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Transcatheter aortic valve implantation with SAPIEN 3 versus surgical aortic valve replacement in patients with symptomatic severe aortic stenosis at low risk of surgical mortality: a cost-utility analysis for Switzerland

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Summary

AIMS OF THE STUDY: The 2021 European Society of Cardiology Guidelines on valvular heart disease recommend transcatheter aortic valve implantation (TAVI) for patients with symptomatic severe aortic stenosis at low surgical risk and age ≥75 years who are suitable for a transfemoral approach (recommendation class IA) based on two large randomised controlled trials (PARTNER 3 and Evolut Low Risk) comparing transcatheter aortic valve implantation with surgical aortic valve replacement (SAVR). Whether such an approach is cost-effective in Switzerland remains unclear. The aim of this cost-utility analysis was to compare transcatheter aortic valve implantation with SAPIEN 3 versus surgical aortic valve replacement in symptomatic severe aortic stenosis patients at low risk of surgical mortality from the perspective of Swiss compulsory health insurance using data from the PARTNER 3 trial (reflecting specifically the safety and efficacy of the SAPIEN 3 TAVI device).

METHODS: A previously published two-stage Markov-based model that captured clinical outcomes from the PARTNER 3 trial was adapted from the perspective of the Swiss compulsory health insurance system, using local or geographically close general population mortality and utility data, unit costs and medical resource use from publicly available sources and based on expert opinion. The model had a lifetime horizon with a 3% yearly discounting factor. The cost–utility analysis estimated changes in both direct healthcare costs and health-related quality-adjusted life years for transcatheter aortic valve implantation compared with surgical aortic valve replacement in patients with symptomatic severe aortic stenosis at low risk of surgical mortality.

RESULTS: Overall, transcatheter aortic valve implantation with SAPIEN 3 resulted in lifetime costs per patient of CHF 79,534 and quality-adjusted life years per patient of 9.64, compared with surgical aortic valve replacement lifetime costs and quality-adjusted life years per patient of CHF 76,891 and 8.96, respectively. Compared with surgical aortic valve replacement, transcatheter aortic valve implantation was estimated to offer an incremental improvement of +0.68 quality-adjusted life years per patient at an increased cost of +CHF 2643 per patient over a lifetime horizon. The incremental cost-effectiveness ratio was CHF 3866 per quality-adjusted life year gained and remained below CHF 50,000 per quality-adjusted life year gained across several sensitivity analyses.

CONCLUSIONS: This analysis suggests that transcatheter aortic valve implantation using the SAPIEN 3 device is likely to be a highly cost-effective alternative for symptomatic severe aortic stenosis patients at a low risk of surgical mortality, treated in the contemporary Swiss setting. These findings may help to inform a holistic approach when making policy decisions for the management of this patient group.

ABBREVIATIONS

CHF:	Swiss franc
EQ-5D(-5L):	European Quality of Life 5 Dimensions (5 Level Version)
ESC:	European Society of Cardiology
PARTNER 3 trial:	Placement of Aortic Transcatheter Valves 3 trial
SAVR:	surgical aortic valve replacement
TAVI:	transcatheter aortic valve implantation

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Introduction

Severe aortic stenosis is a common valvular disease [1] with survival probabilities as low as 50% at two years and 20% at five years [2] without valve replacement. Since its introduction in 2002, transcatheter aortic valve implantation (TAVI) has become the treatment of choice for the treatment of symptomatic severe aortic stenosis in elderly and high-risk surgical patients [3, 4]. Continuous development of the technology improved patients' outcomes, patients' quality of life and reduced complication rates, leading to an unprecedented expansion towards lower-risk patient populations, namely intermediate-risk and low-risk patients [5–8].

The Placement of Aortic Transcatheter Valve Study (PARTNER) 3 trial was a multicentre randomised controlled study in patients with symptomatic severe aortic stenosis considered at low risk of surgical mortality [9–11]. In this study, transfemoral TAVI using the SAPIEN 3 transcatheter heart valve (Edwards Lifesciences) was compared to surgical aortic valve replacement (SAVR) [9–11]. TAVI reduced the composite outcome of death, stroke or rehospitalisation compared with SAVR after 2 years (11.5% vs 17.4%; hazard ratio [HR]: 0.63; 95% confidence interval: 0.45–0.88; p = 0.007) [9, 10] and after 5 years (22.8% vs 27.2%; HR: 0.79; 95% confidence interval: 0.61–1.02; p = 0.07) [11] but slightly short of statistical significance. TAVI also 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. Last, there were no significant between-group differences in major vascular complications, new permanent pacemaker insertions, or moderate or severe paravalvular regurgitation [9–11].

Based on the clinical benefits of TAVI versus SAVR in patients with symptomatic severe aortic stenosis across all risk groups, the latest European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) guidelines on valvular heart disease recommend TAVI in all patients aged 75 years or older who are suitable for a transfemoral approach, regardless of the degree of surgical risk (recommendation class IA) [5, 12].

ESC guidelines were endorsed by the Swiss Society of Cardiology, and the Swiss compulsory health insurance scheme (on the legal basis of the Federal Health Insurance Act [13]) recently added coverage for the TAVI procedures in patients with symptomatic severe aortic stenosis at low surgical risk in their latest policy – effective from 1 July 2023. The regulations state that there should be mandatory coverage for inoperable, high- and intermediate- surgical risk patients, and provisional coverage regarding evidence development for those at low risk. Criteria for reimbursement in Switzerland are based on efficacy, effectiveness, expediency and economic efficiency. While both efficacy and expediency were convincingly shown in previous randomised controlled trials, cost-effectiveness largely depends on national tariffs and prosthesis prices, and thus requires a dedicated cost-utility analysis.

Such evaluations have already been performed in various countries, with publications in France [14], Italy [15], Spain [16], Germany [17], Belgium [18] and the Netherlands [19] all showing the cost-effectiveness of TAVI with SAPIEN 3 compared with SAVR; however data for Switzerland is lacking.

We thus aimed to conduct a cost-utility analysis comparing TAVI with SAPIEN 3 with SAVR in symptomatic severe aortic stenosis patients at low risk of surgical mortality from the perspective of Swiss compulsory health insurance, using data from the PARTNER 3 trial and other relevant sources.

Methods

A cost-utility analysis was built using methodology validated for the French [14], Italian [15], Spanish [16], German [17], Belgian [18] and Dutch [19] populations to estimate changes in both direct healthcare costs and health-related quality of life with the use of TAVI with SAPIEN 3 versus SAVR in symptomatic severe aortic stenosis patients at low risk of surgical mortality (<4% as defined by the Society of Thoracic Surgeons [STS]) from the perspective of the Swiss compulsory health insurance system. Ethical approval of research was not required as this cost-utility analysis was based on data from previously conducted studies and did not include any new studies with human participants.

Model structure

Details of the two-stage model structure and the rationale of the four distinct health states have been described previously [14]. In brief, survival, quality of life, costs and early adverse events (AEs) linked to the TAVI procedure were captured using the 30-day AEs dataset from the PARTNER 3 study [10] in a decision tree (figure 1A). This data was then 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 post-SAVR intervention (figure 1B). The model was considered appropriate for the Swiss context by the authors, based on their clinical and health economics expertise.

Considering that the initial treatment decision has long-term consequences and that symptomatic severe aortic stenosis requires life-long valve replacement, a lifetime horizon (50 years) was selected for the cost-utility analysis. This time horizon was chosen to reflect all possible consequences in individuals with symptomatic severe aortic stenosis over their lifetime.

A discounting factor per year of 3% was applied for both future costs and benefits. Such a discount rate is frequently used in Health Technology Assessment (HTA) reports for the Federal Office of Public Health (FOPH) and is thus accepted by the FOPH [20]. Details for input variable definitions have been published previously [10, 14] and are summarised in the sections below.

The cost-utility model generated total per-patient costs and quality-adjusted life years for each intervention and the incremental cost-effectiveness ratio for TAVI compared with SAVR. Output definitions can be found at www.yhec.co.uk/glossary/. For non-experts of economic evaluation, a reader's guide to facilitate reading and interpretation is recommended [21].

Study overview

The model was informed by the study population of PARTNER 3 (ClinicalTrials.gov number: NCT02675114), a multicentre randomised clinical trial that compared TAVI with transfemoral placement of a third-generation balloon-expandable valve with standard SAVR in patients with symptomatic severe aortic stenosis who were considered at low risk of mortality from surgery (STS-Predicted Risk of Mortality [STS-PROM] score <4%). The trial protocol was designed by the trial sponsor (Edwards Lifesciences) and the steering committee, with guidance from the Food and Drug Administration (FDA). The sponsor funded all trial-related activities and participated in site selection, data collection and monitoring, and statistical analyses. Patients with clinical frailty, bicuspid aortic valves or other anatomical features that increased the risk of complications associated with either surgery or transcatheter aortic valve implantation were excluded. In PARTNER 3, 1000 patients were enrolled, of whom 503 were randomised to TAVI and 497 to SAVR, with "as treated" groups of 496 and 454 patients, respectively [10]. The trial comprised patients with an average age of 73 years and 69% of patients were male.

All-cause mortality was determined from general population normal mortality risk, with relative risks applied from published literature corresponding to each health state. Costs and resources used were based on costing information from Swiss Diagnosis-Related Groups (DRGs), regional tariffs, literature and expert interviews. Utility values used age-adjusted population norms from Germany in the absence of robust Swiss population norms [22], with decrements (disutilities) applied from published literature corresponding to each health state.

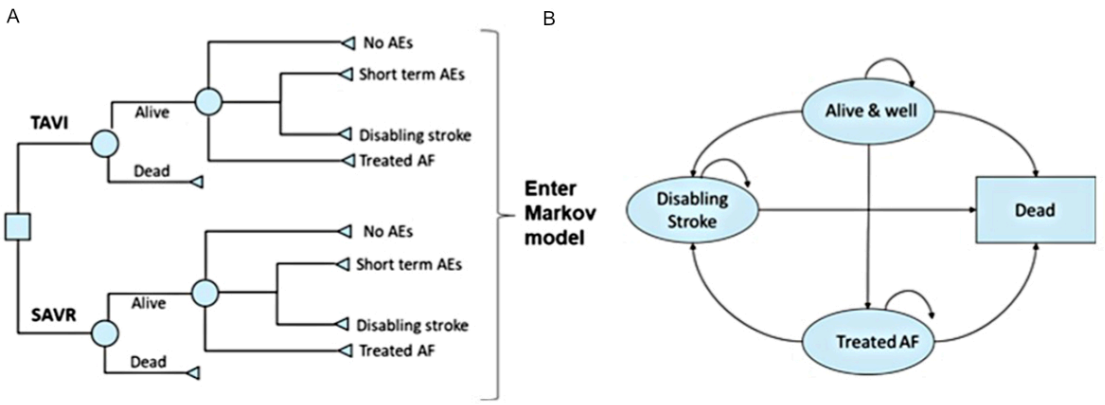
Clinical events

Probabilities of clinical events, such as health state transition probabilities, rehospitalisation rates, aortic reintervention rates and intercurrent events (such as myocardial infarction, bleeding and transient ischaemic attack), used in the model were sourced from the PARTNER 3 trial and from Swiss-specific literature sources when available and relevant (table S1 in the appendix). Monthly transition probabilities between health states for the Markov model were estimated based on data from PARTNER 3 (up to 5-year outcomes) or other literature sources where there were too few events in PARTNER 3 for reliable estimates (table S1). Input data for permanent pacemaker insertion at 30 days was based on PARTNER 3 data for SAVR [10] and estimates from the Swiss TAVI Registry [23] to reflect more recently available SAPIEN 3 TAVI data specific to the Swiss population. Rehospitalisation rates were based on data from the PARTNER 3 study up to 5 years [9–11] and assumed to remain constant over the time horizon of the model thereafter. Reintervention rates were also based on data from the PARTNER 3 study up to 5 years [9–11] and by competing risk estimates for the 73-year-old cohort from a study by Bourguignon et al. from Year 6 onwards [24]. The same reintervention rate was used for both TAVI with SAPIEN 3 and SAVR in the base case; this simplifying assumption allowed best use of the available data.

Survival extrapolation

All-cause mortality was determined from general population normal mortality risk, with relative risks applied from published literature corresponding to each health state. In the base case, transition probabilities were taken from the literature (compared to the general population, relative risks of death with "treated AF" and "disabling stroke" are 1.46 and 2.30, respectively) due to immaturity of survival

Figure 1: The cost-effectiveness model had two stages: (**A**) early adverse events (AE) from the PARTNER 3 trial were captured in a decision tree, which fed into (**B**) a Markov model that captured longer-term outcomes of patients, with four distinct health states: "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", "treated AF" or "dead" at any point during the model time horizon. "Treated AF" = patients have undergone the procedure and survived but developed atrial fibrillation (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 to the "dead" state at any point during the model time horizon. "Dead" is the absorbing state in the model: all patients in the model are at risk of dying due to general all-cause mortality; patients with "treated AF" and "disabling stroke" are at an increased risk of dying. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation. Reproduced from Gilard M, et al. [14]. Value Health 2021doi: https://doi.org/10.1016/j.jval.2021.10.003, under the terms of the Creative Commons licence "Attribution 4.0 International".



data from the PARTNER 3 trial producing clinically implausible estimates (because of the very low rate of death in the study [9–11]). Annual mortality risk for "alive and well" and other relative risks for other health states are shown in table S2 in the appendix.

Health utilities

The PARTNER 3 trial collected EQ-5D-based utilities; however, given that few clinical events were observed, we decided it was more appropriate to consider estimates from the literature. We used age-specific utility values representing population norms from Germany in the absence of Swiss population norms covering all language regions [22]. Disutilities by health state were calculated as weighted averages of disutilities in neighbouring countries, namely Germany [17], France [14] and Italy [15], with weights based on the distribution of main languages in Switzerland, as reported in the Structural Survey of the Federal Statistical Office (FSO). The resulting disutilities were 0.14 for "treated AF" and 0.38 for "disabling stroke" (table S3 in the appendix).

Cost inputs

Costs were based on costing information from Swiss Diagnosis Related Groups (DRGs), regional tariffs and literature. Costs associated with TAVI and SAVR (procedure, complications and long-term) are shown in table 1. Base case procedure cost information was drawn from a composite of SwissDRG version 13.0 AG 2024 [25]: F98B and F98C (TAVI); F03C and F03E (SAVR). The breakdown of TAVI and SAVR procedure costs is shown in table S4 in the appendix. For pacemaker complication costs, in the absence of Swiss-specific data we used data from a German study [31]. To adjust the costs to the Swiss price level, we used purchasing power parity corrections (Germany: 1.544 for 2020 and 1.490 for 2021 [32]). All costs were adjusted to 2022 Swiss franc (CHF) using the Consumer Price Index.

Cost-effectiveness threshold per quality-adjusted life year

In the absence of an official willingness-to-pay threshold for Switzerland, we assumed the cost-effectiveness threshold to be CHF 50,000 per quality-adjusted life year gained.

Sensitivity and scenario analyses

To evaluate uncertainty, 1-way deterministic sensitivity analyses were performed by varying inputs using confidence intervals and ranges from the literature when available, and plausible ranges when data was unavailable (appendix table S5). All parameters were changed and the impact on the results explored. Overall parameter uncertainty was addressed using a probabilistic sensitivity analysis (PSA). Probability distributions for all input parameters were specified and 1000 Monte Carlo simulations were run using random draws of all parameters from within their assigned distributions (appendix table S6).

Finally, several scenario analyses were performed to account for uncertainties not captured by the standard sensitivity analyses. The impact of increased risk of reintervention was explored in Scenario 1, based on data at 5 years from the PARTNER 2 trial [7]. Scenarios 2 and 3 considered parametric survival fitting based on Kaplan-Meier data from the PARTNER 3 trial, utilising various HRs. Among the three parametric distributions considered

Table 1:
Costs associated with transcatheter aortic valve implantation and surgical aortic valve replacement (procedure, complications, long-term).

Unit cost components		Transcatheter aortic valve implantation with SAPIEN 3	Surgical aortic valve replacement	Source
Procedure	Intervention	CHF 45,211	CHF 36,099	Composite of SwissDRG Version 13 [25]: F98B and F98C (TAVI); F03C and F03E (SAVR).
	Rehabilitation	CHF 4934	CHF 9422	SwissDRG ST Reha Version 1.0 / 2022 [26].
Associated with health state	Treated AF – month 1	CHF 6649		SwissDRG AG 2021 [25]: F50B and F50C; + cost of anticoagulation drug and beta-blocker; + outpatient costs calculated as per TARMED [27], expert interview.
	Treated AF ≥ month 2	CHF 93		Cost of anticoagulation drug (20 mg Xarelto) and beta-blocker (5 mg Bilol), assumption of one tablet each per day [28].
	Disabling stroke – month 1	CHF 20,662		Pletscher et al. 2013 [29].
	Disabling stroke ≥ month 2	CHF 3648		
	Alive and well – Year 1 (per month)	CHF 103	CHF 34	TARMED [27], expert interview (CHF 413 per check-up for echocardiography, consultation and report. Assumption of one check-up per year; with TAVI, three check-ups in the first year).
	Alive and well – year 2+ (per month)	CHF 34	CHF 34	
Other costs considered	Myocardial infarction	CHF 8924	CHF 8924	Reinhold et al. 2011. Value adjusted to inflation rate (Dec 2020) using the following converter: [30].
	Pacemaker procedure	CHF 13,176	CHF 13,176	SwissDRG AG 2021 [25]: F17A.
	Pacemaker complications (monthly)	CHF 329	CHF 329	SwissDRG AG 2021 [25]: F17A + TARMED [27], expert interview + Ludwig et al. 2019 [31].
	Rehospitalisation	CHF 9259	CHF 9259	SwissDRG AG 2021 [25]: F62A, F62B, F62C, F62D.
	Reintervention	CHF 50,145	CHF 50,145	Assumed equal to cost of initial procedure plus rehabilitation associated with procedure.

AF: atrial fibrillation; CHF: Swiss franc; DRG: Diagnosis-Related Group; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

(Weibull, Exponential, Gompertz), the Weibull was best in terms of goodness-of-fit statistics, minimising the Akaike information criterion (AIC) and the Bayesian information criterion (BIC), and was adjusted to the survival of the overall Swiss population. In Scenario 2, the HR from the PARTNER 3 trial at two years (HR = 0.75) was used and adjusted to the Swiss population overall mortality. Scenario 3 removed any survival benefit with the SAPIEN 3 valve (HR = 1). Scenario 4 considered utility decrements for each treatment arm from the PARTNER 3 trial – individually extracted at baseline, after 30 days, 6 months and 1 year [33]**.** Scenarios 5 and 6 considered various costing estimates (SAVR based on minimal invasive tariff and assuming inpatient rehabilitation only). Lastly**,** Scenarios 7 to 11 looked at various model time horizons (from 5 to 30 years). All analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

Results

Base case

Compared with SAVR, TAVI is estimated to offer significant benefits by increasing quality-adjusted life years (incremental improvement of +0.68 per patient) at a slightly increased cost (+CHF 2643 per patient) over a lifetime horizon. This represents an incremental cost-effectiveness ratio of CHF 3866 per quality-adjusted life year gained. Overall, TAVI with SAPIEN 3 resulted in lifetime costs per patient of CHF 79,534 and lifetime quality-adjusted life year per patient of 9.64; SAVR in CHF 76,891 and 8.96 quality-adjusted life years respectively.

The estimated incremental cost-effectiveness ratio is much lower than the considered highly-cost-effectiveness threshold of CHF 50,000 per quality-adjusted life year gained (table 2). Further examination of the breakdown of costs for TAVI with SAPIEN 3 versus SAVR revealed that, despite initial higher procedural costs in the model with TAVI, costs with respect to "disabling stroke", "treated AF" and "rehospitalisation" were lower (figure 2).

Probabilistic sensitivity analyses

The findings of the PSA corroborate those of the base case analysis. At the considered highly-cost-effectiveness threshold of CHF 50,000/quality-adjusted life year, TAVI with SAPIEN 3 remained cost-effective compared with SAVR in 99.9% of simulations (figure 3). Even at a lower threshold of CHF 30,000/quality-adjusted life year, TAVI with SAPIEN 3 still had a high probability (97.7%) of being cost-effective (figure 4).

Table 2:
Base case results with acute and lifetime costs.

Summary results		**Transcatheter aortic valve implantation with SAPIEN 3**	**Surgical aortic valve replacement**	**Incremental**
Cost per patient		CHF 79,534	CHF 76,891	CHF 2643
Life years gained (undiscounted)		14.99	14.44	0.55
Life years gained (discounted)		11.67	11.29	0.38
Median survival (years)		17.83	15.92	1.92
Quality-adjusted life years per patient		9.64	8.96	0.68
Incremental cost-effectiveness ratio (ICER)*				CHF 3866
Acute phase cost (first hospitalisation and rehabilitation)	Index hospitalisation	CHF 45,211	CHF 36,099	CHF 9112
	Rehabilitation (inpatient and outpatient)	CHF 4934	CHF 9422	–CHF 4488
	Acute phase costs	**CHF 50,145**	**CHF 45,521**	**CHF 4624**
Additional costs at 1 year	Myocardial infarction	CHF 135	CHF 117	CHF 18
	Costs of pacemaker complications	CHF 457	CHF 139	CHF 318
	Costs of rehospitalisations	CHF 645	CHF 947	–CHF 313
	Reintervention costs	CHF 224	CHF 250	CHF 2
	"Alive and well" health state costs	CHF 1153	CHF 255	CHF 898
	"Treated atrial fibrillation" health state costs	CHF 389	CHF 2785	–CHF 2397
	"Disabling stroke" health state costs	CHF 21	CHF 303	–CHF 283
	Total costs at 1 year	**CHF 53,168**	**CHF 50,314**	**CHF 2854**
Additional lifetime costs	Costs of pacemaker complications	CHF 5474	CHF 1617	CHF 3857
	Costs of rehospitalisations	CHF 1626	CHF 1476	CHF 150
	Reintervention costs	CHF 10,774	CHF 10,149	CHF 624
	"Alive and well" health state costs	CHF 3694	CHF 2674	CHF 1020
	"Treated atrial fibrillation" health state costs	CHF 2223	CHF 4611	–CHF 2388
	"Disabling stroke" health state costs	CHF 2574	CHF 6050	–CHF 3475
Additional lifetime costs		**CHF 26,365**	**CHF 26,577**	**–CHF 212**
Total lifetime costs		**CHF 79,534**	**CHF 76,891**	**CHF 2643**

CHF: Swiss franc.

* Incremental Cost-Effectiveness Ratio (ICER) is defined as the Incremental Cost per patient divided by Incremental quality-adjusted life years gained per patient.

Deterministic sensitivity analyses

Univariate sensitivity analyses showed that TAVI remained cost-effective irrespective of plausible changes in individual model parameters (figure 5). The model was most sensitive to the procedure and the reintervention costs of both strategies, the risk of new onset of AF at 30 days for SAVR, and the starting age of patients entering the model (only those 10 parameters with the greatest influence on the model's results are displayed).

Scenario analyses

The results from the various scenario analyses demonstrated the comparative robustness of the model reported (table 3).

Discussion

This analysis indicates that TAVI with SAPIEN 3 is expected to be a cost-effective valve replacement choice for patients with symptomatic severe aortic stenosis at low risk of surgical mortality in Switzerland. Incremental cost-effectiveness ratio benefits shown in this analysis suggest a cost-effective intervention in the Swiss system, even with a considered cost-effectiveness threshold of CHF 50,000 per quality-adjusted life year. Sensitivity analyses were used to assess uncertainty and the results appeared robust.

The findings of the current analyses are reinforced by other cost-effectiveness studies which show that TAVI with

Figure 2: Cost breakdown for transcatheter aortic valve implantation (TAVI) with SAPIEN 3 and for surgical aortic valve replacement (SAVR). AF: atrial fibrillation; CHF: Swiss franc; MI: myocardial infarction; TIA: transient ischaemic attack.

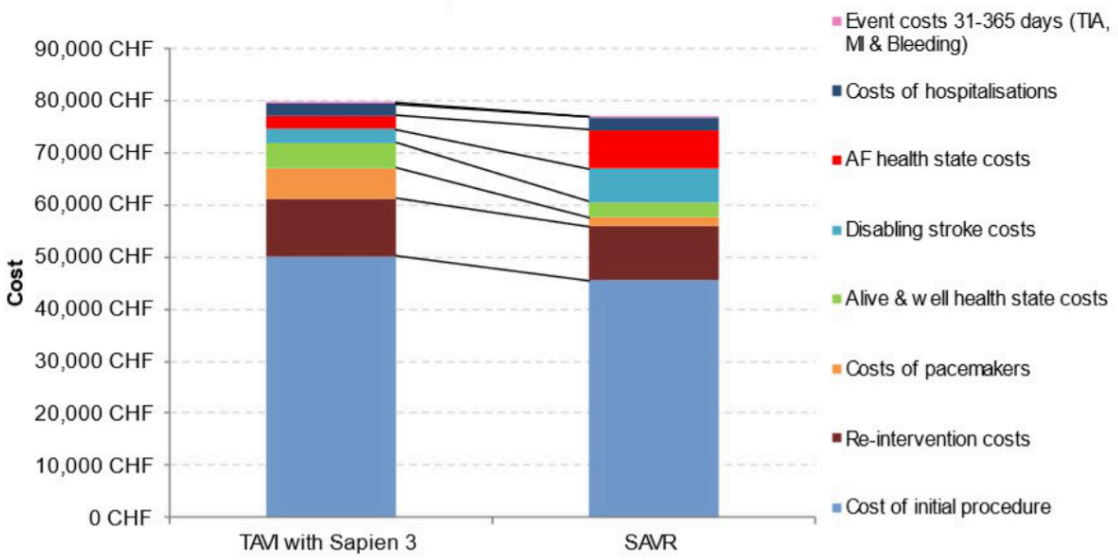
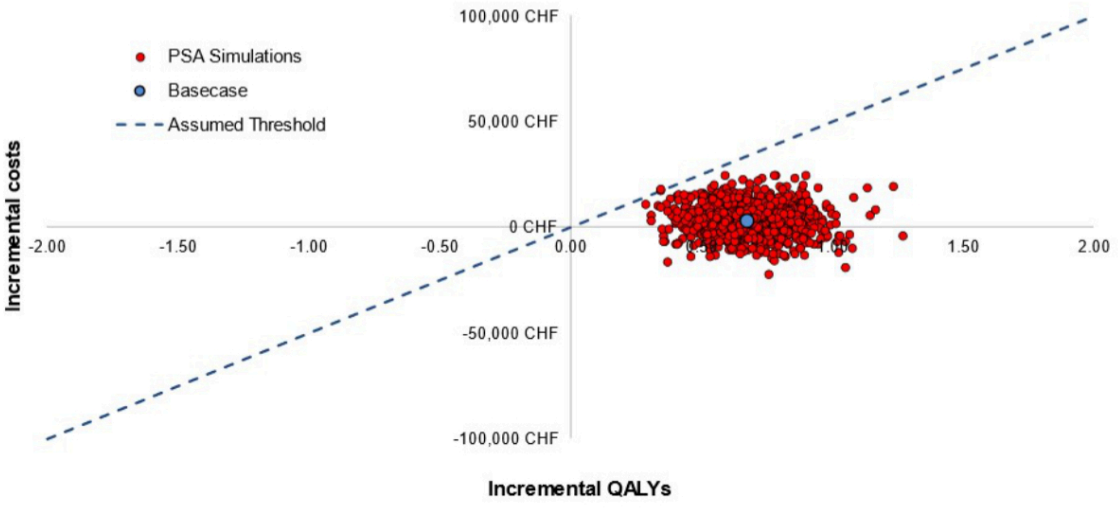


Figure 3: Probabilistic sensitivity analysis (PSA): Cost-effectiveness scatter plot. "Assumed threshold" is the willingness-to-pay threshold that corresponds to Swiss francs (CHF) 50,000 per quality-adjusted life year (QALY) gained. The scatter plot is shown on a cost-effectiveness plane. The cost-effectiveness plane plots incremental QALYs against incremental costs for each probabilistic simulation. As an example, simulations in the top-right quadrant represent simulations in which transcatheter aortic valve implantation (TAVI) is more costly and more effective than surgical aortic valve replacement (SAVR).



SAPIEN 3 is either dominant or cost-effective in patients at low risk of surgical mortality [34–38]. The Swiss findings are also consistent with cost-effectiveness analyses of TAVI with SAPIEN 3 versus SAVR in France [14], Italy [15], Spain [16], Germany [17], Belgium [18] and the Netherlands [19] using the same model structure.

The cost-effectiveness of TAVI in low-risk patients in Switzerland appears to be driven by lower long-term management costs, particularly those costs related to "treated AF" and "disabling stroke"; cost savings in these areas were also seen in France, Italy, Spain, Germany, Belgium and the Netherlands [13–19]. Our analysis showed that initial procedure costs for TAVI with SAPIEN 3 were higher than for SAVR in Switzerland; this was also the case in Italy and Spain, whereas the initial cost for performing TAVI was lower than for SAVR in France, mainly driven by the higher rehabilitation costs that SAVR patients experience.

The results of this cost-effectiveness study in Switzerland are valuable for supporting the use of TAVI as a minimally invasive treatment option in patients with symptomatic severe aortic stenosis at low risk of surgical mortality. Data

Figure 4: Probabilistic sensitivity analysis: Cost-effectiveness acceptability curve. CHF: Swiss franc; QALYs: quality-adjusted life years; TAVI: transcatheter aortic valve implantation.

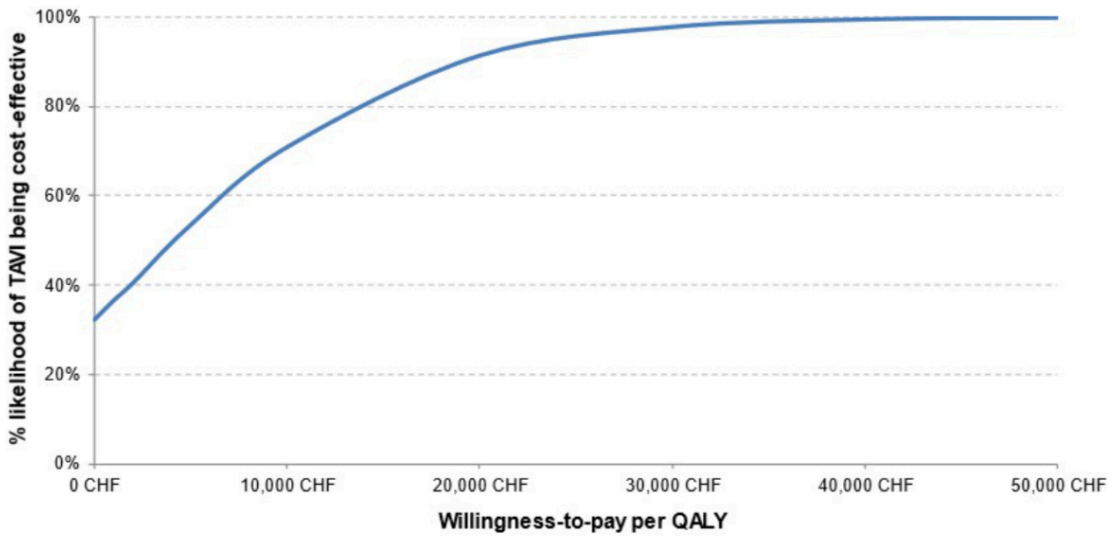
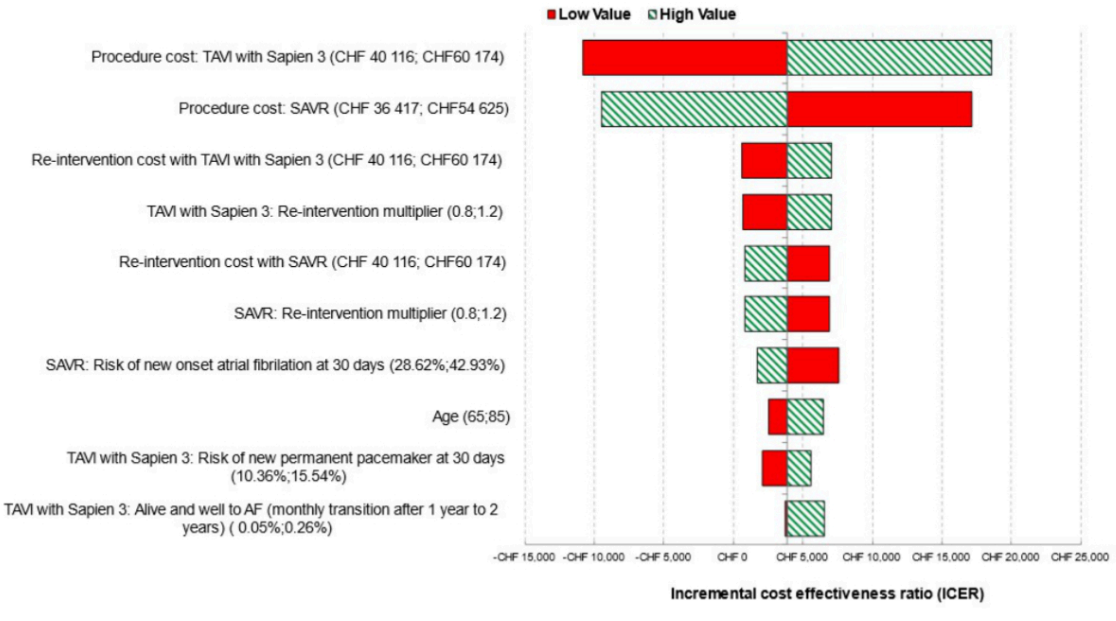


Figure 5: Deterministic sensitivity analysis: Tornado diagram showing the 10 parameters with greatest influence on the model. CHF: Swiss franc; ICER: incremental cost-effectiveness ratio; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation. *Interpretation note:* This chart presents the results of the 10 univariate sensitivity analyses that had the greatest influence on the model ICER. Each analysis is summarised using a horizontal bar which represents the variation in the ICER around a central value corresponding to the base case analysis as the relevant parameter is varied between two plausible but extreme values. The horizontal bars are ordered so that those with the greatest spread (i.e. parameters to which the model output is most sensitive) are at the top of the diagram, and those with the lowest spread at the bottom.



suggests that, with TAVI, rehospitalisation risk is reduced, there is a lower risk of procedural complications and recovery rates improve, resulting in overall quality of life gains. There are also many societal benefits associated with the use of TAVI. Reducing hospital stays as well as resource use (e.g. lower general anaesthesia, less intensive care/ICU stays, improvement in efficiencies during the index hospitalisation) allows for more patients to be treated in the same hospital. The former is an important element as long waiting lists after the COVID-19 pandemic occurred in some countries and an expected increase in number of TAVI procedures due to demographic changes have put health systems, already in high demand, under even further stress [39].

Following the update to the European guidelines [5, 12] and the potential update to the Swiss guidelines, it would be expected that the number of TAVIs will increase in the coming months and years, as large numbers of symptomatic severe aortic stenosis patients at low surgical risk become eligible to benefit from this treatment. It is likely that the TAVI procedure will be further simplified, with shorter admission times and lengths of stay post-procedure, leading to decreasing costs. In this regard, the results of this analysis could inform policymakers on the management of patients with symptomatic severe aortic stenosis in Switzerland and improve access to TAVI for these patients.

Limitations

Some limitations relate to those of any cost-effectiveness analysis and include assumptions made where there is "best fit" data or paucity of data, extrapolations modelled for time horizons beyond the scope of existing input data, and potential for under- and over-estimations due to differences in healthcare systems or by the intervention/treatment selection criteria within a specific system. First, neither utilities nor estimates for annual mortality rates were derived from aortic stenosis patients. Both are likely different in an aortic stenosis population than the average normal population.

Second, the reintervention rate was assumed to stay constant after 22 years; the effect of this assumption on modelled outcomes was thought to be minimal based on an expectation that around 15% of patients would still be alive in the model after this time point, with limited need for reintervention. Nevertheless, uncertainty about the longer-term durability of the TAVI device and consequent reintervention rates in younger patients cannot be disregarded. Third, disutilities were not included for intercurrent events because it would risk them being counted twice with the health state utilities being applied to patients in the "treated AF" and "disabling stroke" states. This was a conservative assumption because, apart from pacemaker complications, rates of intercurrent events were generally lower for TAVI with SAPIEN 3 compared with SAVR [10]. Fourth, the literature data used to calculate the utility decrements for "treated AF" and "disabling stroke" could imply a limitation. The disutilities were calculated through an average weighting of disutilities in neighbouring countries, namely Germany, France and Italy. Although the best available option and methodologically sound, further investigation into disutilities specific to the Swiss population on these conditions may be valuable. Moreover, utilities were taken from population norms in Germany that were recorded 20 years ago; hence, they may not be applicable to current times. Fifth, additional charges *(Zusatzentgelte)*, which would have a greater impact on SAVR costs (transfusion, haemofiltration in acute kidney injury) were not taken into consideration. Sixth, to calculate some costs, such as the rehabilitation costs following a TAVI and SAVR procedure, the "treated AF" cost, the "alive and well" cost and the pacemaker cost, expert interviews were partially relied upon. This was seen as the best available option to localise the cost. The generalisability of the PARTNER 3 results was a limitation. Patients with unfavourable coronary anatomy were excluded from PARTNER 3, so any conclusions cannot be generalised to the overall population with aortic stenosis. In addition, findings from this model cannot be generalised to populations outside of Switzerland. Seventh, variations may occur across regions of Switzer-

Table 3:
Scenario analyses.

No.	Description	Incremental costs (TAVI vs SAVR), in CHF	Incremental quality-adjusted life years (TAVI vs SAVR), in quality-adjusted life years	Incremental cost-effectiveness ratio: CHF / quality-adjusted life year
	Base case	2643	0.68	3866
1	More aggressive reintervention rate for transcatheter aortic valve implantation (PARTNER 2A 5 years)	26,117	0.67	39,267
2	Survival data from PARTNER 3, as reported in the study (HR = 0.75)	5517	1.37	4033
3	Survival data from PARTNER 3, estimating there is no survival benefit (HR = 1)	187	0.48	390
4	Utility from PARTNER 3 EQ-5D-5L (disutility by treatment)	2643	0.34	7866
5	Procedure cost with all SAVRs based on minimal-invasive tariff (F03C)	–9317	0.68	Dominant
6	Only inpatient rehabilitation (no outpatient rehabilitation)	880	0.68	1287
7	Time horizon = 5 years	2407	0.24	9890
8	Time horizon = 10 years	1940	0.43	4468
9	Time horizon = 15 years	1939	0.57	3385
10	Time horizon = 20 years	2329	0.65	3566
11	Time horizon = 30 years	2640	0.68	3862

CHF: Swiss franc; HR: hazard ratio; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

land. Finally, the employment of some of the authors by Edwards Lifesciences could be considered a limitation.

Conclusions

This analysis suggests that TAVI using the SAPIEN 3 device is likely to be a cost-effective alternative for symptomatic severe aortic stenosis patients at a low risk of surgical mortality, treated in the contemporary Swiss setting. The findings are consistent with cost-effectiveness analyses of TAVI with SAPIEN 3 versus SAVR in other European countries using the same model structure. While the initial procedure costs for TAVI with SAPIEN 3 are higher than those of SAVR in Switzerland, the overall cost-effectiveness of TAVI is driven by lower long-term management costs. TAVI with SAPIEN 3 offers efficiency gains by limiting healthcare resource use, reducing postoperative complications and shortening hospital length of stay compared with SAVR, while also meeting patients' preference for a minimally invasive option and improving patients' quality of life. We propose that this analysis is valuable for clinical decision-making and for policymakers specifically considering the 2021 European Society of Cardiology / European Association for Cardio-Thoracic Surgery guidelines that recommend TAVI in all patients ≥75 years who are suitable for a transfemoral approach regardless of the degree of surgical risk.

Data availability statement

Input parameters values used and data generated during this cost-utility study are wholly included within this published article and the associated supplementary material in the appendix.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. *CAW* and *RC* have no direct conflicts of interest to declare; however, Heart Clinic Hirslanden acts as a Centre of Excellence for HeartTeam which receives educational grants from Edwards Lifesciences. *TN* has received research support from the Swiss National Science Foundation (P400PM_191037/1), the Swiss Heart Foundation (FF20079), the Prof. Dr. Max Cloëtta Foundation, the Margarete und Walter Lichtenstein-Stiftung (3MS1038), the University of Basel, University Hospital Basel, and an educational grant from Edwards Lifesciences, as well as speaker honoraria/consulting honoraria from Siemens, Beckman Coulter, Bayer, Ortho Clinical Diagnostics and Orion Pharma, all outside the submitted work. *PC* is an employee of Edwards Lifesciences. *AD* was an employee of Edwards Lifesciences at the time of the study. *MS* received research funding from Edwards Lifesciences, via employment institution. *BF* and *HT* were paid by Edwards Lifesciences as Health Economic consultants for this study.

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Appendix

Table S1. Probabilities of clinical events used in the model.

Clinical events	TAVI with SAPIEN 3	SAVR	Source
At 30 days			
Treated AF	4.1%	35.8%	PARTNER 3 trial [10]; SGK 2021 [23]
New permanent pacemaker	13.0%	4.0%	
Rehospitalisation	3.4%	6.4%	
Disabling stroke	0.0%	0.4%	
Aortic re-intervention	0.0%	0.0%	
Mortality	0.4%	1.1%	
Monthly health states transition probabilities and intercurrent events between 30 days and 1 year			
Alive and well → Treated AF	0.114%	0.155%	PARTNER 3 trial [10]
Alive and well → Disabling stroke	0.004%	0.004%	SAFE [40]
Treated AF → Disabling stroke	0.028%	0.028%	Blum et al. 2022 [41]
TIA	0.092%	0.040%	PARTNER 3 trial [10]
MI	0.018%	0.080%	
Severe or life-threatening bleeding	0.367%	0.120%	
Monthly health states transition probabilities between 1 year 2 years			
Alive and well → Treated AF	0.064%	0.108%	PARTNER 3 trial, 2-year outcomes [9]
Alive and well → Disabling stroke	0.004%	0.004%	SAFE [40]
Treated AF → Disabling stroke	0.028%	0.028%	Blum et al. 2022 [41]
Monthly health states transition probabilities after 2 years			
Alive and well → Treated AF	0.160%	0.024%	PARTNER 3 trial, 5-year outcomes [11]
Alive and well → Disabling stroke	0.004%	0.004%	SAFE [40]
Treated AF → Disabling stroke	0.028%	0.028%	Blum et al. 2022 [41]
Events beyond 30 days (converted to monthly rates in calculations)			
Rehospitalisation at 1 year	4.3%	5.1%	PARTNER 3 trial [10]
Rehospitalisation at 2 years	1.3%	1.2%	PARTNER 3 trial, 2-year outcomes [9]

Rehospitalisation at 3 years and beyond	1.7%	1.6%	PARTNER 3 trial, 5-year outcomes [11]
Aortic re-intervention (converted to monthly rates in calculations)			
From Year 1 to Year 23 onwards	From 0.4% to 8.9%	From 0.4% to 8.9%	PARTNER 3 trial, up to 5 years [9-11] and thereafter Bourguignon et al. 2015 [24]

AF, atrial fibrillation; MI, myocardial infarction; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TIA, transient ischaemic attack.
Note: Transitions for the first month are informed by 30-day rates directly. Transitions for the following 11 months (up to one year) are informed by the 1-year rates (subtracting those known to have occurred in the first 30 days), assuming an equal rate across the 11 months. From Year 2 onwards, the 2-year outcomes from PARTNER 3 were used to inform where possible, using the same method as for transitions up to one year. Where literature was used, it was assumed that the rate of movement between states was constant from Month 1 onwards.

Table S2A. Annual mortality risk for "alive and well" health state.

Annual mortality risk alive and well (by age), years	Males	Females
73	1.8%	1.0%
74	2.0%	1.1%
75	2.1%	1.2%
76	2.3%	1.4%
77	2.5%	1.5%
78	2.8%	1.7%
79	3.1%	2.0%
80	3.5%	2.3%
81	4.0%	2.6%
82	4.6%	3.0%
83	5.3%	3.4%
84	6.1%	4.0%
85	7.0%	4.6%
86	8.1%	5.4%
87	9.3%	6.2%
88	10.5%	7.2%
89	12.0%	8.3%
90	13.5%	9.5%
91	15.1%	10.9%
92	16.9%	12.5%
93	18.7%	14.1%
94	20.7%	15.9%
95	22.8%	17.8%
96	25.0%	19.8%
97	27.5%	21.8%
98	30.4%	24.0%
99	33.9%	26.2%
100	38.1%	28.5%
101	42.9%	30.7%
102	47.9%	33.0%
103	51.7%	35.1%
104	55.6%	38.5%
105	59.7%	42.2%
106	64.0%	45.9%
107	68.3%	49.9%
108	72.6%	54.0%
109	77.0%	58.3%
110	81.2%	62.7%
111	85.1%	67.3%

Annual mortality risk alive and well (by age), years	Males	Females
112	88.8%	71.9%
113	92.0%	76.5%
114	94.6%	81.0%
115	96.7%	85.4%
116	98.2%	89.4%
117	99.1%	93.0%
118	99.7%	95.9%
119	99.9%	98.2%
120	100.0%	100.0%

Source: Life Tables Switzerland [42]. Cohort mortality tables for Switzerland by birth cohort, sex and age published by Federal Statistical Office [42]. Values for birth year 1949.

Table S2B. Excess risk of mortality.

Relative risk of death (HR) associated with treated AF, disabling stroke, compared to the general population of the same age		
Treated AF	HR=1.46	Odutayo et al. 2016 [43]
Disabling stroke	HR=2.30	Gandjour & Stock 2007 [44]

AF, atrial fibrillation; HR, hazard ratio.
Justification Note: No specific Swiss study was found on the excess risk of mortality for both treated atrial fibrillation and disabling stroke. Therefore, for treated atrial fibrillation, we used the value from a meta-analysis including 104 studies involving 9,686,513 patients by Odatuyo et al. [43] in which the HR with atrial fibrillation was 1.46 with a 95% confidence interval of [1.39–1.54]. For disabling stroke, we used an HR estimate of 2.3 from a German study by Gandjour & Stock [44].

Table S3. Disutilities.

Utilities data	TAVI	SAVR	Source
Disutility for treated AF	0.14	0.14	Ali et al. 2017 [45]; Gilard et al. 2022 [13]; Mennini et al. 2022 [15]; Walter et al. 2021 [46]
Disutility for disabling stroke	0.38	0.38	Ali et al. 2017 [45]; Gilard et al. 2022 [14]; Mennini et al. 2022 [15]; Walter et al. 2021 [46]

AF, atrial fibrillation; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Table S4. Breakdown of TAVI and SAVR procedure and rehabilitation costs.

DRG procedure with and without pacemaker				Permanent pacemaker incidence rate	Weighted average
TAVI with SAPIEN 3	F98B	with pacemaker	CHF 55 242	13%	CHF 45 211
	F98C	without pacemaker	CHF 43 719	87%	
SAVR	F03C	with pacemaker	CHF 48 059	4%	CHF 36 099
	F03E	without pacemaker	CHF 35 601	96%	

	Inpatient rehabilitation cost (SwissDRG AG 2021, TR19B [26]; expert interview)	**Inpatient rehabilitation incidence (Mack et al. 2019 [10])**	**Incidence weighted Inpatient rehabilitation cost**	**Outpatient rehabilitation cost (expert interview)**	**Outpatient rehabilitation incidence (Mack et al. 2019 [10])**	**Incidence weighted Outpatient rehabilitation cost**	**Total rehabilitation cost (with incidence)**
TAVI with SAPIEN 3	CHF 11 495	20.9%	**CHF 2 403**	CHF 3 200	79.1%	**CHF 2 531**	**CHF 4 934**
SAVR	CHF 11 495	75.0%	**CHF 8 622**	CHF 3 200	25.0%	**CHF 800**	**CHF 9 422**

DRG, Diagnostic Related Group; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Table S5. Deterministic sensitivity analysis: Input parameters.

Parameter	Base case value	Lower value	Upper value
Age	73	65	85
Proportion male	69%	65%	73%
Discount rate: Costs (1-30 years)	3.0%	0.0%	5.0%
Discount rate: Costs (after 30 years)	3.0%	0.0%	5.0%
Discount rate: Benefits (1–30 years)	3.0%	0.0%	5.0%
Discount rate: Benefits (after 30 years)	3.0%	0.0%	5.0%
TAVI with SAPIEN 3: Mortality risk at 30 days	0.4%	0.3%	0.5%
TAVI with SAPIEN 3: Risk of new onset AF at 30 days	4.1%	3.3%	4.9%
TAVI with SAPIEN 3: Risk of new permanent pacemaker at 30 days	13.0%	10.4%	15.5%
TAVI with SAPIEN 3: Risk of disabling stroke at 30 days	0.0%	0.0%	0.4%
SAVR: Mortality risk at 30 days	1.1%	0.9%	1.3%
SAVR: Risk of new onset AF at 30 days	35.8%	28.6%	42.9%
SAVR: Risk of new permanent pacemaker at 30 days	4.0%	3.2%	4.8%
SAVR: Risk of disabling stroke at 30 days	0.4%	0.4%	0.5%
TAVI with SAPIEN 3: Alive and well to treated AF (monthly transition after from 30 days to 1 year)	0.114%	0.091%	0.137%
TAVI with SAPIEN 3: Alive and well to disabling stroke (monthly transition from 30 days to 1 year)	0.004%	0.003%	0.005%
TAVI with SAPIEN 3: Treated AF to disabling stroke (monthly transition from 30 days to 1 year)	0.028%	0.022%	0.033%

SAVR: Alive and well to treated AF (monthly transition from 30 days to 1 year)	0.155%	0.124%	0.186%
SAVR: Alive and well to disabling stroke (monthly transition from 30 days to 1 year)	0.004%	0.003%	0.005%
SAVR: Treated AF to disabling stroke (monthly transition from 30 days to 1 year)	0.028%	0.022%	0.033%
TAVI with SAPIEN 3: Alive and well to treated AF (monthly transition from 1 year to 2 years)	0.064%	0.051%	0.259%
TAVI with SAPIEN 3: Alive and well to disabling stroke (monthly transition from 1 year to 2 years)	0.004%	0.003%	0.005%
TAVI with SAPIEN 3: Treated AF to disabling stroke (monthly transition from 1 year to 2 years)	0.028%	0.022%	0.033%
SAVR: Alive and well to treated AF (monthly transition from 1 year to 2 years)	0.108%	0.051%	0.130%
SAVR: Alive and well to disabling stroke (monthly transition from 1 year to 2 years)	0.004%	0.003%	0.005%
SAVR: Treated AF to disabling stroke (monthly transition from 1 year to 2 years)	0.028%	0.022%	0.033%
TAVI with SAPIEN 3: Alive and well to treated AF (monthly transition after from 2 years onwards)	0.160%	0.128%	0.192%
TAVI with SAPIEN 3: Alive and well to disabling stroke (monthly transition from 2 years onwards)	0.004%	0.003%	0.005%
TAVI with SAPIEN 3: Treated AF to disabling stroke (monthly transition from 2 years onwards)	0.028%	0.022%	0.033%
SAVR: Alive and well to treated AF (monthly transition from 2 years onwards)	0.024%	0.019%	0.029%
SAVR: Alive and well to disabling stroke (monthly transition from 2 years onwards)	0.004%	0.003%	0.005%
SAVR: Treated AF to disabling stroke (monthly transition from 2 years onwards)	0.028%	0.022%	0.033%
TAVI with SAPIEN 3: Rehospitalisation multiplier	1.0	0.8	1.2
SAVR: Rehospitalisation multiplier	1.0	0.8	1.2
TAVI with SAPIEN 3: Re-intervention multiplier	1.0	0.8	1.2
SAVR: Re-intervention multiplier	1.0	0.8	1.2
Relative risk of death with treated AF	1.46	1.17	1.75

Relative risk of death with disabling stroke (Month 1)	2.30	1.90	2.76
Relative risk of death with disabling stroke (Month 2+)	2.30	1.90	2.76
Relative risk of death with re-intervention TAVI with SAPIEN 3	2.21	1.77	2.66
Relative risk of death with re-intervention SAVR	2.21	1.77	2.65
Hazard ratio mortality vs SAVR: TAVI with SAPIEN 3	0.75	0.35	1.63
Utility decrement: Treated AF	0.14	0.11	0.17
Utility decrement: Disabling stroke	0.38	0.30	0.46
Procedure cost: TAVI with SAPIEN 3	CHF 50145	CHF 40116	CHF 60174
Procedure cost: SAVR	CHF 45521	CHF 36417	CHF 54625
Adverse event cost: TAVI with SAPIEN 3	CHF -	CHF -	CHF 354
Adverse event cost: SAVR	CHF -	CHF -	CHF 1 637
Treated AF cost: Month 1	CHF 6 649	CHF 5 319	CHF 7 979
Treated AF cost: Per month from Month 2	CHF 93	CHF 74	CHF 112
Disabling stroke cost (Month 1): Per month	CHF 20 662	CHF 16 530	CHF 24 794
Disabling stroke cost (Month 2+): Per month	CHF 3 648	CHF 2 918	CHF 4 378
Alive and well cost: Per month (TAVI 1)	CHF 103	CHF 82	CHF 124
Alive and well cost: Per month (TAVI 2+)	CHF 34	CHF 27	CHF 41
Alive and well cost: Per month (SAVR 1)	CHF 34	CHF 27	CHF 41
Alive and well cost: Per month (SAVR 2+)	CHF 34	CHF 27	CHF 41
Permanent pacemaker insertion cost	CHF 13 176	CHF 10 541	CHF 15 811

Pacemaker complications (per month)	CHF 329	CHF 264	CHF 395
Rehospitalisations cost: TAVI with SAPIEN 3	CHF 9 259	CHF 7 407	CHF 11 111
Rehospitalisations cost: SAVR	CHF 9 259	CHF 7 407	CHF 11 111
Re-intervention cost with TAVI with SAPIEN 3	CHF 50 145	CHF 40 116	CHF 60 174
Re-intervention cost with SAVR	CHF 50 145	CHF 40 116	CHF 60 174

AF, atrial fibrillation; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Table S6. Probabilistic sensitivity analysis assumptions.

Parameter	Base case value	Distribution	Parameters	Source
TAVI with SAPIEN 3 – clinical events at 30 days				
All-cause mortality	**0.4%**	Beta	Alpha = 2 / Beta = 494	PARTNER 3 trial [10]; SGK 2021 [23])
New onset of treated AF	**4.1%**	Beta	Alpha = 17 / Beta = 400	
New permanent pacemaker	**13.0%**	Beta	Alpha = 64 / Beta = 432	
Rehospitalisation	**3.4%**	Beta	Alpha = 17 / Beta = 479	
Disabling stroke	**0.0%**	Beta	Alpha = 0 / Beta = 496	
SAVR – clinical events at 30 days				
All-cause mortality	**1.1%**	Beta	Alpha = 5 / Beta = 449	PARTNER 3 trial [10]
New onset of treated AF	**35.8%**	Beta	Alpha = 132 / Beta = 237	
New permanent pacemaker	**4.0%**	Beta	Alpha = 18 / Beta = 436	
Rehospitalisation	**6.4%**	Beta	Alpha = 29 / Beta = 425	
Disabling stroke	**0.4%**	Beta	Alpha = 2 / Beta = 452	
TAVI with SAPIEN 3 – Clinical events from 30 days to 1 year (monthly probability)				
TIA	**0.00%**	Beta	Alpha = 0 / Beta = 496	PARTNER 3 trial [10]
MI	**0.018%**	Beta	Alpha = 1 / Beta = 495	
Severe/life-threatening bleeding	**0.367%**	Beta	Alpha = 20 / Beta = 476	
Rehospitalisation rate	**0.36%**	Gamma	SD = 0.04 (assumption)	

SAVR – Clinical events from 30 days to 1 year (monthly probability)				
TIA	**0.000%**	Beta	Alpha = 0 / Beta = 454	PARTNER 3 trial [10]
MI	**0.080%**	Beta	Alpha = 4 / Beta = 450	
Severe/life-threatening bleeding	**0.120%**	Beta	Alpha = 6 / Beta = 448	
Rehospitalisation rate	**0.43%**	Gamma	SD = 0.04% (assumption)	
TAVI with SAPIEN 3 – Monthly transition probabilities				
Alive and well to treated AF – Month 1 to Month 12	**0.114%**	Beta	Alpha = 5 / Beta = 395	PARTNER 3 trial [9-11]
Alive and well to treated AF – Month 13 to Month 24	**0.064%**	Beta	Alpha = 3 / Beta = 392	
Alive and well to treated AF – Month 25 onwards	**0.160%**	Beta	Alpha = 22 / Beta = 370	
Alive and well to disabling stroke	**0.004%**	Beta	Alpha = 51.7 / Beta = 99 948	SAFE [40]
Treated AF to disabling stroke	**0.028%**	Beta	Alpha = 38.43 / Beta = 138 348	Blum et al. 2022 [41]
SAVR – Monthly transition probabilities				
Alive and well to treated AF – Month 1 to Month 12	**0.155%**	Beta	Alpha = 4 / Beta = 233	PARTNER 3 trial [9-11]
Alive and well to treated AF – Month 13 Onwards	**0.108%**	Beta	Alpha = 3 / Beta = 230	
Alive and well to treated AF – Month 25 onwards	**0.024%**	Beta	Alpha = 2 / Beta = 228	
Alive and well to disabling stroke	**0.004%**	Beta	Alpha = 51.7 / Beta = 99 948	SAFE [40]
Treated AF to disabling stroke	**0.028%**	Beta	Alpha = 38.43 / Beta = 138 348	Blum et al. 2022 [41]

Other clinical events rates for both arms (TAVI and SAVR) – Annual risk				
Rehospitalisation – TAVI Month 13 to Month 24	**1.3%**	Gamma	SD = 0.1% (assumption)	PARTNER 3 trial [9-11]
Rehospitalisation – TAVI Month 24 onwards	**1.7%**	Gamma	SD = 0.2% (assumption)	
Rehospitalisation – SAVR Month 13 to Month 24	**1.2%**	Gamma	SD = 0.1% (assumption)	
Rehospitalisation – SAVR Month 24 onwards	**1.6%**	Gamma	SD = 0.2% (assumption)	
Re-intervention rate – Year 1	**0.5%**	Gamma	SD = 0.05% (assumption)	PARTNER 3 trial [9-11] and thereafter Bourguignon et al. 2015 [24]
Re-intervention rate – Year 2	**0.4%**	Gamma	SD = 0.04% (assumption)	
Re-intervention rate – Year 3	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 4	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 5	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 6	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 7	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 8	**0.6%**	Gamma	SD = 0.06% (assumption)	
Re-intervention rate – Year 9	**0.8%**	Gamma	SD = 0.08% (assumption)	
Re-intervention rate – Year 10	**1.5%**	Gamma	SD = 0.15% (assumption)	
Re-intervention rate – Year 11	**1.8%**	Gamma	SD = 0.18% (assumption)	
Re-intervention rate – Year 12	**2.4%**	Gamma	SD = 0.24% (assumption)	
Re-intervention rate – Year 13	**2.7%**	Gamma	SD = 0.27% (assumption)	
Re-intervention rate – Year 14	**3.2%**	Gamma	SD = 0.32% (assumption)	

Re-intervention rate – Year 15	**3.9%**	Gamma	SD = 0.39% (assumption)	
Re-intervention rate – Year 16	**4.6%**	Gamma	SD = 0.46% (assumption)	
Re-intervention rate – Year 17	**5.5%**	Gamma	SD = 0.55% (assumption)	
Re-intervention rate – Year 18	**6.2%**	Gamma	SD = 0.62% (assumption)	
Re-intervention rate – Year 19	**7.2%**	Gamma	SD = 0.72% (assumption)	
Re-intervention rate – Year 20	**7.6%**	Gamma	SD = 0.76% (assumption)	
Re-intervention rate – Year 21	**7.9%**	Gamma	SD = 0.79% (assumption)	
Re-intervention rate – Year 22	**8.6%**	Gamma	SD = 0.86% (assumption)	
Re-intervention rate – Year 23 onwards	**8.9%**	Gamma	SD = 0.89% (assumption)	
Relative risk of death (HR) associated with treated AF, disabling stroke and re-intervention – for both arms				
Treated AF	**1.46**	Lognormal	SD = 0.146 (assumption)	Odutayo et al. 2016 [43]
Disabling stroke	**2.30**	Lognormal	SD = 0.230 (assumption)	Gandjour & Stock 2007 [44]
Aortic re-intervention	**2.21**	Lognormal	SD = 0.22 (assumption)	PARTNER 3 trial [10]. Procedural deaths (0.4%) compared to monthly mortality risk of general mortality for 73 years old (0.16%)
Disutilities associated to treated AF and disabling stroke – for both arms				
Utility decrement: Treated AF	**0.14**	Gamma	SD = 0.014 (assumption)	Ali et al. 2017 [45]; Gilard et al. 2022 [14]; Mennini et al. 2022 [15]; Walter et al. 2021 [46]
Utility decrement: Disabling stroke	**0.38**	Gamma	SD = 0.038 (assumption)	

Cost of the procedure (incl. rehabilitation)				
TAVI with SAPIEN 3	**CHF 50 145**	Gamma	SD = 5 015 (assumption)	Composite of SwissDRG AG 2024 F98B and F98C (TAVI); F03C and F03E (SAVR) [25] + SwissDRG AG 2021, TR19B [26]
SAVR	**CHF 45 521**	Gamma	SD = 4 552 (assumption)	
Cost of post-operative complications				
Re-intervention with TAVI with SAPIEN 3	**CHF 50 145**	Gamma	SD = 5 015 (assumption)	Assumed equal to cost of initial TAVI procedure plus rehabilitation associated with procedure.
Re-intervention with SAVR	**CHF 50 145**	Gamma	SD = 5 015 (assumption)	
Monthly cost associated to health states (alive & well, Treated AF, disabling stroke)				
Treated AF up to 30 days	**CHF 6 649**	Gamma	SD = 665 (assumption)	SwissDRG AG 2021, F50B and F50C [25]; + cost of anticoagulation drug and beta blocker; + outpatient costs calculated as per Tarmed [27], expert interview
Treated AF – Month 2 onwards	**CHF 93**	Gamma	SD = 9.3 (assumption)	Cost of anticoagulation drug and beta blocker
Disabling stroke (including caregiver) up to 30 days	**CHF 20 662**	Gamma	SD = 2066 (assumption)	Pletscher et al. 2013 [29]
Disabling stroke (including caregiver) – Month 2 onwards	**CHF 3 648**	Gamma	SD = 365 (assumption)	
TAVI with SAPIEN 3: Alive and well up to 1 year	**CHF 103**	Gamma	SD = 10.3 (assumption)	Tarmed [27], expert interview
SAVR: Alive and well up to 1 year	**CHF 34**	Gamma	SD = 3.4 (assumption)	
Alive and well – Month 13 onwards (both arms)	**CHF 34**	Gamma	SD = 3.4 (assumption)	

Other costs considered in the model – for both arms				
Monthly cost of pacemaker complications	**CHF 329**	Gamma	SD = 32.9 (assumption)	SwissDRG AG 2021, F17A [25] + Tarmed [27], expert interview
Rehospitalisation (both arms)	**CHF 9 259**	Gamma	SD = 926 (assumption)	SwissDRG AG 2021, F62A, F62B, F62C, F62D [25]

AF, atrial fibrillation; HR, hazard ratio; MI, myocardial Infarction; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TIA, transient ischaemic attack.