

Economic Value of Transcatheter Valve Replacement for Inoperable Aortic Stenosis

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Aortic stenosis (AS) is a common disease, affecting 2% to 7% of the global population older than 65 years.¹ Although the condition can be asymptomatic for years, when symptoms do appear, untreated patients with severe AS have high mortality (up to 50% within 2 years).^{2,3} Surgical aortic valve replacement (SAVR), in which the sternum is opened to replace the aortic valve, has been shown to improve survival and quality of life in patients with severe, symptomatic AS (SSAS).^{4,5} Despite data supporting the use of SAVR for the treatment of SSAS, at least 30% of patients do not undergo SAVR, because of either patient preference to avoid invasive surgery or ineligibility for surgery as a result of advanced age and associated comorbidities (the latter referred to as inoperable patients).^{6,7} Historically, this population of untreated patients was treated with medical management alone, resulting in 3-year mortality rates as high as 80%.^{8,9} Transcatheter aortic valve replacement (TAVR) is a less invasive method of AVR in which the aortic valve is replaced through either the femoral artery or a small incision in the chest. Clinical trial data have demonstrated that TAVR for inoperable patients extends median survival by approximately 19 months and significantly improves quality of life compared with medical therapy alone,^{10,11} thereby offering an alternative treatment for this patient population. Accordingly, TAVR was first approved for commercialization in Europe in 2007¹² and by the US FDA in 2011 for the treatment of SSAS in inoperable patients.

With commercial approval of TAVR, the volume of these procedures in the United States has grown dramatically. Within Medicare, TAVR grew from 8.9% of all AVR procedures (across all risk groups) in 2012 to 50.3% in 2017.¹³ This rapid growth suggests a need for an analysis of the aggregate economic impact of TAVR treatment on the distribution of social welfare for inoperable patients; this type of study is referred to as social value analysis.¹⁴ These types of studies provide a useful complement to traditional cost-effectiveness analyses, as they incorporate the value to consumers, as well as the value to innovators, allowing policy makers to consider new technologies in a context that is both broad and deep. Inoperable patients who are treated with TAVR realize benefits in the form of increased quantity and quality of life relative to medical management.

ABSTRACT

OBJECTIVES: To project the social value of transcatheter aortic valve replacement (TAVR) for inoperable patients with severe, symptomatic aortic stenosis (SSAS).

STUDY DESIGN: This study used an economic model with parameters obtained from the literature and from US Census Bureau population projections.

METHODS: Our model estimated the economic value that will accrue to inoperable patients with SSAS and to device manufacturers as a result of TAVR utilization. We estimated individual patient value as the monetized gain in quality-adjusted life-years as estimated in the cost-effectiveness literature, net of device costs and cost offsets. We estimated manufacturer value by applying an assumed profit margin to revenue from device sales. We created population-level estimates by combining these individual-level estimates with age-stratified Census Bureau population projections and estimates of the incidence of AS. We assessed model uncertainty through the use of probabilistic sensitivity analyses.

RESULTS: Between 2018 and 2028, approximately 465,000 inoperable Americans with SSAS will be treated with TAVR. These procedures will yield a cumulative social benefit of up to \$48 billion, with roughly 80% of that benefit accruing to patients and 20% accruing to device manufacturers.

CONCLUSIONS: Policy makers and payers should take this social value into account when considering decisions related to the care of inoperable patients with SSAS.

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In addition, firms that manufacture TAVR devices realize benefits by way of profits earned on units sold. Payers may realize both costs (eg, via incremental new spending on TAVR devices) and benefits (eg, cost offsets realized through the avoidance of downstream events, such as postoperative inpatient readmissions). Assessing the value of TAVR to both payers and manufacturers allows for the estimation of the relative share of economic surplus returning to manufacturers (as opposed to consumers), therefore informing a broader discussion regarding optimal incentives for future innovation.

The purpose of this study was to estimate the present and future economic impact of TAVR adoption for inoperable patients with SSAS and for TAVR device manufacturers in the United States, using recently developed approaches for the assessment of economic value.¹⁵⁻²⁰ Using an analysis time frame of 2018 to 2028, we aimed to project the size of the inoperable population with SSAS, estimate the fraction of this population who will receive TAVR, and calculate the economic returns of that utilization, for both the patients and the device manufacturers.

METHODS

Projecting TAVR-Eligible Population From 2018 to 2028

To estimate the future economic impact of TAVR adoption for patients with inoperable SSAS and for TAVR manufacturers, we began by projecting the size of the inoperable population eligible for TAVR treatment.

To determine the number of inoperable patients with SSAS between 2018 and 2028, we first projected the number of patients with SSAS nationally, regardless of surgical risk status. We did this by multiplying current estimates of severe AS incidence rates (stratified by age) by the proportion of patients with severe AS whose disease is symptomatic,^{21,22} and then multiplying the resulting quantity by age-stratified US population projections for each year in the analysis period.²³ Finally, we multiplied the values described earlier by the estimated fraction of patients with SSAS considered inoperable.⁷ The parameters used to perform these calculations are presented in [Table 1](#).^{7,21,22,24-26}

Projecting TAVR Utilization From 2018 to 2028

Only a fraction of incident inoperable SSAS cases are treated with TAVR.^{21,27} As such, we estimated the number of inoperable patients

TAKEAWAY POINTS

Considering the US population between 2018 and 2028, we estimated the annual and cumulative social value accruing to patients and to manufacturers as a result of uptake of transcatheter aortic valve replacement (TAVR) for the treatment of severe, symptomatic aortic stenosis (SSAS) in inoperable patients.

- ▶ In 2018, approximately 39,000 inoperable patients with SSAS were treated with TAVR in the United States.
- ▶ That number is projected to increase as the population ages and as TAVR uptake grows.
- ▶ TAVR treatment of the inoperable population with SSAS will generate approximately \$48 billion in social value between 2018 and 2028, with 80% of that value accruing to patients.

TABLE 1. Epidemiological and Economic Parameters^{7,21,22,24-26}

Parameter	Base Value	SE	Assumed Statistical Distribution	Source
Epidemiological Inputs				
Severe AS incidence				
Aged 18-64 years	0.00016	0.00003	Beta	Calculated via Benjamin et al (2017) table 22-1 ²²
65 years or older	0.00440	0.0009	Beta	Durko et al (2018) ²¹
Proportion with SSAS	0.68	0.039	Beta	Durko et al (2018) ²¹
Inoperable risk fraction, SSAS	0.33	0.032	Binomial	lung et al (2015) ⁷
Economic Inputs				
TAVR uptake among inoperable patients	0.62	0.102		Durko et al (2018) ²¹
Device cost of SAPIEN	\$32,500	N/A	N/A	ECRI Institute data extract ²⁴
Fraction of device cost retained as manufacturer profit	0.80	N/A	N/A	Assumption
QALY gain (relative to medical management)	1.29	0.132	Normal	Reynolds et al (2012) ²⁵
Societal willingness to pay for a QALY	\$150,000	N/A	N/A	Neumann et al (2014) ²⁶
Lifetime cost offsets of SAPIEN (relative to medical management)	\$97,699	\$9969	Normal	Reynolds et al (2012) ²⁵

AS indicates aortic stenosis; N/A, not available; QALY, quality-adjusted life-year; SSAS, severe, symptomatic AS; SE, standard error; TAVR, transcatheter aortic valve replacement.

using TAVR in the future as the product of (1) the projected eligible inoperable population in each year (described previously), and (2) an estimate of the fraction of eligible inoperable patients who ultimately receive TAVR, extracted from the literature.²¹ As a conservative assumption, we assumed that this fraction remains constant over time. We also assumed that individuals can receive the treatment only once.

Calculation of Industry Value

TAVR market share estimates were available for the population with SSAS but not specifically for the inoperable population with SSAS. In addition, the prices of the different TAVR devices for the different SSAS risk groups (inoperable, high risk, and intermediate risk) are

TABLE 2. Incidence Estimates and Net Present Value (\$150,000/QALY) of TAVR Procedures via the TF Approach Accrued to Inoperable Patients and Manufacturers, 2018-2028*

Year	Projected Population Aged 20-64 Years (× 1000)	Projected Population Aged ≥65 Years (× 1000)	Projected Population Total (× 1000)	Patients With Incident SSAS Aged 20-64 Years	Patients With Incident SSAS Aged ≥65 Years	Total Patients With Incident SSAS	Inoperable Patients With Incident SSAS
2018	192,576	56,819	249,394	21,131	170,751	191,882	63,321
2019	193,421	57,850	251,271	21,223	173,849	195,073	64,374
2020	194,266	58,880	253,147	21,316	176,948	198,264	65,427
2021	195,112	59,911	255,023	21,409	180,046	201,455	66,480
2022	195,957	60,942	256,899	21,502	183,144	204,645	67,533
2023	196,802	61,973	258,775	21,594	186,242	207,836	68,586
2024	197,647	63,004	260,652	21,687	189,340	211,027	69,639
2025	198,493	64,035	262,528	21,780	192,438	214,218	70,692
2026	199,338	65,066	264,404	21,873	195,537	217,409	71,745
2027	200,183	66,097	266,280	21,965	198,635	220,600	72,798
2028	201,028	67,128	268,156	22,058	201,733	223,791	73,851
Total	2,164,823	681,706	2,846,529	237,537	2,048,663	2,286,200	754,446

QALY indicates quality-adjusted life-year; SSAS, severe, symptomatic aortic stenosis; TAVR, transcatheter aortic valve replacement; TF, transfemoral.

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*All dollar values are 2017 US\$ and discounted. QALYs are valued at \$150,000.

very similar.²⁴ As such, for the purposes of this analysis, we used the best peer-reviewed cost-effectiveness evidence available, without regard to TAVR device type, and assumed that these results applied to all inoperable patients treated with TAVR.²⁵ Cost-effectiveness results were then employed to calculate patient value (discussed later). As most contemporary TAVR procedures are performed using transfemoral (TF) access, we used cost-effectiveness results from a TF cohort.

We calculated industry revenue by multiplying the device price by the number of TAVR procedures on inoperable patients projected to occur annually between 2018 and 2028. We assumed that device cost would remain constant across years (Table 17^{21,22,24-26}).²⁵ In addition, we conservatively assumed profit—analogue to welfare gains in the context of social value analysis—to be 80% of revenue.²⁸ This is substantially larger than the profit margins of 18% to 29% reported by device manufacturers in recent years.^{29,30} Formally, (undiscounted) industry value in year t was calculated as $N_t \times P \times p$, where N_t denotes the number of procedures, P denotes the device price, and p denotes the profit margin.

Computation of the Monetized QALY Benefit of TAVR

We estimated the monetized value of the quality-adjusted life-year (QALY) gain for each treated inoperable patient by assuming a QALY willingness-to-pay (WTP) value of \$150,000 (Table 17^{21,22,24-26}).^{26,31} A threshold of \$150,000 was chosen because incremental cost-effectiveness ratios (ICERs) above this cutoff are considered low economic value as defined by the American Heart Association and the American College of Cardiology.³² We estimated the total monetized QALY gain for the US inoperable SSAS population in each year as the product of the individual monetized QALY value and the number of TAVR procedures on inoperable patients in each year.

Calculation of Patient Value

To circumvent the complexities of the US insurance market, this analysis used a societal perspective to estimate patient value. In this framework, we computed the net value that an individual obtains from TAVR as the difference between the monetized valuation of the QALY benefit (described previously) and the incremental difference in costs, including differences in the device cost, as well as differences in postprocedural medical expenses. The concept of patient value is thus an amalgamation of value returning to the patient (in the form of improved quality and/or quantity of life) and the change in medical costs borne by payers, which may be either patients themselves or, more typically, commercial or government insurers. For convenience, we refer to this construct as patient value. We extracted the values for cost offsets (including device cost) from the literature (Table 17^{21,22,24-26})²⁵ and converted them to 2017 US\$ using the Medical Consumer Price Index.³³ We assumed a discount rate of 3% consistent with US guidelines.³⁴ Formally, (undiscounted) patient value in year t was calculated as $N_t \times (Q \times WTP - P - C)$, where N_t denotes the number of procedures, Q denotes the QALY gain of TAVR relative to medical management, WTP denotes the WTP value for a QALY, P denotes the device price, and C denotes the estimated cost offsets of TAVR relative to medical management.

Sensitivity and Scenario Analyses

We assessed the model's sensitivity to the joint uncertainty of all input parameters by implementing a probabilistic sensitivity analysis (PSA). In a PSA, model results are iteratively regenerated following resampling of input parameters from assumed statistical distributions, which are derived from published or assumed values (eg, means and CIs) describing the uncertainty of parameter point estimates. We varied QALY gains, lifetime cost offsets, incidence

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Year	Total Inoperable TAVR Patients	Total QALY Gain	Value Accruing to Patients	Value Accruing to Manufacturers
2018	39,069	50,399	\$3,742,866,524	\$937,656,978
2019	39,719	51,237	\$3,694,280,779	\$925,485,354
2020	40,368	52,075	\$3,645,350,062	\$913,227,309
2021	41,018	52,913	\$3,596,135,489	\$900,898,152
2022	41,668	53,752	\$3,546,695,492	\$888,512,523
2023	42,318	54,590	\$3,497,084,762	\$876,084,121
2024	42,967	55,428	\$3,447,355,008	\$863,625,902
2025	43,617	56,266	\$3,397,555,603	\$851,150,235
2026	44,267	57,104	\$3,347,732,618	\$838,668,659
2027	44,916	57,942	\$3,297,929,673	\$826,192,105
2028	45,566	58,780	\$3,248,187,707	\$813,730,826
Total	465,493	600,486	\$38,461,173,718	\$9,635,232,166

rates, the proportion of severe AS that is symptomatic, the proportion of SSAS that is inoperable, and the proportion of inoperable patients with SSAS who receive TAVR. Table 1^{7,21,22,24-26} shows the assumed statistical distributions of the uncertainty parameters and assumptions that governed the PSA. We performed 1000 replications of the model and computed the fraction of these in which estimated societal value exceeded estimated industry value. We also separately present results from a scenario analysis, which uses a WTP value of \$100,000 per QALY in place of the base-case parameter value of \$150,000.

RESULTS

TAVR Uptake Projections

Between 2018 and 2028, approximately 465,000 Americans with inoperable SSAS were projected to receive TAVR. Because the gradual aging of the US population will slowly increase the annual incidence of SSAS, regardless of risk status, the number of inoperable patients with SSAS receiving TAVR was also projected to grow over time. Full projection results are presented in [Table 2](#).

Annual Social Value

In 2018, approximately 39,000 inoperable patients with SSAS were estimated to receive TAVR, resulting in a cumulative gain of about 50,000 QALYs ([Table 2](#)). After accounting for device costs and cost offsets, and using a WTP value of \$150,000 per QALY, approximately \$3.7 billion in patient value was created. By contrast, assuming that firms retain 80% of revenues as profits, approximately \$940 million of the social value accrued to manufacturers. When these values were projected to 2028, we estimated that these undiscounted benefits would increase to \$4.4 billion and \$1.1 million (\$3.2 billion

and \$810 million discounted) in patient value and manufacturer value, respectively.

Cumulative Social Value

Between 2018 and 2028, we projected the total QALY gain among inoperable patients with SSAS to be 600,486 QALYs and the cumulative social value of TAVR (summing over inoperable patients and manufacturers) to be \$48.1 billion. Roughly 80% of that value (\$38.5 billion) accrued to patients and roughly 20% (\$9.6 billion) to manufacturers ([Table 2](#)). Furthermore, we projected that the undiscounted social value will grow over time as the incidence of SSAS increases ([Figure 1](#)²¹).

Sensitivity and Scenario Analysis Results

[Figure 2](#) depicts repeated simulations of the model results following joint draws from the statistical distributions that describe the uncertainty in each of the model parameters (shown in [Table 1](#)^{7,21,22,24-26}). The base-case (deterministic) result is indicated as a single light blue point; the results of each of the 1000 replications are represented as dark blue points. Points appearing above the orange line represent instances in which the value accruing to patients is greater than the value accruing to manufacturers, and points below it indicate the reverse. In 99.8% of the replicated simulations, the economic value to inoperable patients was greater than the economic value to manufacturers.

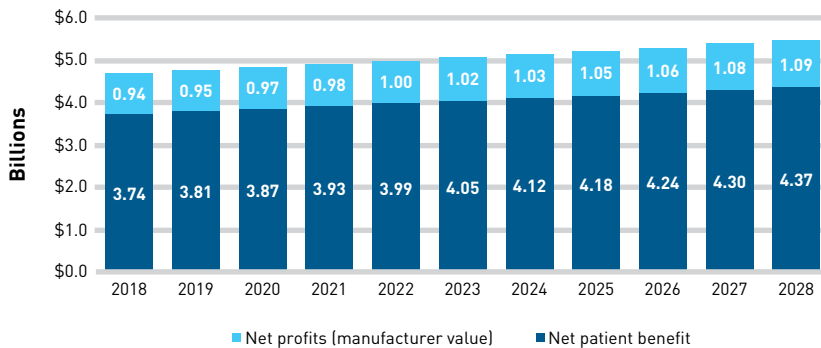
When the WTP for a QALY was assumed to be \$100,000, the cumulative patient value was estimated to fall from \$38.5 billion to \$12.6 billion, and the estimated share of value accruing to manufacturers would rise from 20.0% to 43.3% ([Table 3](#)). When the PSA was conducted using this lower valuation, patient value exceeded manufacturer value in 67.8% of the simulations.

DISCUSSION

Our findings suggest that substantial social value will be created as a result of TAVR treatment for inoperable patients with SSAS over the next decade. Our study projected that up to \$48.1 billion in value will be generated between 2018 and 2028, with roughly 80% of that value accruing to inoperable patients and 20% to manufacturers. A PSA suggested that the portion of social value realized by inoperable patients is likely to exceed the value that will return to manufacturers, as this result was obtained in up to 99.8% of the simulated repetitions.

Prior research has found that TAVR is cost-effective compared with medical management in the inoperable population. Using data from the PARTNER B trial (ClinicalTrials.gov NCT00530894), Reynolds et al found that TAVR would generate a lifetime benefit of 1.29 QALYs per patient, at an incremental cost of \$79,837, resulting in an ICER of \$50,212 per QALY.²⁵ Our study builds on these results by estimating the total social value that TAVR will generate and assessing the distribution of that value between patients and manufacturers. This perspective is useful for payers and policy makers because it

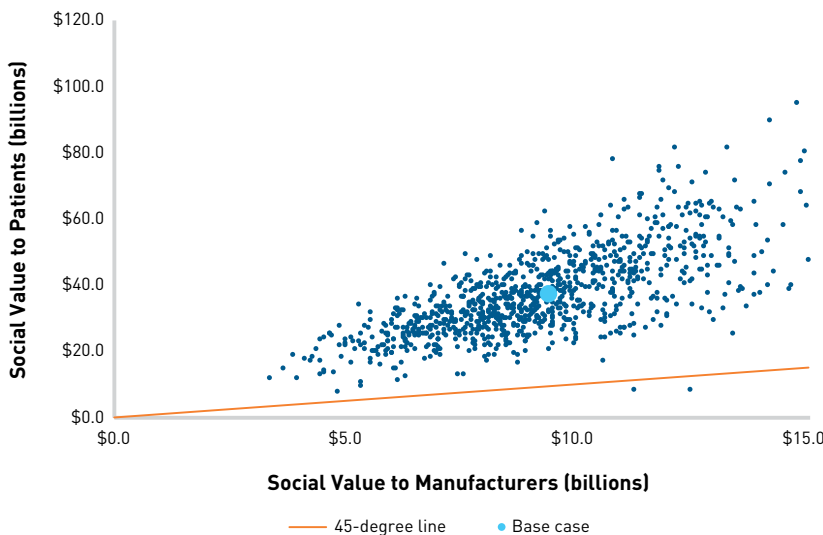
FIGURE 1. Social Value Allocation Among Net Profits and Net Patient Benefits for Inoperable Patients^{21,a}



QALY indicates quality-adjusted life-year; SSAS, severe, symptomatic aortic stenosis.

^aAll dollar values are 2017 US\$; numbers are undiscounted. Net patient benefit for inoperable patients with SSAS is the monetized gain in QALYs at \$150,000 per QALY, net device cost and lifetime cost offsets. The manufacturer value is the profit from device sales, assuming a profit margin of 80%. Both values were estimated based on an uptake of 62% among inoperable patients with SSAS.²¹

FIGURE 2. PSA Results for Inoperable Patients in the Base Case



PSA indicates probabilistic sensitivity analysis; QALY, quality-adjusted life-year; SSAS, severe, symptomatic aortic stenosis.

^aObservations above the 45-degree line indicate replications in which value to patients (net patient benefit) exceeded value to manufacturers (profits); observations below it indicate the reverse. Net patient benefit for inoperable patients with SSAS is the monetized gain in QALYs at \$150,000 per QALY, net device cost and lifetime cost offsets. The manufacturer value is the profit from device sales, assuming a profit margin of 80%. Table 17,^{21,22,24-26} shows the assumed statistical distributions of the uncertainty parameters and assumptions that governed the PSA.

extends the decision-making calculus around TAVR adoption beyond a narrow consideration of short-term costs. In addition, our study informs a larger debate in the literature regarding the relationship between the manufacturer share of economic returns from a new medical technology and incentives for future innovation.^{35,36}

another study found that between 25% and 66% of value accrues to manufacturers for 3 therapies treating multiple sclerosis, depending on modeling assumptions.⁴³ This context suggests that, relative to several therapies, TAVR may generate reasonably large returns to inoperable patients and to society per dollar of manufacturer profit.

Although we observed a large social benefit of TAVR in the inoperable population with SSAS, it is possible that we underestimated the true benefit. First, the data used to inform our study were derived from the use of a first-generation device in the early age of TAVR. Over the past 10 years, there have been substantial improvements in device technology, procedural planning, operator experience, and post-TAVR care, which have been associated with better clinical outcomes and lower resource utilization.³⁷⁻³⁹ Another factor that may also contribute to underestimating the social benefit of TAVR in the inoperable population is the effect of prior undertreatment of this population on our future projection. Durko et al estimated that roughly one-third of inoperable patients with incident SSAS do not receive TAVR.²¹ This value aligns closely with our own comparison of the number of AVR procedures performed annually in the United States with our estimates of the number of annual incident cases (results not shown) and is consistent with previous research.⁴⁰ Furthermore, previous research has suggested that roughly a quarter of patients with SSAS who are offered only SAVR will decline it.⁴¹ Accordingly, it is unknown what fraction of patients who are eligible for TAVR either are not offered it or decline it, thereby leading to the undertreatment of this population. To the extent that patient perception of TAVR as a less invasive alternative grows over time, undertreatment of SSAS may be reduced.⁴² As such, the cost-effectiveness of TAVR in the current era may be greater than previously estimated, and thus our calculations may underestimate the true social value of TAVR in the inoperable population with SSAS.

It is useful to consider our results in the context of other social value studies. Although this study provides the first assessment of the distributional effects on social value for TAVR, informative comparisons are available in the literature. Our estimate of the share of value returning to manufacturers for TAVR (roughly 20%) is nearly identical to the fraction estimated by a recent study on statins.¹⁸ A much lower estimate (2%) was obtained for pediatric vaccines,²⁰ whereas

Of note, TAVR has also been demonstrated to be cost-effective relative to SAVR for operable patients at high⁴⁴ and intermediate⁴⁵ surgical risk. Furthermore, recent clinical trials have demonstrated that TAVR yields substantial benefits relative to SAVR for patients at low surgical risk, who comprise the largest proportion of patients with SSAS.^{46,47} This suggests, first, that the social value of TAVR may extend beyond the inoperable risk group and, second, that this value will be inherently conditional on the degree to which patients and doctors select treatment with TAVR or SAVR. Future research should address these questions directly.

Limitations

This study has several limitations. First, the results rely on projections of unknown future quantities (eg, the percentage of inoperable patients with SSAS who will receive TAVR). We sought to make realistic projections through analysis of data observed in the recent past. However, to the extent that our projections are inaccurate, our estimates may be biased. For example, we assumed the incidence of AS to remain constant, whereas real-world data show that the age-adjusted population incidence of AS decreased in recent years.⁴⁸ Second, we estimated base-case results by incorporating several parameters obtained from the literature into a single economic model. Many of these parameters were estimated with uncertainty, including the QALY benefit and cost offset associated with TAVR usage, as well as the fraction of patients with SSAS considered inoperable. We sought to mitigate this limitation by incorporating the uncertainty associated with each input parameter into a joint PSA. Additionally, as noted previously, the estimated benefit of TAVR for inoperable patients (1.29 QALYs) was obtained from a cost-effectiveness study of an early-generation TAVR device (SAPIEN), as these are the only data available for this patient population.²⁵ Because patient outcomes have improved over time and resource utilization has decreased, we may have underestimated the social value of TAVR by using this data. Third, the data that provided our QALY benefit and cost-offset input parameters considered only TAVR procedures conducted via the TF route²⁵ and did not consider TAVR procedures performed via the less common alternative access routes (eg, transapical). Thus, our results cannot be generalized to TAVR performed via alternative access in this population, although we believe that inoperable patients eligible only for alternative access represent a small portion of the overall population, given that the rates of alternative-access TAVR have decreased substantially over time because of the progressively smaller delivery system of newer-generation TAVR devices.⁴⁹ Finally, our estimate of the cost offsets associated with TAVR for inoperable patients comes from a study that used a 1-year period.²⁵ Thus, our model did not account for any cost differences that might exist beyond this period.

CONCLUSIONS

We sought to estimate the value that will accrue to society—both in aggregate and to different segments of society—as a result of

TABLE 3. Net Present Value (\$100,000/QALY) of TAVR Procedures via the TF Approach Accrued to Inoperable Patients and Manufacturers, 2018-2028^a

Year	Value Accruing to Patients	Value Accruing to Manufacturers
2018	\$1,222,913,395	\$937,656,978
2019	\$1,207,038,889	\$925,485,354
2020	\$1,191,051,669	\$913,227,309
2021	\$1,174,971,705	\$900,898,152
2022	\$1,158,818,087	\$888,512,523
2023	\$1,142,608,686	\$876,084,121
2024	\$1,126,360,395	\$863,625,902
2025	\$1,110,089,348	\$851,150,235
2026	\$1,093,810,596	\$838,668,659
2027	\$1,077,538,391	\$826,192,105
2028	\$1,061,286,111	\$813,730,826
Total	\$12,566,487,273	\$9,635,232,166

QALY indicates quality-adjusted life-year; SSAS, severe, symptomatic aortic stenosis; TAVR, transcatheter aortic valve replacement; TF, transfemoral.

^aAll dollar values are 2017 US\$ and discounted. QALYs are valued at \$100,000.

expected TAVR uptake by inoperable patients with SSAS between 2018 and 2028. We projected that up to \$48.1 billion in social value will be generated, with roughly 80% of that value accruing to patients and the remainder accruing to manufacturers. Future research is needed to assess the social value of TAVR in patients with operable SSAS. ■

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