAR-1 trial, with an initial ICER of £122,000 (Chambers et al., 2009). The committee agreed on a set of model assumptions that led to its preferred ICER of £12,000 (see Table HE79). Clearly, our base-case results in the elective, infrarenal AAA population – EVAR is dominated by OSR – lead to a different conclusion. This is predominantly due to the longer term evidence that are now available and were used to inform the present model, which were not available for TA167. In Table HE79, we present key ways in which our analysis is different to the TA modelling, explaining the rationale and indicating relevant sensitivity analyses for each item. .

Table HE79: Assumptions made in TA167 committee's preferred base-case analysis for elective, infrarenal AAA repair, compared with analogous assumptions made in present model

TA167 preferred assumption	*Alternative assumption used in present model*
Baseline perioperative (30-day) mortality was informed by the EUROSTAR registry	The National Vascular Registry now maintains and reports annual statistics on AAA repair mortality rates in the UK. The use of this UK source for baseline rates makes the present model as applicable to current NHS practice as possible, with the relative treatment effect of EVAR still informed by the available randomised evidence. Alternative values to inform the baseline 30-day mortality rate, all derived from UK sources, were explored in sensitivity analysis but in each case EVAR remained dominated by OSR (see Table HE46).
The hazard of post-operative ("late") mortality unrelated to AAA was 1.072 times higher after EVAR than OSR, for 3 years	The present model focuses on overall survival, rather than AAA-related and non-AAA mortality. Long-term data that were not available at the time of TA167 indicate that overall survival is worse following EVAR compared with OSR (Patel et al., 2016). It is unclear whether this is driven entirely by excess AAA-related mortality. We conducted extensive sensitivity analysis of model inputs for long-term mortality, including using parametric curves to characterise survival (Table HE47), setting the HR to favour EVAR rather than OSR (Figure HE44), and identifying a very unfit population unlikely to experience the long-term benefit associated with OSR (Figure HE45). EVAR remained cost ineffective in all of these analyses.
The hazard of late AAA-related mortality was 1.5 times higher after EVAR than OSR, for the person's lifetime	The present model focuses on overall survival, rather than AAA-related and non-AAA mortality. Long-term data that were not available at the time of TA167 indicate that EVAR has a HR for AAA-related mortality of 3.11 in years 4 to 8, rising to 5.82 after 8 years (Patel et al., 2016). Thus, it is now clear that a lifetime HR of 1.5 is inappropriately optimistic for EVAR. As described above, extreme sensitivity analyses around post-perioperative survival was conducted but did not alter cost-effectiveness conclusions regarding EVAR.
The HR for graft-related reintervention following EVAR, relative to OSR, was 1.5	Long-term data (Patel et al., 2016) were used to inform the EVAR HR for graft-related reintervention. This HR is a notably higher than 1.5 between 6 months and 4 years (12.8 for life-threatening complications, 6.5 for others). Sensitivity analysis removing graft-related complications from the model showed that EVAR remained dominated by OSR (see Table HE50).

TA167 preferred assumption	*Alternative assumption used in present model*
Laparotomy-related reintervention procedures were not modelled	Since TA167, EVAR-1 study data have been re-evaluated to retrospectively capture hernias in its graft-related reintervention results. We therefore explicitly model incidence of hernia, as well as other laparotomy-related procedures by using recent US Medicare data. These complications are more common following OSR. Variation in laparotomy-related reintervention inputs did not have an important influence on the present cost-effectiveness results (see Figure HE40).
There was no difference in the overall primary procedure cost of EVAR and OSR, with the likely additional length of stay and intensive care costs after OSR exactly offsetting the EVAR device cost	Our analysis, using NHS reference costs to "micro-cost" primary procedure resource use in EVAR-1 and IMPROVE, indicates that, while an EVAR procedure is less resource intensive, those cost savings are more than outweighed by the cost of an EVAR graft. Sensitivity analysis showed that EVAR remained cost ineffective even when its device cost was £0, in which case its total procedure cost would be lower than that of OSR (see Figure HE46). Furthermore, using the EVAR-1 trial cost data directly to inform procedure costs (inflated to current prices), rather than using NHS reference costs, does not alter cost-effectiveness conclusions (see Figure HE40).
Follow-up monitoring after EVAR was conducted by ultrasound, with an annual cost of £54	To ensure that our model is consistent with all recommendations made by the present guideline committee, we assume that follow-up scans are conducted using CT rather than ultrasound (see recommendation 1.7.3). Assuming an ultrasound scan is used for this purpose, instead of CT, did not feature among the influential model parameters (see Figure HE40).
All graft-related reintervention procedures incurred the same unit cost of £5,936	The cost of a reintervention is likely to depend on the severity and type of procedure required. Based on the long-term data reporting (Patel et al., 2016), we applied a higher cost of life-threatening graft complications and lower cost for other graft complications. Furthermore, with the addition of laparotomy-related reintervention procedures, specific unit costs were identified ranging from £1,304 to £6,294. Sensitivity analysis removing graft-related complications from the model did not alter cost-effectiveness conclusions (see Table HE50), nor did variation in laparotomy-related reintervention inputs (see Figure HE40).
HRQL recovered to baseline at 6 months after a primary AAA repair or reintervention	The data report a HRQL difference at 3 months that is eradicated by 12 months (Greenhalgh et al., 2005). Given the absence of intermediate data points, assuming a linear recovery from 3 months to the known point of equality at 12 months is a reasonable alternative approach to assuming all recovery occurs at month 6. Variation in HRQL inputs did not have an important influence on cost-effectiveness results (see Figure HE40).

Key: CT, computed tomography; EVAR, endovascular aneurysm repair; HRQL, health-related quality of life; HR, hazard ratio; INMB, incremental net monetary benefit; OSR, open surgical repair

HE.5 Conclusions

Our modelling analyses are the only CUAs to date in AAA that evaluate the cost-effectiveness of EVAR in the elective and emergency settings, for infrarenal and complex aneurysms, and both in people for whom OSR is and is not a suitable intervention.

For the elective repair of unruptured AAAs, our model concludes that EVAR is unlikely to be cost-effective in any circumstance – whether compared with OSR where that is possible, or 'no intervention' where OSR cannot be used, in both infrarenal and complex AAAs. For infrarenal AAAs, the small benefit in perioperative survival with EVAR is more than offset by superior long-term survival following OSR, and the higher cost of EVAR means it is dominated. EVAR is not dominated by OSR for complex AAA; it provides an estimated gain in QALYs, though the true magnitude of this is uncertain, as there are no randomised, comparative data for complex AAA repair. However, the cost of complex EVAR devices is definitely far higher than standard devices, such that its ICER compared with OSR is likely to far exceed £20,000 per QALY gained. Results are generally robust to sensitivity analysis, and neither age, sex, or AAA size alter the base-case conclusions. Our conclusions are largely consistent with previous modelling in this population, based on shorter-term data, though those studies were restricted to infrarenal AAAs.

For the emergency repair of ruptured AAAs, our analysis finds a strategy that uses EVAR where the person's aorta is anatomically suitable, otherwise OSR, is likely to have an ICER below £20,000 per QALY gained compared with using OSR in all cases. Sensitivity analysis identified that this result is highly sensitive to the sex of the patient; the balance of benefits and costs favours EVAR much more strongly in women. Its ICER is actually likely to be worse than £20,000 per QALY gained in younger men (who are more likely to survive an open surgical procedure). The ICER for emergency EVAR is likely to be below £30,000 compared with providing no repair attempt, in people for whom OSR is not a suitable option. In this population, faced with a 100% mortality rate if the ruptured AAA is untreated, the NICE 'end of life' criteria are applicable. Results are sensitive to age of the individual; the EVAR ICER, compared with 'no intervention' is likely to exceed £50,000 per QALY gained in patients aged 84 and older. Our model is the only CUA to adopt a lifetime horizon in emergency patients, limiting the extent to which its results can be directly compared with those of previous analyses.

HE.6 Model parameters

All parameters used in the 'EVAR vs. OSR' model ('fit for OSR' population) are summarised in Table HE80, including details of the distributions and parameters used in probabilistic analysis.

The 'EVAR vs. no intervention' model ('unfit for OSR' population) shares many of these input parameters, however any that are exclusive to this model are summarised in Table HE81.

Table HE80: All parameters in 'EVAR vs. OSR' cost–utility model

Name	*Value (95%CI)*	*Distribution & parameters*	*Source*
BASELINE COHORT			
Cohort age - elective pts (EVAR-1)	74.039 (73.701 ,74.377)	Normal: μ=74.039; σ=0.172	EVAR-1 trial data
Cohort age - emergency pts (IMPROVE)	76.219 (75.62 ,76.818)	Normal: μ=76.219; σ=0.305	IMPROVE trial data
Cohort %male - elective pts (EVAR-1)	0.907 (0.89 ,0.922)	Beta: α=1135.000; β=117.000	EVAR-1 trial data
Cohort %male - emergency pts (IMPROVE)	0.783 (0.75 ,0.815)	Beta: α=480.000; β=133.000	IMPROVE trial data
Cohort AAA size - elective pts (EVAR-1)	6.466 (6.414 ,6.517)	Lognormal: μ=1.866; σ=0.026	EVAR-1 trial data
Cohort AAA size - emergency pts (IMPROVE)	8.389 (8.226 ,8.551)	Lognormal: μ=2.127; σ=0.083	IMPROVE trial data
WAITING TIME (elective repair)			
General lead-in time from referral to surgery (wks)	8 (4 ,12)	Triangular: min=4.000; mode=8.000; max=12.000	Guideline committee
Additional wait time for complex EVAR device (wks)	8 (4 ,12)	Triangular: min=4.000; mode=8.000; max=12.000	Guideline committee
PERIOPERATIVE MORTALITY			
Elective repair			
Infrarenal AAA			
OR, EVAR -v- OSR	0.33 (0.2 ,0.55)	Lognormal: μ=-1.109; σ=0.258	Paravastu et al., 2014
Baseline event rates			
Prob, OSR	0.042 (0.027 ,0.059)	Beta: α=25.000; β=573.000	Brown et al., 2012
Prob, EVAR	0.016 (0.008 ,0.028)	Beta: α=10.000; β=600.000	Brown et al., 2012
NVR: OSR	0.03 (0.021 ,0.039)	Beta: α=38.970; β=1276.030	Nat Vasc Reg, 2016
NVR: EVAR	0.004 (0.002 ,0.007)	Beta: α=11.996; β=2869.004	Nat Vasc Reg, 2016
Complex AAA			
Baseline event rates			
NVR: OSR	0.196 (0.131 ,0.27)	Beta: α=24.368; β=99.958	Nat Vasc Reg, 2016
NVR: EVAR	0.036 (0.026 ,0.047)	Beta: α=40.964; β=1110.036	Nat Vasc Reg, 2016
Effect modifiers			
EVAR			
intercept	-9.21 (-13.592 ,-4.828)	Multivariate Normal	Mani et al., 2015
age, per yr	0.039 (-0.011 ,0.09)	Multivariate Normal	Mani et al., 2015
female	0.187 (-0.79 ,1.166)	Multivariate Normal	Mani et al., 2015

aneurysm diameter, per cm	0.236 (0.051 ,0.421)	Multivariate Normal	Mani et al., 2015
OSR			
intercept	-9.21 (-12.612 ,-5.809)	Multivariate Normal	Mani et al., 2015
age, per yr	0.05 (0.024 ,0.076)	Multivariate Normal	Mani et al., 2015
female	0.082 (-0.402 ,0.566)	Multivariate Normal	Mani et al., 2015
aneurysm diameter, per cm	0.137 (0.032 ,0.243)	Multivariate Normal	Mani et al., 2015
NVR case-mix			
Infrarenal AAA			
EVAR			
Sex (% male)	0.89 (0.878 ,0.901)	Beta: α=2563.110; β=317.890	Nat Vasc Reg, 2016
Age (yrs)	75.517 (75.238 ,75.796)	Normal: μ=75.517; σ=0.142	
AAA diameter (cm)	6.256 (6.224 ,6.288)	Normal: μ=6.256; σ=0.016	
OSR			
Sex (% male)	0.88 (0.862 ,0.897)	Beta: α=1157.120; β=157.880	Nat Vasc Reg, 2016
Age (yrs)	70.175 (69.783 ,70.567)	Normal: μ=70.175; σ=0.200	
AAA diameter (cm)	6.377 (6.331 ,6.423)	Normal: μ=6.377; σ=0.024	
Complex AAA			
EVAR			
Sex (% male)	0.845 (0.824 ,0.866)	Beta: α=973.155; β=177.845	Nat Vasc Reg, 2016
Age (yrs)	73.394 (72.941 ,73.848)	Normal: μ=73.394; σ=0.231	
OSR			
Sex (% male)	0.833 (0.767 ,0.891)	Beta: α=114.167; β=22.833	Nat Vasc Reg, 2016
Age (yrs)	70.652 (69.347 ,71.957)	Normal: μ=70.652; σ=0.666	
Emergency repair			
Infrarenal AAA			
OR, EVAR -v- OSR	0.88 (0.66 ,1.16)	Lognormal: μ=-0.128; σ=0.144	Badger et al., 2017
Baseline event rates			
Prob, OSR	0.394 (0.339 ,0.45)	Beta: α=117.000; β=180.000	IMPROVE trial data
Prob, EVAR	0.37 (0.318 ,0.424)	Beta: α=117.000; β=199.000	IMPROVE trial data
NVR: OSR, infrarenal	0.404 (0.383 ,0.426)	Beta: α=808.000; β=1191.999	Nat Vasc Reg, 2016
NVR: EVAR, infrarenal	0.207 (0.178 ,0.24)	Beta: α=135.620; β=519.550	Nat Vasc Reg, 2016
Complex AAA			
Baseline event rates			
NVR: OSR	0.705 (0.131 ,0.27)	Beta: α=24.368; β=99.958	Nat Vasc Reg, 2016
Effect modifiers			
age	0.065 (0.04 ,0.089)	Multivariate Normal	IMPROVE data
sexf	0.702 (0.118 ,1.287)	Multivariate Normal	IMPROVE data

treat	0.105 (-0.279 ,0.488)	Multivariate Normal	IMPROVE data
treat_sexf	-0.89 (-1.695 ,-0.084)	Multivariate Normal	IMPROVE data
intercept	-5.538 (-7.408 ,-3.669)	Multivariate Normal	IMPROVE data
POST-PERIOPERATIVE MORTALITY			
Elective repair			
Recalibration of general UK mortality			
ln[HR], trial-v-genpop	0.077 (-0.026 ,0.179)	Normal: μ=0.078; σ=0.052	EVAR-1 data & ONS lifetables 1999–2001
Relative effects			
Univariable			
HR, long-term survival: EVAR	1.107 (0.967 ,1.268)	Lognormal: μ=0.102; σ=0.077	EVAR-1 trial data
ln(HR) - DREAM yr-1 to yr-12	0.11 (-0.176 ,0.396)		Van Schaik 2017; Tierney 2007
ln(HR) - EVAR post-perioperative	0.102 (-0.034 ,0.238)		EVAR-1 trial data
ln(HR) - OVER yr-1 to yr-8	0.012 (-0.238 ,0.262)		Lederle 2012; Tierney 2007
Multivariable			
ln[HR], EVAR-v-OSR	0.11 (-0.026 ,0.246)	Multivariate Normal	EVAR-1 trial data
ln[HR], age /yr	0.08 (0.068 ,0.092)	Multivariate Normal	EVAR-1 trial data
ln[HR], female-v-male	0.043 (-0.182 ,0.269)	Multivariate Normal	EVAR-1 trial data
ln[HR], diameter /cm	0.084 (0.013 ,0.155)	Multivariate Normal	EVAR-1 trial data
Centring on EVAR-1			
Female, % of cohort	0.087 (0.065 ,0.111)	Beta: α=50.000; β=526.000	EVAR-1 trial data
Mean diameter, cm	6.477 (6.396 ,6.557)	Lognormal: μ=1.868; σ=0.041	EVAR-1 trial data
Scenario HR			
HR, from 8yrs post-perioperative survival	1.297 (1.035 ,1.627)	Lognormal: μ=0.260; σ=0.150	EVAR-1 trial data
Emergency repair			
Recalibration of general UK mortality			
ln[HR], trial-v-genpop: 0-3 yrs	1.159 (0.867 ,1.416)	Multivariate Normal	IMPROVE & ONS lifetables 2009–2011
ln[HR], trial-v-genpop: 3+ yrs	0.310 (-0.437 ,0.794)	Multivariate Normal	IMPROVE & ONS lifetables 2009–2011
ln[HR], trial-v-genpop: 0-3.5 yrs	1.107 (0.814 ,1.37)	Multivariate Normal	IMPROVE & ONS lifetables 2009–2011
ln[HR], trial-v-genpop: 3.5+ yrs	0.125 (-0.955 ,0.719)	Multivariate Normal	IMPROVE & ONS lifetables 2009–2011
Relative effects			
Univariable			
ln[HR], EVAR-v-OSR: 0-3 yrs	-0.503 (-0.935 ,-0.071)	Multivariate Normal	IMPROVE trial data
ln[HR], EVAR-v-OSR: 3+ yrs	0.461 (-0.16 ,1.081)	Multivariate Normal	IMPROVE trial data
ln[HR], EVAR-v-OSR: 0-3.5 yrs	-0.339 (-0.735 ,0.057)	Multivariate Normal	IMPROVE trial data
ln[HR], EVAR-v-OSR: 3.5+ yrs	0.36 (-0.382 ,1.101)	Multivariate Normal	IMPROVE trial data
Multivariable			
ln[HR], EVAR-v-OSR: 0-3 yrs	-0.508 (-0.942 ,-0.074)	Multivariate Normal	IMPROVE trial data

ln[HR], EVAR-v-OSR: 3+ yrs	0.363 (-0.263 ,0.989)	Multivariate Normal	IMPROVE trial data
ln[HR], age /yr	-0.111 (-0.667 ,0.444)	Multivariate Normal	IMPROVE trial data
ln[HR], female-v-male: 0-3 yrs	0.625 (-0.037 ,1.287)	Multivariate Normal	IMPROVE trial data
ln[HR], female-v-male: 3+ yrs	0.04 (0.015 ,0.065)	Multivariate Normal	IMPROVE trial data
ln[HR], EVAR-v-OSR: 0-3.5 yrs	-0.382 (-0.78 ,0.016)	Multivariate Normal	IMPROVE trial data
ln[HR], EVAR-v-OSR: 3.5+ yrs	0.372 (-0.374 ,1.119)	Multivariate Normal	IMPROVE trial data
ln[HR], age /yr	0.042 (0.017 ,0.067)	Multivariate Normal	IMPROVE trial data
ln[HR], female-v-male: 0-3.5 yrs	0.312 (-0.15 ,0.774)	Multivariate Normal	IMPROVE trial data
ln[HR], female-v-male: 3.5+ yrs	-0.521 (-1.598 ,0.557)	Multivariate Normal	IMPROVE trial data
Centring on IMPROVE			
Female, % of cohort	0.152 (0.103 ,0.208)	Beta: α=27.000; β=151.000	EVAR-1 trial data
Parametric curves			
Elective repair			
Separate models for EVAR and OSR			
Univariable			
EVAR			
Gompertz - constant	-2.985 (-3.173 ,-2.796)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.102 (0.077 ,0.127)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	2.618 (2.462 ,2.774)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.924 (-1.46 ,-0.389)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	2.479 (1.038 ,3.921)	Multivariate Normal	EVAR-1 trial data
OSR			
Gompertz - constant	-2.953 (-3.147 ,-2.759)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.081 (0.054 ,0.107)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	2.612 (2.484 ,2.74)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.586 (-0.9 ,-0.272)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	1.797 (1.116 ,2.478)	Multivariate Normal	EVAR-1 trial data
Multivariable			
EVAR			
Gompertz - age	0.079 (0.062 ,0.096)	Multivariate Normal	EVAR-1 trial data
Gompertz - sex=f	0.138 (-0.169 ,0.444)	Multivariate Normal	EVAR-1 trial data
Gompertz - max diameter	0.104 (0.001 ,0.207)	Multivariate Normal	EVAR-1 trial data
Gompertz - constant	-9.814 (-11.256 ,-8.373)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.129 (0.103 ,0.155)	Multivariate Normal	EVAR-1 trial data
Gamma - age	-0.042 (-0.052 ,-0.032)	Multivariate Normal	EVAR-1 trial data

Gamma - sex=f	-0.098 (-0.25 ,0.054)	Multivariate Normal	EVAR-1 trial data
Gamma - max diameter	-0.06 (-0.108 ,-0.012)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	6.159 (5.346 ,6.971)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.857 (-1.137 ,-0.578)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	2.2 (1.489 ,2.91)	Multivariate Normal	EVAR-1 trial data
OSR			
Gompertz - age	0.082 (0.064 ,0.1)	Multivariate Normal	EVAR-1 trial data
Gompertz - sex=f	-0.061 (-0.393 ,0.272)	Multivariate Normal	EVAR-1 trial data
Gompertz - max diameter	0.066 (-0.032 ,0.165)	Multivariate Normal	EVAR-1 trial data
Gompertz - constant	-9.509 (-10.974 ,-8.043)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.104 (0.076 ,0.131)	Multivariate Normal	EVAR-1 trial data
Gamma - age	-0.052 (-0.064 ,-0.039)	Multivariate Normal	EVAR-1 trial data
Gamma - sex=f	0.017 (-0.176 ,0.21)	Multivariate Normal	EVAR-1 trial data
Gamma - max diameter	-0.019 (-0.08 ,0.043)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	6.555 (5.595 ,7.514)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.678 (-0.93 ,-0.427)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	1.929 (1.347 ,2.51)	Multivariate Normal	EVAR-1 trial data
Single model with treatment variable			
Univariable			
Gompertz - treatment=EVAR	0.104 (-0.032 ,0.239)	Multivariate Normal	EVAR-1 trial data
Gompertz - constant	-3.023 (-3.177 ,-2.869)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.092 (0.074 ,0.11)	Multivariate Normal	EVAR-1 trial data
Gamma - treatment=EVAR	-0.076 (-0.158 ,0.006)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	2.655 (2.54 ,2.771)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.758 (-1.071 ,-0.446)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	2.125 (1.373 ,2.878)	Multivariate Normal	EVAR-1 trial data
Multivariable			
Gompertz - treatment=EVAR	0.112 (-0.024 ,0.248)	Multivariate Normal	EVAR-1 trial data
Gompertz - age	0.08 (0.068 ,0.092)	Multivariate Normal	EVAR-1 trial data
Gompertz - sex=f	0.041 (-0.184 ,0.267)	Multivariate Normal	EVAR-1 trial data
Gompertz - max diameter	0.083 (0.012 ,0.154)	Multivariate Normal	EVAR-1 trial data
Gompertz - constant	-9.685 (-10.713 ,-8.658)	Multivariate Normal	EVAR-1 trial data
Gompertz - gamma	0.116 (0.098 ,0.135)	Multivariate Normal	EVAR-1 trial data
Gamma - treatment=EVAR	-0.077 (-0.155 ,0)	Multivariate Normal	EVAR-1 trial data
Gamma - age	-0.046 (-0.054 ,-0.038)	Multivariate Normal	EVAR-1 trial data

Gamma - sex=f	-0.044 (-0.166 ,0.078)	Multivariate Normal	EVAR-1 trial data
Gamma - max diameter	-0.041 (-0.08 ,-0.002)	Multivariate Normal	EVAR-1 trial data
Gamma - constant	6.351 (5.723 ,6.979)	Multivariate Normal	EVAR-1 trial data
Gamma - ln(sigma)	-0.752 (-0.935 ,-0.568)	Multivariate Normal	EVAR-1 trial data
Gamma - kappa	2.019 (1.58 ,2.457)	Multivariate Normal	EVAR-1 trial data
Emergency repair			
Separate models for EVAR and OSR			
Univariable			
EVAR			
Gompertz - constant	-2.733 (-3.207 ,-2.259)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	0.085 (-0.079 ,0.248)	Multivariate Normal	IMPROVE trial data
Exponential - logscale	-2.533 (-2.782 ,-2.284)	Normal: μ=-2.533; σ=0.127	IMPROVE trial data
OSR			
Gompertz - constant	-2.193 (-2.614 ,-1.773)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	-0.07 (-0.228 ,0.088)	Multivariate Normal	IMPROVE trial data
Exponential - logscale	-2.352 (-2.594 ,-2.111)	Normal: μ=-2.352; σ=0.123	IMPROVE trial data
Multivariable			
EVAR			
Gompertz - age	0.032 (-0.006 ,0.071)	Multivariate Normal	IMPROVE trial data
Gompertz - sex=f	0.036 (-0.605 ,0.676)	Multivariate Normal	IMPROVE trial data
Gompertz - max diameter	-0.02 (-0.034 ,-0.005)	Multivariate Normal	IMPROVE trial data
Gompertz - constant	-3.701 (-6.852 ,-0.551)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	0.126 (-0.044 ,0.296)	Multivariate Normal	IMPROVE trial data
Exponential - age	0.033 (-0.005 ,0.072)	Multivariate Normal	IMPROVE trial data
Exponential - sex=f	0.019 (-0.621 ,0.659)	Multivariate Normal	IMPROVE trial data
Exponential - max diameter	-0.019 (-0.033 ,-0.005)	Multivariate Normal	IMPROVE trial data
Exponential - logscale	-3.536 (-6.697 ,-0.375)	Multivariate Normal	IMPROVE trial data
OSR			
Gompertz - age	0.027 (-0.011 ,0.064)	Multivariate Normal	IMPROVE trial data
Gompertz - sex=f	0.306 (-0.359 ,0.971)	Multivariate Normal	IMPROVE trial data
Gompertz - max diameter	-0.005 (-0.02 ,0.009)	Multivariate Normal	IMPROVE trial data
Gompertz - constant	-3.759 (-6.802 ,-0.716)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	-0.085 (-0.256 ,0.086)	Multivariate Normal	IMPROVE trial data
Exponential - age	0.027 (-0.01 ,0.065)	Multivariate Normal	IMPROVE trial data
Exponential - sex=f	0.305 (-0.361 ,0.97)	Multivariate Normal	IMPROVE trial data

Exponential - max diameter	-0.006 (-0.02 ,0.008)	Multivariate Normal	IMPROVE trial data
Exponential - logscale	-3.983 (-7.008 ,-0.957)	Multivariate Normal	IMPROVE trial data
Single model with treatment variable			
Univariable			
Gompertz - treatment=EVAR	-0.18 (-0.527 ,0.167)	Multivariate Normal	IMPROVE trial data
Gompertz - constant	-2.358 (-2.718 ,-1.998)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	0.002 (-0.111 ,0.115)	Multivariate Normal	IMPROVE trial data
Exponential - treatment=EVAR	-0.18 (-0.527 ,0.166)	Multivariate Normal	IMPROVE trial data
Multivariable			
Gompertz - treatment=EVAR	-0.218 (-0.595 ,0.16)	Multivariate Normal	IMPROVE trial data
Gompertz - age	0.031 (0.004 ,0.057)	Multivariate Normal	IMPROVE trial data
Gompertz - sex=f	0.138 (-0.324 ,0.599)	Multivariate Normal	IMPROVE trial data
Gompertz - max diameter	-0.012 (-0.023 ,-0.002)	Multivariate Normal	IMPROVE trial data
Gompertz - constant	-3.689 (-5.881 ,-1.498)	Multivariate Normal	IMPROVE trial data
Gompertz - gamma	0.017 (-0.103 ,0.136)	Multivariate Normal	IMPROVE trial data
Exponential - treatment=EVAR	-0.219 (-0.596 ,0.158)	Multivariate Normal	IMPROVE trial data
Exponential - age	0.031 (0.004 ,0.057)	Multivariate Normal	IMPROVE trial data
Exponential - sex=f	0.137 (-0.324 ,0.599)	Multivariate Normal	IMPROVE trial data
Exponential - max diameter	-0.012 (-0.022 ,-0.002)	Multivariate Normal	IMPROVE trial data
Exponential - logscale	-3.654 (-5.83 ,-1.477)	Multivariate Normal	IMPROVE trial data
REINTERVENTION (GRAFT)			
Elective repair			
Life-threatening			
OSR, 0-6 months, event prob.	0.03 (0.018 ,0.045)	Beta: α=19.000; β=607.000	Patel et al., 2016
OSR, 0.5-4 years, event prob.	0.004 (0 ,0.01)	Beta: α=2.000; β=568.000	Patel et al., 2016
OSR, 4-8 years, event prob.	0.024 (0.012 ,0.041)	Beta: α=11.000; β=439.000	Patel et al., 2016
EVAR, adjusted HR, 0-6 months	1.08 (0.57 ,2.08)	Lognormal: μ=0.077; σ=0.330	Patel et al., 2016
EVAR, adjusted HR, 0.5-4 years	12.78 (3.01 ,54.23)	Lognormal: μ=2.548; σ=0.738	Patel et al., 2016
EVAR, adjusted HR, 4-8 years	1.41 (0.63 ,3.14)	Lognormal: μ=0.344; σ=0.410	Patel et al., 2016
Serious (not life-threatening)			
OSR, 0-6 months, event prob.	0.03 (0.018 ,0.045)	Beta: α=19.000; β=607.000	Patel et al., 2016
OSR, 0.5-4 years, event prob.	0.014 (0.006 ,0.025)	Beta: α=8.000; β=562.000	Patel et al., 2016
OSR, 4-8 years, event prob.	0.036 (0.021 ,0.055)	Beta: α=16.000; β=428.000	Patel et al., 2016
EVAR, adjusted HR, 0-6 months	2.46 (1.39 ,4.33)	Lognormal: μ=0.900; σ=0.290	Patel et al., 2016
EVAR, adjusted HR, 0.5-4 years	6.45 (3.04 ,13.68)	Lognormal: μ=1.864; σ=0.384	Patel et al., 2016

EVAR, adjusted HR, 4-8 years	1.45 (0.73 ,2.88)	Lognormal: μ=0.372; σ=0.350	Patel et al., 2016
Emergency repair			
OSR, rate/yr	0.208 (0.165 ,0.254)	Beta: α=65.000; β=248.100	Powell et al., 2017
EVAR, adjusted HR	1.12 (0.8 ,1.56)	Lognormal: μ=0.113; σ=0.170	Powell et al., 2017
Severity and type			
0-3 months			
EVAR			
% of events = arterial-related	0.845 (0.753 ,0.919)	Beta: α=60.000; β=11.000	Powell et al., 2017
% arterial events = life-threatening	0.433 (0.312 ,0.559)	Beta: α=26.000; β=34.000	Powell et al., 2017
% laparotomy events = life-threatening	0.111 (0.024 ,0.251)	Beta: α=3.000; β=24.000	Powell et al., 2017
OSR			
% of events = arterial-related	0.649 (0.54 ,0.751)	Beta: α=50.000; β=27.000	Powell et al., 2017
% arterial events = life-threatening	0.66 (0.525 ,0.783)	Beta: α=33.000; β=17.000	Powell et al., 2017
% laparotomy events = life-threatening	0.111 (0.024 ,0.251)	Beta: α=3.000; β=24.000	Powell et al., 2017
3 months+			
EVAR			
% of events = arterial-related	0.868 (0.746 ,0.955)	Beta: α=33.000; β=5.000	Powell et al., 2017
% arterial events = life-threatening	0.333 (0.186 ,0.5)	Beta: α=11.000; β=22.000	Powell et al., 2017
% laparotomy events = life-threatening	0.6 (0.194 ,0.932)	Beta: α=3.000; β=2.000	Powell et al., 2017
OSR			
% of events = arterial-related	0.65 (0.434 ,0.837)	Beta: α=13.000; β=7.000	Powell et al., 2017
% arterial events = life-threatening	0.538 (0.277 ,0.789)	Beta: α=7.000; β=6.000	Powell et al., 2017
% laparotomy events = life-threatening	0.143 (0.004 ,0.459)	Beta: α=1.000; β=6.000	Powell et al., 2017
Total number of reinterventions			
Total AAA reinterventions following elective EVAR	1.634 (1.508 ,1.761)	Normal: μ=1.634; σ=0.065	Patel 2016 (Suppl. Table A9)
Total AAA reinterventions following elective OSR	1.419 (1.277 ,1.561)	Normal: μ=1.419; σ=0.072	Patel 2016 (Suppl. Table A9)
Total reinterventions following emerg EVAR	1.613 (1 ,2)	Triangular: min=1.000; mode=1.613; max=2.000	Powell et al., 2017
Total reinterventions following emerg OSR	1.667 (1 ,2)	Triangular: min=1.000; mode=1.667; max=2.000	Powell et al., 2017
Scenario: pulmonary (elective)			
Prob 30-day pulmonary complication, Open	0.107 (0.066 ,0.156)	Beta: α=19.000; β=159.000	Prinssen et al., 2004
Prob 30-day pulmonary complication, EVAR	0.029 (0.01 ,0.058)	Beta: α=5.000; β=168.000	Prinssen et al., 2004
REINTERVENTION (LAPAROTOMY)			
Elective repair			
EVAR, % serious graft reinterventions caused by hernia	0.095 (0.088 ,0.103)	Beta: α=610.000; β=5781.000	Schermerhorn 2015
OSR, % serious graft reinterventions caused by hernia	0.802 (0.789 ,0.814)	Beta: α=3070.000; β=758.000	Schermerhorn 2015
Lysis of adhesions			

OSR, 0-1 yrs, event prob.	0.006 (0.005 ,0.007)	Beta: α=232.000; β=39734.000	Schermerhorn 2015
OSR, 1-2 yrs, event prob.	0.004 (0.003 ,0.005)	Beta: α=134.000; β=33398.000	Schermerhorn 2015
OSR, 2-5 yrs, event prob.	0.007 (0.006 ,0.007)	Beta: α=220.000; β=33152.000	Schermerhorn 2015
OSR, 5-8 yrs, event prob.	0.005 (0.004 ,0.006)	Beta: α=68.000; β=13287.000	Schermerhorn 2015
EVAR, 0-1 yrs, event prob.	0.001 (0.001 ,0.002)	Beta: α=55.000; β=39911.000	Schermerhorn 2015
EVAR, 1-2 yrs, event prob.	0.001 (0.001 ,0.002)	Beta: α=46.000; β=36188.000	Schermerhorn 2015
EVAR, 2-5 yrs, event prob.	0.003 (0.002 ,0.004)	Beta: α=97.000; β=32087.000	Schermerhorn 2015
EVAR, 5-8 yrs, event prob.	0.003 (0.002 ,0.004)	Beta: α=40.000; β=14387.000	Schermerhorn 2015
Bowel resection			
OSR, 0-1 yrs, event prob.	0.009 (0.008 ,0.01)	Beta: α=371.000; β=39595.000	Schermerhorn 2015
OSR, 1-2 yrs, event prob.	0.007 (0.006 ,0.008)	Beta: α=235.000; β=33297.000	Schermerhorn 2015
OSR, 2-5 yrs, event prob.	0.013 (0.012 ,0.014)	Beta: α=442.000; β=32930.000	Schermerhorn 2015
EVAR, 0-1 yrs, event prob.	0.008 (0.007 ,0.008)	Beta: α=304.000; β=39662.000	Schermerhorn 2015
EVAR, 1-2 yrs, event prob.	0.006 (0.005 ,0.007)	Beta: α=220.000; β=36014.000	Schermerhorn 2015
EVAR, 2-5 yrs, event prob.	0.012 (0.011 ,0.013)	Beta: α=377.000; β=31807.000	Schermerhorn 2015
EVAR, 5-8 yrs, event prob.	0.009 (0.008 ,0.011)	Beta: α=134.000; β=14293.000	Schermerhorn 2015
Other hospitalisation			
OSR, 0-1 yrs, event prob.	0.043 (0.041 ,0.045)	Beta: α=1723.000; β=38243.000	Schermerhorn 2015
OSR, 1-2 yrs, event prob.	0.03 (0.028 ,0.032)	Beta: α=1005.000; β=32527.000	Schermerhorn 2015
OSR, 2-5 yrs, event prob.	0.047 (0.045 ,0.049)	Beta: α=1575.000; β=31797.000	Schermerhorn 2015
OSR, 5-8 yrs, event prob.	0.038 (0.034 ,0.041)	Beta: α=502.000; β=12853.000	Schermerhorn 2015
EVAR, 0-1 yrs, event prob.	0.026 (0.024 ,0.027)	Beta: α=1026.000; β=38940.000	Schermerhorn 2015
EVAR, 1-2 yrs, event prob.	0.02 (0.019 ,0.022)	Beta: α=732.000; β=35502.000	Schermerhorn 2015
EVAR, 2-5 yrs, event prob.	0.041 (0.039 ,0.043)	Beta: α=1325.000; β=30859.000	Schermerhorn 2015
EVAR, 5-8 yrs, event prob.	0.03 (0.027 ,0.032)	Beta: α=427.000; β=14000.000	Schermerhorn 2015
Emergency repair			
% of (bowel resec + adhesions) = bowel resec	0.6 (0.194 ,0.932)	Beta: α=3.000; β=2.000	Powell et al., 2017 (Appendix 1 Table G)
RESOURCE USE & COSTS			
Repair devices			
IMPROVE study			
EVAR, standard stent-graft	5992.566 (5677.168 ,6833.628)	Triangular: min=5677.168; mode=5992.566; max=6833.628	Powell et al., 2015
Open repair stent-graft	654.977 (654.977 ,947.246)	Triangular: min=654.977; mode=654.977; max=947.246	Powell et al., 2015
NHS Supply Chain			

COOK (UK) LTD	6185.57 (5677.168 ,6833.628)	Triangular: min=5677.168; mode=6185.570; max=6833.628	NHS Supply Chain (13/10/17)
BARD LTD (0.6x50 cm, 0.8x50 cm)	832.52 (0 ,0)		NHS Supply Chain (13/10/17)
COOK (UK) LTD	680.41 (0 ,0)		NHS Supply Chain (13/10/17)
GORE-TEX (0.1x30x30 cm)	570.31 (0 ,0)		NHS Supply Chain (13/10/17)
GORE-TEX (0.1x20x20 cm)	625.98 (0 ,0)		NHS Supply Chain (13/10/17)
VASCUTEK LTD	473.05 (0 ,0)		NHS Supply Chain (13/10/17)
VASCUTEK LTD (bifurcated)	648.25 (0 ,0)		NHS Supply Chain (13/10/17)
VASCUTEK LTD	781.86 (0 ,0)		NHS Supply Chain (13/10/17)
Guideline committee			
EVAR, stent-graft	6500 (5500 ,7000)	Triangular: min=5500.000; mode=6500.000; max=7000.000	Guideline Committee
EVAR, custom stent-graft	15685.667 (13750 ,30000)	Triangular: min=13750.000; mode=15685.667; max=30000.000	Guideline Committee
Primary procedure			
EVAR-1 study			
EVAR			
Theatre time (mins), EVAR	191 (186.096 ,195.904)	Normal: μ=191.000; σ=2.502	Brown et al., (2012)
Fluoroscopy duration (mins), EVAR	25 (23.972 ,26.028)	Normal: μ=25.000; σ=0.525	Brown et al., (2012)
Blood products (ml), EVAR	141 (103.745 ,178.255)	Normal: μ=141.000; σ=19.008	Brown et al., (2012)
Preoperative stay (days), EVAR	1.81 (1.625 ,1.995)	Normal: μ=1.810; σ=0.094	Brown et al., (2012)
Postoperative stay (days), EVAR	6.53 (5.555 ,7.505)	Normal: μ=6.530; σ=0.498	Brown et al., (2012)
ITU stay (days), EVAR	0.59 (0.299 ,0.881)	Normal: μ=0.590; σ=0.149	Brown et al., (2012)
HDU stay (days), EVAR	0.83 (0.67 ,0.99)	Normal: μ=0.830; σ=0.082	Brown et al., (2012)
OSR			
Theatre time (mins), OSR	215 (209.568 ,220.432)	Normal: μ=215.000; σ=2.771	Brown et al., (2012)
Fluoroscopy duration (mins), OSR	2 (1.281 ,2.719)	Normal: μ=2.000; σ=0.367	Brown et al., (2012)
Blood products (ml), OSR	863 (781.68 ,944.32)	Normal: μ=863.000; σ=41.491	Brown et al., (2012)
Preoperative stay (days), OSR	2.16 (1.908 ,2.412)	Normal: μ=2.160; σ=0.128	Brown et al., (2012)
Postoperative stay (days), OSR	9.25 (8.178 ,10.322)	Normal: μ=9.250; σ=0.547	Brown et al., (2012)
ITU stay (days), OSR	2.47 (2.433 ,2.507)	Normal: μ=2.470; σ=0.019	Brown et al., (2012)
HDU stay (days), OSR	1.88 (1.656 ,2.104)	Normal: μ=1.880; σ=0.114	Brown et al., (2012)
Unit costs			
Other EVAR consumables, per patient	511.685 (0 ,0)	Gamma: α=15350.000; β=0.033	Brown et al., (2012)
Other OSR consumables, per patient	99 (0 ,0)	Gamma: α=15050.000; β=0.007	Brown et al., (2012)

Operating theatre (hour)	831.081 (0 ,0)	Gamma: α=20080986.932; β=0.000	NHS Scotland 2016 [R142X Vascular Surgery]
Fluoroscopy, 1-20 mins	141.213 (85.1 ,168.4)	Gamma: α=606.638; β=0.233	NHS Reference Costs 2015-16 [IMAGDA RD30Z]
Fluoroscopy, 20-40 mins	138.921 (91.94 ,154.02)	Gamma: α=738.120; β=0.188	NHS Reference Costs 2015-16 [IMAGDA RD31Z]
Fluoroscopy, >40 mins	273.48 (156.05 ,337.47)	Gamma: α=165.406; β=1.653	NHS Reference Costs 2015-16 [IMAGDA RD32Z]
Blood, cost per 450ml (unit)	124.46 (0 ,0)		NHSBT 2017
Complex EVAR , per day	410.08 (244.67 ,397.16)	Gamma: α=381.647; β=1.074	NHS Reference Costs 2015-16 [EL_XS YR03Z]
EVAR, per day	292.461 (135.6 ,391.31)	Gamma: α=61.890; β=4.725	NHS Reference Costs 2015-16 [EL_XS YR04Z]
Open repair, CC score 6+	235.847 (223.9 ,282.47)	Gamma: α=236.053; β=0.999	NHS Reference Costs 2015-16 [EL_XS YQ03A]
Open repair, CC score 0-5	380.67 (172.82 ,505.215)	Gamma: α=21.480; β=17.722	NHS Reference Costs 2015-16 [EL_XS YQ03B]
ITU, per day	1017.029 (778.43 ,1328.69)	Gamma: α=155.411; β=6.544	NHS Reference Costs 2015-16 [CC, Surgical adult, XC06Z]
HDU, per day	717.889 (364.46 ,986.16)	Gamma: α=43.675; β=16.437	NHS Reference Costs 2015-16 [CC, Surgical adult, XC07Z]
Conversion to OSR			
Proportion of EVARs switched to OSR	0.008 (0.003 ,0.016)	Beta: α=5.000; β=624.000	Brown et al., (2012)
IMPROVE study			
EVAR			
Theatre time (mins), EVAR	157 (145.974 ,168.026)	Normal: μ=157.000; σ=5.625	Powell et al., 2015
Routine ward stay (days), EVAR	7 (5.688 ,8.312)	Normal: μ=7.000; σ=0.669	Powell et al., 2017
Transfer to secondary hospital	0.032 (0.015 ,0.054)	Beta: α=10.000; β=306.000	Powell et al., 2015
Secondary hospital days	0.7 (0.193 ,1.207)	Normal: μ=0.700; σ=0.259	Powell et al., 2017
Nursing home (days), EVAR	0 (0 ,0)	Normal: μ=0.000; σ=0.000	Powell et al., 2015
Family doctor visits, EVAR	2.8 (2.37 ,3.23)	Normal: μ=2.800; σ=0.219	Powell et al., 2015
Community nurse visits, EVAR	2.2 (1.461 ,2.939)	Normal: μ=2.200; σ=0.377	Powell et al., 2015
OSR			
Theatre time (mins), OSR	180 (167.717 ,192.283)	Normal: μ=180.000; σ=6.267	Powell et al., 2015
Routine ward stay (days), OSR	7.8 (6.435 ,9.165)	Normal: μ=7.800; σ=0.696	Powell et al., 2017
Transfer to secondary hospital	0.121 (0.087 ,0.161)	Beta: α=36.000; β=261.000	Powell et al., 2015
Secondary hospital days	4.8 (2.4 ,7.2)	Normal: μ=4.800; σ=1.224	Powell et al., 2017
Nursing home (days), OSR	1.8 (0.147 ,21.973)	Lognormal: μ=-1.919; σ=2.239	Powell et al., 2015
Family doctor visits, OSR	2.5 (2.068 ,2.932)	Normal: μ=2.500; σ=0.220	Powell et al., 2015
Community nurse visits, OSR	2.1 (1.258 ,2.942)	Normal: μ=2.100; σ=0.429	Powell et al., 2015

Unit costs (where different to elective)			
Emergency call	6.909 (5.96 ,7.53)	Gamma: α=387.667; β=0.018	NHS Reference Costs 2015-16 [AMB ASC01]
Ambulance (see, treat & convey)	236.44 (210.54 ,255.59)	Gamma: α=551.388; β=0.429	NHS Reference Costs 2015-16 [AMB ASS02]
Investigation & Cat. 5 treatment, general hospital	408.73 (344.02 ,449.67)	Gamma: α=3676.879; β=0.111	NHS Reference Costs 2015-16 [EM T01A VB01Z]
Investigation & Cat. 5 treatment, specialist centre	114.905 (97.29 ,121.75)	Gamma: α=240.951; β=0.477	NHS Reference Costs 2015-16 [EM T02A VB01Z]
Nursing home, per day	152 (76 ,304)		PSSRU 2016 [1.3]
Family doctor, home visit	59 (29.5 ,118)		PSSRU 2016 [10.3]
Community nurse, home visit	10.75 (5.375 ,21.5)		PSSRU 2016 [10.1]
Cost inflator: 2011-12 to 2015-16	1.051 (0 ,0)		PSSRU 2016 (HCHS)
Conversion to OSR			
Proportion of EVARs switched to OSR	0.361 (0.300, 0.423)	Beta: α=84.000; β=149.000	Powell et al., 2017
Monitoring			
IMAGOP, RD21A: Computerised Tomography Scan of one area, with post contrast only, 19 years and over	102.498 (70.75 ,134.97)	Gamma: α=635.064; β=0.161	NHS reference costs - 2015-16
IMAGOP, RD22Z: Computerised Tomography Scan of one area, with pre and post contrast, 19 years and over	118.532 (94.69 ,137.65)	Gamma: α=748.081; β=0.158	NHS reference costs - 2015-16
Ultrasound scan, session (IMAGOP, RD47Z)	57.534 (39.05 ,69.93)	Gamma: α=461.130; β=0.125	NHS reference costs - 2015-16
WF01A: F2F, consultant, follow-up	140.209 (100.18 ,165.1)	Gamma: α=942.162; β=0.149	NHS reference costs - 2015-16
WF01C: non-F2F, consultant, follow-up	72.952 (61.4 ,78.18)	Gamma: α=825.485; β=0.088	NHS reference costs - 2015-16
Follow-up			
EVAR			
Time of first CT scan (OP) (month)	2 (1 ,3)		Guideline committee
No. of OP consultations per year	1		Guideline committee
Maximum number of FU scans	5		Guideline committee
OSR			
Time of first OP consultation (month)	2 (1 ,3)		Guideline committee
No. of OP consultations per year	NA		Guideline committee
Maximum number of FU scans	NA		Guideline committee
Graft reintervention monitoring			
CT scan 1 month before reintervention	1		Guideline committee
CT scan 3 months after reintervention	1		Guideline committee
Reintervention procedures			
Life-threatening, graft			
Life-threatening complication	17089.898	Equal to emergency AAA repair	
Other serious, graft			
EL: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	6811.862 (2666.858 ,8859.458)	Gamma: α=138.719; β=49.105	NHS Spell Costs - 2015-16

EL: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	2720.729 (1853.95 ,3510.86)	Gamma: α=412.157; β=6.601	NHS Spell Costs - 2015-16
EL: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	2376.729 (1523.07 ,2698.36)	Gamma: α=751.625; β=3.162	NHS Spell Costs - 2015-16
EL: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	2011.272 (1181.19 ,2613.33)	Gamma: α=369.674; β=5.441	NHS Spell Costs - 2015-16
NEL: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	12763.105 (9801.09 ,14753.45)	Gamma: α=1232.818; β=10.353	NHS Spell Costs - 2015-16
NEL: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	7704.527 (5620.06 ,8268.34)	Gamma: α=1401.575; β=5.497	NHS Spell Costs - 2015-16
NEL: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	5357.439 (4192.79 ,5971.69)	Gamma: α=1320.420; β=4.057	NHS Spell Costs - 2015-16
NEL: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	4958.278 (2902.08 ,6029.02)	Gamma: α=251.649; β=19.703	NHS Spell Costs - 2015-16
NES: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	1492.36 (869.76 ,1260.67)	Gamma: α=397.828; β=3.751	NHS Spell Costs - 2015-16
NES: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	1557.786 (581.278 ,2478.71)	Gamma: α=29.438; β=52.918	NHS Spell Costs - 2015-16
NES: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	1601.863 (678.21 ,2002.69)	Gamma: α=85.177; β=18.806	NHS Spell Costs - 2015-16
NES: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	1863.624 (1003.26 ,2757.48)	Gamma: α=63.668; β=29.271	NHS Spell Costs - 2015-16
Pulmonary			
EL: DZ20D: Pulmonary Oedema with Interventions	6710.066 (2944.29 ,8254.43)	Gamma: α=206.305; β=32.525	NHS Spell Costs - 2015-16
EL: DZ20E: Pulmonary Oedema without Interventions, with CC Score 6+	3319.343 (2264.1 ,4373.18)	Gamma: α=482.295; β=6.882	NHS Spell Costs - 2015-16
EL: DZ20F: Pulmonary Oedema without Interventions, with CC Score 0-5	2461.491 (1810.66 ,2882.305)	Gamma: α=940.874; β=2.616	NHS Spell Costs - 2015-16
EL: DZ22K: Unspecified Acute Lower Respiratory Infection with Interventions, with CC Score 9+	7080.181 (5505.21 ,8308.5)	Gamma: α=1659.967; β=4.265	NHS Spell Costs - 2015-16
EL: DZ22L: Unspecified Acute Lower Respiratory Infection with Interventions, with CC Score 0-8	4375.059 (3428.2 ,5264.17)	Gamma: α=1436.357; β=3.046	NHS Spell Costs - 2015-16
EL: DZ22M: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 13+	5658.222 (4618.79 ,6828.35)	Gamma: α=1610.990; β=3.512	NHS Spell Costs - 2015-16
EL: DZ22N: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 9-12	3853.994 (3166.43 ,4486.58)	Gamma: α=2295.345; β=1.679	NHS Spell Costs - 2015-16
EL: DZ22P: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 5-8	2859.103 (2489.43 ,3210.28)	Gamma: α=4294.097; β=0.666	NHS Spell Costs - 2015-16
EL: DZ22Q: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 0-4	2004.187 (1744.71 ,2250.35)	Gamma: α=4231.226; β=0.474	NHS Spell Costs - 2015-16
EL: DZ23H: Bronchopneumonia with Multiple Interventions	7742.511 (5725.645 ,8684.87)	Gamma: α=1357.828; β=5.702	NHS Spell Costs - 2015-16
EL: DZ23J: Bronchopneumonia with Single Intervention, with CC Score 11+	6069.102 (4477.17 ,7523.98)	Gamma: α=707.611; β=8.577	NHS Spell Costs - 2015-16

EL: DZ23K: Bronchopneumonia with Single Intervention, with CC Score 0-10	4139.526 (3163.47 ,4870.875)	Gamma: α=1176.607; β=3.518	NHS Spell Costs - 2015-16
EL: DZ23L: Bronchopneumonia without Interventions, with CC Score 11+	5479.992 (4187.53 ,6541.25)	Gamma: α=1321.800; β=4.146	NHS Spell Costs - 2015-16
EL: DZ23M: Bronchopneumonia without Interventions, with CC Score 6-10	3569.571 (2987.22 ,4287.26)	Gamma: α=1865.813; β=1.913	NHS Spell Costs - 2015-16
EL: DZ23N: Bronchopneumonia without Interventions, with CC Score 0-5	2536.481 (1906.95 ,2865.6)	Gamma: α=1656.141; β=1.532	NHS Spell Costs - 2015-16
EL: DZ20D: Pulmonary Oedema with Interventions	1501.086 (391.048 ,2025.33)	Gamma: α=19.958; β=75.213	NHS Spell Costs - 2015-16
EL: DZ20E: Pulmonary Oedema without Interventions, with CC Score 6+	1063.177 (456.03 ,1417.245)	Gamma: α=158.066; β=6.726	NHS Spell Costs - 2015-16
EL: DZ20F: Pulmonary Oedema without Interventions, with CC Score 0-5	587.531 (413.39 ,715.8)	Gamma: α=728.091; β=0.807	NHS Spell Costs - 2015-16
EL: DZ22K: Unspecified Acute Lower Respiratory Infection with Interventions, with CC Score 9+	3597.175 (839.85 ,5063.57)	Gamma: α=26.398; β=136.266	NHS Spell Costs - 2015-16
EL: DZ22L: Unspecified Acute Lower Respiratory Infection with Interventions, with CC Score 0-8	1735.43 (359.83 ,3502.05)	Gamma: α=24.423; β=71.056	NHS Spell Costs - 2015-16
EL: DZ22M: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 13+	2627.965 (591.275 ,5122.78)	Gamma: α=41.617; β=63.146	NHS Spell Costs - 2015-16
EL: DZ22N: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 9-12	1103.675 (529.35 ,1018.53)	Gamma: α=1250.516; β=0.883	NHS Spell Costs - 2015-16
EL: DZ22P: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 5-8	727.316 (488.83 ,762.39)	Gamma: α=1865.178; β=0.390	NHS Spell Costs - 2015-16
EL: DZ22Q: Unspecified Acute Lower Respiratory Infection without Interventions, with CC Score 0-4	507.903 (401.17 ,590.19)	Gamma: α=1878.851; β=0.270	NHS Spell Costs - 2015-16
EL: DZ23H: Bronchopneumonia with Multiple Interventions	2090.556 (926.083 ,2489.77)	Gamma: α=71.558; β=29.215	NHS Spell Costs - 2015-16
EL: DZ23J: Bronchopneumonia with Single Intervention, with CC Score 11+	1094.146 (500.11 ,948.365)	Gamma: α=205.999; β=5.311	NHS Spell Costs - 2015-16
EL: DZ23K: Bronchopneumonia with Single Intervention, with CC Score 0-10	1247.085 (503.06 ,1433.53)	Gamma: α=134.024; β=9.305	NHS Spell Costs - 2015-16
EL: DZ23L: Bronchopneumonia without Interventions, with CC Score 11+	1524.327 (557.793 ,1643.5)	Gamma: α=254.683; β=5.985	NHS Spell Costs - 2015-16
EL: DZ23M: Bronchopneumonia without Interventions, with CC Score 6-10	1060.041 (474.24 ,1289.98)	Gamma: α=371.824; β=2.851	NHS Spell Costs - 2015-16
EL: DZ23N: Bronchopneumonia without Interventions, with CC Score 0-5	782.185 (449.43 ,846.41)	Gamma: α=854.825; β=0.915	NHS Spell Costs - 2015-16
Hernia			
EL: FZ17E, Abdominal Hernia Procedures, 19 years and over, with CC Score 4+	5662.067 (3761.21 ,6562.93)	Gamma: α=929.012; β=6.095	NHS Spell Costs - 2015-16
EL: FZ17F, Abdominal Hernia Procedures, 19 years and over, with CC Score 1-3	4101.312 (3228.55 ,4826.5)	Gamma: α=1690.243; β=2.426	NHS Spell Costs - 2015-16
EL: FZ17G, Abdominal Hernia Procedures, 19 years and over, with CC Score 0	3482.826 (2867.64 ,3863.595)	Gamma: α=3093.211; β=1.126	NHS Spell Costs - 2015-16

NEL: FZ17E, Abdominal Hernia Procedures, 19 years and over, with CC Score 4+	6940.968 (4678.52 ,8558.29)	Gamma: α=687.260; β=10.099	NHS Spell Costs - 2015-16
NEL: FZ17F, Abdominal Hernia Procedures, 19 years and over, with CC Score 1-3	4360.068 (3218.38 ,4844.295)	Gamma: α=1701.159; β=2.563	NHS Spell Costs - 2015-16
NEL: FZ17G, Abdominal Hernia Procedures, 19 years and over, with CC Score 0	3685.25 (2662.26 ,4202.47)	Gamma: α=1052.219; β=3.502	NHS Spell Costs - 2015-16
NES: FZ17E, Abdominal Hernia Procedures, 19 years and over, with CC Score 4+	4096.231 (1552.395 ,3601.82)	Gamma: α=203.551; β=20.124	NHS Spell Costs - 2015-16
NES: FZ17F, Abdominal Hernia Procedures, 19 years and over, with CC Score 1-3	2134.451 (1474.36 ,2402.365)	Gamma: α=972.307; β=2.195	NHS Spell Costs - 2015-16
NES: FZ17G, Abdominal Hernia Procedures, 19 years and over, with CC Score 0	1890.505 (1400.798 ,2396.03)	Gamma: α=439.939; β=4.297	NHS Spell Costs - 2015-16
Lysis of adhesions			
EL: FZ91E, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 9+	6921.13 (2849.47 ,8214.21)	Gamma: α=148.410; β=46.635	NHS Spell Costs - 2015-16
EL: FZ91F, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 5-8	4076.478 (2206.8 ,4645.02)	Gamma: α=656.183; β=6.212	NHS Spell Costs - 2015-16
EL: FZ91G, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 3-4	3262.568 (2096.56 ,3787.9)	Gamma: α=900.574; β=3.623	NHS Spell Costs - 2015-16
EL: FZ91H, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	3421.655 (2320 ,3551.17)	Gamma: α=1953.718; β=1.751	NHS Spell Costs - 2015-16
NEL: FZ91E, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 9+	8305.06 (6719.75 ,9910.63)	Gamma: α=1688.869; β=4.918	NHS Spell Costs - 2015-16
NEL: FZ91F, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 5-8	5013.862 (4283.61 ,5676.63)	Gamma: α=3300.416; β=1.519	NHS Spell Costs - 2015-16
NEL: FZ91G, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 3-4	3743.268 (3139.1 ,4226.26)	Gamma: α=3020.325; β=1.239	NHS Spell Costs - 2015-16
NEL: FZ91H, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	2903.585 (2471.13 ,3206.05)	Gamma: α=4033.556; β=0.720	NHS Spell Costs - 2015-16
NES: FZ91E, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 9+	4663.067 (735.09 ,8498.15)	Gamma: α=17.071; β=273.156	NHS Spell Costs - 2015-16
NES: FZ91F, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 5-8	2838.738 (696.19 ,5583.34)	Gamma: α=20.875; β=135.987	NHS Spell Costs - 2015-16
NES: FZ91G, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 3-4	2162.504 (843.68 ,3591.88)	Gamma: α=36.056; β=59.976	NHS Spell Costs - 2015-16
NES: FZ91H, Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	1585.861 (818.36 ,2294.34)	Gamma: α=132.349; β=11.982	NHS Spell Costs - 2015-16

Bowel resection			
EL: FZ67C, Major Small Intestine Procedures, 19 years and over, with CC Score 7+	13439.447 (8246.98 ,14706.618)	Gamma: α=724.678; β=18.545	NHS Spell Costs - 2015-16
EL: FZ67D, Major Small Intestine Procedures, 19 years and over, with CC Score 4-6	7487.873 (5572.64 ,7950.53)	Gamma: α=2309.692; β=3.242	NHS Spell Costs - 2015-16
EL: FZ67E, Major Small Intestine Procedures, 19 years and over, with CC Score 2-3	5350.145 (4250.14 ,5829.55)	Gamma: α=2881.583; β=1.857	NHS Spell Costs - 2015-16
EL: FZ67F, Major Small Intestine Procedures, 19 years and over, with CC Score 0-1	4317.55 (3578.79 ,4779.21)	Gamma: α=3272.155; β=1.319	NHS Spell Costs - 2015-16
EL: FZ77C, Major Large Intestine Procedures, 19 years and over, with CC Score 3+	6346.206 (4146.86 ,7532.73)	Gamma: α=735.184; β=8.632	NHS Spell Costs - 2015-16
EL: FZ77D, Major Large Intestine Procedures, 19 years and over, with CC Score 1-2	4389.107 (3390.15 ,4931.07)	Gamma: α=1948.843; β=2.252	NHS Spell Costs - 2015-16
EL: FZ77E, Major Large Intestine Procedures, 19 years and over, with CC Score 0	3939.761 (3142.44 ,4602.94)	Gamma: α=1761.161; β=2.237	NHS Spell Costs - 2015-16
NEL: FZ67C, Major Small Intestine Procedures, 19 years and over, with CC Score 7+	15224.266 (10959.27 ,18325.595)	Gamma: α=1033.792; β=14.727	NHS Spell Costs - 2015-16
NEL: FZ67D, Major Small Intestine Procedures, 19 years and over, with CC Score 4-6	9949.293 (7336.73 ,12316.128)	Gamma: α=988.053; β=10.070	NHS Spell Costs - 2015-16
NEL: FZ67E, Major Small Intestine Procedures, 19 years and over, with CC Score 2-3	7035.188 (5424.12 ,7967.74)	Gamma: α=1865.359; β=3.771	NHS Spell Costs - 2015-16
NEL: FZ67F, Major Small Intestine Procedures, 19 years and over, with CC Score 0-1	6346.555 (4516.23 ,7274.55)	Gamma: α=1290.929; β=4.916	NHS Spell Costs - 2015-16
NEL: FZ77C, Major Large Intestine Procedures, 19 years and over, with CC Score 3+	9546.677 (6515.53 ,11903.97)	Gamma: α=616.897; β=15.475	NHS Spell Costs - 2015-16
NEL: FZ77D, Major Large Intestine Procedures, 19 years and over, with CC Score 1-2	6521.316 (4404.253 ,7833.89)	Gamma: α=697.414; β=9.351	NHS Spell Costs - 2015-16
NEL: FZ77E, Major Large Intestine Procedures, 19 years and over, with CC Score 0	5568.019 (3629.85 ,6692.04)	Gamma: α=529.457; β=10.516	NHS Spell Costs - 2015-16
NES: FZ67C, Major Small Intestine Procedures, 19 years and over, with CC Score 7+	5756.419 (1719.53 ,6324)	Gamma: α=105.234; β=54.701	NHS Spell Costs - 2015-16
NES: FZ67D, Major Small Intestine Procedures, 19 years and over, with CC Score 4-6	2943.635 (776.695 ,4191.153)	Gamma: α=48.690; β=60.457	NHS Spell Costs - 2015-16
NES: FZ67E, Major Small Intestine Procedures, 19 years and over, with CC Score 2-3	1597.038 (460.25 ,1976.35)	Gamma: α=92.885; β=17.194	NHS Spell Costs - 2015-16
NES: FZ67F, Major Small Intestine Procedures, 19 years and over, with CC Score 0-1	1121.323 (332.36 ,1612.56)	Gamma: α=89.350; β=12.550	NHS Spell Costs - 2015-16
NES: FZ77C, Major Large Intestine Procedures, 19 years and over, with CC Score 3+	3550.941 (631.79 ,4917.92)	Gamma: α=34.972; β=101.536	NHS Spell Costs - 2015-16
NES: FZ77D, Major Large Intestine Procedures, 19 years and over, with CC Score 1-2	1218.346 (510.3 ,1628.96)	Gamma: α=58.280; β=20.905	NHS Spell Costs - 2015-16
NES: FZ77E, Major Large Intestine Procedures, 19 years and over, with CC Score 0	1236.958 (548.54 ,1702.47)	Gamma: α=41.821; β=29.578	NHS Spell Costs - 2015-16
Other hospitalisation			

EL: FZ91J, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 11+	18386.801 (2925.83 ,23940.325)	Gamma: α=19.504; β=942.742	NHS Spell Costs - 2015-16
EL: FZ91K, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 6-10	4587.811 (1700.07 ,5451.84)	Gamma: α=244.902; β=18.733	NHS Spell Costs - 2015-16
EL: FZ91L, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 3-5	2965.019 (1324.66 ,3754.62)	Gamma: α=344.089; β=8.617	NHS Spell Costs - 2015-16
EL: FZ91M, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 0-2	1861.872 (962.58 ,2262.52)	Gamma: α=541.292; β=3.440	NHS Spell Costs - 2015-16
NEL: FZ91J, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 11+	6343.504 (4347.09 ,7420.425)	Gamma: α=1062.111; β=5.973	NHS Spell Costs - 2015-16
NEL: FZ91K, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 6-10	3845.582 (3241.18 ,4333.3)	Gamma: α=3249.051; β=1.184	NHS Spell Costs - 2015-16
NEL: FZ91L, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 3-5	2762.71 (2388.26 ,2934.85)	Gamma: α=6926.986; β=0.399	NHS Spell Costs - 2015-16
NEL: FZ91M, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 0-2	1878.181 (1665.5 ,2033.53)	Gamma: α=7346.002; β=0.256	NHS Spell Costs - 2015-16
NES: FZ91J, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 11+	1581.703 (551.89 ,2327.02)	Gamma: α=122.806; β=12.880	NHS Spell Costs - 2015-16
NES: FZ91K, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 6-10	963.258 (524.38 ,927.84)	Gamma: α=1421.069; β=0.678	NHS Spell Costs - 2015-16
NES: FZ91L, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 3-5	629.83 (445.67 ,689.2)	Gamma: α=1740.561; β=0.362	NHS Spell Costs - 2015-16
NES: FZ91M, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 0-2	487.351 (377.88 ,563.13)	Gamma: α=1876.570; β=0.260	NHS Spell Costs - 2015-16
DC: FZ91J, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 11+	328.11 (328.11 ,328.11)		NHS Spell Costs - 2015-16
DC: FZ91K, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 6-10	405.379 (199.925 ,637.45)	Gamma: α=81.232; β=4.990	NHS Spell Costs - 2015-16
DC: FZ91L, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 3-5	366.531 (245.46 ,419.75)	Gamma: α=989.901; β=0.370	NHS Spell Costs - 2015-16
DC: FZ91M, Non-Malignant Gastrointestinal Tract Disorders without Interventions, with CC Score 0-2	372.858 (247.06 ,442.55)	Gamma: α=979.737; β=0.381	NHS Spell Costs - 2015-16
HRQL			
Baseline utility value	0.75 (0.731 ,0.768)	Beta: α=1576.923; β=525.641	Greenhalgh et al., 2005

Elective repair			
Primary procedure recovery			
First recovery time point for HRQL update (months)	0 (0 ,0)		Greenhalgh et al., 2005
Months until recovery of HRQL post-surgery	0 (0 ,0)		Greenhalgh et al., 2005
Utility loss @3mo, EVAR	0.027 (0.007 ,0.061)	Beta: α=3.711; β=133.724	Greenhalgh et al., 2005; Epstein et al., 2008; Chambers et al., 2009
Utility loss @12mo, EVAR	0 (0 ,0)		Greenhalgh et al., 2005
Utility difference at 3mos: OSR vs. EVAR	0.05 (0.019 ,0.096)	Beta: α=5.888; β=111.863	Greenhalgh et al., 2005
Utility difference at 12mos: OSR vs. EVAR	0 (0 ,0)		Greenhalgh et al., 2005
Emergency repair			
Primary procedure recovery			
First recovery time point for HRQL update (months)	0 (0 ,0)		Powell et al., 2017
Months until recovery of HRQL post-surgery, EVAR	0 (0 ,0)		Powell et al., 2017
Second recovery time point for HRQL update (months), OSR	0 (0 ,0)		Powell et al., 2017
Months until recovery of HRQL post-surgery, OSR	0 (0 ,0)		Powell et al., 2017
Utility loss @3mo, EVAR	0 (0 ,0)		Calculated value
Utility loss @12mo, EVAR	0 (0 ,0)		Powell et al., 2017
Utility difference at 3mos: OSR vs. EVAR	0.097 (0.031 ,0.163)	Beta: α=7.396; β=68.849	Powell et al., 2017
Utility difference at 12mos: OSR vs. EVAR	0.068 (0.002 ,0.134)	Beta: α=3.733; β=51.157	Powell et al., 2017
Utility difference at 36mos: OSR vs. EVAR	0 (0 ,0)		Powell et al., 2017
Complications			
Graft-related reintervention			
Utility mutliplier, life-threatening AAA reinterv.	0 (0 ,0)		Calculated value
Utility multiplier, other serious AAA reinterv.	0 (0 ,0)		Calculated value
Pulmonary complication			
Utility multiplier, periop. pulmonary complication	0.95 (0.9 ,0.975)		NICE NG78 [Appendix K]
Hernia			
EQ-5D utility before surgery (persistent pain)	0.836 (0.831 ,0.841)	Normal: μ=0.836; σ=0.002	McCormack 2003 (NICE TA83)
EQ-5D utility immediate post surgery period	0.74 (0.713 ,0.767)	Normal: μ=0.740; σ=0.014	McCormack 2003 (NICE TA83)
EQ-5D utility after 1 month	0.82 (0.791 ,0.849)	Normal: μ=0.820; σ=0.015	McCormack 2003 (NICE TA83)
EQ-5D utility after 3 months	0.85 (0.823 ,0.877)	Normal: μ=0.850; σ=0.014	McCormack 2003 (NICE TA83)
Baseline healthy EQ-5D utility	0.952 (0.951 ,0.953)	Normal: μ=0.952; σ=0.001	McCormack 2003 (NICE TA83)
Months living with hernia pre-surgery	5.64 (2.82 ,8.46)		McCormack 2003 (NICE TA83)
Months until recovery of HRQL post-surgery	3 (1.5 ,4.5)		McCormack 2003 (NICE TA83)
Other laparotomy reintervention			
EQ-5D utility before surgery	0.795 (0.749 ,0.841)	Normal: μ=0.795; σ=0.023	Dowson 2013
EQ-5D utility immediate post surgery period	0.331 (0.259 ,0.403)	Normal: μ=0.331; σ=0.037	Dowson 2013

EQ-5D utility after 42 days	0.891 (0.85 ,0.932)	Normal: μ=0.891; σ=0.021	Dowson 2013
Months living with condition pre-surgery	5.64 (2.82 ,8.46)		McCormack 2003 (NICE TA83)
Months until recovery of HRQL post-surgery	1.38 (0.69 ,2.07)		Dowson 2013

1 **Table HE81: All parameters in 'EVAR vs. no intervention' cost–utility model**

Name	*Value (95%CI)*	*Distribution & parameters*	*Source*
BASELINE COHORT			
Cohort age - elective pts (EVAR-2)	76.804 (76.164 ,77.444)	Normal: μ=76.804; σ=0.326	EVAR-2 trial data
Cohort age - emergency pts (IMPROVE)	76.219 (75.62 ,76.818)	Normal: μ=76.219; σ=0.305	IMPROVE trial data
Cohort %male - elective pts (EVAR-2)	0.859 (0.823 ,0.891)	Beta: α=347.000; β=57.000	EVAR-2 trial data
Cohort %male - emergency pts (IMPROVE)	0.783 (0.75 ,0.815)	Beta: α=480.000; β=133.000	IMPROVE trial data
Cohort AAA size - elective pts (EVAR-2)	6.705 (6.607 ,6.803)	Lognormal: μ=1.903; σ=0.050	EVAR-2 trial data
Cohort AAA size - emergency pts (IMPROVE)	8.389 (8.226 ,8.551)	Lognormal: μ=2.127; σ=0.083	IMPROVE trial data
WAITING TIME (elective repair)			
General lead-in time from referral to surgery (wks)	8 (4 ,12)	Triangular: min=4.000; mode=8.000; max=12.000	Guideline committee
Additional wait time for complex EVAR device (wks)	8 (4 ,12)	Triangular: min=4.000; mode=8.000; max=12.000	Guideline committee
PERIOPERATIVE MORTALITY			
Elective EVAR			
Infrarenal AAA			
Prob 30-day mortality: IR, elect EVAR	0.073 (0.039 ,0.115)	Beta: α=13.000; β=166.000	EVAR-2 data
Emergency EVAR			
Estimating 'fitness for OSR' odds ratio			
30-day mortality, EVAR-1	0.016 (0.008 ,0.028)	Beta: α=10.000; β=600.000	Brown et al., 2012
30-day mortality: EVAR, IMPROVE	0.354 (0.303 ,0.408)	Beta: α=112.000; β=204.000	Powell et al., 2015
Elective EVAR			
Complex AAA			
Estimating 'complexity' odds ratio			
NVR EVAR operative mortality, infrarenal	0.004 (0.002 ,0.007)	Beta: α=12.000; β=2870.000	Nat Vasc Reg, 2016
NVR EVAR operative mortality, complex	0.036 (0.026 ,0.047)	Beta: α=41.000; β=1111.000	Nat Vasc Reg, 2016
OR - complex vs infrarenal	0 (4.977 ,15.653)		
Effect modifiers			
Elective EVAR			
intercept	-9.21 (-13.592 ,-4.828)	Multivariate normal	Mani et al., 2015
age, per yr	0.039 (-0.011 ,0.09)	Multivariate normal	Mani et al., 2015
female	0.187 (-0.79 ,1.166)	Multivariate normal	Mani et al., 2015
aneurysm diameter, per cm	0.236 (0.051 ,0.421)	Multivariate normal	Mani et al., 2015
Emergency EVAR			
Ln(OR)s	0 (0 ,0)	: FALSE	

intercept	-4.768 (-7.346 ,0.112)	Multivariate normal	IMPROVE data
age, per yr	0.056 (0.022 ,1.094)	Multivariate normal	IMPROVE data
female	-0.152 (-0.724 ,1.522)	Multivariate normal	IMPROVE data
Cohort % male - IMPROVE - EVAR arm	0.222 (0.178 ,0.269)	Beta: α=70.000; β=246.000	IMPROVE data
Cohort age - IMPROVE - EVAR arm	76.184 (75.366 ,77.001)	Normal: μ=76.184; σ=0.415	IMPROVE data
POST-PERIOPERATIVE & LONG-TERM MORTALITY			
Recalibration of general UK mortality			
ln[HR], trial-v-genpop: 0-5 yrs	1.253 (1.091 ,1.422)	Multivariate Normal	EVAR-2 data & ONS lifetables 1999–2001
ln[HR], trial-v-genpop: 5+ yrs	0.395 (0.079 ,0.776)	Multivariate Normal	EVAR-2 data & ONS lifetables 1999–2001
ln[HR], trial-v-genpop: 0-4.5 yrs	1.264 (1.099 ,1.433)	Multivariate Normal	EVAR-2 data & ONS lifetables 1999–2001
ln[HR], trial-v-genpop: 4.5+ yrs	0.485 (0.195 ,0.867)	Multivariate Normal	EVAR-2 data & ONS lifetables 1999–2001
Relative effects			
Univariable			
ln[HR], EVAR-v-NoInt: 0-5 yrs	-0.252 (-0.505 ,0.002)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 5+ yrs	0.355 (-0.048 ,0.757)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 0-4.5 yrs	-0.299 (-0.561 ,-0.036)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 4.5+ yrs	0.374 (-0.003 ,0.751)	Multivariate Normal	EVAR-2 trial data
Multivariable			
ln[HR], EVAR-v-NoInt: 5 yrs	-0.276 (-0.53 ,-0.022)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 5+ yrs	0.331 (-0.075 ,0.737)	Multivariate Normal	EVAR-2 trial data
ln[HR], age /yr	0.027 (0.01 ,0.044)	Multivariate Normal	EVAR-2 trial data
ln[HR], female-v-male	0.023 (-0.285 ,0.331)	Multivariate Normal	EVAR-2 trial data
ln[HR], diameter /cm	0.056 (-0.04 ,0.152)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 0-4.5 yrs	-0.323 (-0.586 ,-0.06)	Multivariate Normal	EVAR-2 trial data
ln[HR], EVAR-v-NoInt: 4.5+ yrs	0.352 (-0.028 ,0.733)	Multivariate Normal	EVAR-2 trial data
ln[HR], age /yr	0.027 (0.01 ,0.044)	Multivariate Normal	EVAR-2 trial data
ln[HR], female-v-male	0.024 (-0.284 ,0.332)	Multivariate Normal	EVAR-2 trial data
ln[HR], diameter /cm	0.058 (-0.038 ,0.154)	Multivariate Normal	EVAR-2 trial data
Centring on EVAR-2			
Female, % of cohort	0.135 (0.092 ,0.185)	Beta: α=28.000; β=179.000	EVAR-2 trial data
Aneurysm diameter, cm	6.659 (6.523 ,6.795)	Lognormal: μ=1.896; σ=0.069	EVAR-2 trial data
Parametric curves			
Univariable			
EVAR			
Gompertz - constant	-1.827 (-2.09 ,-1.565)	Multivariate Normal	EVAR-2 trial data
Gompertz - gamma	0.062 (0.011 ,0.112)	Multivariate Normal	EVAR-2 trial data

Gamma - constant	1.726 (1.478 ,1.974)	Multivariate Normal	EVAR-2 trial data
Gamma - ln(sigma)	-0.223 (-0.438 ,-0.008)	Multivariate Normal	EVAR-2 trial data
Gamma - kappa	1.257 (0.712 ,1.802)	Multivariate Normal	EVAR-2 trial data
Gamma - sigma	0 (0 ,0)	Multivariate Normal	
Weibull - constant	-1.872 (-2.193 ,-1.552)	Multivariate Normal	EVAR-2 trial data
Weibull - ln(p)	0.143 (0.014 ,0.272)	Multivariate Normal	EVAR-2 trial data
No intervention			
Gompertz - constant	-1.513 (-1.729 ,-1.297)	Multivariate Normal	EVAR-2 trial data
Gompertz - gamma	-0.007 (-0.05 ,0.036)	Multivariate Normal	EVAR-2 trial data
Gamma - constant	1.363 (1.125 ,1.6)	Multivariate Normal	EVAR-2 trial data
Gamma - ln(sigma)	0.041 (-0.091 ,0.172)	Multivariate Normal	EVAR-2 trial data
Gamma - kappa	0.612 (0.24 ,0.983)	Multivariate Normal	EVAR-2 trial data
Gamma - sigma	0 (0 ,0)	Multivariate Normal	
Exponential - logscale	-1.54 (-1.681 ,-1.399)	Multivariate Normal	EVAR-2 trial data
Weibull - constant	-1.62 (-1.879 ,-1.879)	Multivariate Normal	EVAR-2 trial data
Weibull - ln(p)	0.042 (-0.07 ,-0.07)	Multivariate Normal	EVAR-2 trial data
Multivariable			
EVAR			
Gompertz - age	0.019 (-0.006 ,0.043)	Multivariate Normal	EVAR-2 trial data
Gompertz - sex=f	-0.027 (-0.493 ,0.439)	Multivariate Normal	EVAR-2 trial data
Gompertz - max diameter	0.187 (0.04 ,0.335)	Multivariate Normal	EVAR-2 trial data
Gompertz - constant	-4.558 (-6.873 ,-2.243)	Multivariate Normal	EVAR-2 trial data
Gompertz - gamma	0.076 (0.024 ,0.127)	Multivariate Normal	EVAR-2 trial data
Gamma - age	-0.015 (-0.033 ,0.004)	Multivariate Normal	EVAR-2 trial data
Gamma - sex=f	0.047 (-0.312 ,0.405)	Multivariate Normal	EVAR-2 trial data
Gamma - max diameter	-0.139 (-0.248 ,-0.03)	Multivariate Normal	EVAR-2 trial data
Gamma - constant	3.803 (2.105 ,5.502)	Multivariate Normal	EVAR-2 trial data
Gamma - ln(sigma)	-0.299 (-0.542 ,-0.057)	Multivariate Normal	EVAR-2 trial data
Gamma - kappa	1.414 (0.788 ,2.04)	Multivariate Normal	EVAR-2 trial data
Gamma - sigma	0 (0 ,0)	Multivariate Normal	
Weibull - age	0.017 (-0.007 ,0.042)	Multivariate Normal	EVAR-2 trial data
Weibull - sex=f	-0.008 (-0.474 ,0.458)	Multivariate Normal	EVAR-2 trial data
Weibull - max diameter	0.178 (0.031 ,0.324)	Multivariate Normal	EVAR-2 trial data
Weibull - constant	-4.427 (-6.733 ,-2.122)	Multivariate Normal	EVAR-2 trial data
Weibull - ln(p)	0.165 (0.036 ,0.294)	Multivariate Normal	EVAR-2 trial data
No intervention			

Gompertz - age	0.034 (0.011 ,0.057)	Multivariate Normal	EVAR-2 trial data
Gompertz - sex=f	0.196 (-0.215 ,0.606)	Multivariate Normal	EVAR-2 trial data
Gompertz - max diameter	-0.056 (-0.19 ,0.079)	Multivariate Normal	EVAR-2 trial data
Gompertz - constant	-3.977 (-5.866 ,-2.089)	Multivariate Normal	EVAR-2 trial data
Gompertz - gamma	0.007 (-0.038 ,0.051)	Multivariate Normal	EVAR-2 trial data
Gamma - age	-0.031 (-0.053 ,-0.009)	Multivariate Normal	EVAR-2 trial data
Gamma - sex=f	-0.185 (-0.587 ,0.217)	Multivariate Normal	EVAR-2 trial data
Gamma - max diameter	0.047 (-0.087 ,0.181)	Multivariate Normal	EVAR-2 trial data
Gamma - constant	3.673 (1.867 ,5.48)	Multivariate Normal	EVAR-2 trial data
Gamma - ln(sigma)	-0.013 (-0.157 ,0.13)	Multivariate Normal	EVAR-2 trial data
Gamma - kappa	0.749 (0.353 ,1.145)	Multivariate Normal	EVAR-2 trial data
Gamma - sigma	0 (0 ,0)	Multivariate Normal	
Exponential - age	0.033 (0.01 ,0.056)	Multivariate Normal	EVAR-2 trial data
Exponential - sex=f	0.192 (-0.218 ,0.602)	Multivariate Normal	EVAR-2 trial data
Exponential - max diameter	-0.054 (-0.189 ,0.08)	Multivariate Normal	EVAR-2 trial data
Exponential - logscale	-3.901 (-5.72 ,-2.081)	Multivariate Normal	EVAR-2 trial data
Weibull - age	0.035 (0.012 ,0.058)	Multivariate Normal	EVAR-2 trial data
Weibull - sex=f	0.201 (-0.209 ,0.612)	Multivariate Normal	EVAR-2 trial data
Weibull - max diameter	-0.059 (-0.194 ,0.075)	Multivariate Normal	EVAR-2 trial data
Weibull - constant	-4.203 (-6.091 ,-2.315)	Multivariate Normal	EVAR-2 trial data
Weibull - ln(p)	0.073 (-0.04 ,0.186)	Multivariate Normal	EVAR-2 trial data
REINTERVENTION (GRAFT)			
EVAR: % reinterventions = life-threatening	0.5 (0.358 ,0.642)	Beta: α=23.000; β=23.000	Sweeting 2017; Patel 2016
EVAR, 0-6 months, rate/yr	0.253 (0.169 ,0.346)	Beta: α=23.000; β=68.000	Sweeting et al., 2017
EVAR, 0.5-4 years, rate/yr	0.038 (0.022 ,0.059)	Beta: α=16.000; β=400.000	Sweeting et al., 2017
EVAR, >4 years, rate/yr	0.038 (0.017 ,0.068)	Beta: α=8.000; β=202.000	Sweeting et al., 2017
No intervention: rupture rate/yr	0.124 (0.096 ,0.162)	Beta: α=25.668; β=181.332	Brown et al .2012
RESOURCE USE & COSTS			
Repair devices			
IMPROVE study			
EVAR, standard stent-graft	5992.566 (5677.168 ,6833.628)	Triangular: min=5677.168; mode=5992.566; max=6833.628	Powell et al., 2015
Open repair stent-graft	654.977 (654.977 ,947.246)	Triangular: min=654.977; mode=654.977; max=947.246	Powell et al., 2015
NHS Supply Chain			

COOK (UK) LTD	6185.57 (5677.168 ,6833.628)	Triangular: min=5677.168; mode=6185.570; max=6833.628	NHS Supply Chain (13/10/17)
Guideline committee			
EVAR, stent-graft	6500 (5500 ,7000)	Triangular: min=5500.000; mode=6500.000; max=7000.000	Guideline Committee
EVAR, custom stent-graft	15685.667 (13750 ,30000)	Triangular: min=13750.000; mode=15685.667; max=30000.000	Guideline Committee
Primary procedure			
EVAR-1 study			
EVAR			
Theatre time (mins), EVAR	191 (186.096 ,195.904)	Normal: μ=191.000; σ=2.502	Brown et al., (2012)
Fluoroscopy duration (mins), EVAR	25 (23.972 ,26.028)	Normal: μ=25.000; σ=0.525	Brown et al., (2012)
Blood products (ml), EVAR	141 (103.745 ,178.255)	Normal: μ=141.000; σ=19.008	Brown et al., (2012)
Preoperative stay (days), EVAR	1.81 (1.625 ,1.995)	Normal: μ=1.810; σ=0.094	Brown et al., (2012)
Postoperative stay (days), EVAR	6.53 (5.555 ,7.505)	Normal: μ=6.530; σ=0.498	Brown et al., (2012)
ITU stay (days), EVAR	0.59 (0.299 ,0.881)	Normal: μ=0.590; σ=0.149	Brown et al., (2012)
HDU stay (days), EVAR	0.83 (0.67 ,0.99)	Normal: μ=0.830; σ=0.082	Brown et al., (2012)
Unit costs			
Cost inflator: 2008-09 to 2015-16	1.112 (0 ,0)	: FALSE	PSSRU 2016 (HCHS)
Other EVAR consumables, per patient	511.685 (0 ,0)	Gamma: α=15350.000; β=0.033	Brown et al., (2012)
Other OSR consumables, per patient	99 (0 ,0)	Gamma: α=15050.000; β=0.007	Brown et al., (2012)
Operating theatre (hour)	831.081 (0 ,0)	Gamma: α=20080986.932; β=0.000	NHS Scotland 2016 [R142X Vascular Surgery]
Fluoroscopy, 1-20 mins	141.213 (85.1 ,168.4)	Gamma: α=606.638; β=0.233	NHS Reference Costs 2015-16 [IMAGDA RD30Z]
Fluoroscopy, 20-40 mins	138.921 (91.94 ,154.02)	Gamma: α=738.120; β=0.188	NHS Reference Costs 2015-16 [IMAGDA RD31Z]
Fluoroscopy, >40 mins	273.48 (156.05 ,337.47)	Gamma: α=165.406; β=1.653	NHS Reference Costs 2015-16 [IMAGDA RD32Z]
Vascular surgery ward, per day	0 (193.808 ,394.432)		Calculated value
ITU, per day	1017.029 (778.43 ,1328.69)	Gamma: α=155.411; β=6.544	NHS Reference Costs 2015-16 [CC, Surgical adult, XC06Z]
HDU, per day	717.889 (364.46 ,986.16)	Gamma: α=43.675; β=16.437	NHS Reference Costs 2015-16 [CC, Surgical adult, XC07Z]
IMPROVE study			
EVAR			
Theatre time (mins), EVAR	157 (145.974 ,168.026)	Normal: μ=157.000; σ=5.625	Powell et al., 2015
Routine ward stay (days), EVAR	7 (5.688 ,8.312)	Normal: μ=7.000; σ=0.669	Powell et al., 2017
Transfer to secondary hospital	0.032 (0.015 ,0.054)	Beta: α=10.000; β=306.000	Powell et al., 2015
Secondary hospital days	0.7 (0.193 ,1.207)	Normal: μ=0.700; σ=0.259	Powell et al., 2017

Nursing home (days), EVAR	0 (0 ,0)	Normal: μ=0.000; σ=0.000	Powell et al., 2015
Family doctor visits, EVAR	2.8 (2.37 ,3.23)	Normal: μ=2.800; σ=0.219	Powell et al., 2015
Community nurse visits, EVAR	2.2 (1.461 ,2.939)	Normal: μ=2.200; σ=0.377	Powell et al., 2015
Unit costs			
Emergency call	6.909 (5.96 ,7.53)	Gamma: α=387.667; β=0.018	NHS Reference Costs 2015-16 [AMB ASC01]
Ambulance (see, treat & convey)	236.44 (210.54 ,255.59)	Gamma: α=551.388; β=0.429	NHS Reference Costs 2015-16 [AMB ASS02]
Investigation & Cat. 5 treatment, general hospital	408.73 (344.02 ,449.67)	Gamma: α=3676.879; β=0.111	NHS Reference Costs 2015-16 [EM T01A VB01Z]
Investigation & Cat. 5 treatment, specialist centre	114.905 (97.29 ,121.75)	Gamma: α=240.951; β=0.477	NHS Reference Costs 2015-16 [EM T02A VB01Z]
Nursing home, per day	152 (76 ,304)		PSSRU 2016 [1.3]
Family doctor, home visit	59 (29.5 ,118)		PSSRU 2016 [10.3]
Community nurse, home visit	10.75 (5.375 ,21.5)		PSSRU 2016 [10.1]
Critical care, total cost, EVAR	7014.457 (5109.96 ,8918.953)	Gamma: α=84; β=149	Powell et al., 2017
Probabilities			
Prob. EVAR not suitable	0.361 (0.300, 0.423)	Beta: α=25.668; β=181.332	Powell et al., 2017
Prob. extra CT on decision not to intervene	0.500		Guideline committee
Monitoring			
IMAGOP, RD21A: Computerised Tomography Scan of one area, with post contrast only, 19 years and over	102.498 (70.75 ,134.97)	Gamma: α=635.064; β=0.161	NHS reference costs - 2015-16
IMAGOP, RD22Z: Computerised Tomography Scan of one area, with pre and post contrast, 19 years and over	118.532 (94.69 ,137.65)	Gamma: α=748.081; β=0.158	NHS reference costs - 2015-16
Ultrasound scan, session (IMAGOP, RD47Z)	57.534 (39.05 ,69.93)	Gamma: α=461.130; β=0.125	NHS reference costs - 2015-16
WF01A: F2F, consultant, follow-up	140.209 (100.18 ,165.1)	Gamma: α=942.162; β=0.149	NHS reference costs - 2015-16
WF01C: non-F2F, consultant, follow-up	72.952 (61.4 ,78.18)	Gamma: α=825.485; β=0.088	NHS reference costs - 2015-16
EVAR			
Time of first CT scan (OP) (month)	2 (1 ,3)		Guideline committee
No. of OP consultations per year	1		Guideline committee
Maximum number of FU scans	5		Guideline committee
Graft reintervention monitoring			
CT scan 1 month before reintervention	1		Guideline committee
CT scan 3 months after reintervention	1		Guideline committee
Reintervention			
Rupture repair cost	18558.943	Equal to emergency EVAR cost	
Rupture total follow-up cost	1223.799	Equal to emergency EVAR follow up in total	
Rupture mortality before repair is started	0.891 (0.797 ,0.958)	Beta: α=49.000; β=6.000	EVAR-2 trial data
Life-threatening, graft			
Life-threatening complication	12865.540	Equal to emergency EVAR procedure cost	
Other serious, graft			

EL: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	6811.862 (2666.858 ,8859.458)	Gamma: α=138.719; β=49.105	NHS Spell Costs - 2015-16
EL: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	2720.729 (1853.95 ,3510.86)	Gamma: α=412.157; β=6.601	NHS Spell Costs - 2015-16
EL: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	2376.729 (1523.07 ,2698.36)	Gamma: α=751.625; β=3.162	NHS Spell Costs - 2015-16
EL: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	2011.272 (1181.19 ,2613.33)	Gamma: α=369.674; β=5.441	NHS Spell Costs - 2015-16
NEL: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	12763.105 (9801.09 ,14753.45)	Gamma: α=1232.818; β=10.353	NHS Spell Costs - 2015-16
NEL: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	7704.527 (5620.06 ,8268.34)	Gamma: α=1401.575; β=5.497	NHS Spell Costs - 2015-16
NEL: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	5357.439 (4192.79 ,5971.69)	Gamma: α=1320.420; β=4.057	NHS Spell Costs - 2015-16
NEL: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	4958.278 (2902.08 ,6029.02)	Gamma: α=251.649; β=19.703	NHS Spell Costs - 2015-16
NES: YR11A, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 9+	1492.36 (869.76 ,1260.67)	Gamma: α=397.828; β=3.751	NHS Spell Costs - 2015-16
NES: YR11B, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 6-8	1557.786 (581.278 ,2478.71)	Gamma: α=29.438; β=52.918	NHS Spell Costs - 2015-16
NES: YR11C, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 3-5	1601.863 (678.21 ,2002.69)	Gamma: α=85.177; β=18.806	NHS Spell Costs - 2015-16
NES: YR11D, Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	1863.624 (1003.26 ,2757.48)	Gamma: α=63.668; β=29.271	NHS Spell Costs - 2015-16
HRQL			
Baseline utility			
Baseline utility, EVAR [EVAR-2]	0.58 (0 ,0)		Greenhalgh et al., 2005
Baseline utility, No Intervention [EVAR-2]	0.63 (0 ,0)		Greenhalgh et al., 2005
Baseline utility value	0.606 (0.574 ,0.637)	Beta: α=554.739; β=361.394	
Elective repair - recovery			
Baseline, EVAR-1	0.75 (0.731 ,0.768)	Beta: α=1576.923; β=525.641	Greenhalgh et al., 2005
Utility loss @3mo, EVAR	0.027 (0.007 ,0.061)	Beta: α=3.711; β=133.724	Greenhalgh et al., 2005; Epstein et al., 2008; Chambers et al., 2009
Utility loss @12mo, EVAR	0 (0 ,0)		Greenhalgh et al., 2005
Emergency repair - recovery			
Utility multiplier 0-3mo, EVAR	0.964 (0.953 ,0.964)		Calculated value
Utility multiplier 3-12mo, EVAR	0 (0 ,0)		Powell et al., 2017
Complications			
Utility difference at 3mos: OSR vs. EVAR	0.05 (0.019 ,0.096)	Beta: α=5.888; β=111.863	Greenhalgh et al., 2005
Utility multiplier, life-threatening AAA reinterv.	0.936		Calculated value
Utility multiplier, other serious AAA reinterv.	0.978		Calculated value
Rupture total HRQL loss (multiplier)	0.936	Equal to life-threatening graft complications	

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