Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Recommendations
February 2025

In response to an enquiry from the NHSScotland Strategic Planning Board

Transcatheter aortic valve implantation (TAVI) for the treatment of people with symptomatic severe aortic stenosis who are at low surgical risk

Recommendations for NHSScotland

Transcatheter aortic valve implantation (TAVI) should be considered for people with symptomatic severe aortic stenosis who are at low surgical risk. TAVI is likely to be cost effective compared with surgical aortic valve replacement (SAVR) in this population, depending on TAVI device costs. Procurement decisions should be coordinated to ensure that Scotland achieves the best value when purchasing TAVI valves.

Approximately 80% of people with symptomatic severe aortic stenosis are at low surgical risk. Offering TAVI to patients who are at low surgical risk will require increasing the capacity of healthcare services to deliver equitable access to TAVI across NHSScotland. Priority access to TAVI services should be maintained for people in higher surgical risk categories.

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

What were we asked to look at?

We were asked to review the evidence comparing TAVI with SAVR for the treatment of people with symptomatic severe aortic stenosis who are at low surgical risk.

Why is this important?

Aortic stenosis is the most common heart valve disease in adults in Europe.[1, 2] The prevalence of aortic stenosis increases steeply with age and is expected to become more prevalent as the Scottish population gets older.[1] Without intervention, people with symptomatic severe aortic stenosis have a poor prognosis, with an average life expectancy of 2–3 years and survival rates of 15–50% at 5 years after diagnosis.[1]

For people with symptomatic severe aortic stenosis the two main treatment options are SAVR and TAVI. Data from randomised controlled trials (RCTs) in people with symptomatic severe aortic stenosis who are at high or intermediate surgical risk show that TAVI is either as good as or better than SAVR.[1] Approximately 80% of people with symptomatic severe aortic stenosis who are suitable for SAVR are defined as low surgical risk.[3] This review examines the evidence for TAVI compared with SAVR in the low surgical risk population.

What was our approach?

We reviewed the published literature on the clinical effectiveness, cost effectiveness, safety and patient experience of TAVI for the treatment of symptomatic severe aortic stenosis in people at low surgical risk. More information about SHTG Recommendations is available on our website.

What next?

Our recommendations will be used by the NHSScotland Strategic Planning Board to inform decisions on the provision of TAVI across Scotland, including whether TAVI should be offered to people with symptomatic severe aortic stenosis who are at low surgical risk.

Key points from the evidence

Clinical effectiveness and safety

1. Six meta-analyses were selected for review based on their methodological quality, length of follow up, outcomes and primary study designs.[4-9] They included an overlapping set of five RCTs and eight observational studies reporting all-cause mortality after TAVI compared with SAVR in people with symptomatic severe aortic stenosis who are at low surgical risk.

    - A Cochrane review of four RCTs (n=2,818) reported no statistically significant difference in all-cause mortality at 30 days follow up (relative risk (RR) 0.60, 95% confidence interval (CI) 0.33 to 1.44) or 1 year follow up (RR 0.70, 95% CI 0.44 to 1.11).[6]

    - A meta-analysis of three RCTs (n=2,748) found no statistically significant difference in all-cause mortality at 4–5 years follow up (odds ratio (OR) 0.94, 95% CI 0.65 to 1.37).[8] One of the RCTs, the NOTION trial reported consistent findings at 8 and 10 years follow up.[10, 11]

    - A time to event meta-analysis of three RCTs and five observational studies (n=5,444) found no statistically significant difference in all-cause mortality over the first 2 years of follow up (hazard ratio (HR) 1.08, 95% CI 0.89 to 1.31).[9] Meta-analysis of the observational studies found a statistically significantly higher risk of all-cause mortality for the TAVI group compared with the SAVR group between 2 and 8 years follow up (HR 1.51, 95% CI 1.14 to 2.00, n=2,696). These longer term results should be interpreted with caution because observational studies have inherent biases compared with RCTs.

2. Three recently published RCTs (UK TAVI, DEDICATE, NOTION-2) also concluded there were no statistically significant differences in all-cause mortality in comparisons of TAVI and SAVR at 1 year follow up.[12-14]

3. Four out of five RCTs that reported length of hospital stay found that patients who had a TAVI procedure needed to stay in hospital for significantly fewer days than patients who had SAVR.[6, 12, 14] The only RCT that reported a longer hospital stay for TAVI patients (STACCATO) used a higher risk vascular access route for performing TAVI.[6]

4. A meta-analysis of studies in people at low or intermediate surgical risk (n=3,681 low risk patients) found a statistically significant improvement in quality of life for people who had a TAVI procedure compared with people who had SAVR at 30 days follow up. At 1 year follow up there was no statistically significant between group difference in quality of life scores.[15]

5. The six meta-analyses reported that TAVI was associated with statistically significantly higher risks of new pacemaker implantation and paravalvular leaks. In the same meta-analyses, TAVI was associated with significantly lower risks of new onset atrial fibrillation, acute kidney injury and bleeding.

    - A Cochrane review (n=2,748) demonstrated a statistically significantly higher risk of new permanent pacemaker implantation in the TAVI group compared with the SAVR group (HR 3.65, 95% CI 1.50 to 8.87).[6]

    - Two meta-analyses (n=2,611 and n=2,219) reported a seven- to nine-fold higher risk of paravalvular leaks in patients who had TAVI compared with patients who had SAVR.[4, 8] It was unclear whether the severity of these paravalvular leaks affected patient outcomes.

    - The Cochrane review also found statistically significantly lower risks of new onset atrial fibrillation (HR 0.21, 95% CI 0.15 to 0.30), acute kidney injury (HR 0.30, 95% CI 0.16 to 0.58) and any bleeding event (HR 0.31, 95% CI 0.16 to 0.72) in the TAVI group compared with the SAVR group.[6]

    - Safety results were consistent over the long term (more than 1 year follow up), across more recent RCTs and in meta-analyses of observational studies.[4, 8, 12-14]

Cost effectiveness

6. A systematic review of six economic analyses comparing TAVI with SAVR in people with symptomatic severe aortic stenosis who are at low surgical risk, found that TAVI was dominant (more effective and less costly) in one study, cost effective in three studies and not cost effective in one study.[16] The study that reported TAVI was not cost effective was based on older (2010 vs 2018) TAVI devices that may have a different effectiveness and cost profile.

7. Nine primary economic evaluations compared TAVI (using the SAPIEN 3 valve) with SAVR.[17-24]

    - Seven analyses conducted in European countries using local health system cost data found the SAPIEN 3 TAVI valve to be dominant or cost effective (that is, below willingness to pay thresholds) compared with SAVR.[17-19, 21, 23-26] The analyses used outcome data from the PARTNER 3 trial, combined with local costs. Results were stable across time horizons of up to 30 years. TAVI was not cost effective when the analyses were restricted to a time horizon of 5 years.

    - Economic evaluations from the United States (US) and Japanese payer perspectives found that TAVI was dominant or cost effective compared with SAVR.[20, 22]

- Key drivers of cost effectiveness attributed to TAVI are greater survival benefit, fewer complications and lower long term management costs. Higher device and 1 year follow up costs for TAVI are offset by lower healthcare costs over a lifetime time horizon.

8. In 2021, the National Institute for Health and Care Excellence (NICE) published an economic evaluation using data from RCTs and the UK TAVI registry.[27] The NICE model found that TAVI was not cost effective compared with SAVR in people at low surgical risk over a 15-year time horizon.

    - The conflicting results of the NICE evaluation compared with other published economic evaluations can mainly be attributed to higher device procurement costs in the UK (£17,500) compared to other countries.

    - The device price in the UK would need to be lower than £14,800 for TAVI to be cost effective at a willingness to pay threshold of £30,000 per quality adjusted life-year (QALY).[28]

9. An economic analysis from the perspective of the UK NHS (2024) used 4-year follow up data from the Evolut Low Risk trial to compare TAVI using the Evolut self-expanding valve with SAVR.[29] TAVI was cost effective at an assumed UK TAVI valve list price of £17,500 over a lifetime horizon.

    - The improved cost effectiveness of TAVI in this analysis compared with the NICE evaluation can be attributed to the availability of longer follow up data from the Evolut Low Risk trial, which suggests improved survival and outcomes after TAVI that leads to a ten-fold increase in QALYs over a 15-year time horizon.

Patient and social aspects

10. This section describes patient and social aspects relating to TAVI among people who have symptomatic severe aortic stenosis regardless of their surgical risk because the literature rarely reports the level of surgical risk applicable to study participants.

11. A retrospective cohort study (n=10,069) in NHS England found inequalities in access to aortic valve replacement procedures (TAVI or SAVR) for women, people living in more deprived areas and people of African or south Asian descent.[30]

12. A systematic review (n=353) explored patient experiences of having a TAVI procedure.[31]

    - Having an individualised care plan was important to patients because it helped mitigate any disappointment or frustration relating to outcomes after the procedure. When

people felt their treatment goals had been met, they reported improved quality of life even when objective measures suggested minimal change in functional outcomes.

- Some patients experience persistent psychosocial and physical symptoms after their procedure, often because of pre-existing comorbidities. For many people this led to feelings of disappointment, isolation and vulnerability.

13. A systematic review (n=1,096), a qualitative study (n=18) and a cross-sectional study (n=98) explored people's reasons for undergoing treatment for aortic stenosis and factors influencing their decision.[32-34] Patients were often motivated by a strong desire to regain some semblance of a normal life and to continue living independently. The published literature suggests this could be achieved more quickly after TAVI compared with SAVR.

SHTG Council considerations

1. The Council recognised that not all patients who are classed as low surgical risk are suitable for TAVI. The decision on whether TAVI is the best treatment option for each patient is made by a multidisciplinary team as part of the shared decision making process. This ensures that each patient is offered the most appropriate treatment for their individual circumstances.

2. The Council agreed that TAVI was clinically beneficial and offered an improved safety profile compared with SAVR for patients in the low surgical risk group. The Council also agreed that TAVI may lead to an improved procedure related experience for patients compared with SAVR, based on quality of life evidence and qualitative studies.

3. The Council discussed the significance of people who had TAVI being more likely to experience paravalvular leaks compared with SAVR. An invited clinical expert explained that it is difficult to compare rates of paravalvular leaks between the two interventions, and that only moderate or severe leaks were likely to affect patient outcomes. The Council noted that newer TAVI valves had a lower risk of paravalvular leaks.

4. The Council asked the clinical expert for insight into the relative length of hospital stay for patients after TAVI or SAVR. The expert stated that TAVI patients tend to leave hospital after no more than a day in a general ward or outpatient clinic, whereas SAVR patients may require 1–2 days in intensive care and remain on a post-surgical ward for 4–5 days.

5. The Council discussed the UK based evidence on the cost effectiveness of TAVI and how the cost of TAVI devices appeared to be a key driver of the conclusions. The Council highlighted the draft NICE late stage assessment which estimated that TAVI valves would need to cost less than £14,800 for the procedure to be cost effective for patients at all levels of surgical risk.[28] The Council agreed that procurement decisions should be coordinated to ensure that Scotland achieves the best value when purchasing TAVI valves, taking into account the possibility of volume based rebates from device manufacturers.

6. The Council highlighted that patients with symptomatic severe aortic stenosis who are at low surgical risk represent a much larger population than those currently eligible for TAVI in Scotland (inoperable or high surgical risk). The Council recognised that offering TAVI to low surgical risk patients would present challenges for the delivery of TAVI services across NHSScotland because of limited capacity. The Council was clear in their opinion that if capacity were to increase, then access to TAVI should be prioritised based on surgical risk, so that patients who have the fewest alternative treatment options are offered TAVI first.

7. Concerns were voiced by the Council that there appeared to be unequal access to TAVI depending on where people lived, both within Scotland and compared with other areas of the UK and Europe. A clinical expert informed the Council that the number of TAVI procedures per million population was expected to increase nationally, across all TAVI centres, to align with rates in NHS England. They also advised, specifically in relation to the potential unequal access to TAVI within Scotland, that the small number of people getting

TAVI in some board areas could lead to exaggerated differences in TAVI procedures per million population. The Council agreed it was important that there was equal access to TAVI for all suitable patients living in Scotland.

8. The Council understood that patients who are categorised as low surgical risk tend to be younger and have a longer life expectancy than higher risk patients, and that life expectancy for this patient group could exceed the durability of TAVI valves. It was accepted that the results from the NOTION trial after 10 years follow up suggest this may not be an issue with newer TAVI valves.

Contents

Definitions

Aortic stenosis: narrowing of the aortic heart valve caused by calcification. The condition ranges from mild to severe and can be symptomatic or asymptomatic. If left untreated it can lead to heart failure and death.[35]

Surgical aortic valve replacement (SAVR): open heart surgery to remove and replace the aortic valve with a prosthetic valve.[26] SAVR is performed under general anaesthesia and requires cardiopulmonary bypass.

Transcatheter aortic valve implantation (TAVI): a minimally invasive procedure where the aortic valve is functionally replaced by implanting a bioprosthetic replacement valve within the existing valve.[26] The valve is inserted using a catheter passed through the patient's vasculature, most commonly the femoral artery in the groin. Once in place, the valve expands to compress the existing valve against the walls of the aorta.

Introduction

For people with symptomatic severe aortic stenosis the two main treatment options are SAVR and TAVI. SAVR can be performed using different surgical approaches (full sternotomy or less invasive approaches), different kinds of valves and different valve anchoring techniques (sutured and sutureless).[1]

The TAVI procedure involves the minimally invasive insertion of a bioprosthetic valve to functionally replace the existing aortic valve.[1] The bioprosthetic valve is compressed within a dedicated delivery system which, once positioned within the existing aortic valve, expands to compress the native valve against the walls of the aorta. Depending on the patient's anatomy and device characteristics, the TAVI procedure can use one of four access routes. The transfemoral (TF) route is the most common approach. The subclavian/transaxilliary (S/T), transapical (TA) and transaortic (TAo) approaches are used when the patient's anatomy precludes access via the transfemoral route.

Data from RCTs in people with symptomatic severe aortic stenosis who are at high or intermediate surgical risk have found that TAVI is as good or better than SAVR.[1] Recent RCT data from people who are at low surgical risk has initiated debate about whether TAVI should be the primary treatment option for the majority of people with symptomatic severe aortic stenosis, regardless of surgical risk.[5]

Approximately 80% of people with symptomatic severe aortic stenosis who are suitable for surgery are at low surgical risk.[5] This review examines the evidence for TAVI compared with SAVR in patients at low surgical risk.

Defining low surgical risk

The most common surgical risk algorithms are STS Predicted Risk of Mortality (STS-PROM) and EuroSCORE.[1] These tools identify and quantify risk factors that help to predict mortality after cardiac surgery. The exact cutoff values for risk scores vary across the literature and can be arbitrary. In European guidelines, low risk is defined as <4% using both the STS-PROM and EuroSCORE tools.[36]

To estimate the overall surgical risk for each patient, risk scores are used alongside an assessment of frailty and major organ complications (not covered by the scores).[1] A specialised heart team normally conducts this assessment.

Research question

What is the clinical effectiveness, cost effectiveness, safety and patient perspectives of TAVI compared with SAVR for the treatment of people with symptomatic severe aortic stenosis who are at low surgical risk?

Literature search

A systematic search of the secondary literature was carried out between 19 and 24 June 2024 to identify systematic reviews, health technology assessments and other evidence based reports. Medline, Embase and Web of Science databases were searched for systematic reviews and meta-analyses.

The primary literature was systematically searched between 19 and 24 June 2024 using the following databases: Medline, Embase and Web of Science. Results were limited to any study type and English language publications from 2014 onwards.

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

Concepts used in all searches included: symptomatic severe aortic stenosis, low surgical risk, transcatheter aortic valve implantation (TAVI) and transcatheter aortic valve replacement (TAVR). A full list of resources searched, and terms used is available on request.

Health technology description

There are several commercially available TAVI valves that have been approved for use in people with symptomatic severe aortic stenosis who are at low surgical risk (*Table 1*).[37] There are other TAVI valves that have not been specifically approved for use in the low risk patient population. For example, the Navitor Vision (Abbott Medical), Myval Octacor (Meril), Hydra (SMT), Trilogy (Jenavalve) or Allegra TAVI System (Biosensors International). Most TAVI valves are available in a range of sizes and can be used through different vascular access routes to suit individual anatomies.

As shown in *Table 1*, TAVI valves are bioprosthetic devices made from porcine or bovine pericardial tissues. This could mean that TAVI is unacceptable to patients with particular religious beliefs or people who follow a vegetarian or vegan diet.

Table 1: TAVI valves with regulatory approval for use in people with aortic stenosis who are at low surgical risk[37]

Valve	Manufacturer	Valve frame	Valve leaflets	Delivery routes
Balloon expanding				
SAPIEN	Edwards Lifesciences	Stainless steel	Bovine pericardium	TF, TA
SAPIEN 3, SAPIEN 3 Ultra, SAPIEN XT	Edwards Lifesciences	Cobalt chromium	Bovine pericardium	TF, TA, TAo
Self-expanding				
Acurate, Acurate Neo, Acurate Neo 2, Acurate Prime	Boston Scientific	Nitinol	Porcine pericardium	TF, TA
Corevalve Evolut R, Corevalve Evolut Pro, Corevalve Evolut Pro+, Corevalve Evolut FX	Medtronic	Nitinol	Porcine pericardium	TF, S/T, direct aortic

TF = transfemoral; TA = transapical; TAo = Transaortic; S/T = subclavical or transaxilliary

NICE late stage assessment

NICE has produced a draft late stage assessment on the use of TAVI to treat symptomatic severe aortic stenosis in people at any level of surgical risk.[28] The late stage assessment reviews the incremental clinical, economic and non-clinical benefits of different versions of a technology that is already in widespread use in the NHS, in order to determine whether price variations are justified and to inform procurement decisions across NHS England. The late stage assessment does not replace NICE guidance on when to use TAVI, rather the assessment helps to inform which valves to use once the decision to undergo TAVI has been made.[27, 28, 38]

The NICE late stage assessment covers eleven TAVI valves with regulatory approval that are currently in use within NHS England: Acurate Neo 2, Allegra, Corevalve Evolut R, Corevalve Evolut Pro+, Corevalve Evolut FX, Hydra, Myval Octacor, Navitor, SAPIEN 3, SAPIEN 3 Ultra and Trilogy.

The draft late stage assessment recommends:

> '1.1 There is not enough evidence to determine whether incremental innovations can justify price variations between different transcatheter heart valves for transcatheter aortic valve implantation (TAVI) in adults with aortic stenosis.

1.2 Use the least expensive option available that is clinically appropriate for TAVI in the person with aortic stenosis.

1.3 NHS trusts should provide access to a range of valves, so that the most clinically appropriate valve is available for everyone with aortic stenosis.'[28]

The finalised draft of the NICE late stage assessment is expected to be published in 2025.

Epidemiology

Aortic stenosis

People with severe aortic stenosis are likely to develop symptoms associated with narrowing of the aortic valve and the overload of the heart's left ventricle.[1] These symptoms include fainting, exercise-induced chest pain (angina), breathlessness and congestive heart failure.

Aortic stenosis is the most common heart valve disease in adults in Europe.[1, 2] Its prevalence rises steeply with age, affecting approximately 5% of people aged 65, and 12.4% of people aged ≥75.[2] The prevalence of aortic stenosis is likely to increase with progressive ageing of the Scottish population.[1] Currently, 20% of the population is aged 65 or older and this is predicted to rise to 24% by 2030.[1]

Age is a major determinant of surgical risk in people with symptomatic severe aortic stenosis. The 2022 European guidelines recommend TAVI as the preferred intervention for all patients with symptomatic severe aortic stenosis who are aged 75 years or older.[36]

Without intervention, people with symptomatic severe aortic stenosis have a poor prognosis. Average survival is 2–3 years and survival rates are 15–50% at 5 years after diagnosis.[1]

An estimated third of people with symptomatic severe aortic stenosis are not referred for SAVR.[1, 39] The decision whether to refer for surgery or not, appears to be based on perceived operative risk, patient choice or the belief that the condition is not severe enough.[39] Patients who are not referred for surgery are more likely to be older, to have left ventricular dysfunction and to have multiple comorbidities.[1]

A population based modelling study estimated the UK age specific point prevalence of severe aortic stenosis as 1.48% of people aged 55 or older. [3] This equates to an estimated 24,498 people aged ≥55 in Scotland who have severe aortic stenosis. Within this Scottish population, 68.3% (n=16,732) were assumed to have symptomatic disease. The model goes on to estimate that 58.4% (n=9,771) of this symptomatic population are suitable for SAVR and of these symptomatic Scottish patients who are suitable for surgery:

- 6.2% (n=606) are at high surgical risk

- 13.9% (n=1,358) are at intermediate surgical risk
- 79.9% (n=7,808) are at low surgical risk.

Based on the population based modelling study, we calculated the TAVI rate per million population (pmp) in Scotland. We assumed that patients were eligible for surgery and either high, intermediate or low risk, in the proportions outlined in the study. We also assumed that everyone in each risk category would receive TAVI rather than SAVR.

The results of our calculations are presented in *Table 2*. As expected, extending eligibility for TAVI to people with symptomatic severe aortic stenosis at low surgical risk would substantially increase the number of procedures undertaken in Scotland.

Table 2: Approximate number of TAVI procedures pmp in Scotland if eligibility is expanded to other risk categories

Patient population	n TAVI pmp
High risk	112
Intermediate risk	251
Low risk	1,443
High, intermediate and low risk combined	1,806

TAVI in Scotland

In Scotland, TAVI is a treatment option for patients considered unsuitable for surgery (inoperable) or patients considered to be at high surgical risk.[1] SHTG advice in 2019 recommended that TAVI should also be an option for patients at intermediate surgical risk.

There are currently three hospitals that perform TAVI procedures for people living in Scotland:[40]

- Golden Jubilee National Hospital (since 2018)
- Aberdeen Royal Infirmary (since 2019)
- Royal Infirmary of Edinburgh (since 2012).

In 2022–2023 the Scottish Cardiac Audit Programme recorded 575 TAVI procedures in Scotland, representing a 17.8% increase over the previous year.[40] TAVI is currently only available in Scotland to patients who are considered inoperable or at high surgical risk. The cardiac audit data therefore does not include data from patients who are intermediate or low risk.

There is variation in the rate of TAVI procedures across Scottish health boards.[40] In 2022–2023, there were 105 TAVI procedures per million population (pmp) nationally. In the same year, NHS Grampian

reported 165.4 procedures pmp, while NHS Greater Glasgow and Clyde reported 81.8 procedures pmp. In the same year, 40% of TAVI procedures were performed at the Lothian TAVI centre, 36% were performed at the Glasgow centre and 24% were performed in Aberdeen.

The procedure rate in Scotland remains lower than the rest of the UK where there were 113 procedures pmp in 2021–2022. NHS England recommends the use of TAVI for all patients with symptomatic severe aortic stenosis who are over 75 years of age or who are at intermediate or higher surgical risk.

Inequalities

Incidence of aortic stenosis

A retrospective study of patient level administrative data (n=896,274) from Maryland (US) found that black and Hispanic patients had significantly lower incidence of hospitalisation for aortic stenosis compared with white patients (adjusted incidence rate ratio (IRR) 0.45, 95% CI 0.42 to 0.49 for black vs white; adjusted IRR 0.67, 95% CI 0.58 to 0.78 for Hispanic vs white).[41] Black and Hispanic patients with aortic stenosis were younger than white patients and more likely to be female. The study categorised patients as black, white or Hispanic. These categories may not accurately reflect a person's ancestry.

Geographical variation in TAVI procedures

A study comparing the number of TAVI procedures performed in different areas in England found an 11-fold regional variation in the number of procedures pmp (17.4 to 194 procedures pmp).[42, 43] The study authors believe that these differences cannot be explained solely by regional variations in patient demographics.

In 2019, the median waiting time from referral to having a TAVI procedure in NHS England was 20 weeks, with variation across regions from 9 weeks to 35 weeks.[42] In the same year, 299 people died while on a waiting list for a TAVI procedure. If this statistic was extended to cover all 35 TAVI centres in the UK, this would translate to over 500 potentially avoidable deaths per year.

Long waiting times can also lead to clinical deterioration and hospital admissions for patients. A survey of 23 UK TAVI centres found that 22% of TAVI procedures were performed on patients who had already been hospitalised for their condition.[42, 43] The median duration of hospital stay among these patients was 33 days compared with 3 days for people treated before hospitalisation.

In one large TAVI centre, 39% of urgent inpatient procedures were performed on people who had been accepted for TAVI and were on the waiting list but had experienced deterioration before receiving an appointment. According to the Scottish cardiology audit, around 33% of TAVI procedures in Scotland are classed as urgent.[40]

Socioeconomic inequalities

A retrospective cohort study using hospital episode data explored socioeconomic inequalities in access to aortic valve replacement (AVR), including SAVR or TAVI, within NHS England.[30] The study found that people in the most deprived quintile of the index of multiple deprivation (IMD) had significantly lower odds of receiving an AVR procedure compared with people from the least deprived quintile (OR 0.73, 95% CI 0.69 to 0.76). Additionally, a higher proportion of people from the most deprived quintile experienced delays in receiving an AVR procedure (33%) compared with those in the least deprived quintile (26%).

Three studies from the US reported socioeconomic inequalities in access to treatment for aortic stenosis and associated patient outcomes.[44-46]

- People with aortic stenosis who lived in lower income communities had less access to both TAVI and SAVR.[45]
- Patients with aortic stenosis who lived in lower income neighbourhoods were more likely to be female, under 75, have a higher comorbidity burden and be recorded as African American, Hispanic or Native American ($p<0.01$ for all).[44, 45]
- People from lower income areas were more likely to undergo SAVR compared with TAVI (adjusted OR 1.17, 95% CI 1.11 to 1.24).[44]
- Age adjusted rates of TAVI were higher in areas with higher median household income (317.5 TAVI procedures per 100,000 people) compared with lower median income households (170 procedures per 100,000 people). For each $1,000 (£763) decrease in median household income, there were 0.2% fewer TAVI procedures per 100,000 people.[46]
- Compared with people living in areas with the highest income, TAVI patients living in lower income neighbourhoods had a greater risk of needing mechanical ventilation after their procedure (adjusted OR 1.20, 95% CI 1.02 to 1.42).[45]

The findings of these studies from the US may not generalise to Scotland because healthcare funding differs significantly between the two countries.

Ethnicity

The retrospective cohort study Rice et al (2023) also explored inequalities in access to AVR (surgical or TAVI) among different ethnic groups.[30] Ethnicity was nominally self-reported in the data sources and may not accurately reflect the ethnic background of patients.

People from black or south Asian ethnic backgrounds were less likely to receive an AVR compared with people from a white background (OR 0.70, 95% CI 0.60 to 0.82 and OR 0.75, 95% CI 0.69 to 0.82, respectively). People from black (32%) or south Asian (36%) backgrounds were also more likely to experience delays in getting an AVR procedure compared with people from a white background (28%).

Two studies from the US described inequalities in access to TAVI and patient outcomes in people with different ethnic ancestries.[46, 47] Neither study used clear definitions of the genetic heritage of the people included in their analysis.

- Black patients were approximately 2 years younger than white patients who had SAVR or TAVI.[47]
- For every 1% increase in the proportion of black patients living in an area, the number of TAVI procedures decreased by 1.1% (95% CI 0.6% to 1.7%).[46] For every 1% increase in the proportion of Hispanic patients living in an area, the number of TAVI procedures decreased by 1.2% (95% CI 0.2% to 2.2%).
- After TAVI, there was a statistically significantly higher risk of acute kidney injury among patients with Hispanic (OR 1.56, 95% CI 1.24 to 1.96) or Asian or pacific islander ancestry (OR 1.67, 95% CI 1.02 to 2.75) compared with white ancestry.[47]
- After SAVR, there were significantly higher rates of death among black patients compared with white patients (OR 1.36, 95% CI 1.09 to 1.71). Compared with white patients, there were significantly higher rates of bleeding among black (OR 1.25, 95% CI 1.13 to 1.39), Hispanic (OR 1.58, 95% CI 1.39 to 1.8) and Asian or pacific islander (OR 1.52, 95% CI 1.24 to 1.85) patients. There were significantly more cases of acute kidney injury in black patients compared with white patients (OR 1.56, 95% CI 1.4 to1.73).

Gender

The retrospective cohort study using NHS England data found that overall, women were significantly less likely to receive AVR (surgical or TAVI) compared with men (OR 0.65, 95% CI 0.63 to 0.66).[30] There was no statistically significant gender difference in the proportion of people who had delayed AVR.

A retrospective cohort study in France (n=2,429) found that women with severe aortic stenosis were older at diagnosis ($p<0.001$) and had more symptoms than men ($p=0.007$).[48] After age matching, AVR was performed significantly less often in women ($p=0.018$). The 5-year cumulative incidence of AVR was 79% (standard deviation (SD) 2%) for men and 70% (SD 2%) for women ($p<0.001$). Being male was an independent predictor of earlier AVR (within 3 months of diagnosis) in the age matched cohort (OR 1.37, 95% CI 1.11 to 1.69).

A systematic review of five observational studies (n=47,933) found that being female was associated with higher 30-day mortality (OR 1.53, 95% CI 1.31 to 1.79) after a TAVI procedure, but not mortality at 1 year follow up (OR 0.78, 95% CI 0.61 to 1.00).[49] Being female was associated with a higher risk of vascular complications (OR 1.43, 95% CI 1.23 to 1.65) which may explain some of the increased mortality risk. The higher rates of vascular complications were thought to be related to the size of the instruments used during the TAVI procedure and the smaller vascular anatomy of women. The analysis did not adjust for potential confounding factors which may have introduced bias into these results.

An older meta-analysis of four RCTs (n=3,758) found a statistically significant survival advantage for women who had TAVI compared with SAVR at 1 and 2 years follow up.[50] There was no significant difference in mortality between TAVI and SAVR for men. This analysis was based on trials that used earlier generation TAVI valves and recruited patients who were at high surgical risk. As a result, it is unclear if these findings apply to current TAVI valves or patients at low surgical risk.

Clinical effectiveness

Six meta-analyses comparing TAVI with SAVR in people at low surgical risk were reviewed.[4-9] These six analyses were chosen because they:

- analysed only studies recruiting patients at low surgical risk
- were published after 2019 (when the relevant trials had been published)
- are of good methodological quality
- reported outcomes after different lengths of follow up to assess whether treatment effects lasted over time
- described time to event analyses
- included additional outcomes of interest
- compared results from RCTs and observational studies.

Within these analyses, there are a total of five RCTs and eight observational studies, with considerable overlap in included studies across the meta-analyses. All meta-analyses used the Cochrane risk of bias tool to appraise the quality of included RCTs. The five RCTs were unblinded. The unblinded assessment of subjective outcomes, such as quality of life, introduces a high risk of bias for these outcomes. Most trials were sponsored by a manufacturer of TAVI devices.

All six meta-analyses defined low surgical risk as an STS-PROM or EuroSCOREs of <4%. All five RCTs reported a composite primary outcome and all-cause mortality. Other relevant outcomes included cardiac death, cardiovascular events and aortic valve haemodynamic parameters.

The original publication of the Evolut Low Risk trial (Popma et al, 2019) was at high risk of attrition bias because it used a novel Bayesian analysis to predict missing data.[51] Subsequent publications reported the full dataset from the Evolut Low Risk trial (Forrest et al, 2023).[52, 53] The publication used in the six meta-analyses was the earlier publication by Popma et al (2019). The studies by Forrest et al (2023) report results at 3 years follow up, rather than the 30 day and 1 year follow up reported by Popma et al (2019).

Most meta-analyses that included observational studies used the ROBINS-I tool to appraise study quality. Concerns about risk of bias in the observational studies related to confounding, patient selection and missing data. The FinnValve registry study was described as having a high risk of bias

for confounding, patient selection and deviations from intended interventions.[5, 9] The propensity score matched study by Schaefer et al (2019) was regarded as having a high risk of bias for patient selection.[5, 54]

The key characteristics of the RCTs and observational studies reviewed are presented in *Table 3*.

There is some uncertainty about the appropriateness of including the SURTAVI trial low risk subgroup in the meta-analyses. According to the authors of a Cochrane review, the SURTAVI trial investigators felt that participants in their trial, even those with STS-PROM scores less than 4%, were not representative of the low surgical risk population.[6]

The STACCATO trial was ended early because of safety concerns. This RCT was the only one that used a transapical approach to TAVI. The transapical approach is not routine practice in Scotland, with 1.91% of procedures using this access route in 2022–2023.[40]

Table 3: Characteristics of primary studies comparing TAVI with SAVR in people with severe aortic stenosis who are at low risk of surgical complications

Study	Study centres	n	Mean STS-PROM score (TAVI vs SAVR)	Mean age (years)	TAVI valve types	Primary outcome
RCTs included in meta-analyses[6, 26]						
Evolut Low Risk (2019)	Australia, Canada, France, Japan, the Netherlands, New Zealand, US	1,468	1.9% vs 1.9%	73.6	Corevalve*, Corevalve Evolut R, Corevalve Evolut PRO	Composite of all-cause mortality and disabling stroke
NOTION (2015)	Denmark, Sweden	280	2.9% vs 3.1%	79.1	Corevalve*	Composite of all-cause mortality, stroke and myocardial infarction
PARTNER 3 (2019)	US, Canada, Australia, New Zealand, Japan	1,000	1.9% vs 1.9%	73.8	SAPIEN 3	Composite of all-cause mortality, stroke and rehospitalisation
STACCATO (2012)	Denmark	72	3.1% vs 3.4%	81.0	SAPIEN*	Composite of all-cause mortality, major stroke and renal failure
SURTAVI (low risk subgroup) (2017)	US, the Netherlands, Germany, UK, Spain, Switzerland, Sweden, Canada, Denmark	254	2.3% vs 2.3%	75.0	Corevalve*, Corevalve Evolut R	Composite of all-cause mortality and stroke
RCTs not included in meta-analyses						
DEDICATE (2024)[12]	Germany	1,414	1.8% vs 1.9% (medians)	74.0	Acurate Neo, Acurate Neo 2, Lotus Edge,	Composite of all-cause mortality and fatal or non-fatal stroke

					SAPIEN XT, SAPIEN 3, SAPIEN 3 Ultra, Corevalve Evolut R, Corevalve Evolut Pro, Corevalve Evolut Pro+, Portico	
NOTION-2 (2024)[13]	Denmark, Norway, Sweden, Finland, Iceland	370	1.1% vs 1.1% (medians)	71.1	Any valve (physician choice)	Composite of all-cause mortality, stroke or rehospitalisation
UK TAVI (2022)[14]	UK	913	2.6% vs 2.7% (medians)	81 (median)	SAPIEN, SAPIEN XT, SAPIEN 3, Corevalve Evolut, Corevalve Evolut R, Corevalve Evolut Pro, Lotus, Acurate, Acurate Neo, Direct Flow Medical, Portico	All-cause mortality
Observational studies (including registries)						
AVALON registry (2022)[9]	Poland	922**	2.5% vs 2.0%	NR	NR	All-cause mortality
FinnValve registry (2019)[4, 5, 7, 9]	Finland	608**	2.1% vs 1.8%	75.8	Corevalve Evolut R, SAPIEN 3, Acurate Neo, Lotus	Survival
GARY registry (2019)[4, 7]	Germany	20,549	<4% vs 1.8%	71.0	SAPIEN, SAPIEN XT, SAPIEN 3, Corevalve*	Survival
LRT trial (2018)[4]	US	919	1.8% vs 1.6%	73.6	Corevalve*, Corevalve Evolut	All-cause mortality

					R, Corevalve Evolut Pro, SAPIEN 3	
OBSERVANT registry (2016)[5, 7, 9]	Italy	710	2.6% vs 2.5%	80.1	SAPIEN XT, Corevalve*	All-cause mortality
Oh et al (2019)[4]	Korea	261	<4% vs <4%	82.5	NR	Cardiac death
Schaefer et al (2019)[4, 5, 9]	Germany	218**	2.0% vs 2.0%	75.2	First generation devices	All-cause mortality
Vilalta et al (2019)[9]	Spain, Canada	342**	2.6% vs 2.8%	77.7	NR	All-cause mortality, stroke and readmission for heart failure

**First generation TAVI devices that are no longer marketed*

***Propensity matched cohort size rather than the full unmatched cohort size*

NR = not reported

Short term outcomes

A Cochrane review assessed all-cause mortality, cardiac death and rehospitalisation at 30 days and 1 year follow up.[6] The meta-analysis included four RCTs (n=2,818): Evolut Low Risk, NOTION, PARTNER 3 and STACCATO. The STACCATO trial (n=72) was excluded in sensitivity analyses with no substantial effect on the results of the meta-analysis.

Table 4 presents the results of the Cochrane meta-analysis. There were no statistically significant differences in all-cause mortality or cardiac death between the TAVI and SAVR groups within 30 days follow up. Evidence certainty was moderate for these outcomes. At 1 year follow up, the risk of cardiac death was statistically significantly lower for people treated with TAVI.

There was no statistically significant difference between the groups in the rate of rehospitalisation within 30 days. At 1 year follow up, there was a statistically significantly lower risk of rehospitalisation among patients who had TAVI compared with those who had SAVR.

Three RCTs in the Cochrane review reported length of hospital stay as an outcome (PARTNER 3, NOTION, STACCATO). Both the PARTNER 3 and NOTION trial reported a significantly shorter length of hospital stay for patients who had TAVI compared with SAVR. In the PARTNER 3 trial, median length of stay was 3 days (interquartile range (IQR) 2 to 3) for TAVI and 7 days (IQR 6 to 8) for SAVR, giving a mean difference between treatments of 4 or 5 days ($p<0.001$). The NOTION trial reported the median TAVI length of hospital stay as 8.9 days (SD 6.2) and length of stay after SAVR as 12.9 (SD 11.6), giving a mean difference of between 1.8 and 6.2 days ($p<0.001$). The STACCATO trial reported a longer length of stay for TAVI patients compared with SAVR patients. This trial used the higher risk transapical access route when performing TAVI. Evidence certainty for this outcome was very low.

Table 4: Results of a Cochrane meta-analysis comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[6]

Outcome	n participants	n studies	RR (95% CI)
30 days follow up			
All-cause mortality	2,818	4	0.69 (0.33 to 1.44)
Cardiac death	2,818	4	0.71 (0.32 to 1.56)
Rehospitalisation	2,468	2	0.64 (0.39 to 1.06)
1 year follow up			
All-cause mortality	2,748	3	0.70 (0.44 to 1.11)
Cardiac death	2,748	3	0.57 (0.34 to 0.95)
Rehospitalisation	2,468	2	0.63 (0.46 to 0.85)

Long term outcomes

A meta-analysis of three RCTs (Evolut Low Risk, NOTION, PARTNER 3) reported outcomes after 4–5 years follow up (n=2,748).[26] There were no statistically significant differences in all-cause mortality or major cardiovascular events between the TAVI and SAVR groups at 4–5 years follow up (*Table 5*).

There was no statistically significant difference between TAVI and SAVR aortic valve reintervention rates, which suggests that the long term durability of replacement valves is comparable.

Patients in the TAVI group had statistically significantly larger mean aortic valve area compared with the SAVR group at 4–5 years follow up. It is unclear if this difference in aortic valve area is clinically significant.

Table 5: Results from a meta-analysis comparing TAVI and SAVR outcomes at 4–5 years follow up in people with severe aortic stenosis who are at low surgical risk [8]

Outcome	n participants	n studies	Relative effect (95% CI)
All-cause mortality	2,611	3	OR 0.94 (0.65 to 1.37)
Major cardiovascular events	2,611	3	OR 0.96 (0.67 to 1.38)
Aortic valve reintervention	2,611	3	OR 0.93 (0.52 to 1.66)
Aortic valve area (cm^2/m^2)	2,331	2	Mean difference (MD) 0.10 (0.05 to 0.15)
Transvalvular mean gradient (mm Hg)	2,331	2	MD 0.60 (-3.94 to 2.73)

The NOTION trial has collected annual outcomes data for 10 years.[10, 11] Of 280 trial participants, 133 were still alive at 8 years follow up and 100 were alive at 10 years follow up. At 8 and 10 years follow up, there were no statistically significant differences in risk of all-cause mortality between the TAVI and SAVR groups (HR 0.98, 95% CI 0.71 to 1.36 and HR 1.0, 95% CI 0.7 to 1.3, respectively).

The primary composite outcome of all-cause mortality, stroke and myocardial infarction showed no significant differences at 8 and 10 years follow up (HR 1.01, 95% CI 0.74 to 1.40 and HR 1.0, 95% CI 0.7 to 1.3 respectively). At 8 years follow up the trial reported no statistically significant differences between groups in the risk of cardiovascular death (HR 0.93, 95% CI 0.64 to 1.34). This outcome was not reported at 10 years follow up.

Outcomes over time

Two meta-analyses used reconstructed individual patient data and time to event analyses to generate mortality estimates for TAVI compared with SAVR over time.[5, 9]

The most recent meta-analysis included three RCTs (Evolut Low Risk, NOTION, PARTNER 3) and five propensity score matched cohort studies, with a total of 5,444 participants.[9] In the 2 years after TAVI or SAVR, there were no statistically significant differences in mortality risk between the two groups (HR 1.08, 95% CI 0.89 to 1.31). From 2 to approximately 8 years follow up, there was evidence of a statistically significantly higher mortality risk in people who had TAVI compared with SAVR (HR 1.51, 95% CI 1.14 to 2.00).

The meta-analysis authors caution against drawing definitive conclusions from their analysis because the difference in mortality at 2 to 8 years follow up was only reported in meta-analyses of

observational studies, not the RCTs. They also noted a large drop in the number of people at risk after 2 years follow up and that the propensity score matched cohorts still had imbalances in participant characteristics after matching.

The second meta-analysis included the same three RCTs (Evolut Low Risk, NOTION, PARTNER 3) and three observational studies, with a total of 4,169 participants.[5] The results of the meta-analysis are similar to the more recent analysis described above. Mortality hazard ratios initially favoured TAVI over SAVR, but this effect diminished over time. Two years after the procedure, mortality risk was statistically significantly higher in the TAVI group compared with the SAVR group (HR 1.77, 95% CI 1.29 to 2.43).

Limitations noted in this meta-analysis include a lack of long term follow up data from the two largest RCTs, the risk of excluding events that occurred before the landmark cutoff (1 year) and a loss of power by excluding these events. The authors did not comment on any differences in results between RCTs and observational studies.

Comparing results from RCTs and observational studies

Two meta-analysis compared mortality reported in RCTs and observational studies.[4, 7] Both provide little detail on their literature searches and methods.

The most recent meta-analysis included four RCTs (Evolut Low Risk, NOTION, PARTNER 3, SURTAVI) and five observational studies, with a total of 27,276 participants.[4] Results for the meta-analysis using only RCTs, only observational studies and both study designs combined are presented in *Table 6*.

Only the analysis limited to RCTs found statistically significant results favouring TAVI. This contrasts with other meta-analyses of RCTs. This could be because this meta-analysis included the SURTAVI trial that was excluded from other meta-analyses because the authors felt that trial participants were not representative of the low surgical risk population.

Sensitivity analyses excluded studies that fell outside the 95% CI on funnel plots. By excluding the observational study by Schaefer et al, the difference in mortality risk became statistically significant in the observational studies and all studies meta-analyses.

Table 6: Results from a meta-analysis comparing results from RCTs and observational studies for TAVI compared with SAVR in people with severe aortic stenosis who are at low surgical risk[4]

Outcome	RCTs RR (95% CI)	Observational studies RR (95% CI)	All RR (95% CI)
All-cause mortality (30 day)	0.44 (0.20 to 0.98)	0.75 (0.31 to 1.77)	0.64 (0.37 to 1.10)
All-cause mortality (1 year)	0.62 (0.39 to 0.97)	1.02 (0.71 to 1.45)	0.76 (0.51 to 1.12)

The second meta-analysis compared results from RCTs with results from registry studies.[7] The analysis included the same four RCTs (Evolut Low Risk, NOTION, PARTNER 3, SURTAVI) plus three registry studies, with a total of 24,819 participants. The results of the meta-analysis are similar to the more recent analysis reported above.

Recent RCTs (not included in the meta-analyses)

Three RCTs were identified that have not been included in meta-analyses comparing TAVI with SAVR in people at low surgical risk.[12-14] The most likely reason for this is the recent publication date of two of the trials and the definitions of surgical risk used in these trials.

The UK TAVI trial (n=913) was conducted across all UK NHS hospitals that offer TAVI.[14] The trial was originally intended to recruit people with intermediate or high operative risk. Trial participants had a median STS-PROM risk score of 2.6% (IQR 2.0% to 3.4%) which is widely regarded as indicating low surgical risk. The choice of TAVI valve was left to the individual clinician's discretion.

Five people randomised to the TAVI group transferred to the SAVR group and 17 people randomised to surgery crossed over to the TAVI group. Baseline characteristics were well balanced between the two groups. Participants had a median age of 81 years (IQR 78 to 84) and 46.4% were female. At 1 year follow up, 21 people (4.6%) in the TAVI group and 30 people (6.6%) in the SAVR group had died. There were no statistically significant differences in the risk of all-cause mortality or cardiovascular death between the two groups at 1 year follow up (*Table 7*).

The median length of hospital stay for patients who had TAVI was 3 days (IQR 2 to 5). For patients who had SAVR, the median length of hospital stay was 8 days (IQR 6 to 13 days). After their valve replacement, 94.2% of patients who had TAVI were discharged to their own home compared with 82.6% of patients in the surgery group.

Table 7: Results of the UK TAVI trial comparing TAVI with SAVR at 1 year follow up in people with severe aortic stenosis who are at low surgical risk[14]

Outcome	Intervention group (n=458) n events	Control group (n=455) n events	HR (95% CI)
All-cause mortality	21	30	0.69 (0.38 to 1.26)
Cardiovascular death	13	15	0.86 (0.40 to 1.83)

The DEDICATE trial (n=1,414) was conducted across 38 centres in Germany.[12] The trial recruited participants at low or intermediate surgical risk who were eligible for both TAVI and SAVR. The definitions used for low and intermediate surgical risk in this trial were an STS-PROM score of ≤2% for low risk and 2–4% for intermediate risk. The DEDICATE trial was designed as a non-inferiority RCT with a predefined non-inferiority margin of HR 1.14. The trial was not funded by manufacturers of aortic valve devices and participants were treated using any TAVI valve that had regulatory approval.

A total of 1,414 people with symptomatic severe aortic stenosis were recruited. The trial did not recruit consecutive patients because some people requested a specific treatment and were excluded. The baseline characteristics of participants appear well balanced between the two groups, with a median STS-PROM score of 1.8%. Median age was 74 (SD 4) and 57% of participants were male.

Twelve people randomised to the TAVI group switched to the SAVR group and 70 people randomised to SAVR swapped to the TAVI group. To assess the impact of this crossover on the trial results, the authors report both an intention to treat analysis and an as-treated analysis.

The primary outcome was a composite of all-cause mortality and fatal or non-fatal stroke (*Table 8*). At 1 year follow up, the primary outcome was recorded for 5.4% of the TAVI group and 10.0% in the SAVR group (HR 0.53, 95% CI 0.35 to 0.79, p<0.001 for non-inferiority). Results from the as-treated analysis were consistent with the intention to treat analysis.

The median length of hospital stay was 5 days (IQR 4 to 7) for patients who had TAVI and 9 days (IQR 8 to 12) for patients who had SAVR. More patients who had TAVI were discharged directly to their own home (74.7%) compared with SAVR patients (40.4%).

Table 8: Results of the DEDICATE non-inferiority RCT comparing TAVI with SAVR at 1 year follow up in people with severe aortic stenosis who are at low surgical risk[12]

Outcome	Intervention group (n=701) n events	Control group (n=713) n events	HR (95% CI)
All-cause mortality, fatal or non-fatal stroke	37	68	0.53 (0.35 to 0.79)
All-cause mortality	18	42	0.43 (0.24 to 0.73)

The NOTION-2 trial (n=370) was a multicentre RCT conducted in Scandinavia that compared TAVI with SAVR in people aged ≤75 with symptomatic severe aortic stenosis and low surgical risk (STS-PROM score <4%).[13] Unlike previous TAVI trials, NOTION-2 included patients with either tricuspid or bicuspid aortic valves (most trials only included people with tricuspid valves).

A total of 370 people completed the trial, which is less than the predicted sample size needed for statistical power. Of these, 100 participants (27%) had bicuspid aortic valves. Two patients crossed over from the TAVI group to the surgery group, while nine patients crossed over from SAVR to TAVI. The baseline characteristics were well balanced between the groups. Mean age of participants was 71.1 and 42.7% were aged 70 or younger. The mean STS-PROM score was <1%.

Results from the NOTION-2 trial are presented in *Table 9*. There were no statistically significant differences between the groups in the risk of the composite primary outcome (all-cause mortality, stroke or rehospitalisation) with an absolute risk difference of 3.1% at 1 year follow up.

There were no statistically significant differences between groups in rehospitalisation rates. The length of hospital stay was significantly shorter for TAVI patients compared with SAVR patients (median 3 versus 7 days).

For patients who had a bicuspid aortic valve, the risk of the primary outcome was 14.3% in the TAVI group compared with 3.9% in the SAVR group, resulting in an absolute risk difference of 10.4%. While not statistically significant, this result may suggest that people with bicuspid aortic valves should be referred to SAVR rather than TAVI.

Table 9: Results of the NOTION-2 trial comparing TAVI with SAVR at 1 year follow up in people with severe aortic stenosis who are at low surgical risk[13]

Outcome	Intervention group (n=187) % patients	Control group (n=183) % patients	HR (95% CI)
All-cause mortality, stroke or rehospitalisation	10.2	7.1	1.4 (0.7 to 2.9)
Rehospitalisation (procedure related)	1.1	4.0	0.3 (0.06 to 1.3)
Rehospitalisation (valve related)	2.2	1.1	1.9 (0.3 to 10.3)
Rehospitalisation (heart failure related)	0.6	0	–
Length of hospital stay, median days (IQR)	3 (2 to 4)	7 (6 to 9)	4 (4 to 5)

Guidelines

Recommendations from NICE (2021)[27] on interventions for treating aortic valve disease state:

> 'Offer surgery, if suitable (by median sternotomy or minimally invasive surgery), as first-line intervention for adults with severe aortic stenosis, aortic regurgitation or mixed aortic valve disease and an indication for surgery who are at low or intermediate surgical risk. TAVI is not cost effective for people at low or intermediate surgical risk at the current list price.'*[27]

The NICE interventional procedures guidance (IPG) on TAVI does not define the categories of surgical risk for offering TAVI rather than surgery.[38] The IPG states:

> 'Current evidence on the safety and efficacy of transcatheter aortic valve implantation (TAVI) for aortic stenosis is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.'[38]

* When the guidance was published in 2021 the list price for a TAVI valve was £17,500.[27] The NICE late stage assessment, in draft 2025, estimates that TAVI valves would need to be priced at £14,800 or less in order to be cost effective across surgical risk categories.[28]

Safety

Safety outcomes were reported in four of the meta-analyses discussed in the clinical effectiveness section.[4, 6-8]

Short term outcomes

The Cochrane review (n=2,818) reported multiple safety outcomes at 30 days and 1 year follow up (*Table 10*).[6] At 30-days follow up, there was a statistically significantly higher rate of new permanent pacemaker implantation among people who had a TAVI procedure compared with people who had SAVR (HR 3.65, 95% CI 1.50 to 8.87). There were statistically significantly lower rates of new onset atrial fibrillation, acute kidney injury and bleeding in people who had TAVI. These differences remained statistically significant at 1 year follow up.

Table 10: Results of a Cochrane meta-analysis comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[6]

Outcome	n participants	n studies	RR (95% CI)
30 days follow up			
Stroke	2,818	4	0.69 (0.33 to 1.44)
Myocardial infarction	2,748	3	0.82 (0.42 to 1.58)
New pacemaker implantation	2,683	3	3.65 (1.50 to 8.87)
New onset atrial fibrillation	2,683	3	0.21 (0.15 to 0.30)
Acute kidney injury	2,753	4	0.30 (0.16 to 0.58)
Any bleeding	2,753	4	0.31 (0.16 to 0.62)
1 year follow up			
Stroke	2,748	3	0.77 (0.51 to 1.16)
Myocardial infarction	2,748	3	0.78 (0.45 to 1.33)
New pacemaker implantation	2,683	3	3.48 (1.40 to 8.62)
New onset atrial fibrillation	2,683	3	0.26 (0.19 to 0.35)
Any bleeding	2,403	2	0.33 (0.25 to 0.44)

Long term outcomes

The meta-analysis comparing outcomes between TAVI and SAVR at 4–5 years follow up (n=2,748) reported similar findings to the Cochrane analysis.[8] At 4–5 years follow up, the risk of permanent pacemaker implantation remained three times higher and the risk of new onset atrial fibrillation remained 70–80% lower among people who had TAVI.

The meta-analysis reported additional safety outcomes: paravalvular leak, valve thrombosis and endocarditis. The only statistically significant difference between the treatment groups was the risk of paravalvular leaks, which were eight times more likely in people who had TAVI compared with people who had SAVR (*Table 11*).

Table 11: Results for long term safety outcomes (4–5 years) in a meta-analysis comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[8]

Outcome	n participants	n studies	OR (95% CI)
Disabling stroke	2,331	2	0.84 (0.52 to 1.36)
Permanent pacemaker implantation	2,611	3	3.09 (1.36 to 7.01)
Paravalvular leak	2,611	3	8.21 (4.18 to 16.14)
New atrial fibrillation	1,197	2	0.27 (0.17 to 0.30)
Myocardial infarction	1,197	2	0.69 (0.34 to 1.40)
Valve thrombosis	2,331	2	3.11 (0.29 to 33.47)
Endocarditis	2,611	3	0.71 (0.35 to 1.48)

In the NOTION trial (n=280), there were no statistically significant differences between the TAVI and SAVR groups for stroke or myocardial infarction risk at 8 or 10 years follow up.[10, 11] At 8 and 10 years follow up the risk of needing a new permanent pacemaker remained three or four times higher in the TAVI group (42.5% vs 10.9% and 44.7% vs 14.0% respectively). The risk of new onset atrial fibrillation remained significantly lower in the TAVI group at 8 and 10 years follow up (50.0% vs 74.1% and 52.0% vs 74.1%, respectively).

Comparing results from RCTs and observational studies

The most recent meta-analysis comparing outcomes from meta-analyses of RCTs, observational studies and combined study designs reported five safety outcomes (total n=27,276).[4] They found consistent evidence across study designs for a three-to-four-fold increase in the risk of new pacemaker implantation for people who had TAVI compared with people who had SAVR (*Table 12*).

There was consistent evidence from all study designs of a seven-to-nine-fold higher risk of paravalvular leaks with TAVI compared with SAVR. This might be an exaggerated estimate of effect because some of the studies in the analysis used first generation TAVI valves that were more prone to leakage.

Evidence of a reduced risk of acute kidney injury or major bleeding events in people who had TAVI was only found in meta-analyses of RCTs. In meta-analyses of observational studies, the differences were not statistically significant.

Table 12: Results from meta-analyses comparing results from RCTs and observational studies on TAVI compared with SAVR in people with severe aortic stenosis who are at low surgical risk[4]

Outcome	RCTs RR (95% CI)	Observational studies RR (95% CI)	All RR (95% CI)
New pacemaker implantation	3.61 (1.43 to 9.11)	4.31 (1.21 to 15.41)	3.53 (1.90 to 6.55)
Major bleeding	0.29 (0.14 to 0.63)	0.40 (0.11 to 1.53)	0.35 (0.16 to 0.77)
Acute kidney injury	0.27 (0.14 to 0.56)	2.62 (0.05 to 135.37)	0.60 (0.13 to 2.80)
Stroke	0.58 (0.22 to 1.48)	0.79 (0.42 to 1.51)	0.74 (0.46 to 1.18)
Paravalvular leak	9.81 (2.70 to 35.65)	8.97 (2.42 to 33.16)	7.28 (3.83 to 13.81)

Recent RCTs

The UK TAVI, DEDICATE and NOTION-2 trials all report safety outcomes.[12, 14]

In the UK TAVI trial (n=913), at 1 year follow up, there were statistically significantly fewer major bleeding events in the TAVI group compared with the SAVR group (*Table 13*). There was a statistically significantly higher rate of new permanent pacemaker implantation among the TAVI group compared with the SAVR group.

The UK TAVI trial reported a total of 483 adverse events in 252 people (55%) in the TAVI group. In the SAVR group, there were 545 adverse events affecting 255 people (56%). Of these adverse events, 61.5% in the TAVI group and 69.9% in the SAVR group were deemed related to the intervention. Approximately 20% of adverse events were classified as cardiac disorders, 12% as infections and 8–12% related to the surgical or medical procedure.

Table 13: Safety results from the UK TAVI RCT at 1 year follow up, comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[14]

Outcome	Intervention group (n=458) n events	Control group (n=455) n events	HR (95% CI)
Stroke	24	12	1.98 (0.95 to 4.11)
Major bleeding events	33	92	0.33 (0.24 to 0.45)
New pacemaker implantations	65	33	2.05 (1.43 to 2.94)
Infective endocarditis	5	2	2.46 (0.54 to 11.17)
Kidney replacement therapy	3	8	0.37 (0.11 to 1.23)
Myocardial infarction	6	5	1.17 (0.33 to 4.30)
Aortic valve reintervention	10	5	1.98 (0.72 to 5.42)

In the DEDICATE trial (n=1,414), there were statistically significantly lower rates of disabling stroke, new onset atrial fibrillation and major, life threatening or disabling bleeding in the TAVI group compared with the SAVR group (*Table 14*).[12] There was a statistically significantly increased risk of new permanent pacemaker implantation in people in the TAVI group compared with the SAVR group.

Table 14: Safety results from the DEDICATE non-inferiority RCT comparing TAVI with SAVR at 1 year follow up in people with severe aortic stenosis who are at low surgical risk[12]

Outcome	Intervention group (n=701) n events	Control group (n=713) n events	HR (95% CI)
Stroke	20	32	0.61 (0.35 to 1.06)
Disabling stroke	9	21	0.42 (0.19 to 0.88)
Myocardial infarction	7	14	0.51 (0.20 to 1.19)
New onset atrial fibrillation	86	211	0.36 (0.28 to 0.46)
New pacemaker implantation	82	47	1.81 (1.27 to 2.61)
Prosthetic valve dysfunction	11	4	2.44 (0.87 to 8.15)
Endocarditis	4	7	0.66 (0.18 to 2.19)
Prosthetic valve thrombosis	5	2	2.09 (0.50 to 11.64)
Aortic valve reintervention	4	2	1.70 (0.38 to 9.78)
Major, life threatening or disabling bleeding	30	119	0.24 (0.16 to 0.35)
Acute kidney injury	9	17	0.56 (0.24 to 1.21)

In the NOTION-2 trial (n=370), the TAVI group had lower rates of major life threatening bleeding and new onset atrial fibrillation (*Table 15*).[13] There were statistically significantly higher rates of non-disabling stroke and permanent pacemaker implantation in the TAVI group compared with the SAVR group. In the subgroup of patients with bicuspid aortic valves, there was a three-fold higher risk of paravalvular regurgitation compared with patients with a tricuspid aortic valve.

Table 15: Safety results from the NOTION-2 trial comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[13]

Outcome	Intervention group (n=187) % patients	Control group (n=183) % patients	HR (95% CI)
Stroke	5.4	1.6	3.3 (0.9 to 12.0)
Major or life threatening bleeding	4.8	17.5	0.3 (0.1 to 0.5)
Acute kidney injury	0.5	0.5	1.0 (0.1 to 15.5)
New onset atrial fibrillation	3.2	41.7	0.06 (0.03 to 0.2)
New permanent pacemaker implantation	15.1	8.0	2.0 (1.1 to 3.8)
Endocarditis	1.1	1.6	0.6 (0.1 to 3.9)
Myocardial infarction	2.1	1.6	1.3 (0.3 to 5.9)
Aortic reintervention	1.1	2.2	0.5 (0.1 to 2.7)

Device durability

The NOTION trial (n=280) reported valve durability outcomes at 6, 8 and 10 years follow up for patients at low surgical risk (*Table 16*).[10, 11, 26] At all three follow up points, there were statistically significantly more patients in the SAVR group that experienced structural valve deterioration compared with the TAVI group.

By 10 years follow up, the TAVI group showed statistically significantly lower rates of bioprosthetic valve dysfunction. There were no statistically significant differences between the groups in rates of valve related death.

These results are based on TAVI performed with the first generation Corevalve self-expanding valve which is rarely used in current practice.

Table 16: Valve durability in the NOTION trial comparing TAVI with SAVR in people with severe aortic stenosis who are at low surgical risk[10, 11, 26]

Outcome	Intervention group (n=187) % patients	Control group (n=183) % patients	p value
6 years follow up			
Bioprosthetic valve deterioration	56.0	67.0	0.07
Non-structural valve deterioration	54.0	58.0	>0.05
Structural valve deterioration	5.0	24.0	<0.0001
8 years follow up			
Bioprosthetic valve dysfunction	62.0	70.5	0.064
Structural valve deterioration	13.9	28.6	0.0017
Non-structural valve deterioration	54.7	60.7	0.18
Bioprosthetic valve failure	8.7	10.5	0.61
Valve related death	5.0	3.7	0.6
10 years follow up			
Severe structural valve deterioration	1.5	10.0	0.004
Severe bioprosthetic valve dysfunction	20.5	43.0	<0.001
Bioprosthetic valve failure	9.7	13.8	0.3
Valve related death	5.0	3.7	0.6

Patient and social aspects

The literature on people's experiences, preferences, values and motivations relating to TAVI rarely reports the level of surgical risk of study participants. The studies in this section describe patient and social aspects in people who have symptomatic severe aortic stenosis, regardless of their surgical risk.[1, 15, 26, 31-34, 55]

From previous SHTG recommendations

In 2019, SHTG published recommendations on the use of TAVI to treat people with symptomatic severe aortic stenosis who are at intermediate surgical risk.[1] Six qualitative studies were included in the review; three on people's experiences of TAVI and three on factors influencing patient decision making. The key points from the 2019 recommendations are replicated here.

- There is evidence from three qualitative studies of people undergoing TAVI suggesting that:
    - people's experiences before having a TAVI procedure vary. While some people are hopeful that TAVI could improve their lives, others are fearful about facing death because of their weak health. People felt it was important to have a consultation before their TAVI procedure to manage expectations about the procedure and the recovery process.
    - People experience different levels of improvement after TAVI. Some people experience reductions in symptom burden (such as less pain, fatigue and shortness of breath) which leads to improvements in quality of life (eg ability to stay independent or take part in social activities). Other people continue to experience health issues after TAVI that are related to comorbidities or frailty.
    - Support for family caregivers is an important consideration when developing care pathways for TAVI patients, particularly relating to providing information about the recovery process.
- There is evidence from three qualitative studies on people's decision making around undergoing TAVI:
    - among the most common factors influencing the decision making process are people's expectations that TAVI will improve their quality of life and wellbeing, reduce symptoms and extend their lives. Trust in healthcare professionals and the information provided before the procedure are other important factors.
    - Some people are unsure about the benefits or effects of TAVI and require more information and support during the decision making process.
    - In order to provide the most appropriate support, it is important that healthcare professionals are aware of how individual patients make decisions about TAVI.

Quality of life

A meta-analysis compared quality of life among people who had transfemoral TAVI or SAVR and low to intermediate surgical risk.[15] Six out of nine included studies reported quality of life outcomes from trials in people at low surgical risk: NOTION, Evolut Low Risk, PARTNER 3 and UK TAVI (total

n=3,681). Data from the UK TAVI trial was not combined with the other studies in the meta-analysis because it was an outlier compared with the other studies. Quality of life was measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and EuroQol 5-dimension (EQ5D) tools.

At 30 days follow up, KCCQ scores improved more in the TAVI group than the SAVR group (MD 13.56, 95% CI 11.67 to 15.46, p<0.001). There was no statistically significant between group difference in the change in KCCQ scores at 1 year follow up (MD 1.05, 95% CI -0.11 to 2.21, p=0.08).

Similarly, at 30 days follow up, EQ5D scores had improved significantly more in the TAVI group compared with the SAVR group (MD 0.07, 95% CI 0.05 to 0.08, p<0.001). There were no statistically significant differences in the change in EQ5D scores at 12 months follow up (MD 0.01, 95% CI -0.03 to 0.01, p=0.37).

Quality of life in the UK TAVI trial was measured using the EQ5D tool. Quality of life scores improved within 2 weeks of having the TAVI procedure and these benefits were sustained at 1 year follow up. In the SAVR group, quality of life scores were lower 2 weeks after the procedure compared with TAVI patients. Quality of life in the SAVR group improved after 6 weeks but remained lower than in the TAVI group.

A health technology assessment (HTA) reported quality of life results from the PARTNER 3 (n=1,000) and Evolut Low Risk (n=1,468) trials in people with symptomatic severe aortic stenosis who are at low surgical risk.[26] Both trials reported quality of life using the KCCQ score. In the PARTNER 3 trial, the mean KCCQ score change from baseline to 30 days follow up was 18.5 (SD 0.83) in the TAVI group and 2.5 (SD 1.05) in the SAVR group. At 1 year follow up, the change in KCCQ score was 19.4 (SD 0.87) in the TAVI group and 17.4 (SD 0.99) in the SAVR group. In the Evolut Low Risk trial, the mean KCCQ score change from baseline to 30 days follow up was 20.0 (SD 21.1) in the TAVI group and 9.1 (SD 22.3) in the SAVR group.

The NOTION-2 trial (n=370) measured quality of life using the KCCQ score.[13] The score improved from baseline to 30 days follow up by 16% in the TAVI group and by 4% in the SAVR group. By 1 year follow up, quality of life had improved by 17% in both groups, with 85% of patients in each group reporting KCCQ scores associated with fair or better health status.

Experiences of TAVI

A systematic review explored the experiences of older adults (aged ≥64 years) undergoing TAVI.[31] The review authors appraised the quality of the included studies using tools that were appropriate for the different study designs. The studies were judged to be of overall good quality, but had methodological weaknesses, such as an unclear description of the methodologies used and a lack of theory underpinning the research.

The systematic review included 12 studies (n=353), eight of which were qualitative. Study participants had an average age of approximately 81 years and multiple comorbidities, which means the population is likely to have a high surgical risk. The included studies did not report STS-PROM scores for participants.

The review identified four main themes describing the experiences of people who had a TAVI procedure:

- the importance of individualised care plans
- caregiver and family support, communication and education
- persistent psychosocial and physical symptoms
- unique recovery journeys.

These themes are similar to the findings of studies in our previous recommendations on TAVI.[1]

Having an individualised care plan helped clinicians understand patients' goals and mitigated patients' potential feelings of disappointment and frustration if their symptoms did not improve as much as expected after TAVI. People reported a higher quality of life after TAVI when they felt their treatment goals had been met, even when objective data showed only a third of people had experienced improved functional outcomes.

Older adults wanted support, continuity and connection from their healthcare team. People who were having TAVI wanted to discuss the risks and benefits of the procedure, to get an explanation of the recovery process and to develop reasonable expectations of their physical capabilities and quality of life after TAVI. Clarity was important during these discussions because some people described leaving their initial consultation feeling confused about their condition and treatment options. People wanted information about procedure related pain, pain management, the hospital discharge process, symptom monitoring, healthy lifestyles and home support services.

After having a TAVI procedure, some people continued to struggle emotionally. They described feelings of disappointment, loneliness, social isolation and vulnerability. While some people perceived an immediate benefit from their TAVI procedure, others reported persistent breathlessness, fatigue, increased pain and feeling worn out. People often did not realise that while their aortic stenosis symptoms would improve after TAVI, their comorbidities would continue to affect their quality of life and physical abilities.

Individual experiences of the recovery journey varied. Some people experienced a rapid improvement in symptoms within weeks of the procedure. Others had a more prolonged recovery. Overall, people felt optimistic, grateful and self-confident after their procedure, even when they had ongoing symptoms. People reported that they did not regret their decision to have TAVI, even when the outcome was not as good as they had expected.

Making decisions about treatment

A systematic review, a qualitative study and a cross-sectional study explored factors affecting people's decision making about TAVI.[32-34]

The systematic review explored the values and preferences of people deciding whether to have a TAVI procedure.[32] The included studies had methodological limitations, such as inappropriate or unclear sampling and recruitment strategies, and limited descriptions of the data analysis. Eight studies (n=1,096) were included in the review. The average age of study participants ranged from 75 to 86 years. Surgical risk scores varied, were unspecified or were unknown. Where mean STS-PROM scores were reported, participants were at intermediate or high surgical risk.

One study reported considerable variability in people's willingness to accept a potentially shorter duration of effectiveness with TAVI valves compared with SAVR. A subgroup analysis suggested that this variability could be partly explained by people under 60 being more concerned with valve durability than those aged over 60 because of their longer life expectancy.

Most people were willing to accept perioperative mortality risks because they felt that refusing the TAVI procedure and continuing to experience symptoms of aortic stenosis would be a worse outcome. Overall, study participants appeared willing to accept the mortality risk associated with TAVI procedures.

Seven out of eight studies reported improvement in quality of life as a reason for having TAVI. Participants often described quality of life improvement in terms of the ability to do a specific task or activity, to regain or maintain their independence, to restart activities they had stopped and to reconnect with their social networks.

Practical issues relating to having a TAVI procedure were also identified in the review:

- concerns about the longer hospital stay and recovery time with SAVR compared with TAVI
- clinicians were perceived as essential sources of information and guidance during decision making
- the importance of having a trusting relationship with doctors
- living further away from hospitals that offered TAVI resulted in greater difficulties accessing treatment and led to a burden of personal costs incurred from travel, meals and accommodation.

The qualitative study (n=18) used semi-structured interviews to explore people's motivations for having a TAVI procedure.[33] Interviews were conducted in the patient's hospital room the day after their procedure and lasted 20–60 minutes. The timing of the interviews could have affected how participants expressed their expectations for the future.

Eighteen people participated in the study. The mean age of participants was 81.5 years (range 66 to 92 years). Participant STS-PROM scores suggest they were at low to intermediate surgical risk.

For most participants, the motivation for having TAVI was regaining their normal everyday lifestyle. They felt that living with symptomatic severe aortic stenosis had put their lives on hold. Participants described feeling like their bodies had betrayed them. This resulted in feelings of fear, disappointment, frustration and anger. Many people had been forced to stop activities that gave them pleasure and for some this resulted in a sense of loneliness. They welcomed the chance to avoid an increasing dependence on others for daily activities.

Some participants feared dying during the TAVI procedure, but they were willing to accept the risk when they realised it was their chance to regain a normal life and necessary for their survival. Participants described feeling grateful and relieved that they could avoid open heart surgery at their age, but needed reassurance that the new valve would last a long time.

There was a strong desire to continue living independently after the TAVI procedure. Participants expressed belief in their own ability to manage everyday life after TAVI. People said they did not want to become a burden to their families or to be forced to move into a nursing home.

The cross-sectional study used a self-administered questionnaire to explore patients' perspectives on treatment goals and factors influencing treatment choice (n=98).[34] The questionnaire was developed by the clinical team and provided options on a Likert scale. It did not include any open questions. The questionnaire was piloted on 39 people who were not part of the final sample.

The median age of participants was 86 years with the majority (96.9%) aged ≥75 years. Three quarters of participants were female. Participants were at intermediate surgical risk. For most people the treatment goal was to reduce symptom burden (77.6%). Other reasons for having a TAVI procedure included maintaining independence (68.4%), being able to perform a specific activity or hobby (62.2%) and improving prognosis (58.2%).

Factors affecting the decision to undergo TAVI were personal values (54.1%), not wanting to be a burden to family (52.0%), wanting to avoid becoming a burden to society (34.7%) and a lower financial burden (30.6%). Most patients wanted to continue living at home after their procedure (94.9%).

Determining patient preferences

One study used a benefit-risk assessment to determine what features of heart valve interventions were most important to patients (n=93).[55] Ninety-three people were recruited from the mailing lists of Heart Valve Voice, Mended Hearts and the American Heart Association. This recruitment method may have biased the results of the study if people motivated to join these organisations have

different preferences than the wider population. The majority of participants (74.3%) were aged ≥60 years, 57% were female and 93.5% identified as white.

The study used an online survey to identify the level of change in specific attributes of heart valve interventions that patients would be willing to accept in exchange for switching their procedure from invasive to minimally invasive.[55] The attributes assessed included mortality, the risk of non-fatal disabling stroke, regaining independence after a procedure, needing a pacemaker, requiring dialysis and quantity of evidence supporting the procedure.

Table 17 presents a threshold analysis showing the minimum amount of benefit patients would accept or the maximum amount of risk they would tolerate for their preference to be a TAVI procedure. Overall, participants were willing to accept TAVI's reported performance for any attribute in exchange for its lower invasiveness. Older patients (aged ≥60) were more willing to tolerate an increased risk or reduced benefit to avoid having SAVR. Patients placed more value on TAVI's lower mortality rate, reduced procedure invasiveness and quicker return to normal quality of life than the value they placed on the larger quantity of evidence for SAVR or the reduced need for a pacemaker after surgery.

Table 17: Threshold analysis showing minimum benefit or maximum risk before patients prefer TAVI[55]

Attributes	Minimum acceptable benefit or maximum acceptable risk for each characteristic			Reported level of the outcome for TAVI in the literature
	All ages	<60 years	≥60 years	
% people who die within 1 month	12.4%	9.3%	13.2%	1.1%
% people who have a disabling non-fatal stroke rate within 1 month	18.8%	14.1%	20.1%	0.8%
% people who have greater independence within 1 month	5.7%	9.9%	4.5%	47.9%
% people needing a new permanent pacemaker within 1 year	35.3%	27.6%	37.0%	12.3%
% people who need dialysis within1 year	21.0%	13.7%	23.0%	3.2%
n years the procedure has been available and proven to work	0	0	0	10

Organisational issues/context

TAVI procedures are currently undertaken at the Golden Jubilee National Hospital (since 2018), Aberdeen Royal Infirmary (since 2019) and Royal Infirmary of Edinburgh (since 2012).[40]

Patients from the west of Scotland are referred to the Golden Jubilee National Hospital for their TAVI procedure.[40] The Aberdeen Royal Infirmary provides TAVI for patients within NHS Grampian, NHS Highland and NHS Tayside. The Royal Infirmary of Edinburgh accepts referrals from all over Scotland if the patient's nearest hospital does not offer the procedure or if the patient is not a suitable candidate for transfemoral access.

There are 0.55 TAVI centres pmp in Scotland compared with 0.53 centres at a UK level. This is approximately one third of the European average.[42] A survey of UK TAVI centres found that the number of TAVI procedures performed is limited by cardiac catheterisation laboratory capacity and bed numbers (a main or significant factor in 74% and 56% of responses respectively). Limited access to cardiac computed tomography was also a problem for 45% of TAVI centres.

Cost effectiveness

Systematic reviews

Two systematic reviews assessed the cost effectiveness of TAVI compared with SAVR in people with symptomatic severe aortic stenosis who are at low surgical risk.[16, 56] As there is considerable overlap between the studies included in these reviews, only the more comprehensive review is discussed here.[16]

The systematic review included six economic evaluations. One study, developed as part of an HTA in Norway, concluded that TAVI was dominant (that is, TAVI was more effective and less costly than SAVR). Dominance or cost effectiveness of TAVI was demonstrated across a range of scenarios. A 30% increase in the cost of TAVI or a 30% decrease in the cost of SAVR was the estimated threshold at which the analysis results would favour SAVR.

A Danish study found that TAVI was cost effective and represented moderate value based on national willingness to pay (WTP) thresholds. The cost effectiveness of TAVI in patients at low surgical risk was dependent on it providing a long term survival advantage over SAVR.

Two studies found that the cost effectiveness of TAVI was contingent on the type of TAVI device used (self-expanding or balloon expanding). Both evaluations found balloon expanding TAVI to be cost effective at pre-specified WTP thresholds but their conclusions on self-expanding TAVI devices differed. The Australian analysis found self-expanding TAVI to be dominant compared with SAVR. The study from Canada found that the incremental cost effectiveness ratio (ICER) for self-expanding TAVI devices exceeded the local WTP threshold. Both studies used the same data sources and the economic model structure was similar. It is unclear why these studies reached conflicting conclusions.

The only UK based study included in the systematic review found that TAVI was not cost effective compared with SAVR. This study was published in 2010 and was based on first or early generation TAVI devices that are likely to have a different effectiveness and cost profiles to newer valves. The other studies in the systematic review were all published after 2018, when second and third generation TAVI devices were available.

Recent primary economic evaluations

Nine economic evaluations relating to the SAPIEN 3 TAVI device have been published since the systematic review, all of which use outcome data from the PARTNER 3 trial.[17-26]

One analysis from the perspective of the US healthcare system was based on 929 people recruited to the PARTNER 3 trial.[20] This study estimated procedural costs based on resource use and derived health utility scores using the EQ5D questionnaire.

The analysis found TAVI to be less costly and more effective (that is, dominant) than SAVR. There was a 95% probability of the ICER being lower than the $50,000 (£40,673) per QALY (that is, WTP) threshold. TAVI was projected to reduce overall resource costs by $2,030 (£1,591) per patient and lead to an additional 0.05 QALYs per patient compared with SAVR at 2 years follow up. The procedural costs of TAVI were higher than those for SAVR largely because of the cost of the TAVI valve. When factoring in the costs associated with hospital stay, total index hospitalisation costs for TAVI were only marginally higher than those for SAVR. Follow up costs were substantially lower for TAVI compared with SAVR.

A Japanese cost effectiveness analysis also found the ICER for TAVI in low risk patients to be well below the local WTP threshold.[22]

The clinical effectiveness results from the PARTNER 3 trial were applied in six European economic evaluations.[17-19, 21, 23, 24, 26] A cost utility analysis, which used results from the PARTNER 3 trial in combination with a French national hospital claims database, found that TAVI dominated SAVR in people with severe aortic stenosis who are at low surgical risk.[21] The model estimated TAVI to be cost saving by €12,742 (£10,913) per patient and to generate 0.89 QALYs per patient more than SAVR.

Similar models were developed to assess the cost effectiveness of TAVI using SAPIEN 3 valves compared with SAVR in Belgium, Germany, Italy, the Netherlands and Spain.[17-19, 23, 24] The six European economic evaluations used identical models and applied clinical outcomes data from the same trial (PARTNER 3). Direct healthcare costs and long term management costs were adapted based on local estimates.

The results of the European economic analyses are summarised in *Table 18*. TAVI was found to be cost effective (that is, below local WTP thresholds) compared with SAVR in all six analyses. The results are driven by the greater long term survival benefit, fewer complications and lower long term healthcare costs attributed to TAVI.

Base case ICERs in the European analyses were stable across a range of scenarios including time horizons of 5–30 years. TAVI only exceeded the €30,000 (£25,152) per QALY cost effectiveness threshold when applying a 5-year time horizon. Estimates were more favourable for TAVI when applying 2 year survival data from the PARTNER 3 trial (HR 0.75). Across all six European evaluations, the assumptions that led to the greatest increase in ICERs were a more aggressive reintervention rate for TAVI, an increased rate of stroke among TAVI patients and the use of health related quality of life data from PARTNER 3.

An Irish HTA included a model to assess the cost effectiveness of expanding the TAVI care pathway to include people at low and intermediate surgical risk.[26] Evidence from the PARTNER 3 trial was used in the base case analysis for people at low surgical risk. One notable difference between this analysis and the other European studies is that the HTA analysis was limited to a 15 year time

horizon (the expected lifespan of the SAPIEN 3 device), whereas the other evaluations assumed a lifetime horizon.

In the HTA analysis, TAVI had lower expected costs and higher QALY gains compared with SAVR (that is, TAVI was dominant). The cost saving was estimated to be €387 (£331) per patient, alongside a QALY gain of 0.021 per patient. TAVI was cost effective across all scenarios tested.

While the general conclusions of the economic evaluations consistently favour TAVI over SAVR, it is important to note that TAVI valve costs vary between countries. The results of these studies may therefore not be transferable to the UK and Scotland.

Table 18: Summary results of European economic evaluations comparing TAVI with SAVR using outcomes from the PARTNER 3 trial and local healthcare costs[18, 19, 23, 24]

		Belgium[18]	France[21]	Germany[23]	Italy[24]	Netherlands[19]	Spain[17]
Costs at 1 year	TAVI	€33,144 (£28,386)	€26,523 (£22,715)	€26,898 (£23,037)	€33,357 (£28,569)	€36,190 (£30,995)	€27,767 (£23,262)
	SAVR	€31,264 (£26,776)	€29,888 (£25,597)	€19,130 (£16,384)	€29,234 (£25,037)	€29,140 (£24,957)	€16,570 (£13,881)
	Incremental	€1,880 (£1,610)	-€3,365 (-£2,882)	€7,769 (£6,653)	€4,123 (£3,531)	€7,050 (£6,038)	€10,698 (£8,962)
Additional lifetime costs	TAVI	€9,596 (£8,218)	€12,468 (£10,678)	€10,644 (£9,133)	€9,229 (£7,904)	€7,959 (£6,816)	€11,785 (£9,875)
	SAVR	€14,489 (£12,409)	€21,846 (£18,710)	€9,749 (£8,349)	€10,035 (£8,594)	€10,267 (£8,793)	€15,512 (£12,996)
	Incremental	-€4,893 (-£4,190)	-€9,378 (-£8,031)	€896 (£767)	-€806 (-£690)	-€2,308 (-£1,976)	-€3,727 (-£3,123)
Total lifetime costs	TAVI	€42,741 (£35,749)	€38,992 (£33,395)	€37,542 (£32,153)	€42,587 (£36,474)	€44,149 (£37,811)	€39,052 (£32,717)
	SAVR	€45,753 (£39,185)	€51,734 (£44,308)	€28,878 (£24,732)	€39,269 (£33,632)	€39,407 (£33,750)	€32,081 (£26,877)
	Incremental	-€3,013 (-£2,580)	-€12,742 (-£10,913)	€8,664 (£7,420)	€3,317 (£2,840)	€4,742 (£4,061)	€6,971 (£5,840)
QALYs per patient	TAVI	8.89	8.44	8.56	8.94	9.50	8.66
	SAVR	7.89	7.55	7.84	7.83	8.62	7.66
	Incremental	0.94	0.89	0.72	1.11	0.89	1.00
ICER (per QALY)		**TAVI dominant**	**TAVI dominant**	**€12,037 (£10,309)**	**€2,989 (£2,559)**	**€5,346 (£4,578)**	**€6,952 (£5,824)**

NICE economic evaluation

The NICE guideline on heart valve disease published in 2021 included a cost utility analysis comparing TAVI with SAVR in people with severe aortic stenosis at any level of surgical risk.[27] The NICE analysis used a hybrid decision tree model nested within a Markov model. The model predicted the proportion of people progressing to one of nine post-procedural outcomes in the first 30 days, as well as estimating longer term outcomes and costs. A 15-year time horizon was assumed.

Model parameters were informed by a combination of evidence from registries and trial data. Decision tree baseline probabilities were based on the UK TAVI audit data for England, Wales and Northern Ireland in 2020 (containing data from 2007 to March 2020). Relative treatment effects and utilities were based on the PARTNER and Evolut trials of second and third generation TAVI devices. The primary source of cost data was NHS reference costs from 2018–2019. A TAVI valve device cost of £17,500 was assumed in the base case. This was an average price calculated across multiple NHS trusts and different valve brands but was considered to represent the average price paid by participating centres for a TAVI valve in 2020.

TAVI in people who were at low surgical risk was associated with an incremental QALY gain of 0.024 at an incremental cost of £3,300 compared with SAVR. The resulting ICER of £139,799 per QALY means that TAVI is not cost effective at UK QALY WTP thresholds. TAVI was not cost effective in most scenarios tested. Threshold analysis indicated that TAVI would be cost effective at WTP thresholds of £20,000 and £30,000 per QALY if the device price was reduced to £14,800 and £15,000, respectively.

The conclusion of the NICE economic analysis is at odds with the published economic studies conducted in Europe. The primary driver for these diverging conclusions is the difference in device price between countries. The cost of TAVI procurement in the UK is known to be substantially higher than in other countries, such as France and Canada.[57, 58]

Other possible explanations for these diverging results include:

- pooling of treatment effects across all trials and all patients regardless of surgical risk in the NICE model rather than treatment effects from low risk populations only
- an assumption in the NICE model that a higher reintervention rate occurred with TAVI in the low risk group, which directly translates into higher costs and lower QALYs
- reliance by NICE on data from trials with relatively short follow up to model outcomes for a period of 15 years. This contributes to uncertainty in the analysis because some of the assumptions may not hold over time. For example, the assumed permanence of dialysis and stroke health states or the different causes of reintervention for TAVI versus biological valves.

Self-expanding TAVI valves

Two economic evaluations assessed the cost effectiveness of a self-expanding TAVI valve in patients at low surgical risk.[29, 59]

The first study conducted a UK based economic evaluation used 4 year follow up data from the Evolut Low Risk trial to estimate the cost effectiveness of TAVI compared with SAVR from the UK NHS perspective.[29] TAVI provided an incremental benefit of 0.28 QALYs over a lifetime horizon at an incremental cost of £5,021. The resulting ICER of £17,883 per QALY is below the NICE cost effectiveness threshold of £20,000 to £30,000 per QALY.

The longer follow up data from the Evolut Low Risk trial markedly improved the cost effectiveness profile of TAVI compared with SAVR in people at low surgical risk. The survival benefit between years 2 and 4 observed in the Evolut Low Risk trial is a key driver of cost effectiveness this population. When modelled based on 1 and 2 years follow up data from the same trial, TAVI generated incremental QALY gains of 0.14 and 0.17, with ICERs of £35,044 and £28,634 per QALY.

The base case results in this analysis were stable across a range of sensitivity and scenario analyses. While shorter time horizons led to lower incremental QALY gains, incremental costs were also lower, resulting in a relatively stable ICER. In one way sensitivity analyses, variation in the costs of TAVI and SAVR had the greatest effect on the ICER, followed by cohort age and stroke rates.

The base case results assumed a TAVI device cost of £17,500. This was the same as the average reimbursement price included in the NICE evaluation which reached very different conclusions. Diverging ICERs can be attributed primarily to the difference in incremental QALY gains predicted by the two models. The NICE model estimated minimal incremental QALY gains for TAVI (0.024 and 0.018 QALYs in the deterministic and probabilistic results respectively) based on short term outcomes data. The more recent published evaluation predicted QALY gains based on 4 year follow up data from the Evolut Low Risk trial that suggested improved survival.[29] This led to a ten-fold increase in QALYs (0.25) over a 15 year time horizon.

The second study was an analysis based on the French healthcare system assessing the cost effectiveness of the self-expanding Corevalve Evolut R or Corevalve Evolut Pro TAVI valve.[59] These valves were associated with 0.13 additional QALYs over a patient lifetime horizon. The resulting ICER of €6,368 (£5,336) per QALY suggests that TAVI is a cost effective alternative to SAVR. This model used 2 years follow up data from the Evolut Low Risk trial. The base case results did not vary substantially across scenarios testing the impact of shorter time horizons, different sources of utility scores and varying mortality rates.

Real world costs

A retrospective analysis compared costs associated with TAVI and SAVR based on the Medicare records of patients in the US.[25] Patients were categorised as low, intermediate or high surgical risk based on two validated indices, the Hospital Frailty Risk Score (HFRS) and the logEuroScore (LES). In a sample of 8,590 patient records, based on their HFRS, 1,600 people deemed at low risk received TAVI and 1,968 people deemed low risk received SAVR. When surgical risk estimates for the same sample of patient records were based on the LES, there were 1,683 people deemed low risk who received TAVI and 2,849 people who received SAVR.

People who received TAVI had significantly lower costs at discharge and through 1 year of follow up compared with people receiving SAVR (*Table 19*). Cost savings in the TAVI group were primarily driven by lower expenditure during hospitalisation because of a shorter length of stay. The care of people at lower surgical risk also demonstrated reduced costs at follow up after TAVI compared with SAVR. Overall, cumulative 90 day and 1 year costs were lower for TAVI compared with SAVR, regardless of the risk score used.

The differences in costs for both index hospitalisation costs and follow up costs were statistically significant. These findings support a conclusion that TAVI is the dominant treatment strategy, assuming that the clinical outcomes and durability of the TAVI device(s) remains comparable to SAVR.

Table 19: Estimated real world costs for TAVI compared with SAVR in a US population at low surgical risk[25]

Risk score	Technology	Index hospitalisation	Discharge to 30 days	31 to 90 days	91 to 180 days	181 to 360 days
Low risk defined by HFRS	TAVI	$61,845 (£48,477)	$1,637 (£1,283)	$1,955 (£1,532)	$2,089 (£1,637)	$2,943 (£2,306)
	SAVR	$68,968 (£54,061)	$2,922 (£2,290)	$2,185 (£1,712)	$2,540 (£1,991)	$5,136 (£4,025)
	Cost difference	**-$7,123 (-£5,583)**	**-$1,285 (-£1,007)**	**-$230 (-£180)**	**-$451 (-£353)**	**-$2,194 (-£1,719)**
Low risk defined by LES	TAVI	$64,925 (£50,892)	$2,061 (£1,615)	$2,376 (£1,862)	$2,807 (£2,200)	$4,011 (£3,144)
	SAVR	$71,953 (£56,401)	$3,109 (£2,437)	$2,477 (£1,941)	$3,538 (£2,773)	$5,046 (£3,955)
	Cost difference	**-$7,028 (-£5,508)**	**-$1,048 (-£821)**	**-$101 (-£79)**	**-$731 (-£573)**	**-$1,036 (-£812)**

Conclusion

Evidence on the clinical effectiveness and safety of TAVI compared with SAVR in people with symptomatic severe aortic stenosis who are at low surgical risk consists of six meta-analyses and three additional RCTs. The evidence consistently concludes that there is no statistically significant difference in all-cause mortality between TAVI and SAVR in this patient population.

Across meta-analyses and RCTs, there was evidence that people who have TAVI have approximately three times higher risk of needing a permanent pacemaker compared with people who have SAVR.

This is balanced against an increased risk of new onset atrial fibrillation, acute kidney injury and bleeding in people who have SAVR compared with people who have TAVI.

Four RCTs reported that length of hospital stay was significantly shorter after a TAVI procedure compared with SAVR. People who have TAVI often leave hospital within a day of the procedure. People who have SAVR may need time in an intensive care unit and a further 4–5 days on a post-surgical ward.

A meta-analysis found that quality of life was statistically significantly better at 30 days follow up among people who had TAVI compared with SAVR. This difference was not observed at 1 year follow up, suggesting that both procedures may provide similar improvements in quality of life in the longer term.

People's experiences of TAVI, their recovery journey and willingness to accept risk varies between individuals. People were generally motivated to have TAVI so that they could resume a normal life and continue to live independently in their own home.

Evidence from a systematic review, ten economic analyses and Medicare records from the US, indicate that TAVI is either dominant or cost effective compared with SAVR. In contrast, a NICE economic evaluation from 2021 found that TAVI was not cost effective at a TAVI list price of £17,500; the average device cost would need to be lower than £15,000 to be cost effective in people who are at low surgical risk. Device costs are the primary driver of cost effectiveness for TAVI.

Identified research gaps

People with symptomatic severe aortic stenosis who are at low surgical risk are generally younger than people who are considered intermediate or high risk and have a longer life expectancy. It would be advantageous for studies to report on device durability over the long term (10 years or more).

Given the diverging results of the two most recent economic evaluations from a UK NHS perspective, additional economic evaluations using long term data from trials where participants are at low surgical risk would be very helpful. Studies that report on the newer generation balloon-expandable TAVI devices would also be beneficial to inform decision making.

The evidence on patient experiences and decision making appears to be mainly based on people with intermediate or high surgical risk. Studies exploring these aspects specifically in people at low surgical risk would be useful for comparison. Understanding patient experiences and decision making in this population could help tailor interventions and improve patient outcomes, especially if TAVI becomes more widely used in this population.

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Appendix 1: Abbreviations

AVR	aortic valve replacement
CI	confidence interval
EQ5D	EuroQol 5-dimension
HFRS	Hospital Frailty Risk Score
HR	hazard ratio
HTA	health technology assessment
ICER	incremental cost effectiveness ratio
IMD	index of multiple deprivation
IQR	interquartile range
IRR	incidence risk ratio
KCCQ	Kansas City Cardiomyopathy Questionnaire
LES	logEuroScore
MD	mean difference
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OR	odds ratio
PMP	per million population
QALY	quality adjusted life years
RCT	randomised controlled trial
ROBINS-I	risk of bias in non-randomised studies of interventions
RR	relative risk
SAVR	surgical aortic valve replacement
SD	standard deviation
SMD	standardised mean difference
SHTG	Scottish Health Technologies Group
S/T	subclavian/transaxilliary
STS-PROMS	STS Predicted Risk of Mortality
TA	transapical

Tao	transaortic
TAVI	transcatheter aortic valve implantation
TAVR	transcatheter aortic valve replacement
TF	transfemoral
UK	United Kingdom
US	United States
WTP	willingness to pay