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ORIGINAL RESEARCH ARTICLE

Cost-Utility Analysis of TAVI Versus Surgery in Low-Risk Patients with Severe Aortic Stenosis in the UK

Nick Curzen[1,2] · Pascal Candolfi[3] · Philip MacCarthy[4] · Clinton T. Lloyd[5] · Muhammad Aetesam-Ur-Rahman[6] · Tom Bromilow[7] · Valentina Sellitto[8] · Daniel J. Blackman[9]

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Abstract

Background and Objective European guidelines recommend transcatheter aortic valve implantation (TAVI; class IA) for symptomatic severe aortic stenosis (sSAS) in patients aged ≥ 75 years, if a transfemoral approach is possible. Recent cost-utility analyses based on the PARTNER 3 trial have suggested that TAVI with the SAPIEN 3 device is cost effective versus surgical aortic valve replacement (SAVR) in patients at low risk of surgical mortality in several European countries. This cost-utility analysis compares TAVI with SAPIEN 3 versus SAVR in patients with sSAS at low risk of surgical mortality from the UK healthcare system perspective, using 5-year PARTNER 3 trial data.

Methods A two-stage, Markov-based, cost-utility analysis was performed using published and validated methodology to estimate changes in both direct healthcare costs and health-related quality of life for TAVI with SAPIEN 3 versus SAVR in patients with sSAS at low surgical risk from the perspective of the UK healthcare system. The model used a lifetime horizon with a 3.5% yearly discounting factor. Uncertainty was addressed using deterministic and probabilistic sensitivity analyses.

Results Transcatheter aortic valve implantation with SAPIEN 3 generated an incremental health benefit of 0.47 (90% credible interval 0.35–0.60) quality-adjusted life-years per patient compared with SAVR, at an increased cost of £7999 (£852–£15,035 90% credible interval) per patient over a lifetime horizon (incremental cost-effectiveness ratio: £16,979 per quality-adjusted life-year gained). Transcatheter aortic valve implantation has a 63–90% probability of cost effectiveness based on a £20,000–£30,000 willingness-to-pay threshold. Transcatheter aortic valve implantation remained cost effective across most deterministic sensitivity analyses, confirming the relative robustness of the results.

Conclusions Transcatheter aortic valve implantation with SAPIEN 3 has a 63–90% probability of being cost effective compared with SAVR for low-surgical-risk patients with sSAS. These findings may inform policy decision making in the management of this patient group.

✉ Pascal Candolfi
pascal_candolfi@edwards.com

1 Faculty of Medicine, University of Southampton, Southampton, UK

2 Cardiothoracic Unit, University Hospital Southampton NHS Trust, Southampton, UK

3 Edwards Lifesciences Sàrl, Route de l'Etraz 70, 1260 Nyon, Switzerland

4 King's College Hospital, London, UK

5 University Hospitals Plymouth NHS Trust, Plymouth, UK

6 Sheffield Teaching Hospitals NHS FT, Sheffield, UK

7 York Health Economics Consortium, University of York, York, UK

8 Edwards Lifesciences, Milan, Italy

9 Leeds Teaching Hospitals NHS Trust, Leeds, UK

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Key Points for Decision Makers

An increasing body of evidence, combined with recent European and US guideline updates, acknowledge the clinical benefits of transcatheter aortic valve implantation compared with surgical aortic valve replacement for patients with symptomatic severe aortic stenosis, regardless of surgical risk status.

This cost-utility analysis shows that, from the perspective of the UK healthcare system, transcatheter aortic valve implantation with SAPIEN 3 has a 63–90% probability of being cost effective at a £20,000–£30,000 per quality-adjusted life-year willingness-to-pay threshold compared with surgical aortic valve replacement for patients with symptomatic severe aortic stenosis who are at low risk of surgical mortality.

Transcatheter aortic valve implantation with SAPIEN 3 appears to be associated with both clinical and economic benefits compared with surgical aortic valve replacement in patients with symptomatic severe aortic stenosis who are at low risk of surgical mortality. Healthcare providers and policy makers in the UK can use these data to inform their decisions on intervention selection for patients with symptomatic severe aortic stenosis.

1 Introduction

Aortic valve replacement options for the treatment of symptomatic severe aortic stenosis (sSAS) include surgery (surgical aortic valve replacement [SAVR]) or transcatheter aortic valve implantation (TAVI) [1]. Transcatheter aortic valve implantation was initially introduced as a treatment option for sSAS in patients considered inoperable or at high risk of surgical mortality [2], but technical advances and excellent trial outcomes in large randomised controlled trials have expanded the indication. Transcatheter aortic valve implantation is now recommended as an alternative to SAVR in all patients regardless of the surgical risk level, as per the European Society of Cardiology/European Association for Cardio-Thoracic Surgery [3] and American College of Cardiology/American Heart Association Clinical Practice guidelines [4].

In the UK, the latest (2021) National Institute for Health and Care Excellence (NICE) heart valve disease (HVD) guidelines [5] are substantially more restrictive in the use of TAVI than the American College of Cardiology/American Heart Association and European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines. This is partly because (1) NICE guidance needs to account for the cost or cost effectiveness of therapies, and (2) updates in health funding lag behind clinical guidelines updates in the UK, leading to delays in the reimbursement and penetration of TAVI [6, 7]. For example, despite European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines updating in August 2021, TAVI reimbursement for intermediate/low-surgical-risk patients only expanded in January 2023 [8]. This, combined with geographical inequities in the UK, has led to low TAVI penetration, longer waiting times and excess mortality among those awaiting intervention [6].

While the NICE 2021 HVD guidelines [5] concluded that TAVI was not cost effective compared with SAVR in patients at low surgical risk of mortality, these findings are in contrast with other published literature and were calculated from a model that has several limitations. For example, the NICE cost-effectiveness model included heterogeneous sources of mixed indications, types of devices, different valve generations and various TAVI approaches. A 2023 systematic literature review of 42 studies [18] demonstrated that inappropriately combining evidence from different devices, risk groups and access groups can underestimate the economic benefit of the newest generation of TAVI devices, such as the SAPIEN 3 transcatheter heart valve [10–17]. The literature review also reported that SAPIEN 3 was more likely to be found cost effective than other generations of device.

The PARTNER 3 trial was a multicentre randomised controlled study investigating the outcomes of TAVI using the SAPIEN 3 device in patients with sSAS considered at low risk of surgical mortality. Transcatheter aortic valve implantation with SAPIEN 3 resulted in significantly lower rates of stroke and new-onset atrial fibrillation (AF), shorter index hospitalisation, higher functional status and improved quality of life at 30 days. There were also no significant between-group differences in major vascular complications, new permanent pacemaker insertions, or moderate or severe paravalvular regurgitation [19, 20]. The 5-year results of the PARTNER 3 trial found event rates for death, stroke or rehospitalisation remained low with TAVI and very similar to the SAVR arm, reaffirming the SAPIEN 3 device as a meaningful alternative to SAVR for patients with sSAS considered at low risk of surgical mortality [21].

Recently published analyses suggest that TAVI is cost effective versus SAVR in patients at low risk of surgical mortality in France [10], Italy [11], Spain [12], Germany [13], Belgium [14], the Netherlands [15], Sweden [16] and Switzerland [17]. This study involved the development of a cost-utility analysis using 5-year data from the PARTNER 3 trial to assess the value of TAVI with SAPIEN 3 versus SAVR in patients with sSAS and at low risk of surgical

mortality in a UK healthcare setting. The aim was to produce device-specific evidence.

2 Methods

A cost-utility model was built to estimate changes in direct healthcare costs and health-related quality of life with TAVI (using SAPIEN 3) versus SAVR in patients with sSAS with a low risk of surgical mortality (< 4%, as defined by the Society of Thoracic Surgeons [47]), from the perspective of the UK healthcare system. Ethical approval of research was not required as the cost-utility analysis was based on data from existing studies and did not gather any new data from human participants.

2.1 Model Structure

Following a conceptualisation period, the model was built using a two-stage structure: a methodology validated in the French [10], Italian [11], Spanish [12], German [13], Belgian [14], Dutch [15], Swedish [16] and Swiss [17] populations and considered appropriate for a UK context by all authors. Early adverse events (AEs) linked to the TAVI procedure were captured using the 30-day AE dataset from the PARTNER 3 trial [19] in a decision tree (Fig. 1a). These data were subsequently fed into a Markov model that included four distinct health states ('alive and well', 'treated AF', 'disabling stroke' and 'dead') to capture longer term outcomes of patients, post TAVI or SAVR intervention (Fig. 1b). The acute costs associated with a transient ischaemic attack, myocardial infarction and bleed rates were captured between 30 days and 1 year [19].

A lifetime horizon (30 years), and 1-month cycle length was used, with an annual discounting factor of 3.5% applied for both future costs and benefits. A 30-year time horizon was chosen to capture the potential outcomes of people with sSAS over their lifetime. Half-cycle corrections were applied for costs and quality-adjusted life-years (QALYs), with the exception of the procedure costs; all patients will incur these costs, which can be justified given the low risk of surgical mortality.

Health-related quality of life was included in the analysis using QALYs as an endpoint. These were based on the EQ-5D utility values for the different health states in the model, with utility decrements for the AF and stroke health states taken from the published literature and adjusted for age and population norms using Hernández Alava et al. [22].

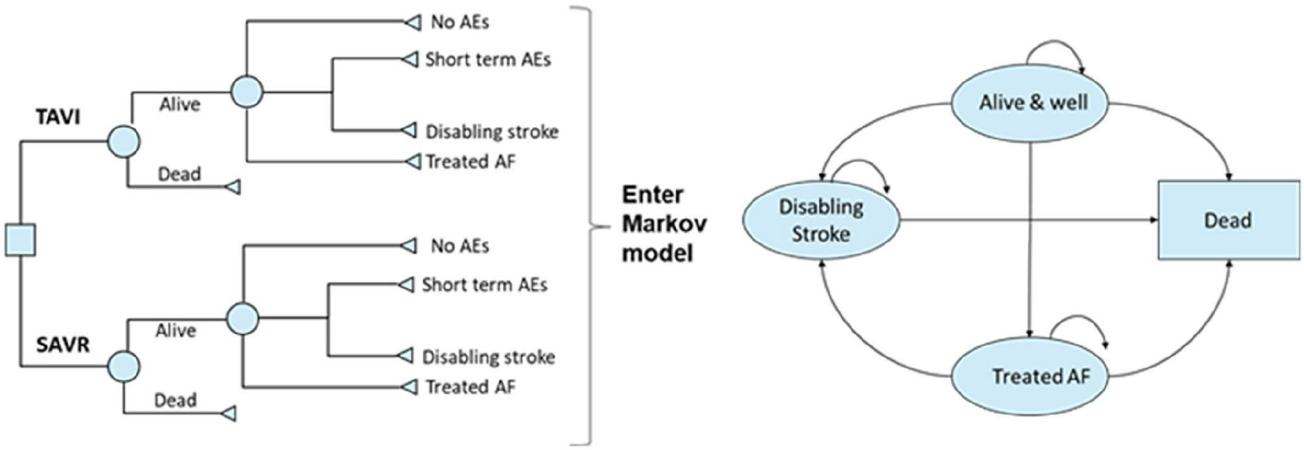

Fig. 1 Cost-effectiveness model had two stages: (**a**) early adverse events (AEs) from the PARTNER 3 trial were captured in a decision tree, which fed into (**b**) a Markov model that captures longer term outcomes of patients. Short-term AEs include new permanent pacemaker, hospitalisation, non-disabling stroke, transient ischaemic attacks, myocardial infarction, bleeding, acute kidney injury with renal replacement therapy and aortic reinterventions. [a]'Alive and well': patients have undergone the procedure and survived with only short-term or no AEs; patients in this health state can transition to 'disabling stroke', 'atrial fibrillation' (AF) or 'dead' at any point during the model time horizon. 'Treated AF': patients have undergone the procedure and survived but developed AF requiring specific treatment; this can either occur within the first 30 days or during the rest of the time horizon of the model, and patients in this health state can transition to 'disabling stroke' or 'dead' at any point during the model time horizon. 'Disabling stroke': patients have undergone the procedure and survived but had a disabling stroke; this can either occur within the first 30 days or during the rest of the time horizon of the model, and patients in this health state can only transition into the 'dead' state at any point during the model time horizon. 'Dead': this is the absorbing state in the model: all patients in the model are at risk of dying because of general all-cause mortality; patients with treated AF and stroke are at an increased risk of dying. *HR* hazard ratio, *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation. Reproduced from Gilard et al. [10], https://doi.org/10.1016/j.jval.2021.10.003 under the terms of the creative commons licence (Creative Commons Attribution License [CC BY])

2.2 Model Inputs

The model was informed by the PARTNER 3 trial population, which excluded patients with clinical frailty, bicuspid aortic valves or other anatomical features that increased the risk of complications associated with either surgery or TAVI, such as aortic insufficiency and aortopathy. In the trial, 503 patients were randomised to TAVI and 497 patients randomised to SAVR, with the 'as treated' groups comprising 496 and 454 patients, respectively [19]. The primary endpoint was a composite of death from any cause, stroke or rehospitalisation at 1 year after the procedure.

2.2.1 Clinical Events

The monthly transition probability from 'alive and well' to 'treated AF' was informed by PARTNER 3 data on new-onset treated AF between 30 days and 5 years (Table 1) [19–26]. This was based on patients who received no treatment for AF to represent those with chronic, rather than acute, AF. For the remaining two health-state transitions,

Table 1 Probabilities of clinical events used in the model

Clinical events	SAPIEN 3	SAVR	Source
At 30 days			
Treated AF	4.1%	35.8%	PARTNER 3 trial [19]
New permanent pacemaker	6.5%	4.0%	PARTNER 3 trial [19]
Rehospitalisation	3.4%	6.4%	PARTNER 3 trial [19]
Disabling stroke	0.0%	0.4%	PARTNER 3 trial [19]
Aortic reintervention	0.0%	0.0%	PARTNER 3 trial [19]
Mortality	0.4%	1.1%	PARTNER 3 trial [19]
Monthly health states transition probabilities and intercurrent events between 30 days and 1 year			
Alive and well → treated AF	0.11%	0.15%	PARTNER 3 trial [19]
Alive and well → disabling stroke	0.02%	0.02%	Public Health England [23]; Hewitt et al. [24]
Treated AF → disabling stroke	0.04%	0.04%	Odutayo et al. [25]
TIA	0.09%	0.04%	PARTNER 3 trial [19]
MI	0.02%	0.08%	PARTNER 3 trial [19]
Severe or life-threatening bleeding	0.4%	0.1%	PARTNER 3 trial [19]
Monthly health states transition probabilities between 1 and 2 years			
Alive and well → treated AF	0.06%	0.11%	PARTNER 3 trial 2-year outcomes [20]
Alive and well → disabling stroke	0.02%	0.02%	Public Health England [23]; Hewitt et al. [24]
Treated AF → disabling stroke	0.04%	0.04%	Odutayo et al. [25]
Monthly health states transition probabilities between 2 and 5 years			
Alive and well → treated AF	0.16%	0.024%	PARTNER 3 trial 5-year outcomes [21]
Alive and well → disabling stroke	0.02%	0.02%	Public Health England [23]; Hewitt et al. [24]
Treated AF → disabling stroke	0.04%	0.04%	Odutayo et al. [25]
Monthly health states transition probabilities after 5 years and beyond			
Alive and well → treated AF	0.16%	0.024%	PARTNER 3 trial 5-year outcomes [21]
Alive and well → disabling stroke	0.02%	0.02%	Public Health England [23]; Hewitt et al. [24]
Treated AF → disabling stroke	0.04%	0.04%	Odutayo et al. [25]
Events beyond 30 days			
Rehospitalisation at 1 year (converted to monthly rates in calculations)	4.3%	5.1%	PARTNER 3 trial [19]
Rehospitalisation at 2 years (converted to monthly rates in calculations)	1.3%	1.2%	PARTNER 3 trial 2-year outcomes [20]
Rehospitalisation at 5 years and beyond (converted to monthly rates in calculations)	1.7%	1.6%	PARTNER 3 trial 5-year outcomes [21]
Aortic reintervention (converted to monthly rates in calculations)			
From year 1 to year 23 onwards	From 0.5% to 8.9%	From 0.5% to 8.9%	PARTNER 3 up to 5 years [21], then Bourguignon et al. [26]

AF atrial fibrillation, *MI* myocardial infarction, *SAVR* surgical aortic valve replacement, *TIA* transient ischaemic attack

the monthly transition probabilities were informed by other literature sources because these events had limited occurrences within PARTNER 3. The transition from 'alive and well' to 'disabling stroke' was informed by Public Health England data from 2007 to 2016 [23] and Hewitt et al. [24]. The transition from 'treated AF' to 'disabling stroke' was informed by a systematic review and meta-analysis involving over 9.5 million participants [25] (Table 1). A simplifying assumption was made that the transitions to "treated AF" and "disabling stroke" remain constant from year 5 onwards in the model. Permanent pacemaker implantation was captured as an intercurrent event between 30 days and 1 year from the PARTNER 3 trial [19].

Other relevant events, such as rehospitalisation rates, were based on the 1-, 2- and 5-year outcome data from PARTNER 3 [19–21]. Reintervention rates because of valve deterioration used PARTNER 3 for the first 5 years of data and Bourguignon et al. for subsequent data [26] (Table 1). In the base case, the same reintervention rate was used for both the TAVI and SAVR arms; this simplifying assumption allowed the best use of the available data. Other reintervention data available for TAVI were used in a scenario analysis [5] but corresponded to a previous generation of TAVR device (SAPIEN XT) so was not deemed appropriate for use in the base case.

Two options were considered for extrapolation of survival. Option 1: transition probabilities were estimated for each health state using general population mortality data and literature reports of hazard ratios (HRs) for death with AF (HR = 1.46) [25], and for death with disabling stroke at 30 days (HR = 5.22) [27] and in the following months (HR = 1.58) [5]. The HRs were sourced through a pragmatic targeted literature search and an assessment made to select the most robust and appropriate source available at the time of the search. Option 2: this consisted of a parametric survival fitting based on Kaplan–Meier data from the 5-year PARTNER 3 study [21] with a choice of six parametric distributions applied (Weibull, exponential, Gompertz, generalised gamma, log-logistic and log-normal). The survival estimates were adjusted using the UK general population survival to ensure that people in the model did not live longer than expected for the general population.

Option 1 was used to determine all-cause mortality estimates in the base case (Table S1 of the Electronic Supplementary Material [ESM]), with Option 2 (parametric survival analysis) explored in scenario analyses. Option 2 was chosen as a scenario rather than the base case because the unadjusted PARTNER 3 study produced clinically implausible estimates in the model owing to a very low rate of death in the study. As previously mentioned, in Option 2, the survival data were adjusted by the general population mortality. General population mortality was predicted to be higher than the PARTNER 3 study by month 1 of the model in the TAVR arm and month 7 in the SAVR arm. Therefore, it was deemed appropriate to reflect the excess risk of death associated with AF and disabling stroke in the model base case [25, 27] in line with previous publications [10–17, 25, 27]. Despite this, the survival outcomes predicted by the model were similar when using Option 1 or 2 (see Fig. S2 of the ESM).

2.2.2 Utilities

Utility values used age-adjusted population utility norms. An EQ-5D index value (time trade-off value set) was used for the age-adjusted population utility norms, specific to the UK population [22]. To account for there being too few events in the PARTNER 3 trial, utility decrements were based on realistic estimates from the literature, estimated utility decrements for AF (− 0.08) and disabling stroke (− 0.39) using data reported by Sullivan et al. [28] and Luengo-Fernandez et al. [29].

2.2.3 Costs

In the base case, procedure costs for TAVI and SAVR were calculated using the same methodology used in the NICE HVD cost-effectiveness model [5]. The NHS Cost Collection [30] price for each procedure was recalculated to include intensive care unit stay, using published average length of stay data. The cost of the valve (TAVI only) and costs of rehabilitation for each procedure were then added to reach the final cost of each procedure. Further details on procedure costs can be found in Table S2 of the ESM.

The majority of cost inputs for health states, short-term complications and long-term complications were sourced from the NHS Cost Collection [30]. However, when the NHS Cost Collection was not applicable (such as for long-term health state costs), inputs were taken from the published literature and inflated to a 2021/22 cost year using the Personal Social Services Research Unit inflation index [31]. Costs associated with the TAVI and SAVR procedures, rehabilitation, complications, health states and other costs are shown in Table 2 [5, 8, 32–34].

2.3 Model Outputs

Details of the model outputs and assumptions have been published previously [10]. All analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). The model generated total per-patient costs and QALYs for each intervention over the patients' lifetime, as well as an incremental cost-effectiveness ratio (ICER) for TAVI with SAPIEN 3 compared with SAVR in a population of UK low-risk patients with sSAS. In the UK, the

Table 2 Costs associated with TAVI and SAVR (procedure, complications, long term) [2021/22 prices]

Unit cost components	TAVI with SAPIEN 3	SAVR	Source
Procedure			
Total cost of initial procedure including rehabilitation	£30,911	£22,890	Based on NICE HVD guidance [5] LR and updated to September 2021/22 prices
Acute post-operative complications			
Re-intervention	£30,911	£30,911	TAVI with SAPIEN 3 as per initial procedure. SAVR arm assumes TAVI replacement (either SAPIEN 3 or Evolut)
Associated with health states			
Treated AF, month 1	£331	£331	NICE pathways [5] NHS improvement [8] Kansal et al. [32]
Treated AF, ≥ month 2	£41.52	£41.52	Kansal et al. [32]
Disabling stroke, month 1	£20,388	£20,388	Xu et al. [33]
Disabling stroke, ≥ month 2	£603	£603	50% of social care costs removed (assumed to be private) in line with method used for NICE guideline NG208 [5]
Alive and well, year 1	£83.02	£83.02	Assumed follow-up consultation required at months 1, 6 and 12. Cost of outpatient appointment based on NHS improvement [8]
Alive and well, year 2+	£27.67	£27.67	Assumed follow-up consultation required at months 1, 6 and 12. Cost of outpatient appointment based on NHS improvement [8]
Other costs considered			
Pacemaker complications (monthly)	£136	£136	Shore et al. [34]
Rehospitalisation	£3758	£3758	NHS improvement [8] (weighted average of NEL for heart failure EB03A-E)

AF atrial fibrillation, *HVD* heart valve disease, *LR* Low-risk, *NEL* non-elective (non-elective HRG codes), *NHS* National Health Service, *NICE* National Institute for Health and Care Excellence, *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation

willingness-to-pay (WTP) threshold is between £20,000 and £30,000 per QALY gained.

Overall parameter uncertainty (or second-order uncertainty) was addressed using a probabilistic sensitivity analysis (Table S3 of the ESM); these results form the base case. Probability distributions for all input parameters were specified. For instance, a beta distribution was applied to proportions and probabilities, a log normal distribution was applied to relative risks and hazard ratios, and a gamma distribution was applied to costs and resource use values (Briggs et al. [43]). We ran 1000 Monte-Carlo simulations using random draws of all parameters from within their assigned distributions, and 90% credible intervals (CIs) were then calculated.

2.4 Sensitivity Analyses

To evaluate uncertainty, univariate deterministic sensitivity analyses were performed by varying inputs using confidence intervals and ranges from the literature when available, and plausible ranges when data were unavailable (Table S4 of the ESM). A ± 20% assumed variation was applied to the base-case values of key model parameters to determine their lower and upper limits. The resulting impact on net monetary benefit, using a £20,000 WTP threshold, was analysed and visualised using a tornado diagram, which ranked the most influential factors affecting cost effectiveness. All parameters were changed and the impact on the results was explored to identify the key drivers of model uncertainty. In addition, we ran 22 deterministic scenario analyses to test a number of assumptions on the clinical inputs, time horizon, the discount factor and the survival data. To understand how the cost of SAPIEN 3 impacts the ICER, we performed a deterministic threshold analysis (Fig. S1 of the ESM) and probabilistic scenarios to assess the robustness of the threshold results. Stochastic uncertainty was not assessed because of the cohort-based nature of the model.

2.5 Model Validation

Clinical experts were introduced to the cost-effectiveness model following its development by health economics specialists, as the methodological framework lies outside their area of expertise. The model's structure, analytical approach and outcomes were subsequently presented and explained to the clinical panel, which comprised six interventional cardiologists and one cardiac surgeon. The experts were invited to evaluate the methodology, the results and particularly the interpretation of those results in the context of the existing clinical literature. Consensus was reached that the interpretation was appropriate and that the potential implications for clinical decision making were both robust and well founded. The model has also been through a stringent

quality assurance process whereby the calculations were checked. The model clinical outcomes were compared with the PARTNER 3 trial data at a 5-year timepoint to ensure internal validity (see the ESM for results).

3 Results

3.1 Base Case (Probabilistic)

Transcatheter aortic valve implantation with SAPIEN 3 is estimated to offer an incremental health benefit of 0.47 (0.35–0.60 CI) QALYs per patient compared with SAVR, at an increased cost of £7999 (£852–£15,035 CI) per patient over a lifetime horizon. This represents a probabilistic ICER of £16,979 per QALY gained (Table 3). At the conventional UK WTP threshold range of £20,000–£30,000 per QALY gained, TAVI with SAPIEN 3 was cost effective compared with SAVR in 63–90% of the simulations in the model (Fig. 2). The deterministic results can be found in Table S5 of the ESM. Detailed examination of the breakdown of costs for TAVI versus SAVR found that the initial procedural costs for TAVI are higher, but the additional lifetime costs were similar and costs related to 'treated AF health state' and 'disabling stroke' are lower (Table 3 and Fig. 3).

3.2 Deterministic Sensitivity Analyses

Univariate deterministic sensitivity analyses demonstrated that TAVI with SAPIEN 3 was cost effective regardless of plausible changes in many of the individual model parameters (Fig. 4). However, the model was most sensitive to the procedural costs of TAVI with SAPIEN 3, procedural costs of SAVR, risk of new onset AF at 30 days with SAVR and

Table 3 Base-case results with acute and lifetime costs (probabilistic)

Summary results	TAVI with SAPIEN 3	SAVR	Incremental
Cost per patient	£42,640	£34,641	£7999
Life-year gained (undiscounted)	12.58	12.04	0.54
QALYs per patient	7.34	6.87	0.47
Incremental cost effectiveness ratio			£16,979
Incremental net monetary benefit (£20,000 per QALY threshold)			£1423
Incremental net health benefit (£20,000 per QALY threshold)			0.07
Acute-phase cost (initial procedure)			
Index hospitalisation (without pacemaker), including rehabilitation	£30,881	£22,863	£8017
Acute-phase costs	£30,881	£22,863	£8017
Additional costs at 1 year			
Bleeding, MI and TIA	£162	£70	£92
Costs of pacemaker complications	£94	£56	£37
Costs of hospitalisations	£259	£391	− £132
Re-intervention costs	£137	£136	£1
Alive and well health state costs	£921	£617	£304
Treated AF health state costs	£36	£274	− £237
Disabling stroke costs	£39	£169	− £131
Death costs	£0	£0	£0
Total costs at 1 year	£32,529	£24,577	£7,952
Additional lifetime costs			
Costs of pacemaker complications	£929	£541	£388
Costs of hospitalisations	£540	£487	£53
Re-intervention costs	£4356	£4058	£298
Alive and well health state costs	£2495	£1790	£705
Treated AF health state costs	£590	£1466	− £876
Disabling stroke costs	£1201	£1722	− £521
Death costs	£0	£0	£0
Additional lifetime costs	£10,111	£10,064	£47
Total lifetime costs	£73,520	£57,504	£16,016

AF atrial fibrillation, *ICER* incremental cost-effectiveness ratio, *MI* myocardial infarction, *QALY* quality-adjusted life-year, *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation, *TIA* transient ischaemic attack

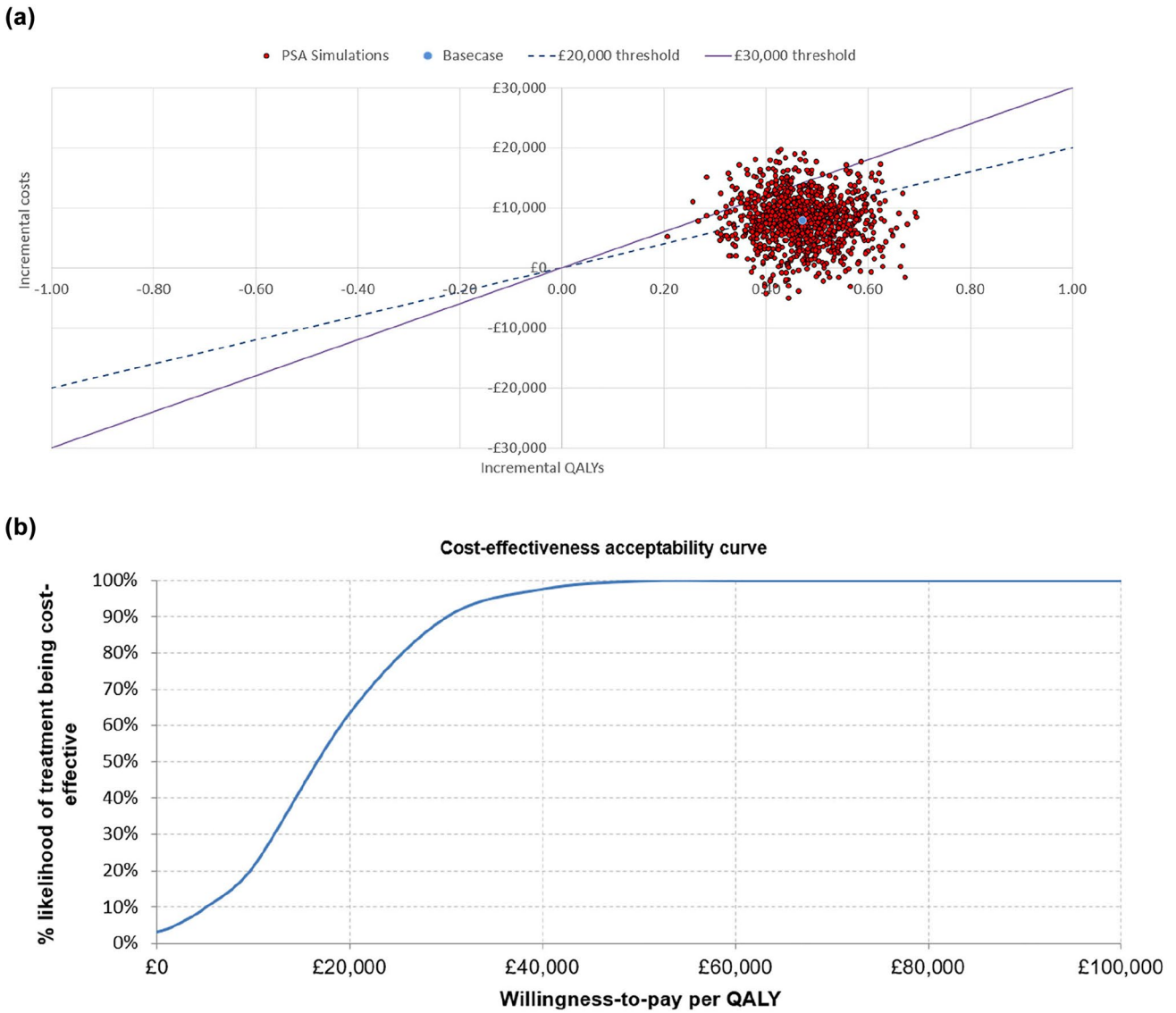

Fig. 2 Probabilistic sensitivity analysis: **a** cost-effectiveness scatter plot; and **b** cost-effectiveness acceptability curve

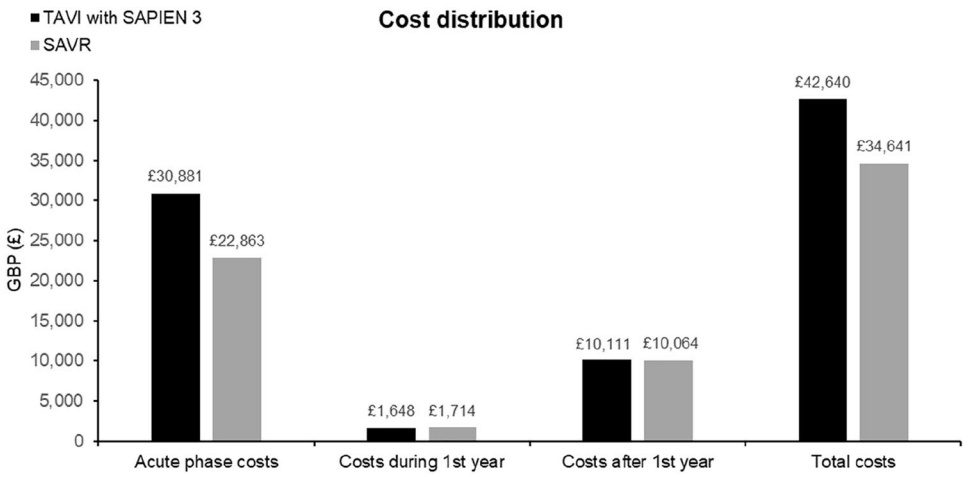

Fig. 3 Cost distribution (probabilistic). The acute-phase category includes the intervention costs and surgery costs. *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation

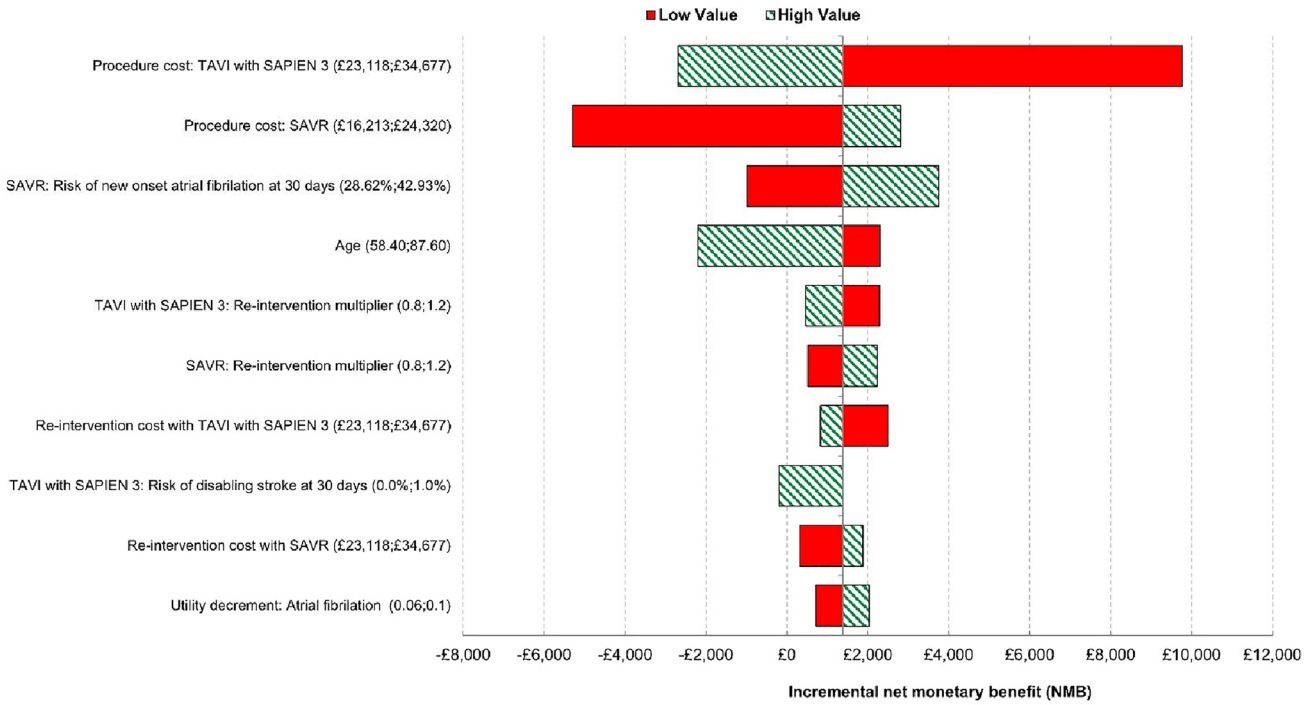

Fig. 4 Tornado diagram showing the ten parameters with greatest influence on the model (deterministic sensitivity analysis). *AF* atrial fibrillation, *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation

age of patients entering the model (Fig. 4). A change in these parameters can lead to the net monetary benefit falling below zero, at a WTP threshold of £20,000/QALY.

3.3 Scenarios

The results from the deterministic scenario analyses demonstrated the comparative robustness of the model (Table 4). Transcatheter aortic valve implantation remained cost effective compared with SAVR in the model when including a more aggressive re-intervention rate for TAVI, an increased risk of stroke, AE costs occurring within 30 days, alternative hospitalisation costs and over various time horizons (Table 4).

The threshold analysis of the SAPIEN 3 valve cost (Fig. S1 of the ESM) demonstrated that the cost of SAPIEN 3 valve would need to be > £23,800 to not be cost effective at the £20,000/QALY threshold or > £28,500 to not be cost effective at the £30,000/QALY threshold. Varying the valve cost from £15,000–£30,000 (from a base-case value of £22,500) moved the ICER from £911 to £33,219 per QALY gained. Probabilistic scenarios were also run on the cost of the SAPIEN valve to assess the robustness of the results. Similar to the deterministic results, the cost of the SAPIEN 3 valve could increase to £23,900 before the probabilistic ICER rose above the £20,000 per QALY threshold (with a 50.1% probability of being cost effective). Similarly, the SAPIEN 3 valve could increase to £28,400 before the probabilistic ICER rose above the £30,000 per QALY threshold (with a 50.1% probability of being cost effective).

4 Discussion

This analysis suggests that TAVI with SAPIEN 3 has a 63–90% probability of being a cost-effective choice for valve replacement in UK patients with aortic stenosis and a low risk of surgical mortality. Transcatheter aortic valve implantation with SAPIEN 3 improves QALYs and increases costs compared with SAVR, leading to a probabilistic ICER of £16,979 per QALY.

The cost-effectiveness results remained robust in most sensitivity analyses at a WTP threshold of £20,000–£30,000 per QALY gained. The unit cost of the SAPIEN 3 valve could increase from £22,500 to £22,900 before the probabilistic ICER rose above the £20,000 per QALY threshold (with a 50.1% probability of being cost effective). Similarly, the SAPIEN 3 valve could increase to £28,400 before the probabilistic ICER rose above the £30,000 per QALY threshold (with a 50.1% probability of being cost effective). The deterministic threshold analysis led to similar results, where SAPIEN 3 could increase to £22,800 and £28,500 before no longer being cost effective at the £20,000 and £30,000 WTP thresholds, respectively.

Table 4 Scenario analyses results (based on deterministic results)

Scenario	Cost difference (TAVI vs SAVR)	QALY difference (TAVI vs SAVR)	ICER
Base case	£7998	0.47	£17,065
Patient starting age 70 years	£7961	0.48	£16,424
Proportion male 54.4%	£7990	0.47	£17,134
Increase in risk of reintervention with TAVI (RR 1.08 from NICE NG208)	£8357	0.47	£17,844
Survival data from PARTNER 3, 5-year KM estimates (gamma distribution, best statistical fit)	£7457	0.31	£23,935
Survival data from PARTNER 3, 5-year KM estimates (Weibull distribution)	£7459	0.31	£23,839
Survival data from PARTNER 3, 5-year KM estimates (log-logistic distribution)	£7463	0.31	£23,705
Increase in risk of stroke to align with PARTNER 3 outcomes (for first 5 years)	£8195	0.44	£18,807
Including adverse event costs within 30 days	£7157	0.47	£15,269
Alternative cost estimates of procedure cost (EY21B for TAVI, elective: £30,911; ED25C for SAVR, elective: £21,638)	£9251	0.47	£19,736
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective short stay: £27,513; ED25C for SAVR, elective: £21,638)	£5589	0.47	£11,924
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective long stay: £34,368; ED25C for SAVR, elective: £21,638)	£12,975	0.47	£27,683
Alternative cost estimates of procedure cost (EY21B for TAVI, elective: £30,911; ED24C for SAVR, elective: £24,142)	£6746	0.47	£14,393
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective short stay: £27,513; ED24C for SAVR, elective: £24,142)	£3085	0.47	£6581
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective long stay: £34,368; ED24C for SAVR, elective: £24,142)	£10,471	0.47	£22,341
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective short stay: £27,513; ED25C for SAVR, non-elective short stay: £15,836)	£11,391	0.47	£24,302
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective long stay: £34,368; ED25C for SAVR, non-elective long stay: £26,486)	£8127	0.47	£17,340
Alternative cost estimates of procedure cost (EY21B for TAVI, non-elective long stay: £34,368; ED24C and ED25C for SAVR, non-elective long stay: £26,621)	£7992	0.47	£17,052
Lower price for SAPIEN 3 device based on NICE NG208 (£17,973)[a]	£3428	0.47	£7314
Alternative disabling stroke cost for month 1 (not excluding 50% of social care costs): £25,322	£7955	0.47	£16,972
Alternative cost of hospitalisation based on NICE NG208 (£2448)[b]	£8026	0.47	£17,123
5-Year time horizon	£7788	0.16	£47,458
10-Year time horizon	£7711	0.31	£25,067
15-Year time horizon	£7799	0.41	£19,061
20-Year time horizon	£7940	0.46	£17,367

AF atrial fibrillation, *ED24C* complex, single heart valve replacement/repair, with CC score 0-5, *ED25C* standard, single heart valve replacement/repair, with CC score 0–5, *EY21B* TAVI using transfemoral approach, with CC score 0–7, *HR* hazard ratio, *ICER* incremental cost-effectiveness ratio, *KM* Kaplan-Meier, *NICE* National Institute for Health and Care Excellence, *QALYs* quality-adjusted life-years, *RR* relative risk, *SAVR* surgical aortic valve replacement, *TAVI* transcatheter aortic valve implantation

[a]£17,500 taken from NICE NG208 [5] and inflated to 2021/22 prices

[b]£2275 taken from NICE NG208 [5] and inflated to 2021/22 prices

A deterministic sensitivity analysis showed that procedural costs (TAVI and SAVR) had the greatest influence on the model's results, followed by SAVR-associated AF risk. In contrast, variations in reintervention rates and costs had a more limited impact, with AF utility decrement having minimal influence. For example, when applying a scenario with an increased TAVI reintervention rate (a RR of 1.08), the resulting deterministic ICER remains below the £20,000 per QALY gained threshold. These findings highlight that procedural costs and clinical complications drive the most substantial changes when adjusting for lower and upper limits.

The results of this study are aligned with a 2024 analysis based on 4-year follow-up data from the Evolut Low Risk trial, which found that TAVI is likely to be cost effective in a UK setting [9]. The Evolut analysis showed that over a lifetime, TAVI was projected to add 0.28 incremental QALYs at an incremental cost of £5021, resulting in an

ICER of £17,883 per QALY gained. The results are also consistent with other analyses that use the same two-stage model structure for patients at low surgical risk in France [10], Italy [11], Spain [12], Germany [13], Belgium [14], Netherlands [15], Sweden [16] and Switzerland [17]. Other cost-effectiveness analyses using PARTNER 3 data report that SAPIEN 3 is cost effective: the Canadian ICER for SAPIEN 3 is CAN $27,196/QALY, the Australian ICER is AUS $3521 [35, 36] and there is a 95% probability that the US ICER would be USD < $50,000 [41]. Transcatheter aortic valve implantation dominance has also been reported in Norway [39] and Ireland [40]. In a cost-effectiveness analysis of TAVI using SAPIEN 3 versus SAVR from a Japanese public healthcare payer perspective, in low-risk patients, the ICER for TAVI was ¥750,417/QALY, which was below the cost-effectiveness threshold of ¥5 million/QALY [42].

In comparison, the findings of this study are discrepant with those reported in the 2021 NICE HVD guidelines [5], which reported that TAVI was not a cost-effective option compared with SAVR in patients at low surgical risk of mortality. The NICE findings were primarily driven by incremental QALY gains for TAVI (+0.024 QALYs) that appear to be very small compared with other published economic evaluations that use 1-year data from the PARTNER 3 trial (+0.1 and +0.2 for the studies by Tam et al. [35] and Zhou et al. [36], respectively).

Concerns regarding these NICE results focus on several issues, namely: (1) outdated assumptions not based on current TAVI practice; (2) combining different valve generations (e.g. second and third); (3) types of TAVI valves (balloon and self-expandable); (4) indications (intermediate-risk and low-risk patients); and (5) TAVI approaches (transfemoral and transapical). These concerns have been described elsewhere [37] and raise uncertainty as to whether the results of the NICE methodology accurately reflect the QALY gains expected with the latest balloon-expandable technology (SAPIEN 3 and SAPIEN 3 Ultra).

Given the continuous evolution of TAVI technology, policy decisions must be guided by the latest evidence on device iterations and procedural advancements. A recent review [38] found that economic evaluations of TAVI often overlook learning effects, technological progress and context-specific factors, leading to outdated or incomplete assessments. Incorporating these factors into policy frameworks is essential for accurate cost-effectiveness evaluations and optimised patient outcomes. As TAVI advances, economic models and reimbursement decisions must be regularly updated to reflect current clinical practice and innovation.

The results of this cost-effectiveness study in the UK support the use of TAVI as a minimally invasive treatment option in patients with sSAS at low risk of surgical mortality, especially when coupled with the substantial clinical benefits previously noted [21]. From a healthcare provider perspective, TAVIs improved outcomes and fewer complications lead to shorter hospital stays and improved capacity, which will positively impact healthcare systems, particularly those with long waiting lists. For policy makers, TAVI's cost effectiveness represents good value for money.

4.1 Limitations

There are some inherent limitations of a cost-effectiveness model, which include assumptions made in the presence of 'best fit' data or paucity of data, extrapolations into time horizons that are modelled beyond the scope of existing input data, and under-estimations and over-estimations potentially caused by differences in healthcare systems or by the criteria for intervention and treatment selection within a specific system. In addition to this, there is the trade-off between capturing the full real-world patient pathway and ensuring the model does not become overly complex. For example, the number of Markov health states was limited to three (excluding death) to reduce the required number of assumptions around transition probabilities. This means that potential health states that did not report statistically significant differences between arms of the PARTNER 3 trial, such as permanent pacemaker (which was instead included as a short-term event) and moderate/severe paravalvular leak, were not included in the Markov model.

The findings of this analysis cannot be generalised to the overall aortic stenosis population because patients with some high-risk features, such as annular calcification and unfavourable coronary anatomy, were excluded from the PARTNER 3 trial. This can also be said for people with bicuspid AS because of them being excluded from the PARTNER 3 trial. There is currently mixed evidence of the safety of TAVI for bicuspid patients, with promising results for SAPIEN 3 [44], but pessimistic results when studied across multiple valve types [45]. Further research needs to be undertaken before concluding whether SAPIEN 3 can be used in this subgroup.

Similarly, the results cannot be generalised to different age groups (such as those under 65 years) because of the mean age in the PARTNER 3 study being 73 ± 5.95 years. Uncertainty about the longer term durability of the TAVI device and consequent re-intervention rates in younger patients cannot be disregarded. Finally, care needs to be taken when attempting to generalise any findings to populations outside the UK and also outside of TAVI using the SAPIEN 3 valve as other TAVI devices have not demonstrated such clinical and economic benefits.

One further limitation is that the survival analysis scenario (mortality option 2, based on Kaplan–Meier estimates at 5 years from the PARTNER 3 trial) was required to be adjusted by the general population mortality because of the trial having few events in both arms. When this

approach is selected, the relative risks of death associated with treated AF and disabling stroke are not included, so people live very slightly longer, reducing the difference in incremental outcomes between TAVI and SAVR moderately. However, both mortality approaches led to similar survival outcomes at both 5 and 10 years (Fig. S2 of the ESM). This aligns with a meta-analysis conducted by Lerman et al. [46]. Further, whilst the use of this option increases the ICER, it is still within the £20,000–£30,000/QALY WTP range.

It should also be noted that the PARTNER 3 trial Kaplan–Meier curves cross (by year 5, SAVR survival is 1.8% higher than TAVI), which suggests that it could be a strong assumption to have a lifetime survival benefit for TAVI [21]. However, the event numbers in each arm are not high enough to draw a strong conclusion from the trial data alone, and the deaths included non-cardiovascular related deaths, including those caused by COVID-19 [21]. This further justifies the use of literature values over the PARTNER 3 trial data for modelling mortality.

5 Conclusions

Using 5-year data from the PARTNER 3 trial, this model estimates that TAVI with SAPIEN 3 has a 63–90% probability of being cost effective versus SAVR in low-risk patients with sSAS when using the £20,000–£30,000 per QALY WTP threshold of the UK healthcare system. Several additional cost scenarios support the cost-effectiveness benefits of TAVI over SAVR in this model. The model appeared to be relatively robust and handled uncertainty introduced via a range of scenarios and sensitivity variables. This analysis using data from the PARTNER 3 trial in conjunction with data from the UK is informative for policy makers and healthcare budget holders.

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Declarations

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Availability of data and material Input parameters values used and data generated during this cost-utility study are wholly included within this article and the associated Electronic Supplementary Material.

Code availability Input parameters values used and data generated during this cost-utility study are wholly included within this article and the associated Electronic Supplementary Material. The code was only used in the model to run a probabilistic and deterministic sensitivity analysis and so will not be made available.

Authors' contributions PC led the project and contributed to the methodology, data analysis and manuscript drafting, and serves as the guarantor, ensuring the integrity and accuracy of the work. VS assisted with model adaptation and manuscript drafting. TB adapted the model, ensured the use of the best methodology and provided a health economics opinion. PMC, DB, CL, MAR and NC provided expert clinical opinion and economic guidance, contributing to the interpretation of results and critical review of the manuscript. All authors reviewed and approved the final version.

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