

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

D Chambers,^{1*} D Epstein,² S Walker,²
D Fayer,¹ F Paton,¹ K Wright,¹
J Michaels,³ S Thomas,³ M Sculpher² and
N Woolacott¹

¹Centre for Reviews and Dissemination, University of York, UK

²Centre for Health Economics, University of York, UK

³Academic Vascular Unit, University of Sheffield, Northern General Hospital, Sheffield, UK

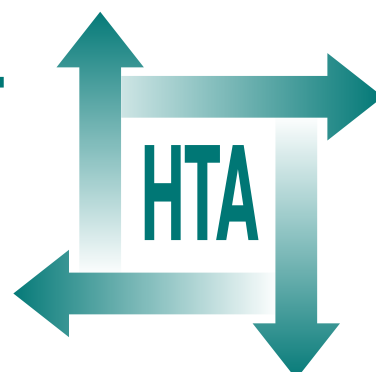
*Corresponding author



Executive summary

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Executive summary

Background

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

Objective

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

Methods

A systematic review of the clinical effectiveness of EVAR was performed. Recent systematic reviews were used to identify randomised controlled trials (RCTs) and other clinical studies. Additional searches (2005–February 2008) were conducted to search for recent RCTs, publications relating to named registries [Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA) and the European Collaborators on Stent–Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) for EVAR, and the National Vascular Database (NVD) for open surgery] and studies on the relationship between patients' baseline risks and outcomes. The following bibliographic databases were searched: BIOSIS Previews,[®]

Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register of Controlled Trials, EMBASE, ISI Proceedings, MEDLINE,[®] MEDLINE[®] In-Process & Other Non-Indexed Citations, Science Citation Index and Zetoc Conferences. Searches were not restricted by language or study design and studies written in any language were eligible for inclusion in the review. Studies of EVAR in patients with asymptomatic or symptomatic and ruptured or unruptured infrarenal AAAs were included. Conventional open repair, non-surgical treatment for AAA (sometimes referred to as 'best medical treatment') or surveillance (sometimes referred to as 'watchful waiting') were the appropriate comparators. Only studies reporting at least one of the following outcomes were included: 30-day mortality rate; aneurysm-related mortality; all-cause mortality; health-related quality of life (HRQoL); adverse effects and complications; and reintervention rates including conversion from EVAR to open procedure and secondary intervention. When appropriate, meta-analysis was employed to estimate a summary measure of treatment effect on relevant outcomes based on intention to treat analyses.

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

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

Results

Clinical effectiveness

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

Compared with open repair, EVAR reduces operative mortality (odds ratio 0.35, 95% CI 0.19 to 0.63) and aneurysm-related mortality over the medium term (hazard ratio 0.49, 95% CI 0.29 to 0.83) but offers no significant difference in all-cause mortality at mid-term follow-up. EVAR was associated with increased rates of complications and reinterventions and these are not offset by any increase in HRQoL.

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

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

Cost-effectiveness

The systematic review of the economic evidence identified six published decision models. Of the five models comparing EVAR and open repair,

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

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

- EVAR is not cost-effective compared with open repair on average given base-case assumptions at a threshold of £30,000 per QALY.
- Results are very sensitive to model assumptions. EVAR may be more cost-effective than open repair if the relative costs of the procedure have fallen, reinterventions are relatively less frequent and follow-up surveillance is currently less intensive compared with the base-case assumptions.
- Results are sensitive to the baseline risk of operative mortality. A subgroup analysis found that EVAR was likely to be cost-effective compared with open repair in patients with poor operative risk and unlikely to be cost-effective in patients with good operative risk. A validated and accepted fitness score is needed to distinguish individual patients by operative risk.
- An exploratory analysis was undertaken to evaluate management options in patients who would not be considered suitable for open surgery, that is, in patients of very poor fitness. This model was based on uncertain data about the natural history of untreated aneurysm. This suggested that the cost-effectiveness of EVAR may be sensitive to aneurysm size and patient's age at operation. Further research in these areas would be important to inform future modelling work.
- Indicative modelling results suggest that EVAR may be cost-effective for small aneurysms (< 5.5 cm) in some patient groups. Ongoing RCTs will provide further evidence relating to these patients. A review of the current

guideline that aneurysms should not be operated on if less than 5.5 cm should then be considered.

Conclusions

Implications for service provision

Based on the results of this assessment of clinical and cost-effectiveness, and using a set of base-case assumptions, open repair is likely to be considered cost-effective compared with EVAR on average in patients considered fit for open surgery. Cost-effectiveness may vary with fitness. EVAR is likely to be more cost-effective than open repair for patients at higher risk of operative mortality. There is considerable uncertainty in this analysis, in particular concerning the relative cost of procedures and rate of reinterventions. An exploratory study suggested that EVAR may be more cost-effective than medical treatment or watchful waiting for some groups of patients unfit for open repair, depending on age and aneurysm size. Evidence does not currently support EVAR for the treatment of ruptured aneurysms.

Suggested research priorities

- Further follow-up of the existing UK trials (EVAR trial 1, EVAR trial 2) should be undertaken.
- The relative procedure costs and device costs should be investigated further.
- Opportunities for individual patient meta-analysis of all RCTs relating to EVAR should be sought.
- Further research is needed on the rates of late complications, reinterventions and

aneurysm-related mortality after EVAR, in particular those associated with the most recent generation of devices.

- The optimal surveillance policy following EVAR should be investigated.
- The extent to which the relative treatment effect of EVAR on operative mortality can be assumed constant across subgroups of patients should be further investigated.
- Research is required into how to implement the best available risk scoring systems for the management of AAA into decision-making in routine clinical practice.
- Research is required into the natural history of untreated AAA to determine more reliably when surgical intervention is optimal. The analysis should investigate the impact of different levels and determinants of patient fitness as well as aneurysm size and anatomy.
- A well-defined and well-conducted RCT of EVAR versus watchful waiting, reflecting current clinical practice, is warranted. However, given the difficulties of conducting RCTs in the management of AAA it is probably advisable that the collection of data through the existing, established registries in the UK, particularly RETA (for EVAR) and NVD (for open repair), should be continued.

Publication

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