Endovascular stents for abdominal aortic aneurysms: a systematic review and economic model

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Date completed: 1st April 2008

Final report 1st April 2008
Source of funding: This report was commissioned by the NIHR HTA Programme on behalf of the National Institute for Health and Clinical Excellence as project number HTA 07/09/01.

Declaration of competing interests:
Three of the co-authors (David Epstein, Jonathan Michaels and Mark Sculpher) have undertaken, and published, previous work on the effectiveness and cost-effectiveness of EVAR devices funded by the NHS Health Technology Assessment Programme. Also Mark Sculpher has undertaken consultancy work for Medtronic in the past in clinical areas unrelated to vascular disease or EVAR.

Acknowledgements
We are grateful to Cheryl Craigs for assistance with protocol development and study selection; to Christian Stock for assistance with the summary figures for the risk modelling studies; to Dr Jaap Buth (EUROSTAR) for giving us access to raw data from the registry; to Dr Buth and the investigators of the ACE, Amsterdam Acute Aneurysm Trial, OVER, NExT ERA and CAESAR studies for their responses to our requests for information; and to the EVAR trial investigators for providing unpublished data on an academic in confidence basis.

The views expressed in this report are those of the authors and not necessarily those of the NIHR HTA Programme. Any errors are the responsibility of the authors.
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1 Definition of terms and list of abbreviations

Glossary

Adverse effects and complications
Includes aneurysm-related outcomes such as rupture and events specific to EVAR, major morbidity, eg. cardiac events, and reintervention including conversion from EVAR to open procedure and secondary intervention.

Aneurysm related mortality
Death of aneurysm-related causes such as rupture. It includes operative mortality and can include, but does not always, postoperative mortality.

Chi-square ($\chi^2$) test
A statistical test used to assess heterogeneity by testing the null hypothesis that the true treatment effects are the same in each study.

Comorbidity
The presence of one or more disorders (or diseases) in addition to a primary disease or disorder

Complications
See adverse effects and complications.

Confidence Interval (CI)
The range of uncertainty about an estimate of a treatment effect. It is the range of values above and below the point estimate that is likely to include the true value of the treatment effect. 95% CI indicates that there is a 95% probability that the CI calculated from a particular study includes the true value of a treatment effect.

Cost-effectiveness analysis
The estimation of the costs and health benefits of mutually exclusive treatment strategies, where the consequences are measured in natural units, such as years of life gained.

Cost-effectiveness acceptability curves (CEAC)
A graphical representation of the probability of an intervention being cost effective over a range of monetary values for the health system’s cost-effectiveness threshold.

Cox proportional hazards analysis
Analysis of one or more risk factors over time on an endpoint such as death.

Device migration
Migration can occur post-implantation when there is any movement or displacement of the stent-graft in relation to the native aorta or renal arteries. The risk of migration increases with
time and can result in the loss of device fixation. To maximize iliac fixation length, the stent-graft is placed at the origin of the hypogastric arteries.

Device migration may not require further treatment and can be monitored or it can result in aneurysm rupture or endoleak, requiring secondary intervention.

**Disutility**
The reduction in health-related quality of life (measured using utilities) compared to a reference such as the general population.

**Endoleak**
Persistence of blood flow outside the endovascular stent-graft but within the aneurysm sac or adjacent vessels in which the graft is deployed.

*Type I:* Perigraft or graft related (proximal anastomosis, distal anastomosis, occluder). Blood flow into the aneurysm sac due to incomplete seal or ineffective seal at the end of the graft. This type of endoleak usually occurs in the early course of treatment, but may also occur later.

*Type II:* Retrograde or collateral (mesenteric, lumbar, renal accessory). Blood flow into the aneurysm sac due to opposing blood flow from collateral vessels. In some circumstance when there are two or more patent vessels a situation of inflow and outflow develops creating an actively blood flow within channel created within the aneurysm sac.

*Type III:* Midgraft (fabric tear, graft dislocation, graft disintegration). Blood flow into the aneurysm sac due to inadequate or ineffective sealing of overlapping graft joints or rupture of the graft fabric. Again, this endoleak usually occurs early after treatment, due to technical problems, or later due to device breakdown.

*Type IV:* Graft porosity. Blood flow into the aneurysm sac due to the porosity of the graft fabric, causing blood to pass through from the graft and into the aneurysm sac.
Endovascular repair
A technique that involves placing a stent–graft prosthesis at the site of the aneurysm. The stent-graft is inserted through a small incision in the femoral artery in the groin, then carried to the site of the aneurysm using catheters and guidewires and placed in position under X-ray guidance.

EUROSTAR registry
A multicentre European database of the outcome of endovascular repair of infra-renal aortic aneurysms.

Fixed effects model
A statistical model that assumes only within-study variation as influencing the uncertainty of results (as reflected in the confidence interval) of a meta-analysis. Variation between the estimates of effect from each study (heterogeneity) does not affect the confidence interval in a fixed effects model.

Hazard ratio
The degree of increased or decreased risk of death or other clinical outcome over a period of time.

Heterogeneity
The differences/variability between the individual studies in the estimates of effects.

Homogeneity
The degree to which the results of studies are similar.

I^2 statistic
A measure to estimate how much of the total variation between the treatment estimates can be attributed to statistical heterogeneity rather than chance. It gives the proportion of the total variation which is due to heterogeneity between study results.

Infrarenal abdominal aortic aneurysm
Weakening of the wall of the aorta can lead to a dilatation of the vessel, or aneurysm in the lower infra-renal part of the abdominal aorta.

Kaplan-Meier survival analysis
A method of analysis that enables calculation of survival time for any given proportion of the sample, the probability of survival and the comparison of the difference in proportions surviving in two groups.

Karnofsky functional autonomy score
Allows patients to be classified as to their functional impairment. This can be used to compare effectiveness of different therapies and to assess the prognosis in individual patients. The lower the Karnofsky score, the worse the survival for most serious illnesses.

Meta-analysis
A method of combining studies to produce an overall summary of the treatment effect across studies (see also fixed effects model and random effects model)

Multiple Regression
A method for estimating the relationship between a dependent variable such as mortality (ie. outcome) and more than one independent explanatory variable such as age or gender. Also referred to as multivariable regression.
Multivariate analysis  Method for estimating jointly the relationship between several dependent variables (outcomes) and several independent explanatory variables.

Neck angulation  Significant aortic neck angulation may predispose to suboptimal outcome after endovascular abdominal aortic aneurysm repair. Defined as severe ($\geq 60$ degrees), moderate (40 to 59 degrees), and mild ($<40$ degrees) aortic neck angulation between the infrarenal aortic neck and the longitudinal axis of the aneurysm.

Odds ratio  A way of comparing whether the odds, or likelihood of a certain event is the same for two groups; the odds refers to the ratio of the number of people having an event to the number not having an event.

Perioperative  Generally refers to the three phases of surgery; preoperative, intraoperative and postoperative, and includes, for example, ward admission, anaesthesia, surgery and recovery.

Quality of life  A concept incorporating all the factors that might impact on an individual’s life, including factors such as the absence of disease or infirmity as well as other factors which might affect their physical, mental and social well-being.

Quality Adjusted Life Year (QALY)  An index of health gain where survival duration is weighted or adjusted by the patient’s (health-related) quality of life during the survival period. QALYs have the advantage of incorporating changes in both quantity (mortality) and quality (morbidity) of life.

Random effects model  A statistical model sometimes used in meta-analysis in which both within-study sampling error (variance) and between study variation are included in the assessment of the uncertainty (confidence interval) of the results of a meta-analysis.

Re-intervention  See adverse effects and complications.

Sensitivity analysis  A mathematical method that examines uncertainty associated with parameter estimated into the analysis to test the robustness of the analysis findings. In one-way sensitivity analysis each parameter is varied individually, for multi-way analysis two or more parameters are varied at the same time, threshold analysis identifies
the critical values above or below which the results of a study vary and analysis of extremes is used to examine the most pessimistic and the most optimistic scenarios. Finally, probabilistic sensitivity analysis attributes distributions of probabilities to uncertain variables that are incorporated within a model.

**Short Form-36 (SF-36)** The SF-36 is a multi-purpose, short-form health survey. It produces an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group.

**Society for Vascular Surgery/International Society for Cardiovascular Surgery (SVS/ISCVS) model** Risk stratification model that includes 3 levels of risk: Level I (age 75-85; stable angina with mild angiographic coronary artery disease (CAD) or normal perfusion scan; ejection fraction 30-50%; chronic obstructive pulmonary disease (COPD) with normal activities of daily living (ADLs); serum creatinine <2mg/dL; estimated mortality from open-surgical repair 3-5%); Level II (age 85-90; stable angina with moderate angiographic CAD or mild-to-moderate abnormal perfusion scan; ejection fraction 20-30%; COPD with moderate-to-severe pulmonary dysfunction; serum creatinine 2-3.5%mg/dL; estimated morality 6-8%); Level III (age >90; Class II-III angina with significant myocardium at risk based on coronary angiography or perfusion scan; ejection fraction <20%; COPD requiring home oxygen; serum creatinine >3.5mg/dL or on chronic dialysis; estimated mortality 8-13%)

**Utility** A measure of the strength of an individual’s preference for a given health state or outcome. Utilities assign numerical values on a scale including 0 (death) to 1 (optimal or ‘perfect’ health), and provide a single number that summarises health-related quality of life. Negative values of utility are feasible

**Weibull model** A specific parametric survival function modelling the relationship between the rate of an event (e.g. death) and time.
List of abbreviations

AAA  Abdominal aortic aneurysm
AHRQ  Agency for Healthcare Research and Quality
ASA  American Society of Anaesthesiologists
CAD/MI  Coronary artery (heart) disease/myocardial infarction
CAESAR  Comparison of surveillance vs. aortic endografting for small aneurysm repair trial
CCI  Charlson Comorbidity Index
CDSR  Cochrane Database of Systematic Reviews
CE  Conformité Européene
CEAC  Cost-effectiveness acceptability curve
CENTRAL  Cochrane Central Register of Controlled Trials
CHE  Centre for Health Economics
CHF  Congestive heart failure
CI  Confidence interval
CINAHL  Cumulative Index to Nursing and Allied Health Literature
COPD  Chronic obstructive pulmonary disease
CPI  Customized Probability Index
CRD  Centre for Reviews and Dissemination
CT  Computed tomography
DARE  Database of Abstract of Reviews of Effects
EQ-5D  EuroQoL - 5 dimensions
EVAR  Endovascular repair
EVPI  Expected value of perfect information
GAS  Glasgow Aneurysm Score
GH  General health perception (SF-36)
HALS  Hand assisted laparoscopic surgery
HR  Hazard ratio
HRQOL  Health related quality of life
HTA  Health Technology Assessment
ICER  Incremental cost-effectiveness ratio
IQR  Interquartile range
ITT  Intention to treat
MASS  Multicentre Aneurysm Screening Study
MeSH  Medical subject headings in the MEDLINE thesaurus
MRC  Medical research council
MRI  Magnetic resonance imaging
NExT ERA  National Expertise Based Trial of Elective Repair of Abdominal Aortic Aneurysms
NHS  National Health Service
NICE  National Institute for Health and Clinical Excellence
NLH  National Library for Health
NRR  National Research Register
NVD  National Vascular Database (currently covering open repair of aneurysms)
OR  Odds ratio
OVER  Open surgery versus endovascular repair trial
PF  Physical function (SF-36)
QALY  Quality adjusted life year
QoL  Quality of Life
RCT  Randomised controlled trial
RETA  The Registry of Endovascular Treatment of Abdominal Aortic Aneurysms
RP  Role physical (SF-36)
SD  Standard deviation
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<tr>
<th>Abbreviation</th>
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<td>SE</td>
<td>Standard Error</td>
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<td>SF-36</td>
<td>Short form 36</td>
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<td>SVS/ISCVS</td>
<td>Society for Vascular Surgery/International Society for Cardiovascular Surgery</td>
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<td>Totally laparoscopic surgery</td>
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<td>Turning Research Into Practice</td>
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<td>UKSAT</td>
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<td>WMD</td>
<td>Weighted mean difference</td>
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2 Executive summary

2.1 Background

Abdominal aortic aneurysms (AAAs) carry a high risk of rupture which is associated with a mortality rate of about 80%. AAAs can be treated by surgical repair to prevent rupture. However, open repair involves significant risks, and approximately 25% of patients with an AAA requiring surgery are considered unfit for open surgery. Endovascular aneurysm repair (EVAR) is a minimally-invasive technique that has been used to treat patients with appropriate aneurysm morphology who are classified as either fit for open repair or as unfit. EVAR is used both as an elective procedure and to treat symptomatic and ruptured aneurysms.

2.2 Objectives

The management options available after diagnosis of AAA can be classified as: immediate elective surgery with open repair; immediate elective surgery with EVAR; surveillance with an option to defer surgery; or a decision to rule out surgery entirely. The objective of this assessment is to determine the clinical and cost-effectiveness of EVAR for repair of infrarenal AAAs in patients at varying levels of risk, including those who are appropriate for open repair and those who are not.

2.3 Methods

A systematic review of the clinical effectiveness of EVAR was performed. Recent systematic reviews were used to identify randomised controlled trials (RCTs) and other clinical studies. Additional searches (2005–Feb 2008) were conducted to search for recent RCTs, publications relating to named registries (registries used were the Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA) and the European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) for EVAR, and the National Vascular Database (NVD) for open surgery), and for studies relating to the investigation of patients’ baseline risks on outcomes. Studies of EVAR in patients with asymptomatic or symptomatic, ruptured or unruptured infrarenal AAAs were included. Conventional open repair, non-surgical treatment for AAA (sometimes referred to as ‘best medical
treatment’) or surveillance (sometimes referred to as ‘watchful waiting’) were the appropriate comparators.

A second systematic review was undertaken to identify and compare existing cost-effectiveness analyses of EVAR compared with open surgery and non-surgical interventions. This review included submissions of economic analyses made by EVAR device manufacturers.

Two new decision models were also developed to inform the review. The first compared the cost-effectiveness of EVAR versus open repair in patients with a large aneurysm (≥5.5 cm) for whom the decision to operate has been taken. The second decision model, complementary to the first, compared options of early surgery (with EVAR or open repair), watchful waiting and no surgical intervention. Both models investigated the cost-effectiveness of the strategies in patients of varying ages, aneurysm size and level of operative fitness. Four fitness levels were defined in the analysis, given a patient’s age and aneurysm size: good, moderate, poor and very poor.

### 2.4 Results

**Clinical effectiveness**

Six RCTs were included in the review. Four compared EVAR and open surgery in patients with unruptured AAAs who were fit for open repair. One RCT compared EVAR with non-surgical management of patients deemed unfit for open repair. A small RCT compared EVAR and open repair in patients with ruptured AAAs. There are five ongoing trials from which results are currently unavailable. The limited data reported by the NVD and RETA registries, and the ‘older’ devices used and non-current data reported by RETA, highlights the importance of the EUROSTAR data and findings. Thirty-four studies evaluated the role of patients’ baseline characteristics in predicting the risks of particular outcomes after EVAR. Three studies evaluated existing scoring systems and one study evaluated the development of a model for assessing risks. However, the majority of the risk modeling studies investigated specific risk factors using multiple regression analysis. The majority of
these studies were based on data from the EUROSTAR registry with likely overlap of patients.

Compared with open repair EVAR reduces operative mortality (OR 0.35 (95% CI 0.19, 0.73) and aneurysm-related mortality over the medium term ( OR 0.49 (95% CI: 0.29, 0.83) but offers no significant difference in all-cause mortality at mid-term follow-up. EVAR was associated with an increased rate of complications and reinterventions and these are not offset by any increase in HRQOL.

There is limited RCT evidence comparing EVAR with non-surgical management in patients unfit for open repair. EVAR trial 2 found no differences in mortality outcomes between groups but this finding cannot be taken as definitive because substantial numbers of patients randomised to non-surgical management crossed over to receive surgical repair of their aneurysm. This may indicate that the benefits of EVAR over no intervention may require more than 4 years follow-up to become apparent.

The results from these trials are complemented by data from registries, in particular the EUROSTAR registry data relating to devices in current use.

Cost-effectiveness

Results of the systematic review of the economic evidence identified six published decision models. Of the five models comparing EVAR and open repair, two were constructed after the operative mortality results of the good quality RCTs were published and considered to be relevant for the decision in the UK. Both concluded that EVAR was not cost-effective on average at a threshold of £20,000 per QALY. One model compared EVAR and no surgical intervention. This model was constructed before the results of the EVAR trial 2 were published. The model concluded that EVAR would be on average more cost effective than no surgical intervention in unfit patients at a threshold of £20,000 per QALY. One model was submitted by a manufacturer (Medtronic). This model concluded that EVAR was
more cost effective than open repair for fit patients at a threshold of £20,000 per QALY.

The main findings of the York economic evaluations (base-case models at a threshold of £20,000 per QALY) are:

- EVAR is not cost-effective for patients of good or moderate fitness, or for patients with small aneurysm, compared with open repair or watchful waiting.

- In patients with poor fitness, EVAR is cost-effective in patients aged between approximately 74 to 78 years in patients with medium or large aneurysm. Open repair is more cost-effective for younger patients, and no surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective in patients aged up to about 83 years in patients with poor fitness and very large aneurysm.

- In patients with very poor fitness and medium or large aneurysm, EVAR is cost-effective in patients aged up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective in patients up to about 78 years with very poor fitness and very large aneurysm.

- Results are sensitive to assumptions and data about the risk of late aneurysm death, particularly in patients with large aneurysms over 6.5 cm, and the hospital cost of the procedures. The modelling of no intervention and watchful waiting is indicative and exploratory, based on assumptions about the natural history of untreated aneurysm in patients anatomically suitable for EVAR.

2.5 Conclusions

2.5.1 Implications for service provision

- Based on the results of this assessment of clinical and cost effectiveness, open repair should be the treatment of choice for patients with AAA who have good or moderate fitness.

- For patients with poorer fitness, whether suitable for open repair or not, EVAR may be cost effective but this will depend upon the patient’s age.

- EVAR cannot currently be recommended for the treatment of ruptured aneurysms.
2.5.2 **Suggested research priorities**

- Further follow-up of the existing UK trials (EVAR trial 1, EVAR trial 2) should be undertaken.
- Opportunities for individual patient meta-analysis of all RCTs relating to EVAR should be sought.
- Further research is needed on the rate of late aneurysm-related mortality after EVAR – in particular that associated with the most recent generations of devices.
- The extent to which the relative treatment effect of EVAR on operative mortality can be assumed constant across sub-groups of patients should be further investigated.
- Research is required into how the implement the best available risk scoring systems for the management of AAA into decision making in routine clinical practice.
- Research is required into the natural history of untreated AAA to determine more reliably when surgical intervention is optimal. The analysis should investigate the impact of different levels and determinants of patient fitness as well as aneurysm size and anatomy.
- A well defined and conducted RCT of EVAR versus ‘watchful waiting’ reflecting current clinical practice is warranted. However, given the difficulties of conducting RCTs in the management of AAA, it is probably advisable that the collection of data through the existing, established registries, particularly RETA (for EVAR) and NVD (for open repair) in the UK should be continued.
3 Background

3.1 Description of health problem

Aortic aneurysms develop when weakening of the vessel wall, often due to atherosclerosis, causes it to bulge, forming a balloon-like projection. This in turn leads to further stretching of the vessel wall and an increase in tension. Eventually, the vessel wall may rupture, leading to massive internal bleeding.

Most aneurysms occur in the abdominal section of the aorta. An abdominal aortic aneurysm (AAA) is defined as an enlargement of the aorta to 1.5 times or more its normal diameter or greater than 3 cm. Most AAAs occur in the lower (infra-renal) part of the abdominal aorta.

Symptoms that may occur as an aneurysm enlarges include a pulsating sensation in the abdomen, back pain and abdominal pain, possibly spreading to the back. Symptomatic AAAs require rapid medical attention. Rupture of an AAA is associated with a mortality rate of about 80 %; even when patients undergo emergency surgery, only about half survive beyond 30 days. The risk of rupture increases with the size of the aneurysm. For example, in the UK Small Aneurysm Trial and associated monitoring study, the number of ruptures per 100 patient years was 0.3, 1.5 and 6.5 for patients with AAAs of diameter $\leq 3.9$ cm, 4.0–4.9 cm and 5.0–5.9 cm, respectively. The rate of rupture may be up to 25 % annually for aneurysms with diameters larger than 6 cm, while a number of studies indicate that without surgery the 5-year survival rate for patients with aneurysms larger than 5 cm is about 20 %.

The main risk factors for AAAs include age, high blood pressure, male sex, smoking and family history. Because most AAAs are asymptomatic, it is difficult to estimate the prevalence of the condition, but screening studies in the UK have estimated a prevalence of 1.3–12.7 % depending on the age group studied and the definition of AAA. AAAs are about 3 times more common in men than in women. The incidence of symptomatic AAA in men is approximately 25/100 000 at age 50, increasing to 78/100 000 in those older than 70 years. The overall incidence of AAAs has increased...
in recent years and is likely to increase further in line with the ageing of the general population.

Most AAAs are detected by chance during clinical examination or investigation (for example, ultrasound or X-ray) for other conditions. Ultrasound screening of the population for early detection of AAAs has been extensively evaluated. In the UK the large Multicentre Aneurysm Screening Study RCT found that screening men aged 65 – 74 reduced the risk of aneurysm related death by 42 % over 4 years.\(^4\) Screening was marginally cost-effective over 4 years and cost-effectiveness was expected to improve substantially over a longer period.\(^5\) National screening programmes are under consideration by the four UK health departments at the time of writing.

### 3.2 Current service provision

AAAs can be treated by surgical repair to prevent rupture. Conventional (‘open’) surgical repair involves making a large incision in the abdomen and inserting a prosthetic graft to replace the damaged section of the aorta. Open repair of AAA carries substantial risk of mortality and morbidity, particularly because many patients with an AAA have significant comorbidities (e.g. heart or kidney disease) that reduce their fitness for surgery. Open repair can also be performed laproscopically: either by hand assisted laproscopic surgery (HALS) or totally laproscopic surgery (TLS). Guidance issued by NICE \(^6\) states that whilst there is adequate evidence of the safety and efficacy of these laproscopic techniques, the technical demands are such that such procedures should not be used without special arrangement for consent and for audit or research.

In current UK clinical practice, elective surgery is generally recommended for aneurysms > 5.5 cm in diameter, as well as for those of diameter > 4.5 cm with an increase in size of > 0.5 cm in the last 6 months. The UKSAT \(^7\) and ADAM \(^8\) trials indicated that there was no mortality advantage of immediate (open) surgical repair over imaging surveillance in patients with aneurysms of less than 5.5 cm diameter. Current guidelines recommend that patients with asymptomatic aneurysms less than 4.5 cm are followed up with ultrasonography every 6 months, whilst aneurysms of 4.5 to 5.5 cm are followed up every 3 or 6 months.
Approximately 25% of patients with an AAA requiring surgery are considered unfit for open surgery. Such patients will be kept under surveillance with an option to defer surgery, or a decision to rule out surgery entirely. As age, fitness and the untreated risk of rupture are evolving over time, the option to defer makes the decision complex and dynamic. It is unclear what the optimum management policy should be in patients considered unfit for open surgery. It may be that a policy to try to improve patient fitness might be effective and patients may be offered medical therapy to reduce risk factors, for example, smoking cessation and blood pressure reduction, but such a policy has not yet been evaluated.

3.3 Description of technology under assessment

Endovascular aneurysm repair (EVAR) is a minimally-invasive technique that involves placing a stent-graft prosthesis at the site of the aneurysm. The stent-graft is inserted through a small incision in the femoral artery in the groin, carried to the site of the aneurysm using catheters and guidewires and placed in position under X-ray guidance. Once in position, the stent-graft is deployed and anchored to the wall of the aorta using a variety of fixing mechanisms. The graft is stronger than the weakened aorta and allows blood to pass through it without creating pressure on the aneurysm. The main types of endovascular stent-grafts are aortic tube grafts (no longer used in the UK), aorto-uni-iliac grafts and aorto-bi-iliac (bifurcated) grafts, with most procedures in the UK using bi-iliac stents. EVAR is carried out under general, regional or local anaesthesia.

EVAR has been used to treat patients both classified as fit for open repair and those classified as unfit. It is used both as an elective procedure and to treat symptomatic and ruptured aneurysms. However, it must be emphasised that EVAR is not suitable for all patients. Patient suitability for EVAR depends on the morphology of the aneurysm. This is assessed by diagnostic imaging, usually computed tomography (CT) scanning and occasionally angiography or magnetic resonance imaging (MRI). In an unselected population of patients with AAA only 55% did not have an absolute morphological contraindication to EVAR.
Potential advantages of EVAR over open repair include reduced time under general anaesthesia, elimination of the pain and trauma associated with major abdominal surgery, reduced length of stay in the hospital and intensive care unit, and reduced blood loss.\textsuperscript{14} Potential disadvantages include the development of endoleaks, which occur when blood continues to flow through the aneurysm because the graft does not seal completely or because of backfilling of the aneurysm from other small vessels arising from the aneurysm wall. Thus, while open repair does not require any special follow-up, patients who have undergone EVAR require regular CT scans to check for the presence of late endoleaks.\textsuperscript{14} In addition, if the EVAR procedure is unsuccessful or complications arise during the procedure, conversion to open repair may be necessary in patients initially considered unfit for open surgery.\textsuperscript{14}

\textit{Prices of endovascular stent grafts}

Endovascular stents are not homogenous products. There are a number of different endovascular stent devices made by different companies and each with different costs. This is further complicated by the fact that different patients who may be fitted with the same company’s device may require different numbers of extensions. The companies who produce them also offer different pricing structures (for example, some charge a price per patient regardless of the number of extensions required while others charge based on the parts required). If the price per patient is not fixed, then ideally the mean price per case should be calculated based on an assessment of the expected number of extension parts required, which in turn depends on the population case-mix. There is also the added complication that individual hospitals often do not actually pay the list price, with manufacturers offering discounts. These considerations make the process of costing a device for the benefits of the economic evaluation complex.

The NICE Methods for Technology Appraisal Guide states that “Where the actual price paid for a resource may differ from the public list price (for example, pharmaceuticals, medical devices), the public list price should be used”.\textsuperscript{15} NICE has received information on the price of devices from four manufacturers of EVAR devices. These are further described below. The prices are summarised in Table 3.2.1
In Medtronic’s submission they stated that

Lombard (Aorfix) have informed NICE that their list price is £5,000 per case (excluding VAT).\(^{17}\)

Gore (Excluder) have stated that

Cook Zenith state that
### Table 3.2.1. Mean list prices per patient for endovascular devices, 2007/2008

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<td>W L Gore - EXCLUDER AAA Endoprosthesis</td>
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<td>Cook Medical - Zenith AAA Endovascular Graft</td>
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<td>Le Maitre - Endologix Powerlink Systems</td>
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*The use and cost of endovascular devices in EVAR trial 18*
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Table 3.2.4.

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Figure 3.2.1.
3.4 Risk score measures for surgical risk

Before any surgical procedure is undertaken the fitness of the patient needs to be assessed. Risk score measures provide numerical scores that have been calculated based on a number of patient factors (e.g., age, gender) that are considered to predict the risk for survival of surgery. Risk scores are assigned to patients; with higher scores indicating greater predicted risk. Low risk scores are not the same as no risk.19 Risk score models vary in complexity and accuracy, but enable comparisons of outcomes to be made between groups of patients, institutions and individual surgeons, whilst taking into account patient-related factors and comorbidity.19 Although there are a wide number of tools in use to measure operative risk, there is no ideal tool and those in use have many limitations; measures are used largely to predict risk in various patient groups rather than individuals, and often the cut-off points between high and low risk are based on costs and the complexity of providing treatment to correct the risk, rather than on the risk itself.20

The main risk scores used in clinical practice, with their roles in predicting risk for EVAR, are outlined below.

American Society of Anaesthesiologists (ASA)

This classification system is widely used, and although it was not originally designed to estimate operative risk, many medical professionals use it as a means of preoperative risk assessment and some have identified it as a predictor of
postoperative morbidity and mortality.\textsuperscript{21} ASA classifies pre-operative physical status, allocating patients to one of five categories based on general medical history and examination not requiring any specific investigations: Class I (normal healthy patient), II (mild systemic disease), III (severe systemic disease but not incapacitating), IV (incapacitating systemic disease that is a threat to life), V (moribund, not expected to survive 24 hours with or without operation). Generally, ASA is effective in predicting mortality when used alone or in conjunction with other parameters, as postoperative mortality rates rise steadily with the ASA grade.\textsuperscript{22} However, there is potential for inter-observer subjective error as it remains a semi-subjective assessment by the anaesthesiologist based on patient comorbidities.\textsuperscript{21}

\textbf{Acute Physiology and Chronic Health Evaluation (APACHE)}

APACHE presents an overall score for physiological variables, age points and chronic health, and has been used extensively in the intensive care setting. It aims to classify patients on the basis of the severity of illness to facilitate comparison of outcome, the evaluation of new therapies and as an indicator of daily progress. APACHE II measures are based on 12 physiologic and laboratory factors, in addition to age and previous health status.

The APACHE-AAA model was developed and internally validated specifically to predict outcome in post-operative AAA patients who are managed in ICU.\textsuperscript{23} However, this model cannot be used for preoperative decision making.\textsuperscript{24}

\textbf{Bayesian Risk Modelling (Customized Probability Index - CPI)}

The CPI accounts for significant clinical risk factors (cardiac and non-cardiac) and current medication use for predicting all cause perioperative morality in patients undergoing all types of open vascular surgery. It identifies nine independent predictors of perioperative mortality; type of vascular surgery, ischaemic heart disease, congestive heart failure, previous stroke, hypertension, renal dysfunction, and chronic pulmonary disease associated with increased risk, and beta-blockers and statin use associated with lower risk). Risk calculated using the sum of scores for surgical risk (0-46 points), medical history (0-67 points), and the score for cardioprotective medication (statins -10 points and beta-blockers -15 points).\textsuperscript{(Kertai et al, 2005 \textsuperscript{25})}

The EVAR trial participants (2007)\textsuperscript{26} were assessed for fitness based on clinicians
decisions using clinical parameters that were integrated into the calculation of the modified CPI.

**Charlson Comorbidity Index (CCI)**

The CCI is a weighted index of comorbidity (number and seriousness of comorbid diseases) which provides a total score: 1 = myocardial infarct, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease and diabetes; 2 = hemiplegia, moderate or severe renal disease, diabetes with end organ damage, any tumour, leukaemia, and lymphoma; 3 = moderate or severe liver disease; 6 = metastatic solid tumour and AIDS. A study looking at survival rates of patients with elective open AAA repair, reported the CCI as a significant independent predictor of lower survival. 

**Comorbidity Severity Score (CSS)**

The Comorbidity Severity Score (CSS) was developed specifically for EVAR risk stratification, and includes a comorbidity severity score (CSS) and an anatomic factor severity score, which includes cardiac disease, pulmonary disease, renal disease, hypertension, and age. The M-CSS has been found to be valid for predicting risk in open repair. When risk scores for open repair were applied to EVAR patients, observed mortality was different, but only statistically significant for the highest risk scores.

**Glasgow Aneurysm Score (GAS)**

The GAS estimates preoperative risk profiles that predict perioperative outcomes after open repair and more recently has been shown to predict perioperative and long-term mortality after EVAR. GAS is calculated using risk score = age in years + 7 points for myocardial disease + 10 points for cerebrovascular disease + 14 points for renal disease + 17 points for shock (not necessarily applicable when elective patients). The GAS separates patients into low or high risk groups, with high risk patients receiving a risk score ≥ 79 points and who might be considered unsuitable for surgery.

**Goldman Cardiac Risk Index (CRI)**
The revised Goldman Cardiac Risk Index (Detsky Index) includes six independent variables. An evaluation of cardiac risk indices for patients undergoing noncardiac surgery carried out by Gilbert et al. (2000)\textsuperscript{31} compared the Detsky Index with the Goldman Index and two other indices. Each index was found to provide a statistically significant degree of stratification ($p<0.001$) and areas under the ROC curves were similar. The models were significantly better than chance for predicting myocardial infarction and death. However, whilst generally, the indices were useful in providing clinical information about risk, but accuracy of the measures was limited.\textsuperscript{31}

**Hardman Scoring Systems**

The Hardman Prognostic Index includes five risk factors; age > 76 years, history of loss of consciousness, ECG evidence of ischemia, haemoglobin < 9 g/dL, and serum creatinine > 0.19 mmol/L. A small study compared the predictive value of the Hardman Index in patients undergoing EVAR and open repair and found that mortality rates increased with rising Hardman scores for both open and EVAR patients.\textsuperscript{32}

**Leiden Score/Modified Leiden Score (M-LS)**

The Leiden Score based on age, gender, presence of myocardial infarction, ST-segment depression, congestive heart failure, renal disease, pulmonary disease and centre specific average surgical mortality. The M-LS is based on the same variables, but ST-segment depression and centre-specific average surgical mortality are not included, and more points are given for severe renal disease. Both the Leiden and M-LS predicted post-operative mortality although their accuracy in predicting post-operative complications is somewhat lower.\textsuperscript{33}

**POSSUM/V-POSSUM** (Physiological & Severity Score for the Enumeration of Mortality & Morbidity/Vascular-POSSUM)

POSSUM has been widely used for assessing outcomes by risk-adjusted analysis in the UK.\textsuperscript{22} It includes a physiological assessment and a measure of operative severity. The physiological assessment includes 12 physiological variables, divided into four grades, which are present at the time of surgery, including age, cardiac history, respiratory history, blood pressure, pulse rate, Glasgow coma score, haemoglobin, wbc, serum urea, serum sodium, serum potassium, and electrocardiogram. The
operative severity section includes 6 variables, divided into 4 grades, which includes operative severity, multiple procedure, total blood loss, peritoneal soiling, presence of malignancy, and mode of surgery.

POSSUM has shown favourable results for mortality and morbidity risk prediction and comparative surgical audit, but does have limitations. In particular, this model and the P-POSSUM model overestimate mortality for low risk procedures. An assessment of the the validity of V-POSSUM and ruptured AAA-POSSUM models and concluded that the two scoring systems were not effective predictors of death after ruptured AAA.

**Vascular-Biochemistry and Haematology Outcome Modelling (V-BOHM)**

The V-BOHM uses data obtained prior to operation to predict outcome, including haemoglobin level, wbc, urea, sodium, potassium, age-on-admission. This model was developed to provide accurate risk prediction for both elective and non-elective AAA surgery (open repair), without the problems often experienced with missing data. An evaluation of the efficacy of the V-BOHM in 2,718 patients and found that the model, which also included age and gender as risk factors, was effective in predicting surgical mortality after both open elective and non-elective AAA repair.

A number of other risk score measures are used in clinical practice, including the British United Provident Association (BUPA) operative grade, Eagle Score, Hospital Prognostic Index, Modified Comorbidity Severity Score (M-CSS), and Prognostic Nutritional Index.
4 Definition of decision problem

4.1 Decision problem
What is the most effective and cost-effective form of management for patients with a diagnosis of AAA: immediate elective surgery with open repair, immediate elective surgery with EVAR, surveillance with an option to defer surgery, or a decision to rule out surgery entirely?

4.2 Overall aims and objectives of assessment
The objective of this assessment is to determine the clinical and cost-effectiveness of endovascular stent-grafts for repair of infrarenal abdominal aortic aneurysms in patients at varying levels of risk, including those who are appropriate for open repair and those who are not. The assessment will build on the information already available, including recent systematic reviews.\textsuperscript{12, 37-39} A particular objective is to seek evidence to clarify areas of uncertainty, for example about longer-term outcomes, about the variables and risk factors that influence the effectiveness and safety of EVAR and whether there are subgroups of patients for whom EVAR is particularly appropriate. Recommendations for further research will reflect identified gaps in the evidence base.

The specific objectives of the cost-effectiveness analysis are:

- to structure an appropriate decision model to characterise patients’ care and subsequent prognosis and the impacts of alternative therapies;
- to populate this model using the most appropriate data identified systematically from published literature and routine data sources;
- to relate intermediate outcomes to final health outcomes, expressed in terms of quality-adjusted life years (QALYs);
- to estimate the mean cost-effectiveness of EVAR compared with standard care (open repair or non-surgical management), based on an assessment of long-term NHS and Personal Social Service costs and quality-adjusted survival;
• consistent with available evidence to report cost-effectiveness of alternative treatments for specific sub-groups of patient. This may include cost-effectiveness by patients underlying risk of particular clinical events.
• to characterise the uncertainty in the data used to populate the model and to present the uncertainty in these results to decision makers.
5 Assessment of Clinical Effectiveness

5.1 Methods for Reviewing Clinical Effectiveness

5.1.1 Search strategy

Recent systematic reviews by Drury et al\textsuperscript{37} and Lederle et al\textsuperscript{38} were used to identify randomised controlled trials (RCTs) and other clinical studies. Additional searches were conducted to identify recent RCTs (2005–7), publications relating to named registries and for studies investigating baseline risks. Searches were not restricted by language or study design.

To identify systematic reviews and guidelines the following databases and web pages were searched/scanned: Cochrane Database of Systematic Reviews, DARE, HTA database, NLH National Library of Guidelines, National Guideline Clearinghouse, NICE web pages.

The following bibliographic databases listed were searched to identify RCTs (2005 to February 2007), risk modelling studies and papers based on Registry data: BIOSIS Previews (R); CINAHL; The Cochrane Central Register of Controlled Trials; EMBASE; ISI Proceedings, MEDLINE(R); MEDLINE(R) In-Process & Other Non-Indexed Citations; Science Citation Index; Zetoc Conferences. Search strategies are given in Appendix 10.1. Searches to identify any ongoing trials were carried out using Clinicaltrials.gov, Current Controlled trials and the National Research Register.

Regular current awareness searches were carried out during the review using both Science Direct and Zetoc. Search alerts were set up for a number of topic-specific journals:

- Annals of Vascular Surgery
- The Asia Pacific Journal of Thoracic & Cardiovascular Surgery
- Cardiovascular Surgery
- European Journal of Vascular Surgery
- European Journal of Vascular and Endovascular Surgery
- Interactive Cardiovascular and Thoracic Surgery
In addition, OvidAutoAlerts were created in both the MEDLINE and EMBASE databases to notify the review team of papers with EVAR in the title, original title, abstract. Current awareness searches were continued until February 2008.

5.1.2 Inclusion and exclusion criteria

Two reviewers independently screened all titles and abstracts. Potentially relevant full paper manuscripts were obtained where possible, and the relevance of each study was assessed independently by two reviewers in accordance with the criteria below. Discrepancies were resolved through discussion, or by referral to a third reviewer when necessary. Studies that did not fulfil all of the criteria were excluded, with reasons for their exclusion documented.

Population

Patients with asymptomatic or symptomatic, ruptured or unruptured infrarenal abdominal aortic aneurysms (AAAs) that were anatomically and clinically suitable for endovascular stent-graft repair (EVAR) were included. The study authors’ definition of aneurysm status and suitability for EVAR were used. Studies of patients with aneurysms of any size were included.

Interventions
Studies identifying elective or emergency EVAR of infrarenal AAAs, using uni-iliac or bi-iliac stent grafts, were included. It was recognised that not all devices evaluated in the research literature would have a CE mark and that several devices would have undergone a number of changes. It was also recognised that manufacturers’ devices would have varying indications for use and contraindications. Hence studies of any EVAR device were eligible but, where data allowed, analysis focussed on devices commonly used in current UK practice.

Comparators

- Studies in which the comparator was one of the following were included:
- For patients in whom conventional open repair was a treatment option (according to study authors’ criteria) conventional open repair was the appropriate comparator.
- For patients in whom conventional open repair was not a treatment option (according to study authors’ criteria) the appropriate comparator was non-surgical treatment for AAA (sometimes referred to as ‘watchful waiting’). Such treatment will vary across studies, but will normally represent best medical care and typically include a range of strategies to manage vascular risk factors, for example smoking cessation, blood pressure reduction and statin therapy.

Outcomes

Only studies reporting at least one of the following outcomes were included:
- 30-day mortality rate
- Aneurysm related mortality
- All cause mortality
- Health-related quality of life (HRQOL)
- Adverse effects and complications. This included aneurysm related outcomes such as rupture and events specific to EVAR e.g. frequency of endoleaks and device migration. Major morbidity, for example, cardiac events, was also assessed.
• Re-intervention rates including conversion from EVAR to open procedure and secondary intervention.

**Study designs**

Estimates of the treatment effect and safety outcomes of EVAR were derived from RCTs and large registries of relevance to UK practice. The registries used were the Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA) and the European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) for EVAR, and the National Vascular Database (NVD) for open surgery).

In order to identify criteria for selecting patients appropriate for EVAR, studies that modelled the spectrum of risk were also reviewed. Risk modelling studies were specific to AAA, focussed on risk of mortality following EVAR, and used appropriate statistical modelling techniques (for example, Kaplan–Meier survival analysis, multiple linear or logistic regression or Cox proportional hazards analysis). Studies were required to be based on a trial, registry or a series of at least 500 patients from developed countries of relevance to UK practice.

**5.1.3 Data extraction strategy**

Data relating to both study design and quality were extracted by one reviewer, using a standardised data extraction form, and checked by a second reviewer. Discrepancies were resolved by discussion, with involvement of a third reviewer when necessary. For studies with multiple publications, those with the greatest number of participants, the longest follow up or the latest publication presenting the largest amount of outcome data were extracted. For registries, this was interpreted to mean the latest report covering all patients in the registry; publications based on an analysis of registry data that were not reports of the registry as a whole were included in the review for completeness but most were not data extracted. Data were extracted on: study details (e.g. study identifier/EndNote ID, author, year, country, setting, number of participants, and fitness), patient characteristics (e.g. age, gender, causal/risk factors, comorbidities, aneurysm size/anatomy), intervention (type of stent-graft),
comparison (details of open repair or medical management), study quality (RCTs and risk model studies), and reported outcomes relating to efficacy and safety as specified above. Careful note was made of definitions used by study authors in relation to fitness for surgery and AAA-related mortality.

5.1.4 Quality assessment strategy
The quality of the individual RCTs and risk model studies was assessed by one reviewer, and independently checked for agreement by a second reviewer. Any disagreements were resolved by consensus and where necessary a third reviewer was consulted. The quality of RCTs was assessed using standard checklists\(^4^0\) that were adapted to incorporate topic-specific quality issues. The quality of risk models was assessed using a checklist adapted by the authors from a checklist used in a previous systematic review of prognostic models.\(^4^1\) The quality of audit/registry data was not assessed because the included registries were chosen for relevance and pre-specified in the protocol.

5.1.5 Data analysis
Data extracted from the studies were tabulated and discussed in a narrative review. The results of the quality assessment were tabulated, and where possible, the effect of study quality on effectiveness data and the findings of the review were discussed. Where appropriate, meta-analysis was employed to estimate a summary measure of treatment effect on relevant outcomes based on intention to treat analyses. Meta-analysis was carried out using fixed effects models, using Review Manager 4.2. A spreadsheet developed by the MRC Clinical Trials Unit, London, was used to estimate hazard ratios where necessary.\(^4^2\) Heterogeneity was explored through consideration of the study populations, methods and interventions, by visualisation of results and, in statistical terms, by the \(\chi^2\) test for homogeneity and the I\(^2\) statistic.
5.2 Results of Review of Clinical Effectiveness

5.2.1 Quantity and quality of research available

Figure 5.2.1: Flow chart of studies through the review process

- Titles and abstracts identified and screened \( n=4691 \)
- Excluded \( n=4012 \)
  - Not relevant \( n=3862^* \)
  - Records of research in progress \( n=150 \)
- Full copies retrieved and screened for inclusion \( n=679 \)
- Excluded \( n=551 \)
  - Patient group not AAA \( n=19 \)
  - RCT but not EVAR vs Open or non-surgical \( n=8 \)
  - Registry other than RETA, EUROSTAR or NVD \( n=3 \)
  - Risk model but not modelling patient risk following EVAR \( n=26 \)
  - Risk model but outcome not relevant \( n=2 \)
  - Risk model with less than 500 patients \( n=94 \)
  - Not RCT, Registry or Risk model \( n=394 \)
  - Duplicate \( n=5 \)

- Total number of studies included \( n=43 \)
  - RCTs \( n=6 \) (19 publications)
  - Risk models \( n=34 \) (36 publications)
  - Registries \( n=3 \) (75 publications)**

*Excluded based on title and abstract

**Most registry publications were not data extracted (see section 5.1.3)

5.2.1.1 Included RCTs

Six RCTs were included in the review. Four of these (DREAM\textsuperscript{43, 44}, EVAR trial \textsuperscript{18, 26}, \textsuperscript{45} and the studies by Cuypers et al.\textsuperscript{46} and Soulez et al.\textsuperscript{47}) compared EVAR and open surgery in patients with unruptured AAAs who were fit for open repair. One RCT
(EVAR trial 2\textsuperscript{48}) compared EVAR with non-surgical management of patients deemed unfit for open repair. A small RCT by Hinchliffe et al.\textsuperscript{49} compared EVAR and open repair in patients with ruptured AAAs.

Table 5.2.1: Quality assessment results for RCTs

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>True randomisation</th>
<th>Adequate concealment of treatment allocation</th>
<th>Outcome assessor blinded</th>
<th>Baseline characteristics comparable between groups</th>
<th>Eligibility criteria reported</th>
<th>Withdrawals or exclusions accounted for</th>
<th>Power calculation reported</th>
<th>Intention to treat analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blankensteijn 2005\textsuperscript{44} DREAM</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cuypers 2001\textsuperscript{46}</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EVAR trial 2 2005\textsuperscript{48}</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EVAR trial 1 2005\textsuperscript{48}</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hinchliffe 2006\textsuperscript{49}</td>
<td>Unclear</td>
<td>No</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Soulez 2005\textsuperscript{47}</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Results of quality assessment of the included RCTs are presented in Table 5.2.1. The main RCTs, DREAM,\textsuperscript{44} EVAR trial 1\textsuperscript{18} and EVAR trial 2,\textsuperscript{48} were all of high quality (positive answers to all quality questions). Some methodological aspects of the remaining RCTs were unclear based on the published reports. The study of EVAR vs open repair for patients with ruptured AAAs\textsuperscript{49} lacked adequate concealment of treatment allocation, perhaps reflecting the ethical and practical problems of conducting an RCT in a setting of emergency surgery. The RCT by Soulez et al.\textsuperscript{47} did not report a sample size calculation and probably lacked statistical power to detect differences in mortality and related outcomes.

In addition to methodological quality issues, these RCTs have a number of limitations that may affect their usefulness in assessing the current clinical effectiveness of EVAR relative to open repair and non-surgical management. Of the four RCTs that compared EVAR and open repair in patients with unruptured aneurysms, those of Cuypers et al.\textsuperscript{46} and Soulez et al.\textsuperscript{47} were small studies and were not designed to assess hard clinical endpoints such as mortality; furthermore, the study of Cuypers et al. was limited to one month of follow-up. Hence the analysis of EVAR versus open repair for unruptured AAAs concentrated on data from the larger RCTs.
These major trials comparing EVAR with open repair, DREAM\textsuperscript{43,44} and EVAR trial 1,\textsuperscript{18,45} randomised patients between November 2000 and December 2003 and between September 1999 and August 2004, respectively. Thus the devices used and other details of the procedures may not represent current best practice. Published results from the two RCTs represent relatively short periods of follow-up (2 years for DREAM and 4 years for EVAR trial 1). The main analyses of EVAR trial 1 were published in 2004 for 30-day operative mortality\textsuperscript{45} and 2005 for 4-year follow-up results\textsuperscript{18} and covered patients randomised up to December 2003. Four-year results for patients randomised up to August 2004 were included in a publication analysing results by patient fitness.\textsuperscript{26} These data were not included in the analyses of mortality outcomes in this review because this was a secondary publication with limited details and because the additional patients were randomised after the official close of recruitment.

Finally, the sample size calculation for DREAM was based on a primary endpoint of short-term mortality and complications and the trial’s power to detect differences in follow-up outcomes is unclear.

The other relevant comparison is between EVAR and continued non-surgical management of patients considered unfit or unsuitable for open repair. The only RCT to have addressed this issue is EVAR trial 2.\textsuperscript{48} Although this was a high-quality RCT in terms of design and methodology, there were problems with its execution. There was a median delay of 57 days between randomisation and procedure in the EVAR arm and 14 patients in this group died before operation (including six from AAA rupture). Forty-seven patients assigned to non-surgical management received surgical aneurysm repair (including 12 who received open repair despite having been classified as unfit for this procedure). These factors complicate the analysis and interpretation of this trial.

The evidence base for EVAR for patients with ruptured AAAs is currently limited to one small pilot trial.\textsuperscript{49} The sample size calculation for this trial was based on recruiting 100 patients, but only 32 patients were randomised, which makes it difficult to draw any firm conclusions from the trial. However, the study showed that it is
possible to conduct a randomised trial in this setting. The ongoing Amsterdam Acute Aneurysm trial (see below) should provide further evidence in due course.\textsuperscript{50}

\textbf{5.2.1.2 Ongoing RCTs}

We received information from investigators of five potentially relevant ongoing RCTs, who we had contacted to request further details and any data that the investigators were willing to include in our review.

ACE\textsuperscript{51} is a French RCT comparing EVAR and open repair in patients aged 50 years and older with an AAA measuring 5 cm or more in diameter (4 cm or more if rapidly growing). The primary outcomes are death and major morbidity and the trial enrolled 600 patients. The trial started in January 2003 with an expected completion date of January 2006. The investigators informed us of a possible first publication in January 2008 (V. David, personal communication) but further details have not been made available.

The Amsterdam Acute Aneurysm Trial is an RCT comparing EVAR and open repair in patients with a ruptured AAA. A paper describing the background, methods and design of the study has been published.\textsuperscript{50} The primary outcome is a composite of death and severe morbidity assessed in hospital and 30 days, 3 months and 6 months post-operatively. Secondary outcomes include HRQOL, length of intensive care stay and cost-effectiveness. The calculated sample size was 40 patients per group. The scheduled end date for the trial is August 2008.

OVER (Open surgery Versus Endovascular Repair) is a large US RCT comparing EVAR and open repair in patients aged 50 years and above with an AAA measuring 5 cm or more in diameter (4.5 cm or more if expanding rapidly).\textsuperscript{52} The primary
outcome is all cause mortality. OVER has an anticipated duration of 9 years and the planned sample size is 900 patients. The expected completion date is October 2011.

NExT ERA (National Expertise Based Trial of Elective Repair of Abdominal Aortic Aneurysms) was a planned pilot study for a national expertise-based RCT comparing EVAR and open repair in Canada. In November 2007, the investigator informed us that the study had been abandoned (T. Mastracci, personal communication).

CAESAR (Comparison of Surveillance vs. Aortic Endografting for Small Aneurysm Repair) is an RCT conducted in Italy to compare EVAR with surveillance (and eventual treatment) in patients with AAAs of diameter 4.1–5.4 cm suitable for EVAR. The design of the study has been published. The primary outcome is all cause mortality. Secondary outcomes include aneurysm related mortality, rupture, perioperative or late complications, conversion to open repair, complications associated with late treatment and HRQOL. A cost analysis is also included. Patients assigned to surveillance are considered for surgery if the aneurysm reaches 5.5 cm in diameter, grows rapidly (>1 cm/year) or becomes symptomatic. The planned sample size is 740 patients. In November 2007, the investigators informed us that 325 patients had been enrolled and results were not expected until the end of 2008 (F. Verzini, personal communication).

5.2.1.3 Included registries

Due to the limited data available from RCTs, and the need for long term data on safety and efficacy for larger numbers of patients, registry databases were also included in the review. Unlike RCTs, which are not powered to allow ad hoc comparisons between subgroups, registries provide the opportunity for various types of secondary analysis to be carried out on a large number of patients. They may also report more realistic results than do RCTs as registry data are obtained from a range of clinical institutions with varying levels of experience and expertise. Indeed, there is evidence to support the validity of registry data, and that such data provides a true representation of a cross-section of patients, methods and hospitals.
The three pre-specified registries included in the review were described in five reports. Two were of EVAR procedures (EUROSTAR\textsuperscript{56, 57} and RETA\textsuperscript{58-60}) and one of open repair (National Vascular Database (NVD))\textsuperscript{19}).

Results from RETA were included in two papers; one reported short-term (30-day) outcome\textsuperscript{60} and the other paper presented mid term results to five years.\textsuperscript{58} Data were also presented in an unpublished report prepared on behalf of the Vascular Surgical Society of Great Britain and Ireland and the British Society of Interventional Radiology.\textsuperscript{59} Data for the NVD registry were reported in the Fourth NVD Report, published on behalf of the Audit and Research Committee of the Vascular Society of Great Britain and Ireland. EUROSTAR data were identified through the progress report for endografts in current use, prepared by the EUROSTAR Data Registry Centre, and the registry’s unpublished protocol paper.

\textit{5.2.1.4 Risk modelling studies}

Thirty-four studies evaluated the role of baseline characteristics on the risks of particular outcomes after EVAR.\textsuperscript{26, 61-93} See Table 5.2.2.
**Table 5.2.2: Overview of Risk Modeling Studies**

<table>
<thead>
<tr>
<th>Study details</th>
<th>Data source</th>
<th>Study dates</th>
<th>Type of study</th>
<th>Development of a risk assessment algorithm</th>
<th>Evaluation/validation of existing risk assessment algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biancari 2006</td>
<td>EUROSTAR</td>
<td>October 1996 to March 2005</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Boult 2007</td>
<td>Australian national audit</td>
<td>1 November 1999 to 16 May 2001</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Brewster 2006</td>
<td>MGH</td>
<td>January 7 1994 to December 31 2005</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown (EVAR trial participants) 2007</td>
<td>EVAR trial 1 and EVAR trial 2</td>
<td>September 1999 to August 2004</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Buth 2000</td>
<td>EUROSTAR</td>
<td>January 1994 to July 1999</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buth 2006</td>
<td>EUROSTAR</td>
<td>January 1994 to March 2001</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brewster 2006</td>
<td>EUROSTAR</td>
<td>June 1996 to March 2001</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buth 2003</td>
<td>Not reported</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cuypers 2000</td>
<td>EUROSTAR</td>
<td>January 1994 to July 1999</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diehm 2007</td>
<td>EUROSTAR</td>
<td>December 1996 to November 2005</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diehm 2007</td>
<td>EUROSTAR</td>
<td>March 1994 to November 2006</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hobo 2006</td>
<td>EUROSTAR</td>
<td>December 1999 to December 2004</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hobo 2007</td>
<td>EUROSTAR</td>
<td>October 1996 to January 2006</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lange 2005</td>
<td>EUROSTAR</td>
<td>1996 to 2004</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2007</td>
<td>EUROSTAR</td>
<td>Patients registered post 1999 inc</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2004</td>
<td>EUROSTAR</td>
<td>6 year period to April 2004</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2006</td>
<td>EUROSTAR</td>
<td>Recruitment began October 1996</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2005</td>
<td>EUROSTAR</td>
<td>May 1994 to December 2003</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2005</td>
<td>EUROSTAR</td>
<td>1994 to 2004</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2006</td>
<td>EUROSTAR</td>
<td>Enrolled 1st December 1996</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifeline Registry of Endovascular aneurysm repair 2002</td>
<td>US Lifeline registry</td>
<td>Not reported</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lottman 2004</td>
<td>EUROSTAR</td>
<td>January 1994 to July 2001</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mohan 2001</td>
<td>EUROSTAR</td>
<td>January 1994 to January 2000</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peppelenbosch 2004</td>
<td>EUROSTAR</td>
<td>Over 6 years up to June 2002</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rimbau 2004</td>
<td>EUROSTAR</td>
<td>January 1994 to August 1998</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ruppert 2006</td>
<td>EUROSTAR</td>
<td>July 1997 to August 2004</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sampram 2003</td>
<td>Cleveland Clinic, Ohio, US</td>
<td>1996 to 2002</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timaran 2007</td>
<td>NIS</td>
<td>2001 to 2004</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Torella 2004</td>
<td>EUROSTAR</td>
<td>May 1994 to June 2002</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>van Eps 2006</td>
<td>EUROSTAR</td>
<td>December 1996 to January 2005</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>van Marrewijk 2004</td>
<td>EUROSTAR</td>
<td>1996 to June 2002</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zarins 2006</td>
<td>AneuRx stent graft trial (40 centres)</td>
<td>1998 to 1999</td>
<td>√</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Massachusetts General Hospital
2 National Surgical Quality Improvement Program
3. The Nationwide Inpatient Sample from the Healthcare Cost and Utilisation Project
The majority of the studies were based on data from the EUROSTAR registry. These studies often investigated a range of potential risk variables such as age and gender and often focused on the investigation of one particular risk factor such as diabetes. However, as there is likely to be overlap of patients between these studies, the number of studies reporting the significance of a factor is not always useful as a guide to the robustness of the evidence. Seven studies are US-based and need to be interpreted within the context of differences in clinical practice between US and UK settings. One study was based on an Australian national audit and one study analysed data from the UK EVAR 1 and 2 trials.

A further caveat concerns the follow up period of the studies included in this section. Generally the studies cover a period of five to ten years, although follow-up of individual patients is generally shorter. Patients are perhaps more ‘typical’ of those in routine clinical practice. However, many of the studies begin in the mid 1990s and this raises issues of older devices and less experience with EVAR.

A final caveat is that the majority of the studies in this section undertook to investigate specific risk factors using multiple regression analysis. As such, statistically significant results can reflect the covariates used in the model which often were not clear from the published reports. Furthermore, these studies highlight risk factors but do not necessarily quantify, for example, the effect of older age on risk of aneurysm related mortality. More useful in this regard were the studies that aimed to develop a risk algorithm or to evaluate an existing algorithm to aid clinical decision making. These studies were few in number and are discussed in section 5.2.4. Studies that both develop or validate an algorithm and discuss individual risk factors are discussed within each relevant section.

Table 5.2.3 details the quality of the risk model studies. Collectively, the studies described the samples in sufficient detail (study characteristics are detailed in Section 5.2.3). Just over half of the studies provided a clear definition of the risk variables under investigation, for example the measurements for a ‘large’ aneurysm or definition of ‘old age’. The weaknesses of the studies were in reporting details of multivariable modeling, particularly outlining the covariates considered to build the model and how these were chosen. Details of any investigations of interaction
between variables were rarely provided. Appropriateness of analysis could not always be ascertained as it was not always clear how continuous variables were handled or whether there were a sufficient number of events to warrant the number of variables under investigation in a study. Finally, nine studies did not present confidence intervals or other measures of uncertainty, making it difficult to assess the precision of any effect measures reported. Overall no studies clearly met all quality criteria, twelve met five or six of the seven criteria and the remainder met fewer than five criteria.
### Table 5.2.3: Risk model studies Quality Assessment

<table>
<thead>
<tr>
<th>Author</th>
<th>Study sample adequately described</th>
<th>Included risk variables clearly defined</th>
<th>Covariates considered to build the multivariate model</th>
<th>Interactions between variables explored</th>
<th>Continuous variables handled appropriately</th>
<th>More than 10 events per included variable</th>
<th>Confidence intervals or other measures of uncertainty presented</th>
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<td>Yes</td>
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5.2.2 Assessment of effectiveness from RCTs

5.2.2.1 EVAR vs. open (unruptured)

Study characteristics

The characteristics of the included RCTs are summarised in Tables 5.2.4 – 5.2.7.

Patients

Four RCTs compared EVAR with open repair in patients with unruptured AAAs: DREAM\(^{43,44}\) (n=351), EVAR trial \(^{118,45}\) (n=1082) and the small RCTs of and the studies by Cuypers et al.\(^{46}\) (n=76) and Soulez et al.\(^{47}\) (n=40) (Table 5.2.4). It should be noted that a later publication of EVAR trial \(^{126}\) reported a larger sample size (n=1252) because patient recruitment had continued until August 2004. However, patient details were not provided and therefore data from this later analysis have not been used in the main analyses in this report nor in Table 5.2.4.

Patients were predominantly male in all RCTs, the percentage of men ranging from 91% to 98% reflecting disease profile. Average age of patients ranged from the late 60s to mid-70s. The four RCTs were relatively homogeneous in terms of average aneurysm diameter: 6.5 cm in EVAR trial 1, 6.0 cm in DREAM, 5.4 cm in Cuypers et al., and 5.2 cm in Soulez et al.

The RCTs varied in their reporting of comorbidity and patient fitness. In all four RCTs the majority of patients were current or ex-smokers. Across the four trials the prevalence of diabetes was 10–16% and of heart disease was 43–68%. Other comorbidities were reported for two or three RCTs respectively (Table 5.2.5).

Patient fitness scores were reported for all four RCTs, but different scoring systems were used. The DREAM investigators\(^{43}\) and Cuypers et al.\(^{46}\) used the ASA classification system; the majority (about two-thirds) of patients in these studies were classified as ASA II. EVAR trial 1 did not report an overall measure of patient fitness in the main publications.\(^{45}\) In a later analysis,\(^{26}\) patients were classified as having good, moderate or poor fitness based on modified Customised Probability Index scores. Of 1252 patients randomised (including some randomised too late for the main
analysis), 579 (46.2%) were classified as ‘good’, 331 (26.4%) as ‘moderate’ and 338 (27.0%) as ‘poor’ fitness.

**Intervention**

Patients receiving EVAR in these four RCTs were recruited between September 1996 and August 2004 (Table 5.2.6), although patients recruited to EVAR trial 1 after December 2003 were not included in the main analysis. They are included in the analysis by fitness. EVAR trial 1 had the latest closing date for recruitment but DREAM had the most recent start (November 2000). The time period covered by the Cuypers trial (1996-1999) limits its relevance to current clinical practice. Delay between randomisation and procedure was similar for the two larger RCTs (median 39 days in DREAM and 43 days in EVAR trial 1), although waiting time ranged up to 183 days in DREAM. A wide range of different devices were used within and between trials. In EVAR trial 1 and DREAM, the most commonly used devices were the Zenith (Cook) and Talent (Medtronic) stent grafts. Information on the effects of device brand on outcomes in RCTs is presented in the last section of 5.2.2.1 headed ‘Analysis by device type’. The majority of patients received bi-iliac stent grafts under general anaesthesia, although in DREAM a substantial minority (40%) received regional anaesthesia. The type of anaesthesia used was not reported in the main publications of EVAR trial 1.

**Comparator**

The comparator intervention in these four RCTs was open repair performed under general anaesthesia according to the centre’s standard procedures. The median time between randomisation and procedure was similar for open repair and EVAR in EVAR trial 1 and DREAM trials but the DREAM trial recorded a high maximum waiting time (260 days; Table 5.2.7).
Table 5.2.4: Basic characteristics of RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Country where study was performed</th>
<th>Number of patients randomised</th>
<th>Age of population</th>
<th>Gender</th>
<th>Aneurysm diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM Blankensteijn 2005&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Multinational The Netherlands and Belgium</td>
<td>351</td>
<td>173.</td>
<td>178.</td>
<td>Mean (SD) 70.1 years (EVAR 70.7(6.6), open 69.6(6.8)) Percentage male (total population) 91.7% (EVAR 93.1%, open 90.4%)</td>
</tr>
<tr>
<td>EVAR trial 1 EVAR trial participants 2005&lt;sup&gt;16&lt;/sup&gt;</td>
<td>UK</td>
<td>1082</td>
<td>543</td>
<td>539</td>
<td>Mean (SD) 74 (SD 6) years (EVAR 74.2 (SD 6.0); open repair 74.0 (SD 6.1)) Percentage male (total population) 91% (EVAR 494 (91%); open repair 489 (91%))</td>
</tr>
<tr>
<td>Cuypers 2001&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Netherlands</td>
<td>76</td>
<td>57</td>
<td>19</td>
<td>Mean (SD) 68.5 years 69 years EVAR 68 years open repair Range 52-82 EVAR 52-81 open repair</td>
</tr>
<tr>
<td>Soulez 2005&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Canada</td>
<td>40</td>
<td>20</td>
<td>20</td>
<td>Mean (SD) 70.5 years 70.3 (SD 6.4) EVAR 71.2 (SD 7.6) open repair</td>
</tr>
</tbody>
</table>
Table 5.2.5: Patient characteristics in RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Smoking history</th>
<th>Diabetes</th>
<th>Heart Disease</th>
<th>Hypertension</th>
<th>Renal disease</th>
<th>Respiratory Disease</th>
<th>Fitness scores</th>
<th>Body Mass Index (BMI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DREAM Blankensteijn 2005</strong>&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Current smokers 209 (59.6%) (EVAR 111 (64.2%), Open 98 (55.1%))</td>
<td>35 (10%) (EVAR 18 (10.4%), Open 17 (9.6%))</td>
<td>154 (43.8%) (EVAR 71 (41%), Open 83 (46.6%))</td>
<td>198 (56.4%) (EVAR 101 (58.4%), Open 97 (54.5%))</td>
<td>28 (8%) (EVAR 13 (7.5%), Open 15 (8.4%))</td>
<td>81 (23%) (EVAR 48 (27.7%), Open 33 (18.5%))</td>
<td>ASA I 81 (23%) (EVAR 37 (21.4%), Open 44 (24.7%)) ASA II 232 (66%) (EVAR 122(70.5%), Open 110(61.8%)) ASA III 38 (10.8%) (EVAR 14 (8.1%), Open 24(13.5%) ASA IV 0</td>
<td>Mean (SD) 26.5(EVAR 26.3(3.4), Open 26.6(4.1))</td>
</tr>
<tr>
<td><strong>EVAR trial 1 EVAR trial participants 2005</strong>&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Current smokers 232 (21%) (EVAR 115 (21%), Open 117 (22%))</td>
<td>111 (10%) (EVAR 49 (9%), open repair 62 (12%))</td>
<td>463 (43%) (EVAR 234 (44%), open repair 229 (43%))</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Mean (SD) 26.4 (EVAR 26.4 (4.6); open repair 26.4 (4.4))</td>
</tr>
<tr>
<td><strong>Cuypers 2001</strong>&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Current smokers 31 (41%)</td>
<td>16%</td>
<td>18 (14%) EVAR 4 (21%) open repair</td>
<td>25 (44%) EVAR history of coronary artery disease 10 (53%) open repair history of coronary artery disease 56% EVAR 12 (63%) open repair</td>
<td>Not reported</td>
<td>28%</td>
<td>17 (30%) COPD -EVAR 4 (21%) COPD - open repair</td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Soulez 2005</strong>&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Current smokers: 8 (20%) EVAR 5 (25%) Open 3 (15%)</td>
<td>6 (15%)</td>
<td>27 (68%)</td>
<td>18 (45%)</td>
<td>CrCl &lt;50mL/min): 6 (15%)</td>
<td>9 (22%)</td>
<td>6 (30%) EVAR 3 (15%) open repair</td>
<td>Mean (SD) 17 (42%) BMI &gt;30</td>
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</tbody>
</table>

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Table 5.2.6: Intervention characteristics in RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or emergency procedure</th>
<th>Type of device (EVAR)</th>
<th>Graft type (EVAR)</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blankensteijn 2005(^4)</td>
<td>November 2000 to December 2003</td>
<td>Median 39 days Range 1 to 183 days</td>
<td>Elective 173 (100%) Emergency 0</td>
<td>Zenith 57 (33.3%) Talent 46 (26.9%) Excluder 37 (21.6%) Other 30 (17.5%)</td>
<td>Uni-iliac (number of patients (%)) 6 (3.5%) Bi-iliac (number of patients (%)) 16 (9.4%) Other Endovascular tube graft 1 (0.6%)</td>
<td>Local (number of patients (%)) 9 (5.3%) Regional (number of patients (%)) 68 (39.8%) General (number of patients (%)) 94 (54.9%)</td>
</tr>
<tr>
<td>EVAR trial 1 EVAR trial participants 2005(^5)</td>
<td>September 1999 to July 1 2004 for main analysis. Additional patients recruited up to August 31 2004 included in some analyses.</td>
<td>Median 43 days (IQR 28-69) Range 28-70 days</td>
<td>Elective 512 (94% of randomised patients) Emergency 0 (0%)</td>
<td>Zenith 261 (51%) (based on n = 512) Talent 167 (33%) (based on n = 512) Excluder 36 (7%) (based on n = 512)</td>
<td>Uni-iliac (number of patients (%)) 51 (10%) (based on n = 512) Bi-iliac (number of patients (%)) 461 (90%) (based on n = 512)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cuypers 2001(^6)</td>
<td>September 1996 to October 1999</td>
<td>Not reported</td>
<td>Not reported</td>
<td>3 patients (5%) Stentor 22 (39%) Vanguard 30 (52%) AneuRx 1 (2%) Lifepath 1 (2%) had open repair</td>
<td>Bi-iliac (number of patients (%)) 57 (100%)</td>
<td>General (number of patients (%)) 57 (100%) patients</td>
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</table>
### Table 1: Details of Included Procedures

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or emergency procedure</th>
<th>Type of device (EVAR)</th>
<th>Graft type (EVAR)</th>
<th>Anaesthesia</th>
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<tr>
<td>Soulez 2005</td>
<td>September 1998 to July 2002</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Talent</td>
<td>Bi-iliac (number of patients (%)) 20 (100%) EVAR patients</td>
<td>Local (number of patients (%)) 1 (5%) EVAR 1 (5%) EVAR General (number of patients (%)) 18 (90%) EVAR</td>
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Table 5.2.7: Comparator characteristics in RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
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<tr>
<th>Author (main publication)</th>
<th>Open repair or non-surgical procedure</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or Emergency procedure</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM Blankenstein 2005&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Open repair Particular open technique used was at the discretion of the surgeon.</td>
<td>November 2000 to December 2003</td>
<td>Median 39 days Range 4 to 260 days</td>
<td>Elective 178(100%)</td>
<td>Local (number of patients (%)&lt;br&gt;1(0.6%) (Crossover to EVAR) Regional (number of patients (%))&lt;br&gt;2(1.1%) (Crossovers to EVAR) General (number of patients (%))&lt;br&gt;171(98.3%) (all patients except 3 crossovers)</td>
</tr>
<tr>
<td>EVAR trial 1 EVAR trial participants 2005&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Open repair</td>
<td>September 1999 to July 1 2004 for main analysis. Additional patients recruited up to August 31 2004 included in some analyses.</td>
<td>Median 35 days (IQR 19-55) Range 20-59 days</td>
<td>Elective 496 (92.0% of randomised patients) Emergency Unclear (possibly 3 (&lt;1%))</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cuypers 2001&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Open repair</td>
<td>September 1996 to October 1999</td>
<td>Not reported</td>
<td>Not reported</td>
<td>General (number of patients (%))&lt;br&gt;19 (100%) patients</td>
</tr>
<tr>
<td>Soulez 2005&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Open repair</td>
<td>September 1998 to July 2002</td>
<td>Not reported</td>
<td>Elective</td>
<td>General (number of patients (%))&lt;br&gt;20 (100%)</td>
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</tbody>
</table>
Results by outcome

30-day mortality

All four RCTs comparing EVAR with open repair in patients with unruptured AAAs (DREAM44, EVAR trial 118 and the studies by Cuypers et al.46 and Soulez et al.47) reported 30-day operative mortality (Figure 5.2.2). Results from a later analysis of EVAR trial 1 based on a larger sample size gave a odds ratio of 0.38 (95% CI: 0.18, 0.80).26 The pooled estimate of effect suggested a significantly lower rate of 30-day mortality in the EVAR group: pooled odds ratio 0.35 (95% CI 0.19, 0.63).

Figure 5.2.2: EVAR vs. open repair. Meta-analysis of RCTs for 30-day mortality.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>EVAR n/N</th>
<th>Open repair n/N</th>
<th>Peto OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cuypers</td>
<td>1/57</td>
<td>1/19</td>
<td>0.26 [0.01, 6.49]</td>
</tr>
<tr>
<td>DREAM</td>
<td>2/171</td>
<td>8/174</td>
<td>0.30 [0.09, 1.04]</td>
</tr>
<tr>
<td>EVAR I</td>
<td>9/532</td>
<td>25/518</td>
<td>0.37 [0.19, 0.73]</td>
</tr>
<tr>
<td>Soulez</td>
<td>0/20</td>
<td>0/20</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>780</td>
<td>731</td>
<td>0.35 [0.19, 0.63]</td>
</tr>
</tbody>
</table>

Total events: 12 (EVAR), 34 (Open repair)
Test for heterogeneity: Chi² = 0.12, df = 2 (P = 0.94), I² = 0%
Test for overall effect: Z = 3.52 (P = 0.0004)

The small Soulez et al. trial did not contribute to this analysis and exclusion of the less relevant data from the Cuyper trial (i.e. a pooled analysis including only the DREAM and EVAR trial 1) produced an almost identical measure of effect: pooled odds ratio 0.35 (95% CI 0.19, 0.64) (Figure 5.2.3).

Figure 5.2.3: EVAR vs. open repair. Meta-analysis of DREAM and EVAR trial 1 RCTs for 30-day mortality.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>EVAR n/N</th>
<th>Open repair n/N</th>
<th>Peto OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM 2004(#4305)</td>
<td>2/171</td>
<td>8/174</td>
<td>0.30 [0.09, 1.04]</td>
</tr>
<tr>
<td>EVAR I 2004(#5085)</td>
<td>9/532</td>
<td>25/518</td>
<td>0.37 [0.19, 0.73]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>703</td>
<td>692</td>
<td>0.35 [0.19, 0.64]</td>
</tr>
</tbody>
</table>

Total events: 11 (EVAR), 33 (Open repair)
Test for heterogeneity: Chi² = 0.09, df = 1 (P = 0.77), I² = 0%
Test for overall effect: Z = 3.42 (P = 0.0004)

AAA-related mortality
The two small RCTs failed to provide information on AAA-related mortality at mid-term follow-up. The DREAM trial and EVAR trial 1 had similar definitions of AAA-related mortality, i.e. death within 30 days of the original procedure or a re-intervention. DREAM was originally designed to detect differences in a primary endpoint of short-term mortality and complications, so its power to detect differences at longer-term follow-up is unclear. Mean duration of medium-term follow-up was about 22 months in DREAM compared with a median of about 35 months (2.9 years) in EVAR trial 1. Maximum follow-up in DREAM was 42 months while 24% of patients in EVAR trial 1 were followed up for 4 years or more. Longer-term data for AAA-related mortality were not available.

Both RCTs reported lower rates of AAA-related mortality in patients treated with EVAR compared with open repair. In DREAM, 3/173 patients in the EVAR group (2.1%) and 9/178 in the open repair group (5.7%) died of aneurysm related causes. The estimated hazard ratio was 0.27 (95% CI: 0.07, 1.00, p = 0.05). The corresponding figures for EVAR trial 1 were 19/543 and 34/539 deaths in the EVAR and open repair groups, respectively. The unadjusted hazard ratio was 0.55 (95% CI: 0.31, 0.96, p = 0.04); hazard ratios adjusted for primary and secondary covariates were similar. Results from a later analysis of EVAR trial 1 based on a larger sample size gave a hazard ratio of 0.60 (95% CI: 0.35, 1.02).26

The pooled estimate for the hazard ratio across the two trials was 0.49 (95% CI: 0.29, 0.83, p = 0.007), confirming a statistically significant benefit of EVAR over open repair for this outcome (Figure 5.2.4).
In a post-hoc analysis, follow-up was divided into the first 6 months after randomisation and the period beyond 6 months. The hazard ratio for the first 6 months was 0.42 (95% CI: 0.21, 0.82), a statistically significant difference favouring the EVAR group. For the later period, the hazard ratio was 1.15 (95% CI: 0.39–3.41), i.e. there was no significant difference between groups; the wide confidence interval reflected the small number of AAA-related deaths during this period.

All cause mortality

Of the four relevant RCTs, only DREAM and EVAR trial 1 provided useful information on all cause mortality at follow-up (2 years in DREAM and 4 years in EVAR trial 1). The trial by Soulez et al.\(^47\) reported only one death during mean follow-up of 29 months following EVAR and 27 months for the open repair group. In the trial by Cuypers et al.\(^46\) patients were only followed up for 30 days. Both main RCTs reported no significant difference in medium-term (35 and 42 months respectively) mortality in patients treated with EVAR compared with open repair. In DREAM, 20/173 patients in the EVAR group and 18/178 in the open repair group died of any cause. The estimated unadjusted hazard ratio was 0.94 (95% CI: 0.50, 1.79, p = 0.86).

The corresponding figures for EVAR trial 1 were 100/543 and 109/539 deaths in the EVAR and open repair groups, respectively. The unadjusted hazard ratio was 0.90 (95% CI: 0.69, 1.18, p = 0.46); hazard ratios adjusted for primary and secondary covariates were similar. Results from a later analysis of EVAR trial 1 based on a larger sample size gave a hazard ratio of 0.93 (95% CI: 0.74, 1.18).\(^{26}\)
In a post-hoc analysis, follow-up was divided into the first 6 months after randomisation and the period beyond 6 months. The hazard ratio for the first 6 months was 0.55 (95% CI: 0.33, 0.93), a statistically significant difference favouring the EVAR group. For the later period, the hazard ratio was 1.10 (95% CI: 0.80–1.52), i.e. there was no significant difference between groups.

A pooled analysis of the two trials confirmed that there was no statistically significant difference between EVAR and open repair for all cause mortality at medium-term follow-up (Figure 5.2.5).

**Figure 5.2.5: EVAR vs. open repair. Meta-analysis of RCTs for all cause mortality at follow-up**
Rupture

The four included RCTs provided limited information on rupture as a separate outcome. The DREAM study\textsuperscript{43, 44} reported that there were no documented postoperative ruptures but there were two sudden deaths following EVAR in which the possibility of rupture was considered but not proved. There were no aneurysm ruptures in either group in the small short-term study by Cuypers et al.\textsuperscript{46} In the small study by Soulez et al.,\textsuperscript{47} there was one rupture in a patient treated with EVAR. In the EVAR trial 1, RCT\textsuperscript{18} three patients randomised to EVAR and seven randomised to open repair had a rupture prior to their surgery. There were two fatal ruptures in the EVAR group and one in the open repair group within 30 days of surgery. After the 30-day point, there were six deaths from rupture in the EVAR group and one in the open repair group. At follow-up, nine patients in the EVAR group were reported with graft rupture as a complication, compared with none in the open repair group.

These limited data suggest that rupture may be more of an issue following EVAR than following open repair.

Endoleak

Across the included RCTs, some form of endoleak occurred at varying frequencies (up to approximately 20\%) following EVAR in those trials reporting this outcome.
Type II endoleaks were most common followed by Type I. The Cuypers et al. study\textsuperscript{46} did not report anything about endoleaks and the DREAM study only reported endoleaks requiring re-intervention in the perioperative period (two (1.2\%) of which one was regarded as a severe complication).\textsuperscript{43}

Table 5.2.8: Occurrence of endoleak in RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Endoleak</th>
<th>Type I endoleak</th>
<th>Type II endoleak</th>
<th>Type III endoleak</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM Blankensteijn 2005\textsuperscript{44}</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>EVAR trial 1 2005\textsuperscript{18}</td>
<td>27 (17 with re-intervention) at follow-up (of 529 EVAR patients with repair completed). Unspecified endoleak reported in 4 patients (4 with re-intervention).</td>
<td>79 (17 with re-intervention) at follow-up (of 529 EVAR patients with repair completed)</td>
<td>8 (4 with re-intervention) at follow-up (of 529 EVAR patients with repair completed)</td>
<td></td>
</tr>
<tr>
<td>Cuypers 2001\textsuperscript{46}</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Soulez 2005\textsuperscript{47}</td>
<td>2 (10%) EVAR</td>
<td>3 (15%) EVAR</td>
<td>Not reported</td>
<td></td>
</tr>
</tbody>
</table>

Device migration

Only the EVAR trial 1 RCT reported on device migration after EVAR. In EVAR trial 1, 12 of 529 patients with a completed EVAR (2.3\%) experienced device migration during follow-up, of which seven required re-intervention.\textsuperscript{18}

Re-interventions

The DREAM and EVAR trial 1 studies compared overall re-intervention rates between patients treated with EVAR and open repair. In DREAM, the risk of re-intervention was significantly higher in the EVAR group for the first 9 months (hazard ratio 2.9, 95\% CI: 1.1, 6.2, p = 0.03) but the groups were not significantly different thereafter (hazard ratio1.1, 95\% CI: 0.1, 9.3, p = 0.95).\textsuperscript{44} Across the medium-term follow-up in EVAR trial 1, the hazard ratio for re-intervention was 2.7 (95\% CI: 1.8, 4.1), indicating a significantly higher risk in the EVAR group.\textsuperscript{18} The 4-year point estimates for re-intervention were 20\% for the EVAR group compared with 6\% for the open repair group.\textsuperscript{18}

Specific re-interventions of interest are shown in Table 5.2.9. Where reported (EVAR trial 1 and Soulez et al.), rates of short-term EVAR-specific re-interventions were similar to rates of re-exploration of open repair. Conversion of EVAR to open repair
within 30 days occurred in 10/531 patients (1.9%) in EVAR trial 1.\textsuperscript{18, 45} Cuypers et al.\textsuperscript{46} reported no conversions after EVAR, while the other two trials did not report this outcome.

### Table 5.2.9: Re-interventions in RCTs of EVAR vs. open repair (unruptured aneurysms)

<table>
<thead>
<tr>
<th>Name of Author</th>
<th>Conversion to open repair (EVAR group only)</th>
<th>Correction of endoleak (EVAR group only)</th>
<th>Re-exploration of open repair (open group only)</th>
<th>Other (specify)</th>
<th>Cumulative rate from K-M curve</th>
<th>Hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM Blankensteijn 2005\textsuperscript{44}</td>
<td>Not reported</td>
<td>2(1.2%) of which 1 was classed as severe (0.6%)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Nine months: 2.9 (95% CI: 1.1 to 6.2, p=0.03) favouring Open</td>
</tr>
<tr>
<td>EVAR trial 1 2005\textsuperscript{18}</td>
<td>10/531 at 30 days (intention-to-treat)</td>
<td>18/531 at 30 days (intention-to-treat)</td>
<td>15/516 at 30 days (intention-to-treat)</td>
<td>Not reported</td>
<td>EVAR 20%; open repair 6% (4-year point estimates)</td>
<td>2.7 (95% CI: 1.8, 4.1)</td>
</tr>
<tr>
<td>Cuypers 2001\textsuperscript{46}</td>
<td>One patient randomised to EVAR received an urgent open AAA repair because of aneurysm rupture prior to receiving EVAR. There were no other conversions to open repair</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Soulez 2005\textsuperscript{47}</td>
<td>Not reported</td>
<td>4 patients</td>
<td>1 patient - operative treatment on an emergency basis with graft limb thrombosis, 7 months after surgery</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

**Short-term adverse events**

Our analysis of major short-term adverse events concentrated on cardiac and cerebrovascular events within 30 days of surgery. The DREAM\textsuperscript{43, 44}, EVAR trial 1\textsuperscript{18, 45} and Soulez et al.\textsuperscript{47} RCTs did not report this information. DREAM reported complications rather than specific events.

Of the trials comparing EVAR and open repair in patients with unruptured AAA, only Cuypers et al. reported on cardiac events: three (5%) in the EVAR group and 2 (11%) in the open repair group.\textsuperscript{46}
Health Related Quality of Life (HRQOL)

All four RCTs reported some details on HRQOL. All used the Medical Outcomes Study short form 36 (SF-36) questionnaire, but different components were reported, making it difficult to synthesise scores across studies. Cuypers et al. and EVAR trial 1 also used the EuroQoL-5D measure. This summary concentrates on inter-group differences.

The DREAM\textsuperscript{95} and Cuypers et al.\textsuperscript{96} RCTs reported results for all eight SF-36 domains and EuroQoL. In DREAM, full results for all time points were not reported. The groups had similar QoL scores at baseline. Three weeks after surgery the open repair group had significantly lower scores for physical function (PF), social functioning and physical role limitations compared with the EVAR group. The physical role limitations score in the open repair group was still significantly lower than that of the EVAR group at 6 weeks. However, at 12 months the open repair group scored significantly higher than the EVAR group for physical function, social functioning, emotional role limitations, bodily pain and general health. EuroQoL-5D scores did not differ between the groups until 6 months but at 6 and 12 months the open repair group had significantly higher scores than the EVAR group.\textsuperscript{95} Cuypers et al. assessed QoL at baseline and after 1 and 3 months.\textsuperscript{96} Groups were similar at baseline. At 1 month the EVAR group had significantly higher scores for physical function, physical role limitations, vitality and bodily pain, and for the usual activities element of EuroQoL. All these differences were no longer present at 3 months. Soulez et al. assessed QoL using the SF-36 questionnaire at baseline, 1, 3, 6, 12, 18 and 24 months. Results for the eight SF-36 domains were presented graphically. The authors reported that there were no significant differences between the groups at any time point.\textsuperscript{47}

The EVAR trial 1 RCT reported EuroQoL-5D weighted index scores and SF-36 physical and mental component summary scores for baseline, 0–3 months, 3–12 months and 12–24 months (Table 5.2.10). The groups were similar at baseline. The EVAR group had higher EuroQoL-5D and physical component summary scores at 0–3 months but differences between groups were not significant at later time points. The mental component summary score did not differ between groups at any time point.\textsuperscript{18}
Overall, these data suggest that there may be a short-term QoL advantage for patients treated with EVAR relative to those who receive an open repair. Longer term QoL data, by contrast, tend to favour open repair. These findings probably reflect the less invasive nature of the intervention in EVAR but also the need for continuing surveillance and the higher rate of complications and re-interventions following EVAR compared with open repair.

Table 5.2.10: Summary of HRQOL data from the EVAR trial 1 RCT

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>HRQOL measure used</th>
<th>Baseline scores mean (SD)</th>
<th>Mean difference between populations at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>EVAR population</td>
<td>Comparator population</td>
</tr>
<tr>
<td>EVAR trial 1 2005&lt;sup&gt;18&lt;/sup&gt;</td>
<td>EuroQol-5D</td>
<td>0.75 (0.22) (541 patients)</td>
<td>0.74 (0.23) (531 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0-3 months: Crude 0.06 (SE 0.02); Adjusted for baseline score 0.05 (SE 0.02)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude -0.01 (SE 0.02); Adjusted for baseline score -0.01 (SE 0.01)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude -0.01 (SE 0.02); Adjusted for baseline score -0.02 (SE 0.02)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SF36 physical component summary</td>
<td>39.92 (5.92) (533 patients)</td>
<td>39.83 (5.90) (534 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0-3 months: Crude 1.68 (SE 0.53); Adjusted for baseline score 1.66 (SE 0.50)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude -0.05 (SE 0.40); Adjusted for baseline score 0.04 (SE 0.37)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude -0.16 (SE 0.44); Adjusted for baseline score -0.15 (SE 0.40)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SF36 mental component summary</td>
<td>43.59 (6.79) (533 patients)</td>
<td>43.95 (6.73) (534 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0-3 months: Crude -0.18 (SE 0.66); Adjusted for baseline score -0.05 (SE 0.66)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude 0.46 (SE 0.46); Adjusted for baseline score 0.41 (SE 0.45)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude -0.22 (SE 0.50); Adjusted for baseline score -0.29 (SE 0.49)</td>
<td></td>
</tr>
</tbody>
</table>

### 5.2.2.2 EVAR versus open repair (ruptured aneurysms)

#### Study characteristics

One RCT compared EVAR and open repair in patients with ruptured AAAs.<sup>49</sup> Only 32 patients were randomised compared with a planned sample size of 100, so it is difficult to draw firm conclusions from the trial. Compared to RCTs of elective EVAR, the patients were similar in age but the patients had larger aneurysms and the proportion of women was slightly higher. Non-commercial stent grafts were used in
patients receiving EVAR. Other study characteristics are shown in Tables 5.2.11–5.2.14.

Table 5.2.11: Basic characteristics of RCT for EVAR vs Open repair in ruptured aneurysm

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Country where study was performed</th>
<th>Number of patients randomised</th>
<th>Age of population</th>
<th>Gender</th>
<th>Aneurysm diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinchliffe 2006(^{15})</td>
<td>UK University Hospital Nottingham</td>
<td>32</td>
<td>15</td>
<td>17</td>
<td>Median EVAR 74 (IQR 68.8-79.5); open 80 (IQR 73.8-83.8) Percentage male (total population) 75% (24/32)</td>
</tr>
</tbody>
</table>

Table 5.2.12: Patient characteristics of RCT for EVAR vs Open repair in ruptured aneurysm

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Smoking history</th>
<th>Diabetes (number of patients (%)</th>
<th>Heart Disease (number of patients (%)</th>
<th>Hypertension (number of patients (%))</th>
<th>Renal disease (number of patients (%))</th>
<th>Respiratory Disease (number of patients (%)</th>
<th>Fitness scores</th>
<th>Body Mass Index (BMI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinchliffe 2006(^{15})</td>
<td>Current smokers 10/32 (31%) Past smokers 11/32 (34%) Never smoked 11/32 (34%)</td>
<td>Not reported</td>
<td>8/32 (25%)</td>
<td>13/32 (41%); measurement tool not reported.</td>
<td>3/32 (9%); 3/32 (9%) with chronic obstructive airways disease.</td>
<td>Not reported</td>
<td>Not applicable to this patient population.</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Table 5.2.13: Intervention characteristics of RCT for EVAR vs Open repair in ruptured aneurysm

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or emergency procedure</th>
<th>Type of device (EVAR)</th>
<th>Graft type (EVAR)</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinchliffe 2006(^{15})</td>
<td>1 September 2002-31 December 2004</td>
<td>Median Time from clinical diagnosis to operation: 75 minutes (IQR 64-126).</td>
<td>Emergency 13 (100%) (13/15 randomised patients underwent EVAR).</td>
<td>All patients received a two piece aortouniiliac stent graft made with Gianturco stents with an uncovered supra-renal component.</td>
<td>Uni-iliac (number of patients (%) 11 (100%) (Of 13 patients who underwent EVAR, 1 was converted to open repair and 1 to axillo-bifemoral graft).</td>
<td>General (number of patients (%) 13 (100%)</td>
</tr>
</tbody>
</table>
Table 5.2.14: Comparator characteristics of RCT for EVAR vs Open repair in ruptured aneurysm

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Open repair or non-surgical procedure</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or Emergency procedure</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinchliffe 200648</td>
<td>Open repair</td>
<td>1 September 2002-31 December 2004</td>
<td>Median Time from clinical diagnosis to operation: 100 minutes (IQR 46-138).</td>
<td>Emergency 15 (100%) (14/17 randomised patients underwent open repair and one patient crossed over from the EVAR group)</td>
<td>General (number of patients (%)) 15 (100%)</td>
</tr>
</tbody>
</table>

**Results**

**30-day mortality**

Of the 15 patients randomised to EVAR, one died before receiving surgery, one was converted to open repair and subsequently died and six died in the perioperative period following EVAR. Thus, on an ITT basis the mortality rate was 8/15 (53%). Of 17 patients randomised to open repair, three died before surgery, two died on the operating table and four died in the perioperative period, giving an ITT mortality rate of 9/17 (53%). Other, longer-term mortality data were not reported.

**Adverse events**

Five of 11 EVAR patients (45%) and 7 of 12 open repair patients (58%) who survived the procedure experienced cardiac events. All events were classified as moderate except for one severe event in the open repair group. One patient in the EVAR group suffered severe cerebrovascular complications, compared with none in the open repair group.49

**5.2.2.3 EVAR versus non-surgical management (patients with unruptured aneurysms considered unfit for open repair)**

**Study characteristics**

EVAR trial 2 48 is the only published RCT in this patient group. This UK RCT compared EVAR (n = 166) and non-surgical management (n = 172) in patients judged to be unfit for open repair. The trial met all quality criteria. The primary endpoint was all cause mortality and secondary endpoints were aneurysm related mortality, HRQOL, postoperative complications and hospital costs. Fourteen patients
randomised to EVAR died before operation (including six from AAA rupture). Forty-seven patients assigned to non-surgical management received surgical aneurysm repair (including 12 who received open repair despite having been classified as unfit for this procedure). These factors complicate the analysis and interpretation of the trial. See tables 5.2.15–5.2.18 for details of patient, intervention and comparator characteristics.
### Table 5.2.15: Basic characteristics of the EVAR trial 2 RCT

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Country where study was performed</th>
<th>Number of patients randomised</th>
<th>Age of population</th>
<th>Gender</th>
<th>Aneurysm diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 2 participants UK</td>
<td>338</td>
<td>Total EVAR Comparator</td>
<td>Mean (SD) 76.4 years (SD 6.45) (based on n=338)</td>
<td>288 (85%) (based on n=339)</td>
<td>Mean (SD) Median 6.4 cm: EVAR, 6.3 cm non-surgical treatment</td>
</tr>
<tr>
<td>EVAR trial 2 participants</td>
<td>166</td>
<td>172</td>
<td>76.8 (SD 6.2) EVAR 76.0 (SD 6.7) non-surgical treatment (Based on n=143)</td>
<td>141 (85%) EVAR 147 (85%) non-surgical treatment (Based on n=143)</td>
<td>86.0-7.4 cm EVAR 6.0-7.0 cm non-surgical treatment</td>
</tr>
<tr>
<td>EVAR trial 2 participants</td>
<td>77.3 (SD 6.8) Zenith device 75.4 (SD 6.1) Talent</td>
<td></td>
<td></td>
<td></td>
<td>Measurement tool used CT scan</td>
</tr>
</tbody>
</table>

### Table 5.2.16: Patient characteristics in EVAR trial 2

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Smoking history</th>
<th>Diabetes</th>
<th>Heart Disease</th>
<th>Hypertension</th>
<th>Renal disease</th>
<th>Respiratory Disease</th>
<th>Fitness scores</th>
<th>Body Mass Index (BMI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 2 participants</td>
<td>Current smokers: 57 (17%)</td>
<td>22 (6%)</td>
<td>233 (69%)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>47 (14%)</td>
<td></td>
<td>Mean (SD) 26.35 (based on n=339)</td>
</tr>
<tr>
<td>EVAR trial 2 participants</td>
<td>Past smokers: 29 (17%) EVAR 28 (16%) non-surgical treatment</td>
<td>259 (77%)</td>
<td>127 (77%) EVAR 132 (77%) non-surgical treatment</td>
<td></td>
<td></td>
<td>Not reported</td>
<td>Other Reported in 26</td>
<td></td>
</tr>
<tr>
<td>EVAR trial 2 participants</td>
<td>Never smoked : 10 (6%)</td>
<td>10 (6%) EVAR 12 (7%) non-surgical treatment</td>
<td>26.35 (based on n=339)</td>
<td></td>
<td></td>
<td></td>
<td>Mean CPI fitness score 10.0 (SD 11.3) for 404 patients (197 EVAR and 207 no intervention). Little difference between randomised groups (details not reported).</td>
<td></td>
</tr>
<tr>
<td>EVAR trial 2 participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Comparison of fitness - 179 patients underwent elective AAA repair in EVAR group and 60 patients in no intervention group: Student's t test: EVAR 10.5 (SD 11.8); No intervention 6.3 (9.6). Significant: p=0.014</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5.2.17: Intervention characteristics in EVAR trial 2

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or emergency procedure</th>
<th>Type of device (EVAR)</th>
<th>Graft type (EVAR)</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 2 2005&lt;sup&gt;56&lt;/sup&gt;</td>
<td>September 1999 to 31st December 2003 (to August 2004 for extra patients included in some of the analyses)</td>
<td>Median 57 days (IQR 39-82) 150 patients randomised to EVAR 163 days (IQR 78-477) 47 patients crossed over from non-surgical treatment group (35 had EVAR, 12 had open repair).</td>
<td>Not reported</td>
<td>Zenith 86 (59) (based on n=150). N=109 in later analysis based on patients randomised up to August 2004.</td>
<td>Uni-iliac (number of patients (%)) 14 (10%) based on n=143 in later analysis based on patients randomised up to August 2004. 7 using Zenith device and 7 using Talent device.</td>
<td>Local (number of patients (%)) Not explicitly reported in main publication.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Talent 31 of 150 (21%). N=34 in later analysis based on patients randomised up to August 2004.</td>
<td>Bi-iliac (number of patients (%)) 131 (87%) (based on n=150)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Excluder 10 of 150 (7%) Other 9 of 150 (6%) AneuRx (Medtronic) 5 of 150 (3%) Quantum (Cordis, Johnson &amp; Johnson, Waterloo, Belgium) 2 of 150 (1%) Bard device (Bard, New Jersey) 1 of 150 (&lt;1%) Anson Aorfix (Lambard Medical, Oxford, UK) 1 of 150 (&lt;1%) EVT (Guidant, Indianapolis) 1 of 150 (&lt;1%) Edwards Lifesciences, Switzerland)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Excluder 10 of 150 (7%) Other 9 of 150 (6%) AneuRx (Medtronic) 5 of 150 (3%) Quantum (Cordis, Johnson &amp; Johnson, Waterloo, Belgium) 2 of 150 (1%) Bard device (Bard, New Jersey) 1 of 150 (&lt;1%) Anson Aorfix (Lambard Medical, Oxford, UK) 1 of 150 (&lt;1%) EVT (Guidant, Indianapolis) 1 of 150 (&lt;1%) Edwards Lifesciences, Switzerland)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 5.2.18: Comparator characteristics in EVAR trial 2

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Open repair or non-surgical procedure</th>
<th>Dates of procedure</th>
<th>Time lapse between randomisation and procedure</th>
<th>Elective or Emergency procedure</th>
<th>Anaesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 2 EVAR trial participants 2005&lt;sup&gt;56&lt;/sup&gt;</td>
<td>Non-surgical procedure</td>
<td>September 1999 to 31st December 2003 (to August 2004 for extra patients included in some analyses)</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
**Results**

30-day mortality  
Short-term mortality is not a meaningful outcome for comparing between EVAR and no surgical intervention. In the EVAR group of EVAR trial 2 \(^{48}\), 13/150 patients who had the procedure (9%) died within 30 days. Of the 47 patients randomised to non-surgical treatment who crossed over to receive EVAR or open surgery, one (2%) died within 30 days.

### AAA-related mortality

In the EVAR trial 2 RCT, there was no significant difference in AAA-related mortality between patients randomised to EVAR and those randomised to non-surgical management. On an ITT basis, 20/166 patients in the EVAR group and 22/172 in the non-surgical management group died of AAA-related causes by 4 years after randomisation, giving a crude hazard ratio of 1.01 (95% CI: 0.55, 1.84, \(p = 0.98\)); hazard ratios adjusted for primary and secondary covariates were similar.\(^{48}\)

### All cause mortality

There was no significant difference in all cause mortality between patients randomised to EVAR and those randomised to non-surgical management. Four years after randomisation, overall mortality was 64%. On an ITT basis, 74/166 patients in the EVAR group and 68/172 in the non-surgical management group died, giving a crude hazard ratio of 1.21 (95% CI: 0.87, 1.69, \(p = 0.25\)); hazard ratios adjusted for primary and secondary covariates were similar.\(^{48}\)
Figure 5.2.7: 

...
Rupture
In EVAR trial 2, 48 nine patients randomised to EVAR had a rupture of their AAA before receiving elective treatment. Of those who received EVAR (178 including patients crossing over from the non-surgical management group), one had a graft rupture following successful treatment. There were 23 ruptures in the non-surgical management group, representing 13.4% of the 172 patients originally randomised to this group. The crude rupture rate was nine per 100 person years. The authors noted that this rupture rate was considerably lower than that reported in other prospective studies monitoring large aneurysm rupture.

Endoleak
Details of endoleaks in patients who received EVAR in the EVAR trial 2 RCT are shown in Table 5.2.19. These figures refer to all patients treated, including those who crossed over from the non-surgical management group.
Table 5.2.19: Occurrence of endoleak in the EVAR trial 2 RCT

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Endoleak</th>
<th>Type I endoleak</th>
<th>Type II endoleak</th>
<th>Type III endoleak</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 2 2005</td>
<td>11 of 178 patients who received EVAR - not ITT (10 complications after EVAR)</td>
<td>23 of 178 patients who received EVAR - not ITT (17 complications after EVAR)</td>
<td>6 of 178 patients who received EVAR - not ITT (5 complications after EVAR)</td>
<td></td>
</tr>
</tbody>
</table>

**Device migration**

The number of patients with device migration in EVAR trial 2 was two out of 178 patients who received EVAR (including crossovers) (1.1%). This was not an ITT analysis.

**Re-interventions**

EVAR trial 2 reported that 14 out of 178 patients (7.9%) who received EVAR (including crossovers) required re-intervention for endoleak, while eight (4.5%) required ‘other surgery’ (unspecified). The overall re-intervention rate during follow-up was 11.5 per 100 person years for EVAR and 1.8 per hundred person years for non-surgical management. By 4 years estimated re-intervention rates were 26% and 4%, respectively (hazard ratio 5.8, 95% CI: 2.4, 14.0, p < 0.0001). This was an ITT analysis, so the re-interventions in the comparator group may represent patients who crossed over to surgical treatment.

The authors noted that the rate of re-interventions in the EVAR group of EVAR trial 2 seemed higher than that observed in the EVAR group of EVAR trial 1 (11.5 vs. 6.9 per 100 person years) but the difference was not statistically significant (hazard ratio 1.4, 95% CI: 0.9, 2.1. p = 0.1).

**Short-term adverse events**

EVAR trial 2 did not report on cardiac and cerebrovascular events within 30 days of surgery.

**HRQOL**

EVAR trial 2 reported the same QoL outcomes as EVAR trial 1. The only statistically significant difference between groups (p = 0.04) favoured the non-
surgical management group for SF-36 physical component summary score at 0–3 months (Table 5.2.20).

Table 5.2.20: Summary of HRQOL data from the EVAR trial 2 RCT

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>HRQOL measure used</th>
<th>Baseline scores mean (SD)</th>
<th>Mean difference between populations at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR trial 22005&lt;sup&gt;18&lt;/sup&gt;</td>
<td>EuroQol-5D Weighted index score</td>
<td>0.58 (SD 0.31) (164 patients)</td>
<td>0.83 (SD 0.28) (171 patients)</td>
</tr>
<tr>
<td>EVAR population</td>
<td>Comparator population</td>
<td>0-3 months: Crude 0.01 (SE 0.05); adjusted for baseline score 0.03 (SE 0.05) (139 patients)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude 0.04 (0.03); adjusted for baseline score 0.06 (0.03) (241 patients)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude 0.05 (0.04); adjusted for baseline score 0.04 (0.04) (156 patients)</td>
<td></td>
</tr>
<tr>
<td>SF36 physical component summary</td>
<td>35.47 (SD 6.63) (160 patients)</td>
<td>35.12 (SD 6.23) (171 patients)</td>
<td>0-3 months: Crude -1.64 (1.00); adjusted for baseline score -1.86 (0.88) (134 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude -0.78 (0.83); adjusted for baseline score -1.11 (0.77) (224 patients)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude -1.47 (1.12); adjusted for baseline score -0.64 (1.04) (130 patients)</td>
<td></td>
</tr>
<tr>
<td>SF36 mental component summary</td>
<td>45.13 (SD 7.92) (160 patients)</td>
<td>46.31 (SD 6.97) (171 patients)</td>
<td>0-3 months: Crude 1.73 (1.47); adjusted for baseline score 2.30 (1.38) (134 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-12 months: Crude 0.08 (1.00); adjusted for baseline score 0.94 (0.95) (224 patients)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-24 months: Crude -0.70 (1.32); adjusted for baseline score 0.50 (1.29) (130 patients)</td>
<td></td>
</tr>
</tbody>
</table>

5.2.2.4 Analysis by device type

A secondary publication from the EVAR trial participants reported an analysis by device type of data from the EVAR trial 1 and EVAR trial 2 RCTs. This analysis compared rates of re-intervention, aneurysm related mortality and all cause mortality in patients who received the Zenith and Talent (n = 187) stent-grafts. In EVAR trial 1 the number of re-interventions per 100 person years was 6.4 for Zenith (n = 318) and 8.6 for Talent (n = 318); there were 0.8 aneurysm related deaths per 100 person years for Zenith and 1.0 for Talent; and deaths from all causes were 5.9 per 100 person years for Zenith and 8.6 for Talent. Statistically there were no significant differences between outcomes with the Zenith and Talent devices. Adjusted hazard ratios were 0.79 (95% CI: 0.51, 1.21) for re-intervention, 0.88 (95% CI: 0.29, 2.65) for aneurysm related mortality and 0.79 (95% CI: 0.53, 1.19) for all cause mortality.
In EVAR trial 2 the number of re-interventions per 100 person years was 9.6 for Zenith (n = 109) and 15.1 for Talent (n = 34); there were 2.8 aneurysm related deaths per 100 person years for Zenith and 4.0 for Talent; and deaths from all causes were 18.5 per 100 person years for Zenith and 23.9 for Talent. Statistically there were no significant differences between outcomes with the Zenith and Talent devices. Adjusted hazard ratios were 0.69 (95% CI: 0.29, 1.62) for re-intervention, 0.94 (95% CI: 0.21, 4.27) for aneurysm related mortality and 0.85 (95% CI: 0.45, 1.60) for all cause mortality.

The DREAM\textsuperscript{44} and Cuypers et al.\textsuperscript{46} studies did not report an analysis by device type, while in the Hinchliffe et al.\textsuperscript{49} and Soulez et al.\textsuperscript{47} studies all EVAR procedures involved the same type of device.

5.2.2.5 Analysis by neck angulation

None of the included RCTs reported data allowing an analysis of outcomes by neck angulation.

5.2.3 Assessment of effectiveness from registries

Study Characteristics

The study characteristics are summarised in Tables 5.2.21 – 5.2.24. NVD and RETA included fewer centres and cases than EUROSTAR (4545 cases from 59 centres for NVD, 1000 cases from 41 centres for RETA, and 8345 from 177 centres for EUROSTAR; Table 5.2.21) and only involved centres from the UK.
Table 5.2.21: Overview of included registries

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Registry Name</th>
<th>Centre entry criteria</th>
<th>Patient entry criteria</th>
<th>Number of patients treated</th>
<th>Dates of procedure</th>
<th>Type of device</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley 2005 10</td>
<td>National Vascular Database (NVD)</td>
<td>Not reported.</td>
<td>Suitable for open repair</td>
<td>Open infrarenal aortic aneurysm surgery; 4545 cases from 59 centres.</td>
<td>Registered 1999 - 31 March 2004</td>
<td>Not applicable</td>
</tr>
<tr>
<td>EUROSTAR Collaborators 2006 11</td>
<td>EUROSTAR</td>
<td>Sufficient expertise in centre, which is involvement in a series of at least 10 stent-graft procedures for AAA. Throughput of at least 10 patients per year and patients managed by a collaborating vascular surgeons and international radiologists.</td>
<td>Minimum age 21 years. Patients with aortic aneurysms &lt;3 cm with iliac aneurysms, pseudo-aneurysms or previous (conventional/endovascular) grafts were excluded. Aortic aneurysms measuring 3-4 cm included if they were associated with iliac aneurysms. Anatomic configuration suitable for stented tube or bifurcated prosthesis: Infrarenal neck length &gt;=1.5 cm and width &lt;2.5 cm. Iliac artery angulation &lt;90 degrees (or correctable angulation). Common iliac artery &lt;1.2 cm in diameter and nonstenotic (&gt;0.6 cm diameter after balloon dilation, if necessary). Elective AAA-operation, without symptoms of rupture or expansion.</td>
<td>8345 cases from 177 European centres.</td>
<td>Not reported. Data collected prospectively up to June 2006. Data relating to 'older' devices excluded from the report.</td>
<td>Zenith: 3290/8304 (39.6%) Talent: 2349/8304 (28.3%) Excluder: 1153/8304 (13.9%) Other: AneuRx: 984/8304 (11.8%) Endolytx: 161/8304 (1.9%) Lifepath: 134/8304 (1.6%) Fortron: 92/8304 (1.1%) EVT: 73/8304 (0.9%) Anaconda: 86/8304 (0.8%)</td>
</tr>
<tr>
<td>Thomas 2005 12, additional data from undated Vascular Surgical Society report 10 and Thomas 2001 10</td>
<td>RETA</td>
<td>Not reported. UK members of the Vascular Surgery Society and British Society of Interventional Radiology registered cases on a voluntary basis.</td>
<td>Age limitations not reported. Aneurysm size not reported. Suitable for open repair; patients classified as fit or unfit for open repair were included. Suitable for EVAR; no criteria specified for elective repair, but majority of cases were asymptomatic (83.2%) or symptomatic (13.5%) AAA. No criteria specified for emergency repair, but small numbers of cases were repair of acute non-ruptured (1.6%) or stable ruptured (1.4%)</td>
<td>1000 cases from 41 centres.</td>
<td>January 1996-March 2000.</td>
<td>Zenith: 144 (14.4%) Talent: 117 (11.7%) Excluder: 19 (1.9%) Other: Ancure 60 (6%) AneuRx: 254 (25.4%) Bard device: 11 (1.1%) Baxter device: 1 (0.1%) Gianturco-Dacron: 123 (12.3%) Gianturco-PTFE: 17 (1.7%) Hol B Endostent: 1 (0.1%) Ivanchev-Malmo: 2 (0.2%) Palmaz/PTFE 54 (6.4%) Stentford 2 (0.2%) Vanguard 174 (17.4%) Missing 11 (1.1%)</td>
</tr>
</tbody>
</table>
**Clinical Expertise**

NVD and RETA did not specify entry requirements for centres to be eligible for inclusion in the registries. It is therefore unclear what level of expertise the surgical teams had with performing EVAR and open repair, which makes it difficult to compare patient outcomes for the different registries and to ascertain whether there may be an association between surgical experience and outcomes. Based on that procedures carried out by specialist teams with a high level of experience in EVAR result in lower mortality rates and fewer adverse events which lead to secondary interventions.\textsuperscript{55} EUROSTAR specifies that centres must have a throughput of at least 10 patients undergoing stent-graft procedures for AAA per year if they are to be included in the registry.

**Data collection**

EUROSTAR data were collected using a case record form which included an informed consent form for signing by the patient. Only surgeons from participating centres who had sufficient expertise (ie. involvement in a series of at least 10 stent-graft procedures for AAA) submitted data to the registry.

Data submitted to the NVD was on a voluntary basis, with almost half the members of the Vascular Society contributing to the database at the time of the report. However, in order to gain a true picture of the outcomes of vascular surgery (eg. AAA repair) throughout Great Britain and Ireland, inclusion of all surgeons performing such operations is needed but at the time of the report external validation to ensure accuracy and completeness of data had not been undertaken.\textsuperscript{19}

Data collection for RETA was also on a voluntary basis and the UK centres submitted cases as they were performed. However, the majority of endovascular repairs in the UK at the time were performed as part of the EVAR trials and cases submitted to RETA at the time of their report were cases performed outside the trial (usually early on in a centres experience to allow entry into the EVAR trials), and as such the full RETA dataset of all cases submitted were less representative of UK practice at the time of the report.
It is unclear whether all participants undergoing EVAR or open repair were included in the registry, but as only certain surgeons were submitting cases, potential sample bias cannot be ruled out.

**Dates of Procedure**

Patients were registered and treated between 1999 and 31 March 2004 for NVD, up to June 2006 for EUROSTAR, and between January 1996 and March 2000 for RETA. Data from the RETA registry are therefore very out of date, which suggests that the results may not be relevant to current practice. This highlights the importance of the data provided by the EUROSTAR registry. The relevance of data is also reflected in the use of ‘older’ types of devices by the RETA registry. The latest report from the EUROSTAR registry explicitly excluded any data relating to ‘older’ devices from their report and included only those patients treated with the newer generation of endografts in current use.

**Procedure Details**

The report from the EUROSTAR registry identified nine devices; Zenith, Talent and Excluder devices being the main ones in use (39.6%, 28.3% and 13.9% respectively) all of which are still in current use. By comparison, RETA data includes 14 devices (4 of which were ‘home made’), the main ones in use being AneuRx, Zenith, and Gianturco-Dacron (‘home made’); 25.4%, 14.4% and 12.3% respectively. However, as mentioned above and in section 3.3, many of the devices used by RETA are no longer in current use. ‘In-house’ (homemade) uni-iliac stents were once the most often used type of graft, but have now been superseded by commercially available and CE marked devices, such as those included in the EUROSTAR registry.

Bi-iliac grafts were the most prevalent form of graft type used by EUROSTAR and RETA; 89.8% and 70.4% respectively. This reflects the increasing use of bi-iliac grafts for EVAR, which appear to be superseding other types of graft such as the aortic tube, the use of which fell due to the number of distal endoleaks associated with this type of device. This again highlights the importance of the EUROSTAR data and its greater relevance to current practice as the RETA registry includes the use of
aortic tube grafts and a smaller percentage of patients received bi-iliac grafts compared to patients in the EUROSTAR registry.

General anaesthesia was reported to be used most often by all three registries (Table 5.2.22).

Table 5.2.22: Procedure details for included registries

<table>
<thead>
<tr>
<th>Study details</th>
<th>Graft type*</th>
<th>Anaesthesia*</th>
</tr>
</thead>
</table>
| Ashley 2005*           | Not applicable         | Local: 1 (0.02%)        
| NVD                    |                         | Regional: Epidural: 34 (0.7%)        
|                        |                         | General: 2461 (54.1%)       
|                        |                         | General + epidural: 1503 (33.1%)       
|                        |                         | TOTAL: 3964 (87.2%)       
|                        |                         | Unspecified: 546 (12%)       |
| EUROSTAR Collaborators 2006* | Bi-iliac: 7497/8345 (89.8%) | Local: 515/8345 (6.2%)       
|                        | Other:                | Regional: 2091/8345 (25.1%)       
|                        | Straight: 156/8345 (1.9%) | General: 5739/8345 (68.8%)       |
|                        | Tapered: 561/8345 (6.7%) |                                                 |
|                        | Unknown: 131/8345 (1.6%) |                                                 |
| Thomas 2005*           | Uni-iliac: 263 (26.4%)  | Regional: 52/993 (5.2%)       
| RETA                   | Bi-iliac: 702 (70.4%)   | General: General alone 908/993       
|                        | Other: Aortic tube 32 (3.2%) | (91.4%)       
|                        | Missing data 3         | General and regional: 32/993 (3.2%)       |

* Number of patients (%)

Patient characteristics

Full details of patient characteristics are given in tables 5.2.23 and 5.2.24.

To be eligible for inclusion in the EUROSTAR registry, patients were required to meet specific entry criteria: age greater than 21 years, and presenting for elective AAA operation without symptoms of rupture or expansion. Patients were excluded if their aneurysms measured <3 cm, and patients with aneurysms measuring 3-4 cm were only included if they were associated with iliac aneurysms. The mean aneurysm diameter for patients included in the registry was 5.84 cm, ranging between 3 and 17.2 cm. The majority of patients were male (93.2%) and the mean age was 72.5 years, ranging between 34 and 100 years. Approximately half of patients had a history of smoking (51.1%), and a high proportion reported a history of heart disease (78.8%) and hypertension (65.5%). Almost half had a history of pulmonary disease (42.3%), a quarter were classed as unfit for open repair, and a quarter considered obese (Table 5.2.24).
Details for gender were available for only 51.4% of patients; however, 90% of this population were male. The median age reported was 73 years, ranging between 44 and 93 years. It was unclear from the registry data what the health status of patients were as no details were provided for comorbidities. However, almost half of patients presented with aneurysms >6 cm and fitness scores indicated that almost a quarter of patients (22.7%) were classified as unfit for open repair. Incomplete reporting of details was one of the shortcomings of this registry as it makes it difficult to make comparisons.

Although the majority of patients were male (84.4%), this figure is almost 10% less than the EUROSTAR population. Mean age was 72.5 years which was comparable to EUROSTAR. The mean aneurysm diameter was not reported, but sizes ranged between <5 cm and >9.9 cm and there was a 1 cm difference between the majority of ruptured and unruptured AAAs.

Only one patient characteristic of interest was reported, which indicated that almost half the population (44.2%) had a history of heart disease.
### Table 5.2.23: Patient characteristics for included registries

<table>
<thead>
<tr>
<th>Study details</th>
<th>Age of population1</th>
<th>Gender (% male)</th>
<th>Aneurysm diameter2</th>
<th>Criteria assessing fitness for surgery/EVAR/open repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley 2005 T NVD</td>
<td>72.5 years (SE  0.12)</td>
<td>3756/4449 (84.4%)</td>
<td>Range</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Majority of unruptured AAAs: 5.0-7.9 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Majority of ruptured AAAs: 6.0-8.9 cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;5 cm: 88 patients</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>5-5.9 cm: 775</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>6-6.9 cm: 1113</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>7-7.9 cm: 588</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8-8.9 cm: 404</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>9-9.9 cm: 136</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;9.9 cm: 109</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Unspecified: 1251</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>EUROSTAR Collaborators 2006 56</td>
<td>72.5 (SD 7.8) years</td>
<td>93.2%</td>
<td>Mean transverse diameter: 5.84 cm (SD 1.16 cm)</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td>Range 34-100 years</td>
<td></td>
<td>Range</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>3.0-17.2 cm</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Thomas 2005 RETA</td>
<td>Median (range) 73 years.</td>
<td>90% (based on 514 cases)</td>
<td>Median 6 cm.</td>
<td>Fitness for EVAR</td>
</tr>
<tr>
<td></td>
<td>Range 44-93 years</td>
<td></td>
<td>42% classified as large aneurysms (&gt; 6 cm).</td>
<td>Based on aneurysm morphology but no specific details reported.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Range 2.5-15 cm.</td>
<td>Fitness for open repair</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fit: patients in ASA grade I-III</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unfit: patients in ASA grades IV or V specified as unfit for open repair because of comorbidity, also those classified as 'fit' by ASA grade but with other features making them high risk (unsuitable) for open repair.</td>
</tr>
</tbody>
</table>

1 Mean age (SD) unless otherwise stated.
2 Mean diameter (cm) unless otherwise stated.
Table 5.2.24: Patient characteristics for included registries (continued)

<table>
<thead>
<tr>
<th>Study details</th>
<th>Smoking history (%)</th>
<th>Diabetes (%)</th>
<th>Heart disease (%)</th>
<th>Hypertension (%)</th>
<th>Renal dysfunction (%)</th>
<th>Respiratory disease (%)</th>
<th>Fitness scores (%)</th>
<th>BMI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley 2005&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Not reported</td>
<td>Not reported</td>
<td>2011 patients (44.2%)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>NVD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EUROSTAR Collaborators</td>
<td>Current smokers</td>
<td>Cardiac:</td>
<td>5337/8142 (65.5%)</td>
<td>1155/8066 (14.3%)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Pulmonary:</td>
<td>ASA I 635/8288 (7.7%)</td>
<td>Not reported</td>
<td>2186/8248</td>
</tr>
<tr>
<td>2006&lt;sup&gt;26&lt;/sup&gt;</td>
<td>1885/8107 (23.3%)</td>
<td>4957/8141 (60.9%)</td>
<td>52/8066 (3.1%)</td>
<td>3419/8079 (42.3%)</td>
<td>not reported</td>
<td>ASA II 3467/8288 (41.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(SVS/ISCVS risk score 2-3)</td>
<td>(SVS/ISCVS risk score 1-3)</td>
<td></td>
<td>131/8066 (1.6%)&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
<td>ASA III 3643/8288 (44%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Past smokers</td>
<td>Cardiopul:</td>
<td>52/8066 (3.1%)</td>
<td>131/8066 (1.6%)&lt;sup&gt;5&lt;/sup&gt;</td>
<td></td>
<td>ASA IV 543/8288 (7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2252/8107 (27.8%)</td>
<td>1436/8038 (17.9%)</td>
<td>5337/8142 (65.5%)</td>
<td>252/8066 (3.1%)</td>
<td></td>
<td>2037/8345 (24.4%)&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SVS/ISCVS risk score 1</td>
<td>(SVS/ISCVS risk score 1-3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(none current, but smoked in last 10 years).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Never smoked</td>
<td>Cardiol:</td>
<td>3537/8142 (65.5%)</td>
<td>1155/8066 (14.3%)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Pulmonary:</td>
<td>ASA I 635/8288 (7.7%)</td>
<td>Not reported</td>
<td>2186/8248</td>
</tr>
<tr>
<td></td>
<td>3970/8107 (49%)</td>
<td>1436/8038 (17.9%)</td>
<td>5337/8142 (65.5%)</td>
<td>252/8066 (3.1%)</td>
<td>not reported</td>
<td>ASA II 3467/8288 (41.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SVS/ISCVS risk score 0 (no tobacco use or none for last 10 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ASA III 3643/8288 (44%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ASA IV 543/8288 (7%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2037/8345 (24.4%)&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thomas 2005&lt;sup&gt;38&lt;/sup&gt;</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>RETA</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Cardiac history (myocardial infarction (MI) <= 6 months ago; MI > 6 months ago; heart failure <= 1 month ago, heart failure > 1 month ago; orthopnoea; angina - controlled/on exertion; angina - uncontrolled/at rest).<sup>4</sup> Creatinine 1.5-3.0mg/dl, creatinine clearance 30-50ml/min (SVS/ISCVS risk score 1).

<sup>7</sup> ASA IV indicating that a patient is too frail to justify open repair.

<sup>5</sup> Creatinine 3.0-6.0mg/dl, creatinine clearance 15-30ml/min (SVS/ISCVS risk score 2).

<sup>6</sup> Creatinine >6.0ml/dl, creatinine clearance <15ml/min or on dialysis or with transplant.

<sup>7</sup> Unfit for open repair when factors other than ASA (eg. obesity, previous laparotomies were considered).
Mortality outcomes

Mortality data from the three registries are summarised in Table 5.2.25. From the study characteristics it can be seen that EUROSTAR provides the most up to date and complete source of data on EVAR.

EUROSTAR

EUROSTAR presented outcomes for short-term (30-day) and long-term (96 months/8 years) mortality, with 190 (2.3%) deaths occurring within 30 days and 789 (9.5%) during the follow-up period. It is unclear from the report whether patients died from aneurysm related or other causes. Kaplan-Meier survival analysis reported the cumulative number of deaths as 979 and mortality rate of 39%. It should be noted, however, that for 30-day outcome 4543 patients were observed out of 5515 expected, 90 patients were observed out of 326 expected for 84 months follow-up, and only 20 patients were observed out of 77 for 96 months follow-up. 111 patients (1.3%) were lost to follow-up, but this will have been included as censored data and accounted for by the Kaplan-Meier survival analysis.

RETA

RETA reported outcomes for short-term (30-day) mortality, aneurysm related mortality at follow-up, and all cause mortality at follow-up (5 years/60 months) (return rates for follow-up data are reported in Table 5.2.17). 58 patients (5.8%) died within 30 days and 9 patients were reported to have died from fatal rupture (aneurysm related mortality) at follow-up (6 (0.8%) at 1 year and 3 (0.8%) at 2 years). A cumulative rate of all cause mortality was not reported, although figures were presented for each year of follow-up; 11.9% mortality in year 1 and 10%, 8% and 7.9% at 2, 3, and 4 years post-procedure.

NVD

Mortality rates following open repair were reported for the 30-day period only, with an overall crude mortality rate of 14.8% (95% CI: 13.7-16.0%). Crude mortality rates for ruptured and unruptured AAAs were 41% (95% CI: 37.7, 44.3%) and 6.8% (95% CI: 5.9, 7.8%) respectively (Table 5.2.25).
### Table 5.2.25: Follow-up and mortality outcomes in included registries

<table>
<thead>
<tr>
<th>Study details</th>
<th>Follow-up</th>
<th>30-day mortality*</th>
<th>Aneurysm related mortality at follow-up*</th>
<th>All cause mortality at follow-up*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley 2005**</td>
<td>Not reported</td>
<td>Crude mortality: Unruptured: 6.8% (95% CI: 5.8-7.8%) Ruptured: 41% (95% CI: 37.7-44.3%) TOTAL: 14.8% (95% CI: 13.7-16.0%)</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>EUROSTAR Collaborators 2006**</td>
<td>Minimum follow-up 30 days Maximum follow-up 96 months (8 years)</td>
<td>190/8345 (2.3%)</td>
<td>Not reported</td>
<td>789/8345 (9.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cumulative rate from K-M curve Number of deaths (cumulative): 979 Proportion deaths: 0.390 Proportion surviving: 0.610 Survival standard error: 0.036</td>
</tr>
<tr>
<td>Thomas 2005**</td>
<td>Minimum follow-up 30 days Maximum follow-up 5 years Return rates for requested follow-up data: 87% at 1 year 77% at 2 years 65% at 3 years 52% at 4 years 51% at 5 years Median follow-up Mean 3.1 years</td>
<td>58/992 (5.8%) Fatal rupture at 1 year 6 (0.8%); fatal rupture at 2 years 3 (0.8%); at 1 year 86/721 (11.9%); missing 7; at risk 728** 1-2 years 37/369 (10%); missing 1; at risk 372 2-3 years 13/162 (8%); at risk 161 3-4 years 5/63 (7.9%); at risk 65 <strong>at end of follow-up period</strong></td>
<td>At 1 year 86/721 (11.9%); missing 7; at risk 728** 1-2 years 37/369 (10%); missing 1; at risk 372 2-3 years 13/162 (8%); at risk 161 3-4 years 5/63 (7.9%); at risk 65 <strong>at end of follow-up period</strong></td>
<td>Published paper reports 11% mortality in year 1 and rates of 10%, 7%, 10% and 8% at 2, 3, 4 and 5 years post-procedure.**</td>
</tr>
</tbody>
</table>
Table 5.2.26: Complications in included registries

<table>
<thead>
<tr>
<th>Study details</th>
<th>Rupture*</th>
<th>Endoleak*</th>
<th>Device migration*</th>
<th>Re-interventions*</th>
<th>Major adverse events (30-day period)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashley 2005 19</td>
<td>Not reported</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>EUROSTAR Collaborators 2006 56</td>
<td>30 days: 4 Follow-up: 37 TOTAL: 41 Cumulative rate from K-M curve at 84 months: Proportion of ruptures: 0.031 Proportion rupture free: 0.969 (SE 0.011)</td>
<td>Cumulative rate from K-M curve 30 days: 496 Follow-up: 827 Total: 1323 Proportion endoleaks: 0.325 Proportion endoleak free: 0.675 (SE 0.021)</td>
<td>30 days: 6 Follow-up: 148 TOTAL: 154</td>
<td>Conversion to open repair 30-day conversion: 75 patients (0.9%) Follow-up conversion: 102 patients (1.2%) TOTAL: 177 patients (2.1%) Cumulative rate from K-M curve: Total number of re-interventions at 84 months: 749 Proportion of secondary interventions: 0.18 Proportion of secondary intervention free: 0.82 Secondary intervention free standard error: 0.013 Total number of re-interventions at 96 months: 1606 Proportion of death and secondary interventions: 0.48 Proportion of secondary intervention free survival: 0.52 (SE 0.022)</td>
<td>Cardiac events: 272 Stroke: Cerebral 57 Systemic complications from operation to discharge: Pulmonary: 174 Renal: 181 Total systemic complications: 928</td>
</tr>
<tr>
<td>Thomas 2005 56</td>
<td>Rupture during deployment 3 (0.3%) 35 Cumulative rate from K-M curve 2% at 5 year follow-up 56</td>
<td>At 30 days 35: Type I: Proximal 54 Distal 19 Type II: 44 Type III: 15 Cumulative rate from K-M curve: Freedom from endoleak 88% at 1 year 80% at 2 years 76% at 3 years 71% at 4 years 68% at 5 years 56</td>
<td>9 (0.9%) with device migration requiring conversion to open repair (immediate outcome) New cases at 1 year follow-up 3/631 New cases at 2 year follow-up 9/331 New cases at 3 year follow-up 0/148 New cases at 4 year follow-up 2/66 56</td>
<td>Conversion to open repair: Immediate outcome: 33/996 (3.3%) Correction of endoleak. Some included under ‘conversion to open repair’. Totals not clearly reported. Cumulative rate from K-M curve Freedom from re-intervention 87% at 1 year 77% at 2 years 70% at 3 years 65% at 4 years 62% at 5 years 56</td>
<td>Cardiac events: 42 (4.2%): myocardial infarction/arrhythmia/left ventricular failure 56 Stroke: 15 (1.5%) cerebrovascular accident/confusion/paraplegia 59 Cumulative rate from K-M curve 30-day rates: 59 Any complication 272/976 (27.8%) Technical complication 55/976 (5.6%) Wound complications 78/976 (8%) Renal failure 40/976 (4.1%) Colonic ischaemia 6/976 (0.6%) Other medical complication 147/976 (15.1%)</td>
</tr>
</tbody>
</table>
Complications (Table 5.2.26)

EUROSTAR$^{56}$

Some form of major adverse event was experienced by 11.1% of patients, with cardiac, pulmonary and renal events being the most significant. By the end of 96 months follow-up only a very small proportion of patients (0.5%) experienced rupture and device migration (1.8%), while 15.9% of patients experienced endoleak. Nine percent of patients required some form of re-intervention at 84 months, increasing to 19.2% at 96 months.

RETA$^{58}$

RETA reported a very small percentage of ruptures during stent deployment (0.35%)$^{59}$ and a cumulative rate of 2% at 5 year follow-up.$^{58}$ One hundred and thirty two cases of endoleak (13.2%) were reported at 30 days$^{58}$, with a cumulative rate of 68% free from endoleak at 5 year follow-up.$^{58}$ A small number of device migrations were reported; 9 (0.9%) at 30 days (requiring conversion to open repair) and 14 over the 4 year follow-up.$^{59}$

Conversion to open repair within 30 days occurred in 3.3% of cases. Kaplan-Meier totals for cumulative rates of re-interventions were not clearly reported, however, the rate at 5 year follow-up was reported as 62%.$^{58}$ This 5 year figure reflects a much higher re-intervention rate than that reported by EUROSTAR at 8 year follow-up (19.2%). Only small numbers of cardiac events and stroke were reported at the 30-day period; 4.2% and 1.5% respectively$^{59}$, but overall 27.8% were reported as having experienced some form of complication (including technical complications and renal failure$^{58}$) (table 5.2.26).

NVD$^{19}$

No data were reported in the NVD registry for occurrence of endoleak and device migration as these complications cannot occur with open repair. No data were presented for rupture rates, re-intervention rates, or major adverse events, which limits analysis of the data and prevents comparison with the EVAR registries.
Resource use

Duration of surgery for open repair (NVD) ranged between <30 minutes and >359 minutes (approximately 6 hours), and between 25 and 720 minutes (12 hours) for EUROSTAR patients and 30 to 540 minutes (9 hours) for RETA. The majority of surgical procedures lasted between 120 and 149 minutes; (21.8%) for NVD patients. By comparison, the mean duration for EUROSTAR patients was 130 minutes and the median for RETA was 150 minutes (Table 5.2.27).

Table 5.2.27: Resource use in included registries

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Length of hospital and ICU stay *</th>
<th>Duration of surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ashley 2005</td>
<td>Unruptured: 13 (SE 0.21)</td>
<td>&lt;30 mins: 9/2326 patients (0.4%) 30-59 mins: 28 patients (1.2%) 60-89 mins: 145 patients (6.2%) 90-119 mins: 356 patients (15.3%) 120-149 mins: 506 patients (21.8%) 150-179 mins: 456 patients (19.6%) 180-209 mins: 363 patients (15.6%) 210-239 mins: 154 patients (6.6%) 240-269 mins: 136 patients (5.8%) 270-299 mins: 65 patients (2.8%) 300-329 mins: 41 patients (1.8%) 330-359 mins: 22 patients (1%) &gt;359 mins: 45 patients (1.9%) Unspecified: 2219 patients</td>
</tr>
<tr>
<td></td>
<td>Ruptured: 15.2 (SE 0.55)</td>
<td></td>
</tr>
<tr>
<td>EUROSTAR Collaborators 2006</td>
<td>5.9 (SD 8.1)</td>
<td>8065 patients Mean duration: 130 (SD 58) mins Range: 25-720 mins</td>
</tr>
<tr>
<td></td>
<td>8169 patients (98 patients with hospital stay &lt;1 day)</td>
<td>Range: 0-183 days</td>
</tr>
<tr>
<td>RETA Thomas 2005</td>
<td>Median: 6 (range 3- &gt;30) 38</td>
<td>Median 150 mins (range 30-540 mins) 39</td>
</tr>
</tbody>
</table>

The mean length of stay for NVD cases was 13 days for unruptured AAAs and 15.2 days for ruptured AAAs. By comparison, EUROSTAR reported a mean of 5.9 days (less than half that of NVD cases), and RETA reported a mean of 6 days.59 The number of days in hospital ranged between 3 and >30 days for RETA, compared to 0 and 183 days for EUROSTAR (Table 5.2.27).

HRQOL measures and costs and length of stay for re-interventions were not reported by the registries.
5.2.4 Assessment of risk factors for adverse outcomes following EVAR

5.2.4.1 Studies evaluating / validating existing risk assessment algorithms

The Leiden score was investigated in one study\textsuperscript{33} but this study had fewer than 500 patients so could not be included in the review. The Hardman score was also investigated in one risk model study but again fewer than 500 patients were included.\textsuperscript{32} Three studies investigated existing risk assessment algorithms and included more than 500 patients.\textsuperscript{26, 61, 88} Biancari et al.\textsuperscript{61} investigated the Glasgow Aneurysm Score (GAS). The GAS was calculated from data entered prospectively according to the formula

\[
\text{Risk score} = \text{age in years} + 7 \text{ points for myocardial disease} + 10 \text{ points for cerebrovascular disease} + 14 \text{ points for renal disease.}
\]

The EVAR Trial Participants\textsuperscript{26} used a modified Customized Probability Index (CPI) score. The range of possible scores was -25 (best) to +57 (worst) and points were allotted for ischaemic heart disease (+13), uncontrolled congestive heart failure (+14), receiving treatment for hypertension (+7), respiratory dysfunction (+7), renal dysfunction (+16), beta-blocker use (-15) and statin use (-10). The GAS and unmodified CPI score are similar and have been shown to be good predictors of immediate post-operative death following elective open repair of AAA.

Timaran et al.\textsuperscript{88} investigated the Charlson Comorbidity Index (CCI) score. The CCI is a validated measure for use with administrative data that correlates with in-hospital mortality after surgical procedures, including AAA repair. The authors first validated the CCI as an independent predictor of in-hospital mortality following EVAR; the CCI was then used to define four surgical risk groups, a CCI score of 0 corresponding to the lowest and 3 to the highest risk.

All three studies assessed the relationship of risk score with 30-day operative mortality; the GAS\textsuperscript{61} and the CPI\textsuperscript{26} were also investigated for their ability to predict
longer term all-cause mortality. Only the CPI was tested for aneurysm-related mortality at follow-up.

Sample sizes of the three studies ranged from 1200 to over 65500 and the data sources used were the EUROSTAR registry, EVAR I RCT and a large US administrative database (Table 5.2.28). The EVAR trial participants\textsuperscript{26} did not report details of the patients studied; the sample included some patients randomised too late for inclusion in the main EVAR I\textsuperscript{18, 45} trial reports but patient characteristics were presumably similar to those reported there. Timaran et al.\textsuperscript{88} did not report a mean age for their population, although an age distribution was reported. Aneurysm diameter was not reported in this study, which makes it difficult to assess whether the population included patients with AAAs smaller than those generally treated in UK practice.
Table 5.2.28: Characteristics of risk modelling studies evaluating/validating existing risk algorithms

<table>
<thead>
<tr>
<th>Author</th>
<th>Data source</th>
<th>Number of patients</th>
<th>Age of population</th>
<th>Gender</th>
<th>Aneurysm diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biancari 2006</td>
<td>Registry - Dates enrolled and/or treated October 1996 to March 2005</td>
<td>5,498 patients: 59.5% co-existing myocardial disease; 5.7% cerebrovascular disease; 18.2% renal disease.</td>
<td>Median age of 72.7 years (IQR 67.3-77.7 years)</td>
<td>Percentage male (total population) 94.1%</td>
<td>Mean (SD) Median aortic diameter 5.6 cm (IQR 5.1-6.3 cm)</td>
</tr>
<tr>
<td>Brown (EVAR trial participants) 2007</td>
<td>Trial - Dates Patients randomised September 1999-August 2004</td>
<td>EVAR trial 1: 1252 (626 randomised to EVAR and 626 to open repair) EVAR trial 2: 404</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Timaran 2007</td>
<td>Registry - Dates enrolled and/or treated 2001-2004</td>
<td>n = 65502</td>
<td>Not reported</td>
<td>Percentage male (total population) 82.9%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Table 5.2.29: Results of risk modelling studies evaluating/validating existing algorithms

a) Glasgow Aneurysm Score (GAS)

<table>
<thead>
<tr>
<th>Author</th>
<th>Risk factor(s) used in model and definitions</th>
<th>30-day mortality</th>
<th>Aneurysm related mortality at follow-up</th>
<th>All cause mortality at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biancari</td>
<td>Glasgow Aneurysm Score (GAS): Risk score = (age in years) + (7 points for myocardial disease) + (10 points for cerebrovascular disease) + (14 points for renal disease). Myocardial disease refers to previously documented myocardial infarction and/or ongoing angina pectoris. Cerebrovascular disease refers to all grades of stroke and includes transient ischaemic attack. Renal disease refers to a history of acute or chronic renal failure and/or a creatinine level above 133umol/l and/or creatinine clearance below 50ml/min. A Society for Vascular Surgery/International Society of Cardiovascular Surgery risk score of 1 or more.</td>
<td>Multivariate analysis showed GAS independently predicted postoperative death (p&lt;0.001). ROC curve showed GAS with area under curve of 0.70 (95% CI: 0.66-0.74, p&lt;0.001) for predicting postoperative death. Best cut-off value 86.6 (sensitivity 56.1%, specificity 76.2%, accuracy 75.6%, positive predictive value 6.4%, and negative predictive value 98.4%).</td>
<td>No risk factors investigated</td>
<td>Multivariate analysis showed overall survival differed significantly among GAS tertiles (ie. &lt;74.4, 74.4-83.6, &gt;83.6) (p&lt;0.001). 5-year overall survival rate for patients with GAS &gt;83.6 = 65.2%.</td>
</tr>
</tbody>
</table>
Table 5.2.29: Results of risk modelling studies evaluating/validating existing algorithms

b) Customized Probability Index (CPI)

<table>
<thead>
<tr>
<th>Author (EVAR trial participants) 2007</th>
<th>Risk factor(s) used in model and definitions</th>
<th>30-day mortality</th>
<th>Aneurysm related mortality at follow-up</th>
<th>All cause mortality at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown</td>
<td>Patients were classified as good, moderate or poor fitness based on a modified Customized Probability Index score (based on cardiovascular disease, respiratory dysfunction, renal dysfunction and medication status). The modification was the exclusion of cerebrovascular disease and by weighting severe aortic stenosis and arrhythmia as risk factors similarly to ischaemic heart disease.</td>
<td>Modified Customized Probability Index score. No significant effect of Customized Probability Index fitness group on benefit of EVAR over open repair in EVAR trial 1 (Good fitness adjusted OR 0.23 (95% CI: 0.06, 0.84), p = 0.027, Moderate fitness adjusted OR 0.70 (95% CI: 0.19, 2.56), p = 0.586, Poor fitness adjusted OR 0.29 (95% CI: 0.07, 1.17), p = 0.882). P value for test of interaction for adjusted model = 0.363</td>
<td>Modified Customized Probability Index score. Mortality rates were 0.9/100 person years for good fitness, 1.2 for moderate fitness and 1.6 for poor fitness. There was no significant effect of fitness group on benefit of EVAR over open repair in EVAR trial 1 (no interaction between fitness score and randomised group). Crude hazard ratios Good fitness 0.49 (95% CI: 0.21, 1.15), p = 0.100, Moderate fitness 0.91 (95% CI: 0.31, 2.70), p = 0.862, Poor fitness 0.60 (95% CI: 0.25, 1.44), p = 0.254</td>
<td>Modified Customized Probability Index score. Mortality rates were 5.3/100 person years for good fitness, 7.7 for moderate fitness and 9.9 for poor fitness. There was no significant effect of fitness group on benefit of EVAR over open repair in EVAR trial 1 (no interaction between fitness score and randomised group). Crude hazard ratios Good fitness 0.76 (95% CI: 0.52, 1.11), p = 0.151, Moderate fitness 1.11 (95% CI: 0.71, 1.75), p = 0.643, Poor fitness 1.02 (95% CI: 0.68, 1.51), p = 0.941</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P value for test of interaction for adjusted model = 0.371</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5.2.29: Results of risk modelling studies evaluating/validating existing algorithms

c) Charlson comorbidity index (CCI)

<table>
<thead>
<tr>
<th>Author</th>
<th>Risk factor(s) used in model and definitions</th>
<th>30-day mortality</th>
<th>Aneurysm related mortality at follow-up</th>
<th>All cause mortality at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timaran 2007</td>
<td>The score is a validated measure for use with administrative data that correlates with in hospital morbidity and mortality after surgical procedures (including elective AAA repairs). Each of the indicated diagnoses is assigned a weight and summed to provide a patient's total score (0 (low risk) to &gt;3 (high risk).</td>
<td>Charlson comorbidity index (CCI) score (0 to &gt;3)</td>
<td>From multivariate regression model OR 1.12 (95% CI 1.06, 1.20) p &lt;0.001</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>A higher CCI score was associated with early death:</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CCI 0 - 1.8%</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CCI 1 - 2.0%</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CCI 2 - 2.2%</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CCI =&gt; 3 3.7%</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p &lt;0.001</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stratified analysis that included only elective EVAR found the per point CCI score to be an independent predictor of in-hospital mortality (OR 1.38, 95% CI 1.29, 1.47)</td>
<td>No risk factors investigated</td>
</tr>
</tbody>
</table>
Study results

Details of the risk scores used in the three studies and results are summarized in Tables 5.2.28 and 5.2.29. One study also assessed other risk factors and results for these factors are discussed in the following section 5.2.4.3.

30-day operative mortality

GAS was found to be an independent predictor of post-operative death. Thirty-day mortality rates were 1.1% for patients with a GAS <74.4, 2.1% for GAS 74.4–83.6 and 5.3% for those with a score >83.6. The best cut-off value was a GAS of 86.6; 30-day mortality was 1.6% in patients with a score below this value and 6.4% in those with a higher score.61 CCI score was also found to be an independent predictor of in-hospital mortality.88 Mortality increased as CCI score increased (odds ratio per point increase 1.12, 95% CI: 1.06, 1.20) and similar results were found in a stratified analysis that included only elective EVAR cases (Table 5.2.29).

Fitness level (good, moderate or poor) as determined from the modified CPI score did not significantly affect the odds ratio for EVAR relative to open repair for 30-day operative mortality.26

Aneurysm-related and all-cause mortality

In the study assessing GAS, median follow-up was 18 months and overall survival differed significantly between the lowest, middle and high GAS groups. The overall 5-year survival rate was 76.7%; patients with a GAS above 83.6 had an overall survival rate of 65.2%.61 The EVAR trial participants found that although aneurysm-related and all-cause mortality rates increased with decreasing fitness, the benefit of EVAR relative to open repair did not differ between fitness groups for either outcome.26 This suggests that the modified CPI score used in this study would not be helpful in identifying patients likely to benefit specifically from EVAR or open repair.
Summary statement

There is evidence from single studies that the GAS and CCI score can independently predict short-term (in-hospital or 30-day) mortality following EVAR. These measures have previously been validated for prediction of mortality risk following open AAA repair. The GAS may also be able to predict longer term mortality risk following EVAR (based on one study). Based on one study, there is no evidence that fitness rating based on a modified CPI score predicts benefit from EVAR compared with open repair.

5.2.4.2 Studies investigating the development of a risk algorithm

One study, described in three papers, focused on the development of an algorithm to assess baseline risks after EVAR. This Australian national audit investigated the role of ASA, age, AAA diameter and morphology, gender, comorbidities, suitability for open repair, sac size change (pre-operative and post-operative, modified ‘Whites grading system’ (aortic neck length <1.5 cm and angulation >45 degrees, thrombus present, aortic sac angulation >60 degrees, severe iliac artery tortuosity, severe iliac artery, calcification), device name and type, patient type (private or public) and smoking status in a group of 961 patients. Patients who underwent elective or semi-urgent (non-ruptured aneurysms) EVAR between 1 November 1999 and 16 May 2001 were enrolled. No risk factors for 30-day mortality were investigated.

Boult et al. (2006) included modified ‘Whites grading system’ to determine whether this variable had a predictive effect on the number of reinterventions and endoleaks reported after EVAR. At mid-term follow-up (i.e. 3 years) no significant effects were reported. Similarly, no significant effect was reported for infrarenal neck diameter as a predictive variable for aneurysm-related death.

Four factors were identified as having a significant impact on survival rates: ASA score, maximum aneurysm diameter, age, and serum creatinine (p<0.001 for each factor). These variables were combined to estimate predicted 3-year and 5-year survival probabilities; ASA II, III or IV; maximum diameter 5, 5.8 or 7.4 cm; age 70, 77 or 83 years; and creatinine 85 or 125 micromoles/litre (see table 5.2.30).
Table 5.2.30: Survival at 3 and 5 years after EVAR predicted by ASA, age and aneurysm size.

From Boult et al. 2007\textsuperscript{62}

<table>
<thead>
<tr>
<th>Additional details</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Predicted survival at 3 years</strong></td>
<td>ASA</td>
<td>Max diameter</td>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>70 years</td>
<td>77 years</td>
<td>83 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Creatinine (μmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>125</td>
<td>85</td>
<td>125</td>
<td>85</td>
<td>125</td>
</tr>
<tr>
<td>ASA II</td>
<td>5 cm</td>
<td>91%</td>
<td>88%</td>
<td>87%</td>
<td>84%</td>
<td>83%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>89%</td>
<td>87%</td>
<td>86%</td>
<td>82%</td>
<td>81%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>87%</td>
<td>83%</td>
<td>82%</td>
<td>77%</td>
<td>77%</td>
</tr>
<tr>
<td>ASA III</td>
<td>5 cm</td>
<td>86%</td>
<td>82%</td>
<td>81%</td>
<td>76%</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>84%</td>
<td>80%</td>
<td>78%</td>
<td>73%</td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>80%</td>
<td>75%</td>
<td>73%</td>
<td>67%</td>
<td>66%</td>
</tr>
<tr>
<td>ASA IV</td>
<td>5 cm</td>
<td>79%</td>
<td>74%</td>
<td>72%</td>
<td>65%</td>
<td>64%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>76%</td>
<td>71%</td>
<td>69%</td>
<td>62%</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>71%</td>
<td>64%</td>
<td>62%</td>
<td>54%</td>
<td>53%</td>
</tr>
<tr>
<td><strong>Predicted survival at 5 years</strong></td>
<td>ASA</td>
<td>Max diameter</td>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>70 years</td>
<td>77 years</td>
<td>83 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Creatinine (μmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>125</td>
<td>85</td>
<td>125</td>
<td>85</td>
<td>125</td>
</tr>
<tr>
<td>ASA II</td>
<td>5 cm</td>
<td>85%</td>
<td>81%</td>
<td>79%</td>
<td>74%</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>83%</td>
<td>79%</td>
<td>77%</td>
<td>72%</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>79%</td>
<td>74%</td>
<td>72%</td>
<td>65%</td>
<td>64%</td>
</tr>
<tr>
<td>ASA III</td>
<td>5 cm</td>
<td>77%</td>
<td>72%</td>
<td>70%</td>
<td>63%</td>
<td>62%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>75%</td>
<td>69%</td>
<td>67%</td>
<td>60%</td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>69%</td>
<td>62%</td>
<td>60%</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td>ASA IV</td>
<td>5 cm</td>
<td>67%</td>
<td>60%</td>
<td>57%</td>
<td>49%</td>
<td>48%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>64%</td>
<td>56%</td>
<td>53%</td>
<td>45%</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>56%</td>
<td>48%</td>
<td>45%</td>
<td>36%</td>
<td>34%</td>
</tr>
</tbody>
</table>

Shading indicates estimates with low certainty. Sample sizes <10 in those regions.

Reprinted from Boult et al. 2007\textsuperscript{62} ©2007, with permission from the European Society for Endovascular Surgery.

Table 5.2.30 indicates that the greatest predicted survival rate would be expected in younger patients (70 years) with lower ASA scores and creatinine levels (85 μmol/L), and smaller aneurysm size (5 cm). Boult et al. (2007)\textsuperscript{62} predicted 91% survival rates for patients at 3 year follow-up and 85% at 5 years. By contrast, patients expected to have lower survival rates were identified as older patients (83 years), with a higher ASA score (ie. IV), higher creatinine levels (125 μmol/L), and larger aneurysm size (7.4 cm). Survival rates for this group of patients were 44% at 3 year follow-up and 25% at 5 years, indicating a difference of 47% for 3-year survival and 60% at 5 years.
between the 2 groups. That is, 15% expected mortality at 5 years for the low risk group and 75% for the high risk group. However, as the authors state, the data presented for patients in the high risk group were unreliable due to the small sample sizes and should be interpreted with caution.

This study was extended\textsuperscript{24} to develop and internally validate an interactive model to evaluate expected outcomes for a particular patient undergoing EVAR. Key predictor variables were identified and their relationship with seventeen success measures was ascertained. Predictor variables were preoperative aneurysm size, age at operation, ASA rating, gender, creatinine, aortic neck angle, infrarenal neck diameter and infrarenal neck length. Success measures included technical and initial clinical success, 3 and 5 year survival, aneurysm related death and early death (30 days), absence from reinterventions (initial and mid-term), graft complications (initial and mid-term), migration, conversion to open repair, rupture and endoleak. Stepwise forward regression using Akaike’s Information Criterion was used to select which of the preoperative variables should be included in each of the success measure models. Initially regressions only included patients who had all preoperative variables. However after significant variables were chosen, the regression model was performed again using as much data as possible. The authors assessed the goodness of fit of each of the 17 outcome models. For each of the final logistic regression models bootstrapping was used to assess the internal model validity.

All outcome models had a reasonable fit with the exception of the outcome model for conversion to open repair. In terms of validation, survival, aneurysm-related deaths, migrations and conversions to open repair performed best in predictive discrimination. Models for survival, migrations and conversions to open repairs performed best in terms of bias corrected R-squared index. The models with the smallest calibration error were 3 and 5 year survival, early deaths and mid-term Type 1 endoleaks. The interactive model is available from http://www.surgeons.org/asernip-s/audit.htm. Users can enter up to eight preoperative variables and review the predicted success rate and confidence intervals. The model can be used at an initial consultation where, for example, information is known about age, ASA, aneurysm diameter, gender and creatinine. Following CT scanning,
measurements could be added on aortic neck angle, infrarenal neck length and infrarenal neck diameter.

5.2.4.3 Studies investigating specific risk factors

Thirty-two studies investigated specific risk factors after EVAR. 62-93 One study 62 has already been discussed above as its main aim was to develop a risk algorithm. However specific risk factors were also discussed and are reported here. Of the three studies discussed in the section on validation of existing algorithms, 26, 61, 88 one also presents further data on specific risk factors and is mentioned in this section. 88 The remaining 30 studies focused exclusively on the evaluation of one or more risk factors after EVAR. Table 5.2.23 details the characteristics of patients in all of the studies included in this section.

Sample size ranged from 676 to 65502. Six studies had fewer than 1000 participants, 62, 63, 75, 87, 92, 93 26 had between 1000 and 6500 participants 64-74, 76-86, 89-91 and one US study had over 65,000 participants. 88 The mean or median age of between 70 and 75 years of age reflected the fact that AAA is predominantly a disease of old age. Equally the higher prevalence of AAAs in men was reflected in the studies with percentages of men ranging from 81.4% to 99.3% where reported. Where reported, mean aneurysm size tended to be between 5.5 cm and 5.9 cm. However not all studies reported the range of aneurysm size and it is likely that some studies contained participants receiving EVAR who would not normally be considered given their aneurysm size under UK current practice.
Table 5.2.31: Risk modelling studies patient characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Age of population</th>
<th>Gender (% male)</th>
<th>Aneurysm diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boulton 2006</td>
<td>961</td>
<td>75.0 (6.9) years</td>
<td>86%</td>
<td>Men 5.8 (1.05) cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Women 5.5 (0.9) cm</td>
</tr>
<tr>
<td>Brewster 2006</td>
<td>873</td>
<td>75.7 (7.6) years</td>
<td>81.4%</td>
<td>5.68 cm (1.06) cm</td>
</tr>
<tr>
<td></td>
<td>2368</td>
<td>72.2 years</td>
<td>99.3%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Buth 2000</td>
<td>1892</td>
<td>70 years</td>
<td>91%</td>
<td>Median 5.6 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 37-90 years</td>
<td></td>
<td>Range 2.8-15 cm</td>
</tr>
<tr>
<td>Buth 2000</td>
<td>1554</td>
<td>70 years</td>
<td>91.4%</td>
<td>Median 5.6 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 37-90 years</td>
<td></td>
<td>Range 2.8-15 cm</td>
</tr>
<tr>
<td>Buth 2002</td>
<td>3075</td>
<td>71.7 years</td>
<td>92.7%</td>
<td>5.66 cm</td>
</tr>
<tr>
<td>Buth 2003</td>
<td>3595</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cuypers 2000</td>
<td>1871</td>
<td>69.7 years</td>
<td>91.8%</td>
<td>5.6 cm</td>
</tr>
<tr>
<td>Diehm 2007</td>
<td>6383</td>
<td>72.4 (SD 7.6)</td>
<td>93.8%</td>
<td>5.87 cm (calculated)</td>
</tr>
<tr>
<td>Diehm 2007</td>
<td>711</td>
<td>No anaemia 74.6 (7.5)</td>
<td>90.9%</td>
<td>No anaemia 5.7(0.97) cm</td>
</tr>
<tr>
<td>Hobo 2006</td>
<td>2846</td>
<td>72.0 (7.5) years</td>
<td>94%</td>
<td>5.8 cm</td>
</tr>
<tr>
<td>Hobo 2007</td>
<td>5183</td>
<td>72.6 years</td>
<td>93.8%</td>
<td>5.9 cm</td>
</tr>
<tr>
<td>Lange 2005</td>
<td>4433</td>
<td>Patients &lt; 80 years</td>
<td>92.7%</td>
<td>Patients &lt; 80 years 94.8% Octogenarians 90.2% (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70.3(6.5) years</td>
<td></td>
<td>Octogenarians 6.2 cm(1.22) (p &lt; 0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Octogenarians 83.4(2.9) years</td>
<td>92%</td>
<td>5.6 cm (SD not reported)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 43-96 years</td>
<td></td>
<td>Max AAA diameter &gt;6 cm: 28.5%</td>
</tr>
<tr>
<td>Leurs 2007</td>
<td>1033</td>
<td>DREAM: 70.6 years</td>
<td>92.7%</td>
<td>DREAM: 6.06 cm (0.89 cm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(6.51)</td>
<td>EUROMAT: 71.6 years (7.67)</td>
<td>EUROMAT: 6.04 cm (1.02 cm)</td>
</tr>
<tr>
<td>Leurs 2004</td>
<td>676</td>
<td>72.1 years (calculated)</td>
<td>93%</td>
<td>5.67 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 43 - 96 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2006</td>
<td>3,499</td>
<td>73.2 years</td>
<td>94.0%</td>
<td>6.1 cm</td>
</tr>
<tr>
<td>Leurs 2005</td>
<td>8017</td>
<td>71.8 years</td>
<td>93.5%</td>
<td>Max AAA diameter &gt;6 cm: 28.5%</td>
</tr>
<tr>
<td>Leurs 2004</td>
<td>4233</td>
<td>Not reported</td>
<td>93.7%</td>
<td>5.8 cm (SD not reported)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 37 - 101 years</td>
<td></td>
<td>Range 4.0-11.0 cm</td>
</tr>
<tr>
<td>Leurs 2006</td>
<td>592</td>
<td>72.3 years</td>
<td>94.1%</td>
<td>5.86 cm</td>
</tr>
<tr>
<td>Lifeline * 2002</td>
<td>1646</td>
<td>73.1 (7.9) years</td>
<td>88.6%</td>
<td>5.57 cm (SD not reported)</td>
</tr>
<tr>
<td>Lifeline * 2005</td>
<td>2664</td>
<td>73.1 (7.8) years</td>
<td>88.6%</td>
<td>5.58 (1.02) cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 45 - 96 years</td>
<td></td>
<td>Range 2.1 - 12.0 cm</td>
</tr>
<tr>
<td>Lottman 2004</td>
<td>3270</td>
<td>Not reported</td>
<td>93%</td>
<td>44% aneurysm diameter of less than 5.5 cm 56% aneurysm diameter of 5.5 cm</td>
</tr>
<tr>
<td>Mohan 2001</td>
<td>2146</td>
<td>Median 70 years</td>
<td>92%</td>
<td>2.1-15.0 (median 3.6) cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 37 – 92 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peppelenbosch 2004</td>
<td>4392</td>
<td>Not reported</td>
<td>93.2%</td>
<td>57.2 cm (SD not reported)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 43 – 109 years</td>
<td></td>
<td>Range 4.0 - 14.5 cm</td>
</tr>
<tr>
<td>Riaimbau 2001</td>
<td>2862</td>
<td>Not reported</td>
<td>92.2%</td>
<td>5.62 cm</td>
</tr>
<tr>
<td>Ruppert 2006</td>
<td>5557</td>
<td>72 years</td>
<td>Not reported</td>
<td>5.85 cm (SD not reported)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range 41 to 100 years</td>
<td></td>
<td>Range 4 cm - 14.5 cm</td>
</tr>
</tbody>
</table>

Final Report 1st April 2008
Across the studies the following risk variables were investigated: age, gender, smoking status, ASA status, pre-existing conditions, renal function, fitness for open procedure, aneurysm size, aortic neck and aneurysm angle, aortic neck length and graft configuration and device type. Each risk variable will be discussed in its own section and each of the five outcomes of 30 day mortality, aneurysm related mortality, all cause mortality, re-intervention and endoleak will be discussed by variable. All studies contributing relevant data to each section will be discussed as appropriate.

Some studies presented odds ratios or hazard ratios whilst others reported a variable as significant or not significant. Details of any numerical data provided can be found in each individual study in the data extraction appendix. Included in each section on a given risk variable is a graphical representation of the evidence. The height of the bars represents sample size and the shading of the bars is the data source. From this it can be determined which variables from which studies and for which outcomes have been found in multivariable regression to be significant or non-significant. It should, however, be noted that studies may be missing on the non-significant sides of the charts. This is due to the fact that they were not reported or were not included in multivariable analysis as they had been found in univariate analyses not to be significant. We are reliant on the reporting of each individual study.
Within the constraints outlined above, an attempt has been made at the end of the risk model section to summarise and interpret the evidence for risk factors and adverse outcomes after EVAR.

**Age**

Twenty-four studies investigated the role of age on adverse outcomes after EVAR. Age was either treated as a continuous variable or dichotomised, for example into under 80 and octogenarians.
Figure 5.2.8  Age and 30-day mortality

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
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<td>65,502</td>
<td>3,075</td>
<td>3,499</td>
<td>4,433</td>
<td>5,167</td>
<td>1,554</td>
</tr>
<tr>
<td>Data source</td>
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<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found age to be an independent risk factor (IRF), while those to the right did not.
* Age 70 years or more; ** Patients < 80 years of age versus octogenarians

Figure 5.2.9  Age and aneurysm-related mortality

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>3,992</td>
<td>4,392</td>
<td>5,892</td>
<td>4,433</td>
<td>961</td>
<td>676</td>
<td>2,664</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>US</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found age to be an independent risk factor (IRF), while those to the right did not.
* Over 70; ** Patients < 80 years of age versus octogenarians
Figure 5.2.10  Age and all-cause mortality

Studies to the left of the vertical line found age to be an independent risk factor (IRF), while those to the right did not.

* Patients < 80 years of age versus octogenarians

Figure 5.2.11  Age and re-intervention

Studies to the left of the vertical line found age to be an independent risk factor (IRF), while those to the right did not.

* Conversion to OR
The evidence showed age to be a risk factor for 30 day mortality. For the outcome of aneurysm related mortality evidence was mixed. All nine studies in this group correctly identified increasing age as an independent risk factor for all cause mortality. Results for re-intervention were almost all analyses of EUROSTAR data and most, but not all, studies concluded that age was not a risk factor. On balance the mainly EUROSTAR based evidence indicate that age is an independent risk factor for type II endoleak or all types of endoleak.

Varying interpretations of old age and the way that data were handled may affect findings and may explain some of the inconsistency in this section’s results.
**Gender**

Eleven studies investigated the role of gender in relation to adverse outcomes after EVAR.\(^62, 63, 65, 66, 71, 81, 83, 84, 88, 89, 91\)

**Figure 5.2.13 Female gender and 30-day mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bath 2000 (b)</td>
<td>1,554</td>
<td>EUROSTAR</td>
<td>1994-1999</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found gender to be an independent risk factor (IRF), while those to the right did not.
Figure 5.2.14  Female gender and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Boult 2007</th>
<th>Lifeline 2005</th>
<th>Torella 2004*</th>
<th>Peppelenbosch 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>961</td>
<td>2,664</td>
<td>3,992</td>
<td>4,392</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>US</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found gender to be an independent risk factor (IRF), while those to the right did not.

* Male not female

Figure 5.2.15  Female gender and all-cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Boult 2007</th>
<th>Lifeline 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>961</td>
<td>2,664</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>US</td>
</tr>
<tr>
<td>Study dates</td>
<td>1999-2001</td>
<td>[5 years]</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found gender to be an independent risk factor (IRF), while those to the right did not.
Figure 5.2.16  Female gender and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
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<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brewster 2006</td>
<td>Boul 2007</td>
<td>Hobo 2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Torella 2004**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peppelenbosch 2004</td>
</tr>
</tbody>
</table>

- **Sample size**: 873 961 2,846 3,992 4,392
- **Data source**: US AUS EUROSTAR EUROSTAR EUROSTAR

Studies to the left of the vertical line found gender to be an independent risk factor (IRF), while those to the right did not.

* Conversion to open repair
** Male not female

Figure 5.2.17  Female gender and endoleak

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buth 2000 (a)</td>
<td>Boul 2007**</td>
<td>Buth 2000 (b) ***</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Boul 2007 ****</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mohan 2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Van Marrewijk 2004</td>
</tr>
</tbody>
</table>

- **Sample size**: 1,892 961 1,554 961 2,146 3,595
- **Data source**: EUROSTAR AUS EUROSTAR AUS EUROSTAR EUROSTAR

Studies to the left of the vertical line found gender to be an independent risk factor (IRF), while those to the right did not.

* Early endoleak
** Male gender and type II endoleak
*** Endoleak at end of procedure
**** Male gender, type I endoleak
The results of the very large recent US-based study and the smaller, older EUROSTAR study provide contradictory results regarding the association between female gender and 30 day mortality. However, given the small number of female patients in most series, the very large study is likely to be more reliable. Therefore there may be a link between female gender and 30 day mortality. There is no indication of any link between female gender and aneurysm-related or all cause mortality. The evidence suggests that gender is not an independent risk factor for re-intervention. There is contradictory evidence regarding association with endoleak.

**Pre-existing conditions**

Nineteen studies investigated the role of pre-existing conditions on adverse outcomes after EVAR. The studies assessed the role of a range of pre-existing conditions, such as pulmonary insufficiency, diabetes, chronic heart failure, obesity, anaemia and hypertension.
**Figure 5.2.18 Pre-existing conditions and 30-day mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leurs 2005 (b)*</td>
<td>6,017</td>
<td>EUROSTAR</td>
<td>1994-2003</td>
<td>Leurs 2006***</td>
<td>3,499</td>
</tr>
<tr>
<td>Van Eps 2006**</td>
<td>5,167</td>
<td>EUROSTAR</td>
<td>1996-2005</td>
<td>Bath 2000 (b)</td>
<td>1,554</td>
</tr>
<tr>
<td>Buth 2000 (b)</td>
<td>3,075</td>
<td>EUROSTAR</td>
<td>1996-2005</td>
<td>Bath 2002*****</td>
<td>3,075</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found pre-existing conditions to be an independent risk factor (IRF), while those to the right did not.

* Diabetes
** Pulmonary impairment
**** Statin use
***** Cardiac status, blood pressure
****** Cardiac status, blood pressure, pulmonary, diabetes, obesity
******* Diabetes, pulmonary status
Figure 5.2.19  Pre-existing conditions and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diehm 2007**</td>
<td>6,383</td>
<td>EUROSTAR</td>
<td>1996-2005</td>
</tr>
<tr>
<td>Peppelenbosch 2004**</td>
<td>4,392</td>
<td>EUROSTAR</td>
<td>1996-2002</td>
</tr>
<tr>
<td>Lifeline 2005***</td>
<td>2,664</td>
<td>US</td>
<td>[5 years]</td>
</tr>
<tr>
<td>Diehm 2007****</td>
<td>6,383</td>
<td>EUROSTAR</td>
<td>1996-2005</td>
</tr>
<tr>
<td>Leurs 2004*****</td>
<td>676</td>
<td>EUROSTAR</td>
<td>1998-2004</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found pre-existing conditions to be an independent risk factor (IRF), while those to the right did not.

* Peripheral vascular disease
** Pulmonary status
*** Hypertension, CAD, MI, CHF, COPD, diabetes
**** Diabetes
***** Pulmonary insufficiency
Figure 5.2.20  Pre-existing conditions and all-cause mortality

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</thead>
<tbody>
<tr>
<td>Sample size</td>
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<td>2,368</td>
<td>711</td>
<td>923</td>
<td>5,892</td>
<td>2,664</td>
<td>1,646</td>
<td>2,862</td>
<td>6,383</td>
<td>4,233</td>
<td>6,017</td>
<td>5,892</td>
<td>2,664</td>
<td>2,862</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found pre-existing conditions to be an independent risk factor (IRF), while those to the right did not.

* Pulmonary disorder
** Pulmonary status
*** Pulmonary function, baseline, diabetes, baseline haemoglobin level
**** COPD, PAD
***** CAD/MI, CHF, COPD
****** COPD, CHF
******* Diabetes in those fit for open-surgery
******** Diabetes
********* Hypertension, diabetes
********** Statin use
*********** Hypertension, carotid artery disease or cardiac disease, hyperlipidaemia, pulmonary status, diabetes in patients unfit for open surgery
### Figure 5.2.21  Pre-existing conditions and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boult 2007*</td>
<td>961</td>
<td>AUS</td>
<td>1999-2001</td>
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<td></td>
</tr>
<tr>
<td>Leurs 2005 (b) **</td>
<td>6,017</td>
<td>EUROSTAR</td>
<td>1994-2003</td>
<td></td>
<td></td>
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<tr>
<td>Leurs 2006 ***</td>
<td>5,892</td>
<td>EUROSTAR</td>
<td>1996-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diehm 2007 ****</td>
<td>6,383</td>
<td>EUROSTAR</td>
<td>1996-2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leurs 2005 (a) *****</td>
<td>4,233</td>
<td>EUROSTAR</td>
<td>1994-2004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peppelenbosch 2004</td>
<td>4,392</td>
<td>EUROSTAR</td>
<td>1996-2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hobo 2006 ******</td>
<td>2,846</td>
<td>EUROSTAR</td>
<td>1999-2004</td>
<td></td>
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</tr>
</tbody>
</table>

Studies to the left of the vertical line found pre-existing conditions to be an independent risk factor (IRF), while those to the right did not.

* Higher number of pre-existing conditions  
** Diabetes  
*** Statin use  
**** Pulmonary status, diabetes  
***** Diabetes leading to re-intervention  
****** Systemic comorbidities
Studies to the left of the vertical line found pre-existing conditions to be an independent risk factor (IRF), while those to the right did not.

* Blood pressure index < 0.87
** Obesity
*** Pulmonary status, diabetes
**** Hypertension, diabetes
***** Cardiac status, blood pressure index for endoleak at completion of procedure
****** Hypertension

The available analyses of EUROSTAR data indicate that cardiac status, high blood pressure and obesity are not independent risk factors for 30 day mortality. The results regarding diabetes and pulmonary impairment as predictors of 30 day mortality are inconsistent.

The analyses for aneurysm related mortality showed inconsistent results for pulmonary status. However the evidence suggested that diabetes is not a risk factor for aneurysm-related mortality and based on one US study hypertension was not found to be a risk factor for aneurysm-related mortality. Evidence on other pre-existing conditions was lacking for this outcome.
There were inconsistent results regarding cardiac disease and all cause mortality after EVAR. The majority of studies found that pulmonary status / COPD was an independent risk factor for all cause mortality after EVAR including both EUROSTAR and US populations. The findings for diabetes as a risk factor for all cause mortality were inconsistent. In one EUROSTAR and one US study hypertension was not found to be a risk factor for all cause mortality. Evidence was lacking on other risk factors.

The available analyses suggest that diabetes is not a risk factor for re-intervention / conversion to open repair.

One Australian study concluded that the higher the number of pre-existing conditions the greater the rates of re-intervention whilst all EUROSTAR studies found that pre-existing conditions did not tend to predict re-intervention

The studies consistently found that pre-existing conditions were not risk factors for endoleak.

**Renal Function**

Eleven studies investigated renal function / renal impairment as a potential risk factor for adverse outcomes in multivariable modelling. Although all outcomes were considered, the outcomes of re-intervention and endoleak were only investigated in one study each.
Figure 5.2.23  Renal function and 30-day mortality

Studies to the left of the vertical line found impaired renal function to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.24  Renal function and aneurysm-related mortality

Studies to the left of the vertical line found impaired renal function to be an independent risk factor (IRF), while those to the right did not.
Figure 5.2.25  Renal function and all-cause mortality

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<tbody>
<tr>
<td>Sample size</td>
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<td>873</td>
<td>1,646</td>
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<td>2,862</td>
</tr>
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<td>Data source</td>
<td>AUS</td>
<td>US</td>
<td>US</td>
<td>US</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found impaired renal function to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.26  Renal function and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>Peppelenbosch 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
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</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
</tr>
<tr>
<td>Study dates</td>
<td>1996-2002</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found impaired renal function to be an independent risk factor (IRF), while those to the right did not.
There was consistent evidence from a small number of studies that renal impairment affects 30 day mortality after EVAR but inconsistent evidence of its effects on aneurysm-related mortality. The balance of evidence suggests renal impairment is an independent risk factor for all cause mortality. Single analyses of EUROSTAR data indicate no link between renal dysfunction and re-intervention or endoleak after EVAR.

**Fitness for open procedure**

Six studies investigated whether patients’ fitness for open procedure determined adverse outcomes after EVAR. Five of these were based on EUROSTAR data\textsuperscript{66, 67, 75, 84, 89} whilst one was based on a national Australian audit.\textsuperscript{62}
Figure 5.2.28  Fitness for open-procedure and 30-day mortality

<table>
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<tr>
<th></th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Bath 2002</td>
<td>Bath 2000 (b)</td>
</tr>
<tr>
<td>Sample size</td>
<td>3,075</td>
<td>1,554</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found lack of fitness for open procedure to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.29  Fitness for open-procedure and aneurysm-related mortality

<table>
<thead>
<tr>
<th></th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Torella 2004</td>
<td>Leurs 2004</td>
</tr>
<tr>
<td>Peppelenbosch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
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</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
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</tbody>
</table>

Studies to the left of the vertical line found lack of fitness for open procedure to be an independent risk factor (IRF), while those to the right did not.
### Figure 5.2.30  Fitness for open-procedure and all-cause mortality

<table>
<thead>
<tr>
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<th>IRF</th>
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</thead>
<tbody>
<tr>
<td>Study</td>
<td>Leurs 2004</td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
<td>676</td>
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<tr>
<td>Study dates</td>
<td>1998-2004</td>
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</table>

Studies to the left of the vertical line found lack of fitness for open procedure to be an independent risk factor (IRF), while those to the right did not.

### Figure 5.2.31  Fitness for open-procedure and re-intervention

<table>
<thead>
<tr>
<th></th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Boult 2007</td>
<td>Torella 2004* Peppelenbosch 2004</td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
<td>3,992 4,392</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found lack of fitness for open procedure to be an independent risk factor (IRF), while those to the right did not.

* Late conversion to OR
There was inconsistent evidence linking fitness and 30 day mortality but the more recent analysis with a larger cohort suggested there might be an association. On balance analyses indicate fitness for open procedure to be linked to aneurysm-related mortality. Evidence was lacking to link fitness for open procedure and all-cause mortality. On balance fitness was not an independent risk factor for re-intervention or endoleak.

**ASA Status**

Twelve studies investigated the role of patients’ ASA status on adverse outcomes after EVAR. The majority of the studies were based on EUROSTAR data.
### Figure 5.2.33  ASA class and 30-day mortality

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
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<td>22,368</td>
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<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>US</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found ASA class to be an independent risk factor (IRF), while those to the right did not.

* ASA III and IV

### Figure 5.2.34  ASA class and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Boult 2007</th>
<th>Leurs 2006 (b)*</th>
<th>Peppelenbosch</th>
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<tbody>
<tr>
<td>IRF</td>
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<td></td>
<td>2004</td>
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<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
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</tbody>
</table>

Studies to the left of the vertical line found ASA class to be an independent risk factor (IRF), while those to the right did not.

* >= ASA III
**Figure 5.2.35  ASA class and all-cause mortality**

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>IRF</td>
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</tr>
<tr>
<td>Not IRF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
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<td>961</td>
<td>923</td>
<td>5,892</td>
<td>22,368</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>AUS</td>
<td>US</td>
<td>EUROSTAR</td>
<td>US</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found ASA class to be an independent risk factor (IRF), while those to the right did not.

*ASA >=III

**Figure 5.2.36  ASA class and re-intervention**

<table>
<thead>
<tr>
<th>Study</th>
<th>Boult 2007</th>
<th>Hobo 2006</th>
<th>Peppelenbosch</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not IRF</td>
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<tr>
<td>Sample size</td>
<td>961</td>
<td>2,846</td>
<td>4,392</td>
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<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found ASA class to be an independent risk factor (IRF), while those to the right did not.
### Figure 5.2.37  ASA class and endoleak

<table>
<thead>
<tr>
<th>Study</th>
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</thead>
<tbody>
<tr>
<td><strong>Sample size</strong></td>
<td>961</td>
<td>961, 2,146</td>
</tr>
<tr>
<td><strong>Data source</strong></td>
<td>AUS</td>
<td>AUS, EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found ASA class to be an independent risk factor (IRF), while those to the right did not.

* Type II  
** Type I

According to EUROSTAR data, ASA class III and IV is predictive of statistically significantly worse 30 day mortality. Evidence for aneurysm related mortality was inconsistent. With the exception of a large US study, all analyses found ASA to be an independent risk factor for all cause mortality. On balance, ASA status was not found to be a significant independent risk factor for re-intervention or endoleak.

### Smoking status

Seven studies investigated smoking status as a risk factor for adverse outcomes after EVAR. 62, 66, 68, 78, 82, 83, 91

The evidence suggests that smoking status is not associated with adverse outcomes after EVAR. However the evidence investigating smoking and mortality after EVAR is very limited.
Studie 5.2.38  Smoking status and 30-day mortality

<table>
<thead>
<tr>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Bath 2000 (b)</td>
</tr>
<tr>
<td>Sample size</td>
<td>1,554</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
</tr>
<tr>
<td>Study dates</td>
<td>1994-1999</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found smoking status to be an independent risk factor (IRF), while those to the right did not.

Studie 5.2.39  Smoking status and aneurysm-related mortality

<table>
<thead>
<tr>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Boult 2007</td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
</tr>
<tr>
<td>Study dates</td>
<td>1999-2001</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found smoking status to be an independent risk factor (IRF), while those to the right did not.
### Figure 5.2.40  Smoking status and all-cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boult 2007</td>
<td></td>
<td>Lottmann 2004</td>
</tr>
</tbody>
</table>

**Sample size**
- Boult 2007: 961
- Lottmann 2004: 3,270

**Data source**
- Boult 2007: AUS
- Lottmann 2004: EUROSTAR

**Study dates**

Studies to the left of the vertical line found smoking status to be an independent risk factor (IRF), while those to the right did not.

### Figure 5.2.41  Smoking status and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boult 2007</td>
<td></td>
<td>Lottmann 2004</td>
</tr>
</tbody>
</table>

**Sample size**
- Boult 2007: 961
- Lottmann 2004: 3,270

**Data source**
- Boult 2007: AUS
- Lottmann 2004: EUROSTAR

**Study dates**

Studies to the left of the vertical line found smoking status to be an independent risk factor (IRF), while those to the right did not.
### Figure 5.2.42  
**Smoking status and endoleak**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td>But 2003*</td>
<td>3,595</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Mohan 2001**</td>
<td>2,146</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Leurs 2005 (a)</td>
<td>4,233</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>But 2000 (b) ***</td>
<td>1,554</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lottmann 2004 ****</td>
<td>3,270</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found smoking status to be an independent risk factor (IRF), while those to the right did not.

* Current smoking decreased risk of type II endoleak
** Those who had stopped > longer ago increased risk of endoleak
*** Negative association between current smoking and endoleak
**** Risk reduction in smokers for late endoleak(type II)

### Aneurysm Size

Nineteen studies investigated aneurysm size as a potential risk factor for adverse outcomes in multivariable modelling.
Figure 5.2.43  Aneurysm size and 30-day mortality

Studies to the left of the vertical line found aneurysm size to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.44  Aneurysm size and aneurysm-related mortality

Studies to the left of the vertical line found aneurysm size to be an independent risk factor (IRF), while those to the right did not.
Figure 5.2.45  Aneurysm size and all-cause mortality

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IRF</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Sample size</td>
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<td>1,033</td>
<td>923</td>
<td>2,664</td>
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<td>US</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>US</td>
<td>US</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aneurysm size to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.46  Aneurysm size and re-intervention

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IRF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Not IRF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
<td>923</td>
<td>703</td>
<td>3,992</td>
<td>4,392</td>
<td>1,871</td>
<td>2,846</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>US</td>
<td>US</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aneurysm size to be an independent risk factor (IRF), while those to the right did not.

* Late conversion to OR
** Conversion to open repair only
Figure 5.2.47  Aneurysm size and endoleak

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
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<td>2,146</td>
<td></td>
<td>4,233</td>
<td>961</td>
<td>2,146</td>
<td>3,595</td>
<td>1,892</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td></td>
<td>EUROSTAR</td>
<td>AUS</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aneurysm size to be an independent risk factor (IRF), while those to the right did not.

* Type I endoleak  
** Type II endoleak  
*** Proximal endoleak  

More recent and larger cohort analysis demonstrates that aneurysm size is an independent risk factor for 30 day mortality. Evidence also suggests it is an independent risk factor for aneurysm-related mortality and all cause mortality.

Evidence for aneurysm size as an independent risk factor for re-intervention and endoleaks was inconsistent.

**Aortic neck and aneurysm angle**

Eight studies investigated aortic neck and angulation as potential risk factors for adverse outcomes in multivariable modelling.\(^62, 66, 72, 76, 78, 83, 84, 89\) With the exception of one Australian study\(^62\) all were based on EUROSTAR populations.
### Figure 5.2.48  Aortic neck/ aneurysm angle and 30-day mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bath 2000 (b)</td>
<td>Hobo 2007</td>
</tr>
<tr>
<td>Sample size</td>
<td>1,554</td>
<td>5,183</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck / angle to be an independent risk factor (IRF), while those to the right did not.

### Figure 5.2.49  Aortic neck/ aneurysm angle and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boul 2007</td>
<td>Hobo 2007</td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
<td>5,183</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck / angle to be an independent risk factor (IRF), while those to the right did not.
Figure 5.2.50  Aortic neck/ aneurysm angle and all-cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boult 2007</td>
<td>Hobo 2007</td>
</tr>
</tbody>
</table>

Sample size  
961  5,183  3,499

Data source  
AUS  EUROSTAR  EUROSTAR

Study dates  

Studies to the left of the vertical line found aortic neck / angle to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.51  Aortic neck/ aneurysm angle and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hobo 2007*</td>
<td>Boult 2007</td>
</tr>
<tr>
<td></td>
<td>Hobo 2007***</td>
<td>Peppelenbosch 2004</td>
</tr>
</tbody>
</table>

Sample size  
5,183  961  3,992  5,183  4,392  3,499

Data source  
EUROSTAR  AUS  EUROSTAR  EUROSTAR  EUROSTAR  EUROSTAR

Study dates  

Studies to the left of the vertical line found aortic neck / angle to be an independent risk factor (IRF), while those to the right did not.

* Long term
** Late conversion to [?]  
*** 30 days
Studies to the left of the vertical line found aortic neck / angle to be an independent risk factor (IRF), while those to the right did not.

The balance of evidence suggests no effect of aortic neck and aneurysm angle on 30 day mortality, aneurysm related mortality or on all cause mortality. Evidence as regards re-intervention and endoleak was mixed allowing no firm conclusions to be drawn.

**Aortic neck length**

Nine studies investigated aortic neck length as a potential risk factor for adverse outcomes in multivariable modelling. With the exception of one Australian study all were based on EUROSTAR populations.
### Figure 5.2.53  Aortic neck length and 30-day mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
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<tbody>
<tr>
<td>Leurs 2006 (a)</td>
<td>3,499</td>
<td>EUROSTAR</td>
<td>1996-2006</td>
</tr>
<tr>
<td>Leurs 2006*</td>
<td>3,499</td>
<td>EUROSTAR</td>
<td>1996-2006</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck length to be an independent risk factor (IRF), while those to the right did not.

* <1 cm vs. > 1.5 cm

### Figure 5.2.54  Aortic neck length and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Data source</th>
<th>Study dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boulton 2007</td>
<td>961</td>
<td>AUS</td>
<td>1999-2001</td>
</tr>
<tr>
<td>Peppelenbosch 2004</td>
<td>4,392</td>
<td>EUROSTAR</td>
<td>1996-2002</td>
</tr>
<tr>
<td>Leurs 2006(a)*</td>
<td>3,499</td>
<td>EUROSTAR</td>
<td>1996-2006</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck length to be an independent risk factor (IRF), while those to the right did not.

* 1.1 – 1.5 cm vs. > 1.5 cm
Figure 5.2.55  Aortic neck length and all-cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boult 2007</td>
<td>Leurs 2006(a)</td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
<td>3,499</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck length to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.56  Aortic neck length and re-intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cuypers 2000*</td>
<td>Torella 2004**</td>
</tr>
<tr>
<td></td>
<td>Boul 2007</td>
<td>Peppelenbosch 2004</td>
</tr>
<tr>
<td>Sample size</td>
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<td>3,992</td>
</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found aortic neck length to be an independent risk factor (IRF), while those to the right did not.

* Conversion to OR
** Late conversion to OR
There was limited evidence available for 30 day mortality. Evidence as regards aneurysm related mortality was inconsistent but none of the EUROSTAR analyses found it to be an independent risk factor. Evidence for all cause mortality was limited but suggestive of no effect. Evidence regarding re-intervention rates was mixed as was the evidence for endoleak with possible differences in types of endoleak.

**Graft Configuration and Device Type**

Ten studies investigated the roles of graft configuration and device type in adverse outcomes after EVAR.
### Figure 5.2.58  Graft configuration/device type and 30-day mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bath 2000 (b)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample size</th>
<th>1,554</th>
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<tbody>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
</tr>
<tr>
<td>Study dates</td>
<td>1994-1999</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found graft configuration/device type to be an independent risk factor (IRF), while those to the right did not.

### Figure 5.2.59  Graft configuration/device type and aneurysm-related mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torella 2004*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peppelenbosch 2004 **</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boult 2007</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample size</th>
<th>3,992</th>
<th>4,392</th>
<th>961</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data source</td>
<td>EUROSTAR</td>
<td>EUROSTAR</td>
<td>AUS</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found graft configuration/device type to be an independent risk factor (IRF), while those to the right did not.

* Old devices
** Association with Stentor and Vanguard devices
Figure 5.2.60  Graft configuration/ device type and all-cause mortality

<table>
<thead>
<tr>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Boult 2007</td>
</tr>
<tr>
<td>Sample size</td>
<td>961</td>
</tr>
<tr>
<td>Data source</td>
<td>AUS</td>
</tr>
<tr>
<td>Study dates</td>
<td>1999-2001</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found graft configuration / device type to be an independent risk factor (IRF), while those to the right did not.

Figure 5.2.61  Graft configuration/ device type and re-intervention

<table>
<thead>
<tr>
<th>IRF</th>
<th>Not IRF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
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</tr>
<tr>
<td>Data source</td>
<td>EUROSTAR US AUS EUROSTAR EUROSTAR</td>
</tr>
</tbody>
</table>

Studies to the left of the vertical line found graft configuration / device type to be an independent risk factor (IRF), while those to the right did not.

* Re-intervention or late conversion to OR
Studies to the left of the vertical line found graft configuration / device type to be an independent risk factor (IRF), while those to the right did not.

*AneuRx, Talent and Fortron devices

**Excluder and Talent for 30 day proximal type I endoleak. Talent and Zenith for long-term proximal type I endoleaks.

*** Device type (tube, tapered or bifurcated)

The evidence relating graft configuration / device type and 30 day and all-cause mortality was too limited to draw conclusions. The balance of evidence suggests that there might be a link between device type and aneurysm-related mortality. Evidence as regards graft configuration / device type and re-intervention and endoleak was inconsistent.
**Summary Statements**

A large number of studies have modelled risk of mortality and other adverse outcomes after EVAR. We do not have definitive evidence on all the risk factors and outcomes explored. The firmest evidence supported the following conclusions.

**30 day mortality**

Increasing age is a risk factor for 30 day mortality and the results of a very large recent US-based study suggest that there may be a link between female gender and this outcome. Cardiac status, high blood pressure and obesity were not found to be independent risk factors for 30 day mortality but there was consistent evidence from a small number of studies that renal impairment affects this outcome. There was a suggestion of a link between fitness and 30 day mortality and according to EUROSTAR data, ASA class III and IV is predictive of statistically significantly worse 30 day mortality. Aneurysm size is likely to be an independent risk factor for 30 day mortality but the balance of evidence suggests no independent effect of aortic neck and aneurysm angle. The evidence relating graft configuration / device type and 30 day mortality was too limited to draw conclusions.

**Aneurysm-related mortality**

There is no indication of a link between female gender and aneurysm-related mortality. The evidence suggested that diabetes and (based on one US study) hypertension were not risk factors for this outcome. Evidence on other pre-existing conditions was lacking. On balance, analyses indicate fitness for open procedure to be linked to aneurysm-related mortality. Aneurysm size is also likely to be an independent risk factor for aneurysm-related mortality. The balance of evidence suggests no effect of aortic neck and aneurysm angle on this outcome but the balance of evidence suggests that there might be a link between device type and aneurysm-related mortality.

**All cause mortality**

Increasing age had a self-evident role in all cause mortality, but there is no indication of any link between female gender and all cause mortality. The majority of studies found that pulmonary status / COPD was an independent risk factor for all cause mortality after EVAR but evidence was lacking or inconsistent on other
comorbidities. The balance of evidence did suggest that renal impairment is an independent risk factor for all cause mortality. With the exception of a large US study, all analyses found ASA to be an independent risk factor for all cause mortality. The very limited evidence suggests that smoking status is not associated with adverse outcomes after EVAR. Aneurysm size is likely to be an independent risk factor for all cause mortality but the balance of evidence suggests no effect of aortic neck and aneurysm angle. The evidence relating graft configuration / device type and all-cause mortality was too limited to draw conclusions.

Re-intervention
The evidence suggests that age and gender were not risk factors for re-intervention. The available analyses suggest that diabetes is not a risk factor for re-intervention / conversion to open repair. One Australian study concluded that the higher the number of pre-existing conditions the greater the rates of re-intervention whilst all EUROSTAR studies found that pre-existing conditions did not tend to predict re-intervention. Single analyses of EUROSTAR data indicate no link between renal dysfunction and re-intervention after EVAR. On balance fitness and ASA status were not independent risk factors for re-intervention.

Endoleak
On balance the evidence indicates that age is an independent risk factor for type II endoleak or all types of endoleak. However, the studies consistently found that pre-existing conditions were not risk factors for endoleak. Single analyses of EUROSTAR data indicate no link between renal dysfunction and endoleak. On balance, fitness and ASA status were not independent risk factors for endoleak.

5.3 Discussion of assessment of clinical effectiveness
Currently, EVAR trial 1, EVAR trial 2 and DREAM studies represent the best randomised evidence for evaluating EVAR. EVAR trial 1 and DREAM provide evidence that EVAR reduces operative mortality compared with open repair in patients considered to be fit for both procedures. EVAR is associated with a reduction in aneurysm related mortality over the medium term (up to 4 years after randomisation in EVAR trial 1 and 2 years in DREAM) but no significant difference
in all cause mortality between EVAR and open repair at mid-term follow-up.

The reason for the failure of the short term benefit of EVAR over open repair to translate into an advantage in the longer term is unclear. One important factor is that patients requiring surgery for AAA are at a high risk of mortality. Because EVAR is a less traumatic surgical procedure than is open repair, then fewer people die as an immediate result of the procedure. However these ‘high risk patients die within a relatively short time scale and so by 4 years post-operatively the mortality rate in patients treated with EVAR or with open repair is the same. Other reasons why the mortality rate in the EVAR treated patients converges with that of the open repair patients include the higher rate of complications and the need for re-interventions in the former group.

The lack of long-term mortality benefit with EVAR was compounded by an increased rate of complications and re-interventions and these were not offset by any increase in HRQOL; possibly due to the increased level of monitoring required with EVAR due to the risk of complications.

Analysis of the EVAR trial data did not find any evidence that a benefit with EVAR over open-repair could be predicted using the CPI score for pre-operative fitness. A large number of studies have modelled risk of mortality and other adverse outcomes following EVAR. These do not provide definitive evidence but age, gender, renal impairment, fitness, ASA class and aneurysm size may be predictive of poorer 30 day survival. There may be a link between fitness for open procedure, aneurysm size and device type and aneurysm related mortality. In terms of all cause mortality, pulmonary status, renal impairment, ASA class and aneurysm size might adversely affect this outcome. We did not consistently find any risk factors for re-intervention. For the outcome of endoleak only age was found to be a possible independent risk factor.

Although measures validated for open repair have been applied to EVAR, and age, aneurysm size, ASA and clinician’s definition of ‘fitness’ do appear to be associated with outcomes, there is currently no fully validated risk scoring tool to assist clinical decision making. One study has produced an internally validated model for predicting
a wide range of short and long-term outcomes following EVAR. The model uses eight variables (aneurysm size, age, ASA score, gender, serum creatinine, aortic neck angle, infrarenal neck diameter and infrarenal neck length) to predict risk of perioperative mortality and morbidity, mid-term survival (3 and 5 years) and need for re-intervention. Further research into subgroups of patients who may benefit particularly from EVAR is warranted.

There is limited RCT evidence comparing EVAR with non-surgical management in patients unfit for open repair. EVAR trial 2 found no differences in mortality outcomes between groups but this finding cannot be taken as definitive because substantial numbers of patients randomised to non-surgical management crossed over to receive surgical repair of their aneurysm, which would be expected to dilute the difference between the arms. In effect, this trial was a comparison of EVAR with delayed aneurysm repair except that the rules governing when to intervene were not defined. A trial designed and conducted specifically to address this question would be helpful.

The results from these trials are complemented by data from registries, in particular the EUROSTAR registry data relating to devices in current use. The 30-day mortality rate of 2.3% in this registry is comparable with the 1.7% in the EVAR arm of the EVAR trial 1 RCT. In the UK NVD19 crude operative mortality following open repair of unruptured aneurysms was 6.8%, compared with 4.7% in the open repair arm of EVAR trial 1. Overall cumulative survival following EVAR was 61% with follow-up of up to 8 years.

The EUROSTAR registry provides a large sample for assessing complications after EVAR with follow-up of up to 7 years in comparison with the relatively small sample available from the trials. The cumulative rate of rupture from EUROSTAR was 3.1%, endoleak 32.5% and re-intervention 18%. Few data on rupture were available from the trials. The rate of endoleak from the trials was lower (about 20%) but the cumulative rate of re-intervention in EUROSTAR was similar to the 4-year point estimate for the EVAR group in EVAR trial 1 (20%) but lower than that from
EVAR trial 2 (26%\textsuperscript{48}), probably reflecting the lower fitness of the patient population in this trial.

Several relevant trials are in progress including ACE (EVAR vs. open repair),\textsuperscript{51} OVER (large RCT similar to EVAR trial 1 in a US population)\textsuperscript{52} and CAESAR (EVAR vs. surveillance for small aneurysms).\textsuperscript{54} A small RCT in Nottingham\textsuperscript{49} indicated that it is feasible to randomise patients with ruptured AAAs to immediate EVAR or open repair and a further trial addressing this patient group (Amsterdam Acute Aneurysm Trial)\textsuperscript{50} is in progress. The overall body of randomised evidence relevant to EVAR is thus expected to increase in the next few years.

5.3.1 Other relevant evidence

Although the clinical review focused on identifying the most rigorous and useful evidence, some study designs were precluded from consideration by the prespecified exclusion criteria. A recent study by Schermerhorn et al.\textsuperscript{98} compared outcomes following EVAR and open repair in large matched cohorts of Medicare recipients in the USA. It is discussed here because of its relevance to the economic model (see section 6.2).

This study used administrative data to identify Medicare beneficiaries who had undergone elective AAA repair during 2001–2004. To control for non-random assignment of patients to procedures, they created matched cohorts of patients after constructing logistic regression models that predicted the likelihood of undergoing EVAR (propensity score). Each patient who underwent EVAR was matched with the patient with the closest propensity score who underwent open repair. The 61,598 patients aged 67 or older who underwent AAA repair were reduced to two matched cohorts with 22,830 patients in each (45,660 patients altogether). The average age of the patients was 76 years and approximately 80% were male. Perioperative (within 30 days) and long-term (during available follow-up) outcomes were evaluated.

Mortality within 30 days was 1.2% after EVAR and 4.8% after open repair (relative risk for open repair 4.00, 95% CI 3.51, 4.56, p < 0.001), an absolute difference of 3.6%. The absolute advantage of EVAR over open repair increased with increasing
age: from 2.1% absolute risk reduction at 67–69 years to 8.5% at 85 years or older. All major perioperative medical complications were less likely after EVAR than after open repair. Conversion from EVAR to open repair was required in 1.6% of patients. Some vascular and abdominal surgical complications were more common after open repair than after EVAR, as were complications related to laparotomy. Mean length of hospital stay was 3.4 days after EVAR and 9.3 days after open repair (p < 0.001).

The early survival benefit from EVAR persisted for about 3 years in the whole population, after which time the survival curves were similar. The benefit lasted less than 18 months in patients aged 67–74 years but for at least 4 years in those aged 85 years and older. Rupture rates were higher in the EVAR group (1.8% vs. 0.5% at 4 years, p<0.001), as were AAA-related re-interventions (9.0% vs. 1.7% at 4 years, p<0.001). Laparotomy-related complications were more frequent in the open repair group (9.7% vs. 4.1% at 4 years, p<0.001).

Important features of this study were that it used a large sample drawn from routine clinical practice, although reflecting practice in the USA rather than the UK. Patients were followed to the 4-year time point, comparable to published data from the EVAR trial 1 RCT. The finding of an early mortality benefit from EVAR but no difference between groups in the longer term is similar to the data from EVAR trial 1 and DREAM trials. The study provides important data on the relationship between age and the benefit of EVAR relative to open repair. It also identified a higher rate of laparotomy-related complications in the open repair group: such complications were not taken into account in previous analyses. This may suggest that the increased risk of non-AAA related re-interventions following open repair may offset the increased risk of AAA-related re-interventions following EVAR.

Limitations of the study reflect its non-randomised design and its reliance on administrative data. The use of propensity scoring produced two cohorts closely matched on known prognostic factors but could not rule out differences between groups in unknown or unmeasured factors with an influence on prognosis. Data on aneurysm size were not available in the administrative database, so it is difficult to say whether the populations included patients not meeting UK guidelines for AAA repair. Similarly, anatomical suitability for EVAR could not be determined.
from the data available, so it is unclear how many patients were assigned to open repair because they were not suitable for EVAR.\textsuperscript{98} While, as noted above, the study reports on surgical complications and laparotomy-related complications and reinterventions, the paper does not report on EVAR-specific complications such as endoleak.

In conclusion, this large observational study\textsuperscript{98} provides data on perioperative and follow-up outcomes from large cohorts of patients treated with EVAR and open repair in routine clinical practice. These data supplement and generally support the findings of RCTs in patients with unruptured AAAs who are fit for both procedures (EVAR trial 1 and DREAM). However, the limitations of observational study design and reliance on administrative data should be borne in mind.
6 Assessment of cost-effectiveness evidence

6.1 Systematic review of existing cost-effectiveness evidence

6.1.1 Methods

A broad range of studies were considered for inclusion in the assessment of cost-effectiveness, including economic evaluations conducted alongside trials and modelling studies. Only full economic evaluations that compared two or more options and considered both costs and consequences were included.

The following databases were searched for relevant published literature: EconLIT, EMBASE, Health Economic Evaluations Databases (HEED), MEDLINE, IDEAS and NHS Economic Evaluation Database (NHS EED). Full details of the main search strategy for this review are presented in Appendix 10.1.

One reviewer assessed all obtained titles and abstracts for inclusion. The quality of the cost-effectiveness studies was assessed according to a checklist updated from that developed by Drummond et al. This information is summarised within the text of the report, alongside a detailed critique of the study and the relevance to the UK NHS. Complete versions of the checklist for each study considered are presented in Appendix 10.2.

6.1.2 Results

The systematic literature search identified 7 studies which met the inclusion criteria for the cost-effectiveness review. The cost-effectiveness review also considered the Medtronic submission to NICE. The following sections provide a detailed critique of the cost-effectiveness evidence from the included studies and an assessment of the quality and relevance of the data from the perspective of the UK NHS. A quality assessment checklist is provided for each study.
6.1.3 Cost-effectiveness studies focusing on the EVAR trial 1 population

Section 6.1.3 considers economic evaluation studies with a focus on a patient population similar to that in EVAR trial 1 (i.e. patients requiring surgery and considered fit for open repair).


Overview

This study was designed to determine whether EVAR is a cost-effective alternative to open surgery in the treatment of abdominal aortic aneurysms. The base-case was defined as 70 year old men with AAA of 5 cm in diameter. This study was conducted before the publication of trial results for either EVAR trial 1 or DREAM.

The authors developed a Markov decision model to compute life time QALYs and costs for a hypothetical cohort of patients who underwent either EVAR or open surgery. In the model, once a patient has undergone a procedure, either EVAR or open surgery, the outcomes include a successful repair or any of a number of complications. Effectiveness, resource use and cost data were derived from the literature. Figure 6.1.1 provides a schematic for the Markov model developed by the authors of this study.
Summary of effectiveness data

Effectiveness data was derived from the literature with preference given to data derived from large multi-centre studies. For open surgery, a large Canadian study was used to derive mortality and morbidity rates. For EVAR, due to there being no randomised controlled trials at the time the study was published, mortality rates were taken as an average of the three largest trials and the occurrence of long-term morbidity was estimated from other sources. It should be noted that their review found EVAR to have lower stroke, myocardial infarction, major amputation and dialysis dependent renal failure rates than open repair during primary admission. For re-interventions, probabilities for both initial procedures were derived from the literature. The study also considered the immediate and late conversions of EVAR to open surgery.

A quality adjustment factor was assigned for each year of survival of a patient who had a major morbidity, for example a quality adjustment factor of 0.4 was used for a patient who had had a major stroke. Quality adjustment for temporary conditions was achieved through subtracting disutilities from the overall quality adjusted life years estimate. Although it is not made clear in the study, it would appear that patients who are experiencing no complications are assigned a utility of 1. This would appear
inappropriate given the age and general ill-health of the patients being considered. Quality adjusted life years were discounted at a rate of 3% per annum. Table 6.1.1 presents some of the key effectiveness parameters used in the study’s model.

### Table 6.1.1 Key effectiveness parameters from Patel et al. 100

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR operative mortality (%)</td>
<td>1.2</td>
<td>Average of three studies Blum et al., 101, Goldstone et al., 102, Zarins et al., 103</td>
</tr>
<tr>
<td>Open repair operative mortality (%)</td>
<td>4.8</td>
<td>Johnston 104</td>
</tr>
<tr>
<td>Conversion of EVAR to open repair during primary procedure (%)</td>
<td>2.0</td>
<td>Weighted average of 4 studies Blum et al., 101, Mialhe et al., 105, Jacobowitz et al., 106, Zarins et al., 103</td>
</tr>
</tbody>
</table>

### Summary of resource utilisation and cost data

The costs were derived from the cost-accounting system at New York Presbyterian Hospital, as well as from the literature. For calculating the costs of the open surgery and EVAR procedures, the major resources consumed were identified and the costs calculated based on the average resource use reported in the literature. Fees for surgeons and radiologists were derived from the Medicare reimbursement rates for the appropriate Current Procedural Terminology codes. The immediate and long term costs of major long-term morbidities, such as stroke, dialysis dependent renal failure and myocardial infarction were derived from the literature. For EVAR rigorous postoperative surveillance was also conducted, with CT scanning at 1 week, 3 and 6 months, 1 year and annually thereafter. The study assumed there was no follow-up surveillance for those patients who underwent open repair. Costs were discounted at a rate of 3% per annum. Table 6.1.2 presents values for some of the key cost parameters used in the model.

### Table 6.1.2 Key resource cost parameters from Patel et al. 100

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial hospitalisation for EVAR procedure</td>
<td>$20,083</td>
<td>Assumptions and literature</td>
</tr>
<tr>
<td>Initial hospitalisation for open repair procedure</td>
<td>$16,016</td>
<td>Assumptions and literature</td>
</tr>
</tbody>
</table>
Summary of cost-effectiveness

For a hypothetical cohort of 70 year old men with AAA of 5 cm in diameter, EVAR produced more QALYs than open surgery (7.95 vs. 7.53 respectively) at a higher lifetime cost ($28,901 vs. $19,314). This yielded an ICER of $22,826 per QALY.

A wide range of sensitivity analyses were also undertaken. It was found that the ICER was sensitive to changes in mortality and morbidity rates of open surgery or EVAR, initial hospitalisation costs of EVAR or open surgery, and the conversion rate of EVAR to open repair during primary procedure. For example it was found that the mortality rate of open surgery had a large effect on the ICER, for example by halving the mortality rate of open surgery from 4.8% to 2.4% (and keeping the operative mortality of EVAR constant) the ICER increased to $43,408. Similarly, if the mortality rate of the EVAR procedure was doubled from 1.2% to 2.4%, keeping the operative mortality of open repair constant) the ICER increased to $30,064.

Table 6.1.3 presents ICERs for the base case and some of the sensitivity analyses performed by the study’s authors.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case</td>
<td>$22,836 per QALY</td>
</tr>
<tr>
<td>Discounted incremental QALYs generated by EVAR compared to open repair</td>
<td>0.42 QALYs</td>
</tr>
<tr>
<td>Discounted incremental cost of EVAR compared to open repair</td>
<td>$9587</td>
</tr>
<tr>
<td>Sensitivity analyses / Alternate assumptions</td>
<td></td>
</tr>
<tr>
<td>If open repair mortality was 2.4% instead of 4.2%</td>
<td>$43,408 per QALY</td>
</tr>
<tr>
<td>Increased initial hospitalisation costs of EVAR to $30,000</td>
<td>$48,046 per QALY</td>
</tr>
<tr>
<td>Increased rate of conversion of EVAR to open repair during primary procedure from 2% to 15%</td>
<td>$50,944 per QALY</td>
</tr>
</tbody>
</table>

Comments

General

Patel et al.\textsuperscript{107} have found that under their base case assumptions EVAR is a cost-effective alternative to open repair in 70 year old men with men with AAAs of 5 cm in diameter.
Internal validity
The largest concern with the Patel et al. study is that the study is based on non-randomised data (as the study pre-dates the publication of the randomised trials) which raises immediate issues over the accuracy of the parameter estimates due to selection bias.

External validity
There are a number of concerns with the Patel et al. study which raises questions over the relevance of the results for the UK setting. Firstly, the study is US based and also dated (it was published in 1999). Secondly, the study makes a larger number of assumptions which do not coincide with evidence provided by the subsequent RCTs (of which the results, it should be noted, were not available at the time). For example, the RCTs found no evidence that the occurrence of stroke and myocardial infarction was different between the treatment groups, 18 but Patel et al. have assumed that it was lower after EVAR, which is one factor causing the results to be in EVAR’s favour. Thirdly, the methods used to account for disutility in the immediate aftermath of the initial procedure will bias against open repair when compared with other studies due to the longer relative period of post intervention disutility assumed in the open repair arm when compared to the EVAR arm than in other studies (the study assumes a loss of 47 days of perfect health for open repair, but a loss of only 11 days of perfect health for EVAR). Subsequent studies, which are discussed at length later in this chapter, found that patients in both arms return to full health within 3 months of either EVAR or open repair. 108, 109 There are also concerns about whether the HRQOL scores are comparable to those used in the other studies, and whether they are appropriate for the UK.

It should also be noted that Patel et al. are evaluating the treatments in a patient population with AAA of diameter of 5 cm, which is smaller than recommended by current guidelines (Chapter 5).
6.1.3.2 Review of Bosch et al. (2002). Abdominal Aortic aneurysms: Cost-effectiveness of Elective Endovascular and Open Surgical Repair

Overview

Bosch et al. performed a cost-utility analysis comparing lifetime costs and QALYs for treatment with EVAR or treatment with open repair. The aim of the study was to evaluate the cost-effectiveness of EVAR compared to open repair.

The authors developed a Markov decision model comparing lifetime costs and QALYs for EVAR and open repair in a cohort of 70 year old men with AAA between 5 and 6 cm in diameter. The clinical effectiveness data for the study were derived from the published literature, which at the time did not include the two largest RCTs (EVAR trial 1 and DREAM). The authors focused on studies with large patient series and cases of both EVAR and open surgery. Resource use and cost estimates were derived from various sources which will be discussed further.

Figure 6.1.2 provides a schematic of the model used by the authors.

Summary of effectiveness data

Due to the absence of RCTs at that time a meta-analysis of the short-term results of studies to compare patients who underwent EVAR with matched patients who underwent open surgery was undertaken. The meta-analysis allowed calculation of the
operative mortality rates for each procedure as well as the rates of complications in the short run (however, it is unclear from the study what length is considered the short run). The meta-analysis found that the most commonly reported systemic and remote complications at 30 days were cardiac, cerebral, renal and pulmonary. It was assumed that these complications had a long term effect which resulted in decreased HRQOL and added long-term costs. They estimated that the probability of systemic-remote complications was considerably lower with EVAR than with open surgery (a probability of 0.13 compared with 0.32 for open repair). Following the initial treatment period, no new systemic complications could occur except when a patient underwent emergent surgical repair. In the long-term an annual average rupture rate of 0.01 for EVAR was used, with no rupture after open repair while for long-term re-intervention rates a rate of 0.08 per year was used for EVAR while 0.01 was used for open surgery. Long-term life expectancy was calculated based on age and sex specific mortality rates from life tables for the US general population, this would seem inappropriate given the general ill-health of the patient population being considered. For patients with major systemic complications, survival was adjusted with an excess mortality rate.

Quality of life weights before treatment and after recovery from either treatment were set similar to those in the general population. To show the effect the treatments had in the short term on quality of life, a 10% reduction in the first month following EVAR was assumed, while a 30% reduction for two months following open surgery was assumed. Long-term quality of life adjustments were also made for patients with cardiac, cerebral, renal or pulmonary complications. Quality adjusted life years were discounted at a rate of 3% per annum

Table 6.1.4 presents values for some of the key parameters used by the authors.

**Table 6.1.4 Key effectiveness parameters from Bosch et al.**

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality of open repair (%)</td>
<td>4.0</td>
<td>Meta-analysis of 9 studies^{111-119}</td>
</tr>
<tr>
<td>Mortality of primary EVAR (%)</td>
<td>3.0</td>
<td>Meta-analysis of 9 studies^{111-119}</td>
</tr>
<tr>
<td>Probability of immediate conversion after EVAR</td>
<td>3.0</td>
<td>Meta-analysis of 9 studies^{111-119}</td>
</tr>
</tbody>
</table>
### Summary of resource utilisation and cost data

The authors included costs for procedures (including patient time productivity costs), morbidity and mortality, and imaging in follow-up. All costs were converted to year 2000 US dollars. Procedure costs included those of the hospital, physician and patient for EVAR, open surgery, percutaneous treatment and emergent surgical repair of rupture. The hospital cost and physician fees were derived from Medicare reimbursement rates by using Diagnosis Related Groups. Patient costs were determined by multiplying the daily wage rate by the number of days spent in hospital. It should be noted that when considering patient costs the authors of the study do not appear to have accounted for other sick days which did not involve hospital stays. For costs for morbidity and mortality, if a major systemic-remote complication occurred during surgery then extra costs were added to the procedure costs. Costs of follow-up included physician visit costs, imaging costs and patient costs. In the model, patients who underwent EVAR were imaged at 3, 6 and 12 months, and annually thereafter. All costs were discounted at 3%. Table 6.1.5 presents some of the key resource costs used in the model.

#### Table 6.1.5 Key resource cost parameters from Bosch et al.\textsuperscript{110}

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular repair procedure</td>
<td>$19,642</td>
<td>Medicare</td>
</tr>
<tr>
<td>Open repair procedure</td>
<td>$23,484</td>
<td>Medicare</td>
</tr>
<tr>
<td>Follow-up imaging (per visit)</td>
<td>$483</td>
<td>Medicare</td>
</tr>
</tbody>
</table>

### Summary of cost-effectiveness

In the base case it was found that EVAR resulted in more QALYs than open repair (6.74 vs. 6.52 respectively) and also more costs ($39,785 vs. $37,606 respectively), resulting in an ICER of $9,905 per QALY. A wide range of sensitivity analysis,
including both one and two-way, were also performed. These found that the results were highly sensitive to the uncertain parameters in the model, such as the systemic complication rate, long-term failure rate and the rupture rate. For example if the annual rate for procedures in follow-up in the EVAR arm was increased from 8 to 12% then the ICER was increased to $56,630 per QALY, and if the rate exceeded 12% then the ICER was more than $100,000 per QALY. Table 6.1.6 presents the ICER for the base case of the model.

Table 6.1.6 Key cost-effectiveness results from Bosch et al.110

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case</td>
<td>$9,905 per QALY</td>
</tr>
<tr>
<td>Discounted incremental QALYs generated by EVAR</td>
<td>0.22 QALYs</td>
</tr>
<tr>
<td>Overall incremental cost of EVAR arm compared to open repair arm</td>
<td>$179</td>
</tr>
<tr>
<td>Sensitivity analyses / Alternate assumptions</td>
<td></td>
</tr>
<tr>
<td>Annual rate for procedures in follow-up after EVAR increased from 8% to 12%</td>
<td>$56,630 per QALY</td>
</tr>
<tr>
<td>Annual long-term failure rate after open surgery decreased from 1% to 0.5%</td>
<td>$54,233 per QALY</td>
</tr>
</tbody>
</table>

**Comments**

**General**
The authors of this study have found that EVAR is likely to be considered cost-effective, given typical thresholds, when compared with open repair in 70 year old men with AAA between 5 and 6 cm in diameter.

**Internal validity**
There are a number of issues with the Bosch et al. study which may have led to the results produced being inaccurate. Firstly, the fact that the values used for the parameters in the model are not based on RCT evidence (as the study pre-dates the subsequent trials) is clearly a major weakness and raises doubts about their relevance.
Secondly, in the absence of better data, the authors have been forced to make a large number of assumptions (e.g. about recovery time, cost of mortality, quality of life, number and type of additional procedures performed etc) thus limiting the robustness of the results. The authors state that the sensitivity analyses conducted test these assumptions and evaluated the influence that any uncertainty in these assumptions may have on the base case ICER. However, as only one and two-way sensitivity analyses were conducted and the results not all presented, they are unlikely to have accurately captured the uncertainty in their assumptions.

*External validity*

There are several issues with the Bosch et al. study beyond those described above which may limit the transferability of the results to a UK setting. Firstly, the inclusion of patients’ costs (productivity costs) may mean that the results of this study difficult to compare with those of the other studies which do not include patient costs in their resource use estimates. Secondly, it should also be noted that the study includes patients with an AAA of between 5 cm and 5.5 cm in diameter. Such patients would not currently be considered for surgery in the UK, where only patients with AAA of above 5.5 cm in diameter are considered for surgery. Thirdly, as the results are based on US population in a US healthcare setting the results may not be transferable to the UK due to the differences in patient population and resource use.

6.1.3.3 Review of Michaels et al. (2005). *Cost-effectiveness of endovascular abdominal aortic aneurysm repair*\(^\text{109}\)

*Overview*

This study evaluated the cost-effectiveness of EVAR compared to open repair, in patients fit for surgery (RC1), or conservative management, in those unfit for surgery (RC2) (This section of the study will be discussed later in this section of the report) . The aim of the study was to determine an optimal strategy for the use of EVAR based on the best available evidence at the time.

Effectiveness and resource use data were based on recent randomised controlled trials (EVAR trial 1 \(^\text{45}\) and DREAM\(^\text{43}\)) as well as a systematic review of the literature. The
study was conducted after the short term (30-day) operative mortality results were published from these trials but before the mid-term results were available. The authors developed a Markov model and used it to consider two separate ‘reference cases’, one of which was similar to the EVAR trial 1 population. They considered fit 70 year old patients with an AAA of 5.5 cm diameter where the choice was between EVAR and Open Surgery (RC1). The primary outcome measure for the cost-effectiveness analysis was the incremental cost per quality adjusted life year (QALY) gained. The authors used a 10 year time horizon. The evaluation was undertaken from the perspective of the National Health Service (NHS).

Figure 6.1. represents the Markov decision model for RC1.

Figure 6.1.3 Schematic of model from Michaels et al. 109. © British Journal of Surgery Society Ltd. Reproduced with permission. Permission is granted by John Wiley & Sons Ltd on behalf of the BJSS Ltd.

Summary of effectiveness data

Short-term operative mortality probabilities were taken from the EVAR trial 1 and DREAM trials.43, 45 The probabilities of re-intervention and complications were derived from a previously conducted systematic review. General mortality was taken
from standardized mortality tables for England and Wales (it should be noted that it is not stated whether these have been adjusted for the poorer health of patients with aneurysms). Aneurysm related mortality was calculated from a previous modelling study.

Utility estimates were based on published figures derived from the EQ5D tariff values for men aged 65 to 74 years old. To account for the lower health-related quality of life initially following surgery, a reduction in keeping with that seen after major surgery was applied for the first 4 weeks after open surgery and the first 2 weeks after EVAR. QALYs were discounted at a rate of 3.5% per annum.

The key effectiveness parameters for the model are reported in Table 6.1.7 below:

### Table 6.1.7 Key effectiveness parameters from Michaels et al. 109

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality of open repair (%)</td>
<td>5.80</td>
<td>EVAR trial 1, DREAM⁴³</td>
</tr>
<tr>
<td>Mortality of primary EVAR in initial 1 month period (%)</td>
<td>1.85</td>
<td>EVAR trial 1, DREAM⁴³</td>
</tr>
<tr>
<td>Probability of conversion of EVAR to open during primary procedure (%)</td>
<td>1.90</td>
<td>NICE review¹²³</td>
</tr>
<tr>
<td>Utility for living patient following treatment</td>
<td>0.8</td>
<td>Health Survey for England 1996¹²⁴</td>
</tr>
</tbody>
</table>

**Summary of resource utilisation and cost data**

Most costs were based on NHS Reference Costs for 2003-2004¹²⁵ with the mean cost being the point estimate. For the probabilistic analysis a normal distribution was assumed with standard deviation based on the assumption that 50 percent of observations were within the published interquartile range. The additional incremental cost of EVAR was estimated from data collected at the Sheffield Teaching Hospital NHS Trust. Follow-up costs for EVAR were based on NHS Reference Costs with the assumption that on average an EVAR patient with have two outpatient visits and two
CT scans per year. After open repair the average cost of a re-intervention in the EVAR arm again used NHS Reference Costs\textsuperscript{125} but was based on the case mix of re-interventions as recorded in the EUROSTAR registry.\textsuperscript{126} All costs have been discounted at a rate of 3.5\% per annum. The key resource cost parameters for the model are reported in Table 6.1.8.

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of open AAA repair</td>
<td>£4,269</td>
<td>NHS Reference Costs\textsuperscript{125}</td>
</tr>
<tr>
<td>Cost of EVAR repair</td>
<td>£8,769</td>
<td>Sheffield Teaching Hospital NHS Trust</td>
</tr>
<tr>
<td>EVAR follow-up cost per month</td>
<td>£41.50</td>
<td>NHS Reference Costs\textsuperscript{125}</td>
</tr>
<tr>
<td>Re-intervention</td>
<td>£4,790</td>
<td>NHS Reference Costs\textsuperscript{125} &amp; EUROSTAR \textsuperscript{126}</td>
</tr>
</tbody>
</table>

### Summary of cost-effectiveness

#### RC1 reference case

The base case results for RC1 showed that EVAR resulted in increased QALYs (0.1 QALYs) when compared to open surgery but also increased costs (£11,449), resulting in an ICER of £110,000 per QALY.

A variety of univariate sensitivity analyses was also undertaken, such as changing the initial incremental cost of the EVAR procedure, altering the discount rate, changing the time horizon, using mortality rates from the systematic review instead of the clinical trials and altering the re-intervention rate. The ICER went as low as £53,773 per QALY when the initial incremental cost of EVAR compared to open surgery was reduced to £0 and as high as £144,552 when the time horizon was increased to 15 years. When the mortality rates were taken from the review instead of the trials, EVAR was dominated by open surgery.
Michaels et al. also undertook a probabilistic sensitivity analysis. All of the simulations generated an ICER of greater than £30,000 per QALY (i.e. the probability of the ICER being less than £30,000 per QALY was 0).

Table 6.1.9 presents the ICER for the RC1 base case as well as some of the sensitivity analyses conducted.

Table 6.1.9 Key cost-effectiveness results from Michaels et al. (RC1)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case</td>
<td>£110,000 per QALY</td>
</tr>
<tr>
<td>Discounted incremental QALYs generated by EVAR (RC1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Discounted incremental cost of EVAR patient compared to open repair patient (RC1)</td>
<td>£11,449</td>
</tr>
</tbody>
</table>

Sensitivity analyses / Alternate assumptions

| Incremental cost of initial EVAR procedure | £53,773 per QALY |
| 15 year time horizon                     | £144,552 per QALY |

Comments

General
Michaels et al. found that EVAR does not appear to be cost-effective in an EVAR trial 1 type patient (i.e. RC1 in their analysis). This is as a result of the high incremental cost and low incremental effectiveness of EVAR, when compared with open surgery.

Internal validity
The Michaels et al. study is based on RCT evidence for the short term operative mortality rates. However, as this study was conducted before mid term results from the RCTs were available, longer term probabilities are based on the results of a review
of the literature\textsuperscript{123} and have not been derived from RCTs. As such they are open to bias and may not accurately reflect those of the patient population being considered.

The study in the base case also only considers a time horizon of 10 years (although this is extended to 15 years in sensitivity analysis). This may not be long enough to capture all the cost and outcome differences between the two trial arms.

\textit{External validity}

The study is a UK based and has been conducted from the perspective of the NHS. However as noted above, not all of the parameters have been estimated from RCTs and are thus open to bias.

\textbf{6.1.3.4 Review of Epstein et al. (2007). Modelling the long term cost-effectiveness of endovascular or open repair for abdominal aortic aneurysm\textsuperscript{108}}

\textbf{Overview}

The study evaluated the cost-effectiveness of EVAR compared to open surgery in a patient population of 74 year old men with a diagnosed AAA of diameter greater than or equal to 5.5 cm. It should be noted that several of the authors of this report were authors of this study.

The authors constructed a Markov decision model to estimate the life time costs and QALYs of male patients aged 74 years old with an AAA of diameter greater than or equal to 5.5 cm. Effectiveness and resource use data used to populate the Markov model were largely drawn from an RCT, EVAR trial 1. The model includes the risks of death from aneurysm, other cardiovascular and non-cardiovascular causes, secondary re-interventions and non-fatal cardiovascular events.

Incremental cost-effectiveness ratios were reported for the base case as well as for a number of sensitivity analyses (e.g. for different starting ages). The probability that EVAR is cost-effective at a threshold of £20,000 per QALY and £40,000 per QALY was also been reported, based on probabilistic sensitivity analyses.
Figure 6.1.4 provides a schematic of the model used in the study.

**Summary of effectiveness data**

The effectiveness data were largely taken from EVAR trial 1 although this has been supplemented by other data sources. Mortality from the initial procedure was calculated from EVAR trial 1. It was assumed that if an EVAR patient converted to open repair during the primary admission then they would have the same long term prognosis as an individual who had originally been allocated to EVAR. Mortality rates after the initial admission were estimated as 3 competing risks; (i) death from an AAA cause, (ii) death from a cardiovascular cause other than AAA, and (iii) death from a non-cardiovascular cause. Patients were also at risk of a non-fatal cardiovascular event or a readmission for a second AAA procedure, all of which were associated with higher costs and lower utilities. The model assumed that the initial operative mortality benefit of EVAR compared with open repair was eroded after two years by additional cardiovascular cause deaths after EVAR, based on the results of EVAR trial 1 and DREAM trial that there was no difference in mid term survival.
between the treatment. The model also assumed that there would be a small but persistent difference in late aneurysm related deaths between the treatments.

It has been assumed that the baseline utility of these patients is the same as that of the age-specific UK general population estimates. There is an initial loss of utility for one month post surgery with open repair resulting in a larger loss (a reduction of 0.094 compared to 0.027 for EVAR). There is also a one month loss of utility for a non-disabling stroke or MI, and a permanent utility decrease following a disabling stroke. In the base case all QALYs were discounted at a rate of 3.5% per annum.

Table 6.1.10 provides a summary of some of the key effectiveness parameters used in the model.

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probability of operative (30-day) mortality for EVAR (%)</td>
<td>5.0</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Probability of operative (30-day) mortality for open repair (%)</td>
<td>1.6</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Probability of conversion to open repair from EVAR during primary admission (%)</td>
<td>0.8%</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Mortality rate from AAA related causes during follow-up with EVAR</td>
<td>6 per 15000 patient months, assumed constant over patient’s life time</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Mortality rate from AAA related causes during follow-up with open repair</td>
<td>1 per 15000 patient months, assumed constant over patient’s life time</td>
<td>EVAR trial 118</td>
</tr>
</tbody>
</table>

**Summary of resource utilisation and cost data**

Resource utilisation and cost data for the initial EVAR or open repair surgery, a conversion to open repair during primary EVAR, and for a secondary readmission for an AAA have all been taken from the EVAR trial. Costs for non-fatal cardiovascular events have been taken from Jones 2004.127
All patients in the EVAR group have been assumed to require hospital outpatient attendances and computed tomography so as to monitor their aneurysm repair. In the base case it was assumed that two surveillance visits would be required in the first year and then one annually thereafter. The costs for these visits and scans have been taken from NHS Reference Costs. In the base case all costs were discounted at a rate of 3.5% per annum. Table 6.1.11 summarises some of the key cost parameters used by the authors in the model.

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR procedure</td>
<td>£10,726</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Open repair procedure</td>
<td>£9,578</td>
<td>EVAR trial 118</td>
</tr>
<tr>
<td>Conversion to open repair during primary EVAR</td>
<td>£42,067</td>
<td>EVAR trial 118</td>
</tr>
</tbody>
</table>

**Summary of cost-effectiveness**

In the base case, EVAR was more costly than open repair by £3800 per patient but was also produced fewer lifetime QALYs than open repair (mean -0.020 QALYs). Therefore under the base case assumptions EVAR was dominated by open repair.

However, the base case assumptions were varied in a series of secondary analyses to reflect alternative evidence and opinions about some of the key parameters in the model. In only one case was the EVAR ICER found to be under £30,000 per QALY. This occurred when the age of the initial cohort was increased from 74 to 82 years old (with a greater absolute difference in operative mortality between the treatments) and the lower long-term rate of cardiovascular death after open surgery was replaced with the assumption that there is no difference in the rate of cardiovascular death after open repair or EVAR.
ICERs for the base case and some of the sensitivity analyses conducted are presented in Table 6.1.12 below.

**Table 6.1.12 Key cost-effectiveness results from Epstein et al.**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case EVAR dominated</td>
<td></td>
</tr>
<tr>
<td>Discounted incremental QALYs generated by EVAR</td>
<td>-0.020 QALYs</td>
</tr>
<tr>
<td>Discounted incremental cost of EVAR arm compared to open repair arm</td>
<td>£3578</td>
</tr>
<tr>
<td>Sensitivity analyses / Alternate assumptions</td>
<td></td>
</tr>
<tr>
<td>Age 82 and no difference in rate of cardiovascular death after open repair or EVAR</td>
<td>£27,000 per QALY</td>
</tr>
<tr>
<td>Same hazard of cardiovascular death following each treatment strategy</td>
<td>£42,000 per QALY</td>
</tr>
<tr>
<td>No difference between EVAR and open repair of the long term rate of AAA related death</td>
<td>£42,000 per QALY</td>
</tr>
</tbody>
</table>

**Comments**

**General**

Epstein et al. found that EVAR was not a cost-effective use of resources in 74 year old male patients with an AAA of diameter of 5.5 cm or greater. Under their base case assumptions they found that EVAR was dominated by open repair (i.e. it had higher costs but worse outcomes).

**Internal validity**

The authors of this study have used RCT evidence to parameterise this model, which is the most preferred form of evidence for NICE. However, they have still had to make assumptions, particularly for the rate of cardiovascular deaths and non-fatal events in the medium term. Assumptions were also made about values of parameters after 4 years as this is the maximum length of follow-up that was available from the
EVAR trial. If these assumptions do not hold then the accuracy of the results will be questionable.

External validity
Epstein et al. have conducted the results from the perspective of the NHS. This is the appropriate perspective for NICE to make decisions. However, as noted above in the internal validity comments, if any of the assumptions made do not hold the relevance of the results to the NHS may be in question. Some data from EVAR trial 1, particularly regarding procedure costs and long term re-intervention rates of current devices, may be dated.

6.1.3.5 Review of Prinssen et al. (2007). Cost-effectiveness of conventional and endovascular repair of abdominal aortic aneurysms: Results of a randomized trial

Overview
The authors conducted a cost-effectiveness analysis of a multicentre randomized trial of EVAR compared with open repair in patients with AAA if greater than or equal to 5 cm in diameter. The analysis is conducted up to 1 year after the original procedure. All the effectiveness and resource use data were taken from the DREAM trial (therefore relevant data from EVAR trial 1 has been excluded).

Summary of effectiveness data
HRQOL was assessed using the EuroQol 5 dimensions questionnaire (EQ-5D). Questionnaires were filled in by the trial patients at baseline (upon randomization), at 3 and 6 weeks, and at 3, 6 and 12 months post-operatively. By using linear interpolation for periods between measurements, quality adjusted survival time was calculated up till one year after inclusion. A small and non-significant benefit of open repair compared to EVAR was found. Table 6.1.13 summarises the QALY outcomes from the two trial arms over a one year period.
Table 6.1.13 Key effectiveness parameters from Prinssen et al. 129

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>QALYs generated by EVAR over 1 year</td>
<td>0.72 QALYs</td>
<td>DREAM\textsuperscript{129}</td>
</tr>
<tr>
<td>QALYs generated by open repair over 1 year</td>
<td>0.73 QALYs</td>
<td>DREAM\textsuperscript{129}</td>
</tr>
</tbody>
</table>

**Summary of resource utilisation and cost data**

Costs associated with treatment and follow-up until one year after inclusion were calculated by multiplying individual patient resource use recorded in the trial by unit costs. All costs were calculated in 2003 Euros.

Costs due to lost productivity were also calculated. This took account of sick leave and travel, as well as other costs incurred by the patients and their families. Table 6.1.14 summarises the average total costs in each trial arm based on a bootstrap estimate.

Table 6.1.14 Key resource cost parameters from Prinssen et al. 129

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average total costs of EVAR patients (from bootstrap)</td>
<td>18,179 Euros</td>
<td>DREAM\textsuperscript{129}</td>
</tr>
<tr>
<td>Average total costs of open repair patients (from bootstrap)</td>
<td>13,886 Euros</td>
<td>DREAM\textsuperscript{129}</td>
</tr>
</tbody>
</table>

**Summary of cost-effectiveness**

The authors found that patients in the EVAR group experienced less QALYs than the open repair group (0.72 QALYs vs. 0.73, respectively) while also incurring more costs (18,179 euros vs, 13,886 respectively). Thus EVAR was dominated by open repair with a one year time horizon.
The authors also conducted a non-parametric bootstrapping approach to evaluate the joint uncertainty in outcomes and costs.

Table 6.1.15 presents the key cost-effectiveness results for the study.

Table 6.1.15 Key cost-effectiveness results from Prinssen et al. 129

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total average cost of EVAR patient over 1 year</td>
<td>18,595 euros</td>
</tr>
<tr>
<td>Total average cost of EVAR patient over 1 year (Bootstrapped)</td>
<td>18,179 euros</td>
</tr>
<tr>
<td>Total average cost of open repair patient over 1 year</td>
<td>13,627 euros</td>
</tr>
<tr>
<td>Total average cost of open repair over 1 year (Bootstrapped)</td>
<td>13,886 euros</td>
</tr>
<tr>
<td>Average QALYs generated by EVAR patient</td>
<td>0.72 QALYs</td>
</tr>
<tr>
<td>Average QALYs generated by open repair patient</td>
<td>0.73 QALYs</td>
</tr>
</tbody>
</table>

**Comments**

**General**

The authors of this study have found that, with a one year time horizon, EVAR is dominated, it has higher costs and lower effectiveness, by open repair in patients with an AAA with diameter of greater than or equal to 5 cm in size. It should be noted that this inclusion criteria is different to EVAR trial 1 where only patients with an AAA of 5.5 cm in diameter or greater were included.

**Internal validity**

The approach taken by the authors of this study raise issues about the validity of the results produced. Most importantly, the short time horizon means that any post 1 year differences between arms have not been captured and these may be important when determining cost-effectiveness. For example, given that mortality was higher in the open repair arm than the EVAR arm, by not extrapolating results the authors may have biased their results against the EVAR arm by not accounting for the fact that
there are more patients still alive at one year and thus more patients who can accrue QALYs over time. They have also ignored differences in complications and mortality that arise after 1 year.

External validity
The study is a Dutch study and as such the results may not be transferable to an NHS setting. The inclusion of patient costs is also not relevant for NICE decision making, however if anything this would be expected to bias the results against open repair due to the observed longer recovery time after the initial procedure in this arm.

6.1.3.6 Review of Medtronic submission. (2007). Endovascular Aneurysm Repair (EVAR) for the treatment of infra-renal Abdominal Aortic Aneurysms (AAA)

Overview
In this study the authors’ conducted a cost-utility analysis comparing EVAR with open repair. The patient population considered was that of EVAR trial 1, i.e. patients with an unruptured infrarenal AAA of at least 5.5 cm in diameter who are considered fit for open surgery. The average age of the population considered was 70 years old and 90% of patients were men.

The authors developed a two stage model to estimate the lifetime cost and QALYs of EVAR and open repair in this patient population. Firstly, a decision tree for the first 30 days post surgery (shown in Figure 6.1.5). Secondly a Markov model from 30 days post surgery until death (shown in Figure 6.1.6).

The figure below represents the short term decision tree for the first 30 days post surgery. As can be seen from Figure 6.1.5, at the end of the first 30 days patients in the EVAR arm will end up in one of 4 states; (i) Successful EVAR with no complications, (ii) EVAR with complications, (iii) Conversion to open surgery, or (iv) Death. Conversely, people in the open repair arm initially may end up in one of 3 states; (i) open repair with no complications, (ii) open repair with complications, or (iii) Death.
from Figure 6.1.5, once patients enter the 30 days post surgery Markov model, then they must be in one of 4 health states; (i) No complications requiring secondary intervention, (ii) Technical complications requiring secondary intervention, (iii) Systemic complications (split into a first year phase and then subsequent years phase), and (iv) Death.
Summary of effectiveness data

The effectiveness data used to parameterise the model were largely been drawn from EVAR trial 1. However, the effectiveness data have been supplemented with data from additional sources.

For the short term model, mortality estimates and the need for secondary intervention were based on data from EVAR trial 1. However, the risk of conversion from EVAR to open surgery is based on clinical expert opinion rather than from the trial (they have used a probability of conversion of 0.2% which is much lower than that used in other studies, for example Epstein et al. where the probability was four times larger at 0.8%, which was taken from EVAR trial 1).

The baseline risk of systemic complications (where systemic complications comprise myocardial infarction, temporary and permanent renal failure, and disabling and non-disabling stroke) for EVAR patients in the first 30 days has been estimated from the EUROSTAR dataset. The relative risk of systemic complications for open surgery versus EVAR has then been taken from a meta-analysis of observational studies and one RCT study (DREAM). The authors have assumed that the incidence rates for systemic complications follow the same pattern as for all cause mortality, i.e. that open repair patients have a higher incidence in the first 30 days post surgery whereas EVAR patients have a higher incidence from 30 days to 18 months post surgery.
Therefore, it has been assumed that over the first 18 months the number of events which occur in the two groups is equal. The authors have achieved this in the model by using the incidence rate of MI and stroke in the general UK population for the open repair group from 30 days to 18 months. Then the relative risk for EVAR was calculated such that the number of events was equal at 18 months. However, it should be noted that the numbers of events in each arm were only equal for MI and strokes and not renal failure which was considered to be closely related to the intervention itself and therefore could only occur in first 30 days, hence there was a higher prevalence of renal failure in the open repair arm. The authors have then assumed that no new systemic complications occur from 18 months onwards.

Long term risk of mortality and secondary interventions were also based on data from EVAR trial 1. The authors considered two scenarios for estimating the difference in late mortality (after 30 days). Firstly, they considered a relative risk for EVAR compared to open repair in late mortality (for any cause) of 1.055, applied for 4 years. The authors stated that this relative risk was calculated from EVAR trial 1 but it was not clear exactly how this has been done. In the second scenario the difference in mortality between the two treatments is only due to AAA mortality, and they estimate a relative risk of 1.18, again based on EVAR trial 1 results for late aneurysm mortality. It should be noted that EVAR trial 1\textsuperscript{18} reported hazard ratios (EVAR relative to open surgery) for aneurysm mortality of 0.42 (95% confidence interval 0.21-0.82) for the first 6 months and 1.15 (0.39 to 3.41) from 6 months to four years in the two periods, and the corresponding hazard ratios for total mortality in the two periods were 0.55 (95% CI 0.33 to 0.93) and 1.10 (0.80 to 1.52), respectively. The study’s authors assumed that from one month post surgery until 4 years the patients experience this as a constant relative risk of death. At 4 years it has been assumed that patients in both arms experience a risk of death similar to that of the background UK population with adjustments for increased incidence of cardiovascular death in an AAA population after surgery.

The risk of patients requiring a secondary intervention is derived from EVAR trial 1 and then supplemented with data from other sources. The total number of secondary interventions was taken from the EVAR trial, the secondary intervention rate was 1.72% per month from 2 to 6 months post surgery in the EVAR arm and 1.03% in
the open, while for post 6 months the rate in the EVAR arm was 0.27% and there were no secondary interventions post 6 months in the open repair arm. However, the percentage of these which were transabdominal, extra-anatomic or trans-femoral has then been derived from other sources, notably EUROSTAR for the EVAR group and expert clinical opinion for the open repair group.

Both patient groups have a constant risk of secondary intervention from the operation until 6 months post it. Post 6 months it is assumed that open repair patients are no longer at risk of secondary interventions while the rate of re-intervention for EVAR patients remain constant over time. The authors have also assumed that patients do not experience disutility from secondary interventions, and have the same prognosis as other patients after the re-intervention.

Utility scores for health states have been taken directly from EVAR trial 1. These found that in the first 3 months post surgery, those in the open repair arm had a lower utility (with a score of 0.67), while following that those in the EVAR arm had a slightly higher utility (with a score of 0.73). From 24 months onwards it was assumed that utility was equal in both arms (although it was age dependent). Disutility scores for the systemic complications have been drawn from several sources.

Table 6.1.16 presents the values used for some of the key parameters in the model.
Table 6.1.16 Key effectiveness parameters from Medtronic submission. 16

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality of open repair (%)</td>
<td>4.19</td>
<td>Brown et al. 26</td>
</tr>
<tr>
<td>Mortality of primary EVAR (%)</td>
<td>1.62</td>
<td>Brown et al. 26</td>
</tr>
<tr>
<td>Probability of conversion of EVAR to open (%)</td>
<td>0.2</td>
<td>Brown et al. 26 and expert opinion</td>
</tr>
<tr>
<td>Mortality all cause (monthly)- EVAR</td>
<td>0.48</td>
<td>EVAR trial 1 18</td>
</tr>
<tr>
<td>Mortality all cause (monthly)- Open repair</td>
<td>0.46</td>
<td>EVAR trial 1 18</td>
</tr>
<tr>
<td>Mortality- AAA related (monthly)- EVAR</td>
<td>0.035</td>
<td>EVAR trial 1 18</td>
</tr>
<tr>
<td>Mortality- AAA related (monthly)- Open repair</td>
<td>0.034</td>
<td>EVAR trial 1 18</td>
</tr>
</tbody>
</table>

Summary of resource utilisation and cost data

The authors also assumed that 50% of follow up scans are now duplex ultrasound and 50% are CT, with the same frequency of monitoring as the EVAR trial 1 protocol. As duplex ultrasound is cheaper than CT this reduced the overall cost of monitoring in the EVAR arm.

The costs for secondary interventions were drawn from NHS Reference Costs. The costs for the same type of intervention (e.g. transabdominal interventions) are
assumed the same for each treatment arm. However, the percentage of each type of intervention, as a proportion of the total number of secondary interventions, differs between the two treatments, with open repair having the highest proportion of the most costly procedures, making the average cost per secondary intervention higher in the open repair group. These percentages have not being based on trial evidence but instead the EUROSTAR registry in the case of the EVAR arm and clinical opinion in the case of the open surgery arm. Table 6.1.17 presents some of the values used for key cost parameters in the model.

Table 6.1.17 Key resource cost parameters from Medtronic submission.  

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of open AAA repair</td>
<td></td>
<td>EVAR trial 1</td>
</tr>
<tr>
<td>Cost of EVAR repair</td>
<td></td>
<td>Multi-centre audit</td>
</tr>
</tbody>
</table>

**Summary of cost-effectiveness**

The authors found that in the base case patients treated with EVAR were expected to receive more QALYs than those treated with open surgery but at a higher cost. This resulted in an incremental cost-effectiveness ratio of £15,681 per QALY for EVAR when compared with open repair.

The study’s authors have also conducted univariate sensitivity analyses for all of the parameters in the model. They used the values for the lower and upper confidence limits of each parameter in the model. They found that the ICER was most sensitive to the short-term relative risk of operative mortality.

Table 6.1.18 presents ICERs for the base case and sensitivity analysis where the short term relative risk of mortality has been varied.
Table 6.1.18 Key cost-effectiveness results from Medtronic submission. 16

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case</td>
<td>£15,681 per QALY</td>
</tr>
<tr>
<td>Discounted incremental QALYs generated by EVAR</td>
<td></td>
</tr>
<tr>
<td>Discounted incremental cost of EVAR patient compared to open repair patient</td>
<td></td>
</tr>
<tr>
<td>Sensitivity analyses / Alternate assumptions</td>
<td></td>
</tr>
<tr>
<td>Lower confidence limit for short-term relative risk of mortality</td>
<td></td>
</tr>
<tr>
<td>Upper confidence limit for short-term relative risk of mortality</td>
<td></td>
</tr>
</tbody>
</table>

Comments

General
The authors of this study have found that under their base case assumptions, EVAR is a cost-effective use of resources when compared with open surgery in the EVAR trial 1 patient population (i.e. patients with an average age of 70 years old, 90% of whom are men and with AAA of at least 5.5 cm in diameter) assuming a cost-effectiveness threshold of £20,000 per QALY.

Internal validity
The first issue relates to assumptions made about the rate of systemic complications (renal, cardiac and cerebrovascular events). In particular, the Medtronic analysis assumed that no new systemic complications occurred after 18 months; that there were no new cases of renal failure after 30 days; and that open repair patients have a higher incidence of all systemic complications after 30 days but EVAR have a higher incidence from 1 to 18 months such that they had equal incidence at 18 months. To test whether these assumptions affected the results, we conducted an additional sensitivity analysis using the Excel model supplied to us by Medtronic. We set the rates of renal failure and cardiovascular complications in the first 30 days and in the long term model to be the same after EVAR and open repair (odds ratios and hazard ratios equal to 1). We found that there was only a small difference (ICER = £18,000)
compared to the Medtronic base case (ICER = £15681) and we conclude that these assumptions do not affect the overall conclusions of the Medtronic model.

Secondly, the authors assume that there is no disutility associated with secondary interventions and no risk of perioperative complications. If these do not hold then the assumptions bias the results in favour of EVAR being cost-effective as EVAR has a higher rate of secondary interventions.

Fourthly, Medtronic also assume that mortality is the same in both arms from 4 years onwards. This model assumption is not supported by the results of the EVAR trial 1 and DREAM trials which both found no difference in survival at 4 years.

**External validity**

In addition to the key issues discussed above there are other issues which may affect the validity of the results for the UK setting. Most importantly, for EVAR resource use,
6.1.3.7 Discussion of EVAR trial 1 type population models

The studies considered above have conflicting results with some finding EVAR to be a cost-effective use of resources (Medtronic 16, Patel et al.,107 Bosch et al. 110) while others finding it a non cost-effective use of resources (Epstein et al., 108 Michaels et al., 109 Prinssen et al. 129). The studies are considered separately below, in light of the evidence provided by the other studies.

Patel et al. 107 have found that under their base case assumptions EVAR is a cost-effective alternative to open repair in 70 year old men with men with AAAs of 5 cm in diameter. This contrasts with UK studies (i.e. Epstein et al.108 and Michaels et al.109) which have found that EVAR is not cost-effective when compared with open repair in similar, if not identical, patient groups. Other authors (e.g. Prinsenn et al.129) have argued that the key reason for the contradictory results produced by Patel et al. is that the combined and lasting mortality and severe morbidity rate used by the authors (1.1% for EVAR versus 9.1% for open repair) was far too optimistic in favour of EVAR and that such a benefit was not shown in EVAR trial 1 or the DREAM trial. As the study is US based, and given the other issues identified it does not appear possible to draw any conclusions from it about the cost-effectiveness of EVAR with regards to a UK NHS setting.

Bosch et al.110 found that EVAR is likely to be considered cost-effective, given typical thresholds, when compared with open repair in 70 year old men with AAA between 5 and 6 cm in diameter. This contrasts with other more recent studies (e.g. Epstein et al. 108 and Michaels at al. 109), which have found EVAR not to be a cost-effective use of resources in similar patient groups. As Bosch et al. has been parameterised based on non RCT data and the study is US based it does not appear reasonable to transfer it conclusions to a UK NHS setting.

Michaels et al.109 found that EVAR does not appear to be cost-effective in an EVAR trial 1 type patient (i.e. RC1 in their analysis). The high incremental cost and low incremental effectiveness of EVAR, when compared with open surgery, in patients who are fit for open surgery (RC1) is consistent with the results of the other recent
study\textsuperscript{108}). However, the study has not made use of mid-term results from EVAR trial 1 as they were not available at the time to the authors

Epstein et al.\textsuperscript{108} found that EVAR was not a cost-effective use of resources in 74 year old male patients with an AAA of diameter of 5.5 cm or greater. Under their base case assumptions they found that EVAR was dominated by open repair (i.e. it had higher costs but worse outcomes). This study was adapted to be used for the economic model presented in Section 6.2 of this report.

Prinssen et al.\textsuperscript{129} found that, with a one year time horizon, EVAR is dominated by open repair (it has higher costs and lower effectiveness) in patients with an AAA with diameter of greater than or equal to 5 cm in size. The approach taken by the authors of this study raise issues about the validity of the results produced. Most importantly, the short time horizon means that any post 1 year differences between arms have not been captured. However, despite there been no extrapolation of results over the patients lifetimes the conclusions to appear to be consistent with those for Epstein et al.\textsuperscript{108} and Michaels et al.\textsuperscript{109} These three papers appear to be the most relevant published studies for a UK perspective.

The authors of the unpublished Medtronic study\textsuperscript{16} found that under their base-case assumptions, EVAR is a cost-effective use of resources when compared with open surgery in the EVAR trial 1 patient population. This contradicts the results found by both Michaels et al.\textsuperscript{109} and Epstein et al.\textsuperscript{108}, which found that in the same population EVAR was not a cost-effective use of resources. Section 6.2 presents a decision model comparing EVAR and open repair that investigates the main assumptions made by each of these authors in more detail. Table 6.1.19 summarises the studies and provides the base case cost-effectiveness results
Table 6.1.19 Summary of studies for EVAR trial 1 type population

<table>
<thead>
<tr>
<th>Study</th>
<th>Summary</th>
<th>Patient population</th>
<th>QALYs</th>
<th>Costs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michaels et al. (RC1) 109</td>
<td>Markov model comparing EVAR with open repair</td>
<td>Fit 70 year old patients with an AAA of 5.5 cm diameter</td>
<td>0.10</td>
<td>£11,449</td>
<td>£110,000 per QALY</td>
</tr>
<tr>
<td>Bosch et al. 110</td>
<td>Markov model comparing EVAR with open repair</td>
<td>70 year old men with AAA between 5 and 6 cm in diameter</td>
<td>0.22</td>
<td>$179</td>
<td>$9,905 per QALY</td>
</tr>
<tr>
<td>Patel et al. 107</td>
<td>Markov model comparing EVAR with open repair</td>
<td>70 year old men with AAA of 5 cm in diameter</td>
<td>0.42</td>
<td>$9587</td>
<td>$22,836 per QALY</td>
</tr>
<tr>
<td>Epstein et al. 108</td>
<td>Markov model comparing EVAR with open repair</td>
<td>Male patients aged 74 years old with an AAA of diameter greater than or equal to 5.5 cm</td>
<td>-0.020</td>
<td>£3578</td>
<td>EVAR dominated</td>
</tr>
<tr>
<td>Prinssen et al. 129</td>
<td>Within trial analysis comparing EVAR with open repair</td>
<td>Fit patients with AAA of greater than or equal to 5 cm in diameter</td>
<td>-0.01</td>
<td>4968 euros</td>
<td>EVAR dominated</td>
</tr>
<tr>
<td>Medtronic 16</td>
<td>Markov model comparing EVAR with open repair</td>
<td>Patients with an average age of 70 years old, 90% of whom are men and with AAA of at least 5.5 cm in diameter</td>
<td></td>
<td></td>
<td>£15,681 per QALY</td>
</tr>
</tbody>
</table>

6.1.4 Cost-effectiveness studies focusing on the EVAR type 2 population

Section 6.1.4 considers economic evaluation studies with a focus on a patient population similar to that in EVAR trial 2 (i.e. patients considered unfit for open repair).

\textbf{Overview}

This study evaluated the cost-effectiveness of EVAR compared to open repair, in patients fit for surgery (RC1), or conservative management, in those unfit for surgery (RC2). The aim of the study was to determine an optimal strategy for the use of EVAR based on the best available evidence at the time. The study was published before the results of the EVAR trial 2 were available.

Effectiveness and resource use data were based on recent randomised controlled trials (EVAR and DREAM) as well as a systematic review of the literature. The authors developed a Markov model and used it to consider two separate ‘reference cases’, one of which, RC1, was discussed in the previous section. In this section we will consider their modelling of 80 year old patients with an AAA of 6.5 cm diameter, who were considered unfit for open surgery, where the choice was between EVAR and conservative management (RC2). The primary outcome measure for the cost-effectiveness analysis was the incremental cost per quality adjusted life year (QALY) gained. The authors used a 10 year time horizon. The evaluation was undertaken from the perspective of the National Health Service (NHS).

The model for RC2 is similar to that of RC1 (Figure 6.1.3), with the surgery arm being replaced by a conservative management arm. Conservative management in this model excludes the option for elective surgery.

\textit{Summary of effectiveness data}

Short-term operative mortality probabilities were taken from the EVAR and DREAM trials (EVAR\textsuperscript{45} and DREAM\textsuperscript{43}). However, it should be noted that these trials were conducted in patient populations who were considered fit for open repair and thus the mortality probability of EVAR found might not be applicable to the less healthy patient population considered here. The probabilities of re-intervention and complications were derived from a previously conducted systematic review. General
mortality was taken from standardized mortality tables for England and Wales. Aneurysm related mortality was calculated from a previous modelling study.

Rupture rates for conservative management were based on three published studies (Cronenwett et al., Bernstein and Chan and Nevitt et al.) and are a function of aneurysm size. Expansion rates were also taken from other studies. It should be noted that these studies are dated (all studies were published before 1992) and may not accurately reflect current natural histories with untreated aneurysm.

Utility estimates were based on published figures derived from the EQ5D tariff values for men aged 65 to 74 years old. To account for the lower health-related quality of life initially following surgery, a reduction in keeping with that seen after major surgery was applied for the first 2 weeks after EVAR. QALYs were discounted at a rate of 3.5% per annum.

The key effectiveness parameters for the model are reported in Table 6.1.20 below:

Table 6.1.20 Key effectiveness parameters from Michaels et al.

<table>
<thead>
<tr>
<th>Key parameters</th>
<th>Values</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality of primary EVAR for 1st month post surgery (%)</td>
<td>1.85</td>
<td>EVAR trial 1 &amp; DREAM</td>
</tr>
<tr>
<td>Probability of conversion of EVAR to open</td>
<td>1.9%</td>
<td>NICE review</td>
</tr>
<tr>
<td>Utility for living patient following treatment</td>
<td>0.8</td>
<td>Health Survey for England</td>
</tr>
</tbody>
</table>

**Summary of resource utilisation and cost data**

Most costs were based on NHS Reference Costs for 2003-2004 with the mean cost being the point estimate. For the probabilistic analysis a normal distribution was assumed with standard deviation based on the assumption that 50 percent of observations were within the published interquartile range. The procedure cost of EVAR was assumed to be the average national NHS reference cost for open surgery.
plus an additional incremental cost of EVAR estimated from data collected at the Sheffield Teaching Hospital NHS Trust. Follow-up costs for EVAR were based on NHS Reference Costs with the assumption that on average an EVAR patient with have two outpatient visits and two CT scans per year. It is not clear from the published paper if patients in the no surgery arm received continuing surveillance. The average cost of a re-intervention in the EVAR arm again used NHS Reference Costs but was based on the case mix of re-interventions as recorded in the EUROSTAR registry. All costs have been discounted at a rate of 3.5% per annum. Table 6.1.21 summarises the key resource cost parameters from the study.

Table 6.1.21 Key resource cost parameters from Michaels et al. 109

<table>
<thead>
<tr>
<th>Key resources</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of EVAR repair</td>
<td>£8,769</td>
<td>Sheffield Teaching Hospital NHS Trust</td>
</tr>
<tr>
<td>EVAR follow-up cost per month</td>
<td>£41.50</td>
<td>NHS Reference Costs 125</td>
</tr>
<tr>
<td>Re-intervention</td>
<td>£4,790</td>
<td>NHS Reference Costs 125 &amp; EUROSTAR 126</td>
</tr>
</tbody>
</table>

**Summary of cost-effectiveness**

**RC2 Reference case**

The base case results for RC2 showed EVAR resulted in increased QALYs (1.64 QALYs) compared to conservative management but also extra costs (£14,077), resulting in an ICER of £8,579 per QALY.

A variety of sensitivity analyses was also undertaken on the RC2 reference case. The ICERs for the RC2 group ranged from £5,215 per QALY (when initial incremental cost of EVAR was reduced to £0) to £19,971 per QALY (when the time horizon was reduced to 5 years).

Michaels et al. also undertook a probabilistic sensitivity analysis. All of the simulations generated an ICER of less than £30,000 per QALY (i.e. the probability of
the ICER being less than £30,000 per QALY was 1). Table 6.1.22 below presents the ICER for the RC2 base case as well as some of the sensitivity analyses conducted.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case (RC2) ICER</td>
<td>£8,579 per QALY</td>
</tr>
<tr>
<td>Discounted mean incremental QALYs generated by EVAR compared to no surgery (RC2)</td>
<td>1.64</td>
</tr>
<tr>
<td>Discounted mean incremental cost of EVAR compared to no surgery (RC2)</td>
<td>£14,077</td>
</tr>
</tbody>
</table>

**Sensitivity analyses / Alternate assumptions**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR procedure costs the same as average cost of open repair</td>
<td>£5,215 per QALY</td>
</tr>
<tr>
<td>5 year time horizon</td>
<td>£19,971 per QALY</td>
</tr>
</tbody>
</table>

**Comments**

**General**

Michaels et al. 109 found that EVAR may be a cost-effective intervention in patients who are unfit for open surgery. With a ten year time horizon they found, that when compared to medical management, EVAR resulted in more QALYs at a higher cost, resulting in an ICER of £8,579 per QALY.

**Internal validity**

This study was conducted before EVAR trial 2 published long term results and has thus instead relied on other sources to parameterise the model. Some of the parameters have been derived from non randomised sources and are thus open to bias. The use of the EVAR trial 1 operative mortality rate also appears inappropriate given the differences between the patient group considered (one that is unfit for open surgery) and the EVAR trial 1 population (all of whom were considered fit for open surgery).
External validity
The study is UK based and has been conducted from the perspective of the NHS. However, estimates of aneurysm growth rates and rupture rates in untreated patients from the literature may not reflect those expected in patients anatomically suitable for EVAR.


Overview
EVAR trial 2 investigated whether EVAR improved survival compared with no intervention in patients who were considered unfit for open repair. Although it was not explicitly a cost-effectiveness study, we review it in this section because the study reported life expectancy and costs, and there have been no other cost-effectiveness analyses published in the light of the results of this trial. The mean age of patients in the EVAR arm was slightly higher than that in the no intervention arm (76.8 years versus 76.0 years respectively). The mean AAA diameter was also marginally larger in the EVAR arm than the no intervention arm (6.4 cm versus 6.3 cm respectively).

In the trial patients were followed up over 4 years and data on mortality, HRQOL (measured by the EQ-5D and the SF36) and resource use were collected over this period.

Summary of effectiveness data
The EVAR trial 2 found that the 30-day operative mortality rate for the EVAR group was 9%. The no intervention group was found to have a rupture rate of 9.0 per 100 person years. By the end of the four years, overall mortality was around 64%, and this did not significantly differ between the two trial arms. The trial also found no significant difference in aneurysm related mortality.
HRQOL data was collected from the EVAR arm patients at 1, 3 and 12 months after the operation, while for the no intervention arm it was collected from the patients at 2, 4 and 13 months after randomisation (this was based on the assumption that it would take one month following randomisation for the EVAR procedure to be performed. No clear and consistent differences in HRQOL between the two trial arms was found.

Summary of resource utilisation and cost data

Resource use and cost estimations were calculated using the same methods as those used in EVAR trial 1 (e.g. data on resource use was collected using CRFs and then multiplied by unit costs to calculate total costs). Resources considered included, among others, initial procedure resource use, hospital stay, secondary AAA procedures, outpatient visits and surveillance using CT.

The study found that the EVAR arm had considerably greater mean hospital costs per patient than those in the no intervention arm (£13,632 versus £4,983 respectively).

Summary of cost-effectiveness

The study found that EVAR did not improve HRQOL over the period, had a high 30-day operative mortality rate, had no 4 year survival benefit, and had considerably higher costs than the no intervention arm. Therefore in the patient group considered (Patients of around 66 years of age with AAA of roughly 6.5 cm in diameter) it appeared that EVAR may be dominated by the no intervention arm (i.e. EVAR has higher costs and worse outcomes).

Comments

General

The EVAR trial 2 investigated whether EVAR improved survival compared with no intervention in patients who were considered unfit for open repair. This study found that EVAR led to no improvement in outcomes but a higher cost.

Internal and external validity
In Chapter 5 several issues which complicate the analysis of the EVAR trial 2 were discussed. These included the long delay between randomisation and procedure and a number of individuals in the no intervention arm who received EVAR or open repair. These raise issues over the validity of the study in terms of whether it accurately captures the costs and benefits of the two strategies (EVAR or no intervention) it aimed to evaluate.

6.1.4.3 Summary of studies considering EVAR trial 2 type population

Table 6.1.23 summarises the results for the two studies considering an EVAR trial 2 type population. Michaels et al.\textsuperscript{109} found EVAR to be a cost-effective use of resources when compared with medical management in AAA patients who are considered unfit for open surgery. The results produced for the RC2 group however do not coincide with the results from EVAR trial 2\textsuperscript{48}, which found the EVAR arm to be dominated by the medical management / no intervention arm (i.e. EVAR was both more costly and with similar survival at 4 years). However as discussed above there were issues with the EVAR trial 2 which may mean its results do not accurately reflect the costs and benefits of the intended strategies. Section 6.2.3 presents an economic model which aims to add to the evidence from the RCT, by bringing together the available evidence costs and outcomes in treated patients with the limited data on natural history in untreated patients, to compare the strategies of surgery, no surgery or watchful waiting.
Table 6.1.23 Summary of studies for EVAR trial 2 type population

<table>
<thead>
<tr>
<th>Study</th>
<th>Summary</th>
<th>Patient population</th>
<th>Incremental QALYs of EVAR</th>
<th>Incremental Costs of EVAR</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michaels et al. (RC2)</td>
<td>Markov model comparing EVAR with medical management</td>
<td>80 year old patients with an AAA of 6.5 cm diameter, who were considered unfit for open surgery</td>
<td>1.64 QALYs</td>
<td>£14,077</td>
<td>£8,579 per QALY</td>
</tr>
<tr>
<td>EVAR trial 2</td>
<td>Within trial analysis comparing EVAR with no intervention</td>
<td>76 year old patients with mean AAA diameter of roughly 6.3 cm who are considered unfit for open repair. cm respectively).</td>
<td>Not stated</td>
<td>£8,649</td>
<td>EVAR dominated by no intervention arm</td>
</tr>
</tbody>
</table>

6.2 Independent Economic Assessment

6.2.1 Introduction

The York economic assessment is divided into two complementary parts. The first part will compare the cost-effectiveness of EVAR versus open repair, in patients with large aneurysms. This analysis assumes that the decision to operate has already been taken.

The second part of the York economic assessment estimates the cost-effectiveness of policies about when, as well as how, the aneurysm repair should be carried out. As well as EVAR and open repair, we consider no surgery and watchful waiting as alternative policies.

In all the analyses, we stratify our results according to three key patient characteristics: age, fitness (risk of operative mortality) and aneurysm size. Each variable affects the parameters of the model, and therefore the decision, in a distinct way. Chapter 5 found age to be a risk factor for operative mortality in most studies and for long term survival, independent of aneurysm diameter and other factors.
Fitness, in this model, represents pre-existing conditions examined in Chapter 5 such as cardiac, pulmonary or renal insufficiency which might be predictive of operative mortality. However, the large number of combinations of potential risk factors and levels would make the presentation of results cumbersome if stratified in this way. It is more convenient to express fitness according to a single scale. In this analysis we define four levels of operative fitness:

- **Good** fitness, or no pre-existing conditions affecting operative mortality
- **Moderate** fitness, with twice the odds of operative mortality, compared with a person of the same age and aneurysm size with good fitness
- **Poor** fitness, with four times the odds of operative mortality, compared with a person of the same age and aneurysm size with good fitness
- **Very poor** fitness, with eight times the odds of operative mortality, compared with a person of the same age and aneurysm size with good fitness

From a clinical perspective, these relative (un)fitness scores could in principle arise from any combination of factors. For example, Chapter 5 showed the evidence on the use of the Glasgow Aneurysm Score (GAS) to predict early and late mortality in EVAR and open repair. Unfortunately, no scoring system has achieved widespread acceptance. Furthermore, in practice, clinicians are skilled at subjectively assessing “fitness” and Chapter 5 showed that these assessments are predictive of both short and long term mortality after surgery. Therefore, for this analysis, we have used a general “fitness” score as defined above.

The structure of Section 6.2 is as follows. Section 6.2.2 describes the methods and results for the York model of EVAR compared with open repair. Section 6.2.3 describes the methods and results of a model for the comparison of surgery with watchful waiting. The chapter concludes with a discussion.

### 6.2.2 Comparison of EVAR and open repair

#### 6.2.2.1 Methods comparing EVAR and open repair in patients with aneurysm of 5.5 cm or more and considered fit for open repair
Overview

The model compares a strategy of open repair with that of EVAR, for patients with a diagnosed AAA of diameter at least 5.5 cm and considered fit for open repair. The perspective of the model is that of the UK NHS. The measure of health benefit is expected quality-adjusted life years (QALY) over the patient’s life time. The price year is 2007 and all costs are measured in UK pounds. Costs and health benefits in future years were discounted at a rate of 3.5% per year. The model is closely based on a previously published model undertaken by some of the assessment team. The main difference is that this model extends the analysis for patients of different ages, fitness levels and aneurysm sizes at the time of the decision to undertake surgery. The base-case model assumed that these factors influenced baseline risks, but that the effect of treatment on operative mortality (odds ratio of EVAR vs open repair) was constant for all patient groups.

The analysis seeks to provide estimates of cost-effectiveness of managements options for all patients in the relevant AAA populations. However, it should be emphasised that most RCT and registry data on EVAR relate to men (see Chapter 5). The cost-effectiveness of EVAR versus open repair in women is explored in a secondary analysis, given the limited data available. Furthermore, untreated rupture rates may differ between men and women and the implications of this are discussed in the model comparing surgery with watchful waiting in Section 6.2.3.

Model structure
The model starts after the decision to operate has been made. The structure is shown in Figure 6.2.1. Patients enter the model and have a primary aneurysm repair procedure (i.e., either EVAR or open repair). Following this, patients may die, convert to open repair, or survive the procedure. Survivors pass into a Markov cohort model to estimate lifetime costs and QALYs. It has been assumed that patients who convert from EVAR to open repair during the primary admission have the same long-term prognosis as patients initially undergoing open repair. Unlike the model shown in Epstein et al.,\textsuperscript{108} this model does not estimate the incidence of cardiovascular complications such as stroke and myocardial infarction, as the clinical review (Chapter 5) found no evidence that the incidence of these events differed between treatments in the short or long term.

**Parameter estimation**

Operative mortality: Equation 1

Estimation of odds ratio of the treatment effect

The treatment effect for operative mortality was obtained from the synthesis of the RCTs reported in Chapter 5 (DREAM\textsuperscript{44}, EVAR trial 1\textsuperscript{18} Cuypers et al. \textsuperscript{46}). The pooled
The odds ratio for 30-day mortality from these trials is 0.35 (95% CI 0.19 to 0.63). The base-case analysis considers the odds ratio for treatment effect to be constant (proportional) for all patient groups. This assumption has been investigated in two studies (see Chapter 5). Brown et al. examined the impact of varying fitness level (assessed by a modified version of the CPI fitness score) on data from the EVAR trial and found no significant interaction (p=0.28) when fitness was considered a continuous variable. Schemerhorn et al. compared operative mortality in a non-randomised cohort of Medicare beneficiaries, adjusting by a propensity score to try to control for selection bias. They found that the odds ratio for treatment effect was similar across all age groups, although the odds ratio tended to be greatest in the youngest (and therefore fittest) patients: the odds ratio for EVAR vs OR for all ages was 0.25 (0.22, 0.28), and for ages 67-69 years was 0.16, (0.13, 0.20).

Estimation of the baseline risk of operative mortality

The probability of operative mortality after EVAR was estimated for different patient groups. This represents the baseline risk of death at 30 days. A logistic regression was constructed, using individual patient data from patients enrolled in EUROSTAR between 1994 and 2006. EUROSTAR data were used because, as described in Chapter 5, these are the most relevant to current clinical practice for EVAR. The explanatory variables were selected from those assessed in Chapter 5: age (continuous), gender, smoking status, ASA status III or IV, pre-existing conditions, renal function, fitness for open procedure, aneurysm size (in 0.5 cm increments), aortic neck and aneurysm angle, aortic neck length and graft configuration and device type. To reflect improved outcomes arising from changes in patient selection, devices and procedures, a variable was included to indicate whether the patient was enrolled after 31 December 1999. The results of the regression are shown in Table 6.2.1 for the statistically significant variables. The predicted probabilities of operative mortality after EVAR and open repair calculated in the base-case model are shown in Table 6.2.2, for patients of good, moderate and poor fitness at various ages and aneurysm sizes. Fitness is defined in a general way as previously described (Section 6.2.1), such that a patient with good fitness of a given age and aneurysm size is assumed to have none of the risk factors in Table 6.2.1, a patient with moderate fitness is assumed to have twice the odds of operative mortality compared with good
fitness and a patient with poor fitness to have four times the odds of operative mortality of a patient with good fitness.

Table 6.2.1. Results of logistic regression of deaths within 30 days of EVAR, from the EUROSTAR data 1994-2006. Equation 1 in Figure 6.2.1

<table>
<thead>
<tr>
<th>Patients included in the model</th>
<th>9667</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>230</td>
</tr>
<tr>
<td>Log likelihood</td>
<td>-992</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>SE (coefficient)</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per year age over or under 74</td>
<td>0.07</td>
<td>1.074</td>
</tr>
<tr>
<td>Per cm in AAA over or under 5.5</td>
<td>0.30</td>
<td>1.347</td>
</tr>
<tr>
<td>Older device</td>
<td>0.43</td>
<td>1.537</td>
</tr>
<tr>
<td>Unfit for open surgery</td>
<td>0.63</td>
<td>1.879</td>
</tr>
<tr>
<td>Renal condition</td>
<td>0.68</td>
<td>1.974</td>
</tr>
<tr>
<td>ASA III or IV</td>
<td>0.70</td>
<td>2.023</td>
</tr>
<tr>
<td>Constant</td>
<td>-4.89</td>
<td></td>
</tr>
</tbody>
</table>
Table 6.2.2. Predicted probabilities of operative mortality after EVAR and open repair in the base-case model in patients of good, moderate and poor fitness, for different ages and aneurysm diameters.

<table>
<thead>
<tr>
<th>Aneurysm 5.5 cm</th>
<th>EVAR</th>
<th>Open repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitness</td>
<td>Age, years</td>
<td>70</td>
</tr>
<tr>
<td>Good</td>
<td>0.006</td>
<td>0.008</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.011</td>
<td>0.016</td>
</tr>
<tr>
<td>Poor</td>
<td>0.022</td>
<td>0.031</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aneurysm 6.5 cm</th>
<th>EVAR</th>
<th>Open repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitness</td>
<td>Age, years</td>
<td>70</td>
</tr>
<tr>
<td>Good</td>
<td>0.008</td>
<td>0.011</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.015</td>
<td>0.021</td>
</tr>
<tr>
<td>Poor</td>
<td>0.030</td>
<td>0.042</td>
</tr>
</tbody>
</table>

Operative mortality after EVAR is estimated from the logistic regression shown in Table 6.2.1, and after open repair assuming the pooled odds ratio estimated in Chapter 5 applies to all patient groups.

Long term model

Chapter 5 found that the early advantage of EVAR in terms of operative mortality diminished over the medium term, with no statistically significant difference in overall survival after about 2 years, based on the results of the EVAR trial \(^\text{18}\) and DREAM trials.\(^\text{44}\) As discussed in Chapter 5, the cause of this erosion of the early survival advantage after EVAR is unclear. One factor may be a greater risk of rupture or aneurysm related death after EVAR compared to open repair. Another factor may be a consequence of the natural variability in the fitness of the population with large AAAs. It may be that open surgery precipitates operative mortality in patients who were already at high risk from other conditions and would have died of other causes in the medium term. It is also possible that it is simply a chance finding in both trials.

To reflect this uncertainty in the reasons for the erosion of the early survival advantage after EVAR, the model was constructed in such a way that different scenarios about patient prognosis following repair of the aneurysm could be explored, based on the available evidence. The overall late mortality rate \(h(t)\) at time \(t\) can be
written as the sum of two competing risks: death from non-aneurysm cause \( h_{\text{Other}} \) (Equation 2) and late death from aneurysm cause \( h_{\text{AAA}} \) (Equation 3):

\[
h(t) = h_{\text{Other}}(t) + h_{\text{AAA}}(t)
\]

Each of these separate risks is discussed below.

**Estimation of the rate of non-aneurysm deaths more than 30 days after aneurysm repair: Equation 2**

The rate of non-aneurysm deaths in the model after than 30 days \( h_{\text{Other}}(t) \) was in turn constructed from the product of three components: the rate of non-aneurysm death in the general population \( h_0(t) \), multiplied by the relative risk in patients with large AAA after aneurysm repair \( \text{HR}_{\text{Large Aneurysm}} \), multiplied by the relative risk after an EVAR procedure, compared to open repair \( \text{HR}_{\text{EVAR}}(t) \). Formally, this can be expressed as:

\[
h_{\text{Other}}(t) = h_0(t) \times \text{HR}_{\text{Large Aneurysm}} \times \text{HR}_{\text{EVAR}}(t)
\]

**Figure 6.2.2. Rates of mortality from non-aneurysm cause after EVAR and open repair used in the base-case model for a patient aged 75, aneurysm 5.5 cm and poor fitness at baseline.**
These three components of non aneurysm death after surgery in the model are illustrated in Figure 6.2.2. Mortality rates in the general population (h0) were estimated from life tables, adjusting for aneurysm-mortality. The parameter HR_{LargeAneurysm} can be thought of as representing the general prognosis for survival free from non-aneurysm death after aneurysm repair, for a person of that fitness and aneurysm size, relative to the general population of that age. The review of risk factors in Chapter 5 found that aneurysm size at the time of the procedure was predictive of the probability of long term survival after EVAR. This is thought to be primarily cardiovascular risk. Brady et al. found a strong association between aneurysm diameter and the risk of non-aneurysm cardiovascular mortality after aneurysm repair in the UK Small Aneurysm Trial and Study: the relative risk of cardiovascular death increased by 31% for each standard deviation increase on a log scale (about 0.8 cm on the natural scale) in aneurysm diameter, after adjusting for other risk factors. We estimated the relationship between risk factors and non-aneurysm deaths using a Cox survival regression based on the EUROSTAR dataset, censoring on AAA deaths. The results of this analysis are shown in Table 6.2.3.

Table 6.2.3. Results of Cox survival analysis of the rate of non-aneurysm deaths more than 30 days following aneurysm repair, from the EUROSTAR data 1994-2006

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>SE(coefficient)</th>
<th>Hazard ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per year of age over 74</td>
<td>0.043</td>
<td>0.004</td>
<td>-</td>
</tr>
<tr>
<td>Unfit for open surgery</td>
<td>0.396</td>
<td>0.076</td>
<td>1.49</td>
</tr>
<tr>
<td>AAA 5.1-5.4 cm</td>
<td>0.185</td>
<td>0.112</td>
<td>1.20</td>
</tr>
<tr>
<td>AAA 5.5-5.9 cm</td>
<td>0.290</td>
<td>0.113</td>
<td>1.34</td>
</tr>
<tr>
<td>AAA 6-6.4 cm</td>
<td>0.429</td>
<td>0.116</td>
<td>1.54</td>
</tr>
<tr>
<td>AAA 6.5+ cm</td>
<td>0.565</td>
<td>0.108</td>
<td>1.76</td>
</tr>
<tr>
<td>Older generation</td>
<td>0.141</td>
<td>0.070</td>
<td>1.15</td>
</tr>
<tr>
<td>Pulmonary condition</td>
<td>0.250</td>
<td>0.067</td>
<td>1.28</td>
</tr>
<tr>
<td>ASA III or IV</td>
<td>0.334</td>
<td>0.070</td>
<td>1.40</td>
</tr>
<tr>
<td>Renal condition</td>
<td>0.332</td>
<td>0.076</td>
<td>1.39</td>
</tr>
</tbody>
</table>

*The hazard ratio is the exponential of the coefficient. The hazard ratio for age is not shown because this is included in the Cox analysis only as an adjustment factor. The model calculates relative risks of non-aneurysm mortality for patients with relevant risk factors compared with mortality rates in the general population of a given age.
In the decision model, patients with small (<5 cm) aneurysms and no other risk factors were assumed to have the same risk of non-aneurysm mortality as the general population of the same age and gender. As shown by the hazard ratios in Table 6.2.3, a patient with a large aneurysm at surgery (5.5 cm) would expect a rate of non-aneurysm death 34% greater than the general population of the same age, and 76% greater if the aneurysm were 6.5 cm or more at surgery.

The clinical review in Chapter 5 found that there were several factors, such as renal insufficiency and ASA class, which were strongly associated with both operative deaths and long term survival. The risk modelling shown in Tables 6.2.1 and 6.2.3 confirms these findings, and furthermore finds that these factors are associated with late non-aneurysm deaths. This correlation between factors predictive of operative death and late non-aneurysm mortality lends support to the hypothesis that open repair is precipitating deaths in the most risky patients. As described above (Section 6.2.1), here we aimed to define fitness in a general way, rather than specifying results for every possible risk factor and combination of factors. However, we need to include the correlation between early and late mortality in the model in order to estimate life expectancy for a patient of a given operative fitness. The best way to estimate this correlation would be to calculate the risk of late non-aneurysm mortality associated with each level of a validated and generally accepted operative risk scoring system. As we do not have such a risk scoring system, we illustrate the model for groups with different levels of operative fitness as follows. We consider patients with renal insufficiency to represent a moderate fitness group, with about twice the odds of operative mortality (odds ratio 1.97, Table 6.2.1) and 40% greater risk of late non-aneurysm mortality (hazard ratio 1.39, Table 6.2.3), and a patient with both renal insufficiency and ASA class III or IV to represent a group with poor fitness, with almost four times the odds of operative mortality (1.97 x 2.02 = 3.99, Table 6.2.1) and almost double the risk of late non-aneurysm mortality (1.39 x 1.40 = 1.95, Table 6.2.3). Further work will be needed to confirm these estimates of the correlation between early and late mortality in different populations using validated risk scoring systems.

**Rate of convergence of survival curves for non aneurysm mortality after EVAR and open repair (HR_{EVAR})**
Given that the EVAR trial 1 and DREAM trial found that the early survival advantage after EVAR was not maintained over the medium term (Chapter 5), it is necessary to estimate the rate of convergence of the survival curves after the primary admission (parameter \( H_{RECVAR} \), see Figure 6.2.2). A large US matched-cohort study (Schermerhorn et al, see Chapter 5)\(^98\) found that both the initial difference in operative mortality of EVAR compared to open repair, and the time taken for the survival curves to meet strongly depended on age: younger patients (67-74) had an absolute difference in operative mortality of less than 2.5% but that the proportion surviving at 18 months was the same after EVAR and open repair. On the other hand, 85 year olds had an absolute reduction of 8.5% and a difference in survival was maintained until 4 years between the groups (Figure 6.2.3). These results suggest that, even though the process causing the survival curves to converge might be unknown, the phenomenon is observed in all patient fitness groups. Furthermore, the benefit of EVAR is prolonged in those patient groups with the greatest difference in operative mortality.

The EVAR trial 1 divided the follow up into the first 6 months after randomisation and the period from 6 months (to allow for delays between randomisation and surgery) and calculated all cause mortality hazard ratios for the two periods to be 0.55 (95% CI 0.33 to 0.93) and 1.10 (0.80 to 1.52) (see Chapter 5). However, the hazard ratio for 6 months onwards is not directly useable in the model as we need the hazard ratio for non-aneurysm related mortality more than 30 days after the procedure. In the intention to treat analysis, the EVAR trial 1 found 81 deaths (7 aneurysm related) more than 30 days after procedure in patients randomised to EVAR and 71 deaths (2 aneurysm related) more than 30 days after procedure in those randomised to open repair.\(^18\) In the base-case model, we assume a hazard ratio of late non-aneurysm death of 1.072 (74 versus 69 deaths) as an estimate of \( H_{RECVAR}(t) \), given that the number of patients and mean length of follow up in the groups were similar. This is assumed to apply to the EVAR group until the non-aneurysm survival curves converge, and for non-aneurysm deaths to be the same in both arms thereafter (\( H_{RECVAR}(t)=1 \)). Sensitivity analysis explored other scenarios.
Figure 6.2.3. Survival of patients undergoing endovascular repair or open repair of abdominal aortic aneurysm, overall and according to age. Source: Schermerhorn et al. 2008, (Reproduced with the permission of NEJM 12 Feb 2008)

Estimation of the rate of late aneurysm related death: Equation 3

Hazard ratio for treatment effect for late aneurysm related deaths

Chapter 5 found that the difference in aneurysm related death between EVAR and open repair is maintained up to 4 years. Nevertheless, even if the rate of late aneurysm death is low, it is important to include it in the model if there is thought there might be a persistent difference between the rates after EVAR and open repair. The hazard ratio (EVAR relative to open repair) for aneurysm related mortality 6 months or more after randomisation estimated by the EVAR trial 1 was 1.15 (95% CI 0.39 to 3.41), with a wide confidence interval because of the few deaths included (see Chapter 5). However, this hazard ratio would seem to underestimate the difference in observed aneurysm related deaths more than 30 days after the primary procedure (7 after EVAR versus 2 after open repair in about 1250 patient years of
follow up in each arm), perhaps because some of the deaths occurred in the first 6 months. For the base-case value in the model, we estimated the hazard ratio (EVAR relative to open repair) from EVAR trial 1 for late aneurysm related deaths occurring more than 30 days after the primary procedure, censoring on other causes of death. This was estimated to be 2.46 (95% CI 0.48 to 12.7). This hazard ratio is not a randomised comparison because of different lengths of time from randomisation to surgery in the two arms. Nevertheless, this estimate is likely to be favourable to EVAR because one of the late AAA deaths in the open repair arm occurred in a patient who had crossed over to EVAR before the primary procedure. Sensitivity analysis explored other estimates.

*Baseline rate of late aneurysm related deaths more than 30 days after EVAR*

Chapter 5 found that baseline aneurysm size was associated with aneurysm related deaths after EVAR in most studies. We estimated the baseline rate of aneurysm related deaths after EVAR occurring after 30 days using the EUROSTAR dataset, for patients enrolled between January 1994 and November 2006, censoring on other cause deaths. Table 6.2.4 shows the data stratified by the date of enrolment and AAA diameter at enrolment. The mean rate of late AAA deaths for recent patients was 0.4% per year in patients with large AAA (5.5 to 6.4 cm) and 1.2% per year in patients with very large AAA > 6.5 cm (Table 6.2.4). These rates are lower than found in an earlier published analysis of the EUROSTAR data, but confirm the earlier finding that rates of late aneurysm mortality after EVAR are strongly associated with aneurysm size at the time of the procedure (see Chapter 5). The higher rate in earlier enrolments might indicate improvement in devices and procedures, but could also arise because patients were followed up for a longer period, with more time for the aneurysm to expand, or more cautious patient selection.
Table 6.2.4. Late aneurysm related deaths, excluding operative mortality in patients undergoing EVAR. EUROSTAR data stratified by enrolment date and baseline AAA diameter

<table>
<thead>
<tr>
<th>Enrolment date</th>
<th>AAA size</th>
<th>N</th>
<th>Deaths by Nov 2006</th>
<th>Patient years at risk</th>
<th>Mean follow up years per patient</th>
<th>Mean rate per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 1 Jan 2000</td>
<td>&lt;5.5 cm</td>
<td>1200</td>
<td>24</td>
<td>4753</td>
<td>3.96</td>
<td>0.5%</td>
</tr>
<tr>
<td></td>
<td>5.5-6.4 cm</td>
<td>786</td>
<td>34</td>
<td>2977</td>
<td>3.79</td>
<td>1.1%</td>
</tr>
<tr>
<td></td>
<td>≥6.5 cm</td>
<td>435</td>
<td>30</td>
<td>1410</td>
<td>3.24</td>
<td>2.1%</td>
</tr>
<tr>
<td>After 1 Jan 2000</td>
<td>&lt;5.5 cm</td>
<td>2296</td>
<td>10</td>
<td>4296</td>
<td>1.87</td>
<td>0.2%</td>
</tr>
<tr>
<td></td>
<td>5.5-6.4 cm</td>
<td>2211</td>
<td>16</td>
<td>4116</td>
<td>1.86</td>
<td>0.4%</td>
</tr>
<tr>
<td></td>
<td>≥6.5 cm</td>
<td>1340</td>
<td>28</td>
<td>2311</td>
<td>1.73</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

It is uncertain whether, for any given patient, the risk of late AAA death is constant, increasing or decreasing with time from surgery. Peppelenbosch et al. estimated that the risk of late aneurysm death tended to increase with time from surgery, using EUROSTAR data for patients enrolled from 1996 to 2002. For patients with large aneurysm (5.5 to 6.5 cm) the rate of late aneurysm death was 0.3% in the first 3 years rising to 2.1% after 4 years. For patients with very large aneurysm (greater than 6.5 cm) the rate was 1% in the first 3 years rising to 8% in the fourth year.

This apparent increase in the risk of death with time from EVAR may be confounded by evolution of devices and surgical technique, as those patients with longest follow up underwent EVAR with the oldest devices. We tried to adjust for this by estimating parametric survival models, including a variable representing the year the device was fitted. Table 6.2.5 shows the results of the parametric survival regression using the EUROSTAR data 1994-2006, for a log-normal, a Weibull and an exponential (constant hazard) distribution. Figure 6.2.4 shows the rate of aneurysm death over time predicted by each regression model (for patient aged 74 with aneurysm 5.5 cm). The Weibull and log normal models estimate similar rates of aneurysm deaths during the first five years, the hazard increasing over time for these patients to a maximum of 0.5%. The Weibull model predicts that the hazard is gradually increasing over time. The log-normal model predicts that the rate is gradually decreasing over time. The average rate (exponential model) for this patient group was 0.33%.
Table 6.2.5. Results of log-normal, Weibull and exponential survival models of the rate of aneurysm deaths more than 30 days following aneurysm repair with EVAR, from the EUROSTAR data. Equation 3 in figure 1

<table>
<thead>
<tr>
<th>Number of observations</th>
<th>8,182</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deaths</td>
<td>142</td>
</tr>
<tr>
<td>Patient months (years)</td>
<td>(19,039)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Lognormal model</th>
<th>Weibull model (base-case)</th>
<th>Exponential model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficient</td>
<td>SE</td>
<td>Coefficient</td>
<td>SE</td>
</tr>
<tr>
<td>Per year age &gt;74</td>
<td>-0.04</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>AAA size 5.5-5.9 cm</td>
<td>-0.48</td>
<td>0.52</td>
<td>0.26</td>
</tr>
<tr>
<td>AAA size 6 -6.4 cm</td>
<td>-0.64</td>
<td>0.69</td>
<td>0.27</td>
</tr>
<tr>
<td>AAA size 6.5+cm</td>
<td>-1.35</td>
<td>1.33</td>
<td>0.22</td>
</tr>
<tr>
<td>Older generation</td>
<td>-0.85</td>
<td>0.82</td>
<td>0.18</td>
</tr>
<tr>
<td>Unfit for open</td>
<td>-0.68</td>
<td>0.64</td>
<td>0.20</td>
</tr>
<tr>
<td>Intercept</td>
<td>9.16</td>
<td>-9.00</td>
<td>-8.53</td>
</tr>
<tr>
<td>Log sigma coefficient</td>
<td>0.81</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Log shape coefficient</td>
<td>0.12</td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Log likelihood</td>
<td>-731</td>
<td></td>
<td>-728</td>
</tr>
<tr>
<td>Log likelihood</td>
<td>-728</td>
<td></td>
<td>-729</td>
</tr>
</tbody>
</table>
Figure 6.2.4. Predicted rate of aneurysm related deaths more than 30 days following aneurysm repair with EVAR for a patient aged 74 years, with an aneurysm diameter 5.5 – 5.9 cm, with a recent EVAR device and fit for open surgery.

Estimated from EUROSTAR data, with an exponential model, a Weibull model and a lognormal model. Dashed lines indicate extrapolation beyond the maximum of 6 years of follow up between year 2000 and 2006

Hence there is considerable uncertainty about the relationship between late aneurysm death and time from surgery. The base-case model assumed that the rate of late aneurysm death was constant from 1 month after surgery (exponential survival model). Sensitivity analyses explored alternative scenarios. An increasing rate might correspond with a belief that the aneurysm continues to expand after EVAR, while a decreasing rate might correspond with a belief that patients at risk will be successfully identified by long term surveillance and receive appropriate treatment.

Illustration of difference in operative, aneurysm and non-aneurysm causes of death between EVAR and open repair in the base-case model

Figure 6.2.5 illustrates how predicted death rates for each cause differ in the base-case model between EVAR and open repair. The figure shows the difference in the cumulative rates of death between the treatments (in patients at risk up to time t), for all cause deaths, AAA deaths and non-AAA death. The initial difference in favour of EVAR is due to a benefit in early operative mortality. There is a continuing
difference in late aneurysm mortality between the treatments. There is also a
difference in late non-aneurysm related deaths due to there being a greater proportion
of patients with poor fitness among survivors of EVAR than survivors of open repair.
This higher rate of mortality persists until the survival curves for non late-aneurysm
death converge, in this case at about 4 years. Although there is a persisting difference
in aneurysm related deaths after the survival curves meet, this has only a small effect
on all cause mortality, because of the relatively high competing risk from deaths for
other causes (Figure 6.2.6).

Figure 6.2.5. Illustration of the difference between the treatments in the cumulative rates of death
(from AAA and non-AAA causes) estimated in the base-case decision model for a patient aged 75
years with large AAA (6.5 cm) and poor fitness.
Figure 6.2.6. Proportion surviving each year free from aneurysm death and all cause death estimated in the decision model for a patient aged 75 years with large AAA (6.5 cm) and poor fitness

Rate of late readmission for complications: Equation 4
Patients are at risk in the model of re-admission for a secondary AAA procedure. We estimate re-admissions, rather than late complications, because for the purpose of the model we are primarily interested in this outcome to predict the use of health care resources. Chapter 5 reported the treatment effect hazard ratio for re-interventions (EVAR relative to open surgery) was 2.7 (95% CI: 1.8, 4.1), but this includes re-interventions in the primary admission, the costs of which are included in the average procedure cost. The rate of readmissions to hospital after discharge from the primary admission was estimated from the EVAR trial 1 data using a Weibull model with deaths as censoring variables. The estimated coefficients of the Weibull model are shown in Table 6.2.6. Like Chapter 5, this regression did not find age and pre-existing conditions to be associated with readmissions, but unlike Chapter 5, also did not find aneurysm size to be a risk factor, perhaps because of the relatively few events.

The base-case model used this regression to predict the rate of readmissions after EVAR to be about 10% per patient-year in the first six months, declining to less than
2.5% per year by 5 years (Figure 6.2.7). The estimated hazard ratio for EVAR compared with open repair using an intention-to-treat analysis was 6.75 (SE 2.56) (Table 6.2.6). This intention to treat analysis may be favourable to EVAR because some readmissions in the open repair randomised group were in patients who had crossed over to EVAR before the primary procedure.

Table 6.2.6. Results of Weibull survival model of the rate of readmissions following aneurysm repair, using individual patient data from the EVAR trial 1. Patients are followed up within randomised groups after discharge from primary procedure. Equation 4.

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>Standard error</th>
<th>Hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of observations</td>
<td>1050</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of readmissions</td>
<td>62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-months (years)</td>
<td>29,415 (2,451)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVAR intervention</td>
<td>1.91</td>
<td>0.38</td>
<td>6.75</td>
</tr>
<tr>
<td>Constant</td>
<td>-6.12</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Log (shape parameter)</td>
<td>-0.53</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

The hazard ratio is the exponential of the coefficient.
Figure 6.2.7 Predicted rate of readmission per year over time (Weibull regression, Table 6.2.6, EVAR trial 1 data).

Dashed lines show the rates of readmission predicted beyond the maximum 4-year follow up available in the EVAR trial 1.

Resource use and costs

Costs are incurred in the model during the primary admission, in surveillance post-surgery and if the patient is readmitted to hospital for an aneurysm related complication.

Costs and resource use during the primary procedures

The costs and resources used in the procedure are shown in Table 6.2.7 for the base-case model. Expected resource use in both procedures is estimated from intention to treat analysis of the EVAR trial 1. As these data are the mean for all the patients in the trial, they include the expected costs of in-hospital complications and mortality. It is possible that given the evolution of devices and procedures, these data do not represent current practice compared with the period 1999 to 2003 when the trial was recruiting. Chapter 5 found that mean total length of stay reported in the most recent registry data was 13 days after open repair and 6 days after EVAR, considerably less than the EVAR arm of the EVAR trial 1. However, the EVAR trial 1 data represent the best available randomised comparison of resource use in the United
Kingdom and so was used for the base-case. A postal survey was conducted in January 2008 of UK hospitals to investigate whether length of stay has changed since the EVAR trial 1. The results are presented in Appendix 10.3. The survey found that length of stay may be currently lower after both EVAR and open repair than in EVAR trial 1, and that the difference in length of stay in general wards may now be greater than estimated by EVAR trial 1. This scenario was explored in sensitivity analysis. It is likely that costs will depend on the risk characteristics of the patient - for example, EVAR trial 2 found that these high risk patients used slightly more hospital resources than patients in the EVAR trial 1. However, the base-case assumed the difference in costs between EVAR and open repair was constant for all patient groups. Chapter 3 presents the list prices of each of the EVAR devices included in this review, where known.

**Intensive care during the primary procedure**

In the base-case, resource use and costs are based on the actual use of intensive care and high dependency units as recorded by the EVAR trial. There is no evidence from the survey in January 2008 that the EVAR trial 1 underestimates the difference between EVAR and open repair in patients’ length of stay in intensive care facilities (Appendix 10.3). However, mean length of stay may not represent the full opportunity cost of these facilities, because some centres require an intensive care bed to be available before commencing a procedure, in case it is needed. The survey results in Appendix 10.3 show that 86% of surgical teams would cancel an open repair procedure if an ICU bed were not available compared with 22% who would cancel an EVAR procedure. This requirement might be a reason for the longer average waiting time for open repair experienced by patients in EVAR trial 1. As well as longer waiting times for aneurysm surgery, this requirement might also affect patients waiting for other surgical procedures as there is a shortage of capacity of intensive care facilities in many surgical centres in the United Kingdom.
### Table 6.2.7. Costs and resources used in the primary procedure.

<table>
<thead>
<tr>
<th>Unit cost</th>
<th>Resource use</th>
<th>£</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVAR</td>
<td>Open</td>
<td>£</td>
</tr>
<tr>
<td></td>
<td>Sources</td>
<td></td>
</tr>
<tr>
<td>Theatre time mins</td>
<td>1593</td>
<td>1794</td>
</tr>
<tr>
<td>Preoperative days</td>
<td>467</td>
<td>541</td>
</tr>
<tr>
<td>ICU days</td>
<td>947</td>
<td>3247</td>
</tr>
<tr>
<td>HDU days</td>
<td>593</td>
<td>1252</td>
</tr>
<tr>
<td>Ward days</td>
<td>1697</td>
<td>2263</td>
</tr>
<tr>
<td>Blood ml</td>
<td>105</td>
<td>575</td>
</tr>
<tr>
<td>Contrast ml</td>
<td>14</td>
<td>0</td>
</tr>
</tbody>
</table>

**Cost £ Resource use £**

<table>
<thead>
<tr>
<th>ISD Scotland cost book 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>52STheatre services R142X 147</td>
</tr>
<tr>
<td>246NHS Ref costs 06/07QZ01A 148</td>
</tr>
<tr>
<td>NHS Ref costs 06/07</td>
</tr>
<tr>
<td>1353XCO5ZTHE</td>
</tr>
<tr>
<td>659XCO5ZHDU</td>
</tr>
<tr>
<td>246NHS Ref costs 06/07 QZ01A</td>
</tr>
<tr>
<td>289National Blood Service 149</td>
</tr>
<tr>
<td>3.5Medtronic 16</td>
</tr>
<tr>
<td>Medtronic</td>
</tr>
</tbody>
</table>

**Total cost of primary procedure 10416 9893**

**Conversion to open repair during primary procedure**

**EVAR trial 1 18, Epstein 2007 108**

**Subsequent to primary procedure (EVAR or open repair)**

| Readmission | 5936 | EVAR trial 1, Epstein 2007 |
| Outpatient visit | 83 | NHS Ref costs speciality 107 |
| Computed tomography | 108 | NHS Ref costs RA10Z |

**Surveillance post surgery**

All patients undergoing EVAR, whether they experience adverse events or not, are assumed to require regular specialist hospital outpatient attendances and computed tomography (CT) scans to monitor their aneurysm repair. In the base-case, based on the results of a survey of UK hospitals participating in the EVAR trials, it was assumed that patients require two surveillance visits during the first year and one visit per year thereafter. Patients who have open repair only require one visit in the first year and none thereafter. A survey was undertaken in January 2008 to update this information as part of this review (Appendix 10.3) which showed that these assumptions are broadly typical of current practice, though the frequency of surveillance tends to diminish with time.
Health-related quality of life (HRQOL)

Chapter 5 reported the EVAR trial 1 results, that HRQOL measured by EQ5D tended to decline in the first 3 months after randomisation but by less after EVAR, with a difference in HRQOL in favour of EVAR after three months of 0.05 (SE 0.02).HRQOL recovered by 3 to 12 months and there was no significant difference between the groups. Based on these findings, the base-case assumed that HRQOL declined by 0.077 in the six month period following open surgery and by 0.027 following EVAR. Patients without the need for re-interventions were assumed to recover to age and sex specific average population values of HRQOL six months after the procedure. Other utility values used in the model are shown in Table 6.2.8

Table 6.2.8 HRQOL values used in the model

<table>
<thead>
<tr>
<th>Mean</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 6 months after successful surgery</td>
<td></td>
</tr>
<tr>
<td>Age ≤ 75 years</td>
<td>0.78</td>
</tr>
<tr>
<td>Age &gt;75</td>
<td>0.75</td>
</tr>
<tr>
<td>Loss of utility for 0-6 months after a procedure</td>
<td></td>
</tr>
<tr>
<td>EVAR procedure</td>
<td>0.027</td>
</tr>
<tr>
<td>Open procedure</td>
<td>0.077</td>
</tr>
<tr>
<td>After readmission</td>
<td>0.077</td>
</tr>
</tbody>
</table>

HRQOL or utility is an index measure of morbidity on a scale of 1 (good health) to 0 (death) with negative utilities feasible.

Cost-effectiveness analysis

Standard decision rules were followed for the cost-effectiveness analysis using expected costs and QALYs. When there are two options under comparison, the incremental cost-effectiveness ratio (ICER) is calculated if both the cost and the benefits of EVAR exceeds open repair. If EVAR is more costly but less effective than the alternative, then EVAR is dominated and no ICER is calculated.
The same decision rule can be expressed in terms of maximising “expected net benefit”. Expected net benefit (NB) for a treatment option is defined as \( \text{NB}(\lambda) = \lambda \times \text{QALYs} - \text{Costs} \), where \( \lambda \) is the threshold cost-effectiveness used by the decision maker. This is the most convenient decision rule when there are 3 or more mutually exclusive strategies being compared, as is the case in the subsequent section, where we compare open surgery, EVAR and watchful waiting. Results are shown for thresholds of £20,000 and £30,000 per QALY.

Results are shown stratified by age, aneurysm size and operative fitness. One-way sensitivity analyses were carried out by varying key parameters in the model. A probabilistic sensitivity analysis, based on the uncertainty in all the parameters of the model, was undertaken to estimate the probability that EVAR is more cost-effective than open repair as a function of the threshold ICER.

Table 6.2.9 shows the uncertainty arising from measurement error in the estimates of each of the parameters used in the base-case model comparing EVAR and open repair. Some parameters have been estimated from regression equations (Equations 1 to 4), and therefore there may be correlations between the coefficients of these equations. The Cholesky matrix was estimated for each risk equation and used to calculate the distribution of the linear predictor for these parameters, assuming the coefficients of these equations follow a joint normal distribution.
### Table 6.2.9. Probability distributions for the parameters used in the probabilistic sensitivity analysis

<table>
<thead>
<tr>
<th>Parameter in the model (75 year old with moderate fitness and aneurysm 5.5 cm)</th>
<th>Mean of value used in model</th>
<th>Mean SE</th>
<th>Alpha</th>
<th>Beta</th>
<th>Distribution</th>
<th>Risk equation (if applicable)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probability operative mortality EVAR</td>
<td>0.011</td>
<td></td>
<td>Joint normal (Cholesky)</td>
<td>Equation 1</td>
<td>EUROSTAR (^{56})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odds ratio EVAR v Open</td>
<td>0.35</td>
<td>-1.05</td>
<td>0.373</td>
<td>Lognormal</td>
<td>Meta-analysis</td>
<td>Chapter 5</td>
<td></td>
</tr>
<tr>
<td>Conversion to open in primary admission</td>
<td>0.008</td>
<td></td>
<td>4</td>
<td>496</td>
<td>Beta</td>
<td></td>
<td>EVAR trial 1 (^{18})</td>
</tr>
<tr>
<td>Non-AAA death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio AAA popn vs general pop</td>
<td>1.86</td>
<td></td>
<td>Joint normal (Cholesky)</td>
<td>Equation 2</td>
<td>EUROSTAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cause hazard ratio after EVAR vs open</td>
<td>1.072</td>
<td>0.070</td>
<td>0.160</td>
<td>Lognormal</td>
<td>EVAR trial 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late AAA death</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio (evar vs open)</td>
<td>2.460</td>
<td>0.900</td>
<td>0.840</td>
<td>Lognormal</td>
<td>EVAR trial 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late AAA death (6month rate)</td>
<td>0.002</td>
<td></td>
<td>Joint normal (Cholesky)</td>
<td>Equation 4</td>
<td>EUROSTAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resource use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost difference EVAR less open, £</td>
<td>523</td>
<td>523</td>
<td>230</td>
<td>Normal</td>
<td>EVAR trial 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard ratio for re-interventions (evar vs open)</td>
<td>6.753</td>
<td>1.910</td>
<td>0.380</td>
<td>Lognormal</td>
<td>EVAR trial 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: where parameters are estimated by risk equations, values are shown in this table for a patient aged 70, with aneurysm of 5.5 cm and moderate fitness


6.2.2.2 Results of York economic assessment: EVAR compared with open repair for patients with large aneurysm (5.5 cm or more) and assessed as fit for open repair

Base-case results of patients with large aneurysm (>5.5 cm) and assessed as fit for open surgery

Table 6.2.10 shows the cost-effectiveness results for EVAR compared with open repair by age, aneurysm size and fitness at baseline. The results of the base-case model suggest that EVAR is unlikely to be more cost-effective than open repair in patients with good or moderate fitness. A 75 year old patient with AAA 6.5 cm, with moderate fitness, would have a predicted operative mortality of about 5.7% after open repair and 2.1% after EVAR (Table 6.2.2). The model suggests this initial advantage would be eroded from other cause mortality after 3 years, and further offset by increased costs and risks of death from complications over the remaining expected lifetime, predicted to be about 5½ years. The expected gain in QALYs is 0.022, the difference in costs is £1,979, and the ICER would be £88,775 (=1979/0.022, Table 6.2.10).

As the ICER is a ratio of incremental costs to incremental QALYs, we observe very high values of the ICER when the expected difference in QALYs between the treatments is close to zero. For example, for patients of moderate fitness, with aneurysm 6.5 cm aged 72.5, the expected difference in costs is £2,128 and the expected difference in QALYs is 0.006, with an ICER of £363,892 (=2128/0.006, Table 6.2.10). For younger patients, aged 70 with aneurysm 6.5 cm, the difference in QALYs is -0.01 and the difference in costs is £2,285, and EVAR is dominated (higher cost and fewer health benefits, Table 6.2.10).

EVAR is predicted to be more cost-effective than open repair in patients with poor fitness at a threshold of £30,000 per QALY. A 75 year old patient, with AAA diameter 5.5 cm, and with poor fitness, but nevertheless considered just suitable for open repair, would have a predicted operative mortality of about 8.5% after open repair and 3.1% after EVAR (Table 6.2.2) and an ICER of £19,105 (Table 6.2.10).
Table 6.2.10. Expected ICER by age, aneurysm size and fitness

### Good fitness

<table>
<thead>
<tr>
<th>Aneurysm Size cm</th>
<th>Age years</th>
<th>70</th>
<th>72.5</th>
<th>75</th>
<th>77.5</th>
<th>80</th>
<th>82.5</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
<tr>
<td>6</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
<tr>
<td>6.5</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
<tr>
<td>7</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
<tr>
<td>7.5</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
<tr>
<td>8</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
<td>Dom</td>
</tr>
</tbody>
</table>

### Moderate fitness

<table>
<thead>
<tr>
<th>Aneurysm Size cm</th>
<th>Age years</th>
<th>70</th>
<th>72.5</th>
<th>75</th>
<th>77.5</th>
<th>80</th>
<th>82.5</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5</td>
<td>118599</td>
<td>71964</td>
<td>50953</td>
<td>39306</td>
<td>31198</td>
<td>26484</td>
<td>22346</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>100770</td>
<td>62304</td>
<td>44748</td>
<td>34921</td>
<td>28008</td>
<td>24047</td>
<td>20485</td>
<td></td>
</tr>
<tr>
<td>6.5</td>
<td>363892</td>
<td>88775</td>
<td>51000</td>
<td>34964</td>
<td>27765</td>
<td>22351</td>
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<tr>
<td>7</td>
<td>115831</td>
<td>56678</td>
<td>37715</td>
<td>27708</td>
<td>22743</td>
<td>18820</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5</td>
<td>162735</td>
<td>63156</td>
<td>39366</td>
<td>28650</td>
<td>22217</td>
<td>18716</td>
<td>15914</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>71042</td>
<td>40766</td>
<td>28805</td>
<td>22269</td>
<td>17997</td>
<td>15516</td>
<td>13485</td>
<td></td>
</tr>
</tbody>
</table>

### Poor fitness

<table>
<thead>
<tr>
<th>Aneurysm Size cm</th>
<th>Age years</th>
<th>70</th>
<th>72.5</th>
<th>75</th>
<th>77.5</th>
<th>80</th>
<th>82.5</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5</td>
<td>26807</td>
<td>22237</td>
<td>19105</td>
<td>16742</td>
<td>14764</td>
<td>13542</td>
<td>12319</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>23454</td>
<td>19631</td>
<td>17053</td>
<td>15125</td>
<td>13499</td>
<td>12552</td>
<td>11578</td>
<td></td>
</tr>
<tr>
<td>6.5</td>
<td>28455</td>
<td>21939</td>
<td>18183</td>
<td>15687</td>
<td>13756</td>
<td>12718</td>
<td>11688</td>
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</tr>
<tr>
<td>7</td>
<td>21560</td>
<td>17373</td>
<td>14841</td>
<td>13071</td>
<td>11694</td>
<td>10955</td>
<td>10218</td>
<td></td>
</tr>
<tr>
<td>7.5</td>
<td>16755</td>
<td>13971</td>
<td>12237</td>
<td>10979</td>
<td>9996</td>
<td>9497</td>
<td>8996</td>
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</tr>
<tr>
<td>8</td>
<td>13304</td>
<td>11392</td>
<td>10196</td>
<td>9303</td>
<td>8607</td>
<td>8284</td>
<td>7967</td>
<td></td>
</tr>
</tbody>
</table>

Fitness is defined as a relative risk of operative mortality, where good fitness indicates no other pre-existing conditions and poor fitness represents 4 times greater odds of operative mortality for a person of a given age and AAA diameter.

ICER is the incremental cost-effectiveness ratio, the difference in expected costs / difference in expected QALYs. Dominated (Dom) means EVAR has less expected benefit and higher cost than open repair.

**Key**

- **ICER > 30001 or EVAR dominated**
- **20001<ICER<30000**
- **ICER<20000**
In general, the ICER of EVAR versus open repair is lower for older patients compared with younger, for patients with greater aneurysm size compared with smaller, and for patients of poorer fitness compared with better fitness (Table 6.2.10). Older patients and those with larger aneurysms and poorer fitness face increased operative mortality, making EVAR relatively more cost effective. However, the EUROSTAR data predicted that the risk of late aneurysm death after EVAR increases with aneurysm size at the time of the procedure (Equation 3, Table 6.2.5), confirming estimates made by studies on earlier EUROSTAR datasets. The increased risk of late aneurysm death causes the ICER of EVAR versus open repair to be greater for patients with aneurysm size of 6.5 cm than for patients with an aneurysm of 6 cm (Table 6.2.10).

Table 6.2.10 shows EVAR might also be cost-effective, compared to open repair, in older patients (80 years or more) with moderate fitness and very large aneurysms (7 cm or more). Although we define fitness in this analysis as “moderate” if patients have few pre-existing conditions relative to other patients of their age, operative mortality would be high in absolute terms for these patients, estimated at 6.7% after EVAR and 17% after open repair. Policies of no surgery or watchful waiting should also be considered for patients with high expected operative mortality, compared with the risk of rupture without surgery. These polices will be evaluated in Section 6.2.3.

**Secondary analyses in model comparing EVAR with open surgery**

In the comparison of EVAR with open repair, in patients for whom the treatment decision has been made, the key scenarios tested were:

- The rate of convergence in the survival curves for EVAR compared with open (HR\textsubscript{EVAR} in the base-case is 1.072, in the sensitivity analysis is 1.055). This value was used by Medtronic in their base-case model.\textsuperscript{16}
- The rate of late aneurysm related deaths (hazard ratio in the base-case is 2.46, in the sensitivity analysis is 1.00). This value was used by Medtronic in their base-case model.
- The relative cost of the initial procedure (EVAR procedure costs £523 more than open repair in base-case, and open repair costs £612 more than EVAR in
The sensitivity analysis). This value was used by Medtronic in their base-case model.

- The treatment effect for operative mortality (odds ratio EVAR vs open repair 0.35 in the base-case, 0.25 in the sensitivity analysis). This odds ratio was reported by a large US matched –cohort study.\textsuperscript{98}

- The baseline odds of operative mortality for both EVAR and open repair are three times greater than the base-case. This might represent outcomes outside specialist centres or in a less selective population. The UKSAT trial found operative mortality after open repair of 5.8\% for patients with average age of 70 and 4.4 cm aneurysm.\textsuperscript{154} The York base-case model predicts operative mortality of 2\% for similar patients (Equation 1, Table 6.2.1).

- The EVAR stent-graft costs more to the NHS on average than assumed in the base-case, see Section 3.3.

---

**The cost-effectiveness of EVAR compared with open repair in women**

The risk equations (Equations 1 to 4) estimated earlier in this section did not find gender to be a significant explanatory variable, and therefore the base-case model does not distinguish between male and female patients, other than to use life tables for men to estimate non-aneurysm mortality in the general population. However, Chapter 5 identified one large study which found an independent effect of gender on 30-day operative mortality (Odds ratio women versus men 1.46, 95\% CI 1.26-1.68).\textsuperscript{88} A secondary analysis explored the cost-effectiveness of EVAR specifically in women, assuming:

- Greater 30-day operative mortality after EVAR in women as estimated by Timaran et al.\textsuperscript{88}

- The average treatment effect (odds ratio) of 30-day mortality of EVAR compared with open repair found by the RCTs in Chapter 5 applies to women

- Using the age-specific non-aneurysm mortality rates (life-tables) for the female general population.
Table 6.2.11 Sensitivity analyses showing incremental cost-effectiveness ratios (ICERs) comparing EVAR and open repair for patients for different fitness, aneurysm size and age

Good and moderate fitness

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Fitness</th>
<th>Age</th>
<th>AAA cm</th>
<th>70</th>
<th>75</th>
<th>80</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ICER</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>York base-case</td>
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<td>46591</td>
<td>118599</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>967319</td>
<td>82865</td>
<td>42380</td>
<td>100770</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Dom Dom Dom</td>
<td>70824</td>
<td></td>
<td></td>
<td>88775</td>
</tr>
<tr>
<td>1</td>
<td>Survival curves converge less rapidly</td>
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<td>Dom</td>
<td>448348</td>
<td>78755</td>
<td>41637</td>
<td>89408</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>354356</td>
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<td>Dom Dom Dom</td>
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ICER is the incremental cost-effectiveness ratio, the difference in expected costs / difference in expected QALYs. Dominated (Dom) means EVAR has less expected benefit and higher cost than open repair.

Key

- ICER > 30001 or EVAR dominated
- 20001<ICER<30000
- ICER<20000
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#### Poor fitness

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ICER is the incremental cost-effectiveness ratio, the difference in expected costs / difference in expected QALYs. Dominated (Dom) means EVAR has less expected benefit and higher cost than open repair.

**Key**

- **ICER > 30001 or EVAR dominated**
- **20001<ICER<30000**
- **ICER<20000**

Final Report 1st April 2008
Table 6.2.11 shows the results of the sensitivity analyses for patients of good, moderate and poor fitness. The sensitivity analyses which have major implications for conclusions compared with the base-case are:

- If the EVAR procedure were cost saving by about £600 compared with open repair, EVAR would be cost-effective for older patients of moderate risk at a threshold of £20,000 to £30,000.
- If there were no difference in late aneurysm deaths (after 30 days) between EVAR and open repair, EVAR would be more cost-effective than open repair in all patients of moderate fitness and older patients with good fitness at a threshold of £30,000.
- If the treatment odds ratio for operative mortality were more favourable to EVAR, EVAR would be more cost-effective than open repair in older patients of moderate fitness, but still unlikely to be cost-effective in patients of good fitness.
- If the baseline odds of operative mortality (affecting both EVAR and open repair) were three times greater than estimated in the base-case, EVAR would be cost-effective compared with open repair in all patients of moderate fitness and older patients of good fitness.
- EVAR would not be cost effective in any of the patient groups considered in this review if the mean list price per patient of the stent graft were the highest of the values quoted by the manufacturers to the York assessment team (Table 3.3.1).
- The analysis for women indicates that EVAR would be unlikely to be cost-effective at a threshold of £20,000 per QALY in women with good fitness, but might be cost-effective in older women of moderate fitness and women with poor fitness. However, it should be emphasised that over 90% of the patients in the RCTs were men and therefore it is difficult to verify the assumption that the average treatment effect applies to women. For this reason this analysis is highly uncertain.
Results of probabilistic sensitivity analysis of the model comparing EVAR and open repair

Table 6.2.12 shows the results of a Monte-Carlo probabilistic sensitivity analysis, to estimate the overall uncertainty that EVAR is more cost-effective than open surgery, given the joint uncertainty in the estimates of all the parameters used in the base-case model. Results are shown for a cost-effectiveness threshold of £20,000 and for £30,000 per QALY. A probability in Table 6.2.12 of more than 0.5 indicates that EVAR was cost-effective in more than half of the Monte-Carlo simulations of the probabilistic model.

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Comparison of York model with Medtronic model of EVAR vs Open repair

The Medtronic model comparing EVAR and open repair was described in Section 6.1. The main differences between the York base-case and the Medtronic base-case models are:

- The difference between EVAR and open repair non-aneurysm cause mortality rates in the medium term
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- The difference in late aneurysm related mortality
- The hospital costs (intensive care, ward and operating theatre time) of the EVAR procedure

The assumptions made by Medtronic\textsuperscript{16} are shown as scenario 4 in Table 6.2.11. In this scenario, there is a slower rate of convergence of the survival curves than the York base-case, a lower relative cost of EVAR and no difference in late aneurysm deaths between EVAR and open surgery. The Medtronic model presented results for a patient aged 70 with an aneurysm size of 5.5 or greater. Fitness was unspecified in the Medtronic model (that is, results were for the average level of fitness in patients in the EVAR trial 1). When these assumptions are used in the York model, the ICER is predicted to be between £11,000 and £24,000 for patients aged 70 of good or moderate fitness (Table 6.2.11, Scenario 4), consistent with the results reported in the Medtronic report \textsuperscript{16} (ICER for average population £15,681).

Figure 6.2.8 illustrates the differences between the assumptions for all cause mortality made in the York Model and the Medtronic model. The figure shows the difference in cumulative deaths between EVAR and open repair predicted by the models. The York model assumed that the initial survival advantage of EVAR for operative mortality would be entirely offset within three years by a relatively higher non-aneurysm death rate after EVAR. This scenario is consistent with the results of EVAR trial 1, DREAM and a large US matched-cohort study.\textsuperscript{98} The predicted survival curve is shown in Figure 6.2.9 for a patient aged 70, with aneurysm 5.5 cm. Furthermore, the York model assumed there would be a small but persistent difference between the treatments in the rates of late aneurysm related deaths. This scenario is consistent with the long term EUROSTAR data.\textsuperscript{84} In contrast, the base-case model by Medtronic assumed a more optimistic scenario: that the rate of convergence of the survival curves would be slightly slower, and the survival curves would not meet. There would be no further difference in deaths beyond four years and, therefore, a long term survival advantage would be maintained in favour of EVAR (Figure 6.2.8). The predicted survival curve when the Medtronic assumptions are used in the York model is shown in Figure 6.2.10.
Figure 6.2.8. A comparison of the difference in cumulative deaths for a patient aged 70 with aneurysm size 5.5 cm and moderate fitness, between EVAR and open repair over time predicted by (a) the York model (b) The Medtronic base-case model.

Figure 6.2.9. Predicted survival curves from the York model for a patient aged 70 with moderate fitness and AAA size 5.5 cm. Survival curves converge by 3 years.
Comparison of York model with other published economic evaluations

The base-case model found that EVAR was not expected to be cost-effective for patients with good or moderate fitness, aged 70 to 75 and aneurysm between 5.5 and 6.5 cm (Table 6.2.10). These results can be compared with the published models for similar patient groups. Section 6.1 found that Michaels et al.\textsuperscript{109} and Epstein et al.\textsuperscript{108} were the published economic evaluations most relevant to the current decision in England and Wales. JA Michaels, DM Epstein and MJ Sculpher are authors of one or both these published papers and authors of this report.

Both Michaels et al.\textsuperscript{109} and Epstein et al.\textsuperscript{108} concluded that EVAR was not expected to be cost-effective in this patient group. However, there were differences between these published models and the York model in the assumptions used to arrive at this conclusion. Michaels et al. found a greater long term benefit in favour of EVAR than the York model, and a greater difference in costs, but was published before the mid term results of the good quality RCTs were available. Epstein et al. was published after the mid term results of the RCTs, and based on these trial results assumed the survival curves for EVAR and open repair would meet by 4 years. The published model has been adapted for use in the York economic evaluation. The main
difference in the parameter values between the models is that Epstein et al. assumed a
greater difference in late aneurysm deaths (hazard ratio EVAR vs open repair 6.0)
than in the York model (hazard ratio 2.46). The York model also used regression
analysis to estimate baseline risks of operative mortality, late aneurysm mortality and
non aneurysm mortality in a wider range of patient groups than Epstein et al.

The next section extends the York model to compare the cost-effectiveness of EVAR,
open repair, watchful waiting and no intervention.
6.2.3 Model comparing immediate elective surgery, watchful waiting and no intervention

6.2.3.1 Methods of model comparing surgery and watchful waiting

Introduction
The objective of this second model was to broaden the nature of the comparisons compared with the first. Specifically, the second model considers when surgery (with EVAR or open repair) might be cost-effective, compared with no surgery or delaying the decision. The model brings together the sparse available evidence about natural history in untreated patients with evidence in treated patients to predict outcomes of a wide range of management policies in patients with diagnosed aneurysm. Given the uncertainties in these data, the model is intended to be exploratory and suggest areas for further research.

Current guidelines for the management of AAA were discussed in Chapter 3. Briefly, patients are observed until the aneurysm reaches 5.5 cm, after which surgical intervention is considered. Patients considered fit for open surgery might be offered EVAR or open surgery; patients considered unfit for open surgery might be offered EVAR or no intervention. However, in practice there is a continuous range of probabilities of operative mortality and the optimum management policy should systematically weigh up all the risks to the patient - that is, operative mortality and late mortality if treated versus the risks of rupture if untreated. Furthermore, a publicly funded healthcare system must also evaluate the use of health-care resources, which are not considered explicitly by the current clinical guidelines. This section presents a decision model to evaluate the cost-effectiveness of surgery, watchful waiting or no surgery, for patients of different ages, operative fitness and aneurysm size.

Description of the watchful waiting strategy
At each consultation with their vascular surgeon, the patient faces four options:

- immediate elective surgery with EVAR
- immediate elective surgery with open repair
- to rule out surgery entirely
• or to delay the decision (watchful waiting).

We assume the patient is evaluated every 6 months in the watchful waiting policy, and patients attend all scheduled follow up visits. We assume that surveillance is discontinued if a decision is made to rule out surgery and there are no subsequent monetary costs to the health-care service. In practice, the patient may return if the aneurysm becomes symptomatic, but we do not model this scenario. The benefits of delaying the decision are that it allows more information on the aneurysm growth rate to be assembled, and preserves the option to commence immediate surgery in the future should the patient’s health state (aneurysm size) worsen. The costs of deferral are the monitoring costs of CT and outpatient attendance, deaths while waiting and a time preference for current benefits rather than future benefits. We assume patients have normal HRQOL for their age while under surveillance, although there is some evidence that patients with diagnosed untreated aneurysm suffer anxiety.

The approach used to model watchful wait is as follows.

• Firstly, the model previously described in Section 6.2.2 to evaluate EVAR vs open surgery was used to estimate the maximum expected net benefit of surgery in patients of a given fitness, for a range of aneurysm sizes (4 cm to 8 cm, in increments of 0.5 cm) and ages (70 years to 85 years, in increments of 6 months).

• Secondly, another model was constructed to evaluate an option of no surgery (that is, natural history, with no treatment and no surveillance) for the same patient groups. This model is described below.

• Finally, a dynamic programme was constructed using these data to estimate the net benefit of a watchful wait strategy, and calculate the optimum policy (EVAR, open repair, no surgery or watchful wait) for each aneurysm size and age.

Model to estimate the natural history of untreated aneurysm

To estimate the natural history of untreated aneurysm a Markov cohort model is used. The aim of the model is to estimate QALYs over the patient’s life time if untreated.
As there is no surveillance and no surgery in this model, there are no costs. The discrete health states are aneurysm sizes, from the size at diagnosis in increments of 0.5 cm, up to a maximum of 10 cm. Rupture rate is conditional on aneurysm size. The mean growth rate and standard deviation, and rupture rate were obtained from a review of the literature on the natural history of untreated aneurysm. It was assumed that aneurysms grow according to a normal probability distribution by 0.5 cm-0.99 cm or 1 cm-1.49 cm per 6 month cycle, or stay the same size (less than 0.49 cm growth) but that aneurysms do not diminish in size. In this model, rupture is assumed to be fatal. Although emergency surgery is possible in cases that reach hospital alive, this scenario is not considered in the model. Patients might die of non-aneurysm causes, depending on current age, current aneurysm size and baseline fitness (Table 6.2.3, Equation 2). Given the absence of evidence on how fitness might evolve over time, and the effect of fitness on aneurysm growth and rupture, it is assumed that fitness is constant over the duration of the model.

Parameter estimation for natural history model

Rupture rate for untreated patients

Untreated patients face a risk of rupture of their aneurysm (Table 6.2.13). It is difficult to measure the risk of rupture in an untreated patient because the natural history is rarely fully observed. Interventions might be considered when the risks of rupture outweigh the operative risk and therefore censoring is not at random. Powell et al conducted a review of the literature and compared the results with estimated rupture rates in the EVAR trial 2. The EVAR trial 2 data are the only data we know of which specifically measured untreated rupture rates in patients suitable for EVAR. Powell et al. found that the patients with large aneurysms (>6 cm) in the EVAR trial 2 had a lower untreated risk of rupture than patients in the other studies, and concluded that this might be due to being anatomically suitable for EVAR (Table 6.2.13). However, there were few patients with further CT after randomisation and so growth after the baseline was not investigated in the EVAR trial 2. This limits the usefulness of these data to model a watchful waiting strategy. For patients with aneurysm <6 cm they found that the rupture rate in EVAR trial 2 was similar to other published estimates. Due to time constraints, the data on rupture rates used in this model were not identified by a systematic review of the literature. However, we
believe we have identified the most important sources of evidence relevant to the UK (Table 6.2.13). We used the estimates from Michaels 1992\(^1\) as the base-case, as these data were available for a wide range of aneurysm sizes and appeared to be broadly consistent with estimates from the EVAR trial.\(^2\)\(^1\) Rupture rates were smoothed with respect to aneurysm size with an exponential function.

Powell et al.\(^{155}\) and Brown et al.\(^{156}\) found that rupture rates tended to be greater in women for a given aneurysm size, though Powell found the result non significant (hazard ratio women v men 1.21 (95% ci 0.77 – 1.90))
Table 6.2.13. Estimates of untreated rupture rates for different sizes of aneurysm: results from review of the literature

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<tbody>
<tr>
<td>Limet 1991 (Case series based on last observed AAA diameter) 157</td>
<td></td>
</tr>
<tr>
<td>&lt;4</td>
<td>0</td>
</tr>
<tr>
<td>4-5</td>
<td>n/a</td>
</tr>
<tr>
<td>&gt;5</td>
<td>0.22</td>
</tr>
<tr>
<td>3-3.9</td>
<td>0.005</td>
</tr>
<tr>
<td>4-4.9</td>
<td>0.010</td>
</tr>
<tr>
<td>5-5.9</td>
<td>0.050</td>
</tr>
<tr>
<td>Michaels 1992 111 (Meta-analysis, based on last observed AAA diameter)</td>
<td></td>
</tr>
<tr>
<td>6-6.9</td>
<td>0.090</td>
</tr>
<tr>
<td>7-7.9</td>
<td>0.125</td>
</tr>
<tr>
<td>8-8.9</td>
<td>0.250</td>
</tr>
<tr>
<td>9-9.9</td>
<td>0.500</td>
</tr>
<tr>
<td>10+</td>
<td>0.900</td>
</tr>
<tr>
<td>Reed 1997 158 (Case series, based on last observed AAA diameter)</td>
<td></td>
</tr>
<tr>
<td>3-3.9</td>
<td>0.000</td>
</tr>
<tr>
<td>4-4.9</td>
<td>0.010</td>
</tr>
<tr>
<td>5-5.9</td>
<td>0.110</td>
</tr>
<tr>
<td>UK SAT 1998 154 (Surveillance arm of RCT)</td>
<td></td>
</tr>
<tr>
<td>4-5.5</td>
<td>0.010</td>
</tr>
<tr>
<td>3-4.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Kim 2007 159 (MASS trial, based on baseline AAA diameter)</td>
<td></td>
</tr>
<tr>
<td>4.5-5.4</td>
<td>0.009</td>
</tr>
<tr>
<td>5.5+</td>
<td>0.063</td>
</tr>
<tr>
<td>Studies of patients refusing or unfit for open repair</td>
<td></td>
</tr>
<tr>
<td>Powell 2008 155 (meta-analysis of 5 studies, based on baseline AAA diameter)  †</td>
<td></td>
</tr>
<tr>
<td>5.0-5.9</td>
<td>0.103</td>
</tr>
<tr>
<td>&gt;=6</td>
<td>0.270</td>
</tr>
<tr>
<td>Powell 2008 155 (EVAR 2 trial, based on baseline AAA diameter)</td>
<td></td>
</tr>
<tr>
<td>5.5-5.9</td>
<td>0.097</td>
</tr>
<tr>
<td>&gt;=6</td>
<td>0.174</td>
</tr>
<tr>
<td>Studies with patients both fit and unfit for open repair</td>
<td></td>
</tr>
<tr>
<td>Brown 2003 (Canadian cohort, men) 156</td>
<td></td>
</tr>
<tr>
<td>5.0-5.9</td>
<td>0.010</td>
</tr>
<tr>
<td>&gt;=6</td>
<td>0.141</td>
</tr>
<tr>
<td>Brown 2003 (Canadian cohort, women) 156</td>
<td></td>
</tr>
<tr>
<td>5.0-5.9</td>
<td>0.039</td>
</tr>
<tr>
<td>&gt;=6</td>
<td>0.223</td>
</tr>
<tr>
<td>Brown 1999 (UKSAT randomised and unrandomised, based on last observed or estimated AAA diameter) 7</td>
<td></td>
</tr>
<tr>
<td>3 – 3.9</td>
<td>0.003</td>
</tr>
<tr>
<td>4- 4.9</td>
<td>0.015</td>
</tr>
<tr>
<td>5- 5.9</td>
<td>0.065</td>
</tr>
</tbody>
</table>

† The 5 studies used in the Powell review 155 were: Jones 1998 160, Powell 1999 161, Conway 2001 162, Lederle 2002 163, Ariz 2004 164

Expansion rate of untreated aneurysm

Table 6.2.14 shows the estimates of the expansion rate of untreated aneurysm from the literature review. Due to time constraints, these data were not identified by a
systematic review of the literature. We used the mean expansion rate from Michaels et al.\textsuperscript{11} as the base-case, as these data were available for a wide range of aneurysm sizes and appeared to be consistent with estimates from the other sources. Not all the studies reported the standard deviation or other measures of variability. We estimated the standard deviation of the expansion rate to be 0.15 cm/6months in aneurysms of 4 to 4.4 cm, a standard deviation of 0.30 cm/6months in aneurysms 4.5 to 6.9 cm and a standard deviation 0.34 cm/6months for aneurysms >7 cm, which seemed roughly consistent with the data on variability of the expansion rate estimated by Kim 2002\textsuperscript{159} UKSAT 1998\textsuperscript{154} and Michaels 1992.\textsuperscript{11} Table 6.2.15 calculates the transition probabilities of moving from the current aneurysm size to one or two sizes larger in one cycle of the natural history model assuming a normal distribution and the mean expansion rate from Table 6.2.14.

Table 6.2.14. Expansion rate of untreated aneurysm, results of review of the literature

<table>
<thead>
<tr>
<th>AAA diameter cm</th>
<th>Median expansion rate cm/yr</th>
<th>Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limet 1991 (Case series based on last observed AAA diameter)\textsuperscript{157}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4</td>
<td>0.53</td>
<td>n/a</td>
</tr>
<tr>
<td>4-5</td>
<td>0.69</td>
<td>n/a</td>
</tr>
<tr>
<td>&gt;5</td>
<td>0.74</td>
<td>n/a</td>
</tr>
<tr>
<td>Michaels 1992 \textsuperscript{11} (Meta-analysis, based on last observed AAA diameter)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-3.9</td>
<td>0.28</td>
<td>53</td>
</tr>
<tr>
<td>4-4.9</td>
<td>0.60</td>
<td>22</td>
</tr>
<tr>
<td>5-5.9</td>
<td>0.68</td>
<td>19</td>
</tr>
<tr>
<td>6-6.9</td>
<td>0.96</td>
<td>5</td>
</tr>
<tr>
<td>7-7.9</td>
<td>1.26</td>
<td>0</td>
</tr>
<tr>
<td>Reed 1997 (Case series) \textsuperscript{158}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>0.21</td>
<td>n/a</td>
</tr>
<tr>
<td>UK SAT 1998 (Surveillance arm of RCT) \textsuperscript{154}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-5.5</td>
<td>0.33</td>
<td>IQR 0.2-0.53 cm</td>
</tr>
<tr>
<td>Kim 2007 (MASS trial, based on baseline AAA diameter)\textsuperscript{159}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-4.4</td>
<td>n/a</td>
<td>0.025</td>
</tr>
<tr>
<td>4.5-5.4</td>
<td>n/a</td>
<td>0.087</td>
</tr>
<tr>
<td>&gt;5.5</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>
Table 6.2.15. Mean and standard deviation (SD) of expansion assumed in the base-case per 6 months, and calculated transition probabilities of expansion in a six month cycle, assuming a normal distribution for aneurysm growth.

### Mean and SD of expansion in 6 months (cm)

<table>
<thead>
<tr>
<th>Aneurysm size at start of 6 month cycle, cm</th>
<th>Mean cm</th>
<th>SD cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0.24</td>
<td>0.15</td>
</tr>
<tr>
<td>4.5</td>
<td>0.28</td>
<td>0.30</td>
</tr>
<tr>
<td>5</td>
<td>0.34</td>
<td>0.30</td>
</tr>
<tr>
<td>5.5</td>
<td>0.40</td>
<td>0.30</td>
</tr>
<tr>
<td>6</td>
<td>0.48</td>
<td>0.30</td>
</tr>
<tr>
<td>6.5</td>
<td>0.57</td>
<td>0.30</td>
</tr>
<tr>
<td>7</td>
<td>0.67</td>
<td>0.30</td>
</tr>
<tr>
<td>7.5</td>
<td>0.80</td>
<td>0.30</td>
</tr>
<tr>
<td>8</td>
<td>0.96</td>
<td>0.35</td>
</tr>
<tr>
<td>8.5</td>
<td>0.96</td>
<td>0.35</td>
</tr>
<tr>
<td>9</td>
<td>0.96</td>
<td>0.35</td>
</tr>
<tr>
<td>9.5</td>
<td>0.96</td>
<td>0.35</td>
</tr>
<tr>
<td>10</td>
<td>0.96</td>
<td>0.35</td>
</tr>
</tbody>
</table>

### Probability of 0-0.5 cm growth, 0.5-1 cm growth and 1 – 1.5 cm growth in 6 months

<table>
<thead>
<tr>
<th>Aneurysm size at start of 6 month cycle, cm</th>
<th>&lt;0.5 cm</th>
<th>0.5-1 cm</th>
<th>&gt;1 cm growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0.96</td>
<td>0.04</td>
<td>0.00</td>
</tr>
<tr>
<td>4.5</td>
<td>0.77</td>
<td>0.23</td>
<td>0.01</td>
</tr>
<tr>
<td>5</td>
<td>0.71</td>
<td>0.28</td>
<td>0.01</td>
</tr>
<tr>
<td>5.5</td>
<td>0.63</td>
<td>0.35</td>
<td>0.02</td>
</tr>
<tr>
<td>6</td>
<td>0.53</td>
<td>0.43</td>
<td>0.04</td>
</tr>
<tr>
<td>6.5</td>
<td>0.41</td>
<td>0.51</td>
<td>0.07</td>
</tr>
<tr>
<td>7</td>
<td>0.31</td>
<td>0.52</td>
<td>0.17</td>
</tr>
<tr>
<td>7.5</td>
<td>0.19</td>
<td>0.53</td>
<td>0.28</td>
</tr>
<tr>
<td>8</td>
<td>0.09</td>
<td>0.46</td>
<td>0.45</td>
</tr>
<tr>
<td>8.5</td>
<td>0.09</td>
<td>0.46</td>
<td>0.45</td>
</tr>
<tr>
<td>9</td>
<td>0.09</td>
<td>0.46</td>
<td>0.45</td>
</tr>
<tr>
<td>9.5</td>
<td>1.00</td>
<td>0.91</td>
<td>0.00</td>
</tr>
<tr>
<td>10</td>
<td>1.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Note: the data on mean aneurysm growth with respect to aneurysm size from Michaels (1992) have been smoothed using an exponential function

Illustration of the predicted rates of mortality of surgical treatment compared with no treatment at each age and aneurysm size

Figure 6.2.11 illustrates the rates of mortality estimated over time in the model for a patient with a starting age of 70, with poor fitness and an initial aneurysm diameter of 4 cm. Without treatment, the aneurysm is predicted to grow exponentially and the risk of rupture increases according to aneurysm diameter (Michaels 1992). Given these estimates of aneurysm growth, and the risk equation estimated from EUROSTAR (Table 6.2.1, Equation 1), the expected operative mortality with EVAR would increase due to increasing age and aneurysm diameter, from about 1.5% at age 70 to 10% after 7 years.
Figure 6.2.11. Illustration of mean rates of operative mortality and rupture estimated over time in the model, for a patient aged 70, with poor fitness and AAA diameter 4 cm at diagnosis. The figure also shows the growth in aneurysm size over time.
Cost-effectiveness analysis using dynamic programming

This section describes how dynamic programming was used to select the most cost-effective option (surgery, no intervention or watchful wait) for patients at each age and aneurysm size, using the results of the models for estimating the net benefits of surgery and the natural history described in the previous sections. The methods are closely based on the work of Driffield and Smith.10

Figure 6.2.12. Management of a patient diagnosed with abdominal aortic aneurysm, showing immediate elective repair, no surgery and watchful waiting strategies

Key to figure: ■ = decision; ● = chance event
This section has 3 parts:

- Firstly, we explain the concepts of dynamic programming, and how the method can be used to simplify the modelling of watchful waiting
- Secondly, we calculate the optimal policy for each aneurysm size in the final time period
- Thirdly, we calculate the optimal policy for each aneurysm size in each of the previous time periods

**Concepts of dynamic programming**

Figure 6.2.12 illustrates the management options. The benefits and costs of the strategies of immediate elective repair versus no surgery depend only on future chance events, such as whether the aneurysm grows slowly or quickly in each cycle, or the patient dies. The previous sections described the Markov models used to estimate patients’ lifetime expected benefits and costs for these two strategies, for any given starting age, aneurysm size and fitness. In principle, we could also use a decision tree or Markov model to calculate a watchful wait strategy. However this would quickly become intractable. The watchful wait strategy is more complex than a decision simply to treat or not treat taken at diagnosis. At each future age and aneurysm size, there are three decision options (immediate surgery, rule out surgery or watchful wait), and an indeterminate time horizon. The problem is dynamic, that is, the optimal strategy depends not just on future chance events but also on decisions made in the light of those events (Figure 6.2.12). This means there are hundreds of possible strategies for watchful waiting (eg, immediate EVAR, wait 6 months then surgery if the aneurysm is 0.5 cm larger, wait 1 year etc), for each starting age and aneurysm size.

To reduce this complexity, we use a dynamic programming formulation to calculate the optimum strategy for each age and aneurysm size. Dynamic programming is based on a simple principle: that if a model has N periods, and we know the optimal choices for each model state (aneurysm size) in the final period N, and we know the probabilities of transition between model states, then we can work backwards to induce the optimal choices for each model state in the previous period (N-1), and so on, until the starting period (t=1). Delaying a decision might have value because it
allows resolution of the uncertainty about whether the aneurysm will grow, which in turn might change the treatment decision. Both surgery and a decision to discharge the patient are irreversible: continuing surveillance with an option to treat in the future if the aneurysm grows might give greater expected benefit than either of these irreversible decisions, which can be compared with the costs of obtaining this information.

*Calculating the optimal policy for each aneurysm size in the final time period*

We begin by assuming that there is a maximum aneurysm size, say 8 cm, above which we will not continue watchful waiting, that is, we will either operate or discharge the patient. 8 cm is arbitrary but as the risk of rupture at this size is 25% per year, and expected growth is over 1¼ cm per year (Michaels 199211) the expected benefits of surveillance beyond this size would be very low. As we assume continued surveillance is not an option, the decision about whether to operate or discharge the patient at any given age when the aneurysm is 8 cm depends on whether the net benefits of surgery are greater than no surgery: the incremental net benefits of surgery vs no surgery will diminish with age (at a given aneurysm size) as operative mortality increases and life expectancy beyond surgery falls. We compare the net benefits of open surgery, EVAR and no surgery to find the maximum age at which it is no longer cost-effective to operate. For example, the base-case model estimates this age to be 85.5 years in patients with poor fitness (incremental costs of EVAR vs no surgery £11,700, incremental benefits 0.30 QALYs, and ICER of £39,000). We present results for thresholds of £20,000 and £30,000 per QALY.

This information tells us that 85 years is the maximum age up to which it is cost-effective to offer surgery. If surgery at age 85.5 is not cost-effective for aneurysm of 8 cm, then it will not be cost-effective for smaller aneurysms, with lower rupture rates but similar operative mortality. This age, 85 years, represents the final period (N) that we need to evaluate the dynamic programme, since watchful waiting can only be more cost-effective than offering no treatment if surgery is a possible future option. In this case there are N = 30 periods, for a starting age in the model of 70 years and a cycle length of 6 months. Although we have shown it is logical to discontinue the option for watchful waiting for all patients at age 85, net benefits of surgery and no
Calculating the optimal policy for each aneurysm size in each of the previous time periods

Given we have calculated the optimum choices for each health state (aneurysm size) at period N, we use backward induction to calculate the optimum choices for each health state in the previous period (t=N-1). Figure 6.2.13 illustrates the numerical solution method with a segment of the decision tree, for a patient of relatively poor operative fitness, perhaps on the margin of eligibility for entry to EVAR trial 1 or the DREAM trial. The right-hand side shows the possible states of health in period N (aged 85). The incremental net benefits for surgery (most cost-effective of EVAR versus open repair) compared to no surgery have been calculated using the decision models for treated and untreated patients previously described; the value for no surgical treatment is always shown as zero (relative to surgery). In the final period there is no option to defer so the decision is merely whether the patient should receive treatment. This decision is straightforward (given the data), depending only on whether the incremental net benefits of surgery are positive (relative to no surgery). At age 85, surgery would only be offered if the aneurysm were 8 cm.

Moving back to period N-1 (age 84.5 years), there is now the additional option to defer treatment. In each state, we compare three possible actions: deferral, treatment and abandonment. If the aneurysm was 7 cm, deferral is calculated as the expected net benefits from waiting another period (6months), when three possible states of health could occur: no growth, growth by 0.5 cm (to 7.5 cm) or growth by 1 cm (to 8 cm). The probabilities of these outcomes were calculated in Table 6.2.15 to be 0.31, 0.52 and 0.17 respectively. The optimal strategy and corresponding expected net benefit in the next period (N) for each outcome have already been calculated: they are zero if the aneurysm is 7 cm or 7.5 cm (no surgery) and £548 if the aneurysm is 8 cm (EVAR). Delaying a decision might have value because it allows resolution of the uncertainty about whether the aneurysm will grow, which in turn would change the treatment decision, with greater benefit than either immediate treatment or never offering surgery. There are three sources of opportunity cost of delaying the decision. Firstly, patients may rupture or die of other causes while waiting. Secondly, there is a...
time preference for current benefits, and so future benefits are discounted. Thirdly, there is a monetary cost of monitoring, which is assumed to be one outpatient visit and CT costing £194. These costs and benefits of delay are expressed in the following formula:

Net benefit of deferral at 7 cm at age 84.5 = 
(1-Pr(death))x e^{r/2} x \{0.35 x 0 + 0.51 x 0 + 0.14 x 548\}-194= -122

where Pr(death) is the probability of death from rupture or other causes for a patient of 7 cm aneurysm, e is the exponential function and r the discount rate (0.035 per year).

So at 7 cm at 84.5 years, the optimal decision is to abandon waiting, as the net benefits are less than no treatment (-£122<0 ). The same decision is reached for smaller aneurysm sizes. For aneurysm size of 7.5 cm at age 84.5, the optimal decision is to wait, with incremental net benefit of £133 compared to no treatment. If the aneurysm reaches 8 cm by the next period, it is cost-effective to operate, otherwise to abandon waiting. For aneurysm size of 8 cm at age 84.5, it is cost-effective to treat with EVAR, with incremental net benefit of £1332 compared with no treatment, given the parameters of the base-case model.

The same algorithm is used to calculate net benefits in for each aneurysm size in period N-2, and the process continues by backward induction until period 1 is reached. In most dynamic programming applications, the main interest is in the decision at period 1 and that the future period calculations are performed merely to inform that decision. In this application, however, we are also interested in the grid of policies for all ages and aneurysm sizes, as this indicates the most cost-effective policy for any patient at diagnosis.
Figure 6.2.13. Illustration of the dynamic programme decision tree for period N and N-1 for a patient of poor operative fitness.

The values shown are the incremental net benefits of deferring the decision (watchful waiting) or immediate treatment compared with abandoning watchful waiting (never offering surgical treatment). The dynamic programme is evaluated from right to left, that is, the cost-effective policies are identified for each state in period N, then each state in period N-1, N-2 etc.

```
5.5cm:
Defer = -194
Treat = -4894
Abandon = 0

6cm:
Defer = -194
Treat = -2994
Abandon = 0

6.5cm:
Defer = -194
Treat = -3872
Abandon = 0

7cm:
Defer = (1-Pr(dth))e^{r/2}x{0.14x548}-194=-122
Treat = -2001
Abandon = 0

7.5cm:
Defer = (1-Pr(dth))e^{r/2}x{0.51x548}-194= 133
Treat = -838
Abandon = 0

8cm:
Defer = (1-Pr(dth))e^{r/2}x548-194 = 133
Treat = 1332
Abandon = 0

Last period N, 85 years

5.5cm:
Treat = -5333
No treat = 0

6cm:
Treat = -3046
No treat = 0

6.5cm:
Treat = -4389
No treat = 0

7cm:
Treat = -2626
No treat = 0

7.5cm:
Treat = -1536
No treat = 0

8cm:
EVAR.
Value = 548
```

EVAR. Value = 0
Never treat.
Value = 0
Never treat.
Value = 0
Never treat.
Value = 0
Never treat.
Value = 0
Never treat.
Value = 0
Never treat.
Value = 0
Never treat.
Value = 0

6.2.3.2 Results of comparison of immediate surgery, watchful waiting and no intervention strategies

Base-case results of model comparing surgery and watchful waiting

Results for patients of good or moderate operative fitness

The base-case model estimated open repair to be more cost-effective than EVAR for patients of good and moderate operative fitness (Table 6.2.10). Including a watchful waiting or no surgery strategy would not alter the conclusion that on average open repair is more cost-effective than EVAR in these patients.

Results of watchful waiting model for patients of poor and very poor operative fitness

Table 6.2.16 shows the optimum policy for patients of poor operative fitness at each age and aneurysm size, under base-case assumptions, and a threshold of £20,000 and £30,000 per QALY. Poor fitness is defined as 4 times the operative mortality of a patient with similar age and aneurysm size but no pre-existing conditions. There is a discontinuity in the policy at 6.5 cm – the model predicts it is cost-effective to treat patients at age 78 years and aneurysm size 6 cm, but not if the aneurysm were 6.5 cm. One reason for this is that the base-case model predicts that the risk of late aneurysm death after EVAR increases considerably at this aneurysm size (Table 6.2.5). Table 6.2.17 shows the results for patients with very poor fitness, defined as eight times the operative mortality of a patient with similar age and aneurysm size but no pre-existing conditions. The results are summarised in Table 6.2.18 for a cost-effectiveness threshold of £20,000 per QALY. If the threshold for cost-effectiveness were £30,000 per QALY, EVAR would be cost-effective for patients with poor and very poor fitness for an older age range compared with a threshold of £20,000 per QALY.
Table 6.2.16. Results of the dynamic programme decision model for patients of poor operative fitness, at thresholds for cost-effectiveness of £20,000 and £30,000

Threshold of £20,000 per QALY, poor fitness

<table>
<thead>
<tr>
<th>Aneurysm size cm</th>
<th>Age 70</th>
<th>Age 71</th>
<th>Age 72</th>
<th>Age 73</th>
<th>Age 74</th>
<th>Age 75</th>
<th>Age 76</th>
<th>Age 77</th>
<th>Age 78</th>
<th>Age 79</th>
<th>Age 80</th>
<th>Age 81</th>
<th>Age 82</th>
<th>Age 83</th>
<th>Age 84</th>
<th>Age 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small 4</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
</tr>
<tr>
<td>4.5</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
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<tr>
<td>5</td>
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<td>O</td>
<td>O</td>
<td>O</td>
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<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
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Threshold of £30,000 per QALY, poor fitness

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Key: O Open repair. E EVAR. W Watchful wait NI. No surgical intervention
Table 6.2.17. Results of the dynamic programme decision model for patients of very poor operative fitness, at a threshold of £20,000 and £30,000 per QALY

Threshold of £20,000 per QALY, very poor fitness

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Threshold of £30,000 per QALY, very poor fitness

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<tr>
<th>Age</th>
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Key: O Open repair. E EVAR. W. Watchful wait NI. No surgical intervention
Table 6.2.18. The management policies predicted by the base-case model to be cost-effective for patients of different levels of fitness at a threshold of £20,000 per QALY

<table>
<thead>
<tr>
<th>Aneurysm size</th>
<th>Good and moderate fitness</th>
<th>Poor fitness</th>
<th>Very poor fitness</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5 to 7.4 cm</td>
<td>EVAR is unlikely to be cost-effective</td>
<td>EVAR is cost-effective approximately between ages 74 to 78. Open repair is more cost-effective for younger patients, and no surgery or waiting until the aneurysm is larger is cost-effective for older patients</td>
<td>EVAR is cost-effective up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients</td>
</tr>
<tr>
<td>7.5 cm and greater</td>
<td>EVAR is more cost-effective than open repair in elderly patients of moderate fitness</td>
<td>EVAR is cost-effective up to about 83 years</td>
<td>EVAR is cost-effective up to about 78 years</td>
</tr>
</tbody>
</table>

6.2.4 Discussion

Conventionally, patients have been classified as fit or unfit for open surgery, and AAA repair has been offered to all patients fit for open surgery with aneurysm size of 5.5 cm or greater. This chapter has presented two models. The first examined EVAR versus open repair in patients according to the conventional classification of fit for open surgery and with large aneurysms of 5.5 cm or greater. The second explored the cost-effectiveness of different policies concerning when, as well as how, surgery should be offered. In both models, results have been presented by age, fitness and aneurysm size at diagnosis. Fitness, in this model, is defined in a general way, so that a person of moderate fitness will have twice the operative mortality of a patient with the same size aneurysm and age with no pre-existing conditions.

Summary of model results: Management of patients with good and moderate operative fitness

The base-case decision models found that EVAR is unlikely to be cost-effective for patients with good or moderate operative fitness, in patients with small or large aneurysms. Under the base-case assumptions, open repair is more cost-effective than EVAR in every patient group considered at a threshold of £20,000 per QALY and EVAR is only cost-effective in the most elderly patients with moderate fitness at a threshold of £30,000 per QALY.
Summary of model results: Management of patients with poor or very poor fitness

Poor fitness has been defined in a general way in this model as four times the odds of operative mortality compared with a patient with the same age and aneurysm size but no pre-existing conditions. Very poor fitness is defined as 8 times the odds of operative mortality of a patient with good fitness.

The base-case model found that EVAR is more cost-effective than open repair for patients of poor or very poor fitness, because the benefit (in absolute terms) of operative mortality is greater, and the survival curves take a longer time to converge than for patients with good or moderate fitness. These results appear to confirm the medium-term analyses conducted by Schemerhorn et al.98 The finding that late aneurysm mortality after EVAR in patients with large aneurysm is much greater than in small aneurysms requires further investigation.84

The conclusion that EVAR is more cost-effective than open repair in patients of poor fitness may be misleading, unless an option of no surgery or delayed surgery is also considered. These options are more difficult to model because the data on the natural history of AAAs are so uncertain. This chapter has presented an exploratory model to explain the decision problem and to highlight areas where further research would be valuable.

When watchful waiting and no intervention are considered for patients with poor fitness, EVAR appears cost-effective between approximate ages of 74 to 78 years in patients with medium to large aneurysms. For younger patients, open repair is more cost-effective, and for older patients, watchful waiting or no intervention is cost-effective. For very large aneurysms EVAR might be cost-effective in patients aged up to about 83 years. In patients with very poor fitness, EVAR is cost-effective in patients aged up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients. For patients with very poor fitness and very large aneurysms EVAR might be cost-effective up to about 78 years.
Comparison of model predictions with results of EVAR trial 1 and DREAM

The results from the decision model (Table 6.2.18) can be compared with the outcomes of the main RCTs. Patients with poor or very poor fitness would very likely be on the margins of eligibility for either EVAR trial 1/DREAM or EVAR trial 2, depending on their age and aneurysm size. The base-case model estimates that open repair would be more cost-effective than EVAR for a large proportion of the patients entered in the EVAR trial 1; that is, in patients with good and moderate fitness, and for younger patients with poor fitness. These results would seem to be consistent with the results of the trials, which found on average insignificant difference in all cause mortality and higher cost.\textsuperscript{18, 43} However, the trials were not powered to undertake formal subgroup analysis, and the results of this model suggest that under base-case assumptions, EVAR might be cost-effective in some groups of older patients with poor fitness.

Comparison of model predictions with results of EVAR trial 2

At up to 4 years follow up, the EVAR trial 2 did not find any benefit for EVAR in the intention to treat analysis (primary adjusted hazard ratio EVAR vs no intervention 1.00, 95\% ci 0.54-1.84), with higher cost in the EVAR group.\textsuperscript{48} The RCT authors concluded EVAR was not effective or cost-effective for patients with very poor fitness. The model results broadly support those of the RCT. The model predicts that EVAR would be less cost effective than no intervention for patients with similar characteristics to those enrolled in EVAR trial 2 \textsuperscript{48} - that is, with very poor fitness, aged 77 (SD 6.2 years) and median aneurysm size 6.4 cm (IQR 6-7.4), Table 6.2.17 and Table 6.2.18.

The model predicts that watchful waiting would be more cost-effective than either EVAR or no intervention in a large proportion of the EVAR trial 2 population – in particular patients with very poor fitness younger than 77 years (Table 6.2.17). A watchful waiting policy was not evaluated by the RCT. However, there were a high proportion of crossovers in the trial - 27\% (47/172) of patients in the no intervention arm had an aneurysm repair by 4 years.\textsuperscript{48} This might indicate a high degree of uncertainty about the optimal management of these patients, such that many clinicians followed a “de facto” watchful waiting policy despite the trial protocol.
Finally, the trial was not powered to formally undertake sub-group analysis. The results of the model suggest that in patients with poor (rather than very poor) fitness, EVAR might be cost-effective for patients with medium to large aneurysm aged between 74 and 78 years old. Given that the treatment effects used in the watchful waiting model were not based on RCT evidence, all the model predictions must be considered indicative and exploratory.

Limitations of the model comparing EVAR and open repair

These conclusions are sensitive to the model assumptions. We discuss the strengths and limitations of the main assumptions in turn.

Firstly, the base-case assumes that the treatment effect is proportional to operative risk; that is, the odds ratio for EVAR vs open repair is constant for all levels of fitness, aneurysm sizes and ages. This implies that the absolute difference between EVAR and open repair in the proportion that dies within 30 days is low in patients at low operative risk. There is some evidence that this assumption is reasonable (Schemerhorn et al., Brown et al., see Chapter 5). Brown et al. found no significant interaction between CPI risk score and treatment effect for the patients in the EVAR trial 1. Schemerhorn et al. also found fairly constant odds ratios across all
age ranges, and therefore the absolute risk reduction (the difference in the operative mortality rate between similar patients) increased with age. Although this comparison used unrandomised data from Medicare, the authors used propensity score matching to compare treatment effects across a much more heterogeneous set of patients than are usually entered in a clinical trial, and in a much larger sample (almost 23,000 patients).

Secondly, the base-case assumes that the initial advantage for EVAR compared with open repair is not sustained in the medium term. For patients at low and moderate risk, with a modest initial difference in operative mortality, the survival curves are predicted to meet between 1 and 3 years after the procedure. This assumption is supported by the results of the EVAR trial 1,18 the DREAM trial43 and Schermerhorn et al.98

Thirdly, the base-case model assumed late aneurysm mortality after EVAR would be low, around 0.3% per year in patients with aneurysm 5 – 5.4 cm, but constant over the patient’s life time. The most recent generations of devices require longer follow up to confirm these results. The base-case model also predicted, from survival analysis of the EUROSTAR data, that late aneurysm mortality after EVAR in patients with large aneurysm (6.5 cm or more) was considerably and significantly greater than patients with small aneurysm (Table 6.2.5: hazard ratio 3.75, SE 0.83), confirming earlier work on this dataset.84 However, patient selection into EUROSTAR may limit its generalisability. AAA diameter is a major determinant of the decision about surgery and is also an independent predictor of suitability for EVAR, so that any results for patients treated by EVAR with large AAA are likely to be based on a highly selective sample of patients. Therefore, this result requires urgent further investigation.

Fourthly, the base-case estimated the use of hospital resources from the EVAR trial 1, as this was recent randomised data relevant to the UK. Other non randomised data, and the survey results in Appendix 10.3, have suggested that some elements of the hospital costs of EVAR procedures, such as length of stay on general wards, may have fallen more rapidly than the costs of open repair since 2003.16,166,167 As discussed in Chapter 3, there is considerable variation in the prices paid for the endovascular stent and accessories.166
Fifthly, the base-case estimated the baseline rate of operative mortality after EVAR conditional on fitness, aneurysm size and age from the EUROSTAR registry, and estimated the rate after open repair using the average odds ratio from a meta-analysis of RCTs (Chapter 5). The predicted rate of operative mortality after open repair is similar to that found by the DREAM and EVAR trial 1 (4.6% and 4.2% respectively), but considerably lower than found by the UKSAT trial in a younger patient group with smaller aneurysms (5.8%). It may be that the EVAR and DREAM trials operated on a more selected patient group, or in more specialist centres, than UKSAT. The base-case analysis assumes that the rates of operative mortality found by EUROSTAR, DREAM and EVAR trial 1 are achievable on average in the UK.

Finally, throughout this analysis, fitness has referred to the risk of operative mortality relative to a patient of that age and aneurysm size with no comorbidities. This has been done because, although fitness is a crucial factor in the analysis, there is no validated risk score system to quantify this risk both for EVAR and open surgery. The development of a recognised risk scoring instrument for operative mortality that is valid for EVAR and open surgery is a matter of urgency.

Limitations of the model comparing surgery with watchful waiting

The watchful waiting model has two sub-models: a model comparing EVAR with open repair, to estimate outcomes with surgery, and a model calculating the natural history of untreated aneurysm to estimate QALYs without any surgical intervention. Therefore, all of the limitations listed above apply to the watchful waiting model. Below, we discuss the additional assumptions required by the natural history model.

The parameters comparing the relative risks of operative mortality, re-interventions and late mortality after open surgery and EVAR were obtained from recent RCTs. However, the model comparing surgery with watchful waiting did not use treatment effects from RCTs. This is because the crossovers, delays and absence of a watchful waiting protocol in EVAR trial 2 make the results difficult to use directly to identify the most cost-effective form of management. Although the UKSAT trial did have a
clear policy for interventions, it did not evaluate EVAR. Therefore, we could not use treatment effects from these two RCTs to inform the model. Instead, the natural history of patients with untreated aneurysms was estimated using rupture rates and growth rates obtained from a review of the literature, and compared with outcomes estimated by the model of EVAR and open repair for patients with the same baseline characteristics.

Given the uncertainties in the data, and the potential for bias in this non-randomised comparison, the decision model and dynamic programme for watchful waiting are intended to be exploratory. Nevertheless, as discussed above, the results appear broadly consistent with those of the EVAR 2 trial, if it is accepted that the crossovers and delays for surgery represent a “de facto” watchful waiting strategy by the trial participants.

It would be difficult to design a RCT which was able to compare all the policies considered in this model and to stratify results by patient characteristics. There is some evidence that rupture rates tend to be greater in women for a given aneurysm size. The optimal treatment policy for women has not been fully addressed in this analysis and requires further work.

In the absence of information about the effectiveness of policies to improve fitness, it is assumed constant (relative to the patient age and aneurysm size) over the patients lifetime. In effect, elective operative mortality worsens because of advancing age and aneurysm growth in these analyses. It may be that fitness can be improved in some patients. The UKSAT trial concluded that one reason for slightly better long term outcomes after early surgery compared with delayed surgery might be that patients were more likely to give up smoking after surgery. The effectiveness of policies with the aim to improve fitness should be a matter for urgent research.

Management of patients with small aneurysms with EVAR

The UKSAT trial is not directly relevant to this evaluation because it did not include EVAR. However, the RCT was important in providing evidence that open
surgery was not effective (and therefore cost-effective) in patients with smaller aneurysm. Under base-case assumptions, the York model suggests that open repair is more cost-effective than EVAR for patients with good or moderate fitness (low operative mortality). Therefore, EVAR would not be cost-effective in patients with small aneurysms, who are also expected to have low operative mortality. On the other hand, as discussed above, the rates of operative mortality found from open repair in UKSAT were higher than expected, and our sensitivity analysis (Table 6.2.11, Scenario 6) suggests that EVAR might be cost-effective in patients of moderate fitness if the operative mortality of UKSAT reflected clinical practice better than the base-case assumptions used in this model. There is, therefore, continuing uncertainty about the cost-effectiveness of EVAR in patients with small aneurysms. The ongoing CAESAR trial comparing EVAR and surveillance is expected to report in 2008 and will provide some evidence relating to this patient group.

Conclusions

The main conclusions of the base-case model at a cost-effectiveness threshold of £20,000 per QALY are:

- EVAR is not cost-effective for patients of good or moderate fitness, or for patients with small aneurysm.
- In patients with poor fitness, EVAR is cost-effective approximately between ages 74 to 78 in patients with medium or large aneurysms. Open repair is more cost-effective for younger patients, and no surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective up to about 83 years in patients with poor fitness and very large aneurysms.
- In patients with very poor fitness, EVAR is cost-effective up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective up to about 78 years in patients with very poor fitness and very large aneurysm.
- Results are sensitive to assumptions and data about the risk of late aneurysm death, particularly in patients with large aneurysms over 6.5 cm, and the cost of the procedures and devices. The modelling of no intervention and watchful waiting is indicative and exploratory, based on assumptions about the natural history of untreated aneurysm in patients anatomically suitable for EVAR.
Further research in these areas would be important to inform future modelling work.
7 Assessment of Factors Relevant to the NHS and Other Parties

EVAR for AAA is already a well established and widely used technology throughout the NHS. It is however a difficult technology to research and hence the evidence base leaves many questions regarding best practice unresolved. This is a rapidly evolving technology, with improved and more specific devices being developed and the range of patients eligible for EVAR is likely to expand as the technology develops. Furthermore, ongoing research into the natural history of AAA will further inform clinical practice. Thus the treatment protocols relating to AAA and EVAR will continue to evolve.

The National Screening Committee for the UK (March 2007) has recommended that AAA screening should be offered to men aged 65, provided that the men invited were given clear information about the risks of elective surgery. Screening will lead to an increase in the number of AAA cases being identified for treatment, particularly small aneurysms. Steps will need to be taken to create networks of vascular surgical services to allow further specialisation, bigger throughput of cases. Provided adequate resources and training are provided the increased volume should reduce the risk of surgery (open or EVAR) as there is evidence correlating volume and quality.168

Irrespective of the potential benefits of EVAR there are a significant proportion of all AAA patients (55% in an unselected series13) who are unsuited to EVAR on grounds of anatomy. Even with developments in EVAR device design it is unlikely that the requirement for open repair will diminish in the near future. It is therefore essential that the NHS maintains provision of, and continues to develop expertise, in open repair.
8 Discussion

8.1 Statement of principal findings

Currently, EVAR trial 1,\textsuperscript{18,45} EVAR trial 2\textsuperscript{48} and the DREAM trial\textsuperscript{43,44} represent the best randomised evidence for evaluating EVAR. In patients fit for both procedures EVAR reduces operative mortality compared with open repair and EVAR is associated with a reduction in aneurysm-related mortality over the medium term but offers no significant difference in all cause mortality between EVAR and open repair at mid-term follow-up.\textsuperscript{************} The lack of long-term mortality benefit with EVAR was compounded by an increased rate of complications and re-interventions and these are not offset by any increase in HRQOL; possibly due to the increased level of monitoring required with EVAR due to the risk of complications.

There is limited RCT evidence comparing EVAR with non-surgical management in patients unfit for open repair. EVAR trial 2\textsuperscript{48} found no differences in mortality outcomes between groups but this finding cannot be taken as definitive because substantial numbers of patients randomised to non-surgical management crossed over to receive surgical repair of their aneurysms.\textsuperscript{************} This may indicate that the benefits of EVAR over ‘watchful waiting’ may only be apparent in the very long-term.

The results from these trials are complemented by data from registries, in particular the EUROSTAR registry data relating to devices in current use.\textsuperscript{56}

Although not formally part of our review the findings of the very large observational study recently published by Schermerhorn et al.\textsuperscript{98} reflect those of the RCTs. Importantly it suggests that, whilst across all age groups the initial benefit of EVAR over open repair diminishes over time, the rate of conversion between the two
treatments is slower in older patients. This suggests that less fit patients may benefit from EVAR more than do fit patients.

Very few data on the use of EVAR for ruptured aneurysms are available and, as yet, it is unclear whether EVAR is an appropriate or beneficial intervention in this indication. An ongoing study\textsuperscript{50} should contribute data to help inform this question.

The base-case decision models developed by the York assessment team found that EVAR is unlikely to be cost-effective for patients with good or moderate operative fitness, in patients with small or large aneurysms. Under base-case assumptions, open repair is more cost-effective in every patient group considered at a threshold of £20,000 per QALY and only in the most elderly patients with moderate fitness at a threshold of £30,000 per QALY. For patients of poor or very poor fitness, the base-case model found that EVAR is more cost-effective than open repair, because the benefit (in absolute terms) of operative mortality is greater, and the survival curves take a longer time to converge than for patients with good or moderate fitness.

The conclusion that EVAR is more cost-effective than open repair in patients of poor fitness may be misleading, unless an option of no surgery or delayed surgery is also considered. These options are more difficult to model because the data on the natural history of AAAs are so uncertain. The York assessment team also presented an exploratory model to explain the decision problem and to highlight areas where further research would be valuable. When watchful waiting and no intervention are considered for patients with poor fitness, EVAR appears cost-effective between approximate ages of 74 to 78 years in patients with medium to large aneurysms. For younger patients, open repair is more cost-effective, and for older patients, watchful waiting or no intervention is cost-effective. For very large aneurysms EVAR might be cost-effective in patients aged up to about 83 years. In patients with very poor fitness, EVAR is cost-effective in patients aged up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients. For patients with very poor fitness and very large aneurysms EVAR might be cost-effective up to about 78 years.
In the model submitted by Medtronic, there is a slower rate of convergence of the survival curves than the York base-case, a lower relative cost of EVAR and no difference in late aneurysm deaths between EVAR and open surgery. The Medtronic model presented results for a patient aged 70 with an aneurysm size of 5.5 or greater. Fitness was unspecified in the Medtronic model (that is, results were for the average level of fitness in patients in the EVAR trial 1). When these assumptions are used in the York model, the ICER is predicted to be between £11,000 and £24,000 for patients aged 70 of good or moderate fitness, consistent with the results reported in the Medtronic report (ICER for average population £15,681).

8.2 strengths and limitations of the assessment

This review of the evidence used established systematic review methods. We defined inclusion and exclusion criteria in advance. We applied a rigorous search strategy to a range of electronic and print sources. We also ensured that the review was kept up to date by using a current awareness strategy. Finally, we quality assessed RCTs before performing a meta-analysis where possible and appropriate. A more definitive analysis would be an individual patient data (IPD) analysis of all completed and currently ongoing trials of EVAR.

We attempted to obtain any extra trial data on EVAR for unruptured aneurysms than that used in a previous systematic review of the RCT literature. Additional analyses of data from the EVAR trials have been published and were also included in the review as appropriate. Our synthesis of the RCT data differs slightly from that of Lederle et al. in that they used odds ratios whereas we used hazard ratios in our meta-analysis to provide a more precise measure of effect. However, this did not affect the findings of the meta-analysis.

The best RCTs included in the review included patients with aneurysms of at least 5.5 cm in diameter. Ongoing trials that have included patients with aneurysms of 5 cm will contribute to the general evidence base of EVAR versus open repair, but will also
specifically inform the debate about the lower aneurysm size limit can be treated beneficially with EVAR. 51, 52

The data from both the RCTs and registries are derived almost entirely from male patients. Although the very high proportion of patients in the studies is representative of patients who develop AAA, the estimates of clinical effect will reflect the treatment of male patients more than female patients.

The registries included in the review were selected based on perceived relevance to the review question. The main strength of registry data is that they may give an indication of outcomes achieved in routine clinical practice. However, it should be noted that some data are old and thus may not reflect current practice. This is particularly the case for the RETA registry, 58 which stopped adding new cases in 2000 when the EVAR trial 1 and EVAR trial 2 studies began. The EUROSTAR registry 56 provides data on a large sample of patients undergoing EVAR, with most data being recorded prospectively. Although probably the strongest source of registry data on EVAR, a possible limitation of EUROSTAR is that it includes relatively few centres from the UK and may not entirely reflect UK practice. The UK NVD 19 currently concentrates on open repair of AAAs almost exclusively and therefore (because patients are not routinely followed up after open repair) includes only short term outcomes (i.e. 30-day mortality) in its published reports.

The studies on risk models provide pointers for further research and show decision makers where data are limited, contradictory or uncertain. The majority of studies assess relationships between pre-operative risk factors and patient outcomes following EVAR. We have provided a narrative and graphical synthesis of these studies and this illustrates which factors have been generally been found to be significant independent risk factors in multivariate analyses. However, there is inconsistency in the combinations of factors used in multivariate models and this supports the decision to use broad categories of patient fitness rather than any specific risk scoring system in the economic model included in this report (see Section 6.2).

A further limitation of most of the included risk modelling studies is that methodology was poorly reported. This, together with a lack of validated quality
assessment tools for such studies, makes it difficult to stratify the studies in terms of quality. We have focused on the studies that evaluated existing risk algorithms\textsuperscript{26, 61, 88} and the one study that developed a risk algorithm from scratch\textsuperscript{24, 62, 94} because these appear to be potentially the most useful for clinical decision making. Further research is required to develop tools to compare possible outcomes of EVAR and alternative strategies (open repair and non-surgical management with or without later surgery).

The modelling undertaken by the York assessment team builds on earlier work undertaken by a subset of authors. In general, a strength of the modelling is that it uses both RCT and registry data in an attempt to identify the most cost-effective form of management for each type of patient (where fitness, age and aneurysm diameter are the key variables characterising patients). This approach highlights the heterogeneity in cost-effectiveness in this area and emphasises that it is not appropriate to define one form of management as the most cost-effective in all types of patients. The modelling approach has also sought to handle the issue of appropriate comparators by presenting two models. The first model assumes (as was the case in EVAR trial 1) that a decision has been taken to operate on a patient, and the question is whether EVAR or open surgery should be provided. The second model widens the comparators by including two additional strategies: watchful waiting and the decision not to intervene.

All models in this area are subject to uncertainty in the assumptions made and the evidence used. These have been dealt with using appropriate sensitivity and scenario analyses. Different perspectives on structural assumptions and choice of evidence also largely explain differences between the York model, those in the published literature and that submitted to NICE by Medtronic. These uncertainties are considered in Section 8.3 below.

### 8.3 Uncertainties

In general, the main uncertainties which may influence this assessment are:

- The uncertainty regarding the natural history of AAA if left untreated.
- The uncertainty regarding the effect size of EVAR in smaller aneurysms. This question is currently being addressed in two ongoing trials ACE and OVER (see section 5.2.1.2)
• The uncertainty regarding the effect size of EVAR compared with ‘watchful waiting’
• The uncertainty regarding the impact of various levels of risk on the outcome following EVAR.

For the economic modelling in particular, there are some specific uncertainties about assumptions and data sources.

• The base-case assumes that the treatment effect is proportional to operative risk; that is, the odds ratio for EVAR vs open repair is constant for all levels of fitness, aneurysm sizes and ages. This implies that the absolute difference between EVAR and open repair in the proportion that dies within 30 days is low in patients at low operative risk. There is some evidence that this assumption is reasonable, see Chapter 5).
• The base-case assumes that the initial advantage for EVAR compared with open repair is not sustained in the medium term. For patients at low and moderate risk, with a modest initial difference in operative mortality, the survival curves are predicted to meet between 1 and 3 years after the procedure. This assumption is supported by the results of EVAR trial 1, the DREAM trial and Schermerhorn et al.
• The base-case model assumes late aneurysm mortality after EVAR would be low, around 0.3% per year in patients with aneurysm 5 – 5.4 cm, but constant over the patient’s life time. It also predicted, from survival analysis of the EUROSTAR data, that late aneurysm mortality after EVAR in patients with large aneurysm (6.5 cm or more) was considerably and significantly greater than patients with small aneurysm confirming earlier work on this dataset. However, patient selection into EUROSTAR may limit its generalisability. AAA diameter is a major determinant of the decision about surgery and is also an independent predictor of suitability for EVAR, so that any results for patients treated by EVAR with large AAA are likely to be based on a highly selective sample of patients.
• The base-case estimated the use of hospital resources from EVAR trial 1, as this was recent randomised data relevant to the UK. Other non-randomised data have suggested that the hospital costs of EVAR procedures may have
fallen more rapidly than the costs of open repair since 2003\textsuperscript{16,166,167} although, as discussed in Chapter 3, there is also considerable variation in the prices paid for the endovascular stent and accessories.\textsuperscript{166}

- The base-case estimated the baseline rate of operative mortality after EVAR conditional on fitness, aneurysm size and age from the EUROSTAR registry\textsuperscript{56} and estimated the rate after open repair using the average odds ratio from a meta-analysis of RCTs. The predicted rate of operative mortality after open repair is similar to that found by the DREAM and EVAR trial 1 (4.6\%\textsuperscript{43} and 4.2\%\textsuperscript{26} respectively), but considerably lower than found by the UKSAT trial in a younger patient group with smaller aneurysms (5.8\%).\textsuperscript{154} It may be that the EVAR and DREAM trials operated on a more selected patient group, or in more specialist centres, than UKSAT.\textsuperscript{154} The base-case analysis assumes that the rates of operative mortality found by EUROSTAR, DREAM and EVAR trial 1 are achievable on average in the UK.

- Throughout this analysis, fitness has referred to the risk of operative mortality relative to a patient of that age and aneurysm size with no comorbidities. This has been done because, although fitness is a crucial factor in the analysis, there is no validated risk score system to quantify this risk both for EVAR and open surgery. It may be that fitness can be improved in some patients, but there has been very little evaluation to date of policies with this objective.

- The model comparing surgery with watchful waiting did not use treatment effects from RCTs. This is because the crossovers, delays and absence of a watchful waiting protocol in EVAR trial 2 make the results difficult to use directly to identify the most cost-effective form of management.\textsuperscript{48} Although the UKSAT trial did have a clear policy for interventions, it did not evaluate EVAR.\textsuperscript{154} Therefore, we could not use treatment effects from these two RCTs to inform the model. Instead, the natural history of patients with untreated aneurysm was estimated using rupture rates and growth rates obtained from a review of the literature, and compared with outcomes estimated by the model of EVAR and open repair for patients with the same baseline characteristics. Given the uncertainties in the data, and the potential for bias in this non-randomised comparison, the decision model and dynamic programme for watchful waiting are intended to be exploratory.
As noted in Chapters 5 and 6, the RCT data on EVAR was predominantly collected in men. Although, Chapter 5 reported that there was no evidence that either baseline risks or treatment effects were influenced by gender, it is feasible that untreated rupture rates may differ between men and women, and this may influence the cost-effectiveness of the management options.
9 Conclusions

- Compared with open repair EVAR reduces operative mortality and aneurysm related mortality over the medium term but offers no significant difference in all cause mortality at mid-term follow-up.

- EVAR is associated with an increased rate of complications and re-interventions and these are not offset by any increase in HRQOL.

- Analysis of the EVAR trial data did not find any evidence that a benefit with EVAR over open-repair could be predicted using the CPI score for pre-operative fitness.

- There is evidence from single studies that the GAS and CCI scores can independently predict in hospital or 30 day mortality after EVAR the GAS may also be able to predict longer term mortality following EVAR.

- A large number of studies have modelled risks for adverse outcomes following EVAR. These do not provide definitive evidence but age, possibly gender, renal impairment, fitness, ASA class and aneurysm size may be predictive of poorer 30 day survival. There may be a link between fitness for open repair, aneurysm size and possibly device type and aneurysm related mortality. In terms of all cause mortality pulmonary status, renal impairment, ASA class and aneurysm size might adversely affect this outcome. We did not consistently find any risk factors for re-intervention. For the outcome of endoleak only age was a possible independent risk factor.

- There is limited RCT evidence comparing EVAR with non-surgical management or ‘watchful waiting’ in patients unfit for open repair. The EVAR II trial found no differences in mortality outcomes between groups but this finding cannot be taken as definitive.

- There is no real evidence that EVAR can be an appropriate or beneficial intervention for ruptured aneurysms.

- EVAR is not cost-effective for patients of good or moderate fitness, or for patients with small aneurysm, compared with open repair or watchful waiting.

- In patients with poor fitness, EVAR is cost-effective between the ages of approximately 74 to 78 years in patients with medium or large aneurysm.
Open repair is more cost-effective for younger patients, and no surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective up to about 83 years in patients with poor fitness and very large aneurysm.

- In patients with very poor fitness, EVAR is cost-effective up to about 74 years. No surgery or waiting until the aneurysm is larger is cost-effective for older patients. EVAR is cost-effective in patients aged up to about 78 years in patients with very poor fitness and very large aneurysm.

- Results are sensitive to assumptions and data about the risk of late aneurysm death, particularly in patients with large aneurysms over 6.5 cm, and the hospital cost of the procedures. The modelling of no intervention and watchful waiting is indicative and exploratory, based on assumptions about the natural history of untreated aneurysm in patients anatomically suitable for EVAR. Further research in these areas would be important to inform future modelling work.

### 9.1 Implications for service provision

Based on the results of this assessment of clinical and cost-effectiveness, open repair should be the treatment of choice for patients with AAA who have good or moderate fitness.

For patients with poorer fitness, whether suitable for open repair or not, EVAR may be cost effective but this will depend upon the patient’s age.

EVAR cannot currently be recommended for the treatment of ruptured aneurysms.

### 9.2 Suggested research priorities

- Further follow-up of the existing UK trials (EVAR trial 1, EVAR trial 2) should be undertaken.
• Opportunities for individual patient meta-analysis of all RCTs relating to EVAR should be sought.
• Further research is needed on the rate of late aneurysm related mortality after EVAR – in particular, in the most recent generations of devices.
• The extent to which the relative treatment effect of EVAR on operative mortality can be assumed constant across sub-groups of patients should be further investigated.
• Research is required into how the implement the best available risk scoring systems for the management of AAA into decision making in routine clinical practice.
• Research is required into the natural history of untreated AAA to determine more reliably when surgical intervention is optimal. The analysis should investigate the impact of different levels and determinants of patient fitness as well as aneurysm size and anatomy.
• A well defined and conducted RCT of EVAR versus ‘watchful waiting’ reflecting current clinical practice is warranted. However, given the difficulties of conducting RCTs in the management of AAA, it is probably advisable that the collection of data through the existing, established registries, particularly RETA (for EVAR) and NVD (for open repair) in the UK should be continued.
10 Appendices

10.1 Literature search strategies

Literature searches were carried out to identify systematic reviews, guidelines, ongoing trials, RCTs, risk modelling studies, reports from specified EVAR Registries and economic studies.

To identify systematic reviews the following were searched:

**Cochrane Database of Systematic Reviews, DARE, HTA database**
Via Cochrane Library issue 4, 2007
Search date: 17th September 2007
Search strategy

#1 (evar):ti,ab,kw or "endovascular stent*":ti,ab,kw or "endovascular repair*":ti,ab,kw or "endovascular treat*":ti,ab,kw or "endovascular surg*":ti,ab,kw
#2 "endovascular aneurysm repair*"
#3 "endoluminal stent*":ti,ab,kw or "endoluminal repair*":ti,ab,kw or "endoluminal treat*":ti,ab,kw or "endoluminal surg*":ti,ab,kw
#4 (#1 OR #2 OR #3)
#5 MeSH descriptor Aortic Aneurysm, Abdominal explode all trees
#6 (AAA):ti,ab,kw or "abdominal aortic aneurysm*":ti,ab,kw or "abdominal aneurysm*":ti,ab,kw
#7 (#5 OR #6)
#8 (#4 AND #7)

To identify guidelines the following databases and webpages were searched/scanned:

**TRIP database**
http://www.tripdatabase.com/index.html
Search date: 11th September 2007

**NLH National Library of Guidelines**
http://www.library.nhs.uk/guidelinesFinder/
Search date 11th September 2007

**National Guideline Clearinghouse**
http://www.guideline.gov/
Search date 29th October 2007

**NICE webpages**
http://www.nice.org.uk/
Search date 29th October 2007
The following bibliographic databases were searched to identify RCTs (2005 to 2007), risk studies and papers based on Registry data.

**BIOSIS Previews (R)**
Via Dialog
Search date: 18th September 2007

S1 131 EVAR/TI,AB,DE
S2 641 ENDOVASCULAR(W)STENT?/TI,AB,DE
S3 506 ENDOVASCULAR(W)REPAIR?/TI,AB,DE
S4 1078 ENDOVASCULAR(W)TREAT?/TI,AB,DE
S5 169 ENDOVASCULAR(W)SURG?/TI,AB,DE
S6 166 ENDOVASCULAR(W)ANEURYSM(W)REPAIR?/TI,AB,DE
S7 155 ENDOLUMINAL(W)STENT?/TI,AB,DE
S8 49 ENDOLUMINAL(W)REPAIR?/TI,AB,DE
S9 51 ENDOLUMINAL(W)TREAT?/TI,AB,DE
S10 5 ENDOLUMINAL(W)SURG?/TI,AB,DE
S11 2497 S1:S10
S12 2931 AAA/TI,AB,DE
S13 2767 ABDOMINAL(W)AORTIC(W)ANEURYSM?/TI,AB,DE
S14 215 ABDOMINAL(W)ANEURYSM?/TI,AB,DE
S15 4836 S12:S14
S16 544 S11 AND S15
S17 3 AAA(W)ENDOGRAFT?/TI,AB,DE
S18 546 S16 OR S17
S19 44179 RANDOM?/TI
S20 45754 TRIAL/TI
S21 36106 DOUBLE(W)BLIND?/AB
S22 3073 SINGLE(W)BLIND?/AB
S23 99005 S19:S22
S24 20 S18 AND S23
S26 11 (EUROSTAR(2W)(REGISTRY OR REGISTER OR PROJECT OR DATABASE OR DATA OR COLLABORAT? OR GROUP?))/TI,AB
S27 16 (EUROSTAR AND (EVAR OR STENT? OR GRAFT? OR ANEURYSM?))/TI,AB
S28 16 RETA/TI,AB
S29 0 REGISTRY(2W)ENDOVASCULAR(W)TREATMENT(2W)ANEURYSMS/TI,AB
S30 1 NATIONAL(W)VASCULAR(W)DATABASE/TI,AB
S31 33 S26:S30
S32 2 (HARDMAN(W)(INDEX OR SCORE? OR SCORING OR MEASURE?))/TI,AB
S33 2 GLASGOW(W)ANEURYSM(W)SCORE?/TI,AB
S34 22 (POSSUM(W)(INDEX OR SCORE? OR SCORING OR MEASURE?))/TI,AB
S35 1 MODIFIED(W)LEIDEN(W)SCORE/AB
S36 1 MODIFIED(W)COMORBIDITY(W)SEVERITY(W)SCORE/AB
S37 26 S32:S36
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CINAHL - Cumulative Index to Nursing & Allied Health Literature
Via Ovid
Search date: 10th September 2007
Database coverage: 1982 to August Week 5 2007
Search strategy:

12323 (RISK? OR MORTALITY OR SURVIVAL OR DEATH)/TI
131 EVAR/TI,AB,DE
641 ENDOVASCULAR(W)STENT?/TI,AB,DE
506 ENDOVASCULAR(W)REPAIR?/TI,AB,DE
1078 ENDOVASCULAR(W)TREAT?/TI,AB,DE
169 ENDOVASCULAR(W)SURG?/TI,AB,DE
166 ENDOVASCULAR(W)ANEURYSM(W)REPAIR?/TI,AB,DE
155 ENDOVASCULAR(W)STENT?/TI,AB,DE
49 ENDOVASCULAR(W)REPAIR?/TI,AB,DE
51 ENDOVASCULAR(W)TREAT?/TI,AB,DE
5 ENDOVASCULAR(W)SURG?/TI,AB,DE
3 AAA(W)ENDOGRAFT?/TI,AB
2499 S39:S49
71 S38 AND S50
134 S25 OR S31 OR S37 OR S51
1453415 (RAT OR RATS OR MOUSE OR MICE OR HAMSTER OR
HAMSTERS OR ANIMAL OR ANIMALS OR DOG OR DOGS OR CAT OR
CATS OR BOVINE
OR SHEEP OR FLY OR FLIES OR FISH OR FISHES OR BAT OR BATS OR BEE
OR BEES OR GRASS OR GRASSES OR FOSSIL OR FOSSILS OR/lichens OR MUSHROOM OR MUSHROOMS)/AB,TI
129 S52 NOT S53
534304 ANIMAL
4001770 HUMAN
413787 S55 NOT (S55 AND S56)
129 S54 NOT S57
17 11 and 16 (144)
18 AAA endograft$.ti,ab. (3)
19 17 or 18 (147)
20 vascular surgery/ (477)
21 20 and 16 (119)
22 19 or 21 (197)
23 exp clinical trials/ (47023)
24 clinical trial.pt. (22538)
25 (clinic$ adj trial$).tw. (11002)
26 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$3 or mask$3)).tw. (6495)
27 randomi?ed control$ trial$.tw. (9627)
28 random assignment/ (16139)
29 random$ allocat$.tw. (1061)
30 placebo.tw. (9144)
31 placebos/ (3742)
32 quantitative studies/ (3400)
33 allocat$ random$.tw. (62)
34 or/23-33 (65834)
35 22 and 34 (17)
36 (EUROSTAR adj2 (registry or register or project or database or data or collaborat$ or group$)).ti,ab. (3)
37 (EUROSTAR and (evar or stent$ or graft$ or aneurysm$)).ti,ab. (3)
38 reta.ti,ab. (2)
39 registry of endovascular treatment of aneurysms.ti,ab. (0)
40 national vascular database.ti,ab. (0)
41 36 or 37 or 38 or 39 or 40 (5)
42 (Hardman adj (index or score$ or scoring or measure$)).ti,ab. (0)
43 Glasgow aneurysm score$.ti,ab. (0)
44 (POSSUM adj (index or score$ or scoring or measure$)).ti,ab. (4)
45 Modified Leiden Score.ti,ab. (0)
46 Modified Comorbidity Severity Score.ti,ab. (0)
47 42 or 43 or 44 or 45 or 46 (4)
48 risk assessment/ (9540)
49 risk factors/ (21665)
50 survival analysis/ (4131)
51 mortality/ (5604)
52 roc curve/ (1418)
53 "Sensitivity and Specificity"/ (10462)
54 (risk$ or mortality or survival or death).ti. (47061)
55 (roc curve$ or sensitivity or specificity).ab. (10517)
56 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 (89143)
57 EVAR.ti,ab. (25)
58 endovascular stent$.ti,ab. (83)
59 endovascular repair$.ti,ab. (93)
60 endovascular treat$.ti,ab. (94)
61 endovascular surg$.ti,ab. (17)
62 endovascular aneurysm repair$.ti,ab. (24)
63 endoluminal stent$.ti,ab. (12)
64 endoluminal repair$.ti,ab. (6)
65 endoluminal treat$.ti,ab. (3)
The Cochrane Central Register of Controlled Trials
Via Cochrane Library 2007, issue 4
Search date: 11th September 2007
Search strategy

#1 (evar):ti,ab,kw or "endovascular stent*":ti,ab,kw or "endovascular repair*":ti,ab,kw or "endovascular treat*":ti,ab,kw or "endovascular surg*":ti,ab,kw in Clinical Trials (52)
#2 "endovascular aneurysm repair*":ti,ab,kw or "endoluminal stent*":ti,ab,kw or "endoluminal repair*":ti,ab,kw or "endoluminal treat*":ti,ab,kw or "endoluminal surg*":ti,ab,kw in Clinical Trials (21)
#3 (#1 OR #2) (84)
#4 (AAA*):ti,ab,kw or "abdominal aortic aneurysm*":ti,ab,kw or "abdominal aneurysm*":ti,ab,kw in Clinical Trials (507)
#5 MeSH descriptor Aortic Aneurysm, Abdominal explode all trees (395)
#6 (#4 OR #5) (728)
#7 (#3 AND #6) (60)
#8 "AAA endograft*":ti,ab,kw in Clinical Trials (0)
#9 (#7 or #8) (60)
#10 MeSH descriptor Vascular Surgical Procedures explode all trees (4141)
#11 (#6 and # 10) (141)
#12 (#9 or #11) (161)
#13 (#12), from 2005 to 2007

EMBASE
Via Ovid
Database coverage: 1980 to 2007 Week 35
Search date: 6th September 2007
Search strategy:

--------------------------------------------------------------------------------
1 EVAR.ti,ab. (422)
2 endovascular stent$.ti,ab. (1345)
3 endovascular repair$.ti,ab. (1373)
4 endovascular treat$.ti,ab. (2990)
5 endovascular surg$.ti,ab. (385)
6 endovascular aneurysm repair$.ti,ab. (438)
7 endoluminal stent$.ti,ab. (280)
8 endoluminal repair$.ti,ab. (171)
9 endoluminal treat$.ti,ab. (140)
10 endoluminal surg$.ti,ab. (24)
or/1-10 (6306)
11 AAA$.ti,ab. (5101)
12 exp aorta aneurysm/ (15874)
13 abdominal aortic aneurysm$.ti,ab. (6740)
14 abdominal aneurysm$.ti,ab. (515)
15 or/12-15 (18921)
16 11 and 16 (2246)
17 AAA endograft$.ti,ab. (14)
18 17 or 18 (2254)
19 vascular surgery/ (10955)
20 and 16 (1022)
21 19 or 21 (3162)
22 clinical trial/ (469549)
23 randomized controlled trial/ (146648)
24 randomization/ (23723)
25 single blind procedure/ (6886)
26 double blind procedure/ (65699)
27 crossover procedure/ (19208)
28 placebo/ (103122)
29 randomi?ed controlled trial$.tw. (25624)
30 rct.tw. (169)
31 random allocation.tw. (584)
32 randomly allocated.tw. (9232)
33 allocated randomly.tw. (1293)
34 (allocated adj2 random).tw. (547)
35 single blind$.tw. (6783)
36 double blind$.tw. (78511)
37 ((treble or triple) adj blind$).tw. (122)
38 placebo$.tw. (100415)
39 prospective study/ (68159)
40 or/23-40 (619632)
41 case study/ (5041)
42 case report.tw. (106789)
43 abstract report/ or letter/ (443249)
44 or/42-44 (553223)
45 41 not 45 (598087)
46 limit 47 to yr="2005 - 2007" (134)
47 (EUROSTAR adj2 (registry or register or project or database or data or collaborat$ or group$)).ti,ab. (50)
48 (EUROSTAR and (evar or stent$ or graft$ or aneurysm$)).ti,ab. (62)
49 reta.ti,ab. (11)
50 registry of endovascular treatment of aneurysms.ti,ab. (1)
51 national vascular database.ti,ab. (7)
52 or 49 or 50 or 51 or 52 or 53 (80)
53 (Hardman adj (index or score$ or scoring or measure$)).ti,ab. (9)
54 Glasgow aneurysm score$.ti,ab. (19)
55 (POSSUM adj (index or score$ or scoring or measure$)).ti,ab. (86)
56 Modified Leiden Score.ti,ab. (2)
57 Modified Comorbidity Severity Score.ti,ab. (1)
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60 55 or 56 or 57 or 58 or 59 (108)
61 risk assessment/ (151661)
62 risk factor/ (205117)
63 survival rate/ (48556)
64 survival time/ (24668)
65 overall survival/ (3310)
66 survival/ (55421)
67 mortality/ (149265)
68 roc curve/ (1438)
69 "Sensitivity and Specificity"/ (37627)
70 (risk$ or mortality or survival or death).ti. (238237)
71 (roc curve$ or sensitivity or specificity).ab. (359551)
72 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 (1014439)
73 EVAR.ti,ab. (422)
74 endovascular stent$.ti,ab. (1345)
75 endovascular repair$.ti,ab. (1373)
76 endovascular treat$.ti,ab. (2990)
77 endovascular surg$.ti,ab. (385)
78 endovascular aneurysm repair$.ti,ab. (438)
79 endoluminal stent$.ti,ab. (280)
80 endoluminal repair$.ti,ab. (171)
81 endoluminal treat$.ti,ab. (140)
82 endoluminal surg$.ti,ab. (24)
83 AAA endograft$.ti,ab. (14)
84 or/73-83 (6314)
85 72 and 84 (1297)
86 48 or 54 or 60 or 85 (1505)
87 from 86 keep 1-1505 (1505)

ISI Proceedings
Via Web of Science
Search date; 18th September 2007
Search strategy

TS=evar (140)
TS=(endovascular SAME (stent* OR repair* OR treat* OR surger*)) (1639)
TS=(endoluminal SAME (stent* OR repair* OR treat* OR surger*)) (241)
#1 or #2 or #3 (1804)
TS=(AAA OR abdominal aortic aneurysm* OR abdominal aneurysm*) (2273)
#5 or #4 (619)

MEDLINE(R)
Via Ovid
Search date: 6th September 2007
Database coverage: 1950 to August Week 5 2007
Search strategy:

1 EVAR.ti,ab. (404)
2 endovascular stent$.ti,ab. (1354)
endovascular repair$.ti,ab. (1394)
endovascular treat$.ti,ab. (2595)
endovascular surg$.ti,ab. (374)
endovascular aneurysm repair$.ti,ab. (417)
endoluminal stent$.ti,ab. (286)
endoluminal repair$.ti,ab. (169)
endoluminal treat$.ti,ab. (126)
endoluminal surg$.ti,ab. (20)
or/1-10 (5920)
AAA$.ti,ab. (5868)
exp aortic aneurysm, abdominal/ (8427)
abdominal aortic aneurysm$.ti,ab. (7979)
abdominal aneurysm$.ti,ab. (713)
or/12-15 (14579)
11 and 16 (1838)
AAA endograft$.ti,ab. (13)
17 or 18 (1846)
vascular surgical procedures/ (16153)
20 and 16 (1121)
or/19 or 21 (2645)
RANDOMIZED CONTROLLED TRIAL.pt. (242026)
CONTROLLED CLINICAL TRIAL.pt. (76175)
RANDOMIZED CONTROLLED TRIALS.sh. (50846)
RANDOM ALLOCATION.sh. (58962)
DOUBLE BLIND METHOD.sh. (93291)
SINGLE BLIND METHOD.sh. (11312)
or/23-28 (410206)
(ANIMALS not HUMANS).sh. (3178675)
29 not 30 (384781)
CLINICAL TRIAL.pt. (441091)
exp CLINICAL TRIALS/ (196388)
(clin$ adj25 trial$).ti,ab. (135407)
((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (92729)
PLACEBOS.sh. (26592)
placebo$.ti,ab. (104970)
random$.ti,ab. (385021)
RESEARCH DESIGN.sh. (49242)
or/32-39 (870519)
40 not 30 (807906)
41 not 31 (442725)
31 or 42 (827506)
22 and 43 (379)
limit 44 to yr="2005 - 2007" (126)
(EUROSTAR adj2 (registry or register or project or database or data or collaborat$ or group$)).ti,ab. (50)
(EUROSTAR and (evar or stent$ or graft$ or aneurysm$)).ti,ab. (60)
reta.ti,ab. (12)
registry of endovascular treatment of aneurysms.ti,ab. (1)
national vascular database.ti,ab. (5)
46 or 47 or 48 or 49 or 50 (77)
(Hardman adj (index or score$ or scoring or measure$)).ti,ab. (11)
Glasgow aneurysm score$.ti,ab. (21)
(POSSUM adj (index or score$ or scoring or measure$)).ti,ab. (85)
Modified Leiden Score.ti,ab. (2)
Modified Comorbidity Severity Score.ti,ab. (1)
52 or 53 or 54 or 55 or 56 (109)
risk assessment/ (81774)
risk factors/ (326347)
survival analysis/ (63460)
mortality/ (27549)
roc curve/ (11339)
"Sensitivity and Specificity"/ (171061)
(risk$ or mortality or survival or death).ti. (313939)
(roc curve$ or sensitivity or specificity).ab. (419309)
58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 (1155607)
EVAR.ti,ab. (404)
endovascular stent$.ti,ab. (1354)
endovascular repair$.ti,ab. (1394)
endovascular treat$.ti,ab. (2595)
endovascular surg$.ti,ab. (374)
endovascular aneurysm repair$.ti,ab. (417)
endoluminal stent$.ti,ab. (286)
endoluminal repair$.ti,ab. (169)
endoluminal treat$.ti,ab. (126)
endoluminal surg$.ti,ab. (20)
AAA endograft$.ti,ab. (13)
vascular surgical procedures/ (16153)
or/67-78 (21316)
66 and 79 (2246)
45 or 51 or 57 or 80 (2470)
from 81 keep 1-2470 (2470)

**MEDLINE(R) In-Process & Other Non-Indexed Citations**
Via Ovid
Search date: September 07, 2007
Search strategy:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EVAR.ti,ab. (37)</td>
</tr>
<tr>
<td>2</td>
<td>endovascular stent$.ti,ab. (66)</td>
</tr>
<tr>
<td>3</td>
<td>endovascular repair$.ti,ab. (74)</td>
</tr>
<tr>
<td>4</td>
<td>endovascular treat$.ti,ab. (127)</td>
</tr>
<tr>
<td>5</td>
<td>endovascular surg$.ti,ab. (15)</td>
</tr>
<tr>
<td>6</td>
<td>endovascular aneurysm repair$.ti,ab. (33)</td>
</tr>
<tr>
<td>7</td>
<td>endoluminal stent$.ti,ab. (9)</td>
</tr>
<tr>
<td>8</td>
<td>endoluminal repair$.ti,ab. (1)</td>
</tr>
<tr>
<td>9</td>
<td>endoluminal treat$.ti,ab. (4)</td>
</tr>
<tr>
<td>10</td>
<td>endoluminal surg$.ti,ab. (1)</td>
</tr>
<tr>
<td>11</td>
<td>or/1-10 (291)</td>
</tr>
<tr>
<td>12</td>
<td>AAA$.ti,ab. (181)</td>
</tr>
</tbody>
</table>
13 abdominal aortic aneurysm$.ti,ab. (185)
14 abdominal aneurysm$.ti,ab. (12)
15 AAA endograft$.ti,ab. (0)
16 or/13-15 (189)
17 11 and 16 (67)
18 RANDOMIZED CONTROLLED TRIAL.pt. (373)
19 CONTROLLED CLINICAL TRIAL.pt. (22)
20 CLINICAL TRIAL.pt. (354)
21 (clin$ adj25 trial$).ti,ab. (4733)
22 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (1686)
23 placebo$.ti,ab. (2174)
24 random$.ti,ab. (17378)
25 or/18-24 (21406)
26 17 and 25 (8)
27 (EUROSTAR adj2 (registry or register or project or database or data or collaborat$ or group$)).ti,ab. (1)
28 (EUROSTAR and (evar or stent$ or graft$ or aneurysm$)).ti,ab. (1)
29 reta.ti,ab. (0)
30 registry of endovascular treatment of aneurysms.ti,ab. (0)
31 national vascular database.ti,ab. (0)
32 27 or 28 or 29 or 30 or 31 (1)
33 (Hardman adj (index or score$ or scoring or measure$)).ti,ab. (2)
34 Glasgow aneurysm score$.ti,ab. (1)
35 (POSSUM adj (index or score$ or scoring or measure$)).ti,ab. (2)
36 Modified Leiden Score.ti,ab. (0)
37 Modified Comorbidity Severity Score.ti,ab. (0)
38 33 or 34 or 35 or 36 or 37 (4)
39 (risk$ or mortality or survival or death).ti. (8672)
40 (roc curve$ or sensitivity or specificity).ab. (12211)
41 39 or 40 (20606)
42 EVAR.ti,ab. (37)
43 endovascular stent$.ti,ab. (66)
44 endovascular repair$.ti,ab. (74)
45 endovascular treat$.ti,ab. (127)
46 endovascular surg$.ti,ab. (15)
47 endovascular aneurysm repair$.ti,ab. (33)
48 endoluminal stent$.ti,ab. (9)
49 endoluminal repair$.ti,ab. (1)
50 endoluminal treat$.ti,ab. (4)
51 endoluminal surg$.ti,ab. (1)
52 AAA endograft$.ti,ab. (0)
53 or/42-52 (291)
54 26 or 32 or 38 or 53 (295)
55 from 54 keep 1-295 (295)

Science Citation Index
Via Web of Science
Search date; 18th September 2007
Three separate searches carried out to identify RCTs, specified Registry reports, risk modelling studies

RCT search strategy (limited to 2005 to 2007)

TS=EVAR (253)
TS=(endovascular SAME (stent* OR repair* OR treat* OR surger*)) (2965)
TS=(endoluminal SAME (stent* OR repair* OR treat* OR surger*)) (252)
TS=(AAA OR abdominal aortic aneurysm* OR abdominal aneurysm*) (2954)
#3 or #2 or #1 (3143)
#5 AND #4 (798)
TS=(RANDOMIZED CONTROLLED-TRIAL or RANDOMISED CONTROLLED-TRIAL) (21120)
TI=(trial* or random*) (40781)
#8 or #7 (55388)
#9 and #6 (121)

Registry reports search strategy, no date limits.

TS=(EUROSTAR SAME (registry OR register OR project OR database OR data OR collaborat* OR group*)) (55)
TS=(EUROSTAR SAME (evar OR stent* OR graft* OR aneurysm*)) (41)
TS=(reta OR "registry of endovascular treatment of aneurysms" OR "national vascular database") (38)
TS=(hardman SAME (index OR score* OR scoring OR measure*)) (12)
TS=("glasgow aneurysm score*" OR "modified leiden score" OR "modified comorbidity severity score") (23)
TS=(possum same (index OR score* OR scoring OR measure*)) (190)
#6 OR #5 OR #4 OR #3 OR #2 OR #1 (313)

Risk modelling studies search strategy, no date limits.

TS=EVAR
TS=(endovascular SAME (stent* OR repair* OR treat* OR surger*))
TS=(endoluminal SAME (stent* OR repair* OR treat* OR surger*))
TS=("AAA endograft**")
#4 OR #3 OR #2 OR #1
TI=(risk* OR mortality OR survival OR death)
#6 and #5 (248 papers)

**Zetoc Conferences**
Search date: 18th September 2007
Series of searches carried out using terms: EVAR, endovascular stents, endovascular repair/treatment/surgery AND aneurysm
(170 papers identified)

To identify any ongoing studies the following were searched:

**Clinicaltrials.gov**
http://clinicaltrials.gov/
Search date: 11th September 2007
Search terms=aneurysm AND endovascular (no date limits)
Results=23

Current Controlled trials
http://www.controlled-trials.com/
Search date: 11th September 2007
Search terms=aneurysm AND endovascular (no date limits)
Results=45

National Research Register
Issue 3, 2007
Search date: 11th September 2007
Search strategy

#1 evar (67)
#2 (endovascular next stent*) (38)
#3 (endovascular next repair*) (49)
#4 (endovascular next treat*) (37)
#5 (endovascular next surger*) (16)
#6 (endoluminal next stent*) (2)
#7 (endoluminal next repair*) (6)
#8 (endoluminal next treat*) (0)
#9 (endoluminal next surger*) (0)
#10 (endovascular next aneurysm next repair*) (60)
#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 (180)
#12 aaa* (104)
#13 (abdominal next aortic next aneurysm*) (196)
#14 (abdominal next aneurysm*) (12)
#15 AORTIC ANEURYSM ABDOMINAL explode all trees (MeSH) (128)
#16 #12 or #13 or #14 or #15 (246)
#17 #11 and #16 (80)
#18 (aaa next endograft*) (1)
#19 (#17 or #18) (80)
#20 VASCULAR SURGICAL PROCEDURES explode tree 1 MeSH) (483)
#21 (#16 and #20) (17)
#22 (#19 or #21) (83)

Economics searches

EconLIT
Via WebSPIRS
Search date: 12th October 2007
Search strategy

#1 EVAR in ti.ab(0 records)
#2 endoluminal(0 records)
#3 endovascular(0 records)
#4 aaa(38 records)
#5 abdominal aortic aneurysm*(5 records)
#6 abdominal aneurysm*(1 records)
#7 aaa endograft*(0 records)
#8 vascular surgery(0 records)
#9 vascular surgical procedure*(0 records)
#10 (abdominal aortic aneurysm*) or (aaa) or (abdominal aneurysm*)(42 records)

EMBASE
Via Ovid
Search date: 11TH October 2007
Search strategy

#1 Health Economics/ (9545)
#2 exp Economic Evaluation/ (91514)
#3 exp Health Care Cost/ (93030)
#4 exp PHARMACOECONOMICS/ (48656)
#5 or/1-4 (176440)
#6 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (206766)
#7 (expenditure$ not energy).ti,ab. (8791)
#8 (value adj2 money).ti,ab. (390)
#9 budget$.ti,ab. (8045)
#10 or/6-9
#11 5 or 10 (305033)
#12 (metabolic adj cost).ti,ab.(356)
#13 ((energy or oxygen) adj cost).ti,ab.(1607)
#14 ((energy or oxygen) adj expenditure).ti,ab. (9073)
#15 or/12-14 (10558)
#16 11 not 15 (302646)
#17 editorial.pt. (198373)
#18 note.pt. 9219980)
#19 letter.pt. (394199)
#20 or/17-19 (812552)
#21 16 not 20 (261791)
#22 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dogs or dog or cats or bovine or sheep).ti,ab,sh. (1900407)
#23 exp animal/ (18204)
#24 Nonhuman/ (2965844)
#25 or/22-24 (3281976)
#26 exp human (5941940)
#27 exp human experiment/ (240151)
#28 26 or 27 (5942804)
#29 25 not (25 and 28) (2713634)
#30 21 not 29 (241038)
#31 EVAR.ti,ab. (430)
#32 endovascular stent$.ti,ab. (1359)
#33 endovascular repair$.ti,ab. (1392)
Technology Assessment Report For The HTA Programme

Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model

#34 endovascular treat$.ti,ab.(3038)
#35 endovascular surg$.ti,ab.(388)
#36 endovascular repair$.ti,ab. (442)
#37 endoluminal stent$.ti,ab.(281)
#38 endoluminal repair$.ti,ab.(171)
#39 endoluminal treat$.ti,ab.(141)
#40 endoluminal surg$.ti,ab.(24)
#41 or/31-40 (6391)
#42 AAA$.ti,ab. (5142)
#43 exp aorta aneurysm/(15998)
#44 abdominal aortic aneurysm$.ti,ab.(6795)
#45 abdominal aneurysm$.ti,ab.(518)
#46 or/42-45
#47 41 and 46
#48 AAA endograft$.ti,ab.(14)
#49 47 or 48 (2282)
#50 vascular surgery/ (11029)
#51 50 and 46 (1030)
#52 49 or 51 (3196)
#53 30 and 52 (138)
#54 limit 53 to yr="2006 - 2008" (24)

HEED
Search date: 11th October 2007
Search strategy

(EVAR OR endovascular OR endoluminal) AND (AAA OR abdominal OR aneurysm OR aneurysms) (57 records retrieved)

IDEAS
Via http://ideas.repec.org/
Search date: 11th October 2007

Series of searches using the following terms: endovascular, aneurysm (3 records retrieved)

MEDLINE
Via Ovid
Search date: 11th October 2007
Search strategy

#1 economics/ (25182)
#2 exp "costs and cost analysis"/(132702)
#3 economics,dental/(1702)
#4 exp "economics, hospital"/(14981)
#5 economics, medical/(6910)
#6 economics, nursing/(3749)
#7 economics, pharmaceutical/ (1842)
#8 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).tw.(248787)
#9 (expenditure$ not energy).tw. (10815)
#10 (value adj1 money).tw.(10)
#11 budget$.tw. (11233)
#12 or/1-11(352654)
#13 ((energy or oxygen) adj cost).ti,ab.(1938)
#14 (metabolic adj cost).ti,ab. (455)
#15 ((energy or oxygen) adj expenditure).ti,ab.(10439)
#16 or/13-15 (12303)
#17 12 not 16 (349802)
#18 EVAR.ti,ab. (423)
#19 endovascular stent$.ti,ab.(1374)
#20 endovascular repair$.ti,ab.(1422)
#21 endovascular treat$.ti,ab. (2632)
#22 endovascular surg$.ti,ab (375)
#23 endovascular aneurysm repair$.ti,ab.(430)
#24 endoluminal stent$.ti,ab. (286)
#25 endoluminal repair$.ti,ab. (169)
#26 endoluminal treat$.ti,ab. (128)
#27 endoluminal surg$.ti,ab.(20)
#28 or/18-27 (6011)
#29 AAA.$ti,ab. (5930)
#30 exp aortic aneurysm, abdominal/(8526)
#31 abdominal aortic aneurysm$.ti,ab.(8061)
#32 abdominal aneurysm$.ti,ab.
#33 or/29-32 (14725)
#34 28 and 33
#35 AAA endograft$.ti,ab.(13)
#36 34 or 35 (1884)
#37 vascular surgical procedures/(16286)
#38 37 and 33 (1148)
#39 36 or 38 (2702)
#40 17 and 39 (134)
#41 limit 40 to yr="2006 - 2007" (27)

**NHS EED**

Via internal CAIRS software
Search date: 10th October 2007
Search strategy

S EVAR
S endovascular(w)stent$
S endovascular(w)repair$
S endovascular(w)treat$
S endovascular(w)surg$
S endovascular(w)aneurysm(w)repair$
S endoluminal(w)stent$
S endoluminal(w)repair$
S endoluminal(w) treat$
S endoluminal(w) surg$
S S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10
S AAA
S aortic(w) aneurysm(w) abdominal
S abdominal(w) aortic(w) aneurysm$
S abdominal(w) aneurysm
S s12 or s13 or s14 or s15
S s11 and s16
S AAA(w) endograft$
S vascular(w) surgical(w) procedures
S s18 or s19
S s17 or s20
(25 records retrieved)
10.2 Quality assessment

Checklists for studies included in the systematic review of existing cost-effectiveness evidence

_Table 10.2.1 Checklist for Patel et al. (1999). The cost-effectiveness of endovascular repair versus open surgical repair of abdominal aortic aneurysms: A decision analysis model[^107]

<table>
<thead>
<tr>
<th>Study question</th>
<th>Grade</th>
<th>Patel et al. (1999)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Costs and effects examined</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selection of alternatives</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. All relevant alternatives are compared (including do-nothing if applicable)</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. The alternatives being compared are clearly described (who did what, to whom, where and how often)</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. The rationale for choosing the alternative programmes or interventions compared is stated</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Form of evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. The choice of form of economic evaluation is justified in relation to the questions addressed</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated?</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effectiveness data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion)</td>
<td>✓</td>
<td>Effectiveness data is drawn from a large range of sources and supplemented with a range of assumptions</td>
<td></td>
</tr>
<tr>
<td>10. Effectiveness data from RCT or review of RCTs</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Potential biases identified (especially if data not from RCTs)</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)</td>
<td>✓</td>
<td>Details are given, i.e. they have taken an average, but such methods are not considered suitable</td>
<td></td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. All the important and relevant resource use included</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. All the important and relevant resource use measured accurately (with methodology)</td>
<td>x</td>
<td>Large number of assumptions made regarding resource use</td>
<td></td>
</tr>
<tr>
<td>15. Appropriate unit costs estimated (with methodology)</td>
<td>?</td>
<td>Unit costs have been taken from the literature and cost accounting system at New York Presbyterian Hospital</td>
<td></td>
</tr>
<tr>
<td>16. Unit costs reported separately from resource use data</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Productivity costs treated separately from other costs</td>
<td>N/A</td>
<td>Productivity costs are not considered</td>
<td></td>
</tr>
<tr>
<td>18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion.</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefit measurement and valuation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. The primary outcome measure(s) for the economic evaluation are clearly stated</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Methods to value health states and other benefits are stated</td>
<td>✓</td>
<td>Methods to value health states are given although they appear inappropriate</td>
<td></td>
</tr>
<tr>
<td>21. Details of the individuals from whom valuations were obtained are given</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decision modelling</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 10.2.2 Checklist for Bosch et al. (2002). Abdominal Aortic aneurysms: Cost-effectiveness of Elective Endovascular and Open Surgical Repair

<table>
<thead>
<tr>
<th>Checkpoint</th>
<th>Grade</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study question</td>
<td>Bosch et al. (2002)</td>
<td></td>
</tr>
<tr>
<td>1. Costs and effects examined</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selection of alternatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. All relevant alternatives are compared (including do-nothing if applicable)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5. The alternatives being compared are clearly described (who did what, to whom, where and how often)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6. The rationale for choosing the alternative programmes or interventions compared is stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Form of evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37. Incremental analysis is reported using appropriate decision rules</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>38. Major outcomes are presented in a disaggregated as well as aggregated form</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>39. Applicable to the NHS setting</td>
<td>❌</td>
<td>US based</td>
</tr>
</tbody>
</table>
7. The choice of form of economic evaluation is justified in relation to the questions addressed.  ✔
8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated?  N/A

### Effectiveness data
9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion)  ✔
10. Effectiveness data from RCT or review of RCTs  ×
11. Potential biases identified (especially if data not from RCTs)  ✔
12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)  ✔

### Costs
13. All the important and relevant resource use included  ✔
14. All the important and relevant resource use measured accurately (with methodology)  ×
15. Appropriate unit costs estimated (with methodology)  ✔
16. Unit costs reported separately from resource use data  ×
17. Productivity costs treated separately from other costs  ×
18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion.  ✔ Costs in year 2000 US dollars

### Benefit measurement and valuation
19. The primary outcome measure(s) for the economic evaluation are clearly stated  ✔
20. Methods to value health states and other benefits are stated  ✔
21. Details of the individuals from whom valuations were obtained are given  ×

### Decision modelling
22. Details of any decision model used are given (e.g. decision tree, Markov model)  ✔ Markov model
23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified  ✔
24. All model outputs described adequately.  ✔ / × Only described adequately for the base-case, all sensitivity analyses given in terms of thresholds

### Discounting
25. Discount rate used for both costs and benefits  ✔ Both discounted at 3%
26. Do discount rates accord with NHS guidance?  × Discounted at 3% per annum, rather than 3.5%
Deterministic analysis
34. The approach to sensitivity analysis is given (e.g. univariate, threshold analysis etc) ✓
35. The choice of variables for sensitivity analysis is justified ✓
36. The ranges over which the variables are varied are stated ✓

Presentation of results
37. Incremental analysis is reported using appropriate decision rules ✓
38. Major outcomes are presented in a disaggregated as well as aggregated form ✓/✗ QALYs and costs are only disaggregated for the base-case analysis
39. Applicable to the NHS setting ✗

Table 10.2.3 Checklist for Michaels et al. (2005). Cost-effectiveness of endovascular abdominal aortic aneurysm repair

<table>
<thead>
<tr>
<th>Study question</th>
<th>Grade</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Costs and effects examined</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td>✓</td>
<td>NHS</td>
</tr>
</tbody>
</table>

Selection of alternatives
4. All relevant alternatives are compared (including do-nothing if applicable) ✓
5. The alternatives being compared are clearly described (who did what, to whom, where and how often) ✓
6. The rationale for choosing the alternative programmes or interventions compared is stated ✓

Form of evaluation
7. The choice of form of economic evaluation is justified in relation to the questions addressed. ✓
8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated? N/A

Effectiveness data
9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion) ✓
10. Effectiveness data from RCT or review of RCTs ✓/✗
11. Potential biases identified (especially if data not from RCTs) ✗ Not discussed in this article
12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies) ✗ Not discussed in this article as most of the parameters are drawn from a NICE review

Costs
13. All the important and relevant resource use included ✓
14. All the important and relevant resource use measured accurately (with methodology) ✓
15. Appropriate unit costs estimated (with methodology) ✓
16. Unit costs reported separately from resource use data ✓
17. Productivity costs treated separately from other costs ✗ This study does not consider productivity costs
18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion. ✓

Benefit measurement and valuation
19. The primary outcome measure(s) for the economic evaluation are clearly stated ✓
20. Methods to value health states and other benefits are stated ✓
21. Details of the individuals from whom valuations were obtained are given ✓

**Decision modelling**
22. Details of any decision model used are given (e.g. decision tree, Markov model) ✓
23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified ✓
24. All model outputs described adequately.

**Discounting**
25. Discount rate used for both costs and benefits ✓
26. Do discount rates accord with NHS guidance? ✓

**Allowance for uncertainty**
27. Details of statistical tests and confidence intervals are given for stochastic data ✗ Parameters are drawn from other studies and no discussion of any statistical tests conducted in these other studies is given here
28. Uncertainty around cost-effectiveness expressed (e.g. confidence interval around incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves).
29. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).
30. Are all appropriate input parameters included with uncertainty?
31. Is second-order uncertainty (uncertainty in means) included rather than first order (uncertainty between patients)?
32. Are the probability distributions adequately detailed and appropriate? ✓ / ✗ Beta distributions have been used appropriately for probabilities, but normal distributions have been used for costs which is inappropriate
33. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).

**Stochastic analysis of decision models**
34. The approach to sensitivity analysis is given (e.g. univariate, threshold analysis etc)
35. The choice of variables for sensitivity analysis is justified
36. The ranges over which the variables are varied are stated

**Deterministic analysis**
37. Incremental analysis is reported using appropriate decision rules
38. Major outcomes are presented in a disaggregated as well as aggregated form ✓ / ✗ Incremental QALYs and costs are disaggregated from one another, but the study does not given the actual level of costs or QALYs for each arm separately
39. Applicable to the NHS setting ✓

| Table 10.2.4 Checklist for Epstein et al. (2007). Modelling the long term cost-effectiveness of endovascular or open repair for abdominal aortic aneurysm |
|-----------------|-----------------|
| ✓ / ✗           | Epstein et al. (2007) |
| Study question  | Study question  |
| Grade           | Grade           |
|Comments         | Comments         |
| Grade           | Grade           |
| Grade           | Grade           |
| Grade           | Grade           |
| Grade           | Grade           |
| Grade           | Grade           |
| Selection of alternatives | Selection of alternatives |
4. All relevant alternatives are compared (including do-nothing if applicable) ✓

5. The alternatives being compared are clearly described (who did what, to whom, where and how often) ✓

6. The rationale for choosing the alternative programmes or interventions compared is stated ✓

Form of evaluation

7. The choice of form of economic evaluation is justified in relation to the questions addressed. ✓

8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated? N/A

Effectiveness data

9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion) ✓

10. Effectiveness data from RCT or review of RCTs ✓

11. Potential biases identified (especially if data not from RCTs)

12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies) N/A

Costs

13. All the important and relevant resource use included ✓

14. All the important and relevant resource use measured accurately (with methodology) ✓

15. Appropriate unit costs estimated (with methodology) ✓

16. Unit costs reported separately from resource use data ✓

17. Productivity costs treated separately from other costs X

18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion. ✓ 2004 UK pounds

Benefit measurement and valuation

19. The primary outcome measure(s) for the economic evaluation are clearly stated ✓

20. Methods to value health states and other benefits are stated X Values are reported in paper but no information on how they were valued is given here, although it is referenced to Kind (1996) so is clearly EQ-5D

21. Details of the individuals from whom valuations were obtained are given X

Decision modelling

22. Details of any decision model used are given (e.g. decision tree, Markov model) ✓

23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified ✓

24. All model outputs described adequately. ✓

Discounting

25. Discount rate used for both costs and benefits ✓

26. Do discount rates accord with NHS guidance? ✓

Allowance for uncertainty

Stochastic analysis of patient-level data

27. Details of statistical tests and confidence intervals are given for stochastic data ✓

28. Uncertainty around cost-effectiveness expressed (e.g. confidence interval around incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves). ✓

29. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data). ✓

Stochastic analysis of decision models

30. Are all appropriate input parameters included with uncertainty? ✓
31. Is second-order uncertainty (uncertainty in means) included rather than first order (uncertainty between patients)? ✔

32. Are the probability distributions adequately detailed and appropriate? ✗ No discussion of probability distributions in the paper although the model code is available on the internet

33. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data). ✔

**Deterministic analysis**

34. The approach to sensitivity analysis is given (e.g. univariate, threshold analysis etc) ✔ They have conducted scenario analyses

35. The choice of variables for sensitivity analysis is justified ✔

36. The ranges over which the variables are varied are stated ✔

**Presentation of results**

37. Incremental analysis is reported using appropriate decision rules ✔

38. Major outcomes are presented in a disaggregated as well as aggregated form ✔ / ✗ Incremental QALYs and costs are disaggregated from one another, but the study does not give the actual level of costs or QALYs for each arm separately

39. Applicable to the NHS setting ✔

---

**Table 10.2.5 Checklist for Prinssen et al. (2007). Cost-effectiveness of conventional and endovascular repair of abdominal aortic aneurysms: Results of a randomized trial**

<table>
<thead>
<tr>
<th>Study question</th>
<th>Grade</th>
<th>Prinssen et al. (2007) Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Costs and effects examined</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td>✗ Viewpoint is not stated but would appear to be societal due to the inclusion of productivity costs (in terms of sick leave)</td>
<td></td>
</tr>
</tbody>
</table>

**Selection of alternatives**

4. All relevant alternatives are compared (including do-nothing if applicable) ✔

5. The alternatives being compared are clearly described (who did what, to whom, where and how often) ✔

6. The rationale for choosing the alternative programmes or interventions compared is stated ✔

**Form of evaluation**

7. The choice of form of economic evaluation is justified in relation to the questions addressed. ✔

8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated? N/A

**Effectiveness data**

9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion) ✔

10. Effectiveness data from RCT or review of RCTs ✔

11. Potential biases identified (especially if data not from RCTs) ✔

12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies) N/A

**Costs**

13. All the important and relevant resource use included ✔
<table>
<thead>
<tr>
<th>Section</th>
<th>Item</th>
<th>Score</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology Assessment Report For The HTA Programme</td>
<td>Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. All the important and relevant resource use measured accurately (with methodology)</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Appropriate unit costs estimated (with methodology)</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Unit costs reported separately from resource use data</td>
<td>✓ / X</td>
<td></td>
<td>Unit costs are reported but resource use data is not</td>
</tr>
<tr>
<td>17. Productivity costs treated separately from other costs</td>
<td>✓ / X</td>
<td></td>
<td>Productivity costs are given separately but are also included in the total cost estimates</td>
</tr>
<tr>
<td>18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion.</td>
<td>✓</td>
<td></td>
<td>2003 Euros</td>
</tr>
<tr>
<td>Benefit measurement and valuation</td>
<td>19. The primary outcome measure(s) for the economic evaluation are clearly stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20. Methods to value health states and other benefits are stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21. Details of the individuals from whom valuations were obtained are given</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Decision modelling</td>
<td>22. Details of any decision model used are given</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(e.g. decision tree, Markov model)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24. All model outputs described adequately.</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Discounting</td>
<td>25. Discount rate used for both costs and benefits</td>
<td>X</td>
<td>Study has only a one year time horizon so even if discounting was performed any changes would be marginal</td>
</tr>
<tr>
<td>Allowance for uncertainty</td>
<td>Stochastic analysis of patient-level data</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>27. Details of statistical tests and confidence intervals are given for stochastic data</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28. Uncertainty around cost-effectiveness expressed (e.g. confidence interval around incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves).</td>
<td>✓ / X</td>
<td>Uncertainty in estimates of incremental costs and QALYs is represented by the presentation of the results of the bootstrapping on the cost-effectiveness plane</td>
</tr>
<tr>
<td></td>
<td>29. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Stochastic analysis of decision models</td>
<td>30. Are all appropriate input parameters included with uncertainty?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31. Is second-order uncertainty (uncertainty in means) included rather than first order (uncertainty between patients)?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32. Are the probability distributions adequately detailed and appropriate?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Deterministic analysis</td>
<td>34. The approach to sensitivity analysis is given</td>
<td>X</td>
<td>(e.g. univariate, threshold analysis etc)</td>
</tr>
<tr>
<td></td>
<td>35. The choice of variables for sensitivity analysis is justified</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>36. The ranges over which the variables are varied are stated</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Presentation of results</td>
<td>37. Incremental analysis is reported using appropriate decision rules</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>38. Major outcomes are presented in a disaggregated as well as aggregated form</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>39. Applicable to the NHS setting</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Table 10.2.6 Checklist for Medtronic submission. (2007). Endovascular Aneurysm Repair (EVAR) for the treatment of infra-renal Abdominal Aortic Aneurysms (AAA)

<table>
<thead>
<tr>
<th>Study question</th>
<th>Grade</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Costs and effects examined</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Selection of alternatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. All relevant alternatives are compared (including do-nothing if applicable)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5. The alternatives being compared are clearly described (who did what, to whom, where and how often)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6. The rationale for choosing the alternative programmes or interventions compared is stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Form of evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. The choice of form of economic evaluation is justified in relation to the questions addressed</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated?</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Effectiveness data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>10. Effectiveness data from RCT or review of RCTs</td>
<td>✓/✗</td>
<td></td>
</tr>
<tr>
<td>11. Potential biases identified (especially if data not from RCTs)</td>
<td>✓/✗</td>
<td></td>
</tr>
<tr>
<td>12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. All the important and relevant resource use included</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>14. All the important and relevant resource use measured accurately (with methodology)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>15. Appropriate unit costs estimated (with methodology)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>16. Unit costs reported separately from resource use data</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>17. Productivity costs treated separately from other costs</td>
<td>✗</td>
<td>Study does not consider productivity costs</td>
</tr>
<tr>
<td>18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion.</td>
<td>?</td>
<td>Costs are in UK pounds but the price year is unclear. Some of the reference costs are for 2005/6 but others are from earlier dates</td>
</tr>
<tr>
<td>Benefit measurement and valuation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. The primary outcome measure(s) for the economic evaluation are clearly stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>20. Methods to value health states and other benefits are stated</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>21. Details of the individuals from whom valuations were obtained are given</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Decision modelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22. Details of any decision model used are given (e.g. decision tree, Markov model)</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>24. All model outputs described adequately.</td>
<td>✓/✗</td>
<td>Costs and QALYs are not always disaggregated</td>
</tr>
<tr>
<td>Discounting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25. Discount rate used for both costs and benefits</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>26. Do discount rates accord with NHS guidance?</td>
<td>✓</td>
<td>Both costs and QALYs are discounted at a rate of 3.5%</td>
</tr>
<tr>
<td>Allowance for uncertainty</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stochastic analysis of patient-level data</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
27. Details of statistical tests and confidence intervals are given for stochastic data ✓ / X

28. Uncertainty around cost-effectiveness expressed (e.g. confidence interval around incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves). ✓

29. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data). ✓

**Stochastic analysis of decision models**

30. Are all appropriate input parameters included with uncertainty? ?

This is unclear from the report but has been done in the model

31. Is second-order uncertainty (uncertainty in means) included rather than first order (uncertainty between patients)? ✓

32. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data). ✓

33. Are the probability distributions adequately detailed and appropriate? ?

This is unclear from the report but has been done in the model

34. The approach to sensitivity analysis is given (e.g. univariate, threshold analysis etc) ✓

Univariate sensitivity analyses have been conducted

35. The choice of variables for sensitivity analysis is justified ✓

36. The ranges over which the variables are varied are stated ✓

**Deterministic analysis**

37. Incremental analysis is reported using appropriate decision rules ✓

38. Major outcomes are presented in a disaggregated as well as aggregated form ✓ / X

QALYs and costs have been disaggregated for the base-case analysis, but only ICERs are reported for the sensitivity analyses

39. Applicable to the NHS setting ✓

---

Table 10.2.7 Checklist for EVAR trial participants. (2005). Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial

<table>
<thead>
<tr>
<th>✓</th>
<th>X</th>
<th>Study question</th>
<th>Grade</th>
<th>EVAR trial participants (2005)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Costs and effects examined</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Alternatives compared</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The viewpoint(s)/perspective of the analysis is clearly stated (e.g. NHS, society)</td>
<td>X</td>
<td>Viewpoint is not clearly stated, although from reading the paper it is clear that it is NHS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Selection of alternatives**

4. All relevant alternatives are compared (including do-nothing if applicable) ✓

5. The alternatives being compared are clearly described (who did what, to whom, where and how often) ✓

6. The rationale for choosing the alternative programmes or interventions compared is stated ✓

**Form of evaluation**

7. The choice of form of economic evaluation is justified in relation to the questions addressed. ✓

8. If a cost-minimisation design is chosen, have equivalent outcomes been adequately demonstrated? ✓

**Effectiveness data**

9. The source(s) of effectiveness estimates used are stated (e.g. single study, selection of studies, systematic review, expert opinion) ✓

10. Effectiveness data from RCT or review of RCTs ✓

---

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<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Potential biases identified (especially if data not from RCTs)</td>
<td>?</td>
</tr>
<tr>
<td>12. Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)</td>
<td>x</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
</tr>
<tr>
<td>13. All the important and relevant resource use included</td>
<td>✓</td>
</tr>
<tr>
<td>14. All the important and relevant resource use measured accurately (with methodology)</td>
<td>✓</td>
</tr>
<tr>
<td>15. Appropriate unit costs estimated (with methodology)</td>
<td>✓</td>
</tr>
<tr>
<td>16. Unit costs reported separately from resource use data</td>
<td>x</td>
</tr>
<tr>
<td>17. Productivity costs treated separately from other costs</td>
<td>x ✓</td>
</tr>
<tr>
<td>Productivity costs were not considered</td>
<td></td>
</tr>
<tr>
<td>18. The year and country to which unit costs apply is stated with appropriate adjustments for inflation and/or currency conversion.</td>
<td>x</td>
</tr>
<tr>
<td><strong>Benefit measurement and valuation</strong></td>
<td></td>
</tr>
<tr>
<td>19. The primary outcome measure(s) for the economic evaluation are clearly stated</td>
<td>x</td>
</tr>
<tr>
<td>20. Methods to value health states and other benefits are stated</td>
<td>✓</td>
</tr>
<tr>
<td>21. Details of the individuals from whom valuations were obtained are given</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Decision modelling</strong></td>
<td></td>
</tr>
<tr>
<td>22. Details of any decision model used are given (e.g. decision tree, Markov model)</td>
<td>NA</td>
</tr>
<tr>
<td>23. The choice of model used and the key input parameters on which it is based are adequately detailed and justified</td>
<td>NA</td>
</tr>
<tr>
<td>24. All model outputs described adequately.</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Discounting</strong></td>
<td></td>
</tr>
<tr>
<td>25. Discount rate used for both costs and benefits</td>
<td>x</td>
</tr>
<tr>
<td>26. Do discount rates accord with NHS guidance?</td>
<td>?</td>
</tr>
<tr>
<td>Discount rate is not stated</td>
<td></td>
</tr>
<tr>
<td><strong>Allowance for uncertainty</strong></td>
<td></td>
</tr>
<tr>
<td>27. Details of statistical tests and confidence intervals are given for stochastic data</td>
<td>✓</td>
</tr>
<tr>
<td>28. Uncertainty around cost-effectiveness expressed (e.g. confidence interval around incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves).</td>
<td>x</td>
</tr>
<tr>
<td>29. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).</td>
<td>x</td>
</tr>
<tr>
<td><strong>Stochastic analysis of decision models</strong></td>
<td></td>
</tr>
<tr>
<td>30. Are all appropriate input parameters included with uncertainty?</td>
<td>NA</td>
</tr>
<tr>
<td>31. Is second-order uncertainty (uncertainty in means) included rather than first order (uncertainty between patients)?</td>
<td>NA</td>
</tr>
<tr>
<td>32. Are the probability distributions adequately detailed and appropriate?</td>
<td>NA</td>
</tr>
<tr>
<td>33. Sensitivity analysis used to assess uncertainty in non-stochastic variables (e.g. unit costs, discount rates) and analytic decisions (e.g. methods to handle missing data).</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Deterministic analysis</strong></td>
<td></td>
</tr>
<tr>
<td>34. The approach to sensitivity analysis is given (e.g. univariate, threshold analysis etc)</td>
<td>NA</td>
</tr>
<tr>
<td>35. The choice of variables for sensitivity analysis is justified.</td>
<td>NA</td>
</tr>
<tr>
<td>36. The ranges over which the variables are varied are stated</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Presentation of results</strong></td>
<td></td>
</tr>
<tr>
<td>37. Incremental analysis is reported using appropriate decision rules</td>
<td>NA</td>
</tr>
<tr>
<td>38. Major outcomes are presented in a disaggregated as well as aggregated form</td>
<td>?</td>
</tr>
<tr>
<td>39. Applicable to the NHS setting</td>
<td>✓</td>
</tr>
</tbody>
</table>
10.3 Survey of health-care resource use after EVAR and open repair

Concerns have been raised by Medtronic \(^{16}\) that the resource use collected from the EVAR trial \(^{1}^{45}\) may no longer accurately reflect current practice. To inform this issue, a postal survey was conducted on behalf of the evaluation team in January 2008 of members of the Vascular Society and the British Society of Interventional Radiology in hospitals where both EVAR and open repair is undertaken. 55 replies were received from 50 centres by 25 March 2008 (it should be noted that there has been some duplication from centres but due to differences in the responses we have treated each response as an individual case). The results of this survey are presented in the table 10.3.1 below.

According to the results of the survey, mean days in both ICU and general wards are lower in 2008 after both open repair and EVAR than were found by the EVAR trial 1, for patients enrolled between 1999 and 2003. The survey results also indicate that length of stay in general wards may have fallen slightly more after EVAR than open repair, but there is no evidence that the difference between EVAR and open repair in the use of HDU and ICU facilities has changed substantially since the EVAR trial 1. The difference in ward length of stay between the treatments in the EVAR trial 1 was 2.3 days, \(^{18}\) and the survey estimates a mean difference in 2008 of 4.3 days. The difference in ICU use estimated by EVAR trial 1 was 1.7 days, \(^{18}\) and the survey estimates a mean difference of 1.1 days.

The EVAR trial 1 found that patients attended on average 2 follow up visits in the first year after EVAR and 1 per year thereafter. \(^{18}\) The results of this survey indicate that this is still current practice but the frequency of surveillance tends to diminish over time.
Table 10.3.1. Results of the survey of resource use after EVAR and open repair

<table>
<thead>
<tr>
<th></th>
<th>EVAR (N= 55 replies)</th>
<th>Open Repair (N= 55 replies)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (proportion)</td>
<td>Median (proportion)</td>
</tr>
<tr>
<td>Prior to EVAR / Open Repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>does a critical care bed have</td>
<td>0.345</td>
<td>0</td>
</tr>
<tr>
<td>to be booked?*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If one is not available would</td>
<td>0.222</td>
<td>0</td>
</tr>
<tr>
<td>the procedure be cancelled?*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard planned post operative arrangements for EVAR / Open Repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days in ICU</td>
<td>0.019</td>
<td>0</td>
</tr>
<tr>
<td>Days in HDU</td>
<td>0.519</td>
<td>1</td>
</tr>
<tr>
<td>Days in General Ward</td>
<td>3.037</td>
<td>3</td>
</tr>
<tr>
<td>Current routine follow-up policy for a patient who has undergone EVAR / Open Repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (appointments per year)</td>
<td>Median (appointments per year)</td>
</tr>
<tr>
<td>Number of follow-up outpatient appointments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>2.000</td>
<td>2</td>
</tr>
<tr>
<td>Year 2</td>
<td>0.759</td>
<td>1</td>
</tr>
<tr>
<td>Year 3</td>
<td>0.648</td>
<td>1</td>
</tr>
</tbody>
</table>
## Number of CT follow-up

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
<th>Follow-up</th>
<th>Cost</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 4</td>
<td>0.623</td>
<td>1</td>
<td>0.073</td>
<td>0</td>
</tr>
<tr>
<td>After year 4</td>
<td>0.635</td>
<td>1</td>
<td>0.073</td>
<td>0</td>
</tr>
</tbody>
</table>

## Number of Ultrasound follow-up

<table>
<thead>
<tr>
<th>Year</th>
<th>Value</th>
<th>Follow-up</th>
<th>Cost</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>1.755</td>
<td>2</td>
<td>0.018</td>
<td>0</td>
</tr>
<tr>
<td>Year 2</td>
<td>0.827</td>
<td>1</td>
<td>0.036</td>
<td>0</td>
</tr>
<tr>
<td>Year 3</td>
<td>0.712</td>
<td>1</td>
<td>0.018</td>
<td>0</td>
</tr>
<tr>
<td>Year 4</td>
<td>0.653</td>
<td>1</td>
<td>0.055</td>
<td>0</td>
</tr>
<tr>
<td>After year 4</td>
<td>0.614</td>
<td>1</td>
<td>0.019</td>
<td>0</td>
</tr>
</tbody>
</table>

* 1 indicates a Yes and 0 a No
10.4 Data extraction tables

10.4.1 Data extraction tables - RCTs

Blankensteijn JD (2005). Two-Year Outcomes after Conventional or endovascular Repair of Abdominal Aortic Aneurysms 11, 44, 95, 169, 170

<table>
<thead>
<tr>
<th>Author (main publication)</th>
<th>Blankensteijn 2005 44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study publications</td>
<td>Main publication Blankensteijn 2005 44; 30-day outcomes from Prinssen 2004 43; quality of life outcomes from Prinssen 2004 45; design and methods Prinssen 2002 109</td>
</tr>
<tr>
<td>Study Name</td>
<td>DREAM</td>
</tr>
<tr>
<td>Country where study was performed</td>
<td>The Netherlands and Belgium</td>
</tr>
<tr>
<td>Centre entry criteria for trial</td>
<td>Surgical teams that had performed at least 5 endovascular procedures were eligible. Teams that had performed fewer than 20 procedures were required to have an experienced proctor assist them during the procedure. Scrub nurses and radiology technicians had to be trained specifically for EVAR. Participating centres required to have a yearly volume of at least 30 conventional AAA repairs and 50 endovascular procedures.</td>
</tr>
<tr>
<td>Patient entry criteria for trial</td>
<td>Age limitations: Not reported Aneurysm size: At least 5 cm in diameter Suitable for open repair: Yes Suitable for EVAR: Yes Elective repair; Non-symptomatic for which an intervention is indicated. Emergency repair: Patients needing emergency repair were excluded. Patients with inflammatory aneurysms, anatomical variations, connective-tissue disease, a history of organ transplantsations or a life expectancy of less than two years were excluded from the study. Patients needed to have an adequate infrarenal neck.</td>
</tr>
<tr>
<td>Number of patients randomised</td>
<td>351 patients of which 339 had an operation according to the randomised assignment.</td>
</tr>
<tr>
<td>Number of patients randomised to EVAR</td>
<td>173. One patient assigned to EVAR underwent Open Repair.</td>
</tr>
<tr>
<td>Number of patients randomised to comparator</td>
<td>178. Five patients assigned to Open Repair underwent EVAR.</td>
</tr>
<tr>
<td>Criteria assessing fitness for surgery/EVAR/open repair</td>
<td>Fitness for EVAR: Determined by endograft dependent anatomical criteria Fitness for open repair: Determined by an internist or cardiologist</td>
</tr>
<tr>
<td>Age of population</td>
<td>Mean (SD): 70.1 years (EVAR 70.7(6.6), Open 69.6(6.8))</td>
</tr>
<tr>
<td>Gender</td>
<td>91.7% male (EVAR 93.1%, Open 90.4%)</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Mean (SD): 6 cm (EVAR 6 cm(0.9) Open 6 cm(0.85))</td>
</tr>
<tr>
<td>Aneurysm anatomy</td>
<td>Not reported</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Current smokers: 209 (59.6%) (EVAR 111 (64.2%), Open 98 (55.1%))</td>
</tr>
<tr>
<td>Diabetes</td>
<td>35 (10%) (EVAR 18 (10.4%), Open 17 (9.6%))</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>154 (43.8%) (EVAR 71 (41%), Open 83 (46.6%))</td>
</tr>
<tr>
<td>Hypertension</td>
<td>198 (56.4%) (EVAR 101 (58.4%, Open 97 (54.5%))</td>
</tr>
<tr>
<td>Renal disease</td>
<td>28 (8%) (EVAR 13 (7.5%), Open 15 (8.4%))</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>81 (23%) (EVAR 48 (27.7%), Open 33 (18.5%))</td>
</tr>
<tr>
<td>Fitness scores</td>
<td>ASA I: 81 (23%) (EVAR 37(21.4%, Open 44(24.7%)) ASA II: 32 (66%)(EVAR 122(70.5%), Open 110(61.8%)) ASA III: 38 (10.8%)EVAR 14 (8.1%), Open 24(13.5%) ASA IV: 0</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>Mean (SD): 26.5(EVAR 26.3(3.4), Open 26.6(4.1))</td>
</tr>
<tr>
<td>Dates of procedure</td>
<td>November 2000 to December 2003</td>
</tr>
<tr>
<td>Time lapse between randomisation and procedure</td>
<td>Median: 39 days Range: 1 to 183 days</td>
</tr>
</tbody>
</table>
Elective or emergency procedure

Elective: 173 (100%)
Emergency: 0

Type of device (EVAR)

Zenith: 7 (33.3%)
Talent: 6 (26.9%)
Excluder: 37 (21.6%)
Other: 30 (17.5%)

Graft type (EVAR)

Uni-iliac: 6 (3.5%)
Bi-iliac: 160 (94%)
Endovascular tube graft: 1 (0.6%)

Anaesthesia

Local: 9 (5.3%)
Regional: 68 (39.8%)
General: 94 (54.9%)

Open repair or non-surgical procedure

Open repair
Particular open technique used was at the discretion of the surgeon.

Dates of procedure

November 2000 to December 2003

Time lapse between randomisation and procedure

Median: 39 days
Range: 4 to 260 days

Elective or Emergency procedure

Elective: 178 (100%)

Anaesthesia

Local: 1 (0.6%) (Crossover to EVAR)
Regional: 2 (1.1%) (Crossovers to EVAR)
General: 175 (98.3%) (all patients except 3 crossovers)

Intention to treat or per protocol

Intention to treat

Method for generating measures of effect

Cox proportional-hazards regression
Used to estimate HRs for reintervention rates

Covariates adjusted for

Not reported

Follow-up

Minimum follow-up: 1 month
Maximum follow-up: 42 months
Mean duration of follow up was 21 months in the open repair group and 22 months in the EVAR group.

30 day mortality

Number of EVAR patients (%) died: 2/171 (1.2%)
Number of comparator patients (%) died: 8/174 (4.6%)

Aneurysm related mortality at follow-up

Defined as death resulting from aneurysm rupture, graft infection or thrombosis; any death occurring within 30 days after the original procedure or a reintervention; or any death occurring more than 30 days after the original procedure or a reintervention but during the same admission.
Number of EVAR patients died: 3/173
Number of comparator patients died: 9/178
Cumulative rate from Kaplan-Meier curve: EVAR 2.1% Open 5.7%

All cause mortality at follow-up

Number of EVAR patients died: 20/173
Number of comparator patients died: 18/178
Cumulative rate from Kaplan-Meier Curve: EVAR 10.3% Open 10.4%

Rupture

No documented postoperative ruptures but rupture was considered a possible cause of death in two patients.
No documented postoperative ruptures.

Endoleak

Not reported

Device migration

Not reported

Re-interventions

Correction of endoleak (EVAR group only)
2 (1.2%) of which 1 was classed as severe (0.6%)
Hazard ratio: Nine months: 2.9 (95% CI: 1.1 to 6.2, p=0.03) favouring Open
> 9 months: 1.1 (95% CI: 0.1 to 9.3, p=0.95)

Major adverse events (30-day period)

Not reported
Quality of Life (QoL) measure used

Medical outcomes study short form (SF-36)
Baseline scores were compared with the scores of the general Dutch population of the same age. Changes in time with QoL scores were calculated relative to the preoperative level. Standardised effect sizes were calculated.

EuroQol-5D
Questionnaire about sexual function reported elsewhere but not data extracted.

Baseline scores

EVAR population mean (SD): Pre-operative score (based on 97% response rate, statistically greater than rate for Open Repair)
PF 70.1(22.8)
SF 70.0(25.3)
RP 52.9(45.5)
RE 60.7(44.0)
MH 68.0(20.1)
VT 60.0(23.3)
BP 71.8(28.2)
GH 62.9(18.5)

Comparator population mean (SD): Preoperative Score (based on 83% response rate)
PF 70.8(22.9)
SF 73.6(22.8)
RP 57.4(44.3)
RE 64.8(44.2)
MH 68.8(19.8)
VT 60.4(20.5)
BP 73.1(27.1)
GH 60.8(18.6)

Follow-up scores

EVAR population mean (SD): Time Points with response rates: 3 weeks (97%), 6 weeks (96%), 3 months (93%), 6 months (95%) and 12 months (94%)

Comparisons with baseline
At 3 weeks EVAR showed a statistically significant decrease compared to baseline on five of the eight SF domains (PF, SF, RP, VT, BP)
At 6 weeks after surgery three (SF, RE, VT) of the five decreased domains had returned to baseline. PF and RP showed a partial but statistically significant recovery.
At 3 months the group had recovered to baseline on all domains. There was a significant increase on MH.
At 12 months there was a statistically significant increase on RE and MH and a decrease on PF.

EuroQol-5D showed a significant decrease 3 weeks after surgery and at 6 weeks recovered to baseline and remained so at 3 months. At 6 months and 12 months there were statistically significant increases compared to baseline.

Comparator population mean (SD): Time points with response rates: 3 weeks (73%), 6 weeks (75%), 3 months (87%), 6 months (87%) and 12 months (91%).

Comparisons with baseline
At 3 weeks Open repair showed a statistically significant decrease on six of the eight SF domains (PF, SF, RP, RE, VT and BP).
At six weeks Open repair showed a partial recovery on all the impaired domains significantly for the PE, SF and VT.
At 3 months open repair recovered to baseline level on all domains. There was a statistically significant increase on MH and on GH.
At 12 months Open repair showed a significantly higher QoL than at baseline on three of the eight domains (SF, RE and MH). All other domains were at baseline level.

Mean difference between populations: EuroQol-5d
3 weeks: EVAR -0.6 Open -0.5 (p=0.857)
6 weeks: EVAR -0.3 Open -0.1 (p=0.426)
3 months: EVAR 0 Open 0.2 (p=0.646)
6 months: EVAR -0.2 Open 0.3 (p=0.005)
12 months: EVAR -0.1 Open 0.5 (p=0.004)

Length of hospital and ICU stay

Mean 6 days, Median 4 days (IQR 3 to 6) p<0.001 for comparison to Open Repair
Mean 0.66 days (16 hours), Median 3 hours (0 to 20) p<0.001 for comparison to Open Repair

Number of days in hospital for open repair population: Mean 13 days, Median 10
days (IQR 8 to 15)
Number of days in ICU for open repair population: Mean 3 days (72 hours), Median 23 hours (IQR 21 to 47)

Duration of surgery
Mean 135 minutes, Median 120 minutes (IQR 105 to 150) \( p \leq 0.001 \) for comparison to Open Surgery.
Duration of surgery for open repair population: Mean 151 minutes, Median 150 minutes (IQR 120 to 170)

Length of stay for reintervention
Not reported

Costs
Not reported

Analysis by type of device
No

Analysis by neck angulation
No

True randomisation
Yes

Adequate concealment of treatment allocation
Yes

Outcome assessor blinded
Yes: An outcome adjudication committee made up of five vascular surgeons assessed the class and severity of complications independently and blinded to treatment. Disagreements were resolved in a plenary consensus meeting.

Baseline characteristics comparable between groups
Yes

Eligibility criteria reported
Yes

Withdrawals or exclusions accounted for
Yes

Power calculation reported
Yes: 80% power to show a reduction of 50% in composite end point of operative mortality and moderate or severe complications at the two-sided 5 percent level with EVAR as opposed to Open Repair. 400 patients were required.

Intention to treat analysis
Yes


Author (main publication)
Cuypers 2001

Study publications
Main publication Cuypers 2001; quality of life data from Lottman 2004.

Country where study was performed
Netherlands

Multicentre
Yes

Centre entry criteria for trial
Not reported

Patient entry criteria for trial
Age limitations: Not reported
Aneurysm size: Larger than 50mm
Suitable for open repair: Yes

Number of patients randomised
76 patients

Number of patients randomised to EVAR
57

Number of patients randomised to comparator
19

Criteria assessing fitness for surgery/EVAR/open repair
Fitness for EVAR: 12-lead ECG and dobutamine stress echocardiogram (DSE).
Exclusion criteria: adverse aneurysm morphology for endografting, contrast allergy, medical conditions precluding open surgery.
Fitness for open repair (specify measurement tool if reported)
12-lead ECG and dobutamine stress echocardiogram (DSE).
Exclusion criteria: adverse aneurysm morphology for endografting, contrast allergy, medical conditions precluding open surgery.
### Technology Assessment Report For The HTA Programme

**Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of population</strong></td>
<td>Mean (SD): 68.5 years</td>
</tr>
<tr>
<td></td>
<td>69 years EVAR</td>
</tr>
<tr>
<td></td>
<td>68 years open repair</td>
</tr>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td></td>
<td>52-82 EVAR</td>
</tr>
<tr>
<td></td>
<td>52-81 open repair</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>92% male</td>
</tr>
<tr>
<td></td>
<td>EVAR - 54 of 57 (95%)</td>
</tr>
<tr>
<td></td>
<td>Open - 16 of 19 (84%)</td>
</tr>
<tr>
<td><strong>Aneurysm diameter</strong></td>
<td>Mean (SD): 5.4 cm</td>
</tr>
<tr>
<td></td>
<td>5.6 cm EVAR</td>
</tr>
<tr>
<td></td>
<td>5.2 cm open repair</td>
</tr>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td></td>
<td>5.2-8.4 cm EVAR</td>
</tr>
<tr>
<td></td>
<td>4.0-6.1 cm open repair</td>
</tr>
<tr>
<td><strong>Aneurysm anatomy</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
<td>Current smokers: 41%</td>
</tr>
<tr>
<td></td>
<td>26 (46%) EVAR</td>
</tr>
<tr>
<td></td>
<td>5 (26%) open repair</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>16%</td>
</tr>
<tr>
<td></td>
<td>8 (14%) EVAR</td>
</tr>
<tr>
<td></td>
<td>4 (21%) open repair</td>
</tr>
<tr>
<td><strong>Heart Disease</strong></td>
<td>46%</td>
</tr>
<tr>
<td></td>
<td>25 (44%) EVAR history of coronary artery disease</td>
</tr>
<tr>
<td></td>
<td>10 (53%) open repair history of coronary artery disease</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td>31 (54%) EVAR</td>
</tr>
<tr>
<td></td>
<td>12 (63%) open repair</td>
</tr>
<tr>
<td><strong>Renal disease</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Respiratory Disease</strong></td>
<td>28%</td>
</tr>
<tr>
<td></td>
<td>17 (30%) COPD - EVAR</td>
</tr>
<tr>
<td></td>
<td>4 (21%) COPD - open repair</td>
</tr>
<tr>
<td><strong>Fitness scores</strong></td>
<td>ASA II: 64%</td>
</tr>
<tr>
<td></td>
<td>34 (60%) EVAR</td>
</tr>
<tr>
<td></td>
<td>15 (79%) open repair</td>
</tr>
<tr>
<td></td>
<td>ASA III: 36%</td>
</tr>
<tr>
<td></td>
<td>23 (40%) EVAR</td>
</tr>
<tr>
<td></td>
<td>4 (21%) open repair</td>
</tr>
<tr>
<td><strong>Body Mass Index (BMI)</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Dates of procedure</strong></td>
<td>September 1996 to October 1999</td>
</tr>
<tr>
<td><strong>Time lapse between</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td>randomisation and</td>
<td></td>
</tr>
<tr>
<td>procedure</td>
<td></td>
</tr>
<tr>
<td><strong>Elective or emergency</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td>procedure</td>
<td>Probably elective, no mention of emergency</td>
</tr>
<tr>
<td><strong>Type of device (EVAR)</strong></td>
<td>3 patients (5%) Stentor</td>
</tr>
<tr>
<td></td>
<td>22 (39%) Vanguard</td>
</tr>
<tr>
<td></td>
<td>30 (52%) AneuRx</td>
</tr>
<tr>
<td></td>
<td>1 (2%) Lifepath</td>
</tr>
<tr>
<td></td>
<td>1 (2%) had open repair</td>
</tr>
<tr>
<td><strong>Graft type (EVAR)</strong></td>
<td>Bi-iliac: 57 (100%)</td>
</tr>
<tr>
<td><strong>Anaesthesia</strong></td>
<td>General: 57 (100%) patients</td>
</tr>
<tr>
<td><strong>Open repair or non-</strong></td>
<td>Open repair</td>
</tr>
<tr>
<td>surgical procedure</td>
<td></td>
</tr>
<tr>
<td><strong>Dates of procedure</strong></td>
<td>September 1996 to October 1999</td>
</tr>
<tr>
<td><strong>Time lapse between</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td>randomisation and</td>
<td></td>
</tr>
<tr>
<td>procedure</td>
<td></td>
</tr>
<tr>
<td><strong>Elective or Emergency</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td>procedure</td>
<td>1 emergency open repair, but analysed as EVAR.</td>
</tr>
<tr>
<td><strong>Anaesthesia</strong></td>
<td>General: 19 (100%) patients</td>
</tr>
<tr>
<td><strong>Intention to treat or</strong></td>
<td>Intention to treat: As randomised, not as treated</td>
</tr>
<tr>
<td>per protocol</td>
<td></td>
</tr>
<tr>
<td><strong>Method for generating</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td>measures of effect</td>
<td></td>
</tr>
<tr>
<td><strong>Covariates adjusted for</strong></td>
<td>Not reported</td>
</tr>
</tbody>
</table>

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Follow-up
Actual follow-up = 30 days

30 day mortality
Number of EVAR patients (%) died: 1 (2%)
Number of comparator patients (%) died: 1 (2%)

Aneurysm related mortality at follow-up
Number of EVAR patients died: 1 (2%) EVAR (pre 30 days)
Number of comparator patients died: 1 (2%) open repair (pre 30 days)
Not reported

All cause mortality at follow-up
Number of EVAR patients died: 2 (2%) pre 30 days
Number of comparator patients died: 1 (2%) pre 30 days

Rupture
Number of EVAR patients (%): One patient randomised to EVAR had an AAA rupture prior to surgery and received urgent open repair.
Number of comparator patients (%): None reported.

Endoleak
Not reported

Device migration
Not reported

Re-interventions
Conversion to open repair (EVAR group only)
One patient randomised to EVAR received an urgent open AAA repair because of aneurysm rupture prior to receiving EVAR. There were no other conversions to open repair

Major adverse events (30-day period)
Number of cardiac events for EVAR patients (%): 3 (5%)
Number of cardiac events for open repair patients (%): 2 (11%)

Quality of Life (QoL) measure used
Medical outcomes study short form (SF-36)

Baseline scores
EVAR population mean (SD): SF-36 (n=54):
  Physical functioning: 68 (SD 24)
  Social functioning: 83 (SD 24)
  Role limitations (physical): 62 (SD 45), (emotional) 64 (SD 48)
  Mental health: 69 (SD 27)
  Vitality: 63 (SD 26)
  Pain: 84 (SD 25)
  General health perceptions: 52 (SD 30)

  EuroQol-5 (n=53):
  Mobility (no problems): 53%; (problems) 47%; (confined to bed) 0%
  Self-care (no problems): 83%; (some problems) 17%; (unable to) 0%
  Usual activities (no problems): 57%; (some problems) 36%; (unable to) 7%
  Pain/Discomfort (none): 62%; (some) 32%; (extreme) 6%
  Anxiety/depression (none): 62%; (some) 30%; (extreme) 8%
  Health self-evaluation (maximum 100): 67 (SD 18)

Comparator population mean (SD)
SF-36 (n=18):
  Physical functioning: 68 (SD 26)
  Social functioning: 78 (SD 20)
  Role limitations (physical): 52 (SD 43), (emotional) 65 (SD 45)
  Mental health: 71 (SD 26)
  Vitality: 68 (26)
  Pain: 83 (SD 30)
  General health perceptions: 53 (SD 19)

  EuroQol-5 (n=18):
  Mobility (no problems): 50%; (problems) 50%; (confined to bed) 0%
  Self-care (no problems): 100%; (some problems) 0%; (unable to) 0%
  Usual activities (no problems): 44%; (some problems) 56%; (unable to) 0%
  Pain/Discomfort (none): 55%; (some) 39%; (extreme) 6%
  Anxiety/depression (none): 50%; (some) 22%; (extreme) 16%
  Health self-evaluation (maximum 100): 61 (SD 17)

Total population mean (SD)
SF-36 Form (n=72):
  Physical functioning: 68
  Social functioning: 81.8
  Role limitations (physical): 59.5; (emotional) 64.3
  Mental health: 69.5
  Vitality: 64.3
  Pain: 83.8
  General health perceptions: 52.3

  EuroQol-5 (n=71):
  Mobility (no problems): 52.2; (problems) 47.8; (confined to bed) 0
Self-care (no problems): 87.3; (some problems) 17 (EVAR); (unable to) 0
Usual activities (no problems): 42.5; (some problems) 41; (unable to) 7 (EVAR)
Pain/Discomfort (none): 60.2; (some) 33.8; (extreme) 6
Anxiety/depression (none): 59; (some) 28; (extreme) 10.5
Health self-evaluation: 65.5

Mean difference between populations
SF-36 Form (n=72):
Physical functioning: 0
Social functioning: 5
Role limitations (physical): 10; (emotional) 1
Mental health: 2
Vitality: 5
Pain: 1
General health perceptions: 1

Follow-up scores
EVAR population mean (SD): 1 month follow-up:
SF-36 (n=52)
Physical functioning: 61 (SD 24), P<0.05 (between group comparisons)
Social functioning: 71 (SD 27)
Role limitations (physical): 44 (SD 42), P<0.05 (between group comparisons); (emotional) 56 (SD 46)
Mental health: 74 (SD 23)
Vitality: 55 (SD 24), P<0.05 (between group comparisons)
Pain: 70 (SD 28), P<0.05 (between group comparisons)
General health perceptions: 47 (SD 26)

EuroQol-5 (n=52):
Mobility (no problems): 42%; (problems) 54%; (confined to bed) 4%
Self-care (no problems): 85%; (some problems) 13%; (unable to) 2%
Usual activities (no problems): 46%, p<0.05 (between group comparisons); (some problems) 42%; (unable to) 12%
Pain/Discomfort (none): 58%; (some) 36%; (extreme) 6%
Anxiety/depression (none): 73%; (some) 23%; (extreme) 4%
Health self-evaluation (maximum 100): 68 (SD 14)

3 month follow-up:
SF-36 (n=52)
Physical functioning: 70 (SD 26)
Social functioning: 86 (SD 16)
Role limitations (physical): 64 (SD 46); (emotional) 79 (SD 37)
Mental health: 73 (SD 23)
Vitality: 63 (SD 26)
Pain: 88 (SD 17)
General health perceptions: 63 (SD 30)

EuroQol-5 (n=50):
Mobility (no problems): 52%; (problems) 46%; (confined to bed) 2%
Self-care (no problems): 86%; (some problems) 12%; (unable to) 2%
Usual activities (no problems): 62%; (some problems) 34%; (unable to) 4%
Pain/Discomfort (none): 60%; (some) 40%; (extreme) 0%
Anxiety/depression (none): 80%; (some) 18%; (extreme) 2%
Health self-evaluation (maximum 100): 67 (SD 18)
Comparator population mean (SD)
1 month follow-up:
SF-36 (n=17):
Physical functioning: 44 (SD 27)
Social functioning: 56 (SD 33)
Role limitations (physical): 13 (SD 25), p<0.01 (within group comparisons relative to preoperatively); (emotional) 40 (SD 46)
Mental health: 63 (SD 25)
Vitality: 39 (SD 25), p<0.01 (within group comparisons relative to preoperatively)
Pain: 45 (SD 32), p<0.01 (within group comparisons relative to preoperatively)
General health perceptions: 54 (SD 24)
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EuroQol-5 (n=17):
Mobility (no problems): 29%; (problems) 65%; (confined to bed) 6%
Self-care (no problems): 82%; (some problems) 12%; (unable to) 6%
Usual activities (no problems): 12%, p<0.01 (within group comparisons relative to preoperatively); (some problems) 53%; (unable to) 35%
Pain/Discomfort (none): 29%; (some) 65%; (extreme) 6%
Anxiety/depression (none): 65%; (some) 29%; (extreme) 6%
Health self-evaluation (maximum 100): 61 (SD 16)

3 month follow-up:
SF-36 (n=17):
Physical functioning: 77 (SD 23)
Social functioning: 83 (SD 16)
Role limitations (physical): 57 (SD 45); (emotional) 69 (SD 43)
Mental health: 77 (SD 24)
Vitality: 64 (SD 26)
Pain: 83 (SD 17)
General health perceptions: 43 (SD 23)

EuroQol-5 (n=17):
Mobility (no problems): 53%; (problems) 47%; (confined to bed) 0%
Self-care (no problems): 88%; (some problems) 6%; (unable to) 6%
Usual activities (no problems): 65%; (some problems) 29%; (unable to) 6%
Pain/Discomfort (none): 59%; (some) 41%; (extreme) 0%
Anxiety/depression (none): 82%; (some) 12%; (extreme) 6%
Health self-evaluation (maximum 100): 61 (SD 17)

Total population mean (SD)
SF-36 Form (n=69) (1 month follow-up):
Physical functioning: 56.8
Social functioning: 67.3
Role limitations (physical): 36.4; (emotional) 52.1
Mental health: 71.3
Vitality: 51.1
Pain: 63.8
General health perceptions: 48.7

EuroQol-5 (n=69):
Mobility (no problems): 38.8; (problems) 56.7; (confined to bed) 4.5
Self-care (no problems): 84.3; (some problems) 12.8; (unable to) 3
Usual activities (no problems): 37.6; (some problems) 44.7; (unable to) 17.7
Pain/Discomfort (none): 50.9; (some) 43.1; (extreme) 6
Anxiety/depression (none): 71; (some) 24.5; (extreme) 4.5
Health self-evaluation: 66.3

SF-36 Form (n=69) (3 month follow-up):
Physical functioning: 71.7
Social functioning: 85.3
Role limitations (physical): 62.3; (emotional) 76.5
Mental health: 74
Vitality: 63.2
Pain: 86.8
General health perceptions: 58.1

Mean difference between populations
SF-36 Form (n=69) (1 month follow-up):
Physical functioning: 17
Social functioning: 15
Role limitations (physical): 31; (emotional) 16
Mental health: 11
Vitality: 16
Pain: 25

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General health perceptions: 7
EuroQol-5 (n=69):
  Mobility (no problems): 13; (problems) 11; (confined to bed) 2
  Self-care (no problems): 3; (some problems) 1; (unable to) 4
  Usual activities (no problems): 34; (some problems) 11; (unable to) 23
  Anxiety/depression (none): 8; (some) 6; (extreme) 2
  Health self-evaluation: 7

SF-36 Form (n=69) (3 month follow-up):
  Physical functioning: 7
  Social functioning: 3
  Role limitations (physical): 7; (emotional) 10
  Mental health: 4
  Pain: 5
  General health perceptions: 20

EuroQol-5 (n=67):
  Mobility (no problems): 1; (problems) 1; (confined to bed) 2
  Self-care (no problems): 2; (some problems) 6; (unable to) 4
  Usual activities (no problems): 3; (some problems) 5; (unable to) 2
  Pain/Discomfort (none): 1; (some) 1; (extreme) 0
  Anxiety/depression (none): 2; (some) 6; (extreme) 4
  Health self-evaluation: 6

Length of hospital and ICU stay
  Number of days in hospital for EVAR population: 5 days (2-21 days)
  Number of days in ICU for EVAR population: 19 hours (8-90 hours)
  Number of days in hospital for open repair population: 11 days (8-50 days)
  Number of days in ICU for open repair population: 21 hours (16-360 hours)

Duration of surgery
  Duration of surgery for EVAR population: 180 mins (65-320 mins)
  Duration of surgery for open repair population: 180 mins (120-270 mins)

Length of stay for reintervention
  Length of stay for EVAR population: Not applicable
  Length of stay for open repair population: Not applicable

Costs
  Not reported

Analysis by type of device
  No

Analysis by neck angulation
  No

True randomisation
  Unclear

Adequate concealment of treatment allocation
  Unclear

Outcome assessor blinded
  Unclear

Baseline characteristics comparable between groups
  Yes
  Aneurysm size and ASA slightly better in open repair group.

Eligibility criteria reported
  Yes

Withdrawals or exclusions accounted for
  Yes

Power calculation reported
  Yes

Intention to treat analysis
  Yes

EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. Lancet 2005;365:2179-2186 18; 45; 171; 9; 26; 97

Author (main publication)
  EVAR trial participants 2005 18

Study publications
  Main publication EVAR trial participants 2005 18. 30-day operative mortality results from EVAR trial participants 2004 11; design and methodology Brown 2004 8; device specific results EVAR trial participants 2007 26; survival by fitness EVAR trial participants 2007 26

Study Name
  EVAR I

Year of Publication
  Year of Publication
<table>
<thead>
<tr>
<th>Country where study was performed</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicentre</td>
<td>Yes</td>
</tr>
<tr>
<td>Centre entry criteria for trial</td>
<td>Centre performed at least 20 EVAR procedures</td>
</tr>
<tr>
<td>Patient entry criteria for trial</td>
<td>Min age 60 years. No max age limit. Aneurysm size: Mean diameter at least 5.5 cm Suitable for open repair: Yes Suitable for EVAR: Yes Emergency repair: Tender aneurysms and contained ruptures eligible if at least 5.5 cm and suitable EVAR equipment available at short notice.</td>
</tr>
<tr>
<td>Number of patients randomised</td>
<td>1082</td>
</tr>
<tr>
<td>Number of patients randomised to EVAR</td>
<td>543</td>
</tr>
<tr>
<td>Number of patients randomised to comparator</td>
<td>539</td>
</tr>
<tr>
<td>Criteria assessing fitness for surgery/EVAR/open repair</td>
<td>Fitness for EVAR: Determined locally by the surgeon, radiologist, anaesthetist and cardiologist. Guidelines on cardiac, respiratory and renal status were provided. Fitness for open repair: Determined locally by the surgeon, radiologist, anaesthetist and cardiologist. Guidelines on cardiac, respiratory and renal status were provided.</td>
</tr>
<tr>
<td>Age of population</td>
<td>Mean: 74 (SD 6) years (EVAR 74.2 (SD 6.0); open repair 74.0 (SD 6.1))</td>
</tr>
<tr>
<td>Gender</td>
<td>91% male (EVAR 494 (91%); open repair 489 (91%))</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Mean (SD) 6.5 cm (EVAR 6.5 (0.9); open repair 6.5 (1.0)) Measurement tool used: Spiral CT scan or conventional CT combined with conventional angiography.</td>
</tr>
<tr>
<td>Aneurysm anatomy</td>
<td>Not reported</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Current smokers: 232 (21%) (EVAR 115 (21%; open repair 117 (22%)) Past smokers: 747 (69%) (EVAR 367 (68%; open repair 380 (70%)) Never smoked: 102 (9%) (EVAR 61 (11%; open repair 41 (8%))</td>
</tr>
<tr>
<td>Diabetes</td>
<td>111 (10%) (EVAR 49 (9%; open repair 62 (12%))</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>463 (43%) (EVAR 234 (44%; open repair 229 (43%))</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Not reported</td>
</tr>
<tr>
<td>Renal disease</td>
<td>Not reported</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>Not reported</td>
</tr>
<tr>
<td>Fitness scores</td>
<td>Reported in 26. Analysis by fitness groups was based on 626 patients randomised to EVAR and 626 randomised to open repair up to 31 August 2004. Patients were classified as good, moderate or poor fitness based on modified Customized Probability Index scores. Good fitness 579 (301 EVAR; 278 open repair) Moderate fitness 331 (160 EVAR; 171 open repair) Poor fitness 338 (164 EVAR; 174 open repair) Missing fitness 4 (1 EVAR; 3 open repair)</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>Mean (SD): 26.4 (EVAR 26.4 (4.6); open repair 26.4 (4.4))</td>
</tr>
<tr>
<td>Dates of procedure</td>
<td>September 1999 to July 1 2004 for main analysis. Additional patients recruited up to August 31 2004 included in some analyses.</td>
</tr>
<tr>
<td>Time lapse between randomisation and procedure</td>
<td>Median: 43 days (IQR 28-60) Range: 28-70 days</td>
</tr>
<tr>
<td>Elective or emergency procedure</td>
<td>Elective: 512 (94% of randomised patients) Emergency: 0 (0%)</td>
</tr>
<tr>
<td>Type of device (EVAR)</td>
<td>Zenith: 261 (51%) (based on n = 512). N = 318 in later analysis based on patients randomised up to August 2004. Talent: 167 (33%) (based on n = 512). N = 187 in later analysis based on patients randomised up to August 2004. Excluder: 36 (7%) (based on n = 512). N = 37 in later analysis based on patients randomised up to August 2004. Quantum or Teramed 10 (2%) (based on n = 512)</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Uni-iliac: 51 (10%) (based on n = 512) Bi-iliac: 461 (90%) (based on n = 512)</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
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Open repair or non-surgical procedure
Open repair

Dates of procedure
September 1999 to July 1 2004 for main analysis. Additional patients recruited up to August 31 2004 included in some analyses.

Time lapse between randomisation and procedure
Median: 35 days (IQR 19-55)
Range: 20-59 days

Elective or Emergency procedure
Elective: 496 (92.0% of randomised patients)
Emergency: Unclear (possibly 3 (<1%))

Anaesthesia
Not reported

Intention to treat or per protocol
Intention to treat: Main analysis, including all randomised patients (EVAR 543; open repair 559). ITT analysis for 30-day mortality based on all randomised patients who underwent aneurysm repair (EVAR 531; open repair 516).
Per protocol: Analysis for 30-day and in-hospital mortality included patients who received the allocated elective treatment, excluding emergency repairs and patients converted from EVAR to open repair during the primary procedure (512 EVAR; 496 open).

Method for generating measures of effect
Cox proportional-hazards regression: Used for all-cause and aneurysm-related mortality
Logistic regression: Used for 30-day operative and in-hospital mortality

Covariates adjusted for
For all-cause mortality and aneurysm-related mortality
Primary covariates: age, sex, FEV1, AAA diameter log (creatinine), statin use at baseline.
Secondary covariates: BMI, smoking status, systolic blood pressure, serum cholesterol concentrations.

For 30-day operative mortality
Age, sex, FEV1, AAA diameter log (creatinine), statin use at baseline, time between randomisation and surgery.

Follow-up
Minimum follow-up: 1 year (at December 31 2004)
Maximum follow-up: Not reported (24% of patients followed up for 4 years as at 31 December 2004).
Median follow-up: 2.9 years (IQR 1.9-4.0) at December 2004

30 day mortality
Number of EVAR patients (%): 9/531 (1.7%) ITT; 8/512 (1.6%) per protocol.
Analysis by fitness groups (based on 626 patients randomised to EVAR up to 31 August 2004)
All patients 10/610 (1.6%)
Good fitness 3/294 (1.0%)
Moderate fitness 4/155 (2.6%)
Poor fitness 3/161 (1.9%)

Number of comparator patients (%): 24/516 (4.7%) ITT; 23/496 (4.6%) per protocol.
Analysis by fitness groups (based on 626 patients randomised to open repair up to 31 August 2004)
Good fitness 11/268 (4.1%)
Moderate fitness 6/162 (3.7%)
Poor fitness 8/163 (4.9%)

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Aneurysm related mortality at follow-up

All deaths within 30 days of any surgery for AAA unless overruled by post-mortem findings or a separate procedure (unrelated to the aneurysm) took place between aneurysm repair and death and was identified as the cause of death. Deaths for which the underlying cause was attributed to ICD codes 1713-19 were also classified as aneurysm-related.

Deaths within 30 days of any aneurysm surgery were categorised as procedure-related. Late complications of aneurysm repair (more than 30 days after operation) were also classified as aneurysm-related procedure deaths.

Number of EVAR patients died
19/543 (3 before surgery, 9 within 30 days of surgery, 7 >30 days after surgery).
Analysis by fitness groups (based on 626 patients randomised to EVAR up to 31 August 2004)
All patients 22/626
Good fitness 8/301
Moderate fitness 6/160
Poor fitness 8/164

Number of comparator patients died
34/539 (7 before surgery, 25 within 30 days of surgery, 2 >30 days after surgery)
Analysis by fitness groups (based on 626 patients randomised to EVAR up to 31 August 2004)
All patients 36/626
Good fitness 15/278
Moderate fitness 7/171
Poor fitness 14/174

Cumulative rate from Kaplan-Meier curve
EVAR 4%; open repair 7% (4-year point estimates)
Hazard ratio: 0.55 (95% CI: 0.31, 0.96).
Analysis by fitness groups (based on 626 patients randomised to EVAR and 626 randomised to open repair up to 31 August 2004)
All patients 0.60 (95% CI: 0.35, 1.02)
Good fitness 0.49 (95% CI: 0.21, 1.15)
Moderate fitness 0.91 (95% CI: 0.31, 2.70)
Poor fitness 0.60 (95% CI: 0.25, 1.44)
Adjusted hazard ratio
Adjusted for primary covariates: 0.55 (95% CI: 0.31, 0.96)
Adjusted for primary and secondary covariates: 0.51 (95% CI: 0.29, 0.92)

Analysis by fitness groups (based on 626 patients randomised to EVAR up to 31 August 2004)
All patients 0.61 (95% CI: 0.36, 1.04)
Good fitness 0.49 (95% CI: 0.21, 1.16)
Moderate fitness 1.00 (95% CI: 0.33, 3.00)
Poor fitness 0.50 (95% CI: 0.21, 1.23)
All cause mortality at follow-up

Number of EVAR patients died: 100/543 (10 before surgery, 9 within 30 days of surgery, 81 >30 days after surgery)
Analysis by fitness groups (based on 626 patients randomised to EVAR up to 31 August 2004)
All patients 138/626
Good fitness 50/301
Moderate fitness 38/160
Poor fitness 50/164

Number of comparator patients died: 109/539 (13 before surgery, 25 within 30 days of surgery, 71 >30 days after surgery)
Analysis by fitness groups (based on 626 patients randomised to open repair up to 31 August 2004)
All patients 145/626
Good fitness 59/278
Moderate fitness 37/171
Poor fitness 49/174

Cumulative rate from Kaplan-Meier Curve: EVAR 26%; open repair 29% (4-year point estimates)
Analysis by fitness groups (based on 626 patients randomised to EVAR and 626 to open repair up to 31 August 2004)
Good fitness 22% (95% CI: 18%, 26%)
Moderate fitness 26% (95% CI: 21%, 32%)
Poor fitness 30% (95% CI: 25%, 36%)
Hazard ratio: 0.90 (95% CI: 0.69, 1.18)

Analysis by fitness groups (based on 626 patients randomised to EVAR and 626 randomised to open repair up to 31 August 2004)
All patients 0.93 (95% CI: 0.74, 1.18)
Good fitness 0.76 (95% CI: 0.52, 1.11)
Moderate fitness 1.11 (95% CI: 0.71, 1.75)
Poor fitness 1.02 (95% CI: 0.68, 1.51)

Adjusted hazard ratio
Adjusted for primary covariates: 0.90 (95% CI: 0.69, 1.19)
Adjusted for primary and secondary covariates: 0.88 (95% CI: 0.67, 1.16)

Rupture

Number of EVAR patients (%): 3 fatal ruptures within 30 days. One further in-hospital death from rupture.
9 with graft rupture at follow-up (of 529 patients with repair completed).
Number of comparator patients (%): 2 fatal ruptures within 30 days. One further in-hospital death from rupture.
0 with graft rupture at follow-up (of 519 patients with repair completed).
Cumulative rate from K-M curve: Not reported
Hazard ratio: Not reported

Endoleak

Type I endoleak: 27 (17 with reintervention) at follow-up (of 529 EVAR patients with repair completed). Unspecified endoleak reported in 4 patients (4 with reintervention).
Type II endoleak: 79 (17 with reintervention) at follow-up (of 529 EVAR patients with repair completed)
Type III endoleak: 8 (4 with reintervention) at follow-up (of 529 EVAR patients with repair completed)
Cumulative rate from K-M curve: Not reported
Hazard ratio: Not applicable

Device migration

12 patients (7 with reintervention) at follow-up (of 529 EVAR patients with repair completed)

Re-interventions

Conversion to open repair (EVAR group only): 10/531 at 30 days (intention-to-treat)
Correction of endoleak (EVAR group only): 18/531 at 30 days (intention-to-treat)
Re-exploration of open repair (open group only): 15/516 at 30 days (intention-to-treat). (16 of 519 patients with open repair completed at follow-up).
Cumulative rate from K-M curve: EVAR 20%; open repair 6% (4-year point estimates)
Hazard ratio: 2.7 (95% CI: 1.8, 4.1)

Major adverse events (30-day period)

Not reported
Quality of Life (QoL) measure used

Medical outcomes study short form (SF-36): Physical component and mental component summary scores reported.

EuroQol-5D

Baseline scores

EVAR population mean (SD)
EQ5D: 0.75 (0.22) (541 patients)
SF36 physical component summary: 39.92 (5.92) (533 patients)
SF36 mental component summary: 43.59 (6.79) (533 patients)

Comparator population mean (SD)
EQ5D: 0.74 (0.23) (531 patients)
SF36 physical component summary: 39.83 (5.90) (534 patients)
SF36 mental component summary: 43.95 (6.73) (534 patients)

Mean difference between populations
EQ5D: 0.01 (SE 0.01)
SF36 physical component summary: 0.08 (SE 0.36)
SF36 mental component summary: -0.35 (SE 0.41)

Follow-up scores

EVAR population mean (SD)
EQ5D
0-3 months: 0.73 (0.21) (238 patients)
3-12 months: 0.71 (0.25) (476 patients)
12-24 months: 0.74 (0.24) (398 patients)

SF36 physical component summary
0-3 months: 37.82 (5.92) (225 patients)
3-12 months: 37.77 (5.73) (466 patients)
12-24 months: 38.17 (5.83) (359 patients)

SF36 mental component summary
0-3 months: 43.86 (7.02) (225 patients)
3-12 months: 44.64 (6.67) (466 patients)
12-24 months: 44.94 (6.43) (359 patients)

Comparator population mean (SD)
EQ5D
0-3 months: 0.67 (0.25) (245 patients)
3-12 months: 0.73 (0.23) (414 patients)
12-24 months: 0.75 (0.25) (371 patients)

SF36 physical component summary
0-3 months: 36.14 (5.45) (242 patients)
3-12 months: 37.81 (5.84) (394 patients)
12-24 months: 38.33 (5.78) (339 patients)

SF36 mental component summary
0-3 months: 44.04 (7.31) (242 patients)
3-12 months: 44.18 (6.81) (394 patients)
12-24 months: 44.76 (6.81) (339 patients)

Mean difference between populations
EQ5D
0-3 months: Crude 0.06 (SE 0.02); Adjusted for baseline score 0.05 (SE 0.02)
3-12 months: Crude -0.01 (SE 0.02); Adjusted for baseline score -0.01 (SE 0.01)
12-24 months: Crude -0.01 (SE 0.02); Adjusted for baseline score -0.02 (SE 0.02)

SF36 physical component summary
0-3 months: Crude 1.68 (SE 0.53); Adjusted for baseline score 1.66 (SE 0.50)
3-12 months: Crude -0.05 (SE 0.40); Adjusted for baseline score 0.04 (SE 0.37)
12-24 months: Crude -0.16 (SE 0.44); Adjusted for baseline score -0.15 (SE 0.40)

SF36 mental component summary
0-3 months: Crude -0.18 (SE 0.66); Adjusted for baseline score -0.05 (SE 0.66)
3-12 months: Crude 0.46 (SE 0.46); Adjusted for baseline score 0.41 (SE 0.45)
12-24 months: Crude -0.22 (SE 0.50); Adjusted for baseline score -0.29 (SE 0.49)

Length of hospital and ICU stay

Number of days in hospital for EVAR population: Mean 10.3 (SD 17.8); Median 7 (IQR 5-10)
Number of days in ICU for EVAR population: Mean 0.7 (SD 3.8) (Intensive therapy, intensive care or cardiac intensive care units)
Number of days in hospital for open repair population: Mean 15.7 (SD 16.9); Median 12 (IQR 9-16)
Number of days in ICU for open repair population: Mean 2.4 (SD 5.9) (Intensive therapy, intensive care or cardiac intensive care units)

Duration of surgery

Duration of surgery for EVAR population: Median 180 min (IQR 140-215)
Duration of surgery for open repair population: Median 200 (IQR 155-240)
Length of stay for reintervention
Not reported

Costs
Costs for EVAR: Primary hospital admission
Main procedure £7569
Hospital stay £3015
Other £235
Total £10819
Secondary procedures, adverse events, scans £2439
Total including 4-year follow-up £13258

Costs for comparator: Primary hospital admission
Main procedure £2811
Hospital stay £9304
Other £89
Total £9204
Secondary procedures, adverse events, scans £741
Total including 4-year follow-up £9945

Analysis by type of device
Reintervention rate, aneurysm-related mortality and all-cause mortality were compared for patients receiving Zenith (N = 318) and Talent (N = 187) endografts. There were no significant differences between devices for any outcome: adjusted hazard ratio 0.79 (95% CI: 0.51, 1.21) for reintervention, 0.88 (95% CI: 0.29, 2.65) for aneurysm-related mortality and 0.79 (95% CI: 0.53, 1.19) for all-cause mortality.

Analysis by neck angulation
No

True randomisation
Yes

Adequate concealment of treatment allocation
Yes

Outcome assessor blinded
Yes: Specifically stated for mortality

Baseline characteristics comparable between groups
Yes

Eligibility criteria reported
Yes

Withdrawals or exclusions accounted for
Yes

Power calculation reported
Yes

Intention to treat analysis
Yes


Author (main publication)
EVAR trial participants 2005

Study publications
Main publication EVAR trial participants 2005; design and methodology Brown 2004; device specific results EVAR trial participants 2007; survival by fitness EVAR trial participants 2007

Study Name
EVAR II

Country where study was performed
UK

Multicentre
Yes

Centre entry criteria for trial
Centre performed at least 20 EVAR procedures

Patient entry criteria for trial
Min age: 60 years
No max age limit
Mean diameter: 5.5 cm or greater
Suitable for open repair: No
Suitable for EVAR: Yes
Emergency repair: Tender aneurysms and contained ruptures eligible if at least 5.5 cm and suitable EVAR equipment available at short notice.

Number of patients randomised
338

Number of patients randomised to EVAR
166

Number of patients randomised to comparator
172

Criteria assessing fitness
Fitness for EVAR: Tender aneurysms and contained ruptures eligible if at least 5.5 cm
for surgery/EVAR/open repair and suitable EVAR equipment available at short notice.

### Age of population

Mean: 76.4 years (SD 6.45) (based on n=338)

- 76.8 (SD 6.2) EVAR
- 76.0 (SD 6.7) Non-surgical treatment
  (Based on n=143)
- 77.3 (SD 6.8) Zenith device
- 75.4 (SD 6.1) Talent

### Gender

288 (85%) male (based on n=339)

- 141 (85%) EVAR
- 147 (85%) non-surgical treatment
  (Based on n=143)

98 of 109 (89.9%) Zenith device
28 of 34 (82.4%) Talent

### Aneurysm diameter

Median 6.4 cm: EVAR, 6.3 cm non-surgical treatment

Range: 6.0-7.4 cm EVAR
6.0-7.0 cm non-surgical treatment

Measurement tool used: CT scan

### Aneurysm anatomy

AAA tender at randomisation (based on n=339):

- 12 patients (4%)
- 4 (2%) EVAR
- 8 (5%) non-surgical treatment
  (Based on n=143)

AAA top neck diameter:

- 2.4 cm (SD 0.3) Zenith device
- 2.4 cm (SD 0.4) Talent

AAA lower neck diameter:

- 2.6 cm (SD 0.3) Zenith
- 2.5 cm (SD 0.5) Talent

AAA neck length:

- 2.8 cm (SD 1.5) Zenith
- 2.8 cm (SD 1.0) Talent

### Smoking history

Current smokers:

- 57 (17%) (based on n=339)
- 29 of 166 (17%) EVAR
- 28 of 172 (16%) non-surgical treatment
  (Based on n=143)

- 27 (19%) (based on n=143)
- 25 of 109 (22.9%) Zenith
- 2 of 34 (5.9%) Talent

Past smokers:

- 259 (77%) (based on n=339)
- 127 of 166 (77%) EVAR
- 132 of 172 (77%) non-surgical treatment

107 (75%) (based on n=143)

- 76 of 109 (69.7%) Zenith
- 31 of 34 (91.2%) Talent

Never smoked: 22 (6%) (based on n=339)

- 10 of 166 (6%) EVAR
- 12 of 172 (7%) non-surgical treatment

### Diabetes

- 47 (14%)

### Heart Disease

- 233 (69%)

### Hypertension

Not reported

### Renal disease

Not reported

### Respiratory Disease

Not reported

### Fitness scores

Reported in 26

Fitness scores were assigned to patients randomised up to August 2004 (c.f. EVAR I).

Mean CPI fitness score 10.0 (SD 11.3) for 404 patients (197 EVAR and 207 no intervention). Little difference between randomised groups (details not reported).

Comparison of fitness - 179 patients underwent elective AAA repair in EVAR group and 60 patients in no intervention group.
Student's t test:
EVAR 10.5 (SD 11.8)
No intervention 6.3 (9.6)
Significant: p=0.014

Body Mass Index (BMI)
Mean (SD): 26.35 (based on n=339)
26.4 (SD 4.9) EVAR
26.3 (SD 4.4) non-surgical treatment
26.85 (based on n=143)
26.9 (SD 5.0) Zenith
26.8 (SD 4.6) Talent

Dates of procedure
September 1999 to 31st December 2003 (to August 2004 for extra patients included in some of the analyses)

Time lapse between randomisation and procedure
Median: 57 days (IQR 39-82) 150 patients randomised to EVAR
163 days (IQR 79-477) 47 patients crossed over from non-surgical treatment group (35 had EVAR, 12 had open repair).

Elective or emergency procedure
Not reported

Type of device (EVAR)
Talent: 31 of 150 (21%). N=34 in later analysis based on patients randomised up to August 2004.
Excluder: 9 of 150 (6%) (AneuRx (Medtronic)
5 of 150 (3%) Quantum (Cordis, Johnson & Johnson, Waterloo, Belgium)
2 of 150 (1%) Bard device (Bard, New Jersey)
1 of 150 (<1%) Anson Aorfix (Lambard Medical, Oxford, UK)
1 of 150 (<1%) EVT (Guidant, Indianapolis)
1 of 150 (<1%) Edwards Lifepath (Edwards Lifesciences, Switzerland)

Graft type (EVAR)
Uni-iliac: 14 (10%) based on n=143 in later analysis based on patients randomised up to August 2004. 7 using Zenith device and 7 using Talent device.
Bi-iliac: 127 (89%) based on n=143 in later analysis based on patients randomised up to August 2004. 102 using Zenith device and 25 using Talent device.

Anaesthesia
Local: Not explicitly reported in main publication.
66 (46%) based on n=143 in later analysis based on patients randomised up to August 2004. 49 using Zenith device and 17 using Talent device.
General: 73 (51%) based on n=143 in later analysis based on patients randomised up to August 2004. 59 using Zenith device and 14 using Talent device. 27 (16%) (47 crossovers)

Open repair or non-surgical procedure
Non-surgical procedure (any relevant details)

Dates of procedure
September 1999 to 31st December 2003 (to August 2004 for extra patients included in some analyses)

Time lapse between randomisation and procedure
Not applicable

Elective or Emergency procedure
Not applicable

Anaesthesia
Not applicable

Intention to treat or per protocol
Main analyses by ITT, as per predefined statistical analysis plan.
Post-hoc per protocol mortality analysis - patients excluded if they contravened their allocated treatment with censorship at the time of protocol violation.

Method for generating measures of effect
Cox proportional-hazards regression

Covariates adjusted for
Primary adjustments for age, sex, FEV1, AAA diameter, log (creatinine), and statin use. Secondary adjustments for variables in primary adjustment, plus BMI, smoking, systolic BP, and serum cholesterol (based on n=339).

Follow-up
Median follow-up: 2.4 years (IQR 1.6-3.6) at December 2004.

30 day mortality
Number of EVAR patients (%) died
13 of 150 (9%) (95% CI: 5-15)
Number of comparator patients (%) died
1 of 47 crossovers (2%)
Aneurysm related mortality at follow-up

Definition of aneurysm-related mortality at follow-up
All deaths within 30 days of any surgery for AAA unless overruled by post-mortem findings or a separate procedure (unrelated to the aneurysm) took place between aneurysm repair and death and was identified as the cause of death. Deaths for which the underlying cause was attributed to ICD codes 1713-19 were also classified as aneurysm-related.

Deaths within 30 days of any aneurysm surgery were categorised as procedure-related. Late complications of aneurysm repair (more than 30 days after operation) were also classified as aneurysm-related procedure deaths.

Number of EVAR patients died: 20 (based on n=166)
(Based on n=143)
7 of 109 (2.8 events per 100 person-years) - Zenith
3 of 34 (4.0 events per 100 person-years) - Talent
Number of comparator patients died: 22
Hazard ratio: 1.01 (95% CI: 0.56-1.84, p=0.98)

Post-hoc comparing EVAR and non-surgical treatment:
1.67 (95% CI: 0.72-3.86) - up to 6 months after randomisation
0.53 (95% CI: 0.20-1.39) - >6 months after randomisation
Adjusted hazard ratio
Primary adjusted: (based on n=339):
1.00 (95% CI: 0.54-1.84, p=1.0)
Secondary adjusted:
0.99 (95% CI: 0.53-1.84, p=0.97)

All cause mortality at follow-up

Number of EVAR patients died: 74 patients (14 prior to EVAR) (based on n=166)
46 of 109 (18.5 events per 100 person-years) - Zenith
18 of 34 (23.9 events per 100 person-years) - Talent
(based on n=143)
Number of comparator patients died: 68 patients
Cumulative rate from Kaplan-Meier Curve: EVAR 66%
non-surgical treatment 62% (4-year point estimates)
Hazard ratio: 1.21 (95% CI: 0.87-1.69, p=0.25) ITT (based on n=339)
Post hoc per protocol analysis:1.07 (95% CI: 0.75-1.52, p=0.70)
Post-hoc comparing EVAR and no intervention:
1.31 (95% CI: 0.70-2.45) - up to 6 months after randomisation
1.18 (95% CI: 0.80-1.73) - >6 months after randomisation
Adjusted hazard ratio
Primary adjusted (based on n=339):1.21 (95% CI: 0.86-1.69, p=0.27)
Secondary adjusted:1.24 (95% CI: 0.88-1.75, p=0.22)

Rupture

Number of EVAR patients (%): 9 prior to elective treatment
1 of 178 patients (includes crossovers) graft rupture after successful treatment
Number of comparator patients (%): 23 - crude rupture rate 9 per 100 person years
(95% CI: 6.0-13.5)

Endoleak

Type I endoleak: 11 of 178 patients who received EVAR - not ITT (10 complications after EVAR)
Type II endoleak: 23 of 178 patients who received EVAR - not ITT (17 complications after EVAR)
Type III endoleak: 6 of 178 patients who received EVAR - not ITT (5 complications after EVAR)

Device migration

Number of patients (%): 2 of 178 patients who received EVAR - not ITT (1%)
Re-interventions

Correction of endoleak (EVAR group only)
14 patients (based on n=178 who received EVAR - not ITT)

16 patients (based on n=143)
5 of 109 (4.6%) Type I - Zenith
1 of 34 (2.9%) Type I - Talent
4 of 109 (3.7%) Type II - Zenith
0 of 34 Type II - Talent
3 of 109 (2.8%) Type III - Zenith
1 of 34 (2.9%) Type III - Talent
0 of 109 Unspecified endoleak - Zenith
2 of 34 (5.9%) Unspecified - Talent

Graft rupture - 1 patient (based on n=178 who received EVAR - not ITT)
Graft kinking - 1 patient
Endotension - 1 patient
Graft thrombosis - 5 patients
Anastomotic aneurysm - 1 patient
Technical problem on graft insertion - 1 patient
Other surgery required - 8 patients

(Based on n=143)
Graft kinking 1 of 109 (0.9%) Zenith device
Endotension 1 of 34 (2.9%) Talent
Graft thrombosis:
1 of 109 (0.9%) Zenith
1 of 34 (2.9%) Talent
Other surgery (cardiac/abdominal or vascular):
5 of 109 (4.6%) Zenith
2 of 34 (5.9%) Talent
Other/unknown reintervention:
2 of 109 (1.6%) Zenith
2 of 34 (5.9%) Talent
Hazard ratio
Reintervention rate - 11.5 per 100 person years (EVAR)
1.8 per 100 person years (non-surgical treatment)
By 4 years: 26% EVAR, 4% non-surgical treatment: HR 5.8 (95% CI: 2.4-14, p=0.0001)

Major adverse events (30-day period)

Not reported

Quality of Life (QoL) measure used

Medical outcomes study short form (SF-36)
EuroQol-5D

Baseline scores

EVAR population mean (SD)
EQ5D Weighted index score: 0.58 (SD 0.31) (164 patients)
SF36 physical component summary: 35.47 (SD 6.63) (160 patients)
SF36 mental component summary: 45.13 (SD 7.92) (160 patients)

Comparator population mean (SD)
EQ5D Weighted index score: 0.63 (SD 0.28) (171 patients)
SF36 physical component summary: 35.12 (SD 6.23) (171 patients)
SF36 mental component summary: 46.31 (SD 6.97) (171 patients)

Mean difference between populations
EQ5D Weighted index score: -0.05
SF36 physical component summary: 0.35
SF36 mental component summary: -1.18
### Follow-up scores

<table>
<thead>
<tr>
<th>Duration</th>
<th>EVAR population mean (SD)</th>
<th>Comparator population mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EQ5D Weighted index score:</td>
<td></td>
</tr>
<tr>
<td>0-3 months</td>
<td>0.57 (SD 0.28)</td>
<td>0.56 (SD 0.29)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>0.64 (SD 0.28)</td>
<td>0.60 (SD 0.26)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>0.65 (SD 0.24)</td>
<td>0.60 (SD 0.30)</td>
</tr>
<tr>
<td>SF36 physical component summary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3 months</td>
<td>33.96 (SD 5.13)</td>
<td>35.60 (SD 5.70)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>34.33(SD 6.10)</td>
<td>35.12 (SD 6.42)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>34.54(SD 5.89)</td>
<td>36.01 (SD 6.92)</td>
</tr>
</tbody>
</table>

### SF36 mental component summary:

<table>
<thead>
<tr>
<th>Duration</th>
<th>EVAR population mean (SD)</th>
<th>Comparator population mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>45.76 (SD 8.65)</td>
<td>44.03 (SD 7.78)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>44.76 (SD 7.21)</td>
<td>44.84 (SD 7.85)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>45.36 (SD 7.20)</td>
<td>44.67 (SD 7.93)</td>
</tr>
</tbody>
</table>

### Comparator population mean (SD)

<table>
<thead>
<tr>
<th>Duration</th>
<th>EQ5D Weighted index score:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>0.01 (SE 0.05)</td>
<td>adjusted for baseline score 0.03 (SE 0.05) (139 patients)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>0.04 (0.03)</td>
<td>adjusted for baseline score 0.06 (0.03) (241 patients)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>0.05 (0.04)</td>
<td>adjusted for baseline score 0.04 (0.04) (156 patients)</td>
</tr>
</tbody>
</table>

### SF36 physical component summary:

<table>
<thead>
<tr>
<th>Duration</th>
<th>EVAR population mean (SD)</th>
<th>Comparator population mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>-1.64 (1.00)</td>
<td>adjusted for baseline score -1.86 (0.88) (134 patients)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>-0.78 (0.83)</td>
<td>adjusted for baseline score -1.11 (0.77) (224 patients)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>-1.47 (1.12)</td>
<td>adjusted for baseline score -0.64 (1.04) (130 patients)</td>
</tr>
</tbody>
</table>

### SF36 mental component summary:

<table>
<thead>
<tr>
<th>Duration</th>
<th>EVAR population mean (SD)</th>
<th>Comparator population mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>1.73 (1.47)</td>
<td>adjusted for baseline score 2.30 (1.38) (134 patients)</td>
</tr>
<tr>
<td>3-12 months</td>
<td>-0.08 (1.00)</td>
<td>adjusted for baseline score 0.94 (0.95) (224 patients)</td>
</tr>
<tr>
<td>12-24 months</td>
<td>-0.70 (1.32)</td>
<td>adjusted for baseline score 0.50 (1.29 (130 patients)</td>
</tr>
</tbody>
</table>

### Length of hospital and ICU stay
- Not reported

### Duration of surgery
- Not reported

### Length of stay for reintervention
- Not reported

### Costs
- Costs per patient of primary procedure and admission to hospital £11,016. Over 4 years £13,632
- Non-surgical treatment: £3,518. Over 4 years £4,983

### Analysis by type of device
- Reported in later publication

### Analysis by neck angulation
- No

### True randomisation
- Yes
### Adequate concealment of treatment allocation
- Yes

### Outcome assessor blinded
- Yes
  *For mortality and aneurysm-related mortality*

### Baseline characteristics comparable between groups
- Yes
  *Although slightly higher percentage in the no intervention group with history of cardiac disease (65% EVAR, 73% no intervention)*

### Eligibility criteria reported
- Yes

### Withdrawals or exclusions accounted for
- Yes

### Power calculation reported
- Yes
  *In addition, post hoc per protocol analysis calculated.*

### Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EVAR</th>
<th>No Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of population</td>
<td>Median 74 (IQR 68.8-79.5); open 80 (IQR 73.8-83.8)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>75% (24/32) male</td>
<td></td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Median 8.5 cm (IQR 8.0-10.0) in patients who had EVAR</td>
<td>Measurement tool used: CT scan</td>
</tr>
<tr>
<td>Aneurysm anatomy</td>
<td>In patients who had EVAR, median supra-renal diameter was 2.8 cm (IQR 2.5-3.1), neck length 1.5 cm (IQR 0.9-2.2) and neck diameter 2.6 cm (IQR 2.3-2.9).</td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td>Current smokers: 10/32 (31%); Past smokers: 11/32 (34%); Never smoked: 11/32 (34%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Heart Disease</td>
<td>8/32 (25%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13/32 (41%); measurement tool not reported.</td>
<td></td>
</tr>
<tr>
<td>Renal disease</td>
<td>3/32 (9%)</td>
<td></td>
</tr>
</tbody>
</table>

### Country where study was performed
- UK
  *University Hospital Nottingham*

### Centre entry criteria for trial
- Not reported
  *Investigator-initiated single centre trial*

### Patient entry criteria for trial
- Min age 50 years
- Exclusion criteria included neck diameter >3.2 cm and neck length <0.5 cm.
- Suitable for open repair: Yes
- Suitable for EVAR: No (Suitability for EVAR was not an entry criterion. Patients randomised to EVAR but found to be unsuitable were given open repair.)
- Emergency repair: Clinically suspected or radiologically confirmed rupture of infra-renal AAA.
- Other patient exclusion criteria: no endovascular team available; full selection of emergency stent-grafts not available; inability to give verbal or written consent; unconscious patient; allergy to radiological contrast, stainless steel or polyester; severe co-morbidity that would preclude intensive care treatment following open repair; previous EVAR; women of child bearing potential not taking contraception; pregnant and lactating women.

### Number of patients

<table>
<thead>
<tr>
<th>Randomised</th>
<th>EVAR</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>15</td>
<td>17</td>
</tr>
</tbody>
</table>

### Criteria assessing fitness for surgery/EVAR/open repair
- Fitness for EVAR: Opinion of the operating surgeon.
- Absolute contra-indications to EVAR: no evidence of aneurysm rupture; juxta-renal aneurysm; neck diameter <3.2 cm; external iliac artery diameter <0.6 cm.
- Relative contra-indications to EVAR: proximal neck length <1 cm; excessive thrombus in the proximal neck; common iliac artery length <2.5 cm; heavily calcified iliac arteries.
- Fitness for open repair: Opinion of the duty consultant vascular surgeon.

---

<table>
<thead>
<tr>
<th><strong>Respiratory Disease</strong></th>
<th>3/32 (9%) with chronic obstructive airways disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fitness scores</strong></td>
<td>Not reported: Not applicable to this patient population.</td>
</tr>
<tr>
<td><strong>Body Mass Index (BMI)</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Dates of procedure</strong></td>
<td>1 September 2002-31 December 2004</td>
</tr>
<tr>
<td><strong>Time lapse between randomisation and procedure</strong></td>
<td>Median</td>
</tr>
<tr>
<td><strong>Elective or emergency procedure</strong></td>
<td>Emergency</td>
</tr>
<tr>
<td><strong>Type of device (EVAR)</strong></td>
<td>All patients received a two piece aortouni-iliac stent graft made with Gianturco stents with an uncovered supra-renal component.</td>
</tr>
<tr>
<td><strong>Graft type (EVAR)</strong></td>
<td>Uni-iliac: 11 (100%) (Of 13 patients who underwent EVAR, 1 was converted to open repair and 1 to axillo-bifemoral graft).</td>
</tr>
<tr>
<td><strong>Anaesthesia</strong></td>
<td>General: 13 (100%)</td>
</tr>
<tr>
<td><strong>Open repair or non-surgical procedure</strong></td>
<td>Open repair</td>
</tr>
<tr>
<td><strong>Dates of procedure</strong></td>
<td>1 September 2002-31 December 2004</td>
</tr>
<tr>
<td><strong>Time lapse between randomisation and procedure</strong></td>
<td>Median</td>
</tr>
<tr>
<td><strong>Elective or Emergency procedure</strong></td>
<td>Emergency</td>
</tr>
<tr>
<td><strong>Anaesthesia</strong></td>
<td>General: 15 (100%)</td>
</tr>
<tr>
<td><strong>Intention to treat or per protocol</strong></td>
<td>Intention to treat: Planned interim analysis reported.</td>
</tr>
<tr>
<td><strong>Method for generating measures of effect</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Covariates adjusted for Follow-up</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>30 day mortality</strong></td>
<td>8/15 (53%) (ITT). Peri-operative mortality of those undergoing EVAR was 6/13 (46%). 9/17 (53%) (ITT). Peri-operative mortality of those undergoing open repair was 6/14 (43%).</td>
</tr>
<tr>
<td><strong>Aneurysm related mortality at follow-up</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>All cause mortality at follow-up</strong></td>
<td>Not reported</td>
</tr>
<tr>
<td><strong>Rupture</strong></td>
<td>Not reported: Not applicable as all patients had ruptured AAA.</td>
</tr>
<tr>
<td><strong>Endoleak</strong></td>
<td>Type I endoleak: 2.</td>
</tr>
<tr>
<td><strong>Device migration</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Re-interventions</strong></td>
<td>Conversion to open repair: 2. Correction of endoleak (EVAR group only): 2. Re-exploration of open repair (open group only): 3 within the first 24 hours.</td>
</tr>
<tr>
<td><strong>Major adverse events (30-day period)</strong></td>
<td>Number of cardiac events for EVAR patients (%) 5 (45%)(based on 11 patients who survived procedure). All events were moderate. Number of cardiac events for open repair patients (%) 7 (58%)(based on 12 patients who survived procedure). 6 events were moderate and 1 severe. Number of EVAR patients (%) suffering stroke 1 (9%)(based on 11 patients who survived procedure) with severe cerebrovascular complications. Number of open repair patients (%) suffering stroke: 0 (0%)</td>
</tr>
<tr>
<td><strong>Quality of Life (QoL) measure used</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Baseline scores</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Follow-up scores</strong></td>
<td>Not applicable</td>
</tr>
<tr>
<td><strong>Length of hospital and ICU stay</strong></td>
<td>Number of days in hospital for EVAR population: Median 10 days (IQR 6-28). Number of days in hospital for open repair population: Median 12 days (IQR 4-52).</td>
</tr>
<tr>
<td><strong>Duration of surgery</strong></td>
<td>Duration of surgery for EVAR population: Median 160 minutes (IQR 150-234). Duration of surgery for open repair population: Median 150 minutes (IQR 141-204).</td>
</tr>
<tr>
<td><strong>Length of stay for reintervention</strong></td>
<td>Not reported</td>
</tr>
</tbody>
</table>
### Technology Assessment Report For The HTA Programme

**Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model**

<table>
<thead>
<tr>
<th>Costs</th>
<th>Not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis by type of device</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Analysis by neck angulation</td>
<td>No</td>
</tr>
<tr>
<td>True randomisation</td>
<td>Unclear</td>
</tr>
<tr>
<td>Adequate concealment of treatment allocation</td>
<td>No</td>
</tr>
<tr>
<td>Outcome assessor blinded</td>
<td>Unclear</td>
</tr>
<tr>
<td>Baseline characteristics comparable between groups</td>
<td>Yes</td>
</tr>
<tr>
<td>Eligibility criteria reported</td>
<td>Yes</td>
</tr>
<tr>
<td>Withdrawals or exclusions accounted for</td>
<td>Yes</td>
</tr>
<tr>
<td>Power calculation reported</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Intention to treat analysis**

Power calculation required 100 patients for trial to have 90% power to detect a reduction in mortality from 50% with open repair to 25% with EVAR.

---

**Soulez et al. Pain and Quality of Life Assessment after Endovascular Versus Open Repair of Abdominal Aortic Aneurysms in Patients at Low Risk. J Vasc Interv Radiol 2005;16(8):1093-1100**

| Author (main publication) | Soulez 2005  
| Country where study was performed | Canada  
| Multicentre | Not reported  
| Centre entry criteria for trial | Not reported  
| Patient entry criteria for trial | Max age 80 years  
| | Aneurysm size: Non-ruptured AAA measuring at least 5 cm in diameter, located below the renal arteries.  
| Number of patients randomised | 40  
| Number of patients randomised to EVAR | 20  
| Number of patients randomised to comparator | 20  
| Criteria assessing fitness for surgery/EVAR/open repair | Fitness for EVAR: Cardiac evaluation according to American College of Cardiology/American Heart Association Guidelines.  
| | Morphologic exclusion criteria: proximal aortic aneurysm neck larger than 30mm in diameter or shorter than 15mm in length, angulation of proximal aneurysm neck greater than 60 degrees, iliac arteries with marked tortuosity or less than 7mm in diameter, AAA extending into both external iliac arteries, dominant inferior mesenteric artery, and a large accessory renal artery >/=3mm with its origin within the aneurysm.  
| | Fitness for open repair (specify measurement tool if reported) Cardiac evaluation according to American College of Cardiology/American Heart Association Guidelines.  
| | Morphologic exclusion criteria: proximal aortic aneurysm neck larger than 30mm in diameter or shorter than 15mm in length, angulation of proximal aneurysm neck greater than 60 degrees, iliac arteries with marked tortuosity or less than 7mm in diameter, AAA extending into both external iliac arteries, dominant inferior mesenteric artery, and a large accessory renal artery >/=3mm with its origin within the aneurysm.  
| Age of population | Mean (SD): 70.5 years  
| | 70.3 (SD 6.4) EVAR  
| | 71.2 (SD 7.6) open repair  

---

Final Report 1st April 2008
| Gender | 39 patients (98%) male  
| 19 of 20 (95%) EVAR  
| 20 of 20 (100%) open repair |
| Aneurysm diameter | Mean (SD): 5.2 cm  
| 5.31 cm (SD 0.48) EVAR  
| 5.09 cm (SD 1.61) open repair |
| Measurement tool used: Spiral computed tomography (CT). |
| Aneurysm anatomy | Neck angulation: Aneurysm neck not greater than 60 degrees. |
| Smoking history | Current smokers: 8 (20%)  
| 5 (25%) EVAR  
| 3 (15%) open repair |
| Past smokers (specify number (%)) patients | 27 (68%)  
| 14 (70%) EVAR  
| 13 (65%) open repair |
| Never smoked (specify number (%)) patients | 5 (12%)  
| 1 (5%) EVAR  
| 4 (20%) open repair |
| Diabetes | Yes: 6 (15%)  
| 1 (5%) EVAR  
| 5 (25%) open repair |
| Heart Disease | Yes: 27 (68%)  
| 13 (65%) EVAR  
| 14 (70%) open repair |
| Hypertension | Yes: 18 (45%)  
| 8 (40%) EVAR  
| 10 (50%) open repair |
| Renal disease | Yes: CrCl < 50mL/min: 6 (15%)  
| 1 (5%) EVAR  
| 5 (25%) open repair |
| Respiratory Disease | Yes: 9 (22%)  
| 6 (30%) EVAR  
| 3 (15%) open repair |
| Fitness scores | Cardiac status NYHA Class 1: 18 (45%)  
| 10 (50%) EVAR  
| 8 (40%) open repair  
| Cardiac status NYHA Class 2: 22 (55%)  
| 10 (50%) EVAR  
| 12 (60%) open repair |
| Body Mass Index (BMI) | Mean (SD): 17 (42%) BMI > 30  
| 8 (40%) > 30 EVAR  
| 9 (45%) > 30 open repair |
| Dates of procedure | September 1998 to July 2002 |
| Time lapse between randomisation and procedure | Not reported |
| Elective or emergency procedure | Not reported  
| Probably elective |
| Type of device (EVAR) | Talent: 20 patients (100%) |
| Graft type (EVAR) | Bi-iliac: 20 (100%) EVAR patients |
| Anaesthesia | Local: 1 (5%) EVAR  
| Regional: 1 (5%) EVAR  
| General: 18 (90%) EVAR |
| Open repair or non-surgical procedure | Open repair |
| Dates of procedure | September 1998 to July 2002 |
| Time lapse between randomisation and procedure | Not reported |
| Elective or Emergency procedure | Elective |
| Anaesthesia | General: 20 (100%) |
| Intention to treat or per | Not reported |
### Protocol

**Method for generating measures of effect**
- Not applicable

**Covariates adjusted for**
- Not reported

**Follow-up**
- Minimum follow-up: 9 months EVAR
- Maximum follow-up: 48 months EVAR
- Median follow-up: Range: 9–48 months EVAR
- Minimum follow-up: 12 months open repair
- Maximum follow-up: 48 months open repair
- Median follow-up: Range: 12–48 months open repair

### 30 day mortality
- Number of EVAR patients (%): 0%
- Number of comparator patients (%): 0%

### Aneurysm related mortality at follow-up
- Number of EVAR patients died: 1 (5%)
- Number of comparator patients died: 0%
- Cumulative rate from Kaplan-Meier curve
  - \( p = 0.80 \); log-rank test (includes survival and reinterventions)

### All cause mortality at follow-up
- Not reported

### Rupture
- Number of EVAR patients (%): 1 (5%)
- Number of comparator patients (%): 0%

### Endoleak
- Type I endoleak: 2 (10%) EVAR
- Type II endoleak: 3 (15%) EVAR

### Device migration
- Not reported

### Re-interventions
- Correction of endoleak (EVAR group only): 4 patients
- Re-exploration of open repair (open group only):
  - 1 patient - operative treatment on an emergency basis with graft limb thrombosis, 7 months after surgery

### Major adverse events (30-day period)
- Not reported

### Quality of Life (QoL) measure used
- Medical outcomes study short form (SF-36)

### Baseline scores
- Not reported

### Follow-up scores
- **EVAR population mean (SD)**
  - Follow-up at 24 months
    - Physical Functioning: 50
    - Role Physical: 48
    - Bodily Pain: 56
    - General Health Perceptions: 58
    - Energy/vitality: 48
    - Social Functioning: 60
    - Role Emotional: 58
    - Mental Health: 58
  - Comparator population mean (SD)
    - Follow-up at 24 months
      - Physical Functioning: 62
      - Role Physical: 66
      - Bodily Pain: 62
      - General Health Perceptions: 66
      - Energy/vitality: 62
      - Social Functioning: 78
      - Role Emotional: 76
      - Mental Health: 70

### Length of hospital and ICU stay
- Number of days in hospital for EVAR population: 4.5 (SD 2.4) days
- Number of days in ICU for EVAR population: 3.4 (SD 11.3) hours
- Number of days in hospital for open repair population: 11.5 (SD 8.1) days
- Number of days in ICU for open repair population: 38.5 (SD 33) hours

### Duration of surgery
- Duration of surgery for EVAR population: 110 (SD 32) minutes
- Duration of surgery for open repair population: 127 (SD 50) minutes
Length of stay for reintervention
Length of stay for EVAR population: 1.7 (SD 5.7) days (aneurysmal disease)
Length of stay for open repair population: 3 (SD 8) days (aneurysmal disease)

Costs  
Not reported

Analysis by type of device  
Not applicable

Analysis by neck angulation  
No

True randomisation  
Unclear

Adequate concealment of treatment allocation  
Unclear

Outcome assessor blinded  
Unclear

Baseline characteristics comparable between groups  
Yes

Eligibility criteria reported  
Yes

Withdrawals or exclusions accounted for  
Yes

Power calculation reported  
No

Intention to treat analysis  
Unclear

10.4.2 Data extraction tables - Registries


<table>
<thead>
<tr>
<th>Author</th>
<th>Ashley 2005 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registry Name</td>
<td>National Vascular Database</td>
</tr>
<tr>
<td>Country/countries included in registry</td>
<td>UK</td>
</tr>
<tr>
<td>Multicentre</td>
<td>59 centres (listed on page 12)</td>
</tr>
<tr>
<td>Centre entry criteria</td>
<td>Not reported</td>
</tr>
<tr>
<td>Patient entry criteria</td>
<td>Suitable for open repair: Yes</td>
</tr>
<tr>
<td>Number of patients treated with comparator</td>
<td>Open infrarenal aortic aneurysm surgery: 4545</td>
</tr>
<tr>
<td>Criteria assessing fitness for surgery/EVAR/open repair</td>
<td>Not reported</td>
</tr>
<tr>
<td>Age of population</td>
<td>Mean 72.5 years (standard error 0.12)</td>
</tr>
<tr>
<td>Gender</td>
<td>3756/4449 patients (84.4%) male</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Range</td>
</tr>
<tr>
<td></td>
<td>Majority of unruptured AAAs: 5.0-7.9 cm</td>
</tr>
<tr>
<td></td>
<td>Majority of ruptured AAAs: 6.0-8.9 cm</td>
</tr>
<tr>
<td></td>
<td>&lt;5 cm: 88 patients</td>
</tr>
<tr>
<td></td>
<td>5-5.9 cm: 775</td>
</tr>
<tr>
<td></td>
<td>6-6.9 cm: 1113</td>
</tr>
<tr>
<td></td>
<td>7-7.9 cm: 588</td>
</tr>
<tr>
<td></td>
<td>8-8.9 cm: 404</td>
</tr>
<tr>
<td></td>
<td>9-9.9 cm: 136</td>
</tr>
<tr>
<td></td>
<td>&gt;9.9 cm: 109</td>
</tr>
<tr>
<td></td>
<td>Unspecified: 1251</td>
</tr>
<tr>
<td>Measurement Tool</td>
<td>Not reported</td>
</tr>
<tr>
<td>Aneurysm anatomy</td>
<td>Not reported</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Not reported</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Not reported</td>
</tr>
<tr>
<td>Heart disease</td>
<td>Cardiac history (myocardial infarction (MI) &lt;= 6 months ago; MI &gt; 6 months ago; heart failure &lt;= 1 month ago, heart failure &gt; 1 month ago; orthopnoea; angina - controlled/on exertion; angina - uncontrolled/at rest): 2011 patients (44.2%)</td>
</tr>
</tbody>
</table>
Hypertension: Not reported  
Renal disease: Not reported  
Respiratory disease: Not reported  
Fitness scores: Not reported  
BMI: Not reported  
Open repair or non-surgical procedure: Open repair  
Dates of procedure: Registered 1999 - 31 March 2004  
Time lapse between registration and procedure: Not reported  
Elective or emergency procedure: 
Elective: Unruptured AAA: 1734 patients  
Crude mortality rate: 6.3% (95% CI: 5.2, 7.6%)  
Emergency: Non-elective unruptured AAA: 423  
Crude mortality rate: 9.2% (95% CI: 6.7, 12.5%)  
Unspecified: Unruptured AAA: 743  
Crude mortality rate: 6.7% (95% CI: 5.1, 8.8%)  
Anaesthesia: 
Local: (0.02%)  
Regional: Epidural: 34 (0.7%)  
General: General: 2461 (54.1%)  
General + epidural: 1503 (33.1%)  
TOTAL: 3964 (87.2%)  
Unspecified: 546 patients (12%)  
Intention to treat or per protocol: Not reported  
Follow-up: Not reported  
30 day mortality: 
Crude mortality rate: 
Unruptured: 6.8% (95% CI: 5.9-7.8%)  
Ruptured: 41% (95% CI: 37.7-44.3%)  
TOTAL: 14.8% (95% CI: 13.7-16.0%)  
Aneurysm related mortality at follow-up: Not reported  
All cause mortality at follow-up: Not reported  
Rupture: Not reported  
Endoleak: Not applicable  
Device migration: Not applicable  
Re-interventions: Not reported  
Major adverse events (30-day period): Not reported  
Quality of Life measure used: Not reported  
Baseline scores: Not reported  
Follow-up scores: Not reported  
Length of hospital and ICU stay: 
Average: 
Unruptured: 13 days (SE 0.21)  
Ruptured: 15.2 days (SE 0.55)  
Duration of surgery: 
<30 mins: 9/2326 patients (0.4%)  
30-59 mins: 28 patients (1.2%)  
60-89 mins: 145 patients (6.2%)  
90-119 mins: 356 patients (15.3%)  
120-149 mins: 506 patients (21.8%)  
150-179 mins: 458 patients (19.6%)  
180-209 mins: 363 patients (15.6%)  
210-239 mins: 154 patients (6.6%)  
240-269 mins: 136 patients (5.8%)  
270-299 mins: 65 patients (2.8%)  
300-329 mins: 41 patients (1.8%)  
330-359 mins: 22 patients (1%)  
>359 mins: 45 patients (1.9%)  
Unspecified: 2219 patients  
Length of stay for reintervention: Not reported  
Costs: Not reported

Author
EUROSTAR Collaborators 2006 56

Registry Name
EUROSTAR

Country/countries included in registry
Europe

Multicentre
177 centres

Centre entry criteria
Sufficient expertise in centre, which is involvement in a series of at least 10 stent-graft procedures for AAA. Throughput of at least 10 patients/year and patients managed by collaborating vascular surgeons and international radiologists.

Patient entry criteria
Minimum age 21 years
Aneurysm size (specify, eg. diameter, length or not reported)
Patients with aortic aneurysms <3 cm with iliac aneurysms, pseudo-aneurysms or previous (conventional/endovascular) grafts were excluded. Aortic aneurysms measuring 3-4 cm included if they were associated with iliac aneurysms.
Anatomic configuration suitable for stented tube or bifurcated prosthesis:
Infrarenal neck length >=1.5 cm and width <2.5 cm.
Iliac artery angulation <90 degrees (or correctable angulation),
Common iliac artery <1.2 cm in diameter and nonstenotic (>0.6 cm diameter after balloon dilation, if necessary).
Elective repair (specify relevant details)
Elective AAA-operation, without symptoms of rupture or expansion.

Number of patients treated with EVAR
8345

Criteria assessing fitness for surgery/EVAR/open repair
Not reported

Age of population
Mean age at operation: 72.5 (SD 7.8) years
Range: 34-100 years

Gender
93.2% male

Aneurysm diameter
Mean transverse diameter: 5.84 cm (SD 1.16 cm)
Range: 3.0-17.2 cm

Measurement Tool
CT scan, intra-arterial digital subtraction arteriogram (IA-DSA), MRI, or Intra-vascular ultrasound (IVUS).

Aneurysm anatomy
Mean aortic neck angulation: 55.8 degrees (SD 35.8 degrees)
Range: 4-240 degrees

Smoking history
Current smokers: 1885/8107 patients (23.3%) (SVS/ISCVS risk score 2/3)
Past smokers: 2252/8107 patients (27.8%) SVS/ISCVS risk score 1 (none current, but smoked in last 10 years)
Never smoked: 3970/8107 patients (49%) SVS/ISCVS risk score 0 (no tobacco use or none for last 10 years)

Diabetes
Yes: 1045/8126 patients (12.9%)

Heart disease
Cardiac: 4957/8141 patients (60.9%) (SVS/ISCVS risk score 1-3)
Carotid: 1436/8038 patients (17.9%) (SVS/ISCVS risk score 1-3)

Hypertension
Yes: 5337/8142 patients (65.5%) (SVS/ISCVS risk score 1-3)

Renal disease
Yes:
1155/8066 patients (14.3%) creatinine 1.5-3.0mg/dl, creatinine clearance 30-50ml/min (SVS/ISCVS risk score 1).
252/8066 (3.1%) patients creatinine 3.0-6.0mg/dl, creatinine clearance 15-30ml/min (SVS/ISCVS risk score 2).
131/8066 (1.6%) patients creatinine >6.0ml/dl, creatinine clearance <15ml/min or on dialysis or with transplant.

Respiratory disease
Pulmonary:
3419/8079 patients (42.3%) (SVS/ISCVS risk score 1-3)

Fitness scores
ASA I: 635/8268 (7.7%)
ASA II: 3467/8288 patients (41.8%)
ASA III: 3643/8288 patients (44%)
ASA IV: 543/8288 (7%) (indicating that a patient is too frail to justify open repair).
2037/8345 patients (24.4%) unfit for open repair when factors other than ASA (eg. obesity, previous laparotomies were considered).

BMI
2186/8248 patients (26.5%) considered obese

Dates of procedure
Not reported
Data related to 'older' devices excluded from the report.

Time lapse between registration and procedure
Not reported
### Type of device (EVAR)

- **Zenith**: 3290/8304 patients (39.6%)
- **Talent**: 2349/8304 patients (28.3%)
- **Excluder**: 1155/8304 patients (13.9%)
- **AneuRx**: 984/8304 patients (11.8%)
- **Endologix**: 134/8304 patients (1.6%)
- **Fortron**: 92/8304 patients (1.1%)
- **EVT**: 73/8304 patients (0.9%)
- **Anaconda**: 66/8304 patients (0.8%)

### Graft type (EVAR)

- **Bi-iliac**: 7497/8345 patients (89.8%)
- **Straight**: 156/8345 patients (1.9%)
- **Tapered**: 561/8345 patients (6.7%)
- **Unknown**: 131/8345 patients (1.6%)

### Anaesthesia

- **Local**: 515/8345 patients (6.2%)
- **Regional**: 2091/8345 patients (25.1%)
- **General**: 5739/8345 patients (68.8%)

### Intention to treat or per protocol

- Intention to treat: According to

### Follow-up

- Minimum follow-up: 30-days
- Maximum follow-up: 96 months (8 years)

### 30 day mortality

- 190/8345 patients (2.3%)

### Aneurysm related mortality at follow-up

- Not reported

### All cause mortality at follow-up

- 789/8345 patients (9.5%) late mortality (ie. after 30 days, up to 96 months)
- Cumulative rate from K-M curve: 979
- Proportion deaths: 0.390
- Proportion surviving: 0.610
- Survival standard error: 0.036

### Rupture

- 30-days: 4
- Follow-up: 37
- TOTAL: 41 (0.5%)
- Cumulative rate from K-M curve
- Freedom from rupture at 84 months: Total number: 41
- Proportion of ruptures: 0.031
- Proportion rupture free: 0.969 (SE 0.011)

### Endoleak

- Cumulative rate from K-M curve
- 30-days: 496
- Follow-up: 827
- Total: 1323
- Proportion endoleaks: 0.325
- Proportion endoleak free: 0.675 (SE 0.021)

### Device migration

- 30-days: 6
- Follow-up: 148
- TOTAL: 154

### Re-interventions

- Conversion to open repair
- 30-day conversion: 75 patients (0.9%)
- Follow-up conversion: 102 patients (1.2%)
- TOTAL: 177 patients (2.1%)
- Cumulative rate from K-M curve
- Freedom from secondary interventions at 84 month follow-up:
  - Total number: 749
  - Proportion of secondary interventions: 0.18
  - Proportion of secondary intervention free: 0.82
  - Secondary intervention free standard error: 0.013

### Major adverse events (30-day period)

- Number of cardiac events: 272
- Number of patients suffering stroke
  - Cerebra: 57
  - Systemic complications from operation to discharge:
    - Pulmonary: 174
    - Renal: 181

### Quality of Life measure used

- Not reported
Baseline scores | Not reported
Follow-up scores | Not reported
Length of hospital and ICU stay | 8169 patients (98 patients with hospital stay ≤1 day)
Mean: 5.9 (SD 8.1) days
Range: 0-163 days
Duration of surgery | 8065 patients
Mean duration: 130 (SD 58) mins
Range: 25-720 mins
Length of stay for reintervention | Not reported
Costs | Not reported

Thomas SM, Beard JD, Ireland M, Ayers S. Results from the prospective Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA): mid term results to five years 2005;29(6):563-570 [58, 60, 59]

Author | Thomas 2005 [58], additional data from undated Vascular Surgical Society report [59] and Thomas 2001 [60]
Registry Name | RETA
Country/countries included in registry | UK
Multicentre | 41 centres submitted cases.
Centre entry criteria | Not reported (UK members of the Vascular Surgery Society and British Society of Interventional Radiology registered cases on a voluntary basis).
Patient entry criteria | Age limitations: Not reported.
Aneurysm size: Not reported.
Suitable for open repair: Yes.
Patients classified as fit or unfit for open repair were included.
Suitable for EVAR: Yes.
Elective repair: No criteria specified but majority of cases were elective repair of asymptomatic (83.2%) or symptomatic (13.5%) AAA.
Emergency repair: No criteria specified but small numbers of cases were repair of acute non-ruptured (1.6%) or stable ruptured (1.4%) AAA.

Number of patients treated with EVAR | 1000 cases from 41 centres.
Criteria assessing fitness for surgery/EVAR/open repair | Fitness for EVAR: Based on aneurysm morphology but no specific details reported.
Fitness for open repair
Fit: patients in ASA grade I-III
Unfit: patients in ASA grades IV or V specified as unfit for open repair because of comorbidity, also those classified as 'fit' by ASA grade but with other features making them high risk (unsuitable) for open repair.
Age of population | Median (range): 73 years.
Range: 44-93 years.
Gender | Percentage male (total population)
90% (based on 514 cases) [59]
Aneurysm diameter | Mean (SD): Median 6 cm.
42% classified as large aneurysms (> 6 cm).
Range: 2.5-15 cm.
Measurement Tool | Not reported
Aneurysm anatomy | Median infra-renal neck length 2.4 cm.
Smoking history | Not reported
Diabetes | Not reported
Heart disease | Not reported
Hypertension | Not reported
Renal disease | Not reported
Respiratory disease | Not reported
Fitness scores | 22.7% (226/997) were classified as unfit for open repair.
699/997 were classified as fit for open repair (ASA I-III).
BMI | Not reported
Dates of procedure  

Time lapse between registration and procedure  
Not reported

Type of device (EVAR)  
Zenith: 144 (14.4%)  
Talent: 117 (11.7%)  
Excluder: 19 (1.9%)  
Ancure 60 (6%)  
AneuRx 254 (25.4%)  
Bard device 11 (1.1%)  
Baxter device 1 (0.1%)  
Gianturco-Dacron ('home made') 123 (12.3%)  
Gianturco-PTFE ('home made') 17 (1.7%)  
Hol B Endostent 1 (0.1%)  
Ivanchev-Malmo ('home made') 2 (0.2%)  
Palmaz/PTFE ('home made') 64 (6.4%)  
Stenford 2 (0.2%)  
Vanguard 174 (17.4%)  
Missing 11 (1.1%)

Graft type (EVAR)  
Uni-iliac: 263 (26.4%)  
Bi-iliac: 702 (70.4%)  
Aortic tube 32 (3.2%)  
Missing data 3

Anaesthesia  
Regional: 52/993 (5.2%)  
General: General alone 908/993 (91.4%)  
General and regional 32/993 (3.2%)

Follow-up  
Minimum follow-up: 30 days  
Maximum follow-up: 5 years

Return rates for requested follow-up data:  
87% at 1 year  
77% at 2 years  
65% at 3 years  
52% at 4 years  
51% at 5 years  
Median follow-up  
Mean 3.1 years

30 day mortality  
58/992 (5.8%)

Aneurysm related mortality  
Fatal rupture at 1 year 6 (0.8%)  
Fatal rupture at 2 years 3 (0.8%)

All cause mortality at follow-up  
At 1 year 86/721 (11.9%); missing 7; at risk 728*  
1-2 years 37/369 (10%); missing 1; at risk 372  
2-3 years 13/162 (8%); at risk 161  
3-4 years 5/63 (7.9%); at risk 65

*at end of follow-up period

Published paper reports 11% mortality in year 1 and rates of 10%, 7%, 10% and 8% at 2, 3, 4 and 5 years post-procedure.

Rupture  
Rupture during deployment 3 (0.3%)  
Cumulative rate from K-M curve: 2% at 5 year follow-up

Endoleak  
Type I endoleak: Proximal 54 within 30 days; Distal 19 within 30 days  
Type II endoleak: 44 within 30 days  
Type III endoleak: 15 within 30 days  
Cumulative rate from K-M curve: Freedom from endoleak  
88% at 1 year  
80% at 2 years  
76% at 3 years  
71% at 4 years  
68% at 5 years

Device migration  
9 (0.9%) with device migration requiring conversion to open repair (immediate outcome)  
New cases at 1 year follow-up 3/631  
New cases at 2 year follow-up 9/331  
New cases at 3 year follow-up 0/148  
New cases at 4 year follow-up 2/56
### Re-interventions
- Conversion to open repair: Immediate outcome: 33/996 (3.3%)
- Correction of endoleak: Some included under ‘conversion to open repair’. Totals not clearly reported.
- Cumulative rate from K-M curve: Freedom from reintervention
  - 87% at 1 year
  - 77% at 2 years
  - 70% at 3 years
  - 65% at 4 years
  - 62% at 5 years

### Major adverse events (30-day period)
- Number of cardiac events for: 42 (4.2%): myocardial infarction/arrhythmia/left ventricular failure.
- Number of patients suffering stroke: 15 (1.5%): cerebrovascular accident/confusion/paraplegia.
- Cumulative rate from K-M curve: 30-day rates:
  - Any complication 272/976 (27.6%)
  - Technical complication 55/976 (5.6%)
  - Wound complications 78/976 (8%)
  - Renal failure 40/976 (4.1%)
  - Colonic ischaemia 6/976 (0.6%)
  - Other medical complication 147/976 (15.1%)

### Quality of Life measure used
- Not applicable

### Baseline scores
- Not applicable

### Follow-up scores
- Not applicable

### Length of hospital and ICU stay
- Median 6 days (range 3- >30)

### Duration of surgery
- Median 150 minutes (range 30-540 minutes)

### Length of stay for reintervention
- Not reported

### Costs
- Not reported
10.4.3 Data extraction tables – Risk models


**Author**
Biancari 2006

**Country where study was performed**
160 centres in Europe

**Type of study**
Evaluation/validation of existing risk assessment algorithm

**Registry**
Glasgow Aneurysm Score (GAS)

**Dates enrolled and/or treated**
October 1996 to March 2005

**Number of patients**
5,498 patients; 59.5% co-existing myocardial disease; 5.7% cerebrovascular disease; 18.2% renal disease.

- 1833 GAS <74.4
- 1832 GAS <74.4-83.6
- 1833 GAS >83.6

**Age of population**
Median age of 72.7 years (IQR 67.3-77.7 years)

**Gender**
94.1% male

**Aneurysm diameter**
Median aortic diameter 5.6 cm (IQR 5.1-6.3 cm)

**Measurement tool used**
CT scan and intra-arterial digital subtraction angiography (DSA)

**Type of device (EVAR)**
- Zenith: 1916 patients (34.8%)
- Talent: 1557 (29.3%)
- Excluder: 737 (13.4%)
- AneuRX: 907 patients (16.5%)
- Lifepath: 119 (2.2%)
- Powerlink (Endologix): 92 (1.7%)
- Fortron: 77 (1.4%)
- EVT: 69 (1.3%)
- Anaconda: 24 (0.4%)

**Graft type (EVAR)**
Not reported

**Anaesthesia**
Not reported

**Risk factor(s) used in model and definitions**
Composite risk score: Glasgow Aneurysm Score (GAS):
Risk score = (age in years) + (7 points for myocardial disease) + (10 points for cerebrovascular disease) + (14 points for renal disease).

- Myocardial disease refers to previously documented myocardial infarction and/or ongoing angina pectoris.
- Cerebrovascular disease refers to all grades of stroke and includes transient ischaemic attack.
- Renal disease refers to a history of acute or chronic renal failure and/or a creatinine level above 133umol/l and/or creatinine clearance below 50ml/min. A Society for Vascular Surgery/International Society of Cardiovascular Surgery risk score of 1 or more.

**Definition of outcomes**
No definition provided.

**Follow-up period**
1, 3, 6, 12, 18 and 24 months, and annually thereafter (median follow-up = 18 months, IQR 6-24 months).

**Methods of analysis**
Univariate analysis was carried out using the Chi-square test for categorical data. The Mann-Whitney test was used for univariate analysis of the distribution of the GAS in subgroups. Receiver-operator operator characteristic (ROC) curves were used to evaluate the performance of the GAS and to identify its best cut-off value in predicting immediate postoperative death.

Multivariate logistic regression with backward selection used to determine independent associations of risk factors with 30-day mortality rate.

Kaplan-Meier analysis with log rank test and multivariate Cox proportional hazards regression analysis with backward selection used to estimate the influence of different variables on long-term outcome (p<0.05 considered statistically significant).
30 day mortality | Aneurysm size: Area under ROC curve 0.65 (95% CI: 0.60-0.70).
Multivariate analysis showed GAS independently predicted postoperative death (p<0.001).

ROC curve showed GAS with area under curve of 0.70 (95% CI: 0.66-0.74, p<0.001) for predicting postoperative death. Best cut-off value 86.6 (sensitivity 56.1%, specificity 76.2%, accuracy 75.6%, positive predictive value 6.4%, and negative predictive value 98.4%.

Aneurysm related mortality at follow-up | No risk factors investigated
All cause mortality at follow-up | Composite risk score: Multivariate analysis showed overall survival differed significantly among GAS tertiles (ie. <74.4, 74.4-83.6, >83.6) (p<0.001).

5-year overall survival rate for patients with GAS >83.6 = 65.2%.

Reintervention | No risk factors investigated
Endoleak | No risk factors investigated

Study sample adequately described | Yes
Included risk variables clearly defined | Yes
Covariates considered to build the multivariate model | Yes
Interactions between variables explored | Yes
Continuous variables handled appropriately | Unclear
More than 10 events per included variable | Yes
Confidence intervals or other measures of uncertainty presented | Yes


Author | Boult 2007 62. Additional data from Boult 2006 94
Country where study was performed | Australia
Type of study | Development of risk assessment algorithm
Specific risk factors following EVAR
Registry | Dates enrolled and/or treated: 1 November 1999-16 May 2001
Australian national audit of EVAR
Number of patients | 961
Age of population | Mean (SD): 75.0 (6.9) years
Gender | 86% male
Aneurysm diameter | Mean (SD): Men 5.8 (SD 1.05) cm, Women 5.5 (SD 0.9) cm
Type of device (EVAR) | Zenith: 788 (82%) (Number calculated from reported %)
Talent: 37 (3.8%) (Number calculated from reported %)
Excluder: 43 (4.5%) (Number calculated from reported %)
Ancure 14 (1.5%) (Number calculated from reported %)
AeurRx 67 (7%) (Number calculated from reported %)
Vanguard 7 (0.7%) (Number calculated from reported %)
Graft type (EVAR) | Not reported
Anaesthesia | Not reported
Risk factor(s) used in model and definitions

- Age
- Gender
- Smoking status (No definition provided)
- Graft configuration and device type (No definition provided)
- ASA (American Society of Anaesthesiology fitness rating I, II, III or IV)
- Pre-existing conditions: Number of co-morbidities (used for reinterventions/complications)
- Fitness for open procedure: American Society of Anaesthesiology (ASA) score was used to assess patient fitness for surgery.
- Renal function (creatinine): Normal: pre-operative creatinine <120 micromol/L; Mid range: pre-operative creatinine 120-159 micromol/L; High: pre-operative creatinine >=160 micromol/L
- Aneurysm size: Maximum aneurysm diameter
- Aortic neck and aneurysm angle: Aortic neck angle >= 45 degrees was considered significant angulation
- Aortic neck length: <1.5 cm; >= 1.5 cm
- Sac size change (pre-operative and post-operative)
- Modified White's grading scale (based on aortic neck length, aortic neck angulation, thrombus present or absent, aortic sac angulation, iliac artery tortuosity and iliac artery calcification)
- Patient type (public or private)

Definition of outcomes

- Aneurysm-related mortality: Death occurring within 30 days of the primary procedure or any secondary procedure, or death from an aneurysm-related cause (e.g. rupture) occurring at any time following the primary procedure.
- All-cause mortality: Includes peri-operative mortality (within 30 days) and deaths during follow-up.
- Endoleak: Type I or II endoleaks.
- Reintervention: Any reintervention or complication detected prior to discharge or at follow-up.

Follow-up period

Annual follow-up due to continue until 2008. Mortality data were obtained in November 2004, September 2005 and August 2006.

Methods of analysis

Logistic regression was used to determine which factors affected the likelihood of complications or reinterventions following EVAR and which aneurysm-related factors affected the occurrence of Type I and II endoleaks. Stratified right censored Kaplan-Meier survival analysis was used to determine which factors significantly influenced all-cause and aneurysm-related mortality using the log rank (Mantel-Haenszel) test. Parametric survival analysis with log-exponential distribution was used to calculate expected 3 and 5-year survival.

30 day mortality

No risk factors investigated

Aneurysm related mortality at follow-up

- Age: No significant effect
- Smoking status: No significant effect
- Graft configuration and device type: No significant effect
- ASA: Significant effect (p = 0.002)
- Renal function (creatinine): No significant effect
- Aneurysm size: Significant effect (p = 0.001)
- Aortic neck and aneurysm angle: No significant effect
- Aortic neck length: Significant effect of infrarenal neck length (p = 0.001)
- Infrarenal neck diameter: no significant effect

All cause mortality at follow-up

- Age: Significant effect on 3 year and 5 year survival (p < 0.001)
- Smoking status: No significant effect
- Graft configuration and device type: No significant effect
- ASA: Significant effect on 3 year and 5 year survival
- Renal function (creatinine): Significant effect on 3 year and 5 year survival
- Aneurysm size: Significant effect on 3 year and 5 year survival
- Aortic neck and aneurysm angle: Significant effect on 3 year and 5 year survival (p = 0.006) but not for 5 year survival (p = 0.093)
No significant effect of infrarenal neck length or aneurysm angle
Aortic neck length
No significant effect on 3 year and 5 year survival
Other (give details)
Combination of ASA score, maximum aneurysm diameter, age and serum creatinine

Predicted 3-year and 5-year survival probabilities are presented for combinations of ASA II, III or IV, maximum diameter 5, 5.8 or 7.4 cm; age 70, 77 or 83 years; and creatinine 85 or 125 micromoles/litre (see below).

**Predicted survival at 3 years**

<table>
<thead>
<tr>
<th>ASA</th>
<th>Max diameter</th>
<th>Age (years)</th>
<th>Creatinine (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70 years</td>
<td>77 years</td>
<td>83 years</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>125</td>
<td>85</td>
</tr>
<tr>
<td>ASA II</td>
<td>5 cm</td>
<td>91%</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>89%</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>87%</td>
<td>83%</td>
</tr>
<tr>
<td>ASA III</td>
<td>5 cm</td>
<td>86%</td>
<td>82%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>84%</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>80%</td>
<td>75%</td>
</tr>
<tr>
<td>ASA IV</td>
<td>5 cm</td>
<td>79%</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>76%</td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>71%</td>
<td>64%</td>
</tr>
</tbody>
</table>

**Predicted survival at 5 years**

<table>
<thead>
<tr>
<th>ASA</th>
<th>Max diameter</th>
<th>Age (years)</th>
<th>Creatinine (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>70 years</td>
<td>77 years</td>
<td>83 years</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>125</td>
<td>85</td>
</tr>
<tr>
<td>ASA II</td>
<td>5 cm</td>
<td>85%</td>
<td>81%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>83%</td>
<td>79%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>79%</td>
<td>74%</td>
</tr>
<tr>
<td>ASA III</td>
<td>5 cm</td>
<td>77%</td>
<td>72%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>75%</td>
<td>69%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>69%</td>
<td>62%</td>
</tr>
<tr>
<td>ASA IV</td>
<td>5 cm</td>
<td>67%</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>5.8 cm</td>
<td>64%</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td>7.4 cm</td>
<td>56%</td>
<td>48%</td>
</tr>
</tbody>
</table>

**Reintervention**

Age: Significant association between increased age and complications or reinterventions: Prior to discharge (p < 0.001); At follow-up (p < 0.001).
Gender: No significant effect
Smoking status: No significant effect
Graft configuration and device type: No significant effect of device type
ASA: Significant association between higher ASA score and complications or reinterventions: Prior to discharge (p < 0.001); At follow-up (p < 0.001).
Pre-existing conditions: Significant association between higher number of pre-existing conditions and complications or reintervention: Prior to discharge (p < 0.001); At follow-up (p = 0.001).
Fitness for open procedure: Significant association between unsuitability for open repair and complications or reinterventions: Prior to discharge (p < 0.001); At follow-up (p < 0.001).
Aneurysm size: Significant association between larger aneurysm size and complications or reinterventions: Prior to discharge (p = 0.031); At follow-up (p = 0.006).
Aortic neck and aneurysm angle: Significant association between greater aneurysm angulation and complications or reinterventions
Prior to discharge no significant effect; At follow-up (p = 0.037).
Aortic neck length: No significant effect of infrarenal neck length and diameter
No significant effect of modified White's grading scale
Endoleak

- Age: No significant effect
- Gender: Male gender
- Type I endoleaks: No significant effect
- Type II endoleaks: Significant association (p = 0.007).
- Smoking status: No significant effect
- Device type: No significant effect
- ASA: Higher ASA score
- Type I endoleaks: No significant effect
- Type II endoleaks: Significant association (p = 0.039).
- Pre-existing conditions: No significant effect
- Fitness for open procedure: No significant effect
- Aneurysm size: Larger aneurysm diameter
- Type I endoleaks: Significant association (p = 0.025)
- Type II endoleaks: No significant effect
- Aortic neck and aneurysm angle: Aortic neck angulation >45 degrees
- Type I endoleaks: Significant association (p = 0.026)
- Type II endoleaks: No significant effect
- Aortic neck length: Shorter infrarenal neck length
- Type I endoleaks: Significant association (p = 0.012)
- Type II endoleaks: No significant effect
- No significant effect of modified White’s grading scale

Study sample adequately described: Yes
- Relevant details included in both papers

Included risk variables clearly defined: Yes
- Most were self-explanatory or definitions were given

Covariates considered to build the multivariate model: Yes
- Variables considered subjective, ambiguous or with highly incomplete data were not entered into statistical analyses.

Interactions between variables explored: Unclear
- Nothing reported about this

Continuous variables handled appropriately: Unclear
- Few details of statistical methodology reported

More than 10 events per included variable: No
- Large numbers of variables included in logistic regression models.

Confidence intervals or other measures of uncertainty presented: No
- Most modelling results reported as p values only.


Author: Brewster 2006

Country where study was performed: USA

Type of study: Specific risk factors following EVAR

Case Series: January 7 1994 to December 31 2005

Name of centre: Massachusetts General Hospital (MGH)

Number of patients: 873

Age of population: Mean (SD): 75.7 (7.6) years
- Range: 49 to 99 years
- 73 (8.4%) patients were aged 65 or less whereas 233 (26.8%) were aged eighty or over.

Gender: 81.4% male

Aneurysm diameter: Mean (SD): 5.68 cm (1.06)

Type of device (EVAR): Zenith: 183 (21%)
- Talent: 0
- Excluder: 110 (12.6%)
- AneuRx 294 (33.7%)
- EVT / Ancure 90 (10.3%)
- Vanguard 39 (4.5%)
- Lifepath 15 (1.7%)
- MGH Custom Made 123 (14.1%)
- Hybrid Custom Made 5 (0.6%)
- Quantum 9 (1%)
- Powerlink 5 (0.6%)
Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model

Graft type (EVAR)
- Uni-iliac: 65 (7.4%)
- Bi-iliac: 785 (90%)
- Tube 23 (2.6%)

Anaesthesia
- Local: A small number (unstated)
- Regional: Over 90% (exact percentage not stated)
- General: A small number < 10% (not stated)

Risk factor(s) used in model and definitions
- Increased age (not defined)
- Device type: Use of first generation (no longer generally available) or current device
- Renal insufficiency (not defined)
- Large AAA is defined as greater than or equal to 5.5 cm

Definition of outcomes
- Aneurysm related mortality: defined as death from any cause within 30 days of the primary EVAR procedure, death less than or equal to 30 days of any secondary reintervention or surgical conversion, or any death due to aneurysm rupture or device complication.
- Secondary reintervention
- Late conversion to open repair

Follow-up period
- At discharge or within 1 month of EVAR, 6, 12 months and yearly thereafter. Mean follow up was 2.25 years with follow up for 5 or more years available for 20% of the patients.

Methods of analysis
- Subgroup comparisons of demographic data were assessed using 2 tailed t tests for continuous variables and chi squared for categorical data. Late outcomes were assessed using Kaplan-Meier life-table analysis and the log rank test was used when comparing subgroups. Stepwise logistic regression was performed to identify variables associated with study endpoints (multivariate analysis). No details of covariates reported.

30 day mortality
- Renal dysfunction was a predictor of mortality risk (OR = 18.4, p = 0.003)
- (It isn’t clear that this was from multivariate analysis)

Aneurysm related mortality at follow-up
- OR = 7.1 (no CI presented) for renal insufficiency
- OR = 1.1 (no CI presented) for large perioperative AAA size
- Small aneurysm 2 (0.5%)
- Large aneurysm 25 (5.7%)
- p < 0.001
- OR = 9.5 (no CI presented) for family history of aneurysmal disease

All cause mortality at follow-up
- OR = 1.1 for increased age (unspecified)
- OR = 14.1 (no CI presented) for renal dysfunction
- OR = 1.1 (no CI presented) for large aneurysm size

Reintervention
- Says female gender a predictor of late conversion to open repair but no OR reported.

Endoleak
- No risk factors investigated

Included risk variables clearly defined
- No

Covariates considered to build the multivariate model
- Not reported
- None of the covariates reported

Interactions between variables explored
- Unclear

Continuous variables handled appropriately
- Unclear

More than 10 events per included variable
- No

Confidence intervals or other measures of
- No

Final Report 1st April 2008
uncertainty presented


Author
Brown (EVAR trial participants) 2007 26

Country where study was performed
UK

Type of study
Evaluation/validation of existing risk assessment algorithm

Trial
Patients randomised September 1999-August 2004 EVAR I and EVAR II RCT

Number of patients
EVAR I: 1252 (626 randomised to EVAR and 626 to open repair) EVAR II: 404

Age of population
Not reported

Gender
Not reported

Aneurysm diameter
Not reported

Type of device (EVAR)
Not reported

Graft type (EVAR)
Not reported

Anaesthesia
Not reported

Risk factor(s) used in model and definitions
Age: Investigated as a risk factor for 30-day mortality in EVAR I (post-hoc analysis) <71 years 71-77 years >77 years
Composite risk score: Patients were classified as good, moderate or poor fitness based on a modified Customized Probability Index score (based on cardiovascular disease, respiratory dysfunction, renal dysfunction and medication status). The modification was the exclusion of cerebrovascular disease and by weighting severe aortic stenosis and arrhythmia as risk factors similarly to ischaemic heart disease.

Definition of outcomes
30-day mortality: not specifically defined in paper. Aneurysm-related mortality: not specifically defined in paper. All-cause mortality: not specifically defined in paper.

Follow-up period
4 years Mean follow-up 3.8 years (minimum 1.3 years)

Methods of analysis
Logistic regression was used to analyse 30-day operative mortality for all patients in EVAR I who had elective aneurysm repair within their randomised group. An interaction term between randomised group and fitness score was included to assess whether the benefit of EVAR varied according to fitness level. Crude and adjusted (for age, sex and aneurysm diameter at randomisation) odds ratios were calculated. A post hoc analysis was performed to investigate any interaction between age (kept as a continuous variable) and randomised group.

Cox regression was used to analyse aneurysm-related and all-cause mortality for all patients in EVAR I within their randomised groups. Crude and adjusted (for age, sex and aneurysm diameter at randomisation) hazard ratios were calculated. An interaction term between randomised group and fitness score was included to assess whether the benefit of EVAR varied according to fitness level.

Kaplan-Meier estimates were used to present all-cause mortality curves truncated at 4 years of follow-up by fitness groups within EVAR I.
### 30 day mortality

Age: EVAR I trial data only

No significant effect of age on benefit of EVAR over open repair in EVAR I

- Age up to 71 years OR 0.33 (95% CI: 0.03, 3.26)
- Age 71-77 years OR 0.32 (95% CI: 0.08, 1.19)
- Age 78 years or older OR 0.41 (95% CI: 0.15, 1.11)

*P = 0.657 (test for interaction).*

Composite risk score: Modified Customized Probability Index score.

No significant effect of Customized Probability Index fitness group on benefit of EVAR over open repair in EVAR I

- Good fitness adjusted OR 0.23 (95% CI: 0.06, 0.84), *p = 0.027*
- Moderate fitness adjusted OR 0.70 (95% CI: 0.19, 2.56), *p = 0.586*
- Poor fitness adjusted OR 0.29 (95% CI: 0.07, 1.17), *p = 0.082*

*P value for test of interaction for adjusted model = 0.363*

### Aneurysm related mortality at follow-up

Composite score: Modified Customized Probability Index score.

Mortality rates were 0.9/100 person years for good fitness, 1.2 for moderate fitness and 1.6 for poor fitness.

There was no significant effect of fitness group on benefit of EVAR over open repair in EVAR I (no interaction between fitness score and randomised group).

Crude hazard ratios
- Good fitness 0.49 (95% CI: 0.21, 1.15), *p = 0.100*
- Moderate fitness 0.91 (95% CI: 0.31, 2.70), *p = 0.862*
- Poor fitness 0.60 (95% CI: 0.25, 1.44), *p = 0.254*

Adjusted hazard ratios
- Good fitness 0.49 (95% CI: 0.21, 1.16), *p = 0.106*
- Moderate fitness 1.00 (95% CI: 0.33, 3.00), *p = 0.999*
- Poor fitness 0.50 (95% CI: 0.21, 1.23), *p = 0.131*

*P value for test of interaction for adjusted model = 0.371*

### All cause mortality at follow-up

Composite risk score: Modified Customized Probability Index score.

Mortality rates were 5.3/100 person years for good fitness, 7.7 for moderate fitness and 9.9 for poor fitness.

There was no significant effect of fitness group on benefit of EVAR over open repair in EVAR I (no interaction between fitness score and randomised group).

Crude hazard ratios
- Good fitness 0.76 (95% CI: 0.52, 1.11), *p = 0.151*
- Moderate fitness 1.11 (95% CI: 0.71, 1.78), *p = 0.643*
- Poor fitness 1.02 (95% CI: 0.68, 1.51), *p = 0.941*

Adjusted hazard ratios
- Good fitness 0.76 (95% CI: 0.52, 1.11), *p = 0.151*
- Moderate fitness 1.13 (95% CI: 0.72, 1.79), *p = 0.595*
- Poor fitness 0.97 (95% CI: 0.65, 1.45), *p = 0.873*

*P value for test of interaction for adjusted model = 0.281*

### Reintervention

No risk factors investigated

### Endoleak

No risk factors investigated

Study sample adequately described

Yes

Included risk variables clearly defined

Yes

Covariates considered to build the multivariate model

Yes

Interactions between variables explored

Yes

Use of specific interaction terms reported.

Continuous variables handled appropriately

Yes

For example, age kept as a continuous variable.

More than 10 events per included variable

Yes

Confidence intervals or other measures of uncertainty presented

Yes
## Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model


<table>
<thead>
<tr>
<th>Author</th>
<th>Bush 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country where study was performed</td>
<td>USA</td>
</tr>
<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
</tr>
<tr>
<td>Registry</td>
<td>Enrolled between 1st May 2001 and 31st December 2004. Enrolled onto the National Surgical Quality Improvement Program (NSQIP) organised through the Department of Veteran Affairs (VA).</td>
</tr>
<tr>
<td>Number of patients</td>
<td>2368 (1580 open repair, 788 EVAR)</td>
</tr>
<tr>
<td>Age of population</td>
<td>Overall mean: 72.2 years EVAR: 72.9 (SD 6.7), (p&lt;0.001) Open: 71.8 (SD 6.4)</td>
</tr>
<tr>
<td>Gender</td>
<td>TOTAL MALE: 2352 (99.3%) EVAR: 1568 (99.2%) Open: 784 (99.4%)</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Not reported</td>
</tr>
<tr>
<td>Type of device (EVAR)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Minimum criteria for entry into study included age &gt;= 60 years. ASA classification 3 or 4. Pre-existing conditions: Comorbid conditions, including history of cardiac, respiratory, or hepatic disease, cardiac revascularization, and low serum albumin (&lt;3.4g/L). Renal function: Elevated creatinine (&gt; or = 2.0mg/dL) based on Revised Cardiac Risk Index</td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>30-day mortality obtained from NSQIP database (National Surgical Quality Improvement Program) 1-year mortality calculated using death dates obtained from Veteran Affairs Beneficiary Identification Record Locator System (BIRLS) and VA Patient Treatment File (PTF). Perioperative complications: adverse cardiac events, renal dysfunction, pulmonary complications, wound complications, neurologic complications, postoperative bleeding requiring transfusion, and graft failure (a return to the operating room - NSQIP guideline).</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>2-year follow-up.</td>
</tr>
<tr>
<td>Methods of analysis</td>
<td>All clinical outcomes were tested for association with type of AAA repair and with the presence of the 6 additional high-risk comorbidities. The effect of type of operation performed was then tested for its unique association with the morbidity and mortality outcomes (30-day, 1-year, any complication), after adjusting for the number of high-risk comorbidities and 20 additional demographic and clinical covariates, using multivariable logistic regression models. Models assessed for goodness of fit by Hosmer-Lemeshow statistic and for discrimination by the c-index. Kaplan-Meier analysis and log rank tests assessed time to death (all-cause mortality only).</td>
</tr>
</tbody>
</table>

### 30 day mortality

Association of type of surgery with outcomes (adjusted for number of high-risk conditions and additional covariates):

- **EVAR (30-day mortality):** OR = 0.65 (95% CI: 0.42,1.03, p=0.067)

No significant association between highest-risk cohort (ASA IV) and 30-day mortality rate (p=0.48), or highest-risk cohort (ASA IV) and 1-year mortality rate (p=0.17).

### Aneurysm related mortality at follow-up

No risk factors investigated

### All cause mortality at follow-up

1-year mortality for type of procedure:

- **EVAR:** OR 0.68 (95% CI: 0.51, 0.91, p=0.0094)

Kaplan-Meier analysis:

Survival advantage in EVAR patients compared with open repair for 2-year follow-up (logrank test X2 = 5.23, p=0.0222)
Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model

Reintervention
No risk factors investigated

Endoleak
No risk factors investigated

Study sample adequately described
Yes

Included risk variables clearly defined
Yes

Covariates considered to build the multivariate model
Not reported

Interactions between variables explored
Unclear

Continuous variables handled appropriately
Yes

More than 10 events per included variable
Yes

Confidence intervals or other measures of uncertainty presented
Yes


Author
Buth 2000

Country where study was performed
90 centres in 15 European countries.

Type of study
Specific risk factors following EVAR

Registry
Dates enrolled and/or treated: January 1994-July 1999
EUROSTAR registry

Number of patients
1892 (362 patients treated before September were recorded retrospectively and the remainder prospectively)

Age of population
Mean (SD): 70 years
Range: 37-90 years

Gender
91% male

Aneurysm diameter
Median 5.6 cm
Range: 2.8-15 cm

Type of device (EVAR)
Zenith: 0%
Talent: 13% (246/1892 calculated)
Excluder: 3% (57/1892 calculated)
Vanguard 42% (795/1892 calculated)
Stentor 17% (322/1892 calculated)
AneuRx 17% (322/1892 calculated)
Cook 4% (76/1892 calculated)
EVT 3% (57/1892 calculated)
Others 1% (19/1892 calculated)

Graft type (EVAR)
Aorto-uni-iliac device 2% (38/1892 calculated)
Modular bifurcation device 89% (1684/1892 calculated); one piece bifurcation device 3% (57/1892 calculated)
Aorto-aortic straight tube endograft 6% (114/1892 calculated)

Anaesthesia
Not reported

Risk factor(s) used in model and definitions
Age: Categorised as <=75 or >75 years.
Gender: Female
ASA medical risk class (I-IV).

Definition of outcomes
Early mortality: mortality within 30 days.
Early endoleak: endoleak detected by angiogram at the end of the procedure or within the first month.

Follow-up period
Outcomes within 30 days of procedure.

Methods of analysis
Paper states that multivariate analysis was performed but methods not reported.

30 day mortality
Significant association between ASA class III and increased 30-day mortality (odds ratio 2.3).
Significant association between ASA class IV and increased 30-day mortality (odds...
Aneurysm related mortality at follow-up: No risk factors investigated
All cause mortality at follow-up: No risk factors investigated
Reintervention: No risk factors investigated
Endoleak: Significant association between age >75 years and occurrence of early endoleak (odds ratio 1.9).

Significant association between female gender and occurrence of early endoleak (odds ratio 1.7).

Study sample adequately described: Yes
Included risk variables clearly defined: No
Covariates considered to build the multivariate model: Not reported
Interactions between variables explored: Unclear
Continuous variables handled appropriately: Unclear
More than 10 events per included variable: Unclear
Confidence intervals or other measures of uncertainty presented: No


Author: Buth 2003
Country where study was performed: 110 European centres
Type of study: Specific risk factors following EVAR
Registry: Dates enrolled and/or treated: not reported.
EUROSTAR registry
Number of patients: 3595 patients (320 with and 3275 without type II endoleak 1 month after EVAR or at any time thereafter).
Age of population: Not reported
Gender: Not reported
Aneurysm diameter: Not reported
Type of device (EVAR): Not reported
Device type not reported for analysis of type II endoleaks.
Graft type (EVAR): Not reported
Anaesthesia: Not reported
Risk factor(s) used in model and definitions:
- Age
- Smoking status
- Aortic neck diameter and length
- Preoperative patency of inferior mesenteric artery
- Ankle-arm blood pressure index (<0.87 or >= 0.87)
Definition of outcomes: Endoleaks (type I, II, III or multiple) were detected by regular imaging during follow-up using contrast-enhanced CT (84% of cases), angiography (4%), magnetic resonance angiography (3%) or duplex ultrasound (8%).
Follow-up period: Patients were followed up at 1, 6, 12, 18 and 24 months and annually thereafter. Mean/maximum follow-up not reported but 2-year cumulative survival rates are reported.
Methods of analysis: Patients were evaluated with respect to age, gender, smoking, obesity, fitness for open repair, ASA physical status classification. The experience of the operating physicians and type of device used were also evaluated. Data on aneurysm morphology (neck diameter and length, aneurysm diameter and angulation) were also analysed.

Discrete data were analysed using chi-squared tests with the Fisher correction in...
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the case of small subgroups. Continuous variables were compared using the Mann-Whitney U test. The incidence of time-dependent variables was compared using a log rank test. Multivariate analysis was performed of selected variables found to be significantly associated with events at the univariate analysis. Multivariate regression analysis was used for binary outcomes and Cox proportional hazards regression was used for multivariate analysis of time-dependent variables.

Factors other than those listed above were included in the multivariate analysis for type II endoleak (see G5) and results are not reported for all factors listed.

30 day mortality
No risk factors investigated

Aneurysm related mortality at follow-up
No risk factors investigated

All cause mortality at follow-up
No risk factors investigated

Reintervention
No risk factors investigated

Endoleak
Significant association between age and risk of type II endoleak (confidence interval 1.01, 1.06, p = 0.001).

Significant association between current smoking and decreased risk of type II endoleak (confidence interval 0.38, 0.87, p = 0.008).

Significant association between length of infrarenal neck and risk of type II endoleak (confidence interval 1.01, 1.03, p = 0.006).

Significant association between preoperative patent inferior mesenteric artery and risk of type II endoleak (confidence interval 1.03, 1.99, p = 0.031).

Significant association between ankle-arm BP index less than 0.87 and reduced risk of type II endoleak (confidence interval 0.23, 0.68, p = 0.0007).

Study sample adequately described
No

Included risk variables clearly defined
No

However, included variables were fairly self-explanatory.

Covariates considered to build the multivariate model
Not reported

Interactions between variables explored
Unclear

Continuous variables handled appropriately
Unclear

More than 10 events per included variable
Yes

320 endoleaks, so the answer appears to be yes, although only variables with a significant association with type II endoleak were reported.

Confidence intervals or other measures of uncertainty presented
Yes

<table>
<thead>
<tr>
<th>Author</th>
<th>Buth 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country where study was performed</td>
<td>Europe (56 centres in 15 countries)</td>
</tr>
<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
</tr>
<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: January 1994-March 1999 EUROSTAR registry</td>
</tr>
</tbody>
</table>

Patients treated before September 1996 were registered retrospectively, with prospective registration after September 1996.

| Number of patients | 1554 (362 registered retrospectively, 1192 registered prospectively) |
| Age of population | Mean (SD): 70 years |
| Gender | 91.4% (1421/1554) male |
| Aneurysm diameter | Median 5.6 cm |
| Measurement tool used | Contrast enhanced CT scanning and usually also angiography |

| Type of device (EVAR) | Talent: 160/1554 (10.3%) |
| | Stentor 330/1554 (21.2%) |
| | Vanguard 741/1554 (47.7%) |
| | EVT 52/1554 (3.3%) |
| | AneuRx 215/1554 (13.8%) |
| | Others 56/1554 (3.6%) |

| Graft type (EVAR) | Aorto-uni-iliac device combined with femorofemoral bypass graft 27/1554 (1.7%) |
| | Modular bifurcation device 1387/1554 (89.3%) |
| | One-piece bifurcation device 42/1554 (2.7%) |
| | Aorto-aortic straight tube endograft 98/1554 (6.3%) |

| Anaesthesia | Not reported |
| Risk factor(s) used in model and definitions | Age: Categorised as <= 65, 65-75 and >= 75 years |
| | Gender: Female |
| | Smoking status: Scored according to the SVS/ISCVS (Society of Vascular Surgery/International Society of Cardiovascular Surgery) scoring system (score 0-3) |

| Device type (brand name) | |
| ASA physical status classification (score I-IV) | |
| Pre-existing conditions: Cardiac status, scored according to the SVS/ISCVS (Society of Vascular Surgery/International Society of Cardiovascular Surgery) scoring system (score 0-3) | |
| Fitness for open procedure (Definition not stated) | |

| Maximum aneurysm diameter |
| Infrarenal neck diameter; Severe angulation of the iliac arteries (definition not stated) |
| Ankle-arm blood pressure index (definition not stated) |

| Procedural aspects (need for adjuvant procedures, duration of procedure; the latter only considered for correlation if it was not thought likely to be a result of the outcome event), experience of the surgical team and date of the procedure were also analysed. |

| Definition of outcomes | 30-day mortality: Mortality within the first post-operative month. |
| Endoleaks: Categorised into types I-IV following the classification of White et al. Endoleaks were divided into those detected at the end of the procedure (documented by completion angiography) and those detected during the first post-operative month. Multivariate results were only reported for the first time period. |

| Follow-up period | Study was limited to events occurring during the first post-operative month. |
| Methods of analysis | Risk factor variables were first correlated with outcome events using the chi-squared test and Mann-Whitney test for continuous parameters (univariate analysis). Significantly associated variables were then selected stepwise (using backward selection) for a multivariate logistic regression model. The model was tested for stability of the coefficients and their standard errors. |
30 day mortality

Age: No significant association reported
Gender: No significant association reported
Smoking status: No significant association reported
No significant association with device type reported

Significant association between ASA class and 30 day mortality
OR 2.3, 95% CI: 1.0, 5.2, p = 0.04 for ASA class III
OR 6.8, 95% CI: 2.7, 17.4, p = 0.0001 for ASA class IV.

No significant association with cardiac status reported
Fitness for open procedure: No significant association reported

No significant association with maximum aneurysm diameter reported
No significant association with infrarenal neck diameter or severe angulation of the iliac arteries reported
Other (give details)
No significant association with ankle and arm blood pressure index reported

Aneurysm related mortality at follow-up
No risk factors investigated

All cause mortality at follow-up
No risk factors investigated

Reintervention
Reinterventions during admission and in the first postoperative month were included in the category of procedure-related and device-related complications but were not analysed separately. No patient factors were significantly associated with this category of complications.

Endoleak
Significant association between age 75 years or older and endoleak at completion of the procedure: OR 1.9, 95% CI: 1.3, 2.9, p = 0.0009.
Significant association between female gender and endoleak at completion of the procedure: OR 1.7, 95% CI: 1.1, 2.7, p = 0.02.
Significant negative association between current smoking and endoleak at completion of the procedure: OR 0.45, 95% CI: 0.2, 0.9, p = 0.02.
No significant association with device type reported for endoleak at completion of the procedure
ASA: No significant association reported for endoleak at completion of the procedure
Pre-existing conditions: No significant association with cardiac status reported for endoleak at completion of the procedure
Fitness for open procedure: No significant association reported for endoleak at completion of the procedure

Study sample adequately described
Yes

Included risk variables clearly defined
Yes
All included variables listed and most were clearly defined or self-explanatory.

Covariates considered to build the multivariate model
Yes

Interactions between variables explored
Unclear
No interaction term reported

Continuous variables handled appropriately
Unclear
Justification was not provided for the way continuous variables were categorised.

More than 10 events per included variable
Yes
For endoleak detected at the end of the procedure
No
For mortality within 1 month (16 variables, 40 events)

Confidence intervals or other measures of uncertainty presented
Yes

Author
Buth 2002

Country where study was performed
101 European institutions

Type of study
Specific risk factors following EVAR

Registry
Dates enrolled and/or treated: June 1996 to March 2001
454 patients from previous studies excluded as data had been enrolled retrospectively in the registry. Only patients with prospective enrolment, which was at least 1 day before the EVAR was performed, were included. EUROSTAR

Number of patients
3075 patients; 2525 normal operative risk (Group A), 399 with conditions indicating unfit for open surgical repair (Group B), 151 with conditions unfit for general anaesthesia necessary for surgical repair (Group C).

Age of population
Mean (SD)
Group A: 70.9 years
Group B: 71.6 years
Group C: 72.6 years
TOTAL: 71.7 years (patients in Group C older than Group A)

Gender
Percentage male (total population)
Group A: 2341 of 2525 (92.7%)
Group B: 368 of 399 (92.2%)
Group C: 142 of 151 (94%)
TOTAL: 2851 (92.7%)

Aneurysm diameter
Mean (SD)
Group A: 5.62 cm (SD 1.06 cm)
Group B: 5.83 cm (SD 1.19 cm) (p less than or equal to 0.001)
Group C: 5.95 cm (SD 1.38 cm) (p less than or equal to 0.001)
TOTAL: 5.66 cm

Measurement tool used: CT scan

Type of device (EVAR)
Zenith: 464 (15.1%)
Talent: 525 (17.1%)
Excluder: 216 (7.0%)
Vanguard: 910 (29.6%)
AneurRx: 794 (25.8%)
EVT/Ancure: 65 (2.1%)
Other: 101 (3.1%)

No statistical differences in the frequency of any device used in patients at high risk.

Graft type (EVAR)
Straight or aortouniiliac:
Group A: 149 (5.9%)
Group B: 37 (9.3%) (p less than or equal to 0.001)
Group C: 17 (11.3%) (p less than or equal to 0.001)
TOTAL: 203 (6.6%)

Anaesthesia
Regional/local anaesthesia:
Group A: 596 (23.6%)
Group B: 112 (28.1%)
Group C: 98 (64.8%) (p less than or equal to 0.001)
TOTAL: 806 (26.2%)

Risk factor(s) used in model and definitions
ASA physical status classification used as general risk indicator (status III/IV). SVS/ISCVS-NA (International Society for Cardiovascular Surgery - North American Chapter) indicated more specific risk factors or condition of different systems: Diabetes, smoking, hypertension, hyperlipaemia, cardiac, carotid, renal, pulmonary (risk score >/=1)

Physician’s prospective assessment of risk according to one of following categories also taken into account: normal medical condition (group A), condition that was unfit for an open surgical repair of the AAA (group B), or condition unfit for general anaesthesia as needed for open repair (group C). Patients with unfit conditions for both open surgery and general anaesthesia categorised in group C. Seven groups of factors define (retrospectively) unfit category: Cardiovascular conditions (including cerebrovascular, status post heart transplant); pulmonary diseases; malignant diseases; abdominal approach and local anatomic factors (eg. previous laparotomies, hostile abdomen, obesity, retroperitoneal fibrosis, abdominal irradiation, inflammatory aneurysm, aortitis, dissections, enterostoma, bladder substitute, uretherostoma, skin infections, osteomyelitis of sternum, peritoneal dialysis, kidney transplant, status post liver transplant, pancreatitis); specified general disorders (eg. hemotologic rheumatoid arthritis, connective tissue disease, hemodialysis, chronic renal failure, peritoneal dialysis, liver disorders, neurologic
disorders, muscle dystrophy, myasthenia, Parkinson's disease, paraplegia, schizophrenia); poor condition - nonspecified general disorders (ASA 4, advanced age, multiple nonspecified comorbidity).

**Ankle-brachial pressure index <0.87.**

**Definition of outcomes**

Primary outcome success (freedom from death, rupture, conversion, and secondary intervention).

Secondary outcome success (freedom from death, rupture, and conversion).

Death rate calculated from the observed data, discarding 1st month deaths and adding deaths as the result of aneurysm rupture.

**Follow-up period**

2-year follow-up

**Methods of analysis**

Association between most relevant clinical variables and different outcome events assessed with multivariate analysis. If subgroup differences statistically significant, odds ratio (OR) were calculated. If outcome event occurred during follow-up period, Cox proportional hazards regression model used and relative risk (RR) calculated.

Cumulative rate of patient survival estimated with life table analysis.

**30 day mortality**

Age of 70 years or more: OR = 3.0 (p=0.0004)

ASA III/IV: OR = 1.9 (p=0.03)

History of cardiac symptoms: p=ns

Pulmonary disorders: p=ns

Diabetes: p=ns

Obesity: p=ns

Renal insufficiency: OR = 2.5 (p=0.0003)

Mortality rate: 77 patients (2.5%) (A vs B/C, p=0.001)

Multivariate analysis (including preoperative and operative variables and risk groups A, B, and C):

Combined risk Groups B/C compared to Group A: OR = 1.8 (p=0.039)

Ankle-brachial index <0.87: p=ns

Experience of team: p=ns

**Aneurysm related mortality at follow-up**

No risk factors investigated

**All cause mortality at follow-up**

Preoperative risk classifications (ASA/SVS) for Groups B/C:

RR = 1.8 (p=0.001)(Exclusion of early deaths at multivariate analysis)

Total for Groups B/C (1st month and late deaths combined):

Cardiac disorders: 28 of 151 (18.5%)

Malignant diseases: 10 of 151 (6.6%)

Stroke: 7 of 151 patients (4.6%)

Pulmonary disorders: 8 of 151 (5.3%)

(Exclusion of early deaths at multivariate analysis)

Aneurysm size

2-year survival rates:

Entire cohort, p=0.0001

Group A, p=0.0001

Groups B/C, p=0.023

(Exclusion of early deaths at multivariate analysis)

Aneurysm diameter: RR = 1.8 (p=0.0002)

(Exclusion of early deaths at multivariate analysis:

Team experience >60 procedures independently associated with late death: RR = 0.6 (p=0.02).

**Reintervention**

No risk factors investigated

**Endoleak**

No risk factors investigated

**Study sample adequately described**

Yes

**Included risk variables clearly defined**

Yes

**Covariates considered to build the multivariate model**

Not reported

**Interactions between variables explored**

Unclear

**Continuous variables**

Yes

Author: Cuypers 2000

Country where study was performed: Europe (65 centres)

Type of study: Specific risk factors following EVAR

Registry: EUROSTAR registry

Number of patients: 1871 (49 with conversion to open repair and 1822 without conversion)

Age of population:
- Mean (SD): 69.7 years for total population
- 72.6 (SD 7.0) for patients with conversion
- 69.6 (SD 8.3) for patients without conversion

Gender:
- 91.8% male; (84%) for patients with conversion; 92% for patients without conversion

Aneurysm diameter:
- Mean (SD): 5.6 cm for total population
- 6.1 (SD 1.2) for patients with conversion
- 5.6 (SD 1.1) for patients without conversion

Graft type (EVAR):
- Uni-iliac: 48/1871 (2.6%)
- Bi-iliac: 1721/1871 (92.0%)
- Tube: 102/1871 (5.5%)

Anaesthesia: Not reported

Risk factor(s) used in model and definitions:
- Age kept as a continuous variable.
- Device type (brand name)
- Pre-existing conditions: Hypertension, smoking, diabetes (not included in multivariate model) and COPD status were defined according to the SVS/ISCVS scoring system (present if score >0). Other risk factors not explicitly defined.
- Aneurysm diameter (continuous variable)
- Proximal neck length and neck diameter (continuous variables).
- Other risk factors analysed included patient factors (gender, ASA classification, weight, smoking status, of which only weight was included in the multivariate analysis), aneurysm morphology, experience of the operating team and year of procedure.

Definition of outcomes: Conversion: all primary (during the initial procedure and within the first post-operative month) and secondary (during follow-up) conversions to open repair.

Follow-up period: Mean follow-up 6 (interquartile range 1-12) months. Follow-up clinical examinations and imaging studies were performed at 1, 3, 6, 12, 18 and 24 months, and annually thereafter.

Methods of analysis: The variables analysed were: patient characteristics (age, gender, ASA classification, weight, hypertension, smoking, diabetes and pulmonary status), aneurysm morphology (angulation of the aortic neck, the aneurysm and iliac arteries, aortic neck diameter and length, maximum aneurysm diameter, common iliac artery diameter and aortic diameter at the level of the bifurcation), operating team experience, year of procedure and type of device.

The association of variables with conversion to open repair was assessed by chi-square analysis for categorical variables. T-tests were used for continuous variables with approximately normal distribution and the Mann-Whitney test was used for other continuous variables. Variables were categorised as patient-, anatomic- or procedure-related and correlations were calculated for each group. Variables that were significantly associated with conversion in the univariate analysis were entered in a multivariate regression model.

30 day mortality: No risk factors investigated

Aneurysm related mortality at follow-up: No risk factors investigated
All cause mortality at follow-up
Reintervention

No risk factors investigated

No significant association between age (continuous variable) and conversion to open repair in multivariate analysis (p = 0.08).

Significant association between EVT and Talent devices and conversion to open repair in multivariate analysis

OR 7.7, 95% CI: 3.19, 18.59 p < 0.01 for EVT

OR 3.4, 95% CI: 1.42, 8.38 p < 0.01 for Talent.

No significant association for other device types.

Significant association between presence of chronic obstructive pulmonary disease and conversion to open repair in multivariate analysis

OR 2.22, 95% CI: 1.12, 4.37, p = 0.02.

No significant association between aneurysm diameter (continuous variable) and conversion to open repair in multivariate analysis (p = 0.14).

Significant association between proximal neck length (continuous variable) and conversion to open repair in multivariate analysis (p < 0.01).

Significant association between weight (continuous variable) and conversion to open repair in multivariate analysis (p = 0.04).

Significant association between presence of chronic obstructive pulmonary disease and conversion to open repair in multivariate analysis

OR 2.22, 95% CI: 1.12, 4.37, p = 0.02.

No significant association between aneurysm diameter (continuous variable) and conversion to open repair in multivariate analysis (p = 0.14).

Significant association between proximal neck length (continuous variable) and conversion to open repair in multivariate analysis (p < 0.01).

Significant association between weight (continuous variable) and conversion to open repair in multivariate analysis (p = 0.04).

Endoleak

No risk factors investigated

Study sample adequately described
Included risk variables clearly defined
Covariates considered to build the multivariate model
Interactions between variables explored
Continuous variables handled appropriately
Continuous variables appear to have been treated as continuous.
More than 10 events per included variable
Only 49 conversions in total.
Confidence intervals or other measures of uncertainty presented


Author

Diehm 2007

Country where study was performed

164 European centres

Type of study

Specific risk factors following EVAR

Registry

Dates enrolled and/or treated: December 1996-November 2005
EUROSTAR registry

Number of patients

6383: Pulmonary status: normal 3650 (57%), impaired 2733 (43%)
Diabetes mellitus: no 5573 (87.3%), yes 810 (12.7%)

Age of population

Mean: 72.4 (SD 7.6) years for total population
Pulmonary status: normal 71.7 (SD 7.9), impaired 73.3 (SD 7.2)
Diabetes mellitus: no 72.4 (SD 7.7), yes 72.1 (SD 7.3)

Gender

93.8% (5985/6383) male

Aneurysm diameter

Mean: 5.87 cm (calculated) for total population
Pulmonary status: normal 5.82 (SD 1.06), impaired 5.94 (SD 1.15)
Diabetes mellitus: no 5.86 (SD 1.11), yes 5.91 (SD 1.13)

Type of device (EVAR)

Zenith: 2409 (37.7%)
Talent: 1757 (27.5%)
Excluder: 883 (13.8%)
AneuRx 895 (14%)
Graft type (EVAR) Not reported
Anesthesia Not reported
Risk factor(s) used in model and definitions Pre-existing conditions: Pulmonary status and diabetes mellitus were classified according to the Society for Vascular Surgery (SVS) risk classification.

For pulmonary function a score of 0 means no pulmonary impairment; scores of 1 to 3 indicate increasing levels of impairment measured by pulmonary function tests and chest radiography.

For diabetes mellitus (DM), a score of 0 indicates normoglycaemia, 1 indicates adult-onset DM controlled by diet, 2 indicates adult-onset DM controlled by insulin and 3 indicates the presence of juvenile-onset DM.

Definition of outcomes
30 day mortality, aneurysm-related mortality, all-cause mortality at follow-up: not specifically defined.

Reintervention: conversion to open repair and all endovascular reinterventions.

Follow-up period Patients were followed up at 1, 3, 6, 12, 18 and 24 months, and annually thereafter. Mean follow-up was 21.1 (SD 18.4) months (range 0-96).

Methods of analysis Patients were classified as good pulmonary status (SVS score 0) or impaired pulmonary status (SVS score 1 to 3). Within the same statistical model, patients were classified as non-diabetic (SVS score 0) or diabetic (SVS score 1 to 3) for a second statistical analysis. Differences between groups were assessed using the Mann-Whitney U test for continuous data and chi-square test for discrete variables. Kaplan-Meier life-table analyses were performed to analyse study endpoints as well as cumulative rates of neck dilatation and type I endoleak.

Multivariate logistic regression analysis (adjusted for smoking, age, gender, comorbidities, fitness for open repair, coexisting common iliac artery aneurysm, neck and aneurysm size, arterial angulation, aneurysm classification, oversizing >= 15% and type of stent-graft) was used to determine independent associations of pulmonary status and DM with 30-day outcomes. Cox proportional hazards models (adjusted for smoking, age, gender, comorbidities, fitness for open repair, coexisting common iliac artery aneurysm, and type of stent-graft) were used to determine independent associations of impaired pulmonary status and DM with 4-year outcomes.

30 day mortality No significant association between pulmonary status and 30-day mortality (p = 0.08).

No significant association between diabetes mellitus and 30-day mortality (p = 0.27).

Aneurysm related mortality at follow-up Significant association between impaired pulmonary status and 4-year aneurysm-related mortality (3.3% normal status vs. 6.8% impaired status, p = 0.006).

No significant association between diabetes mellitus and 4-year aneurysm-related mortality (4.6% no diabetes vs. 6.1% with diabetes, p = NS).

All cause mortality at follow-up Significant association between impaired pulmonary status and 4-year all-cause mortality (19.0% normal status vs. 31.0% impaired status, p < 0.0001).

No significant association between diabetes mellitus and 4-year all-cause mortality (23.4% no diabetes vs. 27.7% with diabetes, p = NS).

Reintervention No significant association between pulmonary status and 30-day conversion to open repair (1.0% normal status vs. 1.1% impaired status, p = 0.93).

No significant association between diabetes mellitus and 30-day conversion to open repair (1.0% no diabetes vs. 1.4% with diabetes, p = 0.21).

No significant association between pulmonary status and 4-year conversion to open repair (5.3% normal status vs. 4.9% impaired status, p = NS).

No significant association between diabetes mellitus and 4-year conversion to open repair (5.4% no diabetes vs. 3.3% with diabetes, p = NS).

Endoleak Significant association between pulmonary status and 4-year type I endoleak (8.1% normal status vs. 9.1% impaired status, p = NS).

No significant association between diabetes mellitus and 4-year type I endoleak (8.5% no diabetes vs. 7.8% with diabetes, p = NS).
### Study sample adequately described
Yes

### Included risk variables clearly defined
Yes

### Covariates considered to build the multivariate model
Yes

### Interactions between variables explored
Unclear

### Continuous variables handled appropriately
Yes

### More than 10 events per included variable
Yes

### Confidence intervals or other measures of uncertainty presented
No

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<table>
<thead>
<tr>
<th>Author</th>
<th>Hobo 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country where study was performed</td>
<td>Europe (131 centres)</td>
</tr>
<tr>
<td>Type of study</td>
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<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: December 1999-December 2004 EUROSTAR registry</td>
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<tr>
<td>Number of patients</td>
<td>2846 patients with follow-up of at least 12 months or reintervention within the first 12 months.</td>
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<td>Age of population</td>
<td>Mean: 72.0 (SD 7.5) years Range: 43-100 years</td>
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<tr>
<td>Gender</td>
<td>94% (2688/2846) male</td>
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<tr>
<td>Aneurysm diameter</td>
<td>Mean (SD): 5.8 cm Range: 4-11 cm</td>
</tr>
<tr>
<td>Measurement tool used</td>
<td>Not explicitly reported. Aneurysm diameter was determined over the minor axis at the site of the largest cross section.</td>
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<tr>
<td>Type of device (EVAR)</td>
<td>Zenith: 1147/2846 (40.3%) Talent: 791/2846 (27.8%) Excluder: 421/2846 (14.8%) AneurRx: 264/2846 (9.3%) Lifepath 67/2846 (2.4%) Fortron 52/2846 (1.8%) Powerlink 51/2846 (1.8%) EVT 36/2846 (1.3%) Anaconda 17/2846 (0.6%)</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Age Gender Type of device (brand name) ASA physical status score (I-IV) Systemic comorbidities (no further details reported). Preoperative aneurysm diameter (categorised as &lt; 5.5 cm, 5.5-6.0 cm, 6.0-6.5 cm and &gt; 6.5 cm). Other risk factors included requirement for an adjuvant procedure and proximal or midgraft endoleak evident at the time of the primary procedure.</td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>Secondary interventions (reinterventions) were categorised as transabdominal (with or without conversion to open repair), extra-anatomic and transfemoral interventions. Results from the multivariate model refer to all interventions.</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>Minimum follow-up 12 months after procedure unless a reintervention occurred before the 12-month visit. Patients were followed up for a mean of 11 (SD 12) months after reintervention (range 0-47 months).</td>
</tr>
</tbody>
</table>
| Methods of analysis | Kaplan-Meier life tables were used to derive cumulative incidence and survival curves for all types of secondary interventions. Relative risk ratios (RR) were
calculated to correlate secondary interventions with their indications at the follow-up visit preceding reintervention. A multivariate Cox proportional hazards model was used to calculate independent associations of baseline (patient and operative) factors with survival free of reintervention during the postoperative and entire follow-up period.

30 day mortality
No risk factors investigated
30-day mortality was investigated using multivariate logistic regression, but results were related to reinterventions and not to patient risk factors.

Aneurysm related mortality at follow-up
No risk factors investigated

All cause mortality at follow-up
No risk factors investigated
All-cause mortality was investigated using multivariate logistic regression, but results were related to reinterventions and not to patient risk factors.

Reintervention
Age: No significant association with secondary interventions.
Gender: No significant association with secondary interventions.
No significant association of device type with secondary interventions.
ASA: No significant association with secondary interventions.
No significant association of systemic comorbidities with secondary interventions.
No significant association of preoperative diameter (with thresholds at 5.5, 6 and 6.5 cm) with secondary interventions.

Independent baseline risk factors for reintervention were requirement for adjuvant procedure ($p = 0.0001$), proximal endoleak ($p = 0.004$) and midgraft endoleak ($p = 0.017$) evident at the primary procedure.

Endoleak
No risk factors investigated

Study sample adequately described
Yes

Included risk variables clearly defined
No
Limited details reported

Covariates considered to build the multivariate model
Yes
Independent associations with outcomes sought

Interactions between variables explored
Unclear

Continuous variables handled appropriately
Unclear

More than 10 events per included variable
Yes
247 reinterventions

Confidence intervals or other measures of uncertainty presented
No
Only $p$ values reported.


Author
Hobo 2007 72

Country where study was performed
159 centres in 18 European countries

Type of study
Specific risk factors following EVAR

Registry
Dates enrolled and/or treated: October 1996 to January 2006 EUROSTAR

Number of patients
5,183 patients: 1,152 with severe neck angulation (SNA), 4,031 without SNA.

Age of population
Overall mean age: 72.6 years, $p<0.0001$
SNA present: 74.3 years (SD 7.5 years)
SNA absent: 72.1 years (SD 7.7 years)

Gender
SNA present: 1040 (90.3%)
SNA absent: 3820 (94.8%)
TOTAL: 4860 male (93.8%)

Aneurysm diameter
Mean AAA sac diameter:
SNA present: 6.38 cm (SD 1.26 cm)
SNA absent: 5.79 cm (SD 1.04 cm)
TOTAL: 5.9 cm, $p<0.0001$
Measurement tool used: CT scan
### Type of device (EVAR)
- Zenith: 2,486 patients (48%)
- Talent: 1,796 patients (34.6%)
- Excluder: 901 patients (17.4%)

### Graft type (EVAR)
- Not reported

### Anaesthesia
- Not reported

### Risk factor(s) used in model and definitions
- Device (brand name)
- Severe neck angulation (SNA) defined as >60 degrees angle between the infrarenal aortic neck and the longitudinal axis of the aneurysm.

### Definition of outcomes
- Complications defined as proximal type I endoleak (short and long term), infrarenal aortic neck dilation, proximal stent-graft migration, and rupture of the aneurysm.
- Proximal neck dilation defined as an increase of at least 0.4 cm compared with the proximal neck diameter at the pre-operative measurement.
- Long-term incidences of proximal type I endoleak, stent-graft migration, aneurysm rupture, secondary interventions, and all-cause and aneurysm-related mortality (no specific definitions).

### Follow-up period
1, 3, 6, 12, 18, and 74 months, then annually thereafter.
Mean follow-up 19.9 (SD 17.9) months.

### Methods of analysis
- Short-term outcome variables were assessed using chi-square, Mann-Whitney, and logistic regression analyses.
- Kaplan-Meier life tables and Cox proportional hazard models used to assess long-term outcome variables. Results presented as adjusted odds ratio (OR) or hazard ratio (HR) with 95% CI (adjusted for age, gender, risk factors, morphological factors, and experience).

### 30 day mortality
- Aortic neck and aneurysm angle
  - OR (adjusted) = 0.89 (95% CI: 0.62-1.30, p=ns)

### Aneurysm related mortality at follow-up
- Aortic neck and aneurysm angle
  - HR (adjusted) = 1.02 (95% CI: 0.75-1.38, p=ns)

### All cause mortality at follow-up
- Aortic neck and aneurysm angle
  - HR (adjusted) = 0.87 (95% CI: 0.72-1.03, p=ns)

### Reintervention
- Secondary intervention (long-term) associated with SNA in patients who received Talent device: HR = 1.54 (95% CI: 1.05-2.24, p=0.0259)
- Aortic neck and aneurysm angle
- Short-term outcomes (30 days): OR (adjusted) = 0.96 (95% CI: 0.64-1.43, p=NS)
- Long-term outcomes (follow-up): OR (adjusted) = 1.29 (95% CI: 1.00-1.67, p=0.0488)

### Endoleak
- Graft configuration and device type
- Short-term outcomes (30 days) (Proximal Type I endoleak):
  - Excluder device: OR (adjusted) = 4.49 (95% CI: 1.31-15.32, p=0.0166)
  - Short-term outcomes (30 days) (Proximal Type I endoleak):
    - Talent device: OR (adjusted) = 2.29 (95% CI: 1.38-3.80, p=0.0014)
    - Long-term outcomes (follow-up) (Proximal Type I endoleak):
      - Talent device: HR (adjusted) = 2.09 (95% CI: 1.27-3.44, p=0.0036)
      - Short-term outcomes (30 days) (Proximal Type I endoleak):
        - Zenith device: OR (adjusted) = 2.62 (95% CI: 1.49-4.63, p=0.0009)
    - Aortic neck and aneurysm angle
      - Short-term outcomes (30 days) (Proximal Type I endoleak):
        - OR (adjusted) = 2.32 (95% CI: 1.60-3.37, p<0.0001)
      - Long-term outcomes (follow-up) (Proximal Type I endoleak):
        - OR (adjusted) = 1.80 (95% CI: 1.25-2.58, p=0.0016)

### Study sample adequately described
- Yes

### Included risk variables clearly defined
- Yes

### Covariates considered to build the multivariate model
- Not reported

### Interactions between variables explored
- Unclear

### Continuous variables handled appropriately
- Yes
More than 10 events per included variable | Yes
---|---
Confidence intervals or other measures of uncertainty presented | Yes


<table>
<thead>
<tr>
<th>Author</th>
<th>Lange 2005</th>
</tr>
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<tbody>
<tr>
<td>Country where study was performed</td>
<td>153 European institutions within the EUROSTAR registry</td>
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<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
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<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: 1996 to 2004 EUROSTAR</td>
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<tr>
<td>Number of patients</td>
<td>4433 patients</td>
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<tr>
<td>Age of population</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>Patients &lt; 80 years 70.3(6.5) years</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 83.4(2.9) years</td>
</tr>
<tr>
<td>Range</td>
<td>Patients &lt; 80 years 43-79 years</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 80-100 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Patients &lt; 80 years 94.8% male</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 90.2% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>Patients &lt; 80 years 5.76 cm(1.04)</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 6.2 cm(1.22) (p &lt; 0.0001)</td>
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<tr>
<td></td>
<td>Measurement tool used between the outer walls on the axial CT slices</td>
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<tr>
<td>Type of device (EVAR)</td>
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</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Uni-iliac: Patients &lt; 80 years 212 (5.1%)</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 54 (7.8%) (p = 0.0038)</td>
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<tr>
<td>Anaesthesia</td>
<td>Local: Patients &lt; 80 years 232 (5.5%)</td>
</tr>
<tr>
<td></td>
<td>Octogenarians 32 (4.6%) NS</td>
</tr>
<tr>
<td>Regional: Patients &lt; 80 years 1012 (24.2%)</td>
<td></td>
</tr>
<tr>
<td>Octogenarians 180 (25.8%) NS</td>
<td></td>
</tr>
<tr>
<td>General: Patients &lt; 80 years 2947 (70.3%)</td>
<td></td>
</tr>
<tr>
<td>Octogenarians 485 (69.6%) NS</td>
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</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Age (patients &gt; 80 years old)</td>
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</table>

**Definition of outcomes**
Deaths occurring within 30 or fewer days of the procedure were categorised as operative deaths and deaths occurring > 30 days were categorised as late deaths. Aneurysm related deaths included 30 day deaths and deaths that occurred as a result of aneurysm rupture, endograft infection or death 1 month or less after a secondary surgical procedure for late complications of the aneurysm.

**Follow-up period**
1, 6, 12, 18, 24 months and annually thereafter. Mean follow up period was 14 months in octogenarians, 19 months in younger patients.

**Methods of analysis**
Differences in findings between the two age groups (< and > 80 years) were assessed by chi squared tests for discrete variables and by t test or Wilcoxon rank sum test for continuous variables. Multivariate regression was used to correct for other risk factors. Life table analyses were conducted for outcomes at follow up and multivariate analysis of time-dependent variables was assessed by Cox proportional hazards.

**30 day mortality**
Age
Patients < 80 years 89(2.1%)
Octogenarians 38 (5.5%)
Adjusted p value 0.0007 OR = 0.48(95% CI: 0.31, 0.73)

**Aneurysm related mortality at follow-up**
Patients < 80 years 117(2.8%)
Octogenarians 49 (7.0%)
Adjusted p value < 0.0001; HR = 2.15(95% CI: 1.52, 3.05)

**All cause mortality at follow-up**
Patients < 80 years 392(9.4%)
Octogenarians 109 (15.9%)
Reintervention

Age: Overall conversion to open repair
- Patients <80 years 95 (2.3%)
- Octogenarians 18 (2.6%)
Adjusted p value NS; HR = 1.35 (95% CI: 0.81, 2.27)

Late conversion to open repair
- Patients <80 years 55 (1.3%)
- Octogenarians 9 (1%)
Adjusted p value NS; HR = 1.03 (95% CI: 0.46, 2.29)

Endoleak

Age: Endoleaks
- Patients <80 years 677 (16.2%)
- Octogenarians 148 (21.2%)
Adjusted p value <0.0001; HR = 1.46 (95% CI: 1.21, 1.76)

Type I - proximal
- Patients <80 years 97 (2.4%)
- Octogenarians 21 (3.2%)
Adjusted p value NS; HR = 1.29 (95% CI: 0.79, 2.12)

Type I - distal
- Patients <80 years 72 (1.8%)
- Octogenarians 17 (2.6%)
Adjusted p value NS; HR = 1.65 (95% CI: 0.94, 2.89)

Type II
- Patients <80 years 140 (3.4%)
- Octogenarians 33 (5.0%)
Adjusted p value 0.0059; HR = 1.87 (95% CI: 1.20, 2.91)

Type III
- Patients <80 years 483 (11.8%)
- Octogenarians 97 (14.8%)
Adjusted p value 0.006; HR = 1.40 (95% CI: 1.10, 1.76)

Study sample adequately described
- Yes
Included risk variables clearly defined
- Yes
Covariates considered to build the multivariate model
- Yes
Interactions between variables explored
- Unclear
Continuous variables handled appropriately
- Yes
More than 10 events per included variable
- Yes
Confidence intervals or other measures of uncertainty presented
- Yes


Author
Leurs 2007

Country where study was performed
Europe-wide

Type of study
Specific risk factors following EVAR

Registry
EUROSTAR: enrolled 1st December 1996 (only patients registered post 1999 included)

Trial
Enrolment commenced in 2000
Dutch Randomised Endovascular Aneurysm Management (DREAM) trial

Number of patients
EUROSTAR: 856
DREAM: 177
Total: 1033 patients

### Age of population
Mean (SD)
- DREAM: 70.6 years (SD 6.51)
- EUROSTAR: 71.6 years (SD 7.67)
- \( p=\text{ns} \)

### Gender
Percentage male (total population)
- DREAM: 165 (93.2%)
- EUROSTAR: 793 (92.6%)
- TOTAL: 958 (92.7%), \( p=\text{ns} \)

### Aneurysm diameter
Mean (SD)
- DREAM: 6.06 cm (SD 0.89 cm)
- EUROSTAR: 6.04 cm (SD 1.02 cm)

### Measurement tool used
- EUROSTAR: computed tomography (CT) and intra-arterial digital subtraction angiography (DSA)
- DREAM: Not reported

### Type of device (EVAR)
- Zenith: 369 (35.7%)
- Talent: 382 (37%)
- Excluder: 114 (11%)
- AneuRx: 89 (8.6%)
- Lifepath: 7 (0.7%)
- Endologix: 8 (0.8%)
- Fortron: 31 (3.0%)
- EVT: 10 (1.0%)
- Anaconda: 21 (2.0%)
- Unknown: 2 (0.2%)

### Graft type (EVAR)
- Uni-iliac: 53 patients (5.1%)
- Bi-iliac: 999 patients (96.7%)
- Straight tube: 11 (1.1%)
- Unknown: 8 (0.8%)

NB: 894 patients included for EUROSTAR graft type, therefore total percentage greater than 100.

### Anaesthesia
- Local (number of patients (%))
  - 94 (9.1%)
- Regional (number of patients (%))
  - 320 (31%)
- General (number of patients (%))
  - 619 (59.9%)

### Risk factor(s) used in model and definitions
- Advanced age (not defined)
- ASA physical status classification I, II, or III (ASA IV patients not included).
- Pre-existing conditions: Co-morbidity: pulmonary impairment (not defined), diabetes (not defined)
- Larger aneurysm diameter at baseline (size not defined)

(Baseline variables included: diabetes, smoking, hypertension, hyperlipaemia, carotid disease, cardiac disease, renal disease, pulmonary disease, but not all variables were analysed).

### Definition of outcomes
- All-cause mortality defined as survival.
- Reintervention defined as secondary intervention or procedure (not defined).

### Follow-up period
1, 3, and 5-year follow-up.

### Methods of analysis
Differences between groups were assessed using Chi-square tests for discrete variables and Wilcoxon rank sum tests for continuous variables.

Multivariate Cox models were used to determine whether baseline and follow-up variables were independently associated with adverse outcomes. (Baseline variables included: diabetes, smoking, hypertension, hyperlipaemia, carotid disease, cardiac disease, renal disease, pulmonary disease, but not all variables were analysed).

Kaplan-Meier analysis was used for survival analysis.

### 30 day mortality
No risk factors investigated

### Aneurysm related mortality at follow-up
No risk factors investigated
All cause mortality at follow-up

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
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<tbody>
<tr>
<td>Age</td>
<td>TOTAL: HR = 1.06 (95% CI: 1.03-1.09, p&lt;0.0001)</td>
<td>DREAM: HR = 1.14 (95% CI: 1.07-1.23, p=0.0002)</td>
</tr>
</tbody>
</table>

Pulmonary impairment (TOTAL):

HR = 1.74 (95% CI: 1.19-2.54, p=0.0046)

Diabetes mellitus (DREAM):

HR = 4.46 (95% CI: 1.41-14.05, p=0.0107)

Larger aneurysm diameter at baseline:

HR = 1.02 (95% CI: 1.01-1.04, p=0.0091)

Reintervention

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>TOTAL: HR = 1.03 (95% CI: 1.00-1.07, p=0.0363)</td>
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</table>

Endoleak

<table>
<thead>
<tr>
<th>Study sample adequately described</th>
<th>Yes</th>
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<tbody>
<tr>
<td>Included risk variables clearly defined</td>
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<tr>
<td>Covariates considered to build the multivariate model</td>
<td>Not reported</td>
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<tr>
<td>Interactions between variables explored</td>
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<td>Continuous variables handled appropriately</td>
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<tr>
<td>More than 10 events per included variable</td>
<td>Unclear</td>
</tr>
<tr>
<td>Confidence intervals or other measures of uncertainty presented</td>
<td>Yes</td>
</tr>
</tbody>
</table>


Author

Leurs 2004  

Country where study was performed

65 centres in Europe

Type of study

Specific risk factors following EVAR

Registry

Dates enrolled and/or treated: 6 year period to April 2004  
EUROSTAR

Number of patients

676 (Group A with aneurysm <5.5 cm 300, Group B with aneurysm 5.5 cm or larger 376)

Age of population

Mean (SD): Group A 71.2 years, Group B 72.8 years (p = 0.0006)  
Overall 72.1 years (calculated)  
Range: Group A 43 to 92 years, Group B 49 to 96 years

Gender

626 (93%) male

Aneurysm diameter

Mean (SD): 5.67 cm (Group A 4.87, Group B 6.32) (p< 0.0001)  
Range: 4 to 10 cm (Group A 4 to 5.4, Group B 5.5 to 10)

Type of device (EVAR)

Excluder: 676 (100%)

Graft type (EVAR)

Bi-iliac: 676 (100%)

Anaesthesia

Local: 78 (12%)  
Regional: 207 (31%)  
General: 391 (58%)

Risk factor(s) used in model and definitions

Age  
Pulmonary insufficiency, hypertension (not defined)  
Fitness for open procedure  
Renal function (creatinine)  
Aneurysm size  
Study cohort was divided into two groups: group A with aneurysms smaller than 5.5 cm and group B with aneurysms of 5.5 cm and larger.

Definition of outcomes

Overall deaths included death related to comorbidity and conditions unrelated to the aneurysm.

Aneurysm related deaths included 30 day deaths and deaths that occurred as a
result of aneurysm rupture, endograft infection or within 1 month after a secondary surgical procedure for late complications of the aneurysm.

Only endoleaks that were identified at 1 month and thereafter were included in the analysis while endoleaks at the completion angiography were not included.

<table>
<thead>
<tr>
<th>Follow-up period</th>
<th>1, 6, 12, 18, 24 months and annually thereafter. Mean duration of follow up was 13.5 months (1 to 60 months).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods of analysis</td>
<td>All variables with a significant correlation with an adverse event and variables appearing clinically related, including size classification, were entered into a multivariate Cox analysis to assess independent associations.</td>
</tr>
<tr>
<td>30 day mortality</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>Aneurysm related mortality at follow-up</td>
<td>Age of the patient was not found to be an independent risk factor for aneurysm related mortality in multivariate analysis. Pulmonary insufficiency was not found to be an independent risk factor for aneurysm related mortality in multivariate analysis.</td>
</tr>
<tr>
<td>All cause mortality at follow-up</td>
<td>Advanced age influenced all cause mortality (HR = 1.05, 95% CI: 1.0, 1.1) Unfitness for open repair influenced all-cause mortality (HR = 2.6, 95% CI: 1.2, 5.6). Large aneurysm size (Group B patients) had a higher risk of all-cause death in multivariate analysis (HR = 2.9, 95% CI: 1.2, 6.7)</td>
</tr>
<tr>
<td>Reintervention</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>Endoleak</td>
<td>No risk factors investigated</td>
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<td>No</td>
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<td>Confidence intervals or other measures of uncertainty presented</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Final Report 1st April 2008

Author
Leurs 2006

Country where study was performed
165 European institutions

Type of study
Specific risk factors following EVAR

Registry
EUROSTAR

Number of patients
3,499 patients:
- 2,822 patients with infrarenal neck length >1.5 cm (group A);
- 485 patients 1.1-1.5 cm (group B);
- 192 patients <=1.0 cm (group C)

Age of population
Mean (SD)
- Group A: 73.2 years (SD 7.7 years)
- Group B: 73.5 years (SD 7.3 years)
- Group C: 72.4 years (SD 7.5 years), p=ns
- Overall Mean: 73.2 years

Gender
Percentage male (total population)
- Group A: 2645 of 2822 (93.7%)
- Group B: 459 of 485 (94.6%)
- Group C: 186 of 192 (96.9%), p=ns
- TOTAL: 3290 (94.0%)

Aneurysm diameter
Mean (SD)
- Group A: 6.13 cm (SD 1.07 cm)
- Group B: 6.22 cm (SD 1.13 cm)
- Group C: 6.29 cm (SD 1.10 cm), p=0.0314
- Overall Mean: 6.1 cm

Measurement tool used:
CT scan and intra-arterial digital subtraction angiography (DSA)

Type of device (EVAR)
Zenith: % not reported
Talent: % not reported

Graft type (EVAR)
Not reported

Anaesthesia
Not reported

Risk factor(s) used in model and definitions
Infrarenal neck length:
>1.5 cm (Group A), 1.1-1.5 cm (Group B), < (Group)

Definition of outcomes
Outcome reporting adhered to guidelines of the Society for Vascular Surgery/American Association for Vascular Surgery (SVS/AAVS). Team experience defined as at least 30 EVAR cases per year.

Follow-up period
1, 3, 6, 12, 18, and 24 months, and annually thereafter.

Methods of analysis
Comparison of patient, morphological, and centre-related characteristics among the 3 infrarenal neck length groups was performed using chi-square tests and Wilcoxon rank-sum tests for categorical and continuous variables, respectively. All variables that differed significantly among the 3 groups according to these univariate analyses were included as covariates in multivariate outcome analyses. Logistic multivariate regression analysis performed for early complications (30-days); OR with 95% CI calculated. For late outcome (1-48 months) multivariate Cox proportional hazard models fitted (hazard ratios (HR) with 95% CI). Kaplan-Meier method, with log-rank analysis present survival curves.

30 day mortality
Aortic neck length
OR Group B v A (adjusted) = 1.77 (95% CI: 1.08, 2.87)
OR Group C v A (adjusted) = 1.40 (95% CI: 0.65, 3.02)

Aneurysm related mortality at follow-up
HR Group B v A (adjusted) = 1.52 (95% CI: 0.50, 4.61)

All cause mortality at follow-up
Aortic neck length
HR Group B v A (adjusted) = 1.20 (95% CI: 0.83, 1.72)
HR Group C v A (adjusted) = 1.45 (95% CI: 0.92, 2.27)

Reintervention
Conversion to open repair (30-days):
OR Group B v A (adjusted) = 0.70 (95% CI: 0.21, 2.36)
OR Group C v A (adjusted) = 1.33 (95% CI: 0.30, 5.84)
Conversion to open repair (48 month follow-up):
HR Group B v A (adjusted) = 1.74 (95% CI: 0.58, 5.28)
HR Group C v A (adjusted) = 0.84 (95% CI: 0.11, 6.43)
Secondly Intervention - Transfemoral (48 month follow-up):
HR Group B v A (adjusted) = 0.73 (95% CI: 0.39, 1.36)
HR Group C v A (adjusted) = 1.13 (95% CI: 0.55, 2.36)

Secondary Intervention - Transabdominal (48 month follow-up):
HR Group B v A (adjusted) = 1.78 (95% CI: 0.66, 4.84)
HR Group C v A (adjusted) = 0.75 (95% CI: 0.10, 5.68)

Secondary intervention - Extra-anatomical (48 month follow-up):
HR Group B v A (adjusted) = 1.53 (95% CI: 0.66, 3.53)
HR Group C v A (adjusted) = 0.50 (95% CI: 0.07, 3.68)

Endoleak

Aortic neck length
Proximal Type I endoleak (30-days):
OR (adjusted) Group B v A = 1.38 (95% CI: 0.80, 2.37)
OR (adjusted) Group C v A = 4.46 (95% CI: 2.61, 7.61)

Proximal Type I endoleak (48 month follow-up):
HR (adjusted) Group B v A = 1.98 (95% CI: 1.16, 3.38)
HR (adjusted) Group C v A = 2.32 (95% CI: 1.17, 4.60)

Distal Type I endoleak (30-days):
OR (adjusted) Group B v A = 0.45 (95% CI: 0.16, 1.24)
OR (adjusted) Group C v A = 0.49 (95% CI: 0.12, 2.05)

Distal Type I endoleak (48 month follow-up):
HR (adjusted) Group B v A = 0.48 (95% CI: 0.19, 1.19)
HR (adjusted) Group C v A = 1.22 (95% CI: 0.52, 2.85)

Type II endoleak (30-days):
OR (adjusted) Group B v A = 0.88 (95% CI: 0.63, 1.23)
OR (adjusted) Group C v A = 0.45 (95% CI: 0.23, 0.89)

Type II endoleak (48 month follow-up):
HR (adjusted) Group B v A = 0.79 (95% CI: 0.56, 1.13)
HR (adjusted) Group C v A = 0.71 (95% CI: 0.40, 1.24)

Type III endoleak (30-days):
OR (adjusted) Group B v A = 0.60 (95% CI: 0.26, 1.40)
OR (adjusted) Group C v A = 0.77 (95% CI: 0.24, 2.51)

Type III endoleak (48 month follow-up):
HR (adjusted) Group B v A = 0.86 (95% CI: 0.47, 1.57)
HR (adjusted) Group C v A = 0.17 (95% CI: 0.02, 1.19)

Study sample adequately described: Yes
Included risk variables clearly defined: Yes
Covariates considered to build the multivariate model: Yes
Interactions between variables explored: Unclear
Continuous variables handled appropriately: Yes
More than 10 events per included variable: Yes
Confidence intervals or other measures of uncertainty presented: Yes

<table>
<thead>
<tr>
<th>Author</th>
<th>Leurs 2005</th>
</tr>
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<tbody>
<tr>
<td>Country where study was performed</td>
<td>163 European centres</td>
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<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
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<tr>
<td>Registry</td>
<td>EUROSTAR</td>
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<tr>
<td>Number of patients</td>
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<tr>
<td>Age of population</td>
<td>With diabetes, mean age = 71.9 years</td>
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<td>Percentage male (total population)</td>
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<td>Max AAA diameter &gt;6 cm:</td>
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<td>Composite risk score</td>
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<td>Definition of outcomes</td>
<td>Intraoperative complications (device-related sequelae, procedural failure, and arterial complications. Postoperative (in-hospital) complications (systemic, procedure- and device-related, and access site/lower limb. Late complications (endoleaks, kinking, thrombosis, and migration occurring after 30 days).</td>
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<tr>
<td>Follow-up period</td>
<td>4-year follow-up. Mean follow-up of 19.36 (SD 18.88) months (range 0-96 months).</td>
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<tr>
<td>Methods of analysis</td>
<td>Odds ratios (HR) (95% CI) calculated for time-independent variables with multivariate logistic regression analysis. Hazard rates (HR) calculated using Cox proportional hazards model for time-dependent characteristics. Models adjusted for patient age, sex, ASA classification, SVS risk factors, obesity, and unfitness for traditional open surgery or general anaesthesia. Life-table analyses and Kaplan-Meier survival estimates used to analyze survival. Statistical significance set at p&lt;0.05.</td>
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<td>30 day mortality</td>
<td>Pre-existing conditions</td>
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<tr>
<td>Aneurysm related mortality at follow-up</td>
<td>No risk factors investigated</td>
</tr>
</tbody>
</table>

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All cause mortality at follow-up
Pre-existing conditions
With diabetes: 67/731 patients (9.16%)
Without diabetes: 452/5286 patients (8.55%)
TOTAL: 519 (8.6%)
HR (adjusted) = 1.15 (95% CI: 0.88-1.50)

Reintervention
Secondary intervention (follow-up):
With diabetes: 71/731 (9.71%)
Without diabetes: 596/5286 (11.09%)
HR (adjusted) = 1.07 (95% CI: 0.83-1.38)

Early conversion (30-days):
With diabetes: 13/731 patients (1.81%)
Without diabetes: 62/5286 patients (1.20%)
OR (adjusted) = 1.57 (95% CI: 0.84-2.95)

Late conversion (follow-up):
With diabetes: 11/731 patients (1.50%)
Without diabetes: 118/5286 patients (2.23%)
HR (adjusted) = 1.02 (95% CI: 0.54-1.91)

Endoleak
Endoleak (30-days):
Total with diabetes: 105/731 (14.36%)
Total without diabetes: 864/5286 (16.35%) (significant between 2 groups, p<0.035)
OR (adjusted) = 0.87 (95% CI: 0.70-1.10)

Endoleak Type I Proximal (30-days):
With diabetes: 22/731 patients (3.01%)
Without diabetes: 160/5286 patients (3.03%)
OR (adjusted) = 0.91 (95% CI: 0.57-1.46)

Endoleak Type I Distal (30-days):
With diabetes: 15/731 patients (2.05%)
Without diabetes: 125/5286 patients (2.36%)
OR (adjusted) = 0.88 (95% CI: 0.51-1.53)

Endoleak Type II (30-days):
With diabetes: 51/731 patients (6.97%)
Without diabetes: 466/5286 patients (8.82%)
OR (adjusted) = 0.86 (95% CI: 0.63-1.17)

Endoleak Type III (30-days):
With diabetes: 12/731 patients (1.64%)
Without diabetes: 125/5286 patients (2.36%)
OR (adjusted) = 0.66 (95% CI: 0.36-1.22)

Endoleak (follow-up):
Total with diabetes: 119/731 (16.28%)
Total without diabetes: 953/5286 (18.03%)
HR (adjusted) = 1.05 (95% CI: 0.87-1.28)

Endoleak Type I Proximal (follow-up):
With diabetes: 20/731 patients (2.74%)
Without diabetes: 157/5286 patients (2.97%)
HR (adjusted) = 1.03 (95% CI: 0.64-1.67)

Endoleak Type I Distal (follow-up):
With diabetes: 27/731 patients (3.69%)
Without diabetes: 218/5286 patients (4.12%)
HR (adjusted) = 1.09 (95% CI: 0.72-1.63)

Endoleak Type II (follow-up):
With diabetes: 67/731 patients (9.17%)
Without diabetes: 563/5286 patients (10.65%)
HR (adjusted) = 0.96 (95% CI: 0.74-1.25)

Endoleak Type III (follow-up):
With diabetes: 28/731 patients (3.83%)
Without diabetes: 227/5286 patients (4.29%)
HR (adjusted) = 1.19 (95% CI: 0.80-1.78)

Study sample adequately described: Yes
Included risk variables clearly defined: Yes

Author: Leurs 2005

Country where study was performed: 147 centres in Europe

Type of study: Specific risk factors following EVAR

Registry: Dates enrolled and/or treated: Between 1994 and 2004 EUROSTAR

Number of patients: 4233 patients

Age of population: Range: 37 to 101 years

Gender: 3967 (93.7%) male

Aneurysm diameter: Mean (SD) 5.8 cm, Range: 4.0-11.0 cm

Measurement tool used: CT scan

Type of device (EVAR): Zenith: 1185 patients (28%), Talent: 892 (21.1%), Excluder: 469 (11.1%), Lifepath: 83 patients (1.5%), EVT/Ancure: 142 patients (3.4%), Others (including Fortron, Anaconda, Endologix, and homemade devices): 164 patients (3.9%), Vanguard/Stentor: 646 patients (1.5%), AneuRx: 672 patients (15.9%)

Graft type (EVAR): Not reported

Anaesthesia: Not reported

Risk factor(s) used in model and definitions: Device to neck diameter ratio >= 1.20

Device main diameter (not defined)

Device related factors: use of aortic extension cuff, absence of proximal bare stent fixation.

Hypertension and smoking (not defined)

Aneurysm diameter (not defined)

Neck diameter and angulation (not defined)

Neck length (not defined)

Definition of outcomes: Dilatation of the infrarenal aneurysm neck was defined as an increase in diameter measured 0.3 cm distally from the lower renal artery - outer wall to outer wall across the minor diameter on the axial CT slice. Growth of aneurysm neck defined as diameter increase of at least 0.4 cm relative to the preoperative measurements on CT.

Device migration diagnosed using judgement of management teams. (Extent of migration not included in analyses as rarely quantified in millimetre device displacement).

Proximal endoleak (endoleaks in the first month not counted).

Follow-up period: Follow-up with plain abdominal radiograph studies performed at 1 month, 1 year, and annually thereafter. Mean or maximum follow-up were not reported.

Methods of analysis: Chi-square tests were used for comparison of discrete variables, and t-test or Wilcoxon rank sum test for continuous variables. Multivariate Cox proportional hazard model was used to determine anatomic and operative variables, with an independent correlation with neck growth and device migration, respectively as the outcome event.

30 day mortality: No risk factors investigated
Aneurysm related mortality at follow-up: No risk factors investigated

All cause mortality at follow-up: No risk factors investigated

Reintervention: No risk factors investigated

Endoleak:
- Smoking status: HR = 0.96 (95% CI: 0.61-1.52, p= 0.87)
- Graft configuration and device type: Without suprarenal fixation system or hooks: HR = 0.75 (95% CI: 0.48-1.15, p= 0.18)
- Device to neck diameter ratio >= 1.20: 0.97 (95% CI: 0.48, 1.56, p=0.63)
- Device main diameter: HR 1.01 (95% CI: 0.89, 1.14, p=0.93)
- Use of aortic extension cuff: HR 0.91 (95% CI: 0.28, 2.88, p=0.87)
- Hypertension: HR = 1.25 (95% CI: 0.83-1.87, p=0.28)
- Aneurysm Diameter: HR = 1.00 (95% CI: 0.99-1.01, p=0.66)
- Neck diameter: HR = 1.04 (95% CI: 0.90-1.19, p=0.63)
- Significant neck angulation (positive correlation): HR = 2.02 (95% CI: 1.37-2.99, p=0.0004)
- Aortic neck length: HR = 0.97 (95% CI: 0.95-0.99, p=0.0043) (negative correlation)

Post operative factors:
- Infrarenal neck dilation: HR 0.85 (95% CI: 0.55, 1.31, p=0.45)
- Migration: HR 3.11 (95% CI: 1.83, 5.30, p=0.0001)

Study sample adequately described: Yes

Included risk variables clearly defined: Yes

Covariates considered to build the multivariate model: Yes

Interactions between variables explored: Unclear

Continuous variables handled appropriately: Unclear

More than 10 events per included variable: Unclear

Confidence intervals or other measures of uncertainty presented: Yes


Author: Leurs 2006

Country where study was performed: 165 institutions in Europe

Type of study: Specific risk factors following EVAR

Registry: Enrolled 1st December 1996 EUROSTAR

Number of patients: 5892 patients, 731 (12.4%) statin users

Age of population:
- Mean (SD)
  - Statin Users: 70.1 yrs (SD 7.3)
  - Non-users: 72.6 cm (SD 1.11 cm), p<0.0001
- TOTAL: 72.3 yrs

Gender:
- Percentage male (total population)
  - TOTAL: 5545 (94.1%), p=ns
  - Statin users: 694 (94.9%)
  - Non-users: 4851 (94.0%)

Aneurysm diameter:
- Overall mean: 5.86 cm
  - Statin users: 5.82 (SD 0.96 cm)
  - Non-users: 5.87 cm (SD 1.11 cm), p=ns

Measurement tool used:
- Computed tomography (CT) and intra-arterial digital subtraction angiography (DSA)

Type of device (EVAR): Not reported

Only commercially available Communautte Europeanne (CE) approved stent grafts
Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model

<table>
<thead>
<tr>
<th>Graft type (EVAR)</th>
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<tbody>
<tr>
<td>Anaesthesia</td>
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<td>Risk factor(s) used in model and definitions</td>
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<td>Age &gt;= 70 yrs</td>
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<td>ASA class greater than or equal to III</td>
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<td>Pre-existing conditions</td>
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<td>Moderate/severe SVS/ISCVS risk score:</td>
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<td>Diabetes</td>
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<td>Smoking</td>
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<td>Hypertension</td>
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<tr>
<td>Cardiac disease</td>
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<tr>
<td>Carotid disease</td>
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<tr>
<td>Renal disease</td>
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<td>Pulmonary disease</td>
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<tr>
<td>Pre-operative statin therapy</td>
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</table>

Definition of outcomes

Death within 30 days of initial procedure defined as operative death. Death after 30 days defined as late death. Aneurysm-related death included 30-day death and death that occurred as a result of aneurysm rupture or endograft infection or within 1 month after a secondary surgical procedure for late complications of the aneurysm.

Follow-up period

1, 3, 6, 12, 18, and 24 months and annually thereafter (mean duration 17 months)

Methods of analysis

Univariate analysis was carried out to correlate the two patient groups with preoperative patient characteristics, comorbidity, risk factors, and aneurysmal morphology at the time of the initial procedure. Differences in baseline characteristics between the two groups were assessed using chi-square test for discrete variables and by Wilcoxon rank sum test for continuous variables.

Multivariate Cox proportional hazard model used to identify effect of statin use on late outcomes with adjustment for potential confounders (ASA class >= III, diabetes, hypertension, cardiac and carotid impairment, obesity and age >70 yrs).

30-day outcomes after EVAR analyzed by multivariate logistic regression, follow-up outcomes assessed by Kaplan-Meier survival analysis.

30 day mortality

No risk factors investigated

Aneurysm related mortality at follow-up

Patient age >70 yrs: HR = 2.38 (95% CI: 1.63, 3.48, p<0.0001)
ASA class >= III: HR = 3.21 (95% CI: 2.27, 4.53, p<0.0001)
Statin use: HR = 0.57 (95% CI: 0.32, 1.03, p=ns)

All cause mortality at follow-up

Patient age >70 yrs: HR = 1.96 (95% CI: 1.62, 2.38, p<0.0001)
ASA class >= III: HR = 1.90 (95% CI: 1.59, 2.28, p<0.0001)
Cardiac status: HR = 1.24 (95% CI: 1.03, 1.49, p=0.022)
Statin use: Adjusted HR = 0.72 (95% CI: 0.54, 0.98, p=0.034)

Reintervention

There was no significant association between statin use and increased risk for conversion: HR (adjusted) 0.98 (95% CI: 0.29, 1.13, p=ns)

Endoleak

No risk factors investigated

Study sample adequately described

Yes

Included risk variables clearly defined

No

Covariates considered to build the multivariate model

Not reported

Interactions between variables explored

Unclear

Continuous variables handled appropriately

Unclear

More than 10 events per included variable

Unclear

Confidence intervals or other measures of uncertainty presented

Yes

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<thead>
<tr>
<th>Author</th>
<th>Lifeline Registry of Endovascular aneurysm repair 2002</th>
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<tbody>
<tr>
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<td>Type of study</td>
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<td>Age of population</td>
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<td>Risk factor(s) used in model and definitions</td>
<td>Age Pre-existing conditions: COPD; CHF; renal failure (not defined) Aneurysm size categorised as &lt;4.0, 4.0-4.9, 5.0-5.9, 6.0-6.9, 7.0-7.9 and &gt; 8.0 cm</td>
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<td>Definition of outcomes</td>
<td>All cause mortality at follow-up (1 year): survival</td>
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<td>Follow-up period</td>
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<td>Methods of analysis</td>
<td>Logistic regression analysis of 1 year survival.</td>
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<tr>
<td>All cause mortality at follow-up</td>
<td>Increasing age associated with reduced one year survival. COPD and congestive heart failure (CHF) associated with reduced one year survival compared to patients with no co-morbidities. Renal failure associated with reduced one year survival compared to patients with no co-morbidities. Increasing aneurysm size associated with reduced one year survival.</td>
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<table>
<thead>
<tr>
<th>Author</th>
<th>Lifeline registry of endovascular aneurysm repair 2005</th>
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<tr>
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<td>Specific risk factors following EVAR</td>
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<td>Registry</td>
<td>Registry established 1998. This report from the Lifeline registry includes 5 year data from clinical trials of four EVAR devices: AnCure, AneuRx, Excluder, and Powerlink.</td>
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<td>Number of patients</td>
<td>2664</td>
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</table>
Age of population: Mean 73.1 (SD 7.8) years
Range: 45 - 96 years

Gender: 88.6% male

Aneurysm diameter: Mean 5.58 (1.02) cm
Range: 2.1 - 12.0 cm

Type of device (EVAR):
- Zenith: 0%
- Talent: 0%
- Excluder: 235/2664 (8.8%)
- AnCure 1040/2664 (39.0%)
- AneuRx 1204/2664 (45.2%)
- Powerlink 185/2664 (6.9%)

Graft type (EVAR): Not reported

Anaesthesia: Not reported

Risk factor(s) used in model and definitions:
- Age: Not specified
- Female gender
- Pre-existing conditions: Coronary artery disease (CAD) or myocardial infarction (MI)
- Congestive heart failure (CHF)
- Hypertension
- Chronic obstructive airways disease
- Diabetes mellitus
- Renal failure (serum creatinine >3 mg)
- Aneurysm size: Not defined

Definition of outcomes:
- Operative mortality: death during initial hospitalisation or up to 30 days post-operative.
- Aneurysm-related death: death from any cause up to 30 days postoperative or up to 30 days after a reintervention for aneurysm or any death due to graft complication or aneurysm rupture.
- All cause mortality: survival
- Aneurysm rupture (not defined)
- Conversion to open repair (not defined)

Follow-up period: At least 5 years. Mean follow-up 2.8 (SD 1.6 years) (maximum 6.7 years)

Methods of analysis: Predictive risk factors for specified outcomes were identified by Cox proportional hazard multivariate logistic regression.

30 day mortality: No risk factors investigated

Aneurysm related mortality at follow-up:
- Age: HR 1.041 (95% CI 1.00, 1.09), p=0.061
- Female gender: HR 1.65 (95% CI 0.71, 3.82), p=0.24
- CAD/MI: HR 2.43 (95% CI 0.58, 10.25), p=0.23
- CHF: HR 2.15 (95% CI 1.00, 4.67), p=0.053
- Hypertension: HR 0.92 (95% CI 0.48, 1.80), p=0.82
- COPD: HR 1.26 (95% CI 0.65, 2.45), p=0.50
- Diabetes mellitus: HR 0.98 (95% CI 0.38, 2.533), p=0.97
- Renal failure: HR 1.78 (95% CI 0.52, 6.01), p=0.36
- Aneurysm size: HR 1.03 (95% CI 1.01, 1.06), p=0.01

All cause mortality at follow-up:
- Age: HR 1.04 (95% CI 1.03, 1.1), p< 0.0001
- Female gender: HR 1.04 (95% CI 0.77, 1.40), p=0.82

Reintervention: No risk factors investigated

Endoleak: No risk factors investigated

Study sample adequately described: Yes

Included risk variables clearly defined: No

Diagnostic criteria for specific comorbidities not stated

Covariates considered to build the multivariate model: Yes

Baseline characteristics

Interactions between variables explored: No

No specific interaction term(s) reported
Continuous variables handled appropriately | Yes
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More than 10 events per included variable | Unclear
Confidence intervals or other measures of uncertainty presented | Yes


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<th>Author</th>
<th>Lottman 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country where study was performed</td>
<td>107 centres in Europe</td>
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<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
</tr>
<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: January 1994 - July 2001 EUROSTAR registry</td>
</tr>
<tr>
<td>Number of patients</td>
<td>3270 (of whom 853 (26%) were smokers)</td>
</tr>
</tbody>
</table>
| Age of population | Range
- 9% were aged 60 yrs or less
- 34% were aged 61-70 years
- 46% were aged 71-80 years
- 11% were aged 80 years or older |
| Gender | 93% male |
| Aneurysm diameter | Range
- 1442 (44%) aneurysm diameter of less than 5.5 cm
- 1748 (56%) aneurysm diameter of 5.5 cm |
| Type of device (EVAR) | Not reported |
| Graft type (EVAR) | Not reported |
| Anaesthesia | Not reported |
| Risk factor(s) used in model and definitions | The study population was divided into two groups: smokers and non-smokers. Smokers were those who did smoke at the time of enrolment (both those who smoked less than one packet a day and those who smoked more than one packet a day. Corresponds to SVS/ICCVS risk score 2 or 3.
Non-smokers were those who did not smoke at enrolment (including those who had smoked in the last 10 years). Corresponds to SVS/ICCVS risk score 0 or 1.
SVS/ICCVS - Society for Vascular Surgery/ International Society for Cardiovascular Surgery |
| Definition of outcomes | Late mortality: death after first 30 days
Reinterventions:
Late reinterventions defined as those after 30 days post-operatively.
Late conversions defined as those after 30 days post-operatively.
Endoleak (type I proximal, Type I distal, type II and Type III) |
| Follow-up period | Median follow-up 12 months (range 0-84 months) |
| Methods of analysis | For outcomes up to 30 days post-operatively differences between the groups were analysed using the Chi-Squared test or the Fisher exact test, or the Rank test for non-parametric data
Outcomes after the first 30 days were analysed using the Kaplan-Meier method. Differences in survival were assessed for significance by means of the log-rank tests. Multivariate Cox proportional hazards models were used to examine the relationship of smoking with late events, adjusted for baseline characteristics: age, gender, morphological data, pre-existing co-morbidity, device, year of operation, and operating team experience. A P value of less than 0.01 was considered statistically significant. |
| 30 day mortality | No risk factors investigated |
| Aneurysm related mortality at follow-up | No risk factors investigated |
| All cause mortality at follow-up | Smoking status: No significant effect of smoking status |
| Reintervention | Smoking status. Late reinterventions: No significant effect of smoking status |
Late conversion: No significant effect of smoking status

Endoleak

Smoking status
Late Endoleak (All)
No significant effect of smoking status

Late Endoleak (Type I proximal)
No significant effect of smoking status

Late Endoleak (Type I distal)
No significant effect of smoking status

Late Endoleak (Type II)
HR 0.64 (95% CI 0.5, 0.9) (association with smoking)

Late Endoleak (Type III)
No significant effect of smoking status

Study sample adequately described Yes
Included risk variables clearly defined Yes
Covariates considered to build the multivariate model Yes
Interactions between variables explored No
No mention of a term for any specific interaction mentioned
Continuous variables handled appropriately No
Age was grouped as >60, 61-70, 71-80, and >80 years. Also other measurements such as aneurysm diameter dichotomised
More than 10 events per included variable Yes
Confidence intervals or other measures of uncertainty presented No


Author Mohan 2001
Country where study was performed European
Type of study Specific risk factors following EVAR
Registry Dates enrolled and/or treated: January 1994 to January 2000 EUROSTAR
Number of patients 2146 (although baseline risk factors assessed in 2194)
Age of population Range: 37 - 92 (median 70)
Gender 92% male
Aneurysm diameter Range: 2.1-15.0 (median 5.6) cm
Type of device (EVAR) Zenith: 6%
Talent: 13%
Excluder: 4%
Vanguard 40%
Stentor 15%
AneuRx 18%
EVT 3%
Other 1%
Graft type (EVAR) Bi-iliac: 92% patients
Anaesthesia Not reported
<table>
<thead>
<tr>
<th>Risk factor(s) used in model and definitions</th>
<th>Age &lt; 65 years; 65-75 years; &gt; 75 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gender male or female</td>
</tr>
<tr>
<td></td>
<td>Smoking (current &gt;20/day; current &lt;20/day; stopped &lt;10 years; stopped &gt; 10 years)</td>
</tr>
<tr>
<td></td>
<td>Device type (trade name)</td>
</tr>
<tr>
<td></td>
<td>Type of aortic device, device diameter and use of aortic cuff.</td>
</tr>
<tr>
<td></td>
<td>ASA classification Class I, II, III or IV</td>
</tr>
<tr>
<td></td>
<td>Pre-existing conditions</td>
</tr>
<tr>
<td></td>
<td>Obesity (not defined)</td>
</tr>
<tr>
<td></td>
<td>Fitness for open procedure (Not defined)</td>
</tr>
<tr>
<td></td>
<td>Aneurysm diameter &lt; 5.0 cm; 5.0-6.0 cm; &gt; 6.0 cm</td>
</tr>
<tr>
<td></td>
<td>Aortic neck and aneurysm angle</td>
</tr>
<tr>
<td></td>
<td>Aortic neck length</td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>Endoleak (all) as identified immediately after stent-graft deployment.</td>
</tr>
<tr>
<td></td>
<td>Endoleak (proximal) as identified immediately after stent-graft deployment.</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>Assessment immediately after stent graft deployment only</td>
</tr>
<tr>
<td>Methods of analysis</td>
<td>The clinical features of patients with endoleak were compared with those of patients without endoleak. Data analysed by Chi-squared test. A multivariate analysis was performed using variables identified from the univariate analysis as being significantly associated with endoleak. A logistic regression model was constructed excluding backward elimination factors not associated with proximal endoleak. Odds ratios (OR) with 95% CI calculated.</td>
</tr>
<tr>
<td>30 day mortality</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>Aneurysm related mortality at follow-up</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>All cause mortality at follow-up</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>Reintervention</td>
<td>No risk factors investigated</td>
</tr>
</tbody>
</table>
Endoleak

Age: All Endoleak
- Less than 65 years (24%): Multivariate analysis OR = 1
- 65-75 years (46%): Multivariate analysis OR = 0.77 (95% CI 0.56, 1.07), p=0.87
- Older than 75 years (30%): Multivariate analysis OR = 1.35 (95% CI 0.96, 1.90), p=0.08

Proximal endoleak: No significant association with age

Gender: All Endoleak
- Female (8%): Multivariate analysis OR = 1
- Male (92%): Multivariate analysis OR = 0.71 (95% CI 1.47, 1.07), p=0.097

Proximal endoleak: No significant association with sex

Smoking status: All endoleak
- Current (>20/day) (10%): Multivariate analysis OR = 1
- Current < 20 /day (19%): No significant association
- Stopped <10 years (29%): No significant association
- Stopped >10 years (43%): Multivariate analysis OR = 1.72 (95% CI 1.10, 2.80), p=0.03

Proximal endoleak: No significant association with smoking status

Graft configuration and device type: No significant association with endoleak or proximal endoleak.

ASA: No significant association with endoleak or proximal endoleak.

Pre-existing conditions
- Obesity: No association with endoleak or proximal endoleak
- Fitness for open procedure: No significant association with endoleak or proximal endoleak
- Aneurysm size: All Endoleak
  - Aneurysm diameter less than 5.0 cm (26%): Multivariate analysis OR = 1
  - Aneurysm diameter 5.0-6.0 cm (49%): Multivariate analysis OR = 1.45 (95% CI 1.06, 1.99), p=0.02
  - Aneurysm diameter more than 6.0 cm (25%): Multivariate analysis OR = 1.60 (95% CI 1.13, 2.27), p=0.008

Proximal endoleak: No significant association with aneurysm size
- Aortic neck and aneurysm angle: No significant association with endoleak or proximal endoleak.
- Aortic neck length: The length of the proximal aortic neck was significantly associated with proximal endoleak: OR 0.93 (95% CI 0.89, 0.96) (p=0.0001).
- Other (give details)
- Experience of surgeon: No significant association with endoleak or proximal endoleak.

<table>
<thead>
<tr>
<th>Study sample adequately described</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Included risk variables clearly defined</td>
<td>Yes</td>
</tr>
<tr>
<td>Covariates considered to build the multivariate model</td>
<td>Yes</td>
</tr>
<tr>
<td>Interactions between variables explored</td>
<td>Unclear</td>
</tr>
<tr>
<td>Continuous variables handled appropriately</td>
<td>No</td>
</tr>
<tr>
<td>More than 10 events per included variable</td>
<td>Age and aneurysm diameter categorised</td>
</tr>
<tr>
<td>Confidence intervals or other measures of uncertainty presented</td>
<td>Yes</td>
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</table>

<table>
<thead>
<tr>
<th>Author</th>
<th>Peppelenbosch 2004</th>
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<tr>
<td>Country where study was performed</td>
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<td>Type of study</td>
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</tr>
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<td>Registry</td>
<td>EUROSTAR Patients enrolled over 6 years up to June 2002</td>
</tr>
<tr>
<td>Number of patients</td>
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<tr>
<td>Age of population</td>
<td>Mean (SD)</td>
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<tr>
<td></td>
<td>Small aneurysms (4.0-5.4 cm) n= 1962, mean age 69.7</td>
</tr>
<tr>
<td></td>
<td>Medium aneurysms (5.5 - 6.4 cm)n=1528, mean age 72.1</td>
</tr>
<tr>
<td></td>
<td>Large aneurysms (&gt;= 6.5 cm)n=902, mean age 73.3</td>
</tr>
<tr>
<td></td>
<td>Range</td>
</tr>
<tr>
<td></td>
<td>Small aneurysms (4.0-5.4 cm) n= 1962, age range 43 - 9469.7</td>
</tr>
<tr>
<td></td>
<td>Medium aneurysms (5.5 - 6.4 cm)n=1528, age range 49 - 109</td>
</tr>
<tr>
<td></td>
<td>Large aneurysms (&gt;= 6.5 cm)n=902, age range 50 - 93</td>
</tr>
<tr>
<td>Gender</td>
<td>Percentage male (total population)</td>
</tr>
<tr>
<td></td>
<td>Small aneurysms (4.0-5.4 cm) 93%</td>
</tr>
<tr>
<td></td>
<td>Medium aneurysms (5.5 - 6.4 cm)93%</td>
</tr>
<tr>
<td></td>
<td>Large aneurysms (&gt;= 6.5 cm) 95%</td>
</tr>
<tr>
<td></td>
<td>Total population % male = 93.2%</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Mean: 57.2 cm (SD not reported)</td>
</tr>
<tr>
<td></td>
<td>Range: 4.0 - 14.5 cm</td>
</tr>
<tr>
<td>Type of device (EVAR)</td>
<td>Zenith: 891 (20.3%)</td>
</tr>
<tr>
<td></td>
<td>Talent: 821 (18.7%)</td>
</tr>
<tr>
<td></td>
<td>Excluder: 341 (7.8%)</td>
</tr>
<tr>
<td></td>
<td>AneuRx n= 877 (20.0%)</td>
</tr>
<tr>
<td></td>
<td>EVT/Ancure n= 150 (3.4%)</td>
</tr>
<tr>
<td></td>
<td>Stentor n= 282 (6.4%)</td>
</tr>
<tr>
<td></td>
<td>Vanguard n= 905 (21%)</td>
</tr>
<tr>
<td></td>
<td>Other/ unknown = 125 (2.9%)</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Aortouni-iliac 193 (4.4%); straight tube 149 (3.4%)</td>
</tr>
<tr>
<td></td>
<td>Bi-iliac: 405 (92.2%)</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Gender</td>
</tr>
<tr>
<td></td>
<td>Graft configuration and device type: A dichotomous categorisation of devices was used, with Stentor and Vanguard as one category and all other devices in the other.</td>
</tr>
<tr>
<td></td>
<td>ASA</td>
</tr>
<tr>
<td></td>
<td>Pre-existing conditions</td>
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<tr>
<td></td>
<td>Fitness for open procedure</td>
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<tr>
<td></td>
<td>Renal function (creatinine)</td>
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<td>Aneurysm size:</td>
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<td>Small aneurysms (4.0-5.4 cm)</td>
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<tr>
<td></td>
<td>Medium aneurysms (5.5 - 6.4 cm)</td>
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<tr>
<td></td>
<td>Large aneurysms (&gt;= 6.5 cm)</td>
</tr>
<tr>
<td></td>
<td>Aortic neck and aneurysm angle</td>
</tr>
<tr>
<td></td>
<td>Aortic neck length</td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>30 day mortality: death within 30 days of initial procedure</td>
</tr>
<tr>
<td></td>
<td>Aneurysm related mortality at follow-up: all operative deaths and those related to aneurysm rupture, endograft infection or within 1 month of a secondary surgical procedure to treat a late complication of the aneurysm</td>
</tr>
<tr>
<td></td>
<td>All cause mortality at follow-up: late deaths that occurred more than 30 days after initial procedure.</td>
</tr>
<tr>
<td></td>
<td>Endoleak: Type I Proximal and Type I distal, type II and Type III. Only endoleaks identified at one month or after included</td>
</tr>
<tr>
<td></td>
<td>Reintervention: late conversion to open repair</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>Mean follow-up 18.4 months (range 1-72 months)</td>
</tr>
<tr>
<td>Methods of analysis</td>
<td>Preoperative patient characteristics, comorbid conditions and aneurysm anatomy at initial procedure and details of procedure and devices were correlated with univariate analysis. Differences in findings between groups were assessed with Chi-squared tests for discrete variables and Mann-Whitney test for continuous variables.</td>
</tr>
</tbody>
</table>
All variables with significant correlation with an adverse outcome were entered into a multivariate Cox analysis.

A dichotomous categorisation of devices was used, with Stentor and Vanguard as one category and all other devices in the other. This variable device category was entered into multivariate analysis irrespective of result of univariate analysis.

Cumulative rates of freedom from aneurysm related death were assessed with life-table analysis. Only rates with SE less than 10% are indicated. Significant differences between study groups were assessed with log-rank testing.

### 30 day mortality
No risk factors investigated

### Aneurysm related mortality at follow-up
Age
Multivariate Hazard ratio (HR) 1.1 (95% CI 1.04, 1.09) (miss print or rounding up of HR?)

Gender: No significant association (multivariate analysis)

Graft configuration and device type: Association with Stentor or Vanguard device: multivariate Hazard ratio (HR) 1.5 (95% CI 1.1, 2.3)

ASA: No significant association (multivariate analysis)

Pulmonary condition: Multivariate Hazard ratio (HR) 1.7 (95% CI 1.1, 2.4)

Association with lack of fitness for open repair: multivariate Hazard ratio (HR) 1.7 (95% CI 1.1, 2.4)

Association with renal insufficiency: multivariate Hazard ratio (HR) 1.8 (95% CI 1.2, 2.7)

Aneurysm related mortality
Association with large aneurysm size: multivariate Hazard ratio (HR) 2.5 (95% CI 1.6, 4.0)

Late aneurysm death
Association with large aneurysm size: multivariate Hazard ratio (HR) 6.0 (95% CI 2.6, 14.1)

Aortic neck and aneurysm angle: No significant association (multivariate analysis)

Aortic neck length: No significant association (multivariate analysis)

### All cause mortality at follow-up
No risk factors investigated

### Reintervention
Age: No significant association (multivariate analysis)

Gender: No significant association (multivariate analysis)

Graft configuration and device type: No significant association (multivariate analysis)

ASA: No significant association (multivariate analysis)

Pre-existing conditions: No significant association (multivariate analysis)

Fitness for open procedure: No significant association (multivariate analysis)

Renal function (creatinine): No significant association (multivariate analysis)

Association with large aneurysm size: multivariate Hazard ratio (HR) 1.6 (95% CI 1.1, 2.3)

Aortic neck and aneurysm angle: No significant association (multivariate analysis)

Aortic neck length: No significant association (multivariate analysis)

### Endoleak
No risk factors investigated.

### Study sample adequately described
Yes

### Included risk variables clearly defined
No

### Covariates considered to build the multivariate model
Yes

### Interactions between variables explored
Unclear

### Continuous variables handled appropriately
Unclear

### More than 10 events per included variable
Unclear

### Confidence intervals or other measures of uncertainty presented
Yes

<table>
<thead>
<tr>
<th>Author</th>
<th>Riambau 2001</th>
</tr>
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<tbody>
<tr>
<td>Country where study was performed</td>
<td>88 centres from European countries</td>
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<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
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<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: Between January 1994 and August 1998</td>
</tr>
<tr>
<td></td>
<td>Patients operated on before July 1996 were included in the retrospective part of the study, and after this date patients were included prospectively.</td>
</tr>
<tr>
<td>Number of patients</td>
<td>2862 patients: 2481 (normal condition), 272 (unfit for open procedure), 109 (unfit for anaesthesia)</td>
</tr>
<tr>
<td>Age of population</td>
<td>Younger than 65 years:</td>
</tr>
<tr>
<td></td>
<td>Normal condition: 600 (24.2%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for open procedure: 58 (21.3%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for anaesthesia: 15 (13.8%)</td>
</tr>
<tr>
<td></td>
<td>TOTAL: 673 (23.5%)</td>
</tr>
<tr>
<td></td>
<td>65-75 years:</td>
</tr>
<tr>
<td></td>
<td>Normal condition: 1157 (46.6%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for open procedure: 113 (41.5%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for anaesthesia: 44 (40.3%)</td>
</tr>
<tr>
<td></td>
<td>TOTAL: 1314 (45.9%)</td>
</tr>
<tr>
<td></td>
<td>Older than 75 years:</td>
</tr>
<tr>
<td></td>
<td>Normal condition: 724 (29.2%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for open procedure: 101 (37.2%)</td>
</tr>
<tr>
<td></td>
<td>Unfit for anaesthesia: 50 (45.9%)</td>
</tr>
<tr>
<td></td>
<td>TOTAL: 875 (30.6%)</td>
</tr>
<tr>
<td>p</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender</td>
<td>TOTAL: 2640 (92.2%) male</td>
</tr>
<tr>
<td>Aneurysm diameter</td>
<td>Overall mean: 5.62 cm</td>
</tr>
<tr>
<td></td>
<td>Normal condition: 5.56 cm (SD 1.07 cm)</td>
</tr>
<tr>
<td></td>
<td>Unfit for open: 5.96 cm (SD 1.19 cm)</td>
</tr>
<tr>
<td></td>
<td>Unfit for anaesthesia: 6.05 cm (SD 1.43 cm), p=0.001</td>
</tr>
<tr>
<td>Measurement tool used</td>
<td>CT scan</td>
</tr>
<tr>
<td>Type of device (EVAR)</td>
<td>Zenith: 239 (8.4%)</td>
</tr>
<tr>
<td></td>
<td>Talent: 383 (13.4%)</td>
</tr>
<tr>
<td></td>
<td>Excluder: 137 (4.8%)</td>
</tr>
<tr>
<td></td>
<td>AneuRX: 707 (24.7%)</td>
</tr>
<tr>
<td></td>
<td>EVT: 127 (4.4%)</td>
</tr>
<tr>
<td></td>
<td>Stentor: 310 (10.8%)</td>
</tr>
<tr>
<td></td>
<td>Vanguard: 892 (31.2%)</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Patients unfit for open surgery and/or unfit for anaesthesia were considered as patients ineligible for elective open repair due to the poor medical conditions. Co-existing diseases (diabetes mellitus, hypertension, hyperlipaemia, cardiac status, carotid disease, renal status, and pulmonary status) reported according to the SVS-ISCV risk score.</td>
</tr>
<tr>
<td>Patients unfit for open surgery or general anaesthesia considered in good medical condition. Patients unfit for open surgery or general anaesthesia considered in poor medical condition.</td>
<td></td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>Early/late mortality (not defined)</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>1, 3, 6, 12, 18, and 24 months, and annually thereafter.</td>
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<tr>
<td>Methods of analysis</td>
<td>Associations between health status and clinical outcome were calculated by age-adjusted mortality rates. Univariate and multivariate regression analysis based on Cox proportional hazards models were used to assess correlations between mortality, co-morbidity, and health status. Exact Fisher’s test was applied to know the correlation between the previous medical condition at entry and the cause of death.</td>
</tr>
<tr>
<td>Survival analysis was calculated by Kaplan-Meier testing.</td>
<td></td>
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<tr>
<td>30 day mortality</td>
<td>No risk factors investigated</td>
</tr>
<tr>
<td>Aneurysm related mortality at</td>
<td>No risk factors investigated</td>
</tr>
</tbody>
</table>
All cause mortality at follow-up

Death among patients, by co-morbidity at baseline:

Hyperlipaemia:
- Patients with normal condition: RR (age-adjusted) = 0.78 (95% CI: 0.6-1.1)
- Patients unfit for open surgery: RR (age-adjusted) = 1.25 (95% CI: 0.7-2.1)

Cardiac disease:
- Normal condition: RR (age-adjusted) = 1.07 (95% CI: 0.8-1.4)
- Patients unfit for open surgery: RR (age-adjusted) = 1.14 (95% CI: 0.6-2.2)

Renal insufficiency:
- Normal condition: RR (age-adjusted) = 1.41 (95% CI: 1.0-2.1)
- Patients unfit for open surgery: RR (age-adjusted) = 1.59 (95% CI: 0.9-2.8)

Pulmonary disease:
- Patients fit for open surgery: RR (age-adjusted) = 1.40 (95% CI: 1.0-1.9)
- Patients unfit for open surgery: RR (age-adjusted) = 1.29 (95% CI: 0.7-2.3)

Diabetes mellitus:
- Patients fit for open surgery: RR (age-adjusted) = 1.66 (95% CI: 1.1-2.5, p<0.05)
- Patients unfit for open surgery: RR (age-adjusted) = 1.42 (95% CI: 0.7-2.8)

There were no significant associations between all-cause mortality at follow-up and smoking (p=0.9), hypertension (p=0.8), or carotid disease (p=0.13).

Reintervention
- No risk factors investigated

Endoleak
- No risk factors investigated

Study sample adequately described
- Yes

Included risk variables clearly defined
- Yes

Covariates considered to build the multivariate model
- Not reported

Interactions between variables explored
- Unclear

Continuous variables handled appropriately
- Yes

More than 10 events per included variable
- Yes

Confidence intervals or other measures of uncertainty presented
- Yes


Author
- Ruppert 2006

Country where study was performed
- 164 collaborating European vascular centres.

Type of study
- Specific risk factors following EVAR
- Main focus of paper is the influence of anaesthesia type on AAA outcomes. Only patient risk factors relate to endoleak rate and these appear to be documented in the text only.

Registry
- Dates enrolled and/or treated
- July 1997 to August 2004
- EUROSTAR

Number of patients
- 5557

Age of population
- Mean (SD): 72 years
- Range: 41 to 100 years

Gender
- Not reported
Aneurysm diameter

Mean (total) 5.85 cm
GA 5.81 cm (1.07)
RA 5.94 cm (1.12)
LA 5.9 cm (1.1)

Range
Total 4 cm to 14.5 cm
GA 4 cm to 13 cm
RA 4 cm to 14.5 cm
LA 4 cm to 10 cm

Type of device (EVAR)

Zenith: 1923 patients (34.6%)
Talent: 1492 (26.8%)
Excluder: 767 (13.8%)
Anaconda 26 (0.5%)
AneuRx 938 (16.9%)
Endologix 116 (2.1%)
EVT 71 (1.3%)
Fortron 82 (1.5%)
Lifepath 115 (2.1%)

Graft type (EVAR)

Bifurcated: 4904 patients (91.6%)
Tube: 108 (2%)
Tapered: 340 (6.4%)

Anaesthesia

Local: 310 patients (6%)
Regional: 1399 (25%)
General: 3848 (69%)

Risk factor(s) used in model and definitions

Age: Not defined
Aneurysm size: Not defined

Definition of outcomes

Not defined

Follow-up period

1, 6, 12, 18 and 24 months and annually thereafter. Mean or median follow up unclear.

Methods of analysis

Multivariate regression analysis for early complications.

30 day mortality

No risk factors investigated

Aneurysm related mortality at follow-up

No risk factors investigated

All cause mortality at follow-up

No risk factors investigated

Reintervention

No risk factors investigated

Endoleak

Advanced age (not specified) was independently associated with endoleak rate (no data provided).

Device type (tube, tapered, or bifurcated) was not independently associated with increased risk for endoleak. However, AneuRx, Talent and Fortron devices were independently associated with increased risk (no data provided).

Aneurysm size independently associated with endoleak rate (no data provided).

Study sample adequately described

No

Included risk variables clearly defined

No

Covariates considered to build the multivariate model

Yes

Interactions between variables explored

Unclear

Continuous variables handled appropriately

Unclear

More than 10 events per included variable

Yes

Confidence intervals or other measures of uncertainty presented

No

Author: Sampram 2003
Country where study was performed: USA
Type of study: Specific risk factors following EVAR
Case Series: 1996-2002
Name of centre: Cleveland Clinic, Ohio, USA.
Number of patients: 703
Age of population: Mean: 75 (SD 8.1) years.
Range: 48-100 years.
Gender: 86% male
Aneurysm diameter: Mean: 5.4 (SD 1.0) cm in minor dimension and 5.8 (SD 1.1) cm in major dimension. Measurement tool used
Preoperative helical computed tomography (CT) with 3 mm axial reconstruction. Angiography and intravascular ultrasound were used when measurements were deemed inaccurate on the basis of CT scans, in the presence of suspected renal or iliac occlusive disease or when required as part of a clinical trial.
Type of device (EVAR): Zenith: 325/703 (46%)
Talent: 39/703 (6%)
AneuRx 203/703 (29%)
Ancure 63/703 (9%)
Other devices 73/703 (10%)
Graft type (EVAR): Not reported
Anaesthesia: Not reported
Risk factor(s) used in model and definitions:
- Age: Per year as continuous variable
- Gender
- Device type (brand name).
- Aneurysm size: Measured on the CT scan with the greatest minor sac dimension on any axial image.
- Non-patient risk factors including procedure date and various procedural variables.
Definition of outcomes:
Reinterventions (secondary procedures): any subsequent procedure, whether percutaneous or open surgical, related to AAA repair or associated complications. Procedures performed because of wound complications were recorded but not analysed.
Follow-up period:
Mean 12.2 (SD 11.7) months, range 0-65 months.
Methods of analysis:
Kaplan-Meier survival analysis was used to express survival, freedom from aneurysm-related death and freedom from reintervention. Cox analysis was used to evaluate time to reintervention for baseline variables (including procedure date, patient demographic parameters and aneurysm size) and procedural details (including device type, placement of renal or aortic stents, hypogastric embolization and use of iliac conduits for access). Hazard ratios (HRs) and associated 95% confidence intervals (CIs) were calculated. Multivariate Cox proportional hazards modelling was used to define independent predictors of reintervention.
30 day mortality:
No risk factors investigated
Aneurysm related mortality at follow-up:
No risk factors investigated
All cause mortality at follow-up:
No risk factors investigated
Reintervention

No significant association between age and risk of reintervention in univariate analysis: HR 1.00, 95% CI: 0.98, 1.03, p = 0.95.

No significant association between male gender and risk of reintervention in univariate analysis: HR 1.10, 95% CI: 0.60, 2.02, p = 0.76.

No significant association between device type and risk of reintervention in univariate analysis: p = 0.32; HRs relative to AneuRx device reported in the paper.

Significant association between minor sac axis and major sac axis and risk of reintervention in univariate analysis HR 1.36, 95% CI: 1.15, 1.62, p <0.001 for minor axis: HR 1.37, 95% CI: 1.16, 1.62, p <0.001 for major axis.

Significant association between minor aneurysm axis and risk of reintervention in multivariate analysis
HR 1.35, 95% CI: 1.13, 1.60 p<0.001.

Significant association between procedure date and aortic stent and risk of reintervention in univariate analysis
HR 1.55, 95% CI: 1.24, 1.94, p <0.001 for date
HR 2.93, 95% CI: 1.35, 6.36, p = 0.007 for aortic stent.

Significant association between procedure date and risk of reintervention in multivariate analysis: HR 1.53, 95% CI: 1.22, 1.92 p <0.001.

No significant association between renal stent, hypogastric embolization or iliac conduit and risk of reintervention in univariate analysis
HR 0.95, 95% CI: 0.38, 2.33, p = 0.90 for renal stent
HR 1.24, 95% CI: 0.66, 2.34, p = 0.50 for hypogastric embolization
HR 1.03, 95% CI: 0.32, 3.25, p = 0.96 for iliac conduit.

Endoleak

No risk factors investigated
Correction of endoleaks included under reinterventions.

Study sample adequately described Yes
Included risk variables clearly defined No
Covariates considered to build the multivariate model Not reported
Interactions between variables explored Unclear
Continuous variables handled appropriately Yes
Age kept as years.
More than 10 events per included variable Yes
128 procedures. Unclear how many variables were included in the final model but answer is probably yes.
Confidence intervals or other measures of uncertainty presented Yes

**Author**

Timaran 2007

**Country where study was performed**

USA

**Type of study**

Specific risk factors following EVAR

Evaluation/validation of existing risk assessment algorithm

**Registry**

The data were from the Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project. This is the largest all-payer inpatient database in the USA. It represents a 20% stratified sample of inpatient admissions to US academic, community and acute care hospitals nationwide (approximately 1000 hospitals in 35 states).

**Number of patients**

65502

**Age of population**

Not reported

4.6% aged 50-59 years; 24.7% aged 80 or over

**Gender**

82.9% male

**Aneurysm diameter**

Not reported

**Type of device (EVAR)**

Not reported

**Graft type (EVAR)**

Not reported

**Anaesthesia**

Not reported

**Risk factor(s) used in model and definitions**

Age categorised as:

- 50-59
- 60-69
- 70-79
- >=80yrs

Gender: Female sex

Composite risk score: The Charlson comorbidity index (CCI) score is a validated measure for use with administrative data that correlates with in hospital morbidity and mortality after surgical procedures (including elective AAA repairs). Each of the indicated diagnoses is assigned a weight and summed to provide a patient’s total score (0 (low risk) to >3 (high risk)).

Emergent or urgent EVAR

Admission during weekend

**Definition of outcomes**

30 day mortality: defined as in hospital mortality (i.e. in hospital for EVAR)

**Follow-up period**

Unclear - in hospital period only

**Methods of analysis**

In-hospital mortality was adjusted for age, sex CCI or risk stratification using multivariate logistic regression analysis. Results expressed as OR with 95% CI.

**30 day mortality**

Age

From multivariate regression model: OR 1.04 (95% CI 1.03, 1.04) \( p < 0.001 \)

Gender: Female sex

From multivariate regression model: OR 1.46 (95% CI 1.26, 1.68) \( p < 0.001 \)

Composite risk score

Charlson comorbidity index (CCI) score (0 to >3)

From multivariate regression model

OR 1.12 (95% CI 1.06, 1.20) \( p < 0.001 \)

A higher CCI score was associated with early death:

- CCI 0 - 1.8%
- CCI 1 - 2.0%
- CCI 2 - 2.2%
- CCI >= 3 3.7%

\( p < 0.001 \)

Stratified analysis that included only elective EVAR found the per point CCI score to be an independent predictor of in hospital mortality (OR 1.38, 95% CI 1.29, 1.47)

Emergent or urgent EVAR

From multivariate regression model

OR 8.25 (95% CI 7.21, 9.44) \( p < 0.001 \)

Admission during weekend

From multivariate regression model

0.719 OR 2.05(95% CI 1.70, 2.47) \( p < 0.001 \)

Aneurysm related mortality at No risk factors investigated

Final Report 1st April 2008
follow-up
All cause mortality at follow-up
Reintervention
Endoleak
Study sample adequately described
Included risk variables clearly defined
Covariates considered to build the multivariate model
Interactions between variables explored
Continuous variables handled appropriately
More than 10 events per included variable
Confidence intervals or other measures of uncertainty presented


<table>
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<tr>
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<td>Country where study was performed</td>
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<tr>
<td>Type of study</td>
<td>Specific risk factors following EVAR</td>
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<tr>
<td>Registry</td>
<td>Dates enrolled and/or treated: May 1994 to June 2002 EUROSTAR</td>
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<tr>
<td>Number of patients</td>
<td>3992 (1224 withdrawn devices versus 2768 current devices)</td>
</tr>
<tr>
<td>Age of population</td>
<td>Mean (SD) 72 (SD 7.9) years for current devices, 70 (SD 7.7) years for withdrawn devices (p &lt; 0.0001)</td>
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<tr>
<td>Gender</td>
<td>Percentage male (total population) 93% (94% current devices, 91% withdrawn devices, p = 0.0002)</td>
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<tr>
<td>Aneurysm diameter</td>
<td>Mean: Current devices 5.7(SD 10.8) and withdrawn devices 5.6(SD 10.5) cm. 206 (7.4%) patients with current devices had aneurysm neck diameters in excess of 2.6 cm and would not have been suitable to receive a withdrawn device.</td>
</tr>
<tr>
<td>Type of device (EVAR)</td>
<td>Zenith: 780 current, 0 withdrawn (10/96 to date) Talent: 739 current, 0 withdrawn (10/96 to date) Excluder; 337 current, 0 withdrawn (1/98 to date) AneuRx 857 current, 0 withdrawn (12/96 to date) EVT 55 current, 51 withdrawn (6/98 to date, 1/95 to 5/98) Stentor 0 current, 277 withdrawn (5/94 to 9/98) Vanguard 0 current, 896 withdrawn (3/96 to date)</td>
</tr>
<tr>
<td>Graft type (EVAR)</td>
<td>Bi-iliac: 3992 (100%)</td>
</tr>
<tr>
<td>Anaesthesia</td>
<td>Not reported</td>
</tr>
<tr>
<td>Risk factor(s) used in model and definitions</td>
<td>Age (Not defined) Male sex Graft configuration and device type: Current versus withdrawn devices Fitness for open procedure: Unfitness for open procedure Diameter and Sac Diameter Neck diameter Aortic neck length Team experience (&gt; 60 cases)</td>
</tr>
<tr>
<td>Definition of outcomes</td>
<td>Aneurysm related mortality defined as late aneurysm related mortality i.e. death due to aneurysm rupture or within 30 days of a secondary intervention. Reintervention: conversion to open repair</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>Follow up time points were 1, 3, 6, 12 and 18 months after surgery and yearly thereafter. Follow up results to 3 years presented.</td>
</tr>
<tr>
<td>Methods of analysis</td>
<td>Independent variables for multivariate analysis were chosen on the basis of significant differences between the two groups at univariate testing (p &lt; 0.001).</td>
</tr>
</tbody>
</table>
Variables included in this analysis were type of device (current or withdrawn), age, male sex, unfitness for OR, team experience, aneurysm diameter, neck length, and neck diameter. Further multivariate analysis included isolated late type II endoleak and related secondary transfemoral interventions as covariates to confirm the role of device type on aneurysm related death. Cox regression with stepwise backward elimination of unrelated factors was used for multivariate analyses.

**30 day mortality**

No risk factors investigated

**Aneurysm related mortality at follow-up**

Older age was associated with aneurysm related death (HR = 1.09, 95% CI: 1.06, 1.12, p < 0.0001). Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that older age was associated with aneurysm related death (HR = 1.09, 95% CI: 1.06, 1.2, p < 0.0001 for 1 year increase above mean).

Male sex was not significantly associated with aneurysm related death.

Current endografts resulted in a significant reduction in aneurysm related death (HR = 0.51; 95% CI: 0.34, 0.75, p = 0.0006). Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that current devices had a protective effect on aneurysm related death (HR = 0.52, 95% CI: 0.35, 0.79, p = 0.001).

Unfitness for open surgery was predictive of aneurysm related death (HR = 2.08, 95% CI: 1.4, 3.1, p = 0.0004). Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that unfitness for open surgery was associated with aneurysm related death (HR = 2.25, 95% CI: 1.5, 3.3, p < 0.0001).

Larger aneurysm diameter was associated with aneurysm related death (HR = 1.03, 95% CI: 1.01, 1.04, p = 0.0004). Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that aneurysm diameter was associated with aneurysm related death (HR = 1.03, 95% CI: 1.01, 1.04, p = 0.0005 for 1mm increase above mean).

Mid neck diameter was not significantly associated with aneurysm related death.

Neck length was not significantly associated with aneurysm related death.

Team experience (> 60 cases) was not significantly associated with aneurysm related death.

**All cause mortality at follow-up**

No risk factors investigated

**Reintervention**

Older age was not significantly associated with late conversion to OR.

Male sex was not significantly associated with late conversion to OR.

Use of current device was significantly associated with late conversion to OR: HR 0.49 (95% CI 0.28, 0.86) p=0.014.

Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that current devices had a protective effect on late conversion to OR (HR = 0.47, 95% CI: 0.27, 0.82, p = 0.008).

Unfitness for OR was not significantly associated with late conversion to OR.

Sac diameter (mm) was significantly associated with late conversion to OR: HR 1.03 (95% CI 1.01, 1.05) p=0.015.

Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that larger aneurysm size (1 mm increase above mean) was associated with late conversion to OR (HR = 1.03, 95% CI: 1.01, 1.05, p = 0.0015).

Mid-neck diameter was significantly associated with late conversion to OR HR 1.10 (95% CI 1.01, 1.20) p=0.027.

Further multivariate analysis with endoleak type II and associated interventions as covariates confirmed that neck diameter(1 mm increase above mean) was associated with late conversion to OR (HR = 1.20, 95% CI: 1.03, 1.22, p = 0.0085).

Neck length was significantly associated with late conversion to OR : HR 0.95 (95% CI 0.92, 0.98) p=0.0003.

Team experience was not significantly associated with late conversion to OR.

**Endoleak**

No risk factors investigated

**Study sample adequately described**

Yes
### Included risk variables clearly defined
Yes

### Covariates considered to build the multivariate model
Yes

### Interactions between variables explored
Unclear

### Continuous variables handled appropriately
Yes

### More than 10 events per included variable
Yes

### Confidence intervals or other measures of uncertainty presented
Yes

---


**Author** Van Marrewijk 2004

**Country where study was performed** 114 European Institutions

**Type of study** Specific risk factors following EVAR

**Registry** Dates enrolled and/or treated: 1996 - June 2002

EUROSTAR.

Of the overall cohort of 4613 patients, 1018 were excluded from this study because of retrospective enrolment, stent graft models other than AneuRx, Excluder, Talent, Vanguard or Zenith, or the presence of type I, III or any combination of endoleaks during follow-up.

**Number of patients** 3595

**Age of population** Mean: 71.2 (SD not reported) (SD not reported)

Range: 37 - 100

**Gender**

94% male

**Aneurysm diameter**

Mean: 5.7 cm (SD not reported)

**Type of device (EVAR)**

Zenith: 879 (24.5%)

Talent: 775 (21.6%)

Excluder: 349 (9.7%)

AneuRx n=833 (23.2%)

Vanguard n=759 (21.1%)

**Graft type (EVAR)**

Not reported

**Anaesthesia**

Not reported

**Risk factor(s) used in model and definitions**

*Only risk factors that were found to be significantly associated with Type II endoleak were reported.*

- Age (Definition not stated)
- Gender (Definition not stated)
- Current smoking
- Device type
- ASA

- Pre-existing conditions
- Obesity (not defined)
- Fitness for open procedure
- Renal function (creatinine) (Definition not stated)
- Aneurysm size (Definition not stated)
- Aortic neck and aneurysm angle (Definition not stated)
- Aortic neck length (Definition not stated)

- Preoperative patency of IMA
- Ankle-Arm Blood pressure index greater or equal to 0.87
- Experience of surgeons

**Definition of outcomes**

Endoleak Type II only

**Follow-up period** 15 months (range 0-72)

**Methods of analysis**

Clinical features of patients with type II endoleak were compared with patients without endoleak (age, gender, smoking status, obesity, fitness for open repair, ASA
grade, experience of surgeon, type of device, aneurysm morphology. Discrete data were analysed using Chi-square test and Fisher correction in case of small subgroups. A multivariate analysis was performed by selecting variables found to be significantly associated with events in the univariate analysis. Continuous variables were compared using the Mann-Whitney U-test. A Cox proportional hazards model was used for multivariate analysis of time-dependent variables.

30 day mortality No risk factors investigated
Aneurysm related mortality at follow-up No risk factors investigated
All cause mortality at follow-up No risk factors investigated
Reintervention No risk factors investigated
Endoleak Association with patients age: p=0.001 (CI 1.01-1.06)
Gender: No significant association
Smoking status: Current smoking association p=0.008 (CI 0.38 - 0.87)
Graft configuration and device type: Device type: no significant association
ASA: No significant association
Obesity: no significant association
Renal insufficiency: No significant association
Aneurysm size: No significant association
Infrarenal neck diameter: No significant association
Length of infrarenal neck association p=0.006 (CI 1.01-1.03)
Preoperative patency of IMA association with p=0.031 (CI 1.03-1.99)
Ankle-arm BP index <=0.87 association with p=0.0007 (CI 0.23-0.68)
Experience of surgeon: no significant association


Author van Eps 2006
Country where study was performed 165 European centres
Type of study Specific risk factors following EVAR
Registry Dates enrolled and/or treated: December 1996 to January 2005 EUROSTAR
Number of patients 5167 patients (4198 (81.2%) had normal renal function, 969 (18.8%) had renal dysfunction)
Age of population Overall mean 72 years
Patients with normal renal function: 71.7(7.6) years
Patients with renal dysfunction: 73.6(7.5) (p <0.001)
Range: Patients with normal renal function 43 to 95 years
Patients with renal dysfunction 45 to 100 years
Gender Overall 4870 (94.3%) male
Patients with normal renal function: 3936 (93.8%)
Patients with renal dysfunction: 934 (96.4%) (p<0.001)
Aneurysm diameter
Mean (SD):
Patients with normal renal function: 5.81(1.08) cm
Patients with renal dysfunction: 5.96(1.17) cm (p < 0.001)
Range:
Patients with normal renal function 4 to 17.2 cm
Patients with renal dysfunction 4 to 14.5 cm

Type of device (EVAR)
Not reported

Graft type (EVAR)
Not reported

Anaesthesia
Not reported

Risk factor(s) used in model and definitions
Age (Not defined)
American Society of Anaesthesiologists Anaesthetic (ASA) risk classification score 
>=3.

According to Society of Vascular Surgery (SVS) stratification model:
Preoperative renal function
0 No known renal disease (serum creatinine <133 umol/ml (less than 1.5 mg/dl) and creatinine clearance >50 ml/min)
1 serum creatinine 133-265 umol/ml (1.5 - 3 mg/dl) and creatinine clearance 30-50 ml/min
2 serum creatinine 265-532 umol/ml (3.0 - 6.0 mg/dl) and creatinine clearance 15-30 ml/min
3 serum creatinine >532 umol/ml and creatinine clearance <15 ml/min or on dialysis or with transplant

Aneurysm size
Pulmonary impairment

Definition of outcomes
Not defined

Follow-up period
Not stated

Methods of analysis
Tests to analyse associations between complications and renal dysfunction were conducted. The model was adjusted for differences found in univariate analysis. Analyses were performed for renal dysfunction (SVS categories 1 to 3) versus no renal dysfunction then further analyses were conducted for less severe renal dysfunction (SVS category 1) versus no renal dysfunction.

ORs were calculated for time-independent outcome variables with multivariable logistic regression analysis.

30 day mortality
Age at operation (not specified) was an independent risk factor for early death (OR = 1.1, 95% CI: 1.0, 1.1) (p < 0.001).
ASA grade 3 or above was an independent risk factor for early death (OR = 2.7, 95% CI: 1.7, 4.2) (p < 0.001).
The 30 day mortality rate in patients with renal dysfunction was significantly higher than those with normal renal function (6.2% versus 2.0%, p < 0.001). An increase of 5.5% was also seen in those with milder forms of renal dysfunction (SVS category 1)

In multivariate analysis preoperative renal dysfunction was an independent risk factor for operative mortality (OR = 2.3, 95% CI: 1.6, 3.3) (p < 0.001).
Aneurysm size was an independent risk factor for early death (unsure of data).
Pulmonary impairment was an independent risk factor for early death (OR = 1.6, 95% CI: 1.1, 2.3, p = 0.012).

Aneurysm related mortality at follow-up
No risk factors investigated

All cause mortality at follow-up
No risk factors investigated

Reintervention
No risk factors investigated

Endoleak
There was no significant association between endoleak and renal dysfunction (16.2% normal renal function versus 15.6% impaired renal function)

Study sample adequately described
Yes

Included risk variables clearly defined
No

Covariates considered to build the multivariate model
Yes

Interactions between variables explored
Unclear

Continuous variables handled appropriately
Unclear

More than 10 events per included variable
No
Endovascular Stents For Abdominal Aortic Aneurysms: A Systematic Review And Economic Model

Confidence intervals or other measures of uncertainty presented Yes


Author Zarins 2006

Country where study was performed USA

Type of study Specific risk factors following EVAR

Aneurysm diameter

Trial Trial Dates: 1998 - 1999
Non-RCT
Prospective multicentre trial of the AneuRx stent graft

Number of patients 923

Age of population

Small AAA (<5.0 cm) mean 71.3 (SD 7.1) years
Medium AAA (5.0 - 5.9 cm) mean 73.4 (SD 7.6) years
Large AAA (>=6.0 cm) mean 74.6 (SD 8.6) years

Gender Percentage male (total population)
Small AAA (<5.0 cm) 90%
Medium AAA (5.0 - 5.9 cm) 88%
Large AAA (>=6.0 cm) 88%

Aneurysm diameter

Mean 5.7 (SD 1.5) cm
Measurement tool used
Maximum transverse aneurysm diameter as measured on the pre-procedure CT scan

Type of device (EVAR)
AneuRx 923 patients (100%)

Graft type (EVAR)
Bi-iliac: 923 patients (100%)

Anaesthesia Not reported

Risk factor(s) used in model and definitions

Age
ASA
Pre-existing conditions: Peripheral vascular disease COPD
Aneurysm size categorised as Small AAA (< 5.0 cm) Medium AAA (5.0 - 5.9 cm) Large AAA (>=6.0 cm)

Definition of outcomes
All cause mortality: survival at 5 years
Aneurysm related death - perioperative and late
Surgical conversion (elective and emergent)

Follow-up period 5 years

Methods of analysis
The outcomes of interest were expressed as Kaplan-Meier estimates with standard errors. Differences between the three categories of aneurysm size (small, medium, large) were determined using the ordered log-rank test. The null hypothesis that the results for all three groups are equal was tested against the ordered alternative hypothesis.

To consider the effect of influential baseline covariates that were out of balance between the three groups, multivariate Cox proportional hazard models were created for outcomes found to be statistically significantly different across the three groups (age, ASA grade, family AAA history, obesity, previous procedures, COPD and PVD).

30 day mortality No risk factors investigated

Aneurysm related mortality at follow-up
PVD: effect on AAA related death at 5 years HR 2.18, p=0.05
Effect of aneurysm size on AAA related death at 5 years HR 2.01, p=0.03

All cause mortality at follow-up
Effect of age on 5 year survival HR 1.05 p<0.0001
Effect of ASA on 5 year survival HR 1.48 p=0.0003
COPD effect on 5 year survival HR 1.84 p<0.0001
PAD effect on 5 year survival 1.50 p=0.002
Effect of aneurysm size on survival at 5 years HR 1.35 p=0.001

Reintervention
Effect of aneurysm size on surgical conversion at 5 years follow-up was HR 1.83, p=0.007
Family history of AAA: effect on surgical conversion at 5 years HR 2.32, p=0.02
| **Endoleak** | No risk factors investigated |
| **Study sample adequately described** | Yes |
| **Included risk variables clearly defined** | Yes |
| **Covariates considered to build the multivariate model** | Yes |
| **Interactions between variables explored** | Unclear |
| **Continuous variables handled appropriately** | No |
| **More than 10 events per included variable** | Yes |
| **Confidence intervals or other measures of uncertainty presented** | No |

Aneurysm size defined but others less clear

See table II

Hazard ratios and/or p values only
### 10.5 Table of excluded studies with rationale

#### Patient group not AAA (19)

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#### RCT but not EVAR vs. open repair or non-surgical management (8)

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<td>Laohapensang 2005</td>
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#### Registry but not EUROSTAR, RETA or NVD (3)

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#### Risk model but not modelling risk following EVAR (26)

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<td>Berry 2001</td>
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Hadjianastassiou 2007
Heller 2000
Hertzer 2005
Hua 2005
Huber 2001
Katz 1997
Koning 2006
Korhonen 2004
Le Manach 2005

Leon Jr 2005
McPhee 2007
Menard 2003
Noel 2001
Ouriel 2005
United Kingdom Small Aneurysm Trial 2002
Wald 2006

Risk model but not modelling relevant outcome (2)
Ouriel 2003
Zarins 2003

Risk model but fewer than 500 patients (94)
Acosta 2007
Alonso-Perez 2001
Alric 2003
Antonello 2007
Aune 2001
Aziz 2003
Azizzadeh 2006
Becker 2001
Biancari 2003
Biebl 2005
Bown 2004
Bui 2003
Bush 1995
Calderwood 2004
Cao 2002
Carpenter 2002
Chaikof 2002
Chang 2003
Chiesa 2006
Cochennec 2007
Conners 2002
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Wolf 2002313
Yii 2003314
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