Cost-Effectiveness of Transcatheter Aortic Valve Replacement With a Self-Expanding Prosthesis Versus Surgical Aortic Valve Replacement

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ABSTRACT

BACKGROUND Previous studies of the cost-effectiveness of transcatheter aortic valve replacement (TAVR) have been based primarily on a single balloon-expandable system.

OBJECTIVES The goal of this study was to evaluate the cost-effectiveness of TAVR with a self-expanding prosthesis compared with surgical aortic valve replacement (SAVR) for patients with severe aortic stenosis and high surgical risk.

METHODS We performed a formal economic analysis on the basis of individual, patient-level data from the CoreValve U.S. High Risk Pivotal Trial. Empirical data regarding survival and quality of life over 2 years, and medical resource use and hospital costs through 12 months were used to project life expectancy, quality-adjusted life expectancy, and lifetime medical costs in order to estimate the incremental cost-effectiveness of TAVR versus SAVR from a U.S. perspective.

RESULTS Relative to SAVR, TAVR reduced initial length of stay an average of 4.4 days, decreased the need for rehabilitation services at discharge, and resulted in superior 1-month quality of life. Index admission and projected lifetime costs were higher with TAVR than with SAVR (differences $11,260 and $17,849 per patient, respectively), whereas TAVR was projected to provide a lifetime gain of 0.32 quality-adjusted life-years ([QALY]; 0.41 LY) with 3% discounting. Lifetime incremental cost-effectiveness ratios were $55,090 per QALY gained and $43,114 per LY gained. Sensitivity analyses indicated that a reduction in the initial cost of TAVR by ~$1,650 would lead to an incremental cost-effectiveness ratio <50,000/QALY gained.

CONCLUSIONS In a high-risk clinical trial population, TAVR with a self-expanding prosthesis provided meaningful clinical benefits compared with SAVR, with incremental costs considered acceptable by current U.S. standards. With expected modest reductions in the cost of index TAVR admissions, the value of TAVR compared with SAVR in this patient population would become high. (Safety and Efficacy Study of the Medtronic CoreValve System in the Treatment of Symptomatic Severe Aortic Stenosis in High Risk and Very High Risk Subjects Who Need Aortic Valve Replacement [Medtronic CoreValve U.S. Pivotal Trial]; NCT01240902) (J Am Coll Cardiol 2016;67:29–38)

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Tранскатетерная аортальная замена (TAVR) быстро стала стандартным методом лечения для пациентов с тяжелым аортальным стенозом (AS), которые не подходят для хирургической аортальной замены (SAVR) (1,2), или как менее инвазивный подход к замене артерий для пациентов с высоким риском для сосудистых осложнений (9). В прошлых исследованиях, используя случайно выбранный случай из баллон-расширяемой системы TAVR, было предложено, что клинический эффект TAVR у ненаркологии пациентов достигается снимыми инкрементными затратами для всех областей здравоохранения в Северной Америке и Европе (5,6). Остается вопрос о согласии, однако, на эффективность TAVR по отношению к хирургическим вмешательствам (7,8).

**METHODS**

**STUDY DESIGN AND PATIENT POPULATION.** As previously reported, the CoreValve U.S. High Risk Pivotal Trial enrolled a total of 795 patients with severe, symptomatic AS who were considered to be at high risk for conventional SAVR. AS was defined as an aortic valve area ≤0.8 cm² or an aortic valve index ≤0.5 cm²/m² and either a mean aortic valve gradient >40 mm Hg or a peak jet velocity >4.0 m/s. All patients were required to have a predicted risk of 30-day mortality ≥15% on the basis of a combination of the Society of Thoracic Surgery risk score and additional, pre-specified factors not included in the risk score (4,10).

Before randomization, all patients were evaluated for anatomic suitability for an iliofemoral (IF) approach using computed tomography angiography. Those patients who were suitable for an IF approach were randomized to IF-TAVR versus SAVR (n = 663), whereas those patients who were not suitable for an IF approach were randomized to TAVR via a non-IF approach, either via the subclavian artery or direct aortic access, versus SAVR (n = 132).

**ANALYTIC OVERVIEW.** We evaluated the cost-effectiveness of TAVR using the CoreValve system compared with SAVR from the perspective of the U.S. health care system. The primary analysis was performed on the as-treated population, which was defined as all randomized patients who underwent attempted valve replacement (4). Patients who expired or withdrew from the study before treatment were therefore excluded. In the event that patients in the as-treated population crossed over to the alternative therapy, they were analyzed on the basis of their originally intended treatment for the reporting of lifetime cost-effectiveness. However, for the reporting of procedural resource use and costs, patients were grouped according to the actual treatment received (per-protocol population).

During the trial, detailed resource utilization and hospital billing data were collected from the time of randomization through death or 12 months. These data were used to determine direct health care costs during the initial 12 months. The current analysis incorporated all available survival and quality-of-life (QOL) data through 2 years. The observed data were then used to project patient-level survival, quality-adjusted survival, and costs over a lifetime.

Abbreviations and Acronyms

- **AS** = aortic stenosis
- **CI** = confidence interval
- **HR** = hazard ratio
- **ICER** = incremental cost-effectiveness ratio(s)
- **ICU** = intensive care unit
- **IF** = iliofemoral
- **LY** = life-year(s)
- **QALY** = quality-adjusted life-year(s)
- **QOL** = quality of life
- **SAVR** = surgical aortic valve replacement
- **STS** = Society of Thoracic Surgeons
- **TAVR** = transcatheter aortic valve replacement

Recently, the CoreValve U.S. High Risk Pivotal Trial reported a significant reduction in 2-year mortality with TAVR using a self-expanding prosthesis (CoreValve, Medtronic, Minneapolis, Minnesota) compared with SAVR in AS patients at high risk for surgical complications (9). Given that previous health economic assessments of TAVR have been derived from a somewhat different patient population that was treated with a different TAVR system, questions regarding the costs and benefits of TAVR relative to SAVR in this new context remain pertinent. The aim of the current study was, therefore, to assess the cost-effectiveness of TAVR using the self-expandable valve system compared with SAVR in high-risk patients.

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perspective. Lifetime cost-effectiveness was then estimated in terms of cost per quality-adjusted life-year (QALY) gained and cost per life-year (LY) gained. All costs are shown in 2013 U.S. dollars, and all future costs and benefits were discounted at 3% (11).

**INDEX PROCEDURE AND ADMISSION COSTS.** Costs for the initial TAVR and SAVR procedures and their associated hospital stays were determined using a combination of hospital billing data and resource-based accounting methods, as described previously (5,12). Procedural costs were calculated by multiplying counts of resource use, as recorded by the study sites, by unit prices derived from 2 study centers. We assumed a commercial price for the self-expandable valve system of $32,000. Ancillary room costs (including overhead, nonphysician personnel costs, and general supplies) were adjusted for measured procedural room time. We assumed that all IF-TAVR procedures would be performed in a cardiac catheterization laboratory environment, and that all SAVR procedures and non-IF TAVR procedures would be performed in an operating room environment.

The remaining nonprocedural costs for each index admission were calculated from hospital bills, when available (n = 505), by multiplying nonprocedural charges by cost-center-specific charge-to-cost ratios obtained from each hospital’s Medicare cost report. When bills were not available (n = 242), costs were estimated using regression models derived separately for TAVR and SAVR patients (R² = 0.72 and 0.74, respectively), from the patients with complete billing data. Covariates for these models included intensive care unit (ICU) and non-ICU length of stay, baseline albumin <3.3 g/dl, in-hospital pacemaker implantation, in-hospital death, and in-hospital stage 3 acute kidney injury.

**FOLLOW-UP HOSPITALIZATION COSTS.** During the initial 12 months of follow-up, hospitalizations for any cause were recorded on case report forms by the study sites. Using available clinical information, each admission was assigned to a Medicare severity-adjusted diagnosis-related group by 1 of 3 study investigators who were blinded to treatment assignment. Costs for these admissions were calculated using hospital billing data (with conversion of charges to costs as previously discussed) when available, or by assigning mean national reimbursement for each respective Medicare severity-adjusted diagnosis-related group to the admission (13).

**PHYSICIAN FEES.** Physician fees for the index procedure were taken from the current Medicare fee schedule for the procedure performed (SAVR, or TAVR via iliofemoral, axillary, or transaortic access) on the basis of the respective Current Procedural Terminology codes. For the index procedure, fees for anesthesiology and transesophageal echocardiographic imaging were also included, where applicable. Fees for daily care were included for the index admission on the basis of measured ICU and non-ICU length of stay. For follow-up admissions, we assumed physician fees would be equal to 20% of the hospital costs (or reimbursement) for each admission (14).

**OTHER COSTS.** Through 12 months, enrolling sites collected data on rehabilitation facility stays, nursing home stays, and major outpatient resource use (emergency department visits, physician office visits, outpatient cardiac testing). We estimated costs for these services using national average per diem rates for residential care and Medicare reimbursement rates for outpatient care on the basis of the Medicare fee schedule.

**LIFE EXPECTANCY ESTIMATION.** Projected survival was estimated separately for the SAVR and TAVR groups. First, survival between months 6 and 24 in the SAVR group was calibrated to expected age and sex-adjusted mortality using U.S. life tables (15). The 6- to 24-month time frame was chosen to minimize the impact of perioperative events and because follow-up data beyond 24 months were sparse at the time of our analysis. A multiplicative factor of 1.15 was derived for SAVR group mortality, relative to age- and sex-matched members of the U.S. population. Patient-level survival beyond 24 months was then projected using the life tables and the calibration factor.

Survival was projected in an analogous fashion for the TAVR group, with the addition of a hazard ratio (HR) comparing TAVR and SAVR group mortality from a landmark survival analysis between months 6 and 24 in the trial. As this empirically derived HR did not differ significantly from unity (HR: 0.86; 95% confidence interval [CI]: 0.58 to 1.27; p = 0.44), we used HR = 1.00 for our base case analysis, but varied this parameter in the sensitivity analysis.

**QUALITY-ADJUSTED LIFE EXPECTANCY.** The EQ-5D questionnaire was administered to all patients at baseline, and at 1-, 6-, 12-, and 24-month follow-ups. Responses to this questionnaire were converted to health state utilities on the basis of a U.S. reference population (16). Through 24 months, quality-adjusted life expectancy was calculated for each patient as the time-weighted average of his or her utility values, with the midpoint between assessments used as the transition between health...
states. Utilities for lifetime projections were estimated using a regression model on the basis of observed data at 24 months. Quality-adjusted life expectancy beyond 24 months was then calculated by multiplying estimated survival in 1-year intervals by predicted utility, adjusted for sex, age, baseline utility, and history of previous cardiac artery bypass graft or stroke.

**LONG-TERM COSTS.** Observed total health care costs between months 6 and 12 of the in-trial period were used to project future costs. Future costs were projected at the patient level on the basis of a regression model of observed 6 to 12 month costs, adjusting for age and sex.

**STATISTICAL ANALYSIS.** Categorical data are reported as frequencies, and continuous data are reported as mean ± SD. Binary and categorical variables were compared using the Fisher exact test. Normally distributed continuous variables were compared using 2-sample Student t tests, and non-normally distributed data were compared using the Wilcoxon rank-sum test. Cost data are reported as both mean and median values and were compared during the in-trial period by 2-sample Student t tests. All probability values were 2-sided. Between-group differences and associated 95% CI for projected life expectancy, quality-adjusted life expectancy, and costs were generated with bootstrap resampling.

Incremental cost-effectiveness ratios (ICER) were calculated as the difference in mean discounted lifetime costs divided by the difference in mean discounted life expectancy or quality-adjusted life expectancy. Bootstrap resampling was used to assess the joint distribution of lifetime cost and survival differences and to graphically represent uncertainty in these parameters on the cost-effectiveness plane. In order to incorporate potential uncertainty in long-term survival effects between TAVR and SAVR, the long-term HR between TAVR and SAVR derived from landmark analysis was also recalculated for each bootstrap replicate.

**Sensitivity and subgroup analyses.** Lifetime cost-effectiveness results were estimated separately for several subgroups of clinical interest, including TAVR access site (IF vs. non-IF), sex, baseline age (dichotomized at 85 years), and Society of Thoracic Surgeons (STS) risk score (dichotomized at 7). Major preplanned sensitivity analyses included variations in the discount rate (from 0% to 5% per year); use of the empirically derived long-term HR for TAVR versus SAVR from landmark analysis (0.86), rather than the assumed value of 1.0; and ignoring costs accrued during subsequent years of life. Additionally, we explored the impact on lifetime cost-effectiveness of potential reductions in the cost of the index TAVR admissions between $1,000 and $10,000.

**RESULTS**

As previously reported, of the 795 patients enrolled in the CoreValve U.S. High Risk Pivotal Trial, a total of 390 underwent attempted TAVR and 357 underwent attempted SAVR and constituted the primary analytic population for our study (4). These patients had a mean age of 83 years, were almost evenly divided between men and women, and had a high burden of comorbid health problems, with mean STS-predicted risk of mortality scores >7 (Online Table 1). There were no important differences in baseline clinical or echocardiographic characteristics between the TAVR and SAVR groups.

**INDEX PROCEDURES AND ADMISSIONS.** Resource utilization and costs incurred during the index TAVR and SAVR hospitalizations are shown in Table 1. Procedure duration and room time were significantly shorter with TAVR. Due to the higher technology cost of the TAVR system compared with a surgical bioprosthesis, TAVR procedures were ~$24,000 more costly than were SAVR procedures. The higher procedure costs were partially offset by significant reductions in ICU and non-ICU length of stay, with a mean reduction in the total length of stay of 4.4 days (95% CI: 3.1 to 5.7; p < 0.001). Despite these cost offsets, total admission costs, including physician fees, remained higher with TAVR by $11,260 per patient (95% CI: $7,143 to $15,378; p < 0.001).

Index admission resource utilization and costs stratified by the access site used for TAVR (as-treated analysis) are shown in Online Tables 2 and 3. For patients treated with SAVR, resource use and costs were similar, regardless of whether they were eligible for TAVR via IF access. In contrast, length of stay, nonprocedural costs, and total admission costs were higher when TAVR was performed via a non-IF, rather than an IF approach. As a result, the difference in index admission costs between TAVR and SAVR was larger for the non-IF subgroup ($23,344 per patient; 95% CI: 13,188 to 33,501; p < 0.001) than for the IF subgroup ($8,787; 95% CI: $4,303 to $13,270; p < 0.001).

**12-MONTH FOLLOW-UP.** At the end of the index admission, TAVR patients were much more likely than SAVR patients to be discharged home (65% vs. 38%; p < 0.001) rather than to short-term rehabilitation or another treatment setting. Otherwise, there were no major differences between the TAVR and SAVR groups.
with respect to health care resource utilization or costs during the 12-month follow-up period (Table 2). Mainly due to a small and not statistically significant difference in residual care costs, total follow-up costs tended to be slightly lower in the TAVR patients (mean difference $2,053, p = 0.52). Cumulative 12-month costs were thus $9,207 per patient higher with TAVR than SAVR ($98,358 vs. $89,151; 95% CI for difference: $1,694 to $18,177; p = 0.02).

**QUALITY OF LIFE.** As previously reported, 12-month mortality was 4.9% lower in the TAVR group than in the SAVR group (14.2% vs. 19.1%) (4), and this absolute difference increased to 6.5% at 2 years (9). In addition to this difference in mortality, QOL was significantly better in the TAVR group at 1-month follow-up, with mean EQ-5D utility scores of 0.79 ± 0.19 in the TAVR group versus 0.67 ± 0.25 in the SAVR group (mean difference: 0.10; 95% CI: 0.07 to 0.14; p < 0.001). At subsequent time points, QOL was significantly improved from baseline to a similar extent in both study groups, with no between-group differences (17).

**LIFETIME PROJECTIONS.** Using observed survival through 24 months and predicted survival thereafter from the calibrated life table approach, we estimated a life expectancy of 6.45 years (95% CI: 6.03 to

### Table 1: Index Admission Resource Use and Costs

<table>
<thead>
<tr>
<th></th>
<th>TAVR (n = 390)</th>
<th>SAVR (n = 357)</th>
<th>Difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure duration, min&lt;sup&gt;†&lt;/sup&gt;</td>
<td>61 ± 35 [55]</td>
<td>221 ± 85 [205]</td>
<td>-161 (-151 to -170)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Room time, min&lt;sup&gt;†&lt;/sup&gt;</td>
<td>216 ± 62 [206]</td>
<td>315 ± 94 [295]</td>
<td>-99 (-87 to -110)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital LOS, days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>3.1 ± 3.3 [2]</td>
<td>4.7 ± 5.9 [3]</td>
<td>-1.6 (-0.9 to -2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-ICU</td>
<td>5.0 ± 5.5 [4]</td>
<td>7.7 ± 8.4 [5]</td>
<td>-2.8 (-1.8 to -3.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-procedure</td>
<td>6.7 ± 5.3 [5]</td>
<td>11.5 ± 10.3 [8]</td>
<td>-4.8 (-3.6 to -5.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>8.1 ± 6.9 [6]</td>
<td>12.5 ± 10.6 [9]</td>
<td>-4.4 (-3.1 to -5.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total ventilator time, h</td>
<td>14.2 ± 64.1 [4.0]</td>
<td>36.2 ± 84.3 [15.5]</td>
<td>-22.0 (-11.1 to -32.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Costs, U.S.$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index procedure</td>
<td>37,920 ± 2,567 [37,320]</td>
<td>14,258 ± 2,749 [13,739]</td>
<td>23,661 (23,280 to 24,043)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonprocedural</td>
<td>27,654 ± 22,981 [21,540]</td>
<td>38,399 ± 30,956 [29,340]</td>
<td>-10,745 (-8,850 to -14,640)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physician fees</td>
<td>4,018 ± 1,070 [3,735]</td>
<td>5,674 ± 1,486 [5,212]</td>
<td>-1,656 (-1,472 to -1,841)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>69,592 ± 24,387 [62,860]</td>
<td>58,332 ± 32,653 [48,952]</td>
<td>11,260 (7,143 to 15,378)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean ± SD (median). *Procedure duration defined as interval from insertion to removal of introducing sheath. Room time defined as interval from when patient entered the procedural room (catheterization laboratory or operating room) to when they left the room.

Cl = confidence interval; ICU = intensive care unit; LOS = length of stay; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

### Table 2: Health Care Resource Use and Costs During 1-Year Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>TAVR (n = 390)</th>
<th>SAVR (n = 357)</th>
<th>Difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up hospitalizations</td>
<td>1.0 ± 1.4</td>
<td>0.8 ± 1.3</td>
<td>0.1 (-0.1 to 0.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0.4 ± 0.8</td>
<td>0.4 ± 0.8</td>
<td>0.0 (-0.1 to 0.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>0.6 ± 1.1</td>
<td>0.5 ± 0.9</td>
<td>0.1 (0.0 to 0.3)</td>
<td>0.06</td>
</tr>
<tr>
<td>Rehabilitation days</td>
<td>9.5 ± 26.3</td>
<td>13.2 ± 22.9</td>
<td>-3.7 (-7.2 to -0.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Other chronic care days</td>
<td>10.3 ± 44.4</td>
<td>8.8 ± 28.9</td>
<td>1.4 (-4.0 to 6.9)</td>
<td>0.60</td>
</tr>
<tr>
<td>Costs, $</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index admission</td>
<td>69,592 ± 24,387 [62,860]</td>
<td>58,332 ± 32,653 [48,952]</td>
<td>11,260 (7,143 to 15,378)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow-up hospitalizations</td>
<td>12,208 ± 22,315 [0]</td>
<td>10,831 ± 18,890 [0]</td>
<td>1,376 (-1,509 to 4,348)</td>
<td>0.37</td>
</tr>
<tr>
<td>Residential care</td>
<td>14,335 ± 33,474 [0]</td>
<td>18,216 ± 30,544 [7,580]</td>
<td>-3,881 (-8,062 to 845)</td>
<td>0.10</td>
</tr>
<tr>
<td>Other outpatient services</td>
<td>2,224 ± 3,059 [1,630]</td>
<td>1,772 ± 2,357 [1,053]</td>
<td>452 (67 to 842)</td>
<td>0.03</td>
</tr>
<tr>
<td>Total follow-up costs</td>
<td>28,766 ± 45,831 [12,425]</td>
<td>30,819 ± 40,411 [17,379]</td>
<td>-2,053 (-8,032 to 4,338)</td>
<td>0.52</td>
</tr>
<tr>
<td>Total 12-month costs</td>
<td>98,358 ± 54,757</td>
<td>89,151 ± 53,828</td>
<td>9,207 (1,694 to 18,177)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values are mean ± SD (median). Abbreviations as in Table 1.
6.88 years) for the TAVR group and 5.92 years (95% CI: 5.47 to 6.35 years) for the SAVR group (difference: 0.52 years; 95% CI: −0.08 to 1.15). After discounting at 3%, these values decreased to 5.47 years, 5.06 years, and 0.41 years, respectively (Table 3). Projected quality-adjusted survival was 20% lower in both groups, and with discounting, the mean difference between groups was 0.32 QALY (95% CI: −0.02 to 0.69) (Table 3).

Given the high background medical costs of the patient population, the TAVR group, by virtue of its longer predicted survival, accrued additional long-term incremental health care costs in our analysis. Consequently, lifetime costs were higher in the TAVR group by $20,488 (95% CI: $6,780 to $35,175) per patient without discounting and $17,849 per patient with discounting (95% CI: $6,815 to $29,166). **COST EFFECTIVENESS.** Distributions of the projected differences in lifetime costs, QALY, and LY are shown in the **Central Illustration.** On the basis of these projections, the ICER for TAVR versus SAVR was $55,090 per QALY gained and $43,114 per LY gained. The ICERs were <$150,000 per QALY or LY gained in approximately 90% of bootstrap replicates (Table 3). **Subgroup and sensitivity analyses.** Lifetime costs, effectiveness, and cost-effectiveness within key subgroups and from major sensitivity analyses are shown in Table 3. The lifetime ICER was slightly more favorable in the majority of patients suitable for IF access than in the full population (lifetime discounted incremental costs: $11,320; incremental QALY: 0.21; ICER: $52,897 per QALY gained), and somewhat less favorable in patients only suitable for non-IF access (incremental costs: $47,703; incremental QALY: 0.76; ICER: $62,767 per QALY gained), although results in the latter group were more uncertain. Potential differences in cost-effectiveness on the basis of sex and STS score were observed, with slightly more favorable point estimates in women and subjects with STS scores <7. The ICER did not vary considerably by age.

In sensitivity analyses, the ICER was not sensitive to variations in the discount rate, to lowering the long-term HR from its assumed value of 1.0 to the observed value of 0.86, or to the exclusion of costs accrued during added years of life (Table 3). Figure 1 illustrates the potential impact of lowering the costs of index TAVR admissions compared with costs for the base case. Each $1,000 reduction in the index TAVR admission cost was found to lower the ICER by ~$3,000 per QALY. As a result, even a modest reduction of ~$1,650 in the cost of the index hospitalization for TAVR was projected to lead to an ICER below $50,000/QALY gained.
Mean incremental 12-month costs and benefits (TAVR – SAVR) are plotted on the cost-effectiveness plane with benefits expressed as QALY (A) or LY (B). Solid circles represent base case estimates, the surrounding open circles represent individual results for 1,000 replications of the study using bootstrap resampling, and the lines represent a willingness to pay threshold of $50,000 per QALY/LY gained (green) or $150,000 per QALY/LY gained (purple). For both effectiveness outcomes, the point estimates are near $50,000 per QALY/LY gained and ~90% of replicates are below $150,000 per QALY/LY gained. See text and Table 3 for additional details. ICER = incremental cost-effectiveness ratio; LY = life-year(s); QALY = quality-adjusted life-year(s); SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.
DISCUSSION

In this patient-level health economic analysis on the basis of empirical data from the CoreValve U.S. High Risk Pivotal Trial, we found that TAVR using a self-expanding prosthesis provided meaningful clinical benefits relative to SAVR, with incremental costs considered acceptable from the perspective of the U.S. health care system. The observed health benefits of TAVR relative to SAVR in this high-risk population included more rapid procedural recovery, superior QOL at 1 month, and lower mortality through 2 years. In a lifetime analysis, we projected discounted gains of 0.32 QALY and 0.41 LY with TAVR, with lifetime incremental costs of ~$18,000 per patient. The resulting ICER of ~$55,000 per QALY gained and ~$43,000 per LY gained are near or below the threshold currently considered to indicate high economic value (<$50,000 per QALY or LY) for cardiovascular therapies in the U.S. health care system (18).

COMPARISON WITH PREVIOUS STUDIES. Previous studies on the cost-effectiveness of TAVR relative to SAVR have generally been on the basis of clinical outcomes from the PARTNER (Placement of Aortic Transcatheter Valves) A study, the only previous randomized controlled trial of TAVR, with cost data drawn from disparate sources (6). As a result, effectiveness estimates in these studies have been largely consistent, but there have been widely divergent conclusions on the cost of TAVR relative to SAVR—in part, on the basis of research methods and in part on the basis of differences in the underlying health care systems.

The current study is not directly comparable to any of the previous studies on this topic, for several reasons. First, ours is the only health economic study focused exclusively on the CoreValve which has potentially important clinical differences compared with the balloon-expandable Sapien valve (Edwards Lifesciences, Irvine, California) studied previously. More importantly, although the PARTNER study and CoreValve U.S. Pivotal Trial had structural similarities, the trials had different entry criteria, enrolled patients with different risk profiles, were conducted at different study centers in different time frames and found different clinical outcomes.

As expected, we found that procedural costs were substantially higher with TAVR than with SAVR, and that those costs were offset by savings from shortened hospital length of stay and a reduced need for post-discharge residential care. In this trial, those offsets were not sufficient for TAVR to achieve overall cost neutrality relative to SAVR, either in the short or long term. The conclusion that TAVR is nonetheless a reasonable value consequently hinges on the observed clinical benefits. These findings have important implications, as TAVR is evaluated in lower-risk AS patients. At current valve prices, length of stay would likely need to be at least 5 to 6 days shorter with TAVR than with SAVR in order to approach cost neutrality.

There were a few notable variations in estimated cost-effectiveness across key subgroups of interest. As seen previously (7), among patients who were suitable only for non-IF access, incremental costs with TAVR versus SAVR were greater than in those patients who were suitable for IF access, mainly because the reduction in length of stay compared with SAVR was much smaller in the non-IF cohort (1.4 vs. 5.0 days). Despite the higher incremental cost, given the substantial gain in projected life expectancy seen in the non-IF subgroup, the ICER for this subgroup was still well below $150,000/QALY—a value that has been recently considered to represent intermediate value in the context of the U.S. health care system (18). It is worth noting that the non-IF patients composed only 16% of the trial population and hence results in this subgroup are uncertain.

There were also possible differences in cost-effectiveness outcomes on the basis of sex, driven...
by a trend toward greater clinical benefits in women and according to STS score. Although more pronounced clinical benefits with TAVR in women than men were also seen in the PARTNER trial (19), we believe that the subgroup results from our analysis must be interpreted with caution, given that statistical testing of the primary survival data showed no significant interactions with these parameters.

**IMPACT OF CHANGING CARE PATTERNS AND OUTCOMES.** Our sensitivity analysis suggests that reductions in the initial hospital costs of TAVR by ~$1,650 per patient would reduce the ICER from its current level to <$50,000 per QALY gained. Although experts have argued that this historical value is no longer a valid reference point for the U.S. health care system (20), it is still frequently cited as a benchmark for high economic value (18). Regardless, we believe that reductions of this magnitude in the cost of TAVR admissions are realistic. TAVR remains a procedure early in its development. The centers performing TAVR in the U.S. trial were all new to the intervention, and extra precautions may have been taken in the context of an investigational device exemption trial. It is reasonable to expect that iterative improvements in TAVR technology in the short to intermediate term, coupled with increased clinical experience, will lead to reduced complication rates (21), more efficient care (22), reduced costs (23), and improved cost-effectiveness relative to SAVR, a much more mature therapy.

**STUDY LIMITATIONS.** The results are on the basis of a single U.S. clinical trial with specific entry criteria and a single TAVR device; one cannot assume that results would be the same in different treatment settings, patient populations, or with different TAVR systems. Although a lifetime horizon is necessary to estimate the full impact of the difference in 2-year mortality, extrapolation of results beyond the period of direct observation introduces uncertainty, particularly in subgroups with limited sample sizes. Nonetheless, we believe that our assumptions about long-term clinical and economic outcomes were appropriately conservative. The long-term durability of the self-expandable valve system is not yet fully known. However, given the advanced starting age of the study population and a projected average life expectancy of 5 to 6 years, on the basis of current worldwide experience, we consider it unlikely that long-term valve performance would alter our results.

**CONCLUSIONS**

On the basis of data from the CoreValve U.S. High Risk Pivotal Trial, we found that TAVR in patients at high risk for complications with SAVR provides important incremental health benefits at reasonable incremental costs and is clearly an acceptable value in the context of the U.S. health care system. With expected improvements in clinical outcomes and efficiency, TAVR with the CoreValve system is likely to provide high economic value in this patient population.

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**PERSPECTIVES**

**COMPETENCY IN SYSTEMS-BASED PRACTICE:** The incremental costs of TAVR relative to SAVR in a clinical trial setting were in a range generally considered acceptable in the United States, and improvements in technology and ancillary care are expected to make TAVR a high-value intervention for carefully specified patients.

**TRANSLATIONAL OUTLOOK:** Future trials should compare the costs and value of TAVR versus SAVR for patients at intermediate surgical risk.


KEY WORDS aortic stenosis, cost-benefit analysis, heart valve prosthesis, quality-adjusted life-years, transcatheter valve therapy

APPENDIX For supplemental tables, please see the online version of this article.