Cost-Effectiveness of Transcatheter Aortic Valve Replacement Compared With Standard Care Among Inoperable Patients With Severe Aortic Stenosis

Results From the Placement of Aortic Transcatheter Valves (PARTNER) Trial (Cohort B)

Matthew R. Reynolds, MD, MSc; Elizabeth A. Magnuson, ScD; Kajjun Wang, PhD; Yang Lei, MSc; Katherine Vilain, MPH; Joshua Walczak, MS; Susheel K. Kodali, MD; John M. Lasala, MD, PhD; William W. O’Neill, MD; Charles J. Davidson, MD; Craig R. Smith, MD; Martin B. Leon, MD; David J. Cohen, MD, MSc; on behalf of the PARTNER Investigators

Background—In patients with severe aortic stenosis who cannot have surgery, transcatheter aortic valve replacement (TAVR) has been shown to improve survival and quality of life compared with standard therapy, but the costs and cost-effectiveness of this strategy are not yet known.

Methods and Results—The PARTNER trial randomized patients with symptomatic, severe aortic stenosis who were not candidates for surgery to TAVR (n=179) or standard therapy (n=179). Empirical data regarding survival, quality of life, medical resource use, and hospital costs were collected during the trial and used to project life expectancy, quality-adjusted life expectancy, and lifetime medical care costs to estimate the incremental cost-effectiveness of TAVR from a US perspective. For patients treated with TAVR, mean costs for the initial procedure and hospitalization were $42 806 and $78 542, respectively. Follow-up costs through 12 months were lower with TAVR ($29 289 versus $53 621) because of reduced hospitalization rates, but cumulative 1-year costs remained higher ($106 076 versus $53 621). We projected that over a patient’s lifetime, TAVR would increase discounted life expectancy by 1.6 years (1.3 quality-adjusted life-years) at an incremental cost of $79 837. The incremental cost-effectiveness ratio for TAVR was thus estimated at $50 200 per year of life gained or $61 889 per quality-adjusted life-year gained. These results were stable across a broad range of uncertainty and sensitivity analyses.

Conclusions—For patients with severe aortic stenosis who are not candidates for surgery, TAVR increases life expectancy at an incremental cost per life-year gained well within accepted values for commonly used cardiovascular technologies.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00530894.

Key Words: aortic stenosis ■ transcatheter valve therapy ■ cost-effectiveness ■ clinical trials

Valvular aortic stenosis occurs most commonly among the elderly and, in the absence of definitive treatment, leads to progressive symptoms, functional decline, and death.1,2 Nonetheless, many patients with severe aortic stenosis do not undergo surgical valve replacement because of both cardiovascular and noncardiovascular comorbidities that result in unacceptable surgical risk.3–5 Recently, the Placement of Aortic Transcatheter Valves (PARTNER) trial reported that in a cohort of patients who were unsuitable for surgical valve replacement (cohort B), transcatheter aortic valve replacement (TAVR), compared with standard nonsurgical care, resulted in a 20% reduction in mortality at 12 months, as well as improved functional status and a reduction in hospital admissions for aortic stenosis.6

Editorial see p 1076
Clinical Perspective on p 1109

New technologies are often cited as a major contributor to increasing healthcare costs.7 Before a new technology or...

Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.

Received July 4, 2011; accepted January 4, 2012.

From the Harvard Clinical Research Institute, Boston, MA (M.R.R., J.W.); Boston VA Healthcare System, Boston, MA (M.R.R.); Saint Luke’s Mid America Heart & Vascular Institute, University of Missouri–Kansas City, Kansas City, MO (E.A.M., K.W., Y.L., K.V., D.J.C.); Columbia-Presbyterian Hospital, New York, NY (S.K.K., C.R.S., M.B.L.); Washington University School of Medicine, St. Louis, MO (J.M.L.); University of Miami School of Medicine, Miami, FL (W.W.O.); and Northwestern University School of Medicine, Chicago, IL (C.J.D.).

Guest Editor for this article was William S. Weintraub, MD.

Correspondence to David J. Cohen, MD, MSc, Saint Luke’s Mid America Heart Institute, University of Missouri-Kansas City School of Medicine, 4401 Wornall Rd, Kansas City, MO 64111. E-mail dcohen@stlukes.org

© 2012 American Heart Association, Inc.

Circulation is available at http://circ.ahajournals.org DOI: 10.1161/CIRCULATIONAHA.111.054072
clinical strategy is widely adopted, it is therefore important to understand the clinical and economic benefits that any increased up-front expenditures may yield. Given the advanced age and multiple comorbid conditions that characterize patients with high surgical risk for surgical valve replacement, the question of whether TAVR can provide meaningful health benefits to the population at an acceptable cost is particularly germane. To address these questions, we conducted a pre-planned health economic study alongside the PARTNER trial, with the goal of understanding the incremental costs and cost-effectiveness of TAVR compared with standard therapy among inoperable patients with severe aortic stenosis.

Methods

Study Population
One-year clinical results from the PARTNER trial (cohort B) have been published previously. Briefly, the trial enrolled adults with severe aortic stenosis, New York Heart Association functional class ≥2, and high surgical risk based on the Society for Thoracic Surgeons risk score or other anatomic or technical factors. These patients were determined not to be suitable surgical candidates on the basis of evaluation by at least 2 surgical investigators and the trial’s executive committee. Patients were randomized to TAVR via the transfemoral route (n = 179) or standard nonsurgical therapy (n = 179), which could include balloon aortic valvuloplasty at the discretion of the treating physician. The study was approved by each enrolling center’s institutional review board, and all patients provided written informed consent. Of the 358 randomized patients, 234 (65%) enrolled at 17 US centers additionally consented to the collection of hospital billing data.

Analytic Overview
All randomized subjects were included in the present study and analyzed according to intention to treat. Our analysis was performed from the perspective of the US healthcare system (ie, a modified societal perspective) and consisted of 2 main components. Data on survival, quality of life, healthcare resource use, and hospital charges were collected through the first 12 months of follow-up (the minimum follow-up duration for the trial) for all patients and were used to calculate survival, quality-adjusted survival, and costs for the trial period. The empirical 12-month data for costs and quality of life, along with all of the available data on survival (up to a maximum of 30 months), were then used to project outcomes beyond the trial, from which estimates of life-years, quality-adjusted life-years (QALYs), and lifetime costs were developed for each patient who survived the trial period. These estimates were then aggregated to calculate average costs and benefits (and their associated distributions) at the treatment-group level.

Determination of Medical Care Costs
Medical care costs were assessed from the perspective of the US healthcare system by use of a combination of resource-based accounting and hospital billing data, as described previously, and are reported in 2010 US dollars. Costs from years before 2010 were converted to 2010 dollars with the medical care component of the Consumer Price Index. Costs from years before 2010 were converted to 2010 dollars with the medical care component of the Consumer Price Index.

TAVR Procedure Costs
For the initial TAVR procedure, study sites recorded procedure duration and counts of major items consumed, such as support wires, guiding catheters, valvuloplasty balloons, Edwards SAPIEN valve systems, temporary pacing catheters, and vascular closure devices. Costs for each procedure were calculated by multiplying item counts by their respective unit prices, determined by the average acquisition costs at a sample of US hospitals. An estimated US commercial price for the Edwards SAPIEN valve system of $30,000 was used for the primary analysis.

Other Index Hospital Costs
Costs for the remainder of each initial hospital stay for TAVR were derived from hospital bills, which were available for 121 of the 175 patients who underwent an attempted TAVR procedure (97% of patients who agreed to participate in billing data collection from 16 US study hospitals). After the exclusion of charges for care received before randomization and charges for the index TAVR procedure itself, all remaining hospital charges were converted to costs by use of cost-center-specific cost-to-charge ratios obtained from each enrolling hospital’s Medicare cost report. When bills were unavailable, the costs of hospital care were estimated with a linear regression model derived from the patients with complete billing data (model $R^2 = 0.84$). Covariates included in the model included total intensive care unit (ICU) and non-ICU length of stay, in-hospital death, in-hospital acute renal failure, and major vascular complication. Use of alternative models, including linear regression of log-transformed costs (with retransformation to natural units), yielded results that were virtually identical.

Follow-Up Hospital Care
Sites collected information on follow-up hospital admissions for any cause at scheduled follow-up visits (1, 6, and 12 months) and on learning of adverse events. Costs for subsequent hospital admissions were calculated from billing data with hospital and cost-center-specific cost-to-charge ratios when bills were available (54% of admissions). When bills were not available (generally because of admission to nonstudy hospitals or to hospitals that do not produce standard billing data), diagnosis, procedure, and adverse event information from the study database were used to assign each admission to a unique Medicare Severity-Adjusted Diagnosis Related Group (MS-DRG). Average reimbursements for each respective MS-DRG, based on 2008 Medicare Provider Analysis and Review (MedPAR) data, were used as the proxy for admission costs in these cases.

Physician Fees
Estimated physician fees for the index TAVR procedure were taken from the Medicare fee schedule and included a primary operator (current fees for surgical aortic valve replacement were used for this unknown value), plus fees for a surgical assistant, cardiac anesthesia (based on measured procedure duration), and intraoperative transesophageal echocardiography. Physician fees for initial consultation and daily care during the remainder of the initial hospital stay and for any additional cardiovascular procedures performed during the index hospitalization (eg, vascular surgery, endovascular stenting) were also taken from the Medicare fee schedule. For follow-up hospitalizations, physician fees were estimated based on the DRG for each admission as described previously.

Other Costs
Data on rehabilitation facility stays, nursing home stays, and outpatient resource use (emergency room visits, physician office visits, outpatient cardiac testing) were collected by the enrolling sites at each study follow-up visit. These measures of resource use were converted to costs using national average per diem rates for residential care and Medicare reimbursement rates for outpatient care based on the Medicare Fee Schedule.

Cost-Effectiveness Analysis
We evaluated cost-effectiveness over a lifetime horizon in terms of both cost per year of life gained (primary analysis) and cost per QALY gained (secondary analysis). These analyses required the projection of life expectancy, quality-adjusted life expectancy, and costs over the anticipated life expectancy of each patient who remained alive at the completion of the trial.

Life Expectancy Estimation
Survival analyses were performed with a locked data set as of September 28, 2010, with a minimum follow-up duration of 12 months, a maximum follow-up duration of 30 months, and mean follow-up duration among survivors of 18 months. To estimate life expectancy for each surviving patient, we used parametric survival models to extrapolate survival probabilities beyond the follow-up time of the trial.
Survival curves were fitted separately for the TAVR and control groups by use of exponential, Weibull, log-normal, log-logistic, logistic, and normal models. Covariates included age, sex, and medical history such as diabetes mellitus, coronary artery disease, peripheral vein disease, myocardial infarction, stroke/transient ischemic attack, prior percuta-
neous coronary intervention, and prior coronary artery bypass graft. To
improve the model fit for the TAVR group and to optimize the resulting
survival projections, we conditioned the model on survival at 3 months
to reduce the influence of periprocedural events not expected to affect
long-term survival. Exponential models were identified as optimal for
both treatment groups based on the Akaike Information Criterion and
Schwarz’s Bayesian Criterion and were used for the primary cost-
effectiveness analysis. Alternative models were used as the basis for
sensitivity analyses (see Statistical Analysis).

From the final survival models, patient-level survival probabilities over
time were generated until the estimated survival probability was
<1%. Individual survival duration was then calculated as the integral
of the survival probability versus time function.

Quality-Adjusted Life Expectancy
Quality of life was assessed directly from patients at baseline, 1, 6,
and 12 months with the EuroQOL (EQ-5D) health status instrument and
contverted to population-level utility weights with a published
algorithm developed for the US population.14 Utility weights are
measures of a person’s strength of preference for his or her state of
health on the basis of a scale from 0 to 1, where 0 represents the
worst possible health state (usually death) and 1 represents ideal
health. 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.15 Missing utility values were estimated by multiple
imputation techniques, taking into account baseline patient charac-
teristics, clinical events, number of hospitalizations, and previous
utility values. Quality-adjusted life expectancy beyond the first year
of follow-up was calculated as the product of projected life expec-
tancy multiplied by the last available utility value for that individual.

Long-Term Costs
Monthly healthcare costs (including hospital costs, physician fees,
outpatient services, and chronic care/rehabilitation costs) beyond the
trial period were estimated on the basis of the last 6 months of observed
costs for each surviving patient by multiplying these cost estimates by
each patient’s projected survival duration beyond the trial.

Statistical Analysis
Categorical data are reported as frequencies, and continuous data are
reported as mean ± SD. Discrete variables were compared by Fisher
exact test. Normally distributed continuous variables were compared
by Student t test, and nonnormally distributed data were compared
with the Wilcoxon rank-sum test. Cost data are reported as both mean
and median values and were compared by t tests, which are
appropriate given the large sample size and our focus on comparing
mean costs between groups (rather than the underlying distribu-
tions).16 All probability values were 2-sided.

For the purposes of the cost-effectiveness analyses, future costs, life
expectancy, and quality-adjusted life expectancy were discounted at 3%
per year, consistent with current guidelines.17 Incremental cost-
effectiveness ratios were calculated as the difference in mean discounted
lifetime costs divided by the difference in mean discounted life expec-
tancy or quality-adjusted life expectancy. Bootstrap resampling18 (5000
replications) was used to assess the joint distribution of lifetime cost
and survival differences and to generate cost-effectiveness acceptability
curves to explore the probability that TAVR would be economically
attractive at any given cost-effectiveness threshold.

In addition to the primary analysis, we performed a number of
sensitivity analyses to explore the impact of key analytic and
structural assumptions on the results of our study. These analyses
included plausible variations in the discount rate and the acquisition
cost of the transcatheter valve; exclusion of all noncardiovascular
care costs; exclusion of the costs of balloon valvuloplasty proce-

Table 1. TAVR Procedural Resource Use and Cost

<table>
<thead>
<tr>
<th>Resource</th>
<th>Use</th>
<th>Unit Cost, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure duration, min</td>
<td>150±84</td>
<td>25.52/min</td>
</tr>
<tr>
<td>TAVR devices, n (%)</td>
<td></td>
<td>30 000</td>
</tr>
<tr>
<td>1</td>
<td>164 (93.7)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10 (5.7)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Valvuloplasty balloons, n</td>
<td>1.3±0.6</td>
<td>462</td>
</tr>
<tr>
<td>Guiding catheters, n</td>
<td>2.7±2.2</td>
<td>51</td>
</tr>
<tr>
<td>Radiographic contrast, mL</td>
<td>132±81</td>
<td>0.14/mL</td>
</tr>
<tr>
<td>Arterial site closure, n (%)</td>
<td>146 (83)</td>
<td>N/A</td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closure device</td>
<td>33 (19)</td>
<td>215</td>
</tr>
<tr>
<td>Procedural costs, $ (median)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Devices</td>
<td>35 400±14 572 (81 631)</td>
<td>. . .</td>
</tr>
<tr>
<td>Room/overhead/personnel</td>
<td>7406±2134 (7018)</td>
<td>. . .</td>
</tr>
<tr>
<td>Total</td>
<td>42 806±15 206 (38 706)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

TAVR indicates transcatheter aortic valve replacement; N/A, not applicable.

Results
Between May 2007 and March 2009, a total of 358 patients with
inoperable aortic stenosis were enrolled at 21 centers (17 US, 3
Canadian, 1 European) and randomized to either TAVR (n=179) or
standard therapy (n=179). Of the 179 patients randomized to TAVR, 175 underwent a TAVR
procedural attempt. Two patients died before their scheduled
procedure, and in 2 other cases, the aortic annulus diameter
was found to be unsuitable for TAVR by intraoperative
transesophageal echocardiography, and the patients were
instead treated with balloon aortic valvuloplasty.

TAVR Procedural Resource Use and Index
Hospitalization Costs
Resource use and costs for the initial TAVR procedures and
their associated hospital stays are summarized in Tables 1 and
2. With few exceptions, the initial procedures used a single
valvuloplasty balloon and a single Edwards-Sapien valve. In
21 patients, 1 or more unplanned procedures were performed,
most commonly a surgical or catheter-based peripheral arte-
rial intervention. The mean TAVR procedural cost, excluding
physician fees, was $42 806 (median $38 706), and the mean
cost for the initial TAVR admission, including physician fees,
was $78 542 (median $67 551). Mean length of stay was 10.1
days, of which 8.6 days were after the procedure.

Follow-Up Resource Use and Costs
Follow-up resource use and costs for the 2 treatment groups are
summarized in Table 3. Over the first 12 months of follow-up,
EQ-5D Scores
Mean baseline EQ-5D utility scores were 0.59 in the TAVR group and 0.57 in the control group. These increased to 0.71 at 30 days and 0.72 at 6 and 12 months in the TAVR group. Among surviving patients in the control group, EQ-5D scores also increased to 0.64 at 30 days, 0.66 at 6 months, and 0.62 at 1 year. The between-group differences in utility weights were statistically significant ($P<0.05$) at each follow-up time point.

Projections Beyond 12 Months
As reported previously, 12-month survival was 70% for the TAVR group versus 50% for the control group, an absolute survival advantage of 20% that was preserved through 2.5 years of follow-up.\textsuperscript{6} Observed survival duration through a maximum of 30 months was 1.25 years with TAVR (95% CI, 1.15–1.36) and 0.88 years (95% CI, 0.78–0.97) with standard therapy, a difference of 0.36 years (95% CI 0.23–0.50). An exponential hazard function best approximated observed survival data for each treatment group based on model goodness-of-fit statistics. Projected survival based on several different hazard functions is displayed along with observed survival in Figure 1.

On the basis of the exponential survival models, total life expectancy for the TAVR group was estimated to be 3.1 years compared with 1.2 years for the control group, a difference of 1.9 years (95% CI, 1.5–2.3 years). This difference decreased to 1.6 years (95% CI, 1.3–1.9 years) after the 3% discount rate was applied. On the basis of these life expectancy projections and the empirical cost data from the last 6 months of follow-up (TAVR $22 429/year; control $35 343/year), lifetime medical care costs beyond the trial were estimated at $43 664 per patient for the TAVR group and $16 282 per patient for the control group.

Cost-Effectiveness Analysis
On the basis of the empirical data for the first 12 months of follow-up and our trial-based survival and cost projections, we estimated a difference in discounted lifetime medical care costs of $79 837 per patient (95% CI, $67 463–$92 349) and a gain in discounted life expectancy of 1.6 years, which resulted in a lifetime incremental cost-effectiveness ratio (ICER) of $50 212 per life-year gained (95% CI, $41 392–$62 591 per life-year gained). Bootstrap simulation demonstrated that the ICER was fairly stable, with 95% of replicates <$60 000 per life-year gained and 100% <$100 000 per life-year gained (Figures 2 and 3).

Sensitivity Analyses
Table 4 summarizes the results of key secondary and sensitivity analyses. Although utility scores were higher at each follow-up

### Table 2. Resource Use and Costs for TAVR Hospitalizations (n=175)

<table>
<thead>
<tr>
<th></th>
<th>Mean±SD (Median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay, d</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>4.0±7.0 (2)</td>
</tr>
<tr>
<td>Non-ICU</td>
<td>6.1±5.4 (9)</td>
</tr>
<tr>
<td>Postprocedure</td>
<td>8.6±9.8 (6)</td>
</tr>
<tr>
<td>Total</td>
<td>10.1±10.1 (7)</td>
</tr>
</tbody>
</table>

Costs, $

TAVR procedure 42 806±15 206 (38 706)
Room and ancillary 30 757±27 484 (22 150)
Physician fees 4979±1697 (4521)
Total for initial hospitalization 78 542±33 799 (67 551)

TAVR indicates transcatheter aortic valve replacement; ICU, intensive care unit.

### Table 3. Cumulative 1-Year Resource Use and Costs

<table>
<thead>
<tr>
<th></th>
<th>TAVR Group (n=179)</th>
<th>Control Group (n=179)</th>
<th>Difference (TAVR-Control) (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up hospitalizations</td>
<td>1.0±1.3</td>
<td>2.2±1.5</td>
<td>−1.1 (−0.8, −1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0.5±0.8</td>
<td>1.7±1.2</td>
<td>−1.2 (−1.0, −1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>0.5±0.8</td>
<td>0.5±0.8</td>
<td>0.1 (−0.1, 0.2)</td>
<td>0.43</td>
</tr>
<tr>
<td>Rehabilitation days</td>
<td>4.6±21.3</td>
<td>3.8±18.7</td>
<td>0.7 (−3.5, 4.9)</td>
<td>0.75</td>
</tr>
<tr>
<td>SNF days</td>
<td>14.4±56.5</td>
<td>7.9±39.5</td>
<td>6.5 (−3.6, 16.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Follow-up hospitalization costs, $</td>
<td>18 074±35 320</td>
<td>45 093±46 943</td>
<td>−27 019 (−35 654, −18 383)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rehabilitation costs, $</td>
<td>4674±21 825</td>
<td>3951±19 209</td>
<td>723 (−3551, 4997)</td>
<td>0.74</td>
</tr>
<tr>
<td>SNF costs, $</td>
<td>4142±16 225</td>
<td>2270±11 344</td>
<td>1 872 (−1038, 4782)</td>
<td>0.21</td>
</tr>
<tr>
<td>Other outpatient costs, $</td>
<td>2400±2584</td>
<td>2308±271</td>
<td>91 (−460, 642)</td>
<td>0.74</td>
</tr>
<tr>
<td>Total follow-up costs, $</td>
<td>29 289±48 542</td>
<td>53 621±53 301</td>
<td>−24 331 (−34 929, −13 735)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total 12-mo costs, $</td>
<td>106 076±60 206</td>
<td>53 621±53 301</td>
<td>52 455 (40 635, 64 275)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

TAVR indicates transcatheter aortic valve replacement; CI, confidence interval; and SNF, skilled nursing facility.
All data are presented as mean±SD.
time point in the TAVR group, mean utility scores in this population remained lower than normal, even after successful TAVR. As a result, the gain in quality-adjusted survival was smaller than the gain in absolute survival, and the cost-utility analysis yielded an ICER of $61,889 per QALY gained (95% CI, $49,551–$78,361 per QALY gained).

These results were relatively insensitive to changes in the discount rate or the assumed acquisition cost of the study device or to the exclusion of costs associated with balloon valvuloplasty procedures from the control group. If the analysis were restricted to only costs related to cardiovascular care, then the lifetime incremental costs of TAVR decreased to ≈$53,000 per patient, with a resulting ICER of $33,860 per life-year and $41,700 per QALY gained. If effectiveness were measured in QALYs, but we assumed no improvement over time in the baseline utility scores for either group, then the ICER for TAVR became less favorable at ≈$83,000 per QALY gained.

Finally, our results were only modestly sensitive to alternative time horizons, alternative hazard functions for TAVR group life expectancy projections, or variations in our estimates of annual costs beyond the first year of follow-up (Figure 1; Table 4). Only an accelerated Gompertz hazard function that yielded 10-year survival of 1% in the TAVR group resulted in an ICER >$60,000 per life-year gained, and >99% of bootstrap simulations yielded ICER results <$100,000 per life-year gained in every scenario examined.

Discussion
In this trial-based analysis, we found that TAVR, performed in a population of patients unsuitable for surgical aortic valve replacement, was associated with procedural costs of ≈$43,000...
and initial hospitalization costs of $78 000. Although follow-up costs through 12 months were significantly lower with TAVR, cumulative 1-year costs remained $55 000 higher per patient with TAVR than with standard, nonsurgical therapy, a difference that increased to $79 000 per patient when costs associated with added years of life were also considered. Over the observed follow-up period, TAVR was associated with a survival benefit of 0.5 years, which increased to 1.9 years (1.6 years after discounting) when the empirical survival data were projected over a lifetime horizon. On the basis of these data, the ICER for TAVR compared with standard care was estimated at $50 200 per year of life gained or $62 000 per QALY gained, results that remained relatively stable across a broad range of uncertainty and sensitivity analyses.

At the present time, there is no explicit cost-effectiveness threshold used for reimbursement policy in the United States, although formal economic assessments are often required in the evaluation of new health technologies in other national health systems. Outpatient hemodialysis has long been referenced as a benchmark for the cost-effectiveness of new medical interventions in the United States, because it has been mandated as a covered benefit under the Medicare program. Recent studies have estimated the cost-effectiveness of hemodialysis for end-stage renal disease at $70 000 per life-year gained. The ICER for TAVR versus standard care of $50 000 per year of life gained from the present study is thus favorable compared to the cost-effectiveness of percutaneous coronary intervention versus medical therapy for patients with stable coronary artery disease or left ventricular assist devices for destination therapy.

In addition to the main results, the present study provides several important insights into the cost-effectiveness of life-extending therapy among the very elderly. First, we found that despite providing substantial cost offsets during the first year of follow-up, among the highly complex, inoperable patients enrolled in this trial, TAVR did not result in long-term cost savings. In fact, our empirically derived projections suggest that the cost difference between TAVR and standard therapy actually increased beyond the first year of follow-up as a result of the greater life-expectancy for the TAVR group coupled with the high cost of ongoing medical care even after successful valve replacement in this uniquely challenging patient population.

The results of the present study were slightly less favorable when expressed as costs per QALY gained rather than costs per life-year gained, even though symptoms, quality of life, and functional status improved more with TAVR than in the control group. This is because the years of life added for the TAVR group were added at less than perfect quality, a finding that would be expected given the patient population under study. If quality of life had not improved with TAVR, as we explored in sensitivity analysis, the ICER would have been substantially higher. Although a 1996 expert panel recommended the use of QALYs as the standard effectiveness measure in health economic analysis, this guidance is not universally accepted both because of imprecision in the methods used to estimate QALYs and because there is both philosophical and political opposition to the notion that

### Table 4. Lifetime Cost-Effectiveness and Selected Sensitivity Analyses

<table>
<thead>
<tr>
<th></th>
<th>Lifetime Costs, $</th>
<th>Life-Years or QALYs</th>
<th>ICER, per LYG</th>
<th>Probability &lt;$50 000</th>
<th>Probability &lt;$100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>Control</td>
<td>Δ</td>
<td>TAVR</td>
<td>Control</td>
</tr>
<tr>
<td>Base case</td>
<td>149 740</td>
<td>69 903</td>
<td>79 837</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>QALYs</td>
<td>149 740</td>
<td>69 903</td>
<td>79 837</td>
<td>2.03</td>
<td>0.73</td>
</tr>
<tr>
<td>Discount rate 0%</td>
<td>156 920</td>
<td>70 915</td>
<td>86 005</td>
<td>3.11</td>
<td>1.23</td>
</tr>
<tr>
<td>Discount rate 5%</td>
<td>146 031</td>
<td>69 295</td>
<td>76 736</td>
<td>2.61</td>
<td>1.18</td>
</tr>
<tr>
<td>Exclude noncardiovascular costs</td>
<td>110 021</td>
<td>56 184</td>
<td>53 837</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>Valve price =$20 000</td>
<td>139 293</td>
<td>69 903</td>
<td>69 390</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>Valve price =$40 000</td>
<td>160 187</td>
<td>69 903</td>
<td>90 284</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>Exclude BAV procedure costs</td>
<td>149 740</td>
<td>67 118</td>
<td>82 623</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>QALYs assuming no QOL improvement from baseline</td>
<td>149 740</td>
<td>69 903</td>
<td>79 837</td>
<td>1.70</td>
<td>0.74</td>
</tr>
<tr>
<td>Gompertz model (life-years)</td>
<td>143 333</td>
<td>69 903</td>
<td>73 430</td>
<td>2.50</td>
<td>1.20</td>
</tr>
<tr>
<td>Accelerated Gompertz model (life-years)</td>
<td>137 420</td>
<td>69 903</td>
<td>67 517</td>
<td>2.23</td>
<td>1.20</td>
</tr>
<tr>
<td>Wellbull model (life-years)</td>
<td>157 726</td>
<td>69 541</td>
<td>88 185</td>
<td>3.14</td>
<td>1.19</td>
</tr>
<tr>
<td>Base case, 10-year horizon</td>
<td>148 180</td>
<td>69 899</td>
<td>78 281</td>
<td>2.71</td>
<td>1.20</td>
</tr>
<tr>
<td>Base case, 5-year horizon</td>
<td>142 680</td>
<td>69 708</td>
<td>72 972</td>
<td>2.46</td>
<td>1.19</td>
</tr>
<tr>
<td>&gt;1-year TAVR costs inflated 25%</td>
<td>160 000</td>
<td>69 903</td>
<td>90 697</td>
<td>2.78</td>
<td>1.20</td>
</tr>
<tr>
<td>&gt;1-year TAVR costs deflated 25%</td>
<td>138 880</td>
<td>69 903</td>
<td>68 977</td>
<td>2.78</td>
<td>1.20</td>
</tr>
</tbody>
</table>

TAVR indicates transcatheter aortic valve replacement; ICER, incremental cost-effectiveness ratio; LYG, life-year gained; QALY, quality-adjusted life-years; BAV, balloon aortic valvuloplasty; and QOL, quality of life.

*All costs and life-years (QALYs) are discounted at 3% per year unless otherwise indicated.
†ICER expressed as dollars per QALY gained.
life-years for one group might be valued differently than life-years for another group (e.g., because of age, disability, or chronic health problems). Indeed, several recent economic studies of life-prolonging cardiovascular therapies have used life-years as the primary measure of effectiveness.23,29,30

Comparison With Previous Studies
To the best of our knowledge, this is the first study to estimate the lifetime cost-effectiveness of TAVR for patients with inoperable aortic stenosis. Wu and colleagues31 used a combination of single-center observational data on survival and quality of life after aortic valve replacement and a computer simulation model based on historical data on the natural history of untreated valve disease to estimate the cost-effectiveness of surgical aortic valve replacement as a function of patient age. They found that for octogenarians, surgical aortic valve replacement resulted in a gain in quality-adjusted life expectancy of ≈5 years and an ICER of $20,000 per QALY.

The results of the present study differ from those of Wu and colleagues31 in several important ways. First, the patient populations in the 2 studies were quite different and, in fact, mutually exclusive. By definition, the patient population in the previous study consisted of patients who were considered to be candidates for valve replacement surgery, whereas the PARTNER cohort B population was specifically selected to exclude such patients. It is therefore not surprising that the projected gain in life expectancy among operative candidates was substantially greater than for nonoperative candidates in the present study. In addition, the present study was based on empirical cost and survival data from a randomized clinical trial that included a parallel control group of comparable patients treated without valve replacement. Given the very large survival benefit observed in the PARTNER trial (cohort B), it appears unlikely that such a study will be repeated, and the control group from our study will remain the benchmark for future clinical and economic evaluations of this technique among inoperable patients.

Study Limitations
Our results should be interpreted in the context of the following limitations. First, the PARTNER trial was conducted with an early-generation transcatheter aortic valve, and for the majority of the enrolling centers, the trial was the investigators’ first experience with TAVR. Outcomes of TAVR procedures and the efficiency of caring for TAVR patients may improve with technological refinements and increased experience. In addition, certain aspects of the care delivered in the PARTNER trial may have differed from typical community practice. For example, the frequent performance of balloon valvuloplasty in the control group of the present trial likely exceeds that used in recent clinical practice. However, results from a sensitivity analysis showed that removing the costs of balloon aortic valvuloplasty procedures (but not their likely benefit on quality of life) had little impact on our findings.

Our long-term projections of survival, quality-adjusted survival, and costs beyond the trial’s time frame are associated with uncertainty. In the absence of external data from a comparable patient population, we relied almost exclusively on observed data from the first 12 to 30 months of follow-up to inform our estimates of future outcomes. Nonetheless, the fact that nearly 50% of all enrolled patients had died by the completion of follow-up renders our estimates of life expectancy quite plausible. Indeed, a recent study32 of 5-year outcomes among Medicare patients with medically managed aortic stenosis reported a life expectancy of 1.4 years among high-risk patients and annual costs of $30,000, results very similar to ours. Our projected life expectancy of 3.1 years for the TAVR group is less certain but probably not an overestimate given that the average life expectancy of an 83-year-old in the United States is roughly 7 years.83

In conclusion, for patients with severe, symptomatic aortic stenosis who are not considered candidates for surgical valve replacement, the PARTNER trial demonstrates that TAVR significantly increases life expectancy at an incremental cost per life-year or QALY gained well within accepted values for commonly used cardiovascular technologies. Further studies will be necessary to evaluate the cost-effectiveness of TAVR for other, lower-risk patient populations and compared with other treatment strategies (e.g., surgical aortic valve replacement).

Sources of Funding
This study was funded by Edwards Lifesciences, Inc.

Disclosures
Dr Reynolds reports receiving research support from Edwards Lifesciences, Biosense Webster, and Sanofi-aventis and consulting income from Biosense Webster, Sanofi-aventis, St. Jude Medical, and Medtronic. Dr Magnuson reports receiving grant support from Eli Lilly, Daichi Sankyo, Sanofi-aventis, and Bristol-Myers Squibb. Dr Kodali reports receiving consulting income from Edwards Lifesciences (clinical proctor). Dr O’Neill reports receiving consulting fees from Medtronic. Dr Davidson reports receiving research support from Edwards Lifesciences and Abbott Vascular and serving on the advisory board of Abbott Vascular. Dr Smith reports receiving research support from Edwards Lifesciences. Dr Leon reports receiving research support from Edwards Lifesciences and consulting income from Medtronic, and he holds stock options in SadrMedica. Dr Cohen reports receiving research support from Edwards Lifesciences, Medtronic, Boston Scientific, Abbott Vascular, MedRad, Merck/Schering-Plough, and Eli Lilly-Daichi Sankyo; consulting income from Schering-Plough, Eli Lilly, Medtronic, and Cordis; and speaking honoraria from Eli Lilly, The Medicines Company, and St. Jude Medical. The other authors report no conflicts.

References


**CLINICAL PERSPECTIVE**

In patients deemed ineligible for cardiac surgery, the Placement of Aortic Transcatheter Valves (PARTNER) trial recently demonstrated a 20% absolute survival difference at 12 months when transcatheter aortic valve replacement (TAVR) was compared with standard nonsurgical therapy. The costs and cost effectiveness of this clinical strategy, which would typically be applied to elderly patients, have not been evaluated previously. Empirical data regarding survival, quality of life, medical resource use, and hospital costs were collected during the PARTNER trial and used to project life expectancy, quality-adjusted life expectancy, and lifetime medical care costs. Average costs for the initial TAVR procedure and hospital stay were $42 806 and $78 542, respectively, but follow-up costs through 12 months were approximately $24 000 lower per patient with TAVR because of higher rates of cardiovascular hospitalization with standard therapy. We projected that over a patient’s lifetime, TAVR would increase life expectancy by 1.9 years (1.6 years after application of a standard 3% discount rate to future costs and benefits) at a discounted lifetime incremental cost of $79 837. The incremental cost-effectiveness ratio for TAVR was thus estimated at $50 200 per year of life gained, or $61 889 per quality-adjusted life-year gained, values generally considered acceptable within the context of the US healthcare system. These estimates were only slightly altered when assumptions about future costs and survival were varied within plausible ranges.

Go to http://cme.ahajournals.org to take the CME quiz for this article.
Cost-Effectiveness of Transcatheter Aortic Valve Replacement Compared With Standard Care Among Inoperable Patients With Severe Aortic Stenosis: Results From the Placement of Aortic Transcatheter Valves (PARTNER) Trial (Cohort B)

Circulation. 2012;125:1102-1109; originally published online February 3, 2012; doi: 10.1161/CIRCULATIONAHA.111.054072
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/125/9/1102

An erratum has been published regarding this article. Please see the attached page for:
/content/128/4/e61.full.pdf

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/
In the article by Reynolds et al, “Cost-Effectiveness of Transcatheter Aortic Valve Replacement Compared With Standard Care Among Inoperable Patients With Severe Aortic Stenosis: Results From the Placement of Aortic Transcatheter Valves (PARTNER) Trial (Cohort B),” which appeared in the March 6, 2012 issue of the journal (Circulation. 2012;125:1102–1109), Dr William W. O’Neill failed to disclose a professional relationship with Edwards Lifesciences, Inc.

The current online version of the article has been corrected. The authors apologize for the omission.