Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Recommendations
July 2022

In response to enquiry from the National Services Division within NHS National Services Scotland

Complex endovascular aneurysm repair

This replaces previous SHTG advice published in May 2018

Recommendations for NHSScotland

Complex endovascular aneurysm repair (C-EVAR) is associated with a limited and low-quality evidence base.

The advantages of C-EVAR remain unclear compared with:

- open surgical repair (OSR), in people for whom OSR is a suitable intervention, and
- non-surgical management, in people for whom OSR is not a suitable intervention.

C-EVAR of complex abdominal aortic aneurysms (AAAs) or thoracoabdominal aneurysms (TAAAs) offers an alternative to OSR and is often considered for patients with perceived moderate/high operative risk.

All patients for whom the use of C-EVAR is being considered should have their case discussed as part of a multidisciplinary team. The consequences of C-EVAR, including uncertainties around reintervention and survival, should be discussed with each patient as part of making a treatment decision.

Within the literature, patient selection between C-EVAR and OSR varies because of a lack of consensus regarding grading of operative risk. NHSScotland should develop a service configuration model that supports a consistent and evidence-based approach to patient assessment and treatment. This will support standardisation of best outcomes for patients and facilitate the collection of outcomes data.

All C-EVAR undertaken should be documented as part of a formal audit and data collection. programme.

NHSScotland is required to consider the Scottish Health Technologies Group (SHTG) recommendations.

What were we asked to look at?

In May 2018, the SHTG published advice on the clinical effectiveness, safety and cost effectiveness of C-EVAR techniques compared with OSR or non-surgical management in patients with a juxtarenal aortic aneurysm (JRAA) or thoracoabdominal aortic aneurysm (TAAA).

The National Services Division (NSD) within NHS National Services Scotland requested that the evidence review and advice is updated to inform their commissioning of future service models.

Why is this important?

The Scottish National Thoraco-Abdominal Aortic Aneurysm and Complex Aortic Service is based in the Royal Infirmary of Edinburgh, NHS Lothian. The service provides care for patients in Scotland requiring assessment and treatment for disease of the aortic arch, thoracic, thoracoabdominal or suprarenal abdominal aorta and other complex aortic conditions. This is a specialist service that is funded and managed by NSD.

NSD has advised that since the publication of SHTG's Advice in 2018, there has been a significant change in clinical practice resulting in greater use of C-EVAR techniques. C-EVAR is available in five boards in NHSScotland, with the centre in NHS Lothian carrying out the most complicated cases.

The increased use of C-EVAR has resulted in increased costs mainly driven by the consumable and device costs. It is important to ensure the service is providing value for money.

NSD has asked that SHTG advice is updated so that they can reach an informed decision on future service models and whether the service fits within a national designation. SHTG advice will shape the new service level agreement and requests to Board Chief Executives and Scottish Government for funding.

What was our approach?

A comprehensive literature search was conducted of evidence published since SHTG's review in 2018. The draft evidence review was subject to peer review. Draft recommendations were presented to the SHTG Council in June 2022, along with the evidence review and peer review comments, for their deliberation.

What next?

The work will be shared with NSD to inform the decisions around the future C-EVAR service model. The advice will also be disseminated to health boards and specialty experts.

Key points

1. Abdominal aortic aneurysms (AAA) develop below the renal arteries of the aorta. Aneurysms that develop above the renal arteries are called thoracic aortic aneurysms (TAAs). Aneurysms that extend from the thoracic section of the aorta into the abdominal section of the aorta are called thoracoabdominal aneurysms (TAAAs). Complex aneurysms involve the branches of the aorta, for example the arteries to organs such as the kidney, liver and bowel. This review is focused on the use of C-EVAR to treat complex AAAs and TAAAs.

2. SHTG advice from 2018 stated that C-EVAR was a novel treatment associated with limited and low-quality evidence. Several systematic reviews have been published since 2018, yet the uncertainties in the evidence about its benefits remain.

3. Systematic reviews which compare outcomes following C-EVAR or OSR all report concerns around the quality of the evidence base. The published literature consists of observational studies within which patient cohorts are often unlikely to be comparable in terms of urgency of treatment (elective/non-elective), aneurysm anatomy, risk profile and other demographics.

4. Guidelines from the National Institute for Health and Care Excellence (NICE) in 2020 summarised nine studies comparing C-EVAR with OSR for the treatment of people with unruptured AAAs. NICE reported that C-EVAR was associated with a shorter procedure time, shorter in-hospital stay, fewer perioperative cardiovascular complications, and a greater chance of discharge to home (as opposed to another hospital or residential care). However, mortality in people who survive the perioperative period was greater in people treated with C-EVAR techniques. NICE reported that C-EVAR and OSR could not be differentiated with regard to perioperative mortality, perioperative complications, duration of critical care and reintervention rate. No evidence was identified comparing the efficacy of EVAR with OSR of ruptured complex AAA.

5. A systematic review, with network meta-analyses (NMA), from 2022 compared treatments for the repair of complex AAA, focusing on juxtarenal aortic aneurysms (JRAA). The interventions evaluated were OSR, fenestrated EVAR (F-EVAR), EVAR with adjuncts (including chimneys and endo-anchors), as well as off-label use of standard EVAR. Twenty-four studies were reviewed including 15 that had been excluded from the NICE review because of quality concerns. In contrast to the NICE review, the authors concluded that there is a perioperative survival benefit for off-label EVAR and F-EVAR compared with OSR, potentially as a result of reduced risk of myocardial infarction (MI). There was no statistically significant difference in perioperative mortality between OSR and chimney-EVAR (Ch-EVAR). The authors note that F-EVAR carries a greater mid-term reintervention risk than OSR, which would have implications for costs and cost effectiveness. Other systematic reviews, in which the evidence base overlapped, similarly reported that F-EVAR and branched-EVAR (B-EVAR) were associated with reduced perioperative mortality, but higher reintervention rates.

6. Five systematic reviews focused specifically on the repair of TAAAs (not included in the NICE guidelines). All reported that a lack of good quality evidence prevented definitive conclusions on the optimal surgical intervention for this cohort of patients. Some reviews suggested possible advantages of C-EVAR over OSR in terms of short-term outcomes, including perioperative mortality, and possibly increased reintervention rates. The conclusions reported in the systematic reviews were not consistent.

7. C-EVAR costs more than OSR or standard EVAR. The cost of the stent graft for C-EVAR is £12,000–£30,000 in the UK depending on the device used. NICE cost-utility analyses found that for patients with complex AAAs, who are fit for OSR, C-EVAR costs more than OSR, but generates more quality-adjusted life years (QALYs). While there is uncertainty about the magnitude of survival gains, C-EVAR devices are often custom made and invariably more expensive, to the extent that C-EVAR is unlikely to be cost effective at conventional thresholds. NICE also reported that C-EVAR cost more and generated less benefit than a no surgical intervention strategy in patients not fit for OSR.

8. High-volume hospitals where surgeons perform a higher number of procedures are associated with lower levels of perioperative mortality. A policy document from NHS England recommends that providers of these techniques should have a projected annual case load of at least 100 aortic procedures, and in excess of 24–30 C-EVAR cases to maintain high levels of expertise in all professionals involved in the care pathway. On this basis, in Scotland, where procedure numbers remain less than 50 per year, C-EVAR should be delivered from a small number of centres, or one centre.

9. C-EVAR is currently conducted in five health boards in NHSScotland. The most complicated cases are referred to the national specialist TAAA service in the Royal Infirmary of Edinburgh, NHS Lothian. This service offers both open and endovascular treatment for patients with diseases of the aortic arch, thoracic, thoracoabdominal or suprarenal abdominal aorta and other complex aortic conditions. As this is a specialist service, C-EVAR delivered here is funded by NSD. C-EVAR delivered from the other NHS boards in not funded by NSD.

SHTG Council considerations

When formulating their recommendations, the Council took into account the published clinical effectiveness, cost effectiveness and safety evidence, as well as the views of topic experts.

1. The Council confirmed that the complex aneurysms included in this review were juxtarenal aortic aneurysms (JRAA), pararenal aortic aneurysms (PRAA), suprarenal aortic aneurysms (SRAA) or TAAA. The treatment of infrarenal aneurysms or aneuryms isolated to the thoracic aorta were not included.

2. The Council noted that the published evidence base consists of lower-level observational studies, the majority of which are prone to selection bias, with patients at higher surgical risk being offered endovascular treatment. The Council supported the need to describe all the available information along with its limitations. The Council also noted that the evidence mostly relates to the elective repair of unruptured aneurysms.

3. The Council highlighted the need for higher-quality evidence, with reference to the forthcoming UK COMplex AneurySm Study (UK-COMPASS) that may help address some uncertainties around this topic (scheduled to complete in 2024). The lack of published information around patient views was also noted.

4. The Council acknowledged that the most robust economic evidence comes from the NICE guidelines on AAA, which excludes TAAAs, and that the analysis was limited by the lack of high-quality clinical effectiveness evidence on C-EVAR.

5. The Council noted that despite the lack of an increased evidence base since the SHTG advice from 2018, there has been an increase in the provision of C-EVAR in NHSScotland. This may be partly explained by the potential advantages offered by C-EVAR, a minimally invasive approach, including shorter hospital stay. People who are treated with OSR will need postoperative care in intensive care units (ICU). The future prevalence of aortic aneurysms (AAs) is likely to increase in association with the ageing population.

6. When someone has a complex AA, the treatment options are OSR, EVAR or conservative treatment. For some people, the potential benefits of surgery (open or endovascular) may not outweigh the potential risks. The Council were in agreement that successful treatment with C-EVAR is likely to be dependent on careful patient selection. Patients will present with different risk profiles and aneurysm anatomies that will determine their best treatment option. They also highlighted that the threshold for aneurysm repair may be different in certain patient groups, for example, aneurysm rupture rates are higher in women.

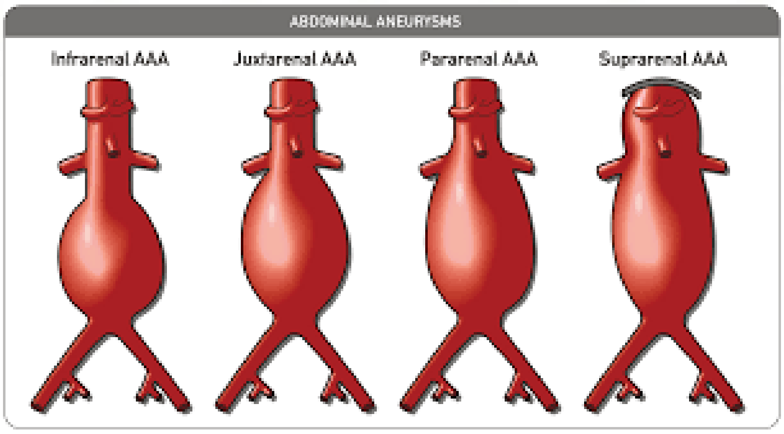
7. The Council noted that the evidence review concluded that high-volume hospitals and surgeons performing higher number of procedures are associated with lower levels of perioperative mortality, and that units in NHSScotland appeared to be doing small numbers of procedures (exact numbers not available).

Contents

Definitions

Abdominal aortic aneurysm (AAA): an aortic aneurysm (AA) that occurs in the abdominal aorta below the kidney arteries. AAAs can be further classified as suprarenal (SRAA), pararenal (PRAA), juxtarenal (JRAA) and infrarenal, as shown in *Figure 1.* An important aspect of endovascular repair is the length of the proximal neck between the renal artery and the aneurysm. This tends to be short in the case of JRAA providing a lower sealing zone margin. In cases of PRAA and SRAA, there is no aortic neck beneath the renal arteries.

Figure 1: Types of abdominal aortic aneurysm



Source: Google Images, labelled for non-commercial reuse

Aortic aneurysm (AA): a bulge (dilation) that occurs in the wall of the aorta, the major blood vessel that carries blood from the heart to the body.[1]

Aortic dissection: an aortic dissection occurs when a tear in the inner layer of the aorta allows blood to rush through the tear, causing the inner and middle layers of the aorta to split (dissect). Aortic dissections are classified into type A and B. Type A dissections are the most common, and occur in the ascending aorta as it leaves the heart. Type A dissections require immediate lifesaving open aortic surgery. A Type B aortic dissection occurs in the descending aorta as it passes down through the chest.[2]

Complex endovascular aneurysm repair (C-EVAR): a technique developed for circumstances when standard EVAR is unfeasible.

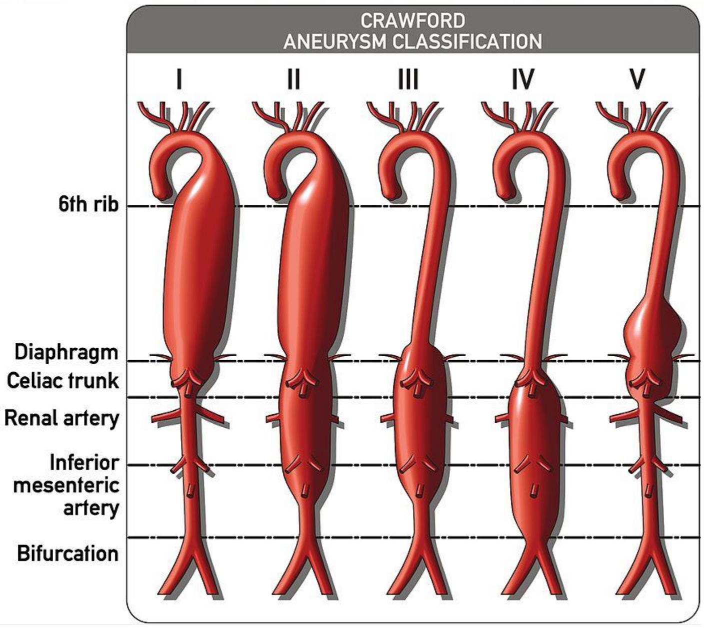
Endovascular aneurysm repair (EVAR): a non-invasive alternative to OSR in which an endograft (stent) is inserted into the affected section of the aorta through the femoral artery under fluoroscopic guidance.[3] EVAR is a potential minimally invasive alternative for patients with severe comorbidities and/or deemed to be at high surgical risk for OSR.

Open surgery repair (OSR): open surgery is the gold standard treatment for AA, including JRAA, in low-surgical-risk patients.[4]

Thoracic aortic aneurysm (TAA): aneurysmal degenerations that occur in the thoracic aorta above the kidney arteries.[5]

Thoracoabdominal aortic aneurysm (TAAA): aneurysms of the descending thoracic aorta extending into the abdominal aorta and involving the celiac, superior mesenteric and renal arteries.[6] These are relatively uncommon in general vascular practice. TAAAs are stratified using the Crawford Classification System based on their distribution within the aorta and this is illustrated in *Figure 2*. According to their relative position in relation to the diaphragm these can be further classified into supradiaphragmatic and infradiaphragmatic.

Figure 2: Crawford aneurysm classification - TAAAs



Source: Google Images, labelled for non-commercial reuse

Introduction

The treatment options for patients with an AA are OSR, EVAR or conservative treatment. For patients with AAAs, a NICE guideline provides criteria for when repair of the aneurysm (either using OSR or EVAR) may be appropriate.[7] The guideline states that when discussing aneurysm repair with people who have an unruptured AAA, clinicians should explain the overall balance of benefits and risks with repair and with conservative management, based on the patient’s current health and their expected future health. The decision on whether repair is preferred over conservative management, should be made jointly by the patient and their clinician, after assessment of factors such as:

- aneurysm size and morphology
- the person’s age, life expectancy, fitness for surgery and any other conditions they have, and

- the risk of AAA rupture if they do not have repair.

OSR has traditionally been regarded as the gold standard for the repair of AAs. Endovascular techniques are being increasingly used, particularly in patients deemed high risk for morbidity and mortality with OSR.[8] Previous reviews of clinical evidence indicated that EVAR was associated with superior perioperative outcomes and similar long-term survival compared with OSR. More recent clinical evidence suggests that, while an early survival benefit of EVAR may still be present, beyond 8 years the survival benefit following OSR may become superior to EVAR. EVAR is associated with a higher rate of reintervention compared with OSR.[9]

Approximately 20% to 30% of otherwise eligible patients are ineligible for standard EVAR because of aortic neck morphology.[10] Most of these patients have an aortic neck situated in the vicinity of the aortic side branches, requiring extensive open surgery. In recent years, complex endovascular stent grafts have increasingly been used to manage anatomically challenging aneurysms, and the off-label use of stent grafts, such as chimney techniques, have been performed.

While multiple high-quality, randomised controlled trials (RCTs) with long-term follow up have been published that compare standard EVAR to OSR, evidence on the use of complex grafts is still evolving.

Research question:

What is the clinical and cost effectiveness of C-EVAR in patients* with JRAA, PRAA, SRAA or TAAA compared with OSR or non-surgical management and how should these technologies be delivered in NHSScotland?

**The patient group includes:*

- *people with unruptured AAAs (elective) and ruptured AAAs (emergency)*
- *people for whom OSR is considered a suitable intervention, and people for whom it is not considered to be a suitable intervention (as a result of medical or anaesthetic contraindications)*

A designated specialist service in NHS Lothian offers both open and endovascular treatment for patients with diseases of the aortic arch, thoracic, thoracoabdominal or suprarenal abdominal aorta and other complex aortic conditions. This service provides interventions that are beyond the scope of this report; for example, standard EVAR (for the treatment of aneurysms isolated to the thoracic or abdominal sections of the aorta), and surgeries of the aortic arch, are not included.

The term 'T-EVAR' (thoracic endovascular aneurysm repair) may be used to describe the treatment of TAAs or TAAAs, but the evidence base for TAA and TAAA is different. T-EVAR for the treatment of TAAs is not in scope. T-EVAR for the treatment of TAAAs is in scope. TAAAs tend to be more complex and difficult to treat than TAAs.

Literature search

A comprehensive search of the secondary literature was carried out between 29 March and 1 April 2022 to identify systematic reviews, health technology assessments and other evidence based reports. Medline, Medline In-Process and the Embase databases were included in the search.

Medline was searched for primary studies, economic studies and patient issues. Results were limited to English language studies from 2018 onwards.

Key websites were searched for guidelines, policy documents, clinical summaries, economic studies and ongoing trials.

Concepts used in all searches included: juxtarenal/thoracoabdominal aortic aneurysm, fenestrated endovascular aneurysm repair (F-EVAR), branched endovascular aneurysm repair (B-EVAR), chimney endovascular aneurysm repair (Ch-EVAR). A full list of resources searched and terms used are available on request.

Health technology description

The main C-EVAR techniques described in the literature are:

- fenestrated endovascular aneurysm repair (F-EVAR)
- branched endovascular aneurysm repair (B-EVAR)
- chimney endovascular aneurysm repair (Ch-EVAR)

Various manufacturers produce the stent grafts used for these techniques. This evidence review does not consider the relative effectiveness of different manufacturers' devices, rather it considers the procedure as a whole compared to OSR or non-surgical management.

F-EVAR is a complex endovascular aneurysm repair technique that uses fenestrated grafts which overcome the problem of an insufficient infrarenal neck for stent graft implantation.[11] These grafts are designed to allow the proximal sealing zone of the stent to incorporate the aorta at the level of the visceral vessel ostia. The flow to the side branches is preserved through fenestrations (holes) in the stent graft fabric.

B-EVAR is a technique which uses branched stent grafts for aneurysms that involve vital aortic side branches such as suprarenal and Type 4 TAAAs or even the precerebral vessels (aortic arch aneurysm).[11] Unlike the fenestrated grafts, which have only premade windows for the visceral artery origins, branched grafts have branches already attached to the body of the endograft, and stent grafts are used to extend from the branches into the visceral arteries. The decision on whether F-EVAR and B-EVAR is more suitable is dependent on the angulations and diameter of the aorta at various segments.

The stents used in F-EVAR and B-EVAR are generally custom made using imaging techniques to determine the aneurysm anatomy. The manufacturing of the stents may take several weeks.[11]

Not all patients with complex aneurysms are suitable for F-EVAR or B-EVAR. Vascular specialists have developed the chimney graft technique (Ch-EVAR, also known as the periscope or snorkel technique) for patients who are deemed unfit for open surgery, but who require urgent intervention and a custom made stent cannot be designed within the time available. Ch-EVAR utilises off-the-shelf stents.

The National Vascular Registry (NVR) annual report for 2021 stated that there were 70 active vascular units in the UK that reported complex AAA repairs to the NVR between 2019 and 2020. Thirty-eight units submitted fewer than 20 procedures over the two years. In 2019, there were 799 procedures, of which 73 were open repairs. Activity was lower in 2020, with units performing 625 complex repairs, of which just 51 were open repairs. Among the 574 endovascular procedures, 349 were F-EVAR and 34 were B-EVAR (the remaining 115 were thoracic repairs).[12]

Epidemiology and current situation in NHSScotland

The patient group of relevance to this review is people with AAAs and TAAAs.

TAAAs and AAAs are multifactorial diseases with both genetic and environmental factors playing a part. Male sex, age and a positive family history are important risk factors. A person's risk is increased if they have other pathologies (for example hypertension and diabetes), if they smoke, or if they have certain congenital diseases or aortic wall infections.[13]

There is a strong relationship between aneurysm size and rupture risk. A ruptured aneurysm leads to life threatening internal bleeding. For AAAs, rupture can lead to death in 80% of cases. For TAAAs greater than 6 cm in diameter, the associated overall mortality rate for rupture is 97% to 100%.[14]

For AAAs, data suggest relatively high rupture risk, particularly with larger aneurysms. Data from 2003 show rupture rates of 3% to 15% for AAAs which are 5 cm to 5.9 cm; 10% to 20% for AAAs which are 6 cm to 6.9 cm; and 20% to 40% for AAAs which are 7 cm to 7.9 cm. A meta-analysis from 2015 reported lower rupture rates for larger AAAs (3.5% for AAAs 5.5 to 6.0 cm; 4.1% for AAAs 6.1 to 7.0 cm; and 6.3% for AAAs >7.0 cm). The authors concluded that the rupture rates commonly reported in the literature may be an over estimation as they are based on out-of-date data. They argue that significant changes have ensued in the treatment of AAA, and there is greater awareness and use of best medical therapy, including antiplatelet, statin and risk factor modification therapy.[15] Rupture rates are higher in women; a health technology assessment from 2013 reported that AAA rupture rates were almost four-fold higher in women than men.[16]

In Scotland, all men aged 65 are invited to attend AAA screening. According to the latest key performance indicators of the Scottish AAA National Screening Programme, Seventy-eight per cent of men who were eligible for screening were tested before age 66 years and 3 months. Of the 26,423 men tested, 312 (1.2%) had a positive result, that is, an aneurysm of 3 cm or greater. Of the 312 men having a positive result, 81.4% were found to have a small aneurysm (3.0–4.4 cm), 9.6% medium (4.5–5.4 cm) and 9% large (5.5 cm or greater). The data in the report were not further classified by aneurysm type. Since the screening programme in Scotland began (2012), 218,122 men in Scotland have been tested and 2,903 (1.3%) have had a positive result.[17]

In Scotland, men with a small or medium-sized aneurysm are invited to attend surveillance appointments to check the size of the aneurysm regularly to monitor any growth. Men with small AAAs are invited to attend annual surveillance scans, while men with medium AAAs are invited to attend quarterly surveillance scans (every three months). Most AAAs grow very slowly, and many men with a small or medium aneurysm never need treatment.[17] Men with large aneurysms (diameter of 5.5 cm or greater) are referred to vascular specialist services for assessment and to discuss treatment options.

TAAAs are less common than AAAs. Unlike AAAs, there is no screening programme for TAAAs. Most TAAAs are detected incidentally when people are undergoing radiology imaging for other clinical reasons. TAAAs are asymptomatic in approximately 95% of people and remain asymptomatic while they silently increase in size. A TAAA greater than 6.0 cm to 6.5 cm in diameter (depending on factors such as the gender of the patient, or the presence of an underlying inherited weakness in the aortic wall), or a TAAA expanding faster than 1 cm per year, is regarded as a life-threatening condition if left untreated. As TAAAs are often detected quite late, this adds to their complexity. Figures from America suggest that up to 10% of deaths from AAs are thoracoabdominal in pathology.[14]

C-EVAR is currently performed in NHS Greater Glasgow and Clyde, NHS Lanarkshire, NHS Tayside, NHS Lothian and NHS Grampian. Following a service review in 2019 by National Services Scotland (NSS) it was recommended that the patient pathway be revised to ensure accessibility and consistency for patients across Scotland. A key component of this revised pathway was to develop a pan-Scotland TAAA and complex aortic surgery multidisciplinary team (MDT), to discuss the optimal treatment strategy for patients with complex AAs.

The most complex procedures tend to be referred to the national specialist TAAA service in the Royal Infirmary of Edinburgh, NHS Lothian. In 2021, 19 C-EVAR procedures were carried out in NHS Lothian (excluding endovascular treatment of TAAA in isolation, which would be a small additional number). This service offers both open and endovascular treatment for patients with diseases of the aortic arch, thoracic, thoracoabdominal or suprarenal abdominal aorta and other complex aortic conditions. As the unit provides a specialist service, C-EVAR delivered here is funded by NSD.

Clinical experts advise that the other units in NHSScotland mostly carry out F-EVAR in people who have AAAs with a short aortic neck not suitable for standard EVAR. Some units carry out B-EVAR for type III and IV TAAA patients. C-EVAR done in the other NHSScotland boards is not funded by NSD, and numbers of procedures undertaken are not readily available.

Clinical effectiveness and safety

Clinical guidelines

NICE guideline (2020)

In March 2020, NICE published a guideline on the diagnosis and management of AAAs.[18] For the treatment of people with unruptured complex AAA, NICE noted that the evidence comparing C-EVAR with OSR was limited in quality and quantity. No RCTs were identified. Nine observational studies met the eligibility criteria, but were described as having ‘nontrivial limitations’. NICE summarised this very low-quality evidence as follows:

- C-EVAR is superior to complex OSR in the following domains:
    - shorter procedure time (two studies comprising 730 participants)
    - fewer perioperative cardiovascular complications (four studies comprising 1,062 participants)
    - shorter duration of hospitalisation (one study comprising 526 participants)
    - a greater chance of discharge to home as opposed to another hospital or residential care (one study comprising 526 participants)
- Complex OSR is superior to C-EVAR in the following domains
    - a lower hazard of death in people who survive the perioperative period (two studies comprising 347 participants)
- C-EVAR and complex OSR cannot be differentiated in the following domains:
    - perioperative mortality (six studies comprising 4,363 participants)
    - perioperative complications (four studies comprising 1,062 participants), including
        - perioperative respiratory complications (four studies comprising 1,062 participants)
        - perioperative renal complications (four studies comprising 1,062 participants)
    - duration of critical care (two studies comprising 730 participants)
    - reintervention rate (one study comprising 204 participants)

No evidence was identified comparing the efficacy of EVAR with OSR of ruptured complex AAA. Based on these findings, NICE make the recommendations detailed in *Table 1.*

Table 1: NICE recommendations on C-EVAR[18]

Repairing unruptured aneurysms: C-EVAR

If open surgical repair and complex EVAR are both suitable options, only consider complex EVAR if:
• the following has been discussed with the person:
  ○ the risks of complex EVAR compared with the risks of open surgical repair
  ○ the uncertainties around whether complex EVAR improves perioperative survival or long-term outcomes, when compared with open surgical repair
• it will be performed with special arrangements for consent and for audit and research that will determine the clinical and cost effectiveness of complex EVAR when compared with open surgical repair, and all patients are entered onto the National Vascular Registry.

For people who have anaesthetic risks and/or medical comorbidities that would contraindicate open surgical repair, only consider complex EVAR if:
• the following has been discussed with the person:
  ○ the risks of complex EVAR compared with the risks of conservative management
  ○ the uncertainties around whether complex EVAR improves perioperative survival or long-term outcomes
• it will be performed with special arrangements for consent and for audit and research that will determine the clinical and cost effectiveness of complex EVAR when compared with conservative management, and all patients are entered onto the National Vascular Registry.

Repairing ruptured aneurysms: C-EVAR
Do not offer complex EVAR to people with a ruptured AAA if open surgical repair is suitable, except as part of a randomised controlled trial comparing complex EVAR with open surgical repair.
NICE research recommendation
What is the effectiveness and cost effectiveness of complex endovascular aneurysm repair (EVAR) versus open surgical repair in people for whom open surgical repair is suitable for: - elective repair of an unruptured AAA or - emergency repair of a ruptured AAA.

Systematic reviews

Eleven systematic reviews were identified and are summarised in *Table 2.* Most of the systematic reviews included studies that had been excluded by the NICE guidelines because of quality concerns. Importantly, in many of the included studies, C-EVAR techniques were only offered if patients were unfit for OSR, and the authors did not attempt to account for such confounding with a form of statistical adjustment. This overview has included these reviews in order to give a complete picture of the existing published evidence base, though the quality concerns remain and are discussed throughout this document.

Table 2: Summary of systematic reviews

Reference	Year	Population	Intervention and comparison	Results
Patel *et al.* [4]	2022	JRAAs (unruptured) ruptured aneurysms were excluded, Ch-EVAR cohorts included urgent operations	OSR v Ch-EVAR v F-EVAR v off-label EVAR	Included 24 observational studies, encompassing 7,854 patients. Perioperative survival benefit for off-label EVAR and F-EVAR as compared to OSR, which is lost by 2.5 year follow up. No perioperative survival benefit to Ch-EVAR compared to OSR.
Sultan *et al.* [14]	2022	TAAAs excluded aneurysm formation post-aortic dissection	EVAR v OSR	No RCTs or controlled clinical trials (CCTs) were identified.
Prapassaro *et al.* [19]	2022	JRAAs and PRAAs included both ruptured and unruptured aneurysms	Ch-EVAR	Included 13 studies, encompassing 1,019 patients. The pooled overall survival, freedom from reintervention and target vessel patency at 3 years was 81.4 % (95% CI 73.8 to 87.9), 85.7% (95% CI 75.6 to 93.5), and 95.1% (95% CI 89.3 to 98.7) respectively. The 30-day mortality rate was 4.9% (95% CI 3.7–6.3%); 4.5% in the elective non-ruptured and 18.6% (8/43) in ruptured cases.
Verzini *et al.* [20]	2021	Post-dissection TAAAs	OSR v B-EVAR and F-EVAR	15 non-comparative studies (seven on OSR, and eight on F-EVAR or B-EVAR), encompassing 1,337 patients, of whom there were 1,068 in the OSR group and 269 in the endovascular repair group. Based on a proportional meta-analysis, the authors report that endovascular repair seems to be a viable alternative for patients unfit for open repair, although the results are not reliable.

Antoniou *et al.* [21]	2021	JRAAs, TRAAs, PRAAs and TAAAs included elective treatment only – so ruptured and symptomatic aneurysms were excluded	OSR v B-EVAR and F-EVAR	11 studies, encompassing 7,061 patients. The evidence is uncertain about the effect of F-EVAR and B-EVAR on perioperative mortality when compared with OSR. Reintervention rates are higher after F-EVAR and B-EVAR.
Rocha *et al.* [22]	2021	TAAAs included elective and urgent repair	B-EVAR, F-EVAR or OSR	Included 71 non-comparative observational studies (24 on B-EVAR or F-EVAR, 47 on OSR). Studies on EVAR included patients with more comorbidities. EVAR was associated with higher rates of spinal cord injury, but similar rates of permanent paraplegia. OSR studies reported higher rates of postoperative dialysis but similar rates of being discharged on permanent dialysis. Perioperative mortality rates were similar.
Mohamed *et al.* [23]	2020	JRAA and PRAA appears to have included elective and urgent together though not specifically stated	F-EVAR	Included 30 observational studies. Early outcomes indicate that F-EVAR is a safe and efficient treatment for patients with PRAA and JRAA. Although long-term outcomes are acceptable, late intervention rate remains high.
He *et al.* [24]	2020	Post-dissection TAAAs	F-EVAR or B-EVAR	Included four non-comparative observational studies. F-EVAR or B-EVAR for the treatment of people with PD-TAAA appears generally feasible based on the limited literature, but endoleaks and reinterventions are frequent.
Jones *et al.* [25]	2019	JRAA elective repairs only	F-EVAR v OSR	Included 27 studies. No significant difference was noted in 30-day mortality; however, F-EVAR was associated with significantly lower morbidity than OSR. Long-term durability is a concern, with far higher reintervention rates after F-EVAR.
Doonan *et al.* [26]	2019	JRAA, PRAA and SRAA	short-neck standard	Included 14 observational studies. EVAR was associated with lower 30-day mortality, acute renal failure, bowel ischaemia and length of stay but with

			EVAR, parallel grafts, F-EVAR and B-EVAR	increased spinal cord ischaemia. High risk of bias of the included studies. Further long-term studies are needed to determine whether these differences persist during long-term follow up.
Rocha *et al.* [27]	2018	TAAAs included elective and urgent repair	B-EVAR or F-EVAR v OSR	Included eight comparative observational studies. Authors concluded that short-term outcomes may be improved in patients undergoing endovascular treatment of TAAA, but note that this is based on evidence limited in quality and quantity.

The most recent systematic review was published in 2022, and includes a NMA.[4] The authors' aim was to compare treatments for the repair of complex AAA, focusing on JRAA. The interventions evaluated in the NMA were OSR, F-EVAR, EVAR with adjuncts (including chimneys and endo-anchors), as well as off-label use of standard EVAR ('off-label' means used in a way not covered by the instructions for use). Studies were eligible for inclusion if they compared outcomes between at least two methods of repair for complex aneurysms. The primary outcome measure was perioperative death, defined either as death within 30 days of the aneurysm repair or death during the same admission as the primary procedure. The literature search (conducted in April 2020) identified 24 retrospective cohort studies and 7,854 patients who underwent OSR, F-EVAR, off-label EVAR or Ch-EVAR. No comparative studies were identified that included EVAR with endo-anchors. The authors noted that all studies were assessed as having a moderate or high risk of bias, and confidence in the network findings was graded as 'low'.

NMA was performed on 23 studies that reported outcomes of aneurysms with short/absent infrarenal neck. Perioperative mortality was reported in 22 studies, and the unweighted pooled perioperative mortality rates were 4.4% for OSR (235 deaths/5,366 patients), 3.1% for F-EVAR (52 deaths/1,654 patients), 4.8% for Ch-EVAR (20 deaths/418 patients), and 0.5% for off-label EVAR (2 deaths/366 patients).

The authors reported that compared with OSR, off-label EVAR and F-EVAR were associated with lower perioperative mortality:

- OSR versus off-label EVAR (relative risk [RR] 0.10, 95% confidence interval [CI] 0.01 to 0.41)
- OSR versus F-EVAR (RR 0.62, 95% CI 0.32 to 0.94)

This difference was not maintained at the mid-term follow up (30 months). There was no statistically significant difference in perioperative mortality between OSR and Ch-EVAR (RR 1.15, 95% CI 0.50 to 2.44).

Secondary outcomes are summarised in *Table 3.*

Table 3: Summary of secondary outcomes reported by Patel *et al* (2022)[4]

Secondary outcome	Number of studies and patients	Main results
Mid-term all-cause mortality	16 studies (3,481 patients with 536 deaths)	SUCRA* scoring rated F-EVAR as the intervention with the best (lowest) mid-term all-cause mortality, followed by OSR, followed by Ch-EVAR, followed by off-label EVAR.
Perioperative renal failure	16 studies (5,690 patients with 868 cases of renal failure)	There were no statistically significant differences in renal failure rates between the four treatment options.
Perioperative MI	17 studies (6,325 patients with 246 MIs reported)	Both off-label EVAR (RR 0.42, 95% CI 0.12 to 0.89) and F-EVAR (RR 0.37, 95% CI 0.16 to 0.62) were associated with a lower risk of perioperative MI than OSR.
Perioperative reintervention	nine studies (3,890 patients with 358 events)	There were no statistically significant differences in perioperative reintervention risk between any of the treatment modalities.
Mid-term reintervention	11 studies (1,336 patients with 135 events)	F-EVAR had a higher rate of mid-term reintervention than OSR (hazard ratio (HR) 1.65, 95% CI 1.04 to 2.66). There were no statistically significant differences between any of the other combinations of complex AAA repair.
Mid-term aneurysm-related mortality	11 studies (2,987 patients and 138 aneurysm-related deaths)	There were no statistically significant differences in mid-term aneurysm-related mortality rates between the four treatment options.

* The SUCRA score is a metric to evaluate which treatment in a network is likely to be the most efficacious in the context of NMA

Based on the findings, the authors concluded that there is a perioperative survival benefit for off-label EVAR and F-EVAR compared with OSR, potentially as a result of reduced risk of MI. The authors concluded that F-EVAR carries a greater mid-term reintervention risk than OSR, with potential implications for cost effectiveness. A lack of comparative data were noted for cases with adverse aortic neck features other than short length.

The included studies were prone to selection bias. For example, F-EVAR was often only offered if patients were unfit for OSR, and Ch-EVAR was only offered if F-EVAR was anatomically not possible or if the cases were urgent. The authors reported that the majority of included studies (17 out of 24) did not attempt to account for confounding. Of the 24 studies included, only five were included in the NICE evidence review.[18] NICE excluded 15 of the studies, mostly because they did not adjust for confounding.

A systematic review by Antoniou *et al.* 2021 included a meta-analysis to explore the comparative outcomes of F-EVAR or B-EVAR with OSR for JRAAs, PRAAs, SRAAs or TAAAs.[21] It included 11 studies (eight of which were included by Patel *et al.*[4]), encompassing 7,061 patients. The results were analysed differently and the inclusion criteria was broader, but the results are largely in agreement with Patel *et al.*:

- Perioperative mortality was lower after F-EVAR and B-EVAR compared with OSR, but the result was not statistically significant (OR 0.56, 95% CI 0.28 to 1.12).
- Overall mortality during follow up was higher following F-EVAR and B-EVAR, but the result was not statistically significant (HR 1.25, 95% CI 0.93 to 1.67).
- Reintervention was significantly higher after endovascular therapy (HR 2.11, 95% CI 1.39 to 3.18).

Antoniou *et al.* noted the issues of quality of the included studies and concluded that:

> The evidence is uncertain about the effect of F/B-EVAR on peri-operative mortality when compared with open repair. There is probably no difference in overall survival, but F/B-EVAR results in an increased reintervention hazard. There is a need for high level evidence to inform decision making and vascular/aortic service provision.

A systematic review by Prapassaro *et al*. (2022) aimed to evaluate the mid- and long-term outcomes of Ch-EVAR.[19] The literature search identified 13 observational studies (nine retrospective cohorts, three comparative and one prospective registry). The authors rated six of the studies as 'poor' and the rest as 'moderate'. The studies encompassed 1,019 patients, 83% of whom were men (mean age was 76 years). One of the studies was included in the review by Patel *et al*. The main results are summarised as follows:

- The 30-day mortality rate was reported in 12 studies, and was 4.9% (95% CI 3.7 to 6.3%), 4.5% (42/914) in the elective non-ruptured and 18.6% (8/43) in ruptured cases.
- The pooled estimate rate of intraoperative type Ia endoleak was 6.0% (95% CI 3.6 to 8.9%), reported in 12 studies.
- Three year overall survival was reported in seven studies (694 patients) and ranged from 69% to 95%. The pooled overall survival at 3 years was 81.4 % (95% CI 73.8 to 87.9%).
- Target vessel patency at 3 years was reported in three studies (126 patients) and ranged from 85.6% to 98%, with a pooled estimate of 95.1% (95% CI 89.3 to 98.7%).
- Three year freedom from reintervention was reported in three studies (90 patients) ranging from 75.8% to 91%. The pooled estimate rate of freedom from reinterventions at 3 years was 85.7% (95% CI 75.6 to 93.5%).

- Nine studies described perioperative stroke, and the pooled estimate rate of perioperative stroke was 2.4% (95% CI 1.5 to 3.5%).

The authors note that the poor methodological quality of the included studies is a major limitation of the review. Heterogeneity was a key weakness, for example in the anatomy of the aneurysms, the baseline characteristics of patients, patient selection, different types of stent and the outcomes reported. The results need to be interpreted with caution.

TAAAs

Five systematic reviews focused specifically on the repair of TAAAs.[14, 20, 22, 24, 27] All reviews stated that a lack of robust evidence makes it difficult to make definitive conclusions on the optimal surgical intervention for this cohort of patients. The most recent review, a Cochrane review by Sultan *et al.,* concluded that because of the lack of RCTs or CCTs, it was not possible to determine the effectiveness or safety of endovascular repair compared with OSR in patients with TAAAs.[14]

In 2018, Rocha *et al.* published a systematic review and meta-analysis which included eight comparative observational studies evaluating the early results of endovascular repair versus OSR of TAAAs.[27] The authors rated the studies as having a high risk of bias. Only two of the eight studies attempted to account for baseline differences between the two groups. After propensity matching in these two studies, no differences were observed in early mortality, spinal cord injury or renal complications after endovascular repair compared with OSR.

In the unmatched observational studies, the endovascular approaches were associated with improved perioperative mortality (RR 0.63, 95% CI 0.45 to 0.87, p=0.006) and less perioperative renal failure requiring dialysis (RR 0.44, 95% CI 0.23 to 0.85, p=0.01). The authors also reported that endovascular approaches were associated with a lower incidence of spinal cord injury in the unmatched studies, but this result was not statistically significant (RR 0.65, 95% CI 0.42 to 1.01, p=0.08). Postoperative stroke rate was reported in three unadjusted studies and was not different between groups (RR 0.81, 95% CI 0.28 to 2.40, p=0.71). Hospital length of stay was reported in four studies and was shorter in the endovascular group (mean difference -4.4 days, 95% CI -6.6 to -1.7, p=0.0009).

Based on these findings, the authors concluded that short-term outcomes may be improved in patients undergoing endovascular treatment of TAAA, but note that this is based on evidence limited in quality and quantity. The authors also discuss the lack of standardisation of reporting of patient and disease characteristics, including aneurysm size, presence of dissection and aneurysm extent.

The same authors published a subsequent systematic review in 2020, including 71 non-comparative observational studies (24 on B-EVAR or F-EVAR, 47 on OSR).[22] The authors noted the included studies were at high risk of bias. They concluded that with regard to the early outcomes of TAAA repair, using either endovascular techniques or OSR was associated with considerable risk of perioperative complications. The studies on EVAR included patients who were older and who had more comorbidities. EVAR was associated with higher rates of spinal cord injury compared with OSR, but similar rates of permanent paraplegia. OSR studies reported higher rates of postoperative dialysis but similar rates of being discharged on permanent dialysis. Perioperative mortality rates were similar.

Two of the systematic reviews evaluated the repair of post-dissection TAAAs. Verzini *et al.* (2021), reviewed open or endovascular repair of post-dissection TAAAs, between January 2009 and February 2020.[20] A proportional meta-analysis was performed for postoperative complications and both early and late mortality and reinterventions. The authors identified 15 non-comparative studies (seven articles on OSR, and eight on F-EVAR or B-EVAR), and combined them using a proportional meta-analysis approach. The studies encompassed 1,337 patients, of whom there were 1,068 in the OSR group (73% males; mean age 58 years) and 269 in the endovascular repair group (78% males; mean age 64 years).

While the authors report that their meta-analysis showed that endovascular repair seems to be a viable alternative for patients unfit for open repair, confidence in this conclusion is low, based on the quality of the included studies and concerns around the methodological robustness of the meta-analysis.

Similarly, He *et al.* (2020) evaluated the literature on F-EVAR and B-EVAR for the repair of post-dissection TAAAs.[24] They pooled the results of four studies (all included in the review by Verzini *et al.*[20]) and concluded that: 'The use of fenestrated/branched stent grafts for the treatment of PD-TAAA appears generally feasible based on the limited literature, but endoleaks and reinterventions are frequent.'[28]

Three other systematic reviews were identified, but the evidence they included overlaps considerably with the systematic reviews already described. Their conclusions do not add to the findings presented above.[23, 25, 26]

Primary studies

A search for primary literature did not identify any RCTs or CCTs. Four additional observational studies that compared outcomes for C-EVAR with OSR were identified. These studies are summarised in *Table 4* (based on study abstracts). Their findings did not affect the conclusions drawn previously. Non-comparative observational studies were excluded.

Table 4: Summary of observational primary studies not included in systematic reviews

Reference	Population	Intervention and comparison	Results
Bootun *et al.* (2022)[29]	JRAA (n=162) 85.8% males	Open repair with a suprarenal clamp positioning (ORSRC) (n=98) versus F-EVAR (n=64)	Patients receiving F-EVAR tended to be older, with a smaller diameter aneurysm. **Length of hospitalization postoperatively** F-EVAR = 10 days, ORSRC = 6 days, p<0.05 **Reintervention** F-EVAR was associated with a greater likelihood of requiring reintervention over time. F-EVAR = 26.6%, ORSRC = 10.2%, p=0.006 **Acute renal impairment on postoperative day 3** F-EVAR = 12.7%, ORSRC = 47.6%, p<0.05 **Renal function deterioration at 1 year** Both interventions had similar rate of renal function deterioration at 1 year. **Mortality at 30 days** F-EVAR = 7.8%, ORSRC = 8.2%, p=0.936 **5-year mortality rate was comparable** F-EVAR = 32.8%, ORSRC = 25.5%, p=0.314
de Guerre *et al.* (2020)[30]	JRAA, PRAA and SRAA (n=2,270)	C-EVAR (n=1,260) versus OSR (n=1,010)	**Perioperative mortality after EVAR** female patients = 6.3%, male patients = 2.4%, p=0.001 **Major complications after EVAR** female patients = 15.9%, male patients = 7.6%, p<0.001 **Perioperative mortality after OSR** female patients = 7.4%, male patients = 5.6%, p=0.3 **Major complications after OSR** female patients = 29.4%, male patients = 27.4%, p=0.53

			Perioperative mortality was significantly lower after EVAR compared with open repair for male patients (2.4% versus 5.6%, p=0.001), this difference was not significant for women (6.3% versus 7.4%, p=0.60) On multivariable analysis, female sex remained independently associated with higher perioperative mortality (OR 2.5, 95% CI 1.3 to 4.9, p=0.007) and major complications (OR 2.0, 95% CI 1.3 to 3.2, p=0.002) in patients treated with EVAR but showed no significant association with mortality (OR 0.9, 95% CI 0.5 to 1.6, p=0.69) or major complications (OR 1.1, 95% CI 0.8 to 1.5, p=0.74) after OSR. The association of female sex with higher perioperative mortality in patients undergoing C-EVAR was reduced when diameter was replaced with aortic size index in the multivariable analysis.
Geisbusch *et al.* (2019)[31]	TAAA (n=2,607, 406 or which were ruptured TAAA)	F-/B-EVAR (n=856) versus OSR (n=1,422) versus hybrid repair (n=354)	The overall raw mortality was 20.5%: 46.1% for ruptured TAAA and 15.9% for non-ruptured TAAA. **In-hospital mortality** Endovascular repair 10.6% (89/839) OSR 23.9% (340/1422) Hybrid repair 30.9% (107/346) In-hospital mortality was significantly reduced when endovascular treatment was performed (RR 0.35, 95% CI 0.24 to 0.51) Complications were more frequent following hybrid repair than OSR and endovascular repair for dialysis, acute mesenteric infarction, bowel resection, acute peripheral limb ischaemia and acute renal artery infarction. MI and acute paraplegia/spinal infarct were more frequent after F-/B-EVAR

Von Meijenfeldt *et al.* (2022)[32]	JRAA (n=455)	OSR (n=258) versus C-EVAR (n=197)	After logistic regression with adjustment for confounders **Major complications within 30 days of treatment** OSR 45% versus C-EVAR 20.8% (OR 3.64, 95% CI 2.25 to 5.89, <0.001) **Minor complications within 30 days of treatment** OSR 33.7% versus C-EVAR 22.8% (OR 2.17, 95% CI, 1.34 to 3.53, p=0.002) **Early mortality** OSR 6.6% versus C-EVAR 2.5% (OR 3.79, 95% CI 1.26 to 11.34, p=0.017)

Patient and social aspects

No studies were identified that reported specifically on patient preferences or experiences in relation to the use of C-EVAR techniques versus OSR.

A 2008 report addressed patient preferences regarding surgical techniques for AAA repair.[33] A total of 237 men aged 65 and over (with an aneurysm diameter between 4.0 and 5.5 cm and not currently considered for imminent aneurysm repair) on the AAA screening programmes at two English acute hospital trusts were asked to state their preference between EVAR and OSR based on an information pack.

Respondents were more than twice as likely to prefer EVAR (46%) to OSR (18%), 14% percent of respondents were equally happy with either treatment and 20% were unsure which of the two methods they preferred. Very few statistically significant variations were identified between respondents in different age groups or based on differences in health or carer status, although the following findings may be worth consideration:

- Respondents in all age groups preferred EVAR to OSR, but younger respondents were marginally more likely to prefer EVAR compared with the other age groups.
- Respondents with a long-term illness or disability were more likely to prefer OSR.
- Respondents that were providing care for others were more likely to prefer EVAR.

The main factor influencing people's preferences was 'the advice of the doctor', while medical history or existing condition, invasiveness of surgery and the risk of postoperative complications were also frequently cited but to a much lesser extent. Just over a third of respondents preferred 'less invasive surgery even with a possible increased risk of postoperative complications' and just under a third said they preferred a lower risk of postoperative complications, even with the need for more invasive surgery, while the other third had no particular preference. Other influencing factors included shorter recovery time, avoiding a stay in intensive care and a shorter hospital stay, and least importance was placed on the size of the scar and the risk of impotency. It should be noted that this study was from 2008, when the long-term outcomes of EVAR (including factors such as durability of the stent) were less well understood.

Volume and outcomes

In 2017 Katsragyris e*t al.* reviewed the literature to investigate the effect of volume of procedures within each hospital on AA repair outcomes.[34] The majority of studies found that high-volume hospitals were associated with lower perioperative mortality of AAA, TAA and TAAA repair. A similar advantage is shown for surgeons who perform a large number of procedures. The volume advantage appears to be less evident for simple endovascular procedures (EVAR), compared to more complex endovascular (F/B-EVAR) and open surgical procedures. Superior outcomes observed in high-volume hospitals may be explained by surgeons undertaking a high volume of cases, but also by more effective management of intra and postoperative complications. Confounding factors to be taken into account are the timing of the studies in relation to positive evolution of outcomes in several high-risk procedures, and patient cohorts selected in regions with very low and very high-volume hospitals only.

A subsequent systematic review published in 2021 mirrors the results of the Katsragyris *et al.* review.[35]

A policy document from NHS England recommends the provision of C-EVAR techniques in arterial centres with a catchment of two million people (typically performing at least 100 aortic procedures annually), and which have a projected annual case load for these specific interventions in excess of 24-30 cases in order to maintain high levels of expertise in all professionals involved in the care pathway.[36]

Ongoing studies

- A Risk-adjusted and Anatomically Stratified Cohort Comparison Study of Open Surgery, Endovascular Techniques and Medical Management for Juxtarenal Aortic Aneurysms: The UK COMplex AneurySm Study (UK-COMPASS). Observational cohort study (n=1,100). A Risk-adjusted and Anatomically Stratified Cohort Comparison Study of Open Surgery, Endovascular Techniques and Medical Management for Juxtarenal Aortic Aneurysms: The UK COMplex AneurySm Study (UK-COMPASS) (nihr.ac.uk)
- Global Fenestrated Anaconda Clinical sTudy (Global FACT). Observational study (prospective cohort; n=160). Global Fenestrated Anaconda Clinical sTudy - Full Text View - ClinicalTrials.gov
- Chimney EndoVascular Aneurysm Sealing Of New Expanded Indication (ChEVAS One). Non-randomised clinical trial, single group assignment (n=11). Chimney EndoVascular Aneurysm Sealing Of New Expanded Indication - Full Text View - ClinicalTrials.gov
- F-BEVAR vs Open Surgery for Complex Abdominal Aortic Aneurysm. Observational study (retrospective cohort, propensity-matched; n=278). F-BEVAR vs Open Surgery for Complex Abdominal Aortic Aneurysm - Full Text View - ClinicalTrials.gov
- Visceral (Kidney and Abdominal Organ) Function After Fenestrated and Branched Endovascular Aneurysm Repair (FEVAR/BEVAR) of Thoracoabdominal Aortic Aneurysms. Non-randomised clinical trial, single group assignment (n=500). Visceral (Kidney and Abdominal Organ) Function After Fenestrated and Branched Endovascular Aneurysm Repair (FEVAR/BEVAR) of Thoracoabdominal Aortic Aneurysms - Full Text View - ClinicalTrials.gov

Cost effectiveness

The available cost effectiveness evidence is limited in terms of generalisability to Scotland. The cost of stent devices is high and ranges from £12,000 to £30,000 in the UK depending on the stent used, while the total cost for the procedure is even higher and can vary substantially.[36]

NICE guideline – economic modelling (2020)

NICE commissioned the development of an economic model to inform its guideline on the diagnosis and management of AAAs.[18] The NICE guideline includes JRAA, PRAA and SRAA when defining complex AAAs, but excludes TAAA. Cost effectiveness conclusions drawn from the model do not apply to TAAA.

Scope and structure of economic models

Two economic models were developed, one comparing EVAR versus OSR, and the other versus no surgical intervention in patients deemed unfit for OSR because of high risk of mortality. The analyses were also divided into subgroups on the basis of aneurysm complexity (infrarenal or complex) and admission type (elective or emergency). Only results for the complex AAA elective repair subgroup fall within the scope of this SHTG assessment.

The two economic models had similar structures. Patients entered the state-transition model after referral for non-emergency AAA repair, initially spending time on the waiting list (if they were considered fit for surgery) and were subject to a risk of death during this time. Patients then go on to receive their intervention (EVAR or OSR), which lasted for one model cycle, during which the patient was at risk of perioperative (30-day) death. Patients who survived the elective procedure transitioned to long-term 'postoperative survival' state, where they were subject to a risk of reintervention to resolve complications, but otherwise remained until death or the end of the model time horizon. Patients in the "no intervention" arm entered the model directly in the "postoperative survival" state and stayed there until mortality because of a ruptured aneurysm or other general causes.

Overall survival and reinterventions

Overall survival was modelled as three distinct parts: waiting time survival, perioperative (30-day) survival, and post-perioperative (long-term) survival. For patients receiving EVAR or OSR, a monthly probability of death of 1% was assumed while on the waiting list and 3% for those found unsuitable for OSR, as observed in the main UK EVAR trials. An average of 2 months on the waiting list was assumed for patients waiting for OSR and an additional month for those waiting for a customised EVAR device.

In the "fit for OSR" population model, 30-day EVAR mortality rates from the UK NVR were used to characterise baseline perioperative mortality rates (3.5%). A measure of relative effect was applied by virtue of an odds ratio (OR 0.33, 95% CI 0.20 to 0.55) derived from a Cochrane meta-analysis, to inform the relative perioperative mortality rate associated with OSR (9.9%). The observed perioperative mortality rate for OSR in the NVR data base was 19.6% but was deemed too high and only used in a scenario analysis. Since both the registry data to inform baseline rates and trial data to inform relative effects was based on standard EVAR, it was assumed that these relative effect data would be transferable to complex aneurysm repair. In the "unfit for OSR" population, the 30-day perioperative mortality rate (40.5%) was obtained by deriving a complexity log-odds ratio using the estimate based on the UK NVR data and applying it to data from the EVAR-2 trial.

For the modelling of long-term postoperative survival in the “fit for OSR” population, data were obtained from a meta-analysis incorporating the results of three RCTs (DREAM, EVAR-1 and OVER), which yielded a HR of 1.049 (95% CI 0.945 to 1.163) for EVAR versus OSR. This HR was then applied to UK general population all-cause mortality data, calibrated to match the OSR arm of the EVAR-1 study. A similar approach was taken in the modelling of the “unfit for OSR” population postoperative survival, where cross-over adjusted data from the EVAR-2 study were used to derive a HR of 0.742 (95% CI 0.571 to 0.964) up to year 4.5 and 1.454 (95% CI 0.997 to 2.199) thereafter. In the “no intervention” arm, similarly to the “fit for OSR” population model, general population all-cause mortality data were calibrated to match the relevant population. Additional effect modifiers for age, sex and aneurysm diameter (5.5 cm, 7.0 cm and 8.5 cm) were also applied in the estimation of mortality risks in subgroup analyses.

Monthly probabilities of life threatening or serious graft-related reinterventions in the economic models were obtained from the EVAR–1 and EVAR–2 studies. Data in the EVAR arm of the “fit for OSR” population model were adjusted down (HR 0.67 95%CI 0.49 to 0.93) to reflect the expected lower rate of complications in current practice compared to trials. In the “no intervention” arm, patients were at annual risk of fatal raptured aneurysm of 12.4% as observed in the EVAR-2 trial.

Utilities and costs

Since a person with an AAA leads a broadly normal life, other than the requirement for monitoring the size of the aneurysm and the risk of rupture, health-related quality of life (HRQoL) was captured in the model as three components: general population HRQoL, reduced HRQoL while recovering from AAA repair and reduced HRQoL while living with a complication and/or recovering from subsequent reintervention. For patients who are unfit for surgery, a utility decrement was assumed upon aneurysm rupture.

The cost of EVAR devices was sourced from NHS Trusts of the NICE guideline committee members. For the endovascular repair of complex aneurysms, custom made EVAR devices are required and these can cost significantly more than off-the-shelf EVAR stent grafts. The unit cost for a C-EVAR device was estimated to be £15,686 in the base case analysis, with an additional £512 for procedure consumables, as opposed to £6,500 for a standard device. The total perioperative cost of C-EVAR, including theatre time and medical care, was found to be £23,628 in the “fit for OSR” population, and £23,507 in the “unfit for OSR” population.

Results

Base case results from the two models are presented in *Tables 5 and 7* below. For patients with complex AAAs, fit for OSR, EVAR was more costly but also generated more QALYs than OSR. The general increase in perioperative mortality rates caused a bigger absolute change in OSR mortality, such that a smaller proportion of OSR patients survive to experience its long-term survival benefits. However, in this population, the total cost of EVAR was substantially higher than for OSR, mainly as a result of the increased cost of EVAR devices required for complex aneurysms.

Table 5: Base case results: NICE cost-utility model in "fit for OSR" population; base case results for complex AAA, elective repair

Strategy	Total (discounted)		Incremental		ICER (£/QALY)
	Costs	QALYs	Costs	QALYs	
OSR	£18,012	6.393			
EVAR	£27,751	6.677	£9,739	0.284	£34,288

Abbreviations: OSR=open surgery repair; EVAR= endovascular aortic repair; QALYs= quality-adjusted life years; ICER=incremental cost-effectiveness ratio;

A range of univariate sensitivity analyses were presented, with three parameters in particular being most influential, device cost, 30-day mortality OR and the post-perioperative mortality HR. In subgroup analyses based on age, gender and aneurysm diameter, the probability of EVAR being cost effective remained low at the £20,000 per QALY threshold, with the highest probability (26%) being in women with aneurysm diameter of 8.5 cm.

Scenario analyses which show the highest variation in the base case ICERs are presented in *Table 6* below.

Table 6: Selected scenario analyses: NICE cost-utility model in 'fit for OSR' population, complex AAA, elective repair

	Scenario	Incremental costs	Incremental QALYs	ICER (£/QALY)
0	Base case	£9,739	0.284	£34,288
1.	Perioperative mortality for OSR – UK NVD – 19.6%	£9,862	0.646	£15,269
2.	Perioperative mortality – OR from casemix-adjusted observational studies for complex AAA (0.90 (95% CI: 0.41-1.98))	£9,526	-0.130	Dominated
3.	Post-perioperative survival – various parametric curves	£9,370-£9,409	0.026-0.097	£97,276-£366,771
4.	Post-perioperative survival – HR from case-mix adjusted observational studies for complex AAA (1.94 (95% CI: 1.15-3.27))	£9,000	-1.219	Dominated
5.	Scenario 2 + scenario 4: using observational data for both peri-operative and post-perioperative survival	£10,267	-1.633	Dominated
6.	General population mortality calibration HR =15, equal	£8,304	0.153	£54,196

	postoperative mortality in the first 8 years, EVAR HR = 1.297 thereafter			
7.	Scenario 6 + complex EVAR device cost equal to standard device cost, £6,500 (as opposed to £15,686)	-£534	0.153	Dominating
8.	Fenestrated EVAR vs OSR*	£10,322	-0.095	Dominated

*Baseline perioperative mortality risk from NVR (3.9%), relative mortality effect from casemix-adjusted observational data (OR for F-EVAR vs. OSR – 0.810 (95%CI: 0.314 – 2.087)) and cost of F-EVAR of £16,502.

Abbreviations: OSR=open surgery repair, NVD= National Vascular Disease registry, OR=odds ratio, AAA=abdominal aortic aneurysm, CI=confidence interval, HR=hazard ratio, EVAR=endovascular aortic repair, QALYs=quality-adjusted life years, ICER=incremental cost-effectiveness ratio;

In the “unfit for OSR” population, as a result of the substantially higher perioperative mortality in the EVAR arm, patients never near the long-term survival in the no treatment arm, resulting in negative life time QALYs for patient treated with EVAR. This, combined with high device costs yielded C-EVAR to be the inferior treatment strategy.

Table 7: Base case results: NICE cost-utility model in “unfit for OSR” population – complex elective AAA, elective repair vs no repair

Strategy	Total (discounted)		Incremental		ICER (£/QALY) Costs
	Costs	QALYs	Costs	QALYs	
No intervention	£1,065	2.324			
EVAR	£23,754	1.523	£22,689	-0.802	Dominated

Abbreviations: EVAR= endovascular aortic repair; QALYs= quality-adjusted life years; ICER=incremental cost-effectiveness ratio;

The base case results were consistent with various sensitivity analyses such as subgroup analyses, threshold analyses for EVAR perioperative mortality rate (5%-50%), exploring various parameter models for long-term postoperative survival, EVAR device cost (£0 to £15,686), lower reintervention rates following EVAR, and assuming higher HRQoL decrement associated with ruptured aneurysms. In all cases EVAR was the dominated treatment strategy and was associated with substantial negative incremental net monetary benefit in comparison with no intervention in this less fit patient group.

On the basis of these overall results, C-EVAR is unlikely to be cost effective at the conventional threshold range of between £20K and £30K per QALY gained. The model results for the “fit for OSR” population were sensitive to changes in three parameters: the complex EVAR device cost, the 30-day mortality OR and the post-perioperative mortality HR. Each of these parameters is subject to substantial uncertainty because of the paucity of data on costs, and the assumption that peri-and post-perioperative mortality rates derived from infrarenal AAAs are transferable to complex AAAs. Threshold analysis found that the average unit cost of a C-EVAR device would need to be below £11,000 for it to be a cost-effective strategy in that population. In the “unfit for OSR” population, all sensitivity analyses results were consistent with the base case results. It is unlikely that C-EVAR could ever be a cost-effective treatment option when compared with no intervention in this patient population, even at device costs of £0, because of higher rates of postoperative mortality and reintervention.

SHTG review - economics (2018)

The SHTG review from 2018 reported on a case-control study from France by Michel *et al*. (2015), which looked at the 30-day costs of F/B-EVAR in comparison with OSR for the treatment of complex AAA and TAAA.[37] In this study, costs were higher with F/B-EVAR (€38,212 (£33,522) compared with €16,497 (£14,472) for OSR, p<0.01) per procedure. After group stratification, costs were higher with F/B-EVAR for PRAA/JRAA (€34,425 (£30,256) versus €14,907 (£13,102), p<0.01) and infradiaphragmatic TAAA (€37,927 (£33,334) versus €17,530 (£15,407), p<0.01), but not different for supradiaphragmatic TAAA (€54,710 (£48,084) versus €44,163 (£38,815), p=0.18). A cost effectiveness analysis was conducted to assess incremental costs per incremental death averted with F/B-EVAR versus OSR. The authors concluded that F/B-EVAR had a higher cost than OSR for a similar clinical outcome. In this study, the prospective cases were significantly older than the controls and comorbidities were generally more frequent, but there was no statistical difference in Charlson comorbidity index between the two cohorts

In an extension study by the same group of authors, 2-year costs (including acute hospital admissions, statutory health insurance, complementary health insurances, and patients' out of pocket expenditures) were higher in the F/B-EVAR group compared with the OSR group (€46,039 (£40,866) versus €22,779 (£20,220), p<0.001).[38] At 2 years, F/B-EVAR was dominated (in other words, more expensive and less effective) by OSR, except in the supradiaphragmatic TAAA subgroup where it is not expected to offer good value for money.

Additional economics literature

The literature search from 2018 was updated, and one additional US costing study published in 2018 was identified (Locham *et al.* 2018).[39] This retrospective study aimed to evaluate the outcomes and cost of OSR compared with endovascular repair of intact TAAA (n=879; 481 endovascular repairs v 398 OSR), using data from a large hospital-based, all-payer healthcare database. The patients undergoing endovascular repair were on average 5 years older (71.2 years v 66.5 years, p<0.001) and were more likely to be female (48% v 42%, p=0.05) and have hypertension (87% v 80%, p=0.009). The authors reported that in-hospital mortality was higher after OSR compared with endovascular repair (14.8% v 5.4%, p<0.001). Secondary outcomes including renal failure (34.7% v 13.5%), paraplegia/spinal cord ischaemia (7.8% v 2.9%), stroke (6.5% v 2.3%), cardiac complications (40.0% v 13.1%), and pulmonary complications (21.6% v 10.2%) were also significantly higher after OSR (all p< 0.05). Median length of stay was 6 days longer in patients undergoing OSR than in those undergoing endovascular repair (11 days v 5 days; p<0.001). Patients were more likely to be discharged home if they were undergoing endovascular compared with open repair (78% v 62%, p<0.001). The authors reported that the unadjusted total hospitalisation cost of OSR was significantly higher compared with F-/B-EVAR (median $44,355 (£35,973) v $36,612 (£29,693), p=0.004), and concluded that this was likely to be driven by longer length of stay and higher morbidity after OSR. The main limitation of this study is the absence of long-term follow up data evaluating factors such as durability and the costs of reinterventions.

Conclusion

Low-quality clinical effectiveness evidence suggests that either F-EVAR or B-EVAR is a clinically acceptable option when it comes to treating people with complex aneurysm anatomies such as JRAAs and TAAAs, particularly in those who are unsuitable for OSR. The absence of longer-term head-to-head comparison data and the high heterogeneity between cohorts, in particular the higher risk profile of those receiving endovascular treatment versus OSR, makes it difficult to make definitive conclusions, or to establish whether these techniques provide a clinical advantage over OSR. Most evidence comes from people receiving elective intervention, rather than those needing urgent care. It is not possible based on the existing evidence to make robust conclusions around the different treatment options in those requiring urgent or elective care.

The systematic reviews consistently reported concerns around the quality of the available published primary studies. C-EVAR techniques were often only offered if patients were unfit for OSR, and most studies included in the reviews did not attempt to account for such confounding with a form of statistical adjustment. Reviews with stricter inclusion criteria with regard to participation and study design were left with unanswered research questions. Conversely, the reviews which were more inclusive tended to caveat their conclusions with concerns around study quality. Several of the systematic reviews combined recently published studies with studies published approximately 10 to 15 years earlier. While this provides a comprehensive overview of the published evidence base, it does not take into account the inevitable improvements and refinements in C-EVAR over time. Overall, while there is a reasonable volume of secondary evidence available, robust conclusions are not possible because of the lack of good quality primary studies.

In some patients, OSR is unfeasible because of surgical risk, and C-EVAR or non-surgical management might be the only options. NICE recommends that C-EVAR is only performed in people with AAAs with special arrangements for consent and for audit and research that will determine the clinical and cost effectiveness of C-EVAR when compared with OSR, and all patients are entered onto the NVR.

NICE concluded that in people with AAAs, C-EVAR techniques were associated with a shorter procedure time, shorter in-hospital stay, fewer perioperative cardiovascular complications, and a greater chance of discharge to home (as opposed to another hospital or residential care). Mortality in people who survive the perioperative period was greater in people treated with C-EVAR techniques. NICE reported that C-EVAR and OSR could not be differentiated with regard to perioperative mortality, perioperative complications, duration of critical care and reintervention rate.

Evidence from other systematic reviews, which included studies rejected by NICE because of quality concerns, reported that there may be a perioperative survival benefit for F-EVAR and B-EVAR (but not Ch-EVAR) over OSR. They also reported that C-EVAR techniques were associated with higher reintervention rates.

No clear conclusions can be made about the cost effectiveness of complex EVAR in people with AAAs and TAAAs because of insufficient underlying clinical evidence. NICE cost-utility analysis found that in people fit for OSR, EVAR generates a gain in QALYs compared to OSR, yet the substantially higher device costs mean that the ICER is likely to exceed conventional cost effectiveness thresholds. NICE analyses also concluded that it is unlikely that EVAR is ever a cost-effective treatment option when compared with no intervention in patients not fit for OSR.

Regarding consensus on how these technologies should be implemented in clinical setting, the evidence is very limited. According to a national multicentre, cross-disciplinary consensus model in which more than 90% of the UK F-EVAR centres participated, there is agreement that F-EVAR should be used when there is moderate risk from OSR and need for suprarenal clamping, but it was less likely to be indicated in patients aged 85 years or more with 5.5-6 cm aneurysms, or short-necked infrarenal AAs.[40]

There appears to be a volume advantage associated with high-volume centres (in excess of 20-30 procedures per year) with regard to perioperative mortality.

Equality and diversity

SHTG advice takes into account equalities considerations across three key stages of the health technology assessment process:

- Topic / technology scoping
- HTA product development stage
- Development of recommendations by SHTG Council

Equalities considerations take into account protected characteristics, additional characteristics and other groups in the population who may experience poor health. Whether such groups can be identified depends on the topic and the evidence available. The outcome of this is reported in our HTAs.

About SHTG Recommendations

SHTG Recommendations are produced to inform a decision at a particular point in time and therefore is not routinely updated. The Recommendation will however be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the Recommendation given. For further information about the SHTG Recommendation process see:

[Scottish Health Technologies Group Products (shtg.scot)]

To propose a topic for SHTG consideration, please visit:

https://shtg.scot/request-advice/

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network www.knowledge.scot.nhs.uk, or by contacting your local library and information service.

A glossary of commonly used terms in health technology assessment is available from htaglossary.net.

Acknowledgements

Reviewers

SHTG Executive would like to thank the following individuals who provided peer review comments on the draft review which were considered by the authors:

- Professor Julie Brittenden, Professor of Vascular Surgery, University of Glasgow
- Mr Roderick Chalmers, Consultant Vascular Surgeon, NHS Lothian
- Dr Andrew Christie, Consultant Interventional Radiologist, NHS Greater Glasgow and Clyde
- Mr Orwa Falah, Consultant Vascular Surgeon and Lead Clinician of the Scottish National service for supra renal and thoracoabdominal Aneurysm, NHS Lothian
- Dr Martin Hennessy, Consultant Interventional Radiologist, NHS Greater Glasgow and Clyde
- Dr Fong Lau, Consultant Interventional Radiologist, University Hospital Hairmyres, NHS Lanarkshire
- Mr Bryce Renwick, Consultant Vascular Surgeon, NHS Grampian
- Dr Iain Robertson, Consultant Interventional Radiologist, NHS Greater Glasgow and Clyde (retired)
- Mr Tamim Siddiqui, Consultant Vascular Surgeon, NHS Lanarkshire
- Mr Andrew Tambyraja, Clinical Director and Consultant Surgeon, Royal Infirmary Edinburgh, NHS Lothian

SHTG Executive would like to thank the following organisation who provided peer review comments on the draft review which were considered by the authors:

- Research Advisory Group for The Aortic Dissection Charitable Trust

Declarations of interest were sought from all reviewers and clinical experts. Reviewers had no role in authorship or editorial control and the views expressed are those of Healthcare Improvement Scotland and the SHTG Council.

SHTG Evidence Review Team

SHTG Executive would like to thank the following individuals and organisations of the Evidence Review Team who provided comments on the draft review which were considered by the authors:

- Ms Janet Bouttell, Research Associate, Health Economics and Health Technology Assessment, Institute of Health and Wellbeing, University of Glasgow
- Dr Paul Campbell, Council Vice Chair, Clinical Director, Clinical Informatics, National Services Scotland
- Mr Ed Clifton, SHTG Unit Head, Healthcare Improvement Scotland
- Mr David Dunkley, Public Partner, Healthcare Improvement Scotland
- Ms Claire Fernie, Public Partner, Healthcare Improvement Scotland
- Ms Karen Macpherson, Lead Health Services Researcher, Healthcare Improvement Scotland
- Dr Ali Mehdi, Council Vice Chair, Consultant Orthopaedic and Trauma Surgeon, NHS Borders
- Dr Neil Smart, Council Chair, Consultant Anaesthetist, NHS Greater Glasgow and Clyde

SHTG Council

SHTG Executive would like to thank the following individuals and organisations on the SHTG Council for developing this Recommendation:

- Dr Paul Campbell, Council Vice Chair, Clinical Director, Clinical Informatics, National Services Scotland
- Mr Ed Clifton, SHTG Unit Head, Healthcare Improvement Scotland
- Mr Mark Cook, Director of Re-imbursement and Government Affairs, Association of British Healthcare Industries
- Mr David Dunkley, Public Partner, Healthcare Improvement Scotland
- Dr Karen Facey, Evidence Based Health Policy Consultant
- Ms Claire Fernie, Public Partner, Healthcare Improvement Scotland
- Ms Alison Harrison, Healthcare Quality and Improvement Directorate, DG Health and Social Care, Scottish Government
- Dr Rodolfo Hernandez, Research Fellow at Health Economics Research Unit, University of Aberdeen

- Mr Colin Marsland, Director of Finance, NHS Shetland
- Dr Ali Mehdi, Council Vice Chair, Consultant Orthopaedic and Trauma Surgeon, NHS Borders
- Dr Neil Smart, Council Chair, Consultant Anaesthetist, NHS Greater Glasgow and Clyde

Healthcare Improvement Scotland development team

- Ms Uzma Aslam, Senior Project Officer, SHTG, Healthcare Improvement Scotland
- Mr Rohan Deogaonkar, Health Economist, SHTG, Healthcare Improvement Scotland
- Ms Maria Petrova Dimitrova, Health Economist, SHTG, Healthcare Improvement Scotland
- Mr Paul Herbert, Information Scientist, SHTG, Healthcare Improvement Scotland
- Ms Jess Kandulu, Programme Manager, SHTG, Healthcare Improvement Scotland
- Ms Joanna Kelly, Lead Author/Health Services Researcher, SHTG, Healthcare Improvement Scotland
- Ms Charis Miller, Information Scientist, SHTG, Healthcare Improvement Scotland
- Mr James Stewart, Public Involvement Advisor, SHTG, Healthcare Improvement Scotland

Published July 2022

Suggested citation: Kelly, J; Aslam, U; Deogaonkar, R; Dimitrova, M; Herbert, P; Stewart, J. (2022). *Complex endovascular aneurysm repair. Glasgow/Edinburgh. NHS Healthcare Improvement Scotland.* *http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/topics_assessed/recommendation_01-20.aspx*

References

1. Mayo Clinic. Aortic aneurysm. [cited 21 April 2022]; Available from: https://www.mayoclinic.org/diseases-conditions/aortic-aneurysm/symptoms-causes/syc-20369472#:~:text=An%20aortic%20aneurysm%20is%20a,Abdominal%20aortic%20aneurysm.
2. Mayo Clinic. Aortic dissection. [cited 21 April 2022]; Available from: https://www.mayoclinic.org/diseases-conditions/aortic-dissection/symptoms-causes/syc-20369496.

3. Circulation Foundation: The Vascular Charity. Endovascular Aneurysm Repair (EVAR). [cited 21 April 2022]; Available from: https://www.circulationfoundation.org.uk/help-advice/abdominal-aortic-aneurysm/endovascular-aneurysm-repair-evar.
4. Patel SR, Ormesher DC, Griffin R, Jackson RJ, Lip GYH, Vallabhaneni SR. Comparison of Open, Standard, and Complex Endovascular Aortic Repair Treatments for Juxtarenal/Short Neck Aneurysms: A Systematic Review and Network Meta-Analysis. Eur J Vasc Endovasc Surg. 2022. Epub 2022/03/01.
5. Mayo Clinic. Thoracic aortic aneurysm. [cited 21 April 2022]; Available from: https://www.mayoclinic.org/diseases-conditions/thoracic-aortic-aneurysm/symptoms-causes/syc-20350188#:~:text=A%20thoracic%20aortic%20aneurysm%20is,to%20the%20body%20(aorta).
6. Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. Annals of cardiothoracic surgery. 2012;1(3):277-85.
7. NICE. Abdominal aortic aneurysm: diagnosis and management. 2020 [cited 2022 Mar 29]; Available from: https://www.nice.org.uk/guidance/ng156/chapter/Recommendations.
8. Buck DB, van Herwaarden JA, Schermerhorn ML, Moll FL. Endovascular treatment of abdominal aortic aneurysms. Nature reviews Cardiology. 2014;11(2):112-23.
9. Antoniou GA, Antoniou SA, Torella F. Endovascular vs. Open Repair for Abdominal Aortic Aneurysm: Systematic Review and Meta-analysis of Updated Peri-operative and Long Term Data of Randomised Controlled Trials. European Journal of Vascular and Endovascular Surgery. 2020;59(385-97).
10. Quatromoni JG, Orlova K, Foley PJ. Advanced Endovascular Approaches in the Management of Challenging Proximal Aortic Neck Anatomy: Traditional Endografts and the Snorkel Technique. Seminars in Interventional Radiology. 2015;32(3):289-303.
11. Scottish Health Technologies Group. Complex endovascular aneurysm repair in patients with juxta-renal or thoraco-abdominal aortic aneurysm. 2018 [cited 2022 Mar 29]; Available from: https://shtg.scot/our-advice/complex-endovascular-aneurysm-repair-in-patients-with-juxta-renal-or-thoraco-abdominal-aortic-aneurysm/.
12. National Vascular Registry. Annual report. 2021.
13. Sakalihasan N, Michel J, B., , Katsargyris A, Kuivaniemi H, Defraigne J-O, Nchimi A*, et al.* Abdominal aortic aneurysms. Nat Rev Dis Primers. 2018;4(34).
14. Sultan S, Concannon J, Veerasingam D, Tawfick W, McHugh P, Jordan F*, et al.* Endovascular versus conventional open surgical repair for thoracoabdominal aortic aneurysms. Cochrane Database of Systematic Reviews. 2022(3).
15. Parkinson F, Ferguson S, Lewis P, Williams IM, Twine CP. South East Wales Vascular Network. Rupture rates of untreated large abdominal aortic aneurysms in patients unfit for elective repair. J Vasc Surg. 2015;16(6):1606-12.
16. Thompson SG, Brown LC, Sweeting MJ, Bown MJ, Kim LG, Glover MJ*, et al.* Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: implications for surveillance intervals and their cost-effectiveness. Health Technol Assess. 2013;17(41):1-118.
17. Public Health Scotland. Scottish Abdominal Aortic Aneurysm Screening Programme Statistics. 2022 [cited 21 April 2022]; Available from: https://publichealthscotland.scot/media/11937/2022-03-01-aaa-publication-report.pdf.
18. National Institute for Health and Care Excellence (NICE). Abdominal aortic aneurysm: diagnosis and management (NG156). 2020 [cited 21 April 2022]; Available from: https://www.nice.org.uk/guidance/ng156.
19. Prapassaro T, Teraa M, Chinsakchai K, Hazenberg C, Hunnangkul S, Moll FL*, et al.* Mid-Term Outcomes of Chimney Endovascular Aortic Aneurysm Repair: A Systematic Review and Meta-analysis. Ann Vasc Surg. 2022;79:359-71. Epub 2021/10/20.
20. Verzini F, Gibello L, Varetto G, Frola E, Boero M, Porro L*, et al.* Proportional meta-analysis of open surgery or fenestrated endograft repair for postdissection thoracoabdominal aneurysms. Journal of Vascular Surgery. 2021;74(4):1377-85.e9.
21. Antoniou GA, Juszczak MT, Antoniou SA, Katsargyris A, Haulon S. Fenestrated or Branched Endovascular versus Open Repair for Complex Aortic Aneurysms: Meta-Analysis of Time to Event Propensity Score Matched Data. Journal of Vascular Surgery. 2021;73(3):1108.

22. Rocha RV, Lindsay TF, Friedrich JO, Shan S, Sinha S, Yanagawa B*, et al.* Systematic review of contemporary outcomes of endovascular and open thoracoabdominal aortic aneurysm repair. Journal of Vascular Surgery. 2020;71(4):1396-412.e12.
23. Mohamed N, Galyfos G, Anastasiadou C, Sachmpatzidis I, Kikiras K, Papapetrou A*, et al.* Fenestrated Endovascular Repair for Pararenal or Juxtarenal Abdominal Aortic Aneurysms: a Systematic Review. Ann Vasc Surg. 2020;63:399-408. Epub 2019/10/21.
24. He Y, Jia S, Sun G, Cao L, Wang X, Zhang H*, et al.* Fenestrated/Branched Endovascular Repair for Postdissection Thoracoabdominal Aneurysms: A Systematic Review with Pooled Data Analysis. Vasc Endovascular Surg. 2020;54(6):510-8.
25. Jones AD, Waduud MA, Walker P, Stocken D, Bailey MA, Scott DJA. Meta-analysis of fenestrated endovascular aneurysm repair versus open surgical repair of juxtarenal abdominal aortic aneurysms over the last 10 years. BJS open. 2019;3(5):572-84.
26. Doonan RJ, Girsowicz E, Dubois L, Gill HL. A systematic review and meta-analysis of endovascular juxtarenal aortic aneurysm repair demonstrates lower perioperative mortality compared with open repair. Journal of Vascular Surgery. 2019;70(6):2054-64.e3.
27. Rocha RV, Friedrich JO, Elbatarny M, Yanagawa B, Al-Omran M, Forbes TL*, et al.* A systematic review and meta-analysis of early outcomes after endovascular versus open repair of thoracoabdominal aortic aneurysms. Journal of Vascular Surgery. 2018;68(6):1936-45.e5.
28. D'Oria M, Wanhainen A, DeMartino RR, Oderich GS, Lepidi S, Mani K. A scoping review of the rationale and evidence for cost-effectiveness analysis of fenestrated-branched endovascular repair for intact complex aortic aneurysms. Journal of Vascular Surgery. 2020;72(5):1772-82.
29. Bootun R, Carey F, Al-Thaher A, Al-Alwani Z, Crawford M, Delbridge M*, et al.* Comparison between open repair with suprarenal clamping and fenestrated endovascular repair for unruptured juxtarenal abdominal aortic aneurysms. J Cardiovasc Surg (Torino). 2022;63(1):44-51. Epub 2021/09/29.
30. de Guerre L, Varkevisser RRB, Swerdlow NJ, Liang P, Li C, Dansey K*, et al.* Sex differences in perioperative outcomes after complex abdominal aortic aneurysm repair. J Vasc Surg. 2020;71(2):374-81. Epub 2019/07/10.
31. Geisbusch S, Kuehnl A, Salvermoser M, Reutersberg B, Trenner M, Eckstein HH. Editor's Choice - Hospital Incidence, Treatment, and In Hospital Mortality Following Open and Endovascular Surgery for Thoraco-abdominal Aortic Aneurysms in Germany from 2005 to 2014: Secondary Data Analysis of the Nationwide German DRG Microdata. European Journal of Vascular & Endovascular Surgery. 2019;57(4):488-98.
32. von Meijenfeldt GCI, Alberga AJ, Balm R, Vahl AC, Verhagen HJM, Blankensteijn JD*, et al.* Results from a nationwide prospective registry on open surgical or endovascular repair of juxtarenal abdominal aortic aneurysms. J Vasc Surg. 2022;75(1):81-9.e5. Epub 2021/07/02.
33. Sheldon H, Garratt E. Patient preferences for alternative surgical techniques for abdominal aortic aneurysm repair: report of a patient survey: Picker Institute Europe. 2008 [cited 25 April 2022]; Available from: https://picker.org/wp-content/uploads/2022/01/Patient-preferences-for-...abdominal-aortic-aneurysm-repair.pdf.
34. Katsargyris A, Klonaris C, Verhoeven EL. Is volume important in aneurysm treatment outcome? The Journal of cardiovascular surgery. 2017;58(2):187-93.
35. Saricilar EC, Iliopoulos J, Ahmad M. A systematic review of the effect of surgeon and hospital volume on survival in aortic, thoracic and fenestrated endovascular aneurysm repair. J Vasc Surg. 2021;74(1):287-95. Epub 2021/02/07.
36. NHS Commissioning Board. Clinical Commissioning Policy: Use of Complex Endovascular Stent Grafts in Abdominal Aortic Aneurysm. 2013 [cited 21 April 2022]; Available from: https://www.england.nhs.uk/wp-content/uploads/2013/04/a04-p-a.pdf.
37. Michel M, Becquemin JP, Clément MC, Marzelle J, Quelen C, Durand-Zaleski I. Editor's Choice – Thirty day Outcomes and Costs of Fenestrated and Branched Stent Grafts versus Open Repair for Complex Aortic Aneurysms. European Journal of Vascular and Endovascular Surgery. 2015;50(2):189-96.

38. Michel M, Becquemin J-P, Marzelle J, Quelen C, Durand-Zaleski I. A Study of the Cost-effectiveness of Fenestrated/branched EVAR Compared with Open Surgery for Patients with Complex Aortic Aneurysms at 2 Years. European Journal of Vascular and Endovascular Surgery. 2018;56(1):15-21.
39. Locham S, Dakour-Aridi H, Nejim B, Dhaliwal J, Alshwaily W, Malas M. Outcomes and cost of open versus endovascular repair of intact thoracoabdominal aortic aneurysm. J Vasc Surg. 2018;68(4):948-55.
40. Cross J, Raine R, Harris P, Richards T. Indications for fenestrated endovascular aneurysm repair. Br J Surg. 2012;99(2):217-24.