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The Evolving Management of Aortic Valve Disease: Trends in the Utilization and Cost of SAVR, TAVR, and Medical Therapy

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THE EVOLVING MANAGEMENT OF AORTIC VALVE DISEASE: TRENDS IN THE UTILIZATION AND COST OF SAVR, TAVR AND MEDICAL THERAPY

by

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THE EVOLVING MANAGEMENT OF AORTIC VALVE DISEASE: TRENDS IN THE UTILIZATION AND COST OF SAVR, TAVR AND MEDICAL THERAPY

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ABSTRACT

Aortic stenosis (AS) and regurgitation (AR) may be treated with surgical aortic valve replacement (SAVR), transcatheter AVR (TAVR), or medical therapy (MT). Data are lacking regarding usage and cost of SAVR, TAVR, and MT for patients hospitalized with aortic valve disease. From the Nationwide Readmissions Database, we determined utilization and cost trends for SAVR, TAVR, and MT in patients with aortic valve disease admitted 2012-2016 for valve replacement, heart failure, unstable angina, non-ST-elevation myocardial infarction, or syncope. From 2012 through 2016, there was a 48.1% increase in the number of patients hospitalized for aortic valve disease annually. Overall, 19.9%, 6.7%, and 73.4% of patients received SAVR, TAVR, and MT, respectively. SAVR decreased from 21.9% in 2012 to 18.5% in 2016; TAVR increased from 2.6% to 12.5%; and MT decreased from 75.5% to 69.0%. In multivariable analysis, likelihood of TAVR relative to SAVR increased 4.57-fold (95% confidence interval 4.21-4.97) with TAVR increasing at the expense of both SAVR and MT. The average 6-month inpatient costs were $59,743 for SAVR, $64,395 for TAVR, and $23,460 for MT. TAVR IA costs decreased over time to become similar to SAVR costs by 2016. The TAVR increase was distributed inequitably, with certain patients more likely to receive TAVR and certain hospitals more likely to provide TAVR. Aggregate costs were higher for TAVR than SAVR and were significantly more expensive than MT alone. With the

expected expansion of indications, equitable and affordable access to TAVR must be addressed to minimize disparities and to optimize patient outcomes.

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LIST OF ABBREVIATIONS

AS	aortic stenosis
AR	aortic regurgitation
SAVR	surgical aortic valve replacement
TAVR	transcatheter aortic valve replacement
MT	medical therapy
US	United States
FDA	Food and Drug Administration
NRD	Nationwide Readmissions Database
AHRQ	Agency for Healthcare Research and Quality
HCUP	Healthcare Cost and Utilization Project
NIS	National Inpatient Sample
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
IA	index admission
CHF	congestive heart failure
UA	unstable angina
NSTEMI	non-ST-elevation myocardial infarction
MNL	multinomial logistic
RRR	relative risk ratio
AME	average marginal effects
CI	confidence interval

CHAPTER 1: INTRODUCTION

Therapies for Aortic Valve Disease

Aortic stenosis (AS) and aortic regurgitation (AR) may be treated with one of three strategies: surgical aortic valve replacement (SAVR), transcatheter aortic valve replacement (TAVR), or medical therapy (MT). The United States (US) Food and Drug Administration (FDA) approved TAVR for the treatment of severe AS in inoperable patients[2] in November 2011, high-risk patients [3,4] in October 2012, and intermediate-risk[5,6] patients in August 2016. Small numbers of TAVR procedures may performed off-label for patients with severe AR[7] or mixed AS and AR[8]. However, definitive data are lacking regarding the actual usage of SAVR, TAVR, and MT for patients hospitalized with aortic valve disease and the characteristics of the patients and hospitals associated with each of these therapies.

Rates of SAVR, TAVR, and MT

Prior studies demonstrate an increase in the number of SAVR and TAVR procedures performed in the US over time. Medicare data for patients over age 65 show an increase in hospitalizations for SAVR from 24,568 in 1989 to 31,380 in 2011[9], and TAVR procedure volumes increased from 4,627 procedures at 198 centers in 2012 to 24,808 procedures at 418 centers in 2015[10]. The relative usage of SAVR and TAVR is also evolving. In the Society of Thoracic Surgeons database, the absolute number of TAVR procedures surpassed SAVR procedures in 2016[11], but the overall rate of SAVR has remained relatively stable[12]. Little is known about trends in patients receiving MT.

To address these gaps in knowledge, we sought to characterize temporal trends in the use of SAVR, TAVR, or MT following admission to US hospitals with a primary or secondary diagnosis of AS or AR from 2012 through 2016. We hypothesized that the usage of TAVR has increased particularly in patients with higher surgical risk and at urban teaching hospitals, while the number of patients receiving MT and the number of high-risk patients undergoing SAVR have decreased.

Costs of SAVR, TAVR, and MT

Data also are lacking regarding the relative costs of SAVR, TAVR, and MT for patients hospitalized with aortic valve disease. Prior studies examining the costs of AS care have yielded varying results. In general, TAVR has been associated with increased up-front costs but decreased post-procedural resource utilization in comparison to SAVR and MT, and follow-up costs have correlated with patients' procedural risk level. Cost effectiveness estimates fluctuate widely, particularly as a result of varying costs in different healthcare systems[13]. In sum, the actual costs of SAVR, TAVR, and MT remain poorly understood.

We examined 6-month total inpatient healthcare expenditures for patients with aortic valve disease admitted from 2012-2016 for valve replacement, heart failure, unstable angina, non-ST-elevation myocardial infarction, or syncope. We also performed multivariable and subgroup analyses to investigate the associations of treatment strategy with costs and inpatient days. In contrast to prior studies, our inclusive nationwide economic approach captured the largest patient population to date across diverse health systems and with numerous payment sources. Furthermore, unlike prior analysis, we sought to compare the costs of SAVR and TAVR to MT. Lastly, we report 5-year temporal trends in the economics of aortic valve disease care. This novel information may facilitate future interventions to address disparities in costs and access to care.

CHAPTER 2: METHODS

Data

Data were obtained from the Nationwide Readmissions Database (NRD), the largest, all-payer inpatient care database of the Agency for Healthcare Research and Quality's (AHRQ's) Healthcare Cost and Utilization Project (HCUP) containing an approximately 20% stratified sample of discharges from all hospitals in 27 US states[14]. Data from the NRD and its sister database, the National Inpatient Sample (NIS), have been used for multiple prior studies evaluating patients who have undergone TAVR[15-18]. From the NRD, we obtained de-identified discharge-level data files from 2012 through 2016. Each discharge record includes patient demographics and comorbidities, hospital characteristics, expected payment source, and discharge status. The NRD also collects primary and secondary (up to 35) discharge diagnoses and primary and secondary (up to 15) procedures based on the International Classification of Diseases, Clinical Modification codes (ICD-9-CM for 2012 through 2015 third quarter, ICD-10-CM for 2015 fourth quarter through 2016). From 2012 through 2016, participation in the HCUP NRD increased from 18 to 27 states. We linked the NRD with cost-to-charge ratio files from the Healthcare Cost Report Information System[19] to convert total charges to total costs. We adjusted total costs for each year to 2016 US dollars using the medical care consumer price index[20].

Study Populations

Patient linkage numbers facilitate tracking individual patients across multiple hospitalizations and between participating states, however, because each annual NRD data set is independent, individual patients cannot be tracked between years. Therefore, the study population included all patients who were admitted with aortic valve disease and discharged from January 1 through June 30 in each calendar year, allowing for 6 months of follow-up for every patient.

In the analysis of the rates of SAVR, TAVR, and MT, the index admission (IA) was defined as the patient's first discharge with a primary or secondary diagnosis of non-rheumatic aortic valve stenosis or regurgitation, which was identified based upon ICD-9-CM (424.1) and ICD-10-CM (I35.0, I35.1, I35.2, I35.8, I35.9) codes, plus at least one of the following procedures or diagnoses: SAVR (ICD-9-CM 35.21, 35.22; ICD-10-CM 02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ), TAVR (ICD-9-CM 35.05, 35.06; ICD-10-CM 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ), congestive heart failure (CHF; ICD-9-CM 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43; ICD-10-CM I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50,40, I50.41, I50.42, I50.43), unstable angina (UA; ICD-9-CM 411.1; ICD-10-CM I20.0), non-ST-elevation myocardial infarction (NSTEMI; ICD-9-CM 410.7 410.70 410.71 410.72; ICD-10-CM I21.4) or syncope (ICD-9-CM 780.2; ICD-10-CM R55) as any of up to 15 procedures or any of up to 35 diagnoses.

Treatment strategy was classified as SAVR, TAVR, or MT. ICD-CM codes were used to identify patients undergoing SAVR and TAVR during the IA or within 180 days of the IA discharge date. Patients not undergoing SAVR or TAVR within 180 days of IA discharge were categorized as receiving MT.

In the analysis of costs, inpatient days, and admissions, IA was defined as a patient's first discharge during which AS/AR (ICD-9-CM 424.1; ICD-10-CM I35.0, I35.1, I35.2, I35.8, I35.9) was a primary or secondary diagnosis, and SAVR (ICD-9-CM 35.21, 35.22; ICD-10-CM 02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ) or TAVR (ICD-9-CM 35.05, 35.06; ICD-10-CM 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ) was performed. For MT, IA was defined as a patient’s first discharge with either a primary diagnosis of AS/AR plus a secondary diagnosis of symptoms or a primary diagnosis of symptoms plus a secondary diagnosis of AS/AR with no SAVR or TAVR performed during the calendar year. Symptoms included congestive heart failure (CHF; ICD-9-CM 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43; ICD-10-CM I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50,40, I50.41, I50.42, I50.43), unstable angina (UA; ICD-9-CM 411.1; ICD-10-CM I20.0), non-ST-elevation myocardial infarction (NSTEMI; ICD-9-CM 410.7 410.70 410.71 410.72; ICD-10-CM I21.4) or syncope (ICD-9-CM 780.2; ICD-10-CM R55). Admissions were excluded from IA if patients died prior to discharge.

We excluded 2011 data because TAVR was not approved in the United States until November of that year; only 21 patients in the NRD underwent TAVR in 2011. This study was exempt from the requirements of the Institutional Review Board at the University of Nebraska Medical Center because the NRD contains no patient-identifiable information.

Variables

In the analysis of the rates of SAVR, TAVR, and MT, the primary independent variable was treatment year. Among explanatory variables, we assessed for patient age (≤64, 65-74, 75-84, ≥85 years), sex, two health status variables constructed by NRD (severity of illness and risk of mortality) and the number of comorbid diagnoses reported during IA (1-10, 11-15, 16-20, 21-35). Age and number of diagnoses were converted to categorical variables because their relationships with SAVR, TAVR, and MT were highly non-linear, even with log transformation; all other predictors were presented as categorical variables by the NRD. Using 3M All Patient Refined Diagnosis Related Groups[21,22], NRD classifies severity of illness into minor (including cases with no comorbidity or complications), moderate, major, and extreme loss of function. Similarly, risk of mortality is categorized into minor, moderate, major, and extreme likelihood of dying.

We also assessed both for patient insurance status (Medicare, Medicaid, private, self-pay, no charge/other) and neighborhood median household income as a proxy of patient socioeconomic status, and county population density as a proxy of urban/rural location. Quartiles of neighborhood median household income for patient ZIP code were defined each year (e.g., in 2016, the quartiles were defined as $1-42,999, $43,000-53,999, $54,000-70,999, and $71,000 or more). NRD also included county population density classification constructed by National Center for Health Statistics (less than 249,999, 250,000-999,999, fringe counties of ≥1 million, central counties of ≥1 million population).

For hospital characteristics, we assessed for ownership (for-profit private; not-for-profit private; government, non-federal), size (small, medium, large per NRD criteria by region and teaching status[23]), and status as an urban teaching hospital (urban non-teaching, rural, urban teaching,).

In the analysis of costs, inpatient days, and admissions, the primary independent variable was treatment strategy (SAVR, TAVR, or MT, as defined in the Methods above). Explanatory variables were similar to those studied in the first analysis but also included Charlson comorbidity index[24], constructed from ICD-9-CM[25] or ICD-10-CM[26] codes, as well as number of inpatient procedures (e.g. echocardiogram, coronary artery bypass surgery, percutaneous coronary intervention). Age, Charlson comorbidity index, and number of procedures were converted to categorical variables because their relationships with 3 outcomes were highly non-linear, even with log transformation; all other predictors were presented as categorical variables by the NRD. We studied 3 outcomes: total costs, inpatient days, and admissions. We analyzed these outcomes in aggregate for all admissions as well as separately for IA only and for 6-month unplanned readmissions only, using the NRD variable for non-elective admissions. We also assessed 5-year temporal trends for these outcomes.

Statistical Analysis

Using Pearson Chi-squared tests, we examined systematic differences in the rates of SAVR, TAVR, and MT between 2012 and 2016, and assessed for systematic differences between treatment strategy and each explanatory variable.

For multivariate analysis, we employed a multinomial logistic (MNL) model to evaluate the factors associated with treatment strategy. We tested two MNL models: the first model used SAVR as the base outcome (which generated two sets of coefficient estimates, TAVR versus SAVR, and MT versus SAVR), and the second model used MT as the base outcome (which generated SAVR versus MT and TAVR versus MT). Coefficients of MNL models were converted to relative risk ratios (RRR)[27,28].

We performed three sensitivity analyses to confirm the validity of our methodology. First, we defined IA using just non-rheumatic AS or AR as any admission diagnosis without considering other conditions (i.e., SAVR, TAVR, CHF, UA, NSTEMI, or syncope). Second, we performed the analysis defining IA using only a primary diagnosis of AS or AR. Third, we repeated the analysis using 3-month and 9-month follow-up periods by allowing IA from January through September or January through March respectively.

Similarly, we examined differences in each variable according to treatment strategy using Pearson Chi-squared tests and analysis of variance. To estimate the effect of treatment strategy on aggregate and IA costs and days, we used a multivariable generalized linear model with a log link function and a gamma distribution (GLM-LG)[29,30]. Given that outcomes were skewed to the right and included outliers, GLM-LG made the distribution of outcomes approximately normal and estimated effects without bias. For unplanned readmission costs and days, we used multivariable two-part models[31-33]. In the first part of the two-part models, logistic regression was used to estimate whether patients had no readmission versus readmission (indicated by zero versus any costs or inpatient days). In the second part of the model, GLM-LG accounted for total costs and LOS conditional upon any positive outcome, given that majority of patients had no readmission[31-33]. For the aggregate number of admissions and binary outcome of any unplanned readmission, we used a negative binomial model and a logistic model, respectively. The coefficients of all estimations were converted into average marginal effects (AME), allowing us to interpret the effect of treatment strategy on outcomes in terms of outcome values (i.e., dollars, inpatient days, number of admissions, and probability of readmission). We performed 2 sensitivity analyses to confirm the validity of our methodology. First, we defined IA that occurred (i) in January only and (ii) between January and March, allowing us to track total costs, inpatient days, and unplanned readmissions for 11 and 9 months, respectively. Second, we estimated total charges instead of total costs.

All analyses were conducted with Stata MP v.16.0 and accounted for the discharge weighting in the HCUP NRD survey design in order to produce nationally-representative estimates.

CHAPTER 3: RESULTS

Trends in SAVR, TAVR, and MT

In the analysis of the rates of SAVR, TAVR, and MT, the sample population included 366,909 patients with IA discharges for aortic valve disease and one of the following procedures or diagnoses: SAVR (n = 64,695), TAVR (n = 18,107), CHF (n = 276,955), UA (n = 11,074), NSTEMI (n = 47,749), or syncope (n = 21,858). The average age was 77.8 years, and 48.7% of the study population was female. Fifty-eight percent (57.9%) of patients had major or extreme loss of function due to severity of illness, and 53.0% of patients had major or extreme likelihood of dying. Eighty-five percent (85.2%), 3.0%, and 9.6% of patients were covered by Medicare, Medicaid, and private insurance, respectively (**Table 1**).

The number of patients hospitalized for aortic valve disease in the first half of each calendar year increased by 48.1% from 57,516 in 2012 to 85,165 in 2016. Overall, from 2012 to 2016, January through June, 71,704 (19.9%), 26,173 (6.7%), and 269,032 (73.4%) patients received SAVR, TAVR, and MT, respectively. In 2012, 21.9%, 2.6%, and 75.5% of patients received each therapy, respectively, however, by 2016, the proportion undergoing SAVR and MT decreased to 18.5% and 69.0%, while the TAVR group increased to 12.5% (**Table 2**).

Therapy Subgroup Analyses

Subgroups stratified by patient, neighborhood, and hospital characteristics showed similar trends (Figures 1 and 2, $P < 0.01$ for all). Of note, among the patients ≥75 years of age, the proportion of patients undergoing TAVR increased rapidly, exceeding the proportion undergoing SAVR in 2016 (Figure 1C, 9.3% for SAVR and 15.1% for TAVR). A similar trend was observed for patients with high severity of illness (i.e., major and extreme loss of function, Figure 1E, 14.5% for SAVR and 17.3% for

TAVR). Furthermore, among women (Figure 2B), patients with high predicted mortality (Figure 2D), and patients hospitalized in a large hospital (Figure 2F) or in a teaching hospital (Figure 2H), the proportions receiving SAVR and TAVR were similar by 2016. The same was true for patients at not-for-profit hospitals (**Figure 3H**), with >20 inpatient diagnoses (**Figure 3B**), or living in an urban area (**Figure 3D**).

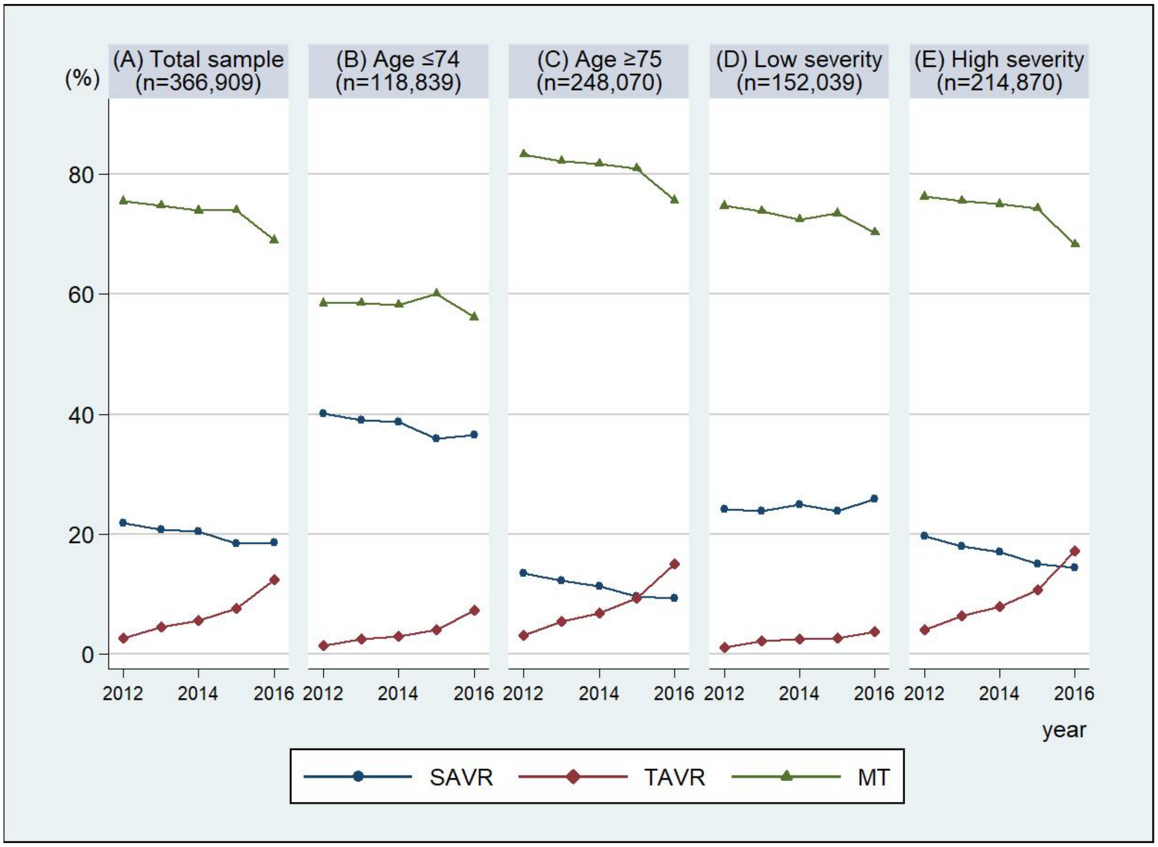

Figure 1. Trends in surgical aortic valve replacement (SAVR), transcatheter aortic valve replacement (TAVR), and medical therapy (MT) from 2012 to 2016: total sample population and stratified by age and severity of illness.

Notes:
(i) Severity of illness: (D) low (minor or moderate loss of function) vs. (E) high (major or extreme loss of function).
(ii) Percentages were adjusted for Healthcare Cost and Utilization Project Nationwide Readmissions Database (HCUP-NRD) discharge weights to generate national estimates.

In multivariable analysis using the MNL model, estimates of TAVR versus SAVR showed that from 2012 to 2016, a patient’s likelihood of receiving TAVR relative to

SAVR increased by 4.57-fold (RRR 4.57, 95% confidence interval [CI] 4.21-4.97) when adjusting for patient, hospital, and neighborhood characteristics. Patients ≥85 years of age (RRR 51.2, 95% CI 46.1-56.7) and those with extreme loss of function (RRR 35.7, 95% CI 29.0-43.8) were most likely to undergo TAVR rather than SAVR. In MNL multivariable analysis for TAVR versus MT, the likelihood of receiving TAVR relative to MT continuously increased from 2012 through 2016 (RRR 4.41 versus 2012, 95% CI 4.08-4.77) (**Table 3**).

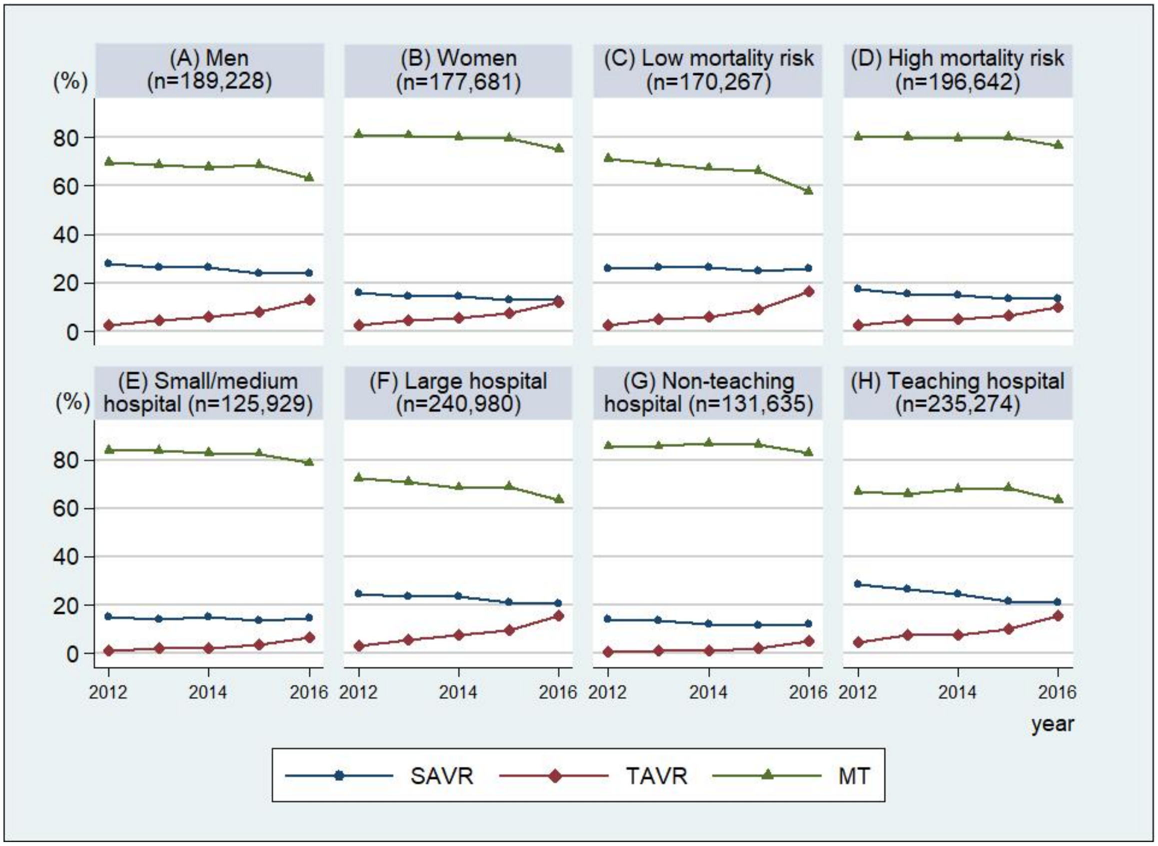

Figure 2. Trends in surgical aortic valve replacement (SAVR), transcatheter aortic valve replacement (TAVR), and medical therapy (MT) from 2012 to 2016: stratified by sex, risk of mortality, hospital size, and hospital teaching status.

Notes:
(i) Risk of mortality: (C) low (minor or moderate likelihood of dying) vs. (D) high (major or extreme likelihood of dying).
(ii) Non-teaching hospital category in panel (G) includes non-teaching hospitals in urban area and any hospitals in rural area.
(iii) Percentages were adjusted for HCUP-NRD discharge weights to generate national estimates.

Therapy Sensitivity Analyses

In the first sensitivity analysis, when we expanded the sample population by defining IA as any admission for AS or AR, regardless of other conditions (i.e., SAVR, TAVR, CHF, UA, NSTEMI or syncope), we captured 244,432 more patients (n = 611,341). Among the additional patients, 98.4% (n = 240,468) patients received MT, and numbers of SAVR and TAVR remained virtually unchanged. The estimates for SAVR vs. TAVR in the multivariate MNL model were similar both in magnitude and statistical significance as compared to the main analysis (**Table 4**). In the second sensitivity analysis, when we restricted the sample population to patients only with a primary diagnosis of AS or AR (n = 101,834), 19.6% of SAVR, 3.8% of TAVR, and 92.9% of MT patients were eliminated. The MNL models in this sensitivity analysis remained similar to the main analysis (data not shown). In the third sensitivity analysis, when we looked at a 3-month window from IA (n = 519,882, SAVR 20.1%, TAVR 6.5%, MT 73.4%) and a 9-month window from IA (n = 195,427, SAVR 19.3%, TAVR 6.6%, MT 74.1%), the rates of each of the 3 therapies and the multivariate MNL model estimates (data not shown) remained similar to the 6-month main analysis.

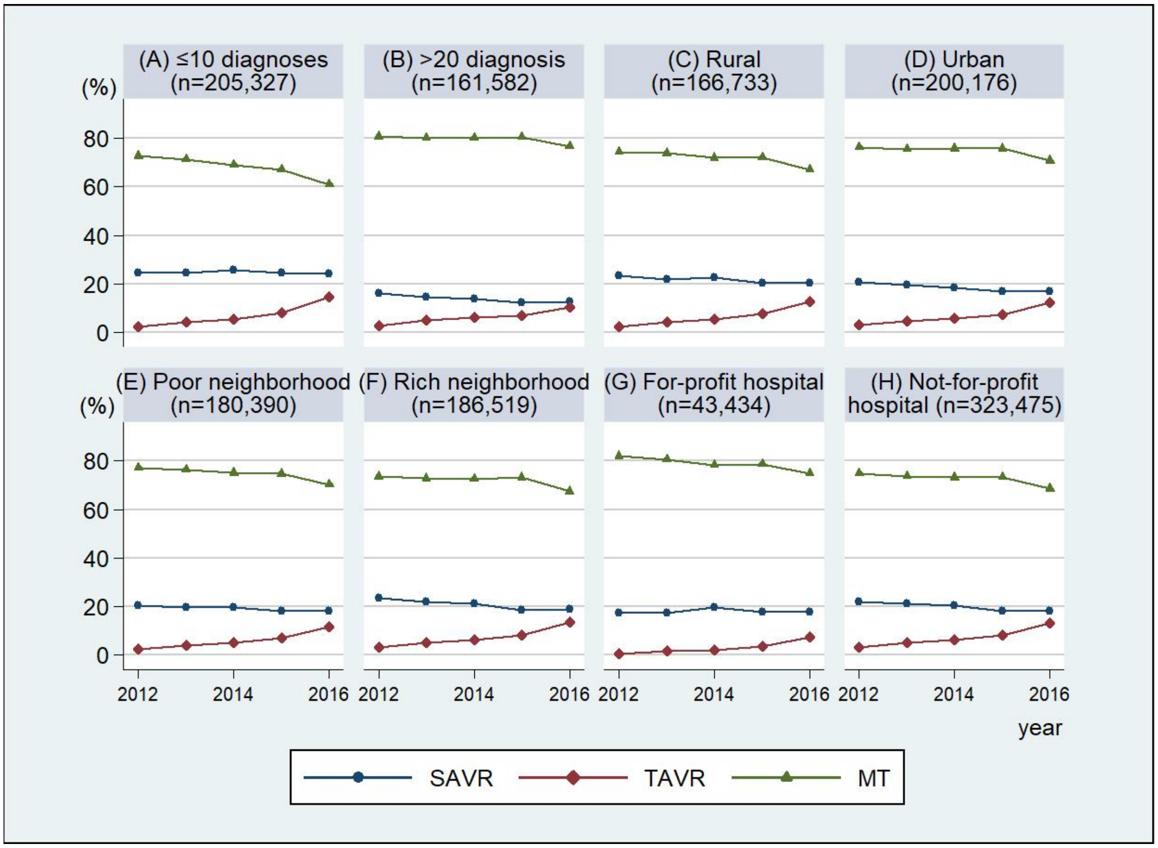

Figure 3. Trends in surgical aortic valve replacement (SAVR), transcatheter aortic valve replacement (TAVR), and medical therapy (MT) from 2012 to 2016: stratified by diagnosis number, hospital location, neighborhood affluence, and hospital not-for-profit status.

Notes:
(i) Percentages were adjusted for HCUP-NRD discharge weights to generate national estimates.
(ii) Diagnosis number: (A) low (10 or fewer diagnoses) vs. (B) high (more than 20 diagnoses).

Trends in Cost, Inpatient Days, and Admissions

In the analysis of costs, inpatient days, and admissions, the study population included 190,563 patients with aortic valve disease, of whom 66,564 (35.6%), 21,902 (10.8%), and 102,097 (53.6%) received SAVR, TAVR, and MT alone, respectively. Patient characteristics are presented in Table 5. Notably, the average age was 76.3 years, 45.0% were female, the average Charlson comorbidity index was 2.1 (SD 0.9), the average number of inpatient procedures was 2.5 (SD 1.2), 53.6% had major or extreme loss of function due to severity of illness, and 47.7% had major or extreme likelihood of dying. Medicare, Medicaid, and private insurance covered 82.0%, 3.1%, and 12.5% of patients, respectively.

The aggregate average 6-month inpatient cost including all admissions was \$40,790±41,730, corresponding to \$59,743 for SAVR, \$64,395 for TAVR, and \$23,460 for MT. However, following IA, the average 6-month cost of readmissions only was \$5505 for SAVR, \$7455 for TAVR, and \$10,013 for MT (Figure 4; $p<0.01$ for all). Among the total study population, the mean number of inpatient days was 10.6±11.5 days for all admissions across 6 months. IA was longer for SAVR (10.0 days) than for TAVR (7.0 day) or MT (5.3 days). However, the average number of unplanned readmission inpatient days was 2.0 for SAVR, 3.0 for TAVR, and 4.3 for MT (Figure 5; $p<0.01$ for all).

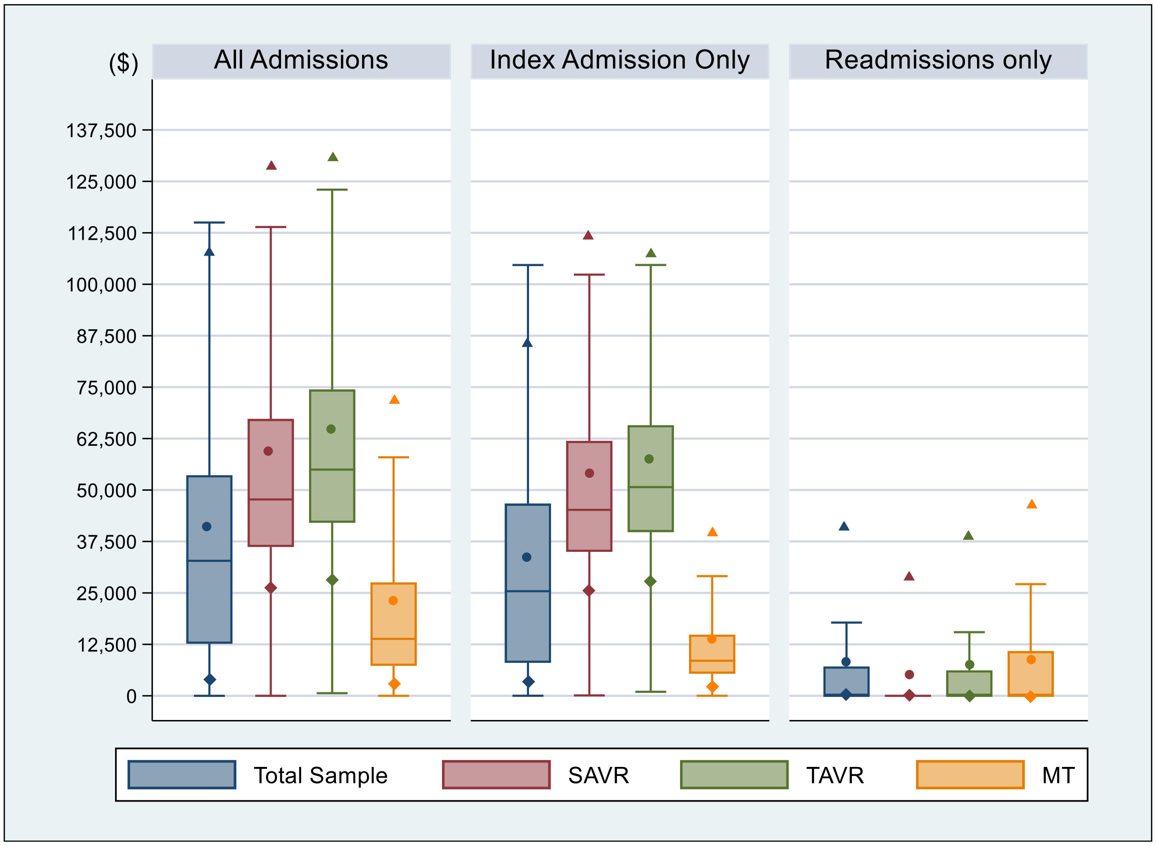

Figure 4. Total costs during all admissions, index admission only, and readmissions only (n=190,563).

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Lower, middle, and upper hinges of box graph represent 25th percentile, 50th percentile (median), and 75th percentile of costs. Lower and upper whiskers represent Tukey's interquartile ranges[34].
(iii) •: mean, ♦: 5th percentile, ▲ : 95th percentile
(iv) All values adjusted for HCUP-NRD discharge weights to generate nationally-representative estimates.

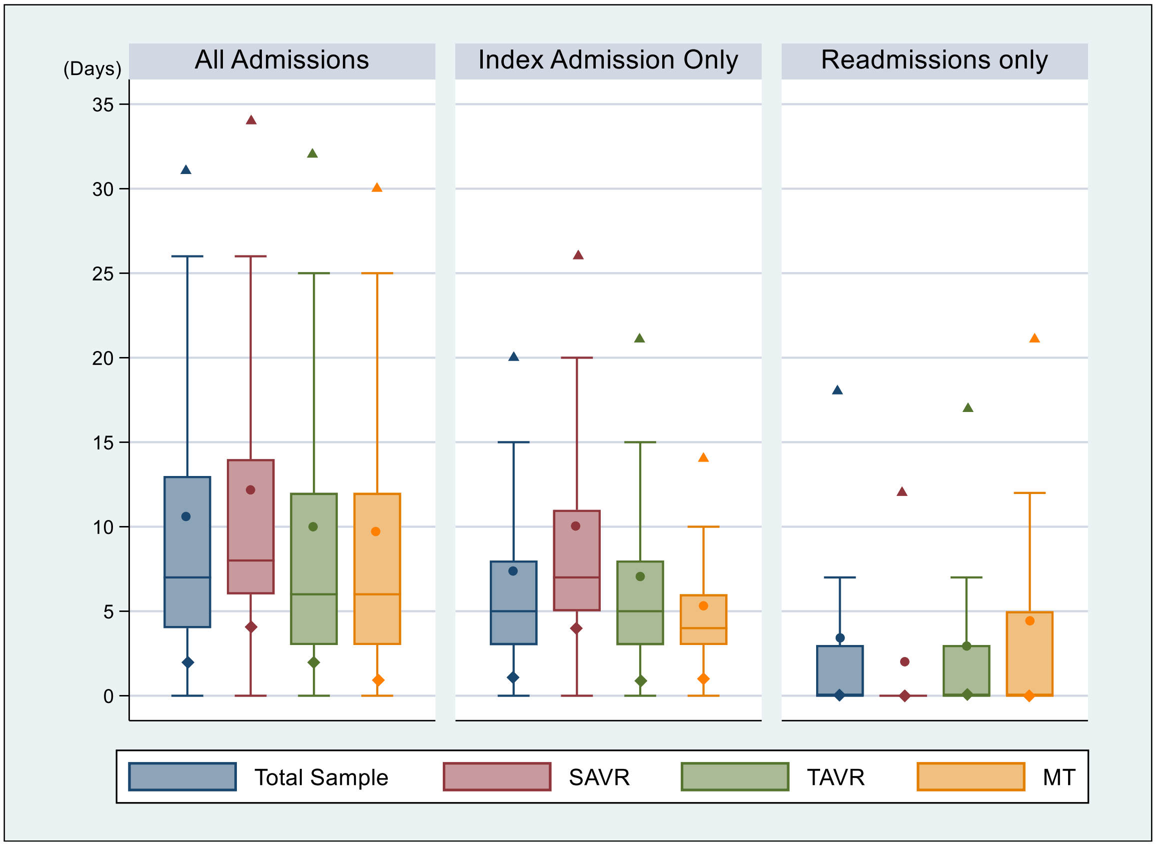

Figure 5. Inpatient days during all admissions, index admission only, and readmissions only (n=190,563).

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Lower, middle, and upper hinges of box graph represent 25th percentile, 50th percentile (median), and 75th percentile of days. Lower and upper whiskers represent Tukey's interquartile ranges[34].
(iii) •: mean, ♦: 5th percentile, ▲ : 95th percentile
(iv) All values adjusted for HCUP-NRD discharge weights to generate nationally-representative estimates.

The average number of total admissions over 6 months was 1.6±1.0, corresponding to 1.3 for SAVR, 1.5 for TAVR, and 1.7 for MT. The probability of any readmission followed the same trend: 0.23 for SAVR, 0.32 for TAVR, and 0.43 for MT ($p<0.01$ for all).

In multivariable analysis (Table 6), compared to patients receiving SAVR, total costs during IA were higher among patients receiving TAVR by $4246 (AME; 95% confidence interval [CI] $3679, $4813) but lower among patients receiving MT by $25,556 (AME; 95% CI -$25,886, -$25,226). However, compared to patients receiving

SAVR, total costs during all unplanned readmissions were higher among patients receiving TAVR by $4044 (AME; 95% CI $3643, $4444) and by $4,164 among patients receiving MT (AME; 95% CI $3888, $4440).

In multivariable analysis for number of inpatient days (Table 7), compared to patients receiving SAVR, IA was shorter by 3.2 days among patients receiving TAVR (AME; 95% CI -3.3, -3.1) and by 2.7 days among patients receiving MT (AME; 95% CI -2.8, -2.6). However, compared to patients receiving SAVR, 6-month unplanned readmission inpatient days were higher by 1.5 days among patients receiving TAVR (AME; 95% CI 1.4, 1.7) and by 1.6 days among patients receiving MT (AME; 95% CI 1.4, 1.7).

In multivariable analysis for number of admissions and any unplanned readmission (Table 8), compared to patients receiving SAVR, the probability of readmission was higher by 0.18 (AME; 95% CI 0.16, 0.19) among patients receiving TAVR and by 0.07 (AME; 95% CI 0.06, 0.07) among patients receiving MT.

The average cost of TAVR IA was higher than SAVR IA from 2012-2016, however, costs of TAVR IA has decreased rapidly after 2013, and the IA cost difference between TAVR and SAVR was not statistically significant in 2016 ($52,487 for TAVR vs. $52,204 for SAVR, p=0.66; Figure 6). Inpatient days and readmission rates for TAVR decreased over time as well. While average IA inpatient days for TAVR (9.2 days) and SAVR (10.3 days) were similar in 2013, by 2016, IA was much shorter for TAVR (5.4 days) than SAVR (9.5 days, p<0.01).

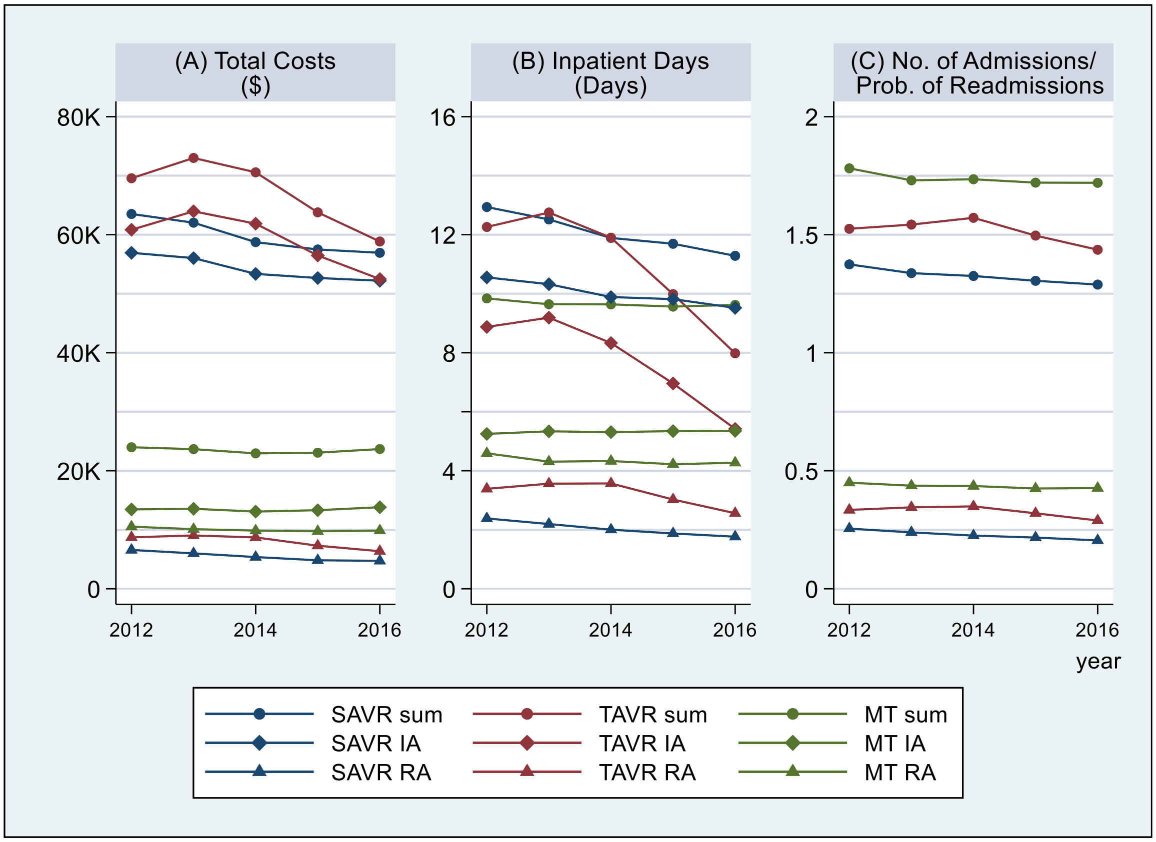

Figure 6. Trends of total costs, inpatient days, and number of admissions from 2012 to 2016 (n=190,563).

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Sum (both IA and RA), IA (index admission), RA (readmissions).
(ii) Mean was adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

Cost Subgroup Analyses

Most results were similar in subgroup analyses. However, during IA only, in comparison to the total study population, the excess cost for TAVR vs. SAVR was less among patients age ≤74 (AME $1334; 95% CI $609, $2528), small and medium size hospitals (AME $3755; 95% CI $2548, $4942), non-teaching hospitals and hospitals in non-metropolitan areas (AME $2940; 95% CI $1674, $4206), and poor neighborhoods (AME $3673; 95% CI $2877, $4470). Conversely, the excess cost of TAVR vs. SAVR IA was most pronounced (AME $13,485; 95% CI $12,427, $14,543) among patients with minor or moderate loss of function.

For inpatient days, TAVR resulted in shorter IA than SAVR (AME -3.2 days, 95% CI, -3.3, -3.1) among the total study population, however this effect was less dramatic among patients with minor or moderate loss of function (AME -0.7, 95% CI -0.9, -0.4). During readmissions, TAVR was actually associated with more inpatient days than SAVR (AME 1.5, 95% CI, 1.4, 1.7) among the total study population, but only a very modest effect was observed in patients with extreme loss of function (AME 0.2, 95% CI, 0.2, 0.2).

Cost Sensitivity Analyses

In the first sensitivity analyses, when we defined IA during January only with 11 months of follow-up or during January through March with 9 months of follow-up, most results were similar to the primary analysis (Table 9). In the second sensitivity analysis, the average aggregate total charge was $155,949±177,656 (Figure 7). Analyses for total charges showed patterns similar to total costs (Table 10).

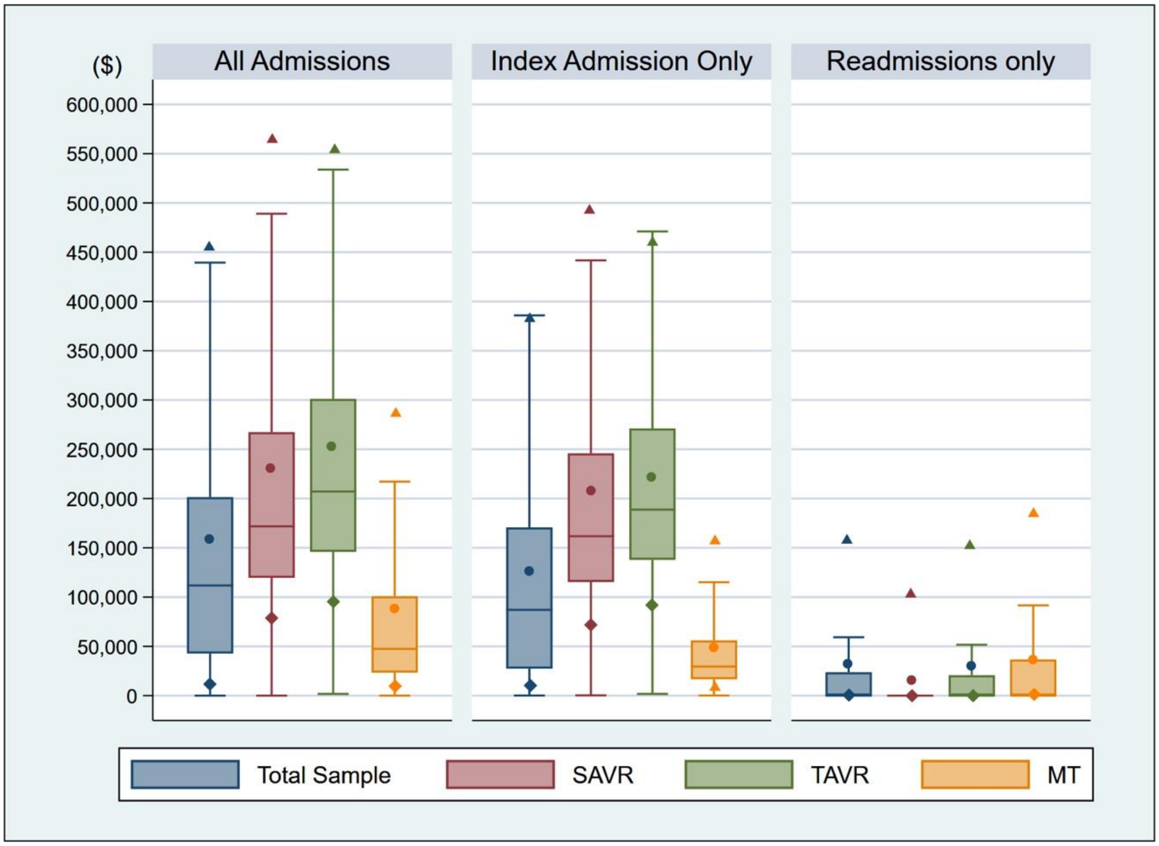

Figure 7. Total charges during all admissions, index admission only, and readmissions only (n=190,563).

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Lower, middle, and upper hinges of box graph represent 25th percentile, 50th percentile (median), and 75th percentile of charges. Lower and upper whiskers represent Tukey's interquartile ranges[34].
(iii) •: mean, ♦: 5th percentile, ▲ : 95th percentile
(iv) All values adjusted for HCUP-NRD discharge weights to generate nationally-representative estimates.

Table 1. Patient characteristics and neighborhood information among total sample population and stratified by treatment strategy (No. (%)).

	Total sample	SAVR	TAVR	MT	p-value
	(n = 366909)	(n = 71704)	(n = 26173)	(n = 269032)	
Age category					p < 0.01
64 or less	47077 (13.2)	20399 (43.9)	1062 (2.1)	25616 (54.0)	-
65-74	71762 (19.6)	24171 (33.9)	3813 (5.0)	43778 (61.1)	-
75-84	117206 (32.0)	22780 (19.7)	10333 (8.3)	84093 (72.0)	-
85 or above	130864 (35.2)	4354 (3.4)	10965 (8.0)	115545 (88.6)	-
Women	177681 (48.7)	24405 (14.1)	12145 (6.4)	141131 (79.5)	p < 0.01
Severity of illness					p < 0.01
Minor loss of function	17761 (4.9)	4918 (27.9)	152 (0.8)	12691 (71.3)	-
Moderate loss of function	134278 (37.2)	32093 (24.0)	3775 (2.7)	98410 (73.3)	-
Major loss of function	164340 (44.5)	27935 (17.3)	10948 (6.4)	125457 (76.3)	-
Extreme loss of function	50530 (13.4)	6758 (14.1)	11298 (21.5)	32474 (64.4)	-
Risk of mortality					p < 0.01
Minor likelihood of dying	21914 (6.1)	11029 (51.0)	1363 (5.6)	9522 (43.4)	-
Moderate likelihood of dying	148353 (40.8)	32363 (22.1)	12622 (7.9)	103368 (70.0)	-
Major likelihood of dying	152437 (41.3)	21673 (14.4)	10519 (6.6)	120245 (79.0)	-
Extreme likelihood of dying	44205 (11.8)	6639 (15.8)	1669 (3.6)	35897 (80.6)	-
Number of diagnoses					p < 0.01
1-10	48545 (13.8)	18923 (39.4)	3011 (5.5)	26611 (55.1)	-
11-15	111841 (30.6)	24060 (21.3)	8277 (6.8)	79504 (71.9)	-
16-20	115774 (31.3)	16990 (14.9)	9137 (7.5)	89647 (77.6)	-
21-35	90749 (24.3)	11731 (13.6)	5748 (6.4)	73270 (80.1)	-
Insurance status					p < 0.01
Medicare	311844 (85.2)	49467 (16.1)	24362 (7.4)	238013 (76.5)	-
Medicaid	11843 (3.0)	3319 (28.6)	244 (2.0)	8280 (69.4)	-
Private	35300 (9.6)	16735 (48.8)	1221 (3.2)	17346 (48.0)	-
Self-pay	2733 (0.8)	824 (30.9)	87 (2.7)	1822 (66.4)	-
No charge/other	5188 (1.4)	1359 (27.4)	259 (5.4)	3570 (67.3)	-
Neighborhood median household income					p < 0.01
Bottom quartile	86423 (24.9)	15393 (17.9)	5117 (5.6)	65910 (76.5)	-
Second quartile	91441 (26.1)	18112 (20.3)	6224 (6.6)	67106 (73.1)	-
Third quartile	94957 (25.5)	19187 (20.8)	7075 (7.2)	68697 (72.0)	-
Top quartile	94087 (23.5)	19012 (20.6)	7757 (7.6)	67319 (71.8)	-
Patient urban-rural classification					p < 0.01
Counties < 249,999	88376 (28.6)	18706 (21.2)	5962 (6.5)	63709 (72.3)	-
Counties 250,000-999,999	78109 (20.6)	16786 (22.0)	5625 (7.0)	55698 (71.0)	-
Fringe counties, ≥1 million	97908 (27.4)	18372 (19.2)	7697 (7.1)	71839 (73.7)	-
Central counties, ≥1 million	102516 (23.4)	17841 (17.4)	6889 (6.4)	77786 (76.2)	-

Notes:

(i) Percentages adjusted for HCUP-NRD discharge weights to generate national estimates, accounting for slight deviation from the percentage calculated from the raw numbers.

(ii) Percentages in total sample are column percentages. Percentages in subsample population (SAVR, TAVR, and MT) are row percentages.

Table 2. Treatment strategy, year, and hospital characteristics among total sample population and stratified by treatment strategy (No. (%)).

	Total sample	SAVR	TAVR	MT	p-value
	(n = 366909)	(n = 71704)	(n = 26173)	(n = 269032)	
Treatment strategy					p < 0.01
SAVR	71704 (19.9)	71704 (100)	0 (0.0)	0 (0.0)	-
TAVR	26173 (6.7)	0 (0)	26173 (100)	0 (0.0)	-
MT	269032 (73.4)	0 (0)	0 (0)	269032 (100)	-
Year					p < 0.01
2012	57516 (18.2)	12290 (21.9)	1557 (2.6)	43669 (75.5)	-
2013	65880 (19.4)	13608 (20.7)	3040 (4.5)	49232 (74.8)	-
2014	69121 (19.7)	14012 (20.5)	4045 (5.6)	51064 (73.9)	-
2015	89227 (21.8)	16247 (18.4)	6904 (7.6)	66076 (74.0)	-
2016	85165 (20.9)	15547 (18.5)	10627 (12.5)	58991 (69.0)	-
Hospital ownership					p < 0.01
Private, investor-owned	43434 (10.7)	7806 (17.9)	1349 (2.9)	34279 (79.2)	-
Private, not-for-profit	283908 (79.2)	57237 (20.6)	21957 (7.2)	204714 (72.2)	-
Government, non-federal	39567 (10.1)	6661 (16.8)	2867 (6.9)	30039 (76.3)	-
Hospital size					p < 0.01
Small	36119 (11.0)	3892 (11.4)	768 (1.9)	31459 (86.7)	-
Medium	89810 (23.1)	14101 (16.1)	4004 (4.1)	71705 (79.8)	-
Large	240980 (65.9)	53711 (22.7)	21401 (8.5)	165868 (68.8)	-
Hospital teaching status					p < 0.01
Urban, non-teaching	109350 (27.6)	15686 (14.9)	2208 (2.0)	91456 (83.1)	-
Rural	22285 (8.3)	1215 (5.7)	237 (1.0)	20833 (93.3)	-
Urban, teaching	235274 (64.1)	54803 (24.0)	23728 (9.5)	156743 (66.5)	-

Notes:

(i) Percentages adjusted for HCUP-NRD discharge weights to generate national estimates, accounting for slight deviation from the percentage calculated from the raw numbers.

(ii) Percentages in total sample are column percentages. Percentages in subsample population (SAVR, TAVR, and MT) are row percentages.

Table 3. Association of year, patient characteristics, and hospital characteristics with treatment strategy (n = 366,909).

	TAVR vs. SAVR	SAVR vs. MT	TAVR vs. MT
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Year			
2012	1 [reference]	1 [reference]	1 [reference]
2013	1.79 (1.64-1.96)	1.00 (0.96-1.04)	1.78 (1.64-1.94)
2014	2.13 (1.95-2.33)	0.96 (0.92-0.99)	2.04 (1.87-2.21)
2015	2.84 (2.61-3.09)	0.90 (0.87-0.94)	2.56 (2.37-2.77)
2016	4.57 (4.21-4.97)	0.96 (0.93-1.00)	4.41 (4.08-4.77)
Age category			
64 or less	1 [reference]	1 [reference]	1 [reference]
65-74	2.64 (2.39-2.92)	1.07 (1.03-1.11)	2.84 (2.57-3.13)
75-84	8.51 (7.72-9.37)	0.62 (0.59-0.64)	5.25 (4.77-5.77)
85 or above	51.2 (46.1-56.7)	0.09 (0.09-0.10)	4.81 (4.37-5.30)
Women	1.29 (1.24-1.34)	0.62 (0.61-0.63)	0.80 (0.77-0.83)
Severity of illness			
Minor loss of function	1 [reference]	1 [reference]	1 [reference]
Moderate loss of function	3.16 (2.61-3.84)	1.89 (1.79-1.99)	5.97 (4.94-7.23)
Major loss of function	17.8 (14.6-21.7)	2.25 (2.12-2.39)	40.2 (33.3-48.8)
Extreme loss of function	35.7 (29.0-43.8)	2.58 (2.38-2.79)	92.0 (75.3-112)
Risk of mortality			
Minor likelihood of dying	1 [reference]	1 [reference]	1 [reference]
Moderate likelihood of dying	0.55 (0.51-0.60)	0.56 (0.53-0.58)	0.31 (0.28-0.33)
Major likelihood of dying	0.16 (0.14-0.17)	0.41 (0.39-0.43)	0.06 (0.06-0.07)
Extreme likelihood of dying	0.01 (0.01-0.01)	0.44 (0.41-0.48)	<0.01 (0.00-0.00)
Number of diagnoses			
1-10	1 [reference]	1 [reference]	1 [reference]
11-15	1.47 (1.38-1.57)	0.44 (0.43-0.46)	0.65 (0.61-0.69)
16-20	1.95 (1.82-2.08)	0.27 (0.26-0.28)	0.53 (0.49-0.56)
21-35	1.58 (1.46-1.70)	0.22 (0.21-0.23)	0.34 (0.32-0.37)
Insurance status			
Medicare	1 [reference]	1 [reference]	1 [reference]
Medicaid	0.57 (0.47-0.68)	0.86 (0.81-0.91)	0.49 (0.41-0.58)
Private	0.48 (0.44-0.53)	1.87 (1.80-1.94)	0.91 (0.83-0.99)
Self-pay	0.65 (0.50-0.85)	0.87 (0.78-0.97)	0.56 (0.44-0.73)
No charge/other	0.72 (0.60-0.85)	1.02 (0.94-1.12)	0.73 (0.62-0.87)
Neighborhood median household income			
Bottom quartile	1 [reference]	1 [reference]	1 [reference]
Second quartile	0.94 (0.89-1.00)	1.34 (1.30-1.38)	1.26 (1.19-1.33)
Third quartile	0.93 (0.88-0.99)	1.43 (1.38-1.47)	1.32 (1.26-1.40)
Top quartile	0.90 (0.84-0.95)	1.61 (1.56-1.67)	1.44 (1.37-1.53)
Patient urban-rural classification			
Counties <249,999	1 [reference]	1 [reference]	1 [reference]
Counties 250,000-999,999	0.93 (0.88-0.99)	0.72 (0.69-0.74)	0.67 (0.63-0.71)
Fringe counties, ≥1 million	1.09 (1.02-1.16)	0.63 (0.61-0.65)	0.68 (0.65-0.72)
Central counties, ≥1 million	0.93 (0.88-0.99)	0.51 (0.50-0.53)	0.48 (0.45-0.51)
Hospital ownership			
Private, investor-owned	1 [reference]	1 [reference]	1 [reference]
Private, not-for-profit	1.33 (1.24-1.43)	0.87 (0.83-0.90)	1.15 (1.08-1.23)
Government, non-federal	1.77 (1.61-1.94)	0.54 (0.52-0.57)	0.96 (0.88-1.04)
Hospital size			
Small	1 [reference]	1 [reference]	1 [reference]
Medium	1.62 (1.45-1.80)	1.57 (1.49-1.65)	2.54 (2.30-2.79)
Large	2.63 (2.38-2.91)	2.88 (2.75-3.02)	7.58 (6.91-8.31)

Hospital teaching status			
Urban, non-teaching	1 [reference]	1 [reference]	1 [reference]
Rural	1.34 (1.13-1.57)	0.28 (0.26-0.30)	0.37 (0.32-0.43)
Urban, teaching	2.85 (2.69-3.02)	2.14 (2.09-2.20)	6.11 (5.78-6.45)

Table 4. Sensitivity analysis: association of year, patient characteristics, and hospital characteristics with treatment strategy in patients admitted with any diagnosis of AS or AR (n = 611,341).

	TAVR vs. SAVR	SAVR vs. MT	TAVR vs. MT
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Year			
2012	1 [reference]	1 [reference]	1 [reference]
2013	1.77 (1.63-1.93)	0.97 (0.94-1.01)	1.72 (1.59-1.86)
2014	2.13 (1.97-2.32)	0.94 (0.91-0.97)	2.00 (1.86-2.17)
2015	2.86 (2.65-3.10)	0.87 (0.84-0.90)	2.49 (2.31-2.68)
2016	4.85 (4.49-5.24)	0.81 (0.78-0.84)	3.94 (3.66-4.23)
Age category			
64 or less	1 [reference]	1 [reference]	1 [reference]
65-74	2.85 (2.59-3.14)	1.04 (1.01-1.08)	2.98 (2.71-3.27)
75-84	9.53 (8.69-10.4)	0.63 (0.61-0.65)	5.98 (5.46-6.54)
85 or above	55.2 (49.9-60.9)	0.11 (0.11-0.12)	6.15 (5.61-6.74)
Women	1.31 (1.26-1.36)	0.60 (0.58-0.61)	0.78 (0.76-0.81)
Severity of illness			
Minor loss of function	1 [reference]	1 [reference]	1 [reference]
Moderate loss of function	3.82 (3.24-4.50)	2.07 (1.99-2.15)	7.90 (6.72-9.29)
Major loss of function	21.6 (18.2-25.5)	2.38 (2.27-2.49)	51.3 (43.5-60.5)
Extreme loss of function	40.8 (34.1-48.9)	2.58 (2.41-2.76)	105 (89-125)
Risk of mortality			
Minor likelihood of dying	1 [reference]	1 [reference]	1 [reference]
Moderate likelihood of dying	0.48 (0.45-0.52)	1.24 (1.20-1.28)	0.60 (0.56-0.64)
Major likelihood of dying	0.13 (0.12-0.14)	1.12 (1.07-1.16)	0.14 (0.13-0.15)
Extreme likelihood of dying	0.01 (0.01-0.01)	1.27 (1.19-1.36)	0.01 (0.01-0.01)
Number of diagnoses			
1-10	1 [reference]	1 [reference]	1 [reference]
11-15	1.35 (1.28-1.43)	0.61 (0.59-0.63)	0.82 (0.78-0.87)
16-20	1.64 (1.55-1.75)	0.42 (0.41-0.44)	0.70 (0.66-0.74)
21-35	1.26 (1.17-1.35)	0.36 (0.35-0.37)	0.45 (0.42-0.48)
Insurance status			
Medicare	1 [reference]	1 [reference]	1 [reference]
Medicaid	0.51 (0.43-0.61)	0.87 (0.83-0.92)	0.45 (0.38-0.53)
Private	0.46 (0.43-0.50)	1.67 (1.62-1.72)	0.78 (0.72-0.84)
Self-pay	0.57 (0.44-0.74)	0.94 (0.86-1.03)	0.54 (0.42-0.70)
No charge/other	0.70 (0.59-0.83)	1.01 (0.94-1.09)	0.71 (0.61-0.83)
Neighborhood median household income			
Bottom quartile	1 [reference]	1 [reference]	1 [reference]
Second quartile	0.97 (0.92-1.02)	1.24 (1.21-1.28)	1.20 (1.14-1.26)
Third quartile	0.96 (0.91-1.01)	1.29 (1.25-1.33)	1.23 (1.17-1.29)
Top quartile	0.96 (0.90-1.01)	1.37 (1.33-1.42)	1.31 (1.25-1.38)
Patient urban-rural classification			
Counties <249,999	1 [reference]	1 [reference]	1 [reference]
Counties 250,000-999,999	0.92 (0.87-0.97)	0.71 (0.69-0.73)	0.65 (0.62-0.68)
Fringe counties, ≥1 million	1.11 (1.05-1.17)	0.64 (0.62-0.66)	0.70 (0.67-0.74)
Central counties, ≥1 million	0.92 (0.87-0.97)	0.52 (0.51-0.54)	0.48 (0.46-0.51)
Hospital ownership			
Private, investor-owned	1 [reference]	1 [reference]	1 [reference]
Private, not-for-profit	1.38 (1.29-1.48)	0.85 (0.82-0.87)	1.17 (1.09-1.24)
Government, non-federal	1.76 (1.61-1.91)	0.56 (0.54-0.59)	0.99 (0.91-1.07)
Hospital size			

Small	1 [reference]	1 [reference]	1 [reference]
Medium	1.65 (1.49-1.83)	1.62 (1.54-1.69)	2.67 (2.43-2.93)
Large	2.74 (2.49-3.01)	2.89 (2.77-3.02)	7.91 (7.25-8.63)
Hospital teaching status			
Urban, non-teaching	1 [reference]	1 [reference]	1 [reference]
Rural	1.32 (1.13-1.54)	0.30 (0.28-0.32)	0.39 (0.34-0.45)
Urban, teaching	2.92 (2.76-3.09)	2.05 (2.00-2.10)	5.99 (5.68-6.30)

Table 5. Patient, hospital, and neighborhood characteristics among total study population and stratified by treatment strategy (No. (%)).

	Total study population (n = 190,563)	SAVR (n = 66,564; 35.6%)	TAVR (n = 21,902; 10.8%)	MT (n = 102,097; 53.6%)	P-value
Age category					< 0.01
≤64	29320 (15.8)	19084 (29.2)	863 (4.0)	9373 (9.3)	-
65-74	41428 (21.7)	22585 (33.5)	3157 (14.3)	15686 (15.3)	-
75-84	60847 (31.9)	21024 (31.5)	8669 (39.7)	31154 (30.5)	-
≥85	58968 (30.6)	3871 (5.8)	9213 (41.9)	45884 (44.8)	-
Women	85231 (45.0)	22444 (34.1)	10042 (46.0)	52745 (52.0)	< 0.01
Charlson comorbidity index					< 0.01
0-1	59104 (31.4)	35263 (53.4)	5452 (24.9)	18389 (18.2)	-
2-3	74157 (39.0)	22386 (33.6)	9296 (42.5)	42475 (41.9)	-
4-5	43635 (22.7)	7234 (10.7)	5500 (25.1)	30901 (30.2)	-
≥6	13667 (6.9)	1681 (2.4)	1654 (7.5)	10332 (9.7)	-
Number of inpatient procedures					< 0.01
0	48881 (25.6)	0 (0)	0 (0.0)	48881 (48.9)	
1-2	49863 (26.2)	10402 (15.8)	8743 (39.4)	30718 (29.7)	
3-4	38493 (20.2)	19959 (30.0)	6293 (29.0)	12241 (11.6)	
≥5	53326 (28.0)	36203 (54.2)	6866 (31.5)	10257 (9.8)	
Severity of illness					< 0.01
Minor loss of function	11720 (6.2)	4295 (6.5)	109 (0.5)	7316 (7.2)	-
Moderate loss of function	75541 (40.2)	29646 (44.6)	2024 (9.4)	43871 (43.4)	-
Major loss of function	78008 (40.8)	26749 (39.9)	6630 (30.5)	44629 (43.4)	-
Extreme loss of function	25294 (12.8)	5874 (8.9)	13139 (59.6)	6281 (6.0)	-
Risk of mortality					< 0.01
Minor likelihood of dying	16450 (8.8)	10225 (15.6)	1220 (5.5)	5005 (5.0)	-
Moderate likelihood of dying	82482 (43.5)	30019 (45.2)	10001 (45.5)	42462 (42.0)	-
Major likelihood of dying	75857 (39.4)	20619 (30.5)	9166 (42.1)	46072 (44.8)	-
Extreme likelihood of dying	15774 (8.3)	5701 (8.7)	1515 (6.9)	8558 (8.3)	-
Insurance status					< 0.01
Medicare	156247 (82.0)	45571 (68.4)	20274 (92.5)	90400 (88.9)	-
Medicaid	6349 (3.1)	2974 (4.2)	202 (0.9)	3173 (2.9)	-
Private	23535 (12.5)	15963 (24.2)	1080 (4.9)	6494 (6.2)	-
Self-pay	1602 (0.9)	755 (1.2)	95 (0.4)	753 (0.7)	-
No charge/other	2829 (1.5)	1301 (2.0)	251 (1.3)	1277 (1.2)	-
Neighborhood median household income					< 0.01
Bottom quartile	43864 (24.2)	14080 (22.0)	4213 (20.5)	25568 (26.3)	-
Second quartile	47721 (26.2)	16770 (26.6)	5212 (25.5)	25739 (26.2)	-
Third quartile	49682 (25.8)	17828 (26.7)	5889 (27.0)	25967 (24.9)	-
Top quartile	49296 (23.8)	17886 (24.7)	6588 (27.0)	24824 (22.6)	-
Patient urban-rural classification					< 0.01
Counties <249,999	46872 (29.0)	17346 (30.4)	5012 (27.5)	24514 (28.4)	-
Counties 250,000-999,999	41545 (21.2)	15607 (22.8)	4707 (21.4)	21231 (20.0)	-
Fringe counties, ≥1 million	51267 (27.5)	17135 (26.5)	6442 (29.1)	27690 (27.8)	-
Central counties, ≥1 million	50879 (22.3)	16476 (20.3)	5741 (22.0)	28662 (23.7)	-
Hospital ownership					< 0.01
Private, investor-owned	22298 (10.6)	7398 (9.9)	1191 (5.0)	13709 (12.2)	-
Private, not-for-profit	148494 (79.8)	53278 (82.0)	18509 (85.7)	76707 (77.1)	-

Government, non-federal	19771 (9.6)	5888 (8.1)	2202 (9.3)	11681 (10.7)	-
Hospital size					< 0.01
Small	16690 (9.8)	3802 (6.6)	725 (3.5)	12163 (13.3)	-
Medium	44326 (22.0)	13304 (19.0)	3528 (14.9)	27494 (25.4)	-
Large	129547 (68.2)	49458 (74.4)	17649 (81.7)	62440 (61.3)	-
Hospital teaching status					< 0.01
Urban, non-teaching	51878 (25.5)	14822 (21.0)	1951 (8.6)	35105 (31.9)	-
Non-metropolitan	9409 (6.8)	1044 (2.2)	178 (1.1)	8187 (10.9)	-
Urban, teaching	129276 (67.7)	50698 (76.8)	19773 (90.2)	58805 (57.2)	-
Year					< 0.01
2012	29235 (17.9)	11323 (19.8)	1239 (6.8)	16673 (18.8)	-
2013	33685 (19.2)	12551 (20.1)	2466 (12.8)	18668 (19.9)	-
2014	35400 (19.4)	13012 (20.2)	3177 (15.3)	19211 (19.7)	-
2015	44847 (21.1)	15114 (20.2)	5730 (24.5)	24003 (21.0)	-
2016	47396 (22.4)	14564 (19.7)	9290 (40.6)	23542 (20.6)	-

Notes:

(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).

(ii) Percentages were adjusted for HCUP-NRD discharge weights to generate national estimates, which accounts for their slight deviation from the percentage calculated from the raw numbers.

(iii) P-values were derived by Pearson Chi-squared tests and analysis of variance.

Table 6. Association of treatment strategy with total cost: total cost during all admissions, index admission only, and readmissions only (n = 190,563).

	All admissions	Index admission only	Readmissions only
	AME in $ (95% CI)	AME in $ (95% CI)	AME in $ (95% CI)
Treatment strategy			
SAVR	-	-	-
TAVR	6559 (5750, 7369)	4246 (3679, 4813)	4044 (3643, 4444)
MT	-22825 (-23360, -22291)	-25556 (-25886, -25226)	4164 (3888, 4440)
Age category			
≤64	-	-	-
65-74	-6058 (-6929, -5187)	-1642 (-2171, -1114)	-3359 (-3905, -2812)
75-84	-8192 (-9077, -7307)	-2660 (-3196, -2125)	-4023 (-4562, -3483)
≥85	-11934 (-12854, -11015)	-4440 (-5008, -3873)	-5113 (-5655, -4571)
Women	305 (-52, 662)	-80 (-305, 144)	274 (88, 460)
Charlson comorbidity index			
0-1	-	-	-
2-3	5435 (4986, 5885)	1670 (1381, 1959)	2829 (2609, 3049)
4-5	9316 (8740, 9892)	3688 (3330, 4046)	4327 (4046, 4609)
≥6	9774 (8928, 10619)	6608 (6073, 7142)	3926 (3519, 4334)
Number of inpatient procedures			
0	-	-	-
1-2	16398 (16015, 16780)	9008 (8800, 9217)	5271 (5056, 5487)
3-4	22607 (22129, 23085)	16623 (16384, 16863)	4838 (4537, 5140)
≥5	30738 (30180, 31295)	30058 (29720, 30397)	2697 (2333, 3061)
Severity of illness			
Minor loss of function	-	-	-
Moderate loss of function	5784 (5116, 6452)	1114 (619, 1609)	2672 (2296, 3048)
Major loss of function	9645 (8891, 10400)	5006 (4449, 5564)	3382 (2965, 3800)
Extreme loss of function	8018 (7025, 9011)	10404 (9596, 11212)	-3632 (-4080, -3185)
Risk of mortality			
Minor likelihood of dying	-	-	-
Moderate likelihood of dying	5264 (4733, 5796)	823 (466, 1181)	3098 (2786, 3410)
Major likelihood of dying	7451 (6770, 8132)	3599 (3145, 4054)	3206 (2830, 3581)
Extreme likelihood of dying	11519 (10334, 12704)	11147 (10269, 12025)	-185 (-709, 340)
Insurance status			
Medicare	-	-	-
Medicaid	4143 (2723, 5563)	2999 (2139, 3860)	942 (221, 1663)
Private	-6078 (-6697, -5458)	-521 (-968, -73)	-3629 (-3928, -3330)
Self-pay	-9276 (-11205, -7346)	-934 (-2812, 945)	-5246 (-5855, -4638)
No charge/other	-6225 (-7638, -4812)	1114 (-151, 2379)	-4852 (-5355, -4349)
Neighborhood median household income			
Bottom quartile	-	-	-
Second quartile	963 (472, 1454)	1253 (948, 1557)	100 (-158, 359)
Third quartile	2015 (1490, 2540)	2719 (2394, 3044)	74 (-192, 339)
Top quartile	4548 (3990, 5107)	5162 (4810, 5514)	495 (202, 788)
Patient urban-rural classification			
Counties <249,999	-	-	-
Counties 250,000-999,999	-386 (-896, 124)	-1013 (-1351, -674)	403 (151, 654)
Fringe counties, ≥1 million	2524 (1938, 3110)	-298 (-663, 68)	2010 (1721, 2300)
Central counties, ≥1 million	7322 (6745, 7900)	4080 (3713, 4447)	2875 (2585, 3166)

Hospital ownership			
Private, investor-owned	-	-	-
Private, not-for-profit	5526 (5048, 6005)	4179 (3886, 4471)	1488 (1238, 1739)
Government, non-federal	12819 (11976, 13662)	6916 (6452, 7379)	4489 (4059, 4919)
Hospital size			
Small	-	-	-
Medium	1090 (411, 1769)	-1367 (-1825, -909)	1120 (826, 1414)
Large	5410 (4786, 6033)	-327 (-754, 99)	3324 (3045, 3603)
Hospital teaching status			
Urban, non-teaching	-	-	-
Non-metropolitan	-69 (-903, 765)	658 (84, 1231)	358 (-19, 736)
Urban, teaching	3302 (2896, 3707)	8 (-249, 265)	2008 (1805, 2211)
Year			
2012	-	-	-
2013	-1233 (-1904, -563)	-403 (-810, 4)	-779 (-1129, -429)
2014	-2953 (-3584, -2321)	-1620 (-2001, -1239)	-1182 (-1531, -833)
2015	-3666 (-4277, -3056)	-1867 (-2244, -1491)	-1458 (-1794, -1123)
2016	-4029 (-4638, -3420)	-1549 (-1929, -1168)	-1804 (-2139, -1470)

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Average marginal effects (AME; $) and 95% confidence interval (CI) were adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

Table 7. Association of treatment strategy with inpatient days: inpatient days during all admissions, index admission only, and readmissions only (n = 190,563).

	All admissions	Index admission only	Readmissions only
	AME in days (95% CI)	AME in days (95% CI)	AME in days (95% CI)
Treatment strategy			
SAVR	-	-	-
TAVR	-2.6 (-2.8, -2.4)	-3.2 (-3.3, -3.1)	1.5 (1.4, 1.7)
MT	-1.7 (-1.8, -1.5)	-2.7 (-2.8, -2.6)	1.6 (1.4, 1.7)
Age category			
≤64	-	-	-
65-74	-1.8 (-2.1, -1.6)	-0.5 (-0.6, -0.4)	-1.2 (-1.4, -1.0)
75-84	-1.6 (-1.9, -1.4)	-0.2 (-0.3, -0.1)	-1.2 (-1.5, -1.0)
≥85	-1.9 (-2.1, -1.6)	0.1 (-0.1, 0.2)	-1.6 (-1.8, -1.4)
Women	0.8 (0.7, 0.9)	0.5 (0.5, 0.6)	0.3 (0.2, 0.3)
Charlson comorbidity index			
0-1	-	-	-
2-3	2.1 (2.0, 2.3)	0.8 (0.7, 0.9)	1.2 (1.1, 1.3)
4-5	3.5 (3.3, 3.6)	1.6 (1.5, 1.7)	1.8 (1.7, 1.9)
≥6	3.5 (3.3, 3.8)	2.3 (2.1, 2.4)	1.5 (1.4, 1.7)
Number of inpatient procedures			
0	-	-	-
1-2	3.1 (3.0, 3.3)	1.1 (1.0, 1.1)	1.9 (1.8, 1.9)
3-4	3.2 (3.1, 3.4)	1.9 (1.9, 2.0)	1.2 (1.0, 1.3)
≥5	4.6 (4.4, 4.8)	5.1 (5.0, 5.2)	0.0 (-0.2, 0.1)
Severity of illness			
Minor loss of function	-	-	-
Moderate loss of function	2.3 (2.1, 2.5)	0.8 (0.7, 0.9)	1.3 (1.2, 1.5)
Major loss of function	3.3 (3.1, 3.6)	1.8 (1.7, 1.9)	1.6 (1.5, 1.8)
Extreme loss of function	0.7 (0.4, 1.0)	2.0 (1.8, 2.2)	-1.3 (-1.4, -1.1)
Risk of mortality			
Minor likelihood of dying	-	-	-
Moderate likelihood of dying	2.3 (2.2, 2.5)	0.8 (0.7, 0.9)	1.3 (1.2, 1.4)
Major likelihood of dying	3.7 (3.5, 3.9)	2.0 (1.9, 2.1)	1.3 (1.1, 1.4)
Extreme likelihood of dying	6.9 (6.5, 7.3)	4.7 (4.5, 4.9)	-0.2 (-0.4, 0.0)
Insurance status			
Medicare	-	-	-
Medicaid	1.6 (1.2, 2.1)	1.1 (0.9, 1.3)	0.3 (0.1, 0.6)
Private	-2.4 (-2.6, -2.2)	-0.6 (-0.7, -0.5)	-1.6 (-1.7, -1.5)
Self-pay	-1.7 (-2.3, -1.1)	0.4 (0.0, 0.8)	-2.0 (-2.3, -1.7)
No charge/other	-1.8 (-2.2, -1.4)	0.2 (-0.1, 0.5)	-1.9 (-2.1, -1.6)
Neighborhood median household income			
Bottom quartile	-	-	-
Second quartile	-0.5 (-0.6, -0.3)	-0.2 (-0.3, -0.1)	-0.2 (-0.3, -0.1)
Third quartile	-0.9 (-1.1, -0.8)	-0.3 (-0.4, -0.3)	-0.5 (-0.6, -0.4)
Top quartile	-1.0 (-1.2, -0.9)	-0.3 (-0.4, -0.2)	-0.6 (-0.7, -0.5)
Patient urban-rural classification			
Counties <249,999	-	-	-
Counties 250,000-999,999	0.3 (0.2, 0.5)	0.0 (-0.1, 0.1)	0.3 (0.2, 0.4)
Fringe counties, ≥1 million	1.6 (1.5, 1.8)	0.5 (0.4, 0.6)	1.0 (0.9, 1.1)
Central counties, ≥ 1 million	1.1 (0.9, 1.2)	0.3 (0.2, 0.4)	0.7 (0.6, 0.8)

Hospital ownership			
Private, investor-owned	-	-	-
Private, not-for-profit	-0.3 (-0.5, -0.2)	-0.3 (-0.4, -0.3)	0.1 (-0.1, 0.2)
Government, non-federal	1.5 (1.3, 1.8)	0.3 (0.2, 0.4)	1.0 (0.9, 1.2)
Hospital size			
Small	-	-	-
Medium	0.9 (0.7, 1.1)	0.2 (0.1, 0.3)	0.6 (0.5, 0.7)
Large	2.4 (2.2, 2.6)	0.6 (0.5, 0.7)	1.5 (1.4, 1.6)
Hospital teaching status			
Urban, non-teaching	-	-	-
Non-metropolitan	0.1 (-0.1, 0.4)	0.2 (0.0, 0.3)	0.0 (-0.1, 0.2)
Urban, teaching	1.4 (1.3, 1.5)	0.3 (0.3, 0.4)	0.9 (0.8, 1.0)
Year			
2012	-	-	-
2013	-0.4 (-0.6, -0.2)	-0.1 (-0.2, 0.0)	-0.3 (-0.5, -0.2)
2014	-0.7 (-0.9, -0.5)	-0.2 (-0.3, -0.1)	-0.4 (-0.6, -0.3)
2015	-1.1 (-1.3, -0.9)	-0.4 (-0.5, -0.3)	-0.5 (-0.7, -0.4)
2016	-1.7 (-1.9, -1.5)	-0.8 (-0.9, -0.7)	-0.7 (-0.9, -0.6)

Notes:

(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).

(ii) Average marginal effects (AME; days) and 95% confidence interval (CI) were adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

Table 8. Association of treatment strategy with aggregate number of admissions and probability of any unplanned readmission (n = 190,563).

	All admissions	Any readmission
	AME in No. (95% CI)	AME in Prob. (95% CI)
Treatment strategy		
SAVR	-	-
TAVR	0.3 (0.2, 0.3)	0.18 (0.16, 0.19)
MT	0.2 (0.2, 0.2)	0.07 (0.06, 0.07)
Age category		
≤64	-	-
65-74	-0.2 (-0.2, -0.1)	-0.06 (-0.07, -0.05)
75-84	-0.2 (-0.2, -0.2)	-0.04 (-0.05, -0.03)
≥85	-0.2 (-0.3, -0.2)	-0.04 (-0.05, -0.03)
Women	0.0 (0.0, 0.0)	0.01 (0.01, 0.02)
Charlson comorbidity index		
0-1	-	-
2-3	0.2 (0.2, 0.2)	0.09 (0.08, 0.09)
4-5	0.3 (0.3, 0.3)	0.13 (0.12, 0.14)
≥6	0.3 (0.2, 0.3)	0.13 (0.12, 0.14)
Number of inpatient procedures		
0	-	-
1-2	0.2 (0.2, 0.2)	0.12 (0.11, 0.12)
3-4	0.0 (-0.1, 0.0)	0.01 (0.00, 0.02)
≥5	-0.3 (-0.3, -0.3)	-0.16 (-0.16, -0.15)
Severity of illness		
Minor loss of function	-	-
Moderate loss of function	0.2 (0.2, 0.2)	0.05 (0.04, 0.07)
Major loss of function	0.1 (0.1, 0.1)	0.02 (0.01, 0.03)
Extreme loss of function	-0.4 (-0.4, -0.4)	-0.28 (-0.29, -0.27)
Risk of mortality		
Minor likelihood of dying	-	-
Moderate likelihood of dying	0.2 (0.1, 0.2)	0.07 (0.06, 0.08)
Major likelihood of dying	0.1 (0.1, 0.1)	0.04 (0.03, 0.05)
Extreme likelihood of dying	0.0 (-0.1, 0.0)	-0.05 (-0.06, -0.03)
Insurance status		
Medicare	-	-
Medicaid	0.0 (0.0, 0.1)	-0.01 (-0.02, 0.01)
Private	-0.3 (-0.3, -0.3)	-0.12 (-0.13, -0.11)
Self-pay	-0.3 (-0.4, -0.3)	-0.16 (-0.19, -0.14)
No charge/other	-0.3 (-0.3, -0.3)	-0.17 (-0.19, -0.16)
Neighborhood median household income		
Bottom quartile	-	-
Second quartile	0.0 (0.0, 0.0)	-0.01 (-0.01, 0.00)
Third quartile	-0.1 (-0.1, 0.0)	-0.02 (-0.03, -0.01)
Top quartile	-0.1 (-0.1, -0.1)	-0.03 (-0.04, -0.03)
Patient urban-rural classification		
Counties <249,999	-	-
Counties 250,000-999,999	0.0 (0.0, 0.1)	0.02 (0.01, 0.03)
Fringe counties, ≥1 million	0.1 (0.1, 0.2)	0.06 (0.05, 0.07)
Central counties, ≥1 million	0.1 (0.1, 0.1)	0.04 (0.03, 0.05)

Hospital ownership		
Private, investor-owned	-	-
Private, not-for-profit	0.0 (0.0, 0.0)	0.01 (0.00, 0.02)
Government, non-federal	0.2 (0.1, 0.2)	0.07 (0.06, 0.08)
Hospital size		
Small	-	-
Medium	0.1 (0.1, 0.1)	0.05 (0.04, 0.06)
Large	0.2 (0.2, 0.2)	0.10 (0.09, 0.11)
Hospital teaching status		
Urban, non-teaching	-	-
Non-metropolitan	0.0 (0.0, 0.0)	0.01 (0.00, 0.02)
Urban, teaching	0.1 (0.1, 0.1)	0.05 (0.05, 0.06)
Year		
2012	-	-
2013	0.0 (-0.1, 0.0)	-0.01 (-0.02, 0.00)
2014	0.0 (-0.1, 0.0)	-0.02 (-0.03, -0.01)
2015	-0.1 (-0.1, 0.0)	-0.02 (-0.03, -0.02)
2016	-0.1 (-0.1, -0.1)	-0.04 (-0.05, -0.03)

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Average marginal effects (AME; in number for total number of admissions, and in probability for any unplanned readmissions) and 95% confidence interval (CI) were adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

Table 9. Total costs, inpatient days, number of admissions, and probability of any unplanned readmission among total study population and stratified by treatment strategy: January as index admission and 11-month follow-up (n = 32,750).

	Total study population	SAVR	TAVR	MT	P-value
	(n = 32,246)	(n =10,040)	(n = 2,892)	(n = 19,314)	
Total costs, mean (SD)					
All admissions	41,566 (46,648)	60,759 (56,359)	67,676 (40,874)	27,704 (35,091)	< 0.01
Index admission only	29,486 (36,481)	53,474 (47,223)	56,681 (29,291)	12,921 (15,326)	< 0.01
Readmissions only	12,081 (28,229)	7,285 (25,436)	10,996 (24,361)	14,784 (29,756)	< 0.01
Inpatient days, mean (SD)					
All admissions	11.9 (12.9)	12.2 (12.8)	11.3 (12.9)	11.7 (12.9)	< 0.01
Index admission only	6.8 (6.6)	9.6 (8.5)	6.8 (6.8)	5.3 (4.7)	< 0.01
Readmissions only	5.1 (10.5)	2.6 (7.9)	4.5 (9.5)	6.4 (11.5)	< 0.01
Admissions, mean (SD)					
Number of all admissions	1.9 (1.4)	1.4 (0.9)	1.7 (1.3)	2.1 (1.5)	< 0.01
Probability of any readmission	0.44 (0.50)	0.27 (0.44)	0.40 (0.49)	0.53 (0.50)	< 0.01

Notes:

(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).

(ii) Mean and standard deviation (SD) were adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

Table 10. Association of treatment strategy with total charges: total charges during all admissions, index admission only, and readmissions only (n = 190,563).

	All admissions	Index admission only	Readmissions only
	AME in $ (95% CI)	AME in $ (95% CI)	AME in $ (95% CI)
Treatment strategy			
SAVR	-	-	-
TAVR	31270 (27915, 34625)	21617 (19305, 23929)	17076 (15415, 18737)
MT	-87112 (-89259, -84964)	-96897 (-98205, -95590)	16321 (15213, 17429)
Age category			
≤64	-	-	-
65-74	-21738 (-25240, -18237)	-4961 (-7051, -2870)	-13283 (-15514, -11053)
75-84	-29995 (-33523, -26467)	-8573 (-10683, -6463)	-15993 (-18201, -13785)
≥85	-44772 (-48419, -41125)	-15820 (-18033, -13607)	-20292 (-22503, -18082)
Women	-299 (-1748, 1149)	-1488 (-2397, -578)	743 (-2, 1487)
Charlson comorbidity index			
0-1	-	-	-
2-3	20377 (18597, 22158)	6051 (4924, 7178)	10928 (10045, 11811)
4-5	35410 (33092, 37728)	13962 (12554, 15369)	16721 (15587, 17856)
≥6	33920 (30583, 37257)	24215 (22093, 26338)	14252 (12650, 15854)
Number of inpatient procedures			
0	-	-	-
1-2	65615 (64118, 67112)	35287 (34488, 36085)	21201 (20352, 22051)
3-4	91037 (89099, 92975)	65769 (64791, 66747)	20136 (18903, 21370)
≥5	123391 (121119, 125663)	120131 (118780, 121482)	11995 (10476, 13514)
Severity of illness			
Minor loss of function	-	-	-
Moderate loss of function	22632 (20073, 25190)	3913 (2010, 5816)	10772 (9339, 12205)
Major loss of function	36482 (33565, 39400)	18175 (16031, 20318)	13282 (11682, 14883)
Extreme loss of function	29339 (25521, 33157)	37867 (34834, 40899)	-13805 (-15541, -12069)
Risk of mortality			
Minor likelihood of dying	-	-	-
Moderate likelihood of dying	19919 (17754, 22084)	2862 (1382, 4342)	11799 (10555, 13043)
Major likelihood of dying	29040 (26306, 31773)	13929 (12103, 15756)	12481 (11000, 13963)
Extreme likelihood of dying	46425 (41765, 51084)	44181 (40779, 47582)	-502 (-2622, 1618)
Insurance status			
Medicare	-	-	-
Medicaid	12874 (7372, 18377)	8569 (5228, 11910)	3029 (244, 5815)
Private	-27208 (-29715, -24702)	-5150 (-6946, -3354)	-14652 (-15843, -13461)
Self-pay	-33036 (-40128, -25943)	-1616 (-8188, 4957)	-19757 (-22282, -17231)
No charge/other	-24453 (-29901, -19006)	3660 (-697, 8018)	-18948 (-20990, -16906)
Neighborhood median household income			
Bottom quartile	-	-	-
Second quartile	-3388 (-5434, -1342)	-476 (-1724, 772)	-1244 (-2316, -173)
Third quartile	-4955 (-7075, -2835)	1017 (-295, 2329)	-2752 (-3826, -1678)
Top quartile	1645 (-608, 3897)	7984 (6576, 9392)	-1860 (-3037, -682)
Patient urban-rural classification			-
Counties <249,999	-	-	-
Counties 250,000-999,999	14521 (12562, 16479)	8916 (7623, 10208)	4977 (4021, 5934)
Fringe counties, ≥1 million	24140 (21956, 26323)	10999 (9633, 12365)	10133 (9057, 11208)
Central counties, ≥1 million	63280 (60989, 65571)	43968 (42500, 45437)	17463 (16328, 18599)

Hospital ownership			
Private, investor-owned	-	-	-
Private, not-for-profit	-74998 (-78052, -71944)	-63610 (-65459, -61761)	-12746 (-14292, -11200)
Government, non-federal	-53847 (-57792, -49902)	-57535 (-59827, -55244)	-3288 (-5256, -1319)
Hospital size			
Small	-	-	-
Medium	25879 (23537, 28220)	15377 (13824, 16929)	6920 (5918, 7922)
Large	56194 (54081, 58307)	31141 (29732, 32551)	18387 (17443, 19331)
Hospital teaching status			
Urban, non-teaching	-	-	-
Non-metropolitan	-39200 (-41946, -36453)	-32480 (-34283, -30678)	-5912 (-7169, -4655)
Urban, teaching	6731 (5025, 8436)	-4641 (-5743, -3538)	6108 (5272, 6944)
Year			
2012	-	-	-
2013	-1203 (-3798, 1392)	1559 (-29, 3147)	-2465 (-3783, -1147)
2014	-4776 (-7282, -2271)	-659 (-2183, 866)	-3379 (-4712, -2046)
2015	1279 (-1205, 3762)	5138 (3619, 6658)	-2566 (-3881, -1252)
2016	519 (-1923, 2960)	7334 (5812, 8856)	-3814 (-5116, -2512)

Notes:
(i) SAVR (surgical aortic valve replacement), TAVR (transcatether aortic valve replacement), MT (medical therapy).
(ii) Average marginal effects (AME; $) and 95% confidence interval (CI) were adjusted for HCUP-NRD discharge weights to generate nationally representative estimates.

CHAPTER 4: DISCUSSION

TAVR Increasing

In nationally-representative sample of 366,909 patients hospitalized for aortic valve disease, IA increased 48.1% from 2012 through 2016. The likelihood of receiving TAVR increased with an RRR of 4.57 relative to SAVR and 4.41 relative to MT, a novel finding. However, not all patients and hospitals absorbed TAVR equally: increasing age, female sex, severity of illness rating, high number of diagnoses, not-for-profit hospital ownership, large hospital size, and teaching hospital status were associated with a higher prevalence of TAVR.

Increasing patient age was associated with increased use of TAVR and decreased use of SAVR. The potential for future growth in TAVR remains enormous due to the high prevalence of aortic valve disease in elderly patients, the overall aging of the US population, and anticipated expansion of TAVR to low-surgical risk patients. Thus, from a public health perspective, knowledge of trends in aortic valve disease is necessary to ensure adequate allocation of medical and financial resources to care for the ever-increasing number of aortic valve patients. Our study showed a 5-year increase of 48.1% in patients hospitalized for aortic valve disease, likely reflecting both the aging of the population and the increased availability of TAVR. A 2013 meta-analysis of 7 studies including 9,723 patients reported a prevalence of AS of 12.4% in patients aged ≥75 years including 3.4% with severe AS[35]. A 2017 meta-analysis of 56 studies in 37 countries including 42,965 patients reported the prevalence of AS to be 4.5%, comprised of 2.8% (95% CI 1.4-4.1%) of patients aged 60-74 years and 13.1% (95% CI 8.2-17.9%) of patients aged >75 years; 19.9% (95% CI 12.8-26.9%) of AS was classified as severe, corresponding to an estimated 781,773 (95% CI 542,923-1,063,142) patients in the US, and >40% of patients did not undergo any sort valve replacement therapy[36].

Increasing severity of illness was associated with a preference for TAVR over SAVR. The evidence supporting this practice is historical: the pivotal randomized controlled trials comparing mortality following TAVR and SAVR showed equipoise for intermediate-risk patients[5,6,37]; for high-risk patients, the trials diverged with one showing equipoise[3] and another showing TAVR to be superior[4]. Recent data regarding low-risk patients[38,39] will likely lead to a future increase in TAVR and decrease in SAVR in this patient population.

Inequitable Distribution

Patients treated at large hospitals and urban teaching hospitals were more likely to undergo valve replacement than patients treated at small hospitals, urban non-teaching hospitals, and rural hospitals; hospitals categorized as not-for-profit and government, non-federal were more likely to provide TAVR but not SAVR than for-profit private hospitals. As new data and procedural techniques emerge rapidly, they are incorporated into clinical practice unequally between different types of hospitals: in our study, the rates of increase in TAVR and decrease in both SAVR and MT confirm that large urban teaching not-for-profit hospitals are far faster to adopt novel evidence-based practices for the treatment of aortic valve disease than their small, rural, non-teaching, or for-profit counterparts. Trends in the care of patients with aortic valve disease require much more research at the national level. Factors limiting access to TAVR must be identified and rectified.

Cost and Cost Effectiveness

Among 190,563 patients with significant aortic valve disease treated from 2012-2016, the average 6-month inpatient costs were $59,743 for SAVR, $64,395 for TAVR, and $23,460 for MT alone. Thus, while the SAVR and TAVR have both been shown to provide a survival benefit over MT for patients with severe aortic stenosis[2,40], the 6-month costs of either intervention clearly exceed the cost of MT.

In aggregate, the costs of SAVR, TAVR, and MT are estimated to total a combined $10.2 billion annually in the US[41]. Several prior studies have examined the costs of aortic valve disease care in selected populations. In the PARTNER trial cohort B of inoperable patients randomized to TAVR or MT, TAVR carried a higher cost for the initial hospitalization ($78,542 versus $42,806 respectively), but MT resulted in follow-up costs almost twice those of TAVR ($29,289 versus. $53,621 respectively)[42]. In 2012, Medicare payments for the 4083 beneficiaries undergoing TAVR totaled $215,770,200, or a median of $49,500 (interquartile range [IQR] $36,900-64,600) per hospitalization, barely less than the $50,400 (IQR $37,400-65,800) for propensity-matched SAVR patients (p<0.01)[43]. Notably, for intermediate-risk trial patients, TAVR incurred ≈$20,000 more than SAVR in procedural costs but $11,377 less (p<0.01) in 2-year follow-up costs[44].

Across several studies, TAVR has been associated with increased procedural costs but decreased post-procedural resource utilization in comparison to SAVR; cost effectiveness estimates vary widely, particularly as a result of varying costs in different healthcare systems[13]. Indeed, assessing cost effectiveness is much more complicated than simply reporting raw costs. The American College of Cardiology typically defines high value interventions as costing <$50,000 per quality-adjusted life year (QALY)[45]. While our study was not able to assess quality of life, we were able to report from our sensitivity analysis that, compared with MT, 11-month costs among all admissions were $33,055 more for SAVR and $39,972 more for TAVR (Appendix Table 1, p<0.01). While either valve replacement modality carries higher-up front costs than MT, as MT is increasingly reserved for only higher-risk patients, their frequent readmissions and on-going medical care may become more expensive than valve replacement procedures.

Previous studies have yielded highly variable findings regarding cost effectiveness. A 2018 hypothetical cost-effectiveness model for intermediate risk patients in the Canadian healthcare system suggested that TAVR added 0.23 QALYs versus SAVR at an incremental cost of $46,083 Canadian per QALY[46]. Conversely, a 2013 hypothetical cost effectiveness analysis for inoperable patients receiving TAVR versus MT estimated an increase in quality-adjusted life expectancy from 1.19 to 1.93 years at an incremental cost of $99,900 per QALY[47]. A 2014 Spanish cost-utility analysis of 207 high-risk patients reported a significant improvement in the cost-effectiveness of TAVR when the price of TAVR devices was reduced by 30%, highlighting the important role of this single expense in the economics of TAVR[48].

Inpatient Duration and Readmission

We found that the average numbers of inpatient days across all admissions over a 6-month period beginning with IA were 12.1 for SAVR, 10.0 for TAVR, and 9.7 for MT, and the average number of admissions were 1.3, 1.5, and 1.7 respectively. In our first sensitivity analysis, when we extended the follow-up period to 11 months, we observed similar results to the main 6-month analysis. Long-term data are lacking, and further studies must test the hypothesis that the up-front costs of SAVR and TAVR are offset by reduced numbers of duration of subsequent readmissions, potentially making valve replacement increasingly cost effective in comparison to MT over several years. Also, as TAVR operators adopt minimalist practices and short hospital stays, TAVR has become less expensive and could become even less expensive than SAVR. Arguing against these hypotheses, an analysis of the National Cardiovascular Data Registry (NCDR) Transcatheter Valve Therapies (TVT) Registry found an increase in all-cause hospitalization and inpatient days in the 1 year post-TAVR compared with the 1 year pre-TAVR: although cardiovascular hospitalizations decreased, non-cardiovascular hospitalizations increased even more[49]. However, when excluding the cost of the TAVR admission, inpatient costs were slightly lower in the post-TAVR year than the pre-TAVR year.

A Field in Economic Flux

From a health systems perspective, an understanding of the costs, inpatient days, and readmission rates associated with different aortic valve disease management strategies is necessary to ensure that resources are appropriately apportioned to provide care for the increasing number of aortic valve disease patients. TAVR continues to supplant both SAVR and MT[1], and the future growth potential for aortic valve therapy is enormous given the high prevalence of aortic valve disease: aortic stenosis is present in up to 4.5% of the population in developed countries with 19.9% classified as severe, and >40% go without valve replacement[36]. Additionally, AR patients may also receive SAVR, TAVR, or MT.

The field of aortic valve disease is in great flux at present with the continued expansion of TAVR, and many changes in the economics of aortic valve disease can be expected. For example, in our study, a greater percentage of TAVR patients than SAVR or MT patients were treated in hospitals characterized as large, not-for-profit, urban teaching, and in affluent neighborhoods, characteristics associated with more expensive hospitalizations in general[50]. While we controlled for disparities in many hospital characteristics in our estimation of costs, the profile of TAVR-capable hospitals is rapidly changing in light of an updated National Coverage Determination by the Center for Medicare and Medicaid Services that significantly reduced the requirements for hospitals to perform TAVR[51].

During our 5-year study period, IA costs and days decreased over time for TAVR but remained stable for SAVR and MT. This observation likely results from the progressively lower risk profile of TAVR patients. However, even at the end of the study period, TAVR was only available for patients at intermediate or greater surgical risk, with intermediate risk approval occurring on August 18, 2016. Given this greater severity of illness among TAVR vs. SAVR patients, we did find more readmission inpatient days and higher readmission rates with TAVR. Looking specifically toward intermediate surgical risk patients, among patients with minor or moderate loss of function, IA was more expensive for TAVR that for SAVR: we may conjecture that the increased costs relate to the higher cost of the TAVR prosthesis than the SAVR prosthesis.

The approval of TAVR for patients at low surgical risk[52] will further alter the economics of aortic valve disease. Additionally, the economic landscape may continue to change with the results of the on-going EARLY TAVR trial (NCT03042104) studying TAVR in severe, asymptomatic aortic stenosis and the TAVR UNLOAD trial studying TAVR in moderate aortic stenosis (NCT02661451). Fortunately, thanks to the availability of the HCUP NRD, this analysis may be repeated with relative ease in to update the assessment of SAVR, TAVR, and MT costs in the future.

Strengths and Limitations

Prior studies have examined the use and economics of SAVR and TAVR, but our novel study also includes the population treated with MT. Furthermore, our unique January-through-June study methodology allowed us to obtain 6-months of post-discharge follow-up data for hundreds of thousands of patients with admissions for aortic valve disease undergoing valve replacement or symptomatic with CHF, UA, NSTEMI, and/or syncope. In contrast, most previous studies of aortic valve disease in HCUP data have employed the NIS, which does not provide unique patient identifiers, thus rendering it impossible to track patients across multiple admissions[53-55]. NIS studies can only examine outcomes per discharge, whereas our NRD methodology allowed 6-month follow-up on a per-patient basis, a more relevant measure for SAVR, TAVR, and MT.

Our study methodology has several important limitations. First, ICD-9-CM codes do not permit differentiation between AS and AR. The prevalence of moderate or severe AR is only approximately 0.5%[56], and AR therapy has changed minimally with the advent of TAVR, so AR is unlikely to have contributed to the trends in therapy observed in this study: the trends observed in this study are principally attributable to AS therapy.

Second, neither ICD-9-CM nor ICD-10-CM codes quantify the severity of aortic valve dysfunction. Most patients with non-severe valve disease do not undergo valve replacement unless SAVR is performed for moderate AS or AR at the time of another cardiac surgery, typically coronary artery bypass grafting. Thus, we recognize the bias that patients with less severe valvular disease will generally be classified in the MT group. To mitigate this bias, we restricted our primary analysis to patients with a concomitant diagnosis suggesting significant AS or AR (i.e., SAVR, TAVR, CHF, UA, NSTEMI, and syncope): as seen in the first therapy trends sensitivity analysis, this concomitant diagnosis eliminated 244,432 patients, 98.4% of whom received medical therapy, suggesting that non-severe aortic valve disease was present. Of course, billing codes cannot determine precisely what fraction of patients hospitalized for aortic valve disease specifically had severe aortic stenosis, the only FDA-approved indication for TAVR. Still, indications will change: the PARTNER 3[38] and Evolut Low Risk[39] trials demonstrated safety and efficacy of TAVR in low-surgical-risk patient; the on-going EARLY TAVR trial (NCT03042104) is studying TAVR in severe, asymptomatic aortic stenosis; and the on-going TAVR UNLOAD trial is studying TAVR in moderate aortic stenosis (NCT02661451). Ultimately, we believe that, because all included patients had both valve disease and an associated procedure or symptom severe enough to qualify as billing diagnoses for hospital admission, the patient populations in the SAVR, TAVR, and MT groups were adequately comparable for a meaningful analysis.

Third, the NRD only captures inpatient data, excluding outpatient, emergency department, and observation visits, which may contribute to overall costs.

Fourth, the NRD does not capture vital status after discharge, so the competing risk of death may influence our observed readmission data.

Fifth, our main analyses used six months of follow-up, and some patients who received MT during the study period may have subsequently undergone SAVR or TAVR, although results did not change appreciably in the sensitivity analyses looking at follow-up to 11 months. Indeed, the population in the cost analysis was smaller than the population in the therapy trends analysis because the cost analysis excluded from the MT group patients who underwent SAVR or TAVR any time during the calendar year, even after 6 months of follow-up. The rare patients undergoing balloon aortic valvuloplasty would also be categorized as receiving MT, but this seems appropriate given the short duration of effect of this procedure. Conclusively, despite these limitations, this study provides important and novel information regarding the variation in use of SAVR, TAVR, and MT in the US.

Conclusions

From 2012 through 2016, the use of TAVR increased at the expense of both SAVR and MT. The greatest use of TAVR was associated with patients at elevated surgical risk and hospitals that were large, not-for-profit, and urban teaching hospitals. Expected expansion of TAVR indications portends continued growth of TAVR and reduction in SAVR and MT. The inequitable distribution of TAVR therapy must be addressed.

For patients admitted with aortic valve disease, 6-month inpatient costs were higher for treatment with TAVR than for treatment with SAVR, and both valve replacement modalities were significantly more expensive than MT. Compared to SAVR, IA was shorter for TAVR and MT, but 6-month readmission inpatient days and the likelihood of readmission were greater for TAVR and MT. IA costs and days decreased over time for TAVR but remained stable for SAVR and MT. The relative cost effectiveness of these 3 treatment modalities requires further study.

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