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Comparison of Endovascular and Open Surgical Repairs for Abdominal Aortic Aneurysm

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions, and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to **epc@ahrq.gov**.

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Structured Abstract

Objectives: Evaluate treatment options for nonruptured abdominal aortic aneurysms (AAA); the relationship of hospital and physician volume to outcomes for endovascular repair (EVAR); affect of patient and AAA factors on outcomes; cost-benefits of treatments.

Data sources: PubMed®, Cochrane Library, FDA, and other electronic websites until May 2006. Reference lists and content experts were used to identify additional reports.

Review Methods: Randomized controlled trials (RCT) of open surgical repair (OSR), EVAR, or active surveillance, systematic reviews, nonrandomized U.S. trials, and national registries were used to assess clinical outcomes. Volume-outcome articles published after 2000 were reviewed if they reported the relationship between U.S. hospital or physician volume and outcomes, were population-based, and the analysis was adjusted for risk factors. Cost studies included at least 50 EVAR and provided data on costs or charges, and cost-effectiveness analyses.

Results: Initial or attained diameter is the strongest known predictor of rupture. The annual risk of rupture is below 1 percent for AAA <5.5 cm in diameter. Among medically ill patients unfit for OSR with AAA ≥5.5 cm, the risk of rupture may be as high as 10 percent per year. Early/immediate OSR of AAA <5.5 cm (two trials n=2,226) did not reduce all-cause mortality compared with surveillance and delayed OSR. Results did not differ according to age, gender, baseline AAA diameter, or creatinine concentration. Two RCT with followup of at least 2 years compared EVAR to OSR for AAA ≥5.5 cm. EVAR reduced postoperative 30-day mortality compared to OSR (1.6 percent EVAR vs. 4.7 percent OSR, RR = 0.34 [0.17 to 0.65]). Early reduction in all-cause mortality with EVAR disappeared before 2 years. Post-operative complications and reinterventions were higher with EVAR. Quality of life differences were small and disappeared after 3-6 months. One RCT of patients with AAA ≥5.5 cm judged medically unfit for OSR (n=338), reported no difference in all-cause mortality or AAA mortality between EVAR and no intervention (HR = 1.21; 95 percent CI 0.87 to 1.69). Forty-eight nonrandomized reports evaluated EVAR. Patient, AAA characteristics, and outcomes were similar to RCT comparing EVAR to OSR. A volume outcome relationship has been shown for OSR, but there are no data adequate to estimate the effect of hospital or physician volume on EVAR outcomes or to identify a volume threshold for policymakers. Immediate OSR for AAA <5.5 cm costs more and does not improve long-term survival compared to active surveillance and delayed OSR. The cost effectiveness of EVAR relative to OSR is difficult to determine. However, compared to OSR for AAA ≥5.5 cm, EVAR has greater in-hospital costs primarily due to the cost of the prosthesis. EVAR has shorter length of stay, lower 30-day morbidity and mortality but does not improve quality of life beyond 3 months or survival beyond 2 years, and is associated with complications, need for reintervention, long-term monitoring, and higher long-term costs. Compared to no intervention in patients medically unfit for OSR, EVAR costs more and does not improve survival or quality of life.

Conclusions: For AAA <5.5 cm in diameter, active surveillance with delayed OSR results in equivalent mortality but lesser morbidity and operative costs due to fewer interventions compared to immediate OSR. For AAA ≥5.5 cm, EVAR has not been shown to improve long-term survival or health status over OSR though peri-operative outcomes are improved. EVAR

does not improve survival in patients who are medically unfit for OSR. EVAR is associated with more complications, need for reintervention, monitoring, and costs compared to OSR or no intervention. U.S. RCT are needed using approved EVAR devices to evaluate patient outcomes.

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Appendix and Evidence Tables for this report are provided electronically at
http://www.ahrq.gov/clinic/tp/aaareptp.htm

Executive Summary

Introduction

An abnormal bulging of the abdominal aorta, called an abdominal aortic aneurysm (AAA) is a potentially serious condition that can lead to death if it ruptures. An AAA is considered present when the maximum diameter of the aorta below the renal arteries (infrarenal AAA) expands to exceed 3.0 cm. In the United States, rupture of AAA accounts for approximately 9,000 deaths annually.[1] Another 30,000-40,000 patients undergo elective surgical repair of asymptomatic AAA to prevent rupture, with perioperative mortality ranging from 2-8 percent.[2,3] Death due to AAA rupture or repair is the thirteenth leading cause of death in the United States and tenth among older men.[4,5]

The majority of AAAs remain asymptomatic for years, though the risk of rupture increases with AAA size. Immediate death can result, and mortality remains between 40 and 60 percent, even when emergency care and repair are undertaken. Management options are primarily based on patient's life expectancy and AAA size and include no treatment, active surveillance and delayed repair, immediate open surgical repair (OSR), and endovascular aneurysm repair (EVAR).

Recent recommendations for AAA screening in high-risk populations along with emerging endovascular methods for repair have led to increased interest in evaluating the effectiveness and adverse effects of treatment options for patients with AAA.

Objectives and Key Questions

The Minnesota Evidence-based Practice Center (EPC) was asked to answer the following questions related to elective treatment of nonruptured AAA that were nominated by America's Health Insurance Plans (AHIP).

1. What are the comparative effectiveness and adverse effects of treatment options of AAA including active surveillance, open repair, and endovascular repair?
2. What is the relationship of volume, both hospital and physician, to the benefits and harms of endovascular procedures to repair AAA?
3. How do the characteristics of the aneurysm (size/location/shape) and the patient (age/gender) affect the benefits and harms of endovascular and open-surgical repair?
4. What are the costs-benefits for each of the procedures?

Methods

Literature Search

For questions 1 and 3 we searched PubMed®, Cochrane Library, Food and Drug Administration (FDA), and other electronic websites from 1990 to October 2005. The following terms were included: abdominal aortic aneurysm, endovascular repair, surveillance, and surgery. Titles and abstracts of identified references were reviewed. For question 2, MEDLINE® was searched for publications about volume-outcome relationships for procedures to repair AAA

published after 1990. Key words included abdominal aortic aneurysm, volume, outcome, and process assessment of health care. For question 4 we used the terms abdominal aortic aneurysm combined with economics, nursing economics, pharmaceutical economics, cost, pharmacoeconomics, cost analysis, cost allocation, cost-benefit analysis, cost control, cost savings, cost of illness, cost sharing, "deductibles and coinsurance," medical savings accounts, health care costs, direct service costs, drug costs, employer health costs, hospital costs, health expenditures, capital expenditures, hospital economics, hospital charges, hospital costs, medical economics, or medical fees. Reference lists and contacts with content experts were used to identify additional reports.

Study Selection Extract Data

For questions 1 and 3, studies were eligible if they were randomized controlled trials or multivariate natural history studies involving AAA, open repair, endovascular repair, or active surveillance and reported clinical outcomes. We included and updated a systematic review of EVAR vs. open repair published by the U.K. National Institute of Clinical Excellence (NICE) as well as nonrandomized U.S. trials or national registries.[6] To assess volume-outcome relations (question 2), articles that met the following criteria were reviewed. The report had to be an original analysis of U.S. data representing repair of unruptured AAA beginning in 1990; the sample had to represent variation between hospitals or surgeons in a community or larger geographic area and present sample statistics representing the relationship between a measure of hospital or physician volume and a beneficial or harmful outcome of AAA repair; the analysis had to attempt to make adjustments for other known risk factors. For question 4, studies had to include at least 50 AAA procedures in each arm, provide data on costs, charges, or reimbursement rates, or be a cost-effectiveness analysis.

Quality Assessment and Strength of Evidence

The methods of Schulz et al. were used to assess the quality of randomized controlled trials (RCT).[7] We determined whether intention-to-treat analysis was utilized and whether published RCT used EVAR devices similar to those available in the United States. We evaluated whether effectiveness of interventions varied according to patient, aneurysm, or device characteristics including: age, race, gender, EVAR device manufacturer, or aneurysm size (small [<5.5 cm] vs. large aneurysm). Data from nonrandomized studies were included to assess relevance and consistency to practice in the United States. Analyses of administrative databases to examine relationships between provider volume and outcomes were evaluated by their ability to represent current practices in the United States, the reliability and validity of 'volume' and outcome measures, and the thoroughness of the regression analyses, including control of key risk factors. Quality of cost studies were based on whether they included relevant costs, used appropriate time frame, and evidence of effectiveness and adverse effects from randomized controlled trials.

Data Extraction

Data regarding study, patient, and device characteristics as well as outcomes were extracted. Outcomes were described as effectiveness (initial clinical success ≤30 days or during initial

hospitalization; short-term (30 days to 6 months), midterm (6 months to 5 years), and long-term >5 years) and adverse effects based on recommendations for reporting of outcomes for open and EVAR by the Society for Vascular Surgery.[8] The primary outcome was midterm all-cause mortality. Additional outcomes included initial all-cause mortality, AAA mortality, AAA rupture, quality of life, and technical measures of EVAR and OSR success. Adverse events and complications included treatment-related mortality and morbidity such as endoleaks, graft rupture, migration, kinking, and need for additional interventions, including OSR.

For question 2 the main outcome that has been studied in relation to provider volume is short-term mortality. All published analyses used regression models of this outcome on retrospectively defined volume measures. Information was abstracted to characterize (1) the study population, (2) volume measures, (3) outcome measures, (4) regression model including covariates used for risk adjustment and handling of clustering of patients within hospitals or surgeons, and (5) adjusted and unadjusted estimates of volume effects. For question 4 we assessed charges, costs, reimbursement rates, hospital and intensive care unit length of stay, incremental cost effectiveness ratios, and quality adjusted life years.

Data Analysis

Descriptive characteristics of patient populations were presented. For results from RCTs we calculated odds ratios (ORs) for categorical variables and weighted risk differences for continuous variables with the corresponding 95 percent confidence intervals. Because of the paucity of RCT, results from each study were evaluated and described and the corresponding statistical parameters for effect size and significance were described. We reported on tests of interaction for predefined subgroups. The preponderance of evidence for relationships between the volume of procedures performed by hospitals and physicians to repair AAA and outcomes has been obtained by secondary regression analysis of administrative databases. Methodological differences, including the definition of volume and outcomes measures, make it difficult to compare results from the different studies. Use of variables to control for pre-procedure risk (case-mix), physician training, and health care system attributes varied. Analytical methods varied as well. Therefore, we did not attempt to do a meta-analysis to combine estimates from different retrospective observational studies. The summary of studies of the volume-outcome relationship was limited to tabulation of individual study characteristics and results. Cost analysis was limited to a review of published findings and discussion of study limitations and strengths.

Results

Comparative Effectiveness of Treatment Options

The strongest known predictor of rupture is AAA diameter. AAA enlargement rate is not consistently independently associated with rupture rate. The annual rate of rupture for AAA <5.5 cm is 1 percent or less. Among individuals refusing or medically unfit for surgical intervention, the 1 year rupture risk may exceed 10 percent in AAA >6 cm and for AAA of >8 cm, the risk may exceed 25 percent at 6 months.

For patients with small AAA (<5.5 cm), two high-quality RCT (n=2,226), the Aneurysm Detection and Management study (ADAM)[9] and the United Kingdom Small Aneurysm Trial (UKSAT)[10] demonstrated that early/immediate OSR of AAA did not reduce all-cause mortality compared with active surveillance and delayed OSR. After a mean followup of approximately 5 years, the overall relative risk (RR) and hazard ratio (HR) for all-cause mortality for ADAM and UKSAT were 1.21 [95 percent confidence interval (CI) 0.95 to 1.54] and 0.94 [95 percent CI 0.75 to 1.17, p=0.56], respectively. Outcomes did not differ between treatment groups according to age, gender, or AAA diameter at baseline. After a mean followup of 8 years in the UKSAT study, no significant difference in mean survival was found between groups (6.5 years for surveillance versus 6.7 for early surgery, p=0.29) although total mortality was lower in the early/immediate OSR (adjusted HR was 0.83 [95 percent CI 0.69 to 1.00, p=0.05]). AAA related mortality was not reduced by early/immediate OSR in the ADAM study (3.3 percent vs. 3.4 percent). In the UKSAT trial, AAA-related deaths (combined ruptured AAA, secondary AAA rupture, and AAA repair deaths) accounted for 19 percent of all deaths in the surveillance group compared to 15 percent for the early OSR group at a mean followup of 8 years. Differences in quality of life measures, when they existed, were small.

Three high-quality multicenter trials compared the outcomes of EVAR with OSR of large AAA (≥5.5 cm) (n = 1,489) in patients judged medically fit for OSR.[11-13] Two trials provided data at 2 years or longer (n = 1,413).[12,13] None of the studies were conducted in the United States. All began recruitment prior to 2000 and some EVAR devices used may not be currently available in the United States EVAR reduced postoperative 30-day mortality compared to OSR (EVAR = 1.6 percent vs. OSR = 4.7 percent RR = 0.34 [95 percent CI 0.17 to 0.65]) and hospital length of stay. Reduction in all-cause mortality seen with EVAR disappeared by 2 years. There was a persistent 3 percent reduction in AAA-related mortality. Outcomes did not differ significantly by treatment for either all-cause or AAA mortality according to age, gender, aneurysm diameter, or renal function though few women were enrolled. In EVAR-1, postoperative complications, included primarily EVAR graft related ruptures, infections, endoleaks, thrombosis, or other surgery required and re-exploration of OSR. These were five times more common with EVAR as with OSR (17.6 vs. 3.3 per 100 person years). The Dutch Randomized Endovascular Aneurysm Management (DREAM) trial reported nearly identical rates of severe (systemic, local-vascular/graft complications or local nonvascular complications) adverse event-free survival in the two groups (16.9 percent [EVAR] versus 19.4 percent [OSR] at year 2). The rate of survival free of moderate or severe complications was similar at two years (65.6 percent for EVAR and 65.9 percent for OSR). In EVAR-1, reinterventions occurred three times as often in the EVAR group, exceeding 20 percent at 4 years. DREAM showed a similar pattern in the first 9 months but then reintervention rates were roughly parallel.

DREAM study data on quality of life and sexual functioning favored EVAR in the early postoperative period, but by 6 months, scores in the OSR group equaled or surpassed those in the EVAR group. In EVAR-1, physical component summary scores in the Short Form-36 (SF-36) were lower with OSR to 3 months, with no differences thereafter. There were no differences at any point in the mental component summary scores. Differences at 3 months did not achieve a level previously determined detectable by patients. EVAR costs were higher than OSR.

The British EVAR-2 study was a methodologically high-quality study and the only RCT that evaluated EVAR versus no intervention for patients with large AAA (≥5.5 cm) and deemed medically unfit for OSR (n = 338). There was a 6 percent higher all-cause mortality in patients receiving EVAR compared with no intervention that did not achieve statistical significance (45

percent vs. 39 percent; HR = 1.21; [95 percent CI 0.87 to 1.69]). AAA rupture occurred in 4 percent of EVAR patients and 12 percent of individuals in the no intervention group (rupture rate in the no intervention group = 9 per 100 person years.) There was no difference in AAA related mortality (12 vs. 13 percent) (HR = 1.01 [0.55 to 1.84]), although nine ruptures and six AAA deaths occurred in the EVAR group prior to elective repair (median time from randomization to EVAR = 57 days). There were no significant differences in mortality for EVAR compared with no intervention according to age, sex, aneurysm diameter, or renal function. The 30-day EVAR mortality was higher in the sicker EVAR-2 patients than those receiving EVAR who were judged medically fit for surgery in EVAR-1 (9 percent versus 2 percent; $p < 0.0001$). If only elective EVAR cases were considered in EVAR-2 the 30-day EVAR mortality was 7 percent. Compared to EVAR-1 patients, there was a greater need for internal iliac artery embolization, blood products, renal dialysis, and longer hospital stay.

Approximately 55 percent of individuals with large AAA screened for trial enrollment in EVAR-1 and 2 were judged to be anatomically suitable for EVAR. The most commonly used EVAR devices in these two trials were Zenith (33-59 percent of devices) and Talent (21 to 33 percent). Over 90 percent of EVAR devices used in these trials were aortobiiliac device systems commercially available in the U.K. at the time of the RCT. Aorto-aortic (tube) grafts were used in the majority of OSR. Selection for EVAR and OSR grafts was based on the discretion of the surgical team. There are no data to determine whether outcomes varied according to device type. The exact make and model of EVAR devices used is not known, and some may not be approved for use or currently available in the United States. Refinements in device, delivery systems, and provider experience may be associated with different outcomes in the United States than reported in these RCTs.

Forty-eight reports of lower methodologic quality than RCT (case series, nonrandomized controlled studies, national registries, and U.S. FDA reports) assessed clinical outcomes of EVAR. While it is not possible to make direct comparisons with RCT, most reports explicitly stated patients were candidates for OSR. Baseline patient characteristics, AAA diameter, 30 day and 2 year overall, and AAA mortality as well as EVAR conversion rates and secondary interventions for included patients were similar to those from EVAR-1 and DREAM. None of these reports assessed EVAR in patients with AAA ≥5.5 cm and considered “medically unfit for OSR” and direct comparisons cannot be made with EVAR-2. One report evaluated outcomes of EVAR and OSR in a “high surgical risk” subgroup of patients entered into any of five nonrandomized multicenter Investigational Device Exemption (IDE) studies leading to U.S. FDA approval of EVAR devices. Patients with AAA ≥5.5 cm were retrospectively categorized as “high surgical risk” based on age >60 years and having at least one cardiac, pulmonary, or renal comorbidity. Inclusion criteria for the IDE studies required that patients were candidates for OSR, though in one study patients were prospectively defined as being poor candidates for OSR or at high risk due to pathophysiologic conditions including creatinine >2.0 mg/dL, disabling COPD, ejection fraction <25 percent, stroke with residual deficit, or myocardial infarction within the past 6 months. Three-quarters of “high-risk” patients had only one comorbid category and less than one percent had all three categories.[14] After 4 years, deaths categorized as due to AAA were similar between EVAR and OSR patients (4.2 percent and 5.1 percent respectively ($p = 0.58$). Overall-survival in EVAR treated patients was 10 percent lower compared to OSR (56 percent vs. 66 percent) though this difference was not statistically significant ($p = 0.23$).

Patient treatment preference according to AAA size and medical fitness for surgical intervention is difficult to ascertain. How the results from published RCTs influence future patient and provider treatment preferences in the United States is not known.

Volume Outcomes

Our search did not find any adequate published studies of the relationship between hospital or physician volume and any outcome of EVAR.

There were several historical studies of the relationship between the volume of OSR done by hospitals and physicians to repair AAA and short-term mortality. Many of these studies represented practices in the 1990s when endovascular repair procedures were being developed and later tested in randomized controlled trials. Studies of the volume-outcome relationship for OSR have not been reported since the widespread adoption of EVAR in the United States. Nevertheless, historical studies of OSR of AAA can serve to inform the design of future studies of EVAR. Studies of OSR have not determined why hospital volume appears to be related to short-term mortality. Surgeon volume and surgeon specialty may explain a large portion of the commonly observed inverse relationship between the volume of OSR done by hospitals and short-term mortality. Very low-volume hospitals often appear to have higher mortality; however, data from low-volume providers is highly variable and statistically imprecise. No previous study carefully controlled all the key risk factors that might confound these observational studies, especially the characteristics of the aneurysms that will be important in studies of EVAR. The type of endograft might be another important factor in studies of EVAR outcomes. The one study of OSR that was able to control for preoperative clinical measures did not find a significant association between hospital volume and mortality. Very low-volume hospitals often appear to have higher mortality; however, data from low-volume providers is highly variable and statistically imprecise. Thus, future studies of EVAR volume in relation to outcomes must strive to take all important covariates into account, and consider the imprecision of outcome data for low-volume providers. Two studies suggested that the volume effect for OSR was relatively consistent in subgroups of patients with different preoperative risks of death.[15,16] However, studies of EVAR should not assume that any volume-outcome relationship will be constant across subgroups of patients. Arbitrary cutpoints for hospital volume that were associated with lower adjusted mortality ranged from 17 to 100 AAA repairs per year in studies of OSR. Investigators used a variety of measures of volume and mortality and did not attempt to analyze their data to find a threshold(s) for the volume effect. If studies of volume-outcome relationships for EVAR are going to be used by payers or policymakers to define volume thresholds for preferential referral, studies should be designed with standardized measures of volume and outcomes, and the nature of relationships between hospital and physician volume and outcomes needs to be characterized more completely.

Costs

Case series focusing on hospital costs generally found that EVAR costs more to perform than OSR, primarily due to the cost of the prosthesis. The high cost of the EVAR prosthesis is partially offset by reduced hospital and intensive care unit length of stay, operating time, and necessity for blood transfusion relative to open surgery. More comprehensive cost analyses noted the higher follow-up costs for EVAR.

None of the Markov cost effectiveness models had accurate data on the complication and reintervention rates associated with EVAR. Although the Michaels et al. study is based on the literature published through September 2004, several case series have come out since then, and data from midterm results of RCTs were not included.[17] Results from ongoing RCTs, comparing EVAR and OSR for large AAA and EVAR versus surveillance for small AAA conducted in the United States have not yet been published.

Data from RCTs demonstrate that for small AAA (<5.5 cm) immediate OSR costs more and does not improve survival compared to active surveillance and delayed elective intervention. For large AAA (≥5.5 cm) among patients unfit for OSR, EVAR has both greater short- and long-term costs, does not improve overall survival or quality of life beyond 1 year, and is associated with complications, need for reintervention, and long-term monitoring compared to OSR or no intervention. EVAR is associated with shorter hospital and intensive care unit length of stay, reduced AAA mortality, and lower 30-day morbidity and mortality, compared to OSR.

The cost effectiveness of EVAR relative to OSR varies by whether an institutional or societal perspective was taken. Third party payers and hospitals each formulate their own institutional perspective on costs and effectiveness that depends on the extent and duration of their responsibility for the financing and/or provision of the patient's health care needs. For third party payers such as Medicare, hospital reimbursement levels are determined by a DRG that does not vary by the type of inpatient procedure (EVAR or OSR) or the cost of the prosthesis.

Conclusions

AAA are associated with considerable morbidity, mortality, and health-care costs. Patients with AAA <5.5 cm have an annual risk of rupture of approximately 1 percent. For AAA <5.5 cm in diameter high-quality RCT results demonstrate that active surveillance with ultrasound and delayed OSR (if AAA attains a diameter of ≥5.5 cm or the patient develops aneurysm related symptoms) results in equivalent mortality but lesser morbidity and operative costs due to fewer interventions compared to immediate OSR. There are no RCTs evaluating EVAR in these patients.

Among individuals refusing or medically unfit for OSR the 1-year rupture risk may exceed 10 percent in AAA >6 cm and for AAA of >8 cm, the risk may exceed 25 percent at 6 months. For AAA ≥5.5 cm and suitable for EVAR, high-quality RCTs have been conducted outside the United States and may have used some EVAR devices that are not approved for use in the United States. Their results demonstrate that, compared to OSR, EVAR is associated with lower perioperative morbidity and mortality and persistent reduction in AAA-defined mortality to 4 years, though the latter may be due, at least in part, to ascertainment bias for later term cause of death. EVAR did not improve longer term overall survival or health status and was associated with greater complications, need for reintervention, long-term monitoring, and costs.

For the minority of patients with AAA ≥5.5 cm and judged medically unfit for OSR, one high-quality RCT conducted in the U.K. and with EVAR devices that may not be approved for use in the United States demonstrated that EVAR did not improve survival or health status and costs more than no intervention.

There are no data adequate to estimate the effect of hospital or physician volume on EVAR outcomes and identify a volume threshold for policymakers. A volume outcome relationship for OSR has been shown for surgery prior to the introduction of EVAR, but none since.

The long-term cost effectiveness of EVAR relative to OSR is difficult to determine because there are no long term (>4 year) outcome data from RCT of EVAR versus OSR conducted in the United States using devices approved by the FDA.

Future Research

- Results from nonrandomized trials, case-series, or FDA reports are inadequate to accurately assess the relative effectiveness and safety of treatments for AAA. The highest priority for future research to guide clinical care is to conduct long-term RCTs in the United States to assess whether RCT results of EVAR conducted in Europe apply to U.S. settings. These include EVAR vs. OSR for AAA $\geq$5.5 cm, EVAR versus active surveillance for AAA <5.5 cm, and EVAR versus no intervention for AAA $\geq$5.5 cm in patients medically unfit for OSR.
- Effective strategies are required to disseminate and implement the findings from published high-quality RCTs to patients, providers, health-care organizations, and payers.
- Additional information on the benefits and risks of treatments in women is needed.
- Refinements in EVAR devices, technique, and interventionist team are required to reduce complications and need for long-term followup.
- Consistent/validated definitions of outcomes including AAA mortality, complications, and need for reintervention are required to assist clinicians, investigators, policymakers, and patients to evaluate relative safety and effectiveness of treatment options. In particular, cause of death ascertainment beyond 30 days or the initial hospitalization is problematic. Reducing ascertainment bias likely requires rigorous adjudication of all death, including use of autopsy and/or post-mortem imaging.
- Conduct RCTs to determine whether medical therapy slows AAA enlargement or rupture.
- Improve data submission, followup, and cause of death ascertainment in registries.
- Improved medical management is needed for patients with large AAA considered as unacceptable surgical risks.
- Specific studies of EVAR are needed to characterize the hospital and physician volume-outcome relationship, if any. The validity of methods used to identify and count EVAR procedures should be examined and reported. Studies should measure volume in a consistent manner and focus on outcomes defined in reporting standards including clinical success, continuing success, complications, and return to preprocedure activity levels. Risk adjustment should include patient demographics, comorbidity, morphology of the aneurysm and access vessels, device characteristics, and any other variables that could have a substantial influence on the outcomes under investigation. Rigorously developed and tested regression models and examination of the sensitivity of results to the method of analysis would be useful. Most likely, representative prospective registries will be needed to perform a proper indepth analysis to determine whether and how the volume of endovascular procedures done by hospitals or physicians to repair AAA relate to beneficial or adverse outcomes. Ideally, future studies would strive to characterize the functional form of volume-outcome relationships and explain why they exist. The volume-mortality relationship for OSR of AAA needs to be reexamined in the EVAR era.
- Future cost analyses studies should include short- and long-term followup data, either collected prospectively on all patients or incorporated from RCTs into Markov models.

- A standardized approach to analyzing costs and effectiveness associated with the two procedures is recommended. Studies should explicitly describe the methods used to calculate costs and should include the following categories: direct medical care costs, institutional overhead costs, patient travel costs, and patients' time and/or lost earnings. The collection of these costs should be carefully itemized and described.
- Studies conducting prospective data collection in the United States taking a societal perspective are needed. Where appropriate, data on the patient's time taken off work or other activities to travel and attend medical appointments, whether on an inpatient or outpatient basis, and to obtain prescriptions are needed.
- Data on United States patient's Quality of Life (QOL), where the treatment of the QOL associated with lost earnings and death is explicitly stated, should also be collected.

Evidence Report

Chapter 1. Introduction

Overview

An abnormal bulging of the abdominal aorta, called an abdominal aortic aneurysm (AAA) is a potentially serious condition that can lead to death if it ruptures. An AAA is considered present when the maximum diameter of the aorta below the renal arteries (infrarenal AAA) expands to exceed 3.0 cm. In the United States rupture of AAA accounts for approximately 9,000 deaths annually.[1] Another 30,000-40,000 patients undergo elective surgical repair of asymptomatic AAA to prevent rupture, with perioperative mortality ranging from 2-8 percent.[2,3] Death due to AAA rupture or repair is the thirteenth leading cause of death in the U.S. and tenth among older men.[4,5]

The majority of AAAs remain asymptomatic for years, though the risk of rupture increases with AAA size. Immediate death can result and mortality remains between 40 and 60 percent, even when emergency care and repair are undertaken. Management options are primarily based on patient's life expectancy and AAA size and include no treatment, active surveillance and delayed repair, immediate open surgical repair (OSR), and endovascular repair (EVAR).

Recent recommendations for AAA screening in high-risk populations along with emerging endovascular methods for repair have led to increased interest in evaluating the effectiveness and adverse effects of treatment options for patients with AAA.

Question 1: What are the comparative effectiveness and adverse effects of treatment options of AAA including active surveillance, open repair, and endovascular repair?
Question 2: What is the relationship of volume, both hospital and physician, to the benefits and harms of endovascular procedures to repair AAA?
Question 3: How do the characteristics of the AAA (size/location/shape) and the patient (age/gender) affect the benefits and harms of EVAR and OSR?
Question 4: What are the costs-benefits for each of the procedures?

Background

The prevalence of AAA found in population-based ultrasound screening studies ranges from 4.2-8.8 percent in men and 0.6-1.4 percent in women.[18] Risk factors for AAA include age, history of regular smoking, family history of AAA, coronary artery disease, hypertension, hypercholesterolemia, and cerebrovascular disease. The overall prevalence of AAA greater than 3.0 cm in "never smokers" ranges from less than 0.2 percent in ages 50-54 to nearly 3 percent in ages 75-79. For "ever smokers" the prevalence ranges from approximately 1 percent to 7 percent across these age groups. Smoking status is also a risk factor for AAA mortality. Negative risk factors for AAA prevalence include female gender, diabetes, and black race.

In a study of 73,451 mostly male U.S. veterans ages 50-79 who did not have a history of AAA, 7.1 percent had an AAA defined as an infrarenal aortic diameter of ≥3.0 cm on ultrasound. More than 90 percent of AAA were considered small (<5.5 cm) and only 0.4 percent were ≥6.0 cm. With each 1 cm decrease in diameter, the number of AAA of that diameter or larger more than doubled.[19] Most aneurysms noted at autopsy were small and asymptomatic and therefore did

not require intervention during the patient's lifetime. However, the natural history of AAA is progressive enlargement. Non-invasive prevention of growth and rupture is primarily limited to smoking cessation and blood pressure control, though the use of aneurysmal pharmacotherapy has recently received attention.[20] Because as many as one in three AAA eventually rupture if left untreated[18] and only 10 to 25 percent of individuals with ruptured AAAs survive through repair, diagnostic and treatment goals are to identify individuals with AAA and target effective treatments possessing low interventional morbidity towards individuals at high risk of rupture.

A recent report from the U.S. Preventive Services Task Force (USPSTF) addressed screening for AAA.[18] The review identified four good or fair quality population-based AAA screening trials; all conducted outside of the U.S. All trials had ORs favoring an association between an invitation to attend screening and a reduction in AAA-related deaths. Pooled analysis of trials showed a reduction for men in AAA-related mortality (OR, 0.57 [CI 0.45 to 0.74]). The 5-year outcomes of AAA screening by smoking history in a cohort of 100,000 men 65-74 years of age demonstrated that 155 AAA deaths could be prevented by screening and elective OSR 138 (89 percent) in "ever smokers." Meta-analysis of the trials demonstrated a nonsignificant reduction in all-cause mortality (OR, 0.98 [95 percent CI 0.95, 1.02]). The evidence report and the USPSTF concluded that "population screening for AAA in men ages 65-74 years appears to reduce AAA-related mortality. Treatment is associated with significant risks for operative deaths and complications. These risks, however, may be acceptable to men with AAAs greater than 5.5 cm."[18,21] Additionally, the USPSTF review of four relevant cost-effectiveness studies of AAA screening yielded an estimated cost-effectiveness ratio of population-based screening compared with no screening that was in the range of other cost effective preventive services.[22] Recommendations for selected screening are likely to lead to increased AAA detection and intervention, particularly of the more prevalent small AAA. Management of AAA will therefore take on increased importance in the future.

The total volume of elective AAA repairs has increased for both OSR and EVAR.[23] Vascular surgeons who repair AAA utilizing both endovascular and open techniques have experienced an increase in aneurysm referrals, while those who have not adopted endovascular skills have seen a decline.[24] Practitioners in interventional radiology, cardiovascular surgery, general surgery, and peripheral vascular surgery are receiving training and purchasing the equipment specifically required to perform AAA endografting. These can include attending 1-3 month training courses at a cost of $30,000 and purchasing portable fluoroscopy units that cost approximately $250,000.[24]

Because the risk of rupture is strongly related to AAA size, management options are generally based on AAA size (small <5.5 cm vs. large ≥5.5 cm) and patient's operative risk (medically fit for OSR versus medically unfit) determined by age and comorbidities. OSR has been considered the gold-standard for prevention of AAA rupture and death. However, it has the mortality risk of major vascular surgery with perioperative complications of about 32 percent including myocardial ischemia, respiratory failure, renal failure, ischemic colitis, spinal cord ischemia and prosthetic graft infection, as well as the cost of this procedure.[22] Therefore, management options that would be equally effective in preventing AAA rupture and prolonging survival, with lower morbidity and similar or reduced health care costs, have been sought.

There are no established criteria for determining acceptable medical fitness for OSR. Because risk factors for AAA include smoking, advanced age, and hypertension, individuals considered candidates for OSR frequently are elderly and have multiple comorbidities including cardiac, pulmonary, or renal disease. Decisions about whether a patient is an acceptable OSR or

EVAR candidate are determined by the perioperative team and incorporate the severity as well as the presence of comorbidities, AAA morphology, the individual surgeon/medical center threshold for acceptable medical fitness and assessment of whether outcomes vary according to gender, AAA, or device characteristics.

As reviewed by others,[25-27] several studies have observed that, on average, in-hospital mortality was inversely associated with the number (volume) of AAA OSR procedures done by hospitals. The mortality appeared to be particularly high for very low volume providers decreasing and eventually leveling off as volume increased. Despite substantial improvement in survival, volume continued to be inversely associated with short-term mortality. In-hospital case fatality rates for OSR in Michigan were reduced from 13.6 percent in 1980 to 5.6 percent in 1990.[28] In California, the in-hospital mortality rate decreased from 11.9 percent to 4.5 percent from 1982 to 1994.[29] Nevertheless, the volume of procedures done in hospitals continued to be inversely associated with mortality in these studies as was originally observed by Luft et al, who analyzed hospital discharge data from 1974-1975.[30]

Given repeated findings of a relationship between volume and mortality for OSR, one might hypothesize that a volume-outcome relationship exists for EVAR as well. Like OSR, EVAR is a technically demanding procedure with inherent risks. However, volume-outcome relationships vary by type of procedure and are not found for all procedures.[30,31] Patient selection criteria, technology, operator skills, and processes of care for endovascular repair differ from open surgical procedures and continue to evolve. Different types of physicians, including interventional radiologists with different training and experience, may be involved in endovascular repairs. As demonstrated elsewhere in this report, short-term mortality is less with EVAR compared to OSR.[6,32,33] Indeed, the 30-day mortality after EVAR now might be less than 2 percent, making it more difficult to detect relationships to hospital or operator volume.

Discussions about cost effectiveness usually begin with a belief that a given approach confers a benefit. The question then is how the cost of achieving that benefit compares to other effects that a similar investment could pay for. Some of the benefits of EVAR appear to occur early in the care process, e.g., fewer complications, reduced hospital length of stay (LOS), etc. Hence they have value primarily where early return to work is crucial. These outcome measures are typically presented as the cost per quality adjusted life year (QALY).

The costs of AAA repair include preoperative costs, hospitalization costs associated with the initial procedure, the costs of the EVAR prosthesis (i.e., graft), and subsequent post operative surveillance, interventions, hospitalizations, and drug treatment. EVAR requires longer term and more intensive monitoring than open repair. OSR of AAA incurs the costs of the surgical team as well as perioperative hospital care. OSR is considered to have greater and more severe early morbidity than EVAR. OSR could result in a longer and more costly length of hospital stay and subsequent greater duration of impaired functional status and quality of life. However, late complications, including rupture, have been rare after open repair. Thus, radiologic, laboratory, and clinician evaluation and costs beyond the perioperative period (approximately 3 months) in the absence of symptoms are minimal.

The main questions in the elective management of AAA are: (1) at what diameter to offer elective repair and (2) do EVAR devices provide a safe and effective treatment option. Additional questions relate to whether outcomes are associated with surgical or medical center volume or OSR or EVAR performed and the relative cost and cost-effectiveness of various options.

Chapter 2. Methods

Topic Assessment and Refinement and Literature Review

We began the review process conferencing with the Agency for Healthcare Research and Quality (AHRQ) and the nominee partner (AHIP) to clarify the project scope and background information. Clinical experts representing areas of vascular surgery, internal medicine, AAA epidemiology, diagnosis and treatment, and systematic review methodology served as members of a technical expert panel (TEP) (Appendix A*.) TEP comments and suggestions clarified the conceptual framework and refined study questions used for the project. Based on our initial conference calls, we developed a comprehensive work plan that covered an assessment and refinement of study questions and proposed literature search and review, inclusion/exclusion criteria, and methods for evaluating the quality of studies and reporting the evidence.

Analytic Framework

An analytic framework was developed that assessed the key questions. The framework describes the logic chain that should be supported by evidence linking management options for AAA to improved outcomes. It takes the perspective of adults presenting with an asymptomatic AAA based on AAA size (small [<5.5 cm] vs. large [≥5.5 cm]) and patient operative risk (medically fit for surgery vs. medically unfit for surgery).

Question 1. What are the comparative effectiveness and adverse effects of treatment options of AAA including active surveillance, open repair, and endovascular repair?

Periodic surveillance, typically with abdominal ultrasound, has been considered reasonable for those with abdominal aortas measuring 3.0-3.9 cm because their risk of rupture is considered very low. For AAA 4.0-5.4 cm in diameter (small AAA) the question existed of whether immediate OSR, compared to ultrasound surveillance with delayed OSR, improves AAA-related mortality and all-cause mortality. For individuals with an AAA >5.5 cm, immediate OSR has been recommended, provided the patient is considered medically fit for OSR.[34]

In 1997, prior to widespread adoption of EVAR, there were an estimated 37,000 OSRs of intact AAA in the United States.[35] During OSR, a vascular graft, comprised of a non-textile synthetic material or a woven synthetic textile that is usually sealed with collagen, gelatin, or albumin is sutured into the aorta. The proximal anastomosis is an end-to-end type and the distal anastomosis is located on the aortic bifuracation, the iliac bifurcations, or the common femoral arteries. Results from several long-term followup studies of individuals undergoing elective OSR for AAA have indicated that the risk of late complications, including secondary rupture, is quite low. In the absence of symptoms, additional evaluation of patients who received OSR is not typically performed.

However, in-hospital mortality rate for repair of intact AAA found in the National Inpatient Sample of community hospitals was 4.2 percent.[4] In-hospital plus 30-day mortality associated with AAA repairs in the elderly fee-for-service Medicare population was estimated to be 5.6

* Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/tp/aaareptp.htm

percent in 1999. Because of perioperative mortality and morbidity (which are likely higher in older/sicker patients), individuals who were considered medically unfit for OSR due to comorbidities and/or advanced age previously underwent no attempt to repair the aneurysm. However, the risk of rupture can be as high as 25 percent per year for AAA with diameters greater than 6 cm.[36]

EVAR consists of the placement of a graft across the aneurysm and fixation to the normal aortic and iliac wall with stents at both ends. Endovascular access is via a transfemoral or transiliac artery approach with the aim of excluding the aneurysm by this graft. The theoretic benefit of EVAR versus OSR is based on the belief that EVAR has lower early morbidity, length of hospital stay, and mortality. Additionally, EVAR may provide long-term effective prevention of AAA rupture, equivalent or increased overall survival, and improved quality of life compared to OSR. These potential benefits of EVAR must be balanced with the need for periodic long-term followup, later-term device failures or complication, need for reinterventions, and costs.

The first report of endoluminal treatment of AAAs in a clinical setting was in 1990.[37] By 2001 the estimated number of EVAR in the United States each year exceeded 12,000.[38] An estimated 40-80 percent of AAA could be amenable to endovascular grafting based on aneurysm size, morphology, and patient surgical risk characteristics.[39,40]

EVAR has involved at least 16 different devices, but only four gained FDA approval and are currently in use in the United States: Cook Incorporated (Zenith); Gore (Excluder); Medtronic (AneuRx); and Endologix (Powerlink). A fifth device, Guidant (Ancure) is no longer available but was used in published reports that are included in this report. Others are, or will soon be, applying for FDA approval including (Talent, Quantum, ENOVUS (formerly Trivascular), and Anaconda).[41] Each device has specific criteria and recommendations regarding the anatomic suitability of an individual patient for a particular graft type. However, one published accepted contraindication to EVAR is a proximal infranal neck either shorter than 15 mm or absent. Other anatomic features include excessive vascular tortuosity or angulation, calcification, or circumferential thrombus. None of these criteria are fixed and often vary by center, interventionalist, and device. There are numerous design and delivery issues unique to each device. The details, available on the FDA websites: (Gore Excluder: www.fda.gov/cdrh/mda/docs/P020004.html; Cook Zenith: www.fda.gov/cdrh/MDA/DOCS/p020018.html; Guidant Ancure: www.fda.gov/cdrh/mda/docs/ p990017s030.html; Endologix PowerLink: www.fda.gov/cdrh/mda/docs/p040002.html, and Medtronic AneuRx: www.fda.gov/cdrh/pdf/p990020.html), are beyond the scope of this project. However, because certain aneurysm characteristics may be associated with additional patient factors, device selection, and clinical outcomes, it is difficult to accurately assess differential rates of outcomes among graft types.

Typically, EVAR devices are modular and allow modification (including selection of size and configuration) by the surgeon or radiologist at the time of placement based on patient, provider, and aneurysm criteria. The most common configurations of endovascular devices now used in the treatment for AAA are the aortobiiliac and aortouniilliac devices. Early developed aorto-tube grafts are no longer marketed in the United States. The endograft is radio-opaque with prespecified markers to aid positioning under fluoroscopic guidance and subsequent radiologic monitoring. It is composed of fabric or expended polytetrafluroethylene, and metal stents and comes loaded in a delivery system. Under fluoroscopic guidance, this introducer system is fed through the iliac arteries by means of catheters and guidewires until the endograft is positioned correctly at the top and bottom of the aneurysmal segment. Removal of the introducer system allows the fixing devices to attach with hooks, radial force/friction, column stiffness, or other

anchors to the aortic wall and hold the graft in place, excluding blood flow from the aneurysm sac and removing pressure from the aneurysm wall.

Imaging guidelines for AAA repair with endovascular stent grafts have been published.[42] These include preprocedural, intraprocedural, and postprocedural imaging and are more extensive than recommended for OSR. The details are beyond the scope of this report. However, two imaging modalities have been recommended no more than 6 months prior to the planned procedure in order to 1) detect or confirm, 2) measure AAA, or 3) evaluate the suitability of the patient for EVAR. Additionally, preoperative evaluation is required because during the procedure it may be determined that EVAR is not possible or complications may result, necessitating OSR.

Recommended preprocedure imaging modalities consist of Thin-Cut Helical/Spiral CT Arteriography (CTA) with multiplanar reconstruction and catheter angiography. The goals of intraprocedural imaging are: (1) to guide and document the appropriate placement of the endovascular stent graft and (2) to evaluate the effectiveness of the stent graft in excluding the AAA. Fluoroscopy and catheter angiography have been considered necessary and sufficient in the vast majority of cases. The goals of postprocedural imaging are to (1) confirm and redocument the appropriate placement status of the stent graft, (2) better assess the effectiveness of the stent graft in initially excluding the AAA (detecting flow in the sac), (3) follow the long-term fate and size of the AAA sac and ensure its stability, (4) detect stent graft failure, and (5) better characterize and follow patients with endoleaks. Current imaging modalities include plain films of the abdomen, CTA, and catheter angiography. The first two have been recommended every 6 months for at least 2 years and CTA annually thereafter (or more frequently if symptoms or device related problems develop). Catheter angiography is not recommended if CTA findings are satisfactory. Excellent technical results are initially characterized by a perfectly canalized blood flow and later by a completely retracted aneurysm wall around the endograft. EVAR use has increased, in part because it is postulated to be less invasive than open repair, results in reduced procedural morbidity, mortality, and hospital and other health care costs, while improving health related quality of life and providing equivalent long-term disease-specific and overall survival to OSR.

Additionally, EVAR may alter the threshold for intervention among individuals because EVAR may be considered an effective and relatively safe option compared to (1) surveillance among individuals with small (≥5.5 cm) AAA in whom the risk of rupture was previously considered too low to justify the morbidity of OSR and (2) no treatment for individuals with large AAA who are judged unfit for surgery due to advanced age or coexisting medical conditions and thus have a risk of rupture-related death that is relatively low compared to mortality from OSR.

EVAR has been associated with unique complications not associated with OSR. These can be related to the device, patient, AAA morphology, or interventionalist. Complications unique to EVAR include stent migration, stent wire fracture, metal fatigue, and endoleak. Because of the potential for these complications to arise and cause serious medical problems or require reintervention, long-term monitoring, following EVAR with CTA, is currently standard practice.

Endoleak is defined by the persistence of blood flow outside the lumen of the endoluminal graft but within the aneurysm sac as determined by an imaging study. An endoleak is evidence of incomplete exclusion of the aneurysm from the circulation. While causes and classifications vary, they may result from an incomplete seal between the endograft and the wall of the blood

vessel, an inadequate connection between stent components, fabric defects, or porosity or retrograde blood flow from patent aortic side branches.[8] Some endoleaks may resolve spontaneously. However, some persistent endoleaks are capable of repressurizing the aneurysm sac and have been associated with late rupture and need for subsequent interventions. Ruptures have been observed in the absence of endoleak. This concept of elevated pressure within the aneurysm sac has been called endotension. Table 1 provides a classification of endoleak.

Table 1. Classification of endoleak[43]

Type	Cause of Perigraft Flow
I	a) Inadequate seal at proximal end of endograft b) Inadequate seal at distal end of endograft c) Inadequate seal at iliac occluder plug
II	Flow from visceral vessel (lumbar, IMA, accessory renal, hypogastric) without attachment site connection
III	a) Flow from module disconnection b) Flow from fabric disruption Minor (<2 mm) Major (≥2 mm)
IV	Flow from porous fabric (<30 days after graft placement)
Endoleak of undefined origin	Flow visualized but source identified

Literature Search and Review Strategy

A literature search was conducted using PubMed®, Cochrane Library, FDA, and other electronic websites from 1990 to October 2005, as well as handsearching of references from retrieved articles and contact with content experts. The following terms were included: abdominal aortic aneurysm, endovascular repair, surveillance, and surgery. Titles and abstracts of identified references were reviewed using standardized data abstraction sheets. The number of excluded studies and reasons for exclusion were noted. Studies meeting preliminary eligibility criteria were retrieved in full for further assessment and data extraction. (See Appendix B* for Exact Search Strings and Appendix C for Lists of Excluded References.) Data extraction forms included information related to study and patient characteristics, interventions, and outcomes.

Study Eligibility and Extract Data

Studies were eligible if they were randomized controlled trials or natural history studies involving AAA, open repair, endovascular repair, or active surveillance and reported clinically relevant outcomes (Figures 1 and 3 on pages 27 and 29). We also included and updated a systematic review of evidence of EVAR vs. open repair for AAA published online and in manuscript form by the U.K. National Institute of Clinical Excellence (NICE). Data from nonrandomized studies and device-specific data available on the FDA website as submitted by manufacturers to the FDA were included to assess relevance and consistency to the United States. This included a report submitted by the Society for Vascular Surgery and published online in April 2006.[14]

* Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/tp/aaareptp.htm

Outcomes

Outcomes were described as effectiveness (initial clinical success ≤30 days or during initial hospitalization), short-term (30 days to 6 months), midterm (6 months to 5 years), long term (>5 years), and adverse effects. These were based on recommendations for reporting of outcomes for open and EVAR by the Society for Vascular Surgery.[8] The primary outcome was midterm all-cause mortality. Additional clinical outcomes included initial all-cause mortality, AAA mortality, AAA rupture, quality of life, and technical measures of EVAR and OSR success. Adverse events included treatment related mortality and morbidity (graft rupture, migration, and kinking) and need for additional interventions (including OSR). Incidences of endoleaks were also noted. Because data from RCT represent level one evidence, their results were emphasized and reported separately from reports using other study designs. Results from the United States that evaluated EVAR approved and available in the United States were highlighted for nonRCT data.

Quality of studies, reduction of bias, and strength of evidence. The methods of Schulz et al. were used to assess the quality of randomized controlled trials (RCT).[7] We determined whether intention-to-treat analysis was utilized, whether results varied by intention-to-treat or per protocol analysis, and whether published RCT used EVAR devices similar to those approved and available in the United States. We evaluated whether effectiveness of interventions varied according to patient, aneurysm, or device characteristics including age, race, gender, EVAR device manufacturer and characteristics (name, tubular, mono or bi-iliac), aneurysm size (small [<5-5.5 cm] vs. large aneurysm) or medical fitness for OSR. Data from nonrandomized studies were included to assess relevance and consistency to practice in the United States. All data were extracted by trained data extractors onto standardized, piloted forms (Appendix D[*]).

Question 2. What is the relationship of volume, both hospital and physician, to the benefits and harms of endovascular procedures to repair AAA?

History of the relationship between hospital volume and operative mortality for OSR.

Volume is believed to be a proxy for one or more structures or processes of care that influence outcomes. However, the structure and processes of care responsible for the volume-outcome relationship in cases of OSR of AAA have not been firmly established. Experience and greater availability of resources in higher volume hospitals could lead to better structure, patient selection, and pre-, intra-, and post-operative processes of care as well as more capable surgeons and support staff. The relationship between hospital volume and survival after OSR of AAA also might depend, in part, on surgeon volume and the type of surgeon (vascular, cardiothoracic, general). Some low-volume providers could perform operations only as necessary or in emergency situations that increase the risk, and a single death could greatly influence the mortality rate of low volume providers.

Conversely, hospitals that somehow achieve better outcomes or those that have a surgeon who specializes in vascular surgery could get more referrals. High volume itself might generate more referrals because information about volume may be more readily available to the community than outcome information. Some providers might be associated with a poor outcome and get fewer referrals. Thus, to some extent, outcome could drive volume rather than vice versa.[44,45] Selective referrals could be augmented by recent policies of purchasers such as the

[*] Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/tp/aaareptp.htm

Leapfrog Group who encouraged preferred use of hospitals in urban areas that perform more than 30 repairs of AAA per year in an effort to improve outcomes.[46]

Policymakers have already used studies of the volume-outcome relationship to set thresholds for preferential referral for OSR. The Leapfrog definition of 'high' volume was based on an investigation that was judged to be the single best report in the literature at the time.[47] This investigation analyzed 3,419 repairs of unruptured AAA done in 116 Veterans Affairs (VA) hospitals (>99 percent male patients) from 1991-1993.[48] Repairs of intact AAA were identified by Patient Management Category algorithms applied to ICD-9-CM codes recorded on discharge abstracts. The validity of this method of case identification wasn't reported. Unadjusted in-hospital mortality was 4.2 ± 3.5 percent in hospitals that performed 32 or more repairs versus 6.7 ± 7.8 percent in hospitals performing fewer than 32 repairs. The basis for selecting 32 as a cutoff was not reported, although it was the mean hospital volume. However, 22 so-called low-volume hospitals had zero mortality in 267 patients. In addition, the published report does not clearly state whether the volume categories were per annum as defined by Leapfrog or over the entire 3-year period of study. Furthermore, many of the operations might have been performed by surgical residents in training. Given these limitations, this study is not adequate for defining a hospital volume threshold for the United States. Investigators only recently demonstrated that hospital volume measured in one time period is related to outcomes in a subsequent period of time.[49] The Leapfrog criterion for a high volume hospital has been increased to 50 or more procedures per year.[50] It is not clear whether this count includes endovascular procedures to repair of AAA or whether the data used to define this threshold represent a period of time before FDA approval and widespread use of endovascular devices.

Adoption of endovascular procedures to repair AAA. The FDA approved the first devices for EVAR in September 1999. A separate International Classification of Diseases procedure code for EVAR was issued in October 2000. By 2001 approximately 36 percent of the repairs of intact AAA were coded as EVAR procedures in the National Inpatient Sample of 986 non-federal community hospitals in 33 states.[51] Those undergoing EVAR rather than OSR tended to be older males with higher prevalence of hypertension and ischemic heart disease and less renal insufficiency or peripheral artery disease.[52] Between May 2001 and September 2003 approximately 38 percent of AAA repairs were coded as endovascular procedures in the VA medical centers. Discharge data from 234 accredited hospitals in Illinois indicated that EVAR was used in approximately 32 percent of all (unruptured and ruptured) AAA cases in 2002.[53] The proportion of AAA repairs done by EVAR was less in women than men. In-hospital mortality for elective EVAR was 2.3 percent in this series of cases from 1995 to 2003, and higher in women than men (5.1 percent vs. 1.7 percent unadjusted for risk or length of stay).

Hospital discharge data representing non-federal hospitals in New York indicated that 40 percent of all repairs of intact AAA in 2001 were EVAR, increasing to more than 50 percent in 2002.[54] There was a corresponding increase of more than 20 percent in the number of hospitals performing EVAR. Compared to patients undergoing OSR, patients having EVAR were older and more likely to have coronary artery disease, hypertension, hyperlipidemia, and diabetes mellitus. In 2002, 60 hospitals in New York performed EVAR. Nearly half did five or fewer procedures, while 12 hospitals did 30 or more. In-hospital mortality rates were 1.9 percent and 0.8 percent respectively. This small difference in mortality was not statistically significant given the relatively small number of hospitals. Furthermore, risk adjustment was not done because the database did not contain patient or physician identifiers, information about the severity of co-morbidities, or information about the aneurysms that were repaired.

Rationale for a volume-outcome relationship for endovascular repair of AAA. There is some evidence of a learning curve for EVAR of AAA. One practice at a tertiary facility analyzed 277 consecutive cases treated from 1994 to 1998 and estimated that approximately 55 cases were required before their technical success rate leveled off at 88 percent.[55] Custom-made endografts were used in two-thirds of these procedures prior to the availability of commercial bifurcated modular endografts for investigational use in 1997. The surgical team and patient selection criteria remained stable during the period of observation, although it is likely they were not trained to perform EVAR and learned as they were developing new procedures and devices. Thus, their experience should not be extrapolated to current EVAR practices where trained physicians use approved devices with less problematic designs. The same referral practice compared 30 procedures done as part of a clinical trial to 230 cases done after FDA approval of the device. Technical success was achieved in 97 percent and 98 percent of these cases. However, procedural complications such as endoleaks, contrast-induced azotemia, access site hematoma, and limb occlusions increased from 11 percent to 18 percent. The increase in complications was attributed not to poorer proficiency over time, but rather to a greater degree of anatomical and morphological difficulty of the cases being referred and treated after FDA approval.[56]

European registry data were grouped according to cumulative experience in 93 hospitals from 1994 to 2000. The EVAR procedures (n=2,863) were grouped as the first 11 performed at a center, cases 12-37, 38-91, and 92 and higher. Unadjusted mortality after 30 days was the same (3-4 percent) in all four groups.[57] There were differences in smoking status, vascular morphology, and types of devices used in the four groups with initial patients appearing to have greater risk. Co-morbidity was not reported. The adjusted hazard of death during continued followup was lower in quartiles three and four (i.e., after 38 cases) compared to first quartile representing early experience. The adjusted hazard ratio for secondary interventions for endoleaks, migration, kinking, thrombosis, stenosis, and rupture was lower in all other quartiles compared to the most inexperienced case quartile. The amount of bias present in these comparisons due to differences in patient selection and censoring (initial cases followed much longer) is not clear. A more recent report based on this registry suggested that devices for earlier EVAR procedures might explain the influence of experience on midterm outcomes.[58] This observation highlights the importance of analyzing data that represent current devices and clinical practices in the United States rather than foreign data on devices that are not being used in the United States.

One should not assume there would be a relationship between EVAR volume and outcome just because there is a learning curve. When development of a new technique is fairly complete, teachers can greatly facilitate learning by experience. Measures of hospital and physician volume typically used in studies are not cumulative counts beginning with initial experience. In fact, volume is often measured during a specified time period ignoring prior experience. Therefore, typical volume measures may reflect a provider's ability to maintain rather than learn skills and effective processes of care. The volume needed to maintain processes of care, skills, and optimal outcomes after a learning curve levels off is not known.

Several randomized controlled trials have required that a certain number of EVAR be done by investigators prior to enrolling patients, but the threshold definitions vary. The EVAR trials required investigator centers to perform at least 20 AAA repair procedures before enrolling patients, whereas investigator teams in the DREAM trial had to have done at least five procedures.[12,59] The Veterans Administration Open Versus Endovascular Repair (OVER) trial

requires a vascular surgeon or interventional radiologist who has performed at least 12 endovascular procedures.[60] Thus, investigator experience required for participation in clinical trials has varied. The bases for these volume criteria were not reported.

Analytical issues. Outcome measures that are based on a smaller number of cases (i.e., low volume) exhibit greater random variation. One is less confident that the outcome measured for low volume providers represents their true or long-term performance. A minimum number of cases per provider is sometimes required to help assure the outcome measurements aren't too unreliable. Regression analyses that weight data points by their variance can help avoid placing undue emphasis on outcomes measured in low-volume providers. Regression analyses generally assume that the variation in outcome measures is homogeneous across all levels of a predictor, which is generally not true when volume is used to predict outcomes. Data transformation, such as taking the logarithm of outcome measures, might make this assumption more tenable. Furthermore, the influence of each hospital or physician on the estimated volume-outcome relationship estimated by regression analysis should be examined.

Patients treated at the same hospital or by the same surgeon may be more likely to have similar outcomes than if the patients were treated by different providers. Thus, outcomes might not be truly independent of each other as is assumed by regression analyses that use the patient as the unit of analysis. This so-called clustering with hospitals and physicians reduces variation in outcomes compared to what would be observed with truly independent measurements.

General estimating equations can be used to calculate confidence intervals and p-values that take clustering into account.[61] This analytical approach is difficult when the outcome data are clustered within more than one variable, e.g., hospital and surgeon volume, and when the size of the clusters, i.e., volume, is correlated with the outcome. In addition, the resulting estimate of relative effects such as an odds ratio is an aggregate or population averaged estimate specific to the mix of clusters in the analysis. Alternatively, random-effects regression models that consider clusters, i.e., hospitals or surgeons, as random variables can account for clustering in the data. Small clusters (low-volume providers) can complicate this approach. Clustering within surgeons and hospitals could be analyzed by hierarchical random-effects models if surgeons don't operate at more than one hospital. If a surgeon(s) represents most of the volume at a hospital, the surgeon and hospital volume will be redundant measures, making it difficult to estimate their separate effects on outcomes. Thus, different methods of analysis of the same data might not produce the same estimate of the effects of volume on outcomes. The method of analysis is an important consideration when comparing studies. Multiple methods of analysis could be employed to see if the results are sensitive to the method of analysis.

The adequacy of risk adjustment is questionable in retrospective studies of databases that did not prospectively collect data on known risk factors. Known risk factors for operative mortality for AAA repairs include the urgency of the operation, presence and severity of renal dysfunction, ischemic heart disease and its treatment with beta-adrenergic blockers and statins, heart failure and chronic obstructive pulmonary disease, advanced age, being female, and several characteristics of the aneurysm such as its diameter and juxtarenal position.[52,62] Unmeasured risk factors could be particularly important for low-volume providers. One unrecognized high risk case can greatly affect the outcomes, and if the variable that made the case high risk wasn't measured, the increased risk would not be controlled. Omission of influential covariates can bias estimates of volume-outcome relationships even if they are balanced across groups. Thus, it is important to examine the risk factors that were taken into consideration in analyses.

All studies of the relationship between provider volumes and outcomes used regression models to analyze the data. Therefore, it is important to know how well the model fits the data and how well the model discriminated the outcomes, such as death or survival. A model with poor discrimination suggests that key risk factors were not measured, hence controlled, in the analysis. The c-statistic is commonly used to examine model discrimination. A c-statistic equal to 1 indicates perfect discrimination whereas a value of 0.5 indicates the model was no better than random predictions of outcomes.

Search Strategy for Pertinent Publications

The MEDLINE® database was searched for publications about volume-outcome relationships for procedures to repair AAA that were published after 1990 when endovascular procedures for repair of AAA became available, at least to investigators. Key words included abdominal aortic aneurysm, volume, outcome, and process assessment health care. Reference lists were searched for additional reports (Figure 2 on page 28).

Study Inclusion and Exclusion Criteria

Articles that met the following criteria were reviewed to summarize study methods and characterize volume-outcome relationships.

- The report had to be an original analysis of data representing repair of unruptured AAA in the endovascular era beginning in 1990.
- The report had to represent practices in the United States.
- The sample had to represent variation between hospitals or surgeons in a community or larger geographic area, thereby excluding single site cases series.
- The report had to present sample statistics (e.g., percentages, odds ratios) representing the relationship between a measure of hospital or physician volume and any good or bad outcome associated with AAA repair.
- The analysis had to attempt to make adjustments for known risk factors in an effort to reduce bias.

Health care systems, physician training, clinical care processes, and procedures to repair AAA have evolved, thus older and foreign data might not represent current practices or outcomes in the United States. Since health care practices including patient selection criteria, referral patterns, and types of devices sold outside the United States could differ from the U.S. in important ways, this review was restricted to studies within the U.S. This restriction corresponds with the presumed interests of U.S. insurance companies that requested this evidence review. Furthermore, inclusion of foreign studies would not address the limitations of U.S. studies, would create concern about extrapolating foreign results to the United States, and would not alter the conclusions of this review. More recent recommendations in the United States to seek out higher volume hospitals could be altering the volume-outcome relationships. In addition, adoption of EVAR in recent years most likely has altered the characteristics of cases being surgically repaired, and perhaps the volume-outcome relationship. This review focused on available data that represented practices and outcomes in the United States in the 1990s and beyond.

Data Extraction

All published analyses regressed an outcome of AAA on retrospectively defined volume measures. A single unblinded reviewer abstracted information from each study to characterize (1) the study population including the time period and geographical region, (2) volume measures, (3) outcome measures, (4) regression model including covariates used for risk adjustment and handling of clustering of patients within hospitals or surgeons, and (5) adjusted and unadjusted estimates of volume effects.

Data Analysis

The preponderance of evidence for relationships between the volume of procedures performed by hospitals and physicians to repair AAA and outcomes has been obtained by secondary regression analysis of administrative databases. Methodological differences make it difficult to compare results from the different studies. For example, investigators defined hospital and physician volume in a variety of ways, often using arbitrary categorizations with varying reference groups. Use of variables to control for pre-procedure risk (case-mix), physician training, and health care system attributes varied. Analytical methods varied as well. Therefore, we did not attempt to do a meta-analysis to combine estimates from different studies. This review was limited to tabulation of individual study characteristics and results.

Question 3: How do the characteristics of the aneurysm (size/location/shape) and the patient (age/gender) affect the benefits and harms of endovascular and open-surgical repair?

It is not known whether patient, aneurysm, provider, or device characteristics differentially affect treatment success rates. As discussed above, patient factors including age, gender, and comorbidities may not only affect the prevalence and size of AAA but also the risk of AAA rupture and/or operative/EVAR related complications. As noted in Question 1, AAA morphology including size, vascular angulation, size of the aortic neck, and/or involvement of renal or iliac vessels may alter the feasibility of repair options and influence outcomes.

Literature Search Strategy and Eligibility Criteria

A literature search strategy was conducted similar to question 1 (Figures 1 and 3 on pages 27 and 29). Emphasis was placed on studies that provided comparative effectiveness of one treatment strategy versus another (especially RCT), conducted in the United States, used devices currently available in the United States, and provided information on clinical outcomes according to AAA size, location, shape, patient age, gender, or race. We updated a systematic review by NICE[63] with emphasis on results from RCTs or studies conducted in the United States.

Outcomes

Data regarding study, patient, and device characteristics, as well as outcomes, were extracted. Outcomes were described as effectiveness (initial clinical success ≤30 days or during initial hospitalization); short-term (30 days to 6 months), midterm (6 months to 5 years), and long-term

(>5 years); and adverse effects based on recommendations for reporting of outcomes for open and EVAR by the Society for Vascular Surgery.[8] The primary outcome was midterm all-cause mortality. Additional outcomes included initial all-cause mortality, AAA mortality, AAA rupture, quality of life, and technical measures of EVAR, and OSR success. Adverse events included treatment related mortality and morbidity including endoleaks, graft rupture, migration, kinking, and need for additional interventions, including OSR. Specific characteristics of AAA and patient included: 1) AAA size (small <5.5 cm; large ≥5.5 cm), shape (sacular vs. fusiform), extension (into iliacs); 2) patient age (<65 vs. ≥65), race (White, Black, Hispanic, other); gender; and 3) device manufacturer and type.

Quality of studies, reduction of bias, and strength of evidence. We used the methods of Schulz et al. to assess the quality of RCT.[7] We attempted to assess whether the effectiveness of interventions varied according to patient, aneurysm, or device characteristics including age, race, gender, EVAR device manufacturer, aneurysm size (<5.5 cm vs. ≥5.5 cm), or aneurysm location. No study quality measures were used for manufacturer submitted data available on the FDA website. We described how patients, AAA, EVAR characteristics, and outcomes compare with those from RCT.

Question 4: What are the costs-benefits for each of the procedures?

From the perspective of cost, different audiences have different concerns. Traditional economic analysis focuses on the cost to the economy of delivering each element of service. However, policy makers may be more interested in the payments they must underwrite than in the economic cost of a procedure. These costs vary somewhat depending on the health care system. For example, in the United States, where Medicare pays for hospital care using a DRG payment approach, differences in the costs of the prosthesis/graft or even in lengths of stay are irrelevant for Medicare because they are all folded into the overall rate paid. However, those differences are very salient to hospitals that must bear them. Likewise in the United Kingdom, working under the National Health System, issues of hospital efficiency are quite important.

The analysis becomes even more complex if a differential survival rate exists across treatments. Unless the results can be expressed in terms like QALYs, which capture both quality of life and survival, the estimated benefit may be exaggerated by comparing quality of life only among survivors.

The classic approach would be to estimate the difference in outcomes across treatments and then divide that by the difference in costs. However, in the case of AAA repair, the outcomes seem to be generally equivalent over the long term. The real difference lies in the short term.

EVAR is considered less invasive and may result in shorter in-hospital and intensive care unit length of stay compared with open repair. However, there are additional costs associated with EVAR. These include the high costs the stent device (which has accounted for over 50 percent of the total in hospital EVAR costs in one analysis) diagnostic cost, primarily because of increased imaging costs with EVAR, and professional fees.[64] Pre and intraprocedural imaging are more extensive with EVAR than open repair. Because of the concern related to EVAR complications or failures, long term radiologic monitoring is required. The complexities of and recommendations for conducting cost-effectiveness analyses comparing treatment options for AAA have been described.[22,65]

Search Strategy Methods

We adopted the search strategy used by the AHRQ report on AAA screening.[22] Our search was conducted within MEDLINE®. Key search terms included abdominal aortic aneurysm combined with economics, nursing economics, pharmaceutical economics, cost, pharmacoeconomics, cost analysis, cost allocation, cost-benefit analysis, cost control, cost savings, cost of illness, cost sharing, "deductibles and coinsurance," medical savings accounts, health care costs, direct service costs, drug costs, employer health costs, hospital costs, health expenditures, capital expenditures, hospital economics, hospital charges, hospital costs, medical economics, or medical fees. We focused on studies reporting on the cost associated with either procedure, EVAR, OSR, or both. This strategy yielded 27 articles published between 2000 and 2005. Six of these studies were eliminated from the analyses as they contained less than 50 patients in either arm of the study (i.e., EVAR or OSR).[66-71] Of the remaining 21 articles, 12 reported on a comparative analysis of EVAR and OSR, two reported on EVAR and Conservative Management (CM) (one of which also reported on EVAR and OSR), three on EVAR only, two on OSR and CM, and three on OSR only (Figure 4 on page 30).

Figure 1. Flow Chart: Question 1—RCTs

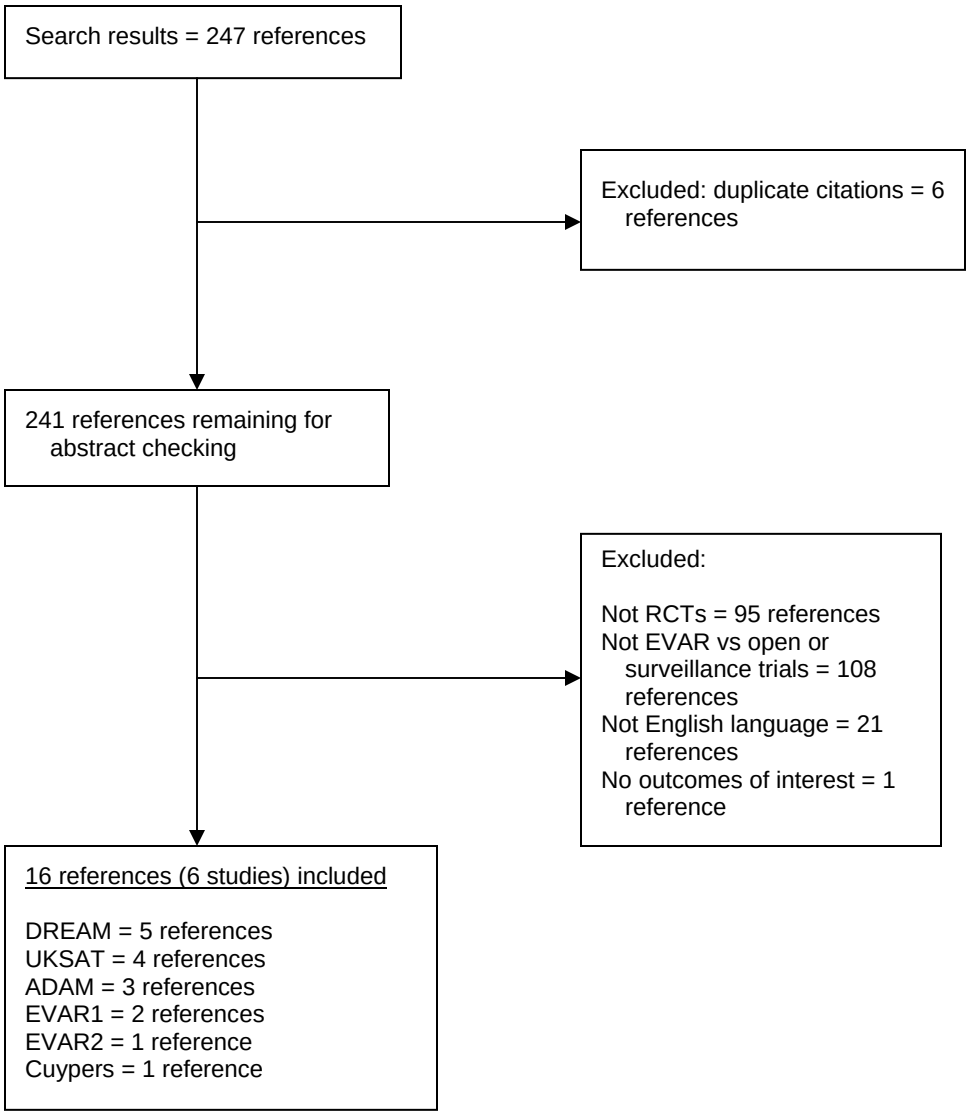


Figure 2. Flow Chart: Question 2—Volume

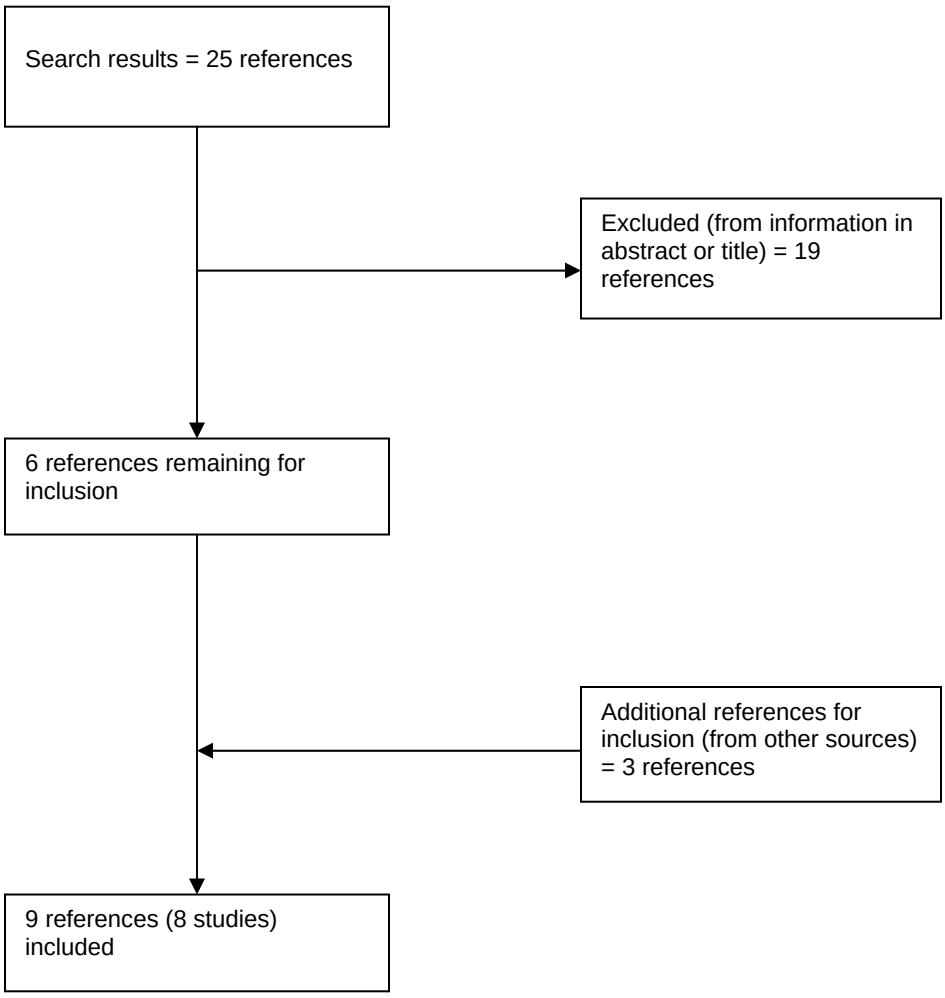


Figure 3. Flow Chart: Question 3—nonRCTs

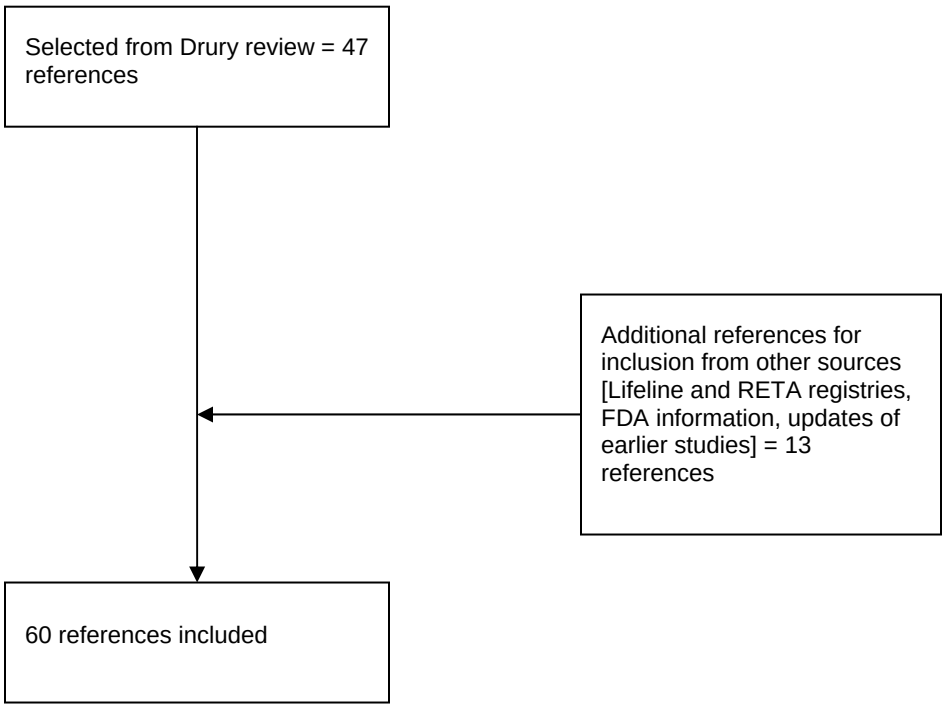
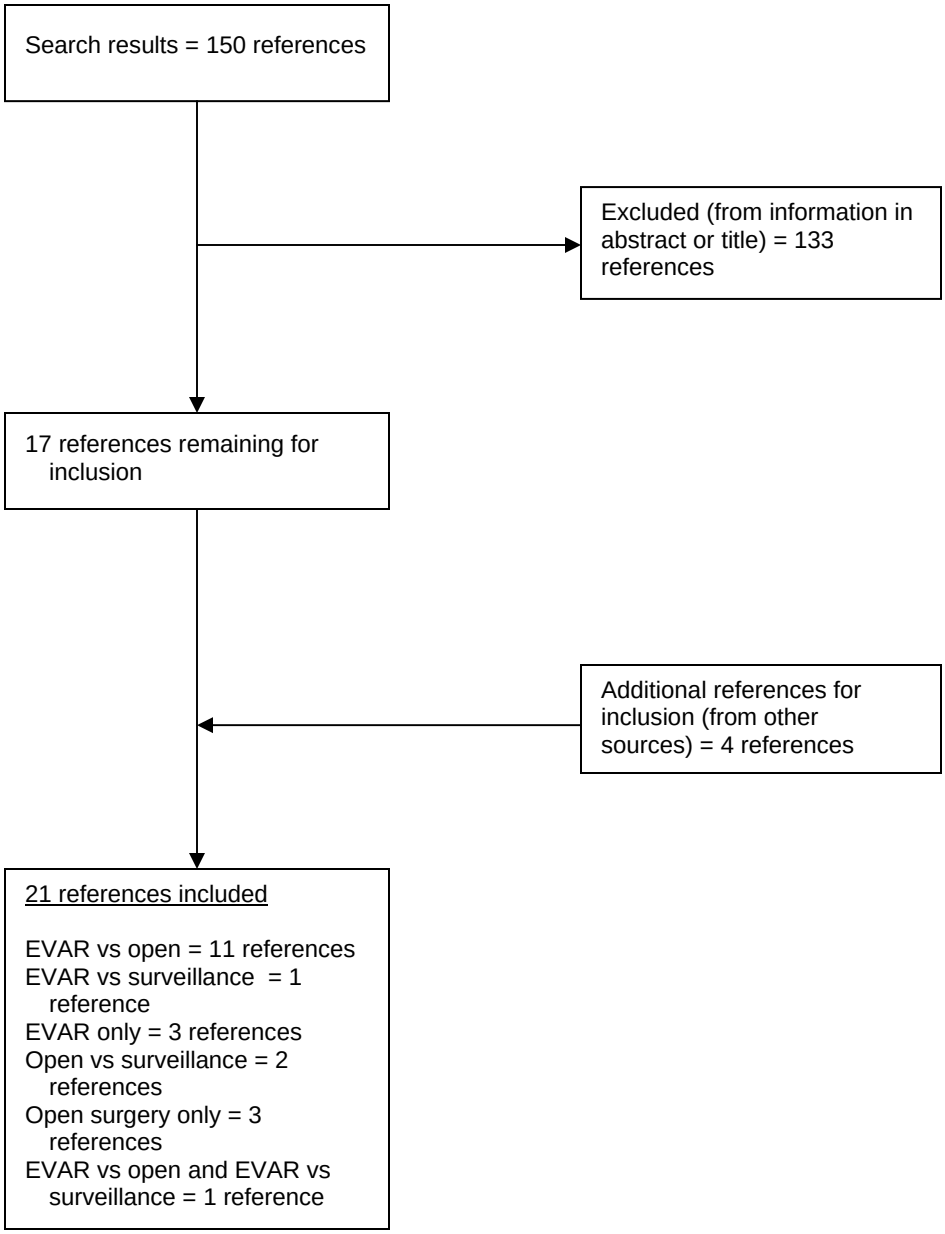


Figure 4. Flow Chart: Question 4—Cost



Chapter 3. Results

Question 1: What are the comparative effectiveness and adverse effects of treatment options of AAA including active surveillance, open repair, and endovascular repair?

Natural History of AAA

Observational studies have assessed the rupture rate of AAA according to diameter and other risk factors among patients followed by surveillance. The results of seven recent studies that assessed the average rate of enlargement and risk of rupture of AAA according to initial or attained size are summarized. Studies were selected, in part, because they represent patients with AAA size or medical conditions where the decision for early intervention is controversial (e.g., small AAA (<5.5 cm) or patients with large AAA (≥5.5) but considered medically unfit for OSR). For individuals with large AAA that are considered OSR candidates, the more relevant question is not based on rupture rate in the absence of intervention but rather on the comparative effectiveness of EVAR vs. OSR. Estimates for AAA rupture or enlargement in an individual may be more variable than the average estimates obtained from these studies.

A population-based study of residents of Rochester, Minnesota, with AAA documented by ultrasound reported on enlargement rate and risk of rupture. Of 181 patients, 103 had more than one ultrasound. The diameter of the AAA increased by a median of 0.21 cm/year. The risk of rupture over 5 years was 0 percent for the 130 patients with an initial AAA <5 cm in diameter and 25 percent for the 46 patients with AAA ≥5 cm.[72] Among variables examined, including age and sex, only the size of the AAA at initial ultrasound was associated with subsequent rupture. A 1 cm larger initial diameter was associated with an approximately 50 percent increase in the adjusted rupture risk. There was no significant association with risk of rupture in relation to the rate of change in size, though the confidence intervals were wide.

An evaluation of 166 patients with small AAA detected by screening reported an annual rupture rate of 0.7 percent for AAA of 3.0 to 4.4 cm and 1.7 percent for AAA 4.5 to 4.9 cm. [73] When patients who underwent elective OSR due to growth rate or attained size were included, the risk of rupture or elective OSR was 2.1 percent and 10.2 percent respectively. An additional report demonstrated that the risk of rupture was very low (2 of 256 patients per year) for AAA <5 cm, even if they grew 1.0 cm or greater per year.[74]

Three studies[9,75,76] used results from patients recruited for RCTs of immediate OSR versus active surveillance and delayed OSR of small AAA to determine the rate of, and risk factors for, rupture of AAA under surveillance. A cohort of 2,257 adults was comprised of patients enrolled in the UKSAT and the associated study for patients ineligible or refusing randomization. After 3 years the annual rate of AAA rupture was 2.2 percent. The risk of rupture was associated with female gender, larger AAA diameter, mean blood pressure, and current smoking. Additional analyses assessed the risk of rupture and last known or estimated AAA diameter categorized as ≤3.9 cm, 4.0 to 4.9 cm, 5.0 to 5.9 cm and ≥6.0 cm. The number of ruptures per 100 patient-years increased from 0.3 for AAA <3.9 cm to 1.5 for AAA 4.0 to 4.9 cm and 6.5 for AAA 5.0 to 5.9 cm. Individuals with AAA ≥6.0 had few person-years of followup because most underwent OSR. The mean diameter preceding rupture was smaller in women (5.0 ± 0.8 cm) than men (6.0 ± 1.4 cm; $p = 0.001$). In the surveillance group of UKSAT, the median aneurysm growth rate was 0.33 cm per year (Inter Quartile Range of 0.20-0.53).

In the surveillance arm of the ADAM trial, the rate of rupture was 0.7 percent per year. Of these ruptures, two were incidental findings at the time of elective repair. Median rate of increase in diameter according to first and last Computed Tomography (CT) readings was 0.32 cm per year (interquartile range = 0.16 to 0.42 cm). The only significant predictor of increased rate of enlargement was a larger initial diameter and the absence of diabetes.[9]

The expansion rates and outcomes for men with very small AAA (3.0 cm to 3.9 cm) found by ultrasound scanning were assessed at five VA Medical Centers participating in the ADAM trial.[76] More than 90 days after the initial screening 790 men had AAA meeting the eligibility diameter and had at least one repeat ultrasound scan. The average followup period was 3.9 years, mean AAA size = 3.3 cm and the median expansion rate = 0.11 cm/year. No expansion was observed in 25 percent of patients and moderate expansion (defined as >0.4 cm/year) was noted in 8.9 percent of the overall group. There were no reported AAA ruptures during the study period. However, the cause of death was available in only 43 percent of patients. Therefore, misclassification or lack of assessment could lead to underreporting of AAA rupture and death. In patients with initial AAA of 3.0 to 3.4 cm, only 23 of 578 (4 percent) had expansion to ≥5 cm and 1.2 percent had OSR. Among 212 men with an AAA of 3.5 to 3.9 cm, 14 percent had expansion to ≥5 cm and 6.6 percent had OSR.

The risk of rupture of large AAA has been poorly understood because most patients with AAA ≥5.5 cm undergo early elective repair. Three studies provided information on patients with large AAA who were considered unfit for OSR or refused OSR. In 1998 Jones reported on rupture rates in a cohort of patients with a large AAA considered unfit for OSR.[77] The annual rupture rate was 12 percent for AAA of 5.0 to 5.9 cm and 14 percent for AAA ≥6 cm.

Lederle and colleagues reported on the rupture rate of large AAA (mean = 6.6 cm) in a cohort of 198 veterans who refused or were considered unfit for elective OSR.[36] Outcome ascertainment was complete for all patients (almost all men) with a 46 percent autopsy rate among the 112 patients who died; 40.2 percent had a probable AAA rupture. The 1-year incidence of probable rupture by initial AAA diameter was 9.4 percent for AAA of 5.5 to 5.9 cm, 10.2 percent for AAA of 6.0 to 6.9 cm, and 32.5 percent for AAA ≥7.0 cm. Among patients who attained an AAA diameter exceeding 8.0 cm, 25.7 percent ruptured within 6 months. In multivariate analysis diameter of the AAA was the strongest predictor of rupture (RR = 1.39 per 1 cm). The median rate of change in AAA diameter was 0.43 cm per year. In multivariate models the rate of change was a nearly significant predictor of probable rupture when last measurement of AAA diameter was also included (RR per 0.1 cm per year = 1.07; 95 percent CI, 0.99-1.15).

The EVAR-2 study was a RCT comparing EVAR to no intervention in 338 patients ≥60 years of age with AAA >5.5 cm and considered medically unfit for OSR. Patients enrolled in the no intervention arm (n=172, though 27 percent underwent intervention to exclude the AAA, including 12 cases of OSR) provide information regarding rupture rates in medically unfit patients at a median followup of 2.4 years. Mean AAA diameter was 6.3 cm. Crude rupture rate in the no intervention group was 9.0 per 100 person years (95 percent CI 6.0-13.5) with a median time to rupture of 98 days. The rupture rate was lower than in the report by Lederle.[36] Overall, 33 percent of patients died, with mortality attributed to AAA rupture occurring in 12 percent.

In summary, the strongest known predictor of rupture is initial or attained AAA diameter. The rate of enlargement has not been consistently independently associated with rupture rates. Evaluating rupture rates based on size or enlargement is complicated by the fact that many patients with larger or more rapidly enlarging AAA receive elective intervention in the absence of symptoms due to concern of rupture and subsequent poor outcomes.

The annual risk of rupture is 1 percent or lower for AAA less than 5.5 cm. These individuals are very unlikely to benefit from elective interventions even if there is low operative morbidity. The 1-year risk of rupture increases with AAA size and may exceed 10 percent in individuals with AAA >6 cm who are judged medically unfit for OSR. AAA of this diameter comprise fewer than 1 percent of AAA detected in screening programs. For AAA that attain a size of >8.0 cm, the risk may exceed 25 percent at 6 months. Based on estimates of rupture risk in the absence of intervention, the potential risks and benefits of early OSR or EVAR can be weighed.

Elective Immediate OSR Versus Active Surveillance for Small Aneurysms (4.0 to 5.5 cm)

Two randomized trials (n=2,226), one in the United States and the other in the United Kingdom, assessed whether immediate elective OSR decreases AAA and overall mortality for patients with small AAA (4.0-5.5 cm), compared to active surveillance with OSR delayed for prespecified AAA conditions: ADAM[9] and the UKSAT.[10] Both studies had similar eligibility requirements and criteria for intervention in the active surveillance group. An RCT conducted in Canada was ended prematurely due to inadequate recruitment and reported no outcomes.

Two trials evaluating early EVAR compared with surveillance have begun recruitment. The Positive Impact of endoVascular Options for Treating Aneurysms earLy (PIVOTAL), a multi-center randomized trial, is scheduled to enroll 1,700 patients with AAA 5.0 cm or less in diameter.[78] The Comparison of surveillance versus Aortic Endografting for Small Aneurysm Repair (CAESAR) trial has a target enrollment of 740 patients with AAA between 4.1 and 5.4 cm.[79]

Baseline Characteristics (Appendix E*, Table E1)

Baseline characteristics and a description of the study protocol are shown in Appendix E, Table E1. ADAM randomized 1,136 patients fit for elective OSR with an AAA between 4.0 to 5.4 cm in diameter out of a total of 5,038 patients screened and referred for recruitment. The majority of patients excluded had AAA outside the eligible parameters, severe comorbid conditions, or were judged to be unlikely to adhere to the study protocol. Patients were randomized to immediate OSR (n=569) or to undergo surveillance (n=567) by ultrasonography or computed tomography (CT) every 6 months. Patients in the surveillance group were followed without repair until: 1) AAA reached 5.5 cm in diameter; 2) enlargement of AAA by at least 0.7 cm in six months or 1.0 cm in 1 year; or 3) the development of symptoms attributable to the AAA by the attending vascular surgeon.

Enrolled patients were ages 50 to 79 years with a mean age of 68 and a baseline mean AAA diameter by CT scan of 4.7 cm. Comorbid conditions included hypertension (56 percent), coronary artery disease (42 percent), and diabetes (10 percent). Past or current smoking status was greater than 90 percent. Patients were overwhelmingly male and white race.

UKSAT randomized 1,090 out of 1,276 eligible patients with non-tender infrarenal AAA between 4.0 to 5.5 cm. Patients fit for elective OSR were randomly assigned to early OSR

* Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/tp/aaareptp.htm

(n=563) or ultrasonographic surveillance (n=527). OSR in the surveillance group was recommended if patients met the following criteria: (1) AAA exceeded 5.5 cm in diameter; (2) enlargement of AAA >1.0 cm per year; (3) AAA became tender; or (4) iliac or thoracic repair of an aneurysm was needed. Patients had a mean age of 69 years (range 60 to 76) and a mean AAA diameter of 4.6 cm. The majority of patients were male (83 percent) and 37 percent were current smokers. Hypertension was prevalent in 38 percent, ischemic heart disease in 40 percent. Over 90 percent of patients had a history of tobacco use with 37 percent still smoking.

Followup and Treatment

The mean duration of followup was 4.9 years for ADAM and 4.6 years for the initial report of the UKSAT. Additional analysis of the UKSAT provided results at a mean followup duration of 8 years (range 6-10). In both trials approximately 60 percent of patients randomized to active surveillance underwent OSR sometime during the trial. The vast majority of delayed OSR were because AAA achieved predetermined criteria; typically AAA size >5.5 cm. In ADAM, AAA repair was performed in 93 percent of patients in the immediate OSR group, 72 percent within 6 weeks after randomization. In the active surveillance group, 62 percent of patients in the surveillance group had undergone AAA OSR by the end of the trial, and 9 percent were performed despite the fact that participants did not meet study criteria for OSR. Rate of repair in the surveillance group increased with the size of the aneurysm at baseline. Four years after randomization, 27 percent of AAA that had measured 4.0 to 4.4 cm at baseline had OSR as compared with 81 percent of those with baseline AAA 5.0 to 5.4 cm.

In UKSAT, 92 percent assigned to early repair had undergone OSR by the end of the trial and 87 percent within 5 months of randomization. Within the surveillance group, 62 percent had undergone repair, (82 percent of all delayed OSR were done according to protocol). The median time to surgery was 2.9 years. At the 8 year mean followup period, an additional 1 percent in the early repair group and 12 percent in the surveillance group had AAA repair. Treatment between the initial and longer followup report did not necessarily adhere to protocol. Approximately one of five patients in the surveillance group (105 of 527) died without undergoing AAA repair.

Results

Mortality (Tables 2 and 3 on pages 42 and 43 and Appendix E*, Table E2)

All-cause mortality. Early/immediate OSR of AAA did not significantly reduce all-cause mortality compared with surveillance in either trial. After a mean followup of approximately 5 years, 27 percent of patients randomized to early OSR had died compared with 25 percent of the surveillance and delayed OSR group. Comparing immediate OSR to surveillance, the RR of death in the ADAM trial was 1.21 [95 percent CI 0.95 to 1.54] and the HR for the UKSAT was 0.94 [95 percent CI 0.75 to 1.17, p=0.56]. After a mean followup of 8 years, the adjusted hazard ratio was 0.83 [95 percent CI 0.69 to 1.00; p <0.05] with an estimated 7.1 and 8.3 deaths per 100 patient years for the early repair and surveillance groups, respectively.

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In UKSAT (but not ADAM) mortality within the first 6 months of randomization was significantly higher in the early repair group compared with patients in the surveillance group (HR of 2.52 [95 percent CI 1.20 to 5.33] and absolute risk difference of 3 percent) (Appendix E*, Table E2). The 30-day mortality rate was approximately 6 percent for patients who underwent elective OSR and did not vary by time of repair. After 3 years, mortality was higher in the surveillance group in UKSAT but not ADAM. At the 8 year followup period, the mean duration of survival in the early OSR group was 6.7 years compared to 6.5 years for the surveillance group. Despite a mortality of 2.7 percent within 30 days of surgery or during hospitalization, the immediate OSR group of ADAM had lower cumulative survival compared to the surveillance and delayed OSR throughout the followup period. Independent predictors of death included higher serum creatinine level, lower weight, diagnosis of Chronic Obstructive Pulmonary Disease (COPD) or diabetes, larger AAA diameter, lower forced expiratory volume in one second, and nonuse of a beta-blocker.

Aneurysm-related mortality and rupture. (Table 2 on page 42) Aneurysm-related mortality was not reduced by early/immediate repair in the ADAM study (3.3 percent vs. 3.4 percent) but as defined differently in UKSAT was lower in the long-term followup report (7.5 percent vs. 11.4 percent.

In ADAM, 0.4 percent in the immediate OSR group and 1.9 percent in the surveillance group had AAA rupture. UKSAT assessed AAA rupture and death from OSR. The latter was defined as occurring within 14 days of OSR. The total rupture rate was 1.6 percent per year in the first 5 years of followup and 3.2 percent per year in the subsequent 3 years. Four percent of patients (8 percent of all deaths) in the surveillance group study died due to ruptured AAA compared to 1.8 percent (4 percent of all deaths) in the early OSR group after 8 years of followup.

Aneurysm related mortality in UKSAT, defined as deaths due to ruptured AAA, secondary AAA rupture, or AAA repair accounted for 19.3 percent vs. 15.3 percent of all deaths in the surveillance and early OSR groups respectively. Death associated with aneurysm-related disorders following OSR occurred in 19 patients, 15 in the surveillance group compared to four in the early repair group ($p < 0.001$). Of these 19 deaths, three resulted from secondary AAA rupture, four from aortoduodenal fistula, and 12 from a ruptured thoracic aortic aneurysm. The risk of rupture was four times as high among women as among men. Additionally, fatal ruptures were more common in women than men; resulting in 14 percent of deaths for women versus 5 percent of deaths for men ($p = 0.001$). However, deaths for women from any cause were similar in the two treatment groups (8.4 percent versus 7.3 percent respectively; $p = 0.99$).

All-cause mortality according to diameter of aneurysm, age, gender, and smoking status. (Table 3 on page 43) Both trials reported no benefit from early OSR of AAA <5.5 cm in diameter or in any subgroup of patients defined by aneurysm diameter at entry. In UKSAT the reported test of interaction was not significant ($p = 0.28$) across AAA size or age ($p = 0.18$) or gender ($p = 0.40$). Calculated risk differences, reported relative risks and tests for interaction from ADAM were not significant and had point estimates favoring surveillance. In UKSAT, the overall death rate for patients who continued to smoke was 12.0 per 100 patient-years compared to 3.8 per 100 patient-years for patients who no longer smoked. However, these results were not reported according to randomized treatment assignment.

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Operative and in-hospital mortality. The age and sex adjusted 30-day and in-hospital operative mortality did not differ in either the UKSAT or ADAM trial between patients receiving immediate OSR or those initially managed with surveillance but receiving delayed OSR. In UKSAT the 30 day operative mortality was 5.8 percent in the early repair group versus 7.1 percent in the group initially managed with surveillance ($p = 0.30$). In-hospital mortality was 5.8 percent and 7.2 percent respectively. Direct comparisons of these percents should be done cautiously because of differences between groups at the time of surgery in terms of age, aneurysm size, and number of tender or ruptured AAA at the time of OSR. In the ADAM study both the 30-day and in-hospital mortality were below 3 percent in the immediate OSR group and the surveillance group. Thus the finding in ADAM of no survival benefit with early OSR was found despite a low total operate mortality in the immediate repair group.

Complications of OSR (Appendix E*, Table E3)

AAA-related hospitalizations (besides those for the elective OSR) occurred more than twice as often for patients undergoing immediate OSR (44.8 percent) versus those randomized to surveillance (22.7 percent). Major complications of OSR with no operative death of unruptured AAA occurred in 4.5 percent of immediate repair patients and 7.6 percent of patients in surveillance who underwent delayed OSR. More than 50 percent of patients in either group who underwent OSR experienced "any complication." Rehospitalizations for complications were slightly higher for early OSR versus surveillance (20.5 percent versus 16.5 percent). Late graft failure occurred in less than 0.5 percent of patients in either arm.

Rupture and Enlargement of Small Aneurysms in Patients Kept Under Ultrasound Surveillance

After nearly 5 years of followup, there were 25 and 14 total ruptures in UKSAT and ADAM, respectively. In ADAM, there were 12 ruptures in the surveillance group, resulting in eight deaths, yielding a rupture rate of 0.7 percent per year of followup of unrepaired aneurysms. The mean risk of rupture in the UKSAT study was 1.0 percent per year. The rate of aneurysm enlargement was 0.32 cm (interquartile range (IQR) 0.16 to 0.42) and 0.33 cm (IQR 0.20 to 0.53) per year for the ADAM and UKSAT surveillance groups, respectively. After 8 years of followup, UKSAT assessed total rupture rates (including AAA ≥5.5 cm and non-fatal ruptures) for two time periods. The total rupture up to the end of the trial was 1.6 percent per year and during the final 3 years of followup the rate was 3.2 percent per year ($p = 0.008$).

UKSAT investigators assessed risk factors associated with AAA rupture in 2,257 patients enrolled in the UKSAT or an associated study who were kept under ultrasound surveillance (data not shown in tables).[75] In addition to UKSAT participants, eligible patients analyzed had aortic diameter <4.0 cm (n=507), or ≥5.5 cm (n=100), refused randomization (n=122), were considered unfit for surgery (n=340), or other reasons (n=98). Ninety-eight percent of patients had initial aneurysm diameters between 3-6 cm. Three-quarters of the ruptures occurred in patients with AAA ≥5 cm in diameter. After 3 years of followup, the annual rate of AAA rupture was 2.2 percent (95 percent CI = 1.7 to 2.8). The risk of rupture was associated with female sex, larger

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initial aneurysm diameter, current smoking, and higher mean blood pressure. Women had a threefold higher risk of aneurysm rupture than men. Crude rupture rate in women was 4.6 per 100 person years vs. 2.0 per 1,000 person years in men.

Quality of Life (Appendix E*, Figures E1-E3 and Appendix E, Table E4)

Any differences in quality of life between treatment groups were small. ADAM utilized the Short Form-36 (SF-36) health status questionnaire in addition to measuring impotence and maximal activity level. The SF-36 scores for the physical and mental subscales are shown in Appendix E, Figure E1. There were no significant differences in any of the subscales between the immediate OSR and surveillance group with the exception of general health. All subscales showed a significant decrease throughout the followup period regardless of treatment group. The general health score was higher ($p < 0.001$) at individual time points from 6 months to 2 years for the immediate OSR group. There were sporadic time point comparisons in other subscales that were significant, mental health at 6 months favoring immediate OSR and physical function at 5 years and role-physical at 6.5 years favoring the surveillance group. These should be interpreted cautiously due to the large number of comparisons. The baseline value for physical functioning was determined to be an independent predictor of mortality during the study duration.

The prevalence of impotence by treatment arm over the study duration is shown in Appendix E, Figure E2. Approximately 40 percent of all patients were impotent before OSR. Following randomization, impotence increased in the immediate OSR group between 18 months to 4 years ($p < 0.03$), with the exception of 12 months. Maximum activity level did not significantly differ between the study groups. A significant interaction between treatment and followup ($p < 0.02$) indicated a greater decline in maximum activity level over time in the immediate repair group.

Health-related quality of life status for UKSAT was assessed by the Medical Outcomes Study short-form 20-item questionnaire. There were no significant differences between groups in the mean change in scores from baseline at 12 months after randomization with the exception in current health perceptions subscale which favored the early repair group. The weighted mean difference in the mean change of scores from baseline between early repair and surveillance was 6.70 [95 percent CI 3.45 to 9.95] (Appendix E, Table E4, Appendix E, Figure E3). Within the surveillance group, mean score changes between baseline and 12 months after randomization for physical functioning, role functioning, social functioning, and bodily pain subscales decreased. In the early OSR group only physical functioning decreased significantly, but the health perceptions subscale improved significantly.

Large Aneurysm (≥5.5 cm) Randomized Controlled Trials

Three RCTs that enrolled patients with AAA $\geq$5.5 cm and considered medically fit for OSR have been completed.[11-13] None were conducted in the United States. EVAR devices used may not have been approved for, or are currently in use, in the U.S. Two of the trials, British Endovascular Aneurysm Repair-1 (EVAR-1) and DREAM, recently published midterm (2-4 year) results. EVAR-1 and DREAM report on procedures performed from 1999-2003. The

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Cuyper's trial objective was to compare cardiac response after EVAR and OSR. Cardiac complications in both groups were assessed up to 1 month postoperatively, and no long-term outcomes were reported. Two additional trials are undergoing recruitment, the Open Versus Endovascular Repair (OVER) in the U.S. and the AnEVARysme de l'aorte abdominal: Chirurgie versus Endoprothese (ACE) project in France. OVER has a recruitment goal of 900 and ACE is planning on enrolling 600 patients. The VA OVER trial will compare procedures done from 2002 to 2007. OVER is unique in that the specific device the patient will receive if randomized to EVAR will be recorded before randomization, thus allowing for subgroup analysis by EVAR compared with randomized controls for that graft. OVER will include a cost-effectiveness analysis of U.S. utilization and costs.

EVAR Versus OSR Patients Who Are Medically Fit for OSR

Study and patient characteristics. (Appendix E*, Table E5). Three trials comparing EVAR with OSR randomized a total of 1,489 patients[11-13] In the largest of the three trials, EVAR-1, 2,068 patients were anatomically eligible for EVAR, of which 52 percent gave consent and were randomized. Reasons for exclusion included: 1) refusal of further assessment following initial screen (n=327); 2) deemed unfit for OSR after local fitness assessment and offered EVAR-2 (n=399); and 3) refusal to participate (n=260).

Eligible patients had to be candidates for either OSR or EVAR based on aneurysm size (at least 5.0 cm) and anatomy as well as surgical risk. Over 90 percent of enrollees were male with an average age of approximately 70 years. Mean AAA diameter ranged from 5.4 cm in the small study by Cuypers to 6.5 cm in EVAR-1. More than 40 percent had a history of cardiac disease, 10-16 percent had diabetes, and the majority a history of tobacco use. All studies reported analyses comparing groups by intention-to-treat. EVAR-1 reported "per protocol" results.

Short-Term Mortality and Morbidity (Table 4 on page 44, Figure 5 on page 49, and Appendix E, Table E6)

EVAR resulted in a lower postoperative 30-day mortality compared to OSR. Pooled 30-day mortality was 1.6 percent for EVAR compared with 4.7 percent for OSR (Risk Difference [RD] = -3, 95 percent CI -5 to -1; RR = 0.34, 95 percent CI 0.17 to 0.65) (Table 4 and Figure 5). In-hospital mortality was similar, 1.9 percent for EVAR vs. 5.8 percent for OSR (RR = 0.32 [0.17 to 0.59]). Of the nine deaths within 30 days in the EVAR group reported in EVAR-1, one occurred after emergency OSR for AAA rupture and one after from rupture following elective OSR. In the OSR group, there was one death after AAA rupture and emergency repair within 30 days.

DREAM reported more severe or moderate systemic operative complications for the OSR group, 26.4 percent versus 11.7 percent for EVAR, an absolute risk reduction of 15 percent [95 percent CI -23 to -7]. A higher rate of pulmonary complications in the OSR group accounted for the majority of this difference. There were significantly more local vascular or implant related complications in the EVAR group, 16.4 percent compared with 8.6 percent for the OSR group (RR = 1.90, 95 percent CI 1.05 to 3.43). In addition, there were three conversions to OSR.

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Endoleaks and Secondary Interventions (Table 5 on pages 45-46 and Appendix E*, Table E6)

Secondary intervention occurred in 9.8 percent of the EVAR group during primary admission in EVAR-1, including ten conversions to OSR and 18 endoleak corrections. The OSR group had 5.8 percent secondary interventions during initial admission, half for re-exploration of OSR.

Midterm Mortality and Morbidity (Table 4 on page 44, Figures 6 and 7 on pages 50 and 51, and Appendix E, Table E6)

In both EVAR-1 and DREAM, reduction in all-cause mortality seen with EVAR at 30 days had disappeared after 2 years (Table 4 and Figure 6). Pooled all-cause mortality was similar between EVAR and OSR groups, 12.7 percent versus 13.2 percent (ARR = -1. 95 percent CI -4 to 3), respectively (DREAM, EVAR-1). It is unclear whether this was just the endovascular group catching up on delayed deaths, or if late mortality will continue to increase with EVAR due to complications or failure to prevent rupture. Both studies reported some advantage for EVAR in aneurysm-related deaths at 2 years (Figure 7), but this may be because all early post-operative deaths (mostly open) are classified as aneurysm-related, whereas late aneurysm-related deaths (mostly EVAR) may be easily misclassified as something else (Table 4 and Figure 6). Overall, 2.5 percent of EVAR deaths were classified as aneurysm-related compared with 5.6 percent for the OSR control, risk reduction of 3 percent [95 percent CI -5 to -1]. The EVAR-1 trial presented results at 4 years after randomization. All-cause mortality was similar between EVAR and OSR, but aneurysm-related mortality continued to be significantly lower in the EVAR group, 3.5 percent versus 6.3 percent (ARR = -3, 95 percent CI -5 to 0). No significant interactions were reported for all-cause or AAA-related mortality with age, sex, AAA diameter, or creatinine concentration subgroups.

In DREAM the rate of survival free of moderate or severe complications was similar in the two groups at two years (65.6 percent [EVAR] versus 65.9 percent [OSR]). No details on specific adverse events, including graft complications were reported. No documented postoperative AAA ruptures were reported, although there was one possible but unconfirmed case.[12]

Midterm Endoleaks and Secondary Interventions (Table 5 on pages 45-46, and Appendix E, Table E6)

At 4 years after randomization, the overall rate of complications in EVAR-1 was five times as common with EVAR compared with OSR, 17.6 vs. 3.3 per 100 person years. However, a large percentage of these complications included radiographic detected endoleaks which are often asymptomatic and do not require a reintervention. Complications occurred in 35 percent of successfully completed EVAR procedures compared to 8.4 percent of OSRs completed [absolute risk difference of 27 percent; 95 percent CI 22 to 31] (Table 5). The most frequent complications were endoleak type 2 (42 percent), endoleak type 1 (15 percent), graft migration (6 percent) and graft thrombosis (6 percent). Reinterventions occurred three times as often in the EVAR group,

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exceeding 20 percent at 4 years in contrast to 6 percent for the OSR group. In DREAM the rate of reintervention after EVAR was almost three times the rate after OSR during the first nine months of followup. Thereafter, reintervention rates similar (Appendix E*, Table E6). Most reinterventions reported in EVAR-1 were endovascular, primarily repairing endoleaks. In the OSR group, reexploration of OSR was the most common re-intervention (44 percent of reinterventions). Overall, 14 EVAR patients required conversion to OSR, including eight completed after initial discharge from the hospital.

Health Related Quality of Life (Appendix E, Figures E4-E8)

The DREAM study reported on quality of life (Appendix E, Figures E4 and E5) and sexual function from the first 153 patients who underwent randomization. The preoperative scores were comparable to the general population of similar age. The physical function but not mental health scores of the SF-36 favored the EVAR group in the early postoperative period, but by six months, scores in the OSR group equaled or surpassed those in the EVAR group.[80,81] Similar findings were reported for sexual function.

In EVAR-1, EQ5D and SF-36 physical component summary scores were lower with OSR to 3 months, with no differences after or at any point in the SF-36 mental component summary scores (Appendix E, Figures E6-E8).

EVAR Versus No Intervention for AAA ≥5.5 cm in Patients Judged Medically Unfit for OSR (Appendix E, Table E7)

Study and patient characteristics. The EVAR-2 study is the only RCT that has evaluated EVAR versus no intervention for AAA ≥5.5 cm among individuals judged to be medically unfit for OSR (Appendix E, Table E7). This study was conducted at the same clinical centers and in parallel with EVAR-1. It enrolled 338 patients at 31 hospitals in the United Kingdom. Each center had to have performed and submitted to the RETA registry at least 20 EVAR procedures. Patients ≥60 years of age, with AAA diameter ≥5.5 cm were considered for participation in the EVAR-1 trial. If they had suitable vascular anatomy for EVAR and were judged medically unfit for major surgery as determined locally by surgeon, radiologist, anesthesiologist, and cardiologist they were offered randomization to EVAR or no intervention. In general, unacceptable surgical risk was due to severe cardiopulmonary conditions. Nearly 90 percent of enrollees were men. The mean age was 76.4 years and mean AAA diameter = 6.3 cm. Local centers could select the graft. Zenith grafts were inserted in 59 percent of patients, Talent in 21 percent, Excluder in 7 percent, and Aneurex in 6 percent. Bifurcated grafts were used in 87 percent of patients. Further description of the grafts was not provided. The mean duration of followup was 3.3 years. One subject randomized to receive EVAR declined and 47 patients randomized to no intervention received treatment with EVAR (35) or OSR (12). The stated reason (n) for repair included rupture (2); tender AAA (11), fast AAA growth (5), became fit for OSR (1), patient preference (14); unknown (14).

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Overall and AAA Related Mortality (Tables 6 and 7 on pages 47 and 48 and Appendix E*, Tables E8 and E9)

All-cause mortality was higher in patients receiving EVAR compared to no intervention though not statistically so (44.6 percent vs. 39.5 percent; HR = 1.21; [95 percent CI 0.87 to 1.69; p = 0.25]) (Table 6). Overall mortality at 4 years for both groups combined was 64 percent according to Kaplan-Meier estimates (Table 7). AAA rupture occurred in 3.9 percent EVAR patients and 12.2 percent in the no intervention group (rupture rate in the no intervention group = 9.0 per 100 person years.) AAA specific mortality was similar between groups (12 vs. 13 percent) (HR = 1.01 [0.55 to 1.84]).

30-day mortality and treatment-related complications. Mortality within 30 days of the primary procedure occurred in 8.7 percent of patients assigned to EVAR and 2.1 percent among the 47 patients in the no intervention group who subsequently underwent either EVAR or OSR (Table 6, and Appendix E, Table E8).

Among patients having a successful EVAR (including the 12 randomized to no intervention) 32.6 percent had a study defined post-intervention complication and 18 percent required reintervention (Tables 6-7 and Appendix E, Table E8). Endoleaks occurred in 18 percent of patients, and there was one graft rupture. The most common reason for reintervention was for repair of endoleaks (mostly type 1). Four-year point estimates for complications were 43 percent vs. 18 percent; EVAR vs. no intervention; for reintervention: 26 percent and 4 percent. Complications following EVAR were comparable in EVAR-1 vs. EVAR-2 patients (43 percent vs. 41 percent). However, the reintervention rate was higher in unacceptable surgical risk EVAR-2 patients (11.5 per 100 person years) compared to EVAR-1 (6.9 per 100 person years).

Health related quality of life. Baseline quality of life scores were lower in EVAR-2 participants compared to EVAR-1 enrollees. There were no differences in quality of life or health status scores between patients assigned to EVAR versus no intervention as measured by the EuroQol 5-D and SF-36 questionnaires (physical and mental components) at any time point among patients who were still alive and completed forms. (Appendix E, Table E9). The authors state that because their results demonstrate that "compared to no intervention EVAR did not show a survival benefit, had little effect on Health Related Quality of Life, was more costly, and involves a continuing need for surveillance and reintervention, they did not see a need to pursue cost-effectiveness modeling at this time (i.e., no intervention was a dominant strategy). Continued monitoring of patients for an additional 6 years is planned."

Patient preferences. There are few data to accurately determine patient treatment preferences according to age, race, AAA size, and comorbid conditions. Determining patient preference by rates or volume of a given procedure is subject to influences by provider or industry. We looked at registries of patients screened for participation in RCTs of OSR versus surveillance and delayed OSR for AAA <5.5 cm, EVAR versus OSR for patients judged medically fit for OSR who have AAA ≥5.5 cm, and EVAR versus no intervention among individuals judged medically unfit for OSR who have AAA ≥5.5 cm. Estimating preferences by these methods is difficult because preferences are not known among patients refusing to be considered for enrollment. Additionally, in the two countries conducting EVAR trials, EVAR

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outside the RCT setting was limited. Patient willingness to participate in and receive EVAR may have been influenced by the opportunity to be treated with otherwise unavailable technology.

Among patients with small AAA and eligible for UKSAT randomization to early OSR or ultrasonographic surveillance, 14 percent refused randomization (reasons not stated). Among those randomized to early OSR 2.3 percent refused surgery. Among those randomized to ultrasonographic screening and delayed OSR 7.2 percent had OSR against protocol. In the ADAM study 2 percent eligible patients refused randomization. In the surveillance group, 9 percent had procedures performed despite the fact that the AAA did not meet criteria for OSR

In DREAM, one percent declined to undergo AAA repair. One patient assigned to OSR crossed over to EVAR. In EVAR-1, 24 percent eligible and offered randomization refused randomization. Stated treatment preferences among those refusing included EVAR (32 percent), OSR (60 percent), no intervention (8 percent), and unknown (2 percent).

Patients who were eligible but refused entry into EVAR-2 were evenly divided between preference for EVAR and no intervention. Eight percent assigned to no intervention subsequently received intervention due to patient preference. Only one patient assigned to EVAR refused. How RCT results will influence preferences in the U.S. is not known.

Table 2. Subgroup mortality for early/immediate elective repair versus surveillance of AAA randomized controlled trials

Outcome, Trials	Early/Immediate Repair, n / N (%)	Surveillance Events, n / N (%)	Death Rate per 100 Patient-Year	Relative Risk (RR) or Hazard Ratio (HR) [95%CI]
Mortality according to baseline aneurysm diameter: Tertile Group 1 (diameter 4.0 to 4.4 cm)				
ADAM,[9] mean followup 4.9 years	37 / 174 (21.5)	32 / 197 (16.2)	NR	RR 1.48 [0.92 to 2.38]
UKSAT,[82] mean followup 4.6 years	63 / 214 (29.4)	53 / 213 (24.9)	7.4 ER; 6.5 S	HR 1.14 [CI NR]
UKSAT,[82] mean followup 8 years	91 / 214 (42.5)	93 / 213 (43.7)	7.1 ER; 7.4 S	HR 0.95 [CI NR]
Mortality according to baseline aneurysm diameter: Tertile Group 2 (diameter 4.5 to 4.8 cm (UKSAT) / 4.9 cm (ADAM))				
ADAM,[9] mean followup 4.9 years	46 / 205 (22.4)	33 / 188 (17.6)	NR	RR 1.27 [0.81 to 1.99]
UKSAT,[82] mean followup 4.6 years	45 / 175 (25.7)	45 / 169 (26.6)	6.3 ER; 6.8 S	HR 0.88 [CI NR]
UKSAT,[82] mean followup 8 years	73 / 175 (41.7)	78 / 169 (46.2)	6.7 ER; 7.9 S	HR 0.84 [CI NR]
Mortality according to baseline aneurysm diameter: Tertile Group 3 (diameter 4.9 cm (UKSAT) / 5.0 cm (ADAM) to 5.4 cm (ADAM) / 5.5 cm (UKSAT))				
ADAM,[9] mean followup 4.9 years	60 / 190 (31.6)	57 / 182 (31.3)	NR	HR 1.02 [0.71 to 1.47]
UKSAT,[82] mean followup 4.6 years	51 / 174 (29.3)	52 / 145 (35.9)	7.4 ER; 9.5 S	HR 0.79 [CI NR]
UKSAT,[82] mean followup 8 years	78/174 (44.8)	83/145 (57.2)	7.5 ER; 10.4 S	HR 0.70 [CI NR]
Mortality according to gender				
UKSAT,[82] Men, mean followup 8 years	201 / 468 (42.9)	210 / 434 (48.4)	7.1 ER; 8.3 S	HR 0.80 [CI NR]
UKSAT,[82] Women, mean followup 8 years	41 / 95 (43.1)	44 / 93 (47.3)	7.3 ER; 8.4 S	HR 0.99[CI NR]
Mortality according to age subgroups, ADAM				
Age 50 to 59 years, mean followup 4.9 years	8 / 47 (17.0)	8 / 51 (15.7)	NR	1.02 [0.38 to 2.73]
Age 60 to 69 years, mean followup 4.9 years	61 / 251 (24.3)	55 / 279 (19.7)	NR	1.34 [0.93 to 1.93]
Age 70 to 79 years, mean followup 4.9 years	74 / 271 (27.3)	59 / 237 (24.9)	NR	1.10 [0.78 to 1.55]
Mortality according to age subgroups, UKSAT				
Age 60 to 66 years, mean followup 8 years	56 / 183 (30.6)	68 / 181 (37.6)	4.7 ER; 6.1 S	0.72 [CI NR]
Age 67 to 71 years, mean followup 8 years	76 / 183 (41.5)	94 / 180 (52.2)	6.7 ER; 9.5 S	0.74 [CI NR]
Age 72 to 76 years, mean followup 8 years	110 / 197 (55.8)	92 / 166 (55.4)	10.0 ER; 9.8 S	1.00 [CI NR]

NR = Not reported

Table 3. All-cause and aneurysm-related mortality for early/immediate elective repair versus surveillance of AAA randomized controlled trials

Outcome, Trials, Followup Period	Early/Immediate Repair (ER) Events, n / N (%)	Surveillance Events, n / N (%)	Death Rate per 100 Patient-Year	Relative Risk (RR) or Hazard Ratio (HR) [95% CI]
All-cause mortality				
ADAM,[9] mean followup 4.9 years	143 / 569 (25.1)	122 / 567 (21.5)	NR	RR 1.21 [0.95 to 1.54]
UKSAT,[10] mean followup 4.6 years	159 / 563 (28.2)	150 / 527 (28.5)	7.0 ER; 7.4 S	HR 0.94 [0.75 to 1.17]
UKSAT,[82] mean followup 8 years	242 / 563 (43.0)	254 / 527 (48.2)	7.1 ER; 8.3 S	HR 0.83 [0.69 to 1.00]
Aneurysm-related mortality, ADAM				
AAA-related	19 / 569 (3.3)	19 / 567 (3.4)	NR	NR
Thoracic aneurysm-related	2 / 569 (<1)	0		
Aneurysm-related mortality, UKSAT *(combined ruptured AAA, secondary AAA rupture, and AAA repair considered underlying cause of death occurring within 14 days after AAA surgery)*				
Mean followup 8 years	37 / 242 deaths (15.3)	49 / 254 deaths (19.3)	NR	NR
Mortality according to time period, UKSAT				
Months 0 to 6	31 / 563 (5.5)	12 / 527 (2.3)	11.4 ER; 4.6 S	HR 2.52 [1.20 to 5.33]
Months >6, mean followup 8 years	211 / 532 (39.7)	242 / 515 (47.0)	6.4 ER; 7.8 S	HR 0.77 [0.63 to 0.93]

* Repair considered underlying cause of death
NR = Not reported

Table 4. Mortality for EVAR versus OSR of AAA randomized controlled trials

Outcome, Trials	EVAR Events, n / N (%)	OSR Events, n / N (%)	Risk Difference, % [95% CI]	Relative Risk [95% CI]
Postoperative 30-day mortality Patient denominators exclude subject deaths, refusals or postponements prior to surgery. DREAM, 6 patients not included in intention-to-treat populations (OSR – 1 death (prior to surgery), 3 refusals; EVAR – 1 death, 1 refusal). EVAR Trial 1, 35 patients not included in intention-to-treat populations (OSR – 14 deaths, 7 refusals, 2 postponed; EVAR – 1 death, 1 refusal, 1 postponed)				
Cuypers[11]	1 / 57 (1.8)	1 / 19 (5.3)	-4 [-14 to 7]	0.33 [0.02 to 5.07]
DREAM[81]	2 / 171 (1.2)	8 / 174 (4.6)	-3 [-7 to 0]	0.25 [0.05 to 1.18]
EVAR-1[13]	9 / 531 (1.7)	24 / 516 (4.7)	-3 [-5 to -1]	0.36 [0.17 to 0.78]
Totals	**12 / 759 (1.6)**	**33 / 709 (4.7)**	**-3 [-5 to -1]**	**0.34 [0.17 to 0.65]**
In-hospital mortality				
DREAM[81]	2 / 171 (1.2)	8 / 174 (4.6)	-3 [-7 to 0]	0.25 [0.05 to 1.18]
EVAR-1[13]	11 / 531 (2.1)	32 / 516 (6.2)	-4 [-7 to -2]	0.33 [0.17 to 0.66]
Totals	**13 / 702 (1.9)**	**40 / 690 (5.8)**	**-4 [-6 to -2]**	**0.32 [0.17 to 0.59]**
Mortality <30 days after primary operation, AAA procedure-related (elective)				
EVAR-1[13]	**7 / 532 (1.3)**	**23 / 518 (4.2)**	**-3 [-5 to -1]**	**0.30 [0.13 to 0.68]**
Mid term (2-year) all-cause mortality				
DREAM[81]	20 / 173 (11.6)	18 / 178 (10.1)	1 [-5 to 8]	1.14 [0.63 to 2.09]
EVAR-1[13]	71 / 543 (13.1)	77 / 539 (14.2)	-1 [-5 to 3]	0.92 [0.68 to 1.24]
Totals	**91 / 716 (12.7)**	**95 / 717 (13.2)**	**-1 [-4 to 3]**	**0.96 [0.73 to 1.25]**
Mid term (4-year) all-cause mortality				
EVAR-1[13]	**100 / 543 (18.4)**	**109 / 539 (20.2)**	**-2 [-7 to 3]**	**0.91 [0.71 to 1.16]**
Mid term (2-year) aneurysm-related mortality				
DREAM[81]	2 / 173 (1.2)	8 / 178 (4.5)	-3 [-7 to 0]	0.26 [0.06 to 1.19]
EVAR-1[13]	16 / 543 (2.9)	32 / 539 (5.9)	-3 [-5 to -1]	0.50 [0.28 to 0.89]
Totals	**18 / 716 (2.5)**	**40 / 717 (5.6)**	**-3 [-5 to -1]**	**0.45 [0.26 to 0.78]**
Mid term (4-year) aneurysm-related mortality				
EVAR-1[13]	19 / 543 (3.5)	34 / 539 (6.3)	-3 [-5 to 0]	0.55 [0.32 to 0.96]
Mid term (2-year) mortality after discharge				
DREAM[81]	17 / 169 (10.1)	9 / 166 (5.4)	5 [-1 to 10]	1.86 [0.85 to 4.04]
Mid term (4-year) mortality >30 days after primary operation				
EVAR-1[13]	81 / 523 (15.5)	71 / 493 (14.4)	1 [-3 to 5]	1.08 [0.80 to 1.44]

Table 5. Complications and endoleaks for EVAR versus OSR of AAA randomized controlled trials

Outcome, Trials	EVAR Events, n / N (%)	OSR Events, n / N (%)	Risk Difference, % [95% CI]	Relative Risk [95% CI]
Number of patients with postoperative 30-day mortality and severe complications (based on standards of the Society of Vascular Surgery/International Society for Cardiovascular Surgery)				
DREAM[81]	8 / 171 (4.7)	17 / 174 (9.8)	-5 [-11 to 0]	0.48 [0.21 to 1.08]
Number of patients with postoperative 30-day mortality and moderate or severe complications				
DREAM[81]	31 / 171 (18.1)	41 / 174 (23.6)	-5 [-14 to 3]	0.77 [0.51 to 1.17]
Systemic complications, moderate/severe	20 / 171 (11.7)	46 / 174 (26.4)	-15 [-23 to -7]	0.44 [0.27 to 0.72]
Systemic complications, severe	6 / 171 (3.5)	19 / 174 (10.9)	-7 [-13 to -2]	0.32 [0.13 to 0.79]
Vascular/implant-related complications, moderate/ severe	28 / 171 (16.4)	15 / 174 (8.6)	8 [1 to 15]	1.90 [1.05 to 3.43]
Vascular/implant-related complications, severe	7 / 171 (4.1)	9 / 174 (5.2)	-1 [-6 to 3]	0.79 [0.30 to 2.08]
Correction of endoleak	2 /171 (1.2)	0 / 174		
Arterial/graft obstruction	11 / 171 (6.4)	5 / 174 (2.9)	4 [-1 to 8]	2.24 [0.79 to 6.31]
Number of patients with a conversion to OSR				
EVAR-1[13] – Secondary intervention during 30 days or primary admission	10 / 531 (1.9)	NA		
DREAM[81]	3 / 171 (1.7)	NA		
Number of patients with secondary interventions (during 30 days or during primary admission)				
EVAR-1[13]	52 / 531 (9.8)	30 / 516 (5.8)	4 [1 to 7]	1.68 [1.09 to 2.60]
Correction of endoleak	18 / 531 (3.4)	1 / 516 (< 1)		
Re-exploration of OSR	NA	15 / 516 (2.9)		
Number of patients with endoleaks and postoperative complications (categories with ≥5 patients): after discharge (4 years)				
EVAR-1[13]	186 / 529* (35.1)	44 / 519* (8.5)	27 [22 to 31]	4.15 [3.06 to 5.63]
Endoleak, type 1	27 / 529 (5.1)	NA		
Endoleak, type 2	79 / 529 (14.9)	NA		
Endoleak, type 3	8/ 529 (1.5)	NA		
Graft rupture	9 / 529 (1.7)	0 / 519		
Graft migration	12 / 529 (2.3)	NA		
Graft kinking or endotension	12 / 529 (2.3)	NA		
Re-exploration of OSR	NA	16 / 519 (3.1)		
Other surgery required	13 / 529 (2.5)	16 / 519 (3.1)	-1 [-3 to 1]	0.80 [0.39 to 1.64]
Number of patients with reintervention: after discharge (4 years)				
EVAR-1[13]	81 / 529* (15.3)	36 / 519* (6.9)	8 [5 to 12]	2.21 [1.52 to 3.21]
Number of patients with endoleaks and postoperative complications with reintervention: after discharge (4 years)				
Endoleak, type 1	17 / 529 (3.2)	NA		

Table 5. Complications and endoleaks for EVAR versus OSR of AAA randomized controlled trials (continued)

Outcome, Trials	EVAR Events, n / N (%)	OSR Events, n / N (%)	Risk Difference, % [95% CI]	Relative Risk [95% CI]
Endoleak, type 2	17 / 529 (3.2)	NA		
Endoleak, type 3	4/ 529 (<1)	NA		
Graft rupture	3 / 529 (<1)	0 / 519		
Graft migration	7 / 529 (1.3)	NA		
Graft kinking or endotension	2/ 529 (<1)	NA		
Re-exploration of OSR	NA	16 / 519 (3.1)		
Other surgery required	13 / 529 (2.5)	16 / 519 (3.1)	-1 [-3 to 1]	0.80 [0.39 to 1.64]

* Based on the number of successful EVARs and OSRs completed
NA = Not applicable

Table 6. Mortality for the EVAR-2 Trial (N=338), EVAR versus no intervention (NI) of AAA

Outcome	EVAR Events, n / N (%)	NI Events, n / N (%)	Hazard Ratio [95% CI]
All-cause mortality	74 / 166 (44.6)	68 / 172 (39.5)	1.21 [0.87 to 1.69]
Aneurysm-related mortality	20 / 166 (12.0)	22 / 172 (12.8)	1.01 [0.55 to 1.84]
Mortality prior to operation	14 / 166 (8.4)	57 / 172 (33.1)	
Mortality <30 days after primary operation. Of the 172 patients in the no intervention group, 125 had no intervention at followup and 47 had AAA repair (35 EVAR and 12 OSR)	13 / 150 (8.7)	1 / 47 (2.1)	
Mortality <30 days after primary operation, AAA procedure-related (elective)	13 / 150 9% [95%CI 5 to 15]	1 / 47 (2.1)	
Mortality >30 days after primary operation	47 / 137 (34.3)	10 / 46 (21.7)	
Total number of patients with complications	58 / 178 33% [95%CI 26 to 40]	NA	
Type of complication			
Endoleak, type 1	10 / 178 (5.6)		
Endoleak, type 2	17 / 178 (9.6)		
Endoleak, type 3	5 / 178 (2.8)		
Graft rupture	1 / 178 (<1)		
Graft migration	2 / 178 (1.1)		
Graft thrombosis	7 / 178 (3.9)		
Other surgery required	8 / 178 (4.5)		
*Total number of patients with reintervention	32 / 178* (18.0) 18% [95%CI 13 to 24]		
Reason for reintervention			
Endoleak, type 1	8 / 178 (4.5)		
Endoleak, type 2	3 / 178 (1.7)		
Endoleak, type 3	3 / 178 (1.7)		
Graft rupture	1 / 178 (<1)		
Graft migration	0		
Graft thrombosis	5 / 178 (2.8)		
Other surgery required	8 / 178 (4.5)		

* Includes 12 patients randomized to No Intervention
NA = Not applicable

Table 7. Kaplan-Meier estimates of mortality and complications according to treatment arm for EVAR versus no intervention of AAA: EVAR-2 randomized controlled trial

1. All-cause mortality *(extracted from graph)*

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=166)	Proportion dying	20%	37%	52%	66%
	Number at risk	129	58	23	6
No intervention (n=172)	Proportion dying	16%	30%	47%	62%
	Number at risk	139	71	29	9

2. Aneurysm-related mortality *(extracted from graph)*

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=166)	Proportion dying	10%	11%	14%	14%
	Number at risk	129	58	23	6
No intervention (n=172)	Proportion dying	8%	10%	19%	19%
	Number at risk	139	71	29	9

3. Complications *(extracted from graph)*: (defined as graft rupture, graft infection, graft migration, endoleaks, graft thrombosis, graft stenosis, renal infarction, anastomotic aneurysm, iliac dilation, technical problem of graft insertion, other surgery required)

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=166)	Proportion with complications	24%	30%	37%	43%
	Number at risk	105	47	14	5
No Intervention (n=172)	Proportion with complications	4%	7%	11%	18%
	Number at risk	137	69	26	7

4. Reinterventions *(extracted from graph)*

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=166)	Proportion with reinterventions	16%	18%	21%	26%
	Number at risk	115	55	20	7
No Intervention (n=172)	Proportion with reinterventions	2%	4%	4%	4%
	Number at risk	137	70	29	9

Figure 5. Endovascular repair versus open repair: 30-day mortality

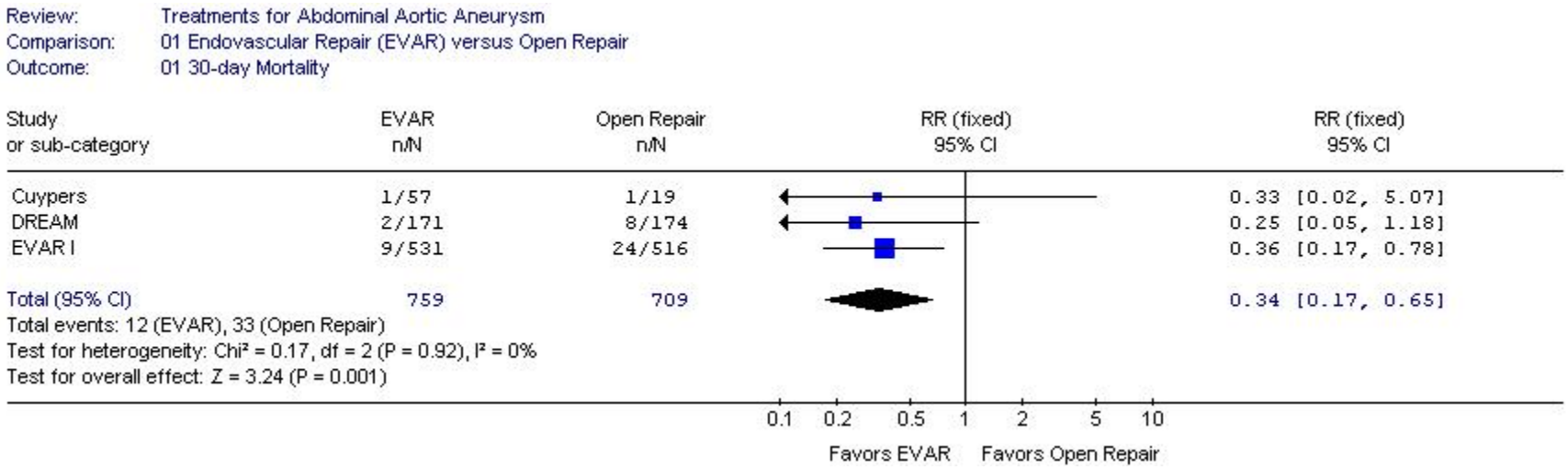


Figure 6. Endovascular repair versus open repair: Midterm all-cause mortality

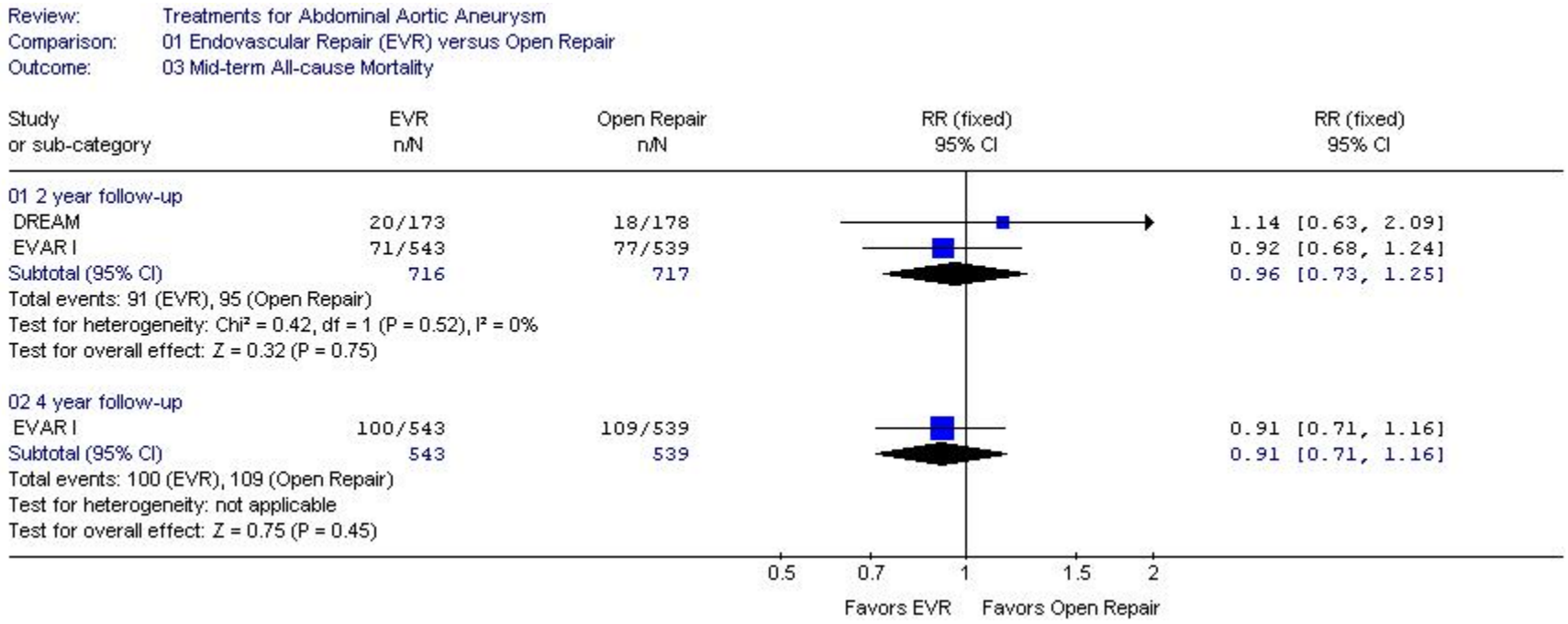
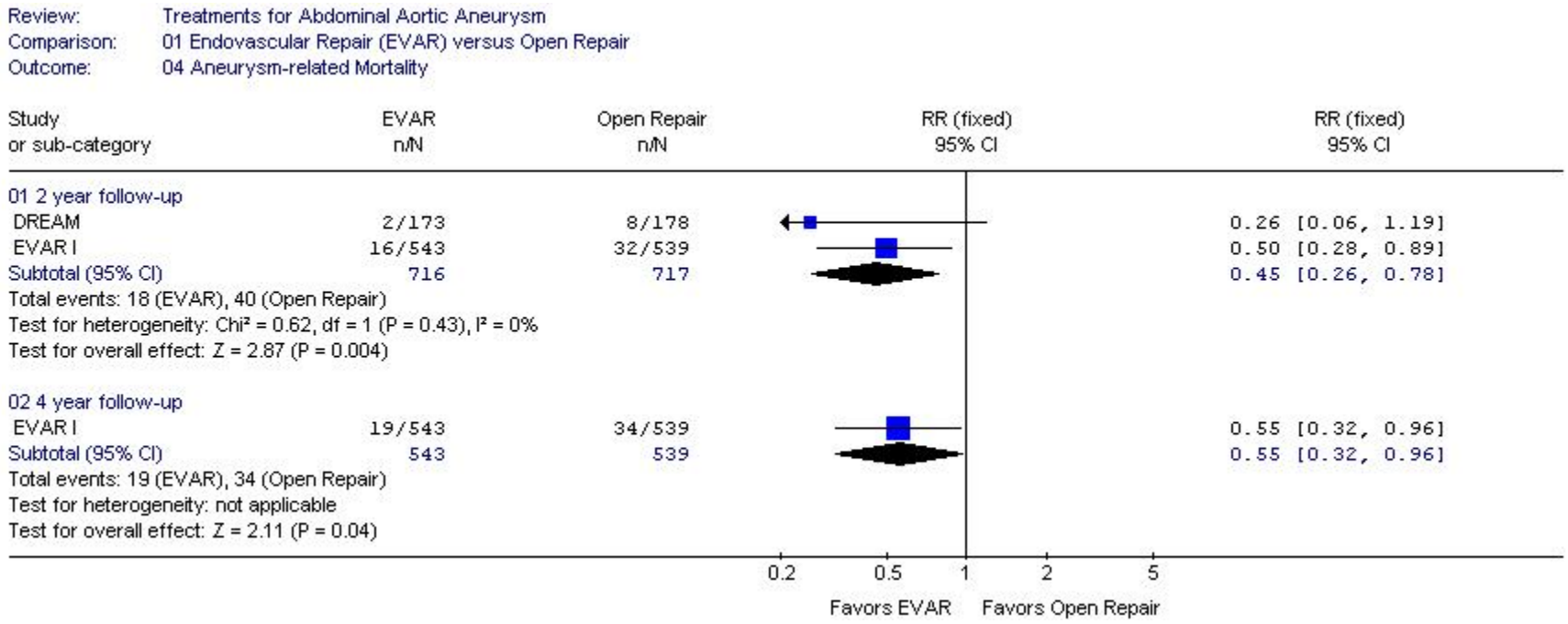


Figure 7. Endovascular repair versus open repair: Aneurysm-related mortality



Evidence from Nonrandomized Controlled Trials, Registries, Case Series, and Comparative Studies Evaluating EVAR

Study and Patient Characteristics

The evidence of the effectiveness and adverse effects of EVAR from sources other than RCTs is based primarily on an update of a recently published systematic review by Drury (http://www.nice.org.uk/pdf/ip/AAA%20stent%20review%20body%20report%20for%20web.pdf.[6] The authors included 47 studies published between 2000 and early 2004 (n=19,160, ranging from 46 to 4,613), including one RCT,[11] nine nonrandomized controlled trials (NRCTs) in comparison to OSR,[54,83-90] 16 comparative (two or more subgroups undergoing EVAR) observational studies,[56,91-105] and 21 case series.[57,106-125] Studies were excluded if they were case series with fewer than 50 patients, not primary studies, assessed ruptured AAA, had insufficient outcomes of interest, or more recent or relevant publications were available. We verified or corrected results from their included studies, summarized findings, updated with data from two recently published national registries, Lifeline (conducted in the U.S., n=2,664)[126] and RETA (n=1,000)[127] and information available on the FDA website from device-specific data. Additionally, we provide information from a post-hoc defined "high-risk subgroup" of patients enrolled in these five mutlicenter investigational device exemption clinical trials leading to FDA approval.[14] Discussion of results from this report are provided under Key Question 3.

Studies were included if the intervention was EVAR, included adults with asymptomatic infrarenal AAA undergoing elective intervention, and assessed clinical outcomes related to efficacy/safety of EVAR. Patients with thoracic and thoraco-abdominal aneurysms and symptomatic or ruptured aneurysms were excluded. Main clinical outcomes included EVAR deployment success, primary and 30-day technical success, aneurysm rupture following successful EVAR, conversion rates (primary and secondary), and secondary interventions. Complications of EVAR were assessed by the frequency of technical problems (stent/graft complications and endoleaks) and major adverse events including 30-day mortality.

Mean ages of the study participants ranged from 65 to 76 years and mean followup times ranged from 7 to 36 months for the studies reporting these variables. AAA diameter ranged from 5 to 7 cm with a mean of 5.8 cm. The average AAA size would be classified as "large." Over 70 percent of studies had a mean followup of at least 12 months, seven with 24 months. Mean followup was not reported in 12 studies. Nearly 90 percent of patients were men. Most had coexisting medical conditions including diabetes (14 percent), hypertension (54 percent), coronary artery disease (59 percent), tobacco use (67 percent), and chronic obstructive pulmonary disease (35 percent).

The methodological quality of included studies reported varied considerably. Reported limitations included lack of detail regarding inclusion/exclusion of study participants, description of dropouts or patients lost to followup, operator experience, and blinding of outcomes assessors. Furthermore, because these studies were not randomized trials, it is not possible to make definitive statements about the relative effectiveness or adverse effects of different endografts. Generally, statistical analyses of study outcomes were not adjusted for confounding factors. The majority of the included studies did not provide a source of funding. Funding was provided by device manufacturers (eight studies),[87,94,95,99,104,105,108,123] and the U.S. government in one.[116]

Results

Mortality

30-day mortality. Fourteen case-control reports, including registries or nonrandomized but controlled trials, compared 30-day mortality of EVAR to OSR.[51,54,84-88,90,126,128-132] There was a higher 30-day mortality in the OSR group, 3.8 percent versus 1.5 percent for EVAR (absolute risk reduction of 2 percent [95 percent CI 2 to 3] favoring EVAR). Incidence and risk reduction in mortality for EVAR were similar to results reported from RCT (Appendix E*, Table E10). The pooled 30-day mortality rate for non-device specific EVAR as reported from both case series and comparative studies was slightly higher than either the RCT or the comparative studies (2.6 percent) and ranged from 0 to 8.4 percent (Appendix E, Table E11).

All-cause and AAA-related mortality. All-cause and AAA-related deaths from reports limited to registries and device-specific studies are shown in Appendix E, Table E12. Mean followup times varied widely or were not reported, limiting interpretation of the results. In the pooled Lifeline registry comprised of device trials conducted in the U.S., 23 percent of patients had died at a mean followup of 34 months, nearly 2 percent due to AAA-defined cause.[126] In data not shown, the overall incidence of AAA-related death was 3.0 percent (range 1.3 percent to 6.8 percent) in three studies (n=1,171) with followup periods ranging from 21 to 36 months. Non-AAA mortality was assessed in eight studies (n=1,228), including one nonRCT. In the nonRCT, using the Talent device, mortality not related to AAA following EVAR was 8.3 percent versus 4.8 percent for OSR at a mean followup of 13 months.[87]

Early and Delayed Aneurysm Rupture (Appendix E, Table E13)

Nine studies (n=8,772) including the four clinical trials comprising Lifeline, reported incidence of early AAA rupture, defined as occurring within 30 days or less following EVAR. The rupture rate was 0.2 percent (16 events) and ranged from 0 percent to 1.6 percent. Delayed rupture, occurring after 30 days postoperatively, was reported in 18 studies (n=9,720). The percent of delayed rupture following EVAR was 0.5 percent during mean followup times ranging from 7 to 72 months. In the device-specific studies, early and late ruptures were reported only for AneuRx device, three (0.3 percent) and ten (0.84 percent), respectively.[124]

Primary and Delayed Conversion to OSR (Appendix E, Table E14)

Primary conversion is defined as conversion to OSR immediately after a failed EVAR procedure. Primary conversion results were reported in 18 studies (n=10,832) including the four clinical trials comprising Lifeline. The overall percentage of patients converting to OSR was 2.2 percent and ranged from 0 to 10 percent. In the device-specific trials, primary conversion ranged from 0 percent for the Excluder device up to 9.7 percent for the EGS.[89,133] In a sub-study of the AneuRx clinical trial, Shames compared EVAR outcomes between men (n=203) and women (n=42) (data not shown).[104] Six women (14 percent) required conversion to OSR compared to one man. Two studies compared early to late experience in performing EVAR. Conversion to

* Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/clinic/tp/aaareptp.htm

OSR for "early experience" was 27 percent and 8.9 percent compared to 4.5 percent and 0 percent for "late experience" in the Flora and Resch studies, respectively.[93,117]

A delayed conversion to OSR was considered to be a conversion after a successful EVAR procedure. The pooled percentage occurrence of delayed conversions from 18 studies (n=10,141) was 1.8 percent with mean followup times ranging from 7 to 72 months. In the device-specific trials, delayed conversion was reported for 38 patients receiving AneuRx (3.2 percent)[124] Only one study had occurrences of delayed conversion greater than 5 percent.[93]

Secondary Intervention Following EVAR (Appendix E*, Table E15)

Secondary intervention was defined by Drury as any surgical or radiological procedure following EVAR that was conducted to maintain exclusion of the aneurysm sac from the circulation or to maintain graft patency. The number and percentage of secondary interventions for 22 studies (n=10,793) are shown in Appendix E, Table E15. Overall, 15.3 percent (range 3.8 to 55.5 percent) of analyzed patients required a secondary procedure within mean followup times ranging from 6 to 72 months. In the device-specific studies, secondary interventions were undertaken for 12 and 13 percent of patients receiving Powerlink and Excluder devices after approximately 2 years, respectively.[133,134] For patients receiving Ancure and EGS devices, 37 percent followed for 5 years required a secondary procedure.[89]

Additional Outcomes

The Drury review assessed clinical outcomes not examined further in our report. These include: (1) deployment success; (2) primary and 30-day technical success; (3) change in aneurysm size during followup; (4) procedural blood loss; (5) length of intensive care unit (ICU) stay; and (6) length of hospital stay. The results are summarized: (http://www.nice.org.uk/pdf/ip/AAA%20stent%20review%20body%20report%20for%20web.pdf).

Successful EVAR deployment, defined as EVAR placement in the correct position without surgical intervention or OSR conversion, was reported in 13 studies (n=5,480).[56,87,89,99,102,103,106,108-110,114,115,120,121,125] Deployment success rate was 97 percent. In two device-specific nonRCTs, success for Ancure/EGS and Talent was 93 percent and 99 percent, respectively.[87,89]

Primary technical success was reported in 11 studies (n=4,998).[56,87,89,92,99,102,103,108,109,112,116,120-122,125] The majority of studies defined this outcome as the successful placement of the endoluminal-stent with complete exclusion of the aneurysm from the circulation.[87,92,99,109,125]

Three studies provided an alternative definition[56,103,116] and four studies[102,108,112,120] provided no definition. Success was verified with either angiogram upon completion or pre-discharge angiograms. Primary technical success varied widely, from 61 to 91 percent, (80 percent overall). One nonRCT (Talent) reported a success of 70 percent.[87] Thirty-day technical success was defined as successful placement of the graft resulting in complete exclusion of the AAA, with or without prior secondary intervention. Overall success was 91 percent in eight studies (n=1,493) and ranged from 77 to 100 percent. Success for the Talent study was 86 percent.[87]

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Increase in AAA size was reported in 14 studies (n=2,509)[83,87,95,96,108-113,121,122,124,135] and ten (n=2,065) reported reduction in AAA[83,95,96,108,110,112,113,121,124,135] following EVAR. Eight studies reported significant change as an increase or decrease of greater than 5 mm.[87,95,110-112,122,124,135] One study defined decrease as a change over 10 mm and increase as a change over 5 mm from preoperative size.[83] The range of increase in the included studies was 0 - 27 percent with an overall average of 7.7 percent. Approximately 44 percent of patients experienced a decrease in AAA (range 11 - 82.5 percent).

Overall procedural blood loss following EVAR was 397 ml, reported in 12 studies (n=2,594).[56,84,85,87-89,96,106,108,110,116,121] Mean blood loss was less for EVAR (414 ml, range 96-783) compared to OSR (1,329 ml range 451-1,800). Mean length of ICU stay with EVAR was less than one-half of OSR (0.7 vs. 1.6 days).[11,84,86-89] The mean length of hospital stay for EVAR from nine nonRCT was also less than one-half that of OSR (4.2 days vs. 9.9 days).

Endoleaks and Complications

Safety of EVAR was assessed according to the incidence of EVAR device-related adverse events, or technical complications. Endoleaks are included in this section although they are not classified as a complication. Endoleaks, detected and classified through radiographic imaging, are often asymptomatic and do not require a reintervention. Complications included stent migrations, fractures, graft-limb thrombosis, graft stenosis, and access artery injury.

Endoleaks (Appendix E*, Tables E16-E18)

Any endoleaks. The incidence of any EVAR endoleaks is shown in (Appendix E, Table E16). Data were extracted from two registries, RETA and Lifeline with additional data from the four clinical trials comprising Lifeline. Within 30 days postoperatively, any endoleaks occurred in nearly one-quarter in the U.S. Lifeline series[126] and 14.6 percent in the European RETA database.[127] For the individual devices, incidences ranged from 13.9 percent AneuRx[124] to 22.7 percent for Powerlink.[134] The incidence was two to three fold as high (42.2 percent) at discharge for combined Ancure and EGS bifurcated devices.[89]

Type I endoleaks. Ten studies (n=2,617) reported occurrences of Type I endoleaks within 30 days following EVAR (Appendix E, Table E17). The overall incidence was 4.2 percent. In the device-specific studies this ranged from 0.9 percent (Powerlink and AneuRx) to 5.8 percent for Talent.[134 87,124] The overall incidence was 3.5 percent (range from 0-14 percent) after one year in 13 studies (n=2,544) reporting. The incidence of Type 1 endoleaks beyond 1 year was 6.7 percent (range 0 to 21.5 percent) for 18 studies reporting (n=7,848).

Type II endoleaks. Eleven studies (n=2,712) reported occurrences of Type II endoleaks within 30 days following EVAR (Appendix E, Table E18). The overall incidence was 10.5 percent with a wide range (1.4-31.2 percent). The percentage of events for the device-specific studies was 1.4 to 19.3 percent for 2 AneuRx studies [102,124] 11.7 percent for Excluder, [133] and 20 percent for Powerlink.[134] The highest number of events occurred in the combined Ancure and EGS study,[89] although this event was reported for bifurcated grafts only. At one year, 14.7 percent of individuals had a Type II endoleak. For the device-specific studies, the 1-year range was 5.4 percent (Talent) up to 21.8 percent (combined Ancure and EGS, bifurcated grafts only).[87,89] After 1 year the percent of events was still 10.2 percent (range 1.0-20.8 percent; 14 studies; n=7,066).

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Type III endoleaks. Type III endoleaks were infrequent. Three studies (n=1,290) reported 30 day outcomes. All 15 events occurred in the RETA registry.[127,133,134] Overall, 4.0 percent had a Type III endoleak after 1 year (nine studies, n=6,599). The majority were from Eurostar.[119] Of the device-specific studies, only AneuRx reported events (8 of 383, 2.1 percent).[124]

Technical complications. (Appendix E*, Table E19). The outcome "any technical complication" for the duration of postoperative hospitalization was reported by the RETA registry.[127] There were 55 events in 976 patients (5.6 percent). Stent migration was defined as caudal displacement greater than 10 mm. Stent migration within 30 days following EVAR or up to discharge occurred in less than 1 percent of patients in the two registries, Lifeline and Eurostar providing data.[120,126] The one year stent migration rate was less than 1 percent for three studies reporting (n=1,599). After 1 year, 4.4 percent had stent migration with a wide range in results (1.7-18.9 percent, eight studies, n=7,027). Stent migration occurred in over 6 percent of patients in the AneuRx device study.[124]

No stent fractures were reported in the 47 included studies by Drury. Stent wire fractures can occur without a full stent fracture and are typically detected by followup x-rays or CT scans. Stent-wire fractures were reported in three studies, two device-specific.[87,108,134] Overall, 17 events in 659 patients occurred (2.6 percent). The Powerlink study reported no stent wire fractures while the Talent reported an incidence of 4.6 percent.[87,134]

Graft-limb thrombosis was reported in five studies (n=659) within 30 days following EVAR (2.4 percent, range 0.7 to 6.3 percent). Incidences for the two device-specific studies were comparable. The overall percentage was similar at 1 year, 2.5, with a range of 0 to 11 percent (11 studies, n=1,657). After 1 year, the incidence increased to 3.8 percent (range 1.9 to 6.1 percent, eight studies, n=6,602). The 1-year incidence for device-specific Powerlink and combined Ancure and EGS reports were 2.1 and 5.4 percent, respectively.[89,134]

Graft stenosis was reported by four studies. Only Eurostar provided data within 30 days (n=2,862) and greater than 1 year (n=4,613) following EVAR (0.3 percent and 1.4 percent respectively). Up to 1 year, the overall incidence of graft stenosis was 2.7 percent in three studies reporting (n=365), including one device-specific study (Powerlink), which reported three events in 192 patients.[134] In data not shown, access artery injury was reported in seven studies (n=2,561) with an overall incidence of 4.8 percent (range 1.4-12.9 percent).[89,92,102-104,109,118,121]

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Question 2. What is the relationship of volume, both hospital and physician, to the benefits and harms of endovascular procedures to repair of AAA?

Results

EVAR of AAA

The literature search did not find any qualifying studies of the association between the volume of endovascular AAA repairs done by hospitals or physicians and any beneficial or harmful outcome.

The only report from the U.S. was based on a statewide discharge database in New York that compared hospitals that did fewer than five EVAR to repair AAA to hospitals doing 30 or more.[54] The crude in-patient mortality rates of 1.9 percent versus 0.8 percent did not differ significantly in this small sample. Investigators were not able to make adjustments for potential differences in risk due to patient, physician, or hospital characteristics.

Analysis of data in a European registry did not find a relationship between 30-day mortality in the first 11 cases versus subsequent cases treated at a medical center.[57] Midterm outcomes were related to center experience. However, methodological issues discussed in the Background section, including use of withdrawn devices that are not used in the U.S. in earlier cases, make it difficult to determine whether these observations would apply to contemporary practice in the U.S.[58]

OSR of AAA

Previous studies of the relationship between hospital and surgeon volume of OSRs and outcomes were reviewed to inform future studies of EVAR. Table 8 on pages 59-64 summarizes studies of relationships between the volume of OSRs of AAA and outcomes in the United States in the 1990s. Endovascular repair was primarily an investigational procedure during this time, and these findings should not be extrapolated to current practice where endovascular procedures are being used to repair a substantial select fraction of the AAA.

Five studies of OSR of AAA used a national sample of hospital discharges, discharges of elderly Medicare enrollees, or operations in VA medical centers.[15,16,136-139] Three investigations analyzed hospital discharges in Maryland, Florida, or New York.[140-142] All studies were retrospective analyses of available databases. The VA study was the only one that had prospectively collected preoperative data including clinical variables.[139] Corresponding with the incidence of AAA, all samples were predominantly elderly males, and data for females is sparse.

Death was the primary outcome in all analyses. In-hospital death was analyzed in five of the eight reports[16,138,140-142] Others included deaths within 30-days to avoid bias that can be introduced by differences in hospital length of stay.[143] Hospital volume was analyzed in all studies. Two studies of Medicare data attempted to estimate each hospital's total volume, not just operations covered by Medicare.[15,136,137] Volume measures reflected periods of time that varied from 1 to 6 years. Some were analyzed as average annual volume, while others reported total volume during the period of study. Half of the studies included a measure of surgeon volume. Only one examined the surgeon's specialty.[138] All studies ignored procedures that were done prior to the period of study as well as the surgeon's experience doing other types of vascular operations.

All studies employed logistic regression models with patients as the unit of analysis. Four studies did not report adjustments for clustering of patients within hospitals (or surgeons).[16,140-142] Two studies utilized hierarchical regression models with hospitals and or surgeons as random effects.[137,139] Age and sex were used as covariates in all analyses except the VA study that was nearly 100 percent male. Race (white versus non-white) was included in six studies.[15,16,136-138,141,142] Two studies did not attempt to include co-morbidities because of concerns about completeness of diagnoses listed on discharge abstracts and the inability to differentiate postoperative complications from preexisting conditions.[141,142] Admission acuity was a covariate in all studies except one that excluded urgent and emergency admissions. Most excluded hospital transfers. Other covariates used by some, but not all, included year to control for time trends, estimated patient income or type of insurance, service intensity of DRGs, hospital length of stay, and characteristics such as bed size, ownership, being a teaching facility for physicians, and urban location. Information about aneurysm characteristics was not available for risk adjustment in any of the eight investigations. Another analysis of the data in Nationwide Inpatient Sample from 1998 to 2001 found that use of low volume hospitals (<10 AAA repairs/year) was associated with race/ethnicity, geographic region, rural setting, Medicaid, and lack of insurance and non-elective admissions.[144] If these variables are also associated with outcomes, they need to be controlled when estimating the effects of volume. Only two studies reported how well their regression model fit the data and three reported how well their model discriminated deaths. Reported c-statistics were modest, ranging from 0.68 to 0.75.

Overall mortality in the studies ranged from 3.5 percent to 5.7 percent. Seven of eight studies reported that significantly lower adjusted mortality was associated with higher volume hospitals. Two studies suggested that the volume effect was relatively consistent in patient subgroups with different preoperative risks of death.[15,16] Cutpoints for hospital volume that were associated with lower adjusted mortality ranged from 17 to 100 AAA OSR per year. These cutpoints were arbitrary and studies did not report analyses specifically to determine a volume threshold(s). The highest volume in the VA study that did not find an association between hospital volume and mortality was 32 procedures per year. This was the only study that prospectively collected and incorporated numerous preoperative clinical variables for risk adjustment. A summary plot of mortality versus volume from all studies was not possible given varying measures of mortality and volume and broad volume categorizations. Some studies only reported risk-adjusted results for volume analyzed as a logarithm-transformed continuous variable.

All three studies that analyzed surgeon volume reported that surgeon volume had an effect that was independent of hospital volume.[137,138,140] One study that reported how surgeon volume altered the effect of hospital volume indicated that the addition of surgeon volume to the regression model greatly reduced, but did not eliminate, the effect of hospital volume.[137] Surgeon volume was inversely related to mortality when surgeon specialty was taken into account in the two studies.[138,142] These studies did not identify a volume cutpoint that could be used to identify surgeons who perform enough AAA repairs to maintain optimal outcomes.

Summary of Results

Adequate studies of the relationship between the volume of EVAR procedures done by hospitals and physicians in the United States have not been reported to date. Most previously published studies of OSRs of AAA done by hospitals and surgeons suggest that there is an inverse relationship between volume and short-term mortality. Whether or not a similar inverse

relationship exists between the volume of EVAR procedures done by hospitals or physicians and mortality or any other outcome has not been established. The poorly defined relationship between the volume of OSR and short-term mortality should not be extrapolated to EVAR. Studies specific to EVAR that address important limitations of previous volume-outcome studies discussed in the Background section are needed to guide policy.

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
Birkmeyer[136] Goodney[15] [1994-1999] All fee-for-service Medicare enrollees over 65 years old who were discharged from a hospital. Mean Age: NR Male: 76%	Death before discharge or within 30 days	Estimated average annual number of AAA repairs over 6 years	Logistic regression with patients as unit of analysis adjusted for clustering Goodness-of-fit: NR Discrimination: NR	Age, sex, race, income, year, acuity of admission, Charlson comorbidity score (19 conditions excluding the indication for surgery and complications)	Overall Annual hospital volume <17 (1900) 17-30 (426) 31-49 (257) 50-79 (156) >79 (80) **Subgroups** Low predicted risk Hospital volume <17 Hospital volume >79 High predicted risk Hospital volume <17 Hospital volume >79	5.7 7.8 5.9 5.2 5.3 4.4 5.6 3.3 12.4 7.4	 Odds ratio reference 0.79 (0.73-0.86) 0.70 (0.64-0.76) 0.71 (0.65-0.78) 0.58 (0.53-0.65)
Birkmeyer[137] [1998-1999] All fee-for-service Medicare enrollees over 65 years old who were discharged from a hospital. Mean Age: NR Male: 77%	Death before discharge or within 30 days	Estimated average annual number of AAA repairs over 2 years	Logistic regression with patients as unit of analysis adjusted for clustering within surgeon and hospital via hierarchical mixed models; surgeon and hospital volume tested in separate and combined models Goodness-of-fit: NR Discrimination: NR	Age, sex, race, income, year, acuity of admission, Charlson comorbidity score (19 conditions excluding the indication for surgery and complications), hospital ownership, teaching status and urban location	Overall Surgeon volume Low <8/year (NR) Med 8-17.5/year (NR) High >17.5/year (NR) Low volume surgeon High volume surgeon Hospital volume <27.5/yr Low surgeon (3279) Medium surgeon (800) High surgeon (218) Hospital volume 27.5-60.5/year Low surgeon (1333) Medium surgeon (642) High surgeon (282)	NR	 6.2 4.6 3.9 Odds ratio 1.65 (1.46-1.86) reference 6.4 5.0 5.2 6.1 4.3 3.9

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s (continued)

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
					Hospital volume >60.5/yr Low surgeon (795) Medium surgeon (379) High surgeon (310) Controlling for hospital volume Low volume surgeon High volume surgeon Hospital volume Low <50/year (NR) High >50/year (NR) Low <50/year High >50/year Controlling for surgeon volume Low volume hospital High volume hospital		 6.0 4.3 3.6 1.40 (1.23-1.59) reference 5.4 4.3 Odds ratio 1.40 (1.23-1.59) reference 1.17 (1.02-1.35) reference

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s (continued)

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
Dimick[16] [1996 & 1997] National Inpatient Sample (stratified random sample of 20% of all discharges from nonfederal hospitals Mean Age: 72 ± 8.1 yrs Male: 79%	In-hospital death	AAA repair procedures done in sample hospitals each year	Logistic regression with patients as unit of analysis not adjusted for clustering. Goodness-of-fit: NR Discrimination: NR	Age, sex, race, acuity of admission, 10 comorbid conditions (Charlson index as modified by Romano). No mention of excluding conditions that might have been complications.	Overall Hospital volume ≤30/year (76 & 91) >30/year (431 & 445) **Subgroups** Age <65 Hospital ≤30/year Hospital >30/year Age <65 & male Hospital ≤30/year Hospital >30/year Age <65 & female Hospital ≤30/year Hospital >30/year Age >65 Hospital ≤30/year Hospital >30/year Age >65 & male Hospital ≤30/year Hospital >30/year Age >65 & female Hospital ≤30/year Hospital >30/year	3.8 4.7 3.1 2.7 1.0 2.5 0.8 3.9 1.9 5.2 3.5 4.6 3.2 7.1 4.4	 Odds Ratio 1.71 (1.37-2.14) reference

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s (continued)

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
Dimick[138] [1997] 60% of National Inpatient Sample that had surgeon identifiers Mean Age: 72±8 years Male: 79%	In-hospital death	AAA repair procedures done in sample hospitals. AAA repairs done by surgeon in all hospitals in sample.	Logistic regression with patients as unit of analysis adjusted for clustering by hospital. Goodness-of-fit: OK Discrimination: c-statistic 0.71	Age, sex, race, acuity of admission, type of procedure code (resection vs. bypass), 10 comorbid conditions (Charlson index as modified by Romano). No mention of excluding conditions that might have been complications.	Overall	4.2	
					Hospital volume		Odds Ratio
					Low <35	5.5	reference
					High ≥35	3.0	0.7 (0.49-0.98)
					Surgeon volume		
					<10	5.6	reference
					≥10	2.5	0.6 (0.40-0.88)
					Surgeon specialty		
					General	5.5	1.76 (1.1-2.9)
					Cardiac	4.0	1.47 (0.85-2.6)
					Vascular	2.2	reference
					Low volume hospital		
					Low volume surgeon	6.5	
					High volume surgeon	3.2	
					General surgeon	6.3	
					Cardiac surgeon	5.9	
					Vascular surgeon	2.7	
					High volume hospital		
					Low volume surgeon	4.2	
					High volume surgeon	2.4	
					General surgeon	4.4	
					Cardiac surgeon	2.5	
					Vascular surgeon	1.9	

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s (continued)

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
Khuri[139] [1991-1997; fiscal years that begin in October] Veterans Affairs medical centers in the prospective National Surgical Risk Study or Surgical Quality Improvement Program Mean Age: 69±6.9 Male: 99%	30-day postoperative mortality	Annual volume per hospital derived as total number of AAA repairs done in a hospital / years hospital contributed to database	Logistic regression with patient as unit of analysis to derive expected number of deaths per hospital, and estimate expected (risk adjusted) mortality Goodness-of-fit: NR C-statistic: 0.75 Mixed effects hierarchical logistic regression; level 1 regression of death on patient characteristics; level 2 regression of hospital volume on risk adjusted mortality	Age, emergency procedure, American Society Anesthesia class, weight loss, albumin, white blood cell count, blood urea nitrogen plus 60 other insignificant factors	Overall Hospital volume 0-3/year (26) 4-6/year (26) 7-10/year (26) 11-32/year (26)	4.7 8.2±17.3 5.3±5.6 4.4±3.0 4.6±2.7	 O/E Ratio 1.75±4.9 0.92±1.0 0.93±0.7 1.08±0.7 p=0.65 Correlation r = -0.11 between hospital O/E and volume p=0.28 Regression coefficient β= -0.028 ±0.021 p=0.10
Dardik[140] [1990-1995] Discharges from nonfederal, acute care hospitals in Maryland excluding urgent and emergent admissions Mean Age: 70±7.5 years Male: 78%	In-hospital death	Total number of elective AAA repairs done by hospitals and surgeons operating in sample hospitals over 6-year period	Logistic regression presumably with patient as unit of analysis, adjustments for clustering not reported Goodness-of-fit: NR Discrimination: NR	Age, sex, race, Medicaid, hypertension, diabetes, chronic obstructive pulmonary disease, cardiac disease, renal disease, smoking history	Overall Hospital volume <50 (30) 50-99 (9) 100 or more (7) Surgeon volume 1 (71) 2-9 (83) 10-49 (56) 50-99 (6) 100 or more (3)	3.5 4.3±0.8 4.2±0.8 2.5±0.5 9.9±3.6 4.9±1.1 2.8±0.5 2.9±0.9 3.8±1.0	 Odds Ratio 2.1 (1.04-4.27) NR reference 3.26 (1.32-8.03) NR reference NR NR

Table 8. Summary of studies of relationships between hospital and surgeon volume and mortality of OSR of unruptured AAA in the 1990s (continued)

Reference(s) [Period of Study] Population	Outcome	Volume	Analysis	Risk Adjustment	Volume Groups (n)	Unadjusted Mortality (%)	Adjusted Volume Effect
Sollano[141] [1990-1995] Discharges from nonfederal, acute care hospitals in New York excluding emergency repairs Age: NR Male: NR	In-hospital death	Total number of nonruptured AAA repairs done in hospitals over 6-year period	Logistic regression with patients as unit of analysis not adjusted for clustering Goodness-of-fit: OK C-statistic: 0.68	Age, sex, race, admission acuity, transfer admission, payer, service intensity weights based on DRG cost ratings were tested	Hospital volume per 100 cases (9,847) Average of hospital volumes 15 (131) 62 (33) 105 (13) 171 (5) 193 (3) 260 (2) 292 (5) 334 (1) 433 (1)	5.5 8.2 5.8 5.5 3.3 4.8 5.4 4.7 3.3 2.6	Odds Ratio 0.82 (0.76-0.90)
Pearce[142] [1992-1996] Discharges from nonfederal, acute care hospitals in Florida Median [IQR] Age: 72 [67-77] Male: 81%	In-hospital death	Annual hospital and surgeon AAA repairs done in sample hospitals	Logistics regression using logarithm of volume measures not adjusted for clustering although presumably patients were the unit of analysis Goodness-of-fit: NR C-statistic: NR	Age, sex, emergency admission, length of stay, year, hospital bed size, teaching status and ownership	Overall Median hospital volume/year 32 [18, 46] (162) Median surgeon volume/year 9 [5, 15] (609) Vascular certification 18% of repairs (62)	5.7	Odds Ratio 0.88* per doubling of volume 0.90* per doubling of volume 0.77* versus not certified for vascular surgery *p <0.01 (CI's NR)

NR = not reported. CI = confidence interval. RR = relative risk. O/E = observed/expected. IQR = interquartile range.

Question 3: How do the characteristics of the aneurysm (size/location/shape) and the patient (age/gender) affect the benefits and harms of endovascular and open-surgical repair?

Aneurysm Location and Morphology

Only elective repair for asymptomatic AAA are considered. Patients enrolled in RCT all had infrarenal AAA. There are no outcomes data based on AAA morphology or classification. The following information is provided to summarize the epidemiology of AAA enrolled in RCTs to serve as a benchmark for estimating relevance to future study design or practice.

In the small aneurysm trials of OSR versus active surveillance, patients were ineligible if they had suprarenal or juxtarenal aneurysm (defined by an anticipated need for reimplantation of a main renal artery). RCT results have not provided outcomes according to AAA morphology class (i.e., whether the aneurysm was confined to the aorta, involved the aortic bifurcation, proximal common iliac arteries, or extended into one or both of the iliac bifurcations). There are no data based on whether AAAs were considered "sacular" versus "fusiform." DREAM provides extensive information on AAA morphology. Nearly 70 percent had cylindrical or fusiform AAA, approximately 60 percent of AAA were considered to involve the aortic bifurcation and have normal iliac arteries, and 18 percent extended into one or both iliac arteries. "Unfavorable features" of the infrarenal neck as defined by an angulation of more than 90 degrees, diameter of more than 18 mm, and a diameter of less than 6 mm or more than 50 percent stenosis was reported in about one-half, while extensive iliac calcification was reported in 70 percent.

Among patients assigned to OSR, nearly 60 percent received a conventional aortoaortic tube graft, while one-third received an aortobiliac (bifurcated graft). Among EVAR patients, more than 90 percent received aortobiiliac EVAR. Parlani evaluated patients with iliac aneurysms versus those without iliac aneurysms and noted no differences in mortality, complications, or need for reinterventions after EVAR.[96]

Aneurysm Size (Small AAA)

Natural History: AAA initial or attained diameter is the biggest known predictor of rupture risk. AAA typically have been classified as small (<5.5 cm) or large. These classifications have been used for inclusion criteria in RCTs and clinical decision making.

The annual rupture rate for AAA <5.5 cm was less than 1 percent in patients enrolled in the active surveillance arm of ADAM and UKSAT. A cohort of 2,257 adults was comprised of patients enrolled in the UKSAT trial and the associated study for patients' ineligible or refusing randomization. After 3 years the annual rate of AAA rupture was 2.2 percent. Additional analyses assessed the risk of rupture and last known or estimated AAA diameter categorized as ≤3.9 cm, 4.0 to 4.9 cm, 5.0 to 5.9 cm, and ≥6.0 cm. The number of ruptures per 100 patient years increased from 0.3 for AAA <3.9 cm to 1.5 and 6.5 for patients with AAAs 4.0 to 4.9 cm and 5.0 to 5.9 cm respectively. A Mayo Clinic study suggested that a 1 cm larger initial diameter was associated with an approximately 50 percent increase in the adjusted rupture risk.

OSR. As noted previously (Question 1) both ADAM and UKSAT analyzed mortality according to treatment arm (early OSR versus surveillance) and age or aneurysm diameter at baseline, based on tertile groups. The adjusted hazard ratio at 8 years followup in UKSAT tended toward a greater benefit of early OSR among younger patients, men, and those with larger

aneurysms. However, neither study demonstrated a significant interaction between treatment group and age baseline, AAA diameter, or gender. The reported test of interaction was not significant across AAA size ($p = 0.28$) or age ($p = 0.18$). Calculated risk differences, reported relative risks, and tests for interaction from ADAM were not significant and had point estimates favoring surveillance. In UKSAT, the overall death rate for patients who continued to smoke was 12.0 per 100 patient years compared to 3.8 per 100 patient years for patients who no longer smoked. Results were not reported according to randomized treatment assignment. Results from ADAM demonstrated that independent predictors of death among all enrollees included higher serum creatinine level, lower weight, diagnosis of COPD or diabetes, larger AAA diameter, lower forced expiratory volume in one second, and nonuse of a beta-blocker. There were few women enrolled in either trial. The test for interaction with gender was not significant in UKSAT ($p = 0.40$). However, fatal ruptures were nearly three times more common in women than men and the risk of AAA rupture was four times higher among women. Greater than 90 percent of enrollees were of white race, and no outcomes according to race were provided.

EVAR. Despite an RCT that reported no benefit in survival or quality of life with immediate OSR versus active surveillance in patients with AAA <5.5 cm there is a possibility that some of these patients might benefit from EVAR, especially if EVAR morbidity is very low. One study recently began recruitment to evaluate EVAR versus surveillance for small AAA. The estimated rupture rate for the surveillance group used in sample size calculations for this trial are higher than reported in the two trials of OSR versus surveillance.

Large AAA

No intervention. The rupture rate for large AAA in patients judged fit for OSR is difficult to determine because most undergo early AAA repair. Lederle reported that the 1-year incidence of probable rupture by initial AAA diameter in those refusing or judged medically unfit for OSR. Rupture rates were 9.4 percent for AAA of 5.5 to 5.9 cm, 10.2 percent for AAA of 6.0 to 6.9 cm, and 32.5 percent for AAA ≥7.0 cm. Among patients who attained an AAA diameter exceeding 8.0 cm, 25.7 percent ruptured within 6 months.[36] The rupture rate among the no intervention group in EVAR-2 was lower than that reported by Lederle. In EVAR-2, (mean AAA = 6.3 cm) AAA rupture occurred in 12.2 percent of individuals in the no intervention group (rupture rate in the no intervention group = 9.0 per 100 person years).

EVAR versus OSR or no intervention. Outcomes of EVAR from randomized controlled trials for large AAA were assessed relative to OSR or no intervention based on whether patients were considered medically fit for OSR. Enrolled patients were all considered candidates for EVAR. However, the proportion of patients with large AAA (i.e., ≥5.5 cm) who might be eligible for EVAR in clinical settings was estimated from the EVAR-1 and 2 trial registries as 54 percent.[13] This is consistent with other reports from EVAR utilization patterns in the U.S. where an estimated 40-80 percent of AAA could be amenable to EVAR based on aneurysm size, morphology, and patient surgical risk characteristics.[39,40] Data from the EVAR-2 trial suggests that approximately one-fifth of patients with large AAA who are EVAR candidates are judged medically unfit for OSR.[145]

Patient characteristics. In trials of EVAR vs. OSR over 90 percent of enrollees were male with an average age of 70 years. Almost all were white. The mean AAA diameter ranged from approximately 5.4 cm in the small study by Cuypers to 6.5 cm in EVAR-1. More than 40 percent

of patients had a history of cardiac disease, 10-16 percent diabetes, and the majority were current or past smokers. No outcomes by race or these selected comorbidities were reported.

Detailed findings from RCTs of EVAR versus OSR or no intervention are described in Question 1. In the DREAM trial the perioperative survival advantage with EVAR as compared with OSR was not sustained after the first postoperative year. In the early postoperative period there was a small quality of life advantage for EVAR. At 6 months and beyond QOL was better after OSR. In the larger EVAR-1 trial, compared with OSR, EVAR offered no advantage in all-cause mortality and health related quality of life, was more expensive, and was associated with a greater number of complications and reinterventions. There was a 3 percent better AAA-related survival with EVAR, though it is possible that cause of death ascertainment was biased against later AAA related deaths in the EVAR group. There were no significant interactions for all-cause or AAA-related mortality with age, sex, aneurysm diameter, or creatinine concentration. Followup time period suggested that hazard ratios for AAA-related mortality, total mortality, complications, and need for intervention began to favor OSR after 6 months.

Patients in EVAR-2 were considered medically unfit for OSR and had large AAA (mean AAA diameter = 6.4 cm; range = 6.0-7.4).[145] Patients were older (76 vs. 70 years) and had worse pulmonary function based on spirometry (FEV_1: 1.6 vs. 2.1L) than patients enrolled in EVAR-1. Baseline blood pressure, serum creatinine, and cholesterol levels as well as the percent males or individuals with diabetes, smoking, or cardiac history appeared similar. The severity or duration of these comorbidities was not described in detail, but 2 year mortality in the no intervention group was greater than 60 percent. In the EVAR-2 trial, EVAR resulted in a 30-day operative mortality of 9 percent in patients unfit for OSR. EVAR did not improve overall or AAA related mortality or quality of life over no intervention and was associated with a need for continued surveillance and reinterventions at increased cost.

There were no significant interactions for the effect of EVAR with age, sex, aneurysm diameter, or creatinine concentration. The 30-day EVAR mortality was higher in the sicker EVAR-2 patients than those receiving endovascular repair who were judged fit for surgery in EVAR-1 (9 percent and versus 1.7 percent; $p < 0.0001$). Additionally, compared to healthy EVAR-1 patients, there was a greater need for internal iliac artery embolization, blood products, renal dialysis, length of hospital stay (and a trend for overall reintervention rate).

A wide range of EVAR devices was used in these trials. Over 90 percent of EVAR procedures used commercially available aortobiiliac device systems while aorto-aortic (tube) grafts were used in the majority of OSRs. Selection for both EVAR and OSR was based on the discretion of the surgical team. The most commonly used EVAR devices were Zenith (33-59 percent of devices) and Talent (27 to 33 percent). Additional description of the devices was not provided. Prior to participating, investigators were required to submit data related to at least 20 completed EVAR procedures.

High Surgical Risk Patients

No randomized trials of EVAR versus OSR have specifically limited recruitment to patients judged to be at high surgical risk due to age, medical comorbidities, or abdominal anatomy (e.g., horseshoe kidney, abdominal adhesions, etc.). As noted previously, patients enrolled in the EVAR and OSR trials were elderly and had numerous comorbid conditions that would result in a limited life expectancy and a relatively high surgical risk. One report enrolled 100 patients believed to be at high risk for complications from OSR and subsequently treated them with the

Zenith AAA EVAR.[131] Pathophysiologic conditions used to determine high risk status included age >80 years, creatinine >2.0 mg/dL, disabling COPD, ejection fraction <25 percent, stroke with residual deficit, medically intractable hypertension, previous renal bypass surgery, or myocardial infarction within the past 6 months. Mean baseline AAA and patient characteristics were not reported and it is not clear how many, if any, of these patients were considered "medically unfit" for OSR. Based on Kaplan-Meir plot estimates, overall survival at 1 year was 92 percent and at 2 years was 78 percent (number at risk not provided). AAA reported survival was estimated at 94 percent for both 1 and 2 year. An additional report evaluated outcomes of EVAR and OSR in a "high surgical risk" subgroup of patients entered into any of five nonrandomized multicenter IDE studies leading to FDA approval of EVAR devices.[14] Patients with AAA ≥5.5 cm were retrospectively categorized as "high surgical risk" based on age >60 years and having at least one cardiac, pulmonary, or renal comorbidity. Inclusion, criteria for the IDE studies required that patients were candidates for OSR, though in one study patients were prospectively defined as being at high risk for OSR complications as noted above. Three-quarters of "high-risk" patients had only one comorbid category and <1 percent had all three categories. There were 14.2 percent endoleaks reported at 30 days, 17.5 percent at 1 year, and 18.9 percent at 4 years. Endograft migration occurred in 2.7 percent at 4 years. Major complications were not reported. After 4 years, deaths categorized as due to AAA were similar between EVAR and OSR patients (4.2 percent and 5.1 percent respectively (p = 0.58). Overall-survival in EVAR treated patients was 10 percent lower compared to OSR (56 percent vs. 66 percent), though this difference was not statistically significant (p = 0.23).

Device-Specific Results from FDA Reports and Lifeline Registry (Tables 9 and 10 on pages 70-72)

Few studies provided an evaluation according to device or patient characteristics. We previously described results from nonrandomized studies of EVAR with description of device-specific results (key question 1 results from nonrandomized trials). A summary of some of these findings is also provided here with attention to reports from the United States (Tables 9 and 10). Pooled results from EVAR devices (n = 3,016) included in the published Lifeline report (Ancure, AneuRx, Excluder, and Powerlink) as well as FDA data related to the Cook-Zenith device and corresponding OSR controls (n = 414) are provided. Information from manufacture/device specific FDA reports is summarized. None represent direct comparisons from randomized trials. Patient or aneurysm factors could influence outcomes. Therefore, it is hazardous to make definitive statements regarding relative safety or effectiveness.

Compared to RCT enrollees, patients receiving EVAR included in these reports had smaller AAA (mean = 5.6 cm). Compared to the listed OSR controls, EVAR patients had slightly smaller AAA (5.6 vs. 5.8 cm), were older (73 vs. 70 years), more frequently male (89 vs. 81 percent), and have a history of coronary artery disease (79 versus 53 percent). Across devices there were no large differences in mean age, AAA diameter, gender, or comorbid conditions.

The number of EVAR devices submitted for FDA review ranged from 121 for Ancure to 416 for AneuRx. The pooled results as well as device-specific data obtained separately from FDA websites indicates that 30-day mortality rates with different devices ranged from 1 percent with Gore Excluder to 4.2 percent with Guidant Ancure. EVAR and OSR 30-day mortality rates were 1.6 and 1.4 percent respectively. Major complications or adverse events within 30 days were not

provided in the Lifeline report but ranged from 13.6 percent in FDA reports with Gore Excluder to 35.6 percent with Guidant Ancure.

Device-Specific Results from Published Nonrandomized Studies

The mean AAA diameter was ≥5 cm in patients included in the nonrandomized-EVAR reports, and available outcomes would be considered related to large AAA. However, three reports describe outcomes of EVAR for small versus large AAA.[94,100,146] Arko reported no significant difference in endoleaks between small, medium, or large AAA (p = 0.41). Ouriel reported that in a cohort of 700 patients treated with EVAR, overall survival, AAA related death, conversion, and Type 1 endoleaks were worse in large (≥5.5 cm) versus small AAA. Similar results from the Eurostar registry were noted by Peppelenbosch.

In the device-specific published studies (which often included additional patients and outcomes data compared to the FDA reports), early and late ruptures were reported only for AneuRx device and were 0.3 and 0.8 percent respectively.[124] Primary conversion ranged from 0 percent for the Excluder device up to 9.7 percent for the EGS. In a sub study of the AneuRx clinical trial, Shames compared EVAR outcomes between men (n = 203) and women (n = 42) (data not shown).[104] Six women (14 percent) required conversion to OSR compared to one man. The incidence of delayed conversions for 18 studies (n = 10,141) was 1.8 percent with mean followup times ranging from 7 to 72 months.

In device-specific trials delayed conversion was reported for 3.2 percent of patients receiving AneuRx. Secondary interventions were undertaken for 12 percent, and 13 percent of patients receiving Powerlink and Excluder devices after approximately 2 years. For patients receiving Ancure and EGS devices, 37 percent followed for 5 years required a secondary procedure.

The incidence of any EVAR endoleaks is shown in Table 9. Data were extracted from two registries, RETA and Lifeline, with additional data from four clinical trials comprising Lifeline. Within 30 days postoperatively, the percentage of any endoleaks for the two registries was 24.7 percent for Lifeline and 14.6 percent for RETA. For the individual devices, incidences ranged from 13.9 percent AneuRx to 22.7 percent for Powerlink. Incidence was 42.2 percent at discharge for combined Ancure and EGS devices. This included only bifurcated grafts.

The overall incidence of Type I endoleaks within 30 days following EVAR was 4.2 percent and ranged from 0.9 percent to 11 percent. The percentage of events in the device-specific studies ranged from 0.9 percent (Powerlink and AneuRx) to 5.8 percent for Talent. Overall incidence of Type III endoleaks within 30 days following EVAR was 1.2 percent in three reports, including Powerlink and Excluder. Powerlink and Excluder reported no Type III endoleaks at any followup period.

There was a wide range in the percentage of Type II endoleaks within 30 days following EVAR (1.4 percent to 19.3 percent in two AneuRx studies, 11.7 percent for Excluder and 20 percent for Powerlink). The highest number of events occurred in the combined Ancure and EGS study, although this event was reported for bifurcated grafts only. In 12 studies (n = 2,598) 14.7 percent had events at 1 year. The range was 5.4 percent (Talent) to 21.8 percent (combined Ancure and EGS, bifurcated grafts only). The Powerlink study reported no stent fractures.

Graft-limb thrombosis was reported in five studies (n = 659) within 30 days following EVAR with an overall incidence of 2.4 percent (range 0.7 percent to 6.3 percent). Incidences for the two device-specific studies were comparable. The 1 year incidence for device-specific Powerlink and combined Ancure and EGS NRCTs were 2.1 percent and 5.4 percent, respectively. Up to 1 year, the overall incidence of graft stenosis was 2.7 percent in three studies reporting, including one device-specific study Powerlink which reported events in 1.6 percent of patients.

Table 9. LIFELINE, FDA, and RCT data for patients undergoing EVAR for AAA

	Pooled LIFELINE* and FDA Cook Zenith (n=3,016)	SVS Outcomes Database "High Risk" (n=565)	FDA Guidant ANCURE (n=121)	FDA Medtronic ANEURX (n=416)	FDA Gore EXCLUDER (n=235)	FDA Endologix POWERLINK (n=192)	FDA Cook ZENITH (n=352**)	DREAM RCT (n=173)	EVAR 1 RCT (n=543)	EVAR 2 RCT (n=166)
Demographics/comorbidities										
Mean age (range)	73	75.7 ± 7.0	73.2 ± 7.1	73 (45-93)	73 (48-91)	73.2 ± 7.0	73.1 ± 7.0	70.7 ± 6.6	74.2 ± 6.8	76.8 ± 6.2
Mean preop AAA diameter	5.6	6.4 ± 0.8	5.8†	5.7†	5.6†	5.2†	5.7†	6.1 ± 0.9	6.5 ± 0.9	6.4† (6.0-7.0)
Male (%)	89	89.2	92.6	89	87	88.5	92.6	93	91	85
CHD (%)	78.6	69.5	65.3	11	62	45.8	36.8 (MI)	40.9	44	65
HTN (%)	64	66.9	62.8	64	NR	63.9	65.2	57.9	SBP =148	SBP=139
DM (%)	12.3	13.8	12.4	12	NR	13.1	13.8	9.9	9	15
COPD (%)	28.3	60.5	39.7	24	26	31.8	23.9	27.5	FEV_1 =2.1	FEV_1=1.6
Smoking Hx (%)	86.5	84.9	90.8	86	89	82.8	86.7	64.9	79	94
Outcomes										
Mortality ≤30 days (%)	1.6	2.8 crude; 2.9‡	4.2	1.7	1.3	1	1.1	1.2	1.7	8.7
Mortality 2 years (%)	13.0	24.6; 26‡	NR	NR	12.8; 13.0‡	NR	8.5††	11.6; 10.3‡	13.1	38.0‡
AAA-related Mortality 2 years (%)	2.0	3.5; 3.8‡	NR	NR	1.7; 2.0‡	NR	1.0††	1.2; 2.1 cumulative rate	2.9	12.0‡
Mortality 4 years (%)	19.9	36.1; 44.0‡	NR	NR	22.1; 23.0‡	NR	NR	NR	18.4; 26.0‡	44.6; 44.0‡
AAA-Mortality 4 years (%)	2.1	3.7; 4.2‡	NR	NR	2.6	NR	NR	NR	3.5; 4.0‡	12.0;14.0‡
Major complications/ adverse events (AEs) ≤30 days (%)	NR	NR	35.6	NR	13.6 Major AEs	18.8 Serious AEs	24.4 AEs	11.7 systemic; 16.4 local	NR	32.6 (58/178 patients with successful EVAR)
Major comp-lications/AEs >30 days (%)	NR	NR	NR	NR	46.8 at 2 years Major AEs	34.9 at 1 year Serious AEs	32.4 at 1 year AEs	16.9 at 2 years	35.2 at 4 years	43.0‡
Primary conversion (%)	2.3	NR	5.8	1.7	0	1.6	0	1.7	1.9	0 (*unfit for OR)*

Table 9. LIFELINE, FDA, and RCT data for patients undergoing EVAR for AAA (continued)

	Pooled LIFELINE* and FDA Cook Zenith (n=3,016)	SVS Outcomes Database "High Risk" (n=565)	FDA Guidant ANCURE (n=121)	FDA Medtronic ANEURX (n=416)	FDA Gore EXCLUDER (n=235)	FDA Endologix POWERLINK (n=192)	FDA Cook ZENITH (n=352**)	DREAM RCT (n=173)	EVAR 1 RCT (n=543)	EVAR 2 RCT (n=166)
Conversions ≤12 months (%)	2.5 (75/3015) 28 post 6 months	NR	7.4	1.9	0 10 post 24 months	2.1	0.85; 2 post 12 months	NR	14 at 4 y	NA
Secondary interventions ≤30 days (%)	15.6 (415/2664) LIFELINE	NR	NR	NR	NR	NR	NR	Reported for 2 endoleaks	9.8	18.0
Secondary interventions ≤12 months (%)	15.4 (464/3015)	NR	NR	6.7	6.4‡‡	9.9	10.3	NR	NR	NR
Secondary intervention >12 months (%)	83, 81,73 re-intervention free: 2, 4, 6 years	NR	NR	NR	5.9‡‡: 12-24 months	NR	3.4	12.5 at 2 years	15.3 at 4 years	26.0‡
Aneurysm rupture ≤12 months (%)	0.17; 14 post 12 months	<1; 2 at 1 year 5 post 12 months	0	0.2	0	0	0.28	None (considered in 2 patients)	NR, AAA deaths only	9 before repair
Endoleaks ≤30 days (%)	NR	14.2	51.8	46.6	21.7	22.7	16.8	2 re-intervention	18 re-intervention	18.0
Endoleaks ≤12 months (%)	NR	17.5	33	17.4	17.3	14.1	3	NR	21.6 at 4 years	NR

* N=2,664; Pooled clinical trial data for ANCURE, ANEURX, EXCLUDER and POWERLINK
** EVAR group comprised of Standard Risk (SR) group (n=200), High Risk group (n=100) and Roll-in group (n=52)
† Based on median of diameter ranges (Interquartile range if provided)
†† SR group only
‡ Estimated from Kaplan-Meier analysis
‡‡ For endoleak and aneurysm size increases
NR Not reported

Table 10. Summaries of LIFELINE, FDA data, and RCT data for patients undergoing OSR (or no intervention) for AAA

	Pooled LIFELINE* and FDA Cook Zenith (n=414)	SVS Outcomes Database "High Risk" (n=61)	FDA Guidant ANCURE (n=111)	FDA Medtronic ANEURX (n=66)	FDA Gore EXCLUDER (n=99)	FDA Endologix POWERLINK (n=66)	FDA Cook ZENITH (n=80)	DREAM RCT (n=174)	EVAR 1 RCT (n=539)	EVAR 2 RCT No Intervention (n=172)
Demographics/comorbidities										
Mean age (range)	69.8	74.2	71.6 ± 7.0	69 (49-85)	70 (51-87)	69.7 ± 7.9	69 ± 7.0	69.5 ± 6.8	74 ± 6.1	76 ± 6.7
Mean preop AAA diameter	5.8	6.6 ± 1.0	5.6**	6.0**	6.0**	5.9**	6.4**	6.0 ± 0.9	6.5 ± 0.9	6.3** (6.0-7.0)
Male gender (%)	81	67.2	76.6	85	74	86.4	88.6	90.2	91	85
CHD (%)	53.4	67.3	61.3	8	54	59.4	28.8 (MI)	46.6	43	73
HTN (%)	69.8	72.1	71.2	56	NR	69.7	83.3	54.0	SBP =147	SBP =138
DM (%)	13	16.4	9.9	9	NR	18.2	15.2	9.8	12	13
COPD (%)	26.6	70.5	29.7	36	25	24.2	17.9	17.8	FEV_1 =2.1	FEV_1 =1.7
Smoking Hx (%)	87.8	77.1	90.1	82	85	85.7	95	54.0	92	93
Outcomes										
Mortality ≤30 days (%)	1.4	4.9 crude; 5.1†	2.7	0	0	6.1	2.5	4.6	4.7	NA
Mortality 2 years (%)	7.8	13.1; 14†	NR	NR	6.1; 7.0†	NR	NR	10.1; 10.4†	14.3; 16.0†	30.0
AAA-related Mortality 2 years (%)	1.2 at 1 year	4.9; 5.2†	NR	NR	2.0; 2.0†	NR	NR	4.5; 5.7 cumulative rate	5.9; 6.0†	11.0†
Mortality 4 years (%)	12.6	24.6; 44.0†	NR	NR	12.1; 15.0†	NR	NR	NR	20.2; 29†	62.0†
AAA-related Mortality, 4 years (%)	NR	4.9; 5.2%†	NR	NR	2.0	NR	NR	NR	6.3; 7.0†	19.0†
Major complications/adverse events (AEs) ≤30 days (%)	NR	NR	44.1	NR	57.0	34.9 Serious AEs	42.5 AEs	26.4 Systemic; 8.6 Local	NR	NR
Major complications/AEs >30 days (%)	NR	NR	NR	NR	66.0	45.5 Serious AEs	51.0 AEs	19.4† at 2 years	8.5; 9.0† at 4 years	18.0† at 4 years
AAA rupture ≤12 months (%)	NR	0	NR	NR	0	NR	NR	0	NR	21 total at 4 years

* Pooled trial data for ANCURE, ANEURX, EXCLUDER and POWERLINK; ** Based on median of diameter ranges; † Estimated from Kaplan-Meier analysis
NR = Not reported

Question 4: What are the costs-benefits for each of the procedures?

Aside from studies developing Markov models to estimate lifetime costs and the cost effectiveness of EVAR and OSR, the majority of studies reviewed for the economic analysis report either on the costs associated with the initial elective procedure (EVAR, OSR, or both) or on costs of followup care for EVAR. If studies reporting on cost also include measures of effectiveness, we report those findings as well as conclusions regarding cost effectiveness.

The results of the two EVAR RCTs for AAA ≥5.5 cm (EVAR vs. OSR and EVAR vs. no intervention) were used as the basis for a cost-effectiveness modeling. With those two exceptions, most of the data on costs or effectiveness (rarely both) come from observational studies, some of which are simply case series with no comparative analysis.

All of the retrospective reviews and prospective case series included in our analyses have taken an *institutional perspective* and report only the costs incurred by the hospital(s) and/or clinics. None take the *societal perspective* of including the cost or quality of life associated with the patient's or caregiver's time lost from work or other activities while hospitalized, traveling, or attending followup visits.

Table 11 on page 79 presents an overview of the included studies. These studies vary not only by type (i.e., RCTs, systematic reviews, Markov models, retrospective reviews, and prospective case series), but also along several substantive dimensions including country, population, time horizon, type of grafts, patient selection criteria, and economic perspective (societal or institutional). A few studies report on hospital incentives supporting the use of these two procedures within the context of their profitability relative to Medicare reimbursement rates for DRGs 110 and 111 (AAA repair with and without complications, respectively).

The costs reported within the studies reviewed also vary by whether they considered direct, indirect, variable, and/or fixed costs. As individual hospital accounting systems do not necessarily follow a standardized approach to allocating costs across departments, the costs reported within this systematic review reflect a variety of costing methodologies. Despite these qualifications, we found a general consensus in the relative costs of EVAR and OSR within each of these studies regardless of the time frame considered.

Results

UKSAT measured and valued direct health service costs for use of UK National Health Service (NHS) resources for participants in their trial. The mean cost of treatment in the early-OSR group was significantly higher than that for ultrasonographic surveillance (£ = 4,978 vs. £3,924; difference = £1,064, CI 799-1,328).[147] It is not clear how these costs would directly relate to U.S. settings. Trials conducted outside the U.S. do not reflect U.S. norms associated with resource valuation, utilization of health care resources, practice variation, and U.S. health care expertise. One cost-effectiveness report used UKSAT data and concluded that despite the negative conclusions of the UK trial, early OSR may be modestly cost effective for patients with small AAAs, particularly younger patients (<72 years of age).[148] Given the higher cost associated with early OSR and the lack of effectiveness regarding survival and quality of life from the UKSAT and ADAM studies (published subsequent to the above cost-effectiveness analysis), it is difficult to accurately conclude that early OSR is cost-effective compared to surveillance with delayed OSR. Although they used different data bases, included different cost elements, were based in different countries with differing health care and payment systems, and focused on

elective and ruptured AAAs, both studies of OSR cost-effectiveness came up with similar findings, an Incremental Cost Effectiveness Ratio (ICER) of about $11,000 per QALY.[142, 155]

With regard to the main comparison of EVAR and OSR, our analyses begins with a discussion of the overall results of the 12 studies providing cost data comparing EVAR and OSR, and then a discussion of the studies reporting on the costs associated with either procedure. Studies include one RCT,[13] one systematic review,[33] seven retrospective reviews, and three Markov models,[17,149,150] one of which is based on the results of one of the other studies.

Regardless of time frame, all studies comparing EVAR and OSR report higher costs associated with EVAR compared to OSR (Table 11 on page 79). Studies relying on Markov models to estimate long-term followup report that the relative cost of EVAR and OSR is very sensitive to the cost of the graft (production costs versus commercial pricing) as well as the need for followup care associated with monitoring, complications, and reinterventions.

Of the 15 studies reporting cost data, four reported on the direct variable costs,[64,147,151,152] excluding the indirect costs that take into account overhead (e.g., utilities) and fixed costs (e.g., new hospital equipment, training). Six of the studies included both direct and indirect costs;[153-158] the remaining five were unclear.[4,51,145,159] Excluded studies are shown in Table 12 on page 80.

Summarizing or comparing the studies reporting on costs is complicated by the variety of approaches taken to calculate costs. Each study includes different elements and combines them differently. Table 13 on pages 81-87 displays what elements were addressed in each of the studies considered, as well as the degree to which the papers fully enumerated what was included in their cost analysis. For example, the vague descriptor "hospital care" included distinctly different subcategories of services from one hospital to another. The majority of the studies did not include pre- or post-operative costs and did not include surgeon fees within the cost of the hospitalization for the initial procedure nor in their total cost estimates. Studies from other countries are hard to translate into the U.S. context. Not only do hospital costs differ, but the basis for the costs is often different. For example, LOS has a different effect on costs in the context of DRGs; it is a cost to the hospital but not to the payer. Focusing on studies reporting hospitalization *costs* (as opposed to *charges*, which tend to be higher), EVAR hospitalization costs for the initial procedure ranged from a low of $16,700 reported by Dryjski et al.[156] to a high of $23,000 in Bertges et al.[153] Although the cost of the EVAR graft reported within Dryjski et al.[156] was among the highest reported in all of the studies, a number of items were explicitly excluded from the cost analysis that led to a relatively low hospitalization cost estimate. These items are anesthesia, respiratory care, pharmacy, radiology, and laboratory tests. Bertges et al., on the other hand, included a very comprehensive itemized list of categories of care in their analyses and thus report higher hospitalization costs of $23,000.[153]

Studies reporting OSR hospitalization *costs* for the initial procedure ranged from a low of $9,000 reported by Dryjski et al.[156] to a high of $18,500 in Bosch et al.[154] This difference is again due in part to Dryjski's explicit exclusion of a number of categories of care as listed above.

Studies reporting hospital *charges* are generally higher than costs, ranging from $45,000 [64] to $50,000[51] for EVAR hospitalizations and $31,000 [64] to $47,000[51] for OSR hospitalizations. The Australian study is on the low end of the scale, reporting costs of approximately $16,000 and $13,400 for EVAR and OSR respectively.[157]

None of the studies reported on the cost of acquiring new equipment or the training required by surgeons to perform EVAR. Both of these items can be quite costly.

EVAR Prosthesis

Since the cohort year also represents the year that the grafts were used, it represents the stage of the technology and to some extent the learning curve associated with the procedure. The majority of the EVAR grafts reported on in these studies received FDA approval in 1999.[67] The cost of some of these grafts may have been discounted or paid for based on production costs at the time the studies were underway. Once grafts became commercially available, they became more expensive. As the driving force behind the majority of the cost of EVAR is the cost of the graft, associated supplies/equipment, and the degree of complications associated with followup, the cohort year relative to the year the grafts became commercially available is important.

Cost estimates for the EVAR graft range from a low of $7,000 reported for a 1997-1999 patient cohort[154] to $13,000 reported for a 2000 patient cohort.[156] The graft accounts for a range of 34 percent to 78 percent of the total hospitalization costs reported in these two studies respectively, with the differences in percentages largely a reflection of how comprehensively the authors itemized costs. Bosch et al. relied on graft costs reported in the literature near the time of commercialization and estimated a relatively low price for the graft relative to the cost of the hospitalization, thus contributing to underestimating the total hospitalization costs for EVAR, underestimating the difference in the cost of EVAR relative to OSR, and underestimating the percent of total hospitalization costs attributable to the graft.[154] In contrast, Dryjski et al. underestimated the cost of the hospitalization relative to the graft by excluding a number of categories of necessary hospital services from the cost estimate.[156]

Reimbursement Issues

The adequacy of Medicare reimbursement for either procedure varies by type of hospital, geographic region, and type of grafts used primarily for EVAR. Several studies report that from a hospital's perspective, reimbursement may not be sufficient to cover the cost of EVAR hospitalization, primarily because the DRG rates were set before EVAR procedure was introduced, thus not taking into account the cost of the prosthesis (graft). Studies published in the late 1990s rely on production costs associated with grafts. Once grafts obtained FDA approval and became commercially available, grafts essentially doubled in price, making it more difficult for hospitals to break even based on Medicare reimbursement rates for AAA repair. As Medicare reimbursement rates for AAA repair do not differentiate between EVAR and OSR, they do not reflect the high cost of the EVAR grafts or differences in length of stay. Hospitals may thus be trading off savings from reduced length of stay against the cost of the EVAR prosthesis.

Measures of Effectiveness (Table 14 on pages 88-89)

Measures of effectiveness include the LOS associated with the initial hospitalization, ICU time, mortality (in-hospital, 30 day) and morbidity, complication, and reintervention rates. EVAR has a shorter LOS associated with the initial hospitalization, range 2.0 days,[151] to 10 days[13] includes preoperative assessments) compared to OSR, range 7.3 days[151] to 15.7 days.[13] The longer length of hospital and ICU length of stay are based on the randomized trials that were conducted in Europe and thus may not be comparable to U.S. settings. Less ICU time is associated with EVAR's initial hospitalization, range 0.6 days[152] to 1.4 days,[156] compared to

OSR, range 2 days[64] to 3.5 days.[151] Thus, EVAR is associated with less resource use in terms of a patient's time spent in the hospital as well as use of the ICU. Because hospital beds are expensive and essentially define the hospital's capacity/ability to serve patients, from the hospital's perspective, EVAR may represent a more efficient use of hospital resources than OSR.

Short-term benefits associated with EVAR include reduced LOS, reduced use of ICU, reduced operative, and 30-day mortality and morbidity. However, results of two RCT comparing EVAR with OSR have provided additional midterm outcome data after 2-4 years of followup. The results from these studies (which were not conducted in the U.S.) indicate that compared to OSR, EVAR reduces AAA related mortality by 3 percent. However, after 2 years there was no difference in overall survival. Differences in health related quality of life were small, may not be clinically noticeable, and disappeared after 3 months. EVAR costs were higher than OSR and were associated with more complications, need for reinterventions, and continued monitoring.

Cost Effectiveness Analyses Using Markov Methodologies (Table 15 on pages 90-92)

Table 15 summarizes three studies that utilized Markov methodologies to analyze differences in the cost and effectiveness of EVAR and OSR over a patient's lifetime[17,149,150] and two studies that compared OSR to conservative treatment. All three of the former found that EVAR was more expensive. Two of the studies were conducted in the U.S. and report that a higher quality of life was associated with EVAR and that the ICERs were $9,905 per QALY and $22,826 per QALY respectively.[149,150] While Bosh, Patel, and Michaels use differing baseline operative mortality rates and QOL measures, they all use 70 year olds with aneurysms between 5 and 6 cm as their baseline reference case. The Patel study used assumptions of effectiveness based on case series data. They conclude that the benefits were worth the cost with the qualification that their results were highly dependent on their assumptions regarding mortality and morbidity. Patel et al. reported that EVAR may be more cost effective than OSR if operative mortality rates were <1.2 percent and the surgical mortality rates were >1.7 percent.[150] However, if the combined mortality and long term morbidity rate of open surgery decreased from 9.1 percent to 4.7 percent, the authors concluded that EVAR may not be cost effective. Bosch et al. also used case series data as the basis for their model; they report the sensitivity of their conclusions to EVAR graft performance in terms of long term failure and rupture rates.[149] They fail, however, to explicitly account for the cost of the EVAR prosthesis by using Medicare reimbursement rates for DRG codes 110 and 111 (AAA repair with and without complications, respectively) to estimate the cost of the initial AAA repair. These DRG codes do not distinguish differences in the cost of AAA repair by procedure (i.e., by EVAR and OSR), and do not include the cost of the EVR prosthesis. Thus, Bosch et al. underestimate the cost of the EVAR initial hospitalization costs relative to OSR and report a conservative estimate of the costs in the cost effectiveness ratio. On the other hand, Bosch includes patients' time lost from work in terms of lost wages in the costs associated with each procedure. As they also estimate the impact of the procedures on the patients' quality of life and include this in the denominator of the cost effectiveness ratio, they have essentially double counted the impact of AAA repair from the patient's perspective.

Although Bosch and Patel varied their analytical assumptions and conducted sensitivity analyses, they did not vary their assumptions simultaneously by employing probabilistic sensitivity analyses to fully test the robustness of their findings as recommended by the U.S. Panel on Cost Effectiveness in Health and Medicine.[160-162]

In a more recent, rigorous approach to Markov modeling, Michaels et al.[17] used data from the EVAR trials and concluded that EVAR was NOT cost effective, in that the extra cost was not worth the gain in QALYs.[17] Their ICER was £110,000 per QALY, which is well above accepted norms for cost effective procedures.[65,160] Michaels et al.[17] found that the cost effectiveness of EVAR and OSR is sensitive to assumptions regarding lower early morbidity for EVAR, higher operative mortality rate for OSR, higher need for followup care for EVAR, higher reintervention/ complication rates for EVAR, e.g., 25-30 percent for EVAR versus 0 percent for OSR, and higher costs associated with care provided to EVAR patients, regardless of time frame.

Michaels et al. point out that there is a time dependent effect.[17] Studies conducted within a relatively short timeframe fail to adequately address the long-term benefits, harm, or costs associated with EVAR. Decreased operative mortality rates associated with EVAR may be offset by higher complication rates later in life. If followup costs associated with complications and reinterventions for EVAR are ignored, then EVAR's low operative mortality rates favor EVAR and may lead to the premature conclusion that EVAR is a cost effective alternative to OSR. This assumption is particularly relevant given the midterm results from RCTs demonstrating that compared with OSR, EVAR offered no advantage in all-cause mortality or health related quality of life and led to a greater number of complications and reinterventions.

In terms of the cost effectiveness of the two procedures, Michaels et al. found that OSR dominates if operative mortality rates are less than 3 percent.[17] OSR is preferred if EVAR's cost/QALY is greater than $30,000 and if operative mortality rates for OSR are between 3 percent and 11 percent. EVAR dominates if operative mortality rates are greater than 40 percent. If EVAR costs are similar to OSR, and/or if EVAR reintervention rates are cut by 50 percent, then EVAR is preferred over OSR. If operative mortality rates are between 11 percent and 40 percent, Michaels et al. report that the outcome of whether EVAR is a cost-effective alternative to OSR is uncertain.[17] Again, this cost effectiveness analysis did not include the midterm results from RCT.

Although Michaels takes the most rigorous approach employing probabilistic sensitivity analyses, they do not explicitly state their assumptions regarding what cost categories they considered for the initial procedure, nor for the cost of the EVAR prosthesis. The authors state that this new technology comes at a considerable price, yet no explicit monetary value was reported, nor was any sensitivity analyses on the cost of the graft and its effect on the cost effectiveness of EVAR relative to OSR conducted.

Michaels also reported that EVAR was cost effective compared to no intervention in individuals with large AAA who were judged medically unfit for OSR.[17] However, they did not use results from EVAR-2 that directly compared EVAR with no intervention.[145] The findings from this RCT demonstrated that EVAR had a considerable 30-day operative mortality in patients already medically unfit for OSR. EVAR did not improve survival compared to no intervention, had little effect on health-related quality of life, and was associated with a need for continued surveillance and reinterventions, at substantially increased cost. Therefore, the authors of EVAR-2 concluded that they saw no reason to pursue cost-effectiveness modeling.

As shown in Table 15, each of these cost-effectiveness models used different levels of specificity when describing how the costs of treatment were calculated. The Michaels study provided almost no guidance about just what went into their calculations.

None of these Markov studies analyzing the cost effectiveness of AAA repair included the less favorable midterm results regarding quality of life, survival, complications, or need for reintervention described above from recently reported RCTs of EVAR versus OSR. Furthermore,

as no RCT studies have been completed within the U.S., the relevance of the cost data incorporated within these Markov studies from other countries is questionable.

Although none of the studies give confidence intervals around the cost effectiveness ratios, the use of probabilistic sensitivity analyses (PSA) and the percent of simulations falling below the reference threshold addresses this issue. However, for those studies not using PSA, because of the large observed variability in operative mortality, EVAR complication rates and the need for reintervention, confidence intervals would help clarify the significance of the point estimate, and the comparability of the reported cost effectiveness ratios. For all of the reasons mentioned above, the cost effectiveness of EVAR versus OSR remains unclear, particularly for specific patient cohorts defined by age, aneurysm size, and comorbidity.

Table 11. Overview of studies

Procedures	Authors (Reference)	Study Type	Publication Year	Cohort Year	Country	Sample Size	Timeframe	Main Cost Results
EVAR, OSR	Bosch[149]	Markov CEA	2002	Not applicable	USA	Not applicable	lifetime	$EVAR >$OSR
	Patel[150]	Markov CEA	1999	Not applicable	USA	Not applicable	lifetime	$EVAR >$OSR
	Michaels[17]	Markov CEA	2005	Not applicable	UK	Not applicable	10 years	$EVAR >$OSR
	EVAR-1[13]	RCT	2005	1999	UK	543, 539	4 years	$EVAR >$OSR
	Angle[151]	Retrospective review	2004	2000-2001	USA	55, 64	Hospital	$EVARh >$OSRh
	Bosch[154]	Retrospective review	2001	1997-1999	USA	181, 273	Hospital	$EVARh >$OSRh
	Clair[152]	Retrospective review	2000	1998	USA	45, 94	Hospital	$EVARh >$OSRh
	Dryjski[156]	Retrospective review	2003	2000	USA	73, 57	Hospital	$EVARh >$OSRh
	Hayter[157]	Retrospective review	2005	1995-2004	Australia	55, 140	Hospital + 1 year followup	$EVAR >$OSR
	Lee[51]	Retrospective review	2004	2001	USA	2565, 4607	Hospital	$EVARh >$OSRh
	Sternbergh[64]	Retrospective review	2000	1996-1997	USA	131, 49	Hospital	$EVARh >$OSRh
	Maher[33]	Systematic review	2003	Not applicable	Not applicable	Not applicable	Not applicable	$EVAR >$OSR
EVAR, CM	Michaels[17]	Markov CEA	2005	Not applicable	UK	Not applicable	10 years	$EVAR >$CM
	EVAR-2[145]	RCT	2005	1999	UK	166, 172	4 years	$EVAR >$CM
EVAR only	Prinssen[159]	Prospective review	2004	1994-2000	Netherlands	77	Followup surveillance	$EVAR only
	Bertges [153]	Retrospective review	2003	2000-2001	USA	221	Hospital	$EVAR only
	Lester[158]	Retrospective review	2001	1994-1999	USA	91	Hospital	$EVAR only
OSR, CM	UKSAT[147]	RCT	1998	1991-1995 UKSAT	UK	563, 527	18 months post randomization	$OSR >$CM
	Schermerhorn[148]	Markov CEA	2000	Not applicable	UK	Not applicable	Lifetime	$OSR >$CM
OSR only	Brox[155]	Retrospective review	2003	1997-2000	USA/Canada	505(US), 552(Canada)	Hospital	$OSR only
	Huber[4]	Retrospective review	2001	1994-1996	USA	16,450	Hospital	$OSR only
	Patel[163]	Markov CEA	2000	Not applicable	USA	Not applicable		$OSR only

CM – Conservative Management, EVARh and OSRh = cost associated with initial hospitalization for EVAR and OSR respectively.

Table 12. Studies excluded from systematic review

Exclusion rationale	Authors (reference)	Study type	Publication year	Cohort year	Sample size	Timeframe	Main cost results
<50 in either arm	Aquino[66]	Prospective	2001	1997-1999	25, 26	Hospital + 1 year followup	Not applicable
	Berman[67]	Prospective	2002	1999-2000	9, 11	Hospital	$EVARh ~ $OSRh
	Birch[68]	Retrospective review	2000	1996-1999	31, 31	Hospital, pred lifetime	$EVAR >$OSR
	Forbes[69]	Retrospective review	2002	1998	7, 31	Hospital +1 year followup	$EVAR >$OSR
	Lottman[70]	RCT	2004	1996-1999	57, 19	Preop, 1 and 3 months postop	Not applicable
	Rosenberg[71]	Retrospective review	2005	2002-2003	34, 54	Hospital	$EVARh ~ $OSRh
No cost information	Drury[6]	Systematic review	2005	Not applicable	Not applicable	Not applicable	Not applicable

EVARh and OSRh = cost associated with initial hospitalization for EVAR and OSR respectively

Table 13. Cost analyses and findings

		EVAR-1 05[13]		Angle 04[151]		Bosch 01[154]		Clair 00[152]	
	Type of cost data (source)	Hospital costs (UK National Health Service)		Hospital costs (unspecified)		Hospital costs (TSI)		Hospital costs (TSI)	
	Type of study	RCT		Retrospective review		Retrospective review		Retrospective review	
	Direct only or direct AND indirect	Unclear		Direct only		Direct and indirect		Direct only	
	Currency	UK pound		U.S. dollar		U.S. dollar, 1999		U.S. dollar	
	Cohort	1999-2003, UK		2000-2001		1997-1999		1998	
		EVAR	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**
----- GRAFTS USED -----	Ancure, Guidant (Menlo Park, CA)	-		✓ "majority"		✓		-	
	AneuRx, Medtronic (Santa Rosa, CA)	✓ 4%		✓ "rest"		-		✓ 100%	
	Excluder, Gore (Flagstaff, AZ)	✓ 7%		-		✓		-	
	Talent, Medtronic (Minneapolis, MN; Santa Rosa, CA)	✓ 33%		-		-		-	
	Vanguard, Boston Scientific (Wayne, NJ)	-		-		✓		-	
	Zenith, Cook (Bloomington, IN; Denmark)	✓ 51%		-		-		-	
	Other commercial grafts	✓ 5%		-		-		-	
	Custom-made stents	-		-		✓ 43%		-	
	Straight, tube type	✓ 10%		✓ 17%	57%	✓ 8%			
	Bifurcated type	✓ 90%		✓ 83%	43%	✓ 64%			
	Other					✓ 27%			
	Ancillary supplies included in graft costs	---		not specified		not specified		yes	
		EVAR	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**
	Initial ER evaluation	-		-		?		✓	
	Preop / preop diagnostics	-		-		?		-	
	Total preop	-		-		?		-	
	Commercial graft / prosthetic device	✓		✓		$7,000	$600	$8,976	$597
	% hospital costs accounted for by graft			58%		34%	3%		
	Operating room	✓		✓		✓		✓	
	Surgeon fees	?		?		-		-	
	Nursing	?		✓		✓		✓	
	Anesthesia	?		?		✓		✓	

Table 13. Cost analyses and findings (continued)

		EVAR-1 05[13]		Angle 04[151]	Bosch 01[154]		Clair 00[152]
	Medical/surgical supplies	?		✓	✓		✓
	Respiratory services/ventilation	?		✓	?		?
	Pharmacy	?		✓	?		✓
	Radiology	?		✓	✓		✓
	Blood/transfusion	✓		?	?		✓
	Laboratory	?		✓	?		✓
	Postop ICU	✓		✓	✓		✓
	Postop ward	✓		✓	✓		?
	Post diagnostic	?		-	?		?
	Allied health, therapy, etc.	?		-	?		?
	"Procedure"	✓		✓	✓		?
	"Hospital," "inpatient hospitalization"	✓		✓	✓		✓
	Patient costs (time, travel, morbidity).	-		-	-		-
	"Other"	✓		?	?		✓
	Total hospitalization	£10,819	£9,204	EVAR =1.74*OSR	$20,716	$18, 484	EVAR = OSR+$7205
	Total preop + hospitalization	-		-	-		-
	Radiology: imaging followup	✓		-	-		-
	Endoleak repair	✓		-	-		-
	Conversion to OSR	✓		-	-		-
	"Adverse events"	✓		-	-		-
	Patient costs (time, morbidity)	✓		-	-		-
	Total followup	£2,439	£741	-	-		-
	GRAND TOTAL	£13,258-4 years	£9,945-4 years	-	-		-

		Dryjski 03[156]	Hayter 05[157]	Lee 04[51]
	Type of cost data (source)	Hospital costs (unspecified)	Hospital costs (Medicare benefits schedule, MBS)	Hospital charges (National Inpatient Sample—NIS)
	Type of study	Retrospective review	Retrospective review	Retrospective review
	Direct only or direct AND indirect	Direct and indirect	Direct and indirect	Direct and indirect
	Currency	U.S. dollar	AU converted U.S. dollar, 2003/04	U.S. dollars, 2001
	Cohort	2000	1995-2004	2001

Table 13. Cost analyses and findings (continued)

		Dryjski 03[156]		Hayter 05[157]		Lee 04[51]	
		EVAR	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**
----- GRAFTS USED -----	Ancure, Guidant (Menlo Park, CA)	✓ 91%		-			
	AneuRx, Medtronic (Santa Rosa, CA)	✓ 9%		-			
	Excluder, Gore (Flagstaff, AZ)	-		✓ 25%		All available	
	Talent, Medtronic (Minneapolis, MN; Santa Rosa, CA)	-		✓ 2%		(National dataset,2001)	
	Vanguard, Boston Scientific (Wayne, NJ)	-		-			
	Zenith, Cook (Bloomington, IN; Denmark)	-		✓ 73%			
	Other commercial grafts	-		-			
	Custom-made stents	-		-			
	Straight, tube type	?			66%	✓	
	Bifurcated type	✓		✓ 100%	34%	✓	
	Other						
	Ancillary supplies included in graft costs?	yes		yes		Not specified	
	Initial ER evaluation	-		-		-	
	Preop / preop diagnostics	-		✓		-	
	Total preop	-		$733	$663	-	
	Commercial graft / prosthetic device	$12,974	$750	$7,765	$363	$10-$12,000	
	% hosp costs accounted for by graft	78%	8%	49%	3%		
	Operating room	✓		✓		?	
	Surgeon fees	-		✓		?	
	Nursing	✓		✓		?	
	Anesthesia	-		✓		?	
	Medical/surgical supplies	?		✓		?	
	Respiratory services/ventilation	-		✓		?	
	Pharmacy	-		✓		?	
	Radiology	-		✓		?	
	Blood/transfusion	?		?		?	
	Laboratory	-		?		?	
	Postop ICU	✓		✓		?	
	Postop ward	✓		✓		?	
	Post diagnostic	?		✓		?	
	Allied health, therapy, etc.	?		✓		?	
	"Procedure"	?		✓		?	
	"Hospital," "inpatient hospitalization"	?		✓		✓	
	Patient costs (time, travel, morbidity).	-		-		-	
	"Other"	?		?		-	

Table 13. Cost analyses and findings (continued)

		Dryjski 03[156]		Hayter 05[157]		Lee 04[51]	
	Total hospitalization	$16,731	$9,042	$15,898	$13,400	$50,346	$47,009
	Total preop + hospitalization	-		$16,631	$14,063	-	
	Radiology: imaging followup	-		✓		-	
	Endoleak repair	-		✓		-	
	Conversion to OSR	-		None needed		-	
	"Adverse events"	-		✓		-	
	Patient costs (time, morbidity)	-		✓		-	
	Total followup	-		$2,013	$59	-	
	GRAND TOTAL	-		$18,644 at 2 years	$14,122 at 2 years	-	

		Sternbergh 00[64]		EVAR2 05[145]		Prinssen 04[159]	Bertges 03[153]
	Type of cost data (source)	Hospital costs (unspecified)		Hospital costs (UK National Health Services)		Hospital costs	Hospital costs (% of charges)
	Type of study	Retrospective review		RCT		Prospective review	Retrospective review
	Direct only or direct AND indirect	Direct only		Unclear		Direct and indirect	Direct and indirect
	Currency	U.S. dollar		UK pound		U.S. dollar	U.S. dollar
	Cohort	1996-1997		1999-2003, UK		1994-2000	2000-2001
		EVAR	**OSR**	**EVAR**	**CM**	**EVAR**	**EVAR**
----- GRAFTS USED -----	Ancure, Guidant (Menlo Park, CA)	-		-		✓ 97%	✓ 86%
	AneuRx, Medtronic (Santa Rosa, CA)	✓ 100%		✓ 6%		-	✓ 14%
	Excluder, Gore (Flagstaff, AZ)	-		✓ 7%		✓ 3%	-
	Talent, Medtronic (Minneapolis, MN; Santa Rosa, CA)	-		✓ 21%		-	-
	Vanguard, Boston Scientific (Wayne, NJ)	-		-		-	-
	Zenith, Cook (Bloomington, IN; Denmark)	-		✓ 59%		-	-
	Other commercial grafts	-		✓ 7%		-	-
	Custom-made stents	-		-		-	-
	Straight, tube type	?		✓ 13%		✓ 17%	
	Bifurcated type	?		✓ 87%		✓ 52%	
	Other					✓ 21%	
	Ancillary supplies included in graft costs?	Not specified		---		---	no

Table 13. Cost analyses and findings (continued)

		Sternbergh 00[64]		EVAR2 05[145]		Prinssen 04[159]	Bertges 03[153]
	Initial ER evaluation	?		-		-	
	Preop / preop diagnostics	✓		-		-	
	Total preop	$1,100	$644	-		-	
	Commercial graft / prosthetic device	$10,200	$653	✓		-	$13,191
	% hospital costs accounted for by graft	51%	6%			-	57%
	Operating room						
	Surgeon fees	-		?		-	
	Nursing	?		?		-	
	Anesthesia	✓		?		-	
	Medical/surgical supplies	✓		?		-	
	Respiratory services/ventilation	?		?		-	
	Pharmacy	✓		?		-	
	Radiology	?		?		-	
	Blood/transfusion	✓		✓		-	
	Laboratory	?		?		-	
	Postop ICU	✓		✓		-	
	Postop ward	✓		✓		-	
	Post diagnostic	✓		?		-	
	Allied health, therapy, etc.	?		?		-	
	"Procedure"	✓		✓		-	
	Hospital," "inpatient hospitalization"	✓		✓		-	
	Patient costs (time, travel, morbidity)	-		-		-	
	"Other"	?		✓		-	
	Total hospitalization	$20,150	$11,698	£11,016	£3,518		$23,042
	U.S. dollars			$17,626	$5,629		
	Total preop + hospitalization	$21,250	$12,342	-		-	
	Radiology: imaging followup	-		✓		✓	
	Endoleak repair	-		✓		✓	
	Conversion to OSR	-		✓		✓	
	"Adverse events"	-		✓		?	
	Patient costs (time, morbidity)	-		✓		-	
	Total followup			£2,616	£1,465	$9,729 (5 years)	
	GRAND TOTAL			£13,632-4 years	£4,983-4 years		

Table 13. Cost analyses and findings (continued)

		Lester 01[158]	Brox 03[155]		Forbes 98[147]		Huber 01[4]
	Type of cost data (source)	Hospital costs (TSI)	Hospital costs (TSI)		Hospital cost (UK National Health Service)		Hospital charges
	Type of study	Retrospective review	Retrospective review		RCT		Retrospective review
	Direct only or direct AND indirect	Direct and indirect	Direct and indirect		Direct only		Direct and indirect?
	Currency	U.S. dollar	U.S. dollar, 2000		UK pound		U.S. dollars, 1996
	Cohort	1994-1999	1997-2000		?		1994-1996
	Treatment	**EVAR**	**OSR-USA**	**OSR-Canada**	**CM**	**OSR**	**OSR**
----- GRAFTS USED -----	Ancure, Guidant (Menlo Park, CA)	✓					
	AneuRx, Medtronic (Santa Rosa, CA)	-					
	Excluder, Gore (Flagstaff, AZ)	✓	Not applicable		Not applicable		Not applicable
	Talent, Medtronic (Minneapolis, MN; Santa Rosa, CA)	-					
	Vanguard, Boston Scientific (Wayne, NJ)	✓					
	Zenith, Cook (Bloomington, IN; Denmark)	-					
	Other commercial grafts	-					
	Custom-made stents	-					
	Straight, tube type	✓ 21%					
	Bifurcated type	✓ 79%					
	Other						
	Ancillary supplies included in graft costs?	Not specified	---		---		---
	Initial ER evaluation	✓	?		?		-
	Preop / preop diagnostics	?	?		?		-
	Total preop	?	?		?		-
	Commercial graft / prosthetic device	-	✓		?		?
	% hospital costs accounted for by graft						
	Operating room	✓	✓		?		?
	Surgeon fees	-	-		?		?
	Nursing	✓	✓		?		?
	Anesthesia	✓	✓		?		?
	Medical/surgical supplies	✓	✓		?		?
	Respiratory services/ventilation	?	✓		?		?

Table 13. Cost analyses and findings (continued)

		Lester 01[158]	Brox 03[155]		Forbes 98[147]		Huber 01[4]
	Pharmacy	✓	✓		?		?
	Radiology	✓	✓		✓		?
	Blood/transfusion	✓	✓		?		?
	Laboratory	✓	✓		?		?
	Postop ICU	✓	✓		?		?
	Postop ward	✓	✓		✓		?
	Post diagnostic	✓	✓		?		?
	Allied health, therapy, etc.	✓	?		?		?
	"Procedure"	✓	✓		✓		?
	"Hospital," "inpatient hospitalization"	✓	✓		✓		✓
	Patient costs (time, travel, morbidity)	-	-		-		-
	"Other"	✓	?		✓		?
	Total hospitalization	✓	$19,000	$16,000	£3,914	£4,978	$35,681
	Total preop + hospitalization	$11,842	?		?		-
	Radiology: imaging followup	-	?		?		-
	Endoleak repair	-	?		?		-
	Conversion to OSR	-	?		?		-
	"Adverse events"	-	?		?		-
	Patient costs (time, morbidity)	-	?		?		-
	Total followup	-	?		?		-
	GRAND TOTAL	-	?		?		-

Key: explicitly included cost ( ); explicitly excluded cost (-); cost not mentioned or inclusion/exclusion uncertain (?).

Table 14. Short-term mortality, hospital, and intensive care unit (ICU) length of stay

	Sternbergh 00[64]		Clair 00[152]		Angle 04[151]		Hayter 05[157]		Lester 01[158]
	EVAR	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**	**EVAR**	**OSR**	**EVAR**
Total N per treatment arm	131	49	45	94	55	64	55	140	91
30-day mortality, n	NR	NR	*see notes*		2	1	1	2	NR
30-day mortality, %					3.6	1.5	1.8	1.4	
In-hospital mortality, n	NR	NR	0	1	NR	NR	NR	NR	1
In-hospital mortality, %	NR	NR	0%	1.0%					1%
Hospital LOS, days (mean)	3.9	8	3.2	9.7	1.96 (1 median)	7.3 (6 median)	6*	10*	3.5
Hospital LOS, range or SD	3.6*	5.8*	1.4*	4.8*	1.5*	8.3*	4 to 24	6 to 46	2.3*
ICU LOS, days (mean)	1.1	2	0.06	2.97	0.09	3.5	0*	1*	
ICU LOS, range or SD	2.0*	2.3*	0.25*	3.02*	0.29*	7.36*	0 to 3	1 to 19	
Notes:	*SD		*SD unless specifically reported as 30-day mortality is assumed to be "in-hospital		*SD		*Median		*SD

	Bosch 01[154]		Dryjski 03[156]		Bertges 03[153]	EVAR1 05[13]		EVAR2 05[145]		Brox 03[155]	
	EVAR	**OSR**	**EVAR**	**OSR**	**EVAR**	**EVAR**	**OSR**	**EVAR**	**AS**	**OSR-U.S.**	**OSR-Canada**
Total N per treatment arm	181	273	73	57	221	543	539	166	172	2.97*	176
30-day mortality, n	NR	NR	NR	NR	NR	9/532	25/518	13/150	1/47	NR	NR
30-day mortality, %						1.7	4.8	8.7	2.1		
In-hospital mortality, n	2	8	3	0	NR	NR	NR	NR	NR		
In-hospital mortality, %	1.1%	2.9%	4							5.2%	5/5%
Hospital LOS, days (mean)	Postop LOS only		4.9	12.6	2.4	10.3	15.7	NR	NR	NR	NR
Hospital LOS, range or SD			13.4*	14.8*		17.8*	16.9*				
ICU LOS, days (mean)	1.2* (1 median)	2.3* (1 median)	1.4	5	NR	0.7	2.4	NR	NR	NR	NR
ICU LOS, range or SD	0.4** 1 to 2	2.1** 1 to 12	7.1*	6.1*		3.8*	5.9*				
Notes:	* Includes only patients staying 1 day or longer *SD		*SD			*SD				* sample size for elective surgeries only	

Table 14. Short-term mortality, hospital, and intensive care unit (ICU) length of stay (continued)

	Bosch 02[149]		Huber 01[4]	Lee 04[51]		Michaels 05[17]			Schermerhorn 00[148]	
	EVAR	OSR	OSR	EVAR	OSR	RC1-EVAR	RC1-OSR	RC2-Nothing	Early Repair	AS
Total N per treatment arm			16450	2565	4607					
30-day mortality, n	NR	NR		NR	NR	NR	NR		NR	NR
30-day mortality, %										
In-hospital mortality, n	NR	NR	691 (est)	33	176	1.85*	5.8*		5.8	7.2
In-hospital mortality, %			4.2	1.3	3.8					
Hospital LOS, days (mean)	NR	NR	10 (8 median)	3.6 (2 median)	8.8 (7 median)	NR	NR		NR	NR
Hospital LOS, range or SD			8.1*	5.9*	7.8*					
ICU LOS, days (mean)	NR	NR	NR	NR	NR	NR	NR		NR	NR
ICU LOS, range or SD										
Notes:	Markov decision model		*SD	*SD		Markov decision model *Probabilities, presumed postoperative, from RCTs			Markov model	

	UKSAT[147]		Patel 99[150]		Prinssen 04[159]
	AS	OSR	EVAR	OSR	EVAR Only
Total N per treatment arm	527	563			77
30-day mortality, n			4.8*	1.2*	NR
30-day mortality, %	7.1%	5.8%			
In-hospital mortality, n					0
In-hospital mortality, %	7.2%	5.8%	4.8	1.2	
Hospital LOS, days (mean)	NR	NR	NR	NR	NR
Hospital LOS, range or SD					
ICU LOS, days (mean)	NR	NR	NR	NR	NR
ICU LOS, range or SD					
Notes:			*Probability		

AS = Active Surveillance

Table 15. Markov models

Source of Costs	**Bosch 2002**[149]		**Patel 1999**[150]		**Michaels 2005**[17]		**Schermerhorn 2000**[148]		**Patel 2000**[163]	
Direct only or direct AND indirect currency	Hospital costs, Medicare reimbursement for DRGs 110 & 111 physician CPT codes Direct and indirect U.S. dollar, 2000		Hospital cost accounting system, Medicare reimbursement rates for physician CPT codes Direct and indirect U.S. dollar, 1997		National Health Service (NHS), Sheffield Teaching Hospitals, NHS Trust Unclear UK £, 2003-2004		Hospital costs (UK NHS), UKSAT Direct UK £ * 1.6 = U.S. $ 1996-97		Hospital cost accounting system, Medicare reimbursement rates, physician CPT codes Unclear U.S. dollar, 1997	
	EVAR	**OSR**	**EVAR**	**OSR**	**RC1-EVAR**	**RC2-Surveillance**	**OSR**	**CM**	**OSR**	**CM**
Reference case	70 years old		70 years old		70 years old	80 years old	60-76 years old		72 years old	
AAA diameter	5-6 cm		5 cm		5.5 cm	6.5 cm	4-5.5 cm		ruptured AAAs	
Risk group (fit or unfit for OSR)	Fit for either procedure		Fit for either procedure		Fit for either	Unfit for OSR	Fit for OSR		Ruptured AAAs	
Time horizon	lifetime		lifetime		10 years		6 years (UK trial) & lifetime		lifetime	
Discount rate	3%		3%		3.50%		3%		3%	
Consumer Price Index (CPI) for inflation	CPI medical care		CPI medical care		?		?		CPI medical care	
Baseline operative mortality rate	3%	4%	1.2%	4.80%	EVAR: 1-85%, OSR: 5-80%	Range 5-80%	5.8% elective		50%	
Quality of Life (QOL) scores	-10% for 30 days	-30% for 60 days	QALY – 11 days	QALY – 47 days	QOL=0.8 each arm; EVAR: QALY – 30 days; OSR: QALY – 14 days		QOL = 0.86 for each arm		QALY – 52 days	
QOL adjustment for complications (Y/N)	Yes		Yes		?		Yes		Yes	
Software	DATA 3.5 (TreeAge)		SMLTREE v2.9		TreeAge Pro		DATA 3.0 (TreeAge)		SMLTREE v2.9	
Probabilistic sensitivity analyses (SA) (Y/N)	No. one & multiple way SA		No. one & multiple way SA		Yes		No. one way SA		No. one & multiple way SA	
Initial ER evaluation	-		-		?		-		✓	✓
Preop / preop diagnostics	-		-		?		-		✓	✓
Total preop	-		-		?		-		OSR = CM	
Graft / prosthetic device	-	-	$8,000	$650	?	?	?		$650	$0
Type of graft / prosthetic device	-	-	Tube 10% bifurc 90%	?	?	?	?	?	?	?

Table 15. Markov models (continued)

Source of Costs	Bosch 2002[149]		Patel 1999[150]		Michaels 2005[17]		Schermerhorn 2000[148]		Patel 2000[163]	
Direct only or direct AND indirect currency	Hospital costs, Medicare reimbursement for DRGs 110 & 111 physician CPT codes Direct and indirect U.S. dollar, 2000		Hospital cost accounting system, Medicare reimbursement rates for physician CPT codes Direct and indirect U.S. dollar, 1997		National Health Service (NHS), Sheffield Teaching Hospitals, NHS Trust Unclear UK £, 2003-2004		Hospital costs (UK NHS), UKSAT Direct UK £ * 1.6 = U.S. $ 1996-97		Hospital cost accounting system, Medicare reimbursement rates, physician CPT codes Unclear U.S. dollar, 1997	
% TC accounted for by graft			40%	4%	?	?	?			
Operating room	?		✓		?	?	✓		✓	
Surgeon fees	✓		✓		?	?	?		✓	
Nursing	?		?		?	?	?		?	
Anesthesia	?		✓		?	?	?		✓	
Medical/surgical supplies	?		✓		?	?	?		?	
Respiratory services/ ventilation	?		?		?	?	?		?	
Pharmacy	?		?		?	?	?		?	
Radiology	?		✓		?	?	✓		?	
Blood/transfusion	?		✓		?	?	?		✓	
Laboratory	?		✓		?	?	?		?	
Postop ICU	?		✓		?	?	?		✓	
Postop ward	?		✓		?	?	?		✓	
Post diagnostic	?		✓		?	?	?		?	
“Procedure”	✓		✓		?	?	✓		?	
“Hospital,” “inpatient hospitalization”	✓		✓		?	?	?		?	
Patient costs (time, travel, morbidity	✓		✓		?	?	?		✓	
Other	?		?		?	?	?		?	
Total hospitalization	$19,642	$23,484	$20,083	$16,016	£?	£?	?		$28,356	$0
Total preop + hospitalization	-	-	-	-			?		?	?
Imaging followup	✓	✓	✓	✓	✓	✓	?		✓	
Total followup	✓	✓	✓	✓			?		?	
GRAND TOTAL	$39,785 lifetime	$37,606 lifetime	$28,901 lifetime	$19,314 lifetime	?	?	$8,000 lifetime	$6,490 lifetime	$36,606 lifetime	$580 lifetime
Net cost	$2,179 more for EVAR		$9,587 more for EVAR		11,449 more for EVAR	14,077 more for EVAR	$1,510 more for early surgery*		$36,026 more for OSR	

Table 15. Markov models (continued)

Source of Costs	Bosch 2002[149]	Patel 1999[150]	Michaels 2005[17]		Schermerhorn 2000[148]	Patel 2000[163]
Direct only or direct AND indirect currency	Hospital costs, Medicare reimbursement for DRGs 110 & 111 physician CPT codes Direct and indirect U.S. dollar, 2000	Hospital cost accounting system, Medicare reimbursement rates for physician CPT codes Direct and indirect U.S. dollar, 1997	National Health Service (NHS), Sheffield Teaching Hospitals, NHS Trust Unclear UK £, 2003-2004		Hospital costs (UK NHS), UKSAT Direct UK £ * 1.6 = U.S. $ 1996-97	Hospital cost accounting system, Medicare reimbursement rates, physician CPT codes Unclear U.S. dollar, 1997
Net benefit	QALYs >0.22 for EVAR	QALYs >0.42 for EVAR	QALYs >0.1 for EVAR	QALYs >1.64 for EVAR	QALYs >0.14 for early surgery	QALYs >3.35 for OSR
Incremental Cost Effectiveness Ratio (ICER)	$9,905/QALY using Medicare reimbursement rates	$22,826 / QALY	£100,000 / QALY	£8,579 / QALY	$10,800 / QALY	$10,754 / QALY

Cost calculation based only on simple conversion from British pounds to U.S. dollars using £1.6 = $1

Chapter 4. Discussion

AAA are associated with considerable morbidity, mortality and health-care costs. Elective OSR has traditionally been considered the intervention of choice to reduce the risk of AAA rupture and improve survival in individuals at high risk of rupture. However, EVAR has become widely used based on belief that it may provide long-term prevention of ruptures with low intervention morbidity and mortality and improved length and quality of life. Approximately one-half of large AAA might be anatomically suitable for EVAR. Results from this systematic review provide the most up-to-date evidence related to the natural history, treatment, and costs associated with asymptomatic nonruptured infrarenal AAA. This report also evaluates evidence related to the relationship of surgical and hospital volume on outcomes for both OSR and EVAR.

AAA is predominantly a condition of older men with a much lower prevalence in younger persons and women. The strongest known predictor of AAA rupture is initial or attained size. Patients with AAA <5.5 cm have an annual risk of rupture of approximately 1 percent. For AAA <5.5 cm in diameter, high-quality RCT results demonstrate that active surveillance with ultrasound and delayed OSR (if AAA attains a diameter of ≥5.5 cm or the patient develops aneurysm related symptoms) results in equivalent mortality but lesser morbidity and operative costs due to fewer interventions compared to immediate OSR. Therefore, for AAA <5.5 cm, active surveillance and delayed OSR if AAA diameter exceed 5.5 cm (or in those that develop symptoms consistent with impending rupture) results in comparable long-term survival and quality of life, fewer OSR, and lower costs than immediate OSR regardless of age or gender. There are no RCT evaluating EVAR in these patients.

Among individuals with large AAA and refusing or medically unfit for OSR, the 1 year rupture risk may exceed 10 percent in AAA >6 cm and for AAA of >8 cm, the risk may exceed 25 percent at 6 months. For AAA ≥5.5 cm and suitable for EVAR, high-quality RCTs have been conducted outside the U.S. and may have used some EVAR devices that are not approved for use in the U.S. Their results demonstrate that compared to OSR for medically fit patients, EVAR is associated with lower perioperative morbidity and mortality and persistent reduction in AAA-defined mortality to 4 years, though the latter may be due, at least in part, to ascertainment bias for later term cause of death. EVAR did not improve longer term overall survival or health status and was associated with greater complications, need for reintervention, long-term monitoring, and costs. Because decisions regarding the risks and benefits of AAA treatments should incorporate a long-term time frame, additional followup information beyond 4 years is needed. There are insufficient data to determine whether outcomes varied according to device type.

For the minority of patients with AAA ≥5.5 cm judged medically unfit for OSR, one high-quality RCT conducted in the U.K. with EVAR devices that may not be approved for U.S. use demonstrated that EVAR did not improve survival at 3 years or health status and costs more than no intervention. More than 60 percent of the no intervention group died indicating that longer followup was unlikely to alter results. Refinements in EVAR devices or provider experience may result in different outcomes. Therefore a RCT conducted in the U.S. with currently approved EVAR devices in these patients is indicated. However, unless results from such a RCT refute findings from EVAR-2, the RCT data provide the highest quality evidence available for treatment decision making and do not support the widespread practice of using EVAR to treat AAA in patients judged to be too sick for OSR. Patient treatment preference is difficult to

ascertain. How the results of RCT influence patient and provider treatment preference in the U.S. is not known.

Data from nonRCT are limited by lack of randomization as well as incomplete followup reporting of entered patients. They cannot be used as substitutes for RCT to evaluate the comparative effectiveness and adverse effects of AAA treatment options. Few studies provided an evaluation according to device or patient characteristics. None represent head to head comparisons from RCT. Furthermore, patient or aneurysm factors could influence outcomes. Therefore, it is hazardous to make definitive statements regarding relative safety or effectiveness. While it is not possible to make direct comparisons with RCT, most reports explicitly stated patients were candidates for OSR. Baseline patient characteristics, AAA diameter, 30 day and 2 year overall, and AAA mortality as well as EVAR conversion rates and secondary interventions for included patients were similar to those from EVAR-1 and DREAM. None of these reports assessed EVAR in patients with AAA ≥5.5 cm and considered "medically unfit for OSR." One report evaluated outcomes of EVAR and OSR in a retrospectively defined "high surgical risk" subgroup of patients entered into any of five nonrandomized multicenter IDE studies leading to FDA approval of EVAR devices. Inclusion criteria for the IDE studies required that patients were candidates for OSR, though in one study patients were prospectively defined as being at high risk for OSR due to age >80 years or other pathophysiologic conditions. It is not known whether any were judged medically unfit for OSR. After 4 years, deaths categorized as due to AAA were similar between EVAR and OSR patients. Overall-survival in EVAR treated patients was 10 percent lower compared to OSR, though this difference was not statistically significant.

Because of the relatively low 30-day procedure related morbidity and mortality, treatment with EVAR of patients with smaller AAA has occurred. Therefore, while the total number of interventions for AAA has remained relatively constant over time, the proportion of patients treated with EVAR has increased. There are no published investigations of relationships between hospital or physician volume and any outcome of EVAR of AAA. Published and ongoing EVAR RCT have required that investigators and their facilities have experience in use of this procedure. The threshold for permitting participation varies from 5 to 20 and were not based on evidence.

The volume of OSR procedures done by hospitals and physicians to repair unruptured AAA was inversely associated with short-term mortality in the 1990s when EVAR procedures were being investigated. Surgeon volume may explain a large portion of the effect of hospital volume, although hospital volume appears to have an effect that is not related to surgeon volume or surgeon specialty. Uncontrolled risk factors might account for some of the volume effects. The one study that was able to control for preoperative clinical measures did not find a significant association between hospital volume and mortality.[139] Otherwise, the reasons for the observed relationships between the volume of procedures done by hospitals or surgeons over a period of time and short-term mortality have not been clearly established. The imprecision inherent in measuring outcomes of very low-volume providers isn't always taken into account and may unduly influence estimates in some studies. Even though policymakers such as the Leapfrog group have somewhat arbitrarily selected cutoffs to define preferred 'high' volume hospitals for OSR of AAA, investigators have not identified optimal thresholds for grouping providers by volume in an effort to improve outcomes. Furthermore, this question needs to be revisited since EVAR has replaced OSR in a substantial percentage of AAA.

The cost effectiveness of EVAR relative to OSR is difficult to determine for several reasons: there are no long term (>4 year) outcome data from RCT of EVAR versus OSR; evolving EVAR technological refinements and provider experience may push EVAR towards being an effective

and cost-effective alternative to OSR; it is difficult to extrapolate the cost experience in one country to that in another with a different health care and payment system; the perspective of the concerned party is critical in such analyses.

Case series focusing on hospital costs generally found that EVAR costs more to perform than OSR, primarily due to the cost of the prosthesis. The high cost of the EVAR prosthesis is partially offset by reduced hospital and intensive care unit length of stay, operating time, and necessity for blood transfusion relative to OSR. More comprehensive cost analyses noted the higher followup costs for EVAR.

None of the Markov cost effectiveness models had accurate data on the complication and reintervention rates associated with EVAR. Although the Michaels et al. study is based on the literature published through September 2004, several case series have come out since then, and data from midterm results of RCTs were not included.[17]

Results from additional RCTs, comparing EVAR and OSR for large AAA and EVAR versus surveillance for small AAA conducted in the U.S. have not yet been published. It is not clear how these costs would directly relate to U.S. settings. Trials conducted outside the U.S. do not reflect U.S. norms associated with resource valuation, utilization of health care resources, practice variation, and U.S. health care expertise. Decisions based on costs may differ with the locus. For example, hospitals may be willing to consider trading higher procedural costs for shorter lengths of stay.

Data from RCTs demonstrate that for small AAA (<5.5 cm) immediate OSR costs more and does not improve survival compared to active surveillance and delayed elective intervention. For large AAA (≥5.5 cm) among patients fit for OSR, EVAR has greater short- and long-term costs, does not improve overall survival or quality of life beyond 1 year, and is associated with greater long-term complications, need for reintervention, and long-term monitoring compared to OSR. EVAR is associated with shorter hospital and intensive care unit length of stay, reduced AAA mortality, and lower 30-day morbidity and mortality, compared with OSR. In patients with AAA ≥5.5 cm and judged medically unfit for OSR, EVAR did not improve survival or quality of life among those who were alive and was associated with higher costs compared to no intervention.

The analyses conducted in the UK reflect concerns relevant to the NHS that may not be as important in a U.S. context. For example, whereas EVAR's potential to free up hospital beds may be important to NHS hospitals pressed for space, in the American context this aspect of EVAR has more salience for hospitals trading off LOS for a more expensive EVAR prosthesis under a fixed payment DRG reimbursement approach.

Other issues regarding the published data used in the Markov models include the transferability of results found in case series studies to different patient populations, e.g., of different aneurysm size. As new clinical devices are continually being introduced in the market, technological improvements may change the mortality and morbidity rates associated with EVAR in particular. The evidence of a learning curve or improvements in device manufacturing associated with EVAR may be associated with a lower long-term mortality, morbidity, and need for monitoring and reintervention that might someday demonstrate that EVAR is a cost effective alternative to OSR. Finally, because the 30-day mortality rates associated with OSR are variable, the significance of the differences in mortality rates between EVAR and OSR is obscured. The variability associated with operative mortality translates to greater uncertainty and higher risk to patients considering OSR. If improvements in long-term morbidity and mortality with EVAR are demonstrated in the future, this may make EVAR a favorable alternative to OSR from the patient's perspective.

When conducting CEA, a common concern among researchers is that one needs to account for the fact that patients who die cost less in terms of health care expenditures than patients who live longer. The treatment arm that results in higher mortality rates would thus have lower costs reflected in the numerator of the cost effectiveness ratio. The standard approach to adjusting the cost effectiveness ratio for deaths is to assume that the QOL associated with death is zero in the denominator.[160] The assumption is that QOL takes into account the disutility associated with morbidity/mortality. As long as the QOL scale also reflects the disutility of lost earnings, solely relying on the QOL to account for deaths in the denominator is permissible. If the QOL scale does not reflect lost earnings, then the numerator must reflect the patients' lost earnings as part of the cost associated with each treatment. Although some might attribute the QOL associated with death as zero, others may think of death as having a higher QOL than other outcomes, such as living with pain.

Different components of cost may have different salience in different national health contexts. When comparing results of economic analyses across countries, there is currently no consensus or standard on how to do this. Simply factoring in the foreign exchange rate, for example, overlooks the variance in utilization and cost estimates across countries due to differences in physician practice patterns, resource valuation, and resource use. Reed et al. discuss the strengths and weaknesses of various methods used to pool cost estimates across countries.[164] Methods are differentiated according to whether measures of effectiveness, resource utilization, and cost are derived from one or multiple countries. Strengths and weaknesses are based on balancing concerns about generalizability, transparency, and statistical power. Tradeoffs exist between trying to keep things simple enough for other researchers to implement (e.g., a one-country costing approach) and losing internal validity associated with a multinational costing approach. One-country costing disrupts the theoretical relationship between relative costs and resource use. Reed et al. note that using relatively high U.S. unit costs overestimates total costs as well as the absolute difference in costs between treatment groups, inflating the numerator of an ICER.[164]

Recommendations for Future Research

- Results from nonrandomized trials, case-series, or FDA reports are inadequate to accurately assess the relative effectiveness and safety of treatments for AAA. The highest priority for future research to guide clinical care is to conduct long-term RCTs in the U.S. to assess whether RCT results of EVAR conducted in Europe apply to U.S. settings. These include EVAR vs. OSR for AAA ≥5.5 cm in patients judged medically fit for OSR (analysis of results according preplanned categories of AAA, operative risk, gender, and device characteristics appears warranted), EVAR versus active surveillance for AAA <5.5 cm, and EVAR versus no intervention for AAA ≥5.5 cm in patients medically unfit for OSR.
- Effective strategies are required to disseminate and implement the findings from published high-quality RCTs to patients, providers, health-care organizations, and payers.
- Additional information on the benefits and risks of treatments in women are needed.
- Refinements in EVAR devices, technique, and interventionist team are required to reduce complications and need for long-term followup.

- Although studies cannot avoid measurement error associated with outcomes resulting from incorporating new devices into them, more research is needed to identify whether outcomes for EVAR vary according to device manufacturer or type and patient or aneurysm characteristics. Ideally, these would be obtained by conducting direct comparison RCTs.
- Consistent/validated definitions of outcomes including AAA mortality; complications, and need for reintervention are required to assist clinicians, investigators, policy makers, and patients to evaluate relative safety and effectiveness of treatment options. In particular, cause of death ascertainment beyond 30 days or the initial hospitalization is problematic. Reducing ascertainment bias likely requires rigorous adjudication of all deaths including use of autopsy and/or post-mortem imaging.
- Conduct RCTs to determine whether medical therapy slows AAA enlargement or rupture. Previous trials were inadequately powered to provide clinically meaningful results.
- Improve data submission, followup, and cause of death ascertainment in registries.
- Improvement in medical management of patients with large AAA considered unacceptable for OSR is needed.
- Specific studies of EVAR are needed to characterize the hospital and physician volume-outcome relationship, if any. The validity of methods used to identify and count EVAR procedures should be examined and reported. Studies should measure volume in a consistent manner and focus on outcomes defined in reporting standards including clinical success, continuing success, complications, and return to preprocedure activity levels. Risk adjustment should include patient demographics, comorbidity, morphology of the aneurysm and access vessels, device characteristics, and any other variables that could have a substantial influence on the outcomes under investigation. Rigorously developed and tested regression models and examination of the sensitivity of results to the method of analysis would be useful. Most likely, representative prospective registries will be needed to perform a proper indepth analysis to determine whether and how the volume of endovascular procedures done by hospitals or physicians to repair AAA relate to beneficial or adverse outcomes. Ideally, future studies would strive to characterize the functional form of volume-outcome relationships and explain why they exist. The volume-mortality relationship for OSR of AAA needs to be reexamined in the EVAR era.
- Future cost analyses studies should include short- and long-term followup data, either collected prospectively on all patients or incorporated from RCTs into Markov models.
- Studies should follow a standardized approach to analyzing costs and effectiveness associated with the two procedures. Studies should explicitly describe the methods used to calculate costs and should include the following categories: direct medical care costs, institutional overhead costs, patient travel costs, and patients' time and/or lost earnings. The collection of these costs should be carefully itemized and described.
- Studies conducting prospective data collection in the United States taking a societal perspective are needed. Where appropriate, data should be collected on the patient's time taken off work or other activities to travel and attend medical appointments, whether on an inpatient or outpatient basis, and to obtain prescriptions.
- Data on United States patient's QOL, where the treatment of the QOL associated with lost earnings and death is explicitly stated, should also be collected.

Conclusions

AAA are associated with considerable morbidity, mortality and health-care costs. Patients with AAA <5.5 cm have an annual risk of rupture of approximately 1 percent. For AAA <5.5 cm in diameter high-quality RCT results demonstrate that active surveillance with ultrasound and delayed OSR (if AAA attains a diameter of ≥5.5 cm or the patient develops aneurysm related symptoms) results in comparable long-term survival and quality of life, fewer OSR, and lower costs than immediate OSR regardless of age or gender. There are no RCTs evaluating EVAR in these patients.

Among individuals refusing or medically unfit for OSR the 1-year rupture risk may exceed 10 percent in AAA >6 cm and for AAA of >8 cm, the risk may exceed 25 percent at 6 months. For AAA ≥5.5 cm and suitable for EVAR, high-quality RCTs have been conducted outside the U.S. and may have used some EVAR devices that are not approved for use in the U.S. Their results demonstrate that, compared to OSR, EVAR is associated with lower perioperative morbidity and mortality and persistent reduction in AAA-defined mortality to 4 years, though the latter may be due, at least in part, to ascertainment bias for later term cause of death. EVAR did not improve longer term overall survival or health status and was associated with greater complications, need for reintervention, long-term monitoring, and costs.

For the minority of patients with AAA ≥5.5 cm and judged medically unfit for OSR, one high-quality RCT conducted in the U.K. and with EVAR devices that may not be approved for use in the U.S. demonstrated that EVAR did not improve survival or health status and costs more than no intervention.

There are no data adequate to estimate the effect of hospital or physician volume on EVAR outcomes and identify a volume threshold for policymakers. A volume outcome relationship for OSR has been shown for surgery prior to the introduction of EVAR, but none since.

The cost effectiveness of EVAR relative to OSR is difficult to determine for several reasons: there are no long term (>4 year) outcome data from RCT of EVAR versus OSR; evolving EVAR technological refinements and provider experience may push EVAR towards being an effective and cost-effective alternative to OSR; it is difficult to extrapolate the cost experience in one country to that in another with a different health care and payment system; and the perspective of the concerned party is critical in such analyses.

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List of Acronyms/Abbreviations

AAA	Abdominal Aortic Aneurysm
ACE	AnEVARysme de l'aorte abdominal: Chirurgie versus Endoprothese
ADAM	Aneurysm Detection and Management
AHIP	America's Health Insurance Plans
AHQR	Agency for Healthcare Research and Policy
ARR	Absolute Risk Reduction
CAESAR	Comparison of surveillance versus Aortic Endografting for Small Aneurysm Repair
CI	Confidence Interval
CM	Conservative Management
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
CTA	Thin-Cut Helical/Spiral CT Arteriography
DREAM	Dutch Randomized Endovascular Aneurysm Management
DRG	Diagnosis Related Group
EGS	Endovascular Aortoiliac Grafting System
EPC	Evidence-based Practice Center
EVAR	Endovascular Repair
FDA	Food and Drug Administration
FEV_1	Forced Expiratory Volume in 1 second
HR	Hazard Ratio
ICD-9-CM	International Classification of Diseases, 9^{th} Revision, Clinical Modification
ICER	Incremental Cost Effectiveness Ratio
ICU	Intensive Care Unit
IDE	Investigational Device Exemption
IQR	Interquartile Range
LOS	Length of Stay
NHS	National Health Service
NICE	National Institute of Clinical Excellence
NRCTs	Nonrandomized Controlled Trials
OSR	Open Surgical Repair
OVER	Open Versus Endovascular Repair
PIVOTAL	Positive Impact of endovascular Options for Treating Aneurysms
PSA	Probabilistic Sensitivity Analysis
QALY	Quality Adjusted Life Years
QOL	Quality of Life
RCT	Randomized Controlled Trials
RD	Risk Difference
RR	Relative Risk
SF-36	Short Form-36
TEP	Technical Expert Panel
UKSAT	United Kingdom Small Aneurysm Trial
USPSTF	U.S. Preventive Services Task Force
VA	Veterans Administration

Appendixes

to

"Comparison of Endovascular and Open Surgical Repairs for Abdominal Aortic Aneurysm"

Prepared by the Minnesota Evidence-based Practice Center
(Contract # 290-02-0009)

Appendix A: Technical Expert Panel Members and Areas of Expertise

TEP Member	Area of Expertise
R. Clement Darling, III, MD	Vascular surgery
Russell Harris, MD, MPH	Internal medicine
Wayne Johnston, MD, FRCSC, FACS	Vascular surgery
Jon S. Matsumura, MD	Vascular surgery

Appendix B: Exact Search Strings

Question 1 (RCTs)

The literature search was done on MEDLINE (via OVID) using the following combination of MeSH headings, keywords, and publication types (search results were limited to clinical trials, clinical trials phase I, clinical trials phase II, clinical trials phase III, clinical trials phase IV, controlled clinical trials, meta analyses, or randomized controlled trials):

(aortic aneurysm/ OR
aortic aneurysm, abdominal/)

AND

((Blood Vessel Prosthesis/ OR
Blood Vessel Prosthesis Implantation/ OR
(endovascular repair.mp. OR
evar.mp. OR
Stents/) OR
(vascular surgical procedures/ OR
open surgery.mp.))

Question 2 (Volume)

The literature search was done on MEDLINE (via OVID) using the following combination of MeSH headings, keywords, and publication types (search results were limited to humans, English language, and years 2000-2005):

((hospital.tw. AND
volume.tw.) AND
((outcome.mp. AND
process assessment health care.sh.) OR
outcome.tw. OR
(mortality.tw. OR
risk.tw. OR
quality.tw.)))

AND

(Aortic Aneurysm, Abdominal/)

Question 4 (Cost)

The literature search (taken from Meenan 2005 [AHRQ report])[17] was done on MEDLINE (via OVID) using the following combination of MeSH headings and keywords (search results were limited to English language, and years 2000-2005):

(aortic aneurysm, abdominal/ OR
(aortic and aneurysm$ and abdom$).ti,ab.)

AND

(ECONOMICS/ OR
economics, nursing/ OR
economics, pharmaceutical/ OR
ec.fs. OR
(econom$ or cost or costs or costing or pharmacoeconomic$).ti,ab. OR
(expenditure$ not energy).ti,ab. OR
"costs and cost analysis"/ OR
cost allocation/ OR
cost-benefit analysis/ OR
cost control/ OR
cost savings/ OR
cost of illness/ OR
cost sharing/ OR
"deductibles and coinsurance"/ OR
medical savings accounts/ OR
health care costs/ OR
direct service costs/ OR
drug costs/ OR
employer health costs/ OR
hospital costs/ OR
health expenditures/ OR
capital expenditures/ OR
economics, hospital/ OR
hospital charges/ OR
hospital costs/ OR
economics, medical/ OR
fees, medical/)

Appendix C: List of Excluded Studies

Question 1: RCTs *(reason for exclusion is provided in italics following each reference)*

Adachi H, Ino T, Mizuhara A, et al. [Clinical significance of selective cerebral perfusion with cold blood on the brain protection]. Nippon Kyobu Geka Gakkai Zasshi 1995 Sep; 43(9):1605-10. (Jap) *Not AAA; not English language*

Adiseshiah M, Bray AJ, Bergeron P, et al. Endoluminal repair of large abdominal aortic aneurysms using PTFE: a feasibility study. J Endovasc Surg 1997 Aug; 4(3):286-9. *Not RCT*

Adriaensen ME, Bosch JL, Halpern EF, et al. Elective endovascular versus open surgical repair of abdominal aortic aneurysms: systematic review of short-term results. Radiology 2002 Sep; 224(3):739-47. *Not RCT*

Alimi YS, Hartung O, Cavalero C, et al. Intestinal retractor for transperitoneal laparoscopic aortoiliac reconstruction: experimental study on human cadavers and initial clinical experience. Surg Endosc 2000 Oct; 14(10):915-9. *Not RCT*

Allen BT, Hovsepian DM, Reilly JM, et al. Endovascular stent grafts for aneurysmal and occlusive vascular disease. Am J Surg 1998 Dec; 176(6):574-80. *Not RCT*

Almgren B, Cars O, Eriksson I, Erlendsdottir H. Pharmacokinetics of dicloxacillin in serum and aortic wall during aneurysmal surgery. Acta Chir Scand 1986 Jan; 152:19-21. *Not EVAR vs open or surveillance trial*

Alric P, Hinchliffe RJ, Wenham PW, et al. Lessons learned from the long-term follow-up of a first-generation aortic stent graft. J Vasc Surg 2003 Feb; 37(2):367-73. *Not RCT*

Amesur NB, Zajko AB, Orons PD, et al. Embolotherapy of persistent endoleaks after endovascular repair of abdominal aortic aneurysm with the ancure-endovascular technologies endograft system. J Vasc Interv Radiol 1999 Oct; 10(9):1175-82. *Not RCT*

Amesur NB, Zajko AB, Orons PD, et al. Endovascular treatment of iliac limb stenoses or occlusions in 31 patients treated with the ancure endograft. J Vasc Interv Radiol 2000 Apr; 11(4):421-8. *Not RCT*

Ariyoshi H, Okuyama M, Okahara K, et al. Expanded polytetrafluoroethylene (ePTFE) vascular graft loses its thrombogenicity six months after implantation. Throm Res 1997 Dec 1; 88(5):427-33. *Not RCT*

Ashoke R, Brown LC, Rodway A, et al. Color duplex ultrasonography is insensitive for the detection of endoleak after aortic endografting: a systematic review. J Endovasc Ther 2005 Jun; 12(3):297-305. *Not EVAR vs open or surveillance trial*

Axelrod DJ, Lookstein RA, Guller J, et al. Inferior mesenteric artery embolization before endovascular aneurysm repair: technique and initial results. J Vasc Interv Radiol 2004 Nov; 15(11):1263-7. *Not EVAR vs open or surveillance trial*

Ayuso JR, de Caralt TM, Pages M, et al. MRA is useful as a follow-up technique after endovascular repair of aortic aneurysms with nitinol endoprostheses. J Magn Reson Imaging 2004 Nov; 20(5):803-10. *Not EVAR vs open or surveillance trial*

Balm R, Eikelboom BC, May J, et al. Early experience with transfemoral endovascular aneurysm management (TEAM) in the treatment of aortic aneurysms. Eur J Vasc Endovasc Surg 1996 Feb; 11(2):214-20. *Not RCT*

Barnes RW, Baker WH, Shanik G, et al. Value of concomitant sympathectomy in aortoiliac reconstruction. Results of a prospective, randomized study. Arch Surg 1977 Nov; 112(11):1325-30. *Not EVAR vs open or surveillance trial*

Batt M, Magne JL, Alric P, et al. In situ revascularization with silver-coated polyester grafts to treat aortic infection: early and midterm results. J Vasc Surg 2003 Nov; 38(5):983-9. *Not EVAR vs open or surveillance trial*

Baum RA, Shetty SK, Carpenter JP, et al. Limb kinking in supported and unsupported abdominal aortic stent-grafts. J Vasc Interv Radiol 2000 Oct; 11(9):1165-71. *Not EVAR vs open or surveillance trial*

Baxendale BR, Baker DM, Hutchinson A, et al. Haemodynamic and metabolic response to endovascular repair of infra-renal aortic aneurysms. Br J Anaesth 1996 Nov; 77(5):581-5. *Not RCT*

Becquemin JP, Haiduc F, Cavillon A. Thrombogenicity of an elastomer-coated aortofemoral Dacron prosthetic graft in humans. Ann Vasc Surg 1994 Sep; 8(5):443-51. *Not EVAR vs open or surveillance trial*

Becquemin JP, Lapie V, Favre JP, et al. Mid-term results of a second generation bifurcated endovascular graft for abdominal aortic aneurysm repair: the French Vanguard trial. J Vasc Surg 1999 Aug; 30(2):209-18. *Not RCT*

Beebe HG, Cronenwett JL, Katzen BT, et al. Results of an aortic endograft trial: impact of device failure beyond 12 months. J Vasc Surg 2001 Feb; 33(2 Suppl):S55-63. *Not RCT*

Bertrand M, Godet G, Koskas F, et al. Endovascular treatment of abdominal aortic aneurysms: is there a benefit regarding postoperative outcome? Eur J Anaesth 2001 Apr; 18(4):245-50. *Not RCT*

Biasi GM, Piglionica MR, Meregaglia D, et al. European multicentre experience with modular device (Medtronic AneuRx) for the endoluminal repair of infrarenal abdominal aortic aneurysms. J Mal Vasc 1998 Dec; 23(5):374-80. *Not RCT*

Blankensteijn JD. Mortality and morbidity rates after conventional abdominal aortic aneurysm repair. Semin Interv Cardiol 2000 Mar; 5(1):7-13. *Not RCT*

Blum U, Voshage G, Beyersdorf F, et al. Two-center German experience with aortic endografting. J Endovasc Surg 1997 May; 4(2):137-46. *Not RCT*

Blum U, Voshage G, Lammer J, et al. Endoluminal stent-grafts for infrarenal abdominal aortic aneurysms. N Engl J Med 1997 Jan 2; 336(1):13-20. *Not EVAR vs open or surveillance trial*

Bolke E, Jehle PM, Storck M, et al. Endovascular stent-graft placement versus conventional open surgery in infrarenal aortic aneurysm: a prospective study on acute phase response and clinical outcome. Clin Chim Acta 2001 Dec; 314(1-2):203-7. *Not RCT*

Bonazzi M, Gentile F, Biasi GM, et al. Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients. A randomised pilot trial. Eur J Vasc Endovasc Surg 2002 May; 23(5):445-51. *Not EVAR vs open or surveillance trial*

Borner G, Ivancev K, Sonesson B, et al. Percutaneous AAA repair: is it safe? J Endovasc Ther 2004 Dec; 11(6):621-6. *Not RCT*

Bove PG, Long GW, Shanley CJ, et al. Transrenal fixation of endovascular stent-grafts for infrarenal aortic aneurysm repair: mid-term results. J Vasc Surg 2003 May; 37(5):938-42. *Not RCT*

Brener BJ, Faries P, Connelly T, et al. An in situ adjustable endovascular graft for the treatment of abdominal aortic aneurysms. J Vasc Surg 2002 Jan; 35(1):114-9. *Not RCT*

Broeders IA, Blankensteijn JD, Gvakharia A, et al. The efficacy of transfemoral endovascular aneurysm management: a study on size changes of the abdominal aorta during mid-term follow-up. Eur J Vasc Endovasc Surg 1997 Aug; 14(2):84-90. *Not RCT*

Broeders IA, Blankensteijn JD, Wever JJ, et al. Mid-term fixation stability of the EndoVascular Technologies endograft. EVT Investigators. Eur J Vasc Endovasc Surg 1999, Oct; 18(4):300-7. *Not RCT*

Brustia P, Renghi A, Gramaglia L, et al. Mininvasive abdominal aortic surgery. Early recovery and reduced hospitalization after multidisciplinary approach. J Cardiovasc Surg 2003 Oct; 44(5):629-35. *Not RCT*

Burtoft JN, Robicsek F, Daugherty HK, et al. Comparative analysis of thrombogenicity and clinical patency between woven and knitted aorto-iliac and aorto-femoral prostheses. ASAIO Trans 1987 Jul-Sep; 33(3):207-11. *Not RCT*

Bush RL, Najibi S, Lin PH, et al. Early experience with the bifurcated Excluder endoprosthesis for treatment of the abdominal aortic aneurysm. J Vasc Surg 2001 Sep; 34(3):497-502. *Not RCT*

Buth J, van Marrewijk CJ, Harris PL, et al. Outcome of endovascular abdominal aortic aneurysm repair in patients with conditions considered unfit for an open procedure: a report on the EUROSTAR experience. J Vasc Surg 2002 Feb; 35(2):211-21. *Not RCT*

Carpenter JP, Anderson WN, Brewster DC, et al. Multicenter pivotal trial results of the Lifepath System for endovascular aortic aneurysm repair. J Vasc Surg 2004 Jan; 39(1):34-43. *Not RCT*

Carpenter JP, Endologix Investigators. Midterm results of the multicenter trial of the powerlink bifurcated system for endovascular aortic aneurysm repair. J Vasc Surg 2004 Nov; 40(5):849-59. *Not RCT*

Carpenter JP, Endologix Investigators. Multicenter trial of the PowerLink bifurcated system for endovascular aortic aneurysm repair. J Vasc Surg 2002 Dec; 36(6):1129-37. *Not RCT*

Cartes-Zumelzu F, Lammer J, Hoelzenbein T, et al. Endovascular placement of a nitinol-ePTFE stent-graft for abdominal aortic aneurysms: initial and midterm results. J Vasc Interv Radiol 2002 May; 13(5):465-73. *Not RCT*

Castronuovo JJ Jr, James KV, Resnikoff M, et al. Laparoscopic-assisted abdominal aortic aneurysmectomy. J Vasc Surg 2000 Aug; 32(2):224-33. *Not RCT*

Chavan A, Cohnert TU, Heine J, Dresler C, Leuwer M, Harringer W, et al. Endoluminal grafting of abdominal aortic aneurysms: experience with the Talent endoluminal stent graft. Eur Radiol 2000; 10(4):636-41. *Not RCT*

Christ F, Gamble J, Raithel P, Steckmeier B, Messmer K. [Preoperative changes in fluid filtration capacity in patients undergoing vascular surgery]. Anaesthesist 1999 Jan; 48(1):9-18. (Ger) *Not RCT; not English language*

Chuter TA, Wendt G, Hopkinson BR, et al. Transfemoral insertion of a bifurcated endovascular graft for aortic aneurysm repair: the first 22 patients. Cardiovasc Surg 1995, Apr; 3(2):121-8. *Not RCT*

Cina CS, Abouzahr L, Arena GO, et al. Cerebrospinal fluid drainage to prevent paraplegia during thoracic and thoracoabdominal aortic aneurysm surgery: a systematic review and meta-analysis. J Vasc Surg 2004 Jul; 40(1):36-44. *Not EVAR vs open or surveillance trial*

Conners MS 3rd, Tonnessen BH, Sternbergh WC 3rd, et al. Does ASA classification impact success rates of endovascular aneurysm repairs? Ann Vasc Surg 2002 Sep; 16(5):550-5. *Not RCT*

Coppi G, Moratto R, Silingardi R, et al. The Italian trial of endovascular AAA exclusion using the Parodi endograft. J Endovasc Surg 1997 Aug; 4(3):299-306. *Not EVAR vs open or surveillance trial*

Coppi G, Pacchioni R, Moratto R, et al. Experience with the Stentor endograft at four Italian centers. J Endovasc Surg 1998 Aug; 5(3):206-15. *Not RCT*

Courbier R, Ferdani M, Jausseran JM, et al. The role of omentopexy in the prevention of femoral anastomotic aneurysm. J Cardiovasc Surg 1992 Mar-Apr; 33(2):149-53. *Not RCT*

Criado FJ, Clark NS, McKendrick C, et al. Update on the Talent LPS AAA stent graft: results with "enhanced talent". Semin Vasc Surg 2003 Jun; 16(2):158-65. *Not RCT*

Criado FJ, Fairman RM, Becker GJ, et al. Talent LPS AAA stent graft: results of a pivotal clinical trial. J Vasc Surg 2003 Apr; 37(4):709-15. *Not RCT*

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Appendix D: Data Extraction Forms

UNIQUE IDENTIFIER #_____

ABDOMINAL AORTIC ANEURYSM (AAA): Surveillance Article Abstraction Form:

Author (first): _____

Journal: _____

Year Publication: _____ Country (ies): _____
(where study was conducted)

Data Abstractor: _____

Case-series **IF YES, STOP**	Yes	No	Unclear
Open study	Yes	No	Unclear
Epidemiologic cohort study	Yes	No	Unclear
RCT: Subjects randomly assigned	Yes	No	Unclear
Study duration $\geq$ 1 month	Yes	No	Unclear

METHODS

Study Design and Conduct

Intention-to-treat analysis	Yes	No	Unclear
Repairs performed by surgical teams with experience (i.e $\geq$ 5 repairs)	Yes	No	Unclear

ASSESSMENT OF STUDY QUALITY

1. RCT - RANDOMIZATION ALLOCATION CONCEALMENT METHOD (circle one)

Clearly adequate: Centralized randomization by telephone, randomization scheme controlled by pharmacy, numbered or coded identical containers administered sequentially, on site computer system which can only be accessed after entering the characteristics of an enrolled participant, sequentially numbered sealed opaque envelopes.

Clearly Inadequate: Alternation (odd-even, etc..), date of birth, date of week

Unclear: Sealed envelopes but not sequentially numbered or opaque, other, list of random numbers read by someone entering patient into trial (open list) *or study noted to be random or "randomization" or "random allocation" but no details provided.*

UNIQUE IDENTIFIER #_____

2. OBSERVATIONAL STUDIES, OTHER (*based on "Systems to Rate the Strength Of Scientific Evidence, AHRQ Publication No. 02-E016, April 2002*)

Score each domain on a scale of 0 (poor, not defined) to 5 (excellent, clearly defined)

Observational Studies Quality Domains/Elements	**Score**
Study question clearly focused and appropriate ***Notes:***	
Description of Study Population ***Notes:***	
Clear definition of intervention ***Notes:***	
Primary/secondary outcomes defined ***Notes:***	
Statistical Analysis: Assessment of confounding attempted Did the analysis adjust for or examine the effects of various factors (i.e., population baseline characteristics, characteristics of surgeons, training, surgical procedures, types of prostheses mentioned/ incorporated into the analyses) ***Notes:***	
Statistical methods used to take into account the effect of more than one variable on the outcome such as multiple regression, multivariate analysis, regression modeling -*see methods in paper* ***Notes:***	
Measure of effect for outcomes and appropriate measure of precision ***Notes:***	
Conclusions supported by results with possible bias and limitations taken into consideration ***Notes:***	
Single versus Multi-site study (*note one of the other*) ***Notes:***	
Patients evaluated with radiographs for outcomes ***Notes:***	
Comorbidities mentioned ***Notes****:*	
Comorbidities incorporated in the analyses ***Notes:***	
Attrition accounted for ***Notes****:*	
Death rates recorded ***Notes:***	

UNIQUE IDENTIFIER #_____

SUBJECTS

Multi-center or single site (*circle one*)

Total # subjects randomized/enrolled _____

	Surveillance	**Surgery (if applicable)**
# Subjects:		
Mean age		
Men: n / N and % (*if provided*)		
Women: n / N and %		
Age < 65* n / N and %		
Age ≥ 65 n / N and %		
Race: white n / N and %		
Race: black n / N and %		
Race: Other n/N and %		
Coronary Disease n/N and %		
Cerebrovascular Disease n/N and %		
Hypertension n/N and %		
Diabetes n/N and %		
COPD n/N and %		
Current smoker n/N and %		
Ever smoked n/N and %		
Blood pressure (mm Hg)		
Systolic		
Diastolic		
Cholesterol, total (mg/dl)		
LDL, (mg/dl)		
HDL, (mg/dl)		
Other n/N and %		
Other n/N and %		

UNIQUE IDENTIFIER #_____

INCLUSION CRITERIA (*write in*)

_____

_____

_____

ABDOMINAL AORTIC ANEURYSM

	Surveillance	**Surgery (if applicable)**
Diameter (cm), mean		
Diameter (cm), median		
Diameter (cm), range		
Diameter subgroups (N) (*write in*)		
Family History n/N and %		
Other		

DROPOUTS PRIOR TO REPAIR

	Did not undergo repair	Reason: Declined	Reason: Died	Reason: Other
Surveillance				
Surgery (if applicable)				

Notes:

UNIQUE IDENTIFIER #_____

PRIMARY/CLINICAL OUTCOMES

(provide SDs, SEs, p-values and confidence intervals when appropriate)

	Surveillance	**Surgery (if applicable)**
Mortality, all-cause, Total n/N and %		
Diameter subgroup (*write in*)		
AAA-related, Total n/N and % (*write in diameter*)		
Mean/Median rate of AAA change		
Rupture of AAA n/N and %		
Attained Rupture rate		
Repair of AAA (all) n/N and %		
Other (*write in)*		
Other n/N and %		
Other n/N and %		

STATUS OF SURVIVING PATIENTS AT END OF STUDY

(provide SDs, SEs, p-values and confidence intervals when appropriate)

	Surveillance	Surgery (if applicable)
Unrepaired AAA n/N and %		
Repaired AAA, exit CT performed n/N and %		
Proximal AAA ≥ 4 cm, n/N and %		
Iliac artery aneurysm ≥ 2.5 cm, n/N and %		
Any aneurysm n/N and %		

COMPLICATIONS

(provide SDs, SEs, p-values and confidence intervals when appropriate)

	Surveillance	Surgery (if applicable)
Major complication with no operative death n/N and %		
Reoperation required n/N and %		
Myocardial infarction n/N and %		
Amputation n/N and %		
Paraplegia n/N and %		
Stroke n/N and %		
Renal dialysis n/N and %		
Pulmonary embolism n/N and %		
Other (*write in*)		
Other (*write in*)		

UNIQUE IDENTIFIER #________________

SURVIVAL DATA (from survival curves i.e. Kaplan Meier)

Write in outcome (all-cause mortality, etc.)________________________

Group (write in)_________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Write in outcome (all-cause mortality, etc.)________________________

Group (write in)_________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Write in outcome (all-cause mortality, etc.)________________________

Group (write in)_________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Write in outcome (all-cause mortality, etc.)________________________

Group (write in)_____

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Quality of Life

Measure:_____

UNIQUE IDENTIFIER #_____

ABDOMINAL AORTIC ANEURYSM (AAA): Open vs. Endovascular Repair RCT Article Abstraction Form:

Author (first): _____

Journal: _____

Year Publication: _____ Country (ies): _____
(where study was conducted)

Data Abstractor: _____

VERIFICATION/SELECTION OF STUDY ELIGIBILITY

Subjects randomly assigned	Yes	No	Unclear
Study duration ≥ 1 month	Yes	No	Unclear
Primary/Clinical outcomes of interest	Yes	No	Unclear

(all-cause/operative mortality; severe complications (systemic complications, hemorrhage, graft complications/infection, thromboembolic complications, obstruction – graft or arterial, QoL measures)

Stop if any of the above is "NO"

METHODS

Study Design and Conduct

Outcome adjudication blinded	Yes	No	Unclear
Intention-to-treat analysis	Yes	No	Unclear
Repairs performed by surgical teams with experience (i.e ≥ 5 repairs) write in mimimum #_____	Yes	No	Unclear

Sponsor's role_____

RANDOMIZATION ALLOCATION CONCEALMENT METHOD (circle one)

Clearly adequate: Centralized randomization by telephone, randomization scheme controlled by pharmacy, numbered or coded identical containers administered sequentially, on site computer system which can only be accessed after entering the characteristics of an enrolled participant, sequentially numbered sealed opaque envelopes.

Clearly Inadequate: Alternation (odd-even, etc..), date of birth, date of week

Unclear: Sealed envelopes but not sequentially numbered or opaque, other, list of random numbers read by someone entering patient into trial (open list) *or study noted to be random or "randomization" or "random allocation" but no details provided.*

UNIQUE IDENTIFIER #_____

PARTICIPANTS

Multi-center or single site (*circle one*)

Total # subjects randomized _____

Period of enrollment _____

	Open Repair Group	**Endovascular Repair Group**
# Subjects:		
Mean age		
Men: n / N and % (*if provided*)		
Women: n / N and %		
Age < 65* n / N and %		
Age ≥ 65 n / N and %		
Race: white n / N and %		
Race: black n / N and %		
Race: Other n/N and %		
Coronary Disease n/N and %		
Cerebrovascular Disease n/N and %		
Hypertension n/N and %		
Diabetes n/N and %		
COPD n/N and %		
Current smoker n/N and %		
Ever smoked n/N and %		
Other n/N and %		
Other n/N and %		

UNIQUE IDENTIFIER #_____

ABDOMINAL AORTIC ANEURYSM

	Open Repair Group	Endovascular Repair Group
Diameter (cm), mean		
Diameter (cm), median		
Diameter (cm), range		
Diameter subgroups *(write in)*		
Family History n/N and %		
Definition arterial candidate **(*write in*)**		

INCLUSION CRITERIA (*write in*)

_____

_____

_____

DROPOUTS PRIOR TO REPAIR

	Did not undergo repair (postponed)	Reason: Declined/ refused	Reason: Died Before surgery	Reason: Other
Open Repair Group				
Endovascular Repair Group				

Notes:

CLINICAL OUTCOMES (provide SDs, SEs, p-values and confidence intervals when appropriate)

	Open Repair Group	Endovascular Repair Group
Mortality		
Mortality, all-cause n/N and %		
AAA-related n/N and %		
Operative Mortality n/N and %		
AAA Complications		
Operative mortality and severe complications: n/N and %		
Rupture of AAA n/N and %		
Repair of AAA (all) n/N and %		
Crossover to open repair n/N and %		
Other (*write in*) n/N and %		
Other (*write in*) n/N and %		

COMPLICATIONS

(provide SDs, SEs, p-values and confidence intervals when appropriate)

	Open Repair Group	Endovascular Repair Group
Systemic, total n/N and %		
Cardiac n/N and %		
Pulmonary n/N and %		
Renal n/N and %		
Cerebrovascular/Spinal cord n/N and %		
Bowel ischemia n/N and %		

Other n/N and %		
Local – vascular or implant related, total; n/N and %		
Hemorrhage n/N and %		
Graft complications n/N and %		
Graft infection n/N and %		
Arterial or graft obstruction n/N and %		
Endovascular leak n/N and %		
Thromboembolic complications n/N and %		
Local – nonvascular, total: n/N and %		
Wound complications n/N and %		
Iatrogenic bowel perforation n/N and %		
Impotence n/N and %		
Claudication n/N and %		
Amputation n/N and %		
Secondary Procedures (*write in*)		
Other (*write in*)		
Other (*write in*)		

HOSPITALIZATION FOR STUDY PROCEDURES

(provide SDs, SEs, p-values and confidence intervals when appropriate

Duration of hospitalization (days) Mean Median Range		
Duration of ICU stay (hrs) Mean Median Range		
Post-op mechanical ventilation n/N and %		
Duration of Post-op mechanical ventilation (hrs) Mean Median Range		

SURVIVAL DATA (from survival curves i.e. Kaplan Meier)

Write in outcome (all-cause mortality, etc.)_____

Group (write in)_____

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

UNIQUE IDENTIFIER #________________

Write in outcome (all-cause mortality, etc.)_________________________

Group (write in)________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Write in outcome (all-cause mortality, etc.)_________________________

Group (write in)________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Write in outcome (all-cause mortality, etc.)_________________________

Group (write in)________________________

Year 1 % = n = N =	Year 2 % n = N =	Year 3 % n = N =
Year 4 % n = N =	Year 4 % n = N =	Year 5 % n = N =
Year _____ % n = N =	Year _____ % n = N =	Year _____ % n = N =

Unique ID: _____

ABDOMINAL AORTIC ANEURYSM (AAA)
Hospital/Surgeon Volumes Abstraction Form

Title: _____

First Author: _____

Journal: _____

Year of Publication: _____ Description of Database: _____

_____

Abstractor: _____

Unique ID: _____

Reference: _____ Group #: _____

Patient Demographics

Number of patients (n,N,%): _____ _____ _____

Age (years,%): _____ _____ Mean: _____ Min: _____ Max: _____ ±SD: _____

±SE: _____

Sex (n,%) Males: _____ _____ Females: _____ _____ Mixed: _____ _____

Unknown: _____ _____

Race (n,%) White: _____ _____ African-American: _____ _____

Other: _____ _____ Describe: _____

Smoking Status: (n,%) _____ _____

Hypertension: (n,%)_____ _____

Diabetes: (n,%)_____ _____

Comments

_____

_____

_____

_____

Patient Inclusion Criteria: _____

_____

Patient Exclusion Criteria: _____

_____

Surgeon Inclusion Criteria: _____

_____

Surgeon Exclusion Criteria: _____

_____

Unique ID: _____

Reference: _____ Group #: _____

Group/Sub-Group Definitions

Group ID	Patients (n)	Define

Unique ID: _____

Reference: _____ Group #: _____

Type of Volume

Hospital Volume

1. Number of patients: _____

2. Number of hospitals: _____

(e.g., low, medium, high)
3. Description: _____

(AAA repair/yr)
4. Define: _____

5. Mean: _____

1. Number of patients: _____

2. Number of hospitals: _____

(e.g., low, medium, high)
3. Description: _____

(AAA repair/yr)
4. Define: _____

5. Mean: _____

Comments

_____

_____

_____

_____

Unique ID: _____

Reference: _____ Group #: _____

1. Number of patients: _____

2. Number of hospitals: _____

(e.g., low, medium, high)
3. Description: _____

(AAA repair/yr)
4. Define: _____

5. Mean: _____

1. Number of patients: _____

2. Number of hospitals: _____

(e.g., low, medium, high)
3. Description: _____

(AAA repair/yr)
4. Define: _____

5. Mean: _____

1. Number of patients: _____

2. Number of hospitals: _____

(e.g., low, medium, high)
3. Description: _____

(AAA repair/yr)
4. Define: _____

5. Mean: _____

Comments

_____

_____

_____

Unique ID: _____

Reference: _____ Group #: _____

Surgeon Volume

Surgeon Demographics

_____ Vascular: (n,%) _____ _____Define: _____

_____ Cardiothoracic: (n,%) _____ _____ Define: _____

_____ General: (n,%) _____ _____ Define: _____

_____ Other: (n,%) _____ _____ Define: _____

_____ Other: (n,%) _____ _____ Define: _____

1. Number of patients: _____

(e.g., low, medium, high)
2. Description: _____

(AAA repair/yr)
3. Define: _____

Mean: _____

Median: _____

1. Number of patients: _____

(e.g., low, medium, high)
2. Description: _____

(AAA repair/yr)
3. Define: _____

Mean: _____

Median: _____

Unique ID: _____

Reference: _____ Group #: _____

1. Number of patients: _____

(e.g., low, medium, high)
2. Description: _____

(AAA repair/yr)
3. Define: _____

Mean: _____

Median: _____

1. Number of patients: _____

(e.g., low, medium, high)
2. Description: _____

(AAA repair/yr)
3. Define: _____

Mean: _____

Median: _____

1. Number of patients: _____

(e.g., low, medium, high)
2. Description: _____

(AAA repair/yr)
3. Define: _____

Mean: _____

Median: _____

Unique ID: _____

Reference: _____ Group #: _____

Intervention

	√	%	x
Open			
EVAR*			
Not Designated			
Other (define):			

*Kind of EVAR: _____

Unique ID: _____

Reference: _____ Group #: _____

Complications

(provide SDs, SEs, p-values and confidence intervals when appropriate)

	Open Repair Group	**Endovascular Repair Group**
Systemic, total n/N and %		
Cardiac n/N and %		
Pulmonary n/N and %		
Renal n/N and %		
Cerebrovascular/Spinal cord n/N and %		
Bowel ischemia n/N and %		
Other n/N and %		
Local – vascular or implant related, total; n/N and %		
Hemorrhage n/N and %		
Graft complications n/N and %		
Graft infection n/N and %		
Arterial or graft obstruction n/N and %		
Endovascular leak n/N and %		
Thromboembolic complications n/N and %		
Local – nonvascular, total**:** n/N and %		
Wound complications n/N and %		
Iatrogenic bowel perforation n/N and %		
Impotence n/N and %		
Claudication n/N and %		
Amputation n/N and %		
Secondary Procedures (*write in*)		

Unique ID: _____

Reference: _____ Group #: _____

Outcomes

Number of patients: _____

Time (days): _____

Define: _____

_____

		%	±SD	±SE	P-Value	95% CI
Overall Mortality						
AAA-Specific Mortality						
Adjusted OR*						
Unadjusted OR						
Adjusted RR*						
Unadjusted RR						
Risk Reduction						
Other (define): _____ _____ _____						

*Adjusted by: _____

_____

Unique ID: _____

Reference: _____ Group #: _____

Outcomes

Type of mortality (define): _____

Comments: _____

_____

_____

_____

_____

Appendix E: Evidence Tables and Figures

Table E1. Characteristics of elective early/immediate repair versus surveillance of abdominal aortic aneurysm (AAA) randomized controlled trials

Study (Year) / Country Repair Groups (# Randomized)	Mean Study Followup	Methodologic Characteristics	Description of Subjects
ADAM (2004)[1] / United States 1. Surveillance (n = 567) 2. Immediate surgery (n = 569)	4.9 years	Randomization: adequate (Schultz) Criteria for surveillance: ultrasonography or computed tomography every 6 months Criteria for surgery in open group: AAA that became symptomatic or reached ≥5.5 cm Type of graft used: not defined Intention-to-treat analysis: yes (patients were not excluded after randomization)	1,136 subjects fit for elective surgery were randomized (5,038 considered for randomization, 46% excluded due to AAA larger than 5.4 or severe comorbidities, 23% refused). Subjects were ages 50 to 79 years old, with AAA 4.0 to 5.4 cm. Patients mean age was 68; male 99%; white race 94%; mean AAA diameter 4.7 cm; family history of AAA was 13%; hypertension 56%; diabetes 10%; history of cardiac disease 42%; tobacco use, ever smoked 94%; tobacco use, current smoking 39%.
UK Small Aneurysm Trial (1998)[2] / United Kingdom 1. Surveillance (n = 527) 2. Early surgery (n = 563)	4.6 years	Randomization: adequate (Schultz) Criteria for surveillance: ultrasonography or computed tomography for AAA 4.0 to 4.9 every 6 months, for AAA 5.0 to 5.5 every 3 months Criteria for surgery in open group: AAA that became symptomatic or reached ≥5.5 cm Type of graft used: prosthetic inlay (92%). Intention-to-treat analysis: yes	1,090 subjects with asymptomatic AAA (non-tender) and were fit for elective surgery were randomized (1,276 eligible for randomization, 15% refused). Subjects were ages 60 to 76 years old, with AAA 4.0 to 5.5 cm. Patients mean age was 69; male 83%; mean AAA diameter 4.6 cm; BMI 25; hypertension 38%; diabetes 3%; ischemic heart disease 40%; tobacco use, ever smoked 94%; tobacco use, current smoking 37%.
Canadian Trial		No details, trial ended prematurely due to inadequate recruitment	107 subjects were randomized

Table E2. Cumulative survival according to treatment arm for surveillance versus elective early/immediate repair of abdominal aortic aneurysm (AAA) randomized controlled trials

ADAM *(extracted from graph, estimated by product-limit method)*

Group		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Surveillance (n=567)	**Survival**	99%	95%	91%	87%	82%	75%	72%	69%
	Number at risk	552	530	513	393	274	183	76	-
Immediate repair (n=569)	**Survival**	96%	93%	88%	83%	78%	73%	66%	61%
	Number at risk	545	526	502	383	264	172	67	-

UK Small Aneurysm Trial *(extracted from graph, estimated by Kaplan-Meier method)*
Survival up to time of surgery

Group		Year 0.5	Year 1	Year 2	Year 3	Year 4	Year 5
Surveillance (n=527)	**Survival**	99%	95%	90%	84%	76%	70%
	Number at risk	484	409	292	197	77	29
Immediate repair (n=563)	**Survival**	99%	90%	86%	78%	63%	-
	Number at risk	91	54	38	32	14	9

UK Small Aneurysm Trial *(extracted from graph, estimated by Kaplan-Meier method)*
Survival after surgery

Group		Year 1	Year 2	Year 3	Year 4	Year 5
Surveillance (n=527)	**Survival**	90%	84%	79%	70%	68%
	Number at risk	241	182	117	60	28
Immediate repair (n=563)	**Survival**	91%	87%	83%	77%	73%
	Number at risk	471	448	385	263	149

Table E3. Outcomes and complications for the ADAM, an early/immediate elective repair versus surveillance of abdominal aortic aneurysm (AAA) randomized controlled trial

Outcome	Early/Immediate Repair, n / N (%)	Surveillance Events, n / N (%)
Rupture, repair, and hospitalization outcomes		
Repair of AAA, ruptured and unruptured	527 / 569 (92.6)	349 / 567 (61.6)
Rupture of AAA	2 / 569 (<1)	11 / 567 (1.9)
Other AAA hospitalizations, no.	255	129
Complications of repair or unruptured AAA: mean followup 4.9 years		
Operative death within 30 days	11 / 526 (2.1)	6 / 340 (1.8)
Operative death within 30 days or hospitalization	14 / 526 (2.7)	7 / 340 (2.1)
Number of patients with any complication	275 / 526 (52.3)	193 / 340 (56.8)
Rehospitalization for complications	108 / 526 (20.5)	56 / 340 (16.5)
Late graft failure	2 / 526 (0.4)	1 / 340 (0.3)
Reoperation required	9 / 526 (1.7)	4 / 340 (1.2)

Table E4. Health-related quality of life measures for elective early/immediate repair versus surveillance of abdominal aortic aneurysm (AAA) randomized controlled trials

UK Small Aneurysm Trial

Outcome	Surveillance (n=480), Baseline Mean (SD)	Surveillance (n=399), Mean Score Change 12 Months After Randomization (SD) (p vs. baseline)	Early Surgery (n=512), Baseline Mean (SD)	Early Surgery (n=391), Mean Score Change 12 Months After Randomization (SD) (p vs. baseline)	Early Surgery vs. Surveillance, Mean Change in Scores from Baseline Weighted Mean Difference [95%CI]
Short Form 20 Health Survey (SF-20) (*subscales 0-100, higher score indicates better quality of life*)					
Physical functioning	66.5 (29.3)	-6.2 (25.5)* (<0.05)	64.2 (30.7)	-3.5 (27.2)* (<0.05)	2.70 [-0.98 to 6.38]
Role functioning	76.7 (37.6)	-4.9 (39.7)* (<0.05)	71.9 (39.5)	-3.9 (36.3)*	1.00 [-4.30 to 6.30]
Social functioning	89.8 (20.4)	-2.2 (20.4)* (<0.05)	89.2 (20.8)	-1.0 (21.2)*	1.20 [-1.70 to 4.10]
Mental health	79.5 (17.0)	0.0 (15.3)*	80.2 (17.2)	0.0 (18.2)*	0.00 [-2.35 to 2.35]
Health perceptions	62.4 (24.6)	-1.0 (22.4)*	62.4 (24.3)	5.7 (24.2)*	6.70 [3.45 to 9.95]
Bodily pain	64.3 (32.1)	-4.7 (36.7)* (<0.05)	64.1 (31.5)	-1.0 (35.3)*	3.70 [-1.32 to 8.72]

*estimated from confidence intervals

ADAM Trial, Maximum activity, Surveillance (SURV) vs. Early Repair (ER)

Time Interval, Years After Randomization	Surveillance, %* Vigorous (# Patients)	Surveillance, %* Moderate (# Patients)	Surveillance, %* Mild (# Patients)	Surveillance, %* Sedentary (# Patients)	Early Repair, %* Vigorous (# Patients)	Early Repair, %* Moderate (# Patients)	Early Repair, %* Mild (# Patients)	Early Repair, %* Sedentary (# Patients)
Baseline SURV n=566 ER n=568	14	50	34	2	11	50	36	3
1 year SURV n=521 ER n=492	11	44	37	8	12	43	39	6
2 years SURV n=483 ER n=458	13	42	34	11	10	41	41	8
3 years SURV n=446 ER n=423	8	39	44	9	8	39	44	9

Table E4. Health-related quality of life measures for elective early/immediate repair versus surveillance of abdominal aortic aneurysm (AAA) randomized controlled trials (continued)

Time Interval, Years After Randomization	Surveillance, %* Vigorous (# Patients)	Surveillance, %* Moderate (# Patients)	Surveillance, %* Mild (# Patients)	Surveillance, %* Sedentary (# Patients)	Early Repair, %* Vigorous (# Patients)	Early Repair, %* Moderate (# Patients)	Early Repair, %* Mild (# Patients)	Early Repair, %* Sedentary (# Patients)
4 years SURV n=333 ER n=317	5	41	42	12	7	38	45	12
5 years SURV n=223 ER n=208	8	39	43	10	5	35	47	13
6 years SURV n=149 ER n=132	4	36	43	17	2	30	44	24
7 years SURV n=60 ER n=55	2	34	47	17	3	20	54	23
7.5 years **	11	26	52	11	4	25	50	21
Maximum activity level did not differ significantly between treatment groups at repeated measure analysis. There was a significant interaction between treatment and followup time ($p < 0.02$) indicating that worsening of maximum activity was greater in the early repair group.								

*estimated from graph
**final assessment

Table E5. Characteristics of endovascular repair (EVAR) versus OSR of abdominal aortic aneurysm (AAA) randomized controlled trials

Study (Year) / Country Repair Groups (# Randomized)	Study Outcome Interval	Methodologic Characteristics	Inclusion Criteria and Description of Subjects
DREAM (2004)[3] / Netherlands and Belgium 1. EVAR (n = 173) 2. Open repair (n = 178)	30 days and 2 years	Randomization: adequate (Schultz)[4] – computer-generated permuted block sequence Experience: Surgeons and radiologists at each center were required to have performed ≥20 EVAR procedures (fewer than 20 required presence of experienced proctor) complying with guidelines issued by Endovascular Safety Committee of the Dutch Society for Vascular Surgery and Dutch Society for Radiology Intention-to-treat analysis: yes Sponsor's role in study: none Grafts used: Zenith 33%; Talent 27%; Excluder 22%; Others 18%	351 subjects anatomically suitable (non-symptomatic infrarenal AAA ≥5.0 cm) for EVAR were randomized. 345 (98%) intention-to-treat (ITT) subjects were included in analyses. 4 declined and 2 died prior to AAA repair. Patients had adequate infrarenal neck and other aortoiliac anatomical configuration suitable for EVAR and a life expectancy ≥2 years Exclusion criteria included juxtarenal or suprarenal AAA, inflammatory AAA (more than wall thickening), bilateral retroperitoneal incision required, sacrifice of both hypogastric arties, various anatomical variations (i.e., horseshoe-kidney, arteries requiring reimplantation), patient unsuitable for laparotomy Characteristics: 92% men; mean age 70; AAA diameter ≥5.0 cm (mean 6.0), range was 5.4 to 6.5 cm; BMI 26.4; diabetes 10%; hypertension 56%; cardiac disease 44%; carotid artery disease 14%; hyperlipidemia 50%; tobacco use 59%
EVAR-1 (2005)[5] / United Kingdom (34 hospitals) 1. EVAR (n = 543) 2. Open repair (n = 539)	30 days and 4 years	Randomization: adequate (Schultz)[4] - 50:50 ratio randomly permuted block sizes constructed by STATA package Experience: Each participating center must have performed ≥20 EVAR procedures according to the UK registry for endovascular treatment of aneurysms (RETA) Intention-to-treat analysis: yes Sponsor's role in study: none Grafts used: Zenith 51%; Talent 33%; Others 16%. Participating centers were free to choose which commercial or in-house devices to use. Use of commercially available devices having undergone certain safety checks was favored. 90% were tubular or bifurcated and the remainder were aortouniiliac	1,082 subjects, ≥60 years age, with an AAA ≥5.5 cm judged anatomically suitable for EVAR were randomized. 1,047 (97%) ITT subjects were included in the analyses. 8 declined, 3 postponed surgery and 24 died prior to AAA repair. Recommended guidelines for patient fitness for open repair and suitability for EVAR-1 or 2 were defined as: no MI ≤3 months, onset of angina ≤3 months, unstable angina at night/at rest, severe valve disease, significant arrhythmia, or uncontrolled CHF Open repair would not be recommended for subjects with the following: unable to walk flight of stairs without shortness of breath; FEV_1 <1.0 L; PO_2 < 8.0 KPa; PCO_2 >6.5 KPa; creatinine 200μmol/L Characteristics: 91% men; mean age 74; AAA diameter ≥5.5 cm (mean 6.5); BMI 26.4; diabetes 10%; history of cardiac disease 43%; current smokers 21%; ever smoked 91%; aspirin use 53%; statin use 33%

Table E5. Characteristics of endovascular repair (EVAR) versus OSR of abdominal aortic aneurysm (AAA) randomized controlled trials (continued)

Study (Year) / Country Repair Groups (# Randomized)	Study Outcome Interval	Methodologic Characteristics	Inclusion Criteria and Description of Subjects
Cuypers (2001)[6] / Netherlands 1. EVAR (n = 57) 2. Open repair (n = 19) *Note: Study's objective was to compare cardiac response between EVAR and OR. Cardiac complications were assessed at 1 hour, day 1, day 7, and day 30 after procedure.* *Outcome assessor was blinded to treatment allocation.*	30 days	Randomization: treatment allocation concealment unclear. A 3:1 ratio for EVAR and OSR was used to increase the experience of the team involved with EVAR and it was also expected that this randomization scheme would increase enrollment to the trial with the greater probability of being allocated to EVAR. Experience: Unclear/not discussed Intention-to-treat analysis: yes Sponsor's role in study: unclear Grafts used: AneuRx (Medtronic)	76 subjects with anatomically suitable AAA >5.0 cm for EVAR were randomized. Exclusion criteria included subjects with adverse aneurysm morphology for EVAR, a contrast allergy and/or medical conditions precluding open surgery. Characteristics: 92% men; mean age 69 (range 52-82); AAA mean 5.5, (mean for EVAR was 5.6 (range 5.2 to 8.4) and 5.2 for OSR (range 4.0 to 6.1)); diabetes 16%; hypertension 43%; coronary artery disease 46%; history of myocardial infarction 33%; previous CABG 24%; previous PTCA 12%; COPD 28%.
OVER (Frank Lederle, Personal communication) United States (40 centers) 1. EVAR 2. Open repair	Up to 8 years	Randomization: adequate (Schultz)[4] - computer generated random numbers Experience: participating investigators must have expertise in open surgery and EVAR and be approved by a study review committee Intention-to-treat analysis: yes Sponsor's role in study: solely funded by the Department of Veterans Affairs Cooperative Studies Program Grafts used: FDA-approved EVAR systems, including ANCURE (Guidant) and AneuRx (Medtronic). Choice of graft to be used will be made prior to randomization by the individual investigator based on that physician's assessment of what graft would be optimal for that patient.	Male and female patients (n=1,260 estimated to be needed) with abdominal aortic aneurysms will be eligible for enrollment if they meet each of the following inclusion criteria: 1) AAA ≥5.0 cm or 2) an iliac aneurysm (associated with an AAA) with a maximum external diameter in any plane of ≥3.0 cm or AAA ≥4.5 cm, if the AAA: a) has increased by 0.7 cm in diameter in 6 months or 1.0 cm in 12 months, as measured from two imaging studies (ultrasound, CT scan, or MRI) within the appropriate interval, the later one within 6 months of randomization, b) is saccular (i.e., a portion of the circumference of the aorta at the level of the aneurysm is considered normal based on CT scan or MRI), or c) is associated with distal embolism. Patients with any of the following will be excluded from the study: 1) previous abdominal aortic surgery; 2) evidence, by imaging test, of AAA rupture; 3) AAA repair is not elective (i.e., urgent or emergent operation, usually due to suspected rupture); or 4) inability or unwillingness to give informed consent or follow study protocol

Table E5. Characteristics of endovascular repair (EVAR) versus OSR of abdominal aortic aneurysm (AAA) randomized controlled trials (continued)

Study (Year) / Country Repair Groups (# Randomized)	Study Outcome Interval	Methodologic Characteristics	Inclusion Criteria and Description of Subjects
ACE France (32 centers to date) Randomization started 01/2003 1. EVAR 2. Open repair	Up to 5 years	Randomization: unclear Experience: Surgeons and radiologists at each center were required to have performed ≥10 EVARs Intention-to-treat analysis: yes Sponsor's role in study: unclear (sponsored by the Programme Hopitalier de Recherche Clinique, section of the Ministry of Health) Grafts used: commercially available devices having undergone certain safety checks were favored	Male and female patients (n=600 estimated to be needed) >50 years of age with abdominal aortic aneurysms ≥5.0 cm with the meeting the following anatomical criteria: 1) healthy upper aneurysmal neck ≥1.5 cm; 2) end of the aneurysmal process ≥1.5 cm proximal to one of the common iliac bifurcation; 3) no significant superior mesenteric artery stenosis; 4) an angle less or equal to 80% of the iliac arteries and aneurysmal neck; or 5) external iliac arteries greater than 6 mm in diameter Patients with severely angulated, heavy calcified, thombotic or aneurysmal upper neck and with aneurysms involving both hypogastric arteries will be excluded

Table E6. Kaplan-Meier estimates of mortality and complications or severe events according to treatment arm for endovascular repair (EVAR) versus OSR of abdominal aortic aneurysm (AAA) randomized controlled trials

1. All-cause mortality

EVAR-1 *(extracted from graph)*

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=543)	Proportion dying	8%	15%	22%	**26%**
	Number at risk	503	316	187	94
OSR (n=539)	Proportion dying	10%	16%	22%	**29%**
	Number at risk	484	314	195	88

DREAM *(extracted from graph)*

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=171)	Proportion dying	3.5%	10.3%	NR	NR
	Number at risk	163	98		
OSR (n=174)	Proportion dying	7%	10.4%	NR	NR
	Number at risk	160	97		

2. Aneurysm-related mortality

EVAR-1 *(extracted from graph)*: (defined as death within 30 days of any surgery for AAA unless overruled by post-mortem findings or if a separate procedure (unrelated to the aneurysm) took place between aneurysm and death and was attributed as the death. Death with underlying cause attributed to ICD10 codes 1713-19 were also classified as aneurysm-related)

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=543)	Proportion dying	2%	3%	4%	**4%**
	Number at risk	503	316	187	94
OSR (n=539)	Proportion dying	6%	6%	7%	**7%**
	Number at risk	484	314	195	88

3. Complications / severe events

EVAR-1 *(extracted from graph)*: Complications (C): Included primarily graft ruptures, graft infections, endoleaks (EVAR specific), graft thrombosis, other surgery required, re-exploration of open repair

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=543)	Proportion with C	25%	30%	36%	**41%**
	Number at risk	386	235	134	67
OSR (n=539)	Proportion with C	5%	5%	7%	**9%**
	Number at risk	466	301	182	82

Table E6. Kaplan-Meier estimates of mortality and complications or severe events according to treatment arm for endovascular repair (EVAR) versus OSR of abdominal aortic aneurysm (AAA) randomized controlled trials (continued)

DREAM *(extracted from graph)*: Severe events (SE): not defined, classified and graded according to the reporting standards of the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery/International Society for Cardiovascular Surgery

Group		Year 1	Year 2	Year 3	Year 4
EVAR (n=171)	Proportion with SE	12%	16.9%	NR	NR
	Number at risk	151	91		
OSR (n=174)	Proportion with SE	15%	19.4%	NR	NR
	Number at risk	146	89		

Table E7. Characteristics of the EVAR 2 Trial (n=338), endovascular repair (EVAR) versus no intervention of abdominal aortic aneurysm (AAA)

Study (Year) / Country Repair Groups (# Randomized)	Study Outcome Interval	Methodologic Characteristics	Inclusion Criteria and Description of Subjects
EVAR-2 (2005)[7] / United Kingdom (31 hospitals) 1. EVAR (n = 166) 2. No Intervention (n = 172)	30 days	Randomization: adequate (Schultz).[4] 50:50 ratio randomly permuted block sizes constructed by STATA package Experience: Each participating center must have performed ≥20 EVAR procedures according to the UK registry for endovascular treatment of aneurysms (RETA) Intention-to-treat analysis: yes Sponsor's role in study: none Grafts used: Zenith 59%; Talent 21%; Excluder 7%; AneuRx 6%; Others 7%. Participating centers were free to choose which commercial or in-house devices to use. Use of commercially available devices having undergone certain safety checks was favored. 87% bifurcated systems.	338 subjects, ≥60 years age, with AAA diameter ≥5.5 cm considered unfit (determined locally by surgeon, radiologist, anesthesiologist, and cardiologist) for major surgery were randomized. Recommended guidelines for patient unfitness for open repair and unsuitability for EVAR 1 were defined as: MI ≤3 months; onset angina ≤3 months; unstable angina at night/at rest; severe valve disease; significant arrhythmia; uncontrolled CHF. In addition, open repair (EVAR 1) would not be recommended for subjects with the following: unable to walk flight of stairs without shortness of breath; FEV_1 <1.0 L; PO_2 <8.0 KPa; PCO_2 >6.5 KPa; creatinine 200µmol/L. In the EVAR group 1 subject declined, 1 was deemed unsuitable and 14 died prior to AAA repair. No subjects were lost to followup. In the No Intervention group, 1 subject was lost to followup. Characteristics: 85% men; mean age 76.4; AAA diameter mean 6.3 [IQR* 6 to 7.4]; AAA tender at randomization 4%; BMI 26.3; diabetes 14%; history of cardiac disease 69%; current smokers 17%; ever smoked 93%; aspirin use 56%; statin use 39%

*IQR = Interquartile range

Table E8. Complications for EVAR-2 trial (n=338), endovascular repair (EVAR) versus no intervention of abdominal aortic aneurysm (AAA)

Outcome	Events, n / N	%
Number of patients with postoperative complications		
All subjects having a successful EVAR*	58 / 178	32.6
Endoleak, type 1	10 / 178	5.6
Endoleak, type 2	17 / 178	9.6
Endoleak, type 3	5 / 178	2.8
Graft rupture	1 / 178	< 1
Graft migration	2 / 178	1.1
Graft thrombosis	7 / 178	3.9
Other surgery required	8 / 178	4.5
Number of patients with reintervention		
All subjects having a successful EVAR*	32 / 178	18.0
Endoleak, type 1	8 / 178	4.5
Endoleak, type 2	3 / 178	1.7
Endoleak, type 3	3 / 178	1.7
Graft rupture	1 / 178	< 1
Graft migration	0	0
Graft thrombosis	5 / 178	2.8
Other surgery required	8 / 178	4.5

* Includes 12 subjects randomized to no intervention

Table E9. Health-related quality of life measures for the EVAR-2 trial (n=338), endovascular (EVAR) versus no intervention of abdominal aortic aneurysm (AAA)

Outcome	EVAR, Mean (SD) (number of patients)	No Intervention, Mean (SD) (number of patients)	Weighted Mean Difference [95% CI]	Difference Adjusted for Baseline Score, Mean (SE) (number of patients)
EQ5D weighted index score (*higher score indicates better quality of life*)				
Baseline	0.58 (0.31) (164)	0.63 (0.28) (171)	-0.05 (SE 0.03) *Crude difference*	*EVAR-2*[1]
0-3 months	0.57 (0.28) (48)	0.56 (0.29) (92)	0.01 [-0.09 to 0.11]	0.03 (0.05) (139) (p = 0.51)
3-12 months	0.64 (0.28) (122)	0.60 (0.26) (120)	0.04 [-0.03 to 0.11]	0.06 (0.03) (241) (p = 0.06)
12-24 months	0.65 (0.24) (88)	0.60 (0.30) (68)	0.05 [-0.04 to 0.14]	0.04 (0.04) (156) (p = 0.30)
SF-36: Physical component summary (*higher score indicates better quality of life*)				
Baseline	35.47 (6.63) (160)	35.12 (6.23) (171)	0.35 (SE 0.71) *Crude difference*	*EVAR-2*[1]
0-3 months	33.96 (5.13) (46)	35.60 (5.70) (89)	-1.64 [-3.54 to 0.26]	-1.86 (0.88) (134) p = 0.04
3-12 months	34.33 (6.10) (116)	35.12 (6.42) (111)	-0.79 [-2.42 to 0.84]	-1.11 (0.77) (224) p = 0.15
12-24 months	34.54 (5.89) (71)	36.01 (6.92) (60)	-1.47 [-3.69 to 0.75]	-0.64 (1.04) (130) p = 0.54
SF-36: Mental component summary (*higher score indicates better quality of life*)				
Baseline	45.13 (7.92) (160)	46.31 (6.97) (171)	-1.18 (SE 0.82) *Crude difference*	*EVAR-2*[1]
0-3 months	45.76 (8.65) (46)	44.03 (7.78) (89)	1.73 [-1.25 to 4.71]	2.30 (1.38) (134) (p = 0.10)
3-12 months	44.76 (7.21) (116)	44.84 (7.85) (111)	-0.08 [-2.04 to 1.88]	0.94 (0.95) (224) (p = 0.32)
12-24 months	45.36 (7.20) (71)	44.67 (7.93) (60)	0.69 [-1.92 to 3.30]	0.50 (1.29) (130) (p = 0.70)

Table E10. Postoperative 30-day mortality for endovascular (EVAR) versus open surgical repair (OSR) of abdominal aortic aneurysm (AAA) nonrandomized controlled trials, and registries

Trials	EVAR Events, n / N (%)	OSR Events, n / N (%)	Risk Difference, % [95% CI]	Relative Risk [95% CI]
Anderson/SPARCS*[8]	19 / 1706 (1.1)	121 / 3063 (4.0)	-3 [-4 to -2]	0.28 [0.17 to 0.46]
Becquemin[9]	2 / 73 (2.7)	2 / 107 (1.9)	1 [-4 to 5]	1.47 [0.21 to 10.17]
Bertrand[10]	6 / 193 (3.1)	12 / 193 (6.2)	-3 [-7 to 1]	0.50 [0.19 to 1.31]
Bolke[11]	0 / 20	1 / 20 (5.0)	-5 [-18 to 8]	0.33 [0.01 to 7.72]
Criado[12]	1 / 240 (< 1)	0 / 126	0 [-1 to 2]	1.58 [0.06 to 38.53]
Elkouri[13]	0 / 94	3 / 261 (1.1)	-1 [-3 to 1]	0.39 [0.02 to 7.56]
Garcia-Madrid[14]	2 / 53 (3.8)	2 / 30 (6.7)	-3 [-13 to 7]	0.57 [0.08 to 3.82]
Greenberg[15]	1 / 200 (<1)	2 / 80 (2.5)	-2 [-6 to 2]	0.20 [0.02 to 2.17]
Hansman[16]	1 / 50 (2.0)	0 / 50	2 [-3 to 7]	3.00 [0.13 to 71.92]
Jordan[17]	6 / 259 (2.3)	12 / 145 (8.3)	-6 [-11 to -1]	0.28 [0.11 to 0.73]
Lee**[18]	33 / 2565 (1.3)	176 / 4607 (3.8)	-3 [-3 to -2]	0.34 [0.23 to 0.49]
LIFELINE Registry†[19]	45 / 2664 (1.7)	4 / 334 (1.2)	0 [-1 to 2]	1.41 [0.51 to 3.90]
Teufelsbauer[20]	7 / 275 (2.5)	23 / 481 (4.8)	-2 [-5 to 0]	0.53 [0.23 to 1.22]
Zeebregts[21]	1 / 92 (1.1)	15 / 194 (7.7)	-7 [-11 to -2]	0.14 [0.02 to 1.05]
Totals	**124 / 8484 (1.5)**	**383 / 9691 (3.8)**	**-2 [-3 to -2]**	**0.37 [0.29 to 0.47]**

* Data from discharge dataset: New York State-Statewide Planning and Research Cooperative System (SPARCS)
** Data from National Inpatient Sample (NIS) database, representing 20% of all-payer stratified sample of nonfederal U.S. hospitals
† Clinical data from four Investigational Device Exemption clinical trials including Carpenter[22] (Matsamura[23] and Moore[24] studies)

Table E11. Mortality following EVAR: Data from nonrandomized clinical trials (non-device specific), case series, and comparative studies

Author (Reference)	Number of Patients				Followup (Months)
	Undergoing EVAR	Number of Deaths (%)	30-Day Deaths* (%)	AAA-Related Deaths (%)	Mean (Range)
Resch 2002[25]	164	NR	7 (4.3)	NR	39 (NR)
Haulon 2003[26]	96	13 (13.5)	2 (2.1)	0	27 (3 to 66)
Burks 2002[27]	95	2 (2.1)	2 (2.1)	0	25 (6 to 44)
Cartes 2002[28]	72	1 (1.4)	1 (1.4)	1 (1.4)	22 (1 to 46)
Alric 2002[29]	88	24 (27.3)	3 (3.4)	6 (6.8)	21 (6 to 68)
Flora 2003[30]	108	11 (10.2)	9 (8.3)	2 (peri-op) + 2 after OSR	20
García-Madrid** 2004[14]	53	5 (9.4)	2 (3.8)	0	19 Median
Zeebregts 2004**[21]	93	11 (11.8) at 2 years	1 (1.1)	0	19
Gilling-Smith 2000[31]	55	8 (14.5)	NR	2 graft -related	18 (3 to 36)
Ohki 2001[32]	239	Unclear (53 of unrelated causes)	20 (8.4)	Unclear (3 after second intervention)	16 (<75)
Parlani 2002[33]	336	NR	4 (1.2)	0 (peri-op)	14 (1 to 46)
Faries 2002[34]	65	11 (16.9)	0	0	13 (6 to 48)
Tutein Nolthenius 2001[35]	77	15 (19.5)	4 (5.2)	0	12 (>12)
Carpenter 2004[22]	227	15 (6.6)	3 (1.3)	1	11 (0 to 41)
Ricco 2003[36]	1012	47 (4.6)	27 (2.7)	NR	11 NR
Becquemin 2000**[9]	73	7 (9.6)	2 (2.7)	2 possibly graft-related	7 (0 to 40)
May 2000[37]	266	NR	NR	NR	6(>6)
Blum 2001[38]	298	3 (1.0)	2 (<1)	2 (<1)	(2 to 50)
Albertini 2001[39]	185	12 (6.5)	12 (6.5)	6 (3.2)	NR
Bertrand 2001**[10]	193	6 (3.1)	6 (3.1)	Unclear	Postoperative period
Bölke 2001**[11]	20	0	0	0	NR
Elkouri 2004**[13]	94	NR	0	NR	NR, postoperative mortality only
Ouriel 2003[40]	704	20% men 22% women at 24 months	11 (1.6)	3.1% men 1.8% women at 24 months	NR
Teufelsbauer 2003**[20]	275	NR	7 (2.5)	NR	NR postoperative mortality only
Total	**4,888**		**125 (2.6)**	**0 to 6.8**	**Postoperative to 39**

* ≤30 days after procedure
** 30-day mortality versus control (open repair) in Appendix E, Table E10
NR = Not reported

Table E12. Mortality following EVAR: Data from registries and device-specific non-randomized clinical trials (NRCTs)

Author (Reference)	Number of Patients				Followup (Months)
	Undergoing EVAR	Number of Deaths (%)	30-Day Deaths* (%)	AAA-Related Deaths (%)	Mean (Range)
RETA database (n=1,000)					
Thomas 2005[41]	1,000	11% year 1 (post-procedure) 10% year 2 7% year 3 10% year 4 8% year 5	57 / 989 (5.8)	6 deaths year 1 (post-procedure)	36 (1 to 60)
Lifeline database (n=2,664): Pooled data from 4 NRCTs					
Lifeline 2005†[19]	2,664	603 (22.6) up to 6 years	45 (1.7)	56 (2.1)	34 (up to 80)
Powerlink Carpenter 2004[22]	192	20 (10.4)	2 (1.0)	1 (<1)	22
Excluder Matsumura[23]	235	33 (14.0)	2 (1.0)	0 from AAA rupture	24
Ancure (n=305) and EGS (n=268); Moore 2003[24]	573	73 / 319 (22.9) Subjects selected for long-term followup**	10 (1.7) Ancure 3/305 (1.0%) EGS 7/268 (2.6%)	0 / 319	5-year update (1 to 60)
AneuRx Zarins 2003[42]	1,193	250 (21.0)	22 (1.8)	30 (2.5)	6-year update
Eurostar database (n=4,613): No mortality data in most recent publication[43]					
Laheij 2002[44]	2,863	257 (9.0)	85 (3.0)	0	NR
Laheij 2000[44]	2442, 245 unfit for surgery and 97 unfit for general anesthesia (GA)	56 unfit for surgery and GA died during followup vs. 157 fit	78 (3.2), 15 unfit for surgery (6%) and 4 unfit for GA (4%)	1 rupture death (unclear if patient was fit or unfit)	12
Data from discharge dataset: New York State-Statewide Planning and Research Cooperative System (SPARCS)					
Anderson 2004†[8]	1,706	NR	19 (1.1)	NR	
Data from National Inpatient Sample (NIS) database, representing 20% of all-payer stratified sample of non-federal U.S. hospitals					
Lee 2004†[18]	2,565	33 (1.3)	33 (1.3)	NR	Postoperative period
Data from University of Alabama-Birmingham vascular registry, "high" vs. "low" risk subjects					
Jordan 2003†[17]	259 130 high 129 low	NR	6 (2.3) high 0 low	0	28
AneuRx Clinical Trial (n=1,193): Data from 19 investigational centers					
Zarins 2003[42]	See Lifeline above for data on all subjects				

Table E12. Mortality following EVAR: Data from registries and device-specific non-randomized clinical trials (NRCTs) (continued)

Author (Reference)	Number of Patients				Followup (Months)
	Undergoing EVAR	Number of Deaths (%)	30-Day Deaths* (%)	AAA-Related Deaths (%)	Mean (Range)
Zenith Clinical Trial (n=200)					
Greenberg 2004†[15]	200	7 (3.5) at 12 months	1 (0.5)	1 (0.5) at 12 months	NR
Talent Clinical Trial (n=471)					
Criado 2001†[45]	471	8 / 462 (1.7)	8 / 462 (1.7)	1 reported	Postoperative period

* ≤30 days after procedure
** Based on implantation date; i.e., the earliest implantations were followed for 5 years.
† 30-day mortality versus control (open repair) in Appendix E, Table E-10
NR = Not reported

Table E13. Early (<30 days post-procedure) and delayed (>30 days post-procedure) aneurysm rupture following EVAR: Data from registries, nonrandomized studies, case series, and comparative studies

Author (Reference)	Number of Patients			Followup (Months)	
	Undergoing EVAR	With Early Rupture (%)	With Delayed Rupture (%)	Mean	Range
RETA Thomas 2005[41]	1,000	2 (0.2)	6 deaths year 1 post-procedure (0.6)	At year 1	NA
LIFELINE 2005[19] 4 NRCTs (below)	2,664	3 (0.1)	15 (0.6)	72*	NR
Powerlink Carpenter 2004[22]	192	0	0	22	NR
Excluder Matsumura 2003[23]	235	0	0	2-year update	24
Ancure (n=305) and EGS (n=268) Moore 2003[24]	319	0	0	5-year update	1 to 60
AneuRx Zarins 2003[42]	1,193	3 (0.3	15 (1.3)	6-year update	NR
Eurostar Laheij 2002[44]	2,863	1 / 2,442 (Laheij 2000)	16 (0.6)	NR	NR
Talent Criado 2003[12]	190	NR	0	13	NR
Albertini 2001[39]	185	3 (1.6)	NR		
Alric 2002[29]	88	NR	2 (2.2)	21	6 to 68
Becquemin 2000[9]	73	NR	0	7	0 to 40
Blum 2001[38]	298	1 (0.3)	4 (1.3)	35	2 to 50
Burks 2002[27]	95	NR	0	25	6 to 44
Carpenter 2004[46]	227	2 (0.9)	NR		
Cartes 2002[28]	72	NR	0	22	1 to 46
Elkouri 2003[47]	100	NR	1 (1)	7	1 to 60
Faries 2002[34]	74	0	0	13	6 to 48
Flora 2003[30]	108	NR	0	20	NR
Gilling-Smith 2000[31]	55	NR	1 (1.8)	18	3 to 36
Moore 2003[24]	684	NR	0	NR	1 to 60
Tutein Nolthenius 2001[35]	77	NR	0	12	>12
Ohki 2001[32]	239	NR	2 (0.8)	16	<75
Ouriel 2003[40]	704	1 (0.1)	3 (0.4)	NR	NR
Parlani 2002[33]	336	see Zannetti	2 (0.6)	14	1 to 46
Ricco 2003[36]	1,012	2 (0.1)	NR		
Zannetti 2001[48]	240	1 (0.4)	NR		
Total (%)		**16 / 8,772 (0.2)**	**52 / 9,720 (0.5)**	**7 to 72**	

* Unclear, studies were to have a minimum of 5-year followup. Kaplan-Meier analyses were done at 6 years
NR = Not reported

Table E14. Primary (immediately following a failed EVAR or <30 days post-procedure) and delayed (secondary or >30 days post-procedure) conversion to OSR following EVAR: Data from registries, nonrandomized studies, case series, and comparative studies

Author (Reference)	Total Number of EVAR	Conversions		Followup (Months)	
		Primary n (%)	Delayed n (%)	Mean	Range
RETA Thomas 2005[41]	1,000	33 / 996 (3.3)	23 (2.3)	36	1 to 60
Lifeline 2005[19]	2,664	68 (2.6)	28 / 2524 (1.1)	72*	NR
Powerlink Carpenter 2004[22]	192	3 (1.6)	1 / 190 (0.5)	22	NR
Excluder Matsumura 2003[23]	235	0	3 (1.3)	2-year update	24
Ancure (n=305) and EGS (n=268); Moore 2003[24]	573	42 (7.3) 16 Ancure (5.2) 26 EGS (9.7)	8 / 319 (2.5)	5-year update	1 to 60
AneuRx Zarins 2003[42]	1,193	11 (0.9)	38 (3.2)	6-year update	NR
Eurostar Vallabhaneni 2001[49]	2,862	47 (1.6)	41 (1.4)	12	0 to 72
Talent Criado 2003[12]	240	NR	5 (2.1)	13	NR
Albertini 2001[39]	185	2 (1.1)	NR		
Alric 2002[29]	88	1 (1.1)	3 (3.4)	21	6 to 68
Becquemin 2000[9]	73	NR	3 (4.1)	7	0 to 40
Bertrand 2001[10]	193	6 (3.1)	NR		
Blum 2001[38]	298	5 (0.8)	8 (2.7)	35	2 to 50
Carpenter 2004[46]	227	3 (1.3)	2 (0.9)	11	0 to 41
Elkouri 2003[47]	100	3 (3.0)	1 (1)	7	1 to 60
Faries 2002[34]	65	NR	2 (3.1)	13	6 to 48
Flora 2003[30] 2 groups (early vs. late)	108 26 early / 82 late	11 (10.0) 7 (27.0) / 4 (4.5)	3 (2.8)	20	NR
Gilling-Smith 2000[31]	55	NR	1 (1.8)	18	3 to 36
Hansman 2003[16]	50	0	1 (2)	NR	NR
May 2000[37]	266	17 (6.4)	NR		
Tutein Nolthenius 2001[35]	77	2 (2.6)	NR		
Ohki 2001[32]	239	NR	5 (2.1)	16	< 75
Ouriel 2003[40]	700	3 (0.4)	29 (4.1)	12	NR
Parlani 2002[33]	336	6 (1.8)	4 (1.2)	14	1 to 46
Resch 2001[50] 2 groups (early vs. late)	164 90 early / 68 late	8 (4.9) 8 (8.9) / 0	15 (9.1)	39	NR
Ricco 2003[36]	1,012	11 (1.1)	4 (0.4)	11	NR
Zannetti 2001[48]	266	6 (2.3)	NR		
Total		**233 / 10,832 (2.2)**	**178 / 10,141 (1.8)**	**7 to 72**	

* Unclear, studies were to have a minimum of 5-year followup. Kaplan-Meier analyses were done at 6 years
NR = Not reported

Table E15. Secondary intervention following EVAR: Data from registries, nonrandomized studies, case series, and comparative studies

Author (Reference)	Total Number of EVAR	Secondary Interventions		Followup (Months)	
		Number	%	Mean	Range
RETA Thomas 2005[41]	996	110 (Short-term)	11.0	36	1 to 60
Lifeline 2005[19]	2,664	487 (415 early)	18.3	72**	NR
Powerlink Carpenter 2004[22]	192	23 (6 early)	12.0	22	NR
Excluder Matsumura 2003[23]	235	31	13.2	2-year update	24
Ancure (n=305) and EGS (n=268); Moore 2003[24]	319	212	37.0	5-year update	1 to 60
AneuRx Zarins 2003[42]	1,193	NR	NR	6-year update	NR
Eurostar Laheij 2002[44]	2,863	410	14.3	NR	NR
Talent Criado 2003[12]	240	9	3.8	13	NR
Alric 2002[29]	88	6	6.8	21	6 to 68
Becquemin 2000[9]	73	16	21.9	7	0 to 40
Blum 2001[38]	298	24	8.1	35	2 to 50
Carpenter 2004[46]	227	17	7.5	11	0 to 41
Cartes 2002[28]	72	10	13.9	22	1 to 46
Elkouri 2003[47]	100	29	29.0	7	1 to 60
Faries 2002[34]	65	17	26	13	6 to 48
Flora 2003[30]	108	28	26.2	20	NR
Gilling-Smith 2000[31]	55	11	20.0	18	3 to 36
Hansman 2003[16]	50	6	12.0	NR	NR
Haulon 2003[26]	96	38	39.6	27	3 to 66
May 2000[37]	266	43	16.2	6	> 6
Tutein Nolthenius 2001[35]	77	22	28.6	12	> 12
Ohki 2001[32]	239	23	9.6	16	< 75
Ouriel 2003[40]	704	173	24.7	NR	NR
Parlani 2002[33]	336	19	5.7	14	1 to 46
Resch 2001[50]	164	91	55.5	39	NR
Ricco 2003[36]	1,012	67	6.6	11	NR
Total	**10,793**	**1,656**	**15.3**	**6 to 72**	

* Unclear, studies were to have a minimum of 5-year followup. Kaplan-Meier analyses were done at 6 years
NR = Not reported

Table E16. Incidence of any EVAR endoleaks: Data from registries, nonrandomized studies, case series, and comparative studies

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
<30 days	**RETA** Thomas 2005[41]	1,000	146	14.6
<30 days	**Lifeline** 2002[51]	1,646	407	24.7
	Total	2,646	553	20.9
At discharge		1,589	451	28.4
3 months		441	90	20.4
6 months		1,403	327	23.3
12 months		1,309	222	17.0
24 months		926	198	21.4
36 months		415	61	14.7
48 months		77	16	20.8
≤30 days	**Powerlink** Carpenter 2004[22]	110	25	22.7
6 months		101	13	12.9
12 months		128	18	14.1
24 months		78	5	6.8
≤30 days	**Excluder** Matsumura 2003[23]	180	39	21.7
12 months		156	27	17.3
24 months		119	24	20.2
Discharge	**Ancure** (n=305) and EGS (n=268); Moore 2003[24]	308*	130	42.2
12 months		262*	79	30.3
24 months		225*	55	24.4
36 months		175*	32	18.3
48 months		101*	15	14.9
60 months		43*	7	16.3
Predischarge	**AneuRx** Zarins 2003[42]	1,103	306	27.7
≤30 days		1,056	147	13.9
6 months		987	135	13.7
12 months		951	132	13.9
24 months		772	129	16.7
36 months		451	63	14.0
48 months		137	19	13.9

* Bifurcated only

Table E17. Incidence of EVAR type I endoleaks: Data from registries, nonrandomized studies, case series, and comparative studies

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
<30 days	**RETA** Thomas 2005[41]	1,000	54	5.4
	Powerlink Carpenter 2004[22]	110	1	0.9
	Excluder Matsumura 2003[23]	180	7	3.9
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	308	12	3.9
	AneuRx Howell 2000[52]	215	2	0.9
	AneuRx Lee 2002[53]	150	5	3.3
	Talent Criado 2003[12]	190	11	5.8
	Gilling-Smith 2000[31]	55	6	10.9
	Becquemin 2000[9]	73	8	11.0
	Parlani 2002[33]	336	3	1.2
	Total	**2,617**	**109**	**4.2**
Up to 1 year	**Powerlink** Carpenter 2004[22]	128	0	0
	Excluder Matsumura 2003[23]	156	2	1.3
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	262	9	3.4
	AneuRx Howell 2000[52]	84	2	2.4
	Talent Criado 2003[12]	159	7	4.4
	Albertini 2001[39]	185	16	8.6
	Blum 2001[38]	298	6	2.0
	Carpenter 2004[46]	227	7	3.1
	Cartes 2002[28]	72	3	4.2
	Hansman 2003[16]	50	1	2.0
	Haulon 2003[26]	91	13	14.3
	Tutein Nolthenius 2001[35]	128	4	3.1
	Ouriel 2003[40]	704	18	2.6
	Total	**2,544**	**88**	**3.5**
>1 year	**Powerlink** Carpenter 2004[22]	78	0	0
	Excluder Matsumura 2003[23]	119	3	2.5
	Ancure(n=305) and **EGS** (n=268); Moore 2003[24]	225	4	1.8
	AneuRx Howell 2000[52]	132	6	4.5
	AneuRx Wolf 2002[54]	189	13	6.9
	AneuRx Zarins 2003[42]	383	10	2.6
	Talent Criado 2003[12]	179	8	4.5
	Alric 2002[29]	88	3	3.4
	Burks 2002[27]	95	0	0.0
	Faries 2002[34]	65	14	21.5

Table E17. Incidence of EVAR type I endoleaks: Data from registries, nonrandomized studies, case series, and comparative studies (continued)

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
	Flora 2003[30]	108	12	11.1
	Fransen 2003[43]	4,613	375	8.1
	Haulon 2003[26]	77	2	2.6
	May 2000[37]	266	21	7.9
	Tutein Nolthenius 2001[35]	128	2	1.6
	Ohki 2001[32]	239	7	2.9
	Ouriel 2003[40]	700	25	3.6
	Resch 2001[50]	164	20	12.2
	Total	**7,848**	**525**	**6.7**

Table E18. Incidence of EVAR type II and III endoleaks: Data from registries, non-randomized studies, case series and comparative studies

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
Type II endoleak				
<30 days	**RETA** Thomas 2005[41]	1,000	44	4.4
	Powerlink Carpenter 2004[22]	110	22	20
	Excluder Matsumura 2003[23]	180	21	11.7
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	308	96	31.2
	AneuRx Howell 2000[52]	215	3	1.4
	AneuRx Lee 2002[53]	150	29	19.3
	Talent Criado 2003[12]	190	16	8.4
	Becquemin 2000[9]	73	9	12.3
	Burks 2002[27]	95	19	20.0
	Gilling-Smith 2000[31]	55	5	9.1
	Parlani 2002[33]	336	22	6.5
	Total	**2,712**	**286**	**10.5**
Up to 1 year	**Powerlink** Carpenter 2004[22]	128	16	12.5
	Excluder Matsumura 2003[23]	156	19	12.2
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	262	57	21.8
	AneuRx Howell 2000[52]	84	8	9.5
	AneuRx Zarins 2003[42]	383	55	14.4
	Talent Criado 2003[12]	185	10	5.4
	Blum 2001[38]	298	9	3.0
	Carpenter 2004[46]	227	18	7.9
	Cartes 2002[28]	30	1	3.3
	Hansman 2003[16]	50	7	14.0
	Haulon 2003[26]	91	9	9.9
	Ouriel 2003[40]	704	173	24.6
	Total	**2,598**	**382**	**14.7**
>1 year	**Eurostar** Fransen 2003[43]	4,613	485	10.5
	Powerlink Carpenter 2004[22]	78	3	4.1
	Excluder Matsumura 2003[23]	119	16	13.4
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	225	38	16.9
	AneuRx Arko 2003[55]	206	40	19.4
	AneuRx Zarins 2003[42]	573	61	10.6
	Alric 2002[29]	88	5	5.7
	Faries 2002[34]	65	3	4.6
	Flora 2003[30]	108	9	8.3

Table E18. Incidence of EVAR type II and III endoleaks: Data from registries, non-randomized studies, case series and comparative studies (continued)

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
	Haulon 2003[26]	77	16	20.8
	May 2000[37]	383	4	1.0
	Tutein Nolthenius 2001[35]	128	8	6.3
	Ohki 2001[32]	239	13	5.4
	Resch 2001[50]	164	23	14.0
	Total	**7,066**	**724**	**10.2**
Type III endoleak				
<30 days	**RETA database** Thomas 2005[41]	1000	15	1.5
	Powerlink Carpenter 2004[22]	110	0	0
	Excluder Matsumura 2003[23]	180	0	0
	Total	**1,290**	**15**	**1.2**
Up to 1 year	**Powerlink** Carpenter 2004[22]	128	0	0
	Excluder Matsumura 2003[23]	156	0	0
	Total	**284**	**0**	**0**
>1 year	**Eurostar** Fransen 2003[43]	4,613	225	4.9
	Powerlink Carpenter 2004[22]	78	0	0
	Excluder Matsumura 2003[23]	119	0	0
	AneuRx Zarins 2003[42]	383	8	2.1
	Alric 2002[29]	88	1	1.1
	Blum 2001[38]	298	5	1.7
	Tutein Nolthenius 2001[35]	77	4	2.3
	Ohki 2001[32]	239	1	0.4
	Ouriel 2003[40]	704	23	3.3
	Total	**6,599**	**267**	**4.0**

Table E19. Incidence of common technical complications of EVAR: Data from registries, nonrandomized studies, case series, and comparative studies

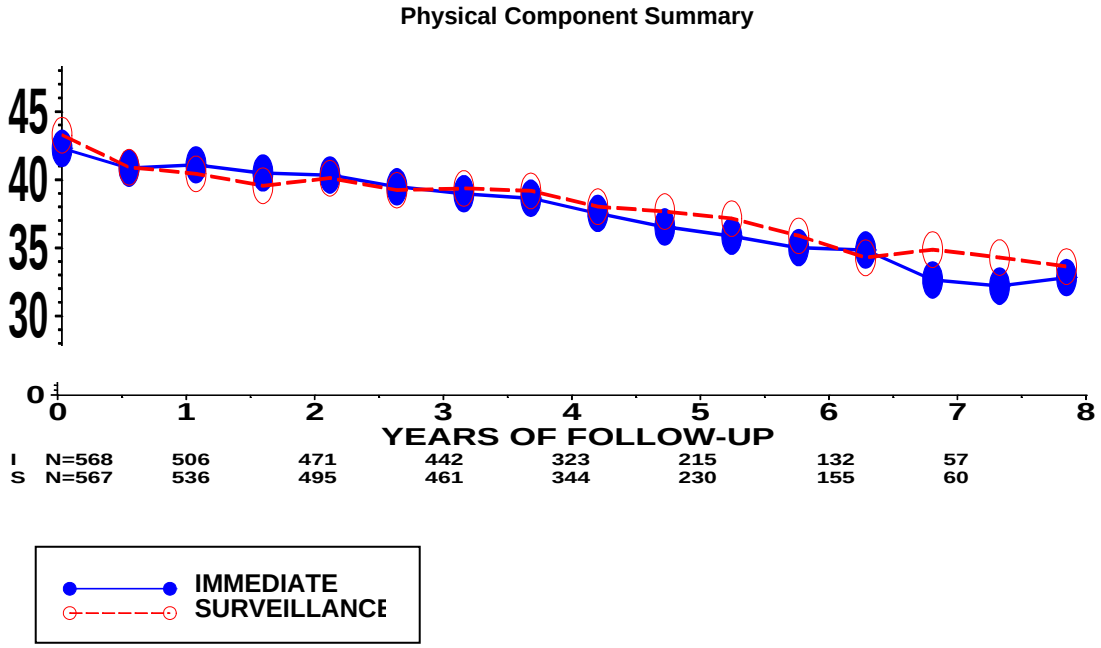
Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
Technical complications, any				
In-hospital	**RETA** Thomas 2005[41]	976	55	5.6
Stent migration				
At discharge	**Lifeline** 2002[51]	1,589	9	0.6
<30 days	**Eurostar** Villabhaneni 2001[49]	2,862	39	1.4
	Total	**4,451**	**40**	**0.90**
3 months	**Lifeline** 2002[51]	441	2	0.4
6 months		1,403	11	0.8
<1 year	**Lifeline** 2002[51]	1,309	2	0.2
	Talent Criado 2003[12]	240	3	1.3
	Hansman 2003[16]	50	1	2.0
	Total	**1,599**	**6**	**0.4**
>1 year	**Lifeline** 2002[51]	926	48	5.2
	Eurostar Fransen 2003[43]	4,613	156	3.4
	AneuRx Zarins 2003[42]	383	13	6.3
	Blum 2001[38]	298	5	1.7
	Flora 2003[30]	108	2	1.9
	Tutein Nolthenius 2001[35]	77	6	8.2
	Ouriel 2003[40]	704	51	7.2
	Resch 2001[50]	164	31	18.9
	Total	**7,027**	**312**	**4.4**
36 months	**Lifeline** 2002[51]	415	30	7.2
48 months		77	7	9
Stent wire fracture				
Up to 1 year	**Powerlink** Carpenter 2004[22]	192	0	0
	Talent Criado 2003[12]	240	11	4.6
	Carpenter 2004[46]	227	6	2.6
	Total	**659**	**17**	**2.6**
Graft limb thrombosis				
<30 days	**Ancure** (n=305) and **EGS** (n=268); Moore 2003[24]	573	17	3.0
	AneuRx Howell 2000[52]	215	5	2.3
	Burks 2002[27]	95	6	6.3
	Lee 2002[53]	150	1	0.7
	Parlani 2002[33]	336	4	1.2
	Total	**1,369**	**33**	**2.4**
<1 year	**AneuRx** Shames 2003[56]	241	10	4.1
	AneuRx Zarins 2000[57]	149	1	0.7
	Albertini 2001[39]	135	2	1.5
	Alric 2002[29]	88	3	3.4

Table E19. Incidence of common technical complications of EVAR: Data from registries, nonrandomized studies, case series, and comparative studies (continued)

Time Point	Author (Reference)	Number of Subjects	Number of Cases	%
	Arko 2003[55]	200	1	0.5
	Ayerdi 2003[58]	96	2	2.1
	Becquemin 2000[9]	73	8	11.0
	Blum 2001[38]	298	4	1.3
	Carpenter 2004[46]	227	0	0.0
	Elkouri 2003[47]	100	4	4.0
	Hansman 2003[16]	50	2	4.0
	Total	**1,657**	**41**	**2.5**
>1 year	**Eurostar** Fransen 2003[43]	4613	152	3.3
	Powerlink Carpenter 2004[22]	192	4	2.1
	Ancure (n=305) and **EGS** (n=268); Moore 2003[24]	573	31	5.4
	Flora 2003[30]	108	2	1.9
	Haulon 2003[26]	96	8	8.3
	Tutein Nolthenius 2001[35]	77	3	2.3
	Ohki 2001[32]	239	7	2.9
	Ouriel 2003[40]	704	43	6.1
	Total	**6,602**	**250**	**3.8**
Graft stenosis				
<30 days	**Eurostar** Villabhaneni 2001[49]	2862	10	0.3
<1 year	**Powerlink** Carpenter 2004[22]	192	3	1.6
	Becquemin 2000[9]	73	4	5.5
	Elkouri 2003[47]	100	3	3.0
	Total	**365**	**10**	**2.7**
>1 year	**Eurostar** Fransen 2003[43]	4,613	66	1.4

Figure E1. ADAM trial: Mean SF-36 scores by treatment group

All scores are 0 to 100, with 100 representing better health. Asterisks for individual time points are for p <.05.



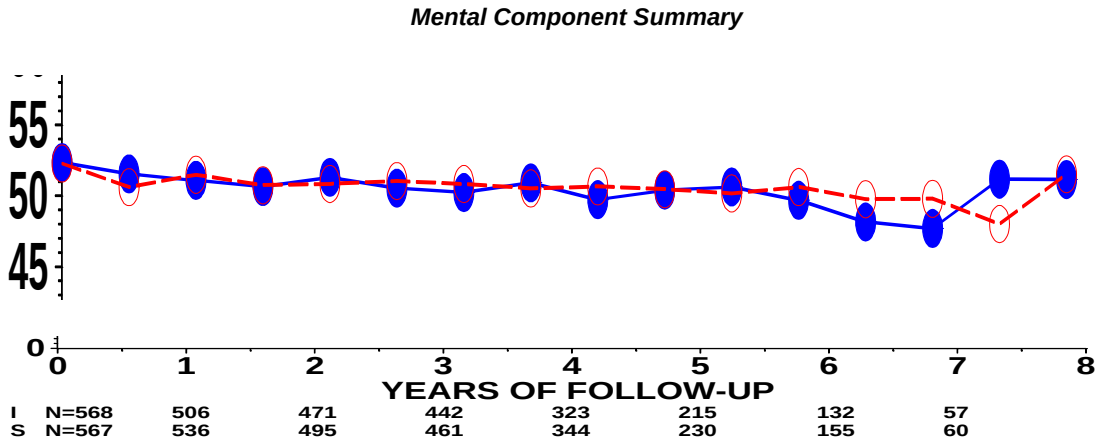


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Figure E2. ADAM trial: Prevalence of impotence by treatment group

Overall, by repeated measures analysis, impotence was significantly increased after randomization in the immediate repair group (p <.03)

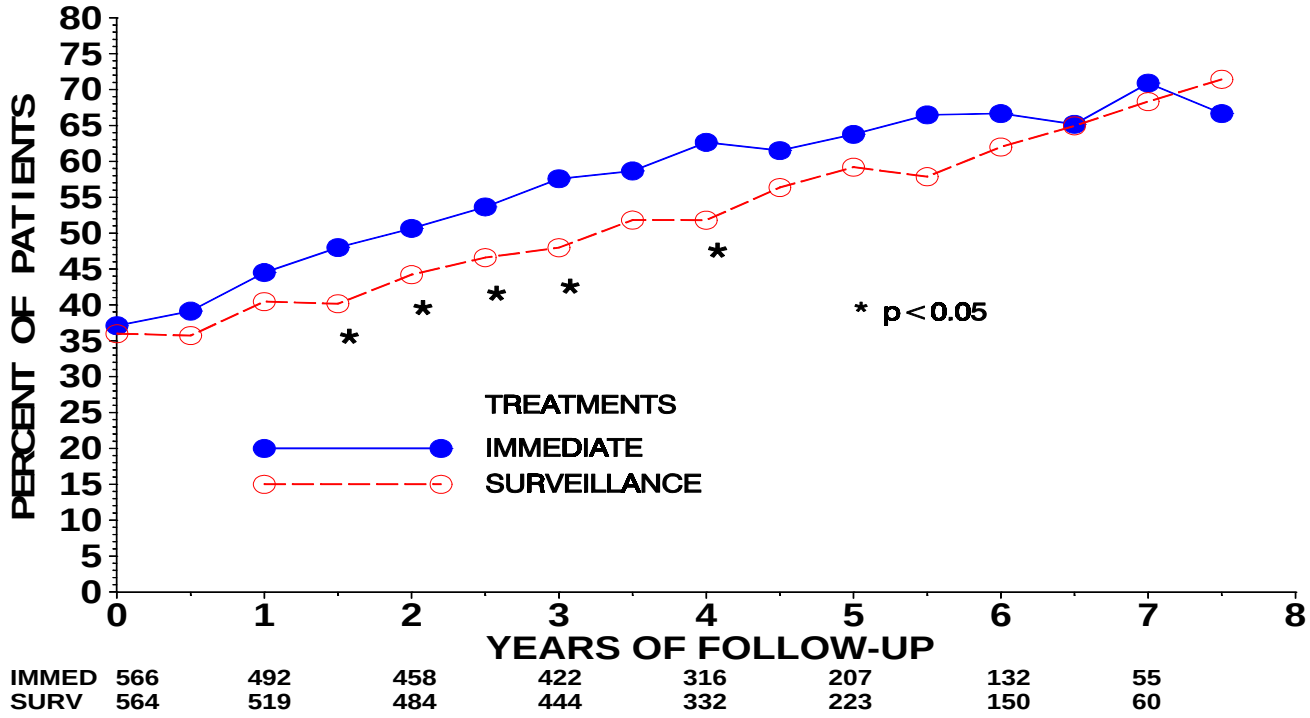

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Figure E3. Immediate open repair of small aneurysms (4.0 to 5.5 cm) vs. surveillance: UKSAT mean change in SF-20 scores from baseline at 12 months

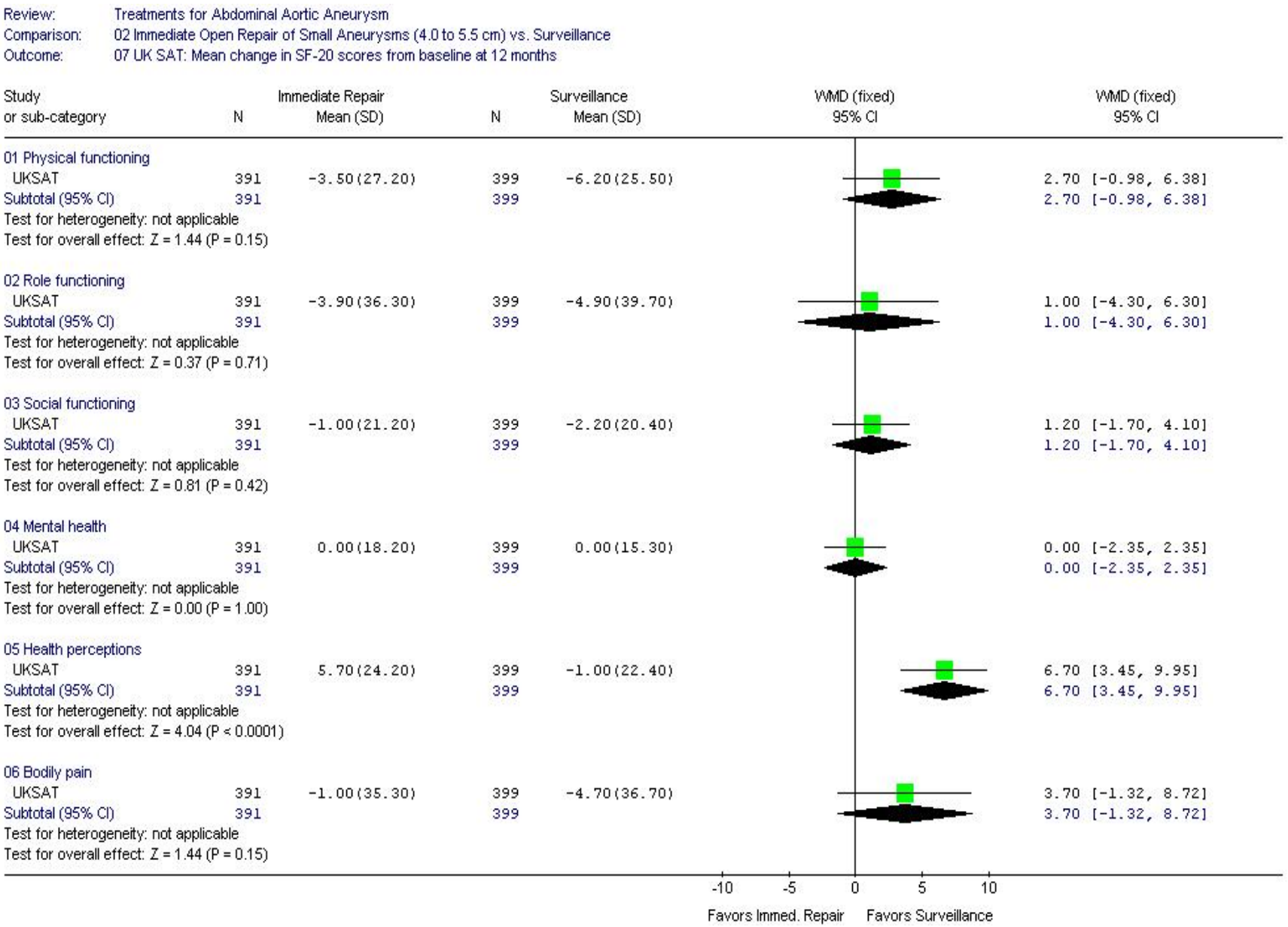


Figure E4. DREAM trial (n = 153): Changes in Short Form-36: Physical function domain over time: Endovascular repair (EVAR) vs. open repair (OR)

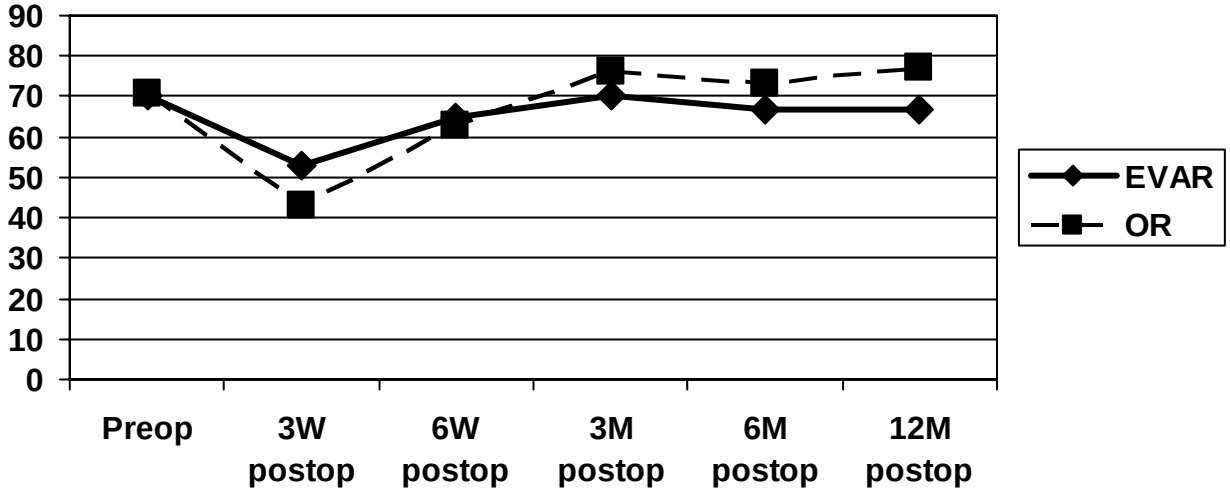


Figure E5. DREAM trial (n = 153): Changes in Short Form-36: Domain of mental health, over time: Endovascular repair (EVAR) vs. open repair (OR)

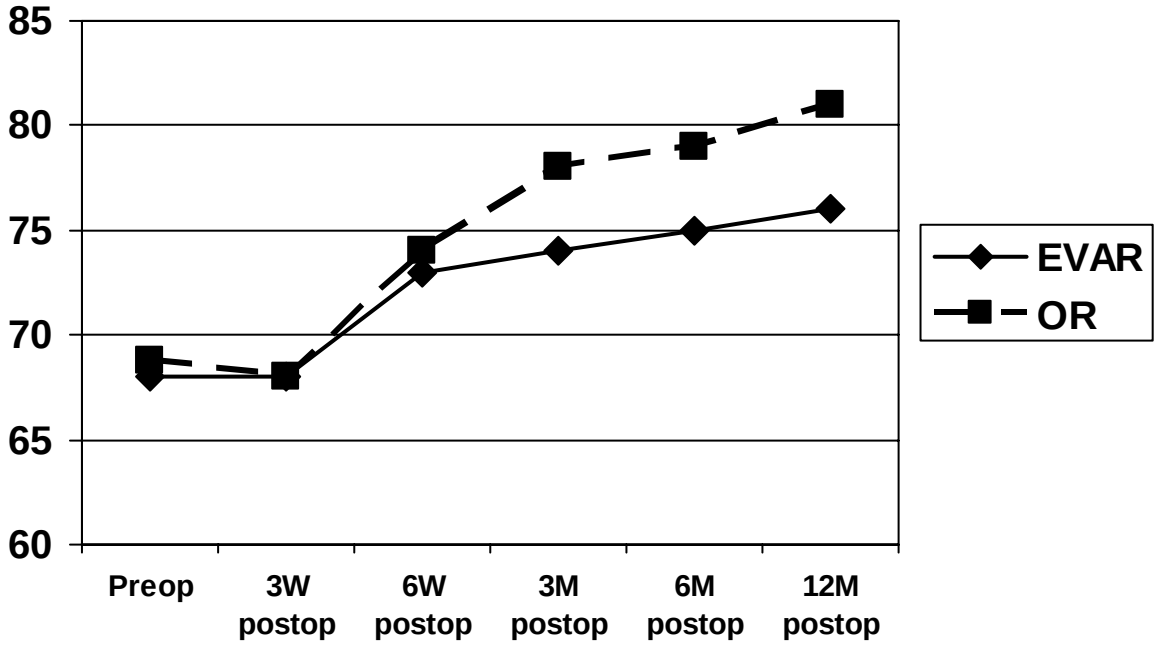


Figure E6. EVAR1 trial: Euro QoL 5-D (EQSD): Endovascular repair (EVAR) vs. open repair (OR)

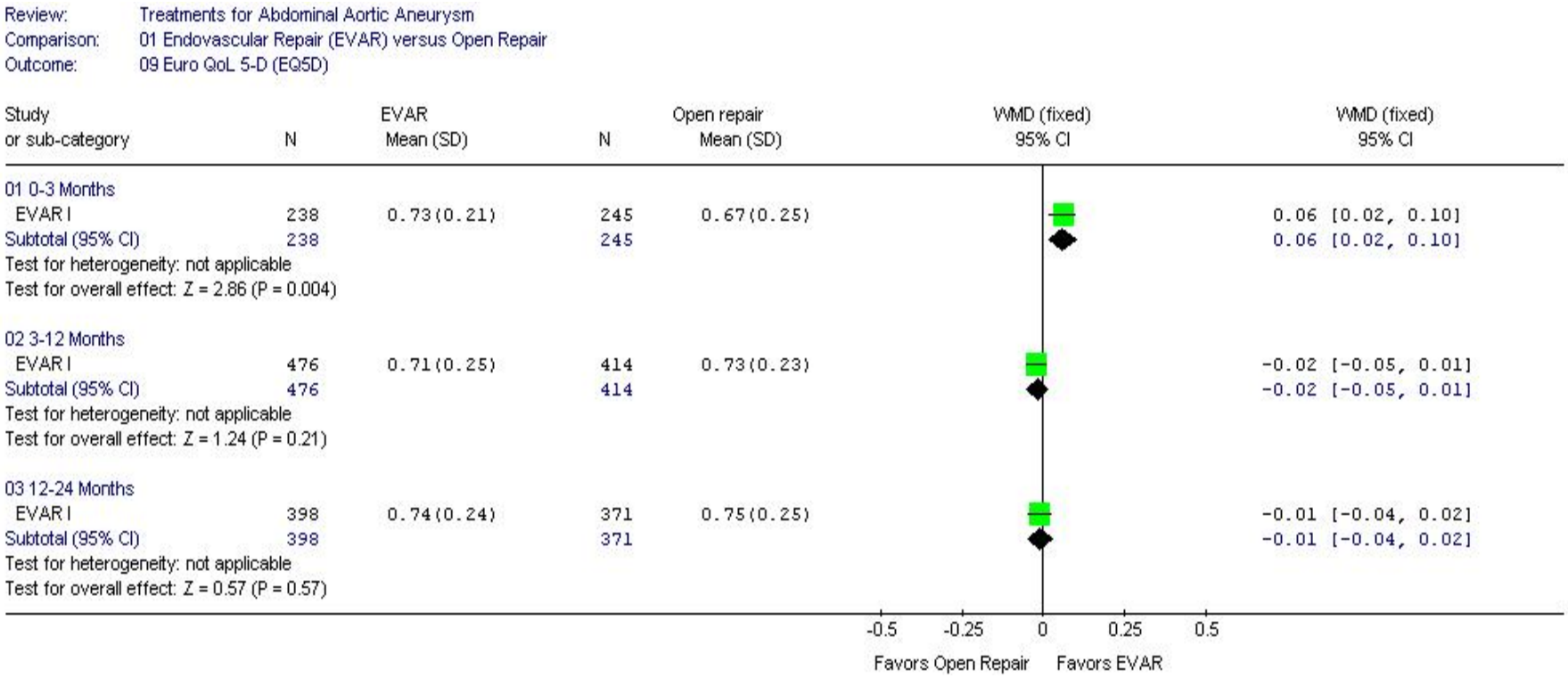


Figure E7. EVAR1 trial: Short Form-36 physical component: Endovascular repair (EVAR) vs. open repair (OR)

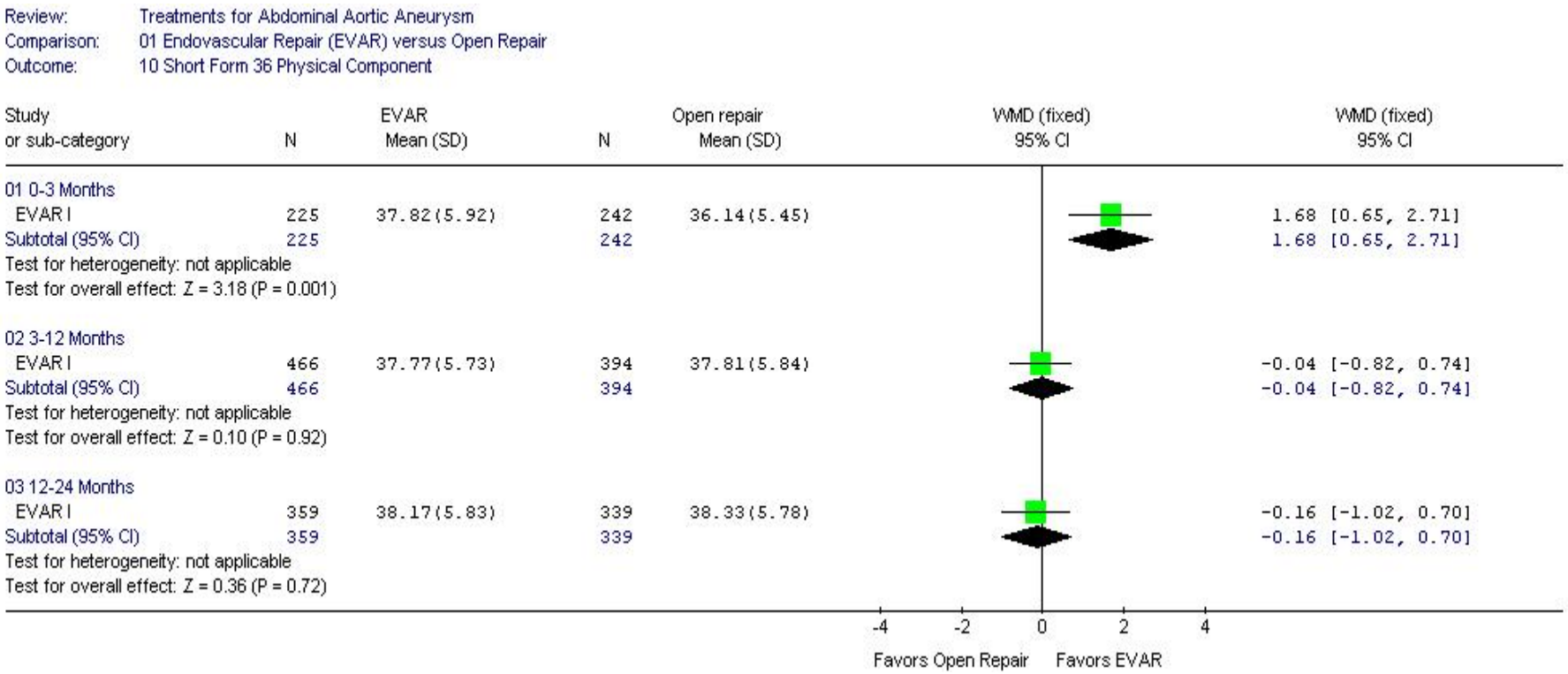
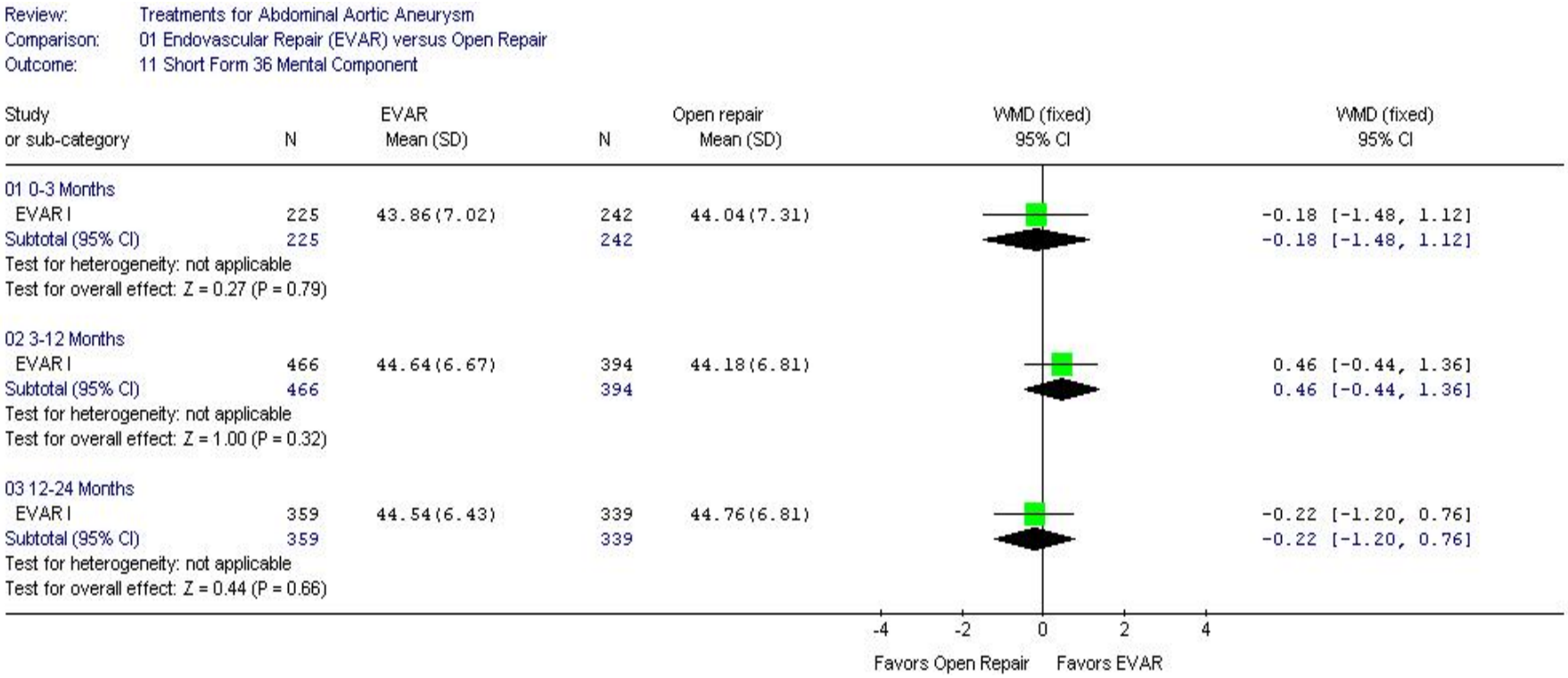


Figure E8. EVAR1 trial: Short Form-36 mental component: Endovascular repair (EVAR) vs. open repair (OR)



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