A Markov decision analysis model to aid the vascular surgeon in the management of a patient with an asymptomatic infra-renal abdominal aortic aneurysm

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Abstract

Introduction

Despite increasing evidence regarding the safety and efficacy of endovascular (EVAR) and open abdominal aortic aneurysm repair, it is often unclear which technique is most appropriate for an individual patient. We have designed a decision analysis model that will predict survival, reintervention rates and other parameters for individual patients.

Methods

A Markov decision analysis model was developed in Microsoft Excel to simulate five management options; EVAR, open repair, best medical therapy or delayed EVAR or open repair at a threshold aneurysm diameter. Probabilities for the model were determined from systematic literature review. The user can assess the impact of adjusting patient-specific risk-factors including aneurysm size, threshold diameter for intervention, operative mortality, hazard ratios for general mortality, reintervention rate and aneurysm rupture rate.

Results

Patient and aneurysm specific variables are entered through a user-friendly data-input sheet and the model generates graphical and descriptive results regarding estimated survival and reintervention rates for the different management options. Individualised survival curves, both aneurysm-related and general mortality curves, cumulative reintervention rates and other key parameters are generated for each management option. The model has been validated against average data published from recent RCTs and examples have been generated based on real and hypothetical patient characteristics.

Conclusions

An easy-to-use computer model has been developed that will provide meaningful information relating to risks and benefits that could assist in shared decision making and obtaining informed consent from patients with aneurysms, and could help to guide policy decisions in respect to patient selection for EVAR.

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OBJECTIVE

Conventional management of abdominal aortic aneurysm is by open repair, and is associated with a mortality rate of 2-6%. Endovascular aneurysm repair (EVAR) is an alternative technique first introduced in 1991. There is a growing body of evidence regarding the safety and efficacy of both techniques, particularly since the publication of several randomised controlled trials (RCT). Despite this however, it is often unclear which technique is most appropriate for an individual patient. In addition it can be very difficult to decide when, if at all, it is most appropriate time to intervene. Consequently a decision analysis model has been developed that will provide survival and reintervention outcome data for an individual patient managed by five different options; open repair, EVAR, best medical therapy and best medical therapy combined with delayed intervention (EVAR or open repair) at a certain level of aneurysm diameter. In addition, a systematic review was performed to determine the required probabilities for the model.

INTRODUCTION

Definition and epidemiology

An abdominal aortic aneurysm (AAA) is defined as an abnormal dilatation of the artery that is 1.5 times the diameter of the normal segment. A diameter of greater than 3 cm is generally regarded as aneurysmal in the abdominal aorta. Most aneurysms are caused by degenerative disease affecting the vessel and this process is most common in the infrarenal segment of the abdominal aorta, accounting for 90-95% of AAAs. Approximately 75% of aneurysms are asymptomatic and are found incidentally during clinical examination or radiographic investigations. Therefore the exact prevalence is unknown but various screening studies have estimated it to be between 1.7%-6% in the older male population.[1-3] The incidence of AAAs is known to increase with age: the incidence rate for males over 50 years is approximately 25/100,000 increasing to 78/100,000 in those over 70 years.[4] AAAs are more common in men than women with a male: female ratio of 3.5-6: 1.[4] Furthermore a number of studies have suggested that the incidence of AAA is actually increasing.[5]

Pathology

Aneurysmal disease is associated with degeneration of the vessel wall with loss of intima and a reduction in the elastin and collagen content of the media. The exact cause of these changes is largely unknown; however the risk factors for atherosclerotic disease (smoking, hypertension, hyperlipidaemia and diabetes mellitus) are thought to be largely responsible.

The natural history of AAA is one of progressive structural deterioration, gradual expansion and eventual rupture. An ectatic abdominal aorta is defined as one that is diffusely and irregularly dilated with a diameter less than 3 cm. One study demonstrated that the median growth rate was 0.65 mm/year with 19% becoming aneurysmal within a 2-year follow-up period.[6] Another study demonstrated expansion rates of 0.09 cm/year for aneurysms 2.6-2.9 cm, 0.16 cm/year for aneurysms 3.0-3.4 cm, and 0.32 cm/year for aneurysms 3.5-3.9cm.[7] Other studies have shown expansion rates of 0.2-0.4 cm/year for aneurysms <4 am diameter, 02-0.5 cm/year for aneurysms 4-5 cm and 0.3-0.7 cm/year for those larger than 5 cm.[8] The UK Small Aneurysm Trial demonstrated that ultrasound surveillance is a safe management option for patients with small abdominal aortic aneurysms (4.0 – 5.5 cm diameter) with an

annual rupture rate of 1%.[9] After 3 years of surveillance, it has been shown that the annual rate of aneurysm rupture is 2.2%.[10,11] 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 %.[136]

Current management strategy

Intervention for AAA is designed to prevent rupture, which is associated with an overall mortality rate of approximately 80%, with only half of those undergoing emergency operation surviving. The UK Small Aneurysm Trial demonstrated that there was no long-term survival advantage from elective surgery on small aneurysms (<5.5 cm diameter).[9] This finding was also supported by the ADAM trial.[137] Therefore current guidelines recommend that a size of 5.5 cm diameter and larger, or >4.5 cm with an increase in size of >0.5 cm in the preceding 6 months before elective treatment is undertaken. Conventional management of AAA is by open repair and when performed electively is associated with a mortality rate of 2-6%. More recently an alternative, less invasive technique for repair of AAA has been developed. This is endovascular repair (EVAR).

The use of EVAR in the treatment of infrarenal abdominal aortic aneurysms was established in 1991 by Parodi et al.[1] Since then, both the technique and devices have been developed so that this procedure may be used in elective, symptomatic and ruptured cases. The technique was initially developed in Europe and subsequently the AneuRx, Ancure and Guidant stent-graft devices were approved by the Food and Drug Administration (FDA) in September 1999.

Early trials have demonstrated lower mortality and early morbidity rates and consequently EVAR has been used with increasing frequency.[3-5] This is particularly true in the case of elderly and high-risk patients for whom traditional open repair carries significant risks. In order to repair an aneurysm by endovascular methods, certain anatomical and morphological criteria must be met. However there are no fixed criteria and they differ between different centres and for different stent-grafts. Typical criteria include: proximal neck length >10mm length, <26mm diameter and <60 degrees angulation; iliac artery diameter <16mm and >7mm. Significant iliac artery tortuosity or calcification, or circumferential thrombus at the proximal neck are usually considered to be contraindications.

Intervention techniques

Open repair of AAA is performed in an operating theatre under general anaesthesia. Access to the abdominal aorta is via a transperitoneal approach through a midline incision. Following retroperitoneal dissection of the aorta, a cross-clamp is placed across the proximal aneurysm neck and across each iliac arteries. An arteriotomy is then made and an interposition Dacron graft (either tube or bifurcated configuration) is sutured into place. The wound is then closed according to standard surgical techniques.

Endovascular aneurysm repair involves positioning of an endograft within the abdominal aorta by a transfemoral or transiliac route with the aim of exclusion of the aneurysm from within the circulation. The procedure is carried out in an operating room or endovascular suite under general or regional anaesthesia. Access to the femoral arteries is achieved by surgical cut-down and the prosthesis is inserted via a preloaded delivery catheter system. One lumen of the catheter is used for guide wire access and flushing, whilst the other lumen contains the deployment line. The delivery system usually has a tapered balloon creating an atraumatic tip during insertion. Radio-opaque markers on the catheter and stent graft allow the endoprosthesis to be manoeuvred into position under fluoroscopic guidance. The stent-graft of appropriate size and configuration is selected on the basis of diagnostic imaging. The stent graft is usually oversized by 10-20% to decrease the incidence of type I endoleak. Following successful insertion of the stent-graft a completion angiogram is performed to document exclusion of the aneurysm from the circulation. The femoral arteriotomies are closed according to standard surgical techniques. Following open repair or EVAR patient is transferred to an appropriate after-care setting for observation.

Prior to undertaking endovascular aneurysm repair, the patient must undergo preoperative contrast-enhanced computed tomographic (CT) scanning to accurately determine aneurysm morphology. A full clinical assessment must also be carried out to identify any risk factors for open and endovascular repair. These two processes are required to ensure that the patient fulfils the clinical and anatomical inclusion criteria for endovascular aneurysm repair.

The lower physiological stress of the minimally invasive endovascular approach is associated with lower morbidity and mortality rates, and consequently is a therapeutic option for high risk patients for whom conventional open repair would not be appropriate. Endovascular

aneurysm repair has been performed not only as an elective procedure, but also on symptomatic and ruptured aneurysms. However, only the technique of elective aneurysm repair has been considered in this review.

Current practice in the UK

There are currently around 40 centres in the UK undertaking EVAR for abdominal aortic aneurysms (AAA). The majority of these centres have been involved in the EVAR 1 trial (randomised controlled trial comparing EVAR to open repair). Before being considered for participation in the trial, a new centre had to submit outcome data on 20 cases.

Commercially-available endovascular stent-grafts are of one of three designs: aortic tube graft, aortic uniiliac graft or aortic biiliac (bifurcated) graft. The stent-graft typically comprises a self-expanding nickel-titanium (nitinol) stent attached to a woven polyester fabric graft. The tube graft is composed of a single structure, whilst the bifurcated grafts are modular and comprise multiple segments. Tube grafts are no longer used in this country. The bifurcated graft consists of a proximal tube, a flow divider, a full-length ipsilateral iliac limb and a short contralateral stump for attachment of the second iliac limb. The stent-grafts are attached to the native aortic wall by a number of metallic wires, hooks and anchors. Additional modular components include aortic and iliac extender cuffs and are used for the treatment of type I endoleaks. The main stent-grafts used in this country are made by Cook (Zenith bifurcated graft, a custom made graft and an aortouniliac device), Medtronic (Talent endograft) and Gore (Excluder).

Potential complications of aneurysm repair

Traditional open surgical repair of abdominal aortic aneurysms is associated with significant morbidity and mortality risks, particularly as there are significant levels of co-morbidity in the relevant population. Common complications of open aneurysm repair include haemorrhage, local wound infections, chest infections, the need for post-operative ventilation and clinical cardiac events. Other less common complications include renal impairment (transient and permanent), lower limb ischaemia and trash foot, colonic ischaemia, graft infection and delayed rupture. In assessing the efficacy and safety of alternative therapeutic

options, i.e. EVAR, it is important to consider all the above outcome measures. However, endovascular repair is also associated with certain other complications such as endoleak, stent migration and stent wire fracture from metal fatigue.

Endoleaks are a well recognised complication following aneurysm repair that is specific to endovascular repair. The classification of endoleaks used in this thesis is that developed by White et al, 1998.[12]

Type Ia - Perigraft leak from poor proximal attachment or seal
Type 1b - Perigraft leak from poor distal attachment or seal
Type II - Collateral backflow / retrograde endoleak
Type III - Mid-graft fabric tear / modular disconnection or poor seal
Type IV - Porosity – graft-wall fabric porosity or suture holes

Decision analysis modelling and randomised controlled trials

Level one evidence, (randomised controlled trial (RCT) data) is widely quoted as the gold standard for research in medicine and there have been a number of such trials that have reported medium-term results on the use of EVAR in the management of abdominal aortic aneurysms. The EVAR 1, DREAM and OVER trials compared the endovascular approach against open repair in aneurysm patients considered medically 'fit' for an open procedure. The EVAR 2 trial compared EVAR to best medical therapy in a group of aneurysm patients deemed 'unfit' for surgical repair. In addition, there are other RCTs that are currently being carried out to assess the role of EVAR in the management of abdominal aortic aneurysms. These trials include the ACE trial in France.

However there are a number of issues regarding the role of RCTs in evaluating the safety and efficacy of new developments such as EVAR. EVAR is a new technique that was only developed in 1991. Consequently such a technique is not stable, but is continually evolving. This has a number of inevitable consequences; firstly operators will have a limited amount of experience, and there is obviously a learning curve associated with any new technique. Secondly the stent-graft device itself has undergone substantial development and the first generation stents which were of a tube-configuration have all been withdrawn from current usage. In addition a significant number of second and third-generation commercially

developed devices have been withdrawn and the devices in use today are undergoing continual modification in response to clinical demand. Therefore a number of participants in the RCTs will have had their aneurysm repaired by devices which are now withdrawn, or modified; a fact that requires consideration when interpreting the results.

Another issue with RCTs is the underlying heterogeneity of the study population. The inclusion and exclusion criteria must be sufficiently relaxed to allow for sufficient recruitment to the trial, whilst at the same time be sufficiently rigorous to minimise heterogeneity. Creation of a homogenous study population generates more robust results which enables their application to more specific cases and sub-groups. Further disadvantage of RCTs are the time and cost factors associated with such a research technique.

Modelling techniques have a number of advantages and disadvantages over RCTs. It is possible assess the outcome of adjusting various parameters within the model, something that is not possible from randomised trials without conducting a new one, with its associated time and expense. Modelling is therefore particularly beneficial for evolving techniques such as EVAR, as the impact of ongoing developments can be assessed more easily. However models are limited by the availability of high quality data that is necessary to generate the required transition probabilities.

The management of a patient with an AAA is a time dependent process, and requires modelling using Markov techniques. A Markov model contains a finite number of states in which a person may be found at any time. Markov processes occur within a discrete length of time. Progression through time occurs in cycles, the length of which is fixed and defined by the creator of the model. During each cycle, a patient makes transitions from one state to another, until either the preset number of cycles has been completed or they reach the state death. Death is an absorbing state which means that once a patient enters this state, they cannot leave.[143]

Despite recent publications of large RCT concerning the use of EVAR, it can be difficult to translate these results to accurately reflect risks and benefits on an individual basis. Decision analysis is a technique used to aid decision-making under conditions of uncertainty by systematically representing and examining all of the relevant information for a decision and the uncertainty around that information. Evidence based medicine is more than just the

application of trial evidence to an individual; it is influenced the fact not every individual will have the same absolute treatment response as a clinical trial and also by the fact that individuals differ in their choices. Each individual will trade off different outcomes against potential adverse consequences (utilities) in making a particular decision.[144]

Therefore the Markov model created has predefined health states in which a patient with an aneurysm can exist and the transition probabilities used do determine movement between the health states are determined from a systematic review of the literature. In addition the user of the model can input patient specific variables so that the model will provide meaningful, individualised information relating to risks and benefits that could assist in shared decision-making and obtaining informed consent from patients with aneurysms, and could help to guide policy decisions in respect to patient selection for EVAR.

METHODS

Creation of the model involved several key areas. These included development of a conceptual model to reflect the clinical management of a patient with an aneurysm, identification of input parameters and transition probabilities, and validation of the model by recent RCT outcome data.

Development of the model

The clinical states, transition probabilities, management options and outcome measures were established from a combination of a systematic literature review and expert opinion from clinicians involved in the care of patients with abdominal aortic aneurysms. The Markov model was developed as a spreadsheet in Microsoft Excel. The model was developed in Microsoft Excel rather than other modelling specific software such as Datapro by TreeAge for several reasons. Firstly once developed it was envisaged that the model would be readily accessible in clinical practice and Microsoft Excel software is available in most NHS Trusts, unlike the TreeAge software. Secondly it was considered that significantly more people would be familiar with Excel than TreeAge and consequently the model would be easier to use in Microsoft Excel.

A user-friendly data input sheet was created to allow the vascular surgeon to enter patient-specific variables so that the results created from the model would be applicable to that particular patient.

The following variables were listed on the data input sheet:

- Patient age
- Operative mortality rate – It was clear from the systematic literature review that there was wide variation in 30-day mortality rate for both open repair and EVAR. In addition there are a variety of scoring methods available to assess the 30-day mortality rate from open aneurysm repair. Consequently the data input sheet contained a pick-list from which the expected 30-day mortality for open repair could be chosen. The pick list contained six different expected mortality rates; these were from a meta-analysis of EVAR 1 trial type patient studies, EVAR 2 trial, an expected value based upon a calculation from a Bayesian risk model[145], an expected value based upon a calculation from the P-POSSUM

risk model[146], the Glasgow aneurysm score[147] and an option to enter the operative mortality rate from the user's own clinical practice. The P-POSSUM risk model was chosen as this had been demonstrated to be as accurate in risk prediction as the V-POSSUM model and the author assumed a greater familiarity amongst model users with the P-POSSUM equation.[148] The data input sheet is therefore divided into three sections. At the top of the data input sheet there are tables containing pick-lists for all the variables required to calculate the expected mortality rate from the three risk models, (Bayesian, Glasgow aneurysm score and P POSSUM). The user of the model can enter data into any or all of the risk prediction tables at the top of the data input sheet. The table in the middle of the data input sheet then displays the mortality rates for the six options so that the model user can compare the expected mortality rates. The table at the bottom of the data input sheet then contains a pick-list of the six thirty-day open surgical mortality rates and it is this value that is then used in the model to calculate the patient's results. The results from the literature review provided a hazard ratio for 30-day mortality rate for EVAR compared to open repair. The 30-day mortality rate for EVAR was then calculated based upon the hazard ratio of the operative mortality rate selected by the model user. For the delayed EVAR and delayed open repair pathways, the patient would have increased in age by the time the procedure was carried out. Consequently the operative mortality rate at the point at which the delayed intervention is carried out is adjusted by an interpolated hazard ratio obtained from the UK Small Aneurysm Trial.

- Hazard ratio for general mortality – The model was programmed to cross-reference the patient's age during that particular cycle against the expected general mortality rate for a person of that age. The general mortality rates referred to in the model are adjusted to reflect the individual patient's co-morbidities. The hazard ratio is generated by the model and is determined by the expected 30-day mortality rate for any particular patient.
- Aneurysm size – The patient's aneurysm size is inputted into the data entry sheet, and this value is then entered into the model. The aneurysm size increases during each cycle according to a table of expansion rates obtained from the literature review. The aneurysm rupture rate is calculated during each cycle by cross-referencing the size at that stage against the probability of rupture for that given size.
- Threshold for aneurysm repair – Two of the five management pathways envisaged during development of the conceptual model involved delaying treatment of the aneurysm until a larger diameter had been reached, at which the probability of death from the procedure

would approach the probability of rupture in a patient with multiple co-morbidities. Therefore the threshold diameter at which the vascular surgeon considered treatment to be of benefit could be entered so that the impact of delaying intervention in that particular patient could be assessed.

- Hazard ratio for rupture rates - The option of manipulating the rupture rate for a given diameter of aneurysm was also included on the data-entry sheet. Although the probabilities of rupture were acquired from a systematic literature review, there was a wide variety of rupture rates that were reported. The model user could therefore alter the likelihood of rupture and assess its impact on the model.
- Discount rate for quality adjusted survival – One of the outcomes from the model is quality adjusted survival. A variable discount rate could be applied to this so that the model user could assess the impact of adjusting the discount rate.
- Anatomical suitability for EVAR – From the systematic review it was noted that there was a wide variety in anatomical requirements in order to undertake an endovascular procedure. It was considered that the anatomical suitability for EVAR would affect the operative mortality rate for EVAR, the primary conversion rate and probability of undergoing a secondary procedure subsequently. Therefore a pick-list of four options for anatomical suitability was created on the data-entry sheet. These options were; very unsuitable, unsuitable, suitable and highly suitable. If very unsuitable was selected then the value corresponding to two standard deviations above the mean for operative mortality rate for EVAR, primary conversion rate and reintervention rate would be returned into the model. Likewise unsuitable would return values one standard deviation above the mean, suitable would return the mean values and highly suitable would return values one standard deviation below the mean. Therefore by adjusting the anatomical suitability for EVAR, the model user would be able to assess the likely success of an endovascular procedure in that patient.

Systematic review

Having devised the conceptual model, a systematic review of the literature was performed to obtain the required transition probabilities.

Search strategy

The search aimed to identify all references relating to the safety and efficacy of using endovascular stents for the treatment of abdominal aortic aneurysms.

Sources searched

Thirteen electronic bibliographic databases were searched, covering biomedical, health-related, science, and social science literature:

- BIOSIS
- Cinahl
- Central Database
- Cochrane Database of Systematic Reviews (CDSR)
- Centre for Reviews and Dissemination (CRD) Databases
- Database of Abstracts of Reviews of Effects (DARE)
- Embase
- Health Technology Assessment (HTA) Database
- Medline
- Medline In Process
- NHS Economic Evaluations Database (NHS EED)
- Science Citation Index
- Social Sciences Citation Index

Search terms

A combination of free-text and thesaurus terms were used. 'Population' terms (for example, abdominal aortic aneurysm, AAA) were combined with 'intervention' terms (for example, EVAR, endovascular aneurysm repair, endovascular stent).

Search restrictions

The searches were restricted to English language articles and restricted to papers published from the year 2000 to November 2009.

Inclusion and exclusion criteria

Types of studies

Randomised controlled trials, controlled clinical trials, comparative observational studies, case series studies, and population-based registries assessing the efficacy and/or safety of EVAR were included. Systematic reviews and single case reports were excluded from the review. Case series comprising less than two hundred patients or contained no primary outcome data of interest were excluded. For studies with multiple publications, those with the greatest number of participants, the longest follow-up, or the latest publications with the most amount of outcome data were included.

Types of participants

Studies including adults with asymptomatic infrarenal abdominal aortic aneurysms undergoing elective intervention were eligible for inclusion. Patients with symptomatic or ruptured aneurysms were excluded from this review.

Types of interventions

Endovascular aneurysm repair of abdominal aortic aneurysms. Thoracic and thoraco-abdominal aortic aneurysms were excluded.

Types of outcome

Efficacy

Main clinical outcomes:

- Successful endograft deployment
- Primary technical success – defined as complete exclusion of the aneurysm from the circulation immediately following completion of the procedure
- Thirty day technical success – defined as complete aneurysm exclusion at thirty days
- Secondary technical success – defined as complete aneurysm exclusion following a secondary intervention
- Aneurysm rupture following successful EVAR
- Changes in size of aneurysm during follow-up

- Primary conversion rate (conversion to open procedure)
- Delayed conversion rate (conversion to open procedure)
- Secondary intervention rate

Other clinical outcomes

- Proportion of population for whom EVAR technically feasible
- Procedural blood loss
- Length of ITU stay
- Total length inpatient stay

Safety

The frequency and type of adverse events were tabulated to assess the safety of EVAR. Safety endpoints were considered in the following categories:

- Technical problems
    - Stent migrations
    - Stent fracture
    - Stent wire fracture
    - Graft limb thrombosis
    - Graft stenosis
    - Graft kinking
    - Endoleak – type I, II and III
    - Access artery injury
    - Contrast reaction
- Major morbidity
    - Thirty day mortality rate
    - Subsequent death from aneurysm and non-aneurysm related causes
    - Cardiac event
    - Renal impairment
    - Graft infection
    - Colonic ischaemia
    - Lower limb ischaemia
    - Minor morbidity
    - Wound infection

Quality assessment strategy

The methodological quality of all full-text reports was assessed by one reviewer using three separate quality assessment forms. The 17-question checklist used to assess the quality of the case series studies (Appendix 2) was adapted from the NHS Centre for Reviews and Dissemination's guidance for those carrying out or commissioning reviews (2001) and from Downs and Black. The 18-question checklist used to assess the quality of the non-randomised controlled trials and comparative observational trials (appendix 3) is also adapted from the NHS Centre for Reviews and Dissemination's guidance for those carrying out or commissioning reviews (2001) and from Downs and Black. The 11-question checklist used to assess randomised controlled trials is a modified version of the Delphi List, a criteria list developed using Delphi consensus methods by Verhagen and colleagues to assess the quality of randomised controlled trials (Appendix 4).

Data extraction strategy

A data extraction form was specifically developed in an Access database to record details of the design of included studies, characteristics of participants, technical aspects of EVAR, and outcome measures of interest. Data extraction was carried out by one reviewer and checked for accuracy by a second. Reviewers were not blinded to the names of study authors, institutions, or publications.

Data synthesis

For binary outcomes the pooled odds ratio and its 95% confidence interval were calculated using a fixed effects model in Review Manager Version 4.2.7. Where significant heterogeneity was indicated the results were recalculated using a random effects model. For continuous outcomes, a weighted mean difference and its 95% confidence interval were calculated, also in Review Manager Version 4.2.7. Where standard deviations were not reported by the authors they were estimated from the interquartile range (if available) using methods described in the Cochrane Reviewers Handbook (based on the width of the interquartile range being equivalent to approximately 1.35 times the standard deviation), in order to calculate a weighted mean difference (WMD). Such calculations make the assumption that the data follows a normal distribution. If this data was also not available, studies were not combined in the meta-analysis. For studies that did not include a comparison group, an overall mean and its 95% confidence interval was calculated.

Validation of the model

The first stage of validation of the model involved building various internal checking systems into it. These systems ensured that for all cycles within the model, no negative figures were generated and that the sum of all the states in which a person could exist totalled one. This was important to check that all patients were accounted for as they progressed through the model and that no patients were being lost or created. Face validity was used to test the results generated by the model against a variety of scenarios. Firstly the 5Y survival outcome results from the model were compared against expected survival for different patient cohorts. Secondly the data from the recent randomised control trials that have published short and medium-term results was used to validate the model. Average patient data from each of the RCTs was used to generate a hypothetical patient that was inputted into the model. The outcomes generated by the model for an average hypothetical patient from each trial were then compared against the published results from that trial. The model was designed to generate results for all the major outcome parameters reported by the trials and therefore the model was validated against all of these.

Thirdly the model contains an anatomical suitability for EVAR parameter, which in turn affects the operative mortality rate and primary conversion rate for EVAR. Consequently a highly anatomically unsuitable aneurysm for EVAR would be expected to generate results for the EVAR pathway that approximated those generated by the open repair pathway. Therefore scenarios in which the anatomical suitability for EVAR was adjusted were also used to validate the model. The methods of sensitivity analysis describe above are known as point-estimate or expected value analysis and are a form of deterministic sensitivity analysis. Other more complex methods of sensitivity analysis such as Monte Carlo simulation, also known as probabilistic sensitivity analysis were considered but not used for several reasons. During Monte Carlo simulation the model will run many times over assigning values that are randomly drawn from probability distributions to the different parameters and consequently the results produced quantify the total impact on uncertainty in the model. However the methods actually used to assess parameter uncertainty within the model did not generate significantly different results and as Monte Carlo simulation required specific programmes such as TreeAge, it was not considered necessary to use such analytical techniques.

The final stage in the validation of the model would involve the application of the model in clinical practice. The model could be used by a variety of vascular surgeons and patients to assess whether the graphical and tabulated results generated were of any benefit in the management process of an individual patient with regards to decision-making and informed consent.

Outcome results generated by the model

From the systematic literature review, five elective management strategies were identified for a patient with an abdominal aortic aneurysm. These were EVAR, open repair, best medical therapy (BMT), delayed open repair at a threshold aneurysm diameter and delayed EVAR at a threshold aneurysm diameter. For each of these management strategies, the model produces graphical and results regarding estimated survival and reintervention rates. Individualised survival curves, quality adjusted survival curves and discounted quality adjusted survival curves are generated for each management option. Health related quality of life data published from the EVAR 1 trial demonstrated no significant reduction in quality of life in the long-term for either open repair or EVAR. Therefore utility estimates were based upon published figures derived from the EuroQol tariff values for male's age 65-74 years in the Health Survey for England 1996. Expected survival at specific time points and estimated median survival are also generated as tabulated results for each option. In addition both aneurysm-related and general mortality curves, cumulative reintervention rate curves and cumulative rupture rate curves are generated for each therapeutic option.

Potential applications for the model

The model is designed to produce individualised results that can be used by a vascular surgeon and patient to make an evidence-based management decision for that particular patient. In particular, for high-risk patients there is likely to be an increase in median survival associated with delayed intervention. By adjusting the threshold aneurysm diameter at which intervention is carried out, the optimal time delay that is associated with either greatest overall survival or greatest median survival can be determined. For example the model could be used at a Multi-Disciplinary Team Meeting in which one could use the model to look at the predicted outcomes based upon patient's clinical and demographic characteristics to decide upon the most appropriate management strategy for an individual patient.

The model could be used to help put the patient in a position where they can weigh up their preferences for the different outcomes and risk distributions; however for this a number of factors need to be considered. There are different potential distributions of risk and individual patients may have differing strength of preference for early vs delayed risks. For example there is an early higher risk of open surgery, but there is a need for more instensive follow-up following endovascular repair with a potentially higher re-intervention rate. A patient may have a particular preference for early or late risk, but the model could be used to show the different risk profiles to help an individual patient make a balanced, informed decision.

In addition, the model may be used as a research tool to assess the likely outcome changes that may occur with a continually evolving relatively new technique such as EVAR.

RESULTS

Systematic review

Type and quantity of evidence available

From the literature search, one hundred and fifty-one papers were identified as being potentially relevant and full papers were obtained and assessed in detail for inclusion. From these, a total of 116 studies were identified for inclusion. There were 6 randomised controlled trials (8 reports), 36 non-randomised controlled trials, 17 comparative observational studies, 44 case series and 11 registry publications.

A summary of the included studies is shown in Table 1

The number of participants in the included studies ranged from 40 to 65506 (total n=146,883) and the mean age (where reported) ranged from 65 to 85 years. The number of patients receiving EVAR ranged from 20 to 65506 (total n=128,374).

Mean follow-up ranged from 1 to 62 months. Seventy two studies had a mean follow-up of 12 months or more, and 21 had a mean follow-up of at least 36 months. The mean follow-up period was not recorded in 33 of the papers.

Forty-one of the primary studies were set in North-America, two were set in Australia, and the rest were set in Europe (6 UK papers and 8 EUROSTAR database publications). In addition, 22 of the studies were multi-centre studies. The device manufacturer funded eight of the studies and one was funded by the US government. The remaining studies did not declare a source of funding.

There appeared to be overlap in the patient populations in the included studies. Some studies, for example, were single-centre reports of patients, some of whom had been included in larger, multi-centre studies. However, the numbers of patients included in the trials was not always clearly reported in these articles. Where possible these studies have been grouped together. It is therefore not possible to give an exact representation of the number of patients who have received EVAR in the included studies.

Table 1 Summary of included studies

Author, Year	RCT/NRCT/ Case series/ Comparative study	Mean age	Enrolled (all interventions)	N° receiving EVAR	Months of follow-up (range)
Aarts 2005[13]	NRCT	NR	215	99	23 (0-73)
Abbruzzese 2008[14]	Case Series	76	565	565	30 (±21)
Anderson 2004[15]	NRCT	NR	4769	1706	NR
Arko 2007[16]	Comp Study	NR	65506	65506	NR
Aune 2007[17]	NRCT	74	504	118	44 (0-117)
Becquemin 2004[18]	Case Series	71	250	250	28
Becquemin 2000[19]	*NRCT*	*70*	*180[a]*	*73*	*7 (0-40)*
Bertrand 2001[20]	NRCT	71	386	193	NR
Blankensteijn 2005[21]	RCT	70	351	173	21 (0-42)
Prinssen 2004[22]	*RCT*	*70*	*351*	*173*	*1*
Blum 2001[23]	Comp study	70	298	298	(2-50)
Bolke 2001[24]	NRCT	72	40	20	NR
Boult 2006[25]	Case Series (R)	75	961	961	NR (5-60)
Boult 2004[26]	*Case Series (R)*	*75*	*950*	*950*	*NR*
Borchard 2005[27]	NRCT	74	166	65	21 (1-74)
Bos 2008[28]	Case Series	72	234	234	27 (1-104)
Verhoeven 2004[29]	*Case Series*	*70*	*308*	*308*	*36 (±22)*
Brewster 2006[30]	Case Series	73	873	873	27
Bush 2007[31]	NRCT	72	2368	788	NR
Cao 2004[32]	NRCT	72	1119	534	33 (13-50)[c]
Cao 2009[33]	*Case Series*	*74*	*349*	*349*	*25 (12-60)*
Cao 2006[34]	*Case Series*	*72*	*649*	*649*	*38*
Parlani 2002[35]	*Comp study*	*70*	*336*	*336*	*14 (1-46)*
Zannetti 2001[36]	*Comp study*	*70*	*266[a]*	*266*	*11 (1-32)*
Carpenter 2004a[37]	Case Series	NR	227	227	11 (0-41)
Chahwan 2006[38]	NRCT	73	677	260	36
Chisci 2009[39]	NRCT	73	187	74	25 (0-39)
Conrad 2009[40]	Case Series	76	832	832	35 (0-113)
Corriere 2004[41]	Case Series	72	220	220	NR
Cuypers 2001[42]	RCT	69	76	57	NR
Dias 2009[43]	Case Series	74	304	304	54
El Sayed 2009[44]	Case Series	NR	444	444	57 (±9)

Author, Year	RCT/NRCT/ Case series/ Comparative study	Mean age	Enrolled (all interventions)	N° receiving EVAR	Months of follow-up (range)
Espinosa 2009[45]	Case Series	73	337	337	59 (12-120)
Espinosa 2005[46]	*Case Series*	*71*	*193*	*193*	*36*
Garcia-Madrid 2004[47]	NRCT	NR	83	53	26
Greenhalgh 2005[d48]	RCT	74	1047	531	35 (23-48)[c]
Greenhalgh 2004[d49]	*RCT*	*74*	*1047*	*531*	*1*
Greenhalgh 2005b[e 50]	RCT	76	238	166	29 (19-43)[c]
Go 2008[51]	Case Series	74	376	376	NR
Hansman 2003[52]	NRCT	72	100	50	NR
Hinchliffe 2004[53]	Case Series	74	269	269	12
Hiramoto 2006[54]	Case Series	76	325	325	30 (1-85)
Hynes 2007[55]	NRCT	75	162	66	23 (±16)
Iannelli 2005[56]	NRCT	75	62	34	14 (12-36)
Jiminez 2007[57]	Case Series	78	574	574	42 (±32)
Jones 2007[58]	Case Series	76	873	873	33
Jordan 2004[59]	NRCT	73	404	259	28
Lederle 2009[60]	RCT	70	881	444	21.6
Lee 2004[61]	NRCT	72	7172	2565	NR
Maldonado 2007[62]	Case Series	73	430	430	36 (2-94)
Maldonado 2004[63]	*Case Series*	*72*	*311*	*311*	*22 (2-72)*
May 2000[64]	Case Series	72	266	266	>6
Mistry 2007[65]	NRCT	66	278	122	33 (0-88)
Moore 2003[66]	NRCT	73	684	573	NR (1-60)
Nevala 2009[67]	Case Series	73	206	206	29 (±20)
Ohki 2001[68]	Case Series	76[b]	239	239	15 (<75)
Ouriel 2003[69]	Comp study	75[b]	704	704	NR
Ouriel 2003[70]	Comp study	75	700[a]	700	12
Park 2006[71]	NRCT	75	410	342	NR
Paolini 2008[72]	NRCT	83	150	81	25 (1-80)
Pitoulias 2009[73]	Case Series	69	617	617	47 (1-94)
Qu 2009[74]	Case Series	72	612	612	62
Qu 2007[75]	*Case Series*	*69*	*378*	*378*	*27 (1-84)*
Ricco 2003[76]	Case Series	72	1012	1012	11
Sahal 2008[77]	NRCT	72	895	452	21.2 (0-136)
Teufelsbauer 2003[78]	*NRCT*	*72*	*756*	*275*	*NR*
Sampaio 2009[79]	Case Series	75	241	241	10 (1-65)

Author, Year	RCT/NRCT/ Case series/ Comparative study	Mean age	Enrolled (all interventions)	N° receiving EVAR	Months of follow-up (range)
Sampaio 2004[80]	*Case Series*	*75*	*241*	*241*	*10 (1-71)*
Elkouri 2003[81]	*Case Series*	*76*	*100*	*100*	*7 (1-60)*
Elkouri 2004[82]	*Case Series*	*74*	*355*	*94*	*NR*
Schermehorn 2008[83]	NRCT	76	22830	22830	NR
Siccard 2006[84]	NRCT	75	565	61	32 (0-123)
Soulez 2005[85]	RCT	70	40	20	27 (12-48)
Szmidt 2007[86]	Case Series	NR	445	445	30
Thomas 2005[87]	Case Series (R)	73	1000	1000	37
Traul 2008[88]	Case series	73	245	245	30 (±18)
Waasdorp 2008[89]	Case Series	71	291	291	4
Herwaarden 2007[90]	*Case series*	*71*	*212*	*212*	*52 (1-109)*
Wald 2006[91]	NRCT	72	6516	2651	NR
Wales 2008[92]	Case Series	73	286	286	16 (0-70)
Vasquez 2004[93]	Comp study	75	212	212	NR
Zeebregts 2004[94]	NRCT	72	286	93	19
EUROSTAR database (n=7043)					
Hobo 2008[95]	Case Series (R)	72	7043	7043	18.6 (0-108)
Koning 2007[96]	*Case Series (R)*	*74*	*5612*	*5612*	*NR*
Marrewijk 2005[97]	*Case series (R)*	*71*	*6787*	*6787*	*21 (0-108)*
Lange 2005[98]	*Case series (R)*	*71*	*4888*	*4888*	*19*
Hobo 2006[99]	*Case Series (R)*	*72*	*2846*	*5846*	*23*
Fransen 2003[100]	*Case Series (R)*	*71*	*4613*	*4613*	*21 (1-72)*
Laheij 2002[101]	*Case Series (R)*	*NR*	*2863[a]*	*2863*	*NR*
Vallabhaneni 2001[102]	*Case Series (R)*	*71*	*2862[a]*	*2862*	*12 (0-72)*
Excluder Clinical Trial(n=334)[a]					
Peterson 2007[103]	NRCT	7	334	235	60

Author, Year	RCT/NRCT/ Case series/ Comparative study	Mean age	Enrolled (all interventions)	N° receiving EVAR	Months of follow-up (range)
Lifeline Registry (n=2998)					
Zarins 2005[104]	NRCT	73	2998	2664	34
Powerlink Clinical Trial (n=349)					
Carpenter 2004[105]	NRCT	73	258	192	NR
Carpenter 2006[106]	NRCT	73	258	192	36
Parmer 2006[107]	NRCT	73	283	283	NR
Wang 2008[108]	NRCT	73	258	192	49 (±20)
Talent Clinical Trial (n=471)					
Criado 2001[109]	Comp study	NR	471	471	NR
Criado 2003[110]	*NRCT*	*76*	*366[a]*	*240*	*13*
Fairman 2004[111]	*Comp study*	*NR*	*237*	*237*	*21*
AneuRx Clinical Trial (n=1193)[a]					
Arko 2002[112]	NRCT	73	497	200	12 (1-60)
Arko 2003[113]	*Comp study*	*73*	*206[a]*	*206*	*32 (3-55)*
Ayerdi 2003[114]	Comp study	73	96	96	12
Howell 2001[115]	Case Series	72	215	215	14
Howell 2000[116]	*Comp study*	*72*	*89[a]*	*89*	*(1-18)*
Lee 2002[117]	Comp study	74	150	150	NR
Lee 2000[118]	*Case Series*	*74*	*67[a]*	*67*	*18*
Ramaiah 2002[119]	Comp study	74	260	260	NR
Shames 2003[120]	Comp study	73	245	245	11 (1-26)
Tonnessen 2005[121]	Comp study	73	130	130	39 (12-72)
Wolf 2002[122]	Comp study	75	189	189	13
Zarins 2000[123]	Case Series	NR	149	149	12 (1-39)
Zarins 2004[124]	Case Series	NR	1193	1193	<48
Zarins 2003[125]	*Case Series*	*73*	*383[a]*	*383*	*36*
Zenith Clinical Trial (n=432)					
Greenberg 2004[126]	NRCT	NR	432	352	NR
Hugl 2007[127]	Case Series	74	366	366	NR
Lalka 2005[128]	Case Series	NR	136	369	36 (1-61)
Total		**73**	**146883**	**128374**	

[a]Excluded from count of enrolled population (all interventions and EVAR) as duplicate series

[b] Some participants may overlap with the Talent and AneuRx clinical trial populations

[c]IQR given for follow-up

[d] EVAR 1 Trial [e] EVAR 2 Trial

NR – Not reported (R) Registry publication

Number and type of excluded studies

Out of the 151 papers initially assessed as potentially relevant for the review, 35 papers were judged as being unsuitable for inclusion in the current review. A summary of the reasons for exclusion is shown in Table 2.

Table 2 Reasons for study exclusion

Reason for exclusion	Number of articles
Not a primary study	4
Small case series (n<200)	1
Insufficient outcome data of interest	6
More recent/relevant publication available	23
Other	1
Total	**35**

Quality of the available evidence

Randomised controlled trials

The results of the quality assessment of the six RCTs (eight papers) is summarised in Table 3. How patients were assigned to treatment groups was reported and random in all of the included RCTs with the exception of the study by Cuypers et al.[45] Patients were randomised to EVAR with a 3:1 ratio, but no information is provided as to the method of randomisation. In the two EVAR trials,[52,53] patients were randomised using a 1:1 ratio in randomly sized permuted blocks. Abdominal aortic aneurysm repair cannot be blinded to the care provider or the patient as it is an invasive procedure, so these checklist items were not applicable. Primary outcome measures were presented as point estimates and measures of variability in all RCTs. In the study by Cuypers et al.[45] there was no record of losses to follow-up and it was unclear whether the procedure was undertaken by an experienced person. The study by Soulez et al also failed to document the level of operator experience. In the remaining studies, the losses to follow-up and level of operator experience were well documented.

Table 3 Summary of the quality assessment of the randomised controlled trials

Criteria	Yes	No	Unclear
Was the assignment to the treatment groups really random?	5	0	1
Was the treatment allocation concealed?	0	N/A	0

Were the groups similar at baseline in terms of prognostic factors?	6	0	0
Were the eligibility criteria specified?	6	0	0
Were the groups treated in the same way apart from the intervention received?	6	0	0
Was the outcome assessor blinded to the treatment allocation?	5	0	1
Was the care provider blinded?	0	N/A	0
Were the patients blinded?	0	N/A	0
Were the point estimates and measures of variability presented for the primary outcome measures?	6	0	0
Was the withdrawal/drop-out rate likely to cause bias?	0	5	1
Did the analyses include an intention-to-treat analysis?	5	0	1
Was the operation undertaken by somebody experienced in performing the procedure	4	0	2

Non-randomised controlled trials

These studies compared a group of patients undergoing EVAR against a group of patients undergoing open repair. A summary of the quality assessment of the 36 non-randomised controlled trials is presented in Table 4.

The participants were generally a representative sample, although the inclusion and exclusion criteria for the studies were only moderately-well documented overall and were only clear in seventeen studies.[22;55;107] Enrolment of patients was reported to be consecutive in twelve studies.[20;22;87;107] and data was collected prospectively in twenty-three studies.[18;87] The level of operator experience was not clearly documented in any of the studies.

Valid outcome measures were used in all studies, although only fifteen considered all outcomes considered important.[71;107] Only five studies provided information on non-respondents or dropouts and in the majority of the remaining studies it was unclear as whether participants lost to follow-up were likely to introduce bias. Analyses were adjusted for confounding factors in only three of the studies.

Table 4 Summary of the quality assessment of the non-randomised controlled trials

Criteria	Yes	No	Unclear
Were participants a representative sample selected from a relevant patient population?	30	0	6

Were the inclusion/exclusion criteria of participants clearly described?	24	4	8
Were participants entering the study at a similar point in their disease progression?	13	9	14
Was selection of patients consecutive?	12	3	21
Was data collection undertaken prospectively?	23	6	7
Were the groups comparable on demographic characteristics and clinical features?	10	23	3
Was the intervention (and comparison) clearly defined?	34	2	0
Was the intervention undertaken by someone experienced at performing the procedure?	0	0	36
Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure? (E.g. access to back-up facilities?	26	0	10
Were all the important outcomes considered?	15	21	0
Were objective (valid and reliable) outcome measure/s used?	36	0	0
Was the assessment of main outcomes blind?	1	4	31
Was follow-up long enough to detect important effects on outcomes of interest?	24	0	12
Was information provided on non-respondents, dropouts?	5	29	2
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; differential drop-out; no description of those lost)	1	5	30
Was length of follow-up similar between comparable groups	18	5	13
Were all the important prognostic factors identified?	27	6	3
Were the analyses adjusted for confounding factors?	3	26	7

Comparative observational studies

These studies compared two or more subgroups of patients undergoing endovascular repair. A summary of the quality assessment of the 24 comparative observational studies is presented in Table 5.

The participants were a representative sample from a relevant population in twenty of the twenty-four studies. The inclusion and exclusion criteria were only clearly described in half of the studies. The groups were only comparable on demographic features in seven of the studies; in three studies, this was not applicable as the groups were set by different demographic or clinical features. Objective outcome measures were used in all studies, although none reported on all important outcome measures of interest. The description of participants lost to follow-up was poorly reported and consequently it was unclear whether

this was likely to introduce bias. Important prognostic factors were reported in eleven studies, and in only four studies were the analyses adjusted for confounding factors.

Table 5 Summary of the quality assessment of the comparative observational studies

Criteria	Yes	No	Unclear
Were participants a representative sample selected from a relevant patient population?	15	0	2
Were the inclusion/exclusion criteria of participants clearly described?	10	4	3
Were participants entering the study at a similar point in their disease progression?	10	3	4
Was selection of patients consecutive?	9	1	7
Was data collection undertaken prospectively?	10	6	1
Were the groups comparable on demographic characteristics and clinical features?	6	7	4
Was the intervention (and comparison) clearly defined?	17	0	0
Was the intervention undertaken by someone experienced at performing the procedure?	1	0	16
Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure? (E.g. access to back-up facilities?	10	0	7
Were all the important outcomes considered?	0	6	11
Were objective (valid and reliable) outcome measure/s used?	17	0	0
Was the assessment of main outcomes blind?	1	16	0
Was follow-up long enough to detect important effects on outcomes of interest?	15	0	2
Was information provided on non-respondents, dropouts?	1	16	0
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; differential drop-out; no description of those lost)	0	1	16
Was length of follow-up similar between comparable groups	12	1	4
Were all the important prognostic factors identified?	8	9	0
Were the analyses adjusted for confounding factors?	2	15	0

Case Series

A summary of the quality assessment of the 55 case series studies is presented in Table 6. The patients were a representative sample selected from a relevant population in two-thirds of the studies. The exclusion and inclusion criteria were only clearly described in a third of

cases. Data collection was prospective in just over half of the studies, but selection of patients was consecutive in a minority of studies. An attempt to blind the outcomes assessors was only made in one study.

The level of experience of the person performing the procedure was only documented in one of the studies reviewed. Although objective outcomes were used by all of the studies, only five studies reported on all outcomes considered important. Information on losses to follow-up was generally reported poorly and therefore it was unclear whether this was likely to introduce any bias.

Table 6 Summary of the quality assessment of the case series

Criteria	Yes	No	Unclear
Were participants a representative sample selected from a relevant patient population?	39	1	15
Are the inclusion/exclusion criteria of patients in the study clearly described?)	24	23	8
Were participants entering the study at a similar point in their disease progression?	11	23	18
Was selection of patients consecutive?	13	1	41
Were all important prognostic factors identified?	27	11	17
Was data collection undertaken prospectively?	29	10	14
Was the recruitment period clearly stated?	52	3	0
Was the intervention that which is being considered in the review? (or was it a significant modification?)	54	0	1
Was an attempt made to blind outcomes assessors?	1	54	0
Was the operation undertaken by someone experienced in performing the procedure?	1	0	54
Did the staff, place, and facilities where the patients were treated provide an appropriate environment for performing the procedure? (e.g. was the intervention undertaken in a centre with the necessary back-up facilities?)	10	0	15
Were objective (valid and reliable) outcome measures used?	54	0	0
Were all the important outcomes considered?	17	38	0
Was follow-up long enough to detect important effects on outcomes of interest?	49	0	6
Was information provided on non-respondents, dropouts?	20	35	0
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; no description of those lost)	1	17	37
Were the main findings clearly described? (to allow replication)	53	0	2

EVAR VERSUS OPEN REPAIR

Major outcomes

30 day outcomes

- **Mortality**

Thirty-day mortality rates are displayed in Tables 8 and 9, and Figure 1. Data from the RCTs[25;45;52] showed a significant reduction in 30-day mortality for EVAR compared to open repair, (OR 0.27; 95% CI 0.15 to 0.51). The results from the NRCTs are concordant with the above findings, showing a significant reduction following EVAR compared to open repair (OR 0.28; 95% CI 0.25 to 0.31).

Table 7 30 day mortality rate for EVAR versus open repair (RCTs)

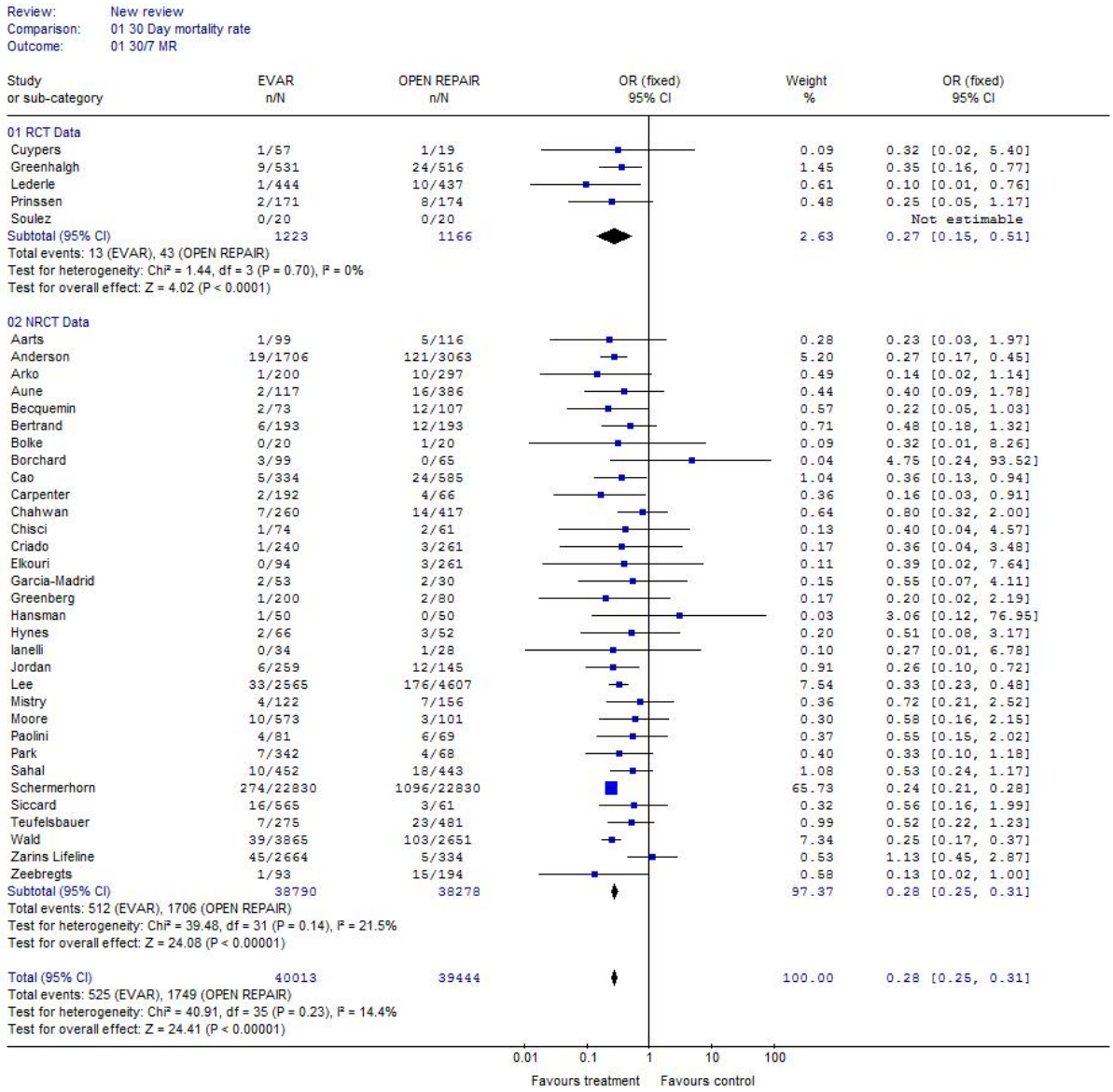
Study ID	EVAR		Open repair	
	n/N	%	n/N	%
Cuypers 2001[42]	1/57	1.8%	1/19	5.3%
Greenhalgh 2004[48]	9/531	1.7%	24/516	4.7%
Lederle 2009[60]	1/444	0.2%	10/437	2.3%
Prinssen 2004[22]	2/171	1.1%	8/174	4.6%
Soulez 2005[85]	0/20	0%	0/20	0%

Table 8 30 day mortality rate for EVAR versus open repair (NRCTs)

Study ID	EVAR		Open repair	
	n/N	%	n/N	%
Aarts 2005[13]	1/99	1.0%	5/116	4.3%
Anderson 2003[15]	19/1706	1.1%	121/3063	4.0%
Arko 2002[16]	1/200	0.5%	10/297	3.4%
Aune 2007[17]	2/117	1.7%	16/386	4.1%
Becquemin 2000[19]	2/73	2.7%	12/107	1.9%
Bertrand 2001[20]	6/193	3.1%	12/193	6.2%
Bolke 2001[24]	0/20	0.0%	1/20	5.0%
Borchard 2005[27]	3/99	3.0%	0/65	0.0%
Cao 2004[32]	5/534	0.9%	24/585	4.1%
Carpenter 2004[37]	2/192	1.0%	4/66	6.1%
Chahwan 2006[38]	7/260	2.7%	14/417	3.5%

Chisci 2009[39]	1/74	1.4%	2/61	3.3%
Criado 2003[110]	1/240	0.4%	0/126	0.0%
Elkouri 2004[82]	0/94	0%	3/261	1.1%
Garcia-Madrid 2004[47]	2/53	3.8%	2/30	6.7%
Greenberg 2004[126]	1/200	0.5%	2/80	2.5%
Hansman 2003[52]	1/50	2.0%	0/50	0.0%
Hynes 2007[55]	2/66	3.0%	3/52	5.8%
Iannelli 2005[56]	0/34	0%	1/28	3.6%
Jordan 2004[59]	6/259	2.3%	12/145	8.3%
Lee 2004[61]	33/2565	1.3%	176/4607	3.8%
Mistry 2007[65]	4/122	3.3%	7/156	4.5%
Moore 2003[66]	10/573	1.7%	3/101	3.0%
Park 2006[71]	7/342	2.0%	4/68	5.3%
Paolini 2008[72]	4/81	4.9%	6/69	8.7%
Sahal 2008[77]	10/452	2.2%	18/443	4.1%
Teufelsbauer 2003[78]	*7/275*	*2.5%*	*23/481*	*4.8%*
Schermehorn 2008[83]	274/22830	1.2%	1096/22830	4.8%
Sicard 2006[84]	16/565	2.9%	3/61	5.1%
Wald 2005[91]	39/3865	1.0%	103/2651	3.9%
Zarins CK 2005[104]	45/2664	1.7%	5/334	1.4%
Zeebregts 2004[94]	1/93	1.1%	15/194	7.7%

Figure 1 30 day mortality rate for EVAR versus open repair: Forest plot



- **Aneurysm rupture**

The primary objective of EVAR is to prevent subsequent rupture and its associated high morbidity and mortality rates. Only four NRCTs reported on early rupture rates occurring in the first 30 days post procedure (see Table 9). The early rupture rate from these studies was 0.1%. Data from the included case series indicated an overall early rupture rate of 0.2% (95% CI 0.1% to 0.3%).

Table 9 Early (<30 days) aneurysm rupture rates following EVAR

Author	Number of patients		Rupture
	EVAR	With rupture	Rate (%)
Carpenter 2006[106]	192	0	0.0
Cao 2004[32]	534	1	0.2
Sicard 2006[84]	565	1	0.2
Zarins 2005[104]	2664	3	0.04

- **Primary conversion to open repair**

This is defined as the number of patients undergoing conversion to open surgery immediately following a failed attempt at endovascular repair.

From the four RCTs[25;52] that reported this outcome, the primary conversion rate averaged 1.2%, (see Table 10). Seventeen NRCTs (see Table 11) reported the primary conversion rate and the results are displayed in Table 10. The overall mean conversion rate was 1.8% (95% CI 1.6% to 1.9%). Data from the 42 case series that reported on this outcome indicated a mean conversion rate of 1.3% (95% CI 1.1% to 1.4%).

Table 10 Primary conversion rates following EVAR (RCTs)

Author	Total number of	Primary conversion	
	EVAR	Number of patients	Rate (%)
Greenhalgh 2005[48]	531	4	0.8
Lederle 2009[60]	444	7	1.6
Prinssen 2004[22]	171	3	1.8
Soulez 2005[85]	20	0	0
	1166	**11**	**0.94**

Table 11 Primary conversion rates following EVAR (NRCTs)

Author	Total number of	Primary conversion	
	EVAR	Number of patients	Rate, % (95% CI)
Arko 2002[13]	200	2	1
Bertrand 2001[20]	193	6	3.1
Borchard 2005[27]	99	0	0
Cao 2004[32]	534	7	1.3

Carpenter 2004[105]	192	3	1.6
Criado 2003[110]	240	1	0.4
Elkouri 2004[82]	94	1	1.1
Garcia-Madrid 2004[47]	53	0	0
Greenberg 2004[126]	200	0	0
Hansman 2003[52]	50	0	0
Ianelli 2005[56]	34	0	0
Jordan 2004[59]	259	1	0.4
Mistry 2007[65]	122	1	0.8
Moore 2003[66]	573	42	7.3
Schermerhorn 2008[83]	22830	365	1.6
Zarins 2005[104]	2664	68	2.6
Zeebregts 2004[94]	93	1	1.1
	28430	**498**	**1.8 (1.6% - 1.9%)**

Longer term outcomes

- **Aneurysm-related mortality**

There were 10 studies that had documented deaths that were directly attributable to the aneurysm. From the DREAM[25] EVAR 1[52] and OVER trials, there was a significant reduction in AAA related deaths in the EVAR group from 30-days post-procedure which was maintained throughout the follow-up period. This difference in aneurysm-related mortality was based entirely on the difference in in-hospital (perioperative) mortality. The OVER trial demonstrated no long term difference in AAA-related death at follow-up to 2 years. The NRCTs demonstrated a non-significant difference between AAA related mortality, 0.9% for EVAR and 1.4% for open repair.

Table 12 Aneurysm-related mortality for EVAR versus open repair

Study ID	**EVAR**		**Open repair**	
	n/N	**%**	**n/N**	**%**
Blankensteijn 2005[21]	**2/173**	**1.2%**	**8/178**	**4.5%**
Greenhalgh 2005[48]	**19/543**	**3.5%**	**34/539**	**6.3%**
Lederle 2009[60]	**6/444**	**1.4%**	**13/437**	**3.0%**
Carpenter 2004[105]	1/192	0.5%	0/66	0%
Chisci 2009[39]	3/71	4.1%	2/61	3.3%
Greenberg 2004[126]	1/200	0.5%	3/80	3.8%

Hynes 2007[55]	2/66	3.3%	3/52	6.1%
Mistry 2007[65]	0/122	0%	0/156	0%
Peterson 2007[103]	2/235	0.9%	0/99	0%
Sicard 2006[84]	5/565	0.9%	0/61	0%

- **Non-aneurysm related mortality**

There were three NRCT (see Table 13) that reported a mortality rate that was not AAA related. Overall, there was a significantly increased rate of death in the EVAR group compared to the open repair group (OR 1.42; 95% CI 1.07 to 1.89).

Table 13 Non-aneurysm related mortality for EVAR versus open repair

Study ID	EVAR		Open repair	
	n/N	%	n/N	%
Cao 2004[32]	101/534	18.9%	78/585	13.3%
Carpenter 2004[105]	19/192	9.9%	9/66	13.6%
Criado 2003[110]	20/240	8.3%	6/126	4.8%

- **All-cause mortality**

Three NRCT (see Table 14) reported total mortality rates at one year, showing no significant difference in mortality in the EVAR group compared to the open repair group (OR 0.81, 95% CI 0.43 to 1.52; p=0.53).

Table 14 All-cause mortality at 1 year for EVAR versus open repair

Study ID	EVAR		Open repair	
	n/N	%	n/N	%
Becquemin 2000[19]	5/73	6.8%	3/107	2.8%
Greenberg 2004[126]	7/200	3.5%	3/80	3.8%
Zeebregts 2004[94]	7/93	7.5%	26194	13.4%

During more prolonged follow up the EVAR 1 trial and OVER trial it was reported that there was no significant difference in mortality rates between the EVAR and open repair groups.

In the EVAR 1 trial at four years, approximately 28% of the study population had died in the EVAR and open repair groups (hazard ratio 0.9, 95% CI 0.69 to 1.19; p=0.46).

At two years, the DREAM trial[47] reported cumulative survival rates of 89.6% following open repair and 89.7% following EVAR, a difference of -0.1 percentage points (95% CI -6.8 to 6.7 percentage points; p=0.86).

In all of the RCTs,[25;52] the initial significant reduction in 30-day mortality rate was lost by one to two years follow up. The EVAR 1 trial[52] reported a hazard ratio for EVAR compared to open repair during the first 6 months of 0.55 (95% CI 0.33 to 0.93) and 1.10 (95% CI 0.80 to 1.52) after 6 months. These findings were similar from the NRCTs with slight difference in favour of EVAR, hazard ratio 1.16 (95% CI 1.02 – 1.33) that just reached significance.

Table 15 All-cause mortality at >1 year for EVAR versus open repair

Study ID	EVAR		Open repair	
	n/N	%	n/N	%
Greenhalgh 2005[49]	**100/543**	**18.4%**	**109/539**	**20.2%**
Lederle 2009[60]	**31/444**	**7.0%**	**43/437**	**9.8%**
Aune 2007[17]	33/118	28%	85/386	22%
Wang 2008[108]	42/192	21.9%	13/66	19.7%
Carpenter 2004[105]	*20/192*	*10.4%*	*9/66*	*13.6%*
Chahwan 2006[38]	41/260	16%	65/417	15%
Garcia-Madrid 2004[47]	5/53	9.4%	6/30	20%
Hynes 2007[55]	14/66	21.2%	8/52	15.1%
Ianelli 2005[56]	3/34	8.8%	3/28	10.7%
Mistry 2007[65]	17/122	13.9%	10/156	6.4%
Paolini 2008[72]	41/81	51%	40/69	58%
Peterson 2007[103]	66/235	28%	19/99	19%
Sahal 2008[77]	214/452	47.3%	192/443	43.3%
Sicard 2006[84]	249/565	44%	21/61	34%
Zarins 2005[104]	819/2664	26%	97/334	29%
Zeebregts 2004[94]	11/93	11.8%	27/194	13.9%

- **Aneurysm rupture rates**

The primary objective of EVAR is to prevent subsequent rupture and its associated high morbidity and mortality rates. Two RCTs and fourteen NRCTs (see Tables 16 and 17, respectively) reported data on delayed rupture rates following EVAR.

Data from the RCTs gave a combined odds-ratio of 5.00 (95% CI 0.58 to 42.94; p=0.14). Of the ten NRCTs, six studies reported delayed rupture rates of 0%. The study by Aune et al, reported the highest rate of 2.5%. Overall the mean rupture rate reported was 1.6% during the studies follow up period. The 30 case series (involving over fifteen thousand patients) that assessed this outcome gave a mean rupture rate of 0.8% over 22 months).

Table 16 Delayed aneurysm rupture rates for EVAR versus open repair (RCT)

Study ID	EVAR		Open repair		Follow-up, months median (IQR)
	n/N	%	n/N	%	
Blankensteijn 2005[21]	0/178	0.0	0/173	0.0	21 (0-42)[a]
Greenhalgh 2005[48]	5/543	0.9	1/539	0.2	35 (23-48)
[a]Mean and range					

Table 17 Delayed aneurysm rupture rates for EVAR versus open repair (NRCT)

Study ID	EVAR		Open repair		Follow-up, months median (IQR)
	n/N	%	n/N	%	
Aune 2007[17]	3/118	2.5	NS	NS	44 (0-117)
Becquemin 2000[19]	0/73	0.0	0/107	0.0	7 (0-40)
Cao 2004[32]	6/529	1.1	0/585	0.0	Not Reported
Chisci 2009[39]	2/74	2.7	0/61	0.0	25 (0-39)
Criado 2003[110]	0/190	0.0	0/240	0.0	Not Reported
Jordan 2004[59]	0/259	0.0	NS	-	Not Reported
Mistry 2007[65]	1/122	0.8	0/156	0.0	32
Moore 2003[66]	0/684	0.0	NS	-	NR (1-60)
Paolini 2008[72]	1/77	1.3	0	0.0	25 (1-80)
Peterson 2007[103]	0/235	0	0/99	0.0	60
Schermerhorn 2008[83]	411/22830	1.8	114/22830	0.5	Not Reported
Sicard 2006[84]	6/565	1.1	0/61	0.0	26(0-123)
Wang 2008[108]	0/192	0.0	0/66	0.0	49 (±20)
Carpenter 2004[105]	*0/192*	*0.0*	*0/66*	*0.0*	*Not Reported*
Zarins 2005[104]	15/2664	0.6	0/334	0.0	34

- **Changes in aneurysm size**

Changes in aneurysm size following endovascular repair were reported in nine NRCTs (see Table 18). Arko 2007[16] defined decrease in size as >10 mm decrease from pre-op size and an increase as >5mm increase from pre-op size, whereas a change in size of 5mm either way was considered a significant increase or decrease in eight studies. Overall, an increase in aneurysm size occurred in 7.9% of patients (95% CI 6.0% to 8.2%). Data from 25 case series indicated that overall 6.5% (95% CI 6.1% to 7.0%) of the EVAR population experienced an increase in size of their aneurysm.

Table 18 Change in aneurysm size following EVAR

Author	Number of cases	Changes in aneurysm size n (%)			Follow-up (mean)
		Increase	No change	Decrease	
Aarts 2005[13]	99	5 (5.1)	79 (79.8)	15 (15.2)	23
Cao 2004[32]	506	39 (7.7)	NR	282 (55.7)	NR
Chisci 2009[39]	74	9 (12)	NR	NR	25
Criado 2003[110]	240	2 (0.8)	NR	NR	13
Elkouri 2004[82]	94	2 (2.1)	28 (29.8)	63 (67)	NR
Greenberg 2004[126]	200	3 (1.5)	NR	NR	NR
Peterson 2007[103]	235	30 (38)	32 (41)	16 (21)	60
Sicard 2006[84]	565	62 (11)	NR	NR	26
Wang 2008[108]	192	20 (10.3)	13 (7)	159 (83)	49 (±20)
Carpenter 2004[105]	*133[d]*	*4(2.0)*	*NR*	*NR*	*22*
Total	**2205**	**172 (7.9)**	**152**	**535**	

[d] n= number of patients who were available for evaluation at 24 months

- **Delayed conversion to open repair**

Any conversion to an open procedure following an initially successful endovascular repair is considered in this section and the results of the studies that reported this outcome are displayed in Tables 19 and 20. From the RCTs[48] the delayed conversion rates were 1.9% 10% respectively and from twelve NRCTs the overall mean delayed conversion rate was 0.6% (95% CI 0.5% to 0.7%).

Table 19 Delayed conversion rates (RCT)

Author	N	Secondary conversions		Follow-up
		n	%	Median (IQR)
Greenhalgh 2005[48]	531	10	1.9	35(23-48)
Soulez 2005[85]	20	2	10	27

Table 20 Delayed conversion rates (NRCTs)

Author	N	Secondary conversions		Follow-up
		n	%	Mean (range)
Aarts 2005[13]	99	2	2.0	23 (0-73)
Becquemin 2000[19]	73	3	4.1	7 (0-40)
Cao 2004[32]	534	19	3.6	33 (13-50)
Chisci 2009[39]	74	2	2.7	25 (0-39)
Criado 2003[110]	240	5	2.1	13 (NS)
Greenberg 2004[126]	200	4	2	NS
Hansman 2003[52]	50	1	2	NS
Ianelli 2005[56]	34	0	34	14 (12-36)
Peterson 2007[103]	235	10	4.3	60
Schermerhorn 2008[83]	22830	91	0.4	NR
Wang 2008[108]	192	3	1.6	49 (±20)
Carpenter 2004[105]	*192*	*3*	*1.6*	*NS*
Zarins 2005[104]	2664	28	1.1	34
	4321	**75**	**0.6%**	
			(95% CI 0.5% - 0.7%)	

- **Secondary intervention rate**

Any procedure (surgical or radiological) that had been carried out to maintain exclusion of the aneurysm sac from the circulation or to maintain graft patency was counted as a secondary procedure and was included in this outcome analysis. The results of the included studies are shown in Tables 21 and 22, and Figure 2.

From the EVAR 1 trial[52] the secondary intervention rate following EVAR was 16.1% compared to 6.9% following open repair (OR 2.57, 95% CI 1.70 to 3.87; p<0.00001). From the DREAM trial[22] the rate of intervention was almost three times the rate after open repair, (hazard ratio 2.9, 95% CI 1.1 to 6.2; p=0.03). From 20 NRCTs the overall secondary

intervention rate following EVAR was 11.7% compared to 2.1%. Overall the odds ratio was in favour of higher reintervention following EVAR (OR 2.87, 95% CI 1.80 to 4.57; p<0.00001).

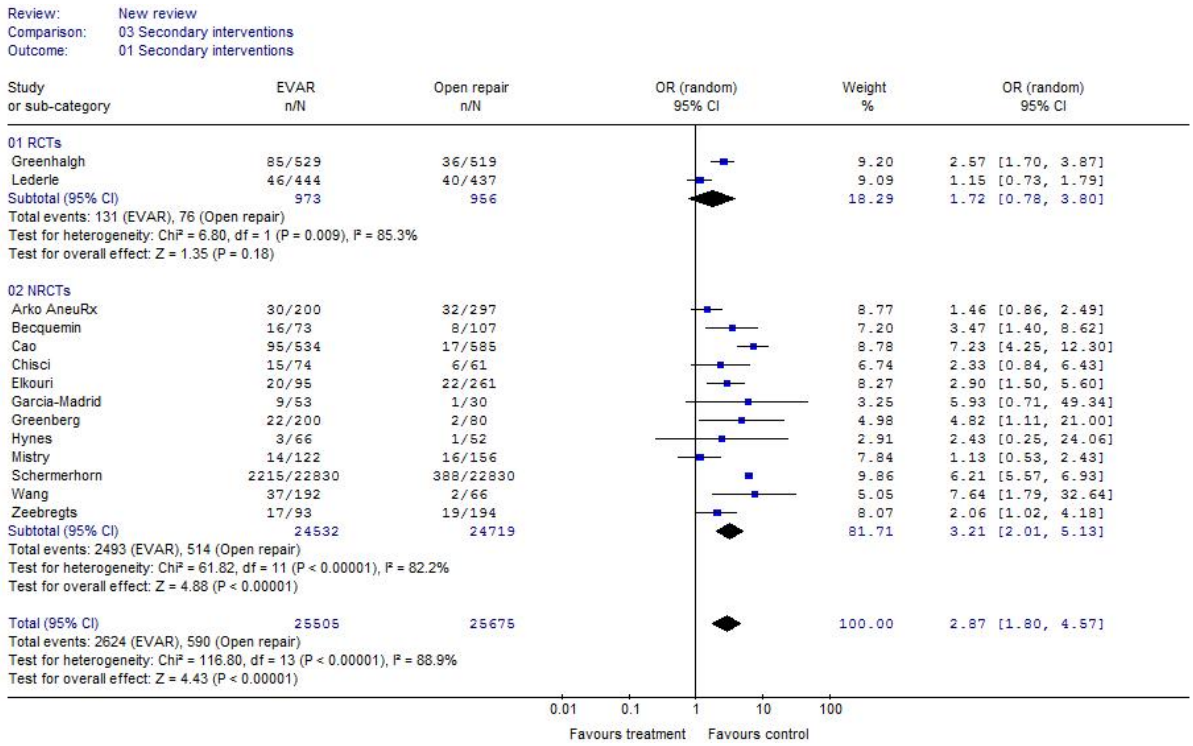
Table 21 Secondary intervention rates for EVAR versus open repair (RCT)

Study ID	EVAR		Open repair		Follow-up, months median (IQR)
	n/N	%	n/N	%	
Greenhalgh 2005[48]	85/529	16.1	36/519	6.9	35 (23-48)
Lederle 2009[60]	46/444	10.4	40/437	9.2	21.6

Table 22 Secondary intervention rates for EVAR versus open repair (NRCT)

Study ID	EVAR		Open repair		Follow-up, months median (IQR)
	n/N	%	n/N	%	
Arko 2002[112]	30/200	15.0	32/297	10.8	12 (1-60)
Aune 2007[17]	27/118	22.9	NS	NS	44 (0-117)
Becquemin 2000[19]	16/73	21.9	8/107	7.5	7 (0-40)
Cao 2004[32]	95/534	18.7	17/585	2.9	NS
Chisci 2009[39]	15/74	20.3	6/61	9.8	25 (0-39)
Criado 2003[110]	9/240	3.8	NS	NS	13 (NS)
Elkouri 2004[82]	20/95	21.1	22/261	3.0	NS
Garcia-Madrid 2004[47]	9/53	17	1/30	3.3	26 (NS)
Greenberg 2004[126]	22/200	11	2/80	2.5	NS
Hansman 2003[52]	6/50	12.0	NS	NS	NS
Hynes 2007[55]	3/66	4.5	1/52	1.9	23 (±16)
Mistry 2007[65]	14/122	11.5	16/156	10	33
Moore 2003[66]	212/573	37.0	NS	NS	NS (1-60)
Paolini 2008[72]	13/77	16.9	NS	NS	25 (1-80)
Park 2006[77]	66/342	19	NS	NS	NS
Peterson 2007[103]	57/235	24.3	NS	NS	60
Schermerhorn 2008[83]	2215/22830	9.7	388/22830	1.7	NS
Wang 2008[108]	37/192	19.3	NS	NS	49 (±20)
Carpenter 2004[105]	*29/192*	*15.1*	*2/66*	*15.1*	*22 (NS)*
Zarins 2005[104]	487/2664	18.2	NS	NS	34
Zeebregts 2004[94]	17/93	18.3	19/194	9.8	19 (NS)

Figure 2 Secondary intervention rates for EVAR versus open repair: Forest plot



Complications

Safety findings are reported according to whether they were endovascular device-related (technical complications) or not (non-technical complications). As outcomes of interest were not reported *a priori* in the majority of studies, in some cases it was not clear whether there were no cases of a complication, or whether the authors had chosen not to report this outcome.

Common technical complications

The incidence of the common technical complications is shown in Table 23 and the results are described below by complication.

- **Stent migration**

A total of 9 studies, reported cases of stent-graft migration following EVAR at <1 year and >1 year. A non-standardised definition of stent-graft migration of either 5mm or 10mm caudal displacement was quoted by most studies which could partly account for the heterogeneity of the results. At < 1 year the incidence was 1.4%, rising to a mean of 2.6% during follow up beyond 1 year.

- **Stent fracture**

There was no report of this adverse event in the included studies.

- **Stent wire fracture**

Only 2 studies reported on the outcome of stent wire fracture. This adverse event was reported from follow-up plain X-rays or CT scans and occurred with an overall incidence of 3.4% during follow-up periods up to 1 year.

- **Graft-limb thrombosis**

During the first 30-days, this was reported to occur in 6.4% of patients by the DREAM trial.[22] During follow up, incidence rates varied from 0.5% to 11.0% amongst the included studies, but the EVAR trial reported a rate of 2.6%.[48]

- **Graft stenosis**

Four studies reported this outcome. Within the first year, one NRCT reported the rate as 5.5%, but one of the EVAR 1 trial52 reported a rate of 0.8% during their follow-up period.

- **Graft kinking**

Four studies reported this outcome, with the RCT reporting a rate of 1.7% during the follow-up period.

- **Type I endoleak**

< 30 days: This adverse event is defined as the occurrence of a type Ia or Ib endoleak in the first 30 days post-EVAR. In seven NRCTs, the incidence of this adverse event ranged from 0.8% to 11.0% with an overall rate of 4.7%.

1 year: Four NRCTs reported 8 (2.3%) cases of type I endoleak during the first year with a range of 0% to 4.4%.

Beyond 1 year: Ten NRCTs reported 69 (3.7%) cases of type I endoleak during follow-up >1Y with a range of 0% to 4.4%. The two RCTs reported rates of 5.5% and 10% during follow-up.

- **Type II endoleak**

<30 days: This adverse event is defined as the occurrence of a type II endoleak in the first 30 days post-EVAR. In 6 NRCTs, the incidences reported ranged from 1.1%[107] to 31.2%,[71] with an overall mean of 17.4%.

1 year: Three NRCTs reported incidences with a range of 5.0%[107] to 21.8%[71] with a mean of 15.3% for this adverse event.

Beyond 1 year: There were 9 NRCT that reported the incidence of type II endoleak beyond 1Y with a mean rate of 14.6%. Two RCTs reported rates of 18.9% and 10% during follow-up.

- **Type III endoleak**

Six NRCTs reported this outcome, with reported incidences between 0% and 11.3%, with an overall mean of 1.8%. The rate reported by one RCT was 1.9% during follow-up.

- **Access artery injury:**

Only two NRCT reported this with rates of 4.1 and 12.9% for arterial injury but did not offer any further definitions for the type of injury sustained. In the case series studies, types of arterial injury were listed as femoral artery damage, iliac artery dissection / injury, external iliac artery rupture, femoral or iliac artery dissection, false femoral aneurysm, femoral artery pseudoaneurysm / iliac dissection. The overall rate of access artery injury was 4.9% from the case series.

- **Contrast reaction**

There was no report of this adverse event in the included studies.

- **'Overall complication' rate**

This was only reported by the EVAR 1 trial.[52] This trial was the only study to consider majority of the technical complications listed above. By 4 years, the proportion of patients with at least one complication following AAA repair was 41% in the EVAR group and 9% in the open repair group. Overall complication rates were 17.6 per 100 person years in the EVAR group and 3.3 per 100 person years in the open repair group, hazard ratio 4.9 (95% CI 3.5, 6.8), p<0.001.

Table 23 Incidence of common technical complications following EVAR (RCT and NRCT)

Complication	Author	EVAR n/N	% (95% CI)
Stent migration			
< 1 year	Criado 2003[110]	3/240	1.3%
	Hansman 2003[52]	1/50	2.0%
	Total	**4/290**	**1.4%**
> 1 year	**Greenhalgh 2005[48]**	**14/529**	**2.6%**
	Aarts 2005[13]	1/99	1.0%
	Borchard 2005[27]	5/99	5.1%
	Greenberg 2004[126]	4/200	2%
	Paolini 2008[72]	1/77	1.3%
	Peterson 2007[103]	0/75	0%
	Wang 2008[108]	8/192	4.3%

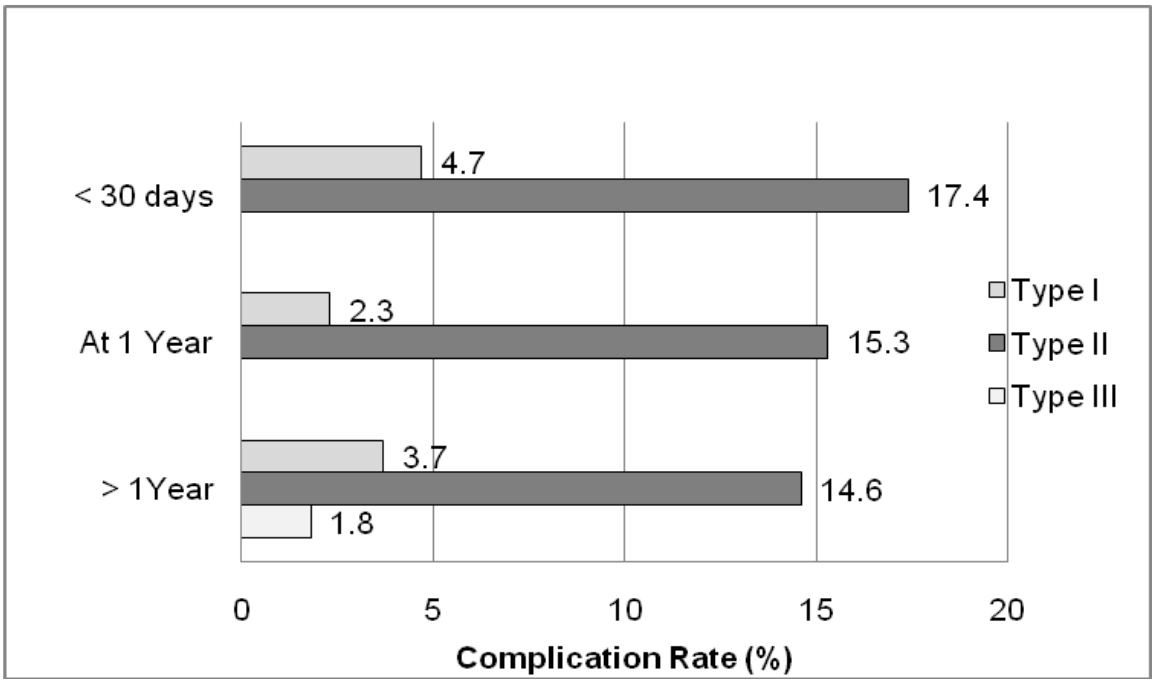
	Carpenter 2006[106]	*5/192*	*2.6%*
	Total	**33/1271**	**2.6%**
Stent wire fracture	Criado 2003[110]	11/240	4.6%
up to 1 year	Greenberg 2004[126]	4/200	2%
	Total	**15/440**	**3.4%**
Graft limb thrombosis			
<30 Days	**Prinssen 2004**[22]	**11/171**	**6.4%**
	Borchard 2005[27]	6/99	6.1%
	Moore 2003[66]	17/573	3.0%
	Total	**34/843**	**4.0%**
<1 year	Arko 2007[17]	1/200	0.5%
	Becquemin 2000[19]	8/73	11.0%
	Hansman 2003[52]	2/50	4.0%
	Ianelli 2005[56]	1/34	2.9%
	Total	**12/357**	**3.4%**
>1 year	**Greenhalgh 2005**[48]	**14/529**	**2.6%**
	Aarts 2005[13]	1/99	1.0%
	Aune 2007[17]	7/118	5.9%
	Borchard 2005[27]	3/99	3.1%
	Chisci 2009[39]	3/74	4.1%
	Hynes 2007[55]	1/66	1.5%
	Moore 2003[66]	31/573	5.4%
	Paolini 2008[72]	2/77	2.6%
	Wang 2008[108]	6/192	3.1%
	Carpenter 2006[106]	*4/188*	*2.1%*
	Total	**68/1827**	**3.7%**
Graft stenosis	Becquemin 2000[19]	4/73	5.5%
<1 year			
>1 year	**Greenhalgh 2005**[48]	**4/529**	**0.8%**
	Carpenter 2004[105]	3/188	1.6%
	Peterson 2007[103]	0/77	0%
	Total	**7/794**	**0.9%**

Graft Kinking	**Greenhalgh 2005[48]**	**9/529**	**1.7%**
>1 year	Borchard 2005[27]	2/99	2.1%
	Carpenter 2006[106]	0/192	0.0%
	Hynes 2007[55]	1/66	1.5%
	Total	**12/886**	**1.4%**
Type I endoleak	Becquemin 2000[19]	8/73	11.0%
< 30 days	Borchard 2005[27]	6/99	6.1%
	Carpenter 2004[105]	1/121	0.8%
	Chisci 2009[39]	3/74	4.1%
	Criado 2003[110]	11/190	5.8%
	Garcia-Madrid 2004[47]	2/53	3.8%
	Moore 2003[66]	12/308	3.9%
	Total	**43/918**	**4.7%**
up to 1 year	Carpenter 2004[105]	0/140	0%
	Criado 2003[110]	7/159	4.4%
	Hansman 2003[52]	1/50	2.0%
	Ianelli 2005[56]	1/34	2.9%
	Total	**9/383**	**2.3%**
>1 year	**Greenhalgh 2005[48]**	**29/529**	**5.5%**
	Soulez 2005[85]	**2/20**	**10%**
	Aarts 2005[13]	4/99	4.0%
	Borchard 2005[27]	2/99	2.1%
	Carpenter 2004[105]	0/90	0%
	Chisci 2009[39]	4/74	5.4%
	Criado 2003[110]	8/179	4.5%
	Garcia-Madrid 2004[47]	1/53	1.9%
	Moore 2003[66]	4/225	1.8%
	Paolini 2008[72]	4/77	5.2%
	Park 2006[71]	11/342	3.2%
	Peterson 2007[103]	0/68	0%
	Total	**69/1855**	**3.7%**
Type II endoleak	Becquemin 2000[19]	9/73	12.3%
<30 days	Borchard 2005[27]	1/99	1.1%
	Carpenter 2004[105]	22/121	18.2%
	Garcia-Madrid 2004[47]	3/53	5.7%

	Criado 2003[110]	16/190	8.4%
	Moore 2003[66]	96/308	31.2%
	Total	**147/844**	**17.4%**
up to 1 year	Criado 2003[110]	8/159	5.0%
	Hansman 2003[52]	7/50	14.0%
	Moore 2003[66]	57/262	21.8%
	Total	**72/471**	**15.3%**
>1 year	**Greenhalgh 2005[48]**	**100/529**	**18.9%**
	Soulez 2005[85]	**2/20**	**10%**
	Aarts 2005[13]	16/99	16.2%
	Borchard 2005[27]	11/99	11.1%
	Chisci 2009[39]	19/74	25.7%
	Carpenter 2004[105]	3/90	3.3%
	Garcia-Madrid 2004[47]	2/53	3.8%
	Moore 2003[66]	38/225	16.9%
	Paolini 2008[72]	4/77	5.2%
	Parks 2006[71]	47/342	13.7%
	Peterson 2007[103]	2/68	2.9%
	Total	**244/1676**	**14.6%**
Type III endoleak	**Greenhalgh 2005[48]**	**10/529**	**1.9%**
>1 year	Aarts 2005[13]	3/99	3.0%
	Borchard 2005[27]	1/99	1.1%
	Carpenter 2004[103]	0/144	0%
	Chisci 2009[39]	1/74	1.4%
	Garcia-Madrid 2004[47]	6/53	11.3%
	Parks 2006[71]	3/342	0.9%
	Total	**24/1340**	**1.8%**
Access artery injury	Borchard 2005[27]	4/99	4.1%
	Moore 2003[66]	74/573	12.9%
	Total	**78/672**	**11.6%**

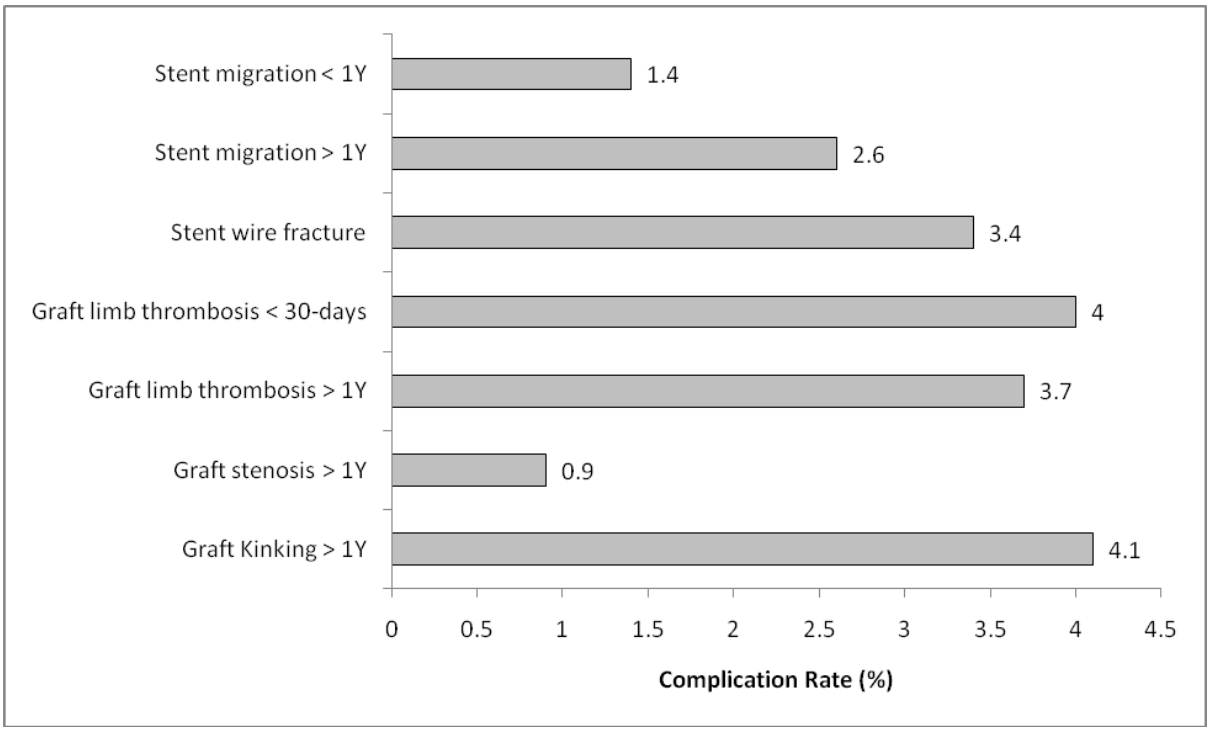
*Results from the RCT trial are stated in bold

Figure 3 Incidence of new or persisting endoleak following EVAR



Results are taken from from the mean of NRCT and RCT data available.

Figure 4 Incidence of technical complications - other



Common non-technical complications

The incidences of the non-technical adverse events are displayed in Table 24. Forest plots are available for selected outcomes in Appendix 2.

- **Cardiac event rate (<30 days)**

From the two RCTs[22;42] that reported this outcome, there was a slight reduction in cardiac events following EVAR, but this difference was not significant, (OR 0.80, 95% CI 0.35 to 1.84; p=0.60). From the 22 NRCTs, there was a significant reduction in cardiac event rate following EVAR, (OR 0.44, 95% CI 0.34 to 0.57; p<0.00001).

- **Renal impairment**

Data from the RCTs indicated that there was no significant difference in renal impairment between the two groups at 30-days, (OR 1.02, 95% CI 0.14 – 7.31). However data from the NRCTs demonstrated a significant reduction in renal impairment in favour of EVAR, (OR 0.52, 95% CI 0.34 – 0.79; p=0.003).

In addition, two NRCTs reported renal impairment rates during follow up of > 1 year and found no significant difference between EVAR and open repair (OR 1.22, 95% CI 0.38 to 3.95; p=0.21).

- **Graft infection**

From the 2 RCT that reported this outcome, there was no significant difference in graft infection rates between the two groups at either 30-days, or during follow-up.

- **Colonic ischaemia**

From both the RCT and NRCT data, there was no significant difference in the rates of graft infection post either procedure. Overall odds ratio for EVAR compared to open repair 0.90 (95% CI 0.76 – 1.08; p=0.26).

- **Lower limb ischaemia:**

This outcome included cases of lower limb ischaemia in the perioperative (<30 day) period only. The incidence of this outcome was reported to vary between 0% and 15.4% following EVAR and 0.9% and 4.0% following open repair. There was no significant difference between EVAR and open repair (OR 0.88, 95% CI 0.47 to 1.64; p=0.69).

- **Pulmonary complications**

From the DREAM trial there was a significant reduction in pulmonary complications following EVAR compared to open repair, (OR 0.25, 95% CI 0.09 to 0.67; p=0.006).

Analysis of the NRCT results also demonstrated a significant reduction in pulmonary complications following EVAR, (OR 0.43, 95% CI 0.40 to 0.46), p<0.00001).

- **Haemorrhage**

From the DREAM trial, there was a non significant reduction in the incidence of haemorrhage following EVAR, (OR 0.5, 95% CI 0.12 to 2.03; p=0.33).

However, a meta-analysis of the NRCT studies demonstrated a significant reduction in haemorrhage following EVAR, (OR 0.23, 95% CI 0.15 to 0.36; p<0.00001).

- **Local wound complications:**

All local wound complications were considered in this section and included haematoma formation, wound infection, lymph leak / lymphocoele, femoral nerve damage. A meta-analysis of the eleven NRCTs that reported this event demonstrated a significantly higher rate of complications after EVAR, (OR 1.37, 95% CI 1.01 to 1.86; p=0.04).

Table 24 Common non-technical complications for EVAR versus open repair

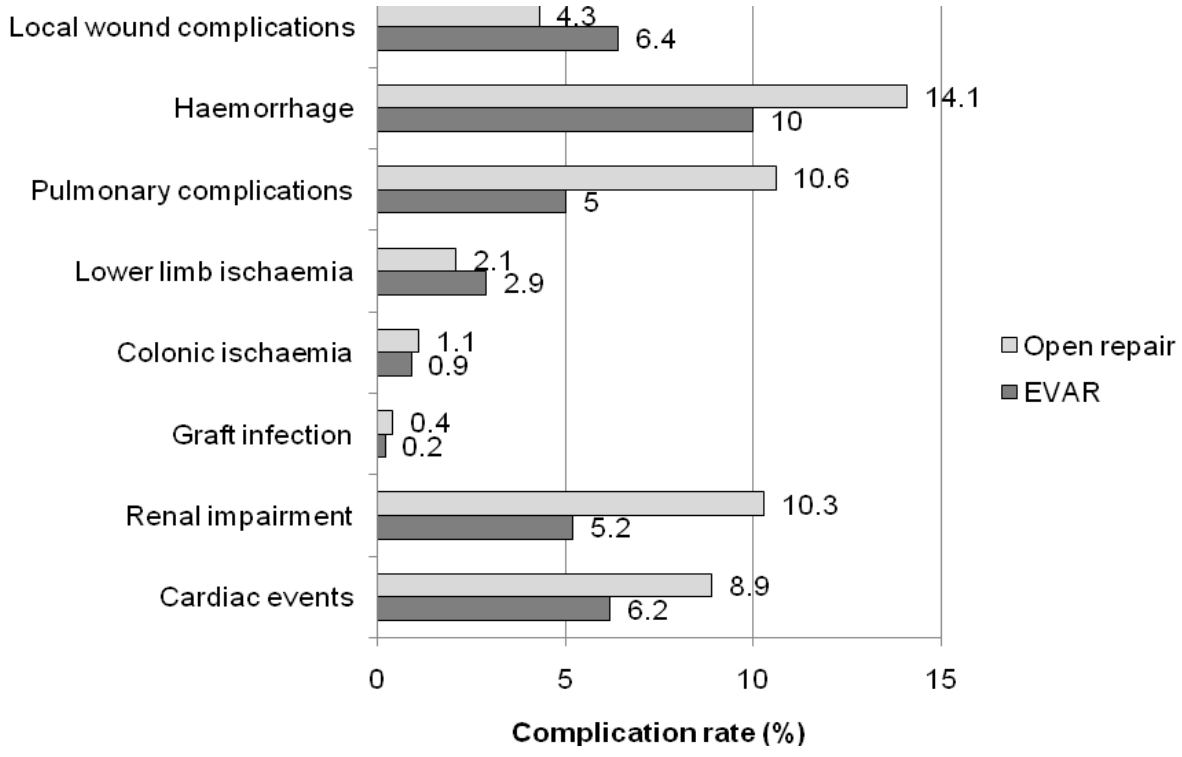
Study ID	EVAR		Open repair		P
	n/N	%	n/N	%	
Cardiac event rate (<30 days)					
Cuypers 2001[42]	**3/57**	**5.3%**	**2/19**	**10.5%**	
Prinssen 2004[22]	**9/171**	**5.3%**	**10/174**	**5.7%**	
Anderson 2003[15]	52/1706	3.0%	230/3063	7.5%	
Arko 2002[112]	10/200	5.0%	15/297	5.1%	
Aune 2007[17]	3/118	2.5%	18/386	4.7%	
Becquemin 2000[19]	2/73	2.7%	7/107	6.5%	
Bertrand 2001[20]	26/193	13.5%	41/193	21.2%	
Bolke 2001[24]	1/20	5.0%	5/20	25.0%	
Borchard 2005[27]	5/99	5.1%	35/65	54%	
Cao 2004[32]	9/534	1.7%	25/585	4.3%	
Chisci 2009[39]	4/74	5.4%	7/61	11.5%	
Criado 2003[110]	3/240	1.3%	4/126	3.2%	
Elkouri 2004[82]	10/94	10.6%	57/261	21.8%	
Garcia-Madrid 2004[47]	2/53	3.8%	1/30	3.3%	
Greenberg 2004[126]	6/200	3.0%	9/80	11.3%	
Hansman 2003[52]	1/50	2.0%	1/50	2.0%	
Ianelli 2005[56]	0/34	0%	2/28	7.1%	
Jordan 2004[59]	8/259	3.1%	9/145	6.2%	
Lee 2004[61]	77/2565	3.0%	320/4607	6.9%	
Moore 2003[66]	56/573	9.8%	23/111	20.7%	<0.01
Park 2006[71]	3/342	0.9%	3/68	4.5%	
Schermerhorn 2008[83]	1598/22830	7%	2146/22830	9.4%	

Wang 2008[108]	16/192	8.3%	12/66	18.1%	
Carpenter 2004[104]	*2/192*	*1.0%*	*5/66*	*7.6%*	
Zeebregts 2004[94]	4/93	4.3%	12/194	6.2%	
Renal impairment (<30 days)					
Prinssen 2004[22]	**2/171**	**1.2%**	**2/174**	**1.1%**	
Arko 2002[112]	1/200	0.5%	1/297	0.3%	
Becquemin 2000[19]	3/73	4.1%	3/107	2.8%	
Bertrand 2001[20]	10/193	5.2%	21/193	10.9%	<0.02
Bolke 2001[24]	3/20	15.0%	4/20	20.0%	
Cao 2004[32]	6/534	1.1%	4/585	0.7%	
Chisci 2009[39]	2/74	2.8%	2/61	3.3%	
Criado 2003[110]	3/240	1.3%	4/126	3.2%	
Elkouri 2004[82]	4/94	4.3%	11/261	4.2%	
Greenberg 2004[126]	5/200	2.5%	9/80	11.3%	
Ianelli 2005[56]	2/34	5.9%	3/28	10.7%	
Moore 2003[66]	31/573	5.4%	2/111	1.8%	
Park 2006[71]	14/342	4.1%	15/68	22.2%	
Schermerhorn 2008[83]	1256/22830	5.5%	2488/22830	10.9%	
Wald 2005[91]	439/2651	6.7%	NR	NR	
Wang 2008[108]	2/192	1.0%	6/66	9.1%	
Renal impairment (>1 year)					
Carpenter 2006[106]	4/190	2.1%	1/62	1.6%	
Greenberg 2004[126]	5/200	2.5%	3/80	3.8%	
Graft infection (< 30 days)					
Prinssen 2004[22]	**1/171**	**0.6%**	**2/174**	**1.1%**	
Graft infection (>1 year)					
Greenhalgh 2005[48]	**1/529**	**0.2%**	**2/519**	**0.4%**	
Chisci 2009[39]	0/74	0%	0/61	0%	
Peterson 2007[103]	1/235	0.4%	0/99	0%	
Schermerhorn 2008[83]	2/22830	0.01%	20/22830	0.09	
Colonic ischaemia (<30 days)					
Prinssen 2004[22]	**1/171**	**0.6%**	**2/174**	**1.1%**	
Aarts 2005[13]	1/99	1.0%	1/116	0.9%	
Borchard 2005[27]	2/99	2.1%	0/65	0%	
Cao 2004[32]	3/534	0.6%	2/585	0.3%	
Chisci 2009[39]	0/74	0%	0/61	0%	

Hansman 2003[52]	1/50	2.0%	0/50	0.0%	
Schermerhorn 2008[83]	228/22830	1.0%	256/22830	1.1%	
Lower limb ischaemia (<30 days)					
Arko 2002[109]	2/200	1.0%	5/297	1.7%	
Cao 2004[32]	8/534	1.5%	14/585	2.4%	
Hansman 2003[52]	0/50	0.0%	2/50	4.0%	
Moore 2003[66]	24/573	4.2%	1/111	0.9%	
Park 2006[71]	15/342	15.4%	NR	NR	
Pulmonary complications (<30 days)					
Prinssen 2004[22]	**5/171**	**2.9%**	**19/174**	**10.9%**	
Aarts 2005[13]	4/99	4.0%	22/116	18.9%	
Anderson 2003[15]	33/1706	1.9%	235/3063	7.7%	
Arko 2002[16]	0/200	0.0%	6/297	2.0%	
Becquemin 2000[19]	3/73	4.1%	14/107	13.1%	<0.05
Bertrand 2001[20]	10/193	5.2%	52/193	26.9%	<0.001
Bolke 2001[24]	2/20	10.0%	4/20	20.0%	
Borchard 2005[27]	5/99	5.1%	19/65	23.2%	
Cao 2004[32]	2/534	0.4%	27/585	4.6%	
Criado 2003[110]	2/240	0.8%	5/126	4.0%	
Elkouri 2004[82]	3/94	3.2%	42/261	16.1%	
Greenberg 2004[126]	2/200	1.0%	13/80	16.3%	
Hansman 2003[52]	1/50	2.0%	5/50	10.0%	
Ianelli 2005[56]	0/34	0%	4/28	14.3%	<0.05
Jordan 2004[59]	2/259	0.8%	9/145	6.2%	
Moore 2003[66]	30/573	5.2%	25/111	22.5%	<0.01
Schermerhorn 2008[83]	1256/22830	5.5%	2488/22830	10.9%	
Wang 2008[108]	5/192	2.6%	11/66	16.7%	
Carpenter 2004[105]	*4/192*	*2.1%*	*5/66*	*6.1%*	
Zeebregts 2004[94]	2/93	2.2%	42/194	21.6%	
Haemorrhage (<30 days)					
Prinssen 2004[22]	**3/171**	**1.8%**	**6/174**	**3.4%**	
Anderson 2003[15]	54/1706	3.2%	321/3063	10.5%	<0.001
Criado 2003[110]	67/240	27.9%	92/126	73.0%	<0.001
Ianelli 2005[56]	0/34	0%	5/28	17.8%	<0.01
Moore 2003[66]	105/573	18.3%	40/111	36.0%	<0.01
Sicard 2006[84]	66/309	21.4%	11/17	64%	
Zeebregts 2004[94]	0/93	0%	23/194	11.9%	

Local wound complications (<30 days)					
Aune 2007[17]	16/118	13.6%	23/386	6.0%	
Becquemin 2000[19]	1/73	1.4%	2/107	1.9%	
Bertrand 2001[20]	13/193	6.7%	14/193	7.3%	
Borchard 2005[27]	16/99	16.1%	3/65	4.6%	
Cao 2004[32]	13/534	2.4%	11/585	1.9%	
Criado 2003[110]	7/240	2.9%	6/126	4.8%	
Elkouri 2004[82]	6/94	6.4%	15/261	5.7%	
Hansman 2003[52]	3/50	6.0%	5/50	10.0%	
Jordan 2004[59]	6/259	2.3%	1/145	0.7%	
Mistry 2007 [65]	5/122	4.1%	10/156	6.4%	
Moore 2003[66]	69/573	12.0%	4/111	3.6%	<0.05
Zeebregts 2004[94]	10/93	10.8%	14/194	7.2%	

Figure 5 Incidence of common non-technical complications: EVAR versus Open repair



Other peri- and post-operative outcomes

Deployment success rate

The success of endograft deployment was documented in 8 studies (see Tables 25 and 26). Success is defined as accurate placement of the graft in the correct position without the need for surgical intervention / open conversion. The only RCT to report this outcome reported a rate of 97%.[48] In seven NRCTs, the deployment success rate ranged from 93%[110] to 100%,[126] and overall averaged 96.5%, (95% CI 95.6% to 97.4%).

Table 25 Successful endograft deployment rate (RCT)

Author	Number of patients (n)		Deployment success
	Undergoing EVAR	Successful deployment	rate (%)
Greenhalgh 2005[48]	543	529	97%

Table 26 Successful endograft deployment rate (NRCT)

Author	Number of patients (n)		
	Undergoing EVAR	Successful deployment	% (95% CI)
Borchard 2005[27]	99	99	100
Criado 2003[110]	240	237	99
Elkouri 2004[82]	94	93	99
Greenberg 2004[126]	200	199	100
Moore 2003[66]	573	531	93
Wang 2008[83]	192	188	98
Carpenter 2004[104]	*192*	*188*	*98*
Zeebregts 2004[94]	93	92	99
	1491	**1439**	**96.5% (95.6% - 97.4%)**

Technical success rate

- **Primary technical success rate**

The primary technical success rate was reported in 6 of the NRCTs and by just one of the RCTs (see Table 27). Studies included in this section had reported success based

either on completion angiograms or on pre-discharge angiograms. Primary technical success was defined as successful placement of the endoluminal-stent with complete exclusion of the aneurysm from the circulation. Where no definition was stated or where an alternative definition was used, there was sufficient data to determine the primary technical success rate as defined at the start of this section.

The success rate averaged 76.7% (95% CI 77.9%, to 84.0%). This success rate was lower than that reported by the case series (83%) because of the variability in definition of this outcome.

Table 27 Primary technical success rate

Author	Number of patients (n)		Technical success rate
	Undergoing EVAR	Technical success	(%, 95% CI))
Soulez 2005[85]	**20**	**20**	**100**
Borchard 2005[27]	99	83	84
Criado 2003[110]	240	168	70
Chisci 2009[39]	74	71	96
Elkouri 2004[82]	94	69	73
Garcia-Madrid 200447	53	48	91
Hynes 2007[55]	66	64	97%
Total	**646**	**523**	**81.0% (71.9% – 79.5%)**

2.2.2 Thirty day technical success

The thirty day technical success rates are displayed in Table 28. This was defined as successful graft placement resulting in complete aneurysm exclusion, with or without prior secondary intervention. The success rate averaged 87% (95% CI 84.4% to 88.7%). This result was similar to that indicated by data from 12 case series, 89% (95% CI 88.7% to 90.7%).

Table 28 Thirty day technical success

Author	Number of patients (n)		Technical success rate
	Undergoing EVAR	Technical success	(%, 95% CI))
Becquemin 2000[19]	73	56	77
Cao 2004[32]	534	479	90
Criado 2003[110]	190	163	86

Greenberg 2004[126]	200	165	83
Total	**997**	**863**	**87% (84.4% – 88.7%)**

- **Blood loss**

The results of blood loss following EVAR or open repair are displayed in Tables 29 and 30. Forest plots are available in Appendix 2.

Blood loss was reported by two RCTs. From the DREAM trial the median blood loss was 250 ml following EVAR and 1500 ml following open repair (WMD -1260 ml, 95% CI -1420 to -1099; p<0.00001). Data from six NRCT (see Table 30) also indicated that there was a significant reduction in blood loss following EVAR (WMD -1130 ml, 95% CI -1519.11 to -741.39; p<0.00001).

Table 29 Procedural blood loss (RCT)

Author	Number of participants	Blood loss in ml Median (IQR)	WMD (CI)
Prinssen 2004[22]			
EVAR	171	250 (100-500)	-1260 (-1420 to -1099)
Open	174	1500 (900-2100)	
Lederle 2009[60]			
EVAR	444	200 (150-400)	
Open	437	1000 (650 – 2000)	

Table 30 Procedural blood loss (NRCT)

Author	Number of participants		Blood loss (ml) EVAR	Blood loss (ml) Open repair
	EVAR	OPEN	Mean (SD)	Mean (SD)
Aarts 2005[13]	99	116	150	1300
Becquemin 2000[19]	73	107	96 (300)	985 (2450)
Bertrand 2001[20]	193	193	650 (1100)	1800 (1600)
Cao 2004[32]	534	585	200 (100-300)[b]	1400 (1000-2100)
Carpenter 2004[126]	192	66	341[b]	1583[b]
Chahwan 2006[38]	260	417	536 (708)	2532 (1982)
Chisci 2009[39]	74	61	400 (400-975)[b]	1550 (1050-1800)
Criado 2003[81]	240	126	345.5 (337.2)	1541.6 (1218.5)
Hansman 2003[52]	50	50	451 (363)	783 (514)

Moore 2003[66]	573	101	400	800
Paolini 2008[72]	81	69	325[b]	2800[b]

[b]Values are median and IQR

- **Length of ITU stay**

The results of length of stay on ITU, where reported, are displayed in Tables 31 and 32.

From four RCTs (see Table 31), there was a significant reduction in ITU stay post EVAR compared to open repair (WMD -1.50 days, 95% CI -1.64 to -1.36; p<00001). From thirteen NRCTs (see Table 32) there was also a significant reduction in ITU stay post EVAR compared to open repair (WMD -0.92 days, 95% CI -1.29 to -0.55; p<0.00001).

Table 31 Length of ITU stay (RCT)

Author	Number of participants		ITU stay, days Mean (SD)	
	EVAR	Open repair	EVAR	Open repair
Cuypers 2001[42]	57	19	0.8 (0.84)[a]	0.9 (3.58)[a]
Greenhalgh 2005[48]	543	539	0.7 (3.8)	2.4 (5.9)
Lederle 2009[60]	444	437	1[a]	4[a]
Prinssen 2004[22]	171	174	1.5 (0.61)	3 (0.80)
Soulez 2005[85]	20	20	0.1 (0.5)	1.6 (1.4)

[a]Value is median

Table 32 Length of ITU stay (NRCT)

Author	Number of participants		ITU stay days Mean (SD)	
	EVAR	Open repair	EVAR	Open repair
Bertrand 2001[20]	193	193	0.9 (1.46)	1.1 (1.47)
Bolke 2001[24]	20	20	1.2[b]	3.4
Borchard 2005[27]	99	65	0.71	2.0
Carpenter 2004[105]	192	66	0.78	4.1
Criado 2003[110]	240	126	0.6[b] (8.67)	2.3 (4.25)
Elkouri 2004[82]	94	261	1 (3.75)	2 (22.25)
Garcia-Madrid 2004[47]	53	30	0.1 (0.06)	1 (0.96)
Hansman 2003[52]	50	50	0.0 (0.3)	1.2 (0.5)

Hynes 2007[55]	66	52	0.5	3.8
Ianelli 2005[56]	34	28	0.65 (.4)	1.73(.6)
Moore 2003[66]	573	101	1.0 [a]	1.1
Park 2006[71]	342	68	0.6	3.8
Sicard 2006[84]	565	61	0.9 (2)	2.1 (2.2)

[a]Median

[b] Statistically significant difference

[c] Calculation excludes medians

- **Length of hospital stay**

The results of length of hospital stay are displayed in Tables 33 and 34. All five of the RCTs reported a significant reduction in length of hospital stay following EVAR compared to open repair (WMD -5.50 days, 95% CI -7.58 to -3.41; p<0.00001). From a meta-analysis of 20 NRCTs, there was also a significant reduction in total hospital stay in the EVAR group compared to the open repair group (WMD -5.12 days, 95% CI -5.74to -4.55; p<0.00001).

Table 33 Length of hospital stay (RCT)

Author	Number of participants		Hospital stay, days Mean (SD)		P
	EVAR	Open	EVAR	Open	
Cuypers 2001[42]	57	19	5 (2-21)[a]	11 (8-50)[a]	<0.01
Greenhalgh 2005[48]	531	516	10.3 (17.8)	15.7 (16.9)	<0.00001
Lederle 2009[60]	444	437	3	7	<0.001
Prinssen 2004[22]	171	174	6 (3-6)[b]	13 (8-15)[b]	<0.01
Soulez 2005[85]	20	20	4 (13)	15 (34)	<0.001

[a] Median and range

[b] IQR

Table 34 Length of hospital stay (NRCT)

Author	Number of participants		Mean length stay, days Mean (SD)		P
	EVAR	Open	EVAR	Open	
Aarts 2005[13]	99	116	7	11	
Anderson 2004[15]	1706	3063	4	10	p<0.001

Arko 2002[112]	200	297	2.8 (2.8)	8.3 (4.5)	
Aune 2007[17]	118	386	4.4	9.2	p<0.01
Becquemin 2000[19]	73	107	7 (2)	13 (7)	p<0.01
Bertrand 2001[20]	193	193	10 (6)	14 (11)	p<0.01
Bolke 2001[24]	20	20	10	14	p<0.01
Borchard 2005[27]	99	65	4	13	p<0.0001
Cao 2004[32]	534	585	2 (2-3)[a]	6 (5-7)[a]	
Carpenter 2004[105]	192	66	3	10	
Chahwan 2006[38]	260	417	3.4	9	p<0.001
Garcia-Madrid 2004[47]	53	30	2 (2-2)[a]	6 (5-7)[a]	
Hansman 2003[52]	50	50	2.3 (1.9)	5.9 (2.2)	p<0.0001
Hynes 2007[55]	66	52	10.2	20.4	p<0.0001
Ianelli 2005[56]	34	28	3.7(.9)	7.3(2.6)	p<0.01
Jordan 2004[59]	259	145	4	12	
Lee 2004[61]	4607	2565	3.6 (5.9)	8.8 (7.8)	
Moore 2003[66]	564	108	2	6	p<0.0001
Paolini 2008[72]	81	69	3 (3.2)	9 (7.6)	
Park 2006[71]	342	68	4.8	11.6	
Schermerhorn 2008[83]	22830	22830	3.4 (4.7)	9.3 (8.1)	
Sicard 2006[84]	565	61	3.5 (4.7)	9.7 (8.8)	p<0.0001
Wald 2005[91]	2651	3865	2	7	
Zeebregts 2004[94]	93	81	9.2 (14)	19.2 (18.2)	

[a]Median and IQR

EVAR IN HIGH RISK PATIENTS

Overview of the trial

The EVAR 2 trial[50] was designed to assess whether EVAR would have an impact on survival in a group of patients deemed unfit for open repair. Therefore, 338 patients were entered into the trial, with 166 participants randomised to EVAR, and 172 to no intervention. However, in the EVAR arm of the trial, 14 patients died before surgery, 1 patient refused, 1 patient was unsuitable for EVAR and 4 patients underwent open repair, leaving 146 patients undergoing EVAR. In the no intervention arm of the trial, 47 of the 172 patients underwent AAA repair (35 by EVAR and 12 by open repair). The results provided below are, therefore displayed by intention to treat where available, but otherwise are stated as by intervention received (per protocol), depending upon what information was provided in the actual paper. A study by Hynes 2007[55] also compared best medical therapy against EVAR, but this was not a randomised trial and patients were selected for each group by the surgeon involved and consequently the groups were not fully matched. The results of this trial have been included for comparison against the EVAR 2 trial.

Major outcomes

Mortality

- **30-day mortality**

Using an intention to treat analysis, the 30-day mortality rate was 8.7% (13/150), but if only elective procedures are taken into account, the operative mortality reduced to 6.8% (10/147). Based upon analysis by intervention received, the 30 day mortality rate was 7.9% (14/178).

From the study by Hynes 2007, the 30-day mortality rate was 3.0%.

- **Mortality AAA related**

Aneurysm-related death based upon all-cause mortality by randomised group, was found to be 12% (20/166) in the EVAR group and 12.8% (22/172) in the no-intervention group, (adjusted hazard ratio 1.00, 95% CI 0.54 to 1.84). The authors undertook a *post hoc* analysis, dividing follow-up into the first 6 months after

randomisation and the period after 6 months. The hazard ratios for AAA related mortality comparing EVAR and non intervention groups were 1.67 (95% CI 0.72 to 3.86) for the first 6 months and 0.53 (95% CI 0.20 to 1.39) for the period after 6 months.

Hynes 2007 reported a 4Y aneurysm related death rate of 33.2% for the group undergoing no intervention and 3.3% in the EVAR group, (p=0.002)

- **All-cause mortality**

The total mortality rates were 44.6% (74/166) for the EVAR group and 39.5% (68/172) for the no-intervention group during the follow-up period. The difference was not statistically significant.

Hynes 2007 reported a 4Y total mortality rate of 82.1% for the no intervention group and 21.2% in the EVAR group (p<0.001).

Aneurysm rupture

Based upon an intention to treat analysis, there was a 3.6% rupture rate pre-EVAR, the median time from randomisation to aneurysm exclusion was 163 days (IQR 78-477). In the perioperative period (<30 days), there was a 2.0% rupture rate and post-EVAR, there were no documented aneurysm ruptures. In the no-intervention group there were 21 ruptures in 172 participants giving a rupture rate of 12.2%. Results are shown in Table 36.

Table 35 Aneurysm rupture rates for EVAR verses no intervention

Time period	EVAR		No intervention	
	n/N	%	n/N	%
Pre-operation	6/166	3.6	21/172	12.2
<30-days post op[a]	3/150	2.0	-	-
<30-days post op[b]	1/178	0.6	0/47	0
>30-days post op	0/137	0	-	-

[a] intention to treat analysis

[b] analysis by treatment received

Conversion to open repair

Based upon analysis by treatment received, during the primary procedure there was just one primary conversion giving a primary conversion rate of 0.6% (1/178). During follow-up there were 2 further conversions equating to a delayed conversion rate of 1.2% (2/178).

Secondary re-intervention rate

According to the paper, the overall intention rate was 11.5 per 100 person years in the EVAR group and 1.8 per 100 person years in the no intervention group. At 4 years 26% of the EVAR group had required at least one intervention compared to only 4% in the no intervention group, (hazard ratio 5.8, 95% CI 2.4 to 14.0; $p<0.001$). However if the significant number of crossovers are considered as secondary interventions in the no-intervention group then the secondary intervention rate in this group becomes considerably greater, (approximately 30%).

Hynes 2007 reported a secondary intervention rate of 4.5% for the EVAR group during the mean follow-up period of 23 months.

Technical complications

The incidence of technical complications associated with EVAR are displayed in Table 36.

Table 36 Incidence of common technical complications in EVAR

Complication	Number of participants	Number of cases	%
Graft infection	178	1	0.6%
Stent migration	178	2	1.1%
Type I endoleak	178	11	6.2%
Type II endoleak	178	23	12.9%
Type III endoleak	178	6	3.4%
Graft thrombosis	178	8	4.5%
Graft stenosis	178	0	0%

Analysis by intention to treat revealed that 58/178 patients developed a complication following an initially successful EVAR equating to a total complication rate of 32.6% in this group during follow-up.

Other peri- and postoperative outcomes

Deployment success rate

From analysis by intention to treat, successful endograft deployment occurred in 89% (143/160) of participants. Analysis by treatment received (per protocol) gives a success rate of 97% (176/181).

Length of Hospital stay

The mean length of hospital stay was 12 days (versus 10 days in fit patients in EVAR group of EVAR 1 trial).

Hynes 2007 reported a mean length of stay of 10.2 days post EVAR.

Expansion and rupture rates

A Medline search on aneurysm expansion rates and rupture rates provided results listed in Tables 37 and 38. The expansion and rupture rates selected for the model were those that corresponded to a 1cm diameter band, and also appeared consistent with the other rates quoted in the literature. The aneurysm expansion rates were then adjusted to monthly rates for use in the Markov model. The aneurysm expansion rates were also adjusted to monthly rates, but were also interpolated to reflect the fact that a 6.9 cm diameter aneurysm would have a higher rupture rate than a 6.1 cm aneurysm.

Table 37 Aneurysm expansion rates

Source	Aneurysm diameter (cm)	Growth rate (cm / Y)
Powel 2004[11]	< 5.0	0.25 - 0.35
Brown 1999[10]	4.5 – 4.9	0.5
Santili 2002[129]	3.0 – 3.9	0.11
Brady 2004[130]	4.0 – 4.5	0.26
Hallin 2001[8]	< 4.0	0.2 - 0.4
	4.0 – 5.0	0.2 - 0.5
	> 5.0	0.3 - 0.7
Stonebridge 1996[131]	< 4.1	0.26
	4.1 – 6.0	0.41
	> 6.0	0.65
Cook 1996[132]	2.5 – 3.9	0.22
	4.0 – 4.9	0.27
	5.0-5.9 cm	0.5
	>6 cm	0.65

Actual expansion rates used in model

Aneurysm diameter (cm)	Growth rate (cm / Y)
3.0-3.9 cm	0.11
4.0 - 4.9 cm	0.27
5.0-5.9 cm	0.5
>6 cm	0.65

Table 38 Aneurysm rupture rates

Source	AAA Diameter	Rupture rate / year
Brown 1998[9]	4.0-5.5	0.0067
Brown 1999[10]	3.0-6.0	0.01
McCarthy 2003[133]	3.5-3.9	0.007
Hallin 2001[8]	<4.0 cm	0.005
	4-5 cm	0.026
	>5 cm	0.06
Powell 2001[11]	4.0-5.5 cm	0.0065
Conway 2001[134]	5.5-5.9 cm	0.36
	6.0-7.0 cm	0.50
	>7.0 cm	0.55
Scott 1998[135]	<5.9 cm	0.008
Aziz 2004[136]	5.0 - 5.9 cm	0.0223
Perko 1993[137]	<6 cm	0.05
	6 cm	0.10
	>6 cm	0.15
Lederle 2002[138]	4.0-5.0 cm	0.006
Lederle 2002[139]	5.5-5.9 cm	0.094
	6.0-6.9 cm	0.102
	7.0 - 7.9 cm	0.325
	>8.0 cm	0.514

Actual rupture rates used in model

Aneurysm diameter (cm)	Rupture rate / year
4.0 - 4.9	0.006
5.0 - 5.9	0.0223
6.0 - 6.9	0.102
7.0 - 7.9	0.325
>8.0	0.514

Validation of the Model

EVAR 1

A hypothetical patient based upon average data from the EVAR 1 trial was generated, and these characteristics were entered into the model. The data input sheet for this patient is displayed in Table 39. The suitability for endovascular repair was set as average, and the hazard ratio for rupture rates was set as 1. The hazard ratio for general mortality is determined by the operative mortality rate and is programmed to return a value of 1 for an EVAR 1 type patient. In addition the discount rate was set to 3% and the threshold aneurysm diameter for delayed intervention was arbitrarily set at 7.5 cm to demonstrate the results generated from the alternative management pathways generated by the model. The results generated from the model are displayed in Figs 6-10 and Table 41.

From Table 42, it can be seen that all-cause mortality, aneurysm-related mortality and post procedure aneurysm rupture rates are very similar between the Markov model and the EVAR 1 trial. At 4 years the number of people with at least 1 reintervention was 20%. However at 4 years the cumulative reintervention rate from the Markov model was 38.9%. This result is higher than that of the EVAR 1 trial because the reintervention rate used in the model is based upon the total number of reinterventions and the rate used assumes that 1 reintervention is performed per person. The EVAR 1 trial reports the reintervention rate as number of people with at least 1 reintervention. In addition the result of 38.9% is similar to extrapolated results from the EUROSTAR registry and NRCT data from the systematic review.

Table 39 Data input sheet with characteristics for hypothetical EVAR 1 patient.

Patient Age	74	
Glasgow Aneurysm Score		Risk factor score
Pt age		74
Shock	No shock	0
Myocardial disease	No Myocardial disease	0
Cerebro-vascular disease	No cerebro-vascular disease	0
Renal disease	No renal disease (urea <20mmol/L)	0

		74
	Mortality risk	0.35
Bayesian mortality Calculation		
Patient age	71 - 75Y	1.001
Gender	Male	0.972
Lowest Blood Pressure	131-140	1.236
ECG	Normal	0.783
Cardiac History	Positive History	1.176
White cell count	6.0 - 6.9	0.551
Bayesian operative MR	0.045	
P-Possum Score		
Physiological score		
Age	>71	4
Cardiac signs	Diuretic, digoxin, antianginal or hypertensive therapy	2
Respiratory history	Dyspnoea on exertion, mild COPD	2
Blood pressure (systolic) (mmHg)	131-170	2
Pulse (bpm)	50-80	1
GCS	15	1
Haemoglobin (g/100ml)	13.0-16.0	1
WCC	4.1-10.0	1
Urea	<7.6	1
Sodium (mmol/l)	>135	1
Potassium (mmol/l)	3.5-5.0	1
ECG	AF (rate 60-90)	4
		21
Operative score		
Operative severity	Major+	8
Multiple procedures	1	1
Total blood loss (ml)	501-999	4
Peritoneal soiling	None	1
Presence of malignancy	None	1
Mode of surgery	Elective	1
P-Possum MR	0.051	16
Enter own Institution MR	0.05	
Operative MR table		
Bayesian	0.045	
EVAR 1 Type Patient	0.044	
EVAR 2	0.264	
Local Institutional MR	0.050	
P-POSSUM	0.051	
Glasgow aneurysm score	0.350	
OPEN Operative MR	EVAR 1 Type Patient	0.044
EVAR operative MR		0.012
Anatomical suitability	Average suitability	0.280

OPEN Operative MR	EVAR 1 Type Patient	0.044
EVAR operative MR		0.012
Anatomical suitability	Average suitability	0.28
Hazard ratio for general mortality	1	
Hazard ratio for rupture rates	1	
Aneurysm Size (cm)	5.5	
Repair Threshold (cm)	7.5	
Discount rate for quality adjusted survival	0.03	

Table 40 Other parameters used in the model with source of data.

Parameter (Probabilities)	**Value**	**Source**	**Comments**
Mortality rate for open conversion	4.4%	Systematic review	Assumption made that open conversion morality rate equals mortality rate of primary open repair
Probability late AAA related death post EVAR	0.040%	Systematic review	Review showed 17/1160 late AAA deaths during follow up. Proportion of late deaths allocated to post intervention
Probability late AAA related death post open repair	0.05%	Systematic review	Review showed 10/539 late AAA deaths over 35 months
Probability death post reintervention	1.31%	Systematic review	Mortality rate assumed to be equivalent to 30-day mortality rate for EVAR
General Mortality	Age related mortality tables		Interim life tables, Government Actuary Department, based on data years 2001-2003
Probability of secondary reintervention	0.74%	Systematic review	Reintervention occurred in 865/5180 over average of 23 months
Probability of primary open conversion of EVAR	0.94%	Systematic review - RCT	Primary conversion occurred in 11/1166
Probability of delayed open conversion of	0.015%	Systematic review	Delayed conversion occurred in 84/4696 during follow up

EVAR			
Utility for living patient following treatment	Age related tariff		Based on Health survey for England 1996 EQ tariff for 65-74 year old men[12]
Discount rate	3%		
Time horizon (months)	120		Model set to display results over 10 Year period

Table 41 Tabulated results from Markov model

Survival

Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.956	0.936	0.913	0.706	0.436	8.750
EVAR	0.988	0.967	0.943	0.730	0.450	9.000
Best medical therapy	0.995	0.967	0.928	0.307	0.096	3.750
Delayed open repair	0.995	0.967	0.928	0.595	0.367	7.000
Delayed EVAR	0.995	0.967	0.928	0.617	0.381	7.417

Quality adjusted survival

Management	6 month	1 Year	5 Years	10 Years
Open repair	0.320	0.692	3.180	5.369
EVAR	0.328	0.713	3.283	5.544
Best medical therapy	0.330	0.713	2.725	3.353
Delayed open repair	0.330	0.713	2.916	4.797
Delayed EVAR	0.330	0.713	2.996	4.910

Discounted quality adjusted survival

Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.318	0.682	1.930	2.963	3.797	4.719
EVAR	0.326	0.702	1.992	3.058	3.921	4.873
Best medical therapy	0.327	0.702	1.894	2.561	2.849	3.069
Delayed open repair	0.327	0.702	1.892	2.762	3.465	4.241
Delayed EVAR	0.327	0.702	1.897	2.800	3.529	4.335

AAA related death

Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.044	0.046	0.049	0.068	0.085
EVAR	0.012	0.015	0.017	0.037	0.055
Best medical therapy	0.001	0.011	0.029	0.505	0.646
Delayed open repair	0.001	0.011	0.029	0.198	0.213
Delayed EVAR	0.001	0.011	0.029	0.172	0.187

Cumulative reintervention rate

Management	6 month	1 Year	5 Years	10 Years
EVAR	0.035	0.077	0.367	0.621
Best medical therapy	0.003	0.007	0.126	0.160
Delayed open repair	0.003	0.007	0.038	0.038
Delayed EVAR	0.003	0.007	0.169	0.377

Cumulative aneurysm rupture rate

Management	1 month	6 month	1 Year	5 Years	10 Years
EVAR	0.000	0.001	0.003	0.013	0.022
Best medical therapy	0.002	0.014	0.036	0.629	0.801
Delayed open repair	0.002	0.014	0.036	0.190	0.190
Delayed EVAR	0.002	0.014	0.036	0.195	0.202

Fig 6 Aneurysm survival curve for hypothetical EVAR 1 patient

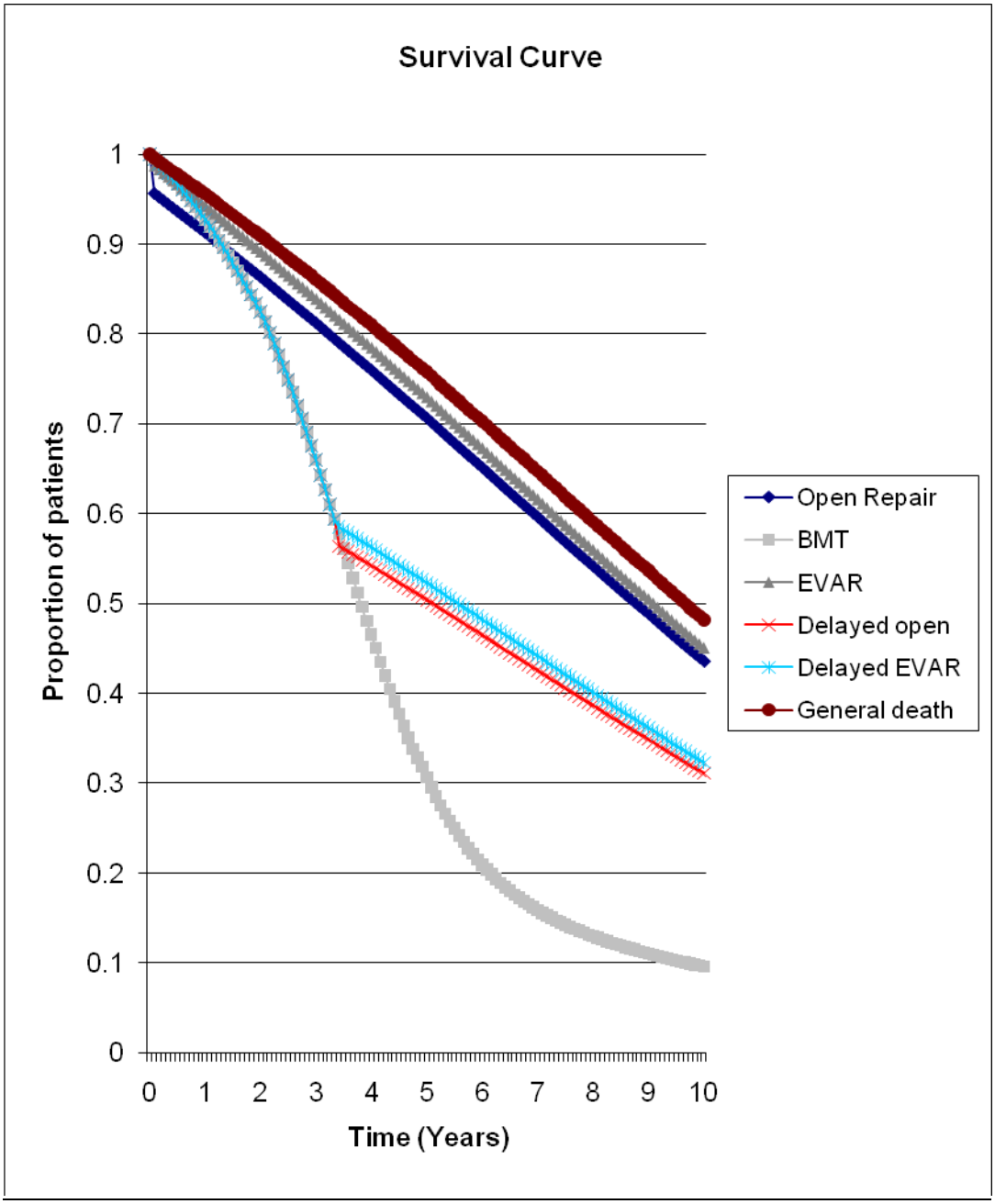


Fig 7 Quality adjusted survival curve for hypothetical EVAR 1 patient

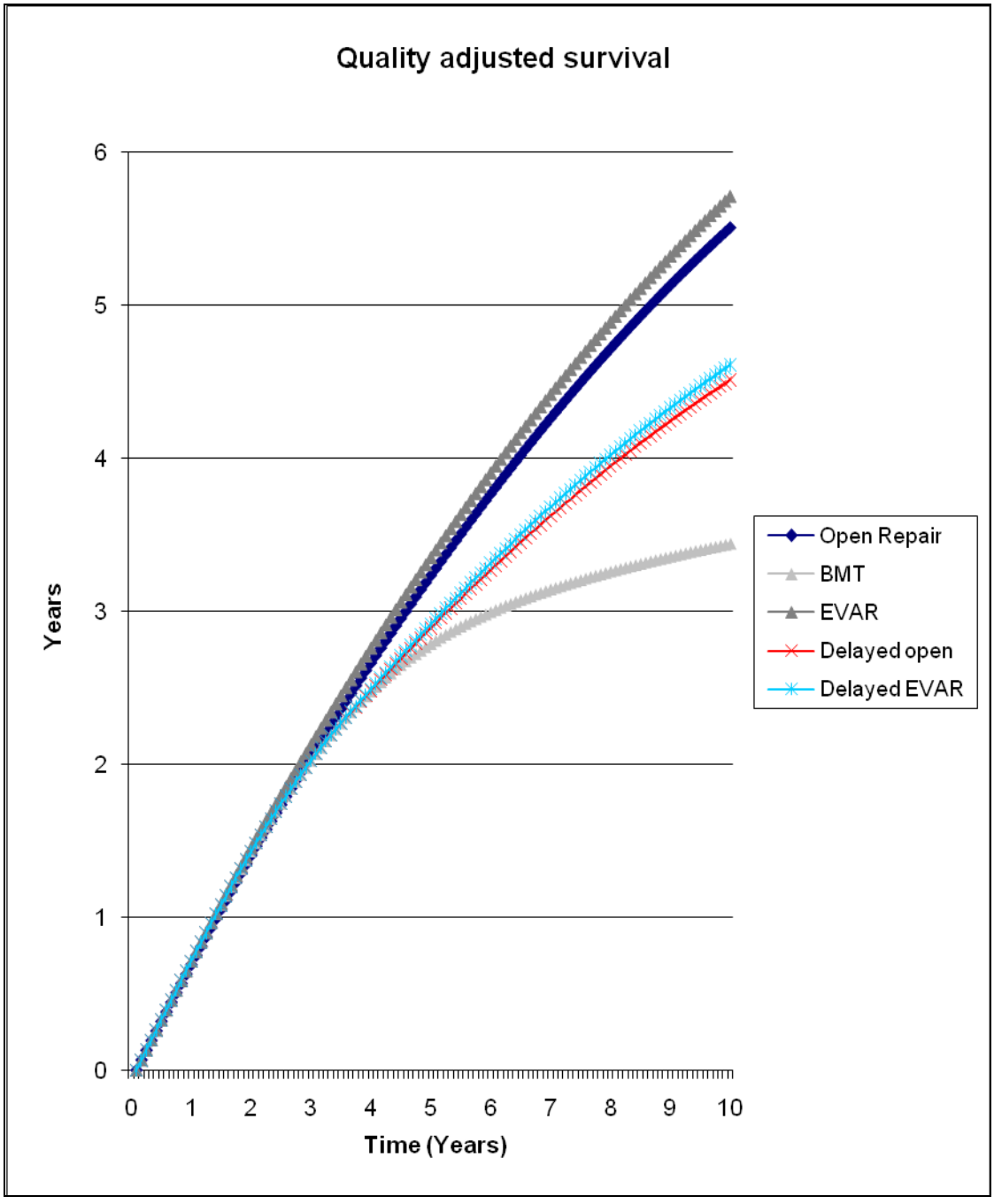


Fig 8 Discounted quality adjusted survival curve for hypothetical EVAR 1 patient

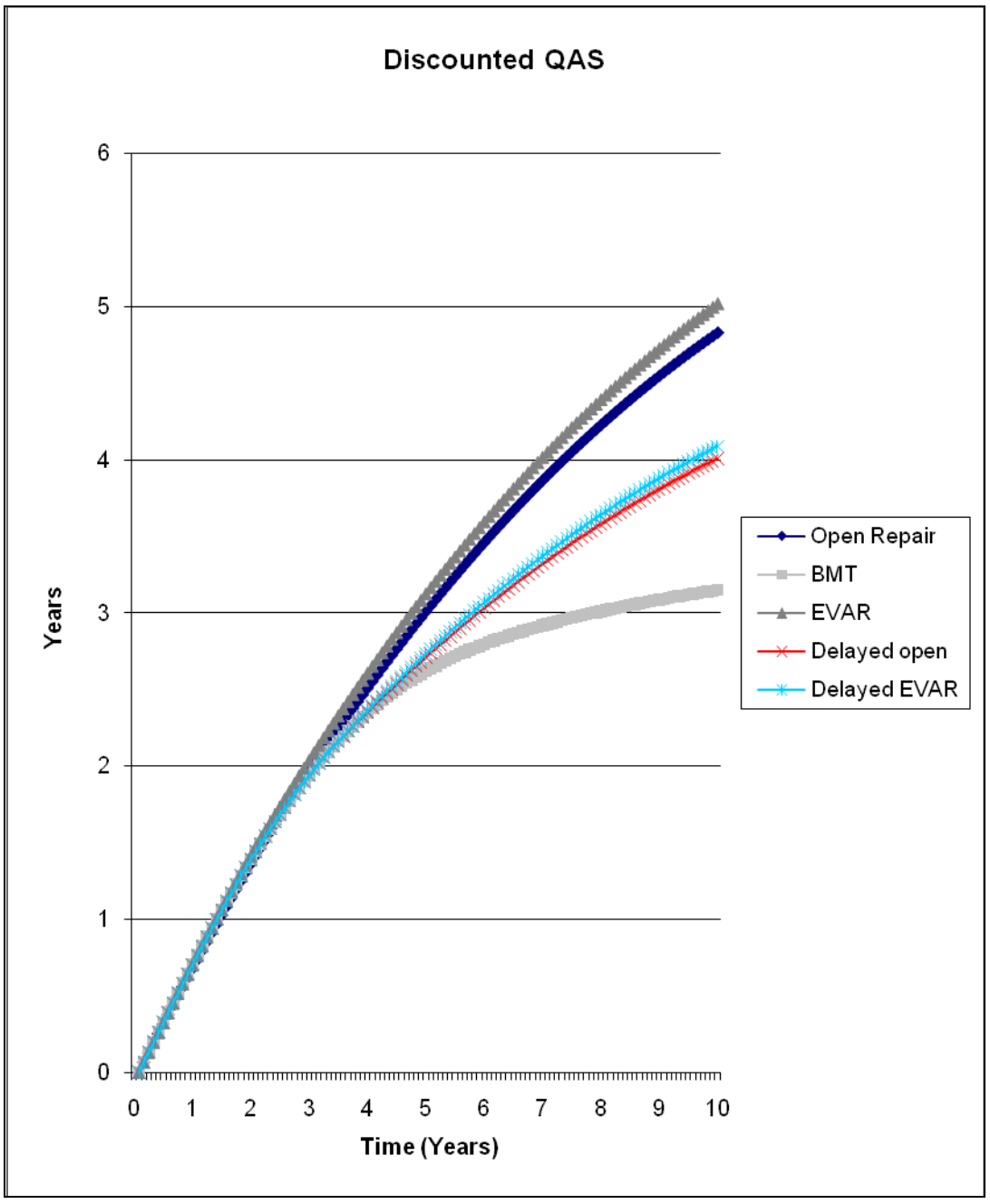


Fig 9 Cumulative aneurysm rupture rate for hypothetical EVAR 1 patient

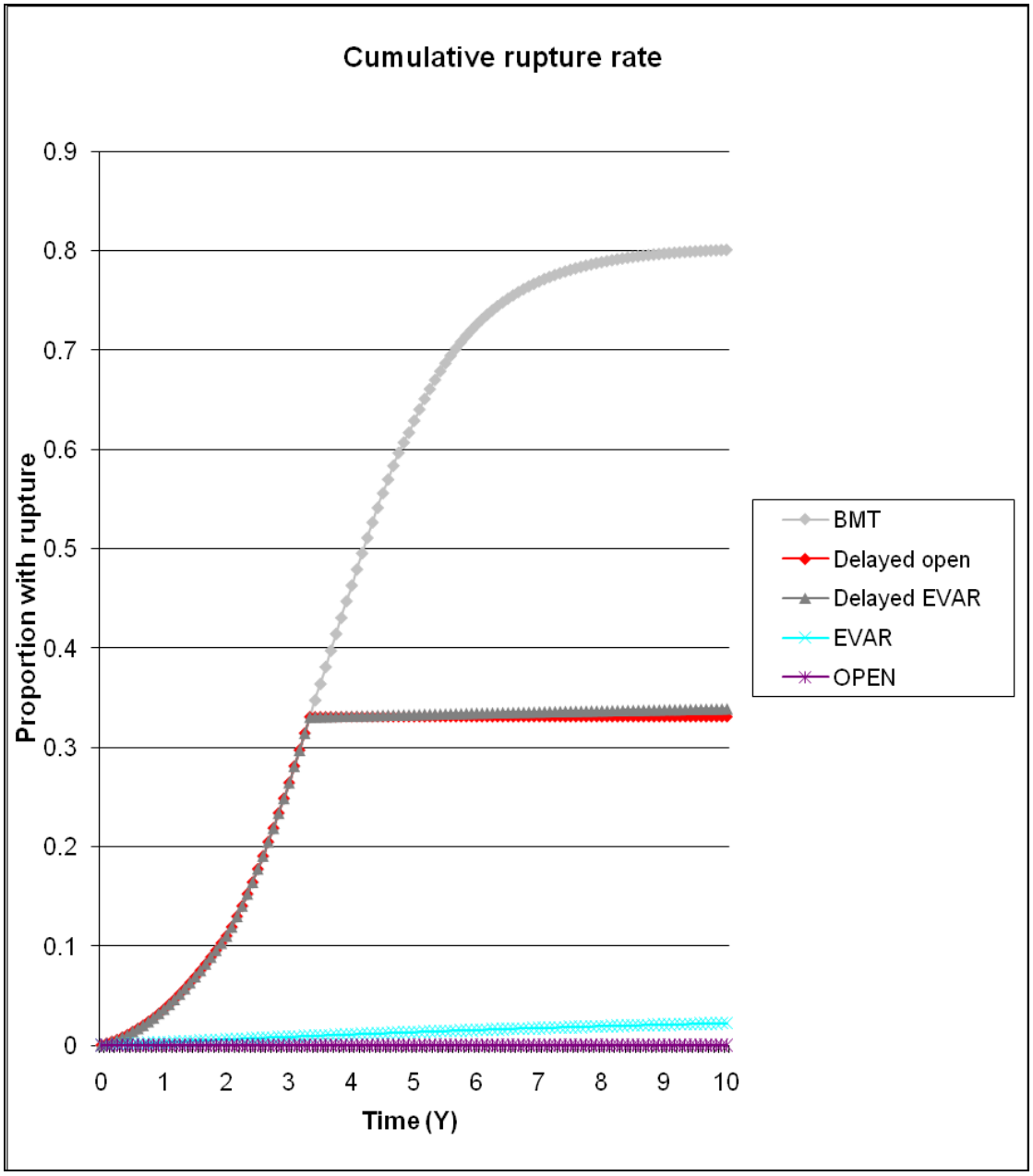


Fig 10 Aneurysm related morality rate for hypothetical EVAR 1 patient

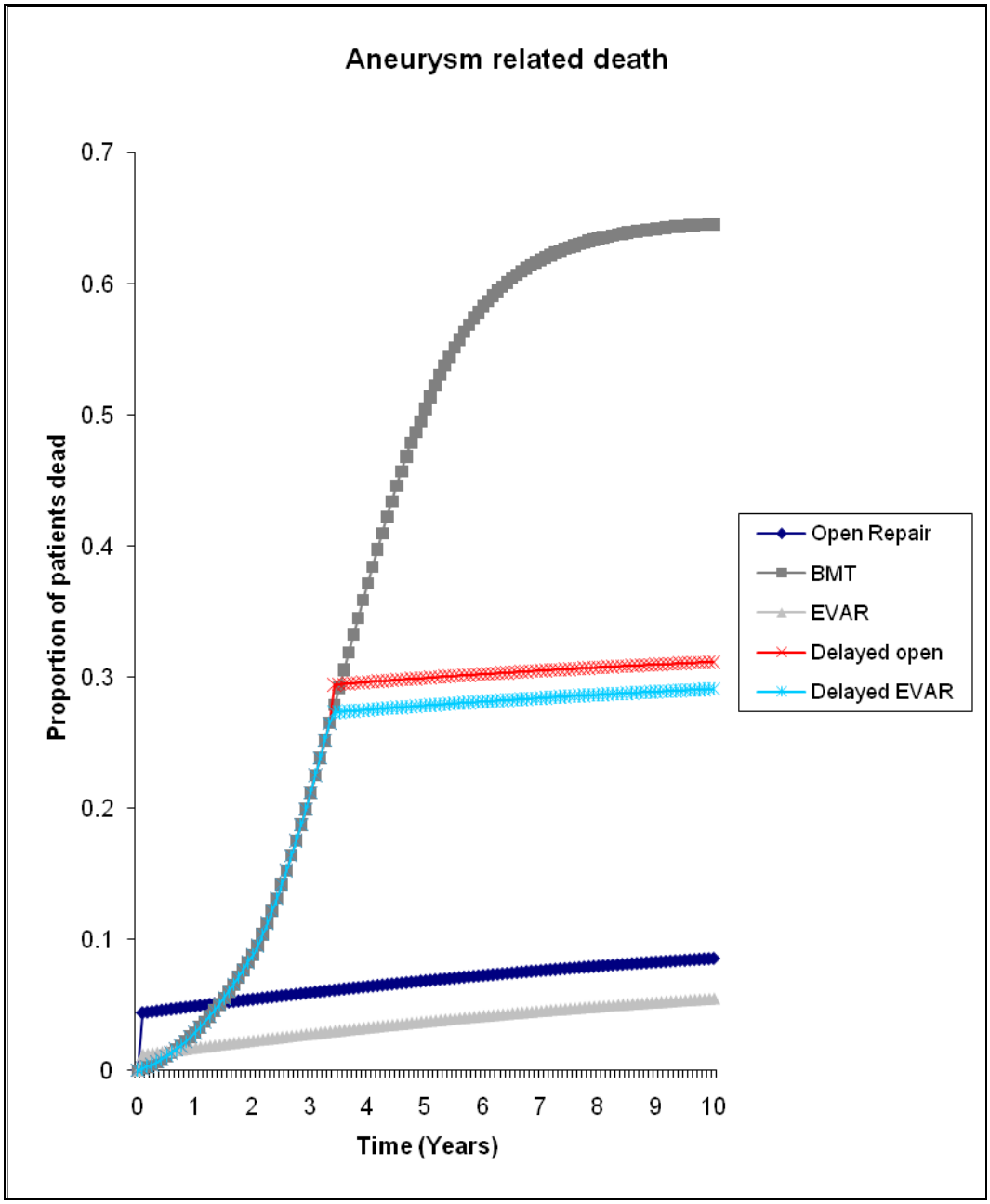


Table 42 Comparison of EVAR 1 and Markov model results.

Outcome measure	Markov model	EVAR 1
All cause mortality at 4Y, EVAR	22.0%	28%
All cause mortality at 4Y, open repair	24.0%	28%
Aneurysm related death at 4Y, EVAR	3.3%	4%
Aneurysm related death at 4Y, open repair	6.4%	7%
Cumulative aneurysm rupture rate at 35 months, EVAR	1.09%	0.92%
Cumulative aneurysm rupture rate at 35 months, open repair	0%	0%
Reintervention rate at 4Y, EVAR	30.1%	20%[a] Approx 38 - 40% from NRCT and EURSTAR registry

[a]reintervention rate stated as number of people with at least 1 reintervention by 4Y. Reintervention rate in Markov model calculated from total number of reinterventions performed over a period of time and rate therefore assumes that 1 reintervention was performed per person. Reintervention rates reported in literature review are very variable and results from the model lie within expected range from other NRCTs and EUROSTAR reports.

EVAR 2

A hypothetical patient based upon average data from the EVAR 2 trial was generated, and these characteristics were entered into the model. The data input sheet for this patient is displayed in Table 43. The suitability for endovascular repair was set as average, and the hazard ratio for rupture rates was set as 1. The hazard ratio for general mortality was programmed to return a value of 3 to reflect the increased mortality rate of this high-co-morbidity population, compared to 'normal' aged matched controls. In addition the discount rate was set to 3% and the threshold aneurysm diameter for delayed intervention was set at 7.0 cm to demonstrate the no-intervention arm of EVAR 2 whereby the patients underwent EVAR if the vascular surgeon thought that the balance between aneurysm rupture and operative mortality rate had been exceeded, or the aneurysm became symptomatic. The results generated from the model are displayed in Figs 11-16 and Table 45.

From Table 46, it can be seen that the results are similar for all-cause mortality, aneurysm related death, cumulative aneurysm rupture rates and reintervention rates between the Markov model and the EVAR 2 trial for both the EVAR and delayed EVAR management options.

Table 43 Data input sheet with characteristics for hypothetical EVAR 2 patient.

Patient Age	76	
Glasgow Aneurysm Score		Risk factor score
Pt age		76
Shock	No shock	0
Myocardial disease	No Myocardial disease	0
Cerebro-vascular disease	No cerebro-vascular disease	0
Renal disease	Renal Disease (urea >20mmol/L)	14
		90
	Mortality risk	**0.62**
Bayesian mortality Calculation		
Patient age	76 - 80Y	1.169
Gender	Male	0.972
Lowest Blood Pressure	131-140	1.236
ECG	Non-normal	1.326
Cardiac History	Positive History	1.176
White cell count	>9.9	1.387

Bayesian operative MR	0.145	
P-Possum Score		
Physiological score		
Age	>71	4
Cardiac signs	Diuretic, digoxin, antianginal or hypertensive therapy	2
Respiratory history	Limiting dyspnoea (one flight), moderate COPD	4
Blood pressure (systolic) (mmHg)	131-170	2
Pulse (bpm)	50-80	1
GCS	15	1
Haemoglobin (g/100ml)	13.0-16.0	1
WCC	4.1-10.0	1
Urea	<7.6	1
Sodium (mmol/l)	>135	1
Potassium (mmol/l)	3.5-5.0	1
ECG	AF (rate 60-90)	4
		23
Operative score		
Operative severity	Major+	8
Multiple procedures	1	1
Total blood loss (ml)	501-999	4
Peritoneal soiling	Free bowel content, pus or blood	8
Presence of malignancy	None	1
Mode of surgery	Elective	1
		23
P-Possum MR	0.2503246	
Enter own Institution MR	0.05	
Operative MR table		
Bayesian	0.145	
EVAR 1	0.047	
EVAR 2	0.264	
Local Institutional MR	0.05	
P-POSSUM	0.250	
OPEN Operative MR	EVAR 2	0.264
EVAR operative MR		0.087
Anatomical suitability	Average suitability	0.28
Hazard ratio for general mortality	3	
Hazard ratio for rupture rates	1	
Aneurysm Size (cm)	6.6	
Repair Threshold (cm)	7	
Discount rate for quality adjusted survival	0.03	

Table 44 Other parameters used in the model with source of data.

Parameter (Probabilities)	Value	Source	Comments
Mortality rate for open conversion	26.4%	Systematic review – from recent RCTs	Assumption made that open conversion morality rate equals mortality rate of primary open repair
Probability late AAA related death post EVAR	0.040%	Systematic review	Review showed 17/1160 late AAA deaths during follow up. Proportion of late deaths allocated to post intervention
Probability late AAA related death post open repair	0.05%	Systematic review	Review showed 10/539 late AAA deaths over 35 months
Probability death post reintervention	1.31%	Systematic review	Mortality rate assumed to be equivalent to 30-day mortality rate for EVAR
General Mortality	Hazard ratio of 3 applied to mortality tables		Interim life tables, Government Actuary Department, based on data years 2001-2003
Probability of secondary reintervention	0.74%	Systematic review	Reintervention occurred in 865/5180 over average of 23 months
Probability of primary open conversion of EVAR	1%	Systematic review - RCT	Primary conversion occurred in 7/702
Probability of delayed open conversion of EVAR	0.015%	Systematic review	Delayed conversion occurred in 84/4696 during follow up
Utility for living patient following treatment	Age related tariff		Based on Health survey for England 1996 EQ tariff for 65-74 year old men[12]
Discount rate	3%		
Time horizon (months)	120		Model set to display results over 10 Year period

Table 45 Tabulated results from Markov model

Survival

Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.7379	0.6870	0.6304	0.2602	0.0474	2.1667
EVAR	0.9139	0.8478	0.7749	0.3095	0.0542	3.0833
Best medical therapy	0.9774	0.8624	0.7205	0.0912	0.0130	1.7500
Delayed open repair	0.9774	0.8624	0.5704	0.2354	0.0429	1.6667
Delayed EVAR	0.9774	0.8624	0.7097	0.2837	0.0497	2.6667

Quality adjusted survival

Management	6 month	1 Year	5 Years	10 Years
Open repair	0.2463	0.5019	1.8441	2.3724
EVAR	0.2897	0.6048	2.2333	2.8529
Best medical therapy	0.3024	0.6165	1.6129	1.7737
Delayed open repair	0.3024	0.5927	1.7915	2.2850
Delayed EVAR	0.3024	0.6111	2.1031	2.6712

Discounted quality adjusted survival

Management	6 month	1 Year	5 Years	10 Years
Open repair	0.2446	0.4947	1.7326	2.1623
EVAR	0.2876	0.5960	2.0984	2.6025
Best medical therapy	0.3001	0.6076	1.5372	1.6684
Delayed open repair	0.3001	0.5844	1.7044	2.0932
Delayed EVAR	0.3001	0.6024	1.9788	2.4411

AAA related death

Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.2621	0.2638	0.2658	0.2760	0.2800
EVAR	0.0861	0.0913	0.0970	0.1263	0.1373
Best medical therapy	0.0089	0.0599	0.1357	0.5138	0.5294
Delayed open repair	0.0089	0.0599	0.3042	0.3134	0.3170
Delayed EVAR	0.0089	0.0599	0.1589	0.1854	0.1953

Cumulative reintervention rate

Management	6 month	1 Year	5 Years	10 Years
EVAR	0.0383	0.0807	0.2978	0.3790
Best medical therapy	0.0150	0.0339	0.1280	0.1317
Delayed open repair	0.0150	0.0210	0.0210	0.0210
Delayed EVAR	0.0150	0.0413	0.2543	0.3339

Cumulative aneurysm rupture rate

Management	1 month	6 month	1 Year	5 Years	10 Years
EVAR	0.0002	0.0013	0.0026	0.0089	0.0113
Best medical therapy	0.0111	0.0749	0.1696	0.6401	0.6583
Delayed open repair	0.0111	0.0749	0.1049	0.1049	0.1049
Delayed EVAR	0.0111	0.0749	0.1057	0.1113	0.1134

Fig 11 Aneurysm survival curve for hypothetical EVAR 2 patient

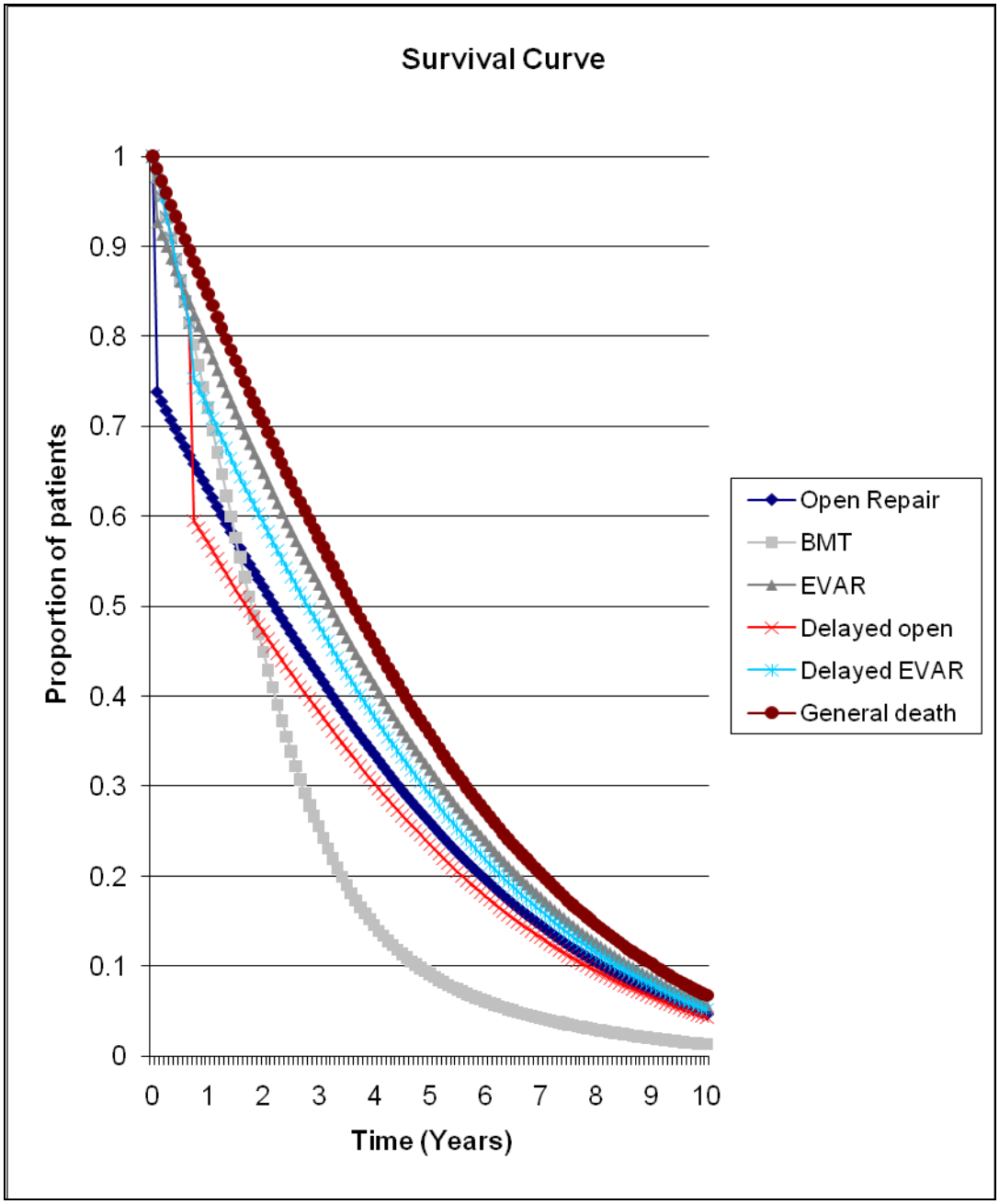


Fig 12 Quality adjusted survival curve for hypothetical EVAR 2 patient

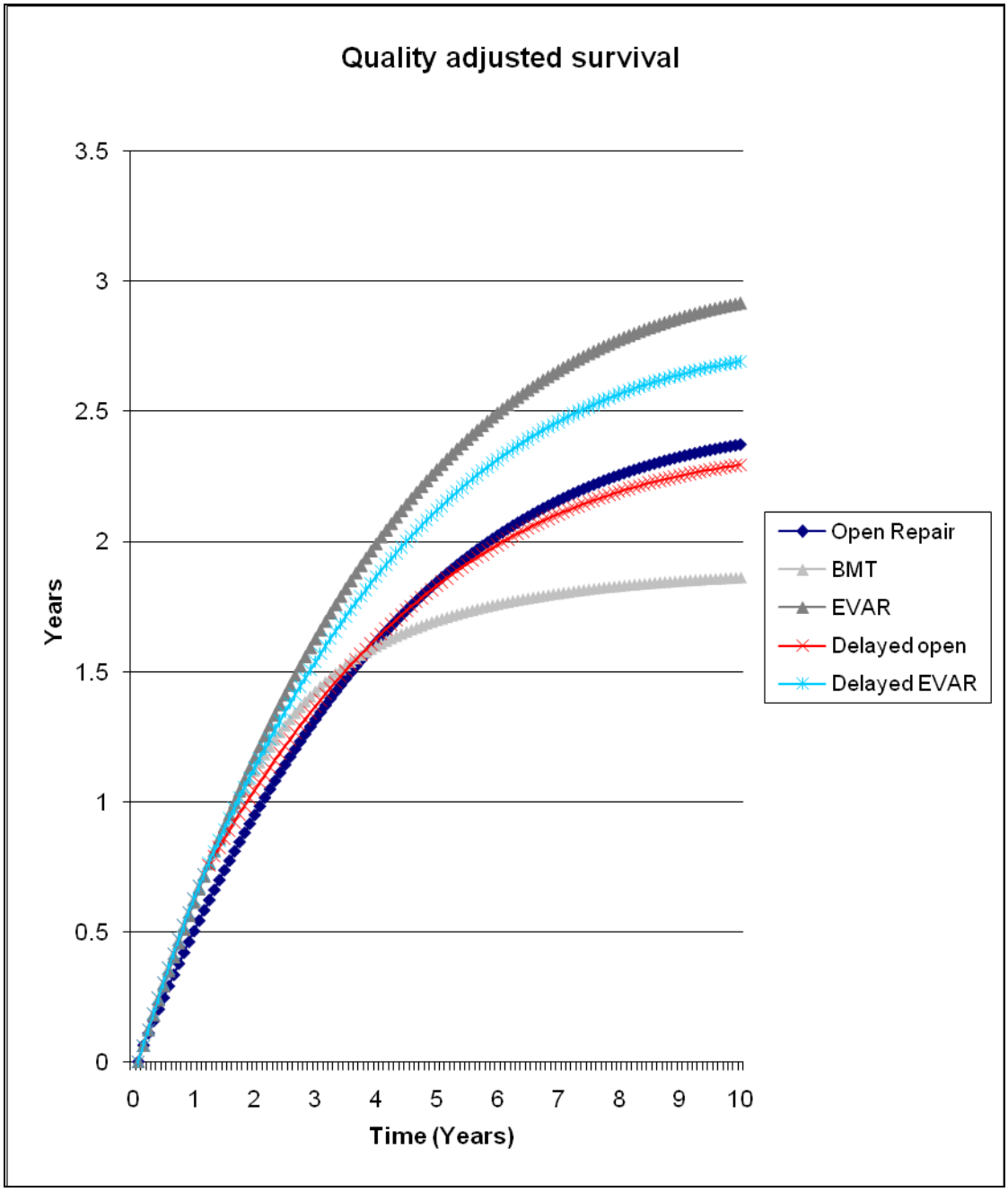


Fig 13 Discounted Quality adjusted survival curve for hypothetical EVAR 2 patient

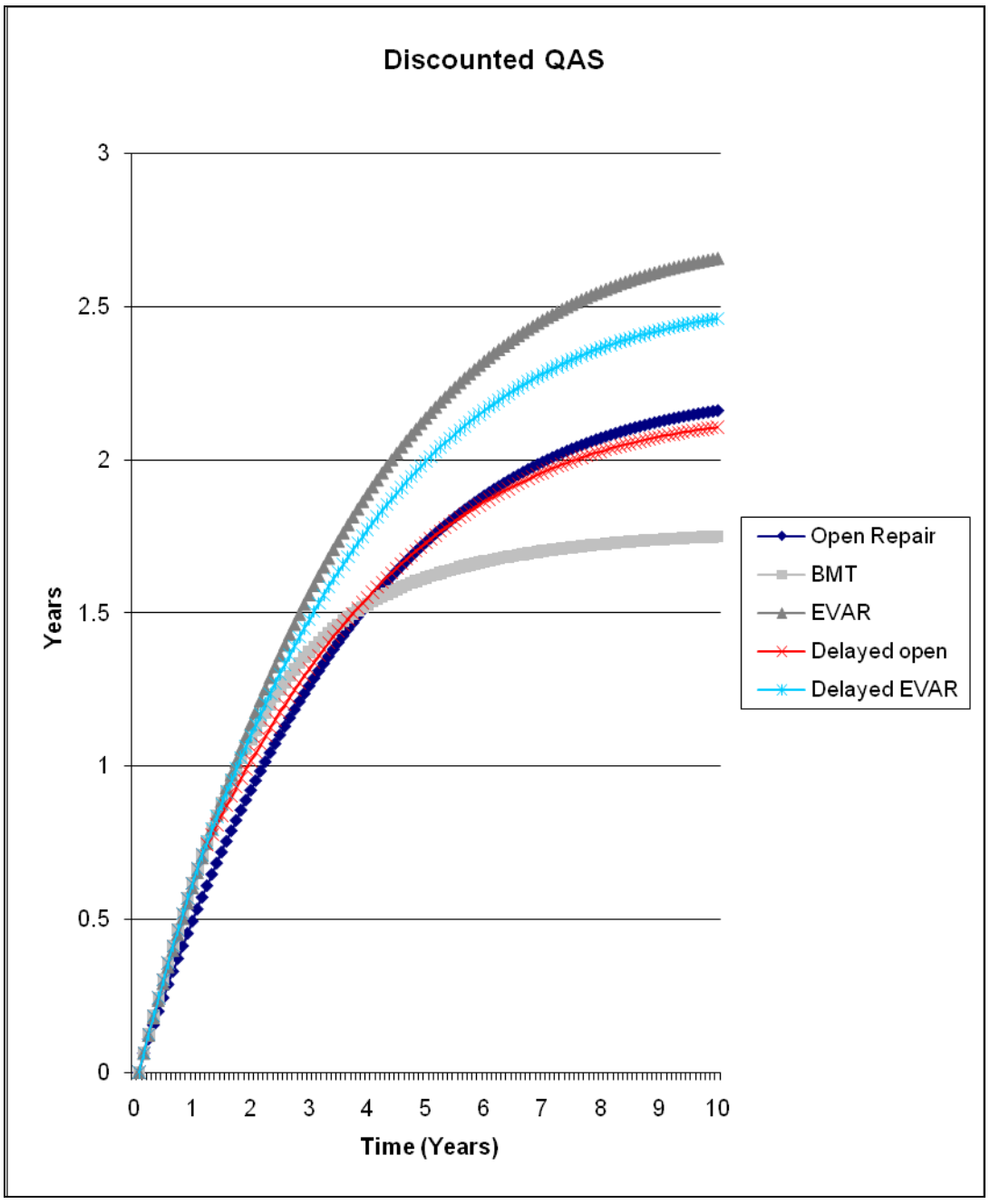


Fig 14 Cumulative reintervention rates for hypothetical EVAR 2 patient

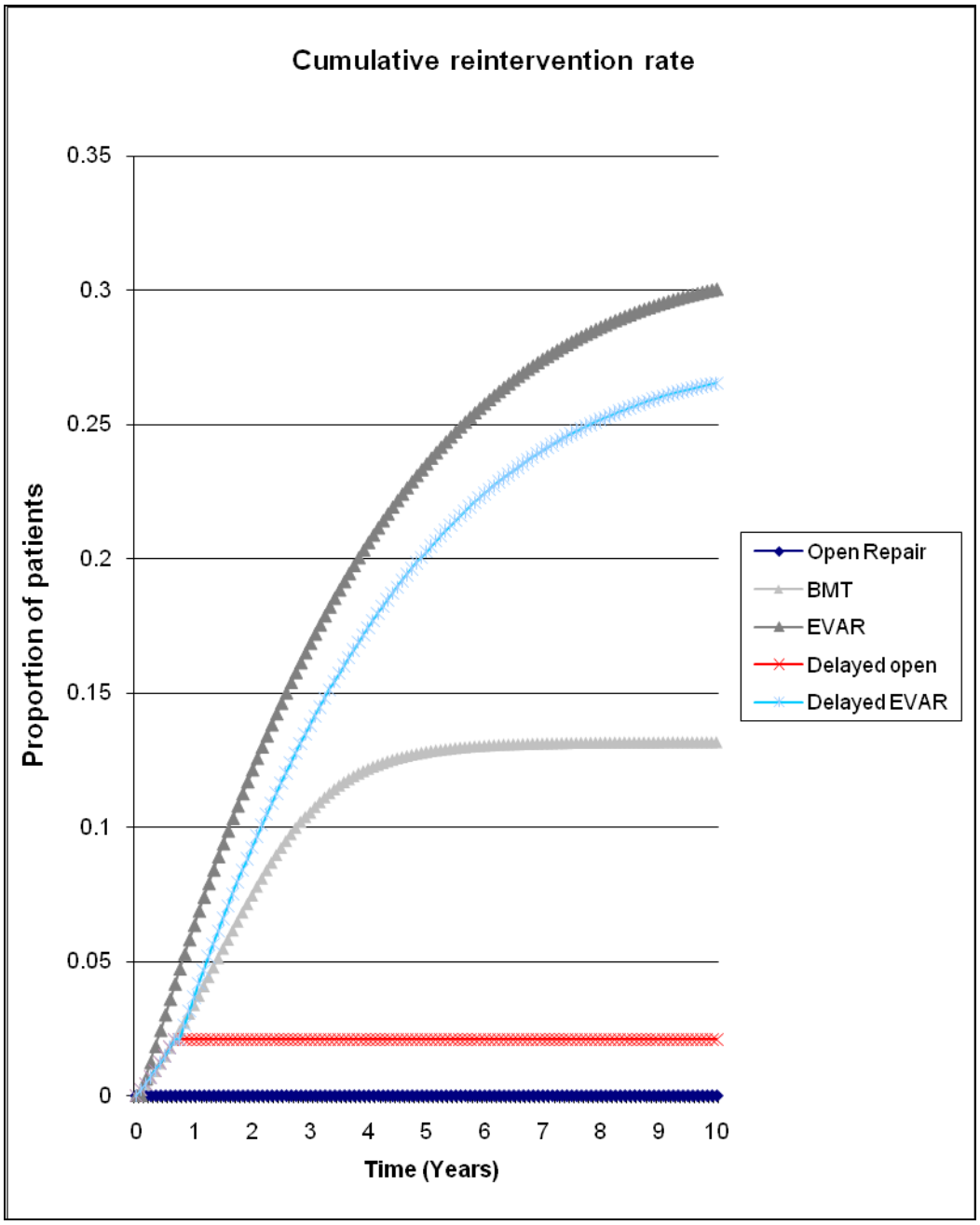


Fig 15 Cumulative aneurysm rupture rate for hypothetical EVAR 2 patient

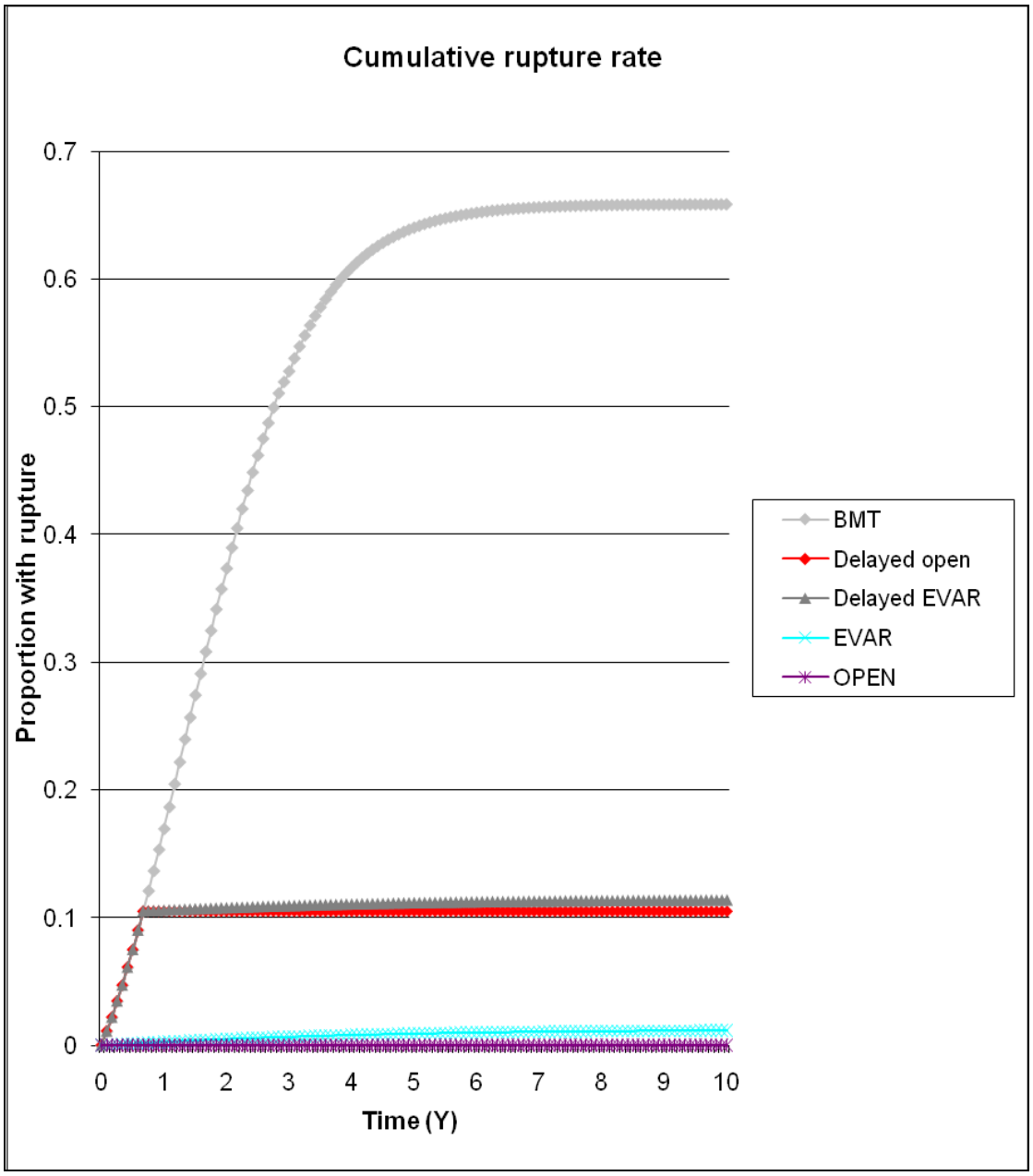


Fig 16 Aneurysm related morality rate for hypothetical EVAR 2 patient

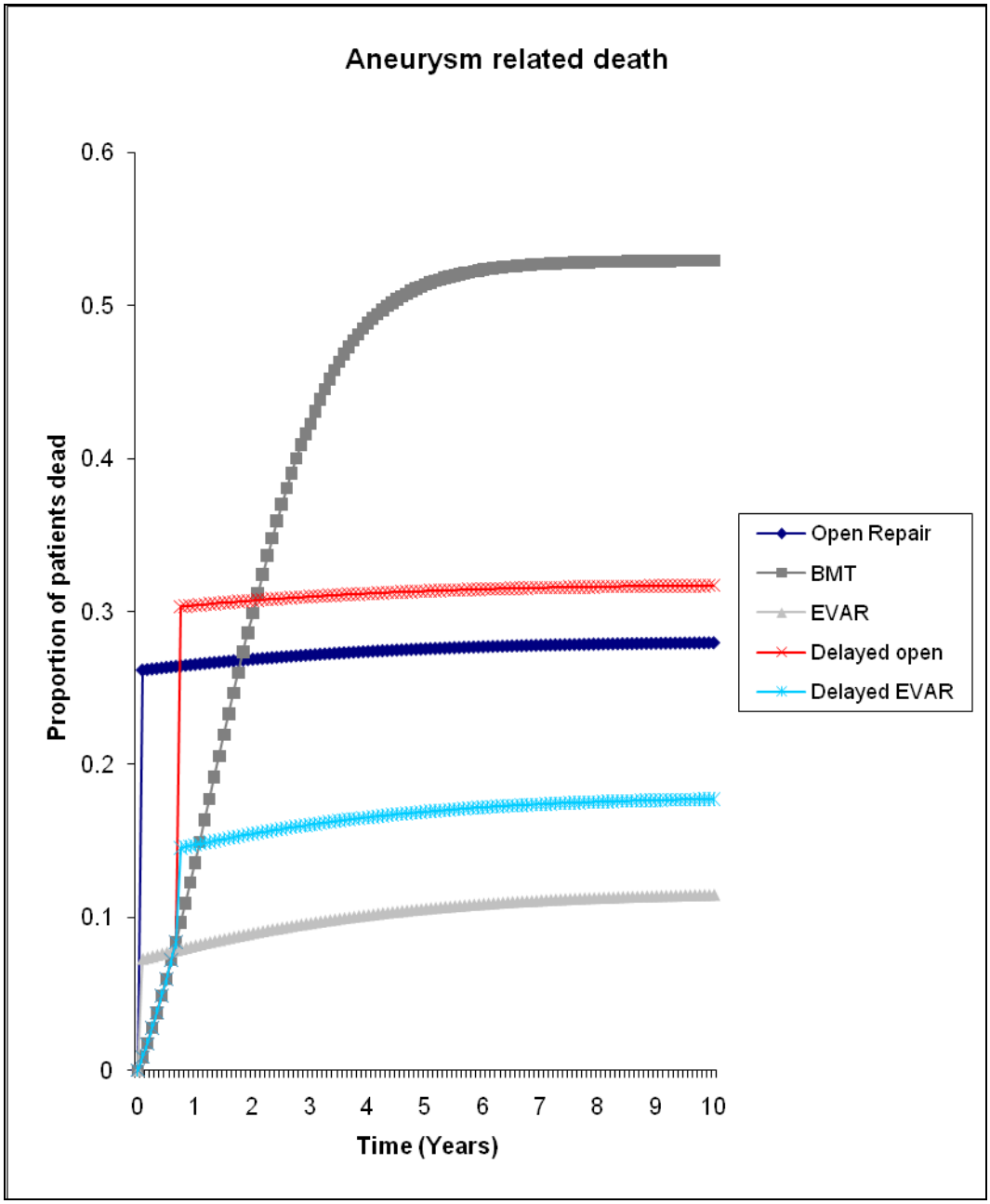


Table 46 Comparison of EVAR 2 and Markov model results.

Outcome measure	**Markov model**	**EVAR 2**
All cause mortality at 4Y, EVAR	58.7%	≈64%
All cause mortality at 4Y, delayed EVAR	64.1%	≈64%
Aneurysm related death at 4Y, EVAR	10.1%	14%
Aneurysm related death at 4Y, delayed EVAR	17.7%	19%
Cumulative delayed aneurysm rupture rate at 29 months, EVAR	0.6%	0.92%
Cumulative aneurysm rupture rate at 29 months, delayed EVAR	13.1%	13.4%
Reintervention rate at 4Y, EVAR	20.6%	20%[a]
Reintervention rate at 4Y, delayed EVAR	15.4%	≈30%[b]

[a]reintervention rate stated as number of people with at least 1 reintervention by 4Y. Reintervention rate in Markov model calculated from total number of reinterventions performed over a period of time and rate therefore assumes that 1 reintervention was performed per person.

[b]Rate stated in EVAR 2 paper is 4%. However rate listed in table above considers crossovers to EVAR arm of trial to have had a reintervention and therefore comparative rate is actually ≈30%.

Adjustment of anatomical suitability

The tabulated survival results and AAA-related mortality results for an aneurysm considered anatomically average for an EVAR are displayed in Table 47a whilst the results for a highly unsuitable aneurysm are displayed in Table 47b. As can be seen from the tables, the results for the EVAR pathway do approximate towards those generated for the open repair pathway for a highly unsuitable aneurysm.

Table 47a Average suitability

			Survival			
Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.948	0.928	0.905	0.700	0.432	8.667
EVAR	0.985	0.965	0.941	0.727	0.448	9.000
Best medical therapy	0.995	0.967	0.928	0.307	0.096	3.750
Delayed open repair	0.995	0.967	0.928	0.589	0.363	6.917
Delayed EVAR	0.995	0.967	0.928	0.616	0.379	7.333

		AAA related death			
Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.052	0.054	0.057	0.076	0.093
EVAR	0.015	0.017	0.020	0.041	0.059
Best medical therapy	0.001	0.011	0.029	0.505	0.646
Delayed open repair	0.001	0.011	0.029	0.205	0.219
Delayed EVAR	0.001	0.011	0.029	0.174	0.190

Table 47b Highly unsuitable

			Survival			
Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.948	0.928	0.905	0.700	0.432	8.667
EVAR	0.974	0.953	0.928	0.715	0.438	8.833
Best medical therapy	0.995	0.967	0.928	0.307	0.096	3.750
Delayed open repair	0.995	0.967	0.928	0.589	0.363	6.917
Delayed EVAR	0.995	0.967	0.928	0.605	0.371	7.167

		AAA related death			
Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.052	0.054	0.057	0.076	0.093
EVAR	0.026	0.029	0.033	0.057	0.078
Best medical therapy	0.001	0.011	0.029	0.505	0.646
Delayed open repair	0.001	0.011	0.029	0.205	0.219
Delayed EVAR	0.001	0.011	0.029	0.186	0.204

Assessment of parameter uncertainty within the model

To assess the parameter uncertainty within the model, a series of alternative scenarios was developed in which certain key variables were adjusted. The mean, upper limit for the 95% confidence interval and lower limit for the 95% confidence interval for each key variable were entered into the model, and the results generated were compared. A fit and healthy patient using average patient characteristics from the EVAR 1 trial was used in each case. The discount rate was set at 3%. The baseline aneurysm size was set to 6.2 cm and the threshold for intervention was set to 7.0 cm.

Operative mortality rate:

The operative mortality rate for open repair was adjusted between the upper and lower 95% confidence intervals obtained from the systematic literature review. The EVAR mortality rate was calculated using the hazard ratio of 0.28 compared to open repair. From Table 48, it can be seen that an operative mortality rate set at the lower 95% confidence interval was only associated with a discounted quality adjusted survival benefit of 0.9 months following open repair and 0.4 months following EVAR at 10 years.

Table 48

Lower 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3210	0.6902	1.9552	3.0018	3.8477	4.7816
EVAR	0.3265	0.7036	1.9972	3.0687	3.9359	4.8948
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8187	2.7424	3.4890	4.3133
Delayed EVAR	0.3247	0.6878	1.8387	2.7848	3.5505	4.3971

Mean

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0489	3.9085	4.8576
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Upper 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3130	0.6703	1.8952	2.9085	3.7275	4.6317
EVAR	0.3238	0.6968	1.9745	3.0303	3.8829	4.8228
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.7894	2.6819	3.4033	4.1998
Delayed EVAR	0.3247	0.6878	1.8283	2.7614	3.5149	4.3457

Reintervention rate:

The results of using the mean and upper and lower 95% confidence limits for reintervention rate are shown in Table 49. It can be clearly be seen that adjustment of the reintervention rate between the upper and lower 95% confidence limits made no difference to the discounted quality adjusted survival results generated by the model.

Table 49

Lower 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0488	3.9084	4.8575
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Mean value

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0489	3.9085	4.8576
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Upper 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9855	3.0489	3.9085	4.8576
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3706

Primary conversion rate:

The results of using the mean and upper and lower 95% confidence limits for primary conversion rate are shown in Table 50. Adjusting the rate of primary conversion for EVAR obviously only affected the EVAR and delayed EVAR results. However there was virtually no difference in 10 year discounted quality adjusted survival for either EVAR or delayed EVAR.

Table 50

Lower 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9852	3.0485	3.9081	4.8570
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Mean

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0489	3.9085	4.8576
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Upper 95% confidence limit

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7002	1.9857	3.0492	3.9089	4.8581
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

Anatomical suitability:

In the data entry sheet there is the option to set how anatomically suitable the particular aneurysm is for endovascular repair. This parameter is in turn set to adjust the 30-day mortality rate for EVAR, the primary conversion rate for EVAR and the reintervention rate following EVAR as these results are likely to be poorer for an

unsuitable aneurysm. The results from a highly anatomically suitable aneurysm and a very unsuitable aneurysm are shown in Table 51. From the model, a fit and healthy patient with a highly anatomically suitable aneurysm would gain 1.6 months discounted quality adjusted survival following an EVAR (1.1 months following a delayed EVAR) compared to a similar patient with a very unsuitable aneurysm for an EVAR.

Table 51

Very unsuitable

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3213	0.6906	1.9532	2.9940	3.8322	4.7535
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8184	2.7390	3.4804	4.2955

Highly suitable

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3261	0.7026	1.9936	3.0627	3.9275	4.8833
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8371	2.7812	3.5450	4.3891

Mortality rate of ruptured AAA:

An 80% mortality rate following rupture of an AAA is widely quoted in the literature. Tables 52 and 53 demonstrate the impact on discounted QAS and AAA-related death of a 70% mortality rate compared to 80% following AAA rupture. These scenarios are based upon an average patient from the EVAR 1 trial. A decrease in the mortality rate by 10% lowers the cumulative AAA-related mortality rate at 10 years by 12.0% for those patients undergoing best medical therapy. The discounted QAS is increased by 3.6 months at 10 years for the best medical therapy group. The AAA-related mortality and discounted QAS rates are also altered for the delayed intervention groups, but the magnitude is less and also dependent upon the threshold size for repair.

Table 52 Mortality rate of AAA rupture 80%

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0489	3.9085	4.8576
Best medical therapy	0.3247	0.6878	1.6916	2.1385	2.3607	2.5656
Delayed open repair	0.3247	0.6878	1.8036	2.7112	3.4448	4.2547
Delayed EVAR	0.3247	0.6878	1.8333	2.7727	3.5321	4.3705

	AAA related death				
Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.0467	0.0491	0.0518	0.0712	0.0882
EVAR	0.0154	0.0178	0.0206	0.0405	0.0579
Best medical therapy	0.0054	0.0349	0.0834	0.6329	0.6931
Delayed open repair	0.0054	0.0349	0.0834	0.1749	0.1898
Delayed EVAR	0.0054	0.0349	0.0834	0.1478	0.1632

Table 53 Mortality rate of AAA rupture 70%

	Discounted quality adjusted survival					
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.3169	0.6799	1.9242	2.9536	3.7857	4.7042
EVAR	0.3251	0.7001	1.9854	3.0489	3.9085	4.8576
Best medical therapy	0.3252	0.6904	1.7328	2.2603	2.5653	2.8667
Delayed open repair	0.3252	0.6904	1.8253	2.7494	3.4964	4.3211
Delayed EVAR	0.3252	0.6904	1.8550	2.8110	3.5837	4.4369

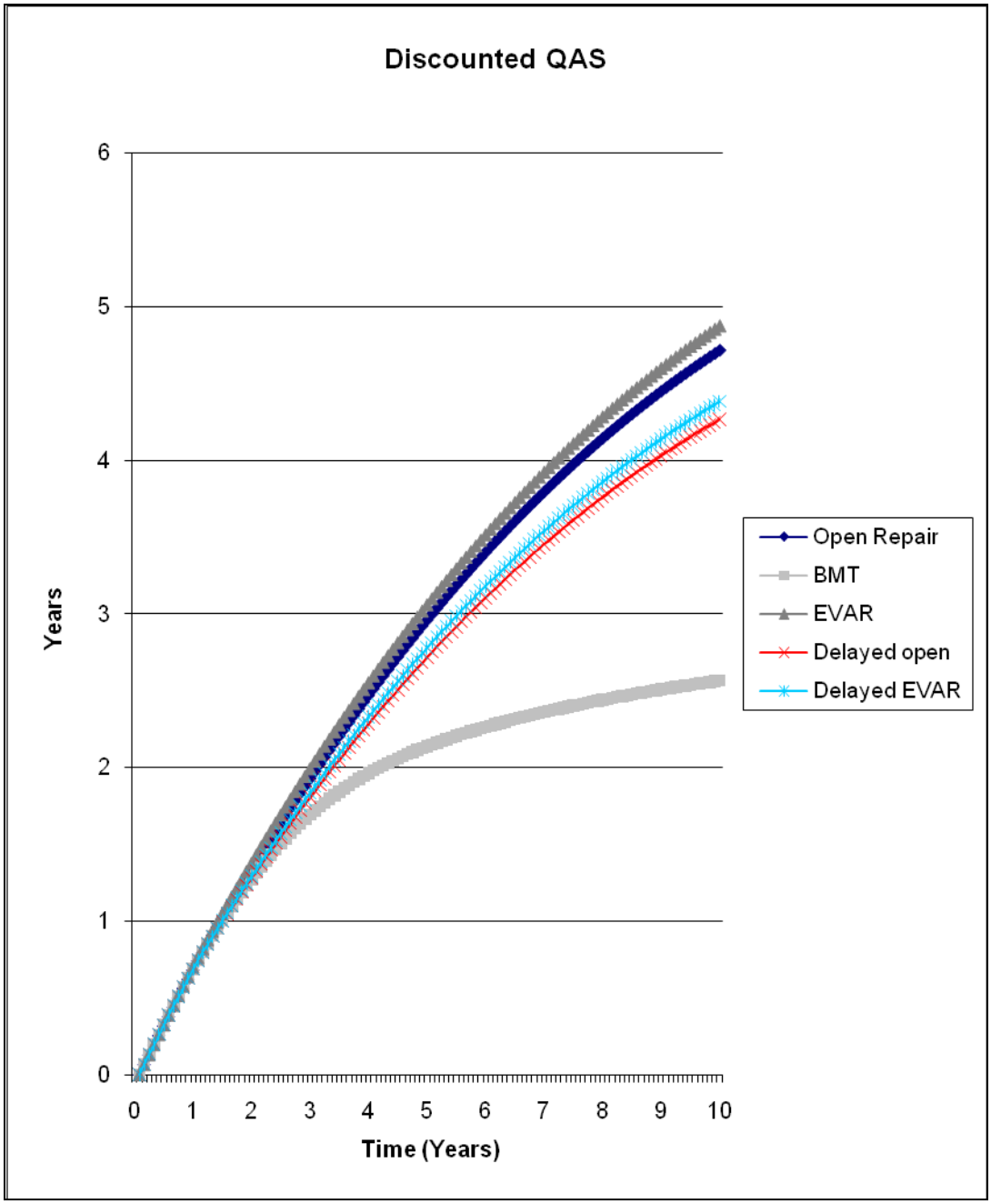
	AAA related death				
Management	1 month	6 month	1 Year	5 Years	10 Years
Open repair	0.0467	0.0491	0.0518	0.0712	0.0882
EVAR	0.0154	0.0178	0.0206	0.0405	0.0579
Best medical therapy	0.0047	0.0306	0.0730	0.5552	0.6100
Delayed open repair	0.0047	0.0306	0.0730	0.1604	0.1756
Delayed EVAR	0.0047	0.0306	0.0730	0.1333	0.1490

Aneurysm rupture rate:

On the data entry sheet, there is the option of adjusting the aneurysm rupture rates. This is because there are a variety of rupture rates quoted in the literature and because the EVAR 2 trial reported a rupture rate of 9 per 100 person years in the no-intervention arm, a rate much lower than used in the Markov model. However as already stated the no-intervention arm of the trial contained a significant number of crossovers to the EVAR arm. The high crossover rate coupled with the relatively small number of patients in the trial means that the natural history of the untreated aneurysm cannot be reliably determined from the EVAR 2 trial. Despite this, the model user has the option of using a lower rupture rate to reflect that seen in the EVAR 2 trial.

The results using aneurysm rupture rates established from the literature review and using these rupture rates multiplied by a hazard ratio of 0.75 are displayed in Fig 17 and 18. The scenarios are again based on an average EVAR 1 trial patient. Lowering the aneurysm rupture rate by 25% was associated with an improved discounted QAS in the best medical group of 2.7 months and a reduction in cumulative aneurysm rupture rate of 3.7% at 10 years. Smaller improvements occur for the delayed open repair and delayed EVAR groups. If patient characteristics for the average EVAR 2 patient are entered into the model then the 10 year discounted QAS is only improved by 1.8 months by a 25% reduction in rupture rates.

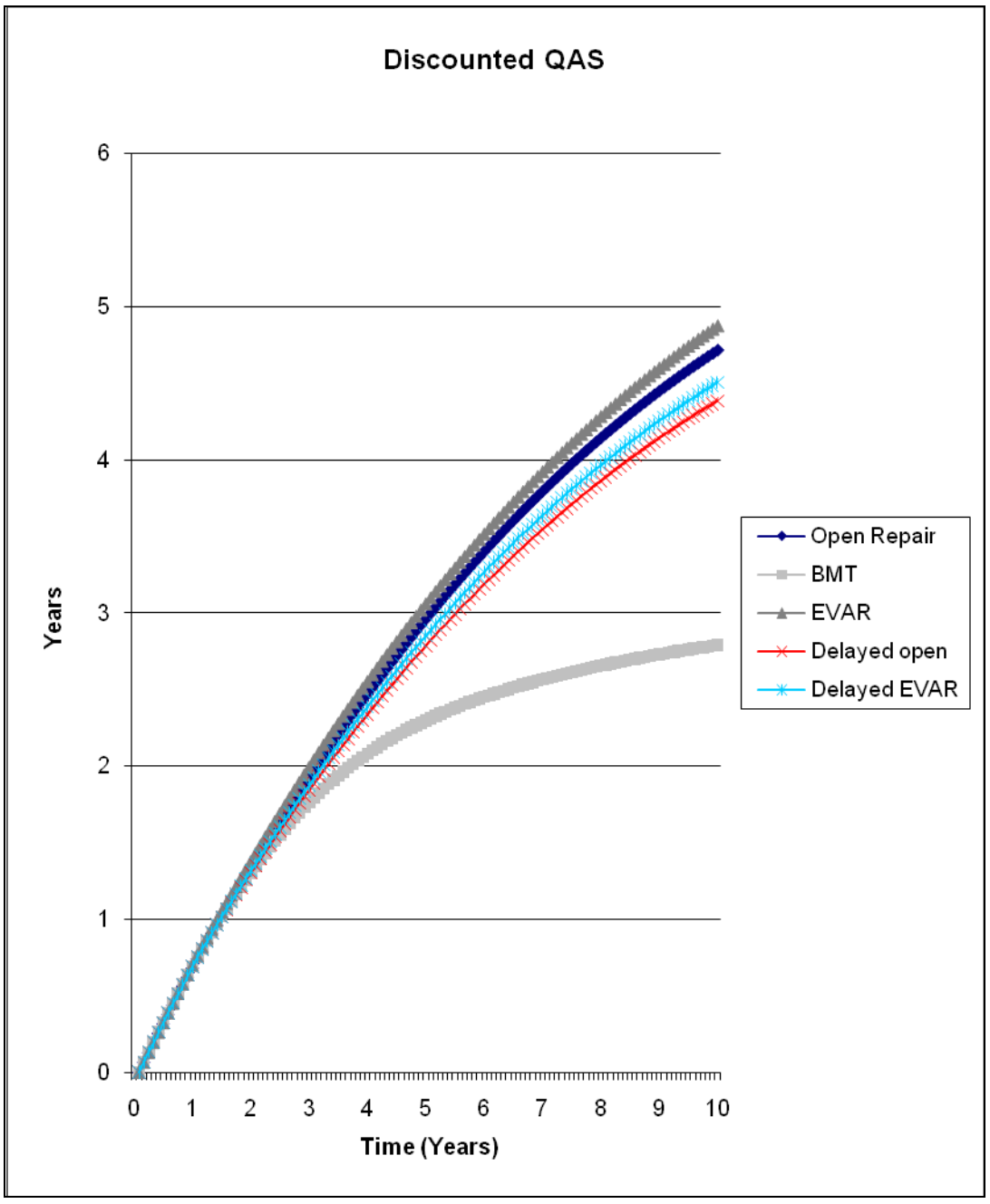
Fig 17 Discounted QAS using evidence based rupture rates (EVAR 1type patient)



Cumulative aneurysm rupture rate

Management	1 month	6 month	1 Year	5 Years	10 Years
EVAR	0.0003	0.0015	0.0030	0.0132	0.0221
Best medical therapy	0.0068	0.0436	0.1042	0.7884	0.8593
Delayed open repair	0.0068	0.0436	0.1042	0.1478	0.1478
Delayed EVAR	0.0068	0.0436	0.1042	0.1559	0.1636

Fig 18 Discounted QAS with evidence based rupture rates reduced by 25% (EVAR 1 type patient)



Cumulative aneurysm rupture rate

Management	1 month	6 month	1 Year	5 Years	10 Years
EVAR	0.0003	0.0015	0.0030	0.0132	0.0221
Best medical therapy	0.0051	0.0329	0.0791	0.7094	0.8271
Delayed open repair	0.0051	0.0329	0.0791	0.1129	0.1129
Delayed EVAR	0.0051	0.0329	0.0791	0.1214	0.1294

Repair threshold:

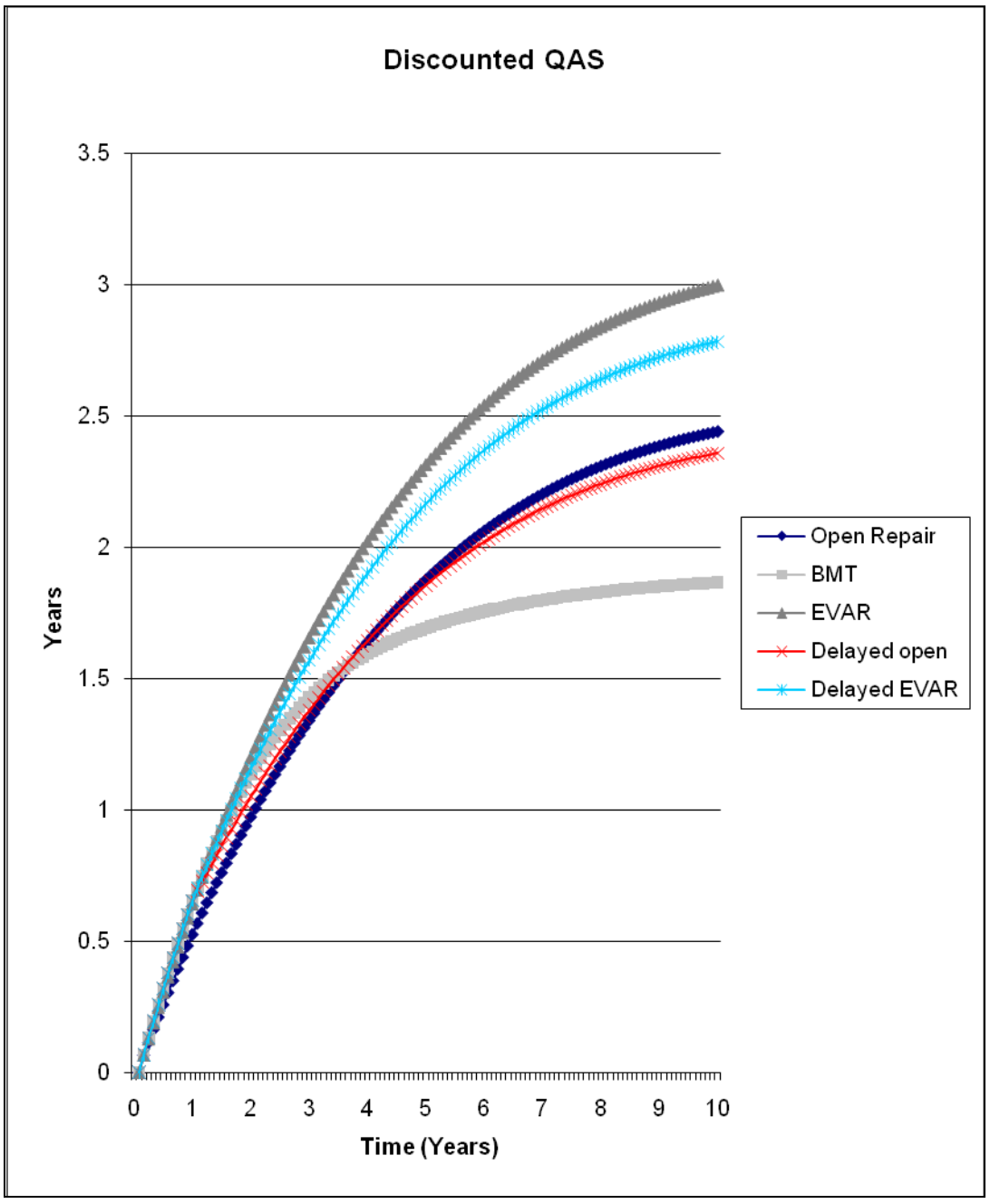
Alternative scenarios to assess the impact of adjusting the threshold at which intervention is carried out were also considered. This time average patient characteristics of an EVAR 2 patient were inputted into the model, with a baseline aneurysm diameter of 6.5cm. The discounted quality adjusted survival curves and tables of discounted QAS rates associated with delayed intervention at 7 cm and 8 cm are displayed in Figs 19 and 20. From the tables and figures it can be seen that adjusting the intervention threshold at which the aneurysm is treated does significantly alter discounted quality adjusted survival for delayed intervention, either EVAR or open repair.

In addition the tables and figures can be used to calculate the discounted quality adjusted survival for each management strategy at any given time point. This then has important management implications. For example, in these scenarios, best medical therapy is associated with a superior discounted QAS compared to EVAR for the first 7 months, and a superior discounted QAS up to 22 months compared to open repair. Therefore the patient will need to live for at least 7 months to gain any benefit from an endovascular procedure and at least 22 months to gain any benefit from an open repair. The survival curves and tabulated results generated from the model give the median survival for an individual patient managed by each of the five options. If endovascular repair is delayed until a threshold size of 7 cm is reached then the patient will need to live for 14 months to gain any benefit from the procedure compared to best medical therapy, but will improve the median survival by 15 months. If an open repair were undertaken at a threshold of 7cm, the patient would not gain any survival advantage until 2Y, and with equal median expected survivals for both strategies of 23 months, the majority of patients would not live long enough to gain any benefit.

If EVAR is delayed until an aneurysm diameter of 8 cm is reached then the patient requires a life expectancy of 3Y and 1 month before any benefit of the procedure is derived. In addition, at an intervention threshold of 8cm immediate open repair is associated with a superior discounted QAS compared to delayed EVAR after survival to 43 months. However from the survival table and curves generated for such a scenarios, (Fig 20), the probability that a patient is alive at 4Y following an open repair is approximately 40%, and therefore only a minority of patients would benefit

from the increased discounted QAS with an open repair over a delayed EVAR in the long term.

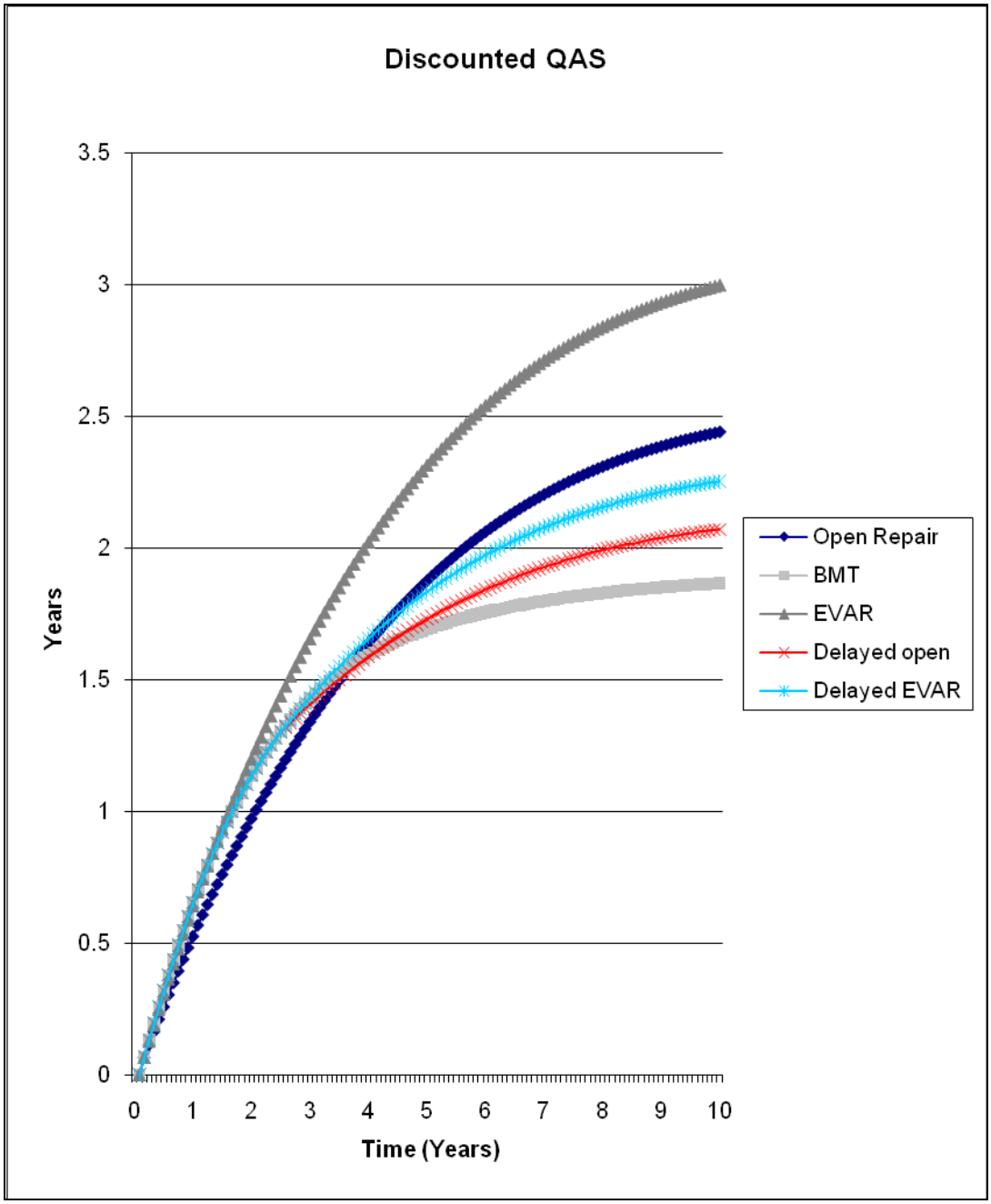
Fig 19 Threshold of 7 cm



Discounted quality adjusted survival

Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.2446	0.4947	1.2632	1.7326	1.9943	2.1623
EVAR	0.2876	0.5960	1.5345	2.0984	2.4078	2.6025
Best medical therapy	0.3012	0.6129	1.3441	1.5757	1.6608	1.7082
Delayed open repair	0.3012	0.6129	1.2971	1.7150	1.9480	2.0975
Delayed EVAR	0.3012	0.6129	1.4619	1.9723	2.2525	2.4289

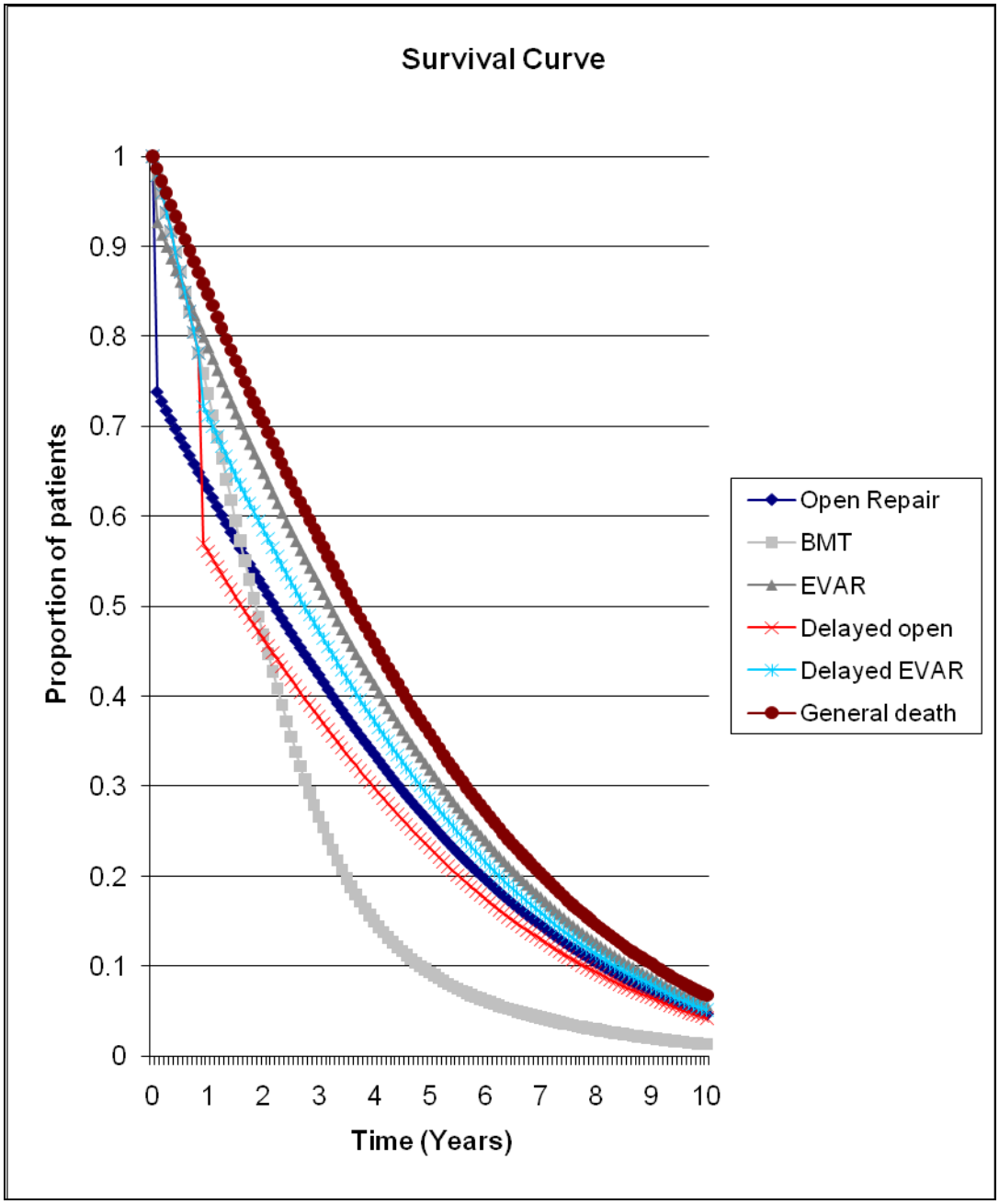
Fig 20 Threshold of 8 cm



Discounted quality adjusted survival

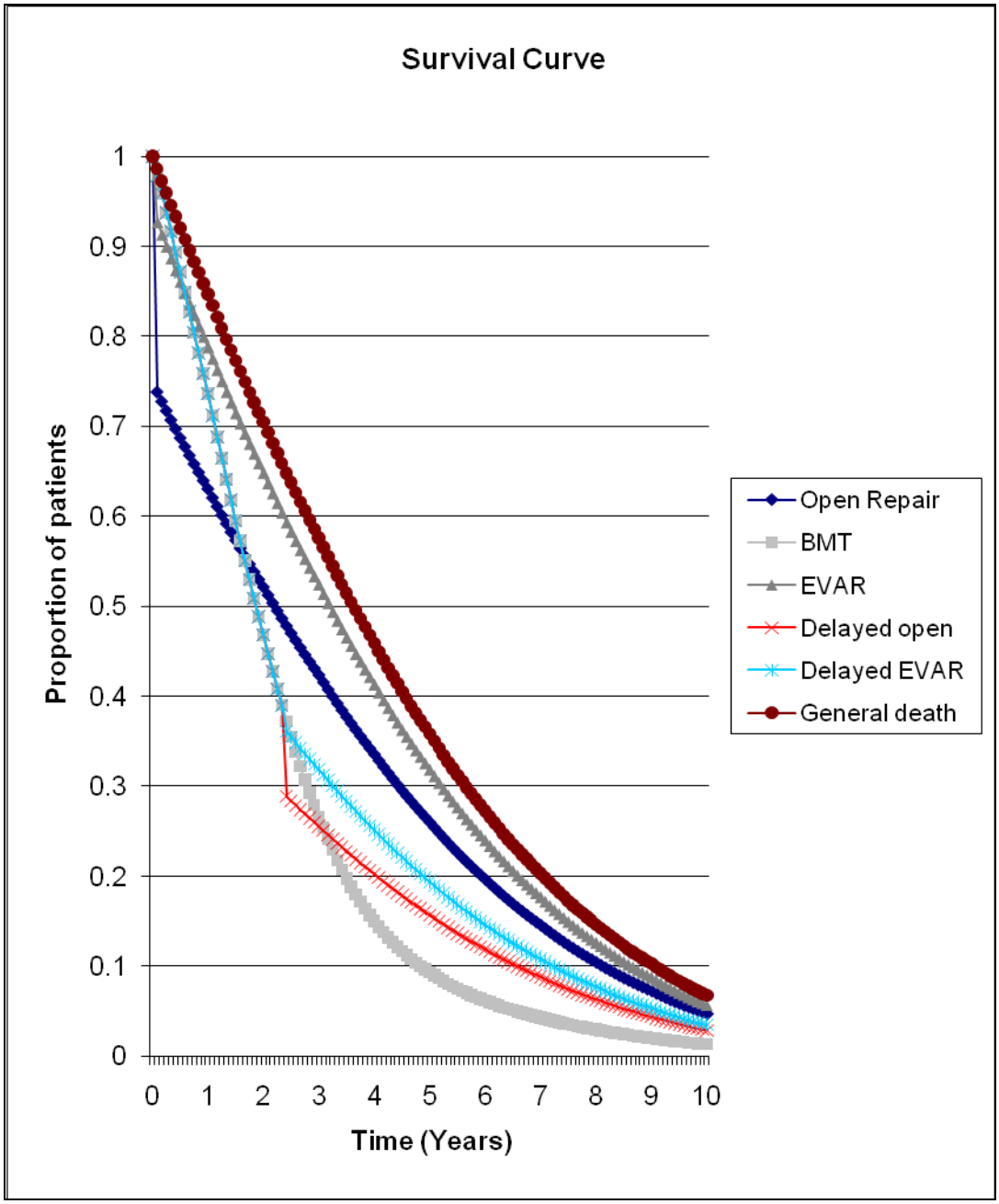
Management	6 month	1 Year	3 Years	5 Years	7 Years	10 Years
Open repair	0.258	0.526	1.341	1.877	2.204	2.442
EVAR	0.307	0.642	1.657	2.317	2.716	3.001
Best medical therapy	0.319	0.653	1.428	1.692	1.799	1.866
Delayed open repair	0.319	0.653	1.407	1.731	1.928	2.072
Delayed EVAR	0.319	0.653	1.433	1.835	2.079	2.253

Fig 21 Survival results for intervention threshold 7 cm



	Survival					
Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.738	0.696	0.649	0.314	0.078	2.583
EVAR	0.927	0.872	0.811	0.384	0.092	3.667
Best medical therapy	0.982	0.886	0.760	0.113	0.021	1.917
Delayed open repair	0.982	0.886	0.577	0.280	0.069	1.917
Delayed EVAR	0.982	0.886	0.732	0.347	0.083	3.167

Fig 22 Survival results for intervention threshold of 8 cm



	Survival					
Management	1 month	6 month	1 Year	5 Years	10 Years	Median
Open repair	0.7379	0.6870	0.6304	0.2602	0.0474	2.1667
EVAR	0.9139	0.8478	0.7749	0.3095	0.0542	3.0833
Best medical therapy	0.9792	0.8721	0.7364	0.0930	0.0130	1.8333
Delayed open repair	0.9792	0.8721	0.7364	0.1570	0.0286	1.8333
Delayed EVAR	0.9792	0.8721	0.7364	0.1902	0.0335	1.8333

Discussion

Until the publication of the DREAM and EVAR and OVER trials, there had been a lack of level one evidence comparing the efficacy and safety of EVAR to open repair. Early publications from population registries (RETA and EUROSTAR) and case series had suggested a lower operative mortality, lower perioperative complications and reduced requirement for hospital beds and critical care for EVAR compared to open repair. These early findings have been supported by the results from the three RCTs listed above and medium term outcome data from the EVAR and DREAM trials has recently been published in addition. The results of the randomised controlled trials represent a broad spectrum of patients with abdominal aortic aneurysms and despite *post hoc* analyses of sub-groups of patients, it can be difficult to apply this evidence base to an individual patient. The EVAR 1, DREAM and OVER trials compared open repair to EVAR in a group of 'healthy' patients and EVAR 2 compared EVAR to best medical therapy in 'unhealthy' patients. However, the majority of patients presenting to a vascular surgeon do not fall neatly into one category or the other and it is in this group of patients that it is most difficult to apply the RCT evidence.

For the Markov decision analysis model, three different modalities of treatment were considered; EVAR, open repair and best medical therapy. The option of delaying either EVAR or open repair until a threshold size for aneurysm diameter was also considered thereby creating five different management pathways. The model contained a data input sheet allowing patient and aneurysm specific variables to be entered so that the results generated were relevant to that particular patient. The model generates both tabulated and graphical results of survival, quality adjusted survival, discounted QAS, aneurysm and non-aneurysm mortality rates cumulative reintervention and cumulative rupture rates for each management option.

One implication for the model is that the tabulated and graphical results can be used to aid the management of a patient with an abdominal aortic aneurysm in a clinical setting. The vascular surgeon can input the patient and aneurysm specific parameters into the model and see the likely outcome for that particular patient in terms of operative mortality, likely survival and discounted quality adjusted survival,

aneurysm and non-aneurysm related mortality, and cumulative rupture and reintervention rates associated with each management option. The surgeon will then be able to explain the different management options to that particular patient and show that patient graphically what is likely to happen to them over the following 10 year period. Where the management options produce similar discounted QAS results, the aneurysm rupture rate and cumulative reintervention rates are likely to play a significant part in the consent process as certain management options are associated with higher rates of subsequent rupture and reintervention.

In addition, by using the model, it is possible for the surgeon and patient to quickly assess the impact of making adjustments to the management process. However the transition probabilities used in the model that are not patient specific are all evidence-based and the model has been validated against the EVAR 1 and 2 trial results. The parameter uncertainty has been studied above by using values from the upper and lower 95% confidence intervals and adjustments to reintervention rate, primary conversion rate and anatomical suitability have little impact on the discounted QAS. Changes to the reintervention rate and anatomical suitability however will obviously alter the likely cumulative reintervention rate generated by the model. In addition adjustment of the operative mortality rate around that expected for that particular patient again has been shown to have little impact on discounted QAS over a 10 Y period.

The results generated by the model are mainly sensitive to patient specific variables. These include age (which affects operative mortality rate and age-related mortality rate), patient specific operative mortality rate (a high operative mortality rate is associated with reduced discounted QAS but the high rate is linked to a high general mortality rate which will also decrease discounted QAS. The results generated for the delayed intervention pathways are also sensitive to the threshold size at which the intervention is performed. This has important clinical consequences; the results generated for a high-risk patient with a reduced life expectancy can be assessed using a variety of threshold sizes to calculate the time-point at which intervention that is expected to be associated with the greatest discounted QAS for that patient.

The model is also moderately sensitive to changes in mortality rate following aneurysm rupture (a reduction in the mortality rate from 80% to 70% is associated with a reduction in cumulative aneurysm rupture rate of 8.3% over 10 years and an increase in discounted QAS of 3.6 months over the same period. This finding implies that even modest improvements in the management of a patient with a ruptured AAA could result in enhanced discounted QAS. However in clinical practice there has been little change in ruptured AAA survival over the last 20 years.

For the base-case scenario for the EVAR1 type patient, the model generated similar results to the randomised controlled trial data. A review of large (>200 patients) case series was conducted to compare the results of the model to results achieved in everyday practice. The case series reported a 30-day mortality rate of 2.5% compared to 1.2% from the model. This difference could be explained by the significant heterogeneity of the case series data as most centres were reporting results on a case-mix of EVAR type 1 and 2 patients and consequently the results would be expected to be inferior to those from RCTs treating only fit and healthy patients. The overall survival results from the model are also similar to those reported in routine practice with the EUROSTAR registry reporting a 5Y overall survival rate of 71.7% compared to 73% from the Markov model. From the model the difference in survival rates between open repair and EVAR converge over time, an observation also reported from the EVAR 1 trial,[48] DREAM trial,[21] Schermerhorn et al[83] and the recent HTA report.[142]

In addition if one compares the rates of AAA related death (~5% over 10 years from the model) against the case series data (~4% over 10 years), then once again the model appears to generate acceptable results compared to routine practice. These results are similar to those reported by the recent HTA report, who reported rates of 0.3% per year.[142] Cumulative intervention rates generated by the model suggested a ten year rate of 62% compared to an extrapolated rate of 74% from the case series. Once again the difference in case mix and difference in management practices between different centres could account for this small difference.

There are a number of limitations associated with the use of this model. The model is limited by the availability of high quality data that is necessary to generate the

required transition probabilities. These probabilities were established from a systematic literature review, but there were a number of limitations noted from the review that generated a few assumptions and uncertainties during model development.

A major limitation of the systematic review relates to the heterogeneity of the study population and unknown criteria for patient selection for EVAR, amongst the NRCT and case series studies. There are two major issues in this respect, the size of aneurysm treated, which determines the risk of rupture in the untreated condition and the case mix of patients regarding age and co-morbidity, which affects the risks associated with open surgical treatment.

Current evidence from the UK Small Aneurysm Trial suggests that surgical intervention is worthwhile if the aneurysm is at least 5.5 cm diameter or greater than 4.5 cm and has increased by 0.5 cm in the 6 months prior to intervention. In many of the reported studies, the inclusion criteria included aneurysms of less than 5.5 cm in diameter. Furthermore, in studies where inclusion criteria are not defined, there is either no documentation of baseline aneurysm size, or the range of aneurysm size extends below 5.5 cm. The expected rupture rate of aneurysms of less than 5.5 cm is in the order of 0.5% per year so that the risks and success rate that would be acceptable are very different from those for patients with larger aneurysms. The data presented do not allow adequate subgroup analysis to determine whether safety and efficacy are related to aneurysm size.

There are also other differences between study populations, with some studies including a significant proportion of patients in whom surgical treatment would be expected to carry high mortality. In those patients with a large aneurysm, co-morbidity or previous abdominal surgery that would add significantly to the risks of conventional treatment, the acceptable risks for EVAR may be considerably higher.

The EVAR 1, DREAM and OVER studies are randomised controlled trials that have addressed a number of these issues. The problem of heterogeneity of the study population was minimised by randomly allocating patients to EVAR or open repair. This resulted in two groups that were well matched, therefore allowing more accurate comparisons between the two groups, as they only differ in terms of treatment

received. All patients in these trials were deemed sufficiently medically fit and anatomically suitable to undergo either procedure. Furthermore, patients were only included in the study if the baseline aneurysm size was 5.0 cm or greater (DREAM) or 5.5 cm or greater (EVAR 1).

Another important consideration in interpreting these results is the issue of operator experience and advances in device technology. Studies included in this review were restricted to papers published from the year 2000 onwards, but the recruitment period in some papers precedes this date by five or more years. Consequently the participants included in this review are undergoing a procedure that may have been carried out by an operator with limited experience in a relatively new technique (EVAR was first introduced in 1991). Furthermore, the level of operator experienced was poorly documented in virtually all of the included studies and the effect of a learning curve for EVAR has been well reported. The level of operator experience was again addressed in the RCTs, as only experienced surgeons and interventional radiologists were included. For the EVAR trials, before being considered for participation in the trial, a new centre must submit outcome data on 20 cases to an independent register (RETA).

There have been substantial improvements in endovascular device technology in recent years. The 'first-generation' stents were home-made tube devices constructed using ePTFE graft material and standard endovascular stents. These are no longer used due to the high level of complications associated with these devices. Further improvements of endovascular prostheses have led to the development of modular bifurcated and aorto-uniiliac devices. These developments coupled with advances in device-delivery systems, have led to a lower incidence of procedural and post-procedural complications. As a consequence, some of the long-term safety and efficacy data relates to devices that are no longer used, whilst there is little medium to long-term data on devices in current usage.

From the RCTs there is a clear reduction in 30-day mortality rate with a mean mortality rate of 3.7% after open repair and 1.1% after EVAR, (OR 0.27, 95% CI 0.15 to 0.51). This result is supported from the findings of the NRCT studies and the low mortality rate from EVAR is in agreement with that reported from published case

series. However, both the EVAR 1 and DREAM studies have demonstrated that during medium-term follow-up, there is no difference in total mortality between EVAR and open repair, and the reduction in aneurysm-related mortality that persists following EVAR is accounted for by the initial lower perioperative mortality rate. These findings are in agreement with results generated by the model, as there is convergence of the survival curves for open repair and EVAR, but the AAA-related mortality curves remain parallel after the first month.

The above would suggest that although initially superior at 30-days, long term there is no survival advantage of EVAR over open repair and in fact the longevity of the EVAR technique remains to be proven. There are several possible explanations to account for the overall higher mortality rate during the first year following EVAR. Open repair may have precipitated the death of frail patients who would have died during the coming year. However it is possible that EVAR is associated with a higher rate of late mortality by failing to prevent late ruptures or by causing complications related to the significantly higher secondary intervention rate. These last two hypotheses are supported by the results from the model as there is both an ongoing risk of late rupture and a significant rate of reintervention following the EVAR or delayed EVAR pathways.

A certain degree of caution needs to be used when interpreting the long-term results generated by the model, particularly for late AAA rupture and reintervention results. There are results from randomised and non-randomised controlled trials that suggest there is an ongoing reintervention requirement and ongoing late rupture rate post EVAR, but the follow-up from such studies is only for approximately 3-4 years at present. The long-term results from the model assumes that the reintervention rate and late rupture rate continue at similar levels beyond the three to four year mark as there is no data at present to support or refute this assumption. It may be that the rate of reintervention declines after a few years, in which case the results from the model would tend to underestimate the benefits of EVAR. However it may be that the rate of reintervention and late aneurysm rupture rate both increase in the long-term, in which case the results from the model would overestimate the benefits of EVAR.

A further limitation of the model is that it uses average rates of expansion and rupture. In practice the expansion and rupture rates are probability distributions and there will be some patients who expand rapidly and rupture prior to their next scan and others who have no change in size or rupture for many years. In addition the decision to delay treatment is not a"once and for all" decision but in reality is reviewed after each scan. Consequently the results of the delayed intervention are limited by the points discussed above.

Nonetheless the medium and long-term results from the model demonstrate that there is a clear need for complete and accurate follow-up for the life of the patient following EVAR.

The technique of EVAR was initially established to treat high-risk surgical candidates for whom open repair would be associated with very significant mortality and morbidity. The EVAR 2 trial addressed this issue by comparing EVAR to best medical therapy in a group of unfit patients. The 30-day mortality result of EVAR in unfit patients was 7.9%, (compared to 1.7% in fit patients). However the rate of aneurysm-related mortality in the no intervention group was found to be significantly lower than that anticipated at the start of the study.

This significantly lower aneurysm-related mortality in the no-intervention group coupled with a higher 30-day mortality post EVAR and high rates of complications, (43% by 4 years) and secondary intervention, (11.5 per 100 person years) negated any potential benefit of EVAR over no intervention in unfit patients. Analysis by intention to treat demonstrated no significant difference in either aneurysm related mortality or total mortality during the follow-up period, leading the trial committee to conclude that there was no survival benefit following EVAR compared to no intervention in unfit patients.

However there are a number of considerations to be made when interpreting these results. It is possible that there may be an element of confounding due to the high rate of crossover of patients on best medical therapy to exclusion by EVAR or surgery. Over twice as many patients underwent late aneurysm repair as died of aneurysm related causes and many of these patients had symptomatic or enlarging aneurysms

that would have increased the aneurysm related mortality had such crossovers not occurred. Therefore the model was designed to include a delayed EVAR management option that would reflect the no intervention arm of EVAR 2, in addition to a best medical therapy option (truly no intervention except for treatment of a ruptured aneurysm).

The model that has been developed is designed as a clinical decision aid and does not consider the issue of cost. In the future the model could be adapted to include cost data to develop a cost-effectiveness model. Such an economic model could help guide policy development and highlight key areas for further research.

Conclusions

An easy-to-use computer model has been developed that will provide meaningful information relating to risks and benefits that could assist in shared decision making and obtaining informed consent from patients with aneurysms, and could help to guide policy decisions in respect to patient selection for EVAR.

APPENDIX 1 Decision analysis trees

Fig 23 Decision tree for Open repair

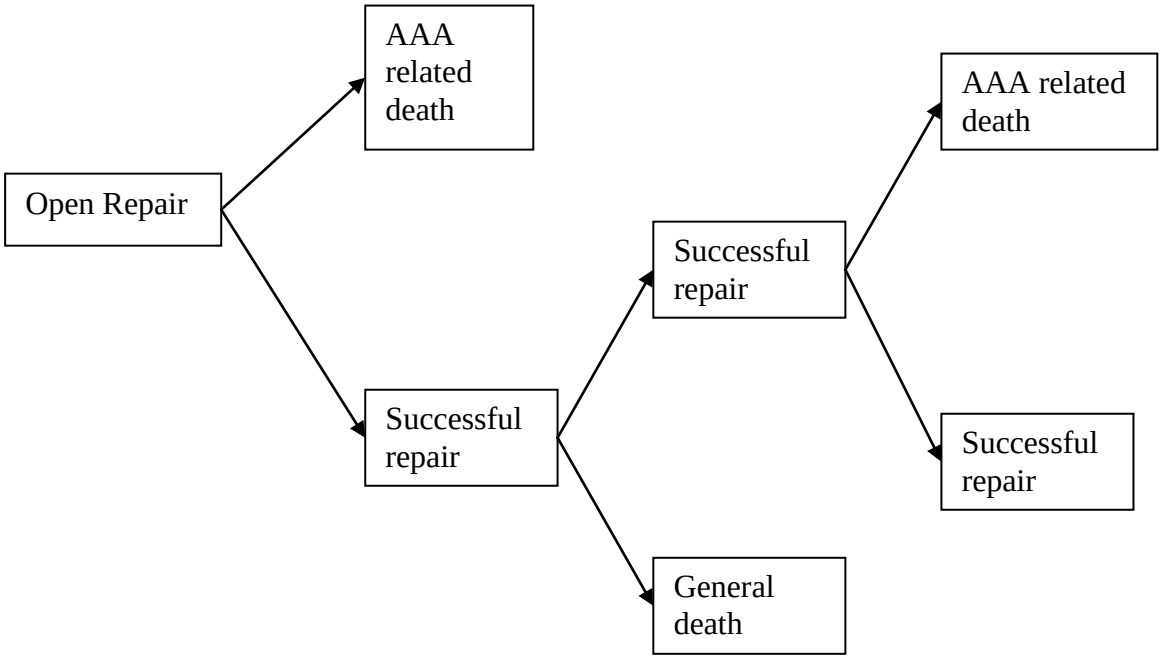


Fig 24 Decision tree for best medical therapy

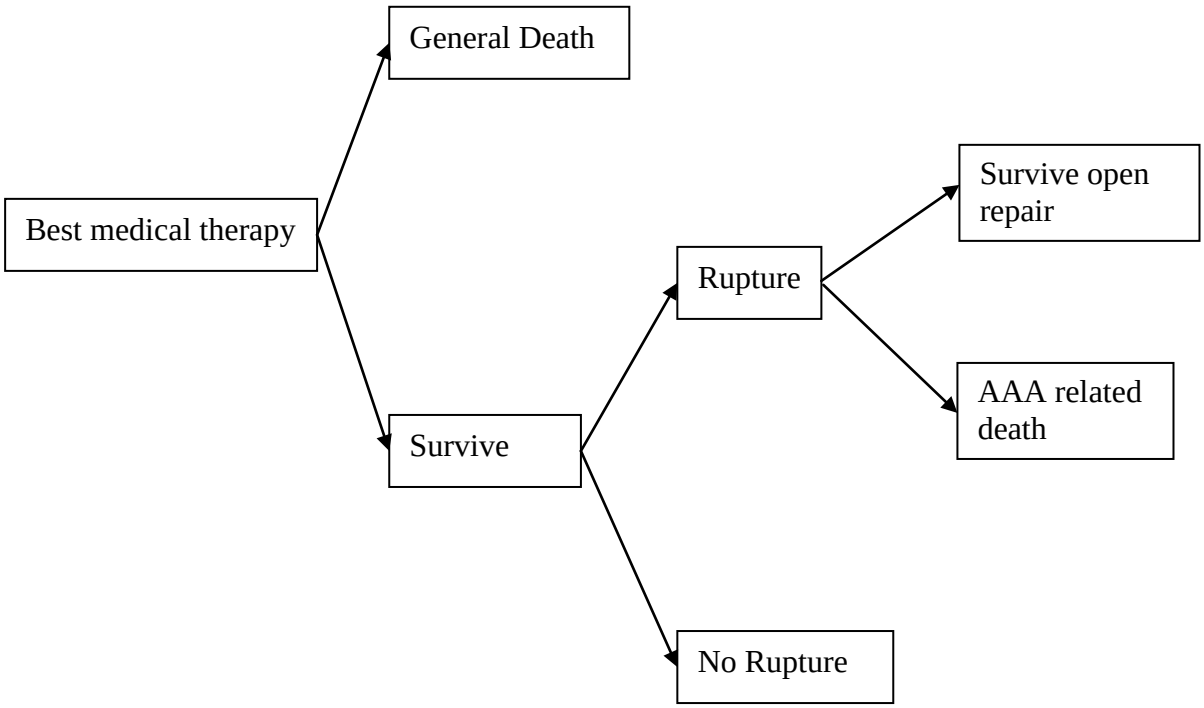


Fig 25 Decision tree for EVAR

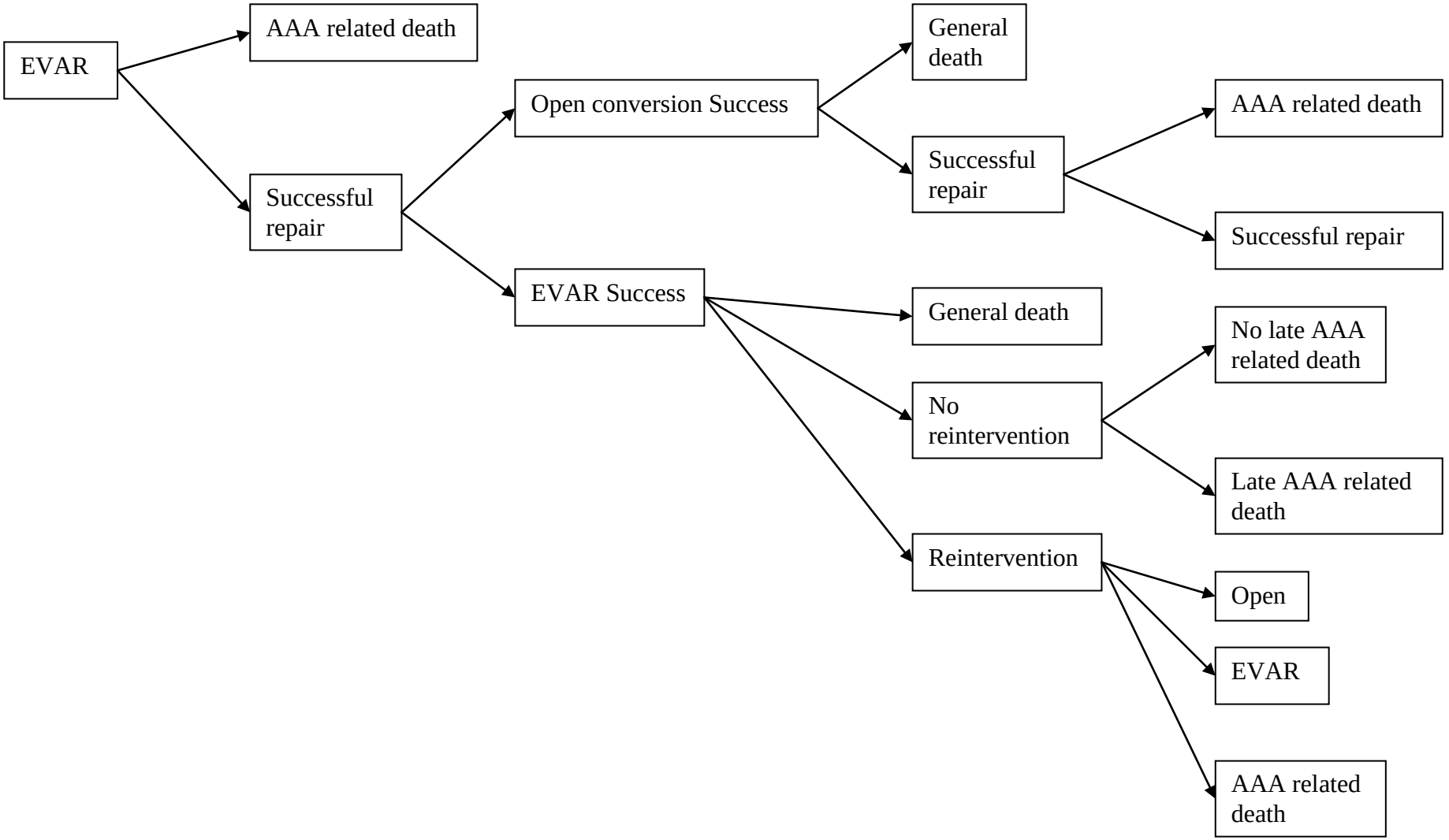
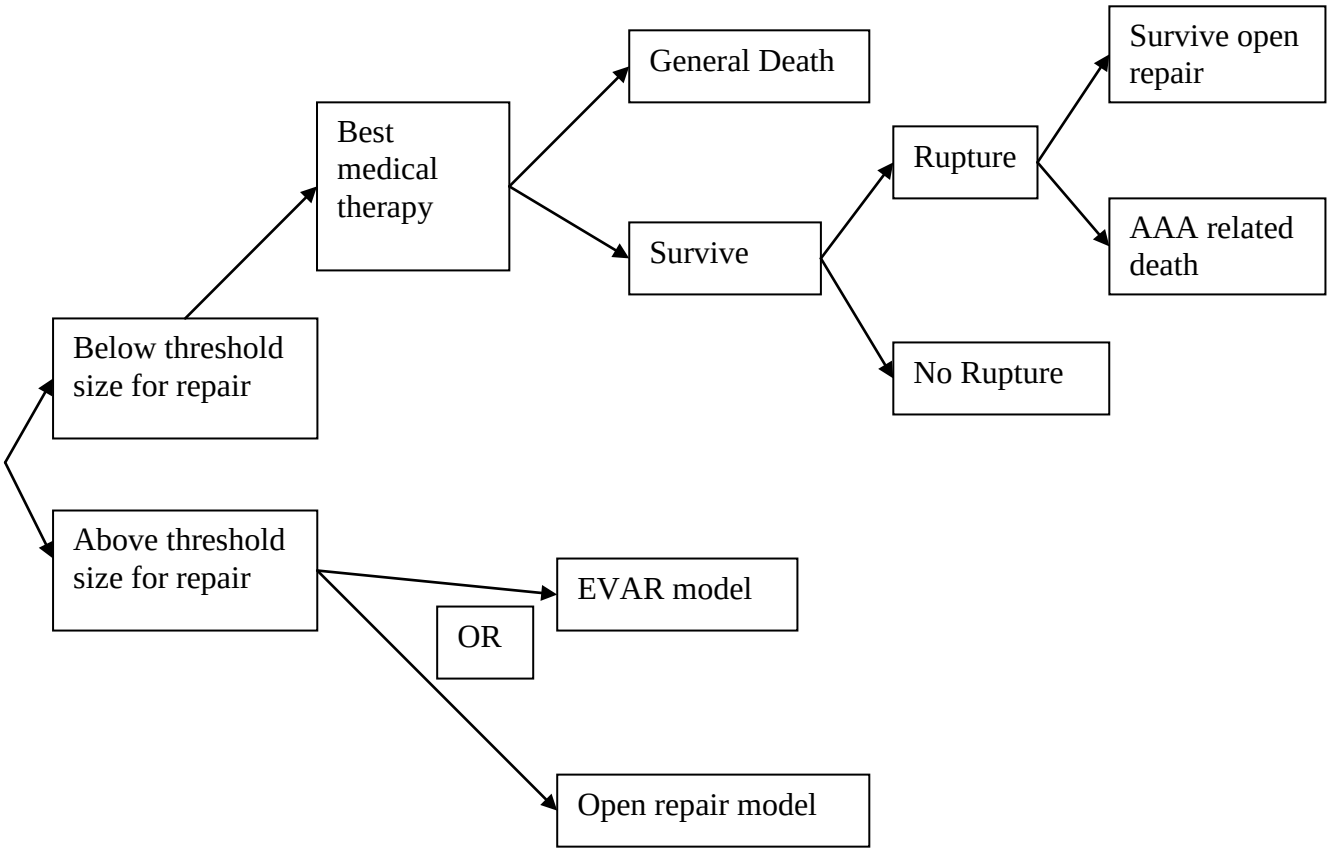


Fig 26 Decision tree for delayed intervention



Appendix 2 Risk models for 30-day mortality rate for open repair

Fig 27 Bayesian risk model for 30-day mortality rate for open repair

Risk Factor	Criteria	Likelihood ratio
Age	< 71 Years	0.469
	71-75 Years	1.001
	76-80 Years	1.169
	>80 Years	2.552
Gender	Male	0.972
	Female	1.214
Lowest Blood Pressure	<81	1.294
	81-100	1.455
	101-110	0.475
	111-130	0.882
	131-140	1.236
	141-150	0.437
	151-160	1.573
	>160	1.001
ECG	Non-normal result	1.326
	Normal	0.783
Cardiac History	No history	0.846
	Positive history	1.176
White cell count	<6.0	1.067
	6.0-6.9	0.551
	7.0-8.9	0.974
	9.0-9.9	0.903
	>9.9	1.387

Posterior odds = Prior odds (0.07) * likelihood

Damped Posterior odds = 0.07 * Likelihood ratio$^{0.8}$

Posterior percentage risk of death = (Damped posterior odds / (1+ Damped posterior odds)

Fig 28 P-POSSUM risk model for 30-day mortality rate for open repair

Physiological score (At time of surgery)

	Score			
Risk Factor	1	2	4	8
Age (Years)	≤60	61-70	≥71	
Cardiac signs Chest X-ray	No failure	Diuretic, digoxin, antianginal or hypertensive therapy	Peripheral oedema; warfarin therapy Borderline cardiomegaly	Raised JVP Cardiomegaly
Respiratory history Chest X-ray	No dyspnoea	Dyspnoea on exertion Mild COPD	Limiting dyspnoea (one flight) Moderate COPD	Dyspnoea at rest (rate ≥30/min) Fibrosis or consolidation
Blood pressure (systolic) (mmHg)	110-130	131-170 100-109	≥171 90-99	≤89
Pulse (beats/min)	50-80	81-100 40-49	101-120	≥121
Glasgow coma score	15	12-14	9-11	≤8
Haemoglobin (g/100ml)	13-16	11.5-12.9 16.1-17.0	10.0-11.4 17.1-18.0	≤9.9 ≥18.1
White cell count (x 10^{12}/l)	4-10	10.1-20.0 3.1-4.0	≥20.1 ≤3.0	
Urea (mmol/l)	≤7.5	7.6-10.0	10.1-15.0	≥15.1
Sodium (mmol/l)	≥136	131-135	126-130	≤125
Potassium (mmol/l)	3.5-5.0	3.2-3.4 5.1-5.3	2.9-3.1 5.4-5.9	≤2.8 ≥6.0
ECG	Normal		Atrial fibrillation	Any other abnormal rhythm or ≥ ectopics / min Q waves or ST/T wave changes

Operative score

	Score			
Risk Factor	1	2	4	8
Operative severity	Minor	Moderate	Major	Major +
Multiple procedures	1		2	>2
Total blood loss (ml)	≤100	101-500	501-999	≥1000
Peritoneal soiling	None	Minor (serous fluid)	Local pus	Free bowel content, pus or blood
Presence of malignancy	None	Primary only	Nodal metastases	Distant metastases
Mode of Surgery	Elective		Emergency resuscitation of >2 h possible. Operation <24 h after admission	Emergency (immediate surgery <2 h needed)

P-POSSUM formula for mortality:

Ln[R/1-R] = -9.065 + (0.1692 * physiological score) + (0.1550 * operative severity score)

Fig 29. Glasgow Aneurysm Score:

Patient age	Add patient age
Presence of shock No shock	Add 17 points Add 0 points
Presence of myocardial disease No myocardial disease	Add 17 points Add 0 points
Presence of cerebro-vascular disease No cerebro-vascular disease	Add 17 points Add 0 points
Presence of renal disease (urea > 20) No renal disease (urea < 20)	Add 17 points Add 0 points

Glasgow aneurysm score mortality rates:

Risk Score	Predicted mortality rate
< 73	15
74 – 82	35
83 – 89	48
90 – 97	62
>97	82

APPENDIX 2 Quality assessment tools

Table 54 Checklist for quality assessment of case series studies on intervention

(adapted from CRD's Guidance for those Carrying out or Commissioning Reviews, 2001 and from Downs and Black, 1998)

Criteria	Yes	No	Unclear	Comments
Were participants a representative sample selected from a relevant patient population?				
Are the inclusion/exclusion criteria of patients in the study clearly described?)				
Were participants entering the study at a similar point in their disease progression?				
Was selection of patients consecutive?				
Were all important prognostic factors identified?				
Was data collection undertaken prospectively?				
Was the recruitment period clearly stated?				
Was the intervention that which is being considered in the review? (or was it a significant modification?)				
Was an attempt made to blind outcomes assessors?				
Was the operation undertaken by someone experienced in performing the procedure?				
Did the staff, place, and facilities where the patients were treated provide an appropriate environment for performing the procedure? (e.g. was the intervention undertaken in a centre with the necessary back-up facilities?)				
Were objective (valid and reliable) outcome measures used?				
Were all the important outcomes considered?				
Was follow-up long enough to detect important effects on outcomes of interest?				
Was information provided on non-respondents, dropouts?				
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; no description of those lost)				
Were the main findings clearly described? (to allow replication)				

Table 55 Checklist for quality assessment of non-randomised studies evaluating interventional procedures.

Items specific for non-randomised comparative studies are in *italic.*

Criteria	Yes	No	Unclear	Not Relevant	Comments
Participants: sample definition and selection					
Were participants a representative sample selected from a relevant patient population?					
Were the inclusion/exclusion criteria of participants clearly described?					
Were participants entering the study at a similar point in their disease progression?					
Was selection of patients consecutive?					
Was data collection undertaken prospectively?					
Were the groups comparable on demographic characteristics and clinical features?					
Intervention:					
Was the intervention (and comparison) clearly defined?					
Was the intervention undertaken by someone experienced at performing the procedure?					
Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure? (E.g. access to back-up facilities?					
Outcome measures:					
Were all the important outcomes considered?					
Were objective (valid and reliable) outcome measure/s used?					
Was the assessment of main outcomes blind?					
Follow-up:					
Was follow-up long enough to detect important effects on outcomes of interest?					
Was information provided on non-respondents, dropouts?					
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; differential drop-out; no description of those lost)					
Was length of follow-up similar between comparable groups					
Analysis:					
Were all the important prognostic factors identified?					
Were the analyses adjusted for confounding factors?					

TABLE 56 Checklist of quality assessment of randomised control trials of an interventional procedure *(adopted from Verhagen et al, 1998)*

Criteria	Yes	No	Unclear	Comments
Was the assignment to the treatment groups really random? *Adequate approaches to sequence generation* computer-generated random tables random number tables *Inadequate approaches to sequence generation* use of alternation, case record numbers, birth dates or week days				
Was the treatment allocation concealed? *Adequate approaches to concealment of randomisation* centralised or pharmacy-controlled randomisation serially-numbered identical containers on-site computer based system with a randomisation sequence that is not readable until allocation other approaches with robust methods to prevent foreknowledge of the allocation sequence to clinicians and patients *Inadequate approaches to concealment of randomisation* use of alternation, case record numbers, birth dates or week days open random numbers lists serially numbered envelopes (even sealed opaque envelopes can be subject to manipulation)				
Were the groups similar at baseline in terms of prognostic factors?				
Were the eligibility criteria specified?				
Were the groups treated in the same way apart from the intervention received?				
Was the outcome assessor blinded to the treatment allocation?				
Was the care provider blinded?				
Were the patients blinded?				
Were the point estimates and measures of variability presented for the primary outcome measures?				
Was the withdrawal/drop-out rate likely to cause bias?				
Did the analyses include an intention-to-treat analysis?				
Was the operation undertaken by someone experienced in performing the procedure?				

Table 57 Checklist for the quality assessment of comparative observational studies

Criteria	Yes	No	Unclear
Were participants a representative sample selected from a relevant patient population?			
Were the inclusion/exclusion criteria of participants clearly described?			
Were participants entering the study at a similar point in their disease progression?[a]			
Was selection of patients consecutive?			
Was data collection undertaken prospectively?			
Were the groups comparable on demographic characteristics and clinical features?[b]			
Was the intervention (and comparison) clearly defined?			
Was the intervention undertaken by someone experienced at performing the procedure?			
Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure? (E.g. access to back-up facilities?			
Were all the important outcomes considered?			
Were objective (valid and reliable) outcome measure/s used?			
Was the assessment of main outcomes blind?			
Was follow-up long enough to detect important effects on outcomes of interest?			
Was information provided on non-respondents, dropouts?			
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; differential drop-out; no description of those lost)			
Was length of follow-up similar between comparable groups			
Were all the important prognostic factors identified?			
Were the analyses adjusted for confounding factors?			

Appendix 4 Forest plots

Figure 30 Cardiac event rate for EVAR versus open repair: Forest plot

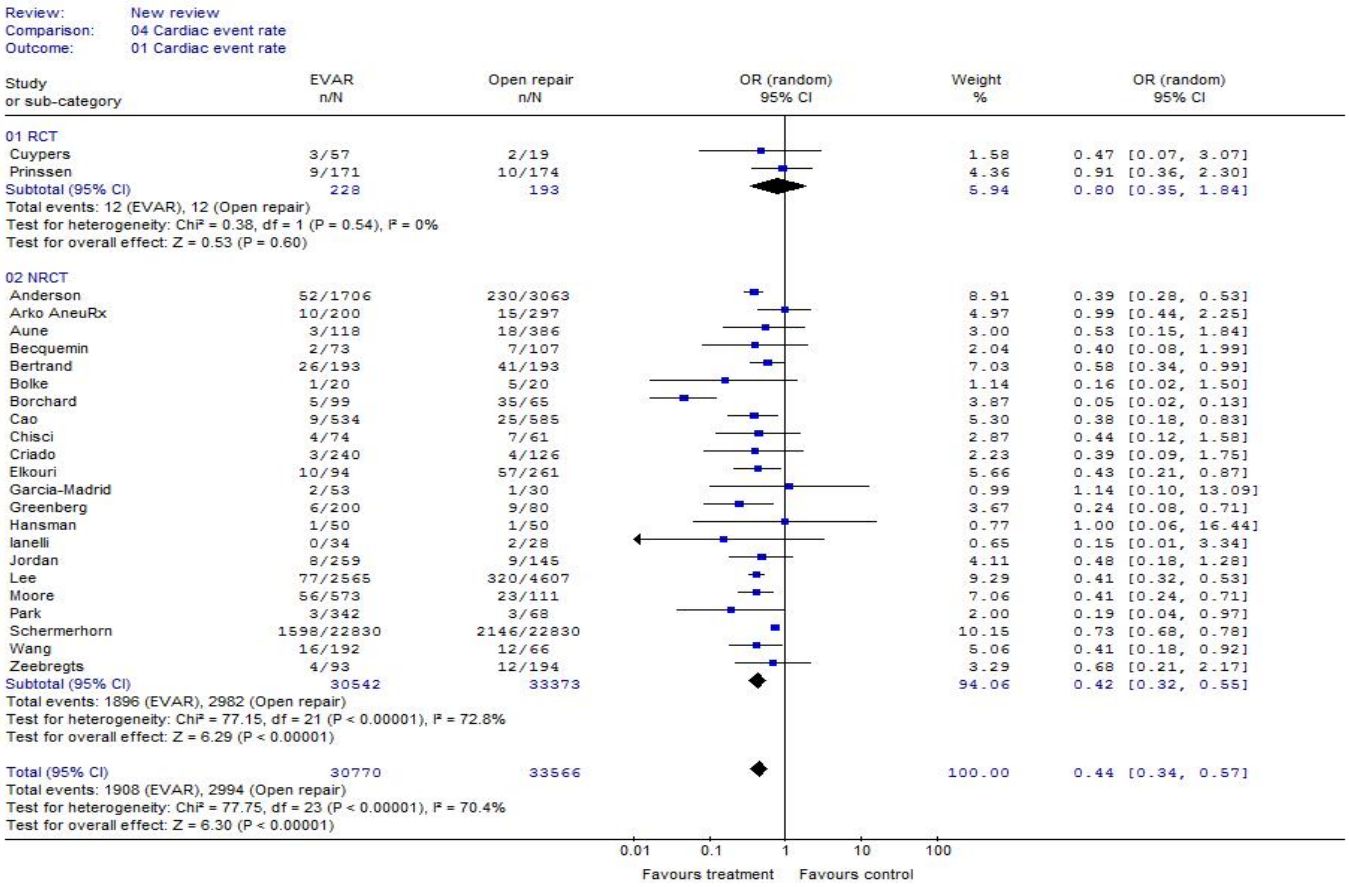


Figure 31 Renal impairment rates for EVAR versus open repair: Forest plot

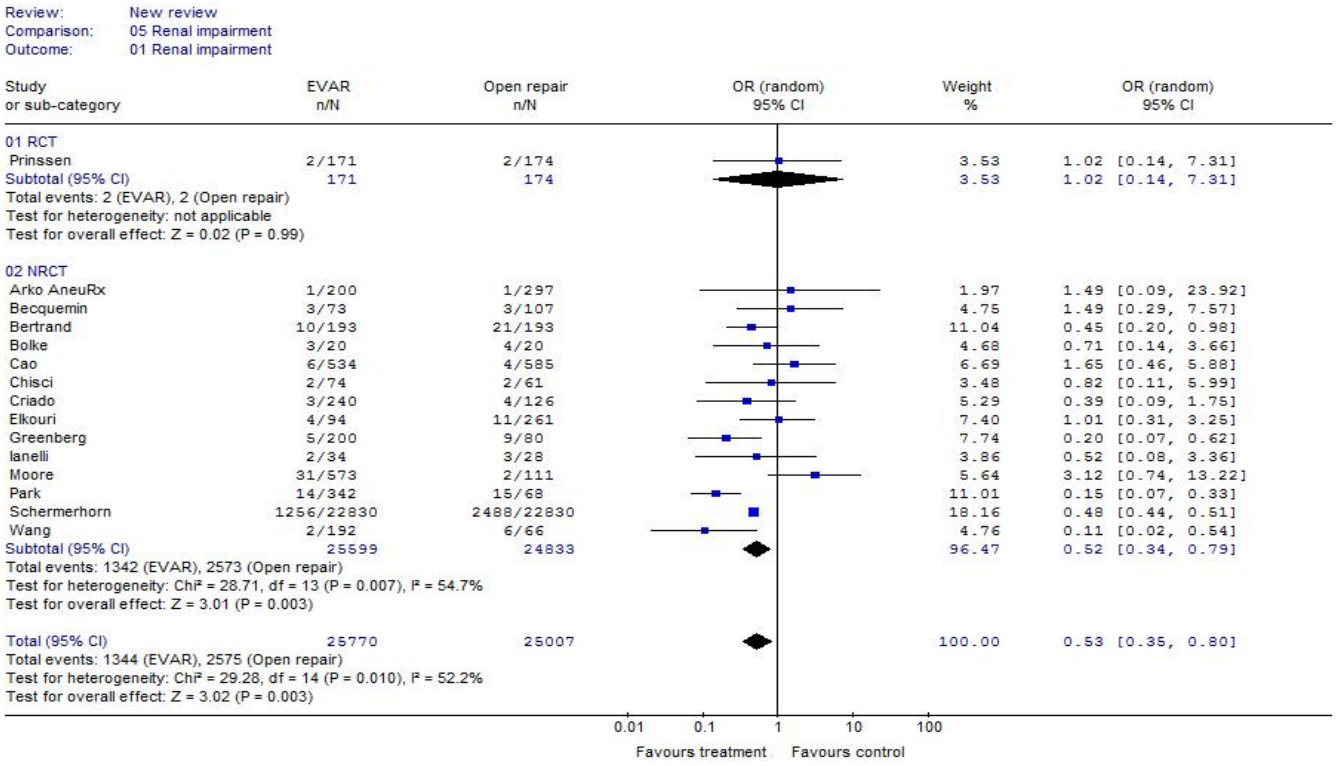


Figure 32 Blood loss for EVAR versus open repair: Forest plot

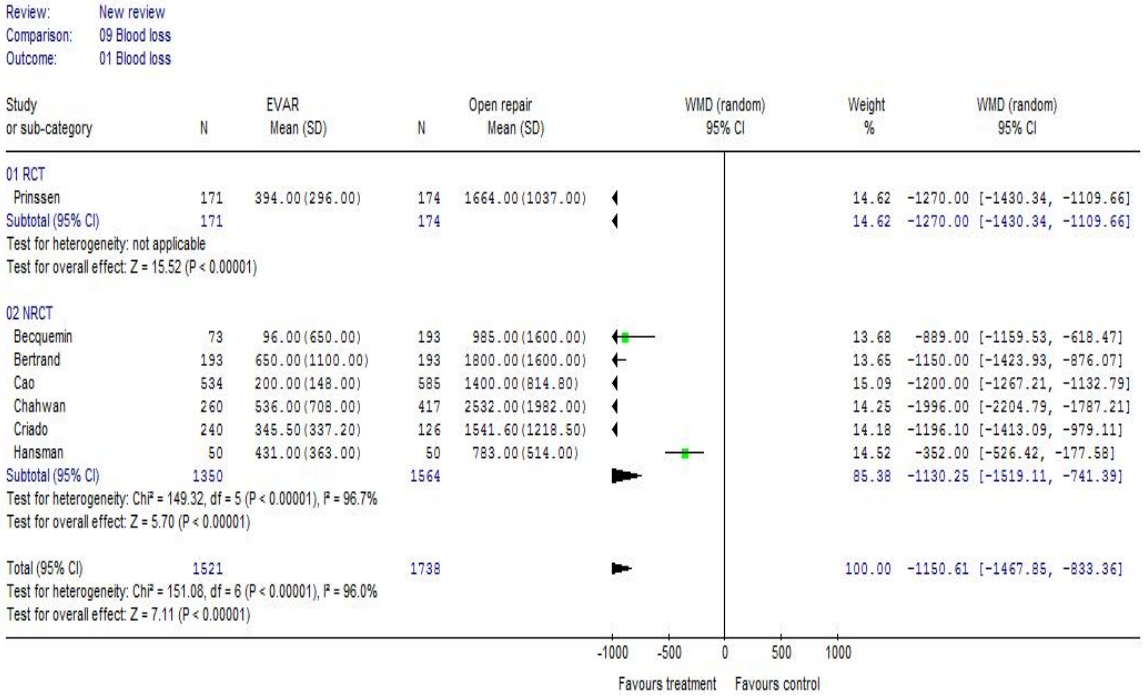


Figure 33 Overall long-term mortality rates following EVAR and open repair

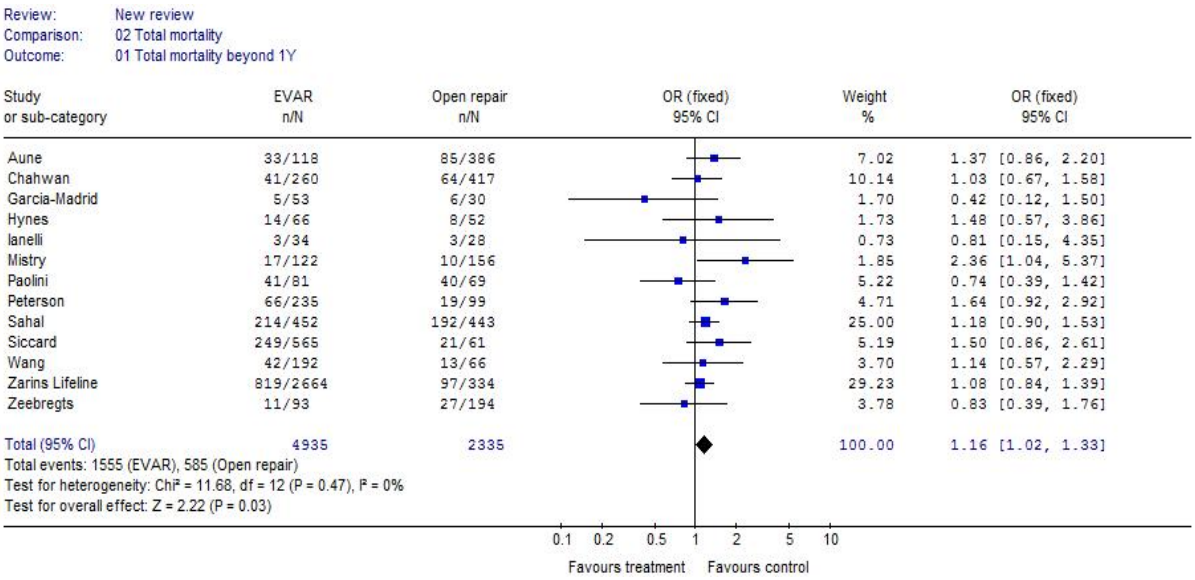


Figure 34 ITU stay for EVAR versus open repair: Forest plot

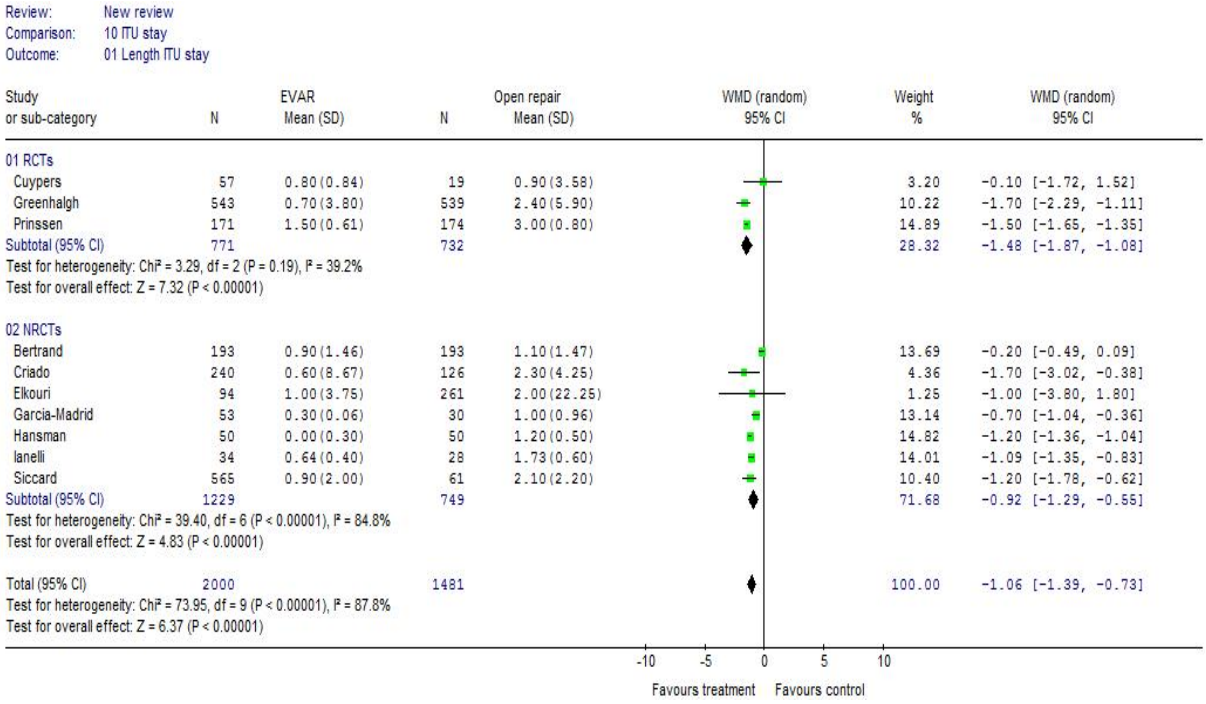
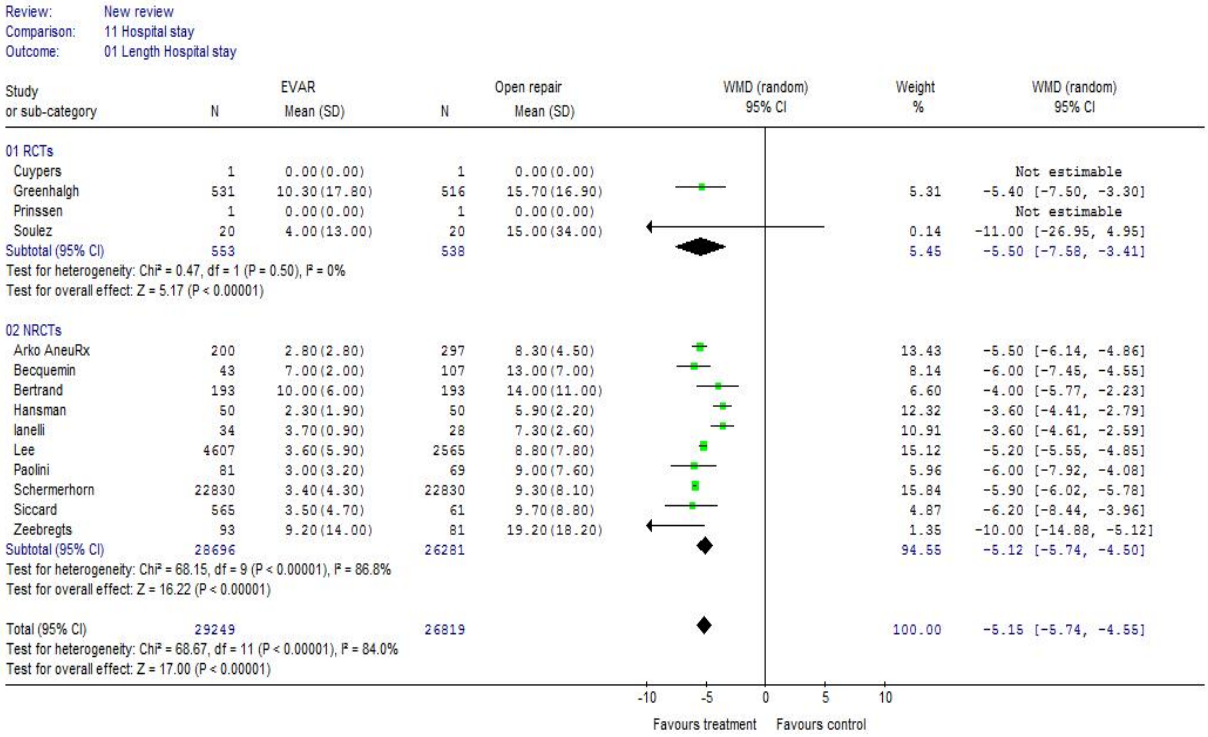


Figure 35 Hospital stay for EVAR versus open repair: Forest plot



APPENDIX 5 List of excluded papers

Akkersdijk 2004
Akkersdijk GJM, Prinssen M, Blankenstejn JD. The impact of endovascular treatment on in-hospital mortality following non-ruptured AAA repair over a decade: A population based study of 16446 patients. Eur J of Vasc Endovasc 2004;28(1);41/46.
Reasons for exclusion: Insufficient outcome data of interest.

Arko 2002
Arko FR, Lee AL, Hill BB, Olcott C, Dalman RL Harrus EJ er al. Aneurysm-related death: Primary endpoint analysis for comparison of open and endovascular repair. J Vasc Surg 2002; 36:297-304.
Reasons for exclusion: Repeat publication from same data series.

Aziz 2003
Aziz I, Lee J, Kopchok G, Donayre C, White R, Virgilio C. Cardiac risk stratification in patients undergoing endoluminal graft repair of abdominal aortic aneurysm: A single-centre experience with 365 patients. J Vasc Surg 2003;38:56-60.
Reasons for exclusion: Uncertain follow-up period, insufficient outcome data of interest.

Berg 2001
Berg P, Kaufmann D, Marrewijk C, Buth J. Spinal cord ischaemia after stent-graft treatment for infra-renal abdominal aortic aneurysms. Analysis of the Eurostar database. Eur J Vasc Endovasc Surg 2001;22:342-347.
Reasons for exclusion: More recent registry publications exist.

Bush 2006
Bush RL, Johnson ML, Collins TC, Henderson WG et al. Open versus endovascular abdominal aortic aneurysm repair in VA hospitals. J Am Coll Surg 2006; 202:577-587.
Reasons for exclusion: Newer publications from same data series exist.

Buth 2000
Buth J, Laheij R. Early complications and endoleaks after endovascular abdominal aortic aneurysm repair: Report of a multicentre study. J Vasc Surg 2000;31:134-46.
Reasons for exclusion: More recent registry publications exist.

Buth 2002
Buth J, Van Marrewijk CJ, Harris PL, Hop WCJ, Riambau V, Laheij RFJ. Outcome of endovascular abdominal aortic aneurysm repair in patients with conditions considered unfit for and open procedure: A report on the EUROSTAR experience. J Vasc Surg 2002; 35:211.
Reasons for exclusion: Later publications from same data series exist.

Carroccio 2002
Carroccio A, Faries P, Morrissey N, Teodorescu V, Burks J, Gravereaux E et al. Predicting iliac limb occlusions after bifurcated aortic stent grafting: anatomic and device-related causes. J Vasc Surg 2002;36:679-684.

Reasons for exclusion: No patient demographics, insufficient outcome data of interest.

Cuypers 2000
Cuypers P, Laheij R, Buth J. Which factors increase the risk of conversion to open surgery following endovascular abdominal aortic aneurysm repair? Eur J Vasc Endovasc Surg 2000;20;183-90.
Reasons for exclusion: More recent registry publications exist.

D'Ayala 2004
D'Ayala M, Dietch JS, Wise L. Complications of endovascular surgery for abdominal aortic aneurysms. Current Surgery 2004; 61(2);163-165.
Reasons for exclusion: No primary data (review article).

Earnshaw 2005
Earnshaw JJ, Murie JA. Mid-term results of endovascular repair of abdominal aortic aneurysm. British Journal of Surgery 2005; 92:925-927.
Reasons for exclusion: No primary outcome data.

Greenberg 2004
Greenberg RK, Deaton D, Sullivan T, Walker E, Lyden SP, Srivastave SD et al. Variable sac behaviour after endovascular repair of abdominal aortic aneurysm: Analysis of core laboratory data. J Vasc Surg 2004; 39:95-101.
Reasons for exclusion: No significant outcome data of interest.

Greenhalgh 2007
The EVAR Trial Participants. Secondary interventions and Mortality following endovascular aortic aneurysm repair: Device specific results from the UK EVAR trials. Eur J Vasc Endovasc Surg 2007; 34, 281-290.
Reasons for exclusion: No new data published compared to previous publications from same series.

Harris 2000
Harris PL, Vallabhaneni SR, Desgranges P, Becquemin J, Marrewijk C, Laheij RFJ. Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: The EUROSTAR experience. J Vasc Surg 2000; 32:39-49.
Reasons for exclusion: Later publications from same series exist.

Harris 2004
Harris PL, Buth J. An update on the important findings from the EUROSTAR EVAR registry. Vascular 2004;12(1);33-38.
Reasons for exclusion: No significant outcome data of interest.

Laheij 2000
Leheij R, Buth J, Harris P, Moll F, Stelter W, Verhoeven E. Need for secondary interventions after endovascular repair of abdominal aortic aneurysms. Intermediate-term follow-up results of a European collaborative registry (EUROSTAR). Br J Surg 2000;87(12):1666-1673.
Reasons for exclusion: More recent publications exist .

Leurs 2004
Leurs LJ, Hobo R, Buth J. The multicentre experience with a third-generation endovascular device for abdominal aortic aneurysm repair. J cardiovasc Surg 2004;45:293-300.
Reasons for exclusion: Large losses to follow up, little outcome data provided, large overlap with other EUROSTAR publications.

Mohan 2001
Mohan I, Laheij R, Harris P. Risk factors for endoleak and the evidence for stent-graft oversizing in patients undergoing endovascular aneurysm repair. Eur J Vasc Endovasc Surg 2001;21:344-349.
Reasons for exclusion: More recent publications exist.

Ouriel 2003
Ouriel K, Clair D, Greenberg R, Lyden S, O'Hara P, Sarac T et al. Endovascular repair of abdominal aortic aneurysms: Device-specific outcome. J Vasc Surg 2003;37:991-8.
Reasons for exclusion: Publication from same data series. No new information included.

Peppelenbosch 2004
Peppelenbosch N, Buth J, Harris PL, Van-Marrewijk C, Fransen G, Ouriel K et al. Diameter of abdominal aortic aneurysm and outcome of endovascular aneurysm repair: Does size matter? A report from EUROSTAR. Journal-of-Vascular-Surgery. 2004; 39(2): 288-297.
Reasons for exclusion: More relevant publications exist.

Rhee 2002
Rhee R, Muluk S, Tzeng E, Missig-Carroll N, Makaroun M. Can the external iliac artery be safely covered during endovascular repair of abdominal and iliac artery aneurysms? Ann Vasc Surg 2002;16:29-36.
Reasons for exclusion: Small study, insufficient outcome data of interest.

Riambau 2001
Riambau V, Laheij R, Garcia-Madrid C, Sanchez-Espin G. The association between co-morbidity and mortality after abdominal aortic aneurysm endografting in patient ineligible for elective open surgery. Eur J Vasc Endovasc Surg 2001;22:265-270.
Reasons for exclusion: More recent publications exist.

Sampram 2003
Sampram ESK, Karafa MT, Mascha EJ, Clair DG, Greenberg RK, Lyden SP et al. Nature, frequency and predictors of secondary procedures after endovascular repair of abdominal aortic aneurysm. J Vasc Surg 2003; 37:930-7.
Reasons for exclusion: Repeat publication from same data series.

Sandridge LC
Sandridge LC, Baglioni AJ, Kongable GL, Harthun NL. Evaluation of the effect of endovascular options on infrarenal abdominal aortic aneurysm repair. Am Surg 2006. Aug; 72(8):700-704.
Reasons for exclusion: Insufficient outcome data of interest.

Schermerhorn 2002
Schermerhorn M, Finlayson S, Fillinger M, Buth J, Marrewijk C, Cronenwett J. Life expectancy after endovascular versus open abdominal aortic aneurysm repair: Results of a decision analysis model on the basis of data from EUROSTAR. J Vasc Surg 2002;36:1112-20.
Reasons for exclusion: No primary data.

Steinmetz 2004
Steinmetz E, Rubin BG, Sanchez LA, Choi ET, Geraghty PJ, Baty J et al. Type II endoleak after endovascular abdominal aneurysm repair: A conservative approach with selective intervention is safe and cost-effective. J Vasc Surg 2004; 39:306-13.
Reasons for exclusion: Only patients with type II endoleak included (n=5).

Sternbergh 2004
Sternbergh W, Money S, Greenberg R, Chutter T. Influence of endograft oversizing on device migration, endoleak, aneurysm shrinkage, and aortic neck dilatation: Results from the Zenith multicentre trial. J Vasc Surg 2004;39:20-6.
Reasons for exclusion: No patient demographics, unclear recruitment period, unclear follow-up, limited outcome data of interest.

Thomas 2001
Thomas S, Gaines P, Beard J. Short-term (30-day) outcome of endovascular treatment of abdominal aortic aneurysm: results of the prospective registry of endovascular treatment of abdominal aortic aneurysms (RETA). Eur J Vasc Endovasc Surg 2001;21:57-64.
Reasons for exclusion: Only 1 month follow-up. 16% population were ruptured or symptomatic AAAs. Newer publications exist.

Timaran 2007
Timaran CH, Veith FJ, Rosero EB, Modrall JG, Arko FR et al. Endovascular aortic aneurysm repair in patients with the highest risk and in hospital mortality in the United States. Arch Surg 2007; 142:520-525.
Reasons for exclusion: Repeat publication from same data series, no new data.

Waasdorp 2005
Waasdorp EJ, de Vries JP, Hobo R, Leurs LJ et al for EUROSTAR collaborators. Aneurysm diameter and proximal aortic neck diameter influence clinical outcome of endovascular abdominal aortic repair: A 4-year EUROSTAR experience. Annals of vascular surgery; 19:755-761
Reasons for exclusion: Repeat publication from same data series, no new data.

Wang 2009
Wang GJ, Carpenter JP. EVAR in small versus large aneurysms: does size influence outcome? Vasc Endovasc Surg 2009;443(3):244-51.
Reasons for exclusion: Repeat publication from same data series, no new data.

Zarins 2000

Zarins C, White R, Fogarty T. Aneurysm rupture after endovascular repair using the AneuRx stent graft. J Vasc Surg 2000;31:960-970.
Reasons for exclusion: Later publications from same series exist. Insufficient outcome data of interest.

Zarins 2000
Zarins C, White R, Hodgson K, Schwarten D, Fogarty T. Endoleak as a predictor of outcome after endovascular aneurysm repair: AneuRx multicenter clinical trial. J Vasc Surg 2000;32:90-107.
Reasons for exclusion: Later publications from same series exist with larger numbers and / or longer follow up.

Zarins 2004
Zarins CK, Bloch DA, Crabtree T, Matsumoto AH, White RA, Fogarty TJ. Aneurysm enlargement following endovascular aneurysm repair: AneuRx clinical trial. Journal-of-Vascular-Surgery. 2004; 39(1): 109-117.
Reasons for exclusion: More relevant publications from same series exist.

Zarins 2006
Zarins CK, Crabtree T, Bloch DA, Arko FR, Ouriel K, White RA. Endovascular aneurysm repair at 5 years: does aneurysm size predict outcome. J Vasc Surg 2006;44:920-30.
Reasons for exclusion: More relevant publications from same series exist.

EVAR DATA FROM NON-CONTROLLED STUDIES

Overview of the efficacy findings from non-controlled studies (Case series and comparative studies)

Deployment success rate

The results from the case series are displayed in the table below. The results were similar to the controlled studies with a success rate of 98%, (95% CI 97.9% to 98.5%).

Table: Successful endograft deployment rate

Author	Number of patients (n)		Deployment success rate %, (95% CI)
	Undergoing EVAR	Successful deployment	
Cao 2006[34]	649	640	99
Carpenter 2004[37]	227	224	99
Criado 2001[109]	471	456	93
Elkouri 2003[81]	100	97	97
Espinosa 2005[46]	193	191	99
Herwaarden 2007[90]	212	209	99
Howell 2001[115]	215	214	100
Howell 2000[116]	*56*[a]	*56*	*100*
Lalka 2005[128]	136	136	100
Lee 2002[117]	150	148	99
Maldonado 2007[62]	430	424	99
May 2000[64]	266	249	94
Qu 2009[74]	612	603	99
Qu 2007[75]	*378*	*372*	*98*
Ramaiah 2002[119]	230	230	100
Zarins 2000[123]	*149*	*147*	*99*
Vallabhaneni 2001[102]	2862	2812	98
Total	**6753**	**6633**	**98% (97.9% - 98.5%)**

[a] n=56 patients who received an AneuRx stent

Technical success rate

- **Primary technical success rate**

Correct stent placement and complete aneurysm exclusion at completion or discharge angiogram was the definition in the majority of the studies. No definition was provided by 4 studies. Four studies stated an alternative definition of technical success. Successful endograft deployment was used by Lee 2002.[117,118] Successful endograft deployment without the need for surgical conversion or death; lack of a persistent (>48 hours) type I or type III endoleak; and a patent graft was used by Okhi 2001.[68] The definition used by Ramaiah 2002[119] was that defined by the Society for Vascular Surgery / International Society for Cardiovascular reporting standards. The success rate averaged 82%, (95% CI 81.3% to 83.0%).

Table: Primary technical success rate

Author	Number of patients (n)		Technical success rate (%, 95% CI)
	Undergoing EVAR	Technical success	

Blum 2001[23]	298	269	90
Boult 2006[25]	961	890	93
Boult 2004[26]	*950*	*853*	*90*
Bos 2008[28]	234	223	95
Carpenter 2004[37]	227	183	81
Criado 2001[109]	471	383	81
Fairman 2004[111]	*109*	*61*	*56*
Espinosa 2009[45]	337	304	90
Hinchliffe 2004[53]	269	240	89
Howell 2001[115]	215	132	61
Howell 2000[116]	*89*	*57*	*64*
Lee 2002[117]	150	93	62
Lee 2000[118]	*67*	*36*	*54*
Zarins 2000[123]	*149*	*94*	*63*
Nevla 2009[67]	206	163	79
Ohki 2001[68]	239	212	89
Ramaiah 2002[119]	260	220	85
Sampaio 2009[80]	241	155	64
Thomas 2005[87]	1000	721	72
Vallabhaneni 2001[102]	2862	2322	81
Wales 2008[92]	286	272	95
Total	**8256**	**6782**	**82% (81.3% – 83.0%)**

- **Thirty day technical success**

The results of the 8 included case series are displayed in the table below. The success rate was 91% (95% CI 90.1% to 92.1%).

Table: Thirty day technical success

Author	Number of patients (n)		Technical success rate, % (95% CI)
	Undergoing EVAR	Technical success	
Boult 2004[26]	950	825	87
Bos 2008[28]	234	228	97
Carpenter 2004[37]	205	179	87
Criado 2001[109]	355[a]	342	96
Elkouri 2003[81]	100	86	86
Howell 2001[115]	215	200	93
Howell 2000[116]	*56[b]*	*53*	*95*
Ramaiah 2002[119]	260	260	100
Zarins 2000[123]	*147*	*121*	*82*
Lee 2000[117]	*67*	*52*	*78*
Thomas 2005[87]	1000	904	90%
Total	**3319**	**3024**	**91% (90.1% - 92.1%)**

a n=355 patients who were available for evaluation
b n=56 patients who received an AneuRx stent

Aneurysm rupture following EVAR

There were 25 case series that had reported the delayed AAA rupture rate following over a mean of 29.5 months follow up, (see table). Overall the mean rupture rate was 1.4% (95% CI 1.2%, 1.5%).

Table: Delayed aneurysm rupture rates following EVAR

Author	Number of patients		Rupture Rate, % (95% CI)	Follow-up (months)	
	Undergoing EVAR	With rupture		Mean	Range

Abbruzzese 2008[14]	565	6	1.1	30	Not reported
Blum 2001[23]	298	4	1.3	35	2-50
Boult 2006[25]	961	12	1.2	NR	5-60
Brewster 2005[30]	873	13	1.5	27	Not reported
Cao 2009[33]	349	2	0.6	25	12-60
Conrad 2009[40]	832	5	0.6	35	0-113
Corriere 2004[41]	220	0	0	NR	Not reported
Dias 2009[43]	304	1	0.3	54	Not reported
Elkouri 2003[81]	100	1	1	7	1-60
Herwaarden 2007[90]	212	7	3.3	52	1-109
Hinchliffe 2004[53]	255	2	0.8	12	Not reported
Hiramoto 2006[54]	325	1	0.3	28	1-85
Hobo 2008[95]	7554	164	2.2	19	(0-108)
Marrewijk 2005[97]	*6787*	*50*	*0.8*	*21*	*0-108*
Hobo 2006[99]	*2846*	*40*	*1.4*	*23*	*Not reported*
Laheij 2002[101]	*2863*	*16*	*0.6*	*NR*	*Not reported*
Howell 2001[115]	215	0	0	14	Not reported
Howell 2000[116]	*89*	*0*	*0*	*13*	*1-18*
Hugl 2007[127]	366	1	0.3	NR	Not reported
Lee 2002[117]	150	0	0	1	Not reported
Lee 2000[118]	*67*	*0*	*0*	*18*	*Not reported*
Ohki 2001[68]	239	2	0.8	16	<75 months
Ouriel 2003[68]	704	3	0.4	NR	Not reported
Parlani 2002[35]	336	2	0.6	14	1-46
Qu 2009[74]	612	1	0.2	62	Not reported
Ramaiah 2002[119]	230	0	0	NR	Not reported
Szmidt 2007[86]	445	3	0.7	30	Not reported
Thomas 2005[87]	1000	11	1.1	37	Not reported
Verhoeven 2004[29]	306	1	0.3	36	Not reported
Zarins 2004[124]	1193	15	1.3	NR	<48
Zarins 2003[125]	*383*	*3*	*0.8*	*36*	*Not reported*
Zarins 2000[123]	*149*	*1*	*0.7*	*12*	*1-39*
Total	**18644**	**257**	**1.4 (1.2%-1.5%)**	**29.5**	**-**

NR – Not reported

Nine studies reported the early AAA rupture rate with a mean of 0.1%, (95% CI 0.1%, 0.2%).

Table: Early (<30 days) aneurysm rupture rates following EVAR

Author	**Number of patients**		**Rupture Rate, % (95%CI)**
	Undergoing EVAR	**With rupture**	
Abbruzzese 2008[14]	565	2	0.4
Blum 2001[23]	298	1	0.3
Carpenter 2004[37]	227	2	0.9
Hobo 2008[95]	7554	5	0.07
Lange 2005[198]	*4191*	*1*	*0.02*
Ouriel 2003[69]	704	1	0.1
Qu 2007[75]	378	1	0.3
Ricco 2003[76]	1012	2	0.1
Zannetti 2001[36]	240	1	0.4
Zarins 2003[125]	1193	3	0.3
Total	**12171**	**18**	**0.1 (0.1%-0.2%)**

NR – Not reported

Changes in aneurysm size

From the 21 case series, 6.5% (95% CI 6.1% - 7.0%) of the EVAR population increased in size (Table 43).

Table: Changes in aneurysm size following EVAR

Author	Number of cases	Changes in aneurysm size n (%)			Follow-up (mean)
		Increase	No change	Decrease	
Arko 2003[113]	206	11 (5.3)	25 (12)	170 (82.5)	32
Bos 2008[28]	234	7 (3.0)	NR	NR	27
Boult 2006[25]	961	96 (10)	231 (24)	634 (66)	NR
Brewster 2006[30]	873	46 (7.8)	375 (43)	452 (49)	27
Carpenter 2004[37]	48[b]	4 (8)[a]	28 (58)	16 (33)	11
Elkouri 2003[81]	97	2 (0.2)	32 (33)	63 (65)	7
El Sayed 2009[44]	438	NR	NR	129 (29)	49
Espinosa 2009[45]	108	7 (6.5)	NR	NR	59
Fairman 2004[111]	16	4 (25)	NR	NR	21
Cao 2009[33]	349	22 (6.3)	169 (48)	158 (45)	25
Parlani 2002[35]	*326[c]*	*21 (6.4)[a]*	*182 (56)*	*127 (39)*	*14*
Dias 2009[43]	304	27 (8.9)	NR	NR	54
Herwaarden 2007[90]	204	15 (7.4)	109 (53)	80 (39)	52
Hobo 2008[95]	7554	910 (12.0)	NR	NR	19
Marrewijk 2005[97]	*6787*	*378 (6)*	*4756 (70)*	*2031 (30)*	*21*
Howell 2000[115]	84	2 (0.9)[a]	59 (27)	23 (11)	14
Hugl 2007[127]	336	12 (3.6)	NR	NR	NR
Jones 2007[58]	873	68 (7.8)	NR	NR	33
Nevla 2009[67]	206	16 (7.8)	64 (31.7)	109 (53.2)	29
Ouriel 2003[69]	700	70 (10)	419 (60)	211 (30)	12
Qu 2009	612	25 (4.0)	NR	NR	62
Zarins 2003[122]	383	46 (12)	138 (36)	199 (52)	36
Lee 2000[115]	67	8 (12)	NR	NR	18
Total	**14653**	**777 (6.5)**	**6542 (55)**	**4200 (35.1)**	**23**

[a] No definition provided
[b] n=48 patients who were available for evaluation at 12 months
[c] n=326 patients with a successfully implanted stent-graft
NR – Not reported

Primary conversion rate

This was reported by 30 studies, (Table 44). The largest single publication is a multicentre study from the EUROSTAR database[100] that reported a primary conversion rate of 0.9%. Overall the mean conversion rate was 1.3% (95% CI 0.9%, 1.2%).

Table: Primary conversion rates

Author	Total number of EVAR	Primary conversion	
		Number of patients	Rate, % (95% CI)
Blum 2001[26]	298	5	0.8
Boult 2006[28]	961	10	1.0
Boult 2004[29]	*950*	*9*	*0.9*

Brewster 2006[31]	873	5	0.6
Cao 2005[35]	649	9	0.2
Parlani 2002[36]	*336*	*6*	*1.8*
Zannetti 2001[37]	*266*	*6*	*2.3*
Carpenter 2004[38]	227	3	1.3
Dias 2009	304	1	0.3
Elkouri 2003[83]	100	3	3
Espinosa 2004[47]	193	1	0.5
Herwaarden 2007[57]	212	2	0.9
Hinchliffe 2004[58]	269	0	0
Hobo 2008	7554	68	0.9
Lange 2005[96]			
Age <80Y	*4191*	*40*	*1.0*
Age >80Y	*697*	*11*	*1.6*
Vallabhaneni 2001[100]	*2862*	*47*	*1.6*
Howell 2001[112]	215	0	0
Howell 2000[113]	*89*	*0*	*0*
Jiminez 2007	574	5	0.9
Lalka 2005[124]	136	0	0
Lee 2002[114]	150	2	1.3
Maldonado 2007[65]	430	6	1.4
Maldonado 2004[66]	*311*	*6*	*1.9*
May 2000[67]	266	17	6.4
Ouriel 2003[76]	700	3	0.4
Pitoulias 2009[73]	625	8	1.3
Qu 2009[74]	612	9	1.5
Qu 2007[75]	*378*	*6*	*1.6*
Ramaiah 2002[119]	260	0	0
Ricco 2003[76]	1012	11	1.1
Shames 2003a[120]	245	7	2.9
Males	203	1	0.5
Females	42	6	14
Thomas 2005[87]	1000	14	1.4
Tonnessen 2005[121]	205	3	1.5
Traul 2008[88]	245	1	0.4
Verhoeven 2004[29]	308	1	0.3
Waasdorp 2008[89]	291	1	0.3
Wales 2008[92]	286	0	0
Zarins 2003[125]	1193	11	0.9
Zarins 2000[123]	*149*	*2*	*1.3*
Total	**20638**	**213**	**1.0 (0.9% - 1.2%)**

[a] Data extracted from Resch 2001[73]

Delayed conversion rate

The results of the 37 case series are displayed in Table 45. The overall mean was 3.7% (95% CI 3.4%, 3.9%). The single largest study from the EUROSTAR database[100] reported a rate of 6.1%. The study with the longest follow-up,[72] which stated a period of at least 60 months, reported a delayed conversion rate of 2.3%.

Table: Delayed conversion rates

Author	Total number of EVAR	Secondary conversions		Follow-up	
		Number	%, (95% CI)	Mean	Range

Abbruzzese 2008[14]	565	4	0.77	30	Not reported
Arko 2003[113]	206	3	1.5	32	3-55
Becquemin 2004[18]	250	11	4.4	28	Not reported
Blum 2001[23]	298	8	2.7	35	2-50
Boult 2006[25]	961	6	0.6	Not reported	5-60
Brewster 2006[30]	852	15	1.8	27	Not reported
Cao 2006[34]	649	29	4.5	38	Not reported
Cao 2009[33]	*349*	*8*	*2.3*	*25*	*12-60*
Parlani 2002[35]	*336*	*4*	*1.2*	*14*	*1-46*
Carpenter 2004[37]	227	2	0.9	11	0-41
Conrad 2009[40]	832	21	2.5	35	0-113
Dias 2009[43]	304	4	0.3	54	Not reported
Elkouri 2003[81]	100	1	1	7	1-60
Fairman 2004[111]	237	6	2.5	21	Not reported
Herwaarden 2007[90]	212	11	5.2	52	1-109
Hobo 2008[95]	7554	462	6.1	19	0-108
Vallabhaneni 2001[102]	*2862*	*41*	*1.4*	*12*	*0-72*
Hobo 2006[99]	*2846*	*40*	*1.4*	*12*	*Not reported*
Howell 2001[115]	215	4	1.9	14	Not reported
Howell 2000[116]	*89*	*2*	*2.2*	*13*	*1-18*
Hugl 2007[127]	366	5	0.3	Not reported	Not reported
Jiminez 2007[57]	569	12	2.1	42	Not reported
Jordan 2004[59]	259	4	1.5	28	Not reported
Lee 2000[118]	67	1	1.5	18	Not reported
Moore 2003[66]	573	2	0.3	Not reported	1-60
Ohki 2001[68]	239	5	2.1	16	<75 months
Ouriel 2003[69]	700	29	4.1	12	Not reported
Pitoulias 2009 [73]	617	39	6.3	47	1-94
Qu 2009[74]	612	14	2.3	62	Not reported
Qu 2007[75]	*366*	*6*	*1.6*	*37*	*1-84*
Ricco 2003[76]	1012	4	0.4	11	Not reported
Thomas 2005[87]	1000	23	2.3	37	Not reported
Verhoeven 2004[29]	308	9	2.9	36	Not reported
Wales 2008[92]	286	0	0	16	0-70
Zarins 2004[124]	1193	42	3.5	Not reported	Not reported
Zarins 2000[123]	*149*	*1*	*0.7*	*12*	*1-39*
Zarins 2003[125]	*383*	*18*	*4.7*	*36*	*Not reported*
Total	**21427**	**791**	**3.7 (3.4% - 3.9%)**	**28**	

Secondary intervention rate

Overall the mean secondary intervention rate from the 42 included case series was 16.2% (95% CI 15.6%, 16.7%). Again, the largest single publication was from the EUROSTAR registry (Hobo 2008), which reported a secondary intervention rate of 16.9%. The study with the longest follow up (54 months) recorded a secondary reintervention rate of 25.6%.

Table: Secondary intervention rates

Author	Total number of EVAR	Secondary interventions		Follow-up	
		Number	% (95% CI)	Mean	Range
Abbruzzese 2008[14]	565	88	15.6	30	Not reported

Arko 2003[113]	206	19	9.2	32	3-55
Becquemin 2004[18]	250	112	44.8	28	Not reported
Blum 2001[23]	298	24	8.1	35	2-50
Bos 2008[28]	234	29	12.4	27	0-104
Verhoeven 2004[29]	*308*	*72*	*23.4*	*36*	*Not reported*
Boult 2006[25]	961	136	14.2	Not reported	5-60
Boult 2004[26]	*950*	*23*	*2.4*	*Not reported*	*Not reported*
Brewster 2006[30]	848	102	12.0	27	Not reported
Cao 2009[33]	349	19	5.4	25	12-60
Parlani 2002[35]	*336*	*19*	*5.7*	*14*	*1-46*
Carpenter 2004[37]	227	17	7.5	11	0-41
Conrad 2009[40]	832	131	15.7	35	0-113
Dias 2009[43]	304	78	26.6	54	Not reported
Herwaarden 2007[90]	212	96	45	52	1-109
Hincliffe 2004[53]	269	21	7.8	12	Not reported
Hiramoto 2006[54]	325	28	8.6	28	1-85
Hobo 2008[95]	7554	1273	16.9	19	0-108
Marrewijk 2005[97]	*6787*	*771*	*11.4*	*21*	*0-108*
Hobo 2006[99]	*2846*	*247*	*8.7*	*12*	*Not reported*
Laheij 2002[101]	*2863*	*410*	*14.3*	*Not reported*	*Not reported*
Howell 2001[115]	215	22	10.2	14	Not reported
Howell 2000[116]	*89*	*11*	*12.4*	*13*	*1-18*
Hugl 2007[127]	366	63	17.2	Not reported	Not reported
Lalka 2005[128]	136	21	12.5	36	1-61
Lee 2002[117]	150	7	4.7	Not reported	Not reported
Lee 2000[118]	*67*	*17*	*24.5*	*18*	*Not reported*
May 2000[64]	266	43	16.2	6	> 6 months
Nevla 2009[67]	206	27	13.1	29	Not reported
Ohki 2001[68]	239	23	9.6	16	<75 months
Ouriel 2003[69]	700	173	24.7	12	Not reported
Pitoulias 2009[73]	617	139	22.5	47	1-94
Qu 2007[75]	366	41	11.2	27	1-84
Ramaiah 2002[119]	230	41	17.8	Not reported	Not reported
Ricco 2003[76]	1021	67	6.6	11	Not reported
Sampaio 2004[80]	241	66	27	10	1-71
Elkouri 2003[81]	*100*	*29*	*29.0*	*7*	*1-60*
Shames 2003[120]	245	36	14.7	11	1-26
Thomas 2005[87]	1000	380	38	37	Not reported
Traul 2008[88]	245	15	6.1	30	
Wolf 2002[122]	189	31	16.4	13	Not reported
Zarins 2003[125]	383	67	17.5	36	Not reported
Zarins 2000[123]	*149*	*21*	*14.1*	*12*	*1-39*
Total	**20338**	**3446**	**16.2 (15.6% - 16.7%)**	**26**	

Procedural blood loss

Studies that reported blood loss following EVAR are displayed in Table 47. The 12 studies were case series with a range of blood loss of 157 ml to 468 ml.

Table: Procedural blood loss

Author	Number of participants	Mean Blood loss (ml)
Bos 2008[28]	234	157

Carpenter 2004[37]	227	350
Fairman 2004[111]		
Complicated neck	153	320
Uncomplicated neck	66	351
Elkouri 2003[81]	100	400
Howell 2001[115]	215	352
Howell 2000[116]	*56* [b]	*428*
Hinchliffe 2004[53]	269	400
Ohki 2001[68]	239	468
Parlani 2002[35]		
EVAR	277	293
AAA and IAA[a]	59	445
Ramaiah 2002[119]		
Early	30	400
Late	230	294
Vasquez 2004[93]		
EVAR	129	255
Renal impairment	83	278
Waasdorp 2008[89]	291	330
Total	**2788**	**341**

[a] Combined abdominal and iliac artery aneurysms
[b] results from late endovascular experience

Length of ITU stay

The results of the ITU length of stay are displayed in Table 48. EVAR was associated with a mean stay of 1 day.

Table: Length of ITU stay

Author	Number of participants	ITU stay (days)
Elkouri 2003[81]	100	1.0 [a]

Length of hospital stay

Sixteen case series reported outcome data on length of hospital stay following EVAR, (Table 49). Overall from the 13 studies the average length of stay following EVAR was 3.8 days.

Table: Length of hospital stay

Author	Number of participants	Mean length stay, days
Ayerdi 2003[114]	96 [a]	
Early EVAR	42	3[b]
Late EVAR	54	2[b]
Bos 2008[28]	234	4.6
Carpenter 2004[37]	227	4
Herwaarden 2007[90]	212	4.3
Howell 2001[115]	215	2
Howell 2000[116]	*89*	

Early EVAR	*33*	*4*
Late EVAR	*56*	*2*
Lange 2005[98]		
Age < 80Y	4191	5.5
Age > 80Y	697	7.3
Ohki 2001[68]	239	4
Parlani 2002[35]	336	
EVAR	277	2
AAA + IAA	59	2
Zannetti 2001[36]	*266*	
EVAR	*240*	*3*
High risk EVAR	*26*	*8*
Ramaiah 2002[119]	260	
Early EVAR	30	4
Late EVAR	230	4
Ricco 2003[76]	1012	9
Samapaio 2004[80]		
Male	212	3
Female	29	4
Elkouri 2003[81]	*100*	*3*
Shames 2003[120]	245	
Male	203	3
Female	42	3
Traul 2008[88]	245	2.3
Total	**8450**	**3.8**

[a]Total number of EVAR participants
[b] Median

Overview of the Safety findings from non-controlled studies (Case series)

Common technical complications

The incidence of the common technical complications is shown in Table 50.

Table: Incidence of common technical complications in EVAR

Complication	Author	Number of participants	Number of cases	%
Stent migration				
<30 days	Hobo 2008[95]	7554	99	1.3%
	Vallabhaneni 2001[102]	*2862*	*39*	*1.4%*
> 1 year	Abbruzzese 2008[14]	565	10	1.8%
	Becquemin 2004[18]	250	4	1.6%
	Blum 2001[23]	298	5	1.7%
	Bos 2008[28]	234	3	1.3%
	Brewster 2006[30]	852	25	2.9%
	Cao 2009[33]	349	17	4.9%
	Herwaarden 2007[90]	212	26	12%
	Hinchliffe 2004[53]	255	6	2.4%
	Hobo 2008[95]	7554	740	9.8%
	Marrewicj 2005[97]	*6787*	*323*	*4.8*

	Hobo 2006[99]	*2846*	*73*	*2.6%*
	Fransen 2003[100]	*4613*	*156*	*3.4%*
	Hugl 2007[127]	366	6	1.6%
	Nevla 2009[67]	206	0	0%
	Ouriel 2003[69]	704	51	7.2%
	Pitoulias 2009[73]	617	60	9.7
	Qu 2009[74]	612	7	1.1%
	Qu 2007[75]	*366*	*6*	*1.6%*
	Tonnessen 2005[121]	130	15	11.5%
	Traul 2008[88]	245	4	1.6%
	Zarins 2000[123]	137	13	9.5%
	Zarins 2003[125]	*383*	*24*	*6.3%*
	Total	**13694**	**994**	**7.3%**
Stent wire fracture up to 1 year	Carpenter 2004[37]	227	6	2.6%
Graft limb thrombosis <30 days	Abbruzzese 2008[14]	565	2	0.4%
	Howell 2000[115]	215	5	2.3%
	Lee 2002[117]	150	1	0.7%
	Parlani 2002[35]	336	4	1.2%
	Wales 2008[92]	286	6	2.1%
	Total	**1552**	**18**	**1.2%**
<1 year	Blum 2001[23]	298	4	1.3%
	Carpenter 2004[37]	227	0	0.0%
	Elkouri 2003[81]	100	4	4.0%
	Shames 2003[120]	241	10	4.1%
	Waasdorp 2008[89]	291	3	1.0%
	Zarins 2000[123]	149	1	0.7%
	Total	**1306**	**22**	**1.7%**
>1 year	Abbruzzese 2008[14]	565	6	1.1%
	Becquemin 2004[18]	250	15	6.0%
	Bos 2008[28]	234	4	0.4%
	Verhoeven 2004[29]	*306*	*15*	*4.9%*
	Cao 2009[33]	349	5	1.4%
	Espinosa 2009[45]	337	4	1.2%
	Go 2008[51]	376	3	0.1%
	Herwaarden 2007[90]	212	3	1.4%
	Hiramoto 2006[54]	325	2	0.6%
	Hobo 2008[95]	7554	352	4.7%
	Marrewicj 2005[97]	*6787*	*267*	*5.4%*
	Hobo 2006[99]	*2846*	*68*	*2.4%*
	Fransen 2003[100]	*4613*	*152*	*3.3%*
	Maldonado 2007[62]	430	16	3.7%
	Maldonado 2004[63]	*287*	*14*	*4.9%*
	Nevla 2009[67]	206	5	2.4%
	Ohki 2001[68]	239	7	2.9%
	Ouriel 2003[69]	704	43	6.1%
	Qu 2009[74]	612	6	1.0%
	Qu 2007[75]	*366*	*8*	*2.2%*
	Thomas 2005[87]	1000	45	4.5%
	Traul 2008[88]	245	5	2.0%

	Total	**13638**	**521**	**3.8%**
Graft stenosis 30 days	Vallabhaneni 2001[102]	2862	10	0.3%
<1 year	Elkouri 2003[81]	100	3	3.0%
>1 year	Becquemin 2004[18]	250	8	3.2%
	Carpenter 2004[37]	188	3	1.6%
	Fransen 2003[100]	4613	66	1.4%
	Qu 2007[75]	366	5	1.4%
	Total	**5417**	**82**	**1.5%**
Stent Kink	Nevla 2009[67]	206	5	2.4%
	Pitoulias 2009[73]	617	59	9.5%
Type I endoleak < 30 days	Boult 2004[26]	950	25	2.6%
	Espinosa 2009[45]	337	4	1.2%
	Go 2008[51]	376	5	1.3%
	Hinchliffe 2004[53]	255	2	0.8%
	Hobo 2008[95]	7554	334	4.4%
	Lange 2005[98]	*4888*	*134*	*2.7%*
	Howell 2000[115]	215	2	0.9%
	Howell 2000[116]	*56*	*2*	*3.6%*
	Lee 2002[117]	150	5	3.3%
	Nevla 2009[67]	206	12	5.8%
	Parlani 2002[35]	336	3	1.2%
	Qu 2007[75]	378	0	0%
	Waasdorp 2008[89]	291	8	2.7%
	Total	**11048**	**400**	**3.6%**
up to 1 year	Blum 2001[23]	298	6	2.0%
	Carpenter 2004[37]	227	7	3.1%
	Go 2008[51]	130	1	0.8%
	Hinchliffe 2004[53]	255	2	0.8%
	Howell 2000[115]	84	2	2.4%
	Moore 2003[66]	262	9	3.4%
	Ouriel 2003[69]	704	18	2.6%
	Total	**1960**	**45**	**2.3%**
>1 year	Becquemin 2004[18]	250	36	14.4%
	Bos 2008[28]	234	5	2.1%
	Boult 2006[25]	961	7	0.7%
	Espinosa 2009[45]	337	4	1.2%
	Herwaarden 2007[90]	212	22	10.4%
	Howell 2000[115]	132	6	4.5%
	Hobo 2008[95]	7554	831	11.0%
	Hobo 2006[99]	*2846*	*144*	*5.1%*
	Fransen 2003[100]	*4613*	*375*	*8.1%*
	May 2000[65]	266	21	7.9%
	Nevla 2009[67]	206	2	1.0%
	Ohki 2001[68]	239	7	2.9%
	Ouriel 2003[69]	700	25	3.6%
	Qu 2009[74]	612	11	1.8%

	Qu 2007[75]	*366*	*10*	*2.7%*
	Sampaio 2004[80]	212	9	4.2%
	Wolf 2002[122]	189	13	6.9%
	Zarins 2003[125]	383	10	2.6%
	Total	**12487**	**1009**	**8.1%**
Type II endoleak <30 days	Boult 2004[26]	950	44	4.6%
	Espinosa 2005[46]	193	7	3.8%
	Hinchliffe 2004[53]	269	13	4.8%
	Howell 2000[115]	215	3	1.4%
	Jones 2007[58]	873	164	18.8%
	Lee 2002[117]	150	29	19.3%
	Parlani 2002[35]	336	22	6.5%
	Waasdorp 2008[89]	291	84	28.9%
	Total	**3277**	**366**	**11.1%**
up to 1 year	Blum 2001[23]	298	9	3.0%
	Carpenter 2004[37]	227	18	7.9%
	Go 2008[51]	130	3	2.3%
	Hinchliffe 2004[53]	269	17	6.3%
	Howell 2000[115]	84	8	9.5%
	Ouriel 2003[69]	704	173	24.6%
	Zarins 2003[125]	383	55	14.4%
	Total	**2095**	**283**	**13.5%**
>1 year	Arko 2003[113]	206	40	19.4%
	Becquemin 2004[18]	250	33	13.2%
	Bos 2008[28]	234	43	18.4%
	Verhoeven 2004[29]	*306*	*26*	*8.5%*
	Brewster 2006[30]	873	161	18.9%
	Espinosa 2009[45]	337	5	1.5%
	Herwaarden 2007[90]	212	25	11.8%
	Hiramoto 2006[54]	325	74	22.8%
	Hobo 2008[95]	7554	1426	18.9%
	Hobo 2006[99]	*2846*	*370*	*13%*
	Fransen 2003[100]	*4613*	*485*	*10.5%*
	May 2000[64]	383	4	1.0%
	Nevla 2009[67]	206	25	12.1%
	Ohki 2001[68]	239	13	5.4%
	Qu 2009[74]	612	26	4.2%
	Qu 2007[75]	*366*	*9*	*2.5%*
	Zarins 2003[125]	573	61	10.6%
	Total	**12004**	**1936**	**16.1%**
Type III endoleak <30 days	Go 2008[51]	376	1	0.3%
	Waasdorp 2008[89]	291	1	0.3%
Type III endoleak >1 year	Becquemin 2004[18]	250	12	4.8%
	Blum 2001[23]	298	5	1.7%
	Bos 2008[28]	234	2	0.9%
	Boult 2006[25]	961	2	0.2%
	Espinosa 2009[45]	337	3	0.9%
	Hobo 2008[95]	7554	525	6.9%
	Hobo 2006[99]	*2846*	*101*	*3.5*

	Fransen 2003[100]	*4613*	*225*	*4.9%*
	Herwaarden 2007[90]	212	7	3.3
	Hiramoto 2006[54]	325	3	0.9%
	Nevla 2009[67]	206	2	1.0%
	Ohki 2001[68]	239	1	0.4%
	Ouriel 2003[69]	704	23	3.3%
	Pitoulias 2009[73]	617	3	0.5%
	Qu 2009[74]	612	0	0%
	Sampaio 2009[79]	241	0	0%
	Zarins 2003[125]	383	8	2.1%
	Total	**13173**	**596**	**4.5%**
Access artery injury	Blum 2001[23]	298	5	1.7%
	Bos 2008[28]	234	20	8.5%
	Espinosa 2004[46]	193	4	2.1%
	Howell 2000[115]	215	4	1.9%
	Howell 2000[116]	*89*	*8* [a]	*9.0%*
	Lange 2005[98]	4888	314	6.4%
	Lee 2002[117]	150	8	5.3%
	Maldonado 2007[62]	430	4	0.9%
	Ricco 2003[76]	1012	19	1.9%
	Shames 2003[120]	241	11	4.6%
	Total	**7661**	**348**	**4.5%**

Common non-technical complications

The incidence of the common technical complications is shown in Table 51.

Table: Incidence of common non-technical complications (Case Series)

Study ID	Number of participants	Number of events	
		Number	%
Mortality rate (<30 days)			
Abbruzzese 2008[14]	565	10	1.8%
Ayerdi 2003[114]	96	0	0.0%
Becquemin 2004[19]	250	5	2.0%
Blum 2001[23]	270	1	0.4%
Bos 2008[28]	234	4	1.7%
Verhoeven 2004[29]	*308*	*2*	*0.6%*
Boult 2006[25]	961	17	1.8%
Boult 2004[26]	*950*	*16*	*1.7%*
Brewster 2006[30]	873	16	1.8%
Cao 2009[33]	557	10	1.8%
Parlani 2002[35]	*336*	*4*	*1.2%*
Zannetti 2001[36]	*266*	*3*	*1.1%*
Carpenter 2004[37]	227	3	1.3%
Conrad 2009[40]	832	13	1.5%
Criado 2001[109]	152	5	3.3%
Dias 2009[43]	304	9	3.0%
Espinosa 2009[45]	337	13	3.9%
Herwaarden 2007[90]	212	5	2.4%
Hinchliffe 2004[53]	269	11	4.1%
Hobo 2008[95]	7554	181	2.4%
Marrewijk 2005[97]	*6787*	*168*	*2.5%*
Lange 2005[98]			
<80Y age	*4191*	*84*	*2.0%*
>80Y age	*697*	*35*	*5.0%*
Laheij 2002[101]	*2863*	*85*	*3.0%*
Vallabhaneni 2001[102]	*2862*	*85*	*3.0%*
Howell 2000[115]	215	0	0.0%
Howell 2000[116]	*89*	*0*	*0.0%*
Lalka 2005[128]	136	0	0.0%
Lee 2002[117]	150	2	1.3%
Lee 2000[118]	*67*	*2*	*3.0%*
Nevla 2009[67]	206	6	2.9%
Ohki 2001[78]	239	20	8.4%
Ouriel 2003[70]	704	11	1.6%
Qu 2009[74]	612	3	0.5%
Qu 2007[75]	*378*	*6*	*1.6%*
Ramaiah 2002[119]	260	2	0.8%
Ricco 2003[76]	891	27	3.0%
Sampaio 2004[80]	241	4	1.7%
Elkouri 2003[81]	*100*	*0*	*0.0%*
Shames 2003[120]	245	4	1.6%
Thomas 2005[87]	1000	58	5.8%
Traul 2008[88]	245	2	0.8%
Vasquez 2004[93]	213	7	3.3%
Wales 2008[92]	286	12	4.2%
Wolf 2002[122]	189	2	1.1%
Zarins 2003[125]	1193	22	1.8%
Zarins 2000[123]	*149*	*2*	*1.3%*
Total	**20718**	**485**	**2.5%**

Mortality - AAA related (range 21-59 months)			
Abbruzzese 2008[14]	565	14	2.5%
Brewster 2006[30]	857	11	1.3%
Conrad 2009[40]	832	21	2.5%
Dias 2009[43]	304	12	4.0%
Espinosa 2009[45]	337	3	0.9%
Hiramoto 2006[54]	325	3	0.9%
Hobo 2008[95]	7554	377	5.0%
Hugl 2007[127]	366	9	2.5%
Ouriel 2003[70]	700	24	3.4%
Pitoulias 2009[73]	617	6	5.9%
Traul 2008[88]	245	2	0.8%
Zarins 2003[125]	383	5	1.3%
Total	**13085**	**487**	**3.7%**
Mortality Non-AAA related (range 12-36 months)			
Ayerdi 2003[114]	96	1	1.0%
Espinosa 2004[47]	193	12	6.2%
Howell 2001[115]	215	12	5.6%
Ohki 2001[68]	239	53	22.2%
Zarins 2000[123]	149	15	10.1%
Total	**892**	**93**	**10.4%**
Mortality – Total (up to 1 year)			
Becquemin 2004[19]	250	15	6.0%
Carpenter 2004[37]	227	15	6.6%
Dias 2009[43]	304	14	4.6%
Elkouri 2003[81]	100	3	3.0%
Ouriel 2003[69]	700	83	11.9%
Shames 2003[120]	241	14	5.8%
Tonnessen 2005[121]	205	17	8.3%
Wolf 2002[122]	189	27	14.3%
Zannetti 2001[36]	266	10	3.8%
Total	**2482**	**198**	**8.0%**
Mortality – Total (>1 year)			
Abbruzzese 2008[14]	565	220	39%
Becquemin 2004[19]	250	43	17.2%
Brewster 2006[30]	873	419	48%
Cao 2009[33]	349	38	10.8%
Conrad 2009[40]	832	247	29.7%
Dias 2009[43]	304	61	20.0%
Espinosa 2009[45]	337	75	25.3%
Herwaarden 2007[90]	212	146	69%
Hiramoto 2006[54]	325	92	28%
Hobo 2008[95]	7554	2141	28.3%
Marrewicj 2005[97]	*6787*	*647*	*9.5%*
Vallabhaneni 2001[102]	*2862*	*655*	*22.9%*
Hugl 2007[127]	366	48	13.1%
Lee 2000[117]	67	15	22.4%
Nevla 2009[67]	206	73	35.5%
Ouriel 2003[69]	704	143	20.3%
Qu 2009[74]	612	124	20.2%
Ricco 2003[76]	891	47	4.6%
Wales 2008[92]	286	28	9.8%
Zarins 2004[124]	1193	250	21.0%
Zarins 2003[125]	*383*	*55*	*14.4%*
Total	**15926**	**4210**	**24.4%**
Cardiac event rate (<30 days)			

Bos 2008[28]	234	5	2.1%
Boult 2004[26]	950	69	7.3%
Elkouri 2003[81]	100	12	12.0%
Lange 2005[98]	4888	167	3.4%
Lee 2002[117]	150	11	7.3%
Nevla 2009[67]	206	10	4.9%
Parlani 2002[35]	336	4	1.2%
Ramaiah 2002[116]	230	6	2.6%
Ricco 2003[76]	1012	8	0.8%
Vasquez 2004[93]	212	15	7.1%
Wales 2008[92]	286	8	2.8%
Zarins 2000[123]	149	5	3.4%
Total	**8753**	**320**	**3.7%**
Renal impairment (<30 days)			
Carpenter 2004[37]	192	2	1.0%
Elkouri 2003[81]	100	3	3.0%
Lange 2005[98]	4888	101	2.1%
Lee 2002[117]	150	2	1.3%
Ramaiah 2002[119]	230	3	1.3%
Ricco 2003[76]	1012	11	1.1%
Vasquez 2004[93]	212	6	2.8%
Wales 2008[92]	286	7	2.4%
Zarins 2000[123]	149	1	0.7%
Total	**7401**	**143**	**1.9%**
Graft infection (< 30 days)			
Parlani 2002[35]	336	1	0.3%
Graft infection (up to 1 year)			
Blum 2001[23]	298	1	0.3%
Criado 2003[109]	240	1	0.4%
Total	**538**	**2**	**0.38%**
Graft infection (>1 year)			
Hiramoto 2006[54]	325	1	0.9%
Hobo 2006[98]	2846	3	0.1%
Howell 2001[115]	215	1	0.5%
Hugl 2007[127]	366	2	0.5%
Total	**3752**	**7**	**0.2%**
Colonic ischaemia (<30 days)			
Carpenter 2004[37]	227	1	0.4%
Hobo 2008[98]	7554	24	0.3%
Maldonado 2007[62]	430	4	0.9%
Ricco 2003[76]	891	3	0.3%
Vasquez 2004[93]	212	3	1.4%
Zarins 2000[123]	149	1	0.7%
Total	**9463**	**36**	**0.4%**
Lower limb ischaemia (<30 days)			
Blum 2001[23]	298	6	2.0%
Ricco 2003[76]	891	16	1.6%
Wales 2008[92]	286	7	2.4%
Vallabhaneni 2001[102]	2862	15	0.5%
Total	**4337**	**44**	**1.0%**
Pulmonary complications (<30 days)			
Bos 2008[28]	234	1	0.4%
Carpenter 2004[37]	227	6	2.6%

Elkouri 2003[81]	100	5	5.0%
Lange 2005[98]	4888	101	2.1%
Lee 2002[117]	150	4	2.7%
Ramaiah 2002[119]	230	3	1.3%
Ricco 2003[76]	891	6	0.7%
Vasquez 2004[93]	212	9	4.2%
Wales 2008[92]	286	9	3.1%
Total	**7218**	**144**	**2.0%**
Haemorrhage (<30 days)			
Nevla 2009[67]	206	20	9.7%
Local wound complications (<30 days)			
Ayerdi 2003[114]	96	1	1.0%
Blum 2001[23]	298	9	3.0%
Carpenter 2004[37]	227	27	11.9%
Elkouri 2003[81]	100	10	10.0%
Espinosa 2004[45]	193	6	3.1%
Howell 2000[115]	215	6	2.8%
Howell 2000[116]	*56*	*3*	5.4%
Ramaiah 2002[119]	230	12	5.2%
Vasquez 2004[93]	212	8	3.8%
Wales 2008[92]	286	3	1.0%
Total	**2277**	**124**	**5.4%**
Spinal Cord Ischaemia(<30 days)			
Maldonado 2007[62]	430	2	0.5%

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