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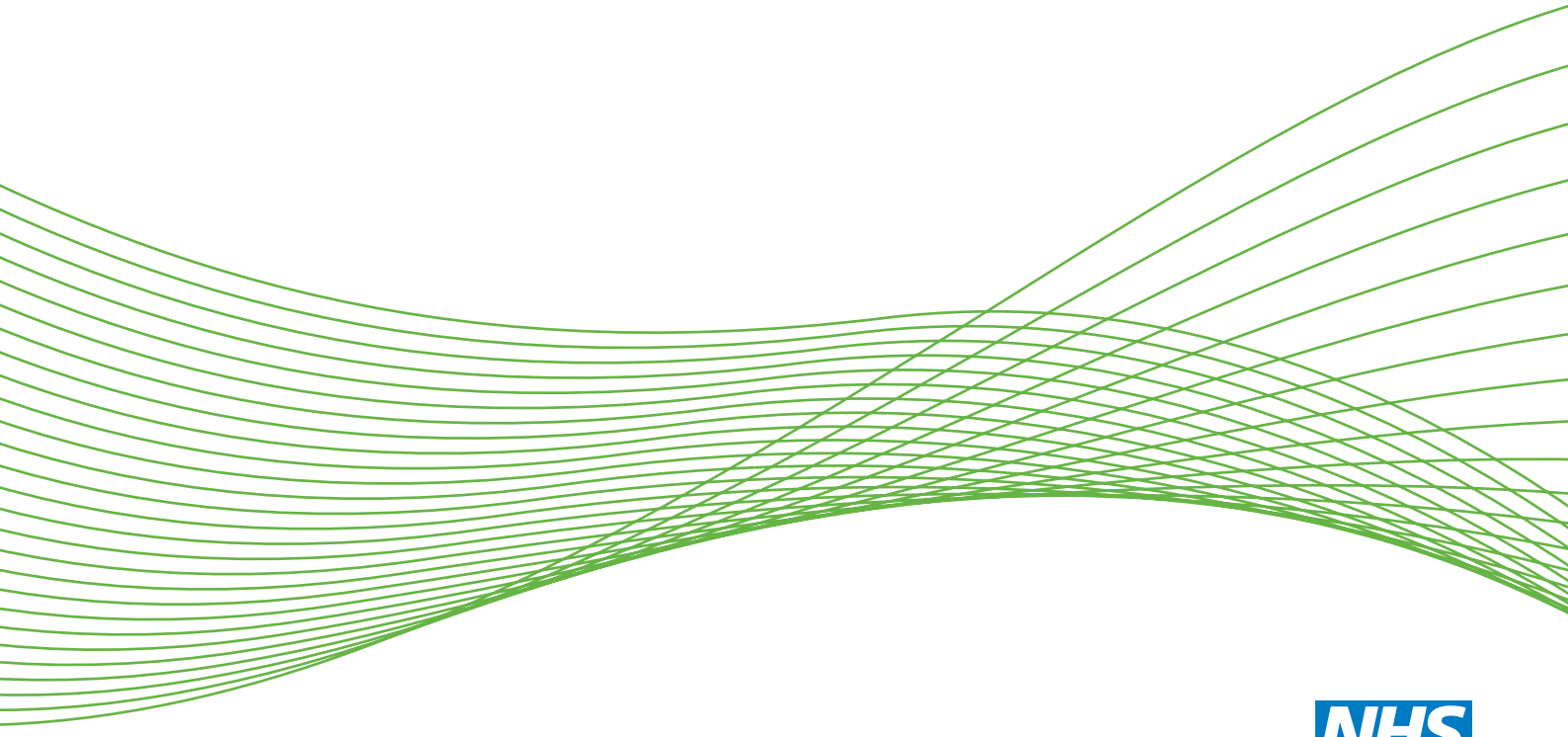

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Abstract

Calculating when elective abdominal aortic aneurysm repair improves survival for individual patients: development of the Aneurysm Repair Decision Aid and economic evaluation

Stuart W Grant,[1] Matthew Sperrin,[2] Eric Carlson,[1] Natasha Chinai,[1] Dionysios Ntais,[2] Matthew Hamilton,[2] Graham Dunn,[2] Iain Buchan,[2] Linda Davies[2] and Charles N McCollum[1]*

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Background: Abdominal aortic aneurysm (AAA) repair aims to prevent premature death from AAA rupture. Elective repair is currently recommended when AAA diameter reaches 5.5 cm (men) and 5.0 cm (women). Applying population-based indications may not be appropriate for individual patient decisions, as the optimal indication is likely to differ between patients based on age and comorbidities.

Objective: To develop an Aneurysm Repair Decision Aid (ARDA) to indicate when elective AAA repair optimises survival for individual patients and to assess the cost-effectiveness and associated uncertainty of elective repair at the aneurysm diameter recommended by the ARDA compared with current practice.

Data sources: The UK Vascular Governance North West and National Vascular Database provided individual patient data to develop predictive models for perioperative mortality and survival. Data from published literature were used to model AAA growth and risk of rupture. The cost-effectiveness analysis used data from published literature and from local and national databases.

Methods: A combination of systematic review methods and clinical registries were used to provide data to populate models and inform the structure of the ARDA. Discrete event simulation (DES) was used to model the patient journey from diagnosis to death and synthesised data were used to estimate patient outcomes and costs for elective repair at alternative aneurysm diameters. Eight patient clinical scenarios (vignettes) were used as exemplars. The DES structure was validated by clinical and statistical experts. The economic evaluation estimated costs, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs) from the NHS, social care provider and patient perspective over a lifetime horizon. Cost-effectiveness acceptability analyses and probabilistic sensitivity analyses explored uncertainty in the data and the value for money of ARDA-based decisions. The ARDA outcome measures include perioperative mortality risk, annual risk of rupture, 1-, 5- and 10-year survival, postoperative long-term survival, median life expectancy and predicted time to current threshold for aneurysm repair. The primary economic measure was the ICER using the QALY as the measure of health benefit.

Results: The analysis demonstrated it is feasible to build and run a complex clinical decision aid using DES. The model results support current guidelines for most vignettes but suggest that earlier repair may be effective in younger, fitter patients and ongoing surveillance may be effective in elderly patients with comorbidities. The model adds information to support decisions for patients with aneurysms outside current indications. The economic evaluation suggests that using the ARDA compared with current guidelines could be cost-effective but there is a high level of uncertainty.

Limitations: Lack of high-quality long-term data to populate all sections of the model meant that there is high uncertainty about the long-term clinical and economic consequences of repair. Modelling assumptions were necessary and the developed survival models require external validation.

Conclusions: The ARDA provides detailed information on the potential consequences of AAA repair or a decision not to repair that may be helpful to vascular surgeons and their patients in reaching informed decisions. Further research is required to reduce uncertainty about key data, including reintervention following AAA repair, and assess the acceptability and feasibility of the ARDA for use in routine clinical practice.

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List of abbreviations

AAA	abdominal aortic aneurysm
ADAM	aneurysm detection and management
AIC	Akaike information criterion
ARDA	Aneurysm Repair Decision Aid
ASA	American Society of Anesthesiologists
AUC	area under the curve
BAR	British Aneurysm Repair
BMI	body mass index
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
DES	discrete event simulation
ECG	electrocardiogram
EED	Economic Evaluations Database
EQ-5D	European Quality of Life-5 Dimensions
EVAR	endovascular aneurysm repair
GAS	Glasgow Aneurysm Score
HR	hazard ratio
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
IPD	individual patient data
LOS	length of stay
LY	life-year
LYG	life-year gained
MI	myocardial infarction
NAAASP	National AAA Screening Programme
NB	net benefit
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NVD	National Vascular Database
NVR	National Vascular Registry
O : E	observed to expected
OPCS	Office of Population Censuses and Surveys
PPI	patient and public involvement
QALY	quality-adjusted life-year
RCT	randomised controlled trial
ROC	receiver operating characteristic
SD	standard deviation
UKSAT	UK Small Aneurysm Trial
VBHOM	Vascular Biochemistry and Haematology Outcome Model
VGNW	Vascular Governance North West
V-POSSUM	Vascular Physiological and Operative Severity Score for enUmeration of Mortality
WCC	white cell count
WTPT	willingness-to-pay threshold

Plain English summary

Abdominal aortic aneurysm (AAA) is a ballooning of the main artery supplying the body; large AAAs may grow until they burst (rupture), at which point 80% of patients die. Currently, repair by major surgery or by inserting a stent–graft is considered if the AAA causes pain or reaches 5.5 cm in diameter for men and 5.0 cm for women. As with all surgery, there are risks associated with repair. These risks must be weighed against the risk of AAA rupture when considering whether or not to treat patients with AAA.

We gathered the best information available on factors that influence the rate of AAA growth, the risk of rupture, the risk of repair and the long-term outcomes of patients who have had a repair. This information was combined using a custom-designed computer program called the Aneurysm Repair Decision Aid (ARDA). The ARDA aims to provide information to help patients and surgeons decide on the best treatment strategy for the AAA. The main information ARDA provides is the expected AAA growth rate and risk of rupture, the chance a patient will need AAA repair, the chance a patient will survive AAA repair and the chance a patient will survive for 5 and 10 years following AAA repair.

We assessed both the clinical and economic impacts of using the ARDA in clinical practice and found that it provides valuable information that could improve decision-making for patients and clinicians.

Scientific summary

Background

Abdominal aortic aneurysm (AAA) is found in 5–8% of men > 65 years. Rupture is responsible for around 7000 deaths per year in the UK. Each year approximately 4000 patients undergo AAA repair in the UK with the aim of preventing premature death due to AAA rupture. Most patients undergoing elective AAA repair are asymptomatic and, as a consequence of the recently implemented NHS AAA Screening Programme, an increasing number are likely to be detected.

The current indication for elective repair is when the aneurysm reaches 5.5 cm in men and 5.0 cm in women. This indication is based on data from randomised controlled trials demonstrating that AAA surveillance is a safe alternative to early repair in patients with AAA in the size range 4.0–5.4 cm. These conclusions were drawn from a population of all patients aged 60–76 years with AAAs over a wide size range, but they do not necessarily apply to individual patients. For example, the indication for elective AAA repair is unlikely to be the same for a fit and healthy patient aged 65 years and an unfit and immobile patient with comorbidities aged 80 years.

Objective

The objective was to develop an Aneurysm Repair Decision Aid (ARDA) to synthesise and simulate several complex processes and decisions in the management of AAA. This is the first stage in demonstrating that it is feasible to construct and run such a complex model to support surgeon and patient decision-making. The aim of the ARDA is to identify the optimal timing of surgery for each individual patient, to maximise survival and facilitate cost-effective use of resources and optimal clinical care.

Methods

This study combines evidence synthesis with original research. A number of separate algorithms were developed to calculate aneurysm growth rate and risk of rupture, risk of perioperative mortality, and life expectancy and survival. These separate algorithms were then combined into the overall ARDA algorithm to provide patients and surgeons with information that may be helpful in making a decision on the optimal time for AAA repair.

Information on risk factors that influence AAA growth and risk of rupture was developed within the National Institute for Health Research Health Technology Assessment-funded RESCAN project. The RESCAN team obtained individual patient data on 15,475 patients under surveillance for AAAs < 5.5 cm in 18 published studies. Although the number of patients with AAAs that rupture in this size range is small, RESCAN is also the best source of information on which to estimate risk of rupture. A random-effects model was used to assess between-patient variability in AAA size and growth rate. Rupture rates were analysed using joint proportional hazards regression to incorporate predicted AAA diameter as a covariate that changed with time. Predictions for AAAs with diameter > 5.5 cm were extrapolated from pooled data across all studies using random-effects meta-analysis. Rupture risk was calculated by Cox proportional hazards regression adjusted for AAA diameter. For AAA diameters outside the range included in the RESCAN project, information on AAA growth and risk of rupture was taken from previously published studies.

Risk of perioperative mortality

Vascular Governance North West (VGNW) data were used to calculate, for each individual patient, the risk of 30-day mortality following endovascular aneurysm repair (EVAR) and elective open surgical repair using a multiple logistic regression model, incorporating patient-specific risk factors. To assess the performance of this model it was validated along with a number of other published models for perioperative mortality (the Glasgow Aneurysm Score, the Vascular Biochemical and Haematological Outcome Model, the Vascular Physiological and Operative Severity Score for enUmeration of Mortality and the Medicare model) in the National Vascular Database (NVD). Subsequently, the NVD was used to develop the British Aneurysm Repair (BAR) score to predict in-hospital mortality following elective AAA repair. Prospectively collected data on all elective AAA repairs were extracted for analysis and a multiple regression model was fitted using the backwards elimination Akaike information criterion. The performance of the BAR score in separate EVAR and open AAA repair subgroups was assessed and both models were validated using contemporary VGNW data. The area under the receiver operating characteristic curve and various measures of calibration were used to assess model performance.

Life expectancy and survival

Prospectively collected data on 4070 elective AAA repairs from VGNW were used to analyse risk factors for long-term survival. Survival data were analysed using the Kaplan–Meier method and differences in survival were compared using the log-rank test. Multivariate Cox proportional hazards models were used to identify significant preoperative prognostic indicators of long-term survival. Although our VGNW data were derived entirely from patients surviving AAA repair, the same model was used to calculate underlying survival in patients who had not yet undergone repair; this survival was subsequently influenced by risk of rupture and perioperative mortality due to elective or emergency repair as appropriate.

Developing the Aneurysm Repair Decision Aid

A discrete event simulation (DES) model was developed to simulate the subsequent life events for each individual patient, starting from age and AAA diameter at initial diagnosis. This approach was selected because it allows the incorporation of all of the above algorithms predicting different aspects of the AAA pathway while also displaying the confidence with which the patient and clinician can interpret any output. The expected growth rate, risk of rupture, risk of dying from other causes, expected time to repair at any given AAA diameter and risk of perioperative mortality and subsequent survival are then simulated 100,000 times for each patient and the median survival and mean costs and quality-adjusted life-years (QALYs) an individual patient could expect are estimated.

Economic evaluation

Use was made of the ARDA to simulate the likely costs, QALYs and cost-effectiveness of the decision to repair and to explore the underlying uncertainty associated with the economic data. The comparator was the current guideline to repair when the aneurysm reaches 5.0 cm (women) or 5.5 cm (men) in diameter. The perspective taken was that of the NHS, social care providers and patients. This viewpoint comprises the key components of a societal perspective. The measure of health benefit for the primary analysis was the QALY. The time horizon for the model is lifetime from identification of the AAA to death from any cause. The lifetime impact was discounted at 3.5%.

The population for the model is people with a confirmed AAA smaller than current thresholds for surgery or people who present with an AAA at or above the current thresholds for surgery. As with the clinical effectiveness analysis, this population is characterised by eight vignettes that describe patients eligible for elective surgical repair.

The DES model developed for the clinical effectiveness analysis was used as the basis for the analysis of the relative cost-effectiveness of the new algorithm. The overall model structure and processes were not changed. The cost and utility values associated with events in the model were added to estimate net costs and QALYs for each of the eight patient vignettes.

Cost and utility data for the economic model were identified from a focused systematic review, review of the NHS reference costs data set and a prospective study of patient records held in the VGNW programme. A focused electronic search was conducted in October 2012 (updated April 2014) to identify studies published between January 2004 and April 2014. This was supplemented by a search of published UK data sets and National Institute for Health and Care Excellence technology appraisals. Titles and abstracts were reviewed by two researchers using predefined inclusion and exclusion criteria and data extraction forms. Descriptive statistics were used to summarise the data to populate the model.

Clinical and service use data for a sample of patients ($n = 118$) included in the VGNW database were reviewed between January 2009 and April 2012 to gather and cost service use information about preoperative, perioperative, and postoperative appointments, scans, and procedures clinically associated with the AAA repair. Descriptive statistics summarised cost data to supplement the systematic review.

For the primary analysis, the model estimated the incremental cost-effectiveness ratio associated with intervening at the aneurysm size identified by the ARDA as maximising QALYs gained. Sensitivity analyses explored data uncertainty and the impact of key assumptions and design choices. A probabilistic sensitivity analysis was conducted for the primary analysis and each of the sensitivity analyses. A cost-effectiveness acceptability analysis estimated the probability that an algorithm to maximise QALYs gained was cost-effective compared with the current guidelines.

Results

Predicting perioperative mortality

The VGNW model included the following risk factors: age, female sex, diabetes, raised serum creatinine level, respiratory disease, antiplatelet medication and open surgery. The area under the curve (AUC) was 0.70 on validation with acceptable calibration. On external validation using the NVD, the VGNW model demonstrated good discrimination with an AUC of 0.71 and acceptable calibration. The BAR model developed on the NVD included the following risk factors: open repair, age, female sex, serum creatinine over 120 µmol/l, cardiac disease, abnormal electrocardiogram (ECG), previous aortic surgery or stent, abnormal white cell count, abnormal serum sodium, AAA diameter and American Society of Anesthesiologists grade. The AUC (bias-corrected) was 0.77 with good calibration. On external validation using VGNW data, the BAR score demonstrated overall excellent discrimination (AUC 0.83) with retained discriminatory ability in procedural subgroups and good calibration.

Survival following abdominal aortic aneurysm repair

Median survival was 8.1 years, with 5- and 10-year survival rates of 70.2% and 41% respectively. The model developed for survival following elective AAA repair using VGNW data included the following risk factors for reduced survival: age, female sex, ischaemic heart disease, abnormal serum sodium, serum creatinine > 120 µmol/l, anaemia and abnormal ECG. Statin and platelet-inhibitory therapy were associated with improved survival.

The Aneurysm Repair Decision Aid

Discrete event simulation achieved reproducible and reliable data that included the following summary information that would be useful to patients and vascular surgeons making a decision on whether or not to repair an asymptomatic AAA of any given size: life expectancy; 1-, 5- and 10-year survival; the risk of dying of rupture; perioperative mortality in the event of EVAR or open surgical repair; the probability that a repair would be undertaken in the patient's lifetime; using current indications (AAA 5.0 cm in women and 5.5 cm in men).

In addition, the ARDA produces the following information based on risks associated with repair at some future date: the risk of dying from other causes; the chances of surviving rupture; predicted AAA growth

rate at the relevant size; risk of rupture over the next 1 year; 1-, 5- and 10-year postoperative survivals; median age for the AAA to reach any given threshold; time to reach any given threshold.

Overall, the economic model indicates high uncertainty in the mean expected costs or QALYs between the new clinical algorithm and current thresholds for surgery. The net costs of the algorithm ranged between a saving of £405 [95% confidence interval (CI) –£17,655 to £13,576] and a net cost of £2716 (95% CI –£13,650 to £22,552). All the vignettes and aneurysm sizes were associated with a net QALY gain, which ranged between 0.006 (95% CI –7.516 to 7.510) and 0.047 (95% CI –8.962 to 9.055). The net costs and QALYs were characterised by wide 95% CIs, which crossed zero. The probability that the new algorithm was cost-effective was around 50% for all of the primary analyses, with a net benefit that ranged between –£1831 (95% CI –£150,921 to £144,164) and £2338 (95% CI –£5110 to £12,425) for vignettes. Again the 95% CIs are wide and cross zero. The sensitivity analysis to explore the impact of using life-years gained, alternative cost and utility estimates did not change this result. Overall, uncertainty in the data inputs indicate that further work is needed to assess whether or not decisions based on the ARDA are likely to be cost-effective.

Conclusion

The ARDA produces detailed information that may be useful to individual patients and their surgeons when considering whether or not to repair an asymptomatic AAA at each surveillance interval after their AAA reaches 4.0 cm in diameter. As the ARDA calculates cost and QALY data, the cost-effectiveness and underlying uncertainty of each potential decision can also be calculated.

As far as the authors are aware this is the first time that DES methodology has been applied in an attempt to facilitate clinical decision-making. The work reported here demonstrates that the ARDA has the potential to be adopted into clinical practice, although additional research and development is required before it can be recommended for routine use in the clinic. It is also important to note that the ARDA is not designed to be used to predict when repair should be undertaken in the future; rather, it should be rerun at each surveillance stage to calculate the consequences of advancing age, observed AAA growth and new comorbidities.

The evidence and results of the clinical effectiveness analysis of the DES model suggest that patient-related preoperative factors should certainly be considered when making clinical decisions regarding elective AAA repair. The overall results of the economic evaluation indicate a high level of uncertainty about whether or not the repair decision with and without the ARDA is cost-effective. This is because of data limitations and a range of modelling assumptions.

The ARDA can be utilised as a decision support tool for patients and clinicians. The information provided can facilitate the patient and clinician in making joint and informed decisions on the timing and appropriateness of intervention. The acceptability of the DES algorithm approach to clinicians and patients needs to be formally tested, as does the feasibility of incorporating it into routine practice. Further research is required to address uncertainty about key parameters and validate the model in other settings. It is vital, going forward, that robust information on the risk of reintervention or complications following both open repair and EVAR be incorporated into the algorithm, as this has important quality-of-life and cost implications.

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The National Institute for Health Research Health Technology Assessment programme.

Chapter 1 Background

Abdominal aortic aneurysm

An aneurysm is defined as a dilatation of a blood vessel by more than 50% of its original diameter. Although aneurysms can affect any blood vessel, the abdominal aorta is most commonly affected. The normal diameter of the abdominal aorta is not usually greater than 2 cm; therefore, an abdominal aortic aneurysm (AAA) is defined as a dilatation of the abdominal aorta to a diameter of greater than 3 cm.

Abdominal aortic aneurysms can be grouped into:

i. those that develop as a result of connective tissue disorders
ii. infective or inflammatory AAAs
iii. late-onset AAAs.

Late-onset AAAs are by far the most common, affecting 5–8% of men over the age of 65 years.[1–4] The prevalence of AAA has been shown to be influenced by increasing age,[2,5,6] male sex,[2,5,7] a history of smoking[8,9] and a family history of AAA.[5,10]

Abdominal aortic aneurysm growth and rupture

Once an AAA develops, the initial dilatation of the aorta leads to an increase in tension of the vessel wall and further growth (law of Laplace).[11] AAA growth rates increase as the AAA gets larger.[12–14] Growth rates have also been shown to be higher in smokers[15–18] and lower in patients taking beta blockers,[19] angiotensin-converting enzyme inhibitors or statins[20,21] and lower in patients with diabetes.[16,18,22,23]

Most AAAs continue to grow until the aneurysm ruptures or is repaired or the patient dies of other causes. Rupture with significant haemorrhage is the most common and devastating complication of AAA. Most patients who suffer AAA rupture die immediately and, even in those who reach hospital and are able to undergo emergency surgery, the operative mortality approaches 50%.[24] AAA rupture causes roughly 7000 deaths/year in the UK, approximately 2.5% of all deaths in men over the age of 65 years.[1] The most significant risk factor for AAA growth and rupture is maximum aneurysm diameter.[25,26]

Detection of abdominal aortic aneurysm

As AAA rupture has such a poor outcome, it is important to identify and repair AAA early. Most patients with AAA experience no symptoms and in the past were identified incidentally on abdominal imaging by ultrasound or computed tomography for other reasons. Ultrasound is non-invasive, pain free and entirely reliable in the detection of AAA.[27] It has been extensively studied as a method of population screening for early detection of AAA. There have been four large randomised controlled trials (RCTs) evaluating screening for AAA;[1–4] a review of these trials concluded that screening was associated with significant reductions in AAA-related mortality in men and a decreased incidence of ruptured aneurysm.[28] The National AAA Screening Programme (NAAASP) was introduced throughout the UK during 2010–13.

Repair of abdominal aortic aneurysm

The primary aim in the management of AAA is to prevent premature death due to AAA rupture. Currently, approximately 4000 elective AAA repairs are performed each year in the UK,[29] a number that is thought to be rising.[30] In patients with symptoms attributable to their AAA, repair should be performed urgently, as these symptoms may represent impending rupture. However, the vast majority of patients are asymptomatic and the clinical decisions are (1) when should the AAA repair be performed? and (2) what method should be used to repair the AAA?

Open or endovascular repair

Open AAA repair is major surgery involving laparotomy, displacing the abdominal viscera, cross-clamping the aorta for at least 40–60 minutes and replacing the aneurysmal aorta with a synthetic graft. Laparoscopic AAA repair is similar in principle to open AAA repair but performed using laparoscopy rather than a laparotomy; it has not been widely adopted because of the difficulty and frequency of complications.[31] Although there are inevitable variations,[32] the mortality following open elective AAA repair is generally accepted as being approximately 5% with some evidence that the 30-day mortality rate is falling.[33,34] In addition to this mortality risk, there is a significant risk of major medical morbidity and laparotomy-related complications.[35]

Endovascular aneurysm repair (EVAR) is performed by catheterising the common femoral arteries on both sides and deploying a stent–graft across the aneurysmal segment of the aorta. The stent–graft then expands, engaging the aortic wall with the blood flow confined within the graft rather than throughout the aneurysmal segment of the aorta. The advantage of EVAR over open AAA repair is that it is considerably less invasive and associated with a lower initial mortality rate and morbidity rates.[35–37] The main disadvantage of EVAR is that the repair is less stable with a substantially higher rate of late AAA-related complications including endoleak, graft displacement, stent fracture and even AAA rupture.[35,38]

There have been a number of comparative studies between open AAA repair and EVAR. The randomised EVAR 1 trial demonstrated that perioperative mortalities were lower in patients who underwent EVAR[39] but found no difference in mid-term or long-term all-cause mortality.[38] EVAR was, however, associated with a more frequent need for AAA-related reinterventions and late AAA ruptures. An additional RCT reported similar perioperative mortality rates to the EVAR 1 trial[35] but again demonstrated no difference in cumulative survival between open surgery and EVAR beyond 2 years.[40] Similar findings have also been reported in a large propensity-matched registry study.[41] There is, therefore, strong evidence that procedure-related mortality may be lower in patients who undergo EVAR, but overall survival is similar from 2 years onwards.

The current indication to repair abdominal aortic aneurysm

The decision on when to perform AAA repair is a balance between the risks of repair and the risk of death due to rupture. It has generally being accepted for many years that patients with large AAAs (> 5.5 cm in men and > 5.0 cm in women) or those with back ache, abdominal loin or groin pain that might be attributed to the AAAs should undergo early or urgent repair.

The current indication for surgery for small asymptomatic AAAs (between 4.0 and 5.5 cm in diameter) is based on two RCTs, the UK Small Aneurysm Trial (UKSAT) and the Aneurysm Detection and Management (ADAM) trial.[42,43] Both trials randomised patients with AAAs between 4.0 and 5.5 cm in diameter to either early AAA repair or ultrasound surveillance with AAA repair when indicated.

Although mortality was initially higher in the immediate repair group, there was no significant difference in mortality between the two groups at 2, 4, 6 and 12 years following randomisation in the UKSAT.[44] In the ADAM trial, the results were similar but follow-up was for a mean of only 4.9 years.[43] A pooled analysis of the two trials confirmed no benefit for early surgery over ultrasound surveillance in AAAs between 4.0 and 5.5 cm.[45] As a result, the established indication was to offer repair of asymptomatic AAAs when the AAA diameter reached 5.5 cm in men. As there is good evidence that women have a greater risk of rupture for a given size of AAA than men,[18] it has become normal practice to repair AAAs in women when diameter reaches 5.0 cm. It is possible that this is a consequence of the generally greater ratio of AAA diameter to normal size in women, as women have smaller aortas.

Can a population-based indication be applied to individuals?

Although the current indication for elective AAA repair is based on well-conducted randomised trials, we question whether or not these population-based findings are applicable to individual patients with AAAs. In the UKSAT, all patients aged 60–76 years were included with the ADAM trial including patients aged 50–79 years. These trials were not designed to determine whether or not the indication for younger patients might be different for that in older patients. Furthermore, although these trials convincingly demonstrate that, within this age, there is no benefit in early surgery for aneurysms in the size range 4.0–5.5 cm, an alternative interpretation of this data is that the true indication for AAA repair in the individual patient might be anywhere within this size range. The timing of repair for a 5.0 cm or 5.5 cm AAA to optimise survival may not be the same for a 60-year-old healthy man and an 80-year-old man with multiple comorbidities. The trials focused on aneurysm size, whereas other factors, such as age, fitness and presence of other comorbidities influence perioperative mortality and long-term survival. There is evidence to support this argument from the subgroup analysis of the UKSAT, as shown in *Table 1*.

This subgroup analysis shows that the number of deaths per 100 person-years following early surgery was highest in the elderly and much lower in those aged 60–66 years. Although this measure of mortality increases with age at surveillance, these findings suggest that across the size range 4.0–5.5 cm there is a mean advantage to patients aged 60–66 years from undergoing early surgery but a disadvantage in patients aged 72–76 years. This is entirely what would be expected and completely compatible with the final conclusion of this study based on all patients aged 60–76 years.

TABLE 1 Subgroup analyses of deaths per 100 person-years from UKSAT[42]

Factor	Surveillance	Early surgery	Hazard ratio[a]	*p*-value[b]
Age (years)				
60–66	5.8	4.7	0.76	0.10
67–71	8.9	6.8	0.80	
72–76	7.6	9.5	1.25	
AAA diameter (cm)				
4.0–4.4	6.5	7.4	1.14	0.26
4.5–4.8	6.8	6.3	0.88	
4.9 –5.5	9.5	7.4	0.79	

a For early-surgery group relative to surveillance group.
b Test of interaction.

Similar results are reported with respect to AAA diameter. For smaller AAAs in the size range 4.0–4.4 cm, the risk of mortality is clearly lower with surveillance than it is with early surgery. However, for larger aneurysms in the size range 4.9–5.5 cm there is a lower risk of death in those patients randomised to early surgery, even though this population included patients aged over 72 years. An alternative conclusion from this study is clearly that in patients aged 60–76 years the optimal indication for AAA repair is somewhere between 4.5 and 4.8 cm and that this indication to repair changes with advancing age.

The current indications for AAA repair based on AAA diameter alone also ignore the following important variables which may influence survival: (1) the patient's life expectancy, (2) factors that influence AAA growth and risk of rupture, (3) factors that influence perioperative mortality and (4) factors that influence long-term survival following elective AAA repair.

Overall aim of the project

This project was designed to gather evidence and explore the potential for the Aneurysm Repair Decision Aid (ARDA) to formalise and improve the current clinical decision processes by calculating the timing of elective AAA repair to optimise survival in individual patients with AAA. The aim of the economic analysis was to explore whether or not adopting the ARDA in place of the existing indications for elective AAA repair would be cost-effective. Although this work is focused on the UK and has implications for the NHS and the NAAASP, this work could be adapted using data from other regions to be similarly relevant to the management of patients with AAA worldwide.

Chapter 2 Research objectives

Aims and objectives

The overall objective was to develop an algorithm (ARDA) to calculate the optimum timing of elective AAA repair to maximise survival in individual patients with AAA.

To develop this algorithm we have undertaken the following steps:

1. development and validation of models to predict the risk of perioperative mortality in elective AAA repair
2. development of a model that predicts long-term survival following elective AAA repair
3. development of an algorithm that calculates the expected AAA growth rate and risk of rupture for each individual patient based on RESCAN data[18]
4. comparison of the clinical effectiveness and cost-effectiveness of decisions based on the ARDA with the current indications for elective AAA repair.

Structure of the report

The data sources used for this research are presented in *Chapter 3*. Patient and public involvement (PPI) in the research is discussed in *Chapter 4*. *Chapter 5* describes the development and validation of models for the prediction of perioperative mortality. *Chapter 6* describes the development of a survival model for elective AAA repair. *Chapter 7* describes the development of the discrete event simulation (DES) model used in the ARDA and provides example patient clinical scenarios (vignettes), which illustrate the information provided by the ARDA. *Chapter 8* describes the methods used to assess the cost-effectiveness of decisions based on the ARDA, with the results of this analysis presented in *Chapter 9*. *Chapter 10* provides a discussion of the strengths and limitations of all of the component studies. Conclusions and research priorities are reported in *Chapter 11*. A list of published papers arising from this work is provided in *Acknowledgements*.

Chapter 3 Data sources

Background

The statistical models and algorithms developed in this project rely on good-quality data. The individual patient data (IPD) used in the development process were made available by the Vascular Governance North West (VGNW) database and the National Vascular Database (NVD). Where appropriate, previously published information was gathered from peer-reviewed papers. The IPD utilised for this project are summarised in *Figure 1*.

The Vascular Governance North West programme

The VGNW database was established as a registry of all vascular procedures in the North West region. The need to implement the quality agenda in specialist surgery was clearly identified following the Bristol inquiry.[46] In April 1999, vascular surgeons in the North West (50 surgeons in 24 units) set up a peer-led clinical governance initiative. Prospective data collection began in February 2000, with surgeons also able to submit retrospective records. The main function of the project was to collect and analyse procedure-specific surgical data. These include open AAA repair (from 1999) and EVAR (from 2006). Fifty-six consultants from the North West region currently participate in this regional audit programme. A full list of all surgeons who have contributed to the VGNW database is given in *Appendix 1*.

At present, data are collected at each hospital: on paper forms, on Microsoft Excel 2010 spreadsheets (version 14.0.6129.5000, Microsoft Corporation, Redmond, WA, USA), or using the web-based data entry tool of the NVD, which has recently evolved into the National Vascular Registry (NVR). Data are transferred to the VGNW audit office at the University Hospital of South Manchester, where it is anonymised and stored in a secure Microsoft Access 2010 database (version 14.0.6129.5000, Microsoft Corporation, Redmond, WA, USA). All the data received directly are submitted to the NVR, with VGNW member surgeons providing nearly 30% of the NVD/NVR data. This VGNW project has also supplied carotid data to the nationwide UK carotid endarterectomy audit and the Greater Manchester Abdominal Aortic Aneurysm Quality Improvement Programme (AAA QIP).

Vascular Governance North West data quality is checked annually by local members of each clinical team to confirm the accuracy and completeness of the data held. Each surgeon is given a summary report of his or her cases and outcomes for cross-checking. Inconsistencies are followed up and resolved by the local VGNW team. Owing to the number of data, 100% checks of individual patient characteristics are not feasible, meaning that inaccuracies in patient risk factor data may be present.

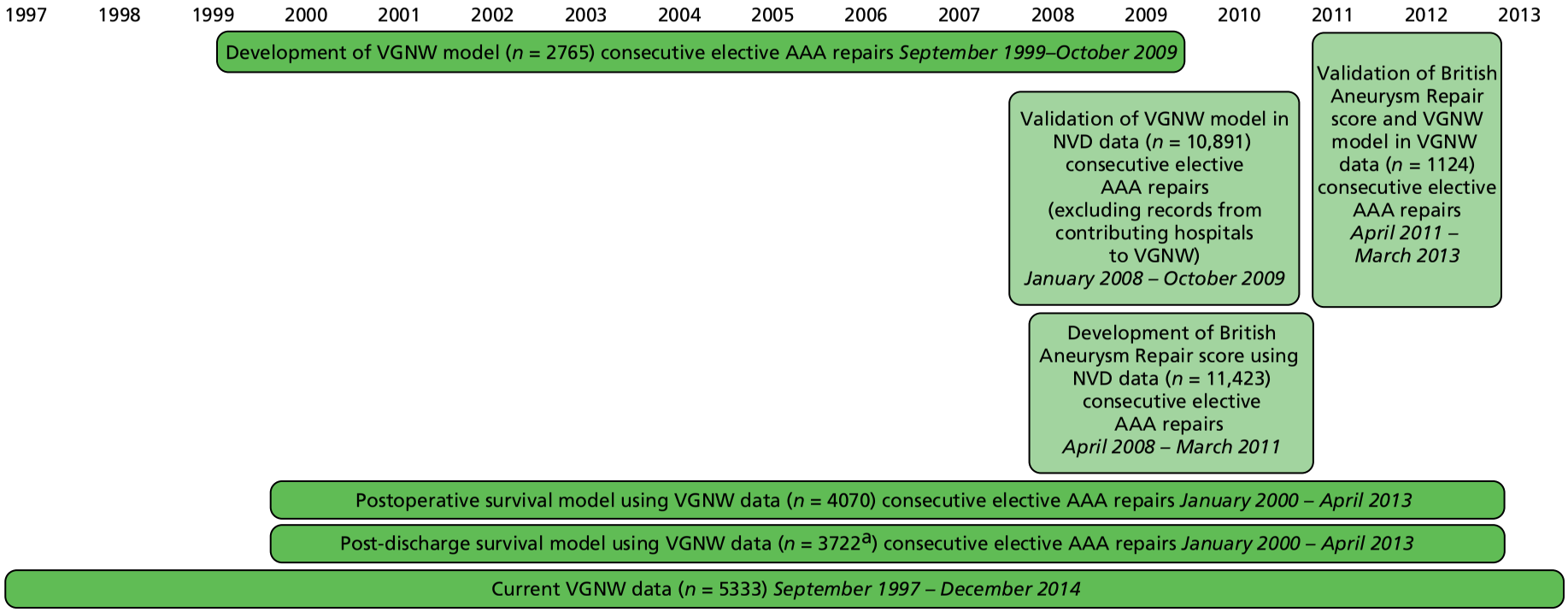


FIGURE 1 Individual patient data used in this project. a, Reduced number of records available because of in-hospital mortality and missing date of discharge information.

The VGNW programme has been granted ethical approval to provide data sets for research purposes. The steering committee of the VGNW approved use of the data for this National Institute for Health Research (NIHR) Health Technology Assessment (HTA) project. These data have been used in the development of models to predict perioperative mortality (see *Chapter 5*) and survival models (see *Chapter 6*). The data fields collected by the VGNW programme for patients undergoing AAA repair are shown in *Appendix 2, Table 43*. At the start of the project, VGNW had preoperative data on over 3600 patients undergoing AAA repair (with 240 who died postoperatively in hospital). Data completeness was variable across all sites, as shown in *Figure 2*.

Owing to the number of hospitals involved and the quality of the data required for the modelling work, the VGNW team sought support from the comprehensive local research network to improve AAA data quality. The comprehensive local research network teams, assisting the local surgical and audit teams, were instrumental in the completion of over 5000 missing data points and of an additional 1700 new patient records. There are now 5333 elective AAA operations recorded in the VGNW database. The number of missing points of data has fallen from 30% to 10%, with improvements in data completeness achieved at all contributing centres. Current data completeness compared with the start of the project is illustrated in *Figure 2*.

Patient mortality status and date of death were also necessary to perform survival analysis. Our PPI group advised against contacting patients directly to gather this information. This decision was taken to avoid upsetting bereaved family members, particularly as the average age at operation of a VGNW patient is 76 years. Survival data were originally for patients who died within 30 days of the operation. To gather long-term follow-up data, an ethical amendment to the VGNW protocol was submitted to the North West regional ethics committee. Section 251 approval was gained from the National Information Governance Board to merge mortality information from the demographic batch service with the VGNW clinical database. This was done using patient NHS numbers and allowed the long-term follow-up mortality status of over 4000 patients to be determined.

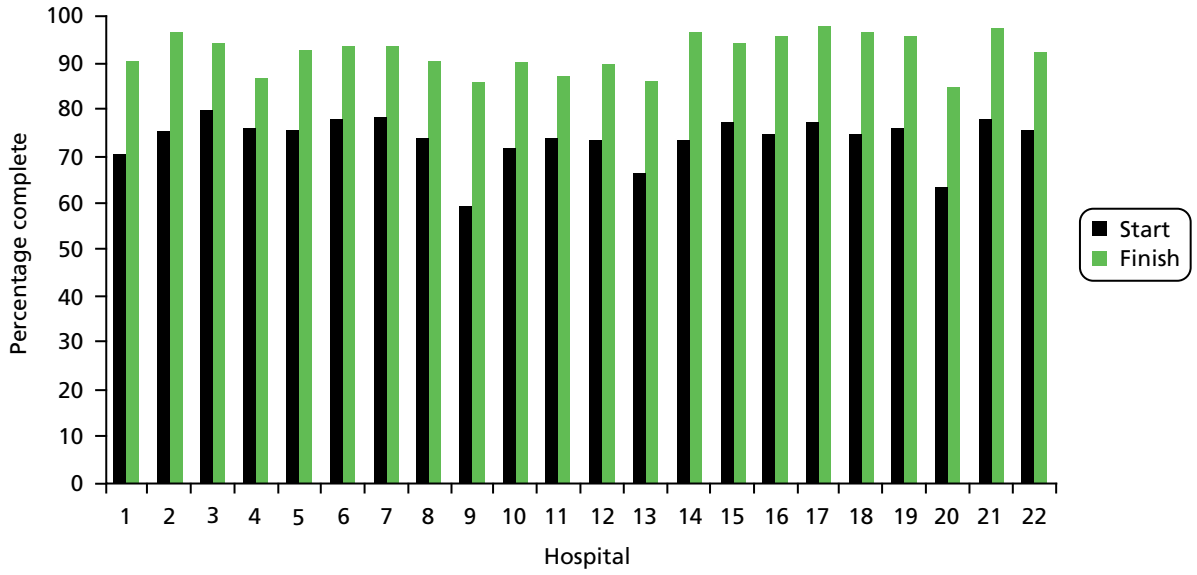


FIGURE 2 Vascular Governance North West data completeness levels at the beginning (2011) and end (2014) of the project by hospital.

The National Vascular Database

The NVD was established in 1997 by the Vascular Society of Great Britain and Ireland, which has a long history of promoting scientific research and clinical excellence in vascular surgery. The NVD was managed by a project co-ordinator, who assisted surgeons, nurses and administrators who input data to the NVD. Contributing surgeons could view activity and outcome reports online to allow local performance to be mapped against national activity in real time. Submission to the NVD was voluntary. Governance of the NVD was the responsibility of the Vascular Society of Great Britain and Ireland. Data were collected on three index procedures: AAA repair, infra-inguinal bypass and amputations. Data collected included patient demographics, comorbidity data, preoperative investigations, intraoperative details and postoperative outcomes. The NVD had a defined minimum data set, and case submission was regularly validated against Hospital Episode Statistics data. No formal validation of clinical data was carried out. For this programme of research; only data on elective AAA repairs were analysed. These data were used in the development of models for perioperative mortality (see *Chapter 5*). The data fields collected by the NVD for AAA surgery along with the minimum data set required for data submission are shown in *Appendix 2, Table 44*. The NVD has subsequently been replaced by the NVR.

Aneurysm growth and risk of rupture

Information on AAA growth and risk of rupture was taken from the previously published NIHR HTA programme-funded RESCAN project.[18,47] The aim of the RESCAN project was to inform the evidence base for choice of appropriate surveillance intervals for small AAAs. Information on AAA growth and risk of rupture was obtained from an analysis of IPD from existing surveillance programmes. IPD were obtained on 15,475 patients under surveillance for small AAA in 18 studies (*Appendix 3*). The data were harmonised with individual AAA diameters in each study analysed using a random-effects model that allowed for between-patient variability in size and growth rates. Rupture rates were analysed by joint proportional hazards regression to incorporate the modelled AAA diameter as a time-varying covariate. Predictions of the risks of AAA exceeding 5.5 cm in diameter, and of rupture, within given time intervals were estimated and pooled across studies in a second stage using random-effects meta-analysis.

The influence of covariates (including demographics and medical and drug history) on aneurysm growth and rupture rates was investigated in each IPD surveillance data set. Growth rates were analysed using longitudinal random-effects modelling, and rupture rates were analysed by Cox proportional hazards regression with adjustment for aneurysm diameter. The effects of covariates were combined across studies in a second stage using random-effects meta-analysis.

The specific data extracted from the RESCAN project are detailed in *Chapter 7*. For AAA diameters outside that included in the RESCAN project, information on AAA growth and risk of rupture was taken from other previously published studies.[47–50]

Chapter 4 Patient and public involvement

Introduction

The NIHR HTA programme encourages the involvement of service users in research.[51] A PPI group was established to ensure the aims of this research met patient needs, to monitor and direct progress and to review outcomes from the project. This chapter reviews the contributions our PPI group made to the project.

The group and setting

The group was established at the inception of the NIHR HTA project and contributed to the design of this research and to our NIHR-HTA grant application. It included 12 AAA patients and three patient relatives supported by appropriate medical staff including the AAA surveillance nurse. It met quarterly at the University Hospital of South Manchester Education and Research Centre.

The membership consists of a consultant vascular surgeon and anaesthetist, two vascular research fellows, a vascular specialist nurse, a research assistant, five patients who have undergone EVAR, three who have undergone open repair (in one case for a ruptured aneurysm), four patients under surveillance who will possibly need repair in the future and three family members of patients (*Appendix 4*). This group met quarterly during the NIHR-HTA project with one of its cochairmen attending the research project's management committee.

The group was initiated by Professor McCollum using the University Hospital of South Manchester AAA surveillance nurse (Helen O'Donnell), to identify interested patients from local AAA preoperative and follow-up clinics. A member of the research team contacted the patients by letter and then by phone to give background information and arrange the first meeting.

Group impact

The involvement of patients in research has been immensely beneficial to the project from its inception. The main purpose of the group was to harness the unique patient perspective of the NHS AAA care pathway to advise on the form taken and content produced by the risk prediction algorithm. Other contributions were review of patient information leaflets (*Appendix 5*), review of research progress reports given during meetings and feedback on the direction of the project, advice on future research agenda and contributions to the management committee by the attendance of the group's chairman.

Important recommendations that the group made included changing the focus of our risk prediction algorithm to produce 5- and 10-year survival rather than median life expectancy, changing the way that the outputs from the algorithm will be communicated with patients, calculating the chance that an operation will be necessary in one's lifetime, pursuing the possibility of presenting an operation window, developing questionnaires for patients in the surveillance programme, reviewing patient information sheets and advising pursuit of section 251 approval to avoid upset of bereaved relatives when gathering long-term follow-up data. The last recommendation was vital to the survival analysis in our project and an unforeseen necessary ethical application highlighted by the patient group. They have also encouraged further work to incorporate the prediction of complications following repair into the ARDA and to produce quality-of-life information (sexual health and mobility).

Chapter 5 Predicting perioperative mortality following elective abdominal aortic aneurysm repair

Background

The risk of short-term mortality following elective AAA repair is dependent on both patient and operative characteristics. The risk of in-hospital mortality following a surgical procedure is commonly estimated using a risk prediction model. A risk prediction model is a mathematical formula that utilises risk factor information to estimate the probability of a patient developing an outcome. Several risk prediction models have been developed and validated for predicting outcomes following AAA repair. A systematic review published in 2008 found that, out of the available risk predication models, the Glasgow Aneurysm Score (GAS) was the most useful model but none was entirely satisfactory.[52,53]

Objective

The aim of the study was to develop and externally validate a suitable risk prediction model for short-term mortality following elective AAA repair. This is used as an input to the ARDA.

Development of a regional model: methods

Data from the VGNW programme on 2765 consecutive AAA repairs carried out between September 1999 and October 2009 were utilised. These data were selected because at the start of the project the VGNW database represented the most reliable large clinical registry data available for elective AAA repairs in the UK. Although including AAA repairs over a wide time period would introduce inevitable temporal effects, this was necessary to provide an adequate sample size for model development and validation.

All variables missing for more than 15% of subjects were excluded from analyses. Missing dichotomous risk factor data were assumed to represent absence of the risk factor and the sample median was substituted for continuous or categorical variables. This imputation approach was adopted for both the perioperative and survival modelling performed on clinical registry data in this project. Although multiple imputation was considered, an understanding of the data collection process identified that multiple imputation would be inappropriate, as the data were known to be missing not at random. Discussions with surgeons and administrators responsible for inputting data indicated that they were likely to leave a field blank if a risk factor was not present.

Patient characteristics for the regional model development cohort are shown in *Table 2*. The outcome for the model was 30-day mortality, defined as death within 30 days following elective AAA repair regardless of cause. Outcome data for patients who died in hospital within 30 days of AAA repair were collected by the VGNW programme; deaths occurring after discharge but within 30 days of AAA repair were captured using the National Strategic Tracing service.

Standard statistical tests were used to calculate odds ratios and 95% confidence intervals (CIs). The data were split randomly, using a simple random sample method without replacement, into a development data set ($n = 1936$, 70.0%) and a validation data set ($n = 829$, 30.0%). A logistic regression analysis was undertaken on the development data set, using the forward stepwise technique, to develop a risk prediction model for 30-day mortality.[54] Candidate variables with $p < 0.100$ were entered into the model and retained if the p-value achieved was below 0.050.

TABLE 2 Association between preoperative characteristics and 30-day mortality after AAA repair in 1936 patients univariate analysis

Characteristic		Patients, *n* (%)	30-day mortality (%)	Odds ratio (95% CI)	*p*-value
Age (years)	< 75	1313 (67.8)	52 (4.0)	Reference	0.001
	≥ 75	623 (32.2)	46 (7.4)	1.93 (1.28 to 2.91)	
Sex	Male	1593 (82.3)	68 (4.3)	Reference	< 0.001
	Female	343 (17.7)	30 (8.8)	2.16 (1.38 to 3.37)	
Ischaemic heart disease	No	1175 (60.7)	55 (4.7)	Reference	0.336
	Yes	761 (39.3)	43 (5.7)	1.22 (0.81 to 1.84)	
History of myocardial infarction	No	1531 (79.1)	68 (4.4)	Reference	0.015
	Yes	405 (20.9)	30 (7.4)	1.73 (1.11 to 2.69)	
Diabetes	No	1764 (91.1)	83 (4.7)	Reference	0.023
	Yes	172 (8.9)	15 (8.7)	1.92 (1.08 to 3.41)	
Respiratory disease	No	1390 (71.8)	56 (4.0)	Reference	< 0.001
	Yes	546 (28.2)	42 (7.7)	1.99 (1.32 to 3.01)	
Obesity	No	1818 (93.9)	86 (4.7)	Reference	0.009
	Yes	118 (6.1)	12 (10.2)	2.28 (1.21 to 4.29)	
Antiplatelet medication	No	950 (49.1)	29 (3.1)	Reference	< 0.001
	Yes	986 (50.9)	69 (7.0)	2.39 (1.54 to 3.73)	
Antianginal medication	No	1640 (84.7)	74 (4.5)	Reference	0.009
	Yes	296 (15.3)	24 (8.1)	1.86 (1.15 to 2.99)	
Antihypertensive medication	No	1005 (51.9)	33 (3.3)	Reference	< 0.001
	Yes	931 (48.1)	65 (7.0)	2.21 (1.44 to 3.39)	
Statin medication	No	1058 (54.6)	51 (4.8)	Reference	0.602
	Yes	878 (45.4)	47 (5.4)	1.11 (0.74 to 1.67)	
Creatinine (μmol/l)	≤ 120	1557 (80.4)	68 (4.4)	Reference	0.005
	> 120	379 (19.6)	30 (7.9)	1.88 (1.21 to 2.94)	
WCC (× 109/l)	≤ 11	1816 (93.8)	91 (5.0)	Reference	0.674
	> 11	120 (6.2)	7 (5.8)	1.19 (0.54 to 2.62)	
Urea (mmol/l)	≤ 9	1680 (86.8)	78 (4.6)	Reference	0.031
	> 9	256 (13.2)	20 (7.8)	1.74 (1.05 to 2.89)	
Haemoglobin (g/dl)	≤ 13	563 (29.1)	46 (8.2)	Reference	< 0.001
	> 13	1373 (70.9)	52 (3.8)	0.44 (0.29 to 0.67)	
Systolic blood pressure (mmHg)	≤ 140	1334 (68.9)	57 (4.3)	Reference	0.018
	> 140	602 (31.1)	41 (6.8)	1.64 (1.08 to 2.47)	
Abnormal ECG	No	1324 (68.4)	62 (4.7)	Reference	0.258
	Yes	612 (31.6)	36 (5.9)	1.28 (0.84 to 1.95)	
Symptomatic aneurysm	No	1176 (60.7)	49 (4.2)	Reference	0.025
	Yes	760 (39.3)	49 (6.4)	1.59 (1.06 to 2.38)	

TABLE 2 Association between preoperative characteristics and 30-day mortality after AAA repair in 1936 patients univariate analysis (*continued*)

Characteristic		Patients, *n* (%)	30-day mortality (%)	Odds ratio (95% CI)	*p*-value
Maximum aneurysm diameter (cm)	≤ 6	712 (36.8)	38 (5.3)	Reference	0.674
	> 6	1224 (63.2)	60 (4.9)	0.91 (0.60 to 1.39)	
Level of aneurysm	Infrarenal	1752 (90.5)	84 (4.8)	Reference	0.038
	Juxta/suprarenal	184 (9.5)	14 (7.6)	1.88 (1.02 to 3.46)	
Type of surgery	EVAR	366 (18.9)	6 (1.6)	Reference	< 0.001
	Open	1570 (81.1)	92 (5.9)	3.72 (1.62 to 8.57)	

CI, confidence interval; ECG, electrocardiogram; WCC, white cell count.

Model performance in the development data set was evaluated by calculating the area under the receiver operating characteristic (ROC) curve[55] and the Hosmer–Lemeshow goodness-of-fit statistic to assess the discrimination and calibration of the model respectively. An area under the ROC curve statistic of 0.5 suggests no discrimination and an area under the curve (AUC) of 1 indicates perfect discrimination. The relative contribution of each variable to the prediction of 30-day mortality was also calculated. To further assess the model's calibration, the cohort was split into low-risk (bottom half of cohort), medium-risk (third quarter of cohort) and high-risk (fourth quarter) groups, based on their predicted probability of 30-day mortality.

The model performance was then tested on the validation data set. Observed and expected rates of 30-day mortality in the development and the validation data set were compared and the ROC curve and the Hosmer–Lemeshow goodness-of-fit statistic were calculated. All statistical analysis was performed with SAS for Windows® version 8.2 (SAS Institute Inc., Cary, NC, USA) and, for all analyses, $p < 0.050$ was considered significant.

The Vascular Governance North West risk prediction model for mortality following elective abdominal aortic aneurysm repair: results

Of the 1936 patients undergoing elective AAA repair in the development data set, 98 (5.1%) died within 30 days. EVAR was performed in 366 patients (18.9%) and open repair in 1570 (81.1%), with 30-day mortality rates of 1.6% and 5.9% respectively. Most procedures ($n = 1752$, 90.5%) were for infrarenal AAA. The majority of patients were men (82.3%) and the median age was 73 years (interquartile range 68–77 years). Increasing age, female sex, history of myocardial infarction (MI), diabetes, obesity, respiratory disease, symptomatic aneurysm, raised serum creatinine concentration, raised urea level, low haemoglobin level and preoperative systolic blood pressure exceeding 140 mmHg, preoperative antiplatelet, antianginal and antihypertensive medications along with the type of aneurysm and whether or not EVAR or open repair was performed were all associated with mortality on univariate analysis, as shown in *Table 2*. These variables were, therefore, included in the logistic regression analysis.

The risk prediction model developed included the following independent risk factors for 30-day mortality: increasing age, female sex, diabetes, raised serum creatinine level, respiratory disease, antiplatelet medication and open surgery (*Table 3*).

TABLE 3 Final logistic regression model for 30-day mortality after AAA repair

Model	Coefficient	Odds ratio (95% CI)	*p*-value
Age (continuous in years)	0.0486	1.05 (1.02 to 1.09)	0.005
Female sex	0.7322	2.08 (1.31 to 3.31)	0.002
Diabetes	0.6620	1.94 (1.07 to 3.51)	0.029
Creatinine (continuous in μmol/l)[a]	0.0073	1.01 (1.00 to 1.01)	0.006
Respiratory disease	0.4718	1.61 (1.05 to 2.46)	0.031
Antiplatelet medication	0.7762	2.17 (1.38 to 3.43)	< 0.001
Open surgery	1.3130	3.72 (1.59 to 8.66)	0.002
Intercept	–9.3431		

a Data were missing for less than 2% of patients.

Vascular Governance North West model performance

The area under the ROC curve for the multivariable prediction model was 0.73 in the development data set. The Hosmer–Lemeshow goodness-of-fit statistic across groups of risk was not statistically significant ($p = 0.118$) demonstrating good model calibration (*Figure 3*). Low-, medium- and high-risk groups were created based on the predicted risk of 30-day mortality. Low-risk patients had a maximum risk of death within 30 days of 3.5%, medium-risk patients had a risk greater than 3.5% but no more than 6.5% and high-risk patients had a risk exceeding 6.5%. Of the 98 observed deaths, 59 (60.2%) occurred in the group predicted to be at high risk. After stratifying the patients into risk groups, the observed versus expected 30-day mortality rates were 2.4% versus 2.0% in low-risk patients ($p = 0.523$), 3.2% versus 4.8% in medium-risk patients ($p = 0.214$) and 12.1% versus 11.1% ($p = 0.617$) in high-risk patients, demonstrating that the model has good calibration in different risk groups.

In the validation data set, 50 patients (6.0%) died within 30 days of intervention. The AUC was 0.70 and the model was well calibrated with a non-significant Hosmer–Lemeshow test ($p = 0.853$), as demonstrated in *Figure 3*. The expected 30-day mortality rate in the validation data set was 5.1%, which did not differ significantly from the 6.0% observed 30-day mortality rate, giving an observed to expected (O : E) ratio of 1.18 ($p = 0.391$). Observed versus expected 30-day mortality rates were 3.2% versus 2.0% in low-risk patients (O : E ratio 1.60; $p = 0.272$), 6.1% versus 5.1% in the medium-risk group (O : E ratio 1.20; $p = 0.671$) and 11.1% versus 10.7% in high-risk patients (O : E ratio 1.04; $p = 0.879$), demonstrating good calibration in clinical subgroups.

The VGNW model incorporates the type of repair (open or EVAR) and six readily available preoperative patient characteristics. The model demonstrates acceptable discriminatory ability on split-data validation with no significant deviation from perfect fit and good calibration.

External validation of the Vascular Governance North West model using the National Vascular Database

External validation is the gold standard for risk prediction model assessment and is used to confirm that the model performs as expected in new but similar patients.[56] An external validation involves assessing a model's calibration, discrimination and clinical validity in a cohort of patients that is different from the cohort used for model development in either location or time.[57] Before a model can be deemed clinically useful it is important that it is externally validated to ensure that there is no overfitting and that adequate

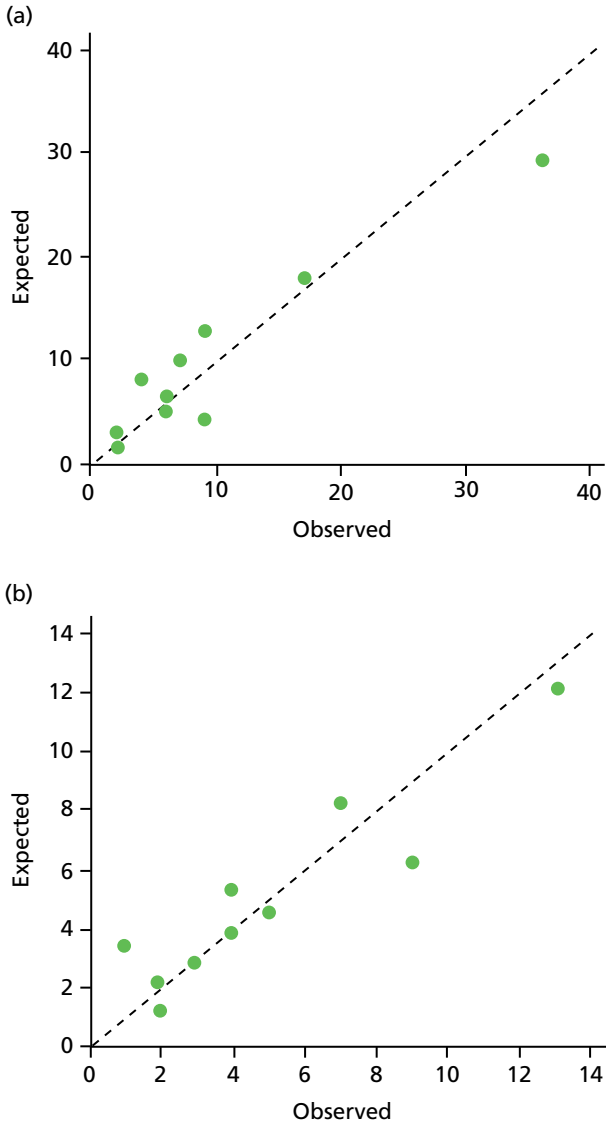


FIGURE 3 Observed and expected 30-day mortality compared for 10 groups of increasing risk in (a) the development data set ($p = 0.118$); and (b) the validation data set ($p = 0.853$). (Hosmer–Lemeshow goodness-of-fit test.)

discrimination and calibration are retained. Therefore, the VGNW model was validated using data from the NVD and its performance was compared with a number of other risk prediction models for AAA repair.

Data on all elective AAA repairs performed between 1 January 2008 and 31 December 2010 from the NVD were included. Records from hospitals in the North West region of England and Wales were excluded, so that there was no overlap with the VGNW model development data set. If these data were included, this might have resulted in an overoptimistic estimation of VGNW model performance. All variables with significant missing data were excluded from the analysis. For retained variables, imputation of missing data was performed as for development of the VGNW model. As 30-day mortality is not collected in the NVD, the primary outcome for the study was in-hospital mortality, defined as any death regardless of cause during the hospital admission for elective AAA repair.

In addition to the VGNW model, other models validated included the Medicare model, the Vascular Physiological and Operative Severity Score for enUmeration of Mortality (V-POSSUM) model, the Vascular Biochemistry and Haematology Outcome Model (VBHOM) and the GAS.[53] The equations used to calculate all of the validated models are included in *Appendix 6*.

As the NVD database was not designed to collect risk factor information necessary for calculation of all the models except the VBHOM, a number of risk factor assumptions were necessary. For the GAS, shock was assumed to be absent in all patients, as only elective cases were included. Myocardial disease included any history of ischaemic heart disease or congestive cardiac failure. Patients were defined as having cerebrovascular disease if they were taking antiplatelet medication (because cerebrovascular disease was not recorded in the NVD) and renal disease was defined as a serum creatinine level exceeding 160 µmol/l. For V-POSSUM, all patients with a history of congestive cardiac failure or ischaemic heart disease in the NVD were assigned a score of 2 for the cardiac component of the physiology score. Respiratory disease was not available in the NVD and was therefore assumed to be absent for all patients. All patients were assumed to have a Glasgow Coma Scale score of 15. For the Medicare model, chronic renal insufficiency was defined as a serum creatinine level exceeding 160 µmol/l, and end-stage renal disease was defined by the need for dialysis. Congestive heart failure included patients who also had any ischaemic heart disease, as these risk factors were not separated out in the NVD. Vascular disease was defined by the need to take antiplatelet medication. For the VGNW model, respiratory disease was assumed to be absent for all patients, as this was not recorded in the NVD.

The ROC curve was calculated to assess the discrimination of each model, with calibration measured by comparing the observed with the expected mortality for equally sized quintiles of ranked predicted risk and by performing a chi-squared test.

Model performance in the National Vascular Database

The validation cohort included 10,891 patients who underwent elective AAA repair. EVAR was performed in 5938 patients (54.5%) and open repair in 4953 (45.5%), with in-hospital mortality rates of 1.3% and 4.7% respectively (overall 2.9%). The patient characteristics of the cohort are shown in *Table 4*. The majority (67.3%) of NVD records were complete for all available and required variables, with only 11.8% of the records missing more than four of the variables required for the analysis. Both the VGNW (AUC 0.71, 95% CI 0.68 to 0.74) and Medicare models (AUC 0.71, 95% CI 0.69 to 0.74) demonstrated fair discrimination, as shown in *Table 5*.[54] The GAS, VBHOM and V-POSSUM all demonstrated lower discrimination with ROC curve values of 0.60 (95% CI 0.56 to 0.63), 0.61 (95% CI 0.58 to 0.64) and 0.62 (95% CI 0.59 to 0.65) respectively.

The VGNW model was the only logistic model that accurately predicted the overall mortality rate in the cohort ($p = 0.066$). The Medicare ($p = 0.006$), V-POSSUM ($p < 0.001$) and VBHOM ($p < 0.001$) all significantly overpredicted the overall mortality rate in the cohort, as shown in *Figure 4*.

As the VGNW and Medicare models were the only models to demonstrate acceptable discrimination, these models were selected to generate the quintiles for further assessment of calibration (*Tables 6* and *7*). The VGNW model demonstrated the best calibration for both data splits, accurately predicting mortality rates in four quintiles. The Medicare model accurately predicted risk in three quintiles for both splits. The V-POSSUM model predicted risk accurately in two quintiles when the data were split using the VGNW model and one quintile when they were split using the Medicare model. The VBHOM did not predict risk accurately in any quintile for either analysis. As the GAS is not a logistic model its calibration could not be assessed.

These results demonstrate that both the VGNW and Medicare models are potentially useful for risk prediction in elective AAA repair in the UK. The other three models assessed (V-POSSUM, VBHOM and GAS) performed poorly in comparison and are therefore not recommended for contemporary risk prediction in elective AAA repair in the UK.

TABLE 4 Data available for patients undergoing elective AAA repair in the NVD

Patient characteristic	Number of patients ($n = 10,891$) (%)
Age > 75 years	4701 (43.2)
Age > 80 years	2010 (18.5)
Women	1388 (12.7)
Diabetes	1209 (11.1)
Cardiac disease[a]	4368 (40.1)
Antiplatelet medication	6725 (61.7)
Statin	7021 (64.5)
Abnormal ECG[b]	2974 (27.3)
Renal dialysis	60 (0.6)
Current smoker	1999 (18.4)
Haemoglobin (g/dl)	
13.0–16.0	7203 (66.1)
11.5–12.9 or 16.1–17.0	2529 (23.2)
< 11.5 or > 17.0	1159 (10.6)
WCC ($\times 10^9$/l)	
4.0–10.0	9505 (87.3)
10.1–20.0 or 3.1–3.9	1328 (12.2)
< 3.0 or > 20.0	58 (0.5)
Urea (mmol/l)	
< 7.6	7897 (72.5)
7.6–10.0	2003 (18.4)
> 10.0	991 (9.1)
Sodium (mmol/l)	
> 135	9733 (89.4)
131–135	991 (9.1)
< 131	167 (1.5)
Potassium (mmol/l)	
3.5–5.0	10,227 (93.9)
3.2–3.4 or 5.1–5.3	454 (4.2)
< 3.2 or > 5.3	210 (1.9)
Creatinine (μmol/l)	
≤ 120	8896 (81.7)
121–160	1431 (13.1)
> 160	564 (5.2)
EVAR	5938 (54.5)

ECG, electrocardiogram; WCC, white cell count.
a Includes history of cardiac failure or ischaemic heart disease.
b Atrial fibrillation, more than five ectopic beats per minute, ischaemic changes or any other abnormal rhythm.

TABLE 5 Discriminatory ability of five risk prediction models for in-hospital mortality assessed in the NVD

Risk model	Area under ROC curve (95% CI)
GAS	0.60 (0.56 to 0.63)
VBHOM	0.61 (0.58 to 0.64)
V-POSSUM	0.62 (0.59 to 0.65)
Medicare	0.71 (0.69 to 0.74)
VGNW	0.71 (0.68 to 0.74)

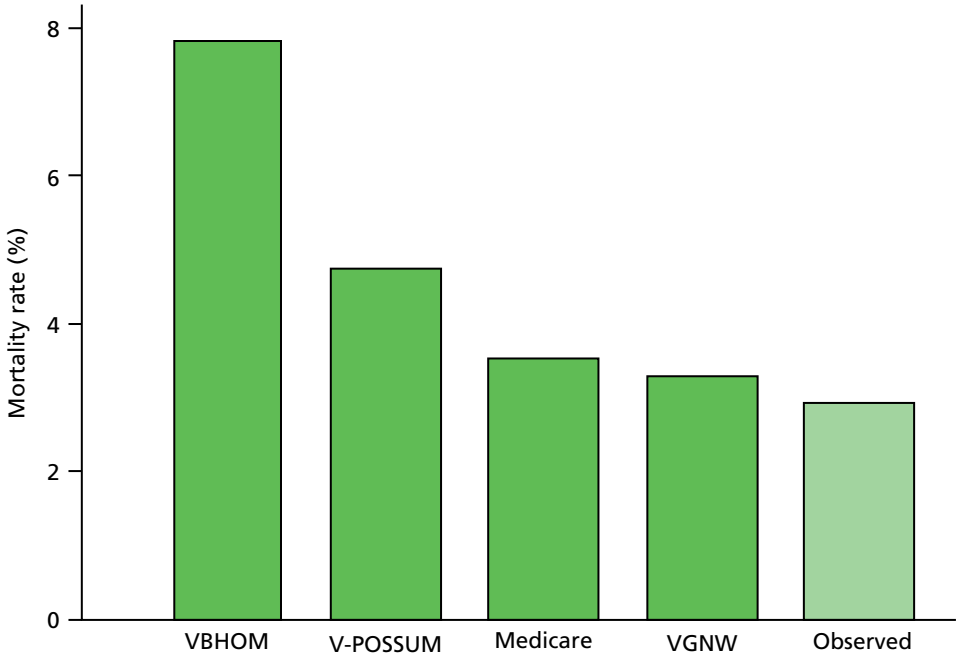


FIGURE 4 Observed and expected in-hospital mortality rates for the VBHOM, V-POSSUM, Medicare and VGNW model for elective AAA repair in the NVD. Dark green, expected; light green, observed.

TABLE 6 Predicted and observed in-hospital mortality rates for elective AAA repair by quintile (derived using the ranked VGNW predicted risk) for the VBHOM, V-POSSUM, Medicare and VGNW in the NVD

Quintile	Number of patients	Predicted mortality (%)				Observed mortality (%)
		VBHOM	V-POSSUM	Medicare	VGNW	
First	2179	6.2[a]	3.6[a]	1.2	0.7	1.2
Second	2175	7.3[a]	4.3[a]	2.0[a]	1.4	1.0
Third	2180	8.3[a]	4.8[a]	3.0[a]	2.3	2.0
Fourth	2178	8.0[a]	5.0	4.2	3.7	3.9
Fifth	2179	9.2[a]	6.1	7.4	8.5[a]	6.4

a $p < 0.05$ versus observed mortality (chi-squared test).

TABLE 7 Predicted and observed in-hospital mortality rates for elective AAA repair by quintile (derived using the ranked Medicare predicted risk) for the VBHOM, V-POSSUM, Medicare and VGNW in the NVD

Quintile	Number of patients	Predicted mortality (%)				Observed mortality (%)
		VBHOM	V-POSSUM	Medicare	VGNW	
First	2188	6.1[a]	3.5[a]	1.0	0.9	1.1
Second	2186	6.9[a]	4.2[a]	1.8[a]	1.5	1.0
Third	2098	7.8[a]	4.3[a]	2.7	2.7	2.2
Fourth	2237	8.2[a]	5.1[a]	4.1[a]	3.9[a]	2.7
Fifth	2182	10.1[a]	6.7	8.1	7.5	7.3

a $p < 0.05$ versus observed mortality (chi-squared test).

A national risk prediction model for mortality following elective abdominal aortic aneurysm repair

Both the VGNW model and Medicare model demonstrated potential suitability for predicting mortality following elective AAA repair. The risk factors in both models were similar, suggesting clinical validity; however, both models only just demonstrated acceptable discrimination. In addition, the compatibility of the models with national vascular practice is potentially limited, as both models contained risk factors not collected by the NVD. Therefore, a decision was made by the research team to explore the development of a model using NVD data.

Prospectively collected data on all elective AAA repairs performed between 1 April 2008 and 31 March 2011 were extracted from the NVD for analysis. The data were cleaned by resolving transcriptional discrepancies and clinical conflicts, removing or transforming aberrant and extreme values and validating procedure type using available Office of Population Censuses and Surveys (OPCS) codes. Records in which the hospital identifier was missing were removed from the study; otherwise all other records were used for model development.

All NVD database variables with 15% or more missing data were excluded from the analysis. For the remaining variables, any missing patient factor was assumed to be absent for categorical variables or replaced with the median value for continuous variables and the mode for ordinal variables. The primary outcome for the study was in-hospital mortality. Continuous variables were dichotomised into abnormal and normal ranges, with the following measurements defined as abnormal: serum > 120 µmol/l; haemoglobin < 11 g/dl for women, < 13 g/dl for men; white cell count (WCC) < 3.0×10^9/l or > 11.0×10^9/l; serum urea > 7.5 mmol/l; serum sodium < 135 mmol/l or > 145 mmol/l; serum potassium < 3.5 mmol/l or > 5.5 mmol/l; systolic blood pressure < 90 mmHg or > 140 mmHg; and highest preoperative heart rate > 80 beats/minute. Cardiac disease included a history of ischaemic heart disease, heart failure or both.

A multiple logistic regression model was fitted including all variables deemed clinically relevant. Backwards model selection using the Akaike information criterion (AIC) was applied.[58] Age and AAA diameter were retained as continuous variables and the linearity assumption was checked using standard diagnostics.[54] Model performance was assessed using bootstrap methodology to sample repeatedly from the complete data set and refit the final multiple logistic regression model 40 times.

Model performance summary statistics were calculated at each stage and averaged over all bootstrapped samples. Model calibration was evaluated using the Hosmer–Lemeshow test (not based on bootstrapped data)[54] and a calibration plot and by dividing the cohort into three groups based on their ranked predicted risk of in-hospital death with goodness of fit between the observed and expected outcomes evaluated using a chi-squared test on 1 degree of freedom. In addition, calibration was also assessed by fitting a

logistic regression model between the predicted and observed outcomes, and model discrimination was evaluated using the AUC.[55] Bias associated with the AUC was calculated using bootstrapping,[59] and DeLong's method for calculating AUC variance was used to calculate the 95% CI for the AUC.[60]

Model performance was also assessed separately for open AAA repair and EVAR subgroup with only within-data diagnostic statistics reported. A p-value < 0.05 was considered significant. All statistical analyses were carried out using R software version 2.14.2 (R Foundation for Statistical Computing, Vienna, Austria). Model selection was done using the MASS package (R Foundation for Statistical Computing, Vienna, Austria),[61] and internal model validation was assessed using the rms package (R Foundation for Statistical Computing, Vienna, Austria).[62]

The British Aneurysm Repair Score

In total, 11,423 records were included in the analysis for model development. The level of missing data in each of the variables included in the final analysis varied between 0% (operation type) and 14.6% (highest preoperative pulse). Overall, there were 6314 records (55.3%) without any missing risk factor data. A summary of patient characteristics is shown in *Table 8*. There were 312 in-hospital deaths after AAA repair, giving an in-hospital mortality rate of 2.7% (95% CI 2.4% to 3.0%).

TABLE 8 Patient characteristics in the NVD cohort used for development of the British Aneurysm Repair score

Characteristic		Frequency/mean	Percentage/SD
Age	≤ 75 years	6450	56.5
	> 75 years	4973	43.5
	Continuous	73.8	7.5
Sex	Male	9926	86.9
	Female	1497	13.1
Diabetes	No	10,052	88.0
	Yes	1371	12.0
Antiplatelet agent	No	3896	34.1
	Yes	7527	65.9
Cardiac disease	No	6682	58.5
	Yes	4741	41.5
Current smoker	No	9222	80.7
	Yes	2201	19.3
Abnormal ECG	No	8181	71.6
	Yes	3242	28.4
Beta blocker	No	7888	69.1
	Yes	3535	30.9
Statin	No	3519	30.8
	Yes	7904	69.2
Systolic BP (mmHg)	90–140	8230	72.0
	< 90 or > 140	3193	28.0
	Continuous	131.5	20.0

TABLE 8 Patient characteristics in the NVD cohort used for development of the British Aneurysm Repair score (*continued*)

Characteristic		Frequency/mean	Percentage/SD
Pulse (bpm)	≤ 80	8727	76.4
	> 80	2696	23.6
	Continuous	74.5	12.6
Haemoglobin	≥ 11 (female) or ≥ 13 (male)	8729	76.4
	< 11 (female) or < 13 (male)	2694	23.6
	Continuous	13.5	1.6
Previous aortic surgery/stent	No	11,089	97.1
	Yes	334	2.9
WCC ($\times 10^9$)	3–11	10,618	93.0
	< 3 or > 11	805	7.0
	Continuous	8	3.5
Urea (mg/dl)	≤ 7.5	8099	70.9
	> 7.5	3324	29.1
	Continuous	7.2	4.7
Serum creatinine (μmol/l)	≤ 120	9281	81.2
	> 120	2142	18.8
	Continuous	103.6	43.3
Sodium (mmol/l)	135–145	10,410	91.1
	< 135 or > 145	1013	8.9
	Continuous	139.6	3.2
Potassium (mmol/l)	3.5–5.5	11,130	97.4
	< 3.5 or > 5.5	293	2.6
	Continuous	4.3	0.4
AAA diameter (cm)	> 6.5	7876	68.9
	≤ 6.5	3547	31.1
	Continuous	6.3	1.1
ASA grade	1	375	3.3
	2	3857	33.8
	3	6788	59.9
	4	403	3.5
Repair type	EVAR	6483	56.8
	Open	4940	43.2

ASA, American Society of Anesthesiologists; BP, blood pressure; bpm, beats per minute; ECG, electrocardiogram; SD, standard deviation.

The final risk prediction model with estimated model coefficients, standard errors, Wald *z*-values, corresponding *p*-values, approximate 95% CI and model equation is shown in *Table 9*. Open AAA repair, age (continuous), female sex, cardiac disease, American Society of Anesthesiologists (ASA) grade and previous aortic surgery or stent were all included. Preoperative investigations included were raised serum creatinine concentration, abnormal WCC, abnormal sodium level and abnormal electrocardiogram (ECG). AAA diameter was also included in the model as a continuous variable.

The Hosmer–Lemeshow chi-squared test did not provide sufficient evidence to reject any assumption of good calibration ($\chi^2 = 2.477$, $p = 0.963$). For the calibration plot displayed in *Figure 5*, the points represent

TABLE 9 Final risk factors by multivariate regression for the British Aneurysm Repair score

Model	Coefficient	Odds ratio (95% CI)	*p*-value
Open AAA repair	1.54192	4.67 (3.6 to 6.13)	< 0.001
Age (years)	0.05396	1.06 (1.04 to 1.07)	< 0.001
Female	0.72735	2.07 (1.56 to 2.72)	< 0.001
Creatinine > 120 µmol/l	0.59902	1.82 (1.40 to 2.35)	< 0.001
Cardiac disease	0.34204	1.41 (1.10 to 1.80)	0.006
Abnormal ECG	0.32107	1.38 (1.07 to 1.77)	0.011
Previous aortic surgery or stent	0.84174	2.32 (1.33 to 3.80)	0.002
Abnormal WCC	0.36911	1.45 (0.95 to 2.13)	0.072
Abnormal sodium	0.31338	1.37 (0.96 to 1.91)	0.076
AAA diameter (cm)	0.13677	1.15 (1.04 to 1.25)	0.003
ASA grade			
Grade 2	0.25229	1.29 (0.56 to 3.72)	0.593
Grade 3	0.74919	2.12 (0.95 to 6.02)	0.104
Grade 4	1.66830	5.3 (2.19 to 15.85)	< 0.001
Intercept	–10.71810		

ASA, American Society of Anesthesiologists.

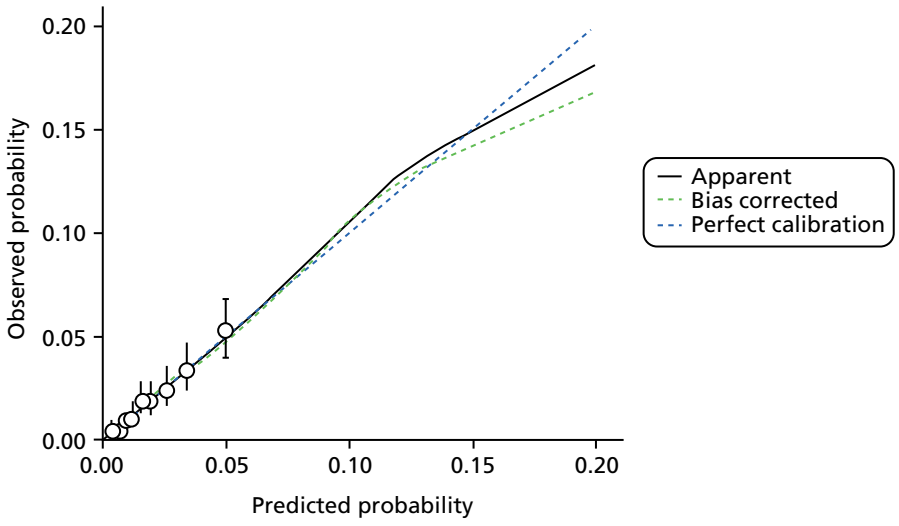


FIGURE 5 Calibration plot comparing observed and predicted in-hospital mortality, which demonstrates good calibration for the British Aneurysm Repair score.

the mean predicted and observed mortality proportion for deciles of predicted probabilities, and error bars represent 95% CIs for the observed mortality. A locally weighted scatterplot smoothing curve (apparent) indicating the general predictive trend, a bias-corrected calibration curve and the line of equality (perfect calibration) are also shown. The bias-corrected calibration curve started to deviate noticeably from the optimal calibration line only for predictions greater than 15%. The bootstrapped intercept and slope of the logistic regression model fitted to the transformed prediction values; observed outcomes were –0.100 and 0.966 respectively, suggesting a minor degree of overfitting.

For the risk group assessment, patients were classified as low risk if their predicted mortality was ≤ 1.5% (5712 patients), medium risk if their predicted mortality was between 1.5% and 3.3% (2856 patients) and high risk if their predicted mortality was greater than 3.3% (2855 patients) (*Table 10*). After risk stratification, the observed versus expected in-hospital mortality rates were 0.84% versus 0.83% in low-risk patients ($p = 0.970$), 2.2% versus 2.3% in the medium-risk group ($p = 0.821$) and 7.0% versus 6.9% ($p = 0.938$) in the high-risk group.

The AUC applied to the data set was 0.781 (95% CI 0.756 to 0.806), which represents good discrimination. Bias-corrected AUC based on the bootstrap method was 0.774; this was 0.007 smaller than the discriminatory ability in the complete data set.

The overall cohort included 4940 open AAA repairs (43.2%) and 6483 EVARs (56.8%). There were 230 in-hospital deaths following open AAA repair (4.7%; 95% CI 4.1% to 5.3%) and 82 deaths following EVAR (1.3%; 95% CI 1.0% to 1.6%). The distributions of the British Aneurysm Repair (BAR) score-predicted mortality risks for open AAA repair and EVAR are shown as density plots in *Figure 6*. Distributions of predicted risks for open AAA repair and EVAR were different, but there was substantial overlap between the subgroups. The model calibration in each group was good, as assessed using the Hosmer–Lemeshow test (open AAA repair: $p = 0.971$, $\chi^2 = 2.293$; EVAR: $p = 0.321$, $\chi^2 = 9.256$). The discrimination in the open AAA repair group was 0.723 (95% CI 0.690 to 0.757) and that in the EVAR group was 0.749 (95% CI 0.698 to 0.800).

The BAR score is made up of 11 preoperative risk factors that are collected easily as part of routine clinical practice. The model demonstrates good calibration and discrimination for all patients undergoing elective AAA repair. The model also demonstrated good performance in open AAA repair and EVAR subgroups. External validation of model performance is required before it can be recommended above other models for the prediction of perioperative mortality.

TABLE 10 Risk group assessment of the British Aneurysm Repair score demonstrates good calibration

Risk group	Total records	Open records	EVAR records	BAR range	Observed mortality	Predicted mortality	*p*-value[a]
Low	5712	918	4794	< 1.5%	0.84	0.83	0.970
Medium	2855	1677	1178	1.5% ≥ BAR ≤ 3.3%	2.2	2.3	0.821
High	2856	2443	413	> 3.3%	7.0	6.9	0.938

BAR, British Aneurysm Repair.
a Chi-squared test (with Yates' continuity correction) for the observed mortality compared with the predicted mortality on 1 degree of freedom.

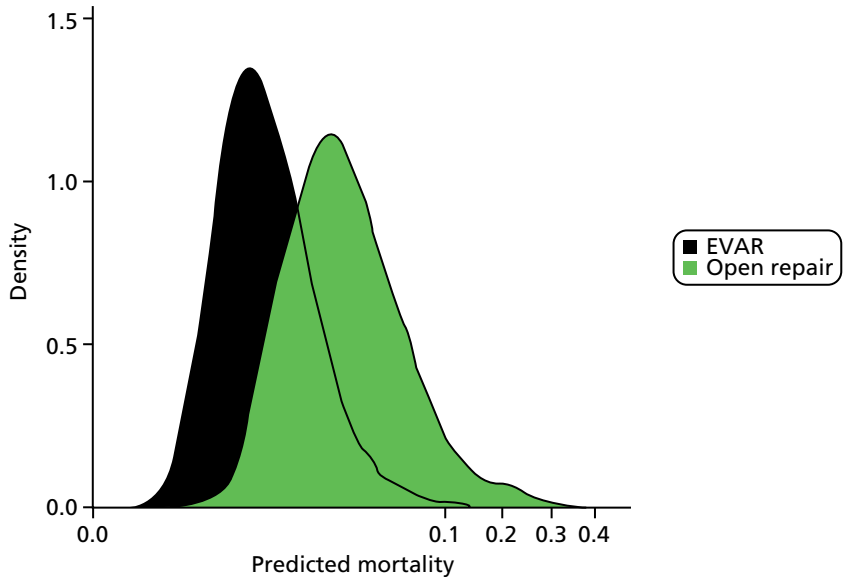


FIGURE 6 British Aneurysm Repair score-predicted mortality density plots for open AAA repair and EVAR subgroups. The horizontal axis has been transformed for better visualisation.

External validation of the British Aneurysm Repair score

To validate the BAR score externally, data were analysed for consecutive elective AAA repairs performed between April 2011 and March 2013 in the VGNW programme. This time period was selected to ensure that no data used for development of either the VGNW model or BAR score were included in the data set.

The data were cleaned by removing duplicate records, correcting transcriptional discrepancies and resolving any clinical or temporal conflicts. Missing data were imputed with the sample median for continuous or ordinal variables and the mode for dichotomous variables. The primary outcome measure used was in-hospital mortality. In addition to the BAR score, the VGNW model and the Medicare model were also validated. Model performance was assessed using measures of calibration and discrimination in the overall cohort and separately in both procedural and sex subgroups.

Discrimination was evaluated by determining the AUC, with AUC variance used for the calculation of AUC 95% CIs. In the overall cohort and procedural subgroups, model calibration has been summarised by calculating the O : E ratio and performing a goodness-of-fit chi-squared test on 1 degree of freedom. Model calibration was further assessed in the overall cohort by dividing the cohort into low-risk (bottom 50%), medium-risk (middle 25%) and high-risk (top 25%) approximate groups based on the model's predicted mortality. Calibration plots for each model based on these groups were produced showing the mean predicted probability of outcome against the observed proportion of outcomes. Approximate 95% CIs for the observed mortality proportions are shown as error bars. The calibration intercepts and slope parameters were also calculated for each model in the overall cohort. All statistical analyses were performed using R version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Data were available on 1124 elective AAA repairs. The mean age of the population was 74.4 years [standard deviation (SD) 7.7 years] and 193 (17.2%) of patients were female. The majority of patients ($n = 759$, 67.5%) underwent EVAR and most patients ($n = 1037$, 92.3%) were asymptomatic. Additional patient characteristic information for this cohort is shown in *Table 11*. There were 32 in-hospital deaths in the cohort, giving an in-hospital mortality of 2.8%. In this cohort of patients, no deaths occurred following discharge but within 30 days of the procedure.

TABLE 11 Patient characteristics for the study population

Risk factor	Frequency (%)	Missing data (%)
Age (years)[a]	74.4 (7.7)	0.2
Female	193 (17.2)	0.0
AAA diameter (cm)[a]	6.3 (1.2)	6.0
Previous aortic surgery/stent	67 (6.0)	1.3
AAA symptoms	87 (7.7)	6.1
Ischaemic heart disease	357 (31.8)	8.5
Previous MI	163 (14.5)	8.5
Cardiac failure	27 (2.4)	9.2
Respiratory disease	199 (17.7)	14.5
Diabetes	162 (14.4)	3.2
Antiplatelet medication	716 (63.7)	0.5
Antihypertensive medication	371 (33.0)	0.5
Statin therapy	778 (69.2)	0.4
Smoking status	–	12.2
Ex-smoker	298 (26.5)	–
Current smoker	246 (21.9)	–
Abnormal ECG	359 (31.9)	5.7
Abnormal sodium	105 (9.3)	11.0
Abnormal potassium	36 (3.2)	10.4
Abnormal urea	308 (27.4)	10.4
Creatinine > 120 µmol/l	186 (16.5)	10.1
Creatinine > 200 µmol/l	21 (1.9)	10.1
Abnormal WCC	82 (7.3)	9.0
Abnormal haemoglobin	296 (26.3)	9.0
ASA grade	–	11.4
1	56 (5.0)	–
2	434 (38.6)	–
3	604 (53.7)	–
4	30 (2.7)	–
Open repair	365 (32.5)	0.0

a Continuous data displayed as mean (SD).

The BAR score-predicted mortality was 2.4%, giving an O : E ratio of 1.2 ($p = 0.509$). The other validated models also demonstrated good overall calibration (VGNW-predicted mortality 3.2%, O : E ratio 0.9; $p = 0.622$; Medicare-predicted mortality 2.8%, O : E ratio 1.0; $p = 0.904$). The calibration plots for the three models are shown in *Figure 7*. The calibration intercept and slope also demonstrated good calibration for all three models, with each unreliability statistic being non-significant (Medicare $p = 0.332$, VGNW $p = 0.756$, BAR $p = 0.581$).

The BAR score demonstrated excellent discrimination in the overall cohort, with an AUC of 0.83 (95% CI 0.76 to 0.89). The discriminative ability of the Medicare and VGNW models was acceptable, with AUCs of 0.78 (95% CI 0.70 to 0.86) and 0.75 (95% CI 0.65 to 0.84) respectively. The ROC curves for the models in the overall cohort are shown in *Figure 8*.

To further check the clinical validity of the modes, performance was assessed in separate procedural and sex subgroups. The in-hospital mortality rates for open AAA repair and EVAR were 6.8% and 0.9% respectively. The predicted mortality in the open AAA repair group was 4.4% (O : E ratio 1.5; $p = 0.148$), 5.4% (O : E ratio 1.3; $p = 0.442$) and 4.9% (O : E ratio 1.4; $p = 0.271$) for the Medicare, VGNW and BAR scores respectively. In the EVAR group the predicted mortality was 2.0% (O : E ratio 0.5; $p = 0.086$), 2.1% (O : E ratio 0.4; $p = 0.059$) and 1.2% (O : E ratio 0.8; $p = 0.615$) for the Medicare, VGNW and BAR scores respectively. In the open AAA repair subgroup, again, only the BAR score demonstrated acceptable discrimination, with an AUC of 0.70 (95% CI 0.61 to 0.78). Both the Medicare and VGNW models demonstrated unacceptable discrimination, with AUCs of 0.68 (95% CI 0.58 to 0.78) and 0.64 (95% CI 0.53 to 0.75). In the EVAR subgroup, only the BAR score demonstrated acceptable discrimination, with an AUC of 0.75 (95% CI 0.55 to 0.95). Both the Medicare and VGNW models demonstrated unacceptable discrimination, with AUCs of 0.66 (95% CI 0.47 to 0.85) and 0.56 (95% CI 0.31 to 0.81) respectively.

The in-hospital mortality for men was 2.8%, and for women it was 3.1%. The predicted mortality for men was 2.4% (O : E ratio 0.9; $p = 0.559$), 2.6% (O : E ratio 0.9; $p = 0.774$) and 1.9% (O : E ratio 0.7%; $p = 0.222$) for the Medicare, VGNW and BAR scores respectively. For women the predicted mortality was

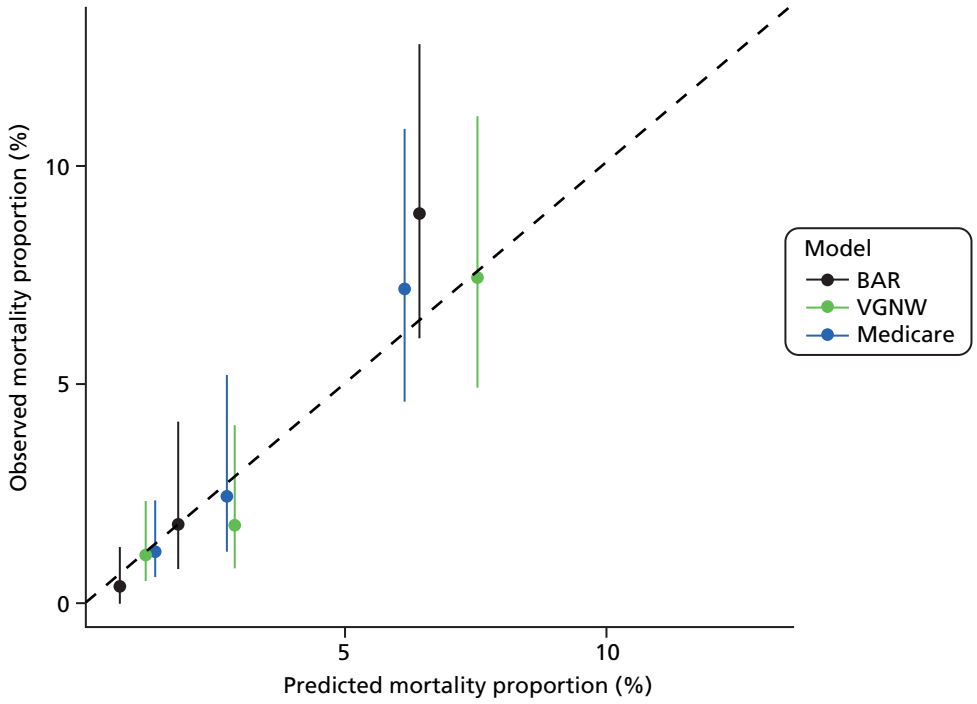


FIGURE 7 Calibration plots for low-, medium- and high-risk groups for the BAR, Medicare and VGNW risk models. The black dashed line is the line of equality that represents perfect calibration. Vertical lines represent 95% binomial CIs of the observed mortality proportion.

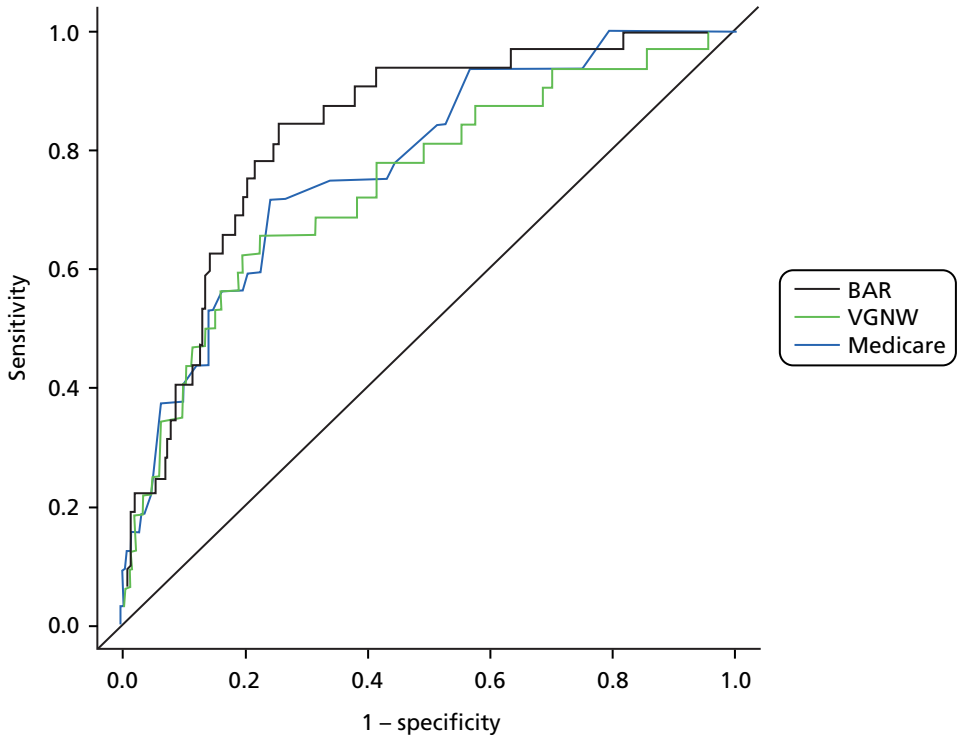


FIGURE 8 Receiver operating characteristic curves for the BAR, Medicare and VGNW risk models in the overall cohort. The diagonal line represents the line of equality.

4.5% (O : E ratio 1.5; $p = 0.429$), 6.2% (O : E ratio 2.0; $p = 0.148$) and 4.8% (O : E ratio 1.5; $p = 0.429$) for the Medicare, VGNW and BAR scores respectively. For men the BAR score demonstrated excellent discriminatory ability, with an AUC of 0.85 (95% CI 0.78 to 0.92). Both the Medicare and VGNW models demonstrated acceptable discrimination, with AUCs of 0.78 (95% CI 0.69 to 0.86) and 0.76 (95% CI 0.65 to 0.86) respectively. For women the Medicare model demonstrated excellent discriminatory ability, with an AUC of 0.88 (95% CI 0.77 to 0.99). The BAR score and VGNW model both demonstrated acceptable discrimination, with AUCs of 0.79 (95% CI 0.67 to 0.91) and 0.76 (95% CI 0.55 to 0.98) respectively.

Summary

Two models (one regional and one national) have been developed for the prediction of perioperative mortality following elective AAA repair. Both models have demonstrated satisfactory performance on external validation. A number of current models have been found to be inadequate for contemporary elective AAA repair. As the BAR score is based on national UK data, demonstrated excellent discriminatory ability overall and retained discriminatory ability in procedural subgroups, this model has been chosen to estimate the risk of in-hospital mortality for the overall algorithm.

Chapter 6 Predicting survival following elective abdominal aortic aneurysm repair

Background

Historically, surgeons have emphasised the in-hospital or 30-day mortality rate after elective AAA repair, and there is a considerable amount of literature published on the topic.[63–66] As the incidence of AAA repair increases with age, with most patients in their eighth decade, often with significant comorbidity,[28] understanding long-term survival is increasingly important. As most patients with AAA are asymptomatic, the principal indication of repair is to prevent rupture and increase survival.

Objective

To identify preoperative risk factors that predict long-term survival following elective AAA repair.

Modelling survival following elective abdominal aortic aneurysm repair: methods

Data from the VGNW programme for all patients who underwent elective AAA repair from January 2000 to April 2013 were included in this analysis. Over this study period there were 87 contributing surgeons across 24 hospitals. Emergency repairs for AAA rupture or repairs of thoracoabdominal aneurysms were excluded. The demographic batch service was used to determine mortality status for all patients up to and including 31 May 2013.

The data were cleaned by first resolving transcriptional discrepancies and clinical conflicts. Aberrant and extreme values were removed or transformed if the cause was inconsistent measurement units. Database variables with significant missing data (15%) were excluded from the analysis. For the remaining variables, any missing patient factor was imputed to the median value for continuous variables and assumed to be absent for categorical variables. The following preoperative measurements were defined as abnormal: serum creatinine concentration > 120 µmol/l; haemoglobin level < 11 g/dl for women and < 13 g/dl for men; WCC $< 3.0 \times 10^9$/l or $> 11.0 \times 10^9$/l; serum urea concentration > 7.5 mmol/l; serum sodium level < 135 mmol/l or > 145 mmol/l; potassium level < 3.5 mmol/l or > 5.5 mmol/l. Ischaemic heart disease included a history of previous MI, angina or both. All analyses and cleaning were performed using R version 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

Survival analyses were performed using the Kaplan–Meier method, and differences in survival were compared using the log-rank test.[67,68] Age and AAA diameter were retained as continuous variables as they did not violate the linearity assumption (checked using standard diagnostics).[54] Individual Cox proportional hazards models were used for univariate analysis of preoperative variables. Variables of clinical significance and those with a *p*-value < 0.2 by univariate analysis were included in a multivariate Cox proportional hazards model to identify significant preoperative prognostic indicators of long-term survival. Backward stepwise selection using AIC was used to optimise this model. Scaled Schoenfield residuals were analysed to ensure the proportional hazards assumptions were not violated for variables associated with long-term survival.[69,70]

Modelling survival following elective abdominal aortic aneurysm repair: results

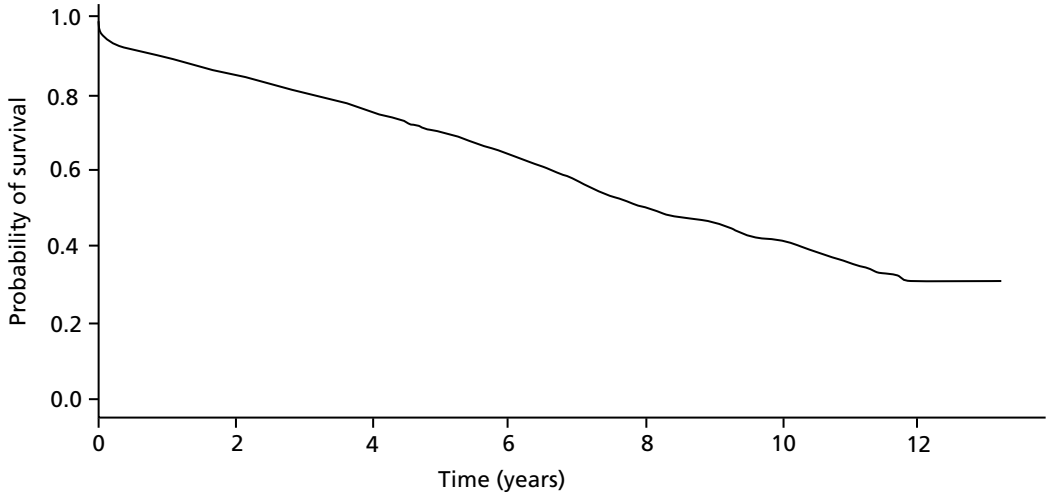
In the 13-year period, 4070 patients underwent AAA repair in the North West region. Of these, 2317 (57%) were by open surgical repair and 1753 (43%) were by EVAR. The mean age was 73.5 years and the majority of patients, 3398 (84%), were men. Patient characteristics are shown in *Table 12*. Overall cohort survival was 70.2% at 5 years and 41% at 10 years, with a median survival of 8.1 years (*Figure 9*). The in-hospital mortality was 5.2% overall, which improved over the study period to a mean of 3.0% during the last 5 years (2009–13). For those patients that survived the perioperative period following open surgical repair or EVAR, the apparent early benefit of EVAR (1-year survival of 88.3% and 91.2% respectively; *Figure 10*) was lost by year 2 of follow-up and at 5 years, 71.3% of patients following open repair were alive compared with 65.4% following EVAR. *Table 12* shows that the main reason for this improved survival following open surgery may be the younger age and lower comorbidities in patients selected for open surgery by the surgeon.

On univariate analysis, increasing patient age, female sex and ischaemic heart disease were all significantly associated with reduced survival. Preoperative investigations associated with reduced survival included abnormal ECG, raised serum concentrations of creatinine and urea, an abnormal serum sodium and anaemia. Larger AAA diameter was also a risk factor for poor survival following repair. Preoperative statin therapy was associated with improved survival long term.

TABLE 12 Patient demographics of the VGNW survival cohort

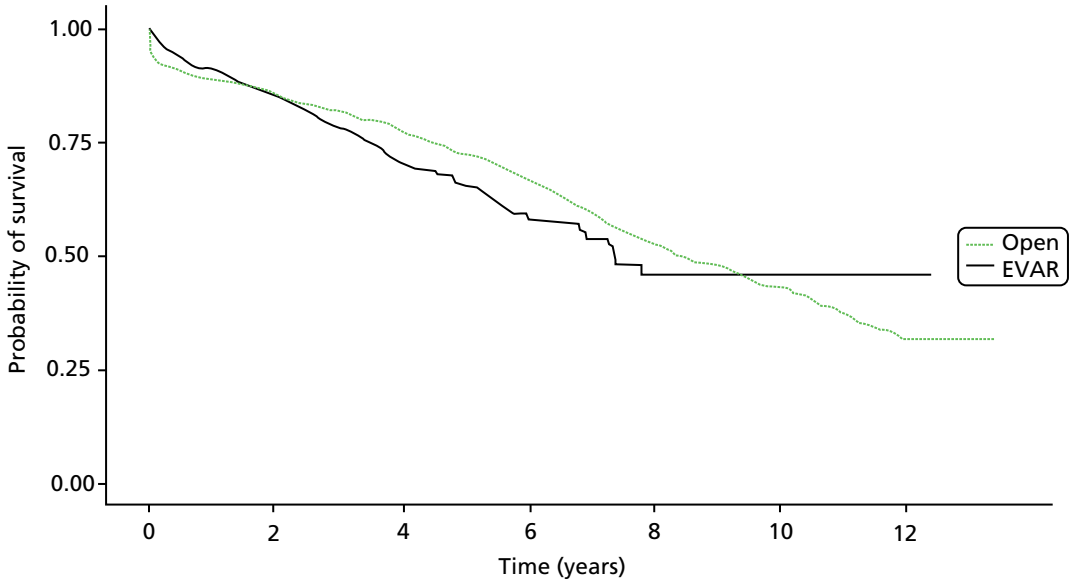
Patient characteristic	All patients ($n = 4070$)	Open repair ($n = 2317$)	EVAR ($n = 1753$)	p-value[a]
Mean (SD) age (years)	73.5 (7.3)	72.1 (7.1)	75.4 (7.1)	< 0.001
Female (%)	16.5	19.5	12.6	< 0.001
Ischaemic heart disease (%)	41.0	35.2	49.2	< 0.001
Diabetes (%)	12.3	10.8	14.5	< 0.001
Previous aortic surgery/stent (%)	5.5	3.4	8.9	< 0.001
Antiplatelet medication (%)	56.4	53.5	60.2	< 0.001
Statin therapy (%)	56.1	50.6	63.4	< 0.001
Antihypertensive medication (%)	40.3	44.0	35.3	< 0.001
Abnormal ECG (%)	31.9	29.0	36.2	< 0.001
WCC ($\times 10^9$/l), < 3 or > 11	6.0	6.5	5.4	0.2
Haemoglobin (g/dl), < 11 (female) or < 13 (male)	24.3	20.9	28.8	< 0.001
Sodium (mmol/l), < 135 or > 145	10.3	10.4	10.2	0.9
Potassium (mmol/l), < 3.5 or > 5.5	3.5	3.7	3.2	0.48
Serum creatinine (μmol/l), > 120	21.4	22.9	20.1	0.05
Urea (mg/dl), > 7.5	30.8	30.0	31.8	0.26
Aneurysm diameter (cm), (SD)	6.5 (1.2)	6.6 (1.3)	6.3 (1.1)	< 0.001
Aneurysm level, infrarenal	92.2	89.2	96.3	–
Aneurysm level, juxta/suprarenal	7.8	10.8	3.7	< 0.001
Symptomatic aneurysm	24.7	34.1	11.8	< 0.001
Aneurysm type, standard	94.5	91.2	99.1	–
Aneurysm type, inflammatory	5.5	8.8	0.9	< 0.001

a Comparison made between open repair and EVAR; student's *t*-test for continuous variables, Pearson's chi-squared test for categorical variables.



Number at risk	4070	2471	1390	822	416	175	37

FIGURE 9 Overall survival following AAA repair of the cohort from day of operation using Kaplan–Meier.



Number at risk	EVAR	1753	1278	824	467	235	123	58	32	17	12	10	6	1	0
	Open	2317	1911	1647	1391	1155	966	764	576	399	268	165	88	36	1

FIGURE 10 Overall survival in patients undergoing open repair or EVAR from date of operation using Kaplan–Meier. No significant survival advantage was noted between the groups ($p = 0.441$).

Multivariate Cox proportional hazards model of prognostic factors for overall survival following AAA repair are shown in *Table 13*. This model was stratified on repair type because of the violation of the proportional hazards assumption demonstrated in *Figure 10*. The patient characteristics significantly associated with reduced survival included increasing age [hazard ratio (HR) 1.05, 95% CI 1.04 to 1.06], female sex (HR 1.32, 95% CI 1.14 to 1.53) and ischaemic heart disease (HR 1.16, 95% CI 1.02 to 1.32). Preoperative statin therapy was associated with improved survival (HR 0.76, 95% CI 0.67 to 0.87). Antiplatelet therapy and diabetes, although included in the model, were not statistically significant predictors of survival ($p = 0.11$ and $p = 0.09$ respectively).

As a sensitivity analysis, multivariate Cox proportional hazard models were prepared on open repair and EVAR patient cohorts separately. These models are shown in *Tables 14* and *15*. Both models include female sex, age, ischaemic heart disease, diabetes, serum creatinine > 120 µmol/l and anaemia. Statin use and abnormal sodium are included in the open repair model while inflammatory aneurysm, antiplatelet use and antihypertensive use are included in the EVAR model. All significant patient characteristics from the separate models are included in the combined model apart from inflammatory aneurysm type, which occurred in very low frequency (0.9% of patients) in the EVAR patient cohort.

TABLE 13 Multivariable risk factors associated with long-term survival after elective AAA repair

Patient characteristic	HR (95% CI)	*p*-value
Female sex	1.32 (1.14 to 1.53)	< 0.001
Age (years)	1.05 (1.04 to 1.06)	< 0.001
Ischaemic heart disease	1.16 (1.02 to 1.32)	0.03
Diabetes	1.17 (0.97 to 1.41)	0.09
Antiplatelet use	0.90 (0.79 to 1.03)	0.11
Statin use	0.76 (0.67 to 0.87)	< 0.001
Abnormal ECG	1.19 (1.05 to 1.36)	< 0.001
Abnormal sodium	1.40 (1.17 to 1.67)	< 0.001
Serum creatinine > 120 µmol/l	1.28 (1.12 to 1.47)	< 0.001
Anaemia	1.30 (1.15 to 1.48)	< 0.001

HR, hazard ratio.
Cox proportional hazards model from date of operation ($n = 4070$).

TABLE 14 Multivariable risk factors for open repair patients associated with long-term survival after elective AAA repair

Patient characteristic	HR (95% CI)	*p*-value
Female sex	1.28 (1.08 to 1.52)	0.004
Age (years)	1.05 (1.04 to 1.07)	< 0.001
Ischaemic heart disease	1.15 (0.99 to 1.34)	0.062
Diabetes	1.23 (0.98 to 1.54)	0.069
Statin use	0.75 (0.65 to 0.87)	< 0.001
Abnormal sodium	1.51 (1.22 to 1.86)	< 0.001
Serum creatinine > 120 µmol/l	1.23 (1.05 to 1.45)	0.010
Anaemia	1.21 (1.03 to 1.42)	0.021

Cox proportional hazards model from date of operation ($n = 2317$).

TABLE 15 Multivariable risk factors for EVAR patients associated with long-term survival after elective AAA repair

Patient characteristic	HR (95% CI)	*p*-value
Female sex	1.48 (1.08 to 2.02)	0.014
Age (years)	1.05 (1.03 to 1.07)	< 0.001
Ischaemic heart disease	1.29 (1.03 to 1.61)	0.027
Diabetes	1.01 (1.00 to 1.02)	0.015
Inflammatory aneurysm	2.58 (1.13 to 5.86)	0.024
Antiplatelet use	0.71 (0.57 to 0.88)	0.002
Antihypertensive use	0.79 (0.62 to 1.00)	0.051
Serum creatinine > 120 µmol/l	1.32 (1.03 to 1.71)	0.031
Anaemia	1.63 (1.30 to 2.05)	< 0.001

Cox proportional hazards model from date of operation ($n = 1753$).

To address the possibility that specific preoperative factors may influence perioperative mortality more than long-term survival and given the extensive analyses already performed on perioperative mortality, a further Cox proportional hazards analysis from the date of discharge from hospital following AAA repair was performed.

In patients surviving to discharge, the median subsequent survival time improved to 8.7 years with 75.0% 5-year survival (*Figure 11*). Multivariate Cox proportional hazards model of prognostic factors for survival following discharge from hospital are shown in *Table 16*. This model did not require stratification on repair type, as the proportional hazards assumption was not violated (*Figure 12*). Interaction terms for type of repair (open versus EVAR) and year of operation were assessed against the variables in this model as EVAR became increasingly used in the later years of this study. In all cases $p < 0.05$ was considered statistically significant.

Increasing age (HR 1.05, 95% CI 1.04 to 1.06), female sex (HR 1.21, 95% CI 1.02 to 1.44), abnormal ECG (HR 1.18, 95% CI 1.02 to 1.36), abnormal sodium (HR 1.37, 95% CI 1.11 to 1.67), creatinine (HR 1.30,

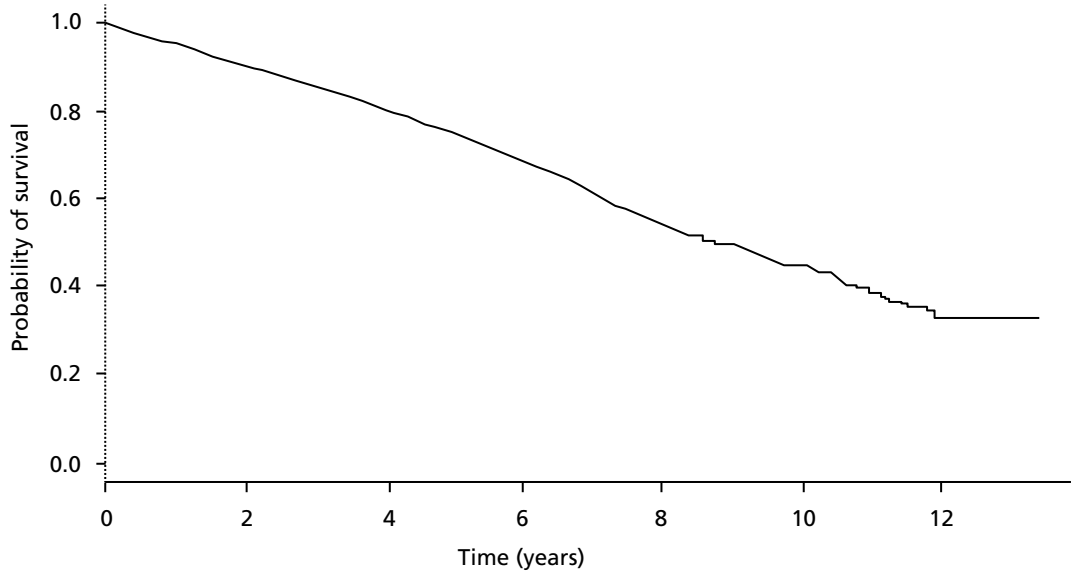
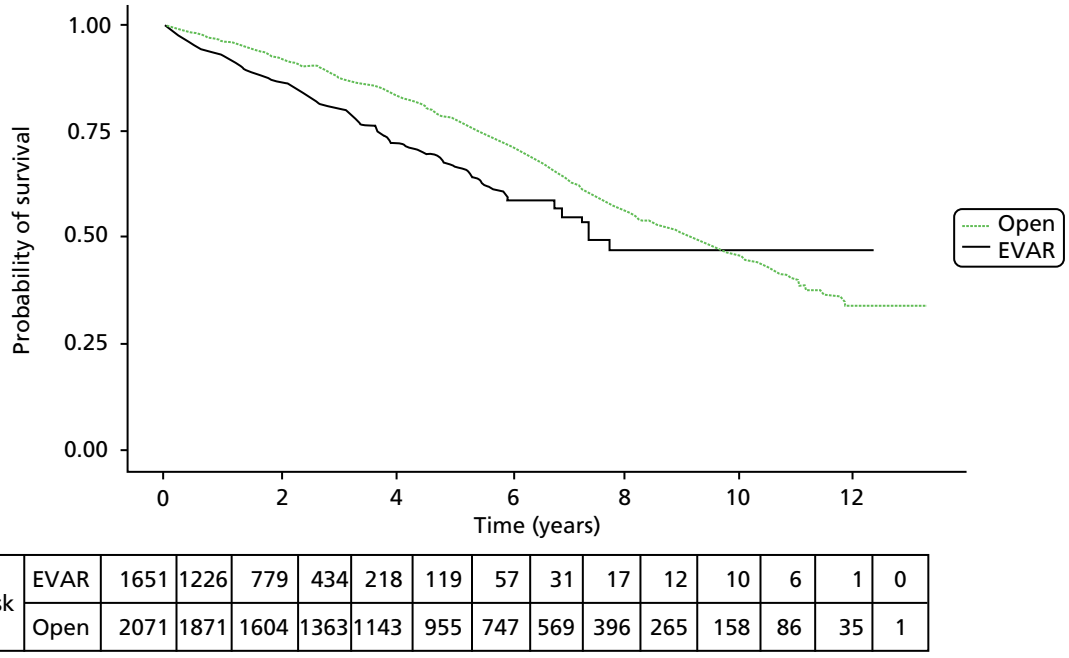


FIGURE 11 Overall survival of the cohort from date of discharge using Kaplan–Meier.

TABLE 16 Multivariable risk factors associated with survival after discharge from hospital following elective AAA repair

Patient characteristic	HR (95% CI)	*p*-value
Open repair	0.70 (0.60 to 0.82)	< 0.001
Female sex	1.21 (1.02 to 1.44)	0.03
Age (years)	1.05 (1.04 to 1.06)	< 0.001
Antiplatelet use	0.85 (0.73 to 0.98)	0.02
Statin use	0.80 (0.69 to 0.92)	< 0.001
Abnormal ECG	1.18 (1.02 to 1.36)	< 0.001
Abnormal sodium	1.37 (1.11 to 1.67)	0.003
Serum creatinine > 120 µmol/l	1.30 (1.12 to 1.51)	< 0.001
Anaemia	1.35 (1.17 to 1.56)	< 0.001

Cox proportional hazards model from date of operation ($n = 3722$).



Number at risk	EVAR	1651	1226	779	434	218	119	57	31	17	12	10	6	1	0
	Open	2071	1871	1604	1363	1143	955	747	569	396	265	158	86	35	1

FIGURE 12 Overall survival in patients undergoing open repair or EVAR from date of discharge using Kaplan–Meier. A significant survival advantage was noted for the open repair group ($p < 0.0001$).

95% CI 1.12 to 1.51) and anaemia (HR 1.35, 95% CI 1.17 to 1.56) were predictive of poor long-term survival. Open repair (HR 0.70, 95% CI 0.60 to 0.82), statin therapy (HR 0.80, 95% CI 0.69 to 0.92) and antiplatelet therapy (HR 0.85, 95% CI 0.73 to 0.98) were predictive of improved long-term survival in patients that survived AAA repair.

In order to include individual patient predicted survival in the DES model, a survival model with a baseline hazard function was required. A Weibull survival model was developed including risk factors identified as in the previous Cox proportional hazards survival models. Backward stepwise AIC model selection was again used to optimise the model.

The Weibull model of prognostic factors for survival following discharge from hospital is shown in *Table 17*. This model did not require stratification on repair type. Female sex (HR 1.02, 95% CI 1.00 to 1.04),

TABLE 17 Weibull model for survival following discharge from hospital following elective AAA repair

Patient characteristic	HR (95% CI)	*p*-value
Open repair	0.97 (0.96 to 0.99)	< 0.001
Female sex	1.02 (1.00 to 1.04)	0.047
Age (years)	0.99 (0.99 to 1.00)	< 0.001
Previous aortic surgery or stent	0.95 (0.91 to 1.00)	0.040
Antiplatelet use	0.98 (0.97 to 1.00)	0.032
Statin use	0.97 (0.96 to 0.99)	0.002
Abnormal ECG	1.02 (1.01 to 1.04)	0.009
Abnormal sodium	1.03 (1.01 to 1.05)	0.009
Serum creatinine > 120 µmol/l	1.03 (1.01 to 1.05)	0.002
Anaemia	1.03 (1.01 to 1.05)	0.001

Baseline parameters: log(scale) = 9.89 ($p < 0001$); log(shape) = 2.23 ($p < 0.001$).

abnormal ECG (HR 1.02, 95% CI 1.01 to 1.04), abnormal sodium (HR 1.03, 95% CI 1.01 to 1.05), creatinine (HR 1.03, 95% CI 1.01 to 1.05) and anaemia (HR 1.03, 95% CI 1.01 to 1.05) were predictive of poor long-term survival. Open repair (HR 0.97, 95% CI 0.96 to 0.99), increasing age (HR 0.99, 95% CI 0.99 to 1.00), previous aortic surgery or stent (HR 0.95, 95% CI 0.91 to 1.00), statin therapy (HR 0.97, 95% CI 0.96 to 0.99) and antiplatelet therapy (HR 0.98, 95% CI 0.97 to 1.00) were predictive of improved survival in those patients that survived to discharge following AAA repair.

Patient age is seen to be protective in this model, but this is accounted for, as the baseline hazard function is monotonically increasing with time which captures the increasing risk of death with increasing age. This increase in risk with time is effectively the patient ageing. Age in this model may represent the healthy-old-person effect where only the healthiest elderly people undergo repair. Alternatively, developing an AAA at an earlier age may indicate more aggressive disease and therefore a poor long-term prognosis.

Summary

Our model has identified preoperative factors such as advancing age, female sex, ischaemic heart disease, abnormal ECG, anaemia, abnormal serum sodium and creatinine as being associated with worse long-term survival following AAA repair. Statin and antiplatelet therapy confer improved survival. This survival model will be incorporated into the final decision aid calculating individual patient indications for AAA repair, as it represents the principal reason for repairing an AAA.

Chapter 7 The Aneurysm Repair Decision Aid

Background

The patient pathway from AAA diagnosis through scheduled surveillance to a decision on repair and ultimately survival following the repair cannot be modelled using standard statistical techniques because the pathway is too complex. In the earlier chapters we illustrated how various components of this pathway can be modelled (AAA growth and rupture rates, perioperative mortality and long-term survival). Each of these elements separately does not allow us to derive optimal intervention strategies for individual patients. This is because the elements interact with each other in a complex manner (for example, once an aneurysm is operated on, it no longer continues to grow nor has a risk of rupture; on the other hand, there is the perioperative and longer-term survival to consider following an intervention).

A DES approach was used as the basis for the ARDA. This approach was chosen as, unlike other approaches, it combines the modelling approaches for each component of the patient pathway into one system. It is a microsimulation approach, that is, a patient with particular baseline demographics is simulated forward in time. A key advantage is that outputs are patient-specific (different outputs would be observed for a patient with different baseline demographics). The system is simulated under different intervention rules (an intervention rule is defined as carrying out AAA repair at a particular aneurysm size). The output of the DES can therefore be used to compare the merits (in terms of a range of outcomes) of the various intervention rules, and hence guide treatment decisions.

Discrete event simulation development and structure

Model development

The DES model was developed in a top-down approach. First, the entire patient journey at a high level was described and discussed by experts. The final description was agreed and coded. Individual modules that described individual components of the model in detail were developed and coded (a module for evaluating AAA growth and a module for calculating the BAR score). Each module was internally assessed for face validity and, where possible, compared with existing implementations (for example, BAR scores were validated against the BAR score web application). The entire DES was then checked for face validity. Further development of the DES code was then undertaken so that cost and health-related quality-of-life outcomes could be simulated in parallel with survival and other clinical data.

Model structure

The code base of the DES algorithm was developed in R. The model is based on an underlying decision rule to consider AAA repair once the AAA has reached a given size. For current practice this rule is to repair when the AAA reaches 5.0 cm diameter for women and 5.5 cm diameter for men. The model was developed to explore the full range of AAA sizes and the potential intervention rules for each size. This includes, as the extreme cases, repairing immediately and not repairing at all. The DES model structure is designed to estimate the consequences of each of these options to reflect the need for management that is tailored to the characteristics and needs of each patient. The DES model informs the decision of when to repair using either open surgery or EVAR but not the decision about which method of repair. This latter decision should be made by the vascular surgeon and patient, not by the ARDA.

The DES uses baseline information about each patient, including age, sex, AAA diameter, comorbidities and blood results. Then, for each patient, the life course of the patient is simulated 100,000 times, starting from their current age and AAA diameter, to construct a distribution of the outcomes that the patient could experience. *Figure 13* gives an overview of the structure of the model.

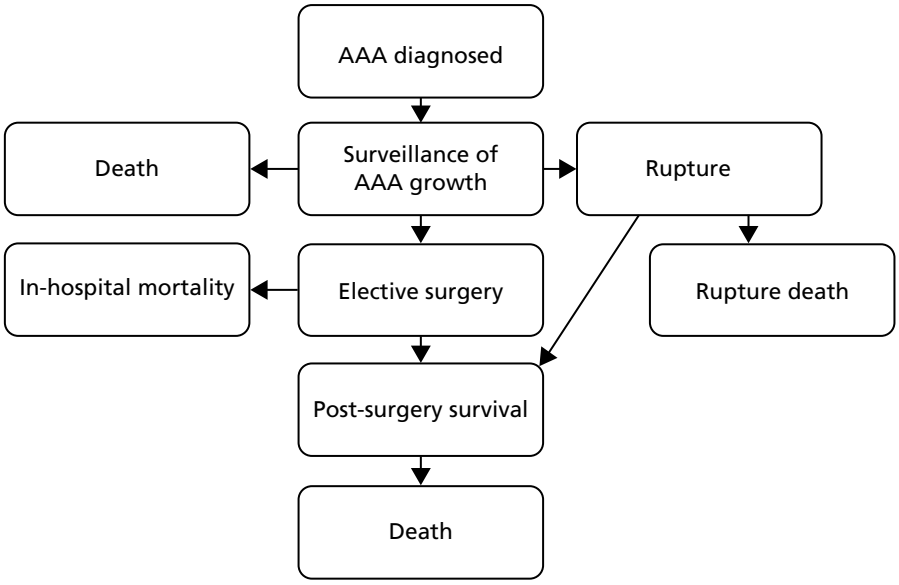


FIGURE 13 Overview of DES model structure.

The DES model starts with a patient with a specified initial age, AAA diameter, clinical and demographic characteristics. Unless a decision is made to repair the AAA immediately, the patient and AAA growth are then monitored through a surveillance programme (in the UK this is generally every 12 months for aneurysms less than 4.4 cm in diameter, after which surveillance is every 3 months). Between surveillance visits, the following events are included in the DES model:

- The patient gets older.
- The AAA grows.
- A rupture of the AAA may occur.
- The patient may die of other causes and exit the model.

The model loops to update the between surveillance events on a 3-monthly basis. At the next surveillance visit the size of the aneurysm may pass the threshold diameter for repair, when immediate repair is indicated.

For those people who have a ruptured AAA, a proportion will die before emergency treatment can be initiated or during emergency repair and will exit the model. Those people who survive emergency repair will then move to the post-surgery survival part of the model.

If the AAA is below the threshold diameter for repair at the surveillance visit, then the patient continues with regular surveillance. If the AAA is at or above the threshold diameter for repair at the surveillance visit, then elective surgery for AAA repair is indicated. Whether surgery is open or EVAR is a decision for the surgeon and patient and is not considered in the DES model of clinical effectiveness. For those patients having elective repair, there is a chance of dying during the inpatient admission. If a patient survives elective surgery and is discharged alive, they move into the post-surgery stage of the model. The patient then remains alive until their date of death (generated from the survival model described in *Chapter 6*) is reached.

Data sources and variable estimation

The DES model is based on the English surveillance programme of an outpatient visit and scan every 12 months until the aneurysm grows to 4.5 cm or more, after which surveillance is every 3 months. This schedule could be optimised,[47] and indeed the ARDA can incorporate different surveillance schedules. While the aneurysm is growing the patient remains under surveillance until a threshold diameter is reached.

The aneurysm grows at a random rate generated from the distributions reported by the RESCAN growth model for AAAs.[18] The growth rate used in the DES model is adjusted for patient characteristics such as smoking, diabetes and sex. Specifically, the growth rate is assumed to follow a normal distribution with a mean and SD derived from the 95% prediction intervals reported in the RESCAN studies and meta analysis.[18] This growth rate is recalculated annually. Annual growth rates are assumed to be independent. The RESCAN analysis[47] includes only growth rates up to an AAA diameter of 5.0 cm. Beyond this, growth rates in this DES model are extrapolated up to 6.0 cm and assumed constant beyond that. For the DES model the annual growth rates are calculated from *Table 18* as follows:

- At the beginning of each year, find the row in the table corresponding to the largest size that has yet been reached (e.g. current diameter = 3.3 cm, use row 3.0 cm; current diameter = 5.5 cm, use row 5.5 cm, current diameter = 6.5 cm, use row 6.0 cm).
- Generate total growth for the year as N [μ, σ^2 (mean and variance respectively)] with means and SDs derived from the table.
- Share this annual growth equally between the 12 months (as the algorithm updates in 3-month time steps).

While the aneurysm is growing, there is a risk of rupture. Rupture probability is also generated from the RESCAN model.[18] Following rupture it is assumed that the probability of mortality is 0.8, otherwise the patient survives emergency repair.[48] Information for rupture rates for small aneurysms comes from the RESCAN data,[18] which was then extrapolated for larger aneurysms. Rupture rates up to 5.0 cm come from table 1 of the RESCAN meta-analysis.[47] Extrapolation assumes rupture probability doubles every 0.5 cm size increase up to 6.5 cm, then switches to the given values for 7.0 cm and 8.0 cm.[49,50] The current data we use are shown in *Table 19*.

While the patient is managed by scheduled surveillance there is also the chance of death from other causes. This was estimated from the age of the patient while in surveillance. The age at 'other cause of death' was generated from the survival models detailed in *Chapter 6*. In this simulation, a patient is assumed to die at that age if he or she reaches that age before another terminal event.

When an AAA grows to a size that it should be repaired using the current intervention rule, and has been observed at that size in scheduled surveillance, the patient is assumed to undergo repair. Following repair, the probability of a perioperative death is calculated from the BAR score,[71] which is influenced by that patient's individual risk factors.

TABLE 18 Growth rates used in the ARDA

	Men		Women	
AAA diameter (cm)	Mean growth rate (cm)	SD	Mean growth rate (cm)	SD
3.0	1.28	0.569	1.46	0.73
3.5	1.86	0.518	1.98	0.63
4	2.44	0.487	2.51	0.533
4.5	3.02	0.513	3.06	0.452
5	3.61	0.592	3.62	0.423
5.5[a]	4.21[a]	0.592[a]	4.22[a]	0.423[a]
6[a]	4.81[a]	0.592[a]	4.82[a]	0.423[a]

a Extrapolated data.

TABLE 19 Rupture rates used in the ARDA

AAA diameter (cm)	Male rupture probability	Female rupture probability
0	0.0005	0.0022
3.5	0.0009	0.0045
4	0.0017	0.0079
4.5	0.0032	0.0147
5	0.0064	0.0297
5.5[a]	0.0128[a]	0.0594[a]
6[a]	0.0256[a]	0.1188[a]
6.5[a]	0.0512[a]	0.2376[a]
7	0.2	0.4
8	0.5	0.5

a Extrapolated data points.

A patient who survives repair remains alive until he or she reaches the age determined by our survival model (see *Chapter 6*).

In some patients, the AAA may never reach the size at which surgery is indicated. In this case, the patient simply dies at the time calculated from the survival model, without undergoing any procedure.

Summary of key assumptions

1. The growth of AAA is assumed to rise by 0.6 cm per year for aneurysms of 5.5–6.0 cm; the SD is assumed to the same as that for an AAA of 5.0 cm diameter. Aneurysm growth rates are assumed to be constant beyond 6.0 cm diameter.
2. The annual growth rate is assumed to be independent within a patient between years (given current size). For example, the growth rate in year 2 depends on the aneurysm size in year 2 but not the growth rate in year 1.
3. To estimate the risk of rupture, it was assumed that reported HRs approximate relative risks, that there is negligible uncertainty in rupture rates and that rupture rate doubles for each subsequent 0.5 cm AAA size beyond 5.0 cm.
4. It was assumed that the patient would have immediate surgery when the threshold AAA diameter is detected.
5. Two-year survival is assumed to be identical for both open surgery and EVAR. The simulations account for this by assuming that the additional perioperative mortality of open surgery is an 'acceleration' of a death that would have happened in the following 2 years had surgery not been undertaken.
6. It was assumed that death from other causes is independent of the AAA and its risk factors.
7. The estimates of in-hospital mortality derived from the BAR score model are accurate. Uncertainty in the parameters in the score was not factored into the DES model.
8. Long-term survival was assumed to be identical regardless of whether or not surgery has been undertaken. There is additional hazard of mortality pre surgery because of the risk of rupture and additional hazard of mortality per surgery driven by the BAR score.
9. It was assumed that a patient's specific risk factors do not change over time. This may not accurately reflect what would occur in routine practice. Operating on patients when they are younger, and thus healthier, may be a large source of benefit of early intervention. The ARDA could also be rerun when a patient's risk factors change.

10. The probability of rupture is calculated annually. At the end of each year, the aneurysm ruptures with the probability derived from the appropriate row of *Table 19*.
11. Growth rates per year are assumed to be normally distributed. Independence between years is currently assumed (e.g. faster than average growth this year does not mean faster than average growth next year) (see *Table 18*).

Results

The results of the DES model and the ARDA are summarised below for each of the eight vignettes evaluated, to allow the reader to assess the value of these outputs in clinical decision-making. The full output definitions are listed in *Appendix 7*. For each vignette a series of patient characteristics were selected. The outputs displayed from the ARDA for each vignette include a plot of median life expectancy based on the AAA size at intervention and a table showing all the outputs calculated by the ARDA. We then show an abbreviated table of outputs, likely to be most useful to surgeons and their patients.

Vignette A

Table 20 reports the patient demographic and clinical characteristics used in vignette A. In this vignette the DES model outputs are reported for two examples. The first is a person with an aneurysm of 4 cm diameter. The second is a person with the same characteristics but an aneurysm of 6.8 cm diameter.

TABLE 20 Patient characteristics for vignette A

Risk factor	Status
Initial age (years)	65
Initial AAA diameter (cm)	4.0/6.8
Sex	Male
Type of repair	Open
Cardiac disease	No
Abnormal ECG	No
Previous aortic surgery or stent	No
Smoker	No
Diabetes	No
BMI (kg/m^2)	30
Antiplatelet medication use	Yes
Statin use	Yes
Anaemia	No
WCC	Normal
Serum sodium	Normal
Serum creatinine	Normal
ASA grade	2

BMI, body mass index.

In this 65-year-old man with an AAA of 4 cm diameter, repair would not be indicated using the current guidelines based on size alone. Based on the AAA growth rate predicted from RESCAN data, it would take a mean of 5.5 years for this individual's aneurysm to reach the current threshold for intervention, with a risk of death due to rupture during that period of just 1% (*Table 21* and *Figure 14*). The patient's life expectancy remains largely unchanged if the repair is carried out at any size between 4.0 and 5.5 cm. The predicted risk of in-hospital death at the time of repair is 1% at both 4 and 5.5 cm but rises to 3% if surgery is delayed by a mean of 8 years until the aneurysm reaches 6.5 cm. The probabilities of survival to 1, 2, 5 and 10 years are all almost identical for repair at 4 cm and 5.5 cm.

Table 22 is based on the same reasonably fit but marginally overweight 65-year-old man but now assumes that his AAA at presentation was 6.8 cm.

Quite clearly, the patient's life expectancy is substantially enhanced if the AAA is repaired immediately compared with no repair, as are his probabilities of surviving for 1, 2, 5 and 10 years. If no repair is undertaken, there is a 64% chance that he will die as a result of aneurysm rupture. As he is young and fit, the risk of perioperative death is only 1%; this result is entirely supportive of our current clinical practice.

TABLE 21 Discrete event simulation model outputs for vignette A with initial AAA diameter of 4.0 cm

	Repair at						
Output	4.0 cm	4.5 cm	5.0 cm	5.5 cm	6.0 cm	6.5 cm	No elective repair
Median life expectancy (years)	76.92	76.95	76.87	76.83	76.81	76.68	75.50
1-year survival	0.97	0.97	0.97	0.97	0.97	0.97	0.97
2-year survival	0.94	0.94	0.94	0.94	0.94	0.94	0.94
5-year survival	0.83	0.83	0.82	0.83	0.83	0.83	0.83
10-year survival	0.60	0.60	0.60	0.60	0.59	0.58	0.51
Other cause of death (prior to repair)	0.00	0.08	0.13	0.19	0.24	0.29	0.53
Death due to rupture	0.00	0.00	0.00	0.01	0.01	0.02	0.38
Rupture survival	0.00	0.00	0.00	0.00	0.00	0.01	0.10
Postoperative survival	0.99	0.91	0.86	0.79	0.73	0.67	NA
Growth rate at size	0.24	0.30	0.36	0.42	0.48	0.48	NA
1-year rupture probability at intervention	0.00	0.00	0.00	0.00	0.01	0.02	NA
Probability of repair	1.00	0.92	0.87	0.81	0.75	0.69	NA
In-hospital mortality on repair	0.01	0.01	0.01	0.02	0.02	0.03	NA
5-year postoperative survival	0.84	0.79	0.76	0.72	0.69	0.65	NA
10-year postoperative survival	0.61	0.51	0.45	0.40	0.34	0.30	NA
Median age at repair (years)	65.00	68.00	69.00	70.50	71.75	73.00	NA
Median years to reach size	0.00	3.00	4.00	5.50	6.75	8.00	NA

NA, not applicable.

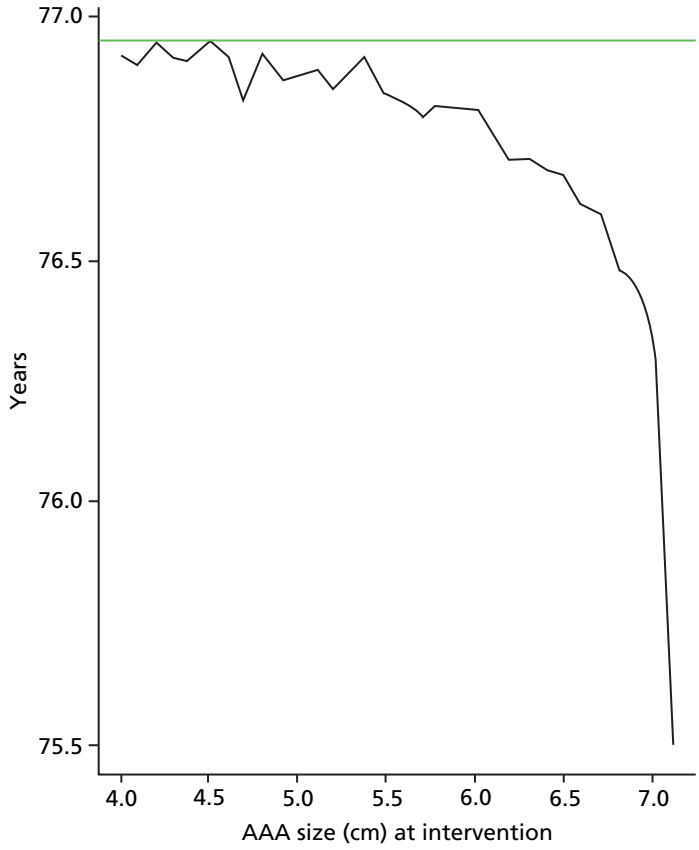


FIGURE 14 Median life expectancy: the ARDA outputs for vignette A with initial AAA diameter of 4.0 cm.

TABLE 22 Aneurysm Repair Decision Aid outputs for vignette A with initial AAA diameter of 6.8 cm

Output	Repair at 6.8 cm	No elective repair
Median life expectancy (years)	76.95	69.75
1-year survival	0.97	0.92
2-year survival	0.94	0.84
5-year survival	0.83	0.47
10-year survival	0.60	0.18
Other cause of death (prior to repair)	0.00	0.20
Death due to rupture	0.00	0.64
Rupture survival	0.00	0.16
Postoperative survival	0.99	NA
Growth rate at size	0.48	NA
1-year rupture probability at intervention	0.02	NA
Probability of repair	1.00	NA
In-hospital mortality on repair	0.01	NA
5-year postoperative survival	0.84	NA
10-year postoperative survival	0.61	NA
Median age at repair (years)	65.00	NA
Median years to reach size	0.00	NA

NA, not applicable.

Vignette B

Table 23 reports the patient demographic and clinical characteristics used in vignette B. In this vignette the DES model outputs are reported for two examples. The first is for a person with an aneurysm of 4 cm diameter. The second is for a person with the same characteristics but an aneurysm of 7.0 cm diameter.

This very different patient, aged 86 years, has an aneurysm that can be repaired by EVAR, but he also has a number of important comorbidities including a history of cardiac disease and a raised serum creatinine. As a result, his ASA grade is 4 and the ARDA predicts a risk of perioperative death of 7% in the case of immediate repair, but rising to 11% if we wait until his AAA reaches 5.5 cm. The outputs of the ARDA (*Table 24*) suggest that there is no benefit in elective repair compared with no elective repair at any aneurysm size.

TABLE 23 Patient characteristics for vignette B

Risk factor	Status
Initial age (years)	86
Initial AAA diameter (cm)	4.0/7.0
Sex	Male
Type of repair	EVAR
Cardiac disease	Yes
Abnormal ECG	Yes
Previous aortic surgery or stent	No
Smoker	No
Diabetes	No
BMI (kg/m^2)	25
Antiplatelet medication use	Yes
Statin use	No
Anaemia	No
WCC	Normal
Serum sodium	Normal
Serum creatinine	Abnormal
ASA grade	4

BMI, body mass index.

TABLE 24 Aneurysm Repair Decision Aid model outputs for vignette B with initial AAA diameter of 4.0 cm

Output	Repair at						No elective repair
	4.0 cm	4.5 cm	5.0 cm	5.5 cm	6.0 cm	6.5 cm	
Median life expectancy (years)	88.74	88.95	89.00	89.00	89.00	89.00	89.00
1-year survival	0.75	0.81	0.81	0.81	0.81	0.81	0.81
2-year survival	0.60	0.62	0.64	0.64	0.64	0.64	0.64
5-year survival	0.26	0.25	0.25	0.27	0.27	0.27	0.27
10-year survival	0.03	0.03	0.03	0.03	0.03	0.03	0.02
Other cause of death (prior to repair)	0.00	0.44	0.62	0.76	0.84	0.89	0.94
Death due to rupture	0.00	0.00	0.01	0.01	0.01	0.02	0.05
Rupture survival	0.00	0.00	0.00	0.00	0.00	0.00	0.01
Postoperative survival	0.93	0.51	0.34	0.21	0.12	0.08	NA
Growth rate at size	0.24	0.30	0.36	0.42	0.48	0.48	NA
1-year rupture probability at intervention	0.00	0.00	0.01	0.01	0.03	0.06	NA
Probability of repair	1.00	0.59	0.44	0.31	0.25	0.22	NA
In-hospital mortality on repair	0.07	0.09	0.10	0.11	0.13	0.14	NA
5-year postoperative survival	0.28	0.20	0.16	0.12	0.10	0.07	NA
10-year postoperative survival	0.04	0.02	0.00	0.00	0.00	0.00	NA
Median age at repair (years)	86.00	89.00	90.00	91.50	92.75	93.75	NA
Median years to reach size	0.00	3.00	4.00	5.50	6.75	7.75	NA

NA, not applicable.

The results shown in *Table 25* refer to the same 86-year-old man outlined in vignette B, but this time assuming that he has presented with an aneurysm 7.0 cm in diameter. As seen in *Table 25*, his probabilities of surviving 1 year and 2 years are higher if he does undergo repair even though repair is associated with a 10% risk of mortality. In this vignette, the risk of rupture within 12 months is calculated at 22%, which is clearly greater than the risk associated with EVAR. However, even following repair, his life expectancy is only an average of 2.6 years. Quite clearly, an 86-year-old man may decide that he does not want to undergo aneurysm repair.

Vignette C

Table 26 reports the patient demographic and clinical characteristics used in vignette C. In this vignette the DES model outputs are reported for two examples. The first is for a person with an aneurysm of 3.8 cm diameter. The second is for a person with the same characteristics but an aneurysm of 5.2 cm diameter.

This vignette assumes a woman aged 70 years. She has an abnormal ECG and is obese with a body mass index (BMI) of 35 kg/m^2. She takes both platelet inhibitory therapy and a statin and has normal full blood count and abnormal serum sodium. The risk of rupture is only 1% if repair is delayed until AAA diameter reaches 4.5 cm. As her risk of in-hospital death is estimated to be 7–8% at the age of 70 or 71 years, but rises to 11% at the age of 74 years, her life expectancy is marginally increased (by approximately 4 months) by repairing this AAA before it reaches 4.5 cm (*Table 27*). As she is obese, her surgeon may advise her to take regular exercise and to diet with a view to losing as much weight as possible in the year before her AAA reaches 4 cm in diameter. Her risk of perioperative death would drop substantially if she were fitter and reduced her weight such that her BMI is below 30 kg/m^2.

TABLE 25 Aneurysm Repair Decision Aid model outputs for vignette B with initial AAA diameter of 7.0 cm

Output	Repair at 7.0 cm	No elective repair
Median life expectancy (years)	88.62	87.75
1-year survival	0.73	0.66
2-year survival	0.58	0.43
5-year survival	0.25	0.06
10-year survival	0.03	0.01
Other cause of death (prior to repair)	0.00	0.37
Death due to rupture	0.00	0.51
Rupture survival	0.00	0.13
Postoperative survival	0.90	NA
Growth rate at size	0.48	NA
1-year rupture probability at intervention	0.22	NA
Probability of repair	1.00	NA
In-hospital mortality on repair	0.10	NA
5-year postoperative survival	0.28	NA
10-year postoperative survival	0.04	NA
Median age at repair (years)	86.00	NA
Median years to reach size	0.00	NA

NA, not applicable.

TABLE 26 Patient characteristics for vignette C

Risk factor	Status
Initial age (years)	70
Initial AAA diameter (cm)	3.8/5.2
Sex	Female
Type of repair	Open
Cardiac disease	No
Abnormal ECG	Yes
Previous aortic surgery or stent	No
Smoker	No
Diabetes	No
BMI (kg/m^2)	35
Antiplatelet medication use	Yes
Statin use	Yes
Anaemia	No
WCC	Normal
Serum sodium	Abnormal
Serum creatinine	Normal
ASA grade	3

BMI, body mass index.

TABLE 27 Aneurysm Repair Decision Aid model outputs for vignette C with initial AAA diameter of 3.8 cm

Output	Repair at							No elective repair
	3.8 cm	4.0 cm	4.5 cm	5.0 cm	5.5 cm	6.0 cm	6.5 cm	
Median life expectancy (years)	77.28	77.22	77.16	76.92	76.50	77.00	77.25	77.25
1-year survival	0.90	0.90	0.94	0.94	0.94	0.94	0.94	0.94
2-year survival	0.86	0.81	0.87	0.87	0.87	0.87	0.87	0.87
5-year survival	0.66	0.65	0.62	0.61	0.65	0.65	0.65	0.66
10-year survival	0.32	0.32	0.32	0.32	0.31	0.30	0.24	0.26
Other cause of death (prior to repair)	0.00	0.10	0.24	0.34	0.44	0.53	0.60	0.76
Death due to rupture	0.00	0.00	0.01	0.01	0.02	0.03	0.05	0.19
Rupture survival	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.05
Postoperative survival	0.93	0.83	0.66	0.55	0.43	0.32	0.23	NA
Growth rate at size	0.20	0.25	0.31	0.36	0.42	0.48	0.48	NA
1-year rupture probability at intervention	0.00	0.00	0.00	0.01	0.02	0.03	0.07	NA
Probability of repair	1.00	0.91	0.78	0.70	0.62	0.57	0.55	NA
In-hospital mortality on repair	0.07	0.08	0.11	0.14	0.19	0.25	0.32	NA
5-year postoperative survival	0.70	0.66	0.60	0.57	0.52	0.51	0.49	NA
10-year postoperative survival	0.35	0.29	0.21	0.17	0.13	0.11	0.09	NA
Median age at repair (years)	70.00	71.00	74.00	75.00	76.50	77.75	79.00	NA
Median years to reach size	0.00	1.00	4.00	5.00	6.50	7.75	9.00	NA

NA, not applicable.

Table 28 and *Figure 15* assume the same woman aged 70 years in vignette C, but her aneurysm is now 5.2 cm. As might be expected, the ARDA calculates her optimal life expectancy if the repair is undertaken immediately, with the probabilities of surviving to 1, 2 and 5 years all higher than if repair is delayed or if the no elective repair decision is taken. In this case, her predicted risk of perioperative death would be 8%. She and her surgeon would have a difficult decision over whether or not it was appropriate and safe to delay surgery for 3–4 months while she pursues a diet and exercise programme with a view to weight loss. Her risk of perioperative death could be reduced if she were able to decrease her weight, although obviously this would be a challenge in only 3 months. However, as the annual risk of rupture is only 1%, a well-motivated 70-year-old woman may decide to pursue an exercise programme and to diet with a view to weight reduction.

Vignette D

Table 29 reports the patient demographic and clinical characteristics used in vignette D. In this vignette the DES model outputs are reported for two examples. The first is for a person with an aneurysm of 4.8 cm diameter. The second is for a person with the same characteristics but an aneurysm of 6.5 cm diameter.

This vignette assumes an 80-year-old man who is fit in every way with the single exception of being a little overweight, with a BMI of 30 kg/m^2. He is ASA grade 2 and his risk of in-hospital death is predicted to be 0.4%. Under these circumstances, his life expectancy is optimised by repairing this AAA early, although there is no important difference in life expectancy if the repair is delayed until the diameter of his

TABLE 28 Aneurysm Repair Decision Aid model outputs for vignette C with initial AAA diameter of 5.2 cm

Output	Repair at				No elective repair
	5.2 cm	5.5 cm	6.0 cm	6.5 cm	
Median life expectancy (years)	77.28	77.20	77.03	76.77	75.50
1-year survival	0.89	0.85	0.93	0.93	0.93
2-year survival	0.86	0.82	0.84	0.85	0.85
5-year survival	0.66	0.65	0.64	0.60	0.53
10-year survival	0.32	0.32	0.31	0.30	0.13
Other cause of death (prior to repair)	0.00	0.06	0.14	0.22	0.51
Death due to rupture	0.00	0.01	0.02	0.05	0.39
Rupture survival	0.00	0.00	0.01	0.01	0.10
Postoperative survival	0.92	0.85	0.74	0.62	NA
Growth rate at size	0.36	0.42	0.48	0.48	NA
1-year rupture probability at intervention	0.01	0.02	0.03	0.07	NA
Probability of repair	1.00	0.94	0.85	0.76	NA
In-hospital mortality on repair	0.08	0.09	0.11	0.14	NA
5-year postoperative survival	0.71	0.69	0.65	0.63	NA
10-year postoperative survival	0.35	0.31	0.26	0.23	NA
Median age at repair (years)	70.00	71.00	72.25	73.50	NA
Median years to reach size	0.00	1.00	2.25	3.50	NA

NA, not applicable.

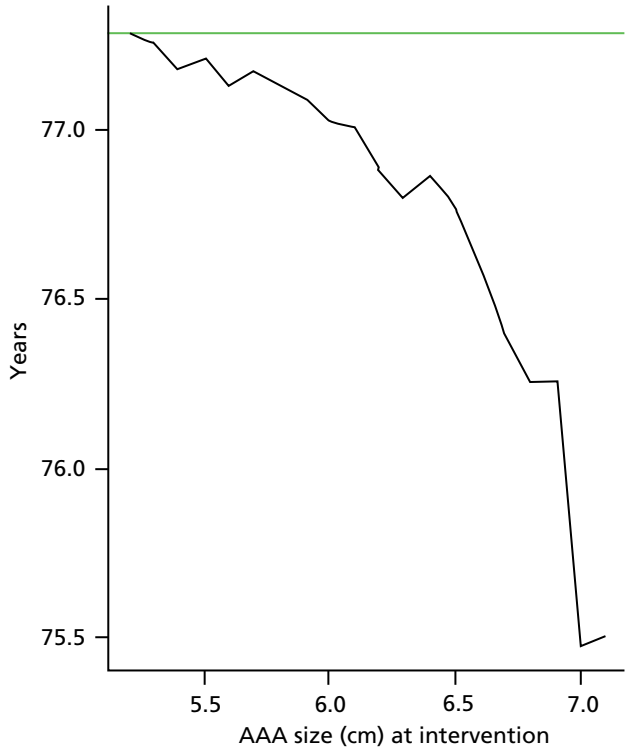


FIGURE 15 Median life expectancy: the ARDA model outputs for vignette C with initial AAA diameter of 5.2 cm.

TABLE 29 Patient characteristics for vignette D

Risk factor	Status
Initial age (years)	80
Initial AAA diameter (cm)	4.8/6.5
Sex	Male
Type of repair	EVAR
Cardiac disease	No
Abnormal ECG	No
Previous aortic surgery or stent	No
Smoker	No
Diabetes	No
BMI (kg/m^2)	30
Antiplatelet medication use	Yes
Statin use	Yes
Anaemia	No
WCC	Normal
Serum sodium	Normal
Serum creatinine	Normal
ASA grade	2

aneurysm is 5.5 cm or more (*Table 30* and *Figure 16*). The probabilities of the patient surviving for 1, 2, 5 and 10 years are all identical in both cases, with only a small deterioration if repair is delayed until the AAA reaches 5.5 cm. Again, this patient and his surgeon may conclude that repair could be delayed until a time convenient for them both. There is the opportunity to improve his general fitness although any improvement in his fitness would have only a marginal effect on perioperative risk.

This final example again refers to the 80-year-old man in vignette D but now assumes that the initial AAA diameter was 6.5 cm. Under these circumstances, the patient's optimal life expectancy is achieved by immediate repair, with the probabilities of surviving for 1, 2, 5 and 10 years all better than would be achieved by no repair (*Table 31*). The anticipated risk of perioperative death is only 0.5%. This verifies our current indication for repair of an AAA at 5.5 cm in diameter for a man of this age.

Summary

The ARDA allows individualised evaluation of the relative benefits of undergoing surgery for AAA at various intervention points. The main strength of this algorithm is that it incorporates information from all stages of the clinical pathway from the growth of the AAA, through to repair, and long-term survival following the intervention. The simulation approach means that CI and other uncertainty measures can be incorporated into the decision being made by patients and their surgeons.

The particular strength of the ARDA is that it is designed to be used at each surveillance stage. Where the ARDA shows that there is no need to repair an AAA, it is not necessary for the patient or the surgeon to decide at what size this AAA should be repaired. The surgeon can advise on an approximate time that the patient may require surveillance, but does not need to indicate the aneurysm size at which a repair should be undertaken. It would not be appropriate to assume that the patient characteristics will be the same in

TABLE 30 Aneurysm Repair Decision Aid model outputs for vignette D with initial AAA diameter of 4.8 cm

Output	Repair at					No elective repair
	4.8 cm	5.0 cm	5.5 cm	6.0 cm	6.5 cm	
Median life expectancy (years)	86.65	86.62	86.56	86.48	86.34	85.75
1-year survival	0.92	0.92	0.92	0.92	0.92	0.92
2-year survival	0.85	0.84	0.84	0.85	0.85	0.85
5-year survival	0.62	0.62	0.61	0.61	0.59	0.59
10-year survival	0.29	0.29	0.28	0.28	0.27	0.09
Other cause of death (prior to repair)	0.00	0.06	0.18	0.27	0.36	0.58
Death due to rupture	0.00	0.00	0.01	0.02	0.03	0.33
Rupture survival	0.00	0.00	0.00	0.00	0.01	0.09
Postoperative survival	1.00	0.93	0.81	0.71	0.60	NA
Growth rate at size	0.30	0.36	0.42	0.48	0.48	NA
1-year rupture probability at intervention	0.00	0.00	0.01	0.02	0.03	NA
Probability of repair	1.00	0.94	0.82	0.71	0.61	NA
In-hospital mortality on repair	0.004	0.004	0.005	0.006	0.007	NA
5-year postoperative survival	0.62	0.60	0.55	0.51	0.47	NA
10-year postoperative survival	0.29	0.26	0.21	0.17	0.14	NA
Median age at repair (years)	80.00	80.75	82.25	83.50	84.75	NA
Median years to reach size	0.00	0.75	2.25	3.50	4.75	NA

NA, not applicable.

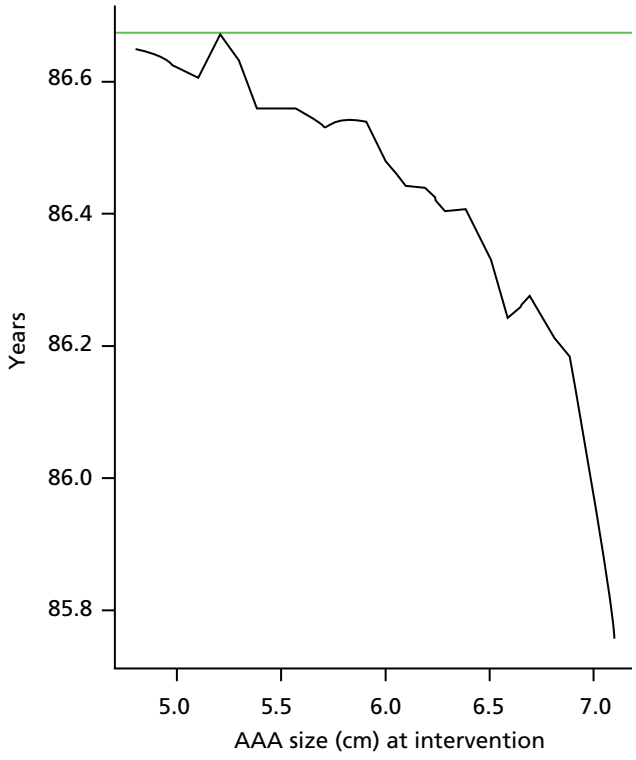


FIGURE 16 Median life expectancy: the ARDA model outputs for vignette D with initial AAA diameter of 4.8 cm.

TABLE 31 Aneurysm Repair Decision Aid model outputs for vignette D with initial AAA diameter of 6.5 cm

Output	Repair at 6.5 cm	No operation
Median life expectancy	86.65	83.75
1-year survival	0.92	0.90
2-year survival	0.85	0.74
5-year survival	0.62	0.27
10-year survival	0.29	0.06
Other cause of death (prior to repair)	0.00	0.31
Death due to rupture	0.00	0.55
Rupture survival	0.00	0.14
Postoperative survival	1.00	NA
Growth rate at size	0.48	NA
1-year rupture probability at intervention	0.03	NA
Probability of repair	1.00	NA
In-hospital mortality on repair	0.005	NA
5-year postoperative survival	0.62	NA
10-year postoperative survival	0.29	NA
Median age at repair (years)	80.00	NA
Median years to reach size	0.00	NA

NA, not applicable.

6 or 12 months. A patient may gain weight, lose weight, suffer a MI, develop angina or develop diabetes in the intervening period. The surgeon and patient merely need to conclude that surveillance should be undertaken in 3, 6 or 12 months as appropriate and to rerun the ARDA at that time. Repair can be scheduled when the ARDA indicates that it is appropriate. A particular advantage of the ARDA is that it provides a wealth of information that can be only vaguely estimated when surgeons talk their patients. The summary ARDA output allows the surgeon to discuss the probability of 1-, 5- and 10-year survival with and without repair. We can indicate the risk of rupture if a repair is not undertaken and can tell a patient how likely it is that a repair would be necessary in any event (at the standard current indication). Finally, the BAR score allows the surgeon to discuss perioperative mortality with greater accuracy than previously.

As the ARDA calculates that only marginal benefit results from repairing smaller AAAs when compared with repair at the current indication (5.5 cm in men and 5.0 cm in women), the patient and surgeon may conclude that taking time to optimise fitness and to reduce the risk of perioperative mortality might be the ideal strategy. Patients also have the choice to delay surgery during this interval, when the AAA is still smaller than the current indication, for reasons of convenience such as holiday or work commitments. On the other hand, a patient may decide that they wish to undergo repair sooner rather than wait until the AAA diameter reaches the current threshold for intervention to reduce anxiety associated with having an AAA. The ARDA provides a range of information to support the patient and their surgeon in making this important decision and optimising care.

Chapter 8 Economic evaluation: methods

Approach

An economic model was used to synthesise clinical and economic data to estimate the incremental cost per unit of outcome of undertaking elective repair at the indication identified by the ARDA. The comparator was the current guideline to repair when the aneurysm reaches 5.0 cm (women) or 5.5 cm (men) diameter. Standard practice also includes informal consideration by the surgeon of other factors such as age and fitness/readiness for surgery. The perspective taken was that of the NHS and social care providers and patients. This viewpoint reflects that recommended by the National Institute for Health and Care Excellence (NICE)[72] and comprises the key components of a societal perspective.

The measure of health benefit for the primary analysis was the quality-adjusted life-year (QALY). Using life-years gained (LYGs) as the measure, health benefit was included in two of the sensitivity analyses.

For the primary analysis, the model estimated the incremental cost-effectiveness ratio (ICER) associated with intervening at the aneurysm size identified by the ARDA as maximising QALYs gained. Sensitivity analysis assessed the ICER if the algorithm was used to minimise costs and whether or not this would change the recommended timing of surgery. Additional sensitivity analyses assessed the impact on the ICER using a number of cost sources including the minimum and maximum costs reported in the NHS reference costs.[73] The time horizon for the model is lifetime from identification of the AAA to death from any cause. The lifetime impact was discounted at 3.5% as recommended by NICE.[72]

Economic model

Population

The population for the model is people with a confirmed AAA, the size of which is below current thresholds for surgery or who present with an AAA at or above the current thresholds for surgery. As with the clinical effectiveness analysis, this population is characterised by eight vignettes that describe typical patients eligible for elective surgical repair (see *Chapter 7*).

Model structure

The DES model developed for the clinical effectiveness analysis (see *Chapter 7*) was used as the basis for the analysis of the relative cost-effectiveness of repair at the indication recommended by the ARDA. The overall model structure and processes were not changed. The cost and utility values associated with events in the model were added to estimate net costs and QALYs. *Figure 17* shows the points at which cost and utility data were added to the model structure.

Embedded within the cost calculations are a number of decision trees. *Figure 18* indicates the pathway for cost estimation for those people whose AAA ruptures and who die at some point between the rupture and postoperative follow-up. *Figure 19* indicates the pathway for estimation of the costs of adverse events (complications and reinterventions) following elective or emergency surgery. The total number of reinterventions and the discount year that applies to each reintervention are calculated by running a once-monthly check for whether or not a reintervention has occurred for the first 6 months after surgery and an annual check thereafter. These checks continue until death. The total number of possible reinterventions is not capped.

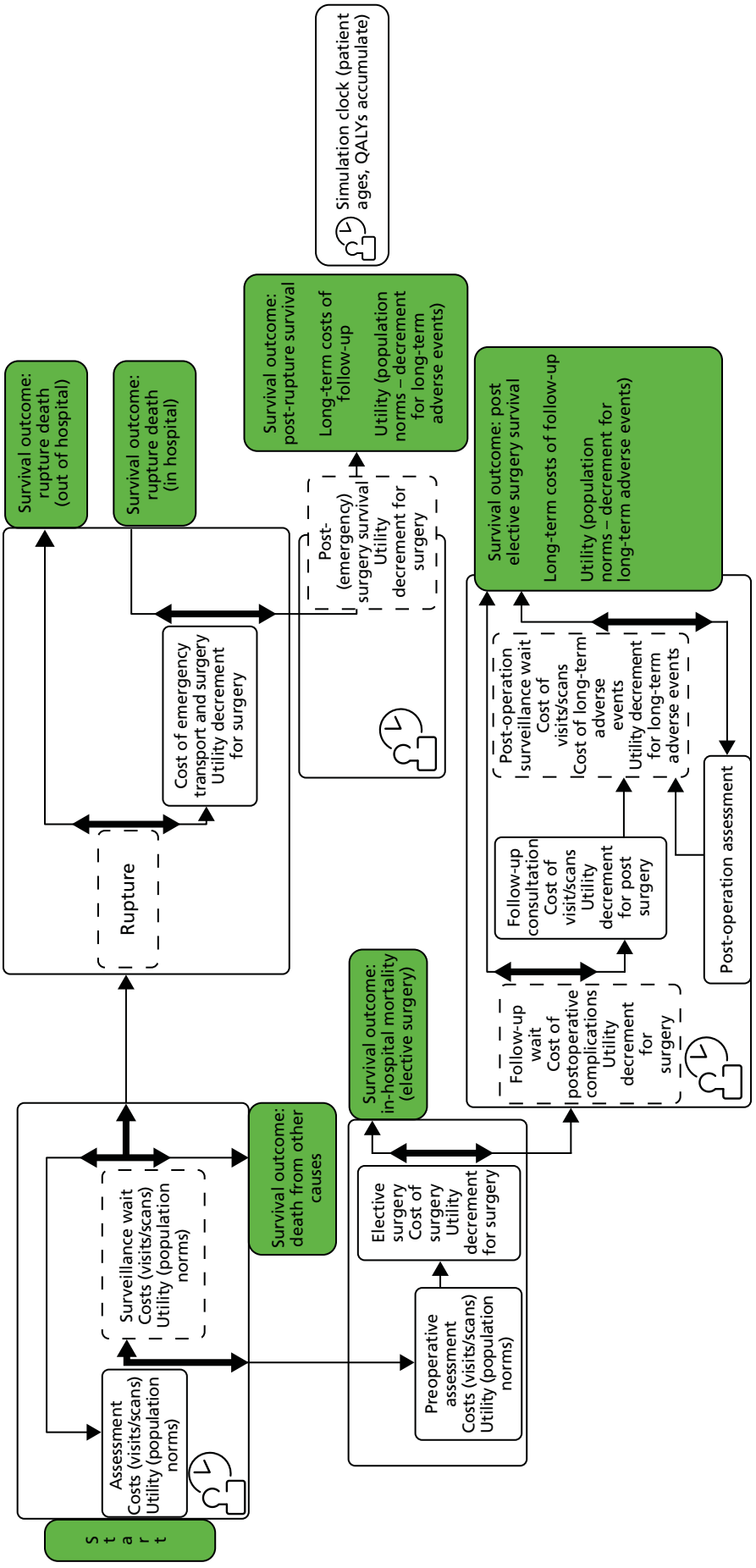


FIGURE 17 Abdominal aortic aneurysm DES model structure adapted for health economic analysis. Dashed border, queue; solid border, activity; solid green boxes, start point/end point.

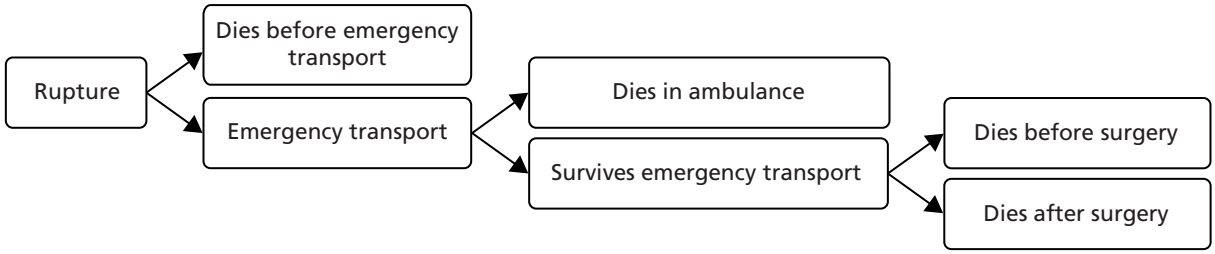


FIGURE 18 Pathway following AAA rupture for those who die following rupture.

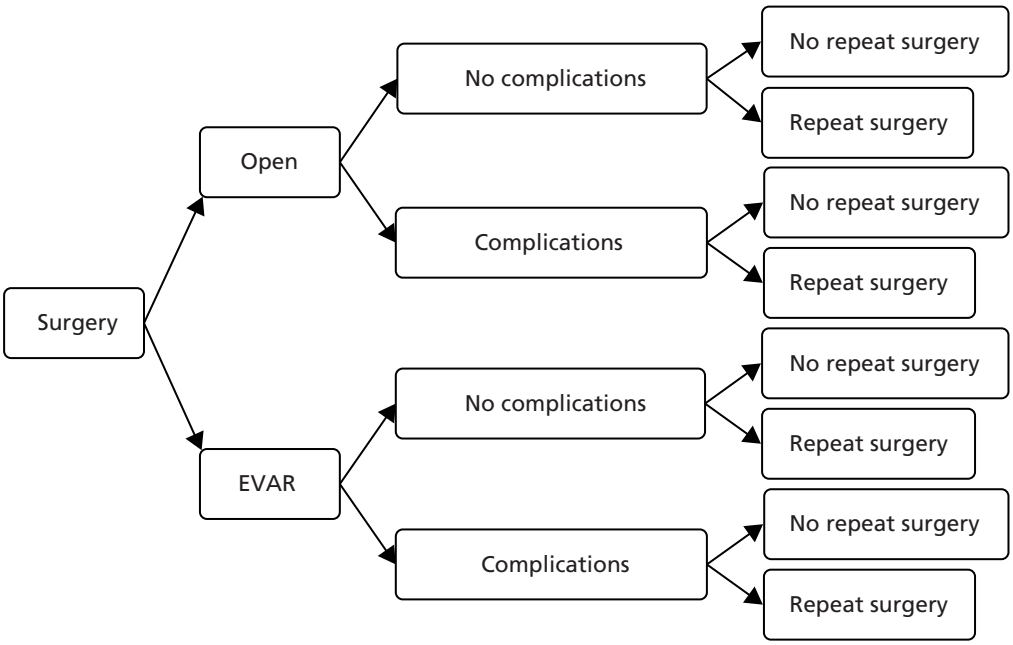


FIGURE 19 Complications and reinterventions following surgery.

Data inputs

The clinical and probability data for the DES model to estimate LYGs are described in *Chapter 7*. AAAs can be treated by open surgical repair or EVAR, and in routine practice the surgeon/patient decision to intervene is made when the risk of repair is considered to be less than the risk of rupture.[74] RCTs have been conducted to compare treatment methods for AAA, with mixed results.[75–78] Cost, utility and cost-effectiveness data have been published for RCTs of AAA repair.[79–81] A number of studies have also explored the costs and outcomes of preoperative surveillance.[82,83] However, less is known about the costs and utilities associated with preoperative assessments and postoperative care. In addition, the existing evidence is primarily from trial settings and patient samples, which may be atypical of those in routine care, collected over a limited follow-up period. These factors mean that the results may not reflect the longer-term costs and outcomes found in routine care.

The clinical algorithm developed and assessed for this project is intended for use in a range of settings. For this reason it is important to assess the costs associated with AAA surveillance and repair in standard care settings. Cost and utility data for the economic model were identified from a focused systematic review of published economic evaluations and population norms for utility values, review of the NHS reference cost data set and a prospective study of patient records held in the VGNW programme.

Systematic review

A focused electronic search was conducted in the Centre for Reviews and Dissemination NHS Economic Evaluations Database (EED) to identify studies that reported service use and/or costs related to AAA surveillance, assessment, repair and postoperative follow-up and utility values associated with these events. This database uses a robust, sensitive search of published literature to identify studies that report economic data[84] and is updated weekly.[85] Given the detailed searches used to identify studies for the NHS EED database, a simple search strategy was used to identify relevant studies for this part of the project. The terms 'aneurysm' and 'aortic' were combined using 'AND'. An initial search indicated that key journal papers already identified for the clinical evaluation and/or known to the authors were identified. However, two reports and monographs published by HTA agencies that were known to the research team were not identified. Accordingly, the search was extended to include the Centre for Reviews and Dissemination HTA database. In addition, the following sources were searched to identify costs and/or utilities of relevant events: published UK data sets (NHS national schedule of reference costs;[73] Personal Social Services Research Unit costs),[86] the EuroQOL website (http://www.euroqol.org/home.html) and NICE technology appraisals.

The technologies for AAA surveillance and repair have evolved in recent years, at the same time as changes to the organisation and provision of health-care services. To take these changes into account and identify data relevant to current practice, the search was restricted to studies published between January 2004 and April 2014. The search was conducted in October 2012 and rerun between February and April 2014. The identified titles and abstracts were reviewed by two researchers (DN and LMD). Predefined inclusion and exclusion criteria were used to select studies for service use and cost data extraction. The inclusion criteria were as follows:

- The study was focused on the surveillance, repair or assessment of AAA.
- The study included any of the following economic data for use in the economic model: details of patient service use or costs; utility values.
- The study was based on primary data collection or systematic review of observational studies.
- The study included data other than charge data used and/or reported resource use or costs relevant to the UK setting.
- Sufficient detail was reported to extract costs and utility values relevant to short- and long-term events related to AAA to populate the economic model.

The data were extracted on pre-defined forms by one researcher (see *Appendix 8*). Descriptive statistics (mean, SD, 95% CI) were used to summarise the data and to derive average values and distributions for the events in the economic model.

Vascular Governance North West programme

The VGNW database is approved by the National Research Ethics Service (09/H1010/2) to gather clinical and service use data about vascular procedures including AAA repair for the purposes of research. The VGNW covers secondary and tertiary care services in the north-west of England and Wales and is part of the NVD. The VGNW team collect data prospectively and check for completeness retrospectively by reviewing patient notes and hospital administrative systems.

A review was done of 118 VGNW patients who received elective treatment for AAA in the north-west of England between January 2009 and April 2012 to gather additional service use information. Pilot data were collected to assess the availability and influence of costing data identified in a systematic review of the cost-effectiveness of AAA repair.[87] After review of initial pilot data, a standard proforma (see *Appendix 9*) was designed to capture preoperative, perioperative and postoperative appointments, scans, and procedures clinically associated with the AAA repair. Data were collected from a mix of district general

and university hospitals by the VGNW team. This cohort is demographically representative of patients in the VGNW database. There was no statistical difference between the age (73.5 years vs. 72.3 years) and proportion of female patients (16.5% vs. 17.8%) in the two populations. The period of interest is from diagnosis of AAA to December 2012. The service use for each patient was multiplied by the relevant unit cost to estimate the costs of events. The unit costs of services were derived from the NHS national schedule of reference costs (2012–13).[73]

The costs of preoperative assessment and preparation for AAA repair and the costs of postoperative follow-up included inpatient admissions, scans and outpatient clinic visits. The costs of scans and outpatient clinic visits were estimated by multiplying the number of visits for scans and assessment appointments by the relevant unit cost. Admissions to hospital for procedures in preparation for AAA repair or needed following AAA repair were estimated in two stages. First, for admissions with a similar length of stay (LOS) to that reported in the NHS reference costs,[73] the observed patient LOS was multiplied by the average unit cost per day. Second, for stays longer than the mean LOS, excess bed-day costs associated with the procedure were applied. The total preoperative and postoperative follow-up cost for each patient was estimated.

Each patient admission for an AAA repair was matched with an associated NHS national schedule of reference cost procedure. This involved classification of open procedures as with or without complication and EVAR procedures by graft type. The admission was costed in the same way as preoperative and postoperative admissions.

Descriptive statistics (mean, SD, 95% CI) were used to summarise the data and to derive average values and distributions for the events in the economic model. The data from VGNW were used to derive costs for preoperative assessment and postoperative follow-up events, to supplement data from the systematic review for the primary analysis. In addition, the VGNW average cost of elective EVAR or open repair was used in the sensitivity analysis.

Analysis of economic model

A probabilistic sensitivity analysis was conducted for the primary analysis and each of the sensitivity analyses. This approach takes into account the uncertainty inherent in each of the estimates of the probability, cost and outcomes associated with the model events and pathways. DES with 100,000 iterations was used to estimate the (expected) costs and outcomes for the probabilistic sensitivity analyses. As described in *Chapter 7*, the DES samples random pathways and the distribution of possible values for each parameter in the decision model. This means that mean costs and outcomes, and measures of variance (standard deviation and 95% CIs) can be estimated to assess the uncertainty inherent in the data used for the model.

These simulated data were used for a cost-effectiveness acceptability analysis. The cost-effectiveness acceptability analysis estimated the probability that undertaking repair at the aneurysm size identified by the ARDA as maximising QALYs gained was cost-effective compared with the current guidelines. This is an approach recommended by NICE for health technology appraisals.[72] The approach revalues effects or outcomes in monetary terms. However, in the UK there is no universally agreed monetary value for the types of outcome measures used in cost-effectiveness analyses. An approach used in health care is to ask the question: what is the maximum amount decision-makers are willing to pay to gain 1 unit of outcome? An analysis of decisions made by NICE suggests a range of implicit values between £15,000 and £30,000 for the amount a decision-maker is prepared to pay to gain 1 QALY.[88]

For this analysis, the outcomes were revalued using a range of maximum willingness-to-pay values from £1 to £50,000 to gain 1 QALY or 1 life-year (LY). These reflect a range of hypothetical willingness-to-pay thresholds (WTPTs) from decision-makers being willing to pay £1 to gain 1 QALY or 1 LY to them being willing to pay £50,000 to gain 1 QALY or 1 LY. The data for the cost-effectiveness acceptability curve (CEAC) are derived by first revaluing each of the 100,000 net outcomes from the simulation by a single WTPT. This is repeated for each WTPT. A net benefit (NB) statistic for each pair of simulated net costs and net outcomes for each WTPT can then be calculated as

$$\mathrm{NB} = (O \times \mathrm{WTPT}) - C, \quad (1)$$

where O = net outcome score and C = net cost. This calculation was repeated for each WTPT. CEACs plot the proportion of simulations in which the NB of an intervention is greater than zero for each WTPT.[89–92]

Sensitivity analysis and key assumptions

One-way and multiple-way sensitivity analyses, varying the measure of health benefit, cost and utility estimates were used to identify whether or not changes would affect the conclusions of the primary analysis. The costs, effects, ICERs and CEACs were re-estimated for each sensitivity analysis. Probabilistic sensitivity analysis was used to assess parameter uncertainty for each of the sensitivity analyses.

A number of simplifying assumptions were used for the primary analysis and these were explored in the sensitivity analyses. It was assumed that the new clinical algorithm would change the timing of surgery but not affect the long-term likelihood of stroke and other disabling events that occur after the postoperative period. This is similar to the approach used in recent UK economic models of the long-term costs of EVAR repair,[79,80] although earlier economic models did include the cost and utility impact of non-fatal stroke and MI.[93] The impact of excluding long-term incidence of disability was explored in the sensitivity analyses by increasing the long-term follow-up costs and adding a decrement to utility. Published population norms and trial data for utility values are available for age bands, rather than by year of age. In addition, the published utility data are not sufficiently detailed to derive utility values for each vignette that are specific to characteristics other than age band and sex. Accordingly, the model assumes that the published utility data for age band and sex adequately reflect the likely utility value for the patients' underlying health status in each vignette. In addition, it is assumed that the average decrements due to surgery are applicable to each of the vignettes. Again, this assumption was tested by varying utility values for each vignette to assess whether or not changes affected the probability that the new clinical algorithm was cost-effective.

Chapter 9 Economic evaluation: data inputs and results

Data inputs

Systematic review

The number of economic studies identified by the search of Centre for Reviews and Dissemination NHS EED, screened and excluded is shown in *Figure 20*. Three additional sources of utility data were identified from the reference lists of papers found by the electronic search.[76,94,95] Costs of hospital visits and admissions were extracted from the NHS reference cost database for 2012/13.[73] Full references of identified papers and a summary of included papers and data extracted are reported in *Appendices 8* and *10*. The derived parameter estimates of utility and cost values are reported in *Table 32*.

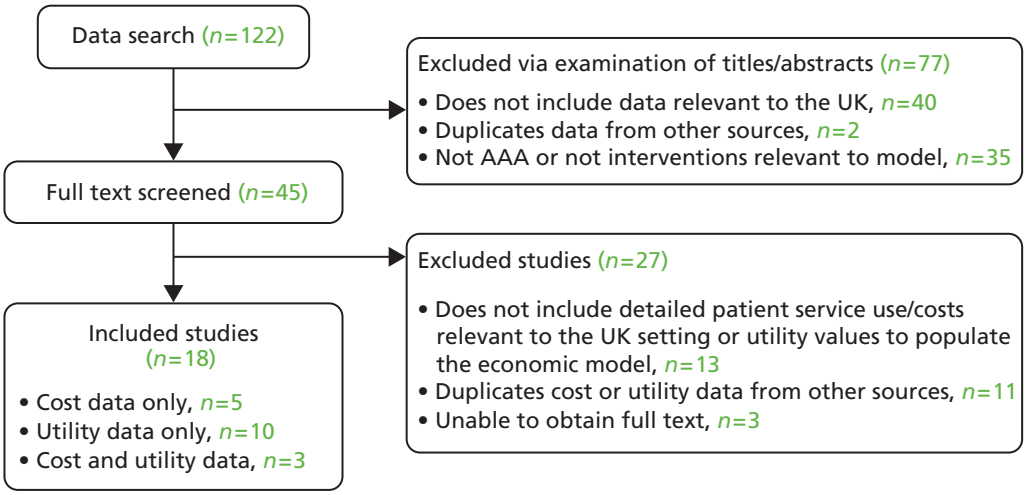


FIGURE 20 Flow diagram of economic studies identified by search of Centre for Reviews and Dissemination NHS EED (excluding duplicate records).

TABLE 32 Perioperative and total hospital preoperative and postoperative costs, 2012–13

	EVAR		Open		All patients	
LOS and costs	*n*	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
VGNW LOS (days)	57	5.95 (4.63)	61	13.16 (9.59)	118	9.68 (8.40)
National LOS (days)[a]	57	3.77 (NA)	61	9.26 (NA)	118	6.61 (NA)
VGNW perioperative costs (£)	57	12,440 (2751)	61	13,380 (4820)	118	12,930 (3970)
National perioperative costs (£)[a]	57	11,856 (NR)	61	9365 (NR)	118	10,569 (NR)
VGNW total preoperative, perioperative and postoperative costs (£)	57	15,580 (4367)	61	15,640 (5336)	118	15,610 (4871)

NA, not applicable; NR, not recorded.
a National LOS and perioperative costs were calculated using a weighted average of NHS reference costs[73] to reflect the patient population sample from VGNW.

Vascular Governance North West

The service use and cost data collected from the VGNW are summarised in *Figures 21* and *22*. *Appendix 11* gives details of service use and costs for preoperative and postoperative visits over the follow-up period. Overall, the average cost of preoperative visits was similar for EVAR and open repair. EVAR was associated with higher costs postoperatively, reflecting a higher number of follow-up visits per year and additional procedures to manage complications.

Overall, the LOS (see *Figure 22*) and associated cost per admission was higher for open repair than for EVAR, which is similar to findings from published trials and to the LOS and costs reported in the NHS references costs.[73] However, *Table 33* illustrates that the average LOS and cost of admissions was higher for people in the VGNW than for those reported in national NHS reference cost data and lower than those reported in the EVAR 1 trial for patients undergoing EVAR but higher for patients undergoing open repair.[73,77]

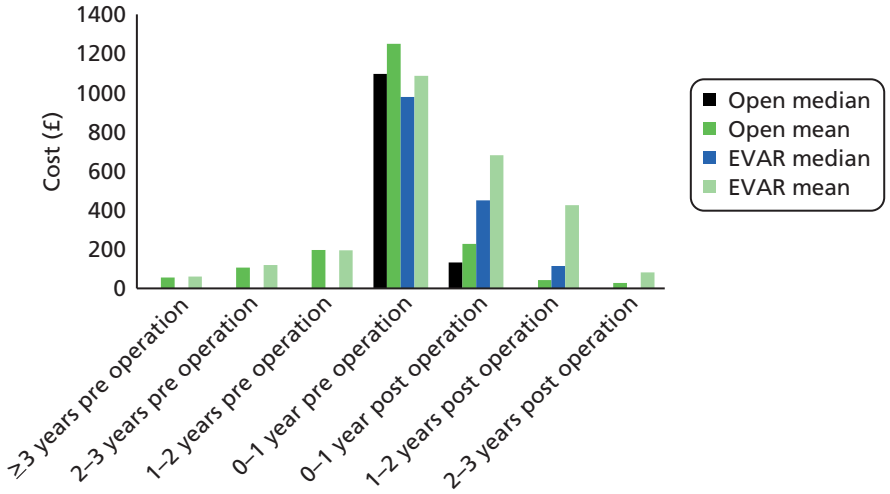


FIGURE 21 Average costs of pre- and postoperative hospital visits and procedures, 2012–13.

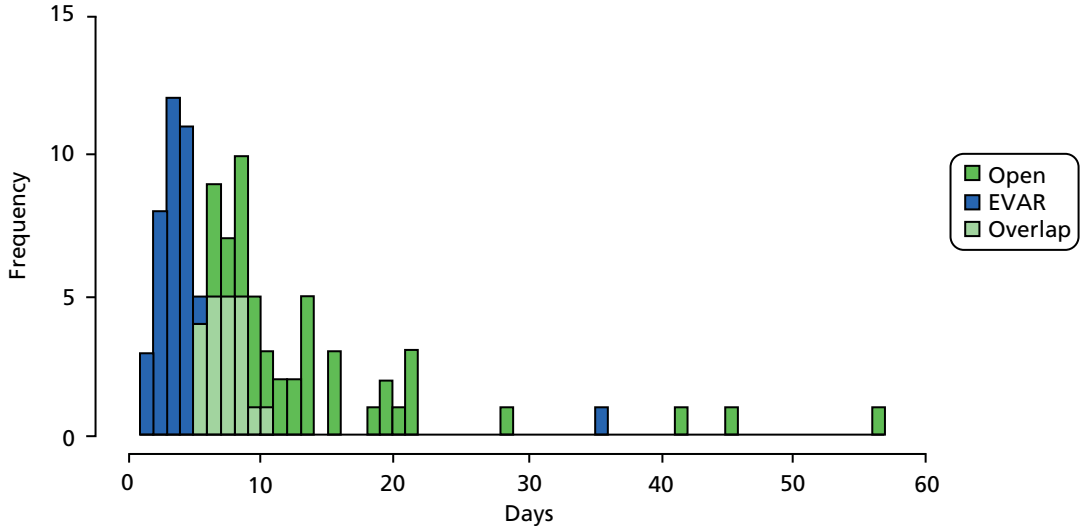


FIGURE 22 Length of inpatient stay for AAA repair.

TABLE 33 Utility parameter estimates for the economic model

Primary analysis	Value	Source
Starting value for model: non-smoker, male		
65–74 years, mean (SD)	0.79 (0.27)	Kind *et al.* 1999[94]
> 75 years, mean (SD)	0.75 (0.29)	Kind *et al.* 1999[94]
Starting value for model: non-smoker, female		
65–74 years, mean (SD)	0.78 (0.25)	Kind *et al.* 1999[94]
> 75 years, mean (SD)	0.71 (0.27)	Kind *et al.* 1999[94]
Elective and emergency postoperative utility decrements (% decrease applied to population norm)[a]		
EVAR 1-month postoperative utility	2.67	Brown *et al.* 2012[79]
EVAR 3-month postoperative utility	5.33	Brown *et al.* 2012[79]
EVAR 12-month postoperative utility	1.33	Brown *et al.* 2012[79]
Open 1-month postoperative utility	9.46	Brown *et al.* 2012[79]
Open 3-month postoperative utility	1.35	Brown *et al.* 2012[79]
Open 12-month postoperative utility	0.00	Brown *et al.* 2012[79]
Sensitivity analysis		
Decrement for 80 > years (% decrease applied to population norm)[b]	8.75	Kind *et al.* 1999;[94] Montreuil *et al.* 2008;[96] Henriksson *et al.* 2005[97]
Starting value for model, minimum (range)	0.67 (0.67–0.90)	Ehlers *et al.* 2009;[98] Szende *et al.* 2014[99]
Starting value for model, maximum (range)	0.90 (0.67–0.90)	Ehlers *et al.* 2009;[98] Szende *et al.* 2014[99]
Elective and emergency 1-month postoperative utility decrements (% decrease applied to population norm)[c]		
EVAR, maximum (range)	0.9 (0.9–8.1)	Brown *et al.* 2012;[79] Epstein *et al.* 2008[93]
EVAR, maximum (range)	8.1 (0.9–8.1)	Brown *et al.* 2012;[79] Epstein *et al.* 2008[93]
Open, maximum (range)	8.7 (8.7–17.3)	Brown *et al.* 2012;[79] Epstein *et al.* 2008[93]
Open, maximum (range)	17.3 (8.7–17.3)	Brown *et al.* 2012;[79] Epstein *et al.* 2008[93]

a The per cent decrement was estimated from the baseline and follow up values reported in the EVAR 1 trial.[79]
b The per cent decrement was estimated as the difference between the utility values for age 70–79 years and that for age > 80 years. The decrement was the average of the decrement calculated from data reported.[96,97]
c The per cent decrement was estimated from the baseline values reported in the EVAR 1 trial[79] and decrements reported here.[93]

Cost and utility parameter estimates for the economic model

Table 34 details the utility parameter estimates used for the model, for the primary economic analysis and the sensitivity analyses. The asymptomatic nature of AAA suggests that the condition will have no direct impact on health status and utility. This means that population norms are likely to reflect health status during the surveillance or active monitoring phase. In addition, available evidence suggests that the health of people having AAA repair returns to preoperative levels in the first year after surgery. Comparison of the UK population norm utility data with those from other European and Scandinavian countries indicates differences in underlying health and utility weights.[99] The values for the UK population are at the lower end of the range of population norm utility estimates (UK = 0.773 for 64–75 years, range = 0.773–0.904).[99] However, the UK population norm utility values for non-smokers[94] lie within the ranges reported at baseline in clinical trials, which are between 0.72 and 0.81 for participants in evaluations of surveillance or surgical repair.[76,78,79,100,101] Economic models that use age-specific population norms report values in the range 0.72–0.87.[80,95–98,102,103] In all but one study[96] the values were derived from the European Quality of Life-5 Dimensions (EQ-5D).

TABLE 34 Probabilities of additional events to estimate costs

Description	Point estimate	Source
Death from rupture before emergency transport	0.40	Expert opinion
Death during emergency transport	0.25	Expert opinion
Death of ruptured patients before emergency surgery	0.33	Expert opinion
Death following emergency surgery	0.34	Thompson *et al.* 2013[83]
EVAR emergency – no or mild complications	0.67	NHS reference costs[73]
EVAR emergency – moderate to severe complications	0.33	
Open emergency – no or mild complications	0.69	
Open emergency – moderate to severe complications	0.31	
EVAR elective – no or mild complications	0.95	
EVAR elective – moderate to severe complications	0.05	
Open elective – no or mild complications	0.83	
Open elective – moderate to severe complications	0.17	
EVAR reintervention probability (0–6 months)	0.02	Brown *et al.* 2012[79]
Open reintervention probability (0–6 months)	0.01	
EVAR reintervention probability (6 months–4 years)	0.03	
Open reintervention probability (6 months–4 years)	0.003	

Table 34 reports the probability data used to estimate weighted average costs for those patients with a ruptured AAA and for the perioperative and postoperative costs of elective AAA repair and *Tables 57* and *58* in *Appendix 12* report the cost of events used in the economic model for the primary and sensitivity analyses.

The main source of cost data for elective or emergency surgical repair and reintervention procedures was the NHS reference costs,[73] to represent the likely national costs that would apply in UK practice. As noted above, the reference cost data indicate lower average costs than those found in the VGNW. The LOS and cost of admissions for primary repair procedures in the VGNW and estimated from the NHS reference cost database (EVAR: mean = 3.5 days, SD = 3.5; open: mean = 5 days, SD = 3.7) were lower than those reported in the UK-based trial of EVAR 1 (EVAR: mean = 10.3 days, SD = 17.8; open: mean = 15.7 days, SD = 16.9).[73,77] The data for the EVAR trial were collected between 1999 and 2004, so may reflect the influence of changes in the organisation and funding of care tending to reduce length of inpatient stay, as well as possible differences in the case mix of patients and patient socio-demographic characteristics. In addition, the shorter stays associated with EVAR may be a result of increased experience and use of the technique during and following the EVAR 1 trial.[79] Accordingly, the NHS reference costs[73] were used as the key source of cost estimates for EVAR and open repair and reinterventions, for both the primary and most of the sensitivity analyses.

Results

Vignette A, male, 65 years, aneurysm 4.0 cm or 6.8 cm, open repair

Tables 35 and *36* report the costs and QALYs found in the primary and sensitivity analyses, with the threshold aneurysm size for surgery. *Figures 23* and *24* present the cost-effectiveness plane and CEAC for the primary analysis. The primary analysis assesses the net costs and QALYs of the ARDA to maximise QALYs compared with standard guidelines (5.5 cm). *Appendix 13* reports the mean costs and QALYs for the primary and sensitivity analyses and the cost-effectiveness planes and CEACs for the sensitivity analyses.

The primary analysis indicates repair of the AAA at a lower size (4 cm) than current guidelines, based on a decision rule of maximising QALYs. Repair at 4 cm is associated with a net saving and gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 23* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, the ARDA will be cost-effective in around 50% of cases. The probability that decisions based on the ARDA are cost-effective was similar in all the sensitivity analyses.

TABLE 35 Net costs, QALYs and probability that the ARDA is cost-effective for vignette A: primary analysis

Economic model outputs	Initial aneurysm size = 4 cm	Initial aneurysm size = 6.8 cm
Threshold size to maximise QALYs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	–172 (–11,644 to 18,275)	162 (–13,823 to 13,793)
Net QALY (95% CIs)	0.047 (–8.962 to 9.055)	0.025 (–9.121 to 9.073)
ICER (£)	NA	6583
Probability cost-effective[a]	0.50	0.51
NB (95% CIs) (£)[a]	–1105 (–173,946 to 168,320)	331 (–176,462 to 176,034)

a WTPT = £20,000 per QALY.

TABLE 36 Net costs, QALYs and probability that the ARDA is cost-effective, vignette A: sensitivity analysis

Economic model outputs	Initial aneurysm size = 4 cm	Initial aneurysm size = 6.8 cm
Sensitivity analysis: outcome is LYGs		
Threshold size to maximise LYGs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	–172 (–11,644 to 18,275)	162 (–13,823 to 13,793)
Net LYGs (95% CIs)	0.079 (–18.079 to 18.122)	0.045 (–18.020 to 18.212)
ICER (£)	NA	3622
Probability cost-effective[a]	0.50	0.50
NB (95% CIs) (£)[a]	–463 (–356,444 to 350,835)	711 (–6976 to 7968)
Sensitivity analysis: decision rule is minimise costs		
Threshold size to minimise costs	7.0 cm	6.9 cm
Net cost (95% CIs) (£)	–172 (–17,585 to 16,938)	–162 (–13,793 to 13,822)
Net QALY (95% CIs)	–0.144 (–8.946 to 8.946)	0.025 (–9.121 to 9.073)
ICER (£)	NA	6583
Probability cost-effective[b]	0.50	0.50
NB (95% CIs) (£)[b]	–1946 (–164,807 to 162,508)	331 (–176,462 to 176,034)

continued

TABLE 36 Net costs, QALYs and probability that the ARDA is cost-effective, vignette A: sensitivity analysis (*continued*)

Economic model outputs	Initial aneurysm size = 4 cm	Initial aneurysm size = 6.8 cm
Sensitivity analysis: low starting utility values and high post-repair decrements		
Threshold size to maximise QALYs	5.1 cm	7.0 cm
Net cost (95% CIs) (£)	–242 (–16,631 to 16,900)	185 (–14,288 to 13,767)
Net QALY (95% CIs)	0.021 (–11.264 to 11.316)	0.107 (0 to 12.853)
ICER (£)	NA	1733
Probability cost-effective[b]	0.50	0.812
NB (95% CIs) (£)[b]	288 (–212,734 to 213,471)	7231 (–7894 to 25,512)
Sensitivity analysis: VGNW costs		
Threshold size to maximise QALYs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	–224 (–11,510 to 19,889)	95 (–14,471 to 14,129)
Net QALY (95% CIs)	0.047 (–8.962 to 9.055)	0.025 (–9.121 to 9.073)
ICER (£)	NA	3858
Probability cost-effective[b]	0.50	0.50
NB (95% CIs) (£)[b]	329 (21,322 to 21,134)	398 (–182,551 to 182,055)
Sensitivity analysis: EVAR 1 costs		
Threshold size to maximise QALYs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	–368 (–6966 to 20,323)	94 (–13,870 to 10,679)
Net QALY (95% CIs)	0.047 (–8.962 to 9.055)	0.025 (–9.121 to 9.073)
ICER (£)	NA	3843
Probability cost-effective[b]	0.49	0.50
NB (95% CIs) (£)[b]	–2574 (–183,909 to 178,683)	399 (–182,930 to 182,008)
Sensitivity analysis: high assessment and follow-up costs, low surgery costs		
Threshold size to maximise QALYs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	59 (–8659 to 14,475)	239 (–9019 to 9234)
Net QALY (95% CIs)	0.047 (–8.962 to 9.055)	0.025 (–9.121 to 9.073)
ICER (£)	1279	9664
Probability cost-effective[b]	0.50	0.50
NB (95% CIs) (£)[b]	–181 (180,785 to 180,689)	–995 (–456,396 to 453,777)
Sensitivity analysis: low assessment and follow-up costs, high surgery costs		
Threshold size to maximise QALYs	4.0 cm	6.9 cm
Net cost (95% CIs) (£)	–300 (–15,794 to 23,284)	98 (–19,518 to 19,326)
Net QALY (95% CIs)	0.047 (–8.962 to 9.055)	0.025 (–9.121 to 9.073)
ICER (£)	NA	3979
Probability cost-effective[b]	0.50	0.50
NB (95% CIs) (£)[b]	–1657 (–183,320 to 179,728)	–395 (–182,602 to 182,865)

NA, not applicable.
a WTPT = £20,000 per LYG.
b WTPT = £20,000 per QALY.

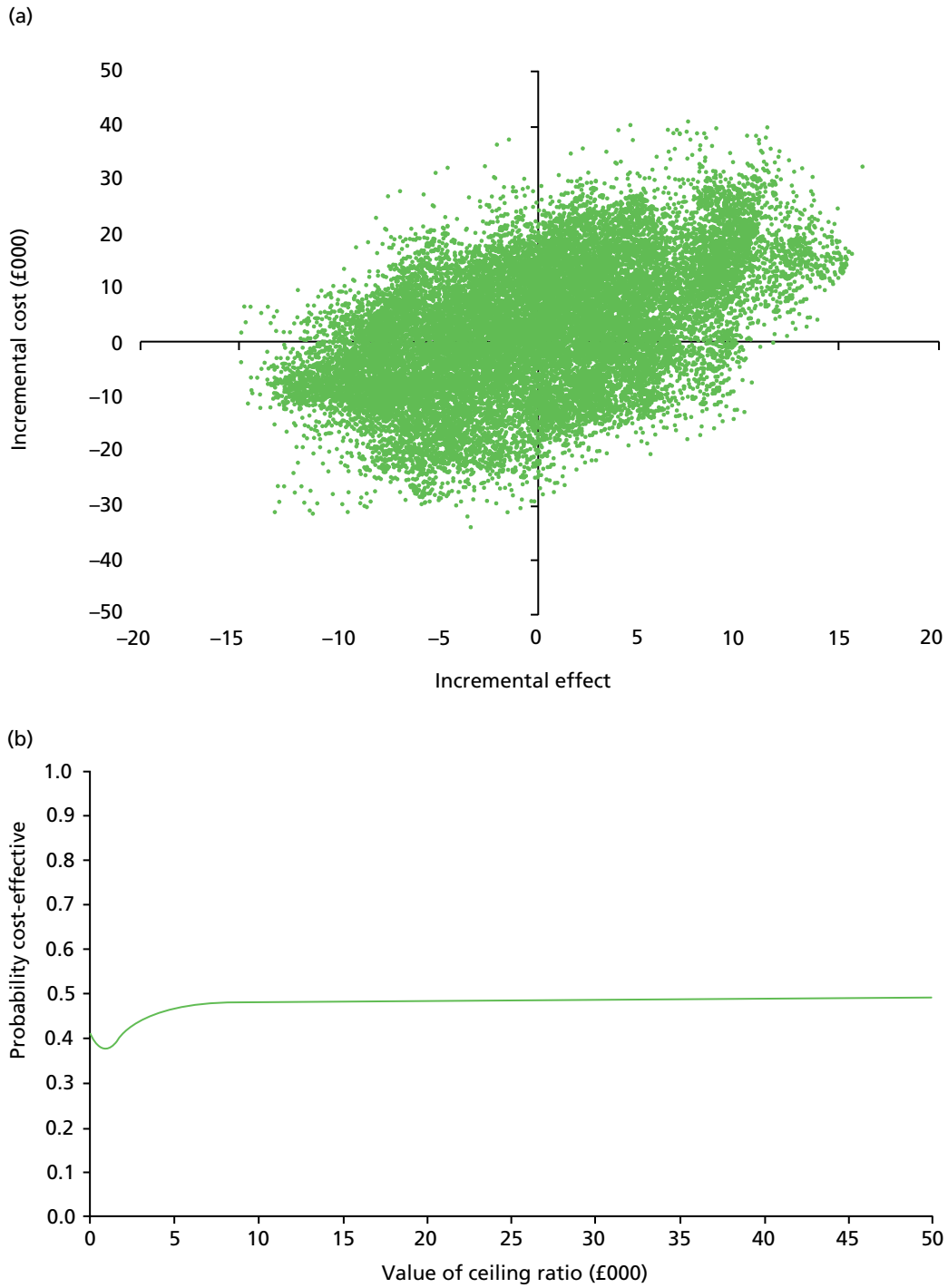


FIGURE 23 Cost-effectiveness plane and CEAC for vignette A at 4.0 cm. (a) Cost-effectiveness plane; and (b) CEAC.

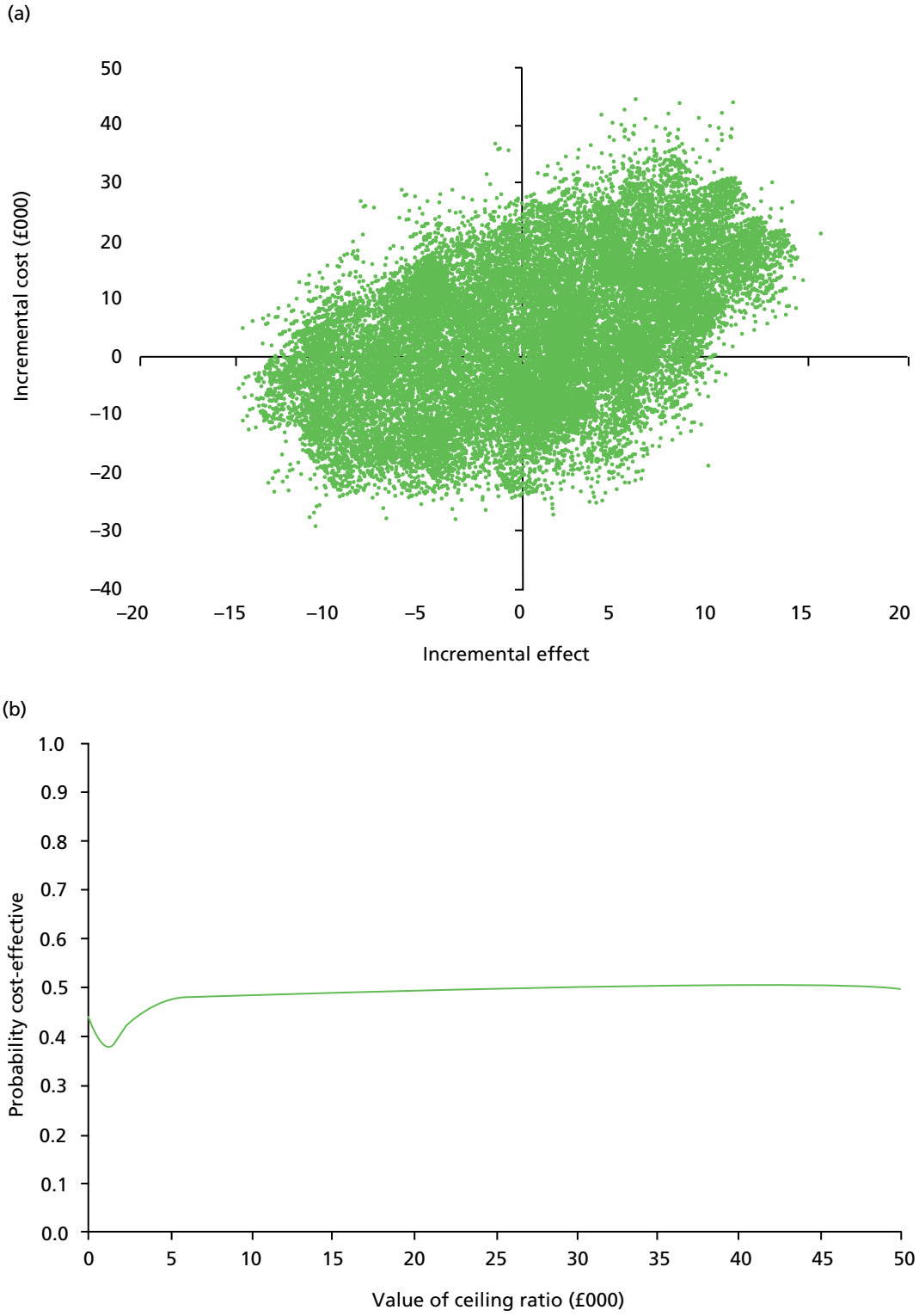


FIGURE 24 Cost-effectiveness plane and CEAC for vignette A at 6.8 cm. (a) Cost-effectiveness plane; and (b) CEAC.

The sensitivity analyses of alternative estimates of the cost parameters and use of LYGs as the outcome measure indicate similar threshold repair sizes to the primary analysis and are associated with high variation in the net costs, net QALYs and NB estimates. If alternative estimates of the utility parameters are used or the decision rule is to choose a threshold that minimises costs, then the threshold size of the AAA at which repair is indicated changes. However, net costs, QALYs and NB estimates are again characterised by high variation and uncertainty.

For an initial aneurysm size of 6.8 cm, the primary analysis indicates repair of the AAA at a similar size (6.9 cm), based on a decision rule of maximising QALYs. This is associated with a net cost and gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 24* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, decisions based on the ARDA information will be cost-effective in around 50% of cases. The probability that the ARDA is cost-effective was similar in all the sensitivity analyses.

Vignette B, male, 86 years, aneurysm 4 cm or 7 cm, endovascular aneurysm repair

Tables 37 and *38* report the costs and QALYs found in the primary and sensitivity analyses, with the threshold aneurysm size for surgery. *Figure 25* presents the cost-effectiveness plane and CEAC for the primary analysis for an initial aneurysm size of 4 cm. For an initial aneurysm size of 7.0 cm, no comparator threshold is available, as the ARDA-recommended threshold equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.

The primary analysis assesses the net costs and QALYs of the ARDA to maximise QALYs compared with standard guidelines (5.5 cm). *Appendix 13* reports the mean costs and QALYs for the primary and sensitivity analyses and the cost-effectiveness planes and CEACs for the sensitivity analyses.

For an initial aneurysm size of 4.0 cm, the primary analysis indicates repair of the AAA at a higher size (6.0 cm) than current guidelines (5.0 cm), based on a decision rule of maximising QALYs. Repair at 6.0 cm is associated with a net saving and gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 25* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, the ARDA will be cost-effective in around 50% of cases. The probability that the ARDA is cost-effective was similar in all the sensitivity analyses.

The sensitivity analyses of alternative estimates of the cost parameters indicate similar threshold repair sizes to the primary analysis and are associated with high variation in the net costs, net QALYs and NB estimates. If alternative estimates of the utility parameters are used, LYGs is used as the outcome measure

TABLE 37 Net costs, QALYs and probability that the ARDA is cost-effective for vignette B: primary analysis

Economic model outputs	Initial aneurysm size = 4.0 cm	Initial aneurysm size = 7.0 cm[a]
Threshold size to maximise QALYs	6.0 cm	7.0 cm
Net cost (95% CIs) (£)	–405 (–17,655 to 13,576)	8591 (699 to 37,110)
Net QALY (95% CIs)	0.017 (–4.940 to 4.926)	2.309 (0 to 6.788)
ICER (£)	NA	NA
Probability cost-effective[b]	0.51	NA
NB (95% CIs) (£)[b]	2338 (–5110 to 12,425)	NA

NA, not applicable.
a No comparator threshold is available as the ARDA-recommended threshold equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.
b WTPT = £20,000 per QALY.

TABLE 38 Net costs, QALYs and probability that the ARDA is cost-effective, vignette B: sensitivity analysis

Economic model outputs	Initial aneurysm size = 4.0 cm	Initial aneurysm size = 7.0 cm[a]
Sensitivity analysis: decision rule is maximise LYGs		
Threshold size to maximise LYGs	7.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–1465 (–21,774 to 7929)	8591 (699 to 37,110)
Net LYGs (95% CIs)	0.086 (–8.009 to 7.847)	3.295 (0 to 10.538)
ICER (£)	NA	NA
Probability cost-effective[b]	0.52	NA
NB (95% CIs) (£)[b]	3186 (–151,866 to 149,092)	NA
Sensitivity analysis: decision rule is minimise costs		
Threshold size to minimise costs	7.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–815 (–17,653 to 8036)	8591 (699 to 37,110)
Net LYGs (95% CIs)	0.017 (–4.972 to 4.888)	3.295 (0 to 10.538)
ICER (£)	NA	NA
Probability cost-effective[b]	0.52	NA
NB (95% CIs) (£)[b]	1147 (–90,143 to 89,875)	NA
Sensitivity analysis: low starting utility values and high post-repair decrements		
Threshold size to maximise QALYs	6.8 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–729 (–17,595 to 9192)	8522 (693 to 36,910)
Net QALY (95% CIs)	0.050 (–6.160 to 6.31)	2.750 (0 to 8.381)
ICER (£)	NA	3471
Probability cost-effective[c]	0.51	NA
NB (95% CIs) (£)[c]	1727 (–113,666 to 117,455)	NA
Sensitivity analysis: VGNW costs		
Threshold size to maximise QALYs	6.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–781 (–17,010 to 15,253)	12,849 (5979 to 27,032)
Net QALY (95% CIs)	0.017 (–4.940 to 4.926)	2.309 (0 to 6.788)
ICER (£)	NA	NA
Probability cost-effective[c]	0.51	NA
NB (95% CIs) (£)[c]	1113 (–98,826 to 100,490)	NA
Sensitivity analysis: EVAR 1 costs		
Threshold size to maximise QALYs	6.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–1023 (–17,074 to 17,073)	16,876 (14,475 to 33,306)
Net QALY (95% CIs)	0.017 (–4.940 to 4.926)	2.309 (0 to 6.788)
ICER (£)	NA	NA
Probability cost-effective[c]	0.51	NA
NB (95% CIs) (£)[c]	1356 (–99,341 to 101,205)	NA

TABLE 38 Net costs, QALYs and probability that the ARDA is cost-effective, vignette B: sensitivity analysis (*continued*)

Economic model outputs	Initial aneurysm size = 4.0 cm	Initial aneurysm size = 7.0 cm[a]
Sensitivity analysis: high assessment and follow-up costs, low surgery costs		
Threshold size to maximise QALYs	6.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–133 (–10,983 to 10,665)	5849 (1271 to 15,782)
Net QALY (95% CIs)	0.017 (–4.940 to 4.926)	2.309 (0 to 6.788)
ICER (£)	NA	NA
Probability cost-effective[c]	0.50	NA
NB (95% CIs) (£)[c]	465 (–99,398 to 98,972)	NA
Sensitivity analysis: low assessment and follow-up costs, high surgery costs		
Threshold size to maximise QALYs	6.0 cm	7.0 cm[a]
Net cost (95% CIs) (£)	–589 (–18,448 to 14,340)	9739 (788 to 35,574)
Net QALY (95% CIs)	0.017 (–4.940 to 4.926)	2.309 (0 to 6.788)
ICER (£)	NA	NA
Probability cost-effective[c]	0.51	NA
NB (95% CIs) (£)[c]	678 (–98,972 to 100,273)	NA

NA, not applicable.
a No comparator threshold is available, as the ARDA-recommended threshold equals the current practice threshold.
b WTPT = £20,000 per LYG.
c WTPT = £20,000 per QALY.

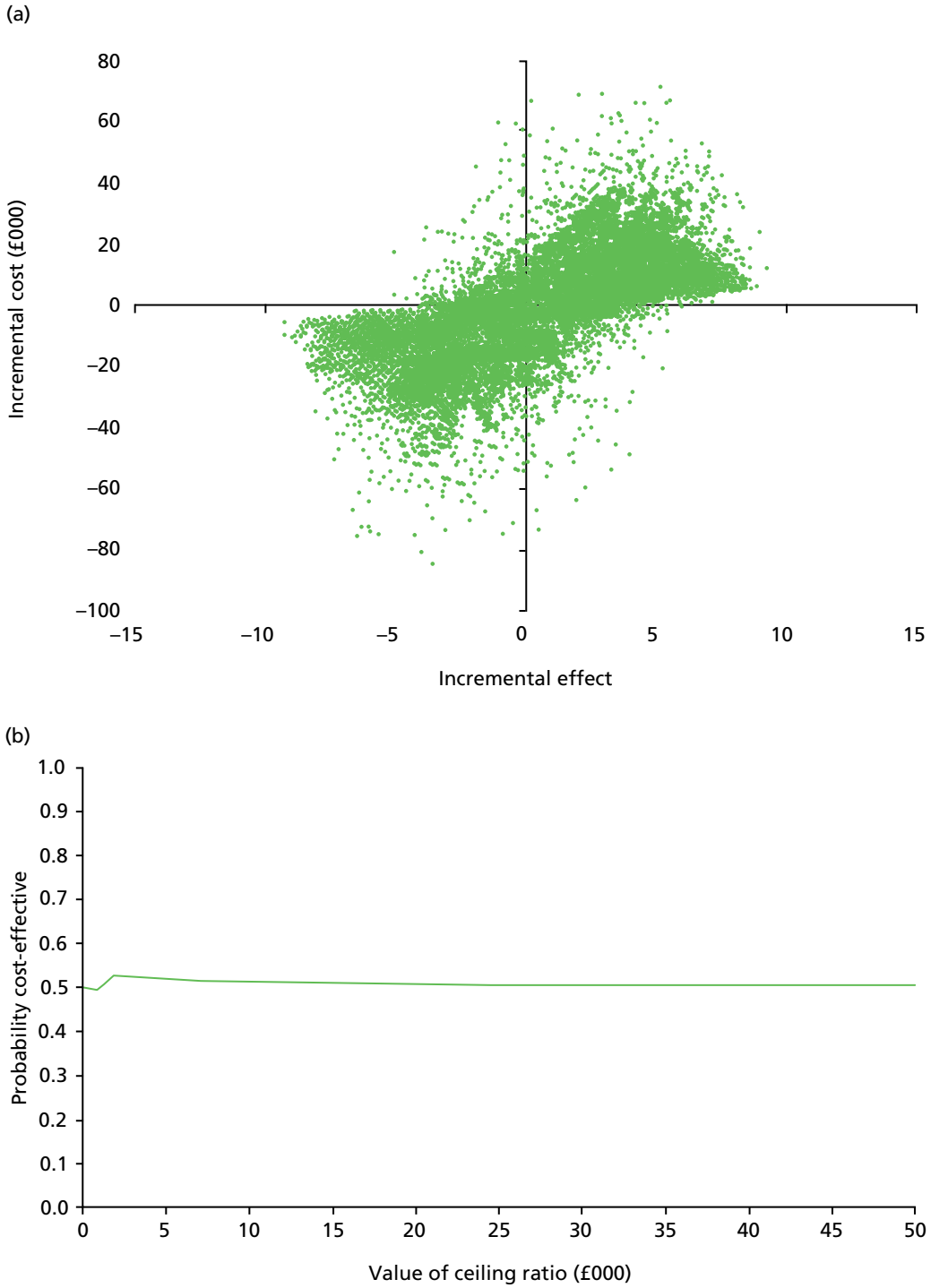


FIGURE 25 Cost-effectiveness plane and CEACs for vignette B at 4.0 cm. (a) Cost-effectiveness plane; and (b) CEAC.

or the decision rule is to choose a threshold that minimises costs, then the threshold size of the AAA at which repair is indicated increases to 6–7 cm. However, net costs, QALYs and NB estimates are again characterised by high variation and uncertainty.

Vignette C, female, 70 years, aneurysm 3.8 cm or 5.2 cm, open repair

Tables 39 and *40* report the costs and QALYs found in the primary and sensitivity analyses, with the threshold aneurysm size for surgery. *Figure 26* presents the cost-effectiveness plane and CEAC for the primary analysis for an initial aneurysm size of 3.8 cm. The primary analysis assesses the net costs and QALYs of the ARDA to maximise QALYs compared with standard guidelines (5.0 cm). *Appendix 13* reports the mean costs and QALYs for the primary and sensitivity analyses and the cost-effectiveness planes and CEACs for the sensitivity analyses.

TABLE 39 Net costs, QALYs and probability that the ARDA is cost-effective for vignette C: primary analysis

Economic model outputs	Initial aneurysm size = 3.8 cm	Initial aneurysm size = 5.2 cm[a]
Threshold size to maximise QALYs	4.0 cm	5.2 cm
Net cost (95% CIs) (£)	2716 (–13,650 to 22,552)	12,790 (5644 to 23,859)
Net QALY (95% CIs)	0.044 (–7.901 to 7.825)	4.962 (0 to 10.756)
ICER (£)	63,361	NA
Probability cost-effective[b]	0.49	NA
NB (95% CIs) (£)[b]	–1831 (–150,921 to 144,164)	NA

NA, not applicable.
a No comparator threshold is available as the ARDA-recommended threshold in the primary analysis equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.
b WTPT = £20,000 per QALY.

TABLE 40 Net costs, QALYs and probability that the ARDA is cost-effective, vignette C: sensitivity analysis

Economic model outputs	Initial aneurysm size = 3.8 cm	Initial aneurysm size = 5.2 cm[a]
Sensitivity analysis: outcome is LYGs		
Threshold size to maximise LYGs	4.0 cm	5.2 cm[a]
Net cost (95% CIs) (£)	2716 (–13,650 to 22,552)	12,790 (5644 to 23,859)
Net LYGs (95% CIs)	0.043 (–14.162 to 14.006)	7.772 (0 to 18.782)
ICER (£)	63,610	NA
Probability cost-effective[b]	0.49	NA
NB (95% CIs) (£)[b]	–1862 (–276,819 to 268,676)	NA
Sensitivity analysis: decision rule is minimise costs		
Threshold size to minimise costs	7.0 cm	7.0 cm
Net cost (95% CIs) (£)	–2322 (–16,948 to 18,669)	–2394 (–17,881 to 22,943)
Net QALY (95% CIs)	–0.13 (–7.72 to 7.36)	–0.37 (–8.11 to 7.84)
ICER (£)	NA	NA
Probability cost-effective[c]	0.51	0.47
NB (95% CIs)[c]	–11 (–141,334 to 135,314)	–4953 (–150,793 to 150,597)

continued

TABLE 40 Net costs, QALYs and probability that the ARDA is cost-effective, vignette C: sensitivity analysis (*continued*)

Economic model outputs	Initial aneurysm size = 3.8 cm	Initial aneurysm size = 5.2 cm[a]
Sensitivity analysis: low starting utility values and high post-repair decrements		
Threshold size to maximise QALYs	5.4 cm	5.3 cm
Net cost (95% CIs) (£)	–514 (–16,590 to 20,082)	63 (–14,051 to 24,204)
Net QALY (95% CIs)	0.03 (–9.48 to 9.57)	0.14 (–9.9 to 10.22)
ICER (£)	NA	444
Probability cost-effective[c]	0.51	0.51
NB (95% CIs) (£)[c]	1121 (–177,022 to 178,786)	2757 (–191,975 to 198,960)
Sensitivity analysis: high assessment and follow-up costs, low surgery costs		
Threshold size to maximise QALYs	4.0 cm	5.2 cm[a]
Net cost (95% CIs) (£)	1942 (–11,252 to 17,168)	11,071 (6242 to 18,141)
Net QALY (95% CIs)	0.04 (–7.90 to 7.83)	4.962 (0 to 10.756)
ICER (£)	43,865	NA
Probability cost-effective[c]	0.49	NA
NB (95% CIs) (£)[c]	–1056 (–160,547 to 155,234)	NA
Sensitivity analysis: low assessment and follow-up costs, high surgery costs		
Threshold size to maximise QALYs	4.0 cm	5.2 cm[a]
Net cost (95% CIs) (£)	3314 (–17,165 to 28,626)	14,365 (5285 to 30,600)
Net QALY (95% CIs)	0.044 (–7.901 to 7.825)	4.962 (0 to 10.756)
ICER (£)	74,858	NA
Probability cost-effective[c]	0.49	NA
NB (95% CIs) (£)[c]	–1831 (–150,921 to 144,164)	NA
Sensitivity analysis: EVAR 1 costs		
Threshold size to maximise QALYs	4.0 cm	5.2 cm[a]
Net cost (95% CIs) (£)	4097 (–16,317 to 23,615)	17,332 (13,221 to 25,740)
Net QALY (95% CIs)	0.044 (–7.901 to 7.825)	4.962 (0 to 10.756)
ICER (£)	92,549	NA
Probability cost-effective[c]	0.49	NA
NB (95% CIs) (£)[c]	–3312 (–163,320 to 153,662)	NA
Sensitivity analysis: VGNW costs		
Threshold size to maximise QALYs	4.0 cm	5.2 cm[a]
Net cost (95% CIs) (£)	3173 (–14,649 to 24,475)	14,367 (7320 to 26,022)
Net QALY (95% CIs)	0.044 (–7.901 to 7.825)	4.962 (0 to 10.756)
ICER (£)	71,675	NA
Probability cost-effective[c]	0.49	NA
NB (95% CIs) (£)[c]	–2288 (–162,109 to 154,481)	NA

NA, not applicable.
a No comparator threshold is available as the ARDA-recommended threshold in the primary analysis equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.
b WTPT = £20,000 per LYG.
c WTPT = £20,000 per QALY.

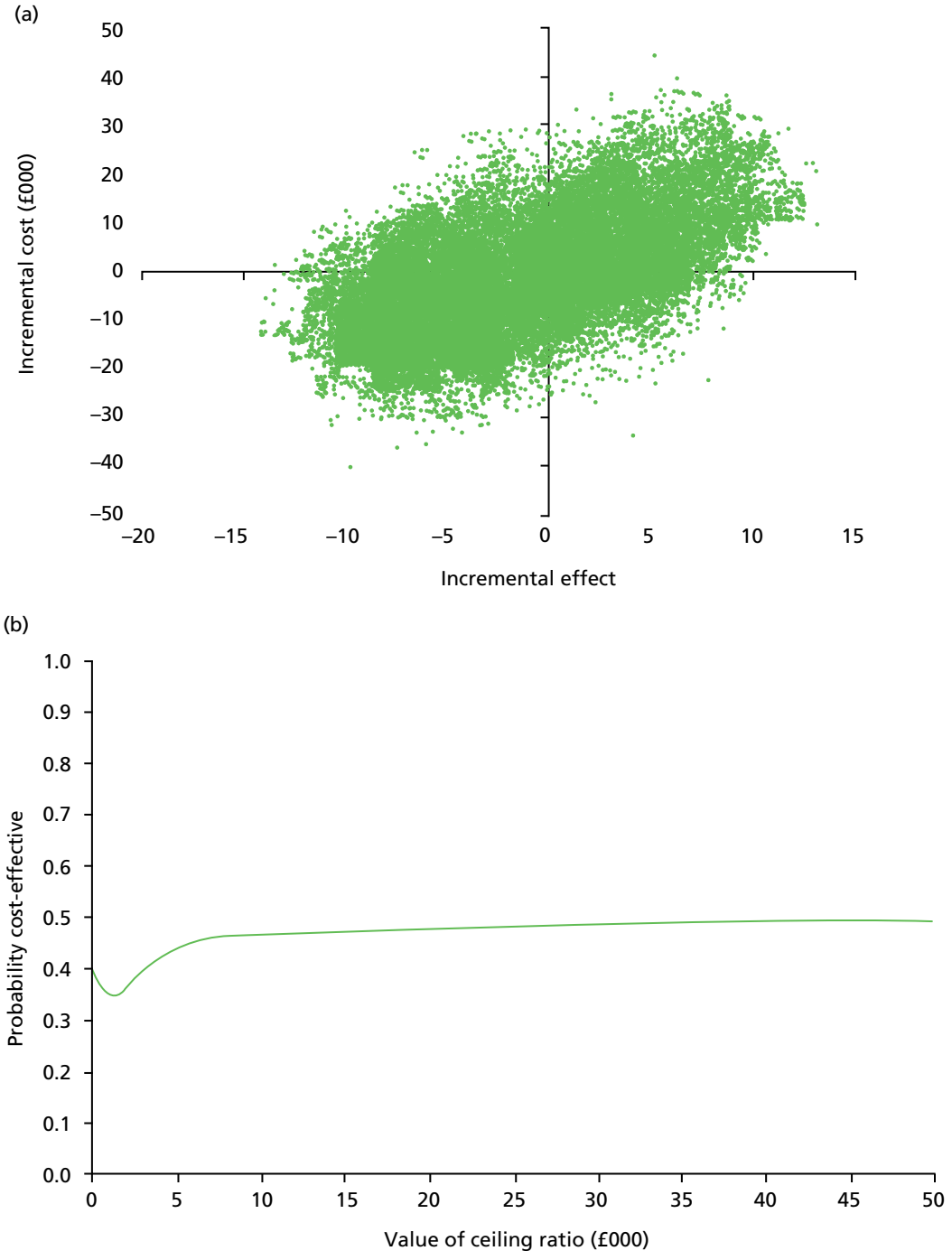


FIGURE 26 Cost-effectiveness plane and CEAC for vignette C at 3.8 cm. (a) Cost-effectiveness plane; and (b) CEAC.

For an initial aneurysm size of 3.8 cm, the primary analysis indicates repair of the AAA at a lower size (4.0 cm) than current guidelines (5.0 cm), based on a decision rule of maximising QALYs. Repair at 4.0 cm is associated with a net cost and gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 26* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, the ARDA will be cost-effective in around 50% of cases. The probability that the ARDA is cost-effective was similar in all the sensitivity analyses.

The sensitivity analysis of using LYGs as the outcome measure indicates the same threshold repair size to the primary analysis and sensitivity analyses relating to costs recommend a minor adjustment to a 3.8 cm threshold size – all are associated with high variation in the net costs, net QALYs and NB estimates. If alternative estimates of the utility parameters are used or the decision rule is to choose a threshold that minimises costs, then the threshold size of the AAA at which repair is indicated increases from 4.0 cm (suggested by the primary analysis) to 5.4 cm or 7.0 cm. However, net costs, QALYs and NB estimates are again characterised by high variation and uncertainty.

For an initial aneurysm size of 5.2 cm in the primary analysis, the ARDA recommended 5.2 cm as the threshold for maximising QALYs.

Vignette D, male, 80 years, aneurysm 4.8 cm or 6.5 cm, endovascular aneurysm repair

Tables 41 and *42* report the costs and QALYs found in the primary and sensitivity analyses, with the threshold aneurysm size for surgery. *Figures 27* and *28* present the cost-effectiveness plane and CEAC for the primary analysis. The primary analysis assesses the net costs and QALYs of the ARDA to maximise QALYs compared with standard guidelines (5.5 cm). *Appendix 13* reports the mean costs and QALYs for the primary and sensitivity analyses and the cost-effectiveness planes and CEACs for the sensitivity analyses.

For an initial aneurysm size of 4.8 cm, the primary analysis indicates repair of the AAA at 4.9 cm, which is slightly lower than standard guidelines (5.5 cm), based on a decision rule of maximising QALYs. Repair at 4.9 cm is associated with net costs and a gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 27* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, the ARDA will be cost-effective in around 50% of cases. The probability that the ARDA is cost-effective was similar in all the sensitivity analyses.

For an initial aneurysm size of 6.5 cm, the primary analysis indicates repair of the AAA at a similar size (6.6 cm), based on a decision rule of maximising QALYs. This is associated with a net cost and gain of QALYs. However, as the 95% CIs and cost-effectiveness plane indicate, there is wide variation in the net costs and QALYs, with the 95% CIs crossing zero. The CEAC in *Figure 28* indicates that if decision-makers are willing to pay £5000 or more to gain 1 QALY, the ARDA will be cost-effective in around 50% of cases.

The sensitivity analyses indicated similar results to the primary analyses for initial aneurysm sizes of 4.8 cm and 6.5 cm, with the exception that making cost minimisation the decision criterion delays recommended intervention until 7.0 cm.

TABLE 41 Net costs, QALYs and probability that the ARDA is cost-effective for vignette D: primary analysis

Economic model outputs	Initial aneurysm size = 4.8 cm	Initial aneurysm size = 6.5 cm
Threshold size to maximise QALYs	4.9 cm	6.6 cm
Net cost (95% CIs) (£)	218 (–29,623 to 39,303)	143 (–32,285 to 39,933)
Net QALY (95% CIs)	0.033 (–7.478 to 7.504)	0.006 (–7.516 to 7.510)
ICER (£)	5799	23,155
Probability cost-effective[a]	0.50	0.50
NB (95% CIs) (£)[a]	535 (–143,900 to 143,655)	–20 (–148,886 to 149,026)

a WTPT = £20,000 per QALY.

TABLE 42 Net costs, QALYs and probability that the ARDA is cost-effective, vignette D: sensitivity analysis

Economic model outputs	Initial aneurysm size = 4.8 cm	Initial aneurysm size = 6.5 cm[a]
Sensitivity analysis: decision rule is to maximise LYGs		
Threshold size to maximise LYGs	4.9 cm	6.7 cm
Net cost (95% CIs) (£)	45 (–31,632 to 39,303)	171 (–32,335 to 39,627)
Net LYGs (95% CIs)	0.039 (–13.735 to 13.841)	0.014 (–13.741 to 13.807)
ICER (£)	1137	12,554
Probability cost-effective[b]	0.50	0.50
NB (95% CIs) (£)[b]	743 (–270,789 to 272,419)	101 (–272,234 to 272,681)
Sensitivity analysis: decision rule is minimise costs		
Threshold size to minimise costs	7.0 cm	7.0 cm
Net cost (95% CIs) (£)	–1047 (–29,946 to 30,834)	–214 (–32,546 to 38,088)
Net QALYs (95% CIs)	–0.18 (–7.51 to 7.347)	–0.117 (–7.692 to 7.42)
ICER (£)	NA	NA
Probability cost-effective[c]	0.49	0.49
NB (95% CIs) (£)[c]	–2579 (–141,491 to 139,155)	–2133 (–150,309 to 146,578)
Sensitivity analysis: low starting utility values and high post-repair decrements		
Threshold size to maximise QALYs	4.9 cm	6.7 cm
Net cost (95% CIs) (£)	242 (–29,717 to 39,216)	74 (–32,999 to 39,564)
Net QALY (95% CIs)	0.08 (–9.57 to 9.65)	0.14 (–9.53 to 9.76)
ICER (£)	3162	517
Probability cost-effective[c]	0.50	0.51
NB (95% CIs) (£)[c]	1289 (–187,079 to 187,361)	2796 (–187,752 to 192,291)

continued

TABLE 42 Net costs, QALYs and probability that the ARDA is cost-effective, vignette D: sensitivity analysis (*continued*)

Economic model outputs	Initial aneurysm size = 4.8 cm	Initial aneurysm size = 6.5 cm[a]
Sensitivity analysis: high assessment and follow-up costs, low surgery costs		
Threshold size to maximise QALYs	4.9 cm	6.6 cm
Net cost (95% CIs) (£)	–770 (–13,163 to 18,156)	178 (–12,247 to 17,906)
Net QALY (95% CIs)	0.038 (–7.365 to 7.445)	0.006 (–7.516 to 7.510)
ICER (£)	NA	NA
Probability cost-effective[c]	0.51	0.50
NB (95% CIs) (£)[c]	1523 (–147,487 to 150,066)	–54 (–150,872 to 150,478)
Sensitivity analysis: low assessment and follow-up costs, high surgery costs		
Threshold size to maximise QALYs	4.9 cm	6.6 cm
Net cost (95% CIs) (£)	785 (–27,275 to 37,503)	–38 (–30,074 to 37,698)
Net QALY (95% CIs)	0.038 (–7.365 to 7.445)	0.006 (–7.516 to 7.510)
ICER (£)	20,834	NA
Probability cost-effective[c]	0.50	0.50
NB (95% CIs) (£)[c]	–31 (150,731 to 150,870)	162 (–153,477 to 153,086)
Sensitivity analysis: EVAR 1 costs		
Threshold size to maximise QALYs	4.9 cm	6.6 cm
Net cost (95% CIs) (£)	2080 (–19,998 to 39,895)	–200 (–24,223 to 39,703)
Net QALY (95% CIs)	0.038 (–7.365 to 7.445)	0.006 (–7.516 to 7.510)
ICER (£)	55,225	NA
Probability cost-effective[c]	0.49	0.50
NB (95% CIs) (£)[c]	–1372 (–151,705 to 148,506)	324 (–151,764 to 152,098)
Sensitivity analysis: VGNW costs		
Threshold size to maximise QALYs	4.9 cm	6.6 cm
Net cost (95% CIs) (£)	1214 (–18,471 to 30,461)	–116 (–19,231 to 30,706)
Net QALY (95% CIs)	0.038 (–7.365 to 7.445)	0.006 (–7.516 to 7.510)
ICER (£)	32,235	NA
Probability cost-effective[c]	0.50	0.50
NB (95% CIs) (£)[c]	–461 (–150,157 to 149,287)	240 (–151,215 to 151,759)

NA, not applicable.
a No comparator threshold is available as the ARDA-recommended threshold in the primary analysis equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.
b WTPT = £20,000 per LYG.
c WTPT = £20,000 per QALY.

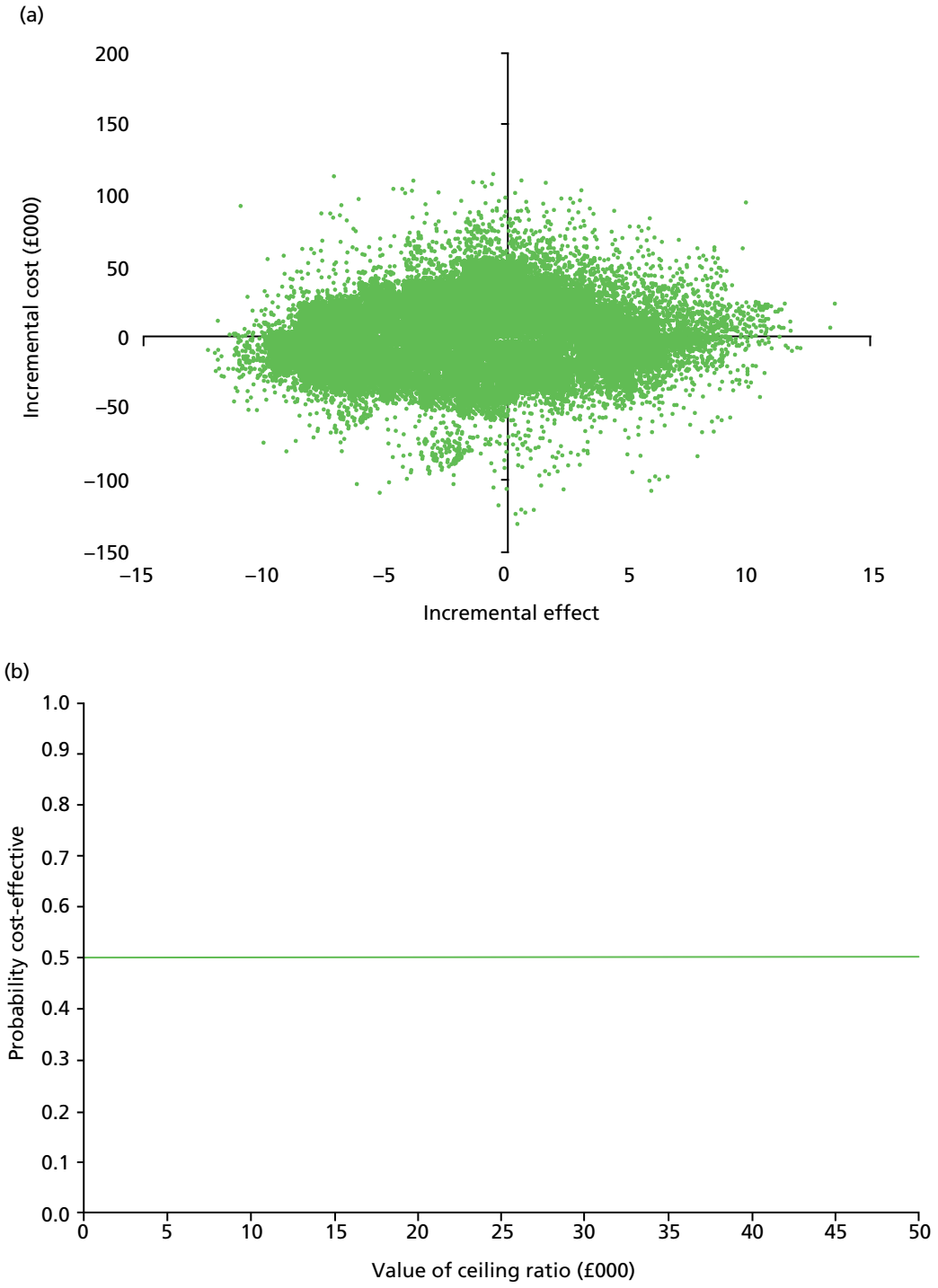


FIGURE 27 Cost-effectiveness plane and CEAC for vignette D at 4.8 cm. (a) Cost-effectiveness plane; and (b) CEAC.

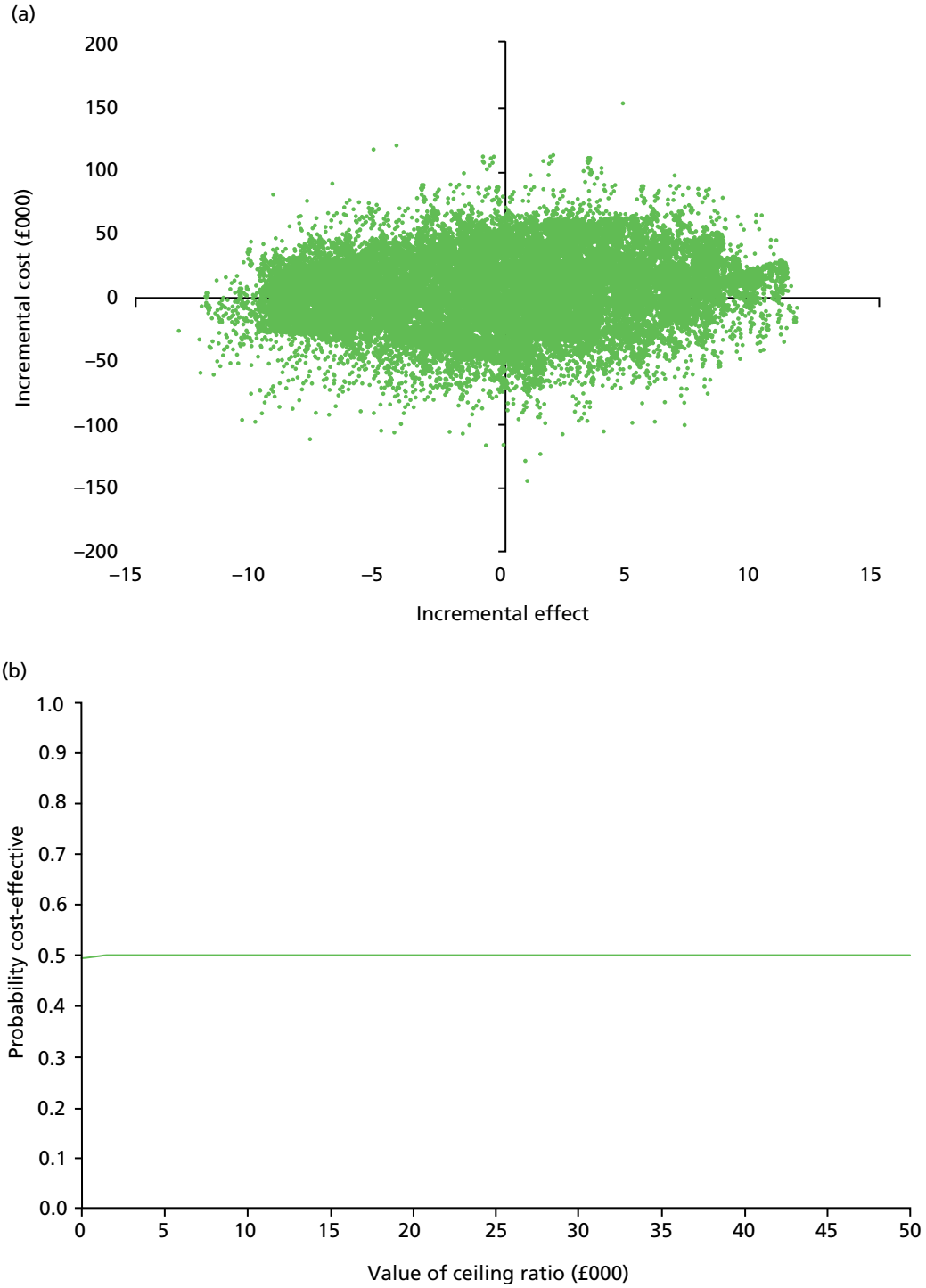


FIGURE 28 Cost-effectiveness plane and CEAC for vignette D at 6.5 cm. (a) Cost-effectiveness plane; and (b) CEAC.

Summary

Overall, the economic model indicates no clear difference in the mean expected costs or QALYs between the ARDA, which formally combines aneurysm size and other factors, and the current thresholds for surgery based on the size of the aneurysm alone. In the primary analysis, the net costs of decisions based on the ARDA information ranged between a saving of £405 (95% CI –£17,655 to £13,576) to a net cost of £2716 (95% CI –£13,650 to £22,552). All the vignettes and aneurysm sizes were associated with a net QALY gain, which ranged between 0.006 (95% CI –7.516 to 7.510) and 0.047 (95% CI –8.962 to 9.055). The net costs and QALYs were characterised by wide 95% CIs, which crossed zero. This is similar to the results found for the analysis of cost-effectiveness and LYGs. The probability that the ARDA-based decisions about timing of repair were cost-effective was around 50% for all of the primary analyses, with a NB that ranged between –£1831 (95% CI –£150,921 to £144,164) and £2338 (95% CI –£5110 to £12,425) for vignettes. Again the 95% CIs are wide and cross zero.

Overall, the results suggest that there is high uncertainty. The wide CIs around the net QALYs gained and net costs generated by this economic analysis reflect the uncertainty in the data and underline the need for reliable data to inform decision aids of this type. As a result of the high level of uncertainty, it was not possible to confidently identify whether the repair indication recommended by the ARDA is likely to be more cost-effective than current guidelines. The sensitivity analysis to explore the impact of using LYGs, alternative costs and utility estimates did not change this result.

Chapter 10 Discussion

Prediction of perioperative mortality

The work on developing models to predict perioperative mortality following elective AAA repair is presented in *Chapter 5*. Prior to this programme of work, several risk prediction models were developed to predict outcomes following AAA repair. A systematic review of risk prediction models for AAA repair published in 2008 found the GAS to be the most useful and consistently validated model.[52] The GAS is a simplified model constructed in 1994 using 500 patients who underwent AAA repair for either intact or ruptured AAA and includes age, shock, myocardial disease, cerebrovascular disease and renal disease.[53] The GAS has since been validated in a number of cohorts,[104–109] but the GAS includes emergency as well as elective AAA repair. As a result, this may mean that it achieves useful discrimination only in populations which include patients undergoing emergency repair. Other models assessed as part of this study include V-POSSUM which was developed using data from 1313 patients who had a range of arterial surgery,[110] the VBHOM which was derived from an earlier cohort of patients in the NVD[111] and the Medicare model which was developed on 45,660 patients who had elective AAA repair between 2001 to 2004 in the USA.[112] Both the V-POSSUM and VBHOM were previously validated.[109,113,114]

In our validation, performed using 10,891 elective AAA repairs, the Medicare model was the only external model to demonstrate fair discrimination, with AUCs > 0.70;[54] the GAS, V-POSSUM and VBHOM were developed from elective and emergency data, and all achieved lower discrimination, with AUCs of 0.60–0.65, which is considered to be poor.[54] The calibration of the V-POSSUM and VBHOM was also poor, indicating that they are not suitable for contemporary elective AAA repair, which is a key finding of this project.

To address the known limitations of existing models, VGNW data were initially used for developing a perioperative risk prediction model, as it contained risk factor data not found in the NVD, such as respiratory disease, and it was thought that the available risk factor data were more accurate. The VGNW model included the following risk factors: age, female sex, diabetes, raised serum creatinine level, respiratory disease, antiplatelet medication and open surgery. The AUC was 0.70 on validation with acceptable calibration. On external validation using the NVD, the VGNW model demonstrated good discrimination with an AUC of 0.71 and acceptable calibration.

Although the VGNW model demonstrated potential for predicting perioperative mortality risk following elective AAA repair, there are a number of limitations. First, the validation data set was relatively small, with only 50 deaths, which may be insufficient for assessing model accuracy.[115] Second, the model was built using regional data. Regional differences in patient populations with regards to health and social deprivation may mean that the model's applicability to other areas in the UK is limited. Third, the model was developed using data collected over a 10-year period during which EVAR was not widely adopted, and outcomes following AAA repair have improved considerably. Case-mix in elective AAA repair has changed significantly over the past 10 years, as can be seen by comparing the patient characteristics of the cohort of patients used to develop the VGNW model and to validate this model using the NVD data (*Tables 2* and *11*). The most significant change was in the procedure type, with over two-thirds of patients undergoing EVAR in the more contemporary cohort, compared with just 18.9% in the earlier cohort used to develop the VGNW model.

To try and improve the generalisability and statistical performance of the perioperative prediction model, the BAR score was developed using NVD data. The BAR score was developed using more efficient statistical methodology and a larger cohort of patients who underwent elective AAA repair over a shorter period of time. The BAR model included the following risk factors: open repair, age, female sex, serum

creatinine over 120 µmol/l, cardiac disease, abnormal ECG, previous aortic surgery or stent, abnormal WCC, abnormal serum sodium, AAA diameter and ASA grade. The AUC (bias-corrected) was 0.77 with good calibration.

Although the BAR score demonstrated improved statistical performance on internal validation compared with the VGNW model, a limitation of the BAR score is that it does not include a history of respiratory disease, as this was not collected in the NVD. Respiratory disease is included in the VGNW model and is viewed as an important predictor of outcomes by the majority of surgeons. Patients with significant respiratory disease will be identified by the ASA grade, which is included in the BAR score, but future models will almost certainly need to include this risk factor. On the final external validation of the VGNW model and BAR score, the BAR score demonstrated improved discriminatory ability on both internal and external validation compared with the VGNW model and demonstrated adequate discrimination in procedural subgroups.

General limitations of the development of the perioperative risk prediction models include potential incomplete case ascertainment. However, data submission to the NVD is improving, and coverage has reached 84%, which compares favourably with administrative data sets such as Hospital Episode Statistics data.[116] Although data cleaning was performed in both the VGNW and NVD databases, inaccuracies were likely to persist. Missing data were more of a problem with NVD. A number of potential risk factors had to be removed prior to any analysis because of significant missing data. For dichotomous risk factors with lower levels of missing data, a single imputation approach was adopted. Based on our in-depth understanding of the data collection process with regards to surgical clinical registries achieved through discussions with database managers and submitting clinicians and administrators, it was decided that missing data were much more likely to reflect absence of the risk factor than to be truly missing. As a result of this, data are therefore unlikely to be missing at random, meaning that other approaches to handling missing data, such as multiple imputation, would be inappropriate. For continuous or ordinal risk factors, either the median or the mean was imputed.

There is a difference in the outcomes the models were designed to predict. The BAR score was developed to predict in-hospital mortality, whereas the VGNW model was designed to predict 30-day mortality. A combined outcome of in-hospital mortality and 30-day mortality is potentially the most appropriate. However, no deaths occurred following discharge but within 30 days of the procedure in the most contemporary cohort of VGNW data. This suggests that the use of in-hospital mortality for perioperative predictive models in this setting is appropriate. Another potential limitation is that centre variation in perioperative mortality is not corrected for in the models we have considered. The issue of how to appropriately combine population-level and centre-level outcome data is an important area of current and future research in risk prediction modelling. Since publication, both the VGNW model and the BAR score have performed well in external validations conducted by other groups.[64,117] The first of these external validations used single-centre data from the UK (VGNW model only) with the second study using data from the Dutch Randomised Endovascular Aneurysm Management (DREAM) trial.[117]

Survival modelling

The work on developing models to predict survival following elective AAA repair is presented in *Chapter 6*. The presented data demonstrate good long-term survival following elective AAA repair in the north-west of England and Wales compared with other historical series.[118,119] This could be as a result of improved standards of care and improved population survival in general. As with all modelling studies using secondary data, there were challenges in terms of the data available, which were collected for other purposes, as they did not include all relevant variables, used uncontrolled designs that may introduce bias and reflected historical rather than current practice. These drawbacks limit the generalisability of this model to other settings and further research is required to validate the model externally.

The NVD did not record long-term outcome, which meant that the survival model used regional data for the north-west of England and Wales (VGNW). There are known geographical differences in population health that could influence survival independently of the method of AAA repair. At present the extent to which the survival model and outputs are generalisable within the UK and internationally is uncertain. The applicability of the survival model to current clinical practice is also uncertain because of the significant changes in clinical practice that have occurred since the early part of the data set with the increase use of EVAR being the most significant change. However, this will continue to be a limitation of studies assessing long-term outcomes until clinical practices stabilise.

Our survival model demonstrates a significant survival benefit at 5 years for patients who underwent open surgery compared with those undergoing EVAR. This contrasts with the published randomised trials in which survival following open repair and EVAR is similar.[38,76,120] This could be a result of differences in the patients selected for EVAR or open repair. Unlike earlier clinical trials, surgeons now undertake EVAR in most patients with suitable anatomy that are unfit for open repair. As more complex EVAR repairs are introduced, the trend for surgeons to reserve open surgery for the fittest patients only is likely to persist.

When modelling survival from the date of discharge, a history of ischaemic heart disease was not included in the model; abnormal preoperative ECG, however, was still a significant risk factor and included in the final survival model. This was presumably a consequence of patients with more significant underlying ischaemic heart disease dying in the early postoperative period.[118,119,121,122] Our finding that statins and antiplatelet therapy improve long-term survival emphasises the importance of these medications in the prevention of late cardiovascular events.[123] That statin use is associated with improved long-term survival is in keeping with previously published reports.[124,125]

The Aneurysm Repair Decision Aid

The DES model represents a novel approach to clinical decision-making in patients with AAA. It allows individualised evaluation of the relative benefits of continued surveillance or repair when patients attend surveillance. This approach contrasts with the current indication for elective AAA repair: a blanket AAA diameter threshold (5.5 cm in men and 5.0 cm in women) for all patients irrespective of individuals' characteristics. The ARDA now includes information from all stages of the clinical pathway: from predicted AAA growth through to repair and finally long-term survival following intervention. This project has demonstrated that it is possible to construct a model that represents and makes explicit a complex decision-making process, using secondary data sources. As the DES model underpinning the ARDA is refined and adapted for use in practice, future simulation can calculate CIs and other uncertainty measures to provide the surgeon and patient with additional information. The DES approach used by the ARDA can and should be updated when new data become available for any parts of the patient pathway. This means that the model can potentially be adapted for other geographical areas or refined as more accurate modelling for AAA growth or risk of rupture becomes available. Even if the patient pathway is altered, the ARDA can be adapted easily.

The model relies on the estimates of perioperative mortality and long-term survival produced by the regression models developed for the project. This means that the limitations of these models also apply to the DES model and the ARDA.

A number of additional assumptions were required to implement the DES/ARDA model. Most of these related to making best use of the data available. There were no data about the growth of AAAs of 5.5 cm and above, and the annual growth rate was assumed to independent from previous years. It was also assumed that death from other causes is independent of the AAA and its risk factors. It is not clear whether or not these assumptions would under- or overestimate life expectancy or the optimal repair size.

To make the model tractable at this development stage, it was assumed that the patient would have immediate surgery when the threshold AAA diameter is detected and that a patient's specific risk factors do not change over time. These assumptions may not accurately reflect what would occur in routine practice. For example, operating on younger and healthier patients may be a benefit of early intervention, which is not accounted for by the model. If there are delays between the decision to repair and the repair taking place, there is a risk of rupture or other adverse events that are not accounted for by the model. It was also assumed that 2-year survival is identical for both open surgery and EVAR. This implies that the additional perioperative mortality of open surgery is an acceleration of a death that would have happened in the following 2 years had surgery not been undertaken.

A limitation of the ARDA is that no information of the risk of reintervention following AAA repair is included in the clinical effectiveness analysis. Reintervention following EVAR and to some extent open AAA repair is an important outcome for both patients and health-care providers. Reintervention following EVAR is thought to be due mainly to AAA morphology and these data were not included in the available data sets used for the clinical effectiveness analysis. In the absence of data to the contrary, it was assumed that reintervention would occur soon after the initial repair. It was also assumed that the impact of reintervention on longer-term survival would be incorporated in the data used to estimate life expectancy. The probability and cost and QALY consequences of reintervention were included in the economic evaluation. However, this was based on published data from clinical trials. As discussed previously, this may not reflect current practice.

Much of the modelling behind the ARDA is based on observational real-world data. This strategy has strengths and limitations. A strength is that effect size estimates are based on the same population of patients that the ARDA will be applied to, whereas randomised trials tend to be conducted in highly selected populations. Effect size estimates are also based on realistic, rather than ideal, conditions. A weakness is that the data are prone to selection bias and confounding by indication. This means that any new clinical decision taken by the ARDA may not have the consequences that the DES modelling indicates.

There are also parts of the pathway where the data are limited. For example, long-term survival is measured following repair. There is no reliable survival information for patients who do not undergo repair. AAA growth rates are currently recalculated annually based on AAA diameter and are assumed to be independent of previous growth rates, an assumption that may not be true as long-term growth trajectories are not yet available.

The outcomes and decision thresholds predicted by the model and reported in *Chapter 7* demonstrate the potential for the model to help support surgeon and patient decision-making. However, the analysis did not include an assessment of uncertainty in the clinical data inputs and outcomes. Further validation of the model structure is required. The economic analysis did include a probabilistic assessment of uncertainty. This illustrated the high level of uncertainty associated with the data currently available.

There are computational limitations. Simulating each individual 100,000 times requires computing power and takes time. The code we use has yet to be optimised and was developed in R, a statistical package, rather than a fast, low-level programming language. We plan software development to address this.

The algorithm is intended to be used at surveillance consultations for patients with AAAs > 4.0 cm in diameter as a decision support tool for patients and clinicians. It is not intended to replace clinical decision-making. It is also not intended to be used to calculate whether open repair or EVAR should be performed. The information provided will help the patient and clinician to make a joint and informed decision on the timing and appropriateness of repair. The algorithm is designed to help the clinician and patient to reach an informed joint decision on whether to operate now, continue surveillance or even discontinue surveillance. As the AAA grows and the patient gets older or acquires new comorbidities, the information available to the algorithm updates; therefore, the algorithm should be rerun at each clinical encounter.

Economic analysis

The economic model used robust, but focused, methods to identify and extract data about the costs and utility associated with decisions on AAA repair. Focusing the electronic search on one database of published economic evaluations may have meant that other relevant papers and data were missed. However, the electronic search strategy, supplemented by hand searching of bibliographies to identify clinical trial reports, identified all the key papers reporting clinical and economic evaluations known to the research team.

The objective of the ARDA was to improve decision-making in the management of patients with AAA. Accordingly, the economic model used costs and utility values derived from national databases where possible. For the primary analysis, the costs of initial elective repair, revision surgery and emergency surgery (the key short-term costs) were estimated from the English NHS reference cost data set[73] to reflect the costs of EVAR and open surgery repair in routine practice. While these are relevant to routine practice in England, they may limit the generalisability of the data to other settings. However, the sensitivity analyses, which incorporated the range of cost estimates found for other settings, suggested that the results were robust.

In the absence of any reliable data from other sources, local data from VGNW were used to estimate NHS resources used in patient care during surveillance and long-term follow-up. However, comparison of the costs of AAA repair between VGNW, the NHS reference costs[73] and those previously published[77] indicate real differences. It is not clear whether or not this would also apply to the costs of surveillance and long-term follow-up. Again the results of the sensitivity analyses suggest that the results of the economic model were robust and the main conclusions were unaffected by different cost estimates.

Published data about population norms were used to estimate the starting utility values for people with AAA to estimate QALYs. Decrements were then applied to account for increasing age and the impact of AAA repair. The strength of this approach is that it may better reflect the values likely to be found in routine practice rather than clinical trials. As most patients with AAA are asymptomatic, AAA may have no direct impact on health status and utility until repair or rupture. Additionally, the UK population norm utility values for non-smokers[94] lie within the ranges reported at baseline in clinical trials on AAA surveillance or surgical repair.[76,78,79,100,101] The approach used in this evaluation is similar to that used in evaluations of the cost-effectiveness of screening and surveillance programmes for AAA.[80,95–98,102,103]

However, there are a number of limitations. The first is that published population norms aggregated utility values for age ranges, rather than by year of age. This means that the starting values for each vignette are approximated to the age specified for that person, which changes over time, as the ageing process is modelled in a stepwise rather than continuous fashion. The UK population norms report utility values for people aged > 75 years, which may overestimate the longer-term benefits if people survive to old age. Published population norms for other settings suggest that the utility values for people aged >80 years are in the region of 9% lower than those in the age range 70–79 years. Sensitivity analyses to explore the impact of alternative utility values indicated that the results of the economic model are robust to changes in the population norm values and decrements applied for ageing and the effects of AAA repair on health status.

Age, sex and smoking status were the only patient attributes used to estimate health-related utility values. As the ARDA is intended to provide information that can inform decisions for individual patients, it should be noted that current estimates of QALYs may be misleading for patients with significant comorbidities.

Comparison of the UK population norm utility data with those from other European and Scandinavian countries indicates differences in underlying health and utility weights.[99] The values for the UK population are at the lower end of the range of population norm utility estimates (UK = 0.773 for 64–75 years, range = 0.773–0.904).[99] Estimates of resource use and costs also appear to vary between countries and

between routine practice and published research on screening, surveillance and AAA repair. This may reduce the generalisability of the results from this economic evaluation to other settings. However, the sensitivity analyses, which incorporated the range of utility values found for other settings, suggested the results were robust to changes in these estimates.

The economic model does not include the long-term costs and utility of non-fatal stroke and other disabling events in the estimation of net costs and QALYs. The impact of these events on life expectancy was incorporated in the survival data used in the model. The exclusion of the costs and utilities of non-fatal adverse events was based on several factors. First, trials of EVAR and open repair indicate no significant difference in the occurrence of these events. Second, the main objective of the algorithm is to determine the timing of AAA repair and to prevent rupture and the need for emergency surgery. Only a higher rate of non-fatal stroke and other disabling events associated with rupture and emergency surgery than the rate of events associated with elective surgery would impact on the value of the algorithm.

Chapter 11 Conclusions and recommendations

Conclusions

The ARDA is a DES algorithm that allows an individualised evaluation of the relative benefits of continued surveillance or repair for patients with AAA. Although it is impossible to report the results for all the possible permutations, AAA repair at 5.0 cm and 5.5 cm for women and men respectively appears to be supported by the algorithm. Young patients at low risk of perioperative mortality would not be harmed but could potentially benefit from earlier repair than the current threshold. Elderly patients with high operative mortalities may benefit from delaying repair beyond the current threshold or not undertaking repair at all.

To inform the DES model, two models for perioperative mortality following elective AAA repair were developed. The regional model (VGNW) included age, female sex, diabetes, renal dysfunction, respiratory disease, open surgery and antiplatelet medication (a surrogate marker for vascular disease) as predictors. The national model (BAR) included 11 risk factors: open repair, age, female sex, creatinine > 120 µmol/l, cardiac disease, abnormal ECG, previous aortic surgery or stent, abnormal WCC, abnormal sodium, AAA diameter and ASA grade. On subsequent external validation, the BAR score outperformed both the VGNW and Medicare models demonstrating excellent discrimination overall and good discrimination in procedural subgroups. This suggests that the BAR score should be adopted for the prediction of perioperative mortality following elective AAA repair; this model was used for the ARDA.

Survival modelling using only preoperative risk factors identified age, female sex, ischaemic heart disease, abnormal ECG, anaemia, abnormal serum sodium and creatinine > 120 µmol/l as predictors of poorer long-term survival following AAA repair with statin and antiplatelet therapy associated with improved survival. These patient-related factors are available and should be considered when making clinical decisions regarding elective AAA repair.

The overall results of the economic evaluation comparing the ARDA to the current indication for elective AAA repair suggest little difference in overall cost, although mean costs may be marginally lower if the ARDA is adopted. The sensitivity analysis to explore the impact of using LYGs, alternative cost and utility estimates did not change this result.

Although the blanket indication for elective AAA repair at 5.0 cm in women and 5.5 cm in men is still applicable to many patients, the ARDA provides surgeons and their patients with the key information they need to make an explicit and informed decision. For younger, fit patients, particularly if AAA repair during their lifetime is almost inevitable, earlier repair improves QALYs and may even be less expensive. For older or unfit patients, repair may be delayed until the AAA diameter increases, or may not be undertaken at all. The ARDA should not be used to influence the decision between open surgery and EVAR repair, as it assumes that this decision is made by the surgeon.

Future research

The discussion in *Chapter 10* identified a number of key limitations in the data that were available to structure and populate the predictive models of perioperative mortality, survival and DES that underpin the ARDA. Assumptions were required to make the DES tractable in this development stage. Further work is required to develop the model for implementation into routine practice, to assess the feasibility and acceptability of the ARDA, to address the data limitations and to develop the processes needed to update the model structure and data as practice changes. Evaluation of the feasibility and acceptability of the ARDA is required followed by rigorous analysis of its clinical effectiveness and cost-effectiveness in routine care.

The ARDA can be characterised as a complex intervention. It reflects and makes explicit a multifactorial decision-making process and synthesises a number of mechanisms (e.g. underlying patient health and demographic characteristics, surveillance, aneurysm growth and rupture, choice of AAA repair procedure and associated mortality and survival). Each component has an independent effect on patient outcomes. In addition, there is the potential for one or more components to mediate or modify the impact of other components on outcome. For example, a patient's underlying health and demographic characteristics may mediate or moderate the rate of aneurysm growth, choice of repair (EVAR or open) and costs and outcomes of AAA repair. There are a range of important and inter-related outcomes that are relevant at differing levels to participants, service providers and policy-makers. The work reported here has developed the ARDA using best evidence and theory. This reflects the first stage of the Medical Research Council guidance for the development and evaluation of complex interventions. The next steps to move towards implementation of the ARDA into routine practice include:

- development work to refine and adapt the ARDA for use in routine practice and improve the evidence base with which to populate the underpinning models
- phased evaluation of the intervention starting with studies to test the acceptability and feasibility of implementing the ARDA, to assess the acceptability and feasibility of alternative evaluation designs and procedures, to develop and assess methods of recruitment and retention of participants, and to estimate sample size. These are required prior to exploratory and definitive trials of clinical effectiveness and cost-effectiveness
- implementation, monitoring and surveillance of the intervention.

Development of the Aneurysm Repair Decision Aid and data inputs

The discussion highlighted a number of assumptions made in the model structure to implement this first phase of the work. In addition, the structure and methods used for the underpinning regression models and DES model require rigorous internal and external validation. This is to ensure that the models reflect routine practice and patient populations, to ensure that bias is minimised and to optimise the accuracy of the outputs. There are also limitations in terms of computing power and time. The ARDA needs to be accessible to both clinicians and patients in terms of the user interface and in computation.

Research priority 1

Further development work is needed to statistically validate the ARDA and underpinning model structures in different settings and populations. Work is also needed to translate the DES model structure from the R statistical package to a fast, low-level programming language that optimises the simulation processes for use in routine practice. A user interface is required to ensure the ARDA is accessible to all those involved in clinical decisions and policy.

Research priority 2

Further systematic review and qualitative work with surgeons, patients and policy-makers is required. This is needed to expand and validate the DES model structure; ensure that it captures all the events that are important to each of these actors; and to develop and test the user interface. For example, it is essential that information that predicts the risk of reintervention or complications following repair (particularly AAA morphology for EVAR) are incorporated into the algorithm as this has important clinical, quality-of-life and cost implications. Processes to routinely identify changes in practice to update the structure of the models incorporated in the ARDA (AAA growth and rupture risk, BAR score and survival models). Perioperative risk models will lose calibration over time.[126] The interval for validating and updating the different models is not known and work is needed to identify this. For the future, the ARDA may need to include new variables and factors that may predict AAA growth, risk of rupture or outcome following repair. Potential risk factors include biomarkers,[127] assessments of functional capacity[128] and genetic analysis.[129] Cardiopulmonary exercise testing assesses individual patient functional capacity and identifies patients at increased risk of perioperative death.[128,130–133] Cardiopulmonary exercise test data may be incorporated into the ARDA in the future if it becomes widely implemented in routine practice.

The outcomes and decision thresholds predicted by the model and reported in *Chapter 7* demonstrate the potential for the model to help support surgeon and patient decision-making. The economic analysis included a probabilistic assessment of uncertainty for the estimates of cost, QALYs and LYGs. This illustrated the high level of uncertainty associated with using the data currently available. As noted in the discussion in *Chapter 10*, the underpinning models for the ARDA use data collected for other purposes. Key issues are that the data are incomplete (owing to missing observations in available data sets and to lack of any data for specific variables), may be inaccurate or biased and may relate to previous rather than current practice and patient populations. To be of use in clinical practice, the data used in the models will need to be updated to reflect changes in patient selection and health as well as changes in repair techniques.

Research priority 3

Research is needed to develop existing databases and registries that use routinely recorded data. This includes methods to extend the scope of the NVD and other relevant data sets, to include key variables required for the ARDA models and to better inform clinical practice in the absence of the ARDA. These include key clinical, service use and cost and patient health status data to reduce uncertainty in the estimates of clinical effectiveness and cost-effectiveness of the ARDA-based decisions. It is also necessary that there is work to identify methods to increase the accuracy and minimise bias in existing data, which can be implemented in the NHS and used in routine data collection. Work to explore the feasibility and acceptability of implementing processes to link the data sets with the ARDA is required, to facilitate the timely and routine updating of the data used by the models.

The economic evaluation conducted in this project assessed the relative cost-effectiveness of decisions to repair AAA based on the ARDA recommendations or current guidelines. It was outside the scope of this research to assess the cost-effectiveness of implementing the ARDA into routine practice. There are likely to be additional costs incurred in the routine use and maintenance of the ARDA. These could be offset by increases in patient health benefit that may also reduce future service costs.

Research priority 4

As the ARDA models are developed and the feasibility and acceptability of implementing them into routine practice are evaluated, the model used for the economic evaluation needs to be extended to explore the potential for the ARDA to be cost-effective.

Phased evaluation of the intervention

This project has established that it is possible to construct a complex decision aid that provides useful information to support patient and surgeon decision-making about the timing of AAA repair. The service user group for the project has had an active role in defining the scope and outputs of the ARDA. However, little is known at this stage about the acceptability and feasibility of implementing the ARDA and associated data requirements in routine practice.

Research priority 5

Mixed-method evaluations are required to qualitatively and quantitatively assess the feasibility of implementing the ARDA and methods to collect and update the data required for the decision tool; barriers and facilitators to implementation; likely adherence with the recommendations of the ARDA; and the acceptability of the tool and its recommendations to patients, surgeons and policy-makers.

If the ARDA and associated data collection and updating processes is demonstrated to be feasible and acceptable, then prospectively collected evidence is required about the long- and short-term clinical effectiveness and cost-effectiveness. While a RCT is seen as the gold standard design to minimise bias and impact of confounding factors, there are also limitations in terms of length, costs and feasibility. The prospective evaluation design needs to be sufficiently robust to identify potentially small but important and relevant effects of the ARDA that may take some time to occur following implementation into practice

and use in any individual patient–surgeon decision. In addition, there are likely to be important effects of selection, allocation and unobservable biases.

Research priority 6a

Mixed-methods research is needed to qualitatively and quantitatively assess the feasibility and acceptability of a RCT, or other prospective study design, to all stakeholders. The research should also identify key confounders and biases and barriers to evaluation and any barriers and facilitators to the recruitment and retention of study centres, staff and participants. A comparison of the specific strengths and weaknesses of alternative designs to evaluate the ARDA and data collection processes in the UK setting is an important component of this stage. A major aim of this research would be to inform the design of the full RCT/controlled non-randomised evaluation of clinical effectiveness and cost-effectiveness.

Research priority 6b

Pilot and/or small exploratory trials are required to test the study design for a full, definitive trial. The main objectives of these trials include assessment of methods to recruit and retain study centres, staff and participants; documentation of likely drop-out rates; exploration of reasons for non-compliance with the study protocol and/or interventions; the feasibility and acceptability of data collection methods and instruments to measure outcomes and service use.

Research priority 6c

Full definitive RCTs/controlled, integrated clinical effectiveness and cost-effectiveness evaluations are needed in the UK setting. The target population and participant sample, intervention and comparator, outcomes and measures need to be clearly described and analysed. The design of the evaluation needs to be evidence based and informed by the work identified in research priorities 1–5. The length of follow-up needs to be sufficient to identify the impact of the ARDA on the decision to repair the AAA and the longer-term impact on survival, service use and costs and patient health benefit.

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Matthew Sperrin (Lecturer, Health Data Science) developed the DES model and drafted the corresponding chapter in this report.

Eric Carlson (Research Assistant, Cardiovascular Surgery) co-ordinated the project and final report, drafted sections of this report, conducted the survival and regional health economic analysis and organised the patient group.

Natasha Chinai (Clinical Research Fellow) advised on the clinical aspects of the survival analysis, drafted the corresponding chapter in this report and provided clinical input for the DES model development.

Dionysios Ntais (Research Associate, Health Economics) conducted the systematic review to inform the economic evaluation (with Matthew Hamilton and Linda Davies), codeveloped the health economic components of the DES, undertook the cost-effectiveness analyses and provided comments and critical input during the drafting of the report.

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Graham Dunn (Professor, Biostatistics) provided statistical guidance on the overall project.

Iain Buchan (Clinical Professor, Public Health Informatics) provided statistical guidance on the overall project and public health implications and edited the report.

Linda Davies (Professor, Health Economics) supervised the health economic modelling work, and (with Dionysios Ntais, Matthew Hamilton and Eric Carlson) wrote the economic evaluation chapters. Linda Davies also had a substantive, critical input to the discussion, conclusion and recommendations for research sections as well as critically reviewing the report overall.

Charles N McCollum (Professor, Surgery) was principal investigator of the project, provided overall direction and supervision for all aspects of the project and edited this report.

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Appendix 1 Vascular Governance North West contributing surgeons

Surgeons who contributed to the Vascular Governance North West database

John Abraham	Maher Hamish	Srinivasa Rao Vallabhaneni
Haytham Al-Khaffaf	Madgi Hanafy	David Reilly
Nile Allaf	Simon Hardy	Steve Richardson
Mohamed Baguneid	Neil Hulton	Graham Riding
Arun Balakrishnan	Riza Ibrahim	Yousef Rouhani
Stephen Blair	Mohideen Jameel	Robert Salaman
John Brennan	David Jones	Mark Scriven
Moatasiem Bukhari	Jos Joseph	James Scurr
John Calvey	Ursula Kirkpatrick	Ferdinand Serracino-Inglott
Colin Chan	Otto Klimach	Raashid Shahbazi
Ramasubramanyan Chandrasekar	Manmohan Madan	Ramanathan Shivalingham
Antonio da Silva	Barun Majumder	Jonathan Smout
Linda De Cossart	Frank Mason	Vince Smyth
Sameh Dimitri	Charles McCollum	William Tait
Susan Drinkwater	Paul Moody	Rashid Tawqeer
Paul Edwards	John Mosley	Nee Beng Teo
Ansy Egun	David Murray	George Thomson
Graeme Ferguson	Jag Naik	Mark Tomlinson
Robert Fisher	Simon Neequaye	Francesco Torella
Jonathan Ghosh	Tom Nicholas	Richard Ward
Martin Greaney	Deji Olojugba	Mark Welch
Andrew Guy	Madu Onwudike	Leith Williams
Mathew Hadfield	Taohid Oshodi	Gerard Williams
	Hisham Osman	Paul Wilson
	Vittorio Perricone	Leszek Wolowczyk
	Chowdary Pratap	Anthony Woodyer
	Asad Rahi	Iraj Zeynali

Appendix 2 Individual patient data

TABLE 43 Data fields collected by the VGNW programme for AAA repair

Data field	Data type
Demographic data	
Hospital	Free text
Surgeon	Free text
Anaesthetist	Free text
Radiologist	Free text
Surname	Free text
First name	Free text
NHS number	Free text
Postcode	Free text
Date of birth	Free text
Sex	List
AAA specific data	
Symptoms	Yes/no
Level	List
Diameter	Free text
Type	List
Comorbidity data	
Ischaemic heart disease	Yes/no
Previous MI	Yes/no
Cardiac failure	Yes/no
Chronic respiratory disease	Yes/no
Dyspnoea	Yes/no
Previous stroke/TIA	Yes/no
Peripheral vascular disease	Yes/no
Diabetes	Yes/no
Antiplatelet medication	Yes/no
Antihypertensive medication	Yes/no
Statin medication	Yes/no
Smoker	List
Preoperative investigations	
Abnormal ECG	Free text
Sodium	Free text
Potassium	Free text

continued

TABLE 43 Data fields collected by the VGNW programme for AAA repair (*continued*)

Data field	Data type
Urea	Free text
Creatinine	Free text
eGFR	Free text
Haemoglobin	Free text
WCC	Free text
Platelets	Free text
Data field	Data type
Operative details	
Admission date	Free text
Procedure date	Free text
Procedure urgency	List
Procedure type	List
Previous aortic surgery/stent	Yes/no
Open surgery details	
Type of repair	List
Clamp level	List
Intraoperative blood loss	Free text
Blood transfusion	Free text
EVAR details	
Graft type	List
Fenestrations	Yes/no
Branched	Yes/no
Scallops	Yes/no
Chimney	Yes/no
Access	List
Adjunct procedure	Yes/no
Intraoperative blood loss	Free text
Blood transfusion	Free text
Contrast volume	Free text
Conversion to open	Yes/no
Endoleak on completion	Yes/no
Device name	Free text
Outcomes	
Return to theatre	Yes/no
Graft limb occlusion	Yes/no
Limb ischaemia	Yes/no

TABLE 43 Data fields collected by the VGNW programme for AAA repair (*continued*)

Data field	Data type
Wound infection	Yes/no
MI	Yes/no
Stroke	Yes/no
Respiratory failure	Yes/no
Renal failure	Yes/no
In-hospital mortality	Yes/no
Discharge date	Free text
Additional comments	Free text

eGFR, estimated glomerular filtration rate; TIA, tertiary ischaemic attack;

TABLE 44 Data fields collected by the NVD for AAA repair

Data field	Data type
Preoperative data	
Patient date of birth[a]	Date
Local patient identifier[a]	Free text
Sex[a]	List
OPCS procedure code[a]	List
Admission date[a]	Date
Admission mode[a]	List
Transfer	Yes/no
Diabetes	Yes/no
Cardiac history	Yes/no
Current smoker	Yes/no
Renal dialysis	Yes/no
Renal transplant	Yes/no
Glasgow Coma Scale	List
Loss of consciousness	Yes/no
Symptomatic aneurysm	Yes/no
Maximum AAA diameter	Free text
AAA screening programme	Yes/no
Surveillance programme	Yes/no
Suitable for EVAR	Yes/no
Fit for open surgery	Yes/no
ECG	List
Other abnormal rhythm	Free text
Antiplatelet agent	Yes/no

continued

TABLE 44 Data fields collected by the NVD for AAA repair (*continued*)

Data field	Data type
Beta-blocker	Yes/no
Statin	Yes/no
Lowest preoperative SBP	Free text
Highest preoperative pulse	Free text
Haemoglobin	Free text
WCC	Free text
Urea	Free text
Creatinine	Free text
Sodium	Free text
Potassium	Free text
Albumin	Free text
INR	Free text
MRSA positive	List
Operative data	
Operation date[a]	Date
ASA grade	List
Operation start time[a]	Date/time
Operation finish time[a]	Date/time
Grade of senior surgeon	List
Timing of surgery	List
Previous aortic surgery/stent	Yes/no
Data field	Data type
AAA surgery	List
EVAR	Yes/no
Type of graft	List
Type of graft other	Free text
Laparoscopic AAA repair	List
Anaesthetic	Check
Grade of anaesthetist	List
Aortic findings	Multilist
Intraoperative blood loss	List
Volume of cell salvage transfused	Text
Open area of necrosis	Yes/no
Wound class	List
Graft used	List
Lowest intraoperative systolic blood pressure	Text
Highest intraoperative pulse	Text

TABLE 44 Data fields collected by the NVD for AAA repair (*continued*)

Data field	Data type
Postoperative data	
AAA reoperation	Yes/no
Any complications	Yes/no
Limb ischaemia	List
Anastomotic complications	Radio
Haemorrhage	Radio
Infection	Multilist
Diagnosis date	Date
Surgical site infection	List
Organism	Free text
Postoperative positive for MRSA	Yes/no
Developed MRSA bacteraemia	Yes/no
Developed *Clostridium difficile* diarrhoea	Yes/no
Wound dehiscence	List
Venous thromboembolism	List
Postoperative stroke	List
Postoperative MI	Yes/no
Postoperative cardiac failure	Yes/no
Postoperative impaired renal function	Yes/no
Need for haemofiltration/dialysis	Yes/no
Postoperative hypotension	Yes/no
Postoperative respiratory failure	Yes/no
Postoperative ischaemic bowel	Yes/no
Other complication	Free text
Destination after operation	List
Return to theatre within 30 days	Yes/no
Discharge status[a]	List
Discharge date[a]	Date
Death date[a]	Date
Death cause[a]	Free text

INR, international normalised ratio; MRSA, meticillin-resistant *Staphylococcus aureus*.
a Fields defined as mandatory for submission by the NVD.

Appendix 3 Studies used in the RESCAN analysis of abdominal aortic aneurysm growth and rupture

TABLE 45 Data taken from the RESCAN published manuscript[18]

Study	Number of patients
Western Australia	685
Bournemouth, UK	677
Chichester, UK	1504
Edinburgh, UK	1052
Gloucestershire, UK	1981
Huntingdon, UK	629
Leeds, UK	267
Leicester, UK	899
Manchester, UK	1095
MASS, UK	1122
Tromsó, Norway	224
PIVOTAL, USA	715
Propranolol, Canada	548
Galdakao, Spain	926
Stirling, UK	457
Gävle, Sweden	243
UKSAT, UK	2227
Viborg, Denmark	224

MASS, Multicentre Aneurysm Screening Study; PIVOTAL, The Positive Impact of Endovascular Options for treating Aneurysms Early.

Appendix 4 Patient and public involvement group membership

TABLE 46 Members of the PPI group

Name	Group position
Helen O'Donnell	Vascular specialist nurse
Nick Wisely	Consultant anaesthetist
Anthony Echersley	Patient
Max Ramsey	Patient
Wendy Ramsey	Patient relative
Ann Pollard	Patient
Doug Claydon	Patient (cochairman)
David Vaughan	Patient
Janet Vaughan	Patient relative
Robert Rolfe	Patient
Malcolm Pythian	Patient
Pat Pythian	Patient relative
Colin Sadler	Patient
Lionel Nuttall	Patient
John Hatton	Patient
David Smith	Patient (cochairman)
Peter Gardiner	Patient

In addition, members of the NIHR-HTA project were present at all meetings, including Charles McCollum, Stuart Grant, Eric Carlson and Natasha Chinai.

Appendix 5 Patient and surgeon information

Surgeon information regarding patient consent for inclusion in VGNW

Please use this as a guide to inform and consent patients eligible for inclusion in the Vascular Governance North West (VGNW) Audit Database.

Vascular surgical specialists throughout the North West are collecting information about patient care during major vascular procedures such as carotid endarterectomy and aortic aneurysm repair. The information includes personal details such as NHS number, name, date of birth and address as well as medical history, operative details, and follow-up data. This information is stored securely as required by the Data Protection Act 1998. We only share this information with the patient's care team or with NHS organizations that can tell us how the patient is in years to come. Best practice is to seek patient permission to hold this information.

Please explain to the patient that the purpose of collecting and holding this information is to allow us to provide reports to individual trusts regarding the volume, the risks, and the outcomes of these repairs. Also, please emphasis that only anonymous data sets are available for research purposes and that they cannot be identified in any way by the researchers.

If a patient consents to have their data included in the VGNW, please record this in the patient's hospital notes using the phrase "This patient has consented to have their data included in the VGNW database". Should a patients wish to have their data removed from the database, please contact Megan Jones, VGNW project coordinator, on 0161 291 5823. The surgical team will be responsible for relaying this request to the VGNW team. Patient data will be removed immediately upon receipt of this request.

VGNW recommends that patients are provided with an information sheet regarding the use of their data (appendix 1) and that this is supported with verbal explanations by a clinician with sufficient expertise.

Patient Information

This information sheet tells you why your local care team would like your permission to store data on your treatment and the outcomes of that treatment in the Vascular Governance North West (VGNW) Audit Database.

Vascular surgical specialists throughout the North West are collecting information about patient care during major vascular procedures such as carotid endarterectomy and aortic aneurysm repair. The information includes personal details such as NHS number, name, date of birth and address as well as medical history details, details about your operation, and follow-up data. This information is stored securely as required by the Data Protection Act 1998. We only share this information with your care team, the Health and Social Care Information Centre (HSCIC) and other central UK NHS bodies to gather information about your health status.

The purpose of collecting and holding this information is to provide reports to hospitals and surgeons regarding the number of procedures they perform, the different patient characteristics that may increase the risk of a specific procedure, and the outcomes of these procedures. Also, this information can be combined with information from future hospital admissions to help surgeons decide on the best treatment strategy to minimize complications and maximize quality and length of life.

Anonymous data sets (with all your personal details removed) will be made available for research purposes. You could not be identified in these data sets. This research is vital to the future development of vascular surgery.

If you do not wish to have your data stored in VGNW or you would like it removed from the database at a later date, please inform your surgeon. They will be responsible for relaying this request to the VGNW team. Your data will be removed immediately upon receipt of this request.

Please contact Megan Jones, VGNW project coordinator, on 0161 291 5823 with any questions or if you would like further information.

Appendix 6 Risk prediction scores in abdominal aortic aneurysm repair

Glasgow Aneurysm Score

(age [continuous in years]) + (17 × shock) + (7 × myocardial disease) + (10 × cerebrovascular disease) + (14 × renal disease). (2)

Vascular Biochemistry and Haematology Outcome Model

−2.257 + (0.1511 × male) + (0.9940 × mode of admission) + (0.05923 × age [continuous in years]) + (0.001401 × serum urea [continuous mmol/l]) − (0.01303 × sodium [continuous mmol/l])− (0.03585 × potassium [continuous mmol/l]) − (0.2278 × haemoglobin [continuous g/dl]) + (0.02059 × WCC [continuous × 109/l]). (3)

Vascular Physiological and Operative Severity Score for enUmeration of Mortality

−6.0386 + (0.1539 × physiology score). (4)

A physiology score calculator is available (http://www.riskprediction.org.uk). The score can be calculated using table 1 in the POSSUM scoring system manuscript.[114]

Medicare model

−5.02 + (0.42 × female sex) + (0.15 × age [70–75 years]) + (0.63 × age [75–80 years]) + (1.14 × age 80 > years) + (0.71 × chronic renal insufficiency) + (0.95 × end-stage renal disease) + (0.55 × congestive heart failure) + (0.30 × vascular disease) + (1.17 × open repair). (5)

Vascular Governance North West model

−9.3431 + (0.0486 × age [continuous in years]) + (0.7322 × female sex) + (0.6620 × diabetes) + (0.0073 × creatinine [continuous in μmol/l]) + (0.4718 × respiratory disease) + (0.7762 × antiplatelet medication) + (1.3130 × open surgery). (6)

Appendix 7 Discrete event simulation model output definitions

TABLE 47 Discrete event simulation model output definitions

Output	Definition
Median life expectancy	***Median age at death of all patient simulations***
1-year survival	Per cent of all patient simulations still alive at 1 year following initiation of the simulation
2-year survival	Per cent of all patient simulations still alive at 2 years following initiation of the simulation
5-year survival	Per cent of all patient simulations still alive at 5 years following initiation of the simulation
10-year survival	Per cent of all patient simulations still alive at 10 years following initiation of the simulation
Other cause of death (prior to repair)	Per cent of all non-AAA patient simulation deaths prior to AAA repair
Death due to rupture	Per cent of all patient simulations with death due to rupture of AAA
Rupture survival	Per cent of all patient simulations with rupture of AAA and discharge from hospital following AAA repair
Postoperative survival	Per cent of all patient simulations that undergo AAA repair and also survive until discharge
Growth rate at size	Mean growth rate (cm/year) of AAA of all patient simulations at designated repair threshold
1-year rupture probability at intervention	Per cent of all patient simulations that would rupture within 1 year following the designated repair threshold
Probability of repair	Per cent of all patients simulations that reach the designated repair threshold
In-hospital mortality on repair	Per cent of all patients simulations that reach the designated repair threshold that die in hospital following elective repair
5-year postoperative survival	Per cent of all patient simulations that reach the designated repair threshold that also are still alive at 5 years following elective repair
10-year postoperative survival	Per cent of all patient simulations that reach the designated repair threshold that also are still alive at 10 years following elective repair
Median age at repair (years)	Median age of all patient simulations that reach the designated repair threshold
Median years to reach size	Median time (years) to reach the designated repair threshold

Appendix 8 Excluded and included economic studies

TABLE 48 Studies excluded by screening titles and abstracts

Reference	Reason for exclusion
Abbotts J, McIntosh H. *Is There a Difference in Operative Mortality Between Endovascular Aneurysm Repair and Open Surgery in Elective Abdominal Aortic Aneurysm?* Glasgow: NHS Quality Improvement Scotland (NHS QIS); 2012	1
Abularrage CJ, Sheridan MJ, Mukherjee D. Endovascular versus 'fast-track' abdominal aortic aneurysm repair. *Vasc Endovascular Surg* 2005;**39**:229–36	1
Arnaoutakis GJ, Hundt JA, Shah AS, Cameron DE, Black JH. Comparative analysis of hospital costs of open and endovascular thoracic aortic repair. *Vasc Endovascular Surg* 2011;**45**:39–45	1
Aune S, Laxdal E, Pedersen G, Dregelid E. Lifetime gain related to cost of repair of ruptured abdominal aortic aneurysm in octogenarians. *Eur J Vasc Endovascular Surg* 2004;**27**:299–304	1
Ballard JL, Abou-Zamzam AM, Teruya TH, Bianchi C, Petersen FF, Quinones W, *et al.* Quality of life before and after endovascular and retroperitoneal abdominal aortic aneurysm repair. *J Vasc Surg* 2004;**39**:797–803	1
Beeman BR, Doctor LM, Doerr K, McAfee-Bennett S, Dougherty MJ, Calligaro KD. Duplex ultrasound imaging alone is sufficient for midterm endovascular aneurysm repair surveillance: a cost analysis study and prospective comparison with computed tomography scan. *J Vasc Surg* 2009;**50**:1019–24	3
Beinfeld MT, Wittenberg E, Gazelle GS. Cost-effectiveness of whole-body CT screening. *Radiology* 2005;**234**:415–22	1, 2
Bisdas T, Wilhelmi M, Haverich A, Teebken OE. Cryopreserved arterial homografts vs silver-coated Dacron grafts for abdominal aortic infections with intraoperative evidence of microorganisms. *J Vasc Surg* 2011;**53**:1274–81	3
BlueCross BlueShield Association. *Special Report: Critical Appraisal of CT Colonography Cost-effectiveness Analyses*. Chicago, IL: BCBS; 2009	3
Brooke BS, Goodney PP, Powell RJ, Fillinger MF, Travis LL, Goodman DC, *et al.* Early discharge does not increase readmission or mortality after high-risk vascular surgery. *J Vasc Surg* 2013;**57**:734–40	3
Canadian Agency for Drugs and Technologies in Health. *Endovascular Therapy for Elective and Ruptured Abdominal Aortic Aneurysm Procedures: A description of Utilization Trends across Canada.* Ottawa, ON: CADTH; 2013	1
Chandra V, Greenberg JI, Al-Khatib WK, Harris EJ, Dalman RL, Lee JT. Cost impact of extension cuff utilization during endovascular aneurysm repair. *Ann Vasc Surg* 2012;**26**:86–92	1
Chen S, Husereau D, Noorani H, Tran K, Boudreau R, Lentle B, *et al.* Portable ultrasound devices in emergency departments. Ottawa, ON: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2006	3
Chisci E, Setacci F, Iacoponi F, De Donato G, Cappelli A, Setacci C. Surveillance imaging modality does not affect detection rate of asymptomatic secondary interventions following EVAR. *Eur J Vasc Endovasc Surg* 2012;**43**:276–81	3
Cote B, Lance JM, LeBrun M. *Population Ultrasound Screening for Abdominal Aortic Aneurysms.* Montreal, QC: Agence d'Evaluation des Technologies et des Modes d'Intervention en Sante (AETMIS); 2010	1
Dachman AH, Flicker MS, Tsoukas AT, Hazra A. Economic impact of extracolonic findings at computed tomographic colonography. *J Comput Assist Tomo* 2008;**32**:497–503	3
del Mar Polo de Santos M, Matos SL, Navarro BM, Alcazar RA. *Systematic Review of the Effectiveness and Safety of Endovascular Treatment of Thoracic Aortic Diseases*. Madrid: Agencia de Evaluacion de Tecnologias Sanitarias (AETS); 2005	3

continued

TABLE 48 Studies excluded by screening titles and abstracts (*continued*)

Reference	Reason for exclusion
Duriseti RS, Brandeau ML. Cost-effectiveness of strategies for diagnosing pulmonary embolism among emergency department patients presenting with undifferentiated symptoms. *Ann Emerg Med* 2010;**56**:321–32	3
Fleisher LA, Corbett W, Berry C, Poldermans D. Cost-effectiveness of differing perioperative beta-blockade strategies in vascular surgery patients. *J Cardiothorac Vasc Anesth* 2004;**18**:7–13	3
Fleming C, Whitlock E, Beil T, Lederle F. *Primary Care Screening for Abdominal Aortic Aneurysm*. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2005	1
Galician Agency for Health Technology Assessment (AVALIA-T). *Efficacy and Effectiveness of Screening for Abdominal Aortic Aneurysm in a Population at Risk. Cost-effectiveness Analysis. Applicability inside the National Healthcare System*. Santiago de ComPostela: Galician Agency for Health Technology Assessment (AVALIA-T); 2008	1
Gazoni LM, Speir AM, Kron IL, Fonner E, Crosby IK. Elective thoracic aortic aneurysm surgery: better outcomes from high-volume centers. *J Am Coll Surg* 2010;**210**:855–60	3
Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther* 2009;**16**:554–64	1
Goodyear SJ, Yow H, Saedon M, Shakespeare J, Hill CE, Watson D, *et al.* Risk stratification by preoperative cardiopulmonary exercise testing improves outcomes following elective abdominal aortic aneurysm surgery: a cohort study. *Periop Med* 2013;**2**	3
Guirguis-Blake JM, Beil TL, Sun X, Senger CA, Whitlock EP. *Primary Care Screening for Abdominal Aortic Aneurysm: A Systematic Evidence Review for the U.S. Preventative Services Task Force*. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2014	1
Ha CD, Calcagno D. Amplatzer Vascular Plug to occlude the internal iliac arteries in patients undergoing aortoiliac aneurysm repair. *J Vasc Surg* 2005;**42**:1058–62	3
Hassan C, Pickhardt P, Laghi A, Kim D, Zullo A, Iafrate F, *et al.* Computed tomographic colonography to screen for colorectal cancer, extracolonic cancer, and aortic aneurysm: model simulation with cost-effectiveness analysis. *Arch Intern Med* 2008;**168**:696–705	1, 3
Haute Autorite de Sante/French National Authority for Health (drafted by the former National Agency for Accreditation and Evaluation in Healthcare). *Stent-grafts in the Treatment of Thoracic Aortic Aneurysm and Dissection*. Paris: Haute Autorite de Sante (French National Authority for Health) (HAS); 2006	3
HAYES, Inc. *Endovascular Repair, Abdominal Aortic Aneurysms*. Lansdale, PA: HAYES, Inc.; 2007	1
HAYES, Inc. *Endovascular Repair of Thoracic Aortic Aneurysms and Dissections*. Lansdale, PA: HAYES, Inc.; 2007	3
HAYES, Inc. *Endovascular Repair of Abdominal Aortic Aneurysms*. Lansdale, PA: HAYES, Inc.; 2009	1
HAYES, Inc. *Thoracic Aortic Aneurysms and Dissections (TAAD)*. Lansdale, PA: HAYES, Inc.; 2011	3
HAYES, Inc. *Endovascular Repair of Abdominal Aortic Aneurysms*. Lansdale, PA: HAYES, Inc.; 2013	1
Institut fuer Qualitaet und Wirtschaftlichkeit im Gesundheitswesen (IQWiG). *Production of an Evidence Report on the Relationship Between the Quantity of Operations Performed in Patients Undergoing Elective Surgery of an Abdominal Aortic Aneurysm and the Quality of Outcome*. Cologne: Institut fuer Qualitaet und Wirtschaftlichkeit im Gesundheitswesen (IQWiG); 2006	1
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Karmy-Jones R, Bloch R, Nicholls S. A comparison of endovascular repair versus open repair of abdominal aortic aneurysms in a community setting. *Innovations* 2009;**4**:261–4	1
Lachat ML, Pecoraro F, Mayer D, Guillet C, Glenck M, Rancic Z, *et al.* Outpatient endovascular aortic aneurysm repair: experience in 100 consecutive patients. *Ann Surg* 2013;**258**:754–9	1
Lee WA, Brown MP, Nelson PR, Huber TS. Total percutaneous access for endovascular aortic aneurysm repair ('Preclose' technique). *J Vasc Surg* 2007;**45**:1095–101	1

TABLE 48 Studies excluded by screening titles and abstracts (*continued*)

Reference	Reason for exclusion
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Mani K, Alund M, Bjorck M, Lundkvist J, Wanhainen A. Screening for abdominal aortic aneurysm among patients referred to the vascular laboratory is cost-effective. *Eur J Vasc Endovasc Surg* 2010;**39**:208–16	1, 2
Mani K, Wanhainen A, Lundkvist J, Lindstrom D. Cost-effectiveness of intensive smoking cessation therapy among patients with small abdominal aortic aneurysms. *J Vasc Surg* 2011;**54**:628–36	3
Mantha S, Foss J, Ellis JE, Roizen MF. Intense cardiac troponin surveillance for long-term benefits is cost-effective in patients undergoing open abdominal aortic surgery: a decision analysis model. *Anesth Analg* 2007;**105**:1346–56	1
Markovic M, Davidovic L, Savic N, Sindjelic R, Ille T, Dragas M. Intraoperative cell salvage versus allogeneic transfusion during abdominal aortic surgery: clinical and financial outcomes. *Vascular* 2009;**17**:83–92	3
McCutcheon BA, Talamini MA, Chang DC, Rose JA, Bandyk DF, Wilson SE. The comparative effectiveness of surgeons over interventionalists in endovascular repairs of abdominal aortic aneurysm. *Ann Surg* 2013;**258**:476–82	3
McIntosh H. *What is the Published Evidence of an Association Between Hospital Volume and Operative Mortality for Surgical Repair (Open and Endovascular) of Unruptured and Ruptured Abdominal Aortic Aneurysms?* Glasgow: NHS Quality Improvement Scotland (NHS QIS); 2012	3
McNally MM, Agle SC, Parker FM, Bogey WM, Powell CS, Stoner MC. Preoperative statin therapy is associated with improved outcomes and resource utilization in patients undergoing aortic aneurysm repair. *J Vasc Surg* 2010;**51**:1390–6	3
Medical Advisory Secretariat. Fenestrated endovascular grafts for the repair of juxtarenal aortic aneurysms: an evidence-based analysis. *Ont Health Technol Assess Ser* 2009;**9**:1–51	3
Medical Advisory Secretariat. Endovascular repair of abdominal aortic aneurysms in low surgical risk patients. *Ont Health Technol Assess Ser* 2009;**10**(Suppl. 1):1–15	1
Medical Advisory Secretariat. Endovascular repair of descending thoracic aortic aneurysm: an evidence-based analysis. *Ont Health Technol Assess Ser* 2005;**5**:1–59	3
Medical Advisory Secretariat. Ultrasound screening for abdominal aortic aneurysm: an evidence-based analysis. *Ont Health Technol Assess Ser* 2006;**6**:1–67	1, 3
Min SI, Min SK, Ahn S, Kim SM, Park D, Park T, *et al.* Comparison of costs of endovascular repair versus open surgical repair for abdominal aortic aneurysm in Korea. *J Korean Med Sci* 2012;**27**:416–22	1
Morimae H, Maekawa T, Tamai H, Takahashi N, Ihara T, Hori A, *et al.* Cost disparity between open repair and endovascular aneurysm repair for abdominal aortic aneurysm: a single-institute experience in Japan. *Surg Today* 2012;**42**:121–6	1
Moysidis T, Lohmann M, Lutkewitz S, Kemmeries G, Kroger K. Cost associated with D-Dimer screening for acute aortic dissection. *Adv Ther* 2011;**28**:1038–44	3
Murphy EH, Beck AW, Clagett GP, DiMaio JM, Jessen ME, Arko FR. Combined aortic debranching and thoracic endovascular aneurysm repair (TEVAR) effective but at a cost. *Arch Surg* 2009;**144**:222–7	3
National Institute for Clinical Excellence (NICE). *Endovascular Stent-Graft Placement in Thoracic Aortic Aneurysms and Dissections*. London: NICE; 2005	3
National Institute for Health and Care Excellence (NICE). *Stent-Graft Placement in Abdominal Aortic Aneurysm*. London: NICE; 2006	2
Narayan P, Wong A, Davies I, Angelini GD, Bryan AJ, Wilde P, *et al.* Thoracic endovascular repair versus open surgical repair: which is the more cost-effective intervention for descending thoracic aortic pathologies? *Eur J Cardiothorac Surg* 2011;**40**:869–74	3
Ni ZH, Luo JF, Huang WH, Liu Y, Xue L, Fan RX, *et al.* Totally percutaneous thoracic endovascular aortic repair with the preclosing technique: a case–control study. *Chin Med J* 2011;**124**:851–5	3

continued

TABLE 48 Studies excluded by screening titles and abstracts (*continued*)

Reference	Reason for exclusion
Noll RE, Tonnessen BH, Kim J, Money SR, Sternbergh WC. Long-term postplacement cost comparison of AneuRx and Zenith Endografts. *Ann Vasc Surg* 2008;**22**:710–15	3
Ohrlander T, Nessvi S, Gottsater A, Dencker M, Acosta S. Influence of preoperative medical assessment prior to elective endovascular aneurysm repair for abdominal aortic aneurysm. *Int Angiol* 2012;**31**:368–75	1
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Pellerin O, Caruba T, Kandounakis Y, Novelli L, Pineau J, Prognon P, *et al.* Embolization of the internal iliac artery: cost-effectiveness of two different techniques. *Cardiovasc Interv Radiol* 2008;**31**:1088–93	3
Pichon Riviere A, Augustovski F, Cernadas C, Ferrante D, Regueiro A, Garcia Marti S. *Elective endovascular repair for aortic abdominal aneurysm*. Ciudad de Buenos Aires: Institute for Clinical Effectiveness and Health Policy (IECS); 2007	1
Pickhardt PJ, Hassan C, Laghi A, Zullo A, Kim DH, Iafrate F, *et al.* Small and diminutive polyps detected at screening CT colonography: a decision analysis for referral to colonoscopy. *Am J Roentgenol* 2008;**190**:136–44	3
Pickhardt PJ, Hassan C, Laghi A, Kim DH. CT colonography to screen for colorectal cancer and aortic aneurysm in the Medicare population: cost-effectiveness analysis. *Am J Roentgenol* 2009;**192**:1332–40	1
Roos H, Falkenberg M, Zachrisson K, Wingren U, Samuelsson O, Jivegard L, *et al. Fenestrated aortic repair of aortic aneurysm*. Gothenburg: The Regional Health Technology Assessment Centre (HTA-centrum), Region Vastra Gotaland; 2010	1
Ryer EJ, Garvin RP, Webb TP, Franklin DP, Elmore JR. Comparison of outcomes with coils versus vascular plug embolization of the internal iliac artery for endovascular aortoiliac aneurysm repair. *J Vasc Surg* 2012;**56**:1239–45	3
Tatsuishi W, Kohri T, Kodera K, Asano R, Kataoka G, Kubota S, *et al.* Usefulness of an enhanced recovery after surgery protocol for perioperative management following open repair of an abdominal aortic aneurysm. *Surg Today* 2012;**42**:1195–200	1
Tawfick WA, O'Connor M, Hynes N, Sultan S. Implementation of the Continuous AutoTransfusion System (C.A.T.S) in open abdominal aortic aneurysm repair: an observational comparative cohort study. *Vasc Endovasc Surg* 2008;**42**:32–9	3
Vogel TR, Nackman GB, Brevetti LS, Crowley JG, Bueno MM, Banavage A, *et al.* Resource utilization and outcomes: effect of transfer on patients with ruptured abdominal aortic aneurysms. *Ann Vasc Surg* 2005;**19**:149–53	1
Vogel TR, Dombrovskiy VY, Haser PB, Graham AM. Has the implementation of EVAR for ruptured AAA improved outcomes? *Vasc Endovasc Surg* 2009;**43**:252–7	1
Vogel TR, Dombrovskiy VY, Graham AM, Lowry SF. The impact of hospital volume on the development of infectious complications after elective abdominal aortic surgery in the Medicare population. *Vasc Endovasc Surg* 2011;**45**:317–24	3
Wanhainen A, Lundkvist J, Bergqvist D, Bjorck M. Cost-effectiveness of screening women for abdominal aortic aneurysm. *J Vasc Surg* 2006;**43**:908–14	1
Warmuth M. *Endovascular repair of aortic aneurysms*. Vienna: Ludwig Boltzmann Institut fuer Health Technology Assessment (LBIHTA); 2013	1
Williams TK, Schneider EB, Black JH, Lum YW, Freischlag JA, Perler BA, *et al.* Disparities in outcomes for Hispanic patients undergoing endovascular and open abdominal aortic aneurysm repair. *Ann Vasc Surg* 2013;**27**:29–37	1

Reasons for exclusion at screening titles and abstracts stage: (1) does not include detailed patient service use/costs relevant to the UK setting or utility values to populate the economic model, (2) duplicates cost or utility data from other sources, (3) does not focus on comparison of interventions for screening, surveillance, repair or assessment of AAA, (4) not English language, (5) unable to obtain full text.

TABLE 49 Studies with full text reviewed and excluded

Reference	Reason for exclusion
Badger SA, Jones C, Murray A, Lau LL, Young IS. Implications of attendance patterns in Northern Ireland for abdominal aortic aneurysm screening. *Eur J Vasc Endovasc Surg* 2011;**42**:434–9	1
Blackhouse G, Hopkins R, Bowen JM, De Rose G, Novick T, Tarride JE, *et al.* A cost-effectiveness model comparing endovascular repair to open surgical repair of abdominal aortic aneurysms in Canada. *Value Health* 2009;**12**:245–52	2
Bonneux L, Cleemput I, Vrijens F, Vanoverloop J, Galloo P, Ramaekers D. *Elective Endovascular Treatment of the Abdominal Aortic Aneurysm (AAA)*. Brussels: Belgian Health Care Knowledge Centre (KCE); 2005	4
Center for Medical Technology Assessment. *Screening for Abdominal Aortic Aneurysm – A Health Economic Assessment*. Linkoping: Center for Medical Technology Assessment (CMT); 2004	4
Flynn K. *Guidance for Screening for Abdominal Aortic Aneurysms in Veterans Health Administration*. Boston, MA: VA Technology Assessment Program (VATAP); 2005	4
Fotis T, Tsoumakidou G, Katostaras T, Kalokairinou A, Konstantinou E, Kiki V, *et al.* Cost and effectiveness comparison of endovascular aneurysm repair versus open surgical repair of abdominal aortic aneurysm: a single-center experience. *J Vasc Nurs* 2008;**26**:15–21	1
Giardina S, Pane B, Spinella G, Cafueri G, Corbo M, Brasseur P, *et al.* An economic evaluation of an abdominal aortic aneurysm screening program in Italy. *J Vasc Surg*. 2011;**54**:938–46	1
Health Care Insurance Board/College voor zorgverzekeringen. *Dutch Randomized Endovascular Aneurysm Management Dream-trial-primary research*. Diemen: Health Care Insurance Board/College voor Zorgverzekeringen (CVZ); 2005	2
Henriksson M, Lundgren F. Decision-analytical model with lifetime estimation of costs and health outcomes for one-time screening for abdominal aortic aneurysm in 65-year-old men. *Br J Surg* 2005;**92**:976–83	2
Henriksson M, Lundgren F, Carlsson P. Informing the efficient use of health care and health care research resources: the case of screening for abdominal aortic aneurysm in Sweden. *Health Econ* 2006;**15**:1311–22	2
Hynes N, Sultan S. A prospective clinical, economic, and quality-of-life analysis comparing endovascular aneurysm repair (EVAR), open repair, and best medical treatment in high-risk patients with abdominal aortic aneurysms suitable for EVAR: the Irish patient trial. *J Endovasc Ther* 2007;**14**:763–76	1
Kapma MR, Groen H, Oranen BI, Van Der Hilst CS, Tielliu IF, Zeebregts CJ, *et al.* Emergency abdominal aortic aneurysm repair with a preferential endovascular strategy: mortality and cost-effectiveness analysis. *J Endovasc Ther* 2007;**14**:777–84	1
Kim LG, Scott AP, Ashton HA, Thompson SG. A sustained mortality benefit from screening for abdominal aortic aneurysm. *Ann Intern Med* 2007;**146**:699–706	2
Kim LG, Thompson SG, Briggs AH, Buxton MJ, Campbell HE. How cost-effective is screening for abdominal aortic aneurysms? *J Med Screen* 2007;**14**:46–52	2
Lederle FA, Stroupe KT. Cost-effectiveness at two years in the VA open versus endovascular repair trial. *Eur J Vasc Endovasc Surg* 2012;**44**:543–8	1
Maceira Rozas MC, Atienza Merino G, Sampedro Morandeira JL. *Efficacy and Effectiveness of Screening for Abdominal Aortic Aneurysm in a High Risk Population. Cost-effectiveness Analysis. Applicability in the National Health Care Service*. Santiago de ComPostela: Galician Agency for Health Technology Assessment (AVALIA-T); 2007	1
Michaels JA, Drury D, Thomas SM. Cost-effectiveness of endovascular abdominal aortic aneurysm repair. *Br J Surg* 2005;**92**:960–7	2
Mundy L, Hiller JE. *Targeted screening for abdominal aortic aneurysm*. Adelaide, SA: Adelaide Health Technology Assessment (AHTA); 2008	2
National Institute for Health and Care Excellence (NICE). *Endovascular Stent-Grafts for the Treatment of Abdominal Aortic Aneurysms*. London: NICE; 2009	2
Perras C, Ho C, Spry C, Argaez C, Fitzsimmons H. *Elective endovascular Abdominal Aortic Aneurysm Repair Versus Open Surgery: A review of the Clinical and Cost-effectiveness*. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2009	2

continued

TABLE 49 Studies with full text reviewed and excluded (*continued*)

Reference	Reason for exclusion
Shahidi S, Schroeder TV, Carstensen M, Sillesen H. Outcome and survival of patients aged 75 years and older compared to younger patients after ruptured abdominal aortic aneurysm repair: do the results justify the effort? *Ann Vasc Surg* 2009;**23**:469–77	1
Sogaard R, Laustsen J, Lindholt JS. Cost-effectiveness of abdominal aortic aneurysm screening and rescreening in men in a modern context: evaluation of a hypothetical cohort using a decision analytical model. *BMJ* 2012;**345**:e4276	1
Stroupe KT, Lederle FA, Matsumura JS, Kyriakides TC, Jonk YC, Ge L, *et al.* Cost-effectiveness of open versus endovascular repair of abdominal aortic aneurysm in the OVER trial. *J Vasc Surg* 2012;**56**:901–9	1
Sultan S, Hynes N. Clinical efficacy and cost per quality-adjusted life-years of pararenal endovascular aortic aneurysm repair compared with open surgical repair. *J Endovasc Ther* 2011;**18**:181–96	1
Swedish Council on Technology Assessment in Health Care. *Screening for Abdominal Aortic Aneurysm*. Stockholm: Swedish Council on Technology Assessment in Health Care (SBU); 2008	1
Tarride JE, Blackhouse G, De Rose G, Novick T, Bowen JM, *et al.* Cost-effectiveness analysis of elective endovascular repair compared with open surgical repair of abdominal aortic aneurysms for patients at a high surgical risk: a 1-year patient-level analysis conducted in Ontario, Canada. *J Vasc Surg* 2008;**48**:779–87	2
Wilt TJ, Lederle FA, MacDonald R, Jonk YC, Rector TS, Kane RL. *Comparison of Endovascular and Open Surgical Repairs for Abdominal Aortic Aneurysm*. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2006	1

Reasons for exclusion at screening full text stage: (1) does not include detailed patient service use/costs relevant to the UK setting or utility values to populate the economic model, (2) duplicates cost or utility data from other sources, (3) not English language, (4) unable to obtain full text.

TABLE 50 Studies with full text reviewed and included

Reference	Type of intervention	Planned or emergency surgery	Type of data extracted
Bowen J, De Rose G, Hopkins R, Novick T, Blackhouse G, Tarride J-E, *et al. Systematic Review and Cost-effectiveness Analysis of Elective Endovascular Repair Compared to Open Surgical Repair of Abdominal Aortic Aneurysms – Interim report*. Toronto, ON: Program for Assessment of Technology in Health (PATH) at McMaster University on behalf of the Medical Advisory Secretariat (MAS); 2005	Surgical repair	Planned	Utility data
Brown LC, Powell JT, Thompson SG, Epstein DM, Sculpher MJ, Greenhalgh RM. The UK EndoVascular Aneurysm Repair (EVAR) trials: randomised trials of EVAR versus standard therapy. *Health Technol Assess* 2012;**16**(9)	Surgical repair	Planned	Utility and cost data
Chambers D, Woolacott N, Fayter D, Paton F, Wright K. Endovascular stents for abdominal aortic aneurysms. *Health Technol Assess* 2009;**13**(48)	Surgical repair	Planned	Utility and cost data
Ehlers L, Overvad K, Sorensen J, Christensen S, Bech M, Kjolby M. Analysis of cost-effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm. *BMJ* 2009;**338**:b2243	Screening	NA	Utility data
Eisenstein EL, Davidson-Ray L, Edwards R, Anstrom KJ, Ouriel K. Economic analysis of endovascular repair versus surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg* 2013;**58**:302–10	Surgical repair	Planned	Utility data
Epstein DM, Sculpher MJ, Manca A, Michaels J, Thompson SG, Brown LC, *et al.* Modelling the long-term cost-effectiveness of endovascular or open repair for abdominal aortic aneurysm. *Br J Surg* 2008;**95**:183–90	Surgical repair	Planned	Utility data
Hayes PD, Sadat U, Walsh SR, Noorani A, Tang TY, Bowden DJ, *et al.* Cost-effectiveness analysis of endovascular versus open surgical repair of acute abdominal aortic aneurysms based on worldwide experience. *J Endovasc Ther* 2010;**17**:174–82	Surgical repair	Emergency	Cost data

TABLE 50 Studies with full text reviewed and included (*continued*)

Reference	Type of intervention	Planned or emergency surgery	Type of data extracted
Henriksson M, Lundgren F. *One-time Screening for Abdominal Aortic Aneurysm in 65-year-old men: a Decision-Analytic Model with Lifetime Estimation of Costs and Health Outcomes*. Linkoping: Center for Medical Technology Assessment (CMT); 2005	Screening	NA	Utility data
IMPROVE Trial Investigators. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ* 2014;**348**:f7661	Surgical repair	Emergency	Cost data
Kapma MR, Dijksman LM, Reimerink JJ, de Groof AJ, Zeebregts CJ, Wisselink W, *et al.* Cost-effectiveness and cost-utility of endovascular versus open repair of ruptured abdominal aortic aneurysm in the Amsterdam Acute Aneurysm Trial. *Br J Surg* 2014;**101**:208–15	Surgical repair	Emergency	Utility data
Lindholt JS, Sorensen J, Sogaard R, Henneberg EW. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *Br J Surg* 2010;**97**:826–34	Screening	NA	Utility data
Montreuil B, Brophy J. Screening for abdominal aortic aneurysms in men: a Canadian perspective using Monte Carlo-based estimates. *Can J Surg* 2008;**51**:23–34	Screening	NA	Utility data
Prinssen M, Buskens E, de Jong SE, Buth J, Mackaay AJ, Sambeek MR, *et al.* Cost-effectiveness of conventional and endovascular repair of abdominal aortic aneurysms: results of a randomized trial. *J Vasc Surg* 2007;**46**:883–90	Surgical repair	Planned	Utility data
Rollins KE, Shak J, Ambler GK, Tang TY, Hayes PD, Boyle JR. Mid-term cost-effectiveness analysis of open and endovascular repair for ruptured abdominal aortic aneurysm. *Br J Surg* 2014;**101**:225–31	Surgical repair	Emergency	Cost data
Spronk S, van Kempen BJ, Boll AP, Jorgensen JJ, Hunink MG, Kristiansen IS. Cost-effectiveness of screening for abdominal aortic aneurysm in the Netherlands and Norway. *Br J Surg* 2011;**98**:1546–55	Screening	NA	Utility data
Thompson S, Brown L, Sweeting M, Bown M, Kim L, Glover M, *et al.* Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: implications for surveillance intervals and their cost-effectiveness. *Health Technol Assess* 2013;**17**(41)	Surveillance	NA	Cost data
Thompson SG, Ashton HA, Gao L, Scott RA, the Multicentre Aneurysm Screening Study Group. Screening men for abdominal aortic aneurysm: 10 year mortality and cost-effectiveness results from the randomised Multicentre Aneurysm Screening Study. *BMJ* 2009;**338**:b2307	Screening	NA	Cost data
Young KC, Awad NA, Johansson M, Gillespie D, Singh MJ, Illig KA. Cost-effectiveness of abdominal aortic aneurysm repair based on aneurysm size. *J Vasc Surg* 2010;**51**:27–32	Surveillance	NA	Utility data

NA, not applicable.

Appendix 9 Vascular Governance North West health economic data collection proforma

Abdominal Aortic Aneurysm Health Economic Proforma

VGNW ID _____

Note –If the patient has indicated they do not wish to participate in the VGNW database, please do not record the data.

Pre-Operative

Was the patient seen pre-operatively relating to the abdominal aortic aneurysm repair to be done? (No=1, Yes=2, Unknown=9) *If the answer is yes, please complete the table below.* ☐

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Location (hospital, GP surgery, etc.)					
Seen By (surgeon, nurse, etc.)					
Tests / Procedure					
Admission/Visit Date	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____
Admitted (yes/no)					
Mode of admission*					
Discharge Date	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____

AAA Operation

What surgical treatment did the patient receive for AAA? (Open Repair =1, EVAR= 2, Other = 3, Don't know = 9) *If the answer is 1 or 2, please complete the table below.* ☐

Admission date (dd/mm/yyyy)	__/__/____
Discharge/Death Date (dd/mm/yyyy)	__/__/____
If no discharge date, is hospital stay ongoing? (yes/no)	
Hospital	
Mode of Admission *	
Admission through A & E? (No=1, Yes=2, Don't know=9)	

In Hospital Post-Operative Care (ward, HTU, etc.)

Location	Admission	Discharge	Location	Admission	Discharge
	__/__/____	__/__/____		__/__/____	__/__/____
	__/__/____	__/__/____		__/__/____	__/__/____
	__/__/____	__/__/____		__/__/____	__/__/____
	__/__/____	__/__/____		__/__/____	__/__/____

Abdominal Aortic Aneurysm Health Economic Proforma

VGNW ID _____

Post-Operative

Was the patient seen for Abdominal Aortic Aneurysm (AAA) related follow-up? (No=1, Yes=2, Don't know=9) *If the answer to is yes, please complete the table below.* ☐

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Location (hospital, GP surgery, etc.)					
Seen By (surgeon, nurse, etc.)					
Tests / Procedure					
Admission/Visit Date	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____
Admitted (yes / no)					
Mode of admission*					
Discharge Date	__/__/____	__/__/____	__/__/____	__/__/____	__/__/____

*Mode of admission: Elective, Urgent, Emergency

Appendix 10 Utility values for economic evaluation

TABLE 51 Utility values extracted from included papers: primary clinical and/or economic evaluations

Lead author; year	Source of utility data	Intervention	*n*	Mean age (years) (SD)	Utility measure	Baseline	30 days	90 days	180 days	1 year
Primary evaluations of planned AAA repair										
Bowen; 2006[100]	Prospective cohort	EVAR	140	76	EQ-5D (mean)	0.77[a,b]	0.66[a,b]	0.76[a,b]	0.79[a,b]	0.75[a,b]
	Prospective cohort	Open repair (high risk)	52	74	EQ-5D (mean)	0.76[a,b]	0.66[a,b]	0.75[a,b]	0.89[a,b]	0.91[a,b]
	Prospective cohort	Open repair (low risk)	143	72	EQ-5D (mean)	0.80[a,c]	0.7[a,c]	0.87[a,c]	0.90[a,c]	0.91[a,c]
Brown; 2012[79]	EVAR 1 RCT	EVAR	541	74	EQ-5D (mean, SD)	0.75 (0.22)[c]	0.73 (0.21)[c]	0.71 (0.25)[c]	NR	0.74 (0.24)[c]
	EVAR 1 RCT	Open	531	74	EQ-5D (mean, SD)	0.74 (0.23)[c]	0.67 (0.25)[c]	0.73 (0.23)[c]	NR	0.75 (0.25)[c]
	EVAR 2 RCT	EVAR	166	77	EQ-5D (mean, SD)	0.58 (0.31)[c]	0.57 (0.28)[c]	0.64 (0.28)[c]	NR	0.65 (0.24)[c]
	EVAR 2 RCT	No repair	172	76	EQ-5D (mean, SD)	0.63 (0.28)[c]	0.56 (0.29)[c]	0.60 (0.26)[c]	NR	0.60 (0.30)[c]
Lederle; 2009[76]	RCT	EVAR	444	69.6 (7.8)	EQ-5D (mean, SD)	0.79 (0.16)	Change from baseline: 1 year = –0.02 (0.16); 2 years = –0.01 (0.19)			
	RCT	Open	437	70.5 (7.8)	EQ-5D (mean, SD)	0.79 (0.16)	Change from baseline: 1 year = –0.00 (0.17); 2 years = –0.02 (0.16)			
Prinssen; 2007[134]	RCT	EVAR	170	64–77 (range)	EQ-5D (mean, 95% CI)	0.76 (0.68 to 0.85)[a]	0.64 (0.56 to 0.72)[a,d]	0.75 (0.68 to 0.82)[a]	0.75 (0.68 to 0.82)[a]	0.77 (0.70 to 0.84)[a]
	RCT	Open	170	63–76 (range)	EQ-5D (mean, 95% CI)	0.72 (0.64 to 0.80)[a]	0.57 (0.46 to 0.68)[a,c]	0.78 (0.72 to 0.84)[a]	0.80 (0.72 to 0.88)[a]	0.82 (0.75 to 0.88)[a]

NR, not reported.
a Estimated from graph.
b Adjusted for baseline differences.
c Unadjusted data.
d Estimated from graph for 3 week postoperative follow-up.

TABLE 52 Utility values extracted from included papers: evidence synthesis of planned AAA repair

Lead author; year	Intervention	Utility value or decrement
Chambers; 2009[80]	EVAR	Decrement for 6 months after EVAR = 0.027[a]
	Open	Decrement for 6 months after surgery = 0.077[a]
	Preoperation	Population norms (UK); see Kind,[94] *Table 54*
Epstein; 2008[93]	EVAR	Decrement for 1 month after surgery = 0.027 (95% CI 0.007 to 0.061)[b]
	Open and reintervention	Decrement for one month after surgery = 0.094 (95% CI 0.065 to 0.128)[b]
	Preoperation	Population norms (UK); see Kind,[94] *Table 54*
Young; 2010[135]	EVAR	12 months postsurgery mean = 0.70 (minimum 0.3, maximum 1)
	Observation	Mean = 0.75 (minimum 0.5, maximum 1)
	Open	12 months postsurgery mean = 0.71 (minimum 0.3, maximum 1)

a Loss of utility for 6 months after surgery; estimated from EVAR 1 RCT (EVAR trial participants, 2005).
b Loss of utility for 1 month after surgery; estimated from EVAR 1 RCT (EVAR trial participants, 2005).

TABLE 53 Utility values extracted from included papers: evidence synthesis of AAA screening or surveillance

Lead author; year	Utility value or decrement
Henriksson; 2005[97]	Decrement for diagnosis of AAA used in sensitivity analysis only = 0.071, gamma distribution (12.6, 0.01)
	Decrement for postoperative state used in sensitivity analysis only = 0.10, gamma distribution (16, 0.01)
	Baseline health state assumed equal to population norms (Sweden); see Burström,[136] *Table 54*
Lindholt; 2010[102]	Elective surgery (assumed decrement for 6 months) = 0.05
	Emergency surgery – no rupture (assumed decrement for 6 months) = 0.1
	Emergency surgery – rupture (assumed decrement for 6 months) = 0.15
	No screen and screen states: population norms (Denmark); see Sørenson,[137] *Table 54*
[a]Montreuil; 2008[96]	Decrement for dialysis = 0.1
	Decrement for MI = 0.07
	Decrement for stroke = 0.25
	Baseline health for age 65–69 years = 0.82
	Baseline health for age 70–79 years = 0.79
	Baseline health for age > 80 years = 0.72
Spronk; 2011[103]	Assumed decrement for two or more operations = 0.1 (0.052 to 0.147)
	Assumed decrement for irreversible adverse event = 0.15 (0.102 to 0.197)
	Baseline health state assumed equal to population norms, derived from Lindholt 2010[102] and reported in Burström[136] (see *Table 54*)

a Reported as estimated from Canadian population norms measured by the Health Utility Index.

TABLE 54 Utility values extracted from published reports of population norms

Lead author; year	Source of utility data	*n*	Age (years)	Utility measure	Utility value
Burström; 2001[136]	Population survey	387	60–69	EQ-5D (mean, SE)	All: 0.80 (0.010); male: 0.83 (0.012); female: 0.78 (0.015)
	Population survey	318	70–79	EQ-5D (mean, SE)	All: 0.79 (0.012); male: 0.81 (0.018); female: 0.78 (0.017)
	Population survey	122	80–88	EQ-5D (mean, SE)	All: 0.74 (0.021); male: 0.74 (0.037); female: 0.74 (0.026)
Kind; 1999[94]	Population survey	484	55–64	EQ-5D (mean, SD)	All: 0.80 (0.26); male: 0.78 (0.28); female: 0.81 (0.26)
	Population survey	488	65–74	EQ-5D (mean, SD)	All: 0.78 (0.26); male: 0.78 (0.28); female: 0.78 (0.25)
	Population survey	314	> 75	EQ-5D (mean, SD)	All: 0.73 (0.27); male: 0.75 (0.28); female: 0.71 (0.27)
Sørenson; 2009[137]	Population survey	2121	60–69	EQ-5D (mean, SD)	Male: 0.883 (0.153); female: 0.839 (0.177)
	Population survey	1408	70–79	EQ-5D (mean, SD)	Male: 0.847 (0.183); female: 0.818 (0.198)

SE, standard error.

Appendix 11 Economic data from Vascular Governance North West

TABLE 55 Cost of pre- and postoperative visits and procedures, VGNW, 2012–13

	Open					EVAR				
		Number of visits		Cost of visits (£)			Number of visits		Cost of visits (£)	
Length of time	*n*	Mean (SD)	Minimum–maximum	Mean (SD)	Minimum–maximum	*n*	Mean (SD)	Minimum–maximum	Mean (SD)	Minimum–maximum
> 3 years pre operation	61	0.30 (0.78)	0–4	53 (144)	0–681	57	0.39 (1.31)	0–8	60 (212)	0–1362
2–3 years pre operation	61	0.66 (1.11)	0–4	107 (191)	0–763	57	0.51 (0.95)	0–4	120 (425)	0–3124
1–2 years pre operation	61	1.05 (1.73)	0–8	196 (487)	0–3470	57	1.28 (1.56)	0–5	195 (273)	0–1509
0–1 year pre operation	61	5.00 (2.29)	1–11	1249 (841)	164–4707	57	5.05 (2.10)	1–10	1085 (628)	119–3582
Average visits/costs before AAA repair	61	7.18 (4.48)	1–16	1640 (1158)	170–6207	57	7.30 (4.32)	1–17	1473 (987)	119–5988
0–1 year post operation	61	1.10 (0.89)	0–3	227 (340)	0–2481	57	2.65 (1.49)	0–7	682 (1248)	0–9564
1–2 years post operation	53	0.25 (0.65)	0–3	42 (120)	0–640	49	0.96 (1.08)	0–5	426 (1794)	0–12,650
2–3 years post operation	44	0.16 (0.75)	0–4	27 (131)	0–740	37	0.59 (0.86)	0–3	81 (123)	0–468
> 3 years post operation	44	0.14 (0.63)	0–4	85 (511)	0–3390	37	0.38 (0.68)	0–3	552 (3114)	0–18,970
Average visits/costs after AAA repair	61	1.62 (1.84)	0–10	617 (701)	86–4774	57	4.2 (2.17)	0–9	1671 (3135)	86–19,290

Appendix 12 Cost parameter estimates for economic models

TABLE 56 Cost parameter estimates for the economic model: primary analysis

Description	Mean	SD	Source
EVAR active monitoring and surveillance, cost per visit per patient (£)	75	36	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR active monitoring diagnostic tests, cost per test per patient (£)	209	144	NHS reference costs,[73] weighted average of procedure codes[a]
Open active monitoring and surveillance, cost per visit per patient (£)	85	45	NHS reference costs,[73] weighted average of procedure codes[a]
Open active monitoring diagnostic tests, cost per test per patient (£)	200	145	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR preoperative assessment, cost per visit per patient (£)	107	113	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR preoperative diagnostic tests, cost per test per patient (£)	104	151	NHS reference costs,[73] weighted average of procedure codes[a]
Open preoperative assessment, cost per visit per patient (£)	84	63	NHS reference costs,[73] weighted average of procedure codes[a]
Open preoperative diagnostic tests, cost per test per patient (£)	61	81	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative assessment, cost per visit per patient (£)	85	34	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative assessment diagnostic tests, cost per test per patient (£)	155	110	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative assessment, cost per visit per patient (£)	95	20	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative assessment diagnostic tests, cost per test per patient (£)	320	232	NHS reference cost,[73] weighted average of procedure codes[a]
EVAR postoperative monitoring, cost per visit per patient (£)	56	33	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative monitoring diagnostic tests, cost per test per patient (£)	129	212	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative monitoring, cost per visit per patient (£)	94	29	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative monitoring diagnostic tests, cost per test per patient (£)	346	192	NHS reference costs,[73] weighted average of procedure codes[a]
Transport costs for emergency surgery/ rupture, cost per visit per patient (£)	201	0	NHS reference costs,[73] weighted average of procedure codes[a]

continued

TABLE 56 Cost parameter estimates for the economic model: primary analysis (*continued*)

Description	Mean	SD	Source
Elective surgery and reintervention surgery cost per finished consultant episode			
EVAR no complications (£)	5608	5188	NHS reference costs,[73] weighted average of procedure codes QZ15G–QZ15J, RC12A–RC13E plus emergency transport costs[73]
EVAR complications (£)	10,675	7475	NHS reference costs,[73] weighted average of procedure codes QZ15D–QZ15F, RC11A–RC11E plus emergency transport costs[73]
Open no complications (£)	8305	1610	NHS reference costs,[73] weighted average of procedure codes QZ01E-QZ01F plus emergency transport costs[73]
Open complications (£)	12,836	2308	NHS reference costs[73], weighted average of procedure codes QZ01C and QZ01D plus emergency transport costs[73]
Emergency surgery cost per finished consultant episode			
EVAR no complications (£)	5934	8947	NHS reference costs,[73] weighted average of procedure codes QZ15G–QZ15J, RC12A–RC13E plus emergency transport costs[73]
EVAR complications (£)	8630	3864	NHS reference costs [73], weighted average of procedure codes QZ15D–QZ15F, RC11A–RC11E plus emergency transport costs[73]
Open no complications (£)	7493	1946	NHS reference costs,[73] weighted average of procedure codes QZ01E and QZ01F plus emergency transport costs[73]
Open complications (£)	12,558	4848	NHS reference costs,[73] weighted average of procedure codes QZ01C and QZ01D plus emergency transport costs[73]

a Relevant codes included consultant-led outpatient attendances and multiprofessional outpatient consultations based on the VGNW data.

TABLE 57 Cost parameter estimates for the economic model: sensitivity analysis

Description	Minimum (SD)	Maximum (SD)	Source
EVAR active monitoring and surveillance, cost per visit per patient (£)	63 (17)	123 (51)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR active monitoring diagnostic tests, cost per test per patient (£)	168 (164)	224 (179)	NHS reference costs,[73] weighted average of procedure codes[a]
Open active monitoring and surveillance, cost per visit per patient (£)	59 (16)	121 (57)	NHS reference costs,[73] weighted average of procedure codes[a]
Open active monitoring diagnostic tests, cost per test per patient (£)	162 (162)	214 (178)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR preoperative assessment, cost per visit per patient (£)	100 (118)	171 (123)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR preoperative diagnostic tests, cost per test per patient (£)	94 (152)	114 (179)	NHS reference costs,[73] weighted average of procedure codes [a]
Open preoperative assessment, cost per visit per patient (£)	72 (63)	134 (75)	NHS reference costs,[73] weighted average of procedure codes[a]
Open preoperative diagnostic tests, cost per test per patient (£)	50 (71)	63 (90)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative assessment, cost per visit (£)	46 (20)	122 (74)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative assessment diagnostic tests, cost per test per patient (£)	82 (27)	162 (133)	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative assessment, cost per visit per patient (£)	52 (13)	£129 (70)	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative assessment diagnostic tests, cost per test per patient (£)	77 (27)	371 (287)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative monitoring, cost per visit per patient (£)	29 (23)	76 (65)	NHS reference costs,[73] weighted average of procedure codes[a]
EVAR postoperative monitoring diagnostic tests, cost per test per patient (£)	115 (321)	152 (324)	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative monitoring, cost per visit per patient (£)	53 (14)	134 (70)	NHS reference costs,[73] weighted average of procedure codes[a]
Open postoperative monitoring diagnostic tests, cost per test per patient (£)	94 (17)	397 (245)	NHS reference costs,[73] weighted average of procedure codes[a]
Transport costs for emergency surgery/ rupture per finished consultant episode (£)	201 (0)	201 (0)	NHS reference costs,[73] weighted average of procedure codes[a]

continued

TABLE 57 Cost parameter estimates for the economic model: sensitivity analysis (*continued*)

Description	Minimum (SD)	Maximum (SD)	Source
Elective surgery and reintervention surgery cost per finished consultant episode			
EVAR no complications, mean (SD) (£)	3429 (2919)	7254 (8329)	NHS reference costs,[73] weighted average of procedure codes QZ15G–QZ15J, RC12A–RC13E plus emergency transport costs[73]
EVAR complications, mean (SD) (£)	6446 (4426)	13,062 (12,849)	NHS reference costs,[73] weighted average of procedure codes QZ15D–QZ15F, RC11A–RC11E plus emergency transport costs[73]
Open no complications, mean (SD) (£)	5895 (299)	9080 (2244)	NHS reference costs,[73] weighted average of procedure codes QZ01E and QZ01F plus emergency transport costs[73]
Open complications, mean (SD) (£)	6562 (795)	14,964 (7096)	NHS reference costs,[73] weighted average of procedure codes QZ01C and QZ01D plus emergency transport costs[73]
VGNW elective surgery cost			
EVAR, mean (SD) (£)	12,440 (2751)		VGNW
Open, mean (SD) (£)	13,380 (4820)		VGNW
EVAR 1 Trial primary procedure cost, inflated to 2012–2013 prices			
EVAR, mean (£)	13,019		Brown *et al.* 2012[79]
Open, mean (£)	11,842		Brown *et al.* 2012[79]
EVAR 1 Trial reintervention procedure cost, inflated to 2012–2013 prices			
Reintervention, mean (SD) (£)	7536 (10,679)		Brown *et al.* 2012[79]
Emergency surgery cost per finished consultant episode			
EVAR no complications, mean (SD) (£)	4052 (9683)	7144 (9735)	NHS reference costs,[73] weighted average of procedure codes QZ15G–QZ15J, RC12A–RC13E plus emergency transport costs[73]
EVAR complications, mean (SD) (£)	5788 (3797)	11,092 (4675)	NHS reference costs, [73] weighted average of procedure codes QZ15D–QZ15F, RC11A–RC11E plus emergency transport costs[73]
Open no complications, mean (SD) (£)	5405 (2228)	8703 (1857)	NHS reference costs, [73] weighted average of procedure codes QZ01E–QZ01F plus emergency transport costs[73]
Open complications, mean (SD) (£)	7962 (4141)	16,390 (6699)	NHS reference costs, [73] weighted average of procedure codes QZ01C and QZ01D plus emergency transport costs[73]

a Relevant codes included consultant-led outpatient attendances and multiprofessional outpatient consultations based on the VGNW data.

Appendix 13 Mean cost and quality-adjusted life-year results

TABLE 58 Mean costs and QALYs: vignette A

Analysis	Algorithm	Standard practice
Primary analysis *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	12,068 (6722 to 25,541)	12,240 (413 to 23,450)
Mean QALY (95% CIs)	7.111 (0.706 to 13.012)	7.064 (0.745 to 12.786)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	14,419 (6569 to 25,764)	14,256 (6689 to 25,757)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)
Sensitivity analysis: outcome is LYGs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	12,068 (6722 to 25,541)	12,240 (413 to 23,450)
Mean LYGs (95% CIs)	12.152 (0.708 to 25.298)	12.073 (1 to 25.190)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	14,419 (6569 to 25,764)	14,256 (6689 to 25,757)
Mean LYGs (95% CIs)	12.113 (0.50 to 25.29)	12.068 (0.50 to 25.290)
Sensitivity analysis: maximise LYGs *Initial aneurysm size: 4.0 cm*		
Threshold size maximise LYGs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	12,068 (6722 to 25,541)	12,240 (413 to 23,450)
Mean LYGs (95% CIs)	12.152 (0.708 to 25.298)	12.073 (1 to 25.190)
Initial aneurysm size: 6.8 cm		
Threshold size maximise LYGs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	14,419 (6569 to 25,764)	14,256 (6689 to 25,757)
Mean LYGs (95% CIs)	12.113 (0.50 to 25.29)	12.068 (0.50 to 25.29)

continued

TABLE 58 Mean costs and QALYs: vignette A (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: decision rule is minimise costs *Initial aneurysm size: 4.0 cm*		
Threshold size to minimise costs	7.0 cm	5.5 cm
Mean cost (95% CIs) (£)	12,068 (407 to 23,030)	12,240 (413 to 23,450)
Mean QALY (95% CIs)	6.920 (0.743 to 12.674)	7.064 (0.745 to 12.728)
Initial aneurysm size: 6.8 cm		
Threshold size to minimise costs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	14,419 (6569 to 25,764)	14,256 (6689 to 25,757)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)
Sensitivity analysis: low starting utility values and high post-repair decrements *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	5.1 cm	5.5 cm
Mean cost (95% CIs) (£)	12,090 (403 to 23,497)	12,225 (401 to 23,399)
Mean QALY (95% CIs)	8.924 (0.982 to 16.109)	8.903 (0.986 to 16.055)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	7.0 cm	6.8 cm
Mean cost (95% CIs) (£)	14,455 (5743 to 25,878)	14,270 (6752 to 25,703)
Mean QALY (95% CIs)	8.901 (0.767 to 16.088)	8.794 (0.249 to 11.573)
Sensitivity analysis: VGNW costs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	13,091 (8377 to 27,845)	13,314 (402 to 25,053)
Mean QALY (95% CIs)	7.111 (0.706 to 13.012)	7.064 (0.745 to 12.786)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	15,988 (8180 to 27,987)	15,893 (8358 to 27,970)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)
Sensitivity analysis: EVAR 1 costs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	14,942 (14,066 to 28,958)	15,309 (419 to 24,257)
Mean QALY (95% CIs)	7.111 (0.706 to 13.012)	7.064 (0.745 to 12.786)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	18,898 (14,009 to 28,690)	18,804 (13,965 to 28,897)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)

TABLE 58 Mean costs and QALYs: vignette A (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: high assessment and follow-up costs low surgery costs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	11,703 (7285 to 20,036)	11,646 (474 to 19,524)
Mean QALY (95% CIs)	7.111 (0.706 to 13.012)	7.064 (0.745 to 12.786)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	12,984 (7279 to 20,294)	12,745 (7181 to 20,006)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)
Sensitivity analysis: low assessment and follow-up costs, high surgery costs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	4.0 cm	5.5 cm
Mean cost (95% CIs) (£)	12,077 (5679 to 31,596)	12,376 (285 to 27,696)
Mean QALY (95% CIs)	7.111 (0.706 to 13.012)	7.064 (0.745 to 12.786)
Initial aneurysm size: 6.8 cm		
Threshold size to maximise QALYs	6.9 cm	6.8 cm
Mean cost (95% CIs) (£)	15,068 (5612 to 31,736)	14,970 (5700 to 31,661)
Mean QALY (95% CIs)	7.093 (0.691 to 12.801)	7.069 (0.691 to 12.801)

TABLE 59 Mean costs and QALYs: vignette B

Analysis	Algorithm	Standard practice
Primary analysis *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	3071 (152 to 16,000)	3476 (151 to 19,975)
Mean QALY (95% CIs)	2.446 (0.196 to 6.539)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	8591 (699 to 37,110)	NA
Mean QALY (95% CIs)	2.309 (0 to 6.788)	NA
Sensitivity analysis: outcome is LYGs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	3071 (152 to 16,000)	3476 (151 to 19,975)
Mean LYGs (95% CIs)	3.704 (0.250 to 10.422)	3.662 (0.250 to 10.501)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean costs (95% CIs) (£)	8591 (699 to 37,110)	NA
Mean LYGs (95% CIs)	2.309 (0 to 6.788)	NA

continued

TABLE 59 Mean costs and QALYs: vignette B (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: maximise LYGs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise LYGs	7.0 cm	5.5 cm
Mean cost (95% CIs) (£)	2660 (152 to 9911)	3476 (151 to 19,975)
Mean LYGs (95% CIs)	3.721 (0.250 to 10.050)	3.662 (0.250 to 10.5018)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise LYGs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	8591 (699 to 37,110)	NA
Mean LYGs (95% CIs)	3.295 (0 to 10.538)	NA
Sensitivity analysis: decision rule is minimise costs *Initial aneurysm size: 4.0 cm*		
Threshold size to minimise costs	7.0 cm	5.5 cm
Mean cost (95% CIs) (£)	2660 (152 to 9911)	3476 (151 to 19,975)
Mean QALY (95% CIs)	2.466 (0.196 to 6.382)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to minimise costs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	8591 (699 to 37,110)	NA
Mean QALY (95% CIs)	2.309 (0 to 6.788)	NA
Sensitivity analysis: low starting utility values and high post-repair decrements *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	6.8 cm	5.5 cm
Mean cost (95% CIs) (£)	2723 (151 to 11,265)	3452 (151 to 11,265)
Mean QALY (95% CIs)	3.241 (0.25 to 8.217)	3.191 (0.250 to 8.350)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	8522 (693 to 36,910)	NA
Mean QALY (95% CIs)	2.750 (0 to 8.381)	NA
Sensitivity analysis: VGNW costs *Initial aneurysm size: 4.0 cm*		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	3059 (149 to 17,377)	4290 (151 to 19,029)
Mean QALY (95% CIs)	2.446 (0.196 to 6.539)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	12,849 (5979 to 27,032)	NA
Mean QALY (95% CIs)	2.31 (0 to 6.775)	NA

TABLE 59 Mean costs and QALYs: vignette B (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: EVAR 1 costs		
Initial aneurysm size: 4.0 cm		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	4026 (152 to 18,162)	5049 (149 to 18,142)
Mean QALY (95% CIs)	2.446 (0.196 to 6.539)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	16,876 (14,475 to 33,306)	NA
Mean QALY (95% CIs)	2.304 (0 to 6.756)	NA
Sensitivity analysis: high assessment and follow-up costs low surgery costs		
Initial aneurysm size: 4.0 cm		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	3246 (186 to 12,724)	3378 (184 to 13,094)
Mean QALY (95% CIs)	2.446 (0.196 to 6.539)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	5849 (1271 to 15,782)	NA
Mean QALY (95% CIs)	2.304 (0 to 6.756)	NA
Sensitivity analysis: low assessment and follow-up costs, high surgery costs		
Initial aneurysm size: 4.0 cm		
Threshold size to maximise QALYs	6.0 cm	5.5 cm
Mean cost (95% CIs) (£)	2777 (96 to 16,485)	3367 (96 to 20,432)
Mean QALY (95% CIs)	2.446 (0.196 to 6.539)	2.450 (0.192 to 6.603)
Initial aneurysm size: 7.0 cm		
Threshold size to maximise QALYs	7.0 cm[a]	NA
Mean cost (95% CIs) (£)	9739 (788 to 35,574)	NA
Mean QALY (95% CIs)	2.307 (0 to 6.802)	NA

NA, not applicable.

a No comparator threshold is available, as the algorithm-recommended threshold in the primary analysis equals the current practice threshold. The reported cost and QALY data are mean and not net costs and QALYs.

TABLE 60 Mean costs and QALYs: vignette C

Analysis	Algorithm	Standard practice
Primary analysis *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	4.0 cm	5.0 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean QALY (95% CIs)	4.967 (0.378 to 10.715)	4.923 (0.38 to 10.565)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	12,790 (5644 to 23,859)	12,790 (5644 to 23,859)
Mean QALY (95% CIs)	4.962 (0 to 10.756)	4.962 (0 to 10.756)
Sensitivity analysis: outcome is LYGs *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	4.0 cm	5.0 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean LYGs (95% CIs)	7.778 (0.5 to 18.804)	7.735 (0.5 to 18.695)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean LYGs (95% CIs)	7.772 (0 to 18.782)	7.772 (0 to 18.782)
Sensitivity analysis: maximise LYGs *Initial aneurysm size: 3.8 cm*		
Threshold size maximise LYGs	4.0 cm	5.0 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean LYGs (95% CIs)	7.778 (0.5 to 18.804)	7.735 (0.5 to 18.695)
Initial aneurysm size: 5.2 cm		
Threshold size maximise LYGs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean LYGs (95% CIs)	7.772 (0 to 18.782)	7.772 (0 to 18.782)
Sensitivity analysis: decision rule is minimise costs *Initial aneurysm size: 3.8 cm*		
Threshold size to minimise costs	7.0 cm	5.0 cm
Mean cost (95% CIs) (£)	6146 (252 to 18,669)	8468 (247 to 20,345)
Mean QALY (95% CIs)	4.791 (0.394 to 10.306)	4.923 (0.38 to 10.565)
Initial aneurysm size: 5.2 cm		
Threshold size to minimise costs	7.0 cm	5.2 cm
Mean cost (95% CIs) (£)	10,396 (829 to 22,943)	12,790 (5644 to 23,859)
Mean QALY (95% CIs)	4.595 (0.381 to 10.463)	4.962 (0 to 10.756)

TABLE 60 Mean costs and QALYs: vignette C (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: low starting utility values and high post-repair decrements *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	5.4 cm	5.0 cm
Mean cost (95% CIs) (£)	11,182 (258 to 22,457)	8493 (245 to 20,324)
Mean QALY (95% CIs)	6.046 (0.5 to 13.077)	6.128 (0.5 to 13.132)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.3 cm	5.2 cm
Mean cost (95% CIs) (£)	12,823 (5628 to 23,954)	12,823 (5628 to 23,954)
Mean QALY (95% CIs)	6.007 (0 to 13,113)	6.007 (0 to 13,113)
Sensitivity analysis: VGNW costs *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	3.8 cm	5.0 cm
Mean cost (95% CIs) (£)	11,184 (254 to 22,552)	8468 (247 to 20,345)
Mean QALY (95% CIs)	4.967 (0.378 to 10.715)	4.923 (0.38 to 10.565)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.3 cm	5.2 cm
Mean cost (95% CIs) (£)	14,367 (7320 to 26,022)	14,367 (7320 to 26,022)
Mean QALY (95% CIs)	4.944 (0 to 10.74)	4.944 (0 to 10.74)
Sensitivity analysis: EVAR 1 costs *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	3.8 cm	5.0 cm
Mean cost (95% CIs) (£)	15,090 (254 to 23,615)	10,993 (248 to 19,890)
Mean QALY (95% CIs)	4.97 (0.393 to 10.723)	4.932 (0.405 to 10.561)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	17,332 (13,221 to 25,740)	17,332 (13,221 to 25,740)
Mean QALY (95% CIs)	4.95 (0 to 10.739)	4.95 (0 to 10.739)
Sensitivity analysis: high assessment and follow-up costs, low surgery costs *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	3.8 cm	5.0 cm
Mean cost (95% CIs) (£)	9707 (294 to 17,168)	7765 (286 to 16,294)
Mean QALY (95% CIs)	4.954 (0.391 to 10.703)	4.916 (0.393 to 10.559)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	11,071 (6242 to 18,141)	11,071 (6242 to 18,141)
Mean QALY (95% CIs)	4.95 (0 to 10.745)	4.95 (0 to 10.745)

continued

TABLE 60 Mean costs and QALYs: vignette C (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: low assessment and follow-up costs, high surgery costs *Initial aneurysm size: 3.8 cm*		
Threshold size to maximise QALYs	3.8 cm	5 cm
Mean cost (95% CIs) (£)	12,547 (167 to 28,626)	9234 (166 to 25,308)
Mean QALY (95% CIs)	4.967 (0.398 to 10.747)	4.940 (0.411 to 10.559)
Initial aneurysm size: 5.2 cm		
Threshold size to maximise QALYs	5.2 cm	5.2 cm
Mean cost (95% CIs) (£)	14,365 (5285 to 30,600)	14,365 (5285 to 30,600)
Mean QALY (95% CIs)	4.945 (0 to 10.766)	4.945 (0 to 10.766)

TABLE 61 Mean costs and QALYs: vignette D

Analysis	Algorithm	Standard practice
Primary analysis *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.9 cm	5.5 cm
Mean cost (95% CIs) (£)	9995 (819 to 39,303)	9776 (766 to 31,854)
Mean QALY (95% CIs)	4.617 (0.301 to 10.111)	4.579 (0.295 to 7.446)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.6 cm	6.5 cm
Mean cost (95% CIs) (£)	9991 (986 to 39,933)	9847 (1040 to 39,567)
Mean QALY (95% CIs)	4.606 (0.376 to 10.124)	4.6 (0.441 to 10.27)
Sensitivity analysis: outcome is LYGs *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.9 cm	5.5 cm
Mean cost (95% CIs) (£)	9995 (819 to 39,303)	9776 (766 to 31,854)
Mean LYGs (95% CIs)	7.363 (0.5 to 18.444)	7.323 (0.5 to 13.841)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.6 cm	6.5 cm
Mean costs (95% CIs) (£)	9991 (986 to 39,933)	9847 (1040 to 39567)
Mean LYGs (95% CIs)	7.329 (0.294 to 18.436)	4.6 (0.441 to 10.27)
Sensitivity analysis: maximise LYGs *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise LYGs	4.9 cm	5.5 cm
Mean cost (95% CIs) (£)	9995 (819 to 39,303)	9776 (766 to 31,854)
Mean LYGs (95% CIs)	7.363 (0.5 to 18.444)	7.323 (0.5 to 13.841)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise LYGs	6.7 cm	6.5 cm
Mean cost (95% CIs) (£)	10,018 (802 to 39,627)	9847 (1040 to 39,567)
Mean LYGs (95% CIs)	7.334 (0.5 to 18.428)	7.32 (0.283 to 18.485)

TABLE 61 Mean costs and QALYs: vignette D (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: decision rule is minimise costs *Initial aneurysm size: 4.8 cm*		
Threshold size to minimise costs	7.0 cm	5.5 cm
Mean cost (95% CIs) (£)	8730 (767 to 30,384)	9776 (766 to 31,854)
Mean QALY (95% CIs)	4.398 (0.299 to 9.984)	4.579 (0.295 to 7.446)
Initial aneurysm size: 6.5 cm		
Threshold size to minimise costs	7.0 cm	6.5 cm
Mean cost (95% CIs) (£)	9633 (753 to 38,088)	9847 (1040 to 39,567)
Mean QALY (95% CIs)	4.483 (0.283 to 10.101)	4.6 (0.441 to 10.27)
Sensitivity analysis: low starting utility values and high post-repair decrements *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.8 cm	5.5 cm
Mean cost (95% CIs) (£)	10,005 (802 to 39,216)	9763 (769 to 31,672)
Mean QALY (95% CIs)	5.887 (0.5 to 13.073)	5.81 (0.498 to 9.651)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.7 cm	6.5 cm
Mean cost (95% CIs) (£)	9952 (990 to 39,696)	9929 (1052 to 40,103)
Mean QALY (95% CIs)	5.8 (0.5 to 13.018)	5.719 (0.505 to 12.917)
Sensitivity analysis: VGNW costs *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.8 cm	5.5 cm
Mean cost (95% CIs) (£)	14,495 (836 to 30,461)	13,281 (767 to 21,885)
Mean QALY (95% CIs)	4.602 (0.3 to 10.073)	4.587 (0.299 to 7.453)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.5 cm	6.5 cm
Mean cost (95% CIs) (£)	14,536 (5636 to 30,706)	14,652 (6620 to 30,927)
Mean QALY (95% CIs)	4.595 (0.344 to 10.121)	4.605 (0.441 to 10.255)
Sensitivity analysis: EVAR 1 costs *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.8 cm	5.5 cm
Mean cost (95% CIs) (£)	18,235 (816 to 39,895)	16,155 (777 to 26,754)
Mean QALY (95% CIs)	4.602 (0.286 to 10.064)	4.562 (0.294 to 7.446)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.5 cm	6.5 cm
Mean cost (95% CIs) (£)	18,280 (14,766 to 39,703)	18,480 (14,767 to 41,008)
Mean QALY (95% CIs)	4.588 (0.322 to 10.124)	4.615 (0.45 to 10.249)

continued

TABLE 61 Mean costs and QALYs: vignette D (*continued*)

Analysis	Algorithm	Standard practice
Sensitivity analysis: high assessment and follow-up costs, low surgery costs *Initial aneurysm size: 4.8 cm*		
Threshold size to maximise QALYs	4.8 cm	5.5 cm
Mean cost (95% CIs) (£)	7400 (1021 to 18,156)	8,170 (957 to 12,078)
Mean QALY (95% CIs)	4.594 (0.303 to 10.082)	4.588 (0.312 to 7.4)
Initial aneurysm size: 6.5 cm		
Threshold size to maximise QALYs	6.6 cm	6.5 cm
Mean cost (95% CIs) (£)	7217 (1474 to 17,906)	7040 (1739 to 17,871)
Mean QALY (95% CIs)	4.599 (0.33 to 10.12)	4.591 (0.440 to 10.242)

Appendix 14 Meeting dates of study committees

Steering Committee

3 February 2012.

16 October 2012.

21 May 2013.

3 September 2013.

27 November 2013.

Management Committee

24 May 2011.

19 December 2011.

24 May 2012.

2 August 2012.

16 October 2012.

21 May 2013.

11 June 2013.

17 June 2013.

25 June 2013.

8 July 2013.

3 September 2013.

7 November 2013.

Patient and public involvement group

20 September 2011.

19 December 2011.

23 July 2012.

26 October 2012.

25 January 2013.

31 May 2013.

13 September 2013.

10 January 2014.

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