SUPPLEMENTARY APPENDIX

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I. METHODS

Methods for Covariate Adjustment

Propensity score matching was selected *a priori* as the method for confounding adjustment. Other methods such as inverse probability of treatment weighting and regression adjustment were explored in preliminary analyses of the entire population on the falsification endpoints and mortality (no subgroups), with very similar results. Given the aim to evaluate subgroups, matching provided a transparent approach to identify small subgroups and evaluate covariate balance within subgroups. In addition, the extreme tails of the propensity distribution would be expected to generate large weights for some patients, which could be highly impactful to subgroup analyses (results may be sensitive to the weight of an individual). To preserve transparency and avoid sensitivity to large weights in the subgroup analyses, propensity matching was used throughout. This did not result in the systematic exclusion of any type of patients, as the propensity score distributions were overlapping. This did result in a reduction in sample size; however, the final sample size was still 10 times larger than previous clinical trials. Starting with very large registry samples that happened to include very different patients, propensity matching allowed us to identify a more comparable population that was still relatively large.

The propensity score was calculated by logistic regression for the probability of receiving transcatheter aortic valve replacement (TAVR), given measured covariates. Overlap in the covariate distribution and propensity scores between study groups was assessed. Since patients at the tails (<5%, >95%) of the propensity distribution were thought to represent individuals with an overwhelming likelihood of treatment with one or another of the two treatments, these patients were excluded. Propensity score matching was conducted in a 1:1 ratio, by greedy matching, using a caliper of 0.20 standard deviations in the linear predictor. The adequacy of the propensity model was confirmed by checking covariate balance before and after matching. Details are provided below.

Models for treatment on outcomes were fit to the matched sample using a robust empirical variance to account for matched pairs. Associations were estimated in pre-specified subgroups, along with 95% confidence intervals and tests of interaction. All subgroups that were tested are shown. To address the potential for unmeasured confounding, the analysis was repeated on two falsification endpoints: urinary tract infection and lower extremity fracture.

II. TABLES

Table S1. Covariate Definitions

Covariate	STS	TVT
Age, median (IQR)	Patient's age in years, at time of surgery	
Female	Patient with female gender identified at birth	
Race		
White	Patient’s race, as determined by the patient or family, includes white	
Black	Patient's race, as determined by the patient or family, includes black/African American. This includes a person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "negro" can be used in addition to "black or African American."	
Hispanic	Patient's race, as determined by the patient or family, includes Hispanic, Latino, or Spanish ethnicity	
Other	Patient's race, as determined by the patient or family, does not include white, black, or Hispanic	
Commercial insurance	Commercial insurance refers to all indemnity (fee-for-service) carriers and Preferred Provider Organizations (e.g., Blue Cross and Blue Shield).	
Body surface area, median (IQR)	Calculated as SQRT: (height [cm] x weight [kg]/3600)	
Dialysis	Patient is currently undergoing dialysis, including hemodialysis, peritoneal dialysis, and continuous veno-venous hemofiltration	
Prior MI	Patient has had at least one documented previous MI at any time prior to this surgery	
Recent	MI occurred ≤21 days	MI occurred <30 days
Old	MI occurred >21 days	MI occurred ≥30 days
Prior CV surgeries	Patient had open heart cardiac surgeries prior to this procedure. This includes open heart coronary artery bypass, or valve replacement/repairs.	

Resuscitation	Patient required CPR within one hour before the start of the operative procedure which includes the institution of anesthetic management.	"Sudden" cardiac arrest is the sudden cessation of cardiac activity so that the victim becomes unresponsive, with no normal breathing and no signs of circulation. If corrective measures are not taken rapidly, this condition progresses to sudden death. Cardiac arrest should be used to signify an event as described above that is reversed, usually by CPR, and/or defibrillation or cardioversion, or cardiac pacing. Sudden cardiac death should not be used to describe events that are not fatal.
Creatinine clearance, median (IQR)	Indicate the creatinine level closest to the date and time prior to the procedure, but prior to anesthetic management in mg/dL.	
Pre-operative atrial fibrillation/flutter	Indicate whether atrial fibrillation or flutter was present within thirty days of the procedure.	
LVEF, median (IQR)	Most recent determination prior to the surgical intervention documented on a diagnostic report. If a percentage range is reported, whole number mean is reported.	
Heart failure symptoms <2 weeks	Physician documentation that the patient has been in a state of heart failure within the past 2 weeks. Heart failure is defined as physician documentation or report of any of the following clinical symptoms of heart failure described as unusual dyspnea on light exertion, recurrent dyspnea occurring in the supine position, fluid retention; or the description of rales, jugular venous distension, pulmonary edema on physical exam, or pulmonary edema on chest x-ray presumed to be cardiac dysfunction. A low ejection fraction alone, without clinical evidence of heart failure does not qualify as heart failure.	
None or Class I	Patient has cardiac disease but without resulting limitations of ordinary physical activity. Ordinary physical activity (e.g., walking several blocks or climbing stairs) does not cause undue fatigue, palpitation, dyspnea, or anginal pain. Limiting symptoms may occur with marked exertion.	
Class II	Patient has cardiac disease resulting in slight limitation of ordinary physical activity. Patient is comfortable at rest. Ordinary physical activity such as walking more than two blocks or climbing more than one flight of stairs results in limiting symptoms (e.g., fatigue, palpitation, dyspnea, or anginal pain).	
Class III	Patient has cardiac disease resulting in marked limitation of physical activity. Patient is comfortable at rest. Less than ordinary physical activity (e.g., walking one to two level blocks or climbing one flight of stairs) causes fatigue, palpitation, dyspnea, or anginal pain.	

Class IV	Patient has dyspnea at rest that increases with any physical activity. Patient has cardiac disease resulting in inability to perform any physical activity without discomfort. Symptoms may be present even at rest. If any physical activity is undertaken, discomfort is increased.	
Chronic lung disease	Patient has a history of chronic lung disease with severity documented as one of the following:	
None	No documented chronic lung disease	
Mild	Mild: FEV1 60% to 75% of predicted, and/or on chronic inhaled or oral bronchodilator therapy.	
Moderate	Moderate: FEV1 50% to 59% of predicted, and/or on chronic steroid therapy aimed at lung disease	
Severe	Severe: FEV1 <50% predicted, and/or Room Air pO2 < 60 or Room Air pCO2 > 50.	
Home oxygen use	Patient uses supplemental oxygen at home.	
Prior stroke	Patient has a history of stroke (i.e., any confirmed neurological deficit of abrupt onset caused by a disturbance in blood flow to the brain) that did not resolve within 24 hours.	Defined as an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction.
Cerebrovascular disease without prior CVA	Patient has a history of loss of neurological function that was abrupt in onset but with complete return of function within 24 hours.	Patient has a history of a transient ischemic attack, defined as a transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia, without acute infarction.
Diabetes	History of diabetes mellitus according to the American Diabetes Association criteria regardless of duration of disease or need for antidiabetic agents.	
None	No treatment for diabetes	
Insulin	Insulin treatment (includes any combination with insulin).	
Non-insulin	Oral agent treatment (includes oral agent with/without diet treatment).	
CAD: # diseased vessels	Number of diseased major native coronary vessel systems: LAD system, circumflex system, and/or right system with ≥50% narrowing of any vessel preoperatively. Left main disease (≥50%) is counted as TWO vessels (LAD and circumflex, which may include a ramus intermedius). For example, left main and RCA would count as three total.	
Left main CAD	Left main CAD is present when there is ≥50% compromise of vessel diameter preoperatively.	
Pre-operative IABP/inotropes	Patient had a mechanical assist device in place at the start of the procedure. Medications the patient received 24 hours prior to the procedure.	

Prior shock	Patient was, at the time of procedure, in a clinical state of end organ hypoperfusion due to cardiac failure according to the following criteria: persistent hypotension (systolic blood pressure <80–90 or mean arterial pressure 30 mmhg lower than baseline) and severe reduction in cardiac index (<1.8 without support or <2.2 with support).
Hypertension	Patient has a diagnosis of hypertension, documented by one of the following: a. Documented history of hypertension diagnosed and treated with medication, diet and/or exercise b. Prior documentation of blood pressure >140 mmHg systolic or 90 mmHg diastolic for patients without diabetes or chronic kidney disease, or prior documentation of blood pressure >130 mmHg systolic or 80 mmHg diastolic on at least 2 occasions for patients with diabetes or chronic kidney disease c. Currently on pharmacologic therapy to control hypertension.
Immunosuppression	Indicate whether immunocompromise is present due to immunosuppressive medication therapy within 30 days preceding the operative procedure or existing medical condition (see training manual). This includes, but is not limited to systemic steroid therapy, anti-rejection medications, and chemotherapy. This does not include topical steroid applications, one time systemic therapy, inhaled steroid therapy or preoperative protocol.
Aortic insufficiency (moderate/severe)	Highest severity of aortic insufficiency between 12 months prior to the procedure and start of the procedure. Moderate: Qualitative Measurements: Angiographic grade of 2+; Color Doppler jet width greater than mild but no signs of severe aortic regurgitation (insufficiency); Dopplar vena contracta width 0.3–0.6 cm. Quantitative Measures (cath or echo): Regurgitant volume 30-59 ml/beat; Regurgitant fraction 30–49%;Regurgitant orifice area 0.10–0.29 cm(2) Severe: Qualitative Measurements: Angiographic grade of 3–4+; Color Doppler jet width (Central jet) >65% of LVOT; Dopplar vena contracta width >0.6 cm. Quantitative Measures (cath or echo): Regurgitant volume ≥60 ml/beat; Regurgitant fraction ≥50%; Regurgitant orifice area ≥0.30 cm(2)
Mitral insufficiency (moderate/severe)	Severity of mitral valve regurgitation according to the American Society of Echocardiography Guidelines integrated approach.
Tricuspid insufficiency (moderate/severe)	Evidence of tricuspid valve regurgitation.
ICD	Patient had a previous implant of an ICD. This does not include lead placement only.

Prior PCI	Previous PCI was performed any time prior to this surgical procedure. PCI refers to those treatment procedures that unblock narrowed coronary arteries without performing surgery. PCI may include, but is not limited to: 1. Balloon catheter angioplasty, percutaneous transluminal coronary angioplasty (PTCA) 2. Rotational atherectomy 3. Directional atherectomy 4. Extraction atherectomy 5. Laser atherectomy 6. Intracoronary stent placement
Peripheral vascular disease	Patient has a history of peripheral arterial disease (includes upper and lower extremity, renal, mesenteric, and abdominal aortic systems). This can include: 1. Claudication either with exertion or at rest 2. Amputation for arterial vascular insufficiency 3. Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping) 4. Documented aortic aneurysm with or without repair 5. Positive noninvasive test (e.g., ankle brachial index ≤0.9, ultrasound, magnetic resonance, or computed tomography imaging of >50% diameter stenosis in any peripheral artery (i.e., renal, subclavian, femoral, iliac) or angiographic imaging. Peripheral arterial disease excludes disease in the carotid or cerebrovascular arteries.
Aortic valve mean gradient, median (IQR)	Highest MEAN gradient (in mmHg) across the aortic valve obtained from an echocardiogram or angiogram preoperatively between 12 months to start of procedure.

Status (elective, urgent)	Clinical status of the patient prior to entering the operating room: Elective: The patient's cardiac function has been stable in the days or weeks prior to the operation. The procedure could be deferred without increased risk of compromised cardiac outcome. Urgent: Procedure required during same hospitalization in order to minimize chance of further clinical deterioration. Examples include but are not limited to: Worsening, sudden chest pain, CHF, acute myocardial infarction (AMI), anatomy, IABP, unstable angina (USA) with intravenous (IV) nitroglycerin (NTG) or rest angina. Emergent: Patients requiring emergency operations will have ongoing, refractory (difficult, complicated, and/or unmanageable) unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except cardiac surgery. An emergency operation is one in which there should be no delay in providing operative intervention. Emergent Salvage: The patient is undergoing CPR en route to the OR or prior to anesthesia induction or has ongoing ECMO to maintain life.
Hematocrit	Pre-operative hematocrit level at the date and time closest to surgery but prior to anesthetic management (induction area or operating room).
Pre-op total albumin, median (IQR)	The total albumin closest to the date and time prior to surgery but prior to anesthetic management (induction area or operating room).
Prior CABG	Patient had a previous coronary bypass graft prior to the current admission.
Prior aortic valve replacement	Patient had a previous surgical aortic valve replacement prior to the current admission.
PA systolic pressure, median (IQR)	Highest PA systolic pressure recorded prior to SAVR or TAVR procedure.
Mitral stenosis	Patient has mitral stenosis present.
Cardiac presentation	Worst type of angina present prior to this procedure: 1. No symptoms; 2. Symptoms unlikely to be ischemia; 3. Stable angina; 4. Unstable angina; 5. Non-ST Elevation MI; 6. ST Elevation MI
CAD = coronary artery disease; CPR = cardiopulmonary resuscitation; CV = cardiovascular; CVA = cerebrovascular accident; FEV1 = forced expiratory volume in 1 second; IABP = intra-aortic balloon pump; IQR = interquartile range; LAD = left anterior descending; LVEF = left ventricular ejection fraction; MI = myocardial infarction; RCA = right circumflex artery; SQRT = square root; STS = Society of Thoracic Surgeons; TVT = Transcatheter Valve Therapy (Registry)	

Table S2. Baseline Characteristics Before and After Matching

Continuous variables are reported as medians, along with the 25th and 75th percentiles, and categorical variables include the number and percent in a category. Standardized differences were computed to summarize covariate balance across the SAVR and TAVR interventions.

	Before Propensity Matching				After Propensity Matching		
	Overall (N=40,528)	**SAVR (N=22,618)**	**TAVR (N=17,910)**	**SD TAVR vs. SAVR**	**SAVR (N=4,732)**	**TAVR (N=4,732)**	**SD TAVR vs. SAVR**
Age, median (IQR)	81 (76,85)	80 (75,84)	83 (79,87)	52.87%	82 (77,85)	81 (77,85)	-1.01%
Female	19,008 (46.9)	10,270 (45.4)	8,738 (48.8)	6.78%	2,278 (48.1)	2,256 (47.7)	-0.93%
Race				11.57%			2.70%
White	37,210 (91.8)	20,708 (91.6)	16,502 (92.1)		4,355 (92.0)	4,354 (92.0)	
Black	1,332 (3.3)	730 (3.2)	602 (3.4)		151 (3.2)	165 (3.5)	
Hispanic	1,215 (3.0)	633 (2.8)	582 (3.2)		159 (3.4)	145 (3.1)	
Other	771 (1.9)	547 (2.4)	224 (1.3)		67 (1.4)	68 (1.4)	
Commercial insurance	24,612 (60.7)	13,415 (59.3)	11,197 (62.5)	6.58%	2,890 (61.1)	2,861 (60.5)	-1.26%
Body surface area, median (IQR)	1.9 (1.7,2.0)	1.9 (1.7,2.1)	1.8 (1.7,2.0)	-23.17%	1.9 (1.7,2.1)	1.9 (1.7,2.0)	0.04%
Dialysis	1,511 (3.7)	752 (3.3)	759 (4.2)	4.79%	186 (3.9)	179 (3.8)	-0.77%
Prior MI				37.36%			2.21%
Recent	2,637 (6.5)	2,188 (9.7)	449 (2.5)		161 (3.4)	173 (3.7)	
Old	7,853 (19.4)	3,695 (16.3)	4,158 (23.2)		954 (20.2)	924 (19.5)	
Prior CV surgeries	10,080 (24.9)	4,132 (18.3)	5,948 (33.2)	34.69%	1,484 (31.4)	1,406 (29.7)	-3.58%
Resuscitation	139 (0.3)	102 (0.5)	37 (0.2)	-4.27%	16 (0.3)	15 (0.3)	-0.37%
Creatinine clearance, median (IQR)	1.1 (0.9,1.4)	1.1 (0.9,1.4)	1.1 (0.9,1.5)	9.89%	1.1 (0.9,1.4)	1.1 (0.9,1.5)	-0.32%
Pre-operative atrial fibrillation/flutter	13,542 (33.4)	5,135 (22.7)	8,407 (46.9)	52.60%	1,619 (34.2)	1,572 (33.2)	-2.10%
LVEF, median (IQR)	55.0 (45.0,55.0)	55.0 (50.0,55.0)	55.0 (45.0,55.0)	-12.74%	55.0 (45.0,55.0)	55.0 (45.0,55.0)	-1.10%
Heart failure symptoms <2 weeks				83.18%			4.28%
None or Class I	11,246 (27.7)	10,731 (47.4)	515 (2.9)		447 (9.4)	335 (7.1)	
Class II	5,847 (14.4)	3,336 (14.7)	2,511 (14.0)		947 (20.0)	995 (21.0)	
Class III	17,282 (42.6)	6,137 (27.1)	11,145 (62.2)		2,499 (52.8)	2,509 (53.0)	
Class IV	6,153 (15.2)	2,414 (10.7)	3,739 (20.9)		839 (17.7)	893 (18.9)	
Chronic lung disease				27.62%			1.62%

None	23,777 (58.7)	14,719 (65.1)	9,058 (50.6)		2,793 (59.0)	2,784 (58.8)	
Mild	7,349 (18.1)	3,938 (17.4)	3,411 (19.0)		872 (18.4)	866 (18.3)	
Moderate	4,957 (12.2)	2,256 (10.0)	2,701 (15.1)		564 (11.9)	558 (11.8)	
Severe	4,445 (11.0)	1,705 (7.5)	2,740 (15.3)		503 (10.6)	524 (11.1)	
Home oxygen use	3,373 (8.3)	985 (4.4)	2,388 (13.3)	32.02%	385 (8.1)	378 (8.0)	-0.54%
Prior stroke	4,476 (11.0)	2,263 (10.0)	2,213 (12.4)	7.47%	524 (11.1)	506 (10.7)	-1.22%
Cerebrovascular disease without prior CVA	6,940 (17.1)	2,849 (12.6)	4,091 (22.8)	27.08%	725 (15.3)	712 (15.0)	-0.77%
Diabetes				10.95%			1.45%
None	23,485 (57.9)	12,558 (55.5)	10,927 (61.0)		2,726 (57.6)	2,743 (58.0)	
Insulin	1,141 (2.8)	751 (3.3)	390 (2.2)		137 (2.9)	126 (2.7)	
Non-insulin	6,060 (15.0)	3,433 (15.2)	2,627 (14.7)		745 (15.7)	746 (15.8)	
CAD: # diseased vessels				16.17%			0.95%
None	13,277 (32.8)	6,686 (29.6)	6,591 (36.8)		2,292 (48.4)	2,326 (49.2)	
1	7,528 (18.6)	4,031 (17.8)	3,497 (19.5)		770 (16.3)	757 (16.0)	
2	7,249 (17.9)	4,446 (19.7)	2,803 (15.7)		520 (11.0)	512 (10.8)	
3	12,474 (30.8)	7,455 (33.0)	5,019 (28.0)		1,150 (24.3)	1,137 (24.0)	
Left main coronary artery disease	5,351 (13.2)	3,408 (15.1)	1,943 (10.8)	-12.59%	424 (9.0)	434 (9.2)	0.74%
Pre-operative IABP/inotropes	1,172 (2.9)	644 (2.8)	528 (2.9)	0.60%	128 (2.7)	123 (2.6)	-0.66%
Prior shock	215 (0.5)	129 (0.6)	86 (0.5)	-1.25%	28 (0.6)	31 (0.7)	0.81%
Hypertension	36,907 (91.1)	20,624 (91.2)	16,283 (90.9)	-0.94%	4,291 (90.7)	4,285 (90.6)	-0.43%
Immunosuppression	3,250 (8.0)	1,198 (5.3)	2,052 (11.5)	22.38%	363 (7.7)	344 (7.3)	-1.53%
Aortic insufficiency (moderate/severe)	7,949 (19.6)	4,700 (20.8)	3,249 (18.1)	-6.67%	956 (20.2)	947 (20.0)	-0.47%
Mitral insufficiency (moderate/severe)	10,333 (25.5)	3,951 (17.5)	6,382 (35.6)	42.03%	1,166 (24.6)	1,125 (23.8)	-2.02%
Tricuspid insufficiency (moderate/severe)	7,354 (18.1)	2,488 (11.0)	4,866 (27.2)	42.04%	803 (17.0)	783 (16.5)	-1.13%
ICD	1,510 (3.7)	465 (2.1)	1,045 (5.8)	19.50%	185 (3.9)	179 (3.8)	-0.66%
Prior PCI	11,650 (28.7)	5,188 (22.9)	6,462 (36.1)	29.12%	1,278 (27.0)	1,233 (26.1)	-2.15%
Peripheral vascular disease	10,312 (25.4)	4,711 (20.8)	5,601 (31.3)	23.97%	1,138 (24.0)	1,113 (23.5)	-1.24%
Aortic valve mean gradient, median (IQR)	42.0 (34.0,50.0)	42.0 (33.0,51.0)	42.0 (35.0,49.0)	-4.68%	42.0 (35.0,52.0)	42.0 (36.0,52.0)	0.46%
Status (elective, urgent)	30,806 (76.0)	14,542 (64.3)	16,264 (90.8)	67.02%	3,871 (81.8)	3,813 (80.6)	-3.14%

Hematocrit	36.0 (32.4,39.3)	36.6 (33.0,40.0)	35.4 (31.5,39.0)	-21.51%	36.0 (32.3,39.5)	36.0 (32.1,39.6)	0.27%
Pre-op total albumin, median (IQR)	3.7 (3.5,4.0)	3.7 (3.5,4.0)	3.7 (3.5,3.9)	-8.00%	3.7 (3.5,4.0)	3.7 (3.5,4.0)	-0.50%
CAD requiring CABG	19,967 (49.3)	14,447 (63.9)	5,520 (30.8)	-70.15%	1,565 (33.1)	1,523 (32.2)	-1.89%
Prior aortic valve replacement	1,316 (3.2)	654 (2.9)	662 (3.7)	4.51%	219 (4.6)	214 (4.5)	-0.51%
PA systolic pressure, median (IQR)	41.0 (37.0,45.0)	41.0 (36.0,41.0)	41.0 (39.0,50.0)	29.44%	41.0 (37.0,46.0)	41.0 (37.0,46.0)	1.09%
Mitral stenosis	2,069 (5.1)	673 (3.0)	1,396 (7.8)	21.47%	204 (4.3)	220 (4.6)	1.63%
Cardiac presentation	4,316 (10.6)	3,662 (16.2)	654 (3.7)	-42.90%	285 (6.0)	295 (6.2)	0.88%
SD = standardized difference; All other abbreviations can be found in Table S1.							

III. FIGURES

Figures S1. Consort Diagram

This figure displays the beginning study population, through exclusions, to the final study population.

CABG = coronary artery bypass grafting; PS = propensity score; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; TVT = Transcatheter Valve Therapy (Registry)

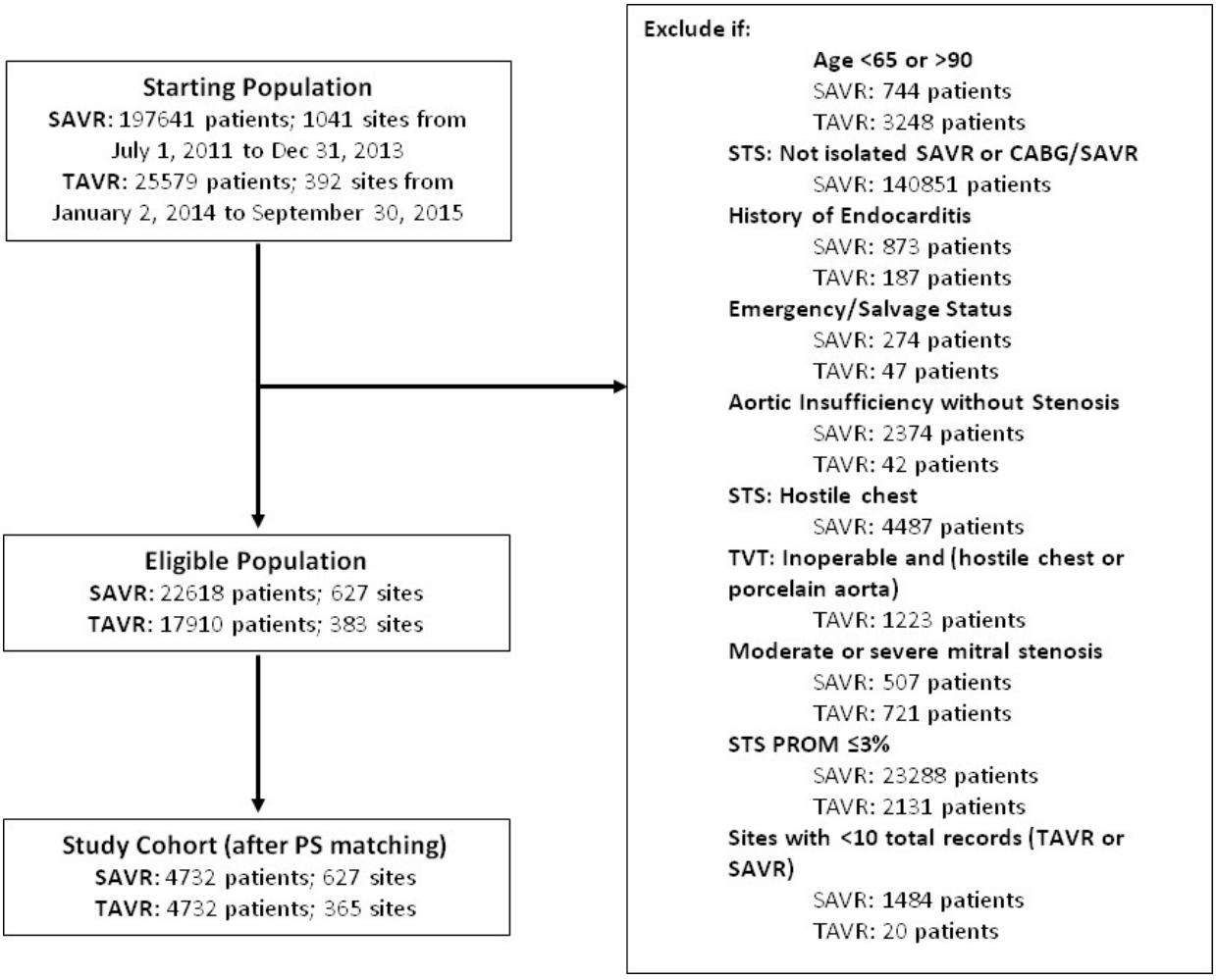
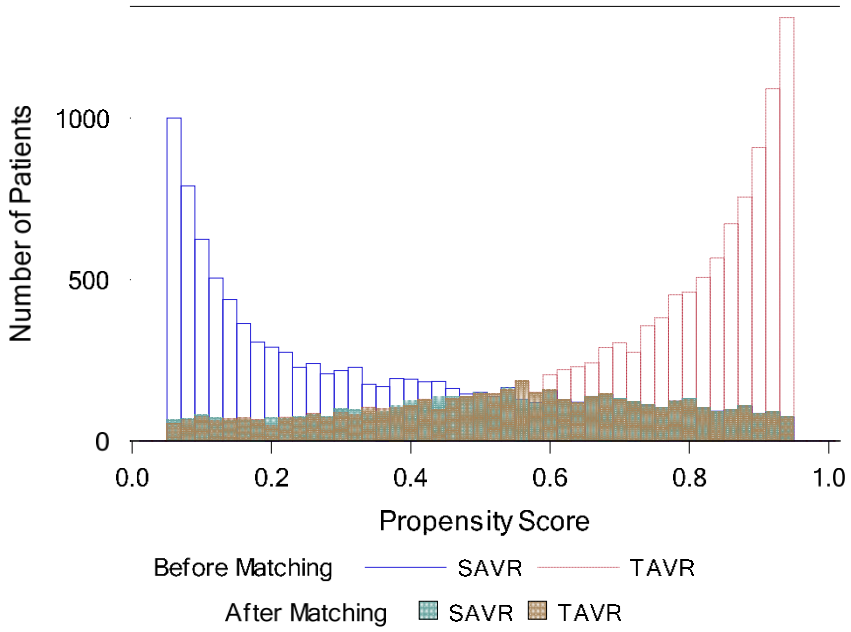


Figure S2. Propensity Distribution

Propensity distribution: A) before matching; and B) after matching (zoomed in; exclusion of propensities<0.05 and >0.95 already applied). The distribution of propensity scores demonstrates overlap, in that some patients could be identified at any level of the propensity score in both treatment arms.

SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement

A)



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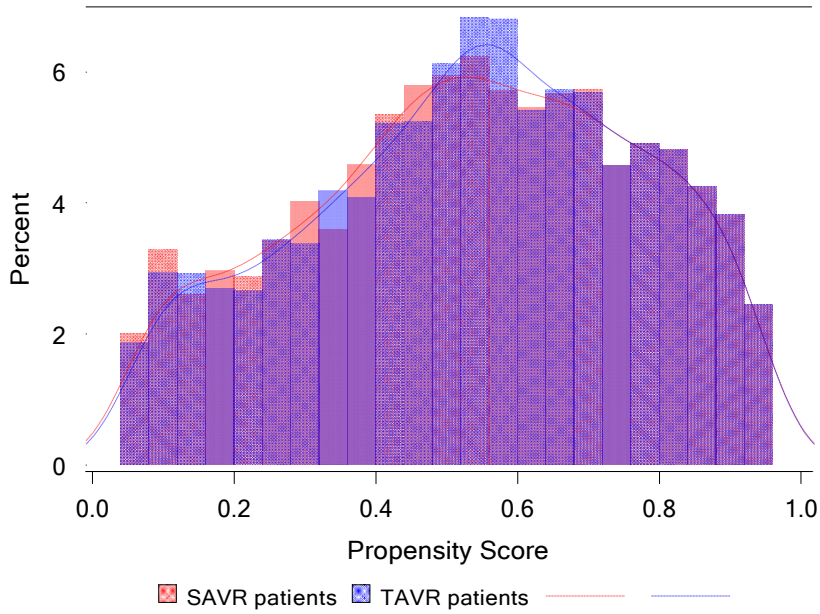


Figure S3. Exploration of Balance after Propensity Score Matching
Standardized differences on the matched population (SAVR n=4732, TAVR n=4732). Prior to matching, extreme imbalances are observed between TAVR and SAVR patients, and these are resolved by matching.
CABG = coronary artery bypass grafting; CAD = coronary artery disease; CV = cardiovascular; CVA = cerebrovascular accident; MI = myocardial infarction; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement

Figure S4. Boxplots of Absolute Standardized Differences
Boxplots of absolute standardized differences (percent), for all covariates (54 including categorical levels), across all 35 pre-specified subgroups (1,890 total). The horizontal line indicates the ideal threshold of 10%. Balance within subgroups is not guaranteed by propensity matching, unless the propensity score is sufficiently flexible (with respect to interactions between covariates and subgroups). We investigated balance within the subgroups of interest. Complete tables (1,890 rows) are available upon request and were used to examine balance. Standardized differences above 10% were addressed by adding interactions to the propensity model (i.e., an imbalanced covariate within a subgroup has a unique relationship to the propensity within that subgroup and, therefore, requires an interaction). A few factors remained >10% but did not exhibit a clinically relevant difference. The final result is summarized in the boxplot below.

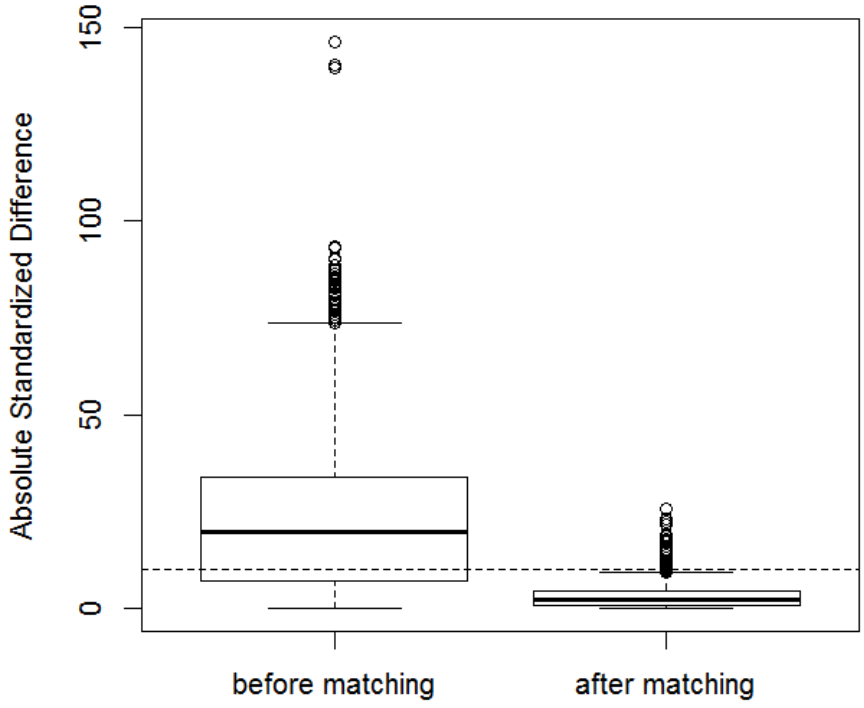
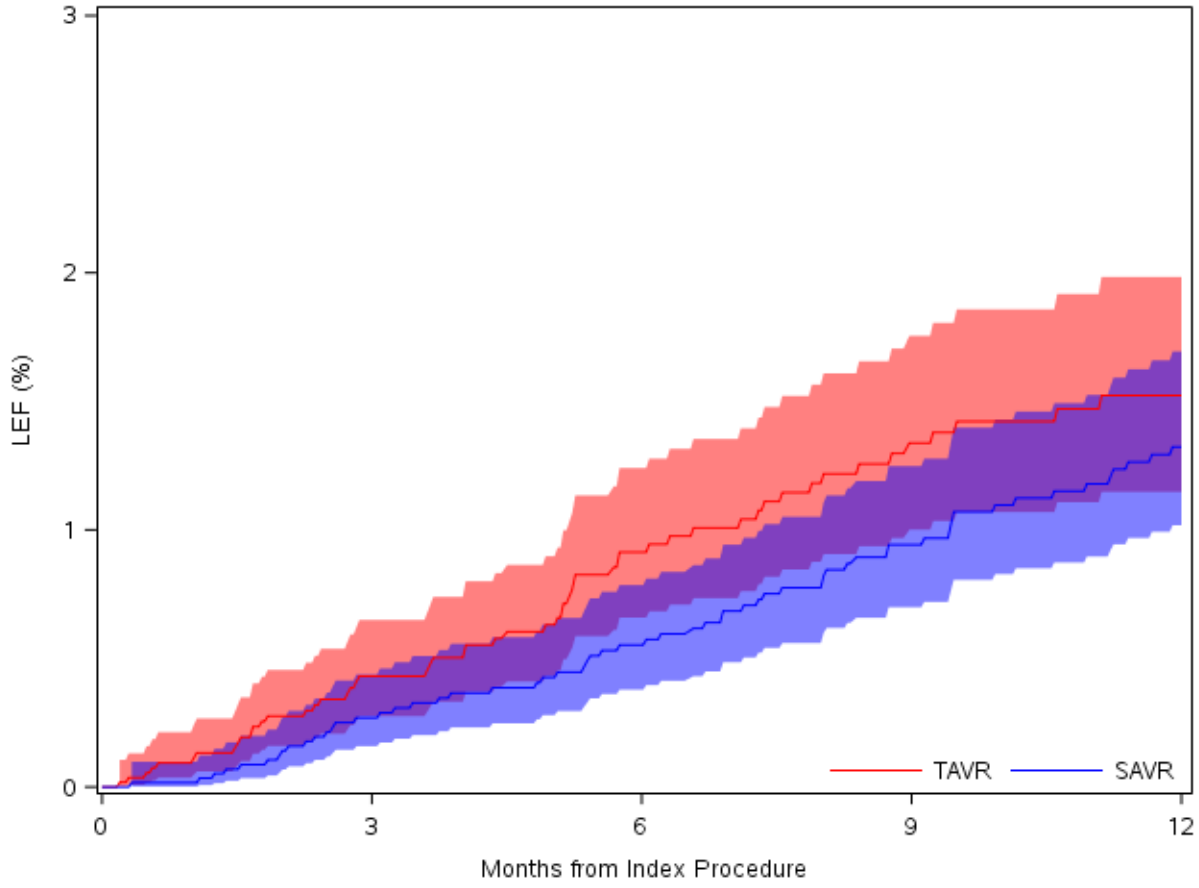


Figure S5. Falsification Endpoints

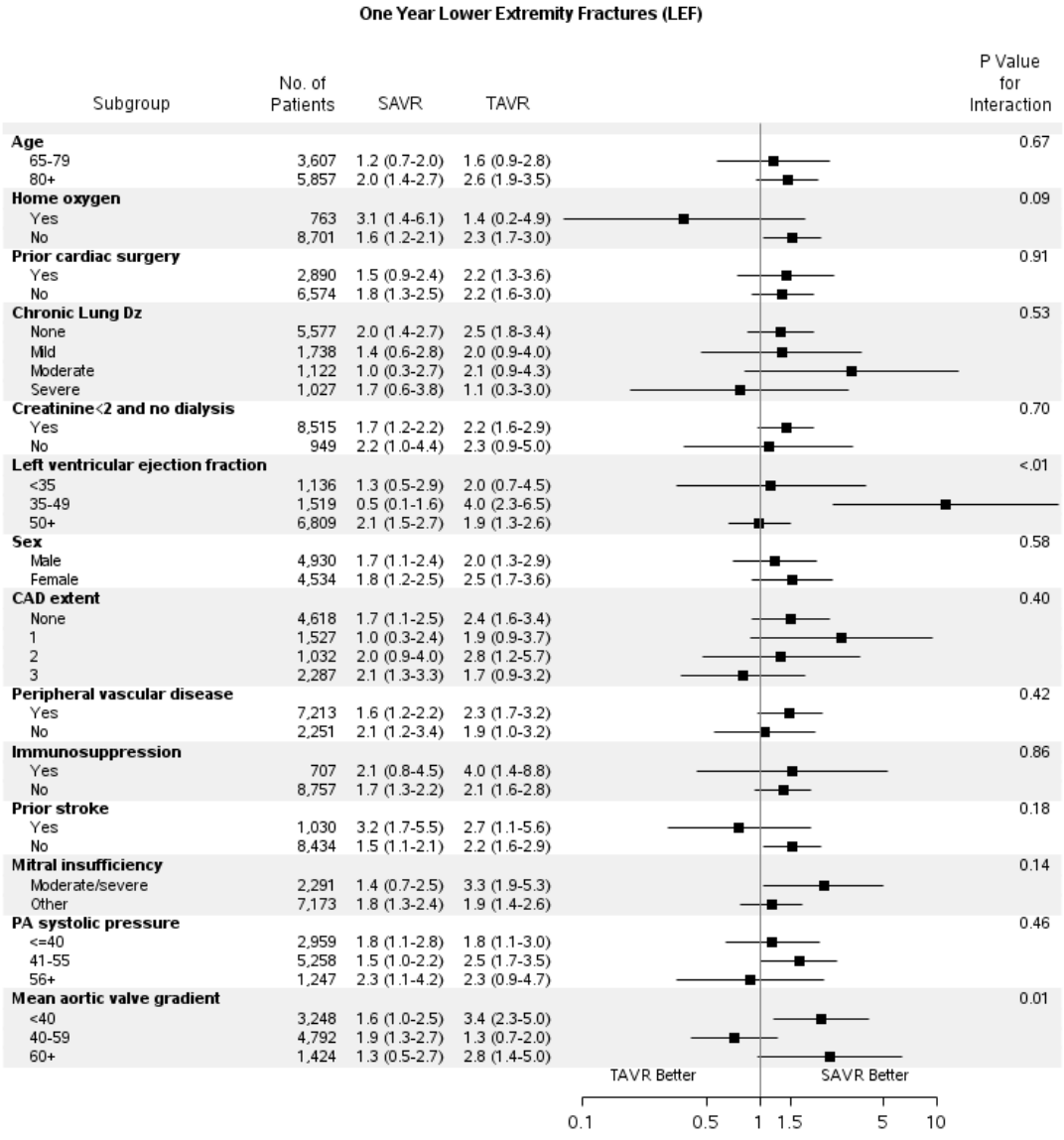
Falsification endpoints for LEF and UTI were identified as endpoints that should not be effected, causally, by TAVR versus SAVR. However, UTI would be related to potential sources of confounding in the TAVR versus SAVR comparison, such as factors related to general health (TAVR patients being generally sicker), access to preventative health care and support, or different health care (some hospitals, regions, or health systems providing better care). These sources of unmeasured confounding could be revealed by a non-zero association between TAVR versus SAVR on the endpoint of UTI, or systematic patterns across subgroups. LEF and UTI are displayed as follows: A) LEF cumulative incidence curve; B) LEF forest plot; C) UTI cumulative incidence curve; and D) UTI forest plot. The confidence intervals generally overlap one, and the point estimates are not systematically different from one.

CAD = coronary artery disease; Dz = disease; LEF = lower extremity fracture(s); PA = pulmonary artery; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; UTI = urinary tract infection

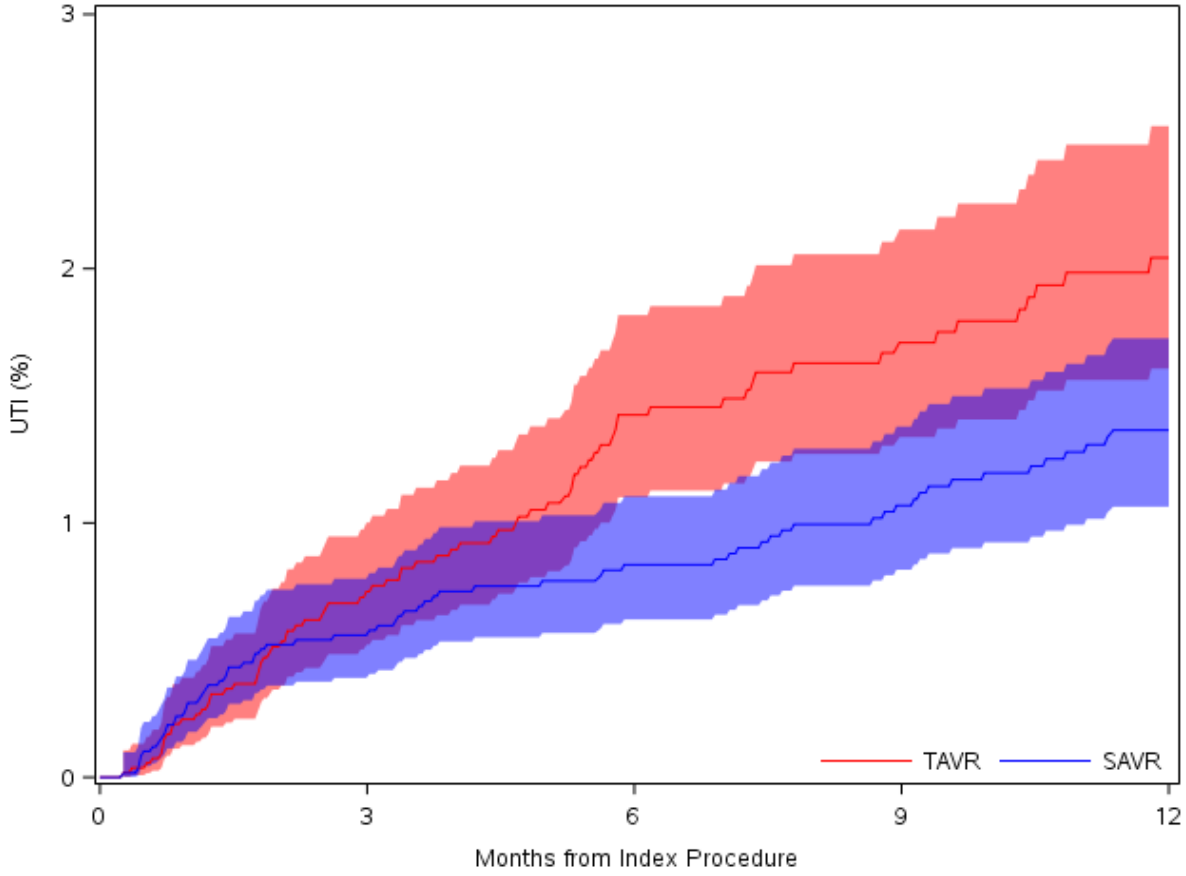
A.



B.


One Year Lower Extremity Fractures (LEF)
Subgroup
No. of Patients
SAVR
TAVR
P Value for Interaction
Age 0.67
65-79 3,607 1.2 (0.7-2.0) 1.6 (0.9-2.8)
80+ 5,857 2.0 (1.4-2.7) 2.6 (1.9-3.5)
Home oxygen 0.09
Yes 763 3.1 (1.4-6.1) 1.4 (0.2-4.9)
No 8,701 1.6 (1.2-2.1) 2.3 (1.7-3.0)
Prior cardiac surgery 0.91
Yes 2,890 1.5 (0.9-2.4) 2.2 (1.3-3.6)
No 6,574 1.8 (1.3-2.5) 2.2 (1.6-3.0)
Chronic Lung Dz 0.53
None 5,577 2.0 (1.4-2.7) 2.5 (1.8-3.4)
Mild 1,738 1.4 (0.6-2.8) 2.0 (0.9-4.0)
Moderate 1,122 1.0 (0.3-2.7) 2.1 (0.9-4.3)
Severe 1,027 1.7 (0.6-3.8) 1.1 (0.3-3.0)
Creatinine<2 and no dialysis 0.70
Yes 8,515 1.7 (1.2-2.2) 2.2 (1.6-2.9)
No 949 2.2 (1.0-4.4) 2.3 (0.9-5.0)
Left ventricular ejection fraction <.01
<35 1,136 1.3 (0.5-2.9) 2.0 (0.7-4.5)
35-49 1,519 0.5 (0.1-1.6) 4.0 (2.3-6.5)
50+ 6,809 2.1 (1.5-2.7) 1.9 (1.3-2.6)
Sex 0.58
Male 4,930 1.7 (1.1-2.4) 2.0 (1.3-2.9)
Female 4,534 1.8 (1.2-2.5) 2.5 (1.7-3.6)
CAD extent 0.40
None 4,618 1.7 (1.1-2.5) 2.4 (1.6-3.4)
1 1,527 1.0 (0.3-2.4) 1.9 (0.9-3.7)
2 1,032 2.0 (0.9-4.0) 2.8 (1.2-5.7)
3 2,287 2.1 (1.3-3.3) 1.7 (0.9-3.2)
Peripheral vascular disease 0.42
Yes 7,213 1.6 (1.2-2.2) 2.3 (1.7-3.2)
No 2,251 2.1 (1.2-3.4) 1.9 (1.0-3.2)
Immunosuppression 0.86
Yes 707 2.1 (0.8-4.5) 4.0 (1.4-8.8)
No 8,757 1.7 (1.3-2.2) 2.1 (1.6-2.8)
Prior stroke 0.18
Yes 1,030 3.2 (1.7-5.5) 2.7 (1.1-5.6)
No 8,434 1.5 (1.1-2.1) 2.2 (1.6-2.9)
Mitral insufficiency 0.14
Moderate/severe 2,291 1.4 (0.7-2.5) 3.3 (1.9-5.3)
Other 7,173 1.8 (1.3-2.4) 1.9 (1.4-2.6)
PA systolic pressure 0.46
<=40 2,959 1.8 (1.1-2.8) 1.8 (1.1-3.0)
41-55 5,258 1.5 (1.0-2.2) 2.5 (1.7-3.5)
56+ 1,247 2.3 (1.1-4.2) 2.3 (0.9-4.7)
Mean aortic valve gradient 0.01
<40 3,248 1.6 (1.0-2.5) 3.4 (2.3-5.0)
40-59 4,792 1.9 (1.3-2.7) 1.3 (0.7-2.0)
60+ 1,424 1.3 (0.5-2.7) 2.8 (1.4-5.0)
TAVR Better
SAVR Better
0.1
0.5
1
1.5
5
10

C.



D.

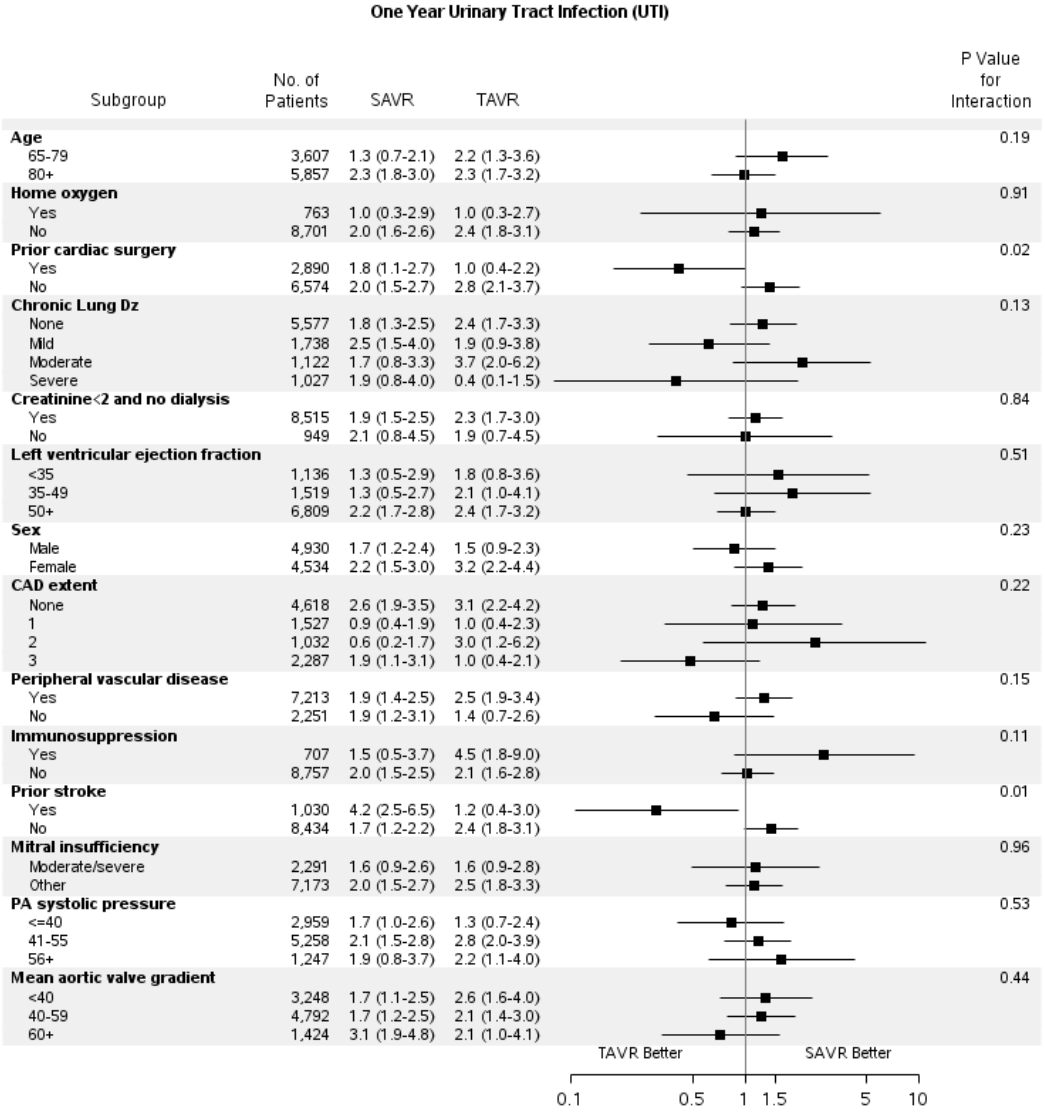

One Year Urinary Tract Infection (UTI)
Subgroup
No. of Patients
SAVR
TAVR
P Value for Interaction
Age 0.19
65-79 3,607 1.3 (0.7-2.1) 2.2 (1.3-3.6)
80+ 5,857 2.3 (1.8-3.0) 2.3 (1.7-3.2)
Home oxygen 0.91
Yes 763 1.0 (0.3-2.9) 1.0 (0.3-2.7)
No 8,701 2.0 (1.6-2.6) 2.4 (1.8-3.1)
Prior cardiac surgery 0.02
Yes 2,890 1.8 (1.1-2.7) 1.0 (0.4-2.2)
No 6,574 2.0 (1.5-2.7) 2.8 (2.1-3.7)
Chronic Lung Dz 0.13
None 5,577 1.8 (1.3-2.5) 2.4 (1.7-3.3)
Mild 1,738 2.5 (1.5-4.0) 1.9 (0.9-3.8)
Moderate 1,122 1.7 (0.8-3.3) 3.7 (2.0-6.2)
Severe 1,027 1.9 (0.8-4.0) 0.4 (0.1-1.5)
Creatinine<2 and no dialysis 0.84
Yes 8,515 1.9 (1.5-2.5) 2.3 (1.7-3.0)
No 949 2.1 (0.8-4.5) 1.9 (0.7-4.5)
Left ventricular ejection fraction 0.51
<35 1,136 1.3 (0.5-2.9) 1.8 (0.8-3.6)
35-49 1,519 1.3 (0.5-2.7) 2.1 (1.0-4.1)
50+ 6,809 2.2 (1.7-2.8) 2.4 (1.7-3.2)
Sex 0.23
Male 4,930 1.7 (1.2-2.4) 1.5 (0.9-2.3)
Female 4,534 2.2 (1.5-3.0) 3.2 (2.2-4.4)
CAD extent 0.22
None 4,618 2.6 (1.9-3.5) 3.1 (2.2-4.2)
1 1,527 0.9 (0.4-1.9) 1.0 (0.4-2.3)
2 1,032 0.6 (0.2-1.7) 3.0 (1.2-6.2)
3 2,287 1.9 (1.1-3.1) 1.0 (0.4-2.1)
Peripheral vascular disease 0.15
Yes 7,213 1.9 (1.4-2.5) 2.5 (1.9-3.4)
No 2,251 1.9 (1.2-3.1) 1.4 (0.7-2.6)
Immunosuppression 0.11
Yes 707 1.5 (0.5-3.7) 4.5 (1.8-9.0)
No 8,757 2.0 (1.5-2.5) 2.1 (1.6-2.8)
Prior stroke 0.01
Yes 1,030 4.2 (2.5-6.5) 1.2 (0.4-3.0)
No 8,434 1.7 (1.2-2.2) 2.4 (1.8-3.1)
Mitral insufficiency 0.96
Moderate/severe 2,291 1.6 (0.9-2.6) 1.6 (0.9-2.8)
Other 7,173 2.0 (1.5-2.7) 2.5 (1.8-3.3)
PA systolic pressure 0.53
<=40 2,959 1.7 (1.0-2.6) 1.3 (0.7-2.4)
41-55 5,258 2.1 (1.5-2.8) 2.8 (2.0-3.9)
56+ 1,247 1.9 (0.8-3.7) 2.2 (1.1-4.0)
Mean aortic valve gradient 0.44
<40 3,248 1.7 (1.1-2.5) 2.6 (1.6-4.0)
40-59 4,792 1.7 (1.2-2.5) 2.1 (1.4-3.0)
60+ 1,424 3.1 (1.9-4.8) 2.1 (1.0-4.1)
TAVR Better
SAVR Better
0.1
0.5
1
1.5
5
10

Figure S6. Discharge to Home
Forest plot of patients discharged to home and associated patient characteristics.
CAD = coronary artery disease; Dz = disease; PA = pulmonary artery; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement

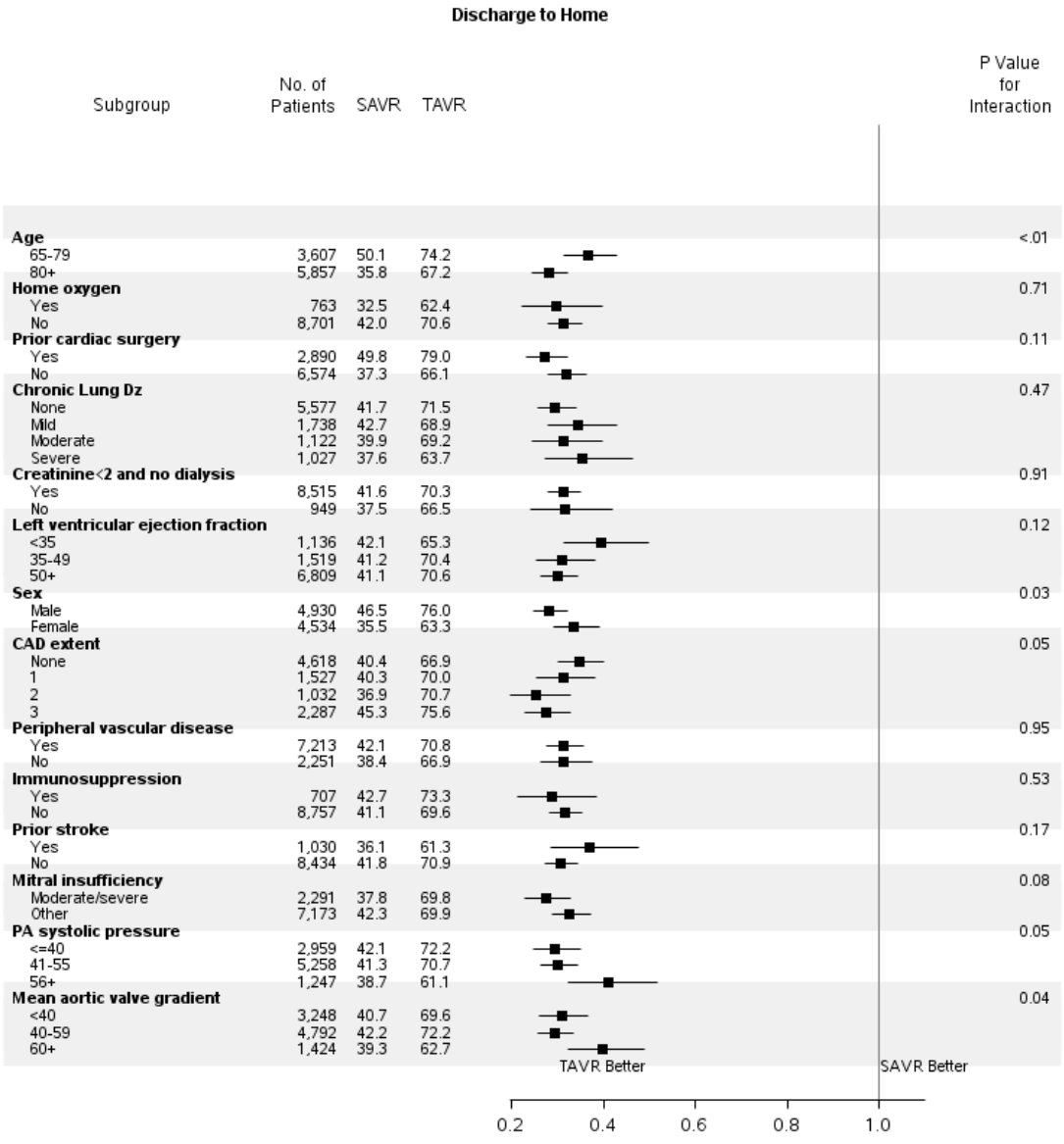


Figure S7. One-year Stroke

Patients suffering a 1-year stroke, and associated patient characteristics.
CAD = coronary artery disease; Dz = disease; PA = pulmonary artery; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement

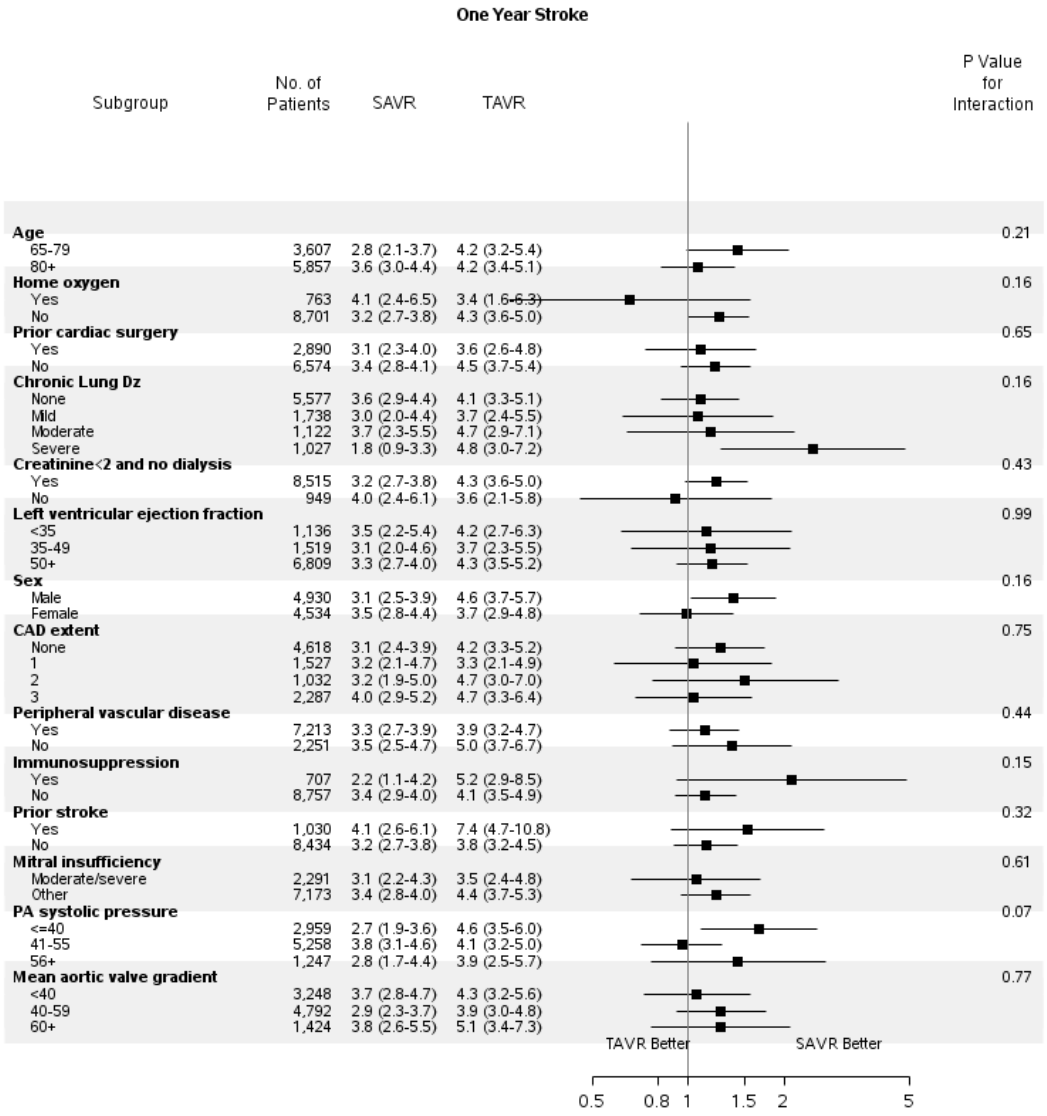


Figure S8. Proportion (%) of DAOH by Treatment Group
Proportion (%) of DAOH according SAVR versus TAVR.
DAOH = days alive and out of hospital; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement