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Valve-in-valve transcatheter aortic valve implantation versus repeat surgical aortic valve replacement in patients with a failed aortic bioprosthesis

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KEYWORDS

- degenerative valve
- TAVI
- valve-in-valve

Abstract

Background: Limited data are available regarding clinical outcomes of valve-in-valve (ViV) transcatheter aortic valve implantation (TAVI) following the United States Food and Drug Administration approval of ViV TAVI in 2015.

Aims: The aim of this study was to evaluate in-hospital, 30-day, and 6-month outcomes of ViV TAVI versus repeat surgical aortic valve replacement (SAVR) in patients with a failed aortic bioprosthetic valve.

Methods: This retrospective cohort study identified patients who underwent ViV TAVI or repeat SAVR utilising the Nationwide Readmission Database from 2016 to 2018. Primary outcomes were all-cause readmission (at 30 days and 6 months) and in-hospital death. Secondary outcomes were in-hospital stroke, pacemaker implantation, 30-day/6-month major adverse cardiac events (MACE), and mortality during readmission. Propensity score-matching (inverse probability of treatment weighting) analyses were implemented.

Results: Out of 6,769 procedures performed, 3,724 (55%) patients underwent ViV TAVI, and 3,045 (45%) underwent repeat SAVR. ViV TAVI was associated with lower in-hospital all-cause mortality (odds ratio [OR] 0.42, 95% confidence interval [CI]: 0.20-0.90, p=0.026) and a higher rate of 30-day (hazard ratio [HR] 1.46, 95% CI: 1.13-1.90, p=0.004) and 6-month all-cause readmission (HR 1.54, 95% CI: 1.14-2.10, p=0.006) compared with repeat SAVR. All secondary outcomes were comparable between the two groups.

Conclusions: ViV TAVI was associated with lower in-hospital mortality but higher 30-day and 6-month all-cause readmission. However, there was no difference in risk of in-hospital stroke, post-procedure pacemaker implantation, MACE, and mortality during 30-day and 6-month readmission compared with repeat SAVR, suggesting that ViV TAVI can be performed safely in carefully selected patients.

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Abbreviations

CI	confidence interval
HR	hazard ratio
MACE	major adverse cardiac events
OR	odds ratio
SAVR	surgical aortic valve replacement
TAVI	transcatheter aortic valve implantation
ViV	valve-in-valve

Introduction

The most significant limitation of bioprosthetic valves is structural deterioration over time, including regurgitation and restenosis[1]. With increased implantation of bioprosthetic valves, the management of prosthesis-related complications, including failed bioprosthetic valves, is evolving[2]. Traditional therapy for patients presenting with a failed aortic bioprosthetic valve was repeat surgical aortic valve replacement (SAVR), as SAVR is a class I recommendation from both European and American guidelines[3,4]. Isolated repeat SAVR for degenerated bioprosthetic valves accounts for ~7% of all aortic valve procedures[5]. However, repeat surgical procedure has been shown to have increased 30-day mortality, postoperative stroke, and pacemaker implantation because of advanced age, risk profile, and increased adhesions from the previous procedure compared with primary SAVR[6].

Transcatheter aortic valve implantation (TAVI) is now the recommended modality for treatment of severe native aortic stenosis in high-risk surgical patients as well as being non-inferior to surgery in low- and intermediate-risk patients[4,6]. Valve-in-valve (ViV) TAVI is used as a therapeutic option for failed aortic bioprosthetic valves, particularly in patients with high or prohibitive surgical risk[4,7]. Small retrospective studies have shown shorter post-procedural stay, lower bleeding risk, and less acute kidney injury with ViV TAVI compared with repeat SAVR[8,9]. A meta-analysis comparing ViV TAVI with repeat SAVR showed better outcomes at 30 days without any differences at one year[10]. One study published using the Nationwide Readmission Database (NRD) from 2012-2016 showed improved short-term outcomes with ViV TAVI; however, this study does not represent contemporary practice[11]. There are limited data available evaluating trends and outcomes of ViV TAVI compared with repeat SAVR with a failed bioprosthetic valve following the Food and Drug Administration (FDA) approval for ViV TAVI. Our study aimed to investigate in-hospital, 30-day, and 6-month clinical outcomes following ViV TAVI versus repeat SAVR.

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Methods

DATA SOURCE

The study utilised data from the NRD from 2016 to 2018[12,13]. We did not use the database before 2016 as it used International Classification of Diseases, Ninth Edition codes. Additionally, the FDA approved the CoreValve® (Medtronic, Minneapolis, MN, USA) and the SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) in 2015 for ViV TAVI. The NRD consists of all-payer databases for the Healthcare Cost and Utilization Project, established by the Agency for Healthcare Research and Quality. It is a nationally representative database comprising discharge records from 28 states, with approximately 35 million weighted discharges annually (excluding rehabilitation and long-term acute care facilities), regardless of the payer. The NRD represents approximately 58.2% of all U.S. hospitalisations. The study was exempt from the Cleveland Clinic institutional review board approval requirement as the database contained de-identified data sets with prior ethics committee approval.

STUDY POPULATION (Figure 1)

We queried the NRD 2016 to 2018 using the International Classification of Diseases, Tenth Revision (ICD-10; Z95.2)[14] to identify all adults (≥18 years) with a history of prosthetic valves. We excluded hospitalisations with concomitant mitral, pulmonary, and tricuspid valvular diseases and a diagnosis of infective endocarditis[15] to identify patients with only an aortic prosthetic heart valve. This exclusion strategy was not followed in the prior study published using NRD data[11]. We utilised ICD-10-PCS codes to identify patients who underwent TAVI or SAVR. After excluding patients aged <18 years, we created two study cohorts, one for in-hospital and 30-day outcomes after excluding discharges in December to allow for a complete 30-day follow-up period, and the second for 6-month outcomes after excluding discharges from July to December to have complete 6-month follow-up. Additionally, we excluded patients who underwent concomitant

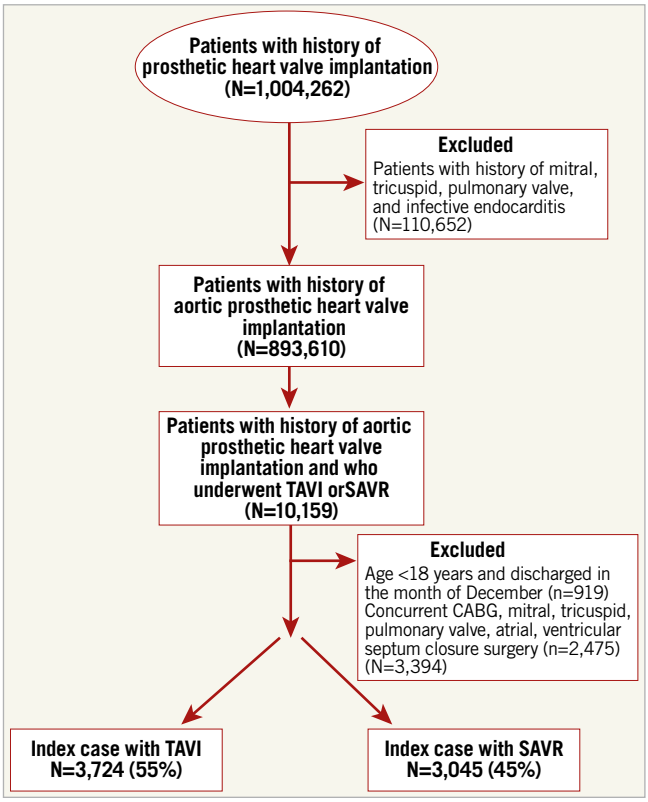


Figure 1. *Flow chart of patient selection. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation*

coronary artery bypass graft (CABG), mitral, tricuspid, or pulmonary valve, atrial or ventricular septum closure surgeries[16] to arrive at the final cohort of patients with aortic prosthetic valves who underwent either TAVI or SAVR alone.

PATIENT AND HOSPITAL CHARACTERISTICS

We used NRD variables to identify each patient's age (in years), gender, median household income, primary payer (Medicare, Medicaid, private insurance), day of admission (weekend/weekday), and type of admission (elective/non-elective). We used ICD-10-CM codes to define the prior history of myocardial infarction, stroke/transient ischaemic attack (TIA), ischaemic cardiomyopathy, chronic heart failure, atrial fibrillation, prior history of percutaneous coronary intervention (PCI), prior history of CABG, and history of defibrillator/pacemaker. Elixhauser comorbidities were used to define hypertension, diabetes, hyperlipidaemia, valvular disease, peripheral vascular disease (PVD), smoker, alcohol abuse, obesity, chronic pulmonary disease, renal failure, liver disease, cancer, fluid and electrolyte imbalance, and coagulopathy. Under hospital characteristics, we included hospital size according to the number of beds (small/medium/large), teaching hospital, location of hospital (urban/non-urban), and ownership of hospital (private vs non-profit settings). Hospital volume was calculated by adding all the weighted admissions with TAVI or SAVR at each hospital, and was divided into low versus high procedure volume hospitals based on an annual procedure volume of 10.

STUDY OUTCOMES

The primary outcome for this study was all-cause readmission (30 days and 6 months) and in-hospital mortality. We defined readmission as hospital admission for any principal diagnosis from the discharge date of the index admission. In the case of multiple readmissions, only the first readmission from the index admission discharge date was counted. The secondary outcomes were major adverse cardiac events (MACE), mortality, major bleeding or vascular complications, non-cardiac infection, procedural complications, as well as resource utilisation which comprised length of stay (LOS) and total cost (in US dollars) during 30-day and 6-month readmission. In-hospital outcomes of interest were acute stroke, cardiorespiratory complications, vascular complications, major bleeding, pacemaker implantation, LOS, and cost. Mortality over 30 days and 6 months includes death during hospitalisation, while out-of-hospital death is not registered in the database. In-hospital LOS was defined as post-procedure, after excluding days from admission to the procedure. The definitions of all composite outcomes are given in **Supplementary Appendix 1**. We showed a trend of utilisation of procedures and their 30-day readmission over quarters. We showed predictors of 30-day, 6-month all-cause readmission in ViV TAVI and repeat SAVR. A subgroup analysis was also performed for 30-day all-cause readmission, stratified by gender, type of primary expected payer, presence or absence of renal failure, presence or absence of heart failure, bed size of the hospital (small/medium/large), and hospital by procedural volume to look for sources of heterogeneity. The definitions and ICD codes of outcome variables are given in **Supplementary Table 1**. ICD-10 codes used to select the final cohort and outcomes have been published previously[14-16].

STATISTICAL ANALYSIS

After assessing the distribution, continuous variables are presented as means with standard deviation or median with interquartile range, while categorical variables are presented as a frequency in percentages. Baseline patient and hospital characteristics were compared between ViV TAVI and repeat SAVR using the chi-square test for categorical variables and the Student's t-test or Wilcoxon rank-sum test.

We created two propensity models (model 1 was for in-hospital and 30-day outcomes, and model 2 was for 6-month outcomes), as the sample sizes of the two cohorts were different. Propensity scores were used to match patients with ViV TAVI to repeat SAVR. A non-parsimonious multivariable logistic regression model was developed to estimate the propensity score for receiving ViV TAVI compared with repeat SAVR using clinically meaningful variables as planned **(Supplementary Appendix 2, Supplementary Appendix 3)**. Then, a double-robust method was used to generate treatment weights, and the inverse probability of treatment weighting was used to match TAVI with SAVR using generalised linear models[17]. On the matched cohort, multivariable regression analysis was done for robustness. Logistic regression analysis was used to calculate the odds ratio (OR) with a 95% confidence interval (CI) for in-hospital outcomes. Cox regression was used for 30-day and 6-month outcomes to calculate the hazard ratio (HR) with a 95% CI.. The global test of proportionality assumption was not violated (global test p=0.243). For the length of stay and cost, linear regression was done to derive the coefficient. The balance of variables before and after matching is described in **Supplementary Figure 1** and **Supplementary Figure 2**. We used logistic regression for predictors of all-cause readmission. Details of the models are given in **Supplementary Appendix 4**.

A Kaplan-Meier graph was constructed for all-cause readmission. To calculate a trend p-value for proportions, we conducted logistic regression for binary outcomes with outcomes of interest as the dependent variable and the year as the independent variable, adjusted for age and gender. All p-values were two-sided with a conventional significance threshold of $p<0.05$.

UNMEASURED BIAS ANALYSIS AND VALIDITY OF STUDY

To evaluate the robustness of our findings, we conducted a falsification endpoint and an "E-value" analysis for 30-day and 6-month readmission and in-hospital mortality[18]. E-value identifies the minimum strength of association that unmeasured confounders would need to have with both treatment and outcome, conditional on measured covariates, to explain the observed association fully. This estimates what the relative risk would have to be for any unmeasured confounder to overcome the observed association of study intervention with study outcomes. In the falsification method, we selected an alternative outcome that may not be expected to be causally

affected by the treatment being studied[19]. Then, we assessed whether study intervention (ViV TAVI) affects alternative outcomes by using a similar method to assess other study outcomes. If no treatment effect is seen for the alternative outcome, it supports but does not prove that there may be a causal treatment effect for the study outcomes. Thus, a successful falsification analysis can strengthen the causal claims between study intervention and outcome in the observational study. We chose a composite of gastrointestinal and urinary tract infection readmission as an alternative outcome and studied the effect of interventions.

All statistical analyses were conducted using appropriate weighting, stratifying, and clustering samples to obtain national estimates using the svy package of Stata, version 16.1 (StataCorp, College Station, TX, USA). The information on the weighting technique is described in **Supplementary Appendix 5**.

Results

From the period 2016 to 2018, we included a total of 6,769 patients in the study who underwent a procedure for a failed aortic bioprosthetic valve, of whom 3,724 (55%) underwent ViV TAVI compared with 3,045 patients (45%) who had repeat SAVR **(Table 1)**. Of these, 1,908 (53.8%) patients with ViV TAVI and 1,640 (46.8%) patients with repeat SAVR had a complete 6-month follow-up.

BASELINE CHARACTERISTICS (Table 1)

In females, ViV TAVI was performed more than repeat SAVR (48.9% vs 38.9%, p<0.001). The patients who underwent ViV TAVI were elderly (79±9.1 vs 65±13.4 years, p<0.001). The repeat SAVR cohort had a higher prevalence of peripheral vascular disease, obesity, liver disease, alcohol abuse, and coagulopathy. The ViV TAVI cohort had a higher prevalence of patients with hypertension, diabetes, hyperlipidaemia, prior history of MI, stroke/TIA, ischaemic cardiomyopathy, chronic heart failure, atrial fibrillation, prior history of PCI, prior history of CABG, history of defibrillator or pacemaker, chronic pulmonary disease, cancer, and chronic renal failure. ViV TAVI was performed more in hospitals with higher procedural volume compared with repeat SAVR. There was no difference in the type of admission, hospital bed size, teaching status of the hospital, or hospital ownership between the ViV TAVI group and the repeat SAVR group.

IN-HOSPITAL OUTCOMES (Table 2, Supplementary Table 2)

ViV TAVI was associated with lower in-hospital mortality (1.2% vs 3.4%, OR 0.42, 95% CI: 0.20-0.90, p=0.026), major bleeding (29.7% vs 67.7%, OR 0.10, 95% CI: 0.04-0.21, p<0.001), and cardiorespiratory complications (9.3% vs 26.5%, OR 0.32, 95% CI: 0.15-0.69, p=0.004). ViV TAVI was also associated with lower post-procedure median length of stay compared with repeat SAVR (4 days vs 10 days, adjusted coefficient = –4.75, 95% CI: –8.61 to –0.90, p=0.016). Differences in other in-hospital outcomes including acute stroke, vascular complications, pacemaker implantation, and cost were not statistically significant.

30-DAY AND 6-MONTH READMISSION OUTCOMES (Table 3, Supplementary Table 3)

Patients who underwent ViV TAVI were found to have increased hazards of 30-day and 6-month all-cause readmission compared with repeat SAVR patients (30-day: 16.1% vs 11.5%, HR 1.46, 95% CI: 1.13-1.90, p=0.004; 6-month: 33.8% vs 24.5%, HR 1.54, 95% CI: 1.14-2.10, p=0.006). The Kaplan-Meier graphs of 30-day and 6-month readmission are shown in **Figure 2A** and **Figure 2B**, respectively. In ViV TAVI, 0.95% of patients died during 30-day readmission, and 1.6% of patients died during 6-month readmission while, in repeat SAVR, 0.27% of patients died during 30-day readmission, and 0.4% of patients died during 6-month readmission. There was no difference in the rates of MACE, mortality, procedural complications, and length of stay during 30-day and 6-month readmission between the two groups. However, ViV TAVI was associated with a higher risk of major bleeding/vascular complications and non-cardiac infection than repeat SAVR.

REASONS FOR 30-DAY AND 6-MONTH ALL-CAUSE READMISSION (Supplementary Table 4, Supplementary Table 5)

In ViV TAVI, within 30 days, 219 (36.62%) readmissions were due to cardiac aetiologies, and 379 (64.88%) readmissions were due to non-cardiac aetiologies. Within 6 months, 304 (47.2%) readmissions were due to cardiac aetiologies, and 344 (52.8%) readmissions were due to non-cardiac aetiologies. In repeat SAVR, within 30 days, 115 (34.02%) readmissions were due to cardiac aetiologies, and 223 (65.98%) readmissions were due to non-cardiac aetiologies. Within 6 months, 231 (57%) readmissions were due to cardiac aetiologies, and 171 (42.5%) readmissions were due to non-cardiac aetiologies.

PREDICTORS OF 30-DAY AND 6-MONTH ALL-CAUSE READMISSION

For ViV TAVI and repeat SAVR, ORs of significant predictors of all-cause readmission are described in **Table 4**, and ORs of all variables included in the multivariable model are given in **Supplementary Table 6.** For ViV TAVI, fluid and electrolyte imbalance, heart failure, atrial fibrillation, chronic kidney disease (CKD), PVD, diabetes, discharge to other facilities (compared with home discharge), and LOS were significant predictors of 30-day or 6-month readmission. For repeat SAVR, primary expected payer (Medicare/Medicaid), chronic lung disease, pulmonary circulation disorder, CKD, diabetes, discharge to other facilities, and LOS were significant predictors of 30-day or 6-month readmission.

SUBGROUP ANALYSIS (Supplementary Table 7)

We conducted a subgroup analysis to investigate the source of heterogeneity in the difference in 30-day readmission. None of the proposed subgroups showed an interaction except the primary expected payer (p for interaction=0.013).

Table 1. Baseline characteristics of ViV TAVI and repeat SAVR.

			ViV TAVI (N=3,724) (55%)	Repeat SAVR (N=3,045) (45%)	*p*-value
Demographics	Age, years (mean±SD)		79±7.8	65±11.2	<0.001
	Female		1,820 (48.9%)	1,185 (38.9%)	<0.001
Primary payer	Medicare		3,334 (89.5%)	1,862 (61.1%)	<0.001
	Medicaid		54 (1.5%)	221 (7.2%)	
	Private insurance		224 (6.0%)	813 (26.7%)	
Median household income	0-25th		762 (20.5%)	767 (25.2%)	0.01
	26-50th		1,065 (28.6%)	878 (28.8%)	
	51-75th		1,039 (27.9%)	775 (25.5%)	
	76-100th		813 (21.8%)	577 (19%)	
Comorbidities	Hypertension		3,289 (88.3%)	2,527 (83%)	<0.001
	Diabetes		1,350 (36.3%)	905 (29.7%)	<0.001
	Hyperlipidaemia		2,641 (70.9%)	1,930 (63.4%)	<0.001
	Peripheral vascular disease		963 (25.8%)	1,105 (36.3%)	<0.001
	Prior history of MI		462 (12.4%)	216 (7.1%)	<0.001
	Stroke/TIA		682 (18.3%)	451 (14.8%)	0.015
	Ischaemic cardiomyopathy		2,631 (70.6%)	1,323 (43.4%)	<0.001
	Chronic heart failure		2,983 (80.1%)	1,386 (45.5%)	<0.001
	Atrial fibrillation		1,464 (39.3%)	948 (31.1%)	<0.001
	Prior history of PCI		659 (17.7%)	207 (6.8%)	<0.001
	Prior history of CABG		957 (25.7%)	241 (7.9%)	<0.001
	History of defibrillator/pacemaker		900 (24.2%)	355 (11.7%)	<0.001
	Obesity		670 (18%)	862 (28.3%)	<0.001
	Chronic pulmonary disease		1,147 (30.8%)	753 (24.7%)	<0.001
	Chronic renal failure		1,415 (38%)	575 (18.9%)	<0.001
	Chronic liver disease		125 (3.4%)	159 (5.2%)	0.008
	Cancer		177 (4.8%)	63 (2.1%)	<0.001
	Coagulopathy		664 (17.8%)	1,179 (38.7%)	<0.001
	Smoker		1,439 (38.6%)	1,113 (36.5%)	0.229
	Alcohol abuse		53 (1.4%)	84 (2.8%)	0.004
	Elixhauser Comorbidity Index	1	3 (0.1%)	25 (0.8%)	<0.001
		2	70 (1.9%)	90 (2.9%)	
		≥3	3,607 (96.9%)	2,883 (94.7%)	
	Transapical approach		101 (2.7%)	NA	
Preprocedural LOS, median (IQR)			0 (0-2)	0 (0-2)	0.690
Type of admission	Elective		2,629 (70.6%)	2,160 (70.9%)	0.872
	Non-elective		1,095 (29.4%)	885 (29.1%)	
Hospital characteristics					
Hospital bed size	Small		297 (8%)	258 (8.5%)	0.351
	Medium		741 (19.9%)	664 (21.8%)	
	Large		2,642 (70.9%)	2,075 (68.2%)	
Teaching hospital			3,056 (82.1%)	2,420 (79.5%)	0.241
Urban hospitals			2,235 (60%)	1,673 (55%)	0.04
Private, non-profit			3,013 (80.9%)	2,362 (77.6%)	0.06
Hospitals by procedure volume	Low volume (<10)		1,575 (43.3%)	1,502 (49.3%)	<0.001
	High volume (≥10)		2,149 (56.7%)	1,543 (50.7%)	

CABG: coronary artery bypass graft; IQR: interquartile range; LOS: length of stay; MI: myocardial infarction; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement; TIA: transient ischaemic attack; ViV TAVI: valve-in-valve transcatheter aortic valve implantation

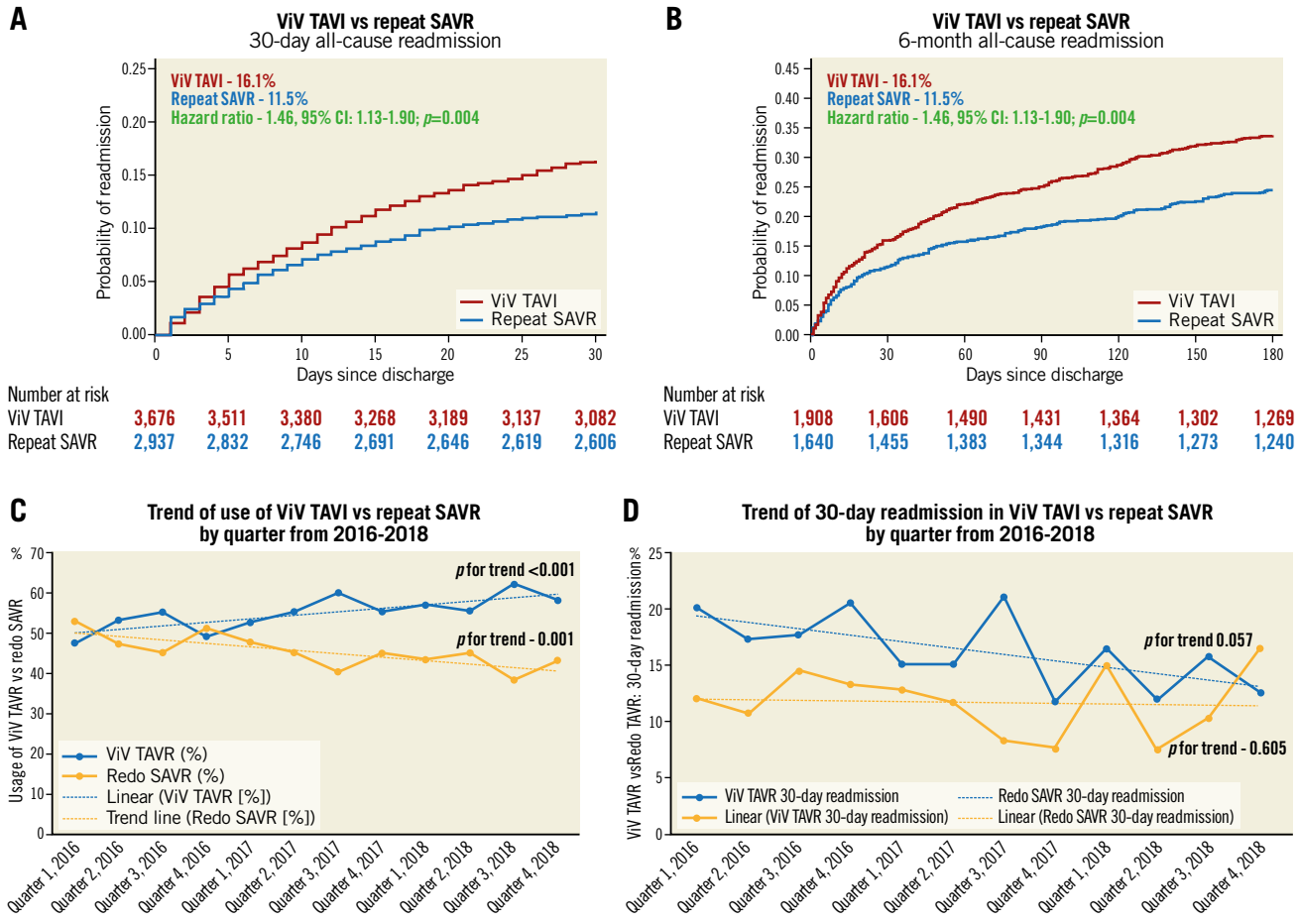


Figure 2. *30-day and 6-month readmission, trends of utilisation and 30-day readmission in ViV TAVI vs repeat SAVR. A) Kaplan-Meier graph of 30-day readmission between ViV TAVI and repeat SAVR. B) Kaplan-Meier graph of 6-month readmission between ViV TAVI and repeat SAVR. C) Trend of utilisation of ViV TAVI and repeat SAVR. D) Trend of 30-day readmission in ViV TAVI and repeat SAVR. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation; ViV: valve-in-valve*

TREND OF THE UTILISATION OF PROCEDURES AND READMISSION (Figure 2C, Figure 2D, Supplementary Table 8)

From 2016 to 2018, utilisation of ViV TAVI increased by 6.6% per quarter (p for trend <0.001), and repeat SAVR decreased by 6.1% per quarter (p for trend=0.001). From 2016 to 2018, the rate of 30-day all-cause readmission remained unchanged in repeat SAVR (p for trend=0.605), but there was an inclination towards a decreasing trend of 30-day readmission in ViV TAVI (p for trend=0.057).

UNMEASURED BIAS ANALYSIS

In the "E-value" analysis, the observed OR of 0.42 for in-hospital mortality, HR of 1.46 for 30-day readmission, and HR of 1.54 for 6-month readmission could be explained by an unmeasured confounder that was associated with both the treatment and the outcome by OR of 4.19-fold, HR of 2.28-fold, and HR of 2.45-fold each, respectively, above the measured confounders, but weaker confounding could not do so. The rate of the falsification endpoint remained similar between the two interventions (HR 1.39, 95% CI: 0.28-6.88, p=0.688).

Discussion

In this most extensive, multicentric, real-world, propensity score-matched analysis comparing ViV TAVI and repeat SAVR for failed bioprosthetic valves, ViV TAVI was associated with 58% lower in-hospital mortality, but 46% and 54% higher all-cause readmission at 30 days and 6 months, respectively **(Central illustration)**. ViV TAVI was associated with lower post-procedure cardiorespiratory complications and major bleeding compared with repeat SAVR. There was no difference in vascular complications, stroke, or post-procedure pacemaker implantation during index admission between the groups. Reduced overall in-hospital complications led to lesser resource utilisation (more home discharges and lower LOS) during index admission with ViV TAVI. There was no difference in MACE, mortality, or procedural complications, but a higher rate of major bleeding or vascular complications and non-cardiac infection (a composite of pneumonia, sepsis, and bacteraemia) during 30-day and 6-month readmission in ViV TAVI. From 2016 to 2018, the utilisation of ViV TAVI for failed bioprosthetic aortic valves increased, and repeat SAVR trended down. There was an inclination towards

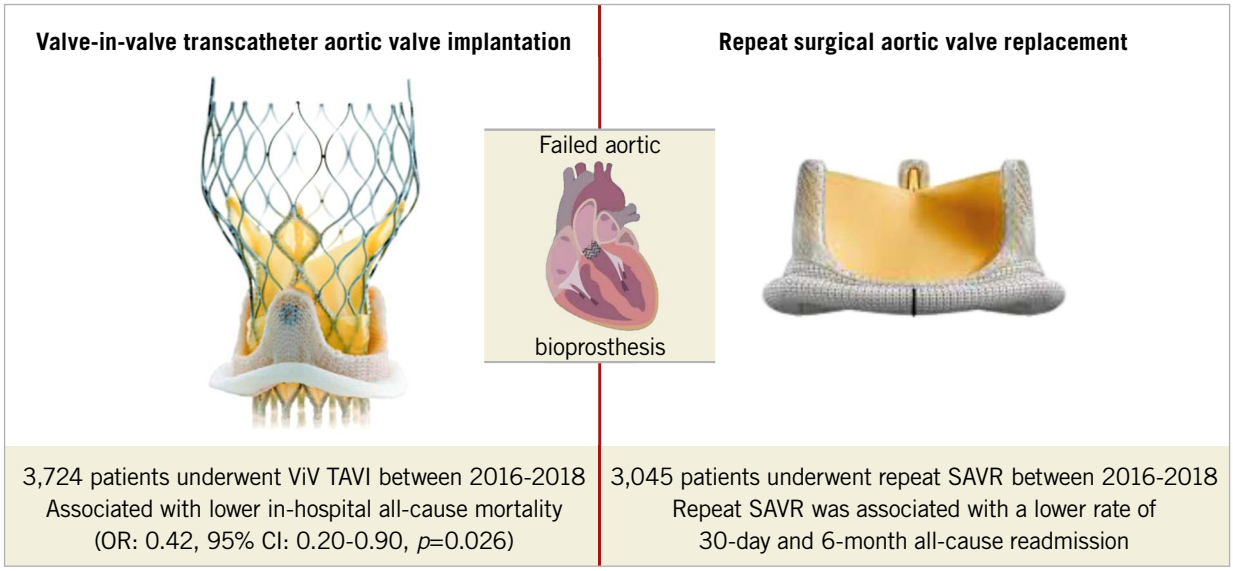
Table 2. In-hospital outcomes for ViV TAVI versus repeat SAVR.

		ViV TAVI N=3,724 (55%)	Repeat SAVR N=3,045 (45%)	OR@	95% CI		*p*-value
Disposition	Home	1,875 (50.3%)	1,135 (37.3%)	3.20	1.11	9.23	0.031
	Others◊	1,787 (48%)	1,795 (58.9%)				
Rehabilitation transfer		600 (16.1%)	774 (25.4%)	0.67	0.22	2.05	0.483
Discharged alive		3,676 (98.7%)	2,941 (96.6%)				
Clinical outcomes							
Death		46 (1.2%)	103 (3.4%)	0.42	0.20	0.90	0.026
Acute stroke		362 (9.7%)	294 (9.7%)	1.49	0.59	3.75	0.398
Cardiorespiratory# complications		347 (9.3%)	808 (26.5%)	0.32	0.15	0.69	0.004
Vascular complications		121 (3.3%)	133 (4.4%)	0.39	0.10	1.59	0.190
Major bleeding¶		1,107 (29.7%)	2,062 (67.7%)	0.10	0.04	0.21	<0.001
Procedural outcomes							
Pacemaker implantation**		479/2,824 (17%)	249/2,690 (9.3%)	3.81	0.62	23.54	0.150
Resource utilisation				**Coefficient**	**95% CI**		***p*-value**
Length of stay, days* (median, IQR)		4 (2-11)	10 (6-18)	–4.75	–8.61	–0.90	0.016
Total cost, U.S. dollars (median, IQR)		56,801 (42,947-77,280)	60,460 (43,213-87,687)	–5,556	–25,984	14,872	0.594

@Double robust method (inverse probability treatment weighting and multivariable regression). ◊Others - includes short-term facility, skilled nursing facility, home health care. #Cardiorespiratory complications - composite of pneumothorax, other respiratory complications including aspiration pneumonia, need of mechanical ventilation, post-procedural cardiogenic shock, use of vasopressors, use of mechanical circulatory support, cardiac arrest, cardiac tamponade, pericardial effusion, haemopericardium, pericardiocentesis, cardiotomy, pericardiotomy, thoracotomy. ¶Major bleeding - composite of gastrointestinal bleeding, postoperative bleeding, genitourinary bleeding, epistaxis, haemoptysis, intracranial haemorrhage, haemoperitoneum, other haemorrhages, blood transfusion. *LOS is post procedure - from day of procedure to discharge (after excluding days from admission to occurrence of procedure). **For pacemaker implantation outcome we excluded patients with history of defibrillator or pacemaker.
CI: confidence interval; IQR: interquartile range; OR: odds ratio; SAVR: surgical aortic valve replacement; ViV TAVI: valve-in-valve transcatheter aortic valve implantation

a decreasing trend of 30-day readmission in ViV TAVI but this remained unchanged in repeat SAVR from 2016 to 2018.

Bioprosthetic valve utilisation has been increasing for the management of severe aortic stenosis in patients undergoing surgery[20,21]. Compared with mechanical valves, bioprosthetic valves are associated with fewer thrombotic complications and the possible avoidance of long-term anticoagulation in addition to their superior haemodynamic profile[20]. Also, an ageing population is presenting for aortic valve replacement, leading to higher use of bioprosthetic valves than mechanical valves[21]. However,



Central illustration. *Valve-in-valve transcatheter aortic valve implantation versus repeat surgical aortic valve replacement in patients with a failed aortic bioprosthesis. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation; ViV: valve-in-valve*

Table 3. 30-day and 180-day readmission outcomes for ViV TAVI versus repeat SAVR.

30-day readmission outcomes						
	ViV TAVI N=3,676 (55.6%)	Repeat SAVR N=2,941 (44.4%)	HR@	95% CI		*p*-value
Clinical outcomes						
All-cause readmission	598 (16.1%)	338 (11.5%)	1.46	1.13	1.90	0.004
MACE◊	181 (4.8%)	92 (3.1%)	1.06	0.66	1.73	0.805
Mortality*	35 (0.95%)	<10 (0.27%)	1.59	0.45	5.60	0.471
Major bleeding/vascular complications◊◊	125 (3.4%)	37 (1.3%)	2.31	1.30	4.08	0.004
Non-cardiac infection#	54 (1.4%)	37 (1.2%)	2.63	1.33	5.20	0.005
Procedural complications**	49 (1.3%)	28 (1%)	1.41	0.61	3.26	0.416
Resource utilisation			**Coefficient@**	**95% CI**		***p*-value**
Length of stay, days (median, IQR)	5 (2-8)	5 (3-8)	1.33	–0.51	3.17	0.157
Total cost, U.S. dollars (median, IQR)	10,386 (6,712-22,700)	9,491 (6,151-17,036)	11,767	3,672	19,862	0.004
6-month readmission outcomes						
	ViV TAVI N=1,908 (53.8%)	**Repeat SAVR N=1,640 (46.8%)**	**HR@**	**95% CI**		***p*-value**
Clinical outcomes						
All-cause readmission	644 (33.8%)	402 (24.5%)	1.54	1.14	2.10	0.006
MACE◊	175 (9.2%)	105 (6.4%)	0.84	0.51	1.39	0.499
Mortality*	30 (1.6%)	<10 (0.4%)	2.76	0.49	15.61	0.249
Major bleeding/vascular complications◊◊	118 (6.2%)	49 (3%)	1.91	0.95	3.81	0.068
Non-cardiac infection#	88 (4.6%)	24 (1.5%)	9.15	4.00	20.91	<0.001
Procedural complications**	40 (2.1%)	39 (2.4%)	0.82	0.40	1.68	0.580
Resource utilisation			**Coefficient@**	**95% CI**		***p*-value**
Length of stay, days (median, IQR)	5 (2-7)	4 (3-7)	0.94	–1.18	3.06	0.384
Cost, U.S. dollars (median, IQR)	10,539 (6,483-20,132)	10,742 (6,753-19,124)	4,516	–3,471	12,504	0.268

@Double robust method (inverse probability treatment weighting and multivariable regression). ◊MACE - composite of MI, stroke, heart failure, cardiogenic shock, cardiac arrest, arrhythmia or death within 30 days. Arrythmia - composite of ventricular tachycardia, fibrillation, supraventricular tachycardia, atrial flutter, fibrillation, complete heart block. ◊◊Major bleeding - composite of gastrointestinal bleeding, postoperative bleeding, genitourinary bleeding, epistaxis, haemoptysis, intracranial haemorrhage, haemoperitoneum, other haemorrhages, blood transfusion or vascular complications. #Non-cardiac infection - composite of bacteraemia, sepsis, pneumonia. * Mortality - includes only in-hospital death; out-of-hospital death is not available in database. **Procedural complications - composite of valvular complications, iatrogenic complications, pericardial complications, pacemaker implantation, wound dehiscence, AKI, pericardiotomy, cardiotomy, or thoracotomy. 30-day myocardial infarction, stroke, pacemaker implantation, vascular complications, valvular complications, gastrointestinal bleeding, wound dehiscence, AKI, pericardial complications weighted numbers are less than 10; hence, not reported as per HCUP guidelines. AKI: acute kidney injury; CI: confidence interval; HR: adjusted hazard ratio; MACE: major adverse cardiovascular events; MI: myocardial infarction

bioprosthetic valves have been associated with shorter durability as they are prone to degeneration, making them more vulnerable to reoperation[20]. There are limited data available on the long-term durability of the bioprosthetic valve[22]. Repeat SAVR has traditionally been performed in cases of failed bioprosthetic valves. ViV TAVI, an emerging technology, is recommended for patients at high or prohibitive surgical risk in the guidelines[3,4], which explains the higher age, higher number of females, and higher baseline comorbidities in the ViV TAVI group compared with the repeat SAVR group. These comorbidities are independently associated with higher morbidity and mortality as they are part of the Society of Thoracic Surgeons (STS) PROM or EuroSCORE II risk calculation prior to the procedure.

Despite the patients in the ViV TAVI group having higher baseline comorbidities, ViV TAVI was associated with improved in-hospital outcomes, including all-cause mortality, cardiorespiratory complications, and bleeding compared with repeat SAVR in the current analysis. These combined led to less resource utilisation (i.e., more and earlier discharges to home). These results are consistent with previously published data showing improved short-term outcomes with ViV TAVI using the 2016 database[11]. In our analysis, newer-generation valves may have been utilised during the study period, which may have been associated with better outcomes[23]. Hence, the previous study may not represent contemporary outcomes reflecting the most current practices. Additionally, the previous study did not exclude patients with other valvular diseases, leading to the inclusion of patients who did not exclusively have a history of aortic bioprosthetic heart valve implantation[11]. Furthermore, a previously published meta-analysis and a propensity score-matched analysis also showed

Table 4. Predictors of 30-day and 6-month all-cause readmission for ViV TAVI and repeat SAVR.

Predictors for ViV TAVI				
30-day predictors	**OR**	**95% CI**		***p*-value**
Fluid and electrolyte imbalance	1.60	1.18	2.17	0.002
Heart failure	1.55	1.05	2.28	0.026
Discharged to other facilities*	1.55	1.14	2.11	0.005
Atrial fibrillation	1.37	1.06	1.78	0.017
Chronic kidney disease	1.36	1.00	1.86	0.052
Length of stay (per 5 days)	1.08	1.02	1.15	0.015
6-month predictors	**OR**	**95% CI**		***p*-value**
Atrial fibrillation	1.89	1.39	2.57	<0.001
Rehabilitation transfer	1.70	1.13	2.56	0.011
Diabetes	1.55	1.07	2.25	0.02
Discharge to other facilities	1.54	1.12	2.11	0.007
Peripheral vascular disease	1.41	1.00	1.99	0.051
Fluid and electrolyte imbalance	1.41	1.00	1.98	0.047
Low-volume hospital	1.34	0.99	1.81	0.059
Predictors for repeat SAVR				
30-day predictors	**OR**	**95% CI**		***p*-value**
Medicare/Medicaid vs private insurance	1.97	1.24	3.13	0.004
Chronic lung disease	1.81	1.22	2.68	0.003
Pulmonary circulation disorder	1.78	1.08	2.93	0.023
Chronic kidney disease	1.62	1.05	2.49	0.029
Length of stay (per 5 days)	1.07	1.01	1.15	0.032
6-month predictors	**OR**	**95% CI**		***p*-value**
Chronic kidney disease	1.79	1.13	2.84	0.013
Chronic lung disease	1.59	1.05	2.39	0.027
Diabetes	1.54	1.05	2.27	0.027
Discharge to other facilities	1.51	0.96	2.39	0.075

*Other facilities include skilled nursing facility, short-term facility.
CI: confidence interval; OR: odds ratio; SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation; ViV: valve-in-valve

reduced LOS with ViV TAVI compared with repeat SAVR, similar to our study[8,10]. We demonstrated that ViV TAVI was associated with similar odds of pacemaker placement during the index hospitalisation, although evidence from previously published studies and meta-analysis suggested an increased risk of pacemaker implantation in patients undergoing ViV TAVI[8-10]. Further, our study reported that 17% of the ViV TAVI population required permanent pacemaker implantation, slightly less than other studies reporting 18-25% pacemaker use[9,10].

There was no major difference in the rates of MACE, mortality, or stroke between the two groups over 6-month follow-up. This is consistent with a previously published meta-analysis[10]. Contrary to previously published studies, we demonstrated higher all-cause readmission rates with ViV TAVI at short-term (30 days) and medium-term follow-up (6 months)[8,11]. To confirm these results, we conducted a falsification endpoint and "E-value" analysis to assess the impact of unmeasured confounders. "E-value" (unmeasured bias) analysis showed that an unmeasured confounder requires higher association with both treatment and outcome conditioned on measured covariates, and successful falsification endpoint analysis indicates less chance of having residual confounders to explain away the measured effect. Several plausible reasons could explain the higher readmission rate in the ViV TAVI group. The average age of patients included in the ViV TAVI group was significantly higher compared with previous studies[8,11]. Age is an independent predictor of poor prognosis, and the older population has been associated with slightly worse outcomes[24]. In addition, there were nearly 49% females included in the ViV TAVI group, which is higher than previously published studies. Female gender has been associated with higher short-term adverse outcomes and 30-day readmission rates[8,11,13,25]. Similarly, in the subgroup of females, a higher 30-day all-cause readmission rate was revealed. Finally, almost all the comorbidities (i.e., hypertension, diabetes, etc.) were significantly higher in the ViV TAVI group, suggesting a higher STS risk score than previously published studies[8,11,26].

We observed a significant rise in the procedural volume for ViV TAVI during the study period. This may lead to improved operator experience and eventually even better outcomes, as shown by a decreasing readmission trend in each quarter in this study. Additionally, the subgroup analysis in hospitals with higher procedural volume showed no difference in 30-day readmission between the two groups, again indicating improved operator experience at high-volume centres. Newer-generation valves with fluoroscopic markers, repositionability, or retrievability may also help to improve valve-related outcomes.

Limitations

This study has several limitations which must be considered when interpreting the results. First, NRD is an administrative database that carries an inherent selection bias and the potential for miscoding. However, the Agency for Healthcare Research and Quality (AHRQ) has quality control measures to secure best coding practices, to ensure that linkage to state-level data is verified and reliable, and to establish internal validation of diagnosis codes through multiple audits. Second, we did not have information on primary aortic valve manufacturer/sizing, anatomical characteristics of the replaced valve (leaflet length, internal stent diameter, supra-annular positioning of the implant, etc.), type of implanted valve in TAVI (CoreValve/Evolut/SAPIEN XT/SAPIEN 3), access site (percentage of non-femoral access), list of antiplatelet or antithrombotic agents, echocardiographic parameters (e.g., valve area, valve gradient, post-procedural effective orifice area, patient-prosthesis mismatch), and left ventricular ejection fraction. We may not have accounted for all the confounding factors even though we performed propensity-matched and unmeasured bias analyses. Smaller valve sizes (preferentially used in repeat SAVR) were associated with higher patient-prosthesis mismatch and worse outcomes[27]. Newer techniques such as bioprosthetic

valve fracture may help to improve outcomes by reducing transvalvular gradients[8]. Third, we could not calculate the STS PROM risk score or EuroSCORE II, which can help to determine the risk of patients undergoing ViV TAVI versus repeat SAVR. Fourth, we could not assess outcomes such as acute kidney injury (AKI) and paravalvular leak (PVL) as AKI may occur before the procedure, and codes for PVL could be related to a failed bioprosthesis rather than post-procedure PVL. Despite these limitations, this analysis demonstrates clinical outcomes in an unselected patient population from the most current nationally available database, and the multi-institutional sample makes our results generalisable.

Conclusions

This analysis demonstrated that the use of ViV TAVI significantly increased during the study period, and was associated with lower in-hospital mortality and morbidity but higher 30-day and 6-month all-cause readmission compared with repeat SAVR in a propensity score-matched cohort. There were no differences in the post-discharge short-term or medium-term MACE, mortality during readmission, stroke, pacemaker implantation, or procedural complications between the two groups. However, there was an increased risk of major bleeding/vascular complications and non-cardiac infections in ViV TAVI compared with repeat SAVR. ViV TAVI can be performed safely in carefully selected patients. The choice to proceed with ViV TAVI versus repeat SAVR should be a shared decision based on available expertise, the individual patient, and valve characteristics until randomised clinical trials with longer follow-up garner more data concerning long-term clinical outcomes in this patient subset.

Impact on daily practice

Currently, repeat SAVR is a class I indication for patients presenting with a failed aortic bioprosthetic valve. ViV TAVI is used in patients with high or prohibitive surgical risk. Our study showed that utilisation of ViV TAVI increased significantly from 2016 to 2018. ViV TAVI was associated with a higher 30-day and 6-month readmission rate than repeat SAVR, but the trend of readmission was declining. ViV TAVI was associated with lower odds of in-hospital mortality and morbidity, and a similar incidence of post-procedural pacemaker implantation compared with repeat SAVR. ViV TAVI was associated with no difference in post-discharge MACE, stroke, mortality, or procedural complications but higher major bleeding/vascular complications during 30-day and 6-month readmission than repeat SAVR. Our results suggest that ViV TAVI can be performed safely in carefully selected patients, based on available expertise, the individual patient, and valve characteristics until further insights are available from randomised clinical trials.

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Conflict of interest statement

A. Kalra is the Chief Executive Officer and Creative Director of makeadent.org. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Definitions of outcomes.

Supplementary Appendix 2. Variables used in propensity model 1 for in-hospital outcomes and 30-day outcomes.

Supplementary Appendix 3. Variables used in propensity model 2 for 180-day outcomes.

Supplementary Appendix 4. Information on weighting sample.

Supplementary Appendix 5. Model building for predictors of all-cause readmission.

Supplementary Figure 1. Balance of covariates before and after matching for in-hospital and 30-day outcomes.

Supplementary Figure 2. Balance of covariates before and after matching for 6-month outcomes.

Supplementary Table 1. CODES of variables and outcomes.

Supplementary Table 2. Breakdown of procedural complications of in-hospital outcomes.

Supplementary Table 3. Breakdown of 30-day outcomes.

Supplementary Table 4. Reasons for 30-day readmission.

Supplementary Table 5. Reasons for 6-month readmission.

Supplementary Table 6. Multivariable model for predictors of 30-day and 6-month readmission in ViV TAVI and repeat SAVR.

Supplementary Table 7. Subgroup analysis for 30-day readmission in ViV TAVI versus repeat SAVR.

Supplementary Table 8. Trend of use of ViV TAVI, repeat SAVR and 30-day readmission by quarter from 2016-2018.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244EIJ-D-21-00472

Supplementary data

Supplementary Appendix 1. Definitions of outcomes

Stroke – a composite of acute ischaemic, acute postoperative and acute haemorrhagic stroke.

Cardio-respiratory complication – a composite of pneumothorax, other respiratory complications including aspiration pneumonia, need of mechanical ventilation, post-procedural cardiogenic shock, use of vasopressors, use of mechanical circulatory support, cardiac arrest, cardiac tamponade, pericardial effusion, haemopericardium, pericardiocentesis, cardiotomy, pericardiotomy, thoracotomy.

Vascular complications – a composite of vessel repair, injury.

Major bleeding – a composite of gastrointestinal bleeding, urinary bleeding, haemoptysis, epistaxis, intracranial bleeding, postoperative bleeding, unspecified bleeding.

Major adverse cardiac events (MACE) – a composite of MI, stroke, heart failure, cardiogenic shock, cardiac arrest, arrhythmia, death during the first readmission.

Arrhythmia – a composite of ventricular tachycardia, fibrillation, supraventricular tachycardia, atrial flutter, fibrillation, complete heart block.

Major bleeding/vascular complications – a composite of major bleeding as described above, vascular complications and need of blood transfusion during second admission.

Non-cardiac infection - a composite of pneumonia, bacteraemia, sepsis.

Procedural complications – a composite of valvular complications, iatrogenic complications, pericardial complications, pacemaker implantation, wound dehiscence, AKI, pericardiotomy, cardiotomy, or thoracotomy.

Falsification endpoint – a composite of gastrointestinal infection and urinary tract infection.

Supplementary Appendix 2. Variables used in propensity model 1 for in-hospital outcomes and 30-day outcomes

Variables used to generate propensity score

Age, gender, primary payer, median household income, hypertension, hyperlipidaemia, peripheral vascular disease, ischaemic cardiomyopathy, prior CABG, history of defibrillator or pacemaker, stroke, TIA, atrial fibrillation, chronic heart failure, chronic lung disease, chronic liver disease, chronic kidney disease, alcohol abuse, coagulopathy, Elixhauser Comorbidity Index, hospital categorisation by procedural volume and hospital location.

Variables in the double robust method

All variables to generate propensity score, diabetes, obesity, prior PCI, admission (elective/non-elective), fluid and electrolyte imbalance, day of admission (weekday/weekend), teaching status of hospital, hospital by bed size.

Supplementary Appendix 3. Variables used in propensity model 2 for 180-day outcomes

Variables used to generate propensity score

Age, gender, hypertension, diabetes, hyperlipidaemia, peripheral vascular disease, ischaemic cardiomyopathy, stroke, TIA, chronic heart failure, chronic pulmonary disease, chronic liver disease, chronic renal failure, history of percutaneous coronary intervention, coronary artery bypass graft, atrial fibrillation.

Variables in the double robust method

All variables to generate propensity score, obesity, admission (elective/non-elective), fluid and electrolyte imbalance, day of admission (weekday/weekend), teaching status of hospital, hospital by bed size.

Supplementary Appendix 4. Model building for predictors of all-cause readmission

First, we conducted univariable logistic regression for all covariates. Covariates with $p<0.15$ and clinically meaningful covariates were selected in the final model. A similar method was used for 30-day, 6-month readmission for ViV TAVI and repeat SAVR, separately.

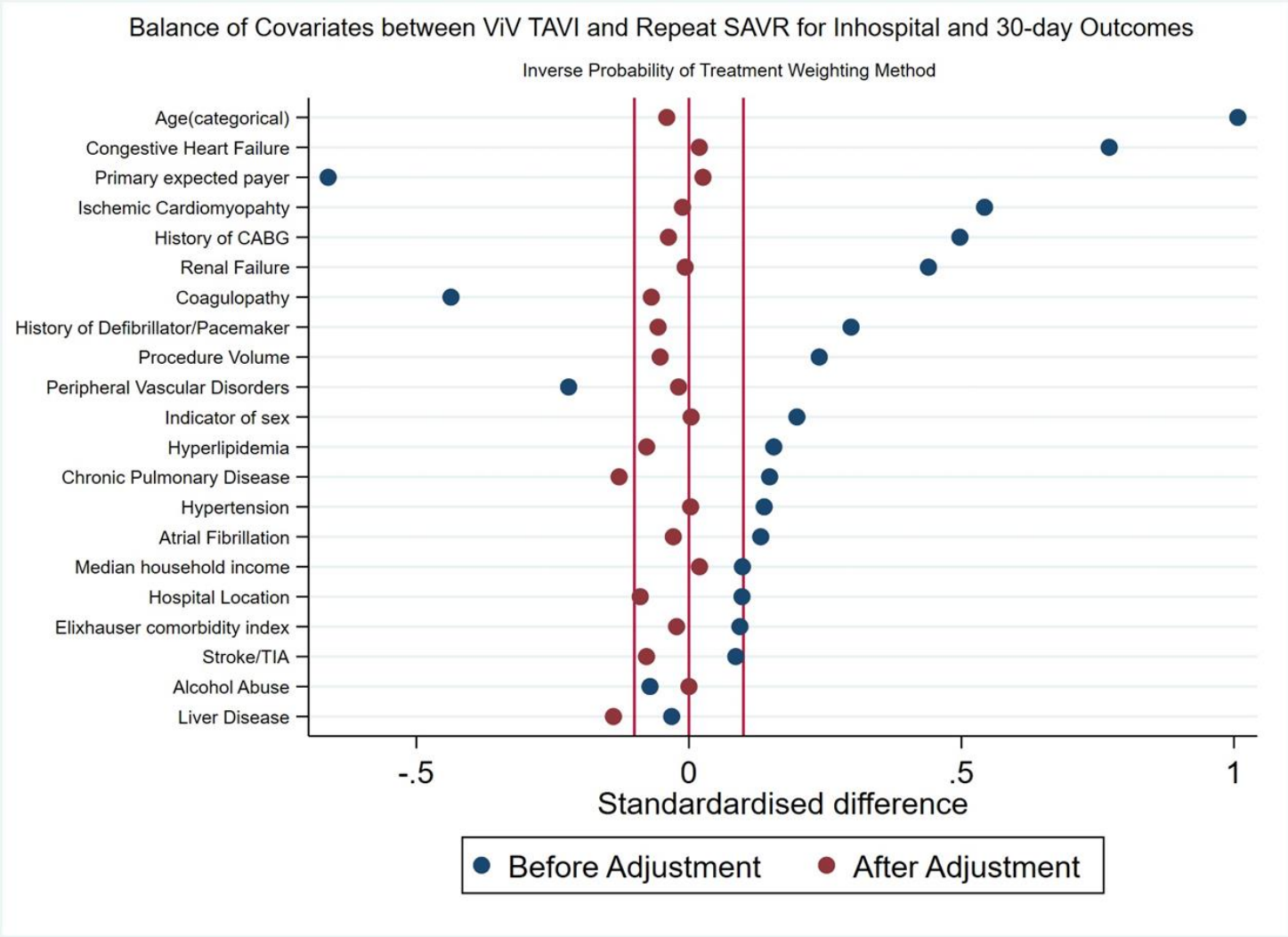
Supplementary Appendix 5. Information on weighting sample

To determine discharge-level weights, the number of discharges for the target universe and the sampling frame were summarised by stratum. Each stratum was defined by hospital characteristics (census region, urban/rural location, hospital teaching status, size of the hospital defined by the number of beds, type of ownership) and patient characteristics (sex and five age groups [0, 1-17, 18-44, 45-64, and 65 and older]). Within each stratum, *s*, each NRD inpatient admission received a weight:

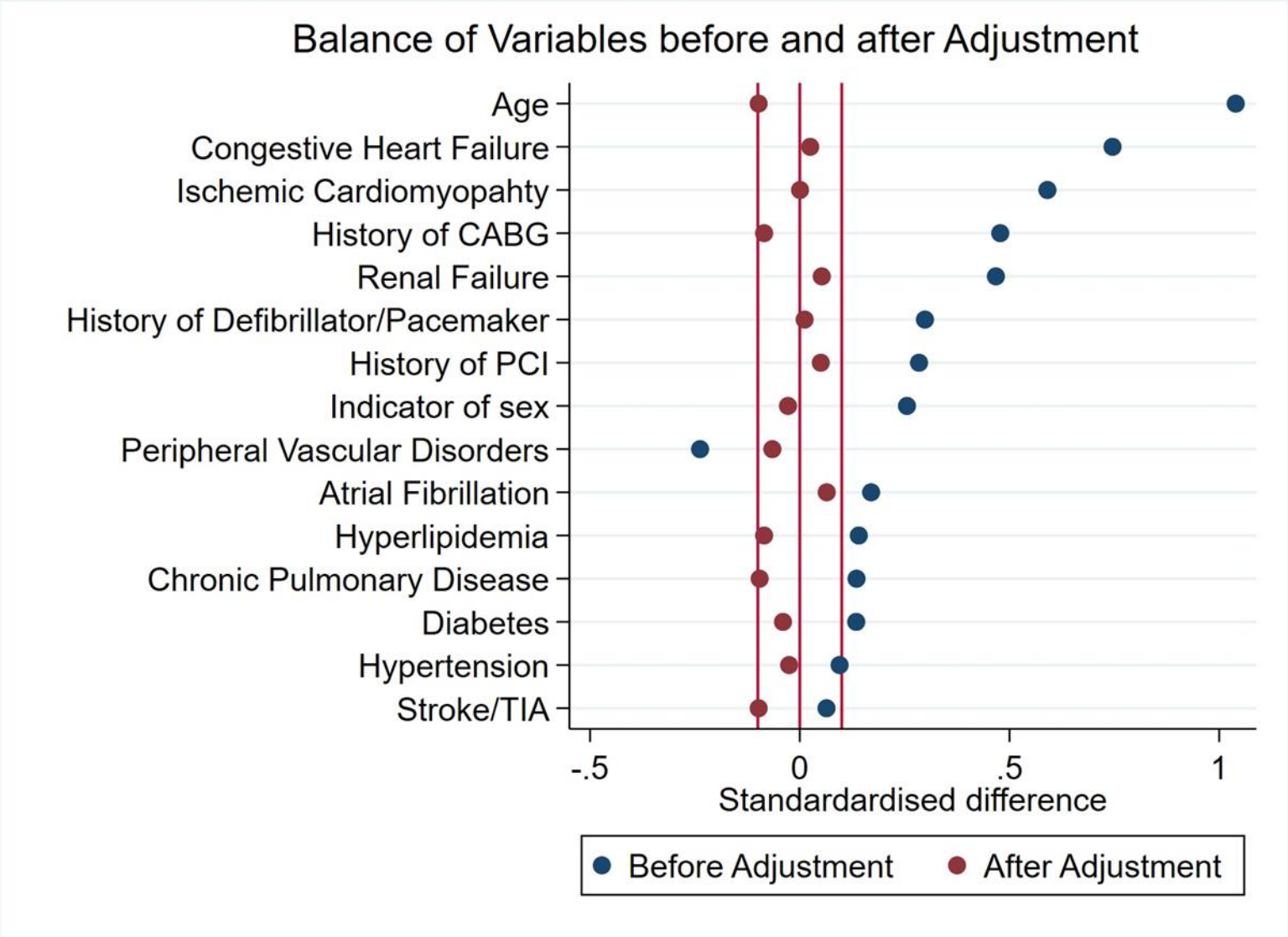
$$DISCWT_{i,j} = Ns(universe)_{i,j} \div Ns(sample)_{i,j}$$

where $Ns(universe)_{i,j}$ represents the number of inpatient discharges at community hospitals that were not a rehabilitation or LTAC hospital in the universe within stratum *s* for sex *i* and age group *j*; $Ns(sample)_{i,j}$ is the number of inpatient discharges in the sampling frame for sex *i* and age group *j*. Age group *j* included ages 0, 1-17, 18-44, 45-64, and 65 and older. Therefore, each discharge's weight ($DISCWT_{i,j}$) is equal to the number of inpatient discharges it represents in stratum *s* for sex *i* and age group *j* during that year.

(https://www.hcup-us.ahrq.gov/db/nation/nrd/Introduction_NRD_2010-2018.jsp#weights)



Supplementary Figure 1. Balance of covariates before and after matching for in-hospital and 30-day outcomes.



Supplementary Figure 2. Balance of covariates before and after matching for 6-month outcomes.

Supplementary Table 1. CODES of variables and outcomes.

Variables	ICD-10 CODES
History of prosthetic heart valve	Z95.2
Mitral valve disease	I05, I34
Tricuspid valve disease	I07, I36, Q22.4, Q22.8, Q22.9
Pulmonary valve disease	I37, Q22.0 – Q22.3
Mitral and tricuspid valve disease	I08.1
Infective endocarditis	I33.0, I33.9, I38
TAVR	02RF37H 02RF38H 02RF3J 02RF3KH, 02RF37Z 02RF38Z 02RF3JZ 02RF3KZ
SAVR	02RF07Z 02RF08Z. 02RF0KZ 02RF47Z 02RF48Z. 02RF4JZ 02RF4KZ 02RF0JZ
Coronary artery bypass surgery	02100, 02110, 02120, 02130
Mitral valve surgery	02UG07Z, 02NG0ZZ, 027G04Z, 02QG0ZZ, 02UG08Z, 02UG0JZ, 02UG0KZ, 025G0ZZ, 027G0DZ, 027G0ZZ, 02BG0ZX, 02BG0ZZ, 02RG07Z, 02RG08Z, 02RG0JZ, 02RG0KZ, 02VG0ZZ, 02CG0ZZ, 02WG07Z, 02WG08Z, 02WG0JZ, 02WG0KZ
Tricuspid valve surgery	02WH0KZ, 02WH07Z, 02WH0JZ, 027H04Z, 02RH08Z, 02TH0ZZ, 02RH0JZ, 02RH07Z, 02BH0ZZ, 02BH0ZX, 027H0ZZ, 027H0DZ, 025H0ZZ, 02UH0KZ, 02UH0JZ, 02UH08Z, 02UH07Z, 02QH0ZZ, 02NH0ZZ
Pulmonary valve surgery	02UJ0KZ, 027J04Z, 02NJ0ZZ, 02QJ0ZZ, 02UJ07Z, 02UJ08Z, 02UJ0JZ, 027J0DZ, 027J0ZZ, 02BJ0ZX, 02BJ0ZZ, 02RJ07Z, 02RJ0JZ, 02CJ0ZZ, 027J04Z, 02RJ08Z, 02RJ0KZ, 02WJ08Z, 02WJ0JZ, 02WJ07Z, 02WJ0KZ
Atrioventricular septum closure	02Q5, 02QM
Prior MI	I25.2
Prior PCI	Z98.61
Prior CABG	Z95.1
Prior pacemaker	Z950
Cardiogenic shock	R57.0
Ischaemic heart disease	I24.8, I24.9, I25.1, I25.10, I25.11, I25.110, I25.111, I25.118, I25.119, I25.2, I25.5, I25.6, I25.8, I25.810, I25.89, I25.9, I25.82, I25.83,

	I25.84, I25.41, I25.42, I25.700, I25.701, I25.708, I25.709, I25.710, I25.711, I25.718, I25.719, I25.720, I25.721, I25.728, I25.729, I25.730, I25.731, I25.738, I25.739, I25.790, I25.791, I25.798, I25.799
Stroke/TIA	I69.3, Z86.73
Atrial fibrillation	I48, I48.0, I48.1, I48.2, I48.4, I48.91
Outcomes	
Acute PE	I82.619, I82.629, I82.609, I82.A19, I82.B19, I82.C19 I82.290, I82.890, I82.90 I26.99, I26.92
Respiratory complication	
Pneumothorax	J95.811
Other iatrogenic respiratory complications (including postoperative aspiration pneumonia)	J95.89, J95.88
AKI	N170, N171, N172, N178, N179, N19, N990, R34
HD	5A1D70Z, 5A1D80Z, 5A1D90Z
Open cardiac surgery	
Pericardiotomy	02CN0ZZ 02NN0ZZ 0W9D00Z 0W9D0ZX 0W9D0ZZ 0WCD0ZZ
Cardiotomy	02C60ZZ 02C70ZZ 02C80ZZ 02C90ZZ 02CK0ZZ 02CL0ZZ 02PA0YZ 02WA0YZ
Thoracotomy	0W9800Z 0W980ZZ 0W9830Z 0W983ZZ 0W9840Z 0W984ZZ 02JA0ZZ 0WJC0ZZ 0W9C00Z 0W9C0ZZ 0WCC0ZZ
Pericardial complications	
Cardiac tamponade	I314
Haemopericardium	I312
Need of pericardiocentesis	0W9C30Z, 0W9C3ZZ 0W9D30Z, 0W9D3ZX, 0W9D3ZZ 0W9D40Z, 0W9D4ZX, 0W9D4ZZ
Post-procedural cardiogenic shock	T8111x
In-hospital cardiac arrest	5A12012
Mechanical ventilation >24 hrs	5A1955Z, 5A1945Z
Vasopressor use	3E030XZ, 3E033XZ, 3E040XZ, 3E043XZ, 3E050XZ, 3E053XZ, 3E060XZ, 3E063XZ
Acute stroke	
Intracranial bleed	TRUNK I60, I61, I62, I690, I691, I692
Systemic embolism	I63, G46
Haemorrhagic stroke	I61, I629
Postoperative stroke or TIA	I97810, I97811, I97820, I97821

Valve-related complications	
Moderate to severe paravalvular leak (regurgitation) of valve	T8203, T82223
Displacement of valve	T8202, T82222
Infection of valve	T826
Breakdown of valve	T8201, T82221
Unspecified valve complications	T8209, T82228
Bleeding	
Postoperative haemorrhage or haematoma	I97418, I97618, I97620, I97621, I97638, D62, L7602, L7622, L7632, M96811, M96831, M96841
Blood transfusion	30243N0 30243N1 30243P0 30243P1 30243H0 30243H1 30240N0 30240N1 30240P0 30240P1 30240H0 30240H1 30230H0 30230H1 30230N0 30230N1 30230P0 30230P1 30233N0 30233N1 30233P0 30233P1
Haemoperitoneum	K66.1
GI bleed	K2211, K250, K252, K254, K256, K2901, K2921, K2931, K2941, K2951, K2961, K2971, K2981, K2991, K260, K262, K264, K266, K270, K272, K274, K276, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K51011, K51211, K51311, K51411, K51511, K51811, K51911, K50011, K50111, K50811, K50911, K625, K5521
GU bleed	R31.0, R31.9
Haemoptysis	R04.2
Epistaxis	R04.0
Unspecified haemorrhage	R58
Intracranial bleed	I60, I61, I62, I690, I691, I692

Elixhauser comorbidities were used for the rest of the baseline variables.

Supplementary Table 2. Breakdown of procedural complications of in-hospital outcomes.

Procedural outcomes	ViV TAVI (N=3,724)		Repeat SAVR (N=3,045)		OR	95% CI		*p*-value
Cardiac tamponade/effusion	45	1.2%	73	2.4%	0.40	0.13	2.27	0.489
Pericardiocentesis	44	1.2%	11	0.4%	2.61	0.99	6.86	0.053
Any pericardial complications	64	1.7%	79	2.6%	0.72	0.48	1.08	0.109
Cardiothoracic surgery	16	0.4%	169	5.6%	0.10	0.05	0.22	<0.001

Supplementary Table 3. Breakdown of 30-day outcomes.

	ViV TAVI (N=3,676)		Repeat SAVR (N=2,941)		HR	95% CI		*p*-value
Arrhythmia	39	1.0%	35	1.2%	1.22	0.52	2.90	0.649
Atrial fibrillation	18	0.5%	26	0.9%	0.50	0.20	1.30	0.154
Stroke	17	0.5%	<10	0.3%	2.68	0.67	10.72	0.163
Heart failure readmission	94	2.5%	41	1.4%	0.55	0.27	1.11	0.094
Death	35	0.9%	<10	0.3%	1.61	0.45	5.81	0.465
Gastrointestinal bleeding	12	0.3%	<10	0.3%	1.65	0.40	6.84	0.488
Major bleeding	47	1.3%	14	0.5%	1.83	0.70	4.81	0.218
Vascular complications	14	0.38 %	<10	0.07%	Not able to compute due to lack of enough events			
Pacemaker implantation*	25/2,507	1.0%	<10/2,446	0.12%	Not able to compute due to lack of enough events			

Hazard ratio (HR) of outcome with <10 events should be interpreted carefully due to lack of sufficient events of the outcome of interest; chance of type 2 error is present.

* We excluded patients who had pacemaker or defibrillator and who had pacemaker implantation during index admissions from denominator.

Supplementary Table 4. Reasons for 30-day readmission.

	TAVI (598)	Percentage	**Repeat SAVR (338)**	Percentage
Cardiac	**219**	**36.62%**	**115**	**34.02%**
Iatrogenic complications	<10	NA	<10	NA
Complete heart block	11	1.84%	<10	NA
Ventricular tachycardia/fibrillation	<10	NA	<10	NA
Atrial fibrillation	18	3.01%	26	7.69%
Supraventricular tachycardia	<10	NA	<10	NA
Sick sinus syndrome	<10	NA	<10	NA
AV block	12	2.01%	<10	NA
Syncope	<10	NA	<10	NA
Haemopericardium/tamponade	<10	NA	<10	NA
Heart failure	90	15.05%	39	11.54%
Myocardial infarction	<10	NA	<10	NA
Vascular complications	15	2.51%	<10	NA
Valvular complications	<10	NA	<10	NA
Pacemaker implantation	25	4.18%	<10	NA
Chest pain	<10	NA	13	3.9%
Shortness of breath	0	0%	<10	NA
Palpitation	0	0%	<10	NA
Non-cardiac	**379**	**64.88%**	**223**	**65.98%**
Stroke	17	3%	<10	NA
Wound dehiscence	0	0%	<10	NA
Respiratory complications	<10	NA	<10	NA
Acute kidney injury	<10	NA	<10	NA
COPD exacerbation	11	2%	<10	NA
Pneumonia	11	2%	<10	NA
Bacteraemia	<10	NA	<10	NA
Sepsis	41	7%	28	8.28%
Cellulitis	15	3%	<10	NA
Gastrointestinal infection	10	2%	<10	NA
Urinary tract infection	<10	NA	<10	NA
Major bleeding	47	8%	13	3.85%
Blood transfusion	90	15%	29	8.58%
Deep vein thrombosis	<10	NA	<10	NA
Pulmonary embolism	<10	NA	<10	NA

Note: numbers do not sum up to total 100% due to weighted numbers. Cell size of some causes are less than 10, which is not reported as per HCUP guidelines.

NA: not available due to event number being less than 10

Supplementary Table 5. Reasons for 6-month readmission.

	TAVI (644)		Repeat SAVR (402)	
Cardiac	**304**	**47.2%**	**231**	**57%**
Iatrogenic complications	<10	NA	<10	NA
Complete heart block	12	1.9%	<10	NA
Ventricular tachycardia/fibrillation	<10	NA	<10	NA
Atrial fibrillation	35	5.4%	45	11%
Supraventricular tachycardia	<10	NA	10	2%
Sick sinus syndrome	<10	NA	<10	NA
AV block	14	2.1%	<10	NA
Syncope	<10	NA	<10	NA
Haemopericardium/tamponade	<10	NA	16	4%
Heart failure	167	25.9%	75	19%
Myocardial infarction	22	3.4%	<10	NA
Vascular complications	20	3.1%	<10	NA
Valvular complication	<10	NA	<10	NA
Pacemaker implantation	39	6.1%	21	5%
Chest pain	<10	NA	13	3.2%
Shortness of breath	0	0%	<10	NA
Palpitation	0	0%	<10	NA
Non-cardiac	**344**	**52.8%**	**171**	**42.5%**
Stroke	32	5%	18	5%
Wound dehiscence	<10	NA	<10	NA
Respiratory complications	<10	NA	<10	NA
Acute kidney injury	15	2.3%	<10	NA
COPD exacerbation	15	2.3%	<10	NA
Pneumonia	30	4.7%	10	2%
Bacteraemia	<10	NA	<10	NA
Sepsis	91	14.2%	44	11%
Cellulitis	10	1.5%	<10	NA
Gastrointestinal infection	11	1.7%	<10	NA
Urinary tract infection	12	1.9%	<10	NA
Major bleeding	87	13.5%	31	8%
Blood transfusion	143	22.2%	53	13%
Deep vein thrombosis	<10	NA	<10	NA
Pulmonary embolism	<10	NA	<10	NA

Note: numbers do not sum up to total 100% due to weighted numbers. Cell size of some causes are less than 10, which is not reported as per HCUP guidelines.

NA: not available due to event number being less than 10

Supplementary Table 6. Multivariable model for predictors of 30-day and 6-month readmission in ViV TAVI and repeat SAVR.

Valve-in-valve transcatheter aortic valve implantation				
30-day predictors	**OR**	**95% CI**		***p*-value**
Age	0.99	0.97	1.01	0.348
Female gender	1.14	0.86	1.52	0.357
Diabetes	1.20	0.91	1.59	0.193
Stroke	1.08	0.77	1.53	0.651
Prior MI	0.61	0.39	0.93	0.021
Heart failure	1.55	1.05	2.28	0.026
Atrial fibrillation	1.37	1.06	1.78	0.017
Chronic kidney disease	1.36	1.00	1.86	0.052
Elixhauser Comorbidity Index	0.94	0.86	1.03	0.155
Low procedure volume hospital	1.22	0.94	1.57	0.136
Rehabilitation transfer	1.41	0.97	2.05	0.075
Discharged to other facilities	1.55	1.14	2.11	0.005
Length of stay (per 5 days)	1.08	1.02	1.15	0.015
Fluid and electrolyte imbalance	1.60	1.18	2.17	0.002
6-month predictors	**OR**	**95% CI**		***p*-value**
Age	0.99	0.98	1.01	0.43
Female gender	1.13	0.83	1.53	0.449
Medicare/Medicaid vs private insurance	0.63	0.36	1.10	0.105
Diabetes	1.55	1.07	2.25	0.02
Peripheral vascular disease	1.41	1.00	1.99	0.051
Prior MI	0.57	0.37	0.88	0.011
Stroke	1.16	0.82	1.64	0.414
Heart failure	1.34	0.87	2.04	0.182
Atrial fibrillation	1.89	1.39	2.57	<0.001

Chronic lung disease	1.25	0.87	1.79	0.22
Chronic kidney disease	1.24	0.89	1.73	0.196
Elixhauser Comorbidity Index	0.93	0.84	1.03	0.183
Private hospital	0.92	0.64	1.33	0.67
Low volume hospital	1.34	0.99	1.81	0.059
Rehabilitation transfer	1.70	1.13	2.56	0.011
Discharge to other facilities	1.54	1.12	2.11	0.007
Length of stay (per 5 days)	1.05	0.97	1.14	0.241
Elective vs non-elective admission	1.11	0.78	1.57	0.561
Weekend vs weekday admission	1.29	0.75	2.23	0.361
Fluid and electrolyte imbalance	1.41	1.00	1.98	0.047

Repeat surgical aortic valve replacement

30-day predictors	**OR**	**95% CI**		***p*-value**
Age	0.99	0.97	1.01	0.19
Female gender	0.90	0.64	1.26	0.535
Medicare/Medicaid vs private insurance	1.97	1.24	3.13	0.004
Diabetes	1.35	0.87	2.09	0.183
Stroke	0.66	0.37	1.17	0.153
Heart failure	1.29	0.88	1.88	0.197
Prior CABG	1.37	0.79	2.39	0.258
Chronic lung disease	1.81	1.22	2.68	0.003
Chronic kidney disease	1.62	1.05	2.49	0.029
Pulmonary circulation disorder	1.78	1.08	2.93	0.023
Elixhauser Comorbidity Index	0.92	0.82	1.03	0.133
Rehabilitation transfer	0.62	0.39	0.98	0.039
Discharge to other facilities	1.36	0.90	2.07	0.145
Length of stay (per 5 days)	1.07	1.01	1.15	0.032

Elective vs non-elective admission	1.12	0.70	1.79	0.64
Weekend vs weekday admission	1.25	0.67	2.33	0.483
6-month predictors	**OR**	**95% CI**		***p*-value**
Age	1.00	0.99	1.02	0.672
Female	0.88	0.61	1.27	0.499
Medicare/Medicaid vs private insurance	1.25	0.78	2.01	0.353
Higher household income	1.18	0.82	1.70	0.372
Diabetes	1.54	1.05	2.27	0.027
Ischaemic cardiomyopathy	1.00	0.68	1.48	0.995
Prior PCI	1.30	0.63	2.69	0.48
Chronic lung disease	1.59	1.05	2.39	0.027
Chronic kidney disease	1.79	1.13	2.84	0.013
Elixhauser Comorbidity Index	0.97	0.88	1.08	0.595
Large hospital (bed size)	1.37	0.91	2.05	0.133
Non-teaching	1.34	0.85	2.12	0.208
Non-private hospital	1.21	0.79	1.85	0.379
Discharge to other facilities	1.51	0.96	2.39	0.075
Length of stay (per 5 days)	1.04	0.95	1.13	0.415
Elective vs non-elective admission	1.27	0.82	1.98	0.282
Weekend vs weekday admission	1.49	0.85	2.62	0.161
Fluid and electrolyte imbalance	1.15	0.76	1.72	0.511

Supplementary Table 7. Subgroup analysis for 30-day readmission in ViV TAVI versus repeat SAVR.

Subgroups	aHR	95% CI		*p*-value	*p*-value for interaction
Gender					
Male	1.34	0.91	1.97	0.139	0.319
Female	1.65	1.07	2.53	0.023	
Primary expected payer					
Medicare/Medicaid	1.30	0.97	1.73	0.076	**0.013**
Private insurance	3.45	1.49	7.99	0.004	
Heart failure					
Absent	1.41	0.87	2.30	0.163	0.823
Present	1.46	1.03	2.07	0.032	
Renal failure					
Absent	1.43	0.99	2.06	0.054	0.44
Present	1.49	0.95	2.34	0.079	
Hospital by procedural volume					
Low volume hospital*	1.78	1.18	2.66	0.006	0.221
High volume hospital**	1.16	0.77	1.75	0.477	

* Low procedural volume – lower four quintiles in procedural volume.
** Higher procedural volume – highest fifth quintile in procedural volume.
aHR: adjusted hazard ratio; CI: confidence interval

Supplementary Table 8. Trend of use of ViV TAVI, repeat SAVR and 30-day readmission by quarter from 2016-2018.

	ViV TAVI (%)	Viv-TAVI 30-day readmission	Repeat SAVR (%)	Repeat SAVR 30-day readmission
Quarter 1, 2016	47.4%	20.1%	52.6%	12.0%
Quarter 2, 2016	52.9%	17.3%	47.1%	10.7%
Quarter 3, 2016	55.0%	17.7%	45.0%	14.5%
Quarter 4, 2016	49.0%	20.5%	51.0%	13.3%
Quarter 1, 2017	52.4%	15.0%	47.6%	12.8%
Quarter 2, 2017	55.0%	15.0%	45.0%	11.6%
Quarter 3, 2017	59.8%	21.0%	40.2%	8.3%
Quarter 4, 2017	55.2%	11.7%	44.8%	7.6%
Quarter 1, 2018	56.8%	16.4%	43.2%	14.9%
Quarter 2, 2018	55.3%	11.9%	44.7%	7.4%
Quarter 3, 2018	61.9%	15.8%	38.1%	10.3%
Quarter 4, 2018	58.0%	12.5%	43.0%	16.4%
	p for trend <0.001	*p* for trend - 0.057	*p* for trend - 0.001	*p* for trend - 0.605
	Rate of increase by quarter - 6.6%	Rate of decrease by quarter - 3.69%	Rate of decrease by quarter - 6.1%	Rate of decrease by quarter - 1.27%