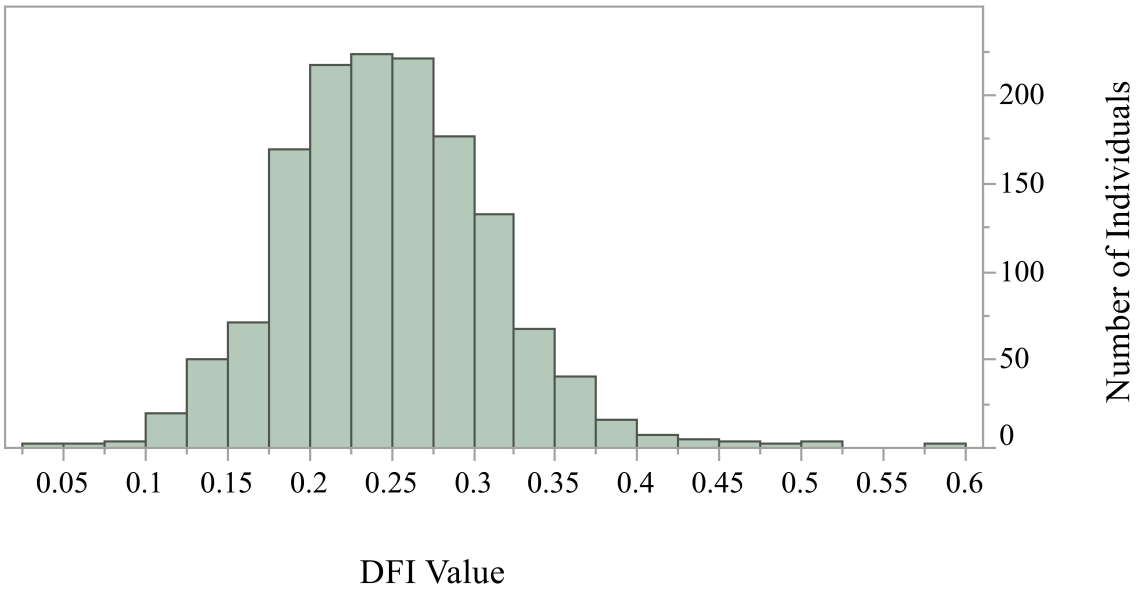
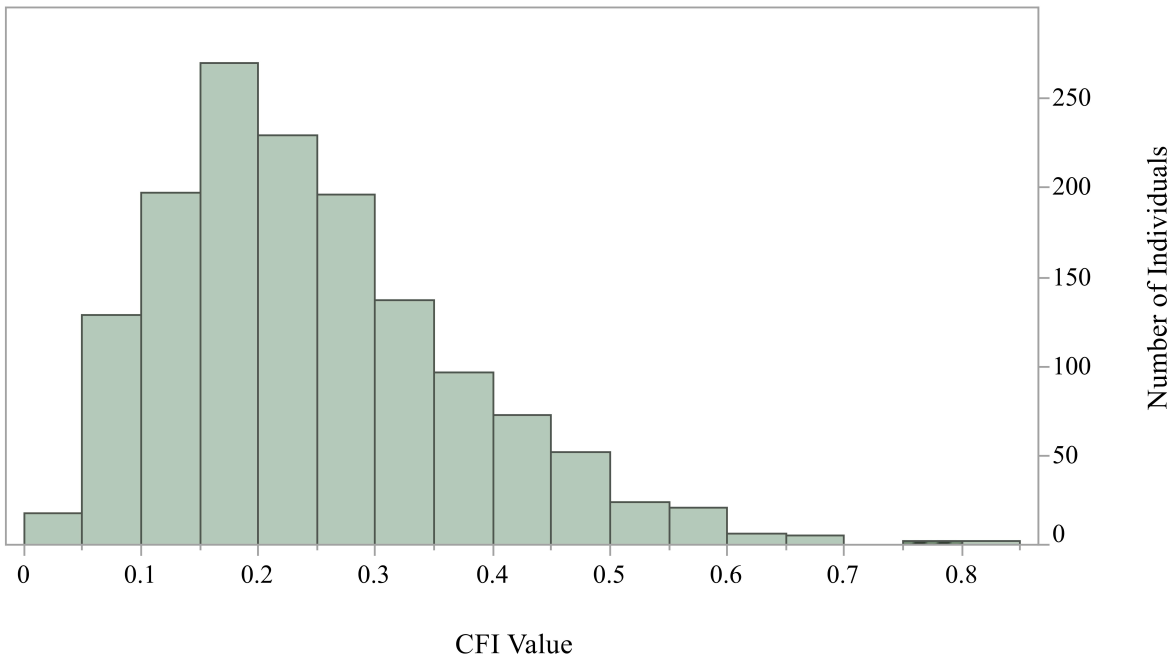
SUPPLEMENTAL MATERIAL

Supplemental Figure I: Histogram of Deficit-Based Frailty Index in the Overall Cohort



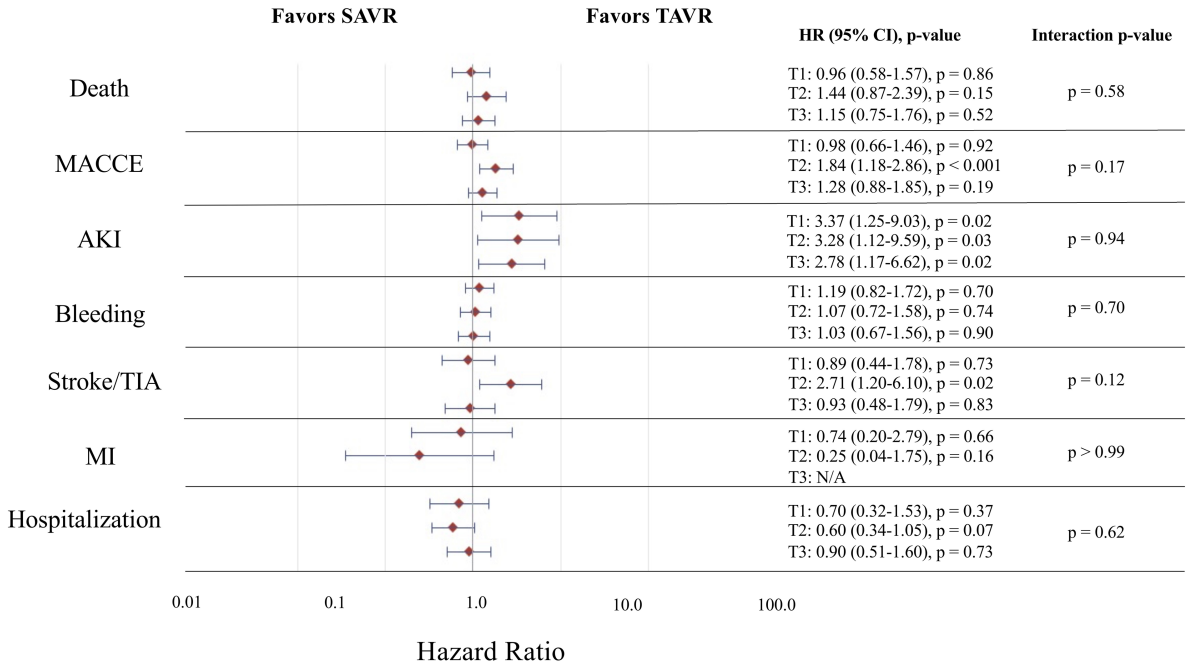
Displayed is a histogram showing the number of individuals with each deficit-based-frailty index (DFI) value in the overall CoreValve studies cohort. The mean DFI value was 0.25 ± 0.06 (range 0.04 to 0.59). Individuals in tertile 1 had a DFI ≤ 0.22, those in tertile 2 had a DFI 0.23-0.27, and those in tertile 3 had a DFI ≥ 0.28.

Supplemental Figure II: Histogram of the Phenotype-based Frailty Index in the Overall Cohort



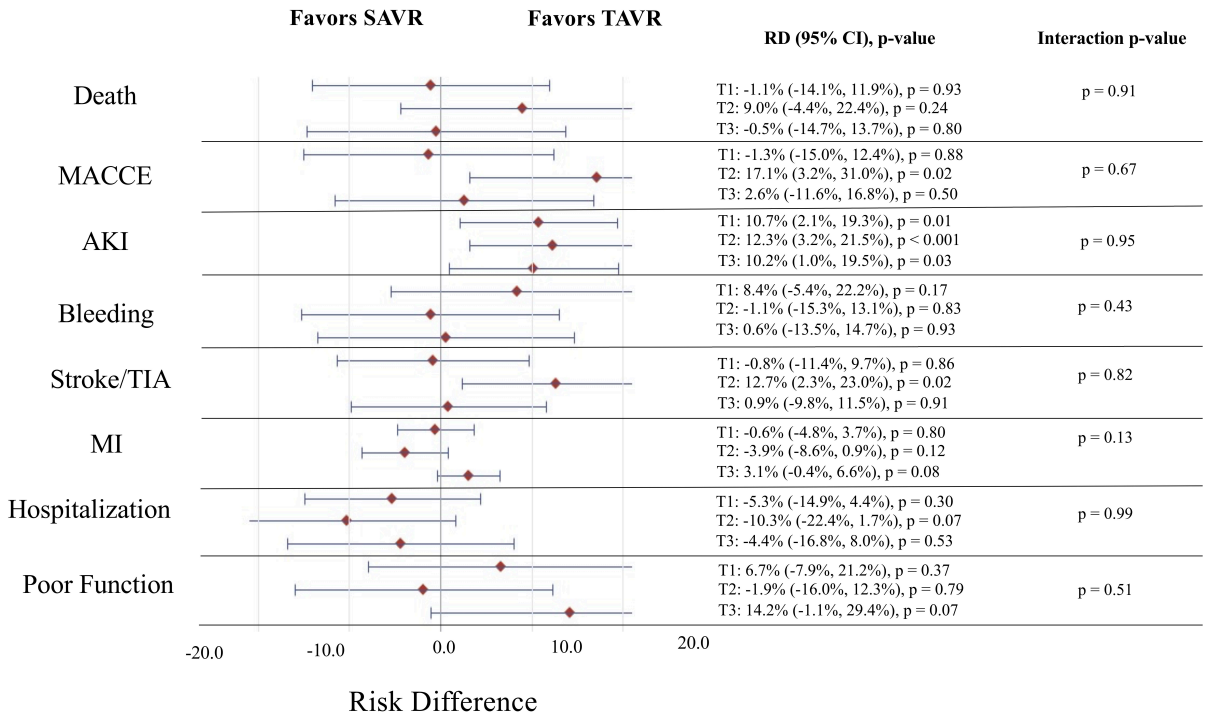
Displayed is a histogram showing the number of individuals with each phenotype-based-frailty index (PFI) value in the overall CoreValve studies cohort. The mean PFI value was 0.25 ± 0.12 (range 0.03 to 0.82). Individuals in tertile 1 had a PFI ≤ 0.18, those in tertile 2 had a PFI 0.19-0.28, and those in tertile 3 had a PFI ≥ 0.29.

Supplemental Figure III: Relative Treatment Effect for TAVR vs. SAVR in the linked CoreValve High Risk Trial by DFI Tertile and Trial Outcome



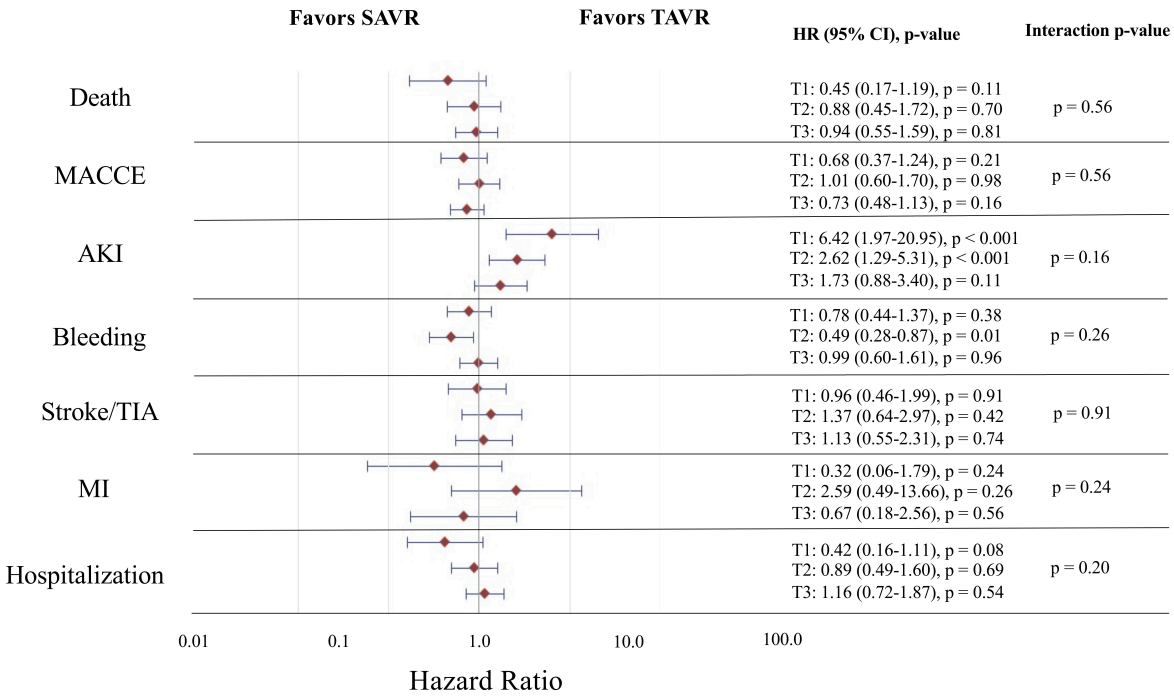
Represents the relative treatment effect for TAVR vs. SAVR in the Medicare linked CoreValve High Risk Trial by DFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted hazard ratio and the horizontal blue lines indicate the 95% confidence interval for the adjusted hazard ratio for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, Society of Thoracic Surgeons Risk score, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, myocardial infarction, coronary artery bypass grafting, congestive heart failure, presence of pacemaker or implantable defibrillator, aortic calcification, and presence of atrial fibrillation or flutter. There were insufficient numbers of individuals with MI in tertile 3 to calculate a hazard ratio. AKI = acute kidney injury, AVR = aortic valve reintervention, DFI = deficit-based frailty index, HR = hazard ratio, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, N/A = not applicable, TIA = transient ischemic attack.

Supplemental Figure IV: Absolute Treatment Effect for TAVR vs. SAVR in the linked CoreValve High Risk Trial by DFI Tertile and Trial Outcome



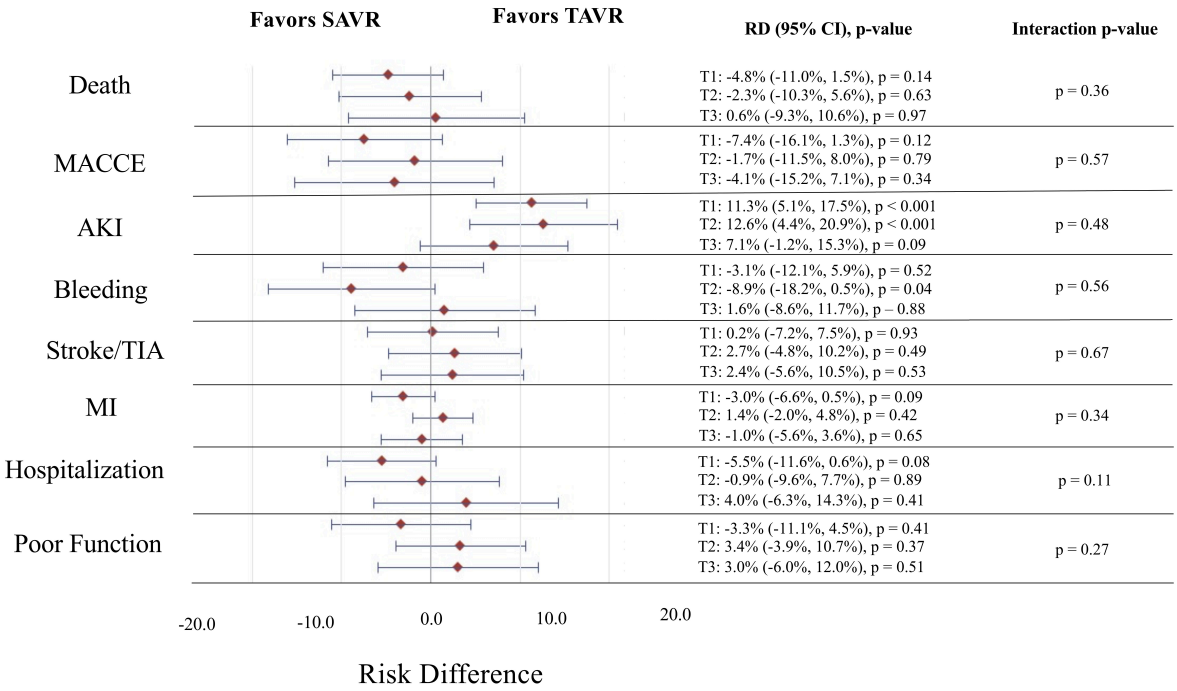
Represents the absolute treatment effect for TAVR vs. SAVR in the Medicare linked CoreValve High Risk Trial by DFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted risk difference and the horizontal blue lines indicate the 95% confidence interval for the adjusted risk difference for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, Society of Thoracic Surgeons Risk score, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, myocardial infarction, coronary artery bypass grafting, congestive heart failure, presence of pacemaker or implantable defibrillator, aortic calcification, and presence of atrial fibrillation or flutter. AKI = acute kidney injury, AVR = aortic valve reintervention, poor function = functional impairment or death by 6 months, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, RD = risk difference, PFI = phenotype-based frailty index, TIA = transient ischemic attack.

Supplemental Figure V: Relative Treatment Effect for TAVR vs. SAVR in the linked SURTAVI Trial by DFI Tertile and Trial Outcome



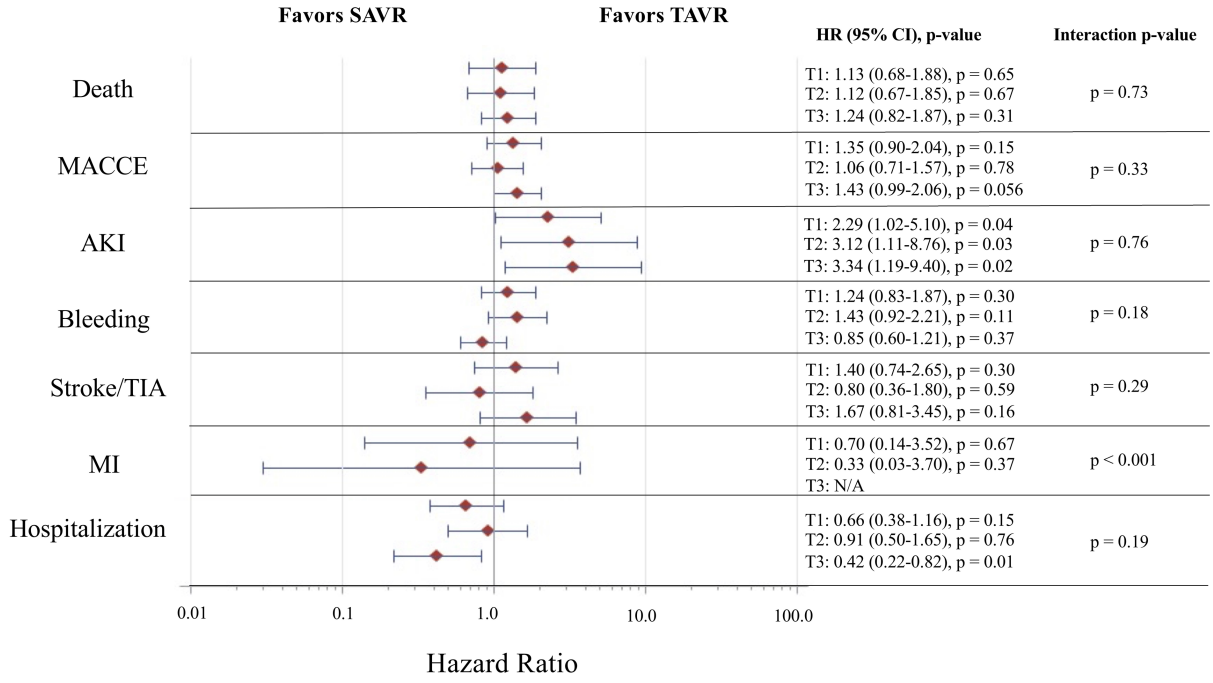
Represents the relative treatment effect for TAVR vs. SAVR in the Medicare linked SURTAVI trial by DFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted hazard ratio and the horizontal blue lines indicate the 95% confidence interval for the adjusted hazard ratio for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, diabetes, hypertension, peripheral vascular disease, coronary artery disease, pacemaker or implantable defibrillator, congestive heart failure, myocardial infarction, prior stroke, prior transient ischemic attack, receipt of percutaneous coronary intervention, aortic calcification, and atrial fibrillation or flutter. AKI = acute kidney injury, AVR = aortic valve reintervention, DFI = deficit-based frailty index, HR = hazard ratio, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, TIA = transient ischemic attack.

Supplemental Figure VI: Absolute Treatment Effect for TAVR vs. SAVR in the linked SURTAVI Trial by DFI Tertile and Trial Outcome



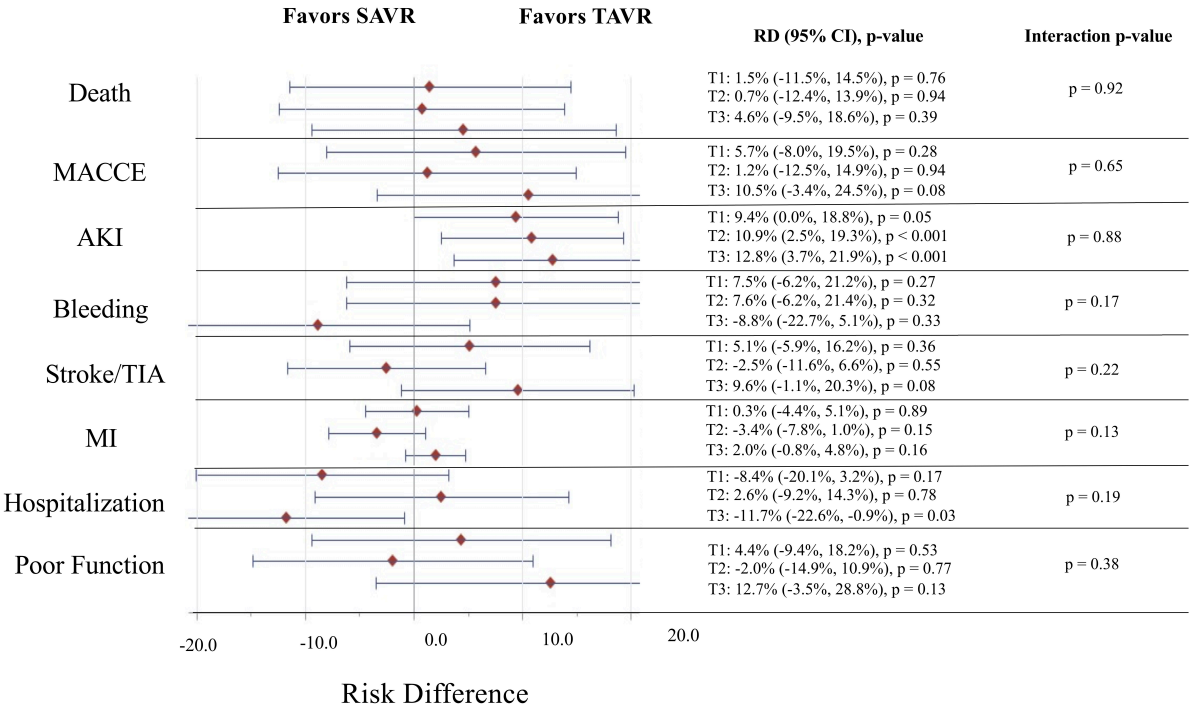
Represents the absolute treatment effect for TAVR vs. SAVR in the Medicare linked SURTAVI Trial by DFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted risk difference and the horizontal blue lines indicate the 95% confidence interval for the adjusted risk difference for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, diabetes, hypertension, peripheral vascular disease, coronary artery disease, pacemaker or implantable defibrillator, congestive heart failure, myocardial infarction, prior stroke, prior transient ischemic attack, receipt of percutaneous coronary intervention, aortic calcification, and atrial fibrillation or flutter. AKI = acute kidney injury, AVR = aortic valve reintervention, DFI = deficit-based frailty index, poor function = functional impairment or death by 6 months, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, RD = risk difference, TIA = transient ischemic attack.

Supplemental Figure VII: Relative Treatment Effect for TAVR vs. SAVR in the linked CoreValve High Risk Trial by PFI Tertile and Trial Outcome



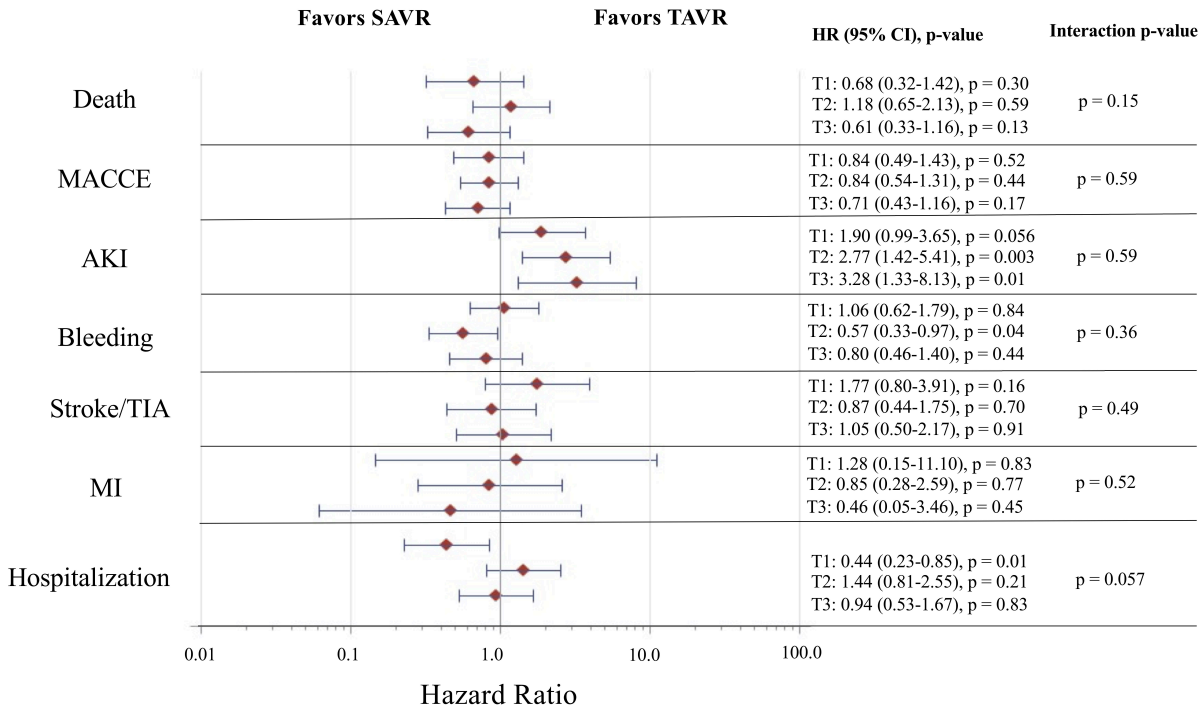
Represents the relative treatment effect for TAVR vs. SAVR in the Medicare linked CoreValve High Risk Trial by PFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted hazard ratio and the horizontal blue lines indicate the 95% confidence interval for the adjusted hazard ratio for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each PFI tertile are provided to the right of the forest plot. The p-value for the interaction of PFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, history of diabetes mellitus, hypertension, immunotherapy, myocardial infarction, coronary artery bypass grafting, and congestive heart failure. There were insufficient numbers of individuals with MI in tertile 3 to calculate a hazard ratio. AKI = acute kidney injury, AVR = aortic valve reintervention, HR = hazard ratio, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, N/A = not applicable, PFI = phenotype-based frailty index, TIA = transient ischemic attack.

Supplemental Figure VIII: Absolute Treatment Effect for TAVR vs. SAVR in the linked CoreValve High Risk Trial by PFI Tertile and Trial Outcome



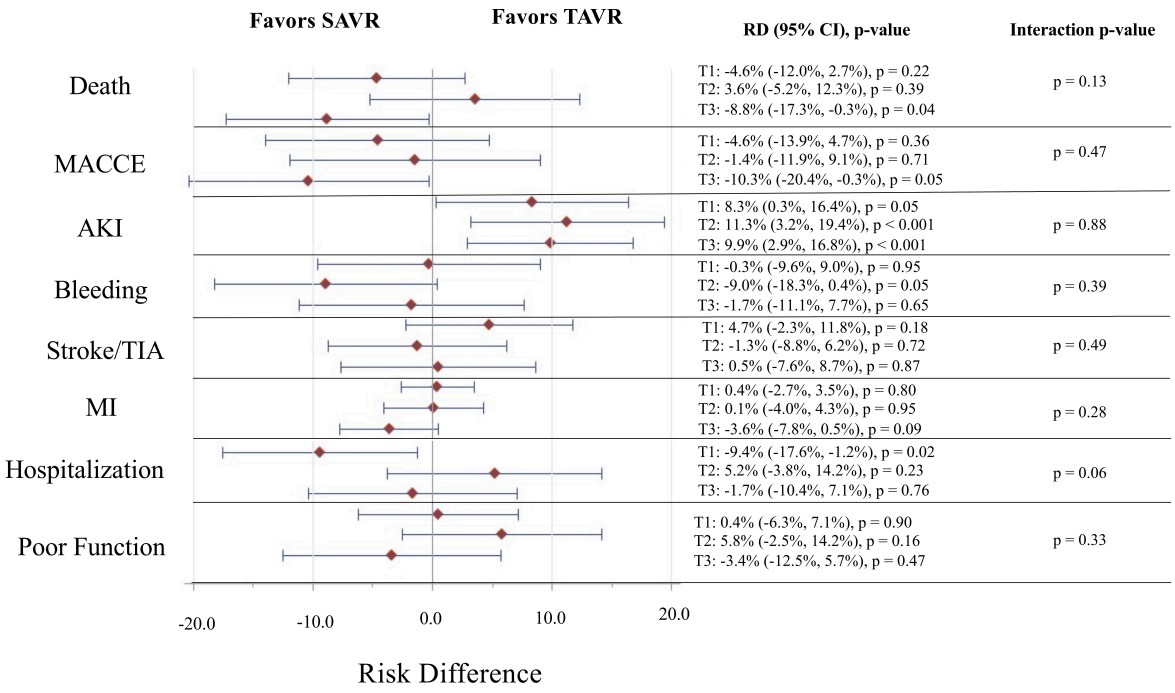
Represents the absolute treatment effect for TAVR vs. SAVR in the Medicare linked CoreValve High Risk Trial by PFI tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted risk difference and the horizontal blue lines indicate the 95% confidence interval for the adjusted risk difference for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each PFI tertile are provided to the right of the forest plot. The p-value for the interaction of PFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, history of diabetes mellitus, hypertension, immunotherapy, myocardial infarction, coronary artery bypass grafting, and congestive heart failure. AKI = acute kidney injury, AVR = aortic valve reintervention, poor function = functional impairment or death by 6 months, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, RD = risk difference, PFI = phenotype-based frailty index, TIA = transient ischemic attack.

Supplemental Figure IX: Relative Treatment Effect for TAVR vs. SAVR in the linked SURTAVI Trial by PFI Tertile and Trial Outcome



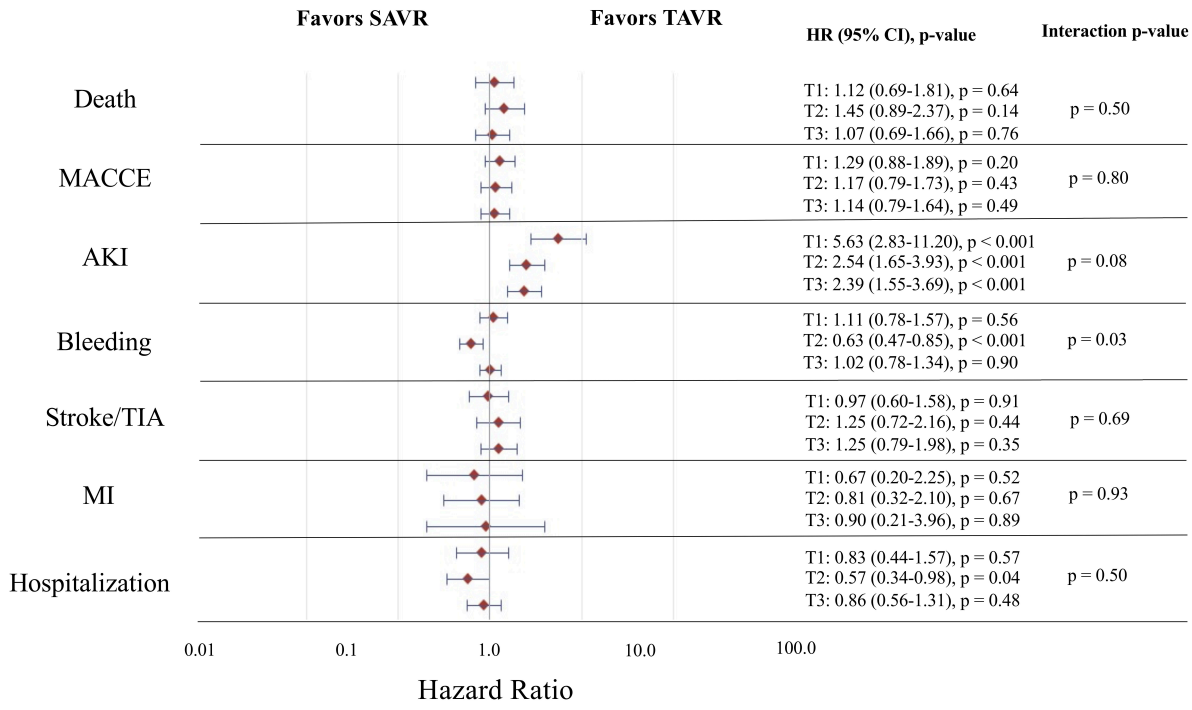
Represents the relative treatment effect for TAVR vs. SAVR in the Medicare linked SURTAVI Trial by PFI Tertile and Trial Outcome. The red diamonds indicate the point estimate for the adjusted hazard ratio and the horizontal blue lines indicate the 95% confidence interval for the adjusted hazard ratio for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each PFI tertile are provided to the right of the forest plot. The p-value for the interaction of PFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery disease, coronary artery bypass grafting, and congestive heart failure. There were insufficient numbers with MI in tertile 3 to calculate a hazard ratio. AKI = acute kidney injury, AVR = aortic valve reintervention, HR = hazard ratio, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, N/A = not applicable, PFI = phenotype-based frailty index, TIA = transient ischemic attack.

Supplemental Figure X: Absolute Treatment Effect for TAVR vs. SAVR in the linked SURTAVI Trial by PFI Tertile and Trial Outcome



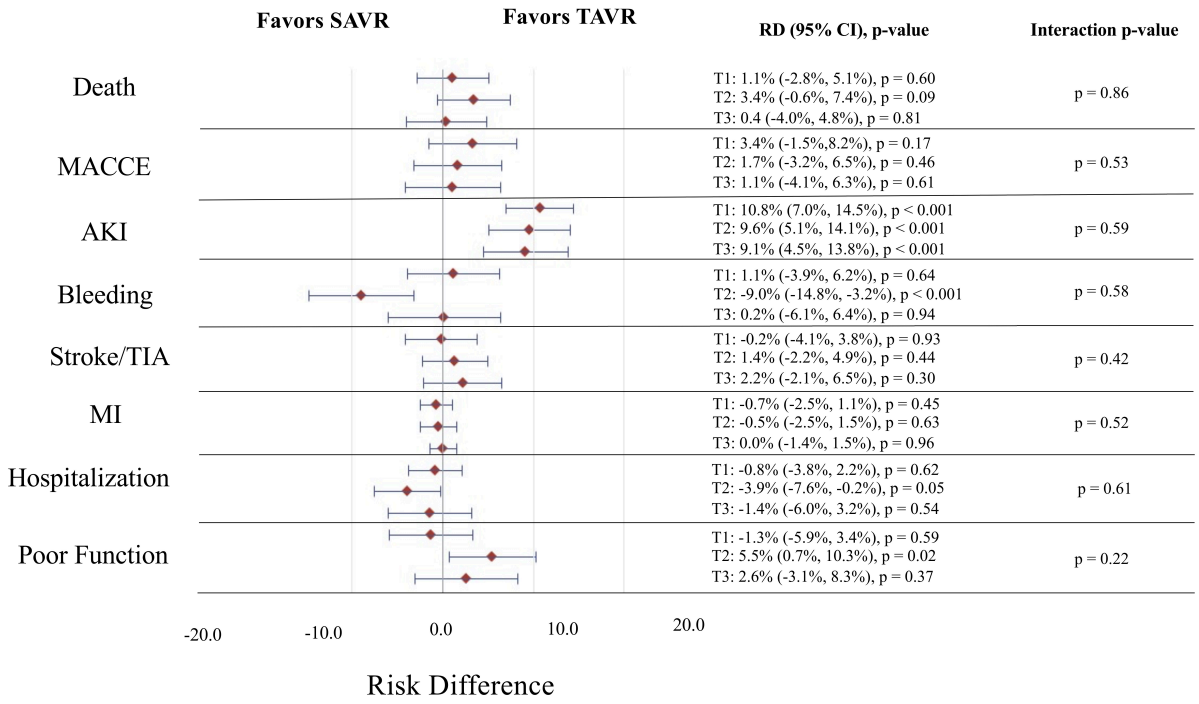
Represents the absolute treatment effect for TAVR vs. SAVR in the Medicare linked SURTAVI Trial by PFI Tertile and Trial Outcome. The red diamonds indicate the point estimate for the adjusted risk difference and the horizontal blue lines indicate the 95% confidence interval for the adjusted risk difference for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each PFI tertile are provided to the right of the forest plot. The p-value for the interaction of PFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery disease, coronary artery bypass grafting, and congestive heart failure. AKI = acute kidney injury, AVR = aortic valve reintervention, poor function = functional impairment or death at 6 months, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, RD = risk difference, PFI = phenotype-based frailty index, TIA = transient ischemic attack.

Supplemental Figure XI: Relative Treatment Effect for TAVR vs. SAVR in the Unlinked Combined Trial Data by DFI Tertile and Trial Outcome



Represents the relative treatment effect for TAVR vs. SAVR in the non-Medicare linked, combined CoreValve SURTAVI and High Risk trials by DFI Tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted hazard ratio and the horizontal blue lines indicate the 95% confidence interval for the adjusted hazard ratio for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, prior stroke and TIA, immunosuppressive therapy, coronary artery disease, coronary artery bypass grafting, receipt of percutaneous coronary intervention, pacemaker or implantable defibrillator, congestive heart failure, atrial fibrillation and flutter, and aortic calcification. AKI = acute kidney injury, DFI = deficit-based frailty index, HR = hazard ratio, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, TIA = transient ischemic attack.

Supplemental Figure XII: Absolute Treatment Effect for TAVR vs. SAVR in the Unlinked Combined Trial Data by DFI Tertile and Trial Outcome



Represents the absolute treatment effect for TAVR vs. SAVR in non-Medicare linked, combined CoreValve SURTAVI and High Risk trials by DFI Tertile and trial outcome. The red diamonds indicate the point estimate for the adjusted risk difference and the horizontal blue lines indicate the 95% confidence interval for the adjusted risk difference for each outcome. The estimates, 95% confidence intervals, and p-values for TAVR vs. SAVR within each DFI tertile are provided to the right of the forest plot. The p-value for the interaction of DFI tertile and treatment group (i.e. TAVR vs. SAVR) for each given outcome is provided. Estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, prior stroke and TIA, immunosuppressive therapy, coronary artery disease, coronary artery bypass grafting, receipt of percutaneous coronary intervention, pacemaker or implantable defibrillator, congestive heart failure, atrial fibrillation and flutter, and aortic calcification. AKI = acute kidney injury, DFI = deficit-based frailty index, poor function = functional impairment or death at 6 months, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, RD = risk difference, TIA = transient ischemic attack.

Supplemental Table I: Demographic, procedural, risk score, and comorbidity variables included in baseline CoreValve trial assessments

Variable Domain	Variable
Demographics	Age
	Sex
Comorbidities	Diabetes mellitus
	Hypertension
	Peripheral vascular disease
	Prior cerebrovascular event or transient ischemic attack
	Coronary artery disease
	History of myocardial infarction
	Prior percutaneous coronary intervention
	Prior coronary artery bypass grafting
	History of pacemaker or implantable defibrillator
	Congestive heart failure
	Atrial flutter or fibrillation
	History of cirrhosis
	Connective tissue diseases
	Use of immunosuppressive therapy
Risk scores	Society of Thoracic Surgeons risk score
	Logistic EuroSCORE
	Charlson comorbidity index
Procedural variables	Number of valves implanted
	Arterial access site
	Severity of aortic calcification
	Presence of a chest wall deformity or hostile mediastinum

Supplemental Table II: Definition of Endpoints Used in the CoreValve Studies

Variable	High Risk	SURTAVI
Primary Outcome	All cause mortality @ 12 mo	All cause death or disabling stroke @ 12 mo
Acute Kidney Injury	N/A	Stage 1 – Increase in serum creatinine to 150-199% (1.5-1.9 x increase compared with baseline) OR increase of ≥ 0.3 mg/dl (≥26.4 µmol/L) OR urine output <0.5 ml/kg/hour for >6 but <12 hours Stage 2 – Increase in serum creatinine to 200-299% (>2.0-2.9 x increase compared with baseline) OR urine output <0.5 ml/kg/hour for >12 but < 24 hours Stage 3 – Increase in serum creatinine to ≥300% (> 3 x increase compared with baseline) OR serum creatinine of > 4.0 mg/d (≥354 µmol/L) with an acute increase of at least 0.5 mg/dl (44 µmol/L) OR urine output <0.3 ml/kg/hour for >24 hours OR anuria for > 12 hours Patients receiving renal replacement therapy are considered stage 3 irrespective of other criteria. Stage 2 and 3 AKI is considered a serious adverse event.
Aortic Reintervention	Any surgical or percutaneous interventional catheter procedure that repairs, otherwise alters or adjusts, or replaces a previously implanted valve. In addition to surgical reoperations, balloon dilatation, interventional manipulation, repositioning, or retrieval, and other catheter-based interventions for valve-related complications are also considered reinterventions.	Any surgical or percutaneous interventional catheter procedure that repairs, otherwise alters or adjusts, or replaces a previously implanted valve. In addition to surgical reoperations, balloon dilatation, interventional manipulation, repositioning, or retrieval, and other catheter-based interventions for valve-related complications are also considered reinterventions.
Bleeding	Life Threatening or Disabling Bleeding • Fatal bleeding OR • Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome OR • Bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR • Bleeding associated with a drop in hemoglobin of ≥5 g/dl or whole blood or packed red blood cells (RBCs) transfusion ≥4 units Major bleeding • Bleeding associated with either associated with a drop in the hemoglobin level of at least 3.0 g/dl or requiring transfusion of two or three units of whole blood RBC AND does not meet criteria of life-threatening or disabling bleeding	Life-threatening or disabling bleeding • Fatal bleeding (BARC type 5) OR • Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome (BARC type 3b) OR • Bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR • Overt source of bleeding with drop in hemoglobin of ≥5 g/dL or whole blood or packed red blood cells transfusion ≥4 units (BARC type 3b) Major Bleeding • Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0g/dL or requiring transfusion of 2-3 units of whole blood/RBC, or causing hospitalization or permanent injury or requiring surgery AND • Does not meet criteria of life-threatening or disabling bleeding Minor Bleeding • Any bleeding worthy of clinical mention (eg. access site hematoma) that does not qualify as life-threatening, disabling or major "Overt" source of bleeding is defined by any of the following criteria being met: • Reoperation after closure of sternotomy for the purpose of controlling bleeding (BARC Type 4) • Chest tube output:

		• 2 L within a 24 hour period (BARC Type 4) OR • > 350 cc within 1st hr. post op OR • ≥ 250 cc. 2nd hr. post op OR • > 150 cc 3rd hr. post op • Bleeding from the vascular system outside of the access site (TAVR) • Bleeding from an access site that requires an intervention (TAVR) • Bleeding from the vascular system outside of the surgical site (Surgical replacement)
Death	<u>All-cause Death:</u> All deaths from any cause after a valve intervention. This includes all cardiovascular and non-cardiovascular deaths. <u>Cardiovascular Death:</u> • Any death due to a cardiac cause (e.g. MI, cardiac tamponade, worsening heart failure) • Unwitnessed death and death of unknown cause • All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure. Death caused by non-coronary vascular conditions such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease. <u>Non-cardiovascular death:</u> • Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma. <u>Valve-related death:</u> • Any death caused by prosthetic valve dysfunction, valve thrombosis, embolism, bleeding event, or implanted valve endocarditis; or related to reintervention on the operated valve.	<u>All-cause mortality:</u> All deaths from any cause after a valve intervention. This includes all cardiovascular and non-cardiovascular deaths. <u>Cardiovascular mortality:</u> Cardiovascular death will be defined according to the Valve Academic Research Consortium (VARC)-2; Updated Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation (TAVI); 2012-10-09. A death meeting any one of the following criteria: • Death due to proximate cardiac cause (eg. myocardial infarction, cardiac tamponade, worsening heart failure) • Death caused by non-coronary vascular conditions such as neurological events, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease • All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure • All valve-related deaths including structural or non-structural valve dysfunction or other valve-related adverse events • Sudden or unwitnessed death • Death of unknown cause <u>Non-cardiovascular mortality:</u> Any death in which primary cause of death is clearly related to another condition (eg. trauma, cancer, suicide) NOTE: All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, any unexpected death even in subjects with coexisting potentially fatal non-cardiac disease (eg. Cancer, infection) are classified as cardiac
Myocardial Infarction	<u>Peri-procedural MI (≤72 hours after the index procedure)</u> • New ischemic symptoms (e.g. chest pain or shortness of breath) or new ischemic signs (e.g. ventricular arrhythmias, new or worsening heart failure, new ST-segment changes – either elevation >1 mm or depression >1 mm in two or more contiguous leads, hemodynamic instability; or imaging evidence of new loss of viable myocardium or new wall motion abnormality) • Elevated cardiac biomarkers evidence, (preferably CK-MB) within 72 hours after the index procedure, consisting of two or more post-procedure samples that are 6-8 hours apart with a 20% increase in the second sample and a peak value exceeding 10x the	N/A

	99th percentile upper reference limit (URL) or a peak value exceeding 5x the 99th percentile URL and with new pathological Q waves in at least 2 contiguous leads. <u>Spontaneous MI (>72 hours after the index procedure) including any of the following:</u> • Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile URL, together with evidence of myocardial ischemia with at least one of the following: -ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block); -New pathological Q waves ≥2 contiguous leads; -Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality • Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood. • Pathological findings of an acute myocardial infarction.	
Neurologic event	<u>Stroke Diagnostic Criteria:</u> • Rapid onset of a focal or global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke • Duration of a focal or global neurological deficit ≥24 hours; OR <24 hours, if therapeutic intervention(s) were performed (e.g. thrombolytic therapy or intracranial angioplasty); OR available neuroimaging documents a new hemorrhage or infarct; OR the neurologic deficit results in death • No other readily identifiable non-stroke cause for the clinical presentations (e.g. brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences)* • Confirmation of the diagnosis by at least one of the following: -Neurology or neurosurgical specialist -Neuroimaging procedure (MR or CT scan or cerebral angiography) -Lumbar puncture (spinal fluid analysis diagnostic of intracranial hemorrhage) <u>Stroke Definitions</u> *Transient ischemia attack* ▪ A new focal neurologic deficit with rapid symptom resolution (usually 1-2 hours), and always within 24 hours. ▪ Neuroimaging without tissue injury	<u>Diagnostic Criteria</u> • Acute episode of a focal or global neurological deficit with at least one of the following: change in level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke • *Stroke:* duration of a focal or global neurological deficit ≥ 24 hours; OR < 24 hours available neuroimaging documents a new hemorrhage or infarct; OR the neurologic deficit results in death • *TIA:* duration of a focal or global neurological deficit <24 hours, any variable neuroimaging does not demonstrate a new hemorrhage or infarct • No other readily identifiable non-stroke cause for the clinical presentations (eg. brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences) to be determined by or in conjunction with designated neurologist • Confirmation of the diagnosis by at least one of the following: ○ Neurology or neurosurgical specialist ○ Neuroimaging procedure (CT scan or brain MRI), but stroke be diagnosed on clinical grounds alone <u>Stroke Classification</u> • Ischemic: an acute episode of focal cerebral, spinal or retinal dysfunctions caused by infarction of the central nervous system tissue • Hemorrhagic: an acute episode of focal cerebral, spinal or spinal dysfunctions caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage

	Stroke (diagnosed as above, preferably with positive neuroimaging study) • Minor: Modified Rankin <2 at 30 and 90 days • Major: Modified Rankin ≥2 at 30 and 90 days	<u>Stroke Definitions</u> • Disabling stroke: an modified Rankin score (mRS) of 2 or more at 90 days and an increase in at least one mRS category from an individual's pre-stroke baseline • Non-disabling stroke: an mRS score of < 2 at 90 days or one that does not result in an increase in at least one mRS category from an individual's pre-stroke baseline

Supplemental Table III: Technique used to construct a deficit-based frailty index

In-person measure	Number of Points Assigned
Anemia requiring transfusion	1 point
Albumin < 3.3 g/dL	1 point
Unplanned weight loss	1 point
Fall in the last 6 months	1 point
Grip strength below threshold (right or left)	1 point
Absence of independent living	1 point
Absence of independent bathing	1 point
Absence of independent dressing	1 point
Absence of independent toileting	1 point
Absence of independent feeding	1 point
Urinary incontinence	1 point
Society of Thoracic Surgeons lung disease severity scale	1 point for severity = severe 0.67 points for severity = moderate 0.33 point for severity = mild
Body mass index (BMI)	1 point for BMI < 18.5 or > 30 kg/m^2 0.5 points for BMI 25-30 kg/m^2
5-minute walk time	1 point for ≤ 33rd percentile 0.67 points for 34-66th percentile 0.33 points for 67-100th percentile
Mini-mental status examination (MMSE)	1 points for MMSE < 18 0.5 point for MMSE 18-23
Diabetes mellitus	1 point
Stroke or transient ischemic attack	1 point
Hypertension	1 point
Coronary artery disease (includes coronary artery disease, receipt of coronary artery bypass grafting, percutaneous coronary intervention, or prior myocardial infarction)	1 point
Congestive heart failure	1 point
Atrial fibrillation or flutter	1 point
Cirrhosis of the liver	1 point
Connective tissue disease	1 point
Peripheral vascular disease	1 point
Serum creatinine (Cr)	0.33 point for Cr < 0.9 mg/dL 0.67 points for Cr 0.9-1.4 mg/dL 1 point for Cr > 1.4 mg/dL
Kansas City Living with Cardiomyopathy Overall Score	1 point for ≤ 33rd percentile 0.67 points for 34-66th percentile 0.33 points for 67-100th percentile
Standard Form-12 (or 36) Physical Component Scale	1 point for ≤ 33rd percentile 0.67 points for 34-66th percentile 0.33 points for 67-100th percentile
Standard Form-12 (or 36) Mental Component Scale	1 point for ≤ 33rd percentile 0.67 points for 34-66th percentile 0.33 points for 67-100th percentile
Aortic calcification	1 point if severe 0.67 points if moderate 0.33 point if mild
Diffusion lung capacity for oxygen (DLCO)	1 point for ≤ 33rd percentile 0.67 points for 34-66th percentile 0.33 points for 67-100th percentile

To construct a deficit-based frailty index according to the Rockwood approach, individuals were assigned point values for each frailty-related deficit based on the technique by Searle SD, Mitniski A, Gahbauer EA, Gill TM, and Rockwood. A standard procedure for creating a frailty index. *BMC Geriatrics.* 2008;8:24. The sum of total points met for a given person was divided by the total number of possible points to create a frailty index for each individual. All points were assigned using in-person measures from the baseline assessment of CoreValve trial participants.

Supplemental Table IV: ICD-9-CM claims used to create the Segal phenotype-based frailty index

Component	ICD-9-CM Diagnosis Codes
Chronic heart failure	39891 402x1 404x3 428x
Parkinson`s disease	3320
Arthritis	7140 7141 7142 71430 71431 71432 71433 7144 71481 71489 7149 7200 71500 71504 71509 71510 71511 71512 71513 71514 71515 71516 71517 71518 71520 71521 71522 71523 71524 71525 71526 71527 71528 71530 71531 71532 71533 71534 71535 71536 71537 71538 71580 71589 71590 71591 71592 71593 71594 71595 71596 71597 71598 V134
Cognitive impairment	2900 29010 29011 29012 29013 29020 29021 2903 29040 29041 29042 29043 2908 2909 2930 2931 2940 2941 29410 29411 29420 29421 2948 2949 3100 3102 3108 31081 31089 3109 3310 3311 33111 33119 3312 33182 797
Depression	3090 3091 30922 30923 30924 30928 30929 3093 3094 30982 30983 30989 3099 29383 29600 29601 29602 29603 29604 29605 29606 29610 29611 29612 29613 29614 29615 29616 29620 29621 29622 29623 29624 29625 29626 29630 29631 29632 29633 29634 29635 29636 29640 29641 29642 29643 29644 29645 29646 29650 29651 29652 29653 29654 29655 29656 29660 29661 29662 29663 29664 29665 29666 2967 29680 29681 29682 29689 29690 29699 3004 311
Falls	E8800 E8801 E8809 E8810 E8811 E882 E8830 E8831 E8832 E8839 E8840 E8841 E8842 E8843 E8844 E8845 E8846 E8849 E885 E8850 E8851 E8852 E8853 E8854 E8859 E8860 E8869 E888 E8880 E8881 E8888 E8889 E9681 E9870 E9871 E9872 E9879
Impaired mobility	V463
Musculoskeletal problems	7130 7131 7132 7133 7134 7135 7136 7137 7138 71600 71601 71602 71603 71604 71605 71606 71607 71608 71609 71620 71621 71622 71623 71624 71625 71626 71627 71629 71629 71630 71631 71632 71633 71634 71635 71636 71637 71638 71639 71640 71641 71642 71643 71644 71645 71646 71647 71648 71649 71650 71651 71652 71653 71654 71655 71656 71657 71658 71659 71660 71661 71662 71663 71664 71665 71666 71667 71668 71680 71681 71862 71683 71684 71685 71686 71687 71688 71689 71690 71691 71692 71693 71694 71695 71696 71697 71698 71699 71810 71811 71812 71813 71814 71815 71817 71818 71819 71820 71821 71822 71823 71824 71825 71826 71827 71828 71829 71850 71851 71852 71853 71854 71855 71856 71857 71858 71859 71860 71865 71870 71871 71872 71873 71874 71875 71876 71877 71878 71879 71880 71881 71882 71883 71884 71885 71886 71887 71888 71889 71890 71891 71892 71893 71894 71895 71897 71898 71899 71900 71901 71902 71903 71904 71905 71906 71907 71908 71909 71910 71911 71912 71913 71914 71915 71916 71917 71918 71919 71920 71921 71922 71923 71924 71925 71926 71927 71928 71929 71930 71931 71932 71933 71934 71935 71936 71937 71938 71939 71940 71941 71942 71943 71944 71945 71946 71947 71948 71949 71950 71951 71952 71953 71954 71955 71956 71957 71958 71959 71960 71961 71962 71963 71964 71965 71966 71967 71968 71969 7197 71970 71975 71976 71977 71978 71979 71980 71981 71982 71983 71984 71985 71986 71987 71988 71989 71990 71991 71992 71993 71994 71995 71996 71997 71998 71999 7201 7202 72081 72089 7209 7210 7211 7212 7213 72141 72142 7215 7216 7217 7218 72190 72191 7220 72210 72211 7222 72230 72231 72232 72239 7224 72251 72252 7226 72270 72271 72272 72273 72280 72281 72282 72283 72290 72291 72292 72293 7230 7231 7232 7233 7234 7235 7236 7237 7238 7239 72400 72401 72402 72403 72409 7241 7242 7243 7244 7245 7246 72470 72471 72479 7248 7249 73300 73301 73302 73393 73309 7331 73310 73311 73312 73313 73314 73315

	73316 73319 73393 73394 73395 73396 73397 73398 V1351 4350 4351 4352 4353 4358 4359
Paranoia	29381 29382 29500 29501 29502 29503 29504 29505 29510 29511 29512 29513 29514 29515 29520 29521 29522 29523 29524 29525 29530 29531 29532 29533 29534 29535 29540 29541 29542 29543 29544 29545 29550 29551 29552 29553 29554 29555 29560 29561 29562 29563 29564 29565 29570 29571 29572 29573 29574 29575 29580 29581 29582 29583 29584 29585 29590 29591 29592 29593 29594 29595 2970 2971 2972 2973 2978 2979 2980 2981 2982 2983 2984 2988 2989
Mycoses	1100 1101 1102 1103 1104 1105 1106 1108 1109 1110 1111 1112 1113 1118 1119 1120 1121 1122 1123 1125 11282 11284 11285 11289 1129 1141 1143 1149 11500 11509 11510 11519 11590 11599 1160 1161 1162 1170 1171 1172 1173 1174 1175 1176 1177 1178 1179 118
Urinary tract infections	03284 59000 59001 59010 59011 5902 5903 59080 59081 5909 5950 5951 5952 5953 5954 59581 59582 59589 5959 5970 59780 59781 59789 59800 59801 5990
Gout or other crystal-induced arthropathy	2740 27400 27401 27402 27403 27410 27411 27419 27481 27482 27489 2749 71210 71211 71212 71213 71214 71215 71216 71217 71218 71219 71220 71221 71222 71223 71224 71225 71226 71227 71228 71229 71230 71231 71232 71233 71234 71235 71236 71237 71238 71239 71280 71281 71282 71283 71284 71285 71286 71287 71288 71289 71290 71291 71292 71293 71294 71295 71296 71297 71298 71299
Skin and soft tissue infections	0201 0210 0220 0311 03285 035 0390 6800 6801 6802 6803 6804 6805 6806 6807 6808 6809 68100 68101 68102 68110 68111 6819 6820 6821 6822 6823 6824 6825 6826 6827 6828 6829 684 6850 6851 6860 68600 68601 68609 6861 6868 6869
Chronic skin ulcer	7070 70700 70701 70702 70703 70704 70705 70706 70707 70709 7071 70710 70711 70712 70713 70714 70715 70719 70720 70721 70722 70723 70724 70725 7078 7079
Pneumonia	00322 0203 0204 0205 0212 0221 0310 0391 0521 0551 0730 0830 1124 1140 1144 1145 11505 11515 11595 1304 1363 4800 4801 4802 4803 4808 4809 481 4820 4821 4822 4823 48230 48231 48232 48239 4824 48240 48241 48242 48249 4828 48281 48282 48283 48284 48289 4829 483 4830 4831 4838 4841 4843 4845 4846 4847 4848 485 486 5130 5171
Charlson Comorbidity Index	
Component	**ICD-9-CM Diagnosis Codes**
Timing: Prior to or on the procedure date	
Myocardial infarction	"412"
Peripheral vascular disease	"441x","4439","7854","V434"
Cerebrovascular disease	"438"
Dementia	"290x"
Chronic pulmonary disease	"490","491","492","493","494","495","496","500","501","502","503","504","505, "5064"
Rheumatologic disease	"725","7100","7101","7104","7140","7141","7142", "71481"
Peptic ulcer disease	"5314x","5315x","5316x","5317x","5324x","5325x","5326x","5327x","5334x","5335x","5336x","5337x","5344x","5345x","5346x","5347x"
Mild liver disease	"5716x","5712","5714","5715"
Diabetes (mild to moderate)	"2500x","2501x","2502x","2503x","2507x"
Diabetes with chronic complications	"2504x","2505x","2506x"

Hemiplegia or paraplegia	"342x","3441"
Renal disease	"582x","588x","5830","5831","5832","5833","5834","5835","5836","5837","585","586"
Moderate or severe liver disease	"4560x","4561x","4562x", "5722","5723","5724","5725","5726","5727","5728","5729","5730","5731","5732","5733","5734","5735","5736","5737","5738","5739","5740","5741","5742","5743","5744","5745","5746","5747","5748","5749","5750","5751","5752","5753","5754","5755","5756","5757","5758","5759","5760","5761","5762","5763","5764","5765","5766","5767","5768","5769","5770","5771","5772","5773","5774","5775","5776","5777","5778","5779","5780","5781","5782","5783","5784","5785","5786","5787","5788","5789","5790","5791","5792","5793","5794","5795","5796", "5797","5798","5799","5800","5801","5802","5803","5804","5805","5806","5807","5808","5809","5810","5811","5812","5813","5814","5815","5816","5817","5818","5819","5820","5821","5822","5823","5824","5825","5826","5827","5828"
Timing: Prior to the procedure date	
Myocardial infarction	"410xx"
Congestive heart failure	"428x"
Cerebrovascular disease	"430x","431x","432x","433x","434x","435x","436x","437x"
Peptic ulcer disease	"5310x","5311x","5312x","5313x","5320x","5321x","5322x","5323x","5330x","5331x","5332x","5333x","5340x","5341x","5342x","5343x","5319","5329","5339","5349"
Any malignancy, including lymphoma and leukemia	"140x","141x","142x","143x","144x","145x","146x","147x","148x","149x","150x","151x","152x","153x","154x","155x","156x","157x","158x","159x","160x","161x","162x","163x","164x","165x","166x","167x","168x","169x","170x","171x","172x","174x","175x","176x","177x","178x","179x","180x","181x","182x","183x","184x","185x","186x","187x","188x","189x","190x","191x","192x","193x","194x","195x","200xx","201xx","202xx","203xx","204xx","205xx","206xx","207xx", "208xx"
Metastatic solid tumor	"196x","197x","198x","199x"
AIDS	"042x","043x","044x"
Peripheral vascular disease	ICD-9-CM procedure code "3848"

International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) claims used to create the Segal phenotypic frailty index (PFI) as per Segal JB, Chang HY, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a Claims-based Frailty Indicator Anchored to a Well-established Frailty Phenotype. *Med Care* 2017;55:716-722.

Supplemental Table V: Characteristics of Linked and Non-Linked Individuals Included in the EXTEND Study

Characteristic	Linked group (N = 4230)	Non-linked group (N = 1072)	p-value
Age (years)	83.0 ± 6.7	82.4 ± 7.1	0.02
Female sex — no. (%)	1939 (45.8)	478 (44.6)	0.47
Body Mass Index (kg/m^2)	28.2 ± 6.2	28.3 ± 6.4	0.14
New York Heart Association class — no. (%)			0.69
Class II	811 (19.2)	218 (20.3)	
Class III	2781 (65.7)	696 (20.0)	
Class IV	638 (15.1)	158 (19.9)	
Society of Thoracic Surgeons Risk Score (%)	7.9 ± 4.5	7.5 ± 4.4	0.02
Logistic EuroSCORE (%)	19.5 ± 14.6	20.0 ± 15.7	0.0011
Diabetes mellitus — no. (%)			
All	1585 (37.5)	400 (37.3)	0.94
Controlled by insulin	545 (12.9)	143 (13.3)	0.68
History of hypertension — no. (%)	3955 (93.5)	1000 (93.3)	0.80
Peripheral vascular disease — no. (%)	1787 (42.4)	474 (44.2)	0.28
Prior stroke — no. (%)	496 (11.7)	113 (10.6)	0.28
Prior transient ischemic attack — no. (%)	425 (10.1)	93 (8.7)	0.19
Cardiac risk factors— no. (%)			
Coronary artery disease	3189 (75.4)	813 (75.8)	0.76
Prior coronary-artery bypass surgery	1315 (31.1)	320 (29.9)	0.46
Prior percutaneous coronary intervention	1468 (34.7)	364 (34.0)	0.65
Balloon Valvuloplasty	417 (9.9)	98 (9.1)	0.53
Pre-Existing Pacemaker of Implantable Cardioverter-Defibrillator	818 (19.3)	234 (21.8)	0.07
Prior myocardial infarction	1025 (24.2)	252 (23.5)	0.63
Congestive heart failure	4126 (97.5)	1033 (96.4)	0.04
Prior atrial fibrillation or atrial flutter	1711 (40.5)	427 (39.9)	0.73

Reproduced with permission from Strom JB, Faridi KF, Butala NM, Zhao Y, Tamez H, Valsdottir LR, Brennan JM, Shen C, Popma JJ, Kazi DS, Yeh RW. Use of Administrative Claims to Assess Outcomes and Treatment Effect in Randomized Clinical Trials for Transcatheter Aortic Valve Replacement: Findings from the EXTEND Study. Circulation. 2020 Jul 21; 142(3):203-213. Represents a comparison of individuals linked and non-linked to Medicare claims in the US CoreValve Pivotal Trials dataset as part of the Extending Trial-Based Evaluations of Medical Therapies Using Novel Sources of Data (EXTEND) study. The 4230 linked individuals includes 600 individuals from the CoreValve High Risk trial, 421 from the US CoreValve Extreme Risk study, 915 from the High Risk Continued Access Study, and 1,005 from Surgery or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients (SURTAVI) trial. The non-linked group represents the baseline characteristics of individuals whose CoreValve study data could and could not be linked to Medicare claims. All values are listed as means ± standard deviations unless otherwise indicated. no. = number.

Supplemental Table VI: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked CoreValve study participants across DFI tertiles in the overall cohort

Characteristic	N obs	DFI Tertile 1 (N = 479)	DFI Tertile 2 (N = 468)	DFI Tertile 3 (N = 463)	p-value
Demographics					
Age (years)	1410	82.7 ± 5.7	81.7 ± 6.0	80.9 ± 6.4	< 0.001
Female sex – no. (%)	1410	230 (48.0)	197 (42.1)	199 (43.0)	0.14
Risk Scores					
Society of Thoracic Surgeons Risk Score	1410	4.9 ± 2.0	5.8 ± 2.4	7.0 ± 3.2	< 0.001
Logistic EuroSCORE	1408	13.6 ± 9.7	14.8 ± 10.2	16.5 ± 12.3	< 0.001
Charlson comorbidity index	590	4.2 ± 1.8	4.7 ± 2.0	5.5 ± 2.1	< 0.001
Comorbidities					
Diabetes mellitus – no. (%)					
Total	1410	85 (17.8)	195 (41.7)	267 (57.7)	< 0.001
Controlled by insulin	1410	19 (4.0)	51 (10.9)	91 (19.7)	< 0.001
History of hypertension – no. (%)	1410	437 (91.2)	448 (95.7)	452 (97.6)	< 0.001
Peripheral vascular disease – no. (%)	1410	119 (24.8)	177 (37.8)	256 (55.3)	< 0.001
Prior stroke – no. (%)	1410	16 (3.3)	41 (8.8)	80 (17.3)	< 0.001
Immunosuppressive therapy – no. (%)	1408	33 (6.9)	36 (7.7)	49 (10.6)	0.10
Prior transient ischemic attack – no. (%)	1410	21 (4.4)	39 (8.3)	73 (15.8)	< 0.001
Cardiac risk factors – no. (%)					
Coronary artery disease	1410	269 (56.2)	343 (73.3)	377 (81.4)	< 0.001
Prior CABG	1410	96 (20.0)	126 (26.9)	121 (26.1)	0.02
Prior PCI	1410	92 (19.2)	129 (27.6)	184 (39.7)	< 0.001
Pacemaker or Implantable Defibrillator	1410	42 (8.8)	75 (16.0)	97 (21.0)	< 0.001
Prior myocardial infarction	1410	56 (11.7)	89 (19.0)	123 (26.6)	< 0.001
Congestive Heart Failure	1410	241 (50.3)	332 (70.9)	391 (84.5)	< 0.001
Atrial flutter or fibrillation	1410	86 (18.0)	162 (34.6)	251 (54.2)	< 0.001
Procedural Variables					
Treatment assignment - no. (%)					
TAVR	1410	243 (50.7)	247 (52.8)	232 (50.1)	0.69
SAVR		236 (49.3)	221 (47.2)	231 (49.9)	
Presence of a calcified aorta – no. (%)	1410				< 0.001
No calcification		102 (21.3)	54 (11.5)	33 (7.1)	
Mild calcification		266 (55.5)	227 (48.5)	226 (48.8)	
Moderate calcification		85 (17.8)	147 (31.4)	141 (30.5)	
Severe calcification		26 (5.4)	40 (8.6)	63 (13.6)	
Arterial access site – no. (%)					0.03
Femoral	721	224 (46.8)	212 (45.3)	196 (42.3)	
Non-Femoral		19 (4.0)	35 (7.5)	35 (7.6)	

A DFI was able to be calculated in 1,410 individuals in the total cohort. Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a DFI ≤ 0.22, those in tertile 2 had a DFI 0.23-0.27, and those in tertile 3 had a DFI ≥ 0.28. CABG = coronary artery bypass grafting, DFI = deficit-based frailty index, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table VII: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked CoreValve High Risk study participants across DFI tertiles

Characteristic	N obs	DFI Tertile 1 (N = 204)	DFI Tertile 2 (N = 194)	DFI Tertile 3 (N = 193)	p-value
Demographics					
Age (years)	591	84.9 ± 6.0	83.5 ± 6.1	81.8 ± 6.3	< 0.001
Female sex – no. (%)	591	105 (51.5)	90 (46.4)	86 (44.6)	0.36
Risk Scores					
Society of Thoracic Surgeons Risk Score	591	6.8 ± 2.8	7.3 ± 2.8	8.2 ± 3.7	< 0.001
Logistic EuroSCORE	590	17.3 ± 12.6	18.0 ± 12.3	19.3 ± 13.7	0.28
Charlson comorbidity index	590	4.3 ± 1.8	5.0 ± 2.0	5.7 ± 2.2	< 0.001
Comorbidities					
Diabetes mellitus – no. (%)					
Total	591	43 (21.1)	88 (45.4)	109 (56.5)	< 0.001
Controlled by insulin	591	< 11	25 (12.9)	43 (22.3)	< 0.001
History of hypertension – no. (%)	591	188 (92.2)	189 (97.4)	187 (96.9)	0.03
Peripheral vascular disease – no. (%)	591	57 (27.9)	82 (42.3)	107 (55.4)	< 0.001
Prior stroke – no. (%)	591	13 (6.4)	31 (16.0)	34 (17.6)	< 0.001
Immunosuppressive therapy – no. (%)	589	11 (5.4)	19 (9.8)	24 (12.5)	0.04
Prior transient ischemic attack – no. (%)	591	18 (8.8)	29 (15.0)	31 (16.1)	0.06
Cardiac risk factors – no. (%)					
Coronary artery disease	591	135 (66.2)	147 (75.8)	159 (82.4)	< 0.001
Prior CABG	591	62 (30.4)	62 (32.0)	60 (31.1)	0.94
Prior PCI	591	62 (30.4)	74 (38.1)	83 (43.0)	0.03
Pacemaker or Implantable Defibrillator	591	30 (14.7)	47 (24.2)	47 (24.4)	0.02
Prior myocardial infarction	591	39 (19.1)	55 (28.4)	61 (31.6)	0.01
Congestive Heart Failure	591	120 (58.8)	139 (71.7)	166 (86.0)	< 0.001
Atrial flutter or fibrillation	591	54 (26.5)	77 (39.7)	121 (62.7)	< 0.001
Procedural Variables					
Treatment assignment - no. (%)					
TAVR	591	111 (54.4)	101 (52.1)	96 (49.7)	0.65
SAVR		93 (45.6)	93 (47.9)	97 (50.3)	
Presence of a calcified aorta – no. (%)	591				< 0.001
No calcification		38 (18.6)	19 (9.8)	< 11	
Mild calcification		96 (47.1)	90 (46.4)	91 (47.2)	
Moderate calcification		54 (26.5)	52 (26.8)	68 (35.2)	
Severe calcification		16 (7.8)	33 (17.0)	26 (13.5)	
Arterial access site – no. (%)	307				0.42
Femoral		93 (45.6)	75 (38.7)	79 (40.9)	
Non-Femoral		18 (8.8)	26 (13.4)	16 (8.3)	

A DFI was able to be calculated in 591 individuals in the High Risk trial cohort. Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a DFI ≤ 0.25, those in tertile 2 had a DFI

0.26-0.30, and those in tertile 3 had a DFI ≥ 0.31. CABG = coronary artery bypass grafting, DFI = deficit-based frailty index, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table VIII: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked SURTAVI participants across DFI tertiles

Characteristic	N obs	DFI Tertile 1 (N = 273)	DFI Tertile 2 (N = 280)	DFI Tertile 3 (N = 266)	p-value
Demographics					
Age (years)	819	82.1 ± 5.3	80.7 ± 5.6	78.9 ± 5.4	< 0.001
Female sex – no. (%)	819	127 (46.5)	114 (40.7)	104 (39.1)	0.18
Risk Scores					
Society of Thoracic Surgeons Risk Score	819	4.3 ± 1.4	4.7 ± 1.5	5.2 ± 1.6	< 0.001
Logistic EuroSCORE	818	11.9 ± 7.4	12.9 ± 8.9	12.8 ± 8.7	0.31
Comorbidities					
Diabetes mellitus – no. (%)					
Total	819	46 (16.9)	98 (35.0)	163 (61.3)	< 0.001
Controlled by insulin	819	11 (4.0)	23 (8.2)	53 (19.9)	< 0.001
History of hypertension – no. (%)	819	245 (89.7)	267 (95.4)	261 (98.1)	< 0.001
Peripheral vascular disease – no. (%)	819	60 (22.0)	110 (39.3)	136 (51.1)	< 0.001
Prior stroke – no. (%)	819	< 11	16 (5.7)	35 (13.2)	< 0.001
Immunosuppressive therapy – no. (%)	819	12 (4.4)	30 (10.7)	22 (8.3)	0.02
Prior transient ischemic attack – no. (%)	819	< 11	14 (5.0)	33 (12.4)	< 0.001
Cardiac risk factors – no. (%)					
Coronary artery disease	819	146 (53.5)	182 (65.0)	220 (82.7)	< 0.001
Prior CABG	819	49 (18.0)	53 (18.9)	57 (21.4)	0.58
Prior PCI	819	41 (15.0)	62 (22.1)	83 (31.2)	< 0.001
Pacemaker or Implantable Defibrillator	819	16 (5.9)	38 (13.6)	36 (13.5)	0.002
Prior myocardial infarction	819	26 (9.5)	41 (14.6)	46 (17.3)	0.03
Congestive Heart Failure	819	126 (45.8)	186 (66.4)	228 (85.7)	< 0.001
Atrial flutter or fibrillation	819	34 (12.5)	75 (26.8)	138 (51.9)	< 0.001
Procedural Variables					
Treatment assignment - no. (%)	819				0.52
TAVR		133 (48.7)	139 (49.6)	142 (53.4)	
SAVR		140 (51.3)	141 (50.4)	124 (46.6)	
Presence of a calcified aorta – no. (%)	819				< 0.001
No calcification		66 (24.2)	35 (12.5)	23 (8.7)	
Mild calcification		154 (56.4)	152 (54.3)	136 (51.1)	
Moderate calcification		41 (15.0)	81 (28.9)	77 (29.0)	
Severe calcification		12 (4.4)	12 (4.3)	30 (11.3)	
Arterial access site – no. (%)	414				0.24
Femoral		125 (45.8)	130 (46.4)	130 (48.9)	
Non-Femoral		< 11	< 11	12 (4.5)	

A DFI was able to be calculated in 819 individuals in the SURTAVI trial cohort. There were insufficient numbers to calculate a Charlson comorbidity index. Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a DFI ≤ 0.20, those in tertile 2 had a DFI 0.21-0.25, and those in tertile 3 had

a DFI ≥ 0.26. CABG = coronary artery bypass grafting, DFI = deficit-based frailty index, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table IX: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked CoreValve study participants across PFI tertiles in the overall cohort

Characteristic	N obs	Tertile 1 (N = 481)	Tertile 2 (N = 481)	Tertile 3 (N = 480)	p-value
Demographics					
Age (years)	1442	76.6 ± 5.6	82.7 ± 4.2	85.9 ± 4.0	< 0.001
Female sex – no. (%)	1442	156 (32.4)	206 (42.8)	273 (56.9)	< 0.001
Risk Scores					
Society of Thoracic Surgeons Risk Score	1442	4.8 ± 2.1	5.7 ± 2.5	7.1 ± 3.0	< 0.001
Logistic EuroSCORE	1440	12.3 ± 9.8	15.2 ± 10.5	17.2 ± 11.6	< 0.001
Charlson comorbidity index	599	5.1 ± 2.1	5.1 ± 2.0	4.9 ± 2.2	0.36
Comorbidities					
Diabetes mellitus – no. (%)					
Total	1442	216 (44.9)	192 (39.9)	152 (31.7)	< 0.001
Controlled by insulin	1442	82 (17.1)	43 (8.9)	39 (8.1)	< 0.001
History of hypertension – no. (%)	1442	458 (95.2)	457 (95.0)	452 (94.2)	0.74
Peripheral vascular disease – no. (%)	1437	208 (43.2)	165 (34.3)	188 (39.2)	0.02
Prior stroke – no. (%)	1441	47 (9.8)	38 (7.9)	53 (11.0)	0.24
Immunosuppressive therapy – no. (%)	1440	47 (9.8)	40 (8.3)	33 (6.9)	0.27
Prior transient ischemic attack – no. (%)	1441	38 (7.9)	52 (10.8)	45 (9.4)	0.30
Cardiac risk factors – no. (%)					
Coronary artery disease	1442	360 (74.8)	329 (68.4)	324 (67.5)	0.02
Prior CABG	1442	165 (34.3)	115 (23.9)	73 (15.2)	< 0.001
Prior PCI	1442	129 (26.8)	141 (29.3)	142 (29.6)	0.58
Pacemaker or Implantable Defibrillator	1442	60 (12.5)	76 (15.8)	83 (17.3)	0.10
Prior myocardial infarction	1442	107 (22.3)	85 (17.7)	84 (17.5)	0.11
Congestive Heart Failure	1442	225 (46.8)	348 (72.4)	414 (86.3)	< 0.001
Atrial flutter or fibrillation	1441	155 (32.2)	169 (35.1)	185 (38.5)	0.12
Procedural Variables					
Treatment assignment - no. (%)	1442				
TAVR		237 (49.3)	269 (55.9)	235 (49.0)	0.051
SAVR		244 (50.7)	212 (44.1)	245 (51.0)	
Presence of a calcified aorta – no. (%)	1439				0.03
No calcification		82 (17.0)	65 (13.5)	49 (10.2)	
Mild calcification		250 (52.0)	243 (50.5)	239 (50.0)	
Moderate calcification		108 (22.5)	130 (27.0)	142 (29.6)	
Severe calcification		41 (8.5)	42 (8.7)	48 (10.0)	
Arterial access site – no. (%)	740				0.78
Femoral		210 (43.7)	239 (49.7)	200 (41.7)	
Non-Femoral		27 (5.6)	30 (6.2)	34 (7.1)	

Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a PFI ≤ 0.18, those in tertile 2 had a PFI 0.19-0.28, and those in tertile 3 had a PFI ≥ 0.29. CABG = coronary artery bypass grafting, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, PFI =

phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table X: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked CoreValve High Risk study participants across PFI tertiles

Characteristic	N obs	Tertile 1 (N = 201)	Tertile 2 (N = 202)	Tertile 3 (N = 197)	p-value
Demographics					
Age (years)	600	78.7 ± 6.7	84.3 ± 4.4	87.4 ± 3.8	< 0.001
Female sex – no. (%)	600	68 (33.8)	100 (49.5)	115 (58.4)	< 0.001
Risk Scores					
Society of Thoracic Surgeons Risk Score	600	6.4 ± 2.9	7.6 ± 2.9	8.3 ± 3.4	< 0.001
Logistic EuroSCORE	599	17.5 ± 14.2	18.7 ± 12.5	18.5 ± 12.2	0.64
Charlson comorbidity index	599	5.1 ± 2.1	4.9 ± 2.0	4.9 ± 2.2	0.50
Comorbidities					
Diabetes mellitus – no. (%)					
Total	600	99 (49.3)	82 (40.6)	62 (31.5)	0.0014
Controlled by insulin	600	33 (16.4)	23 (11.4)	18 (9.1)	0.08
History of hypertension – no. (%)	600	188 (93.5)	199 (98.5)	185 (93.9)	0.02
Peripheral vascular disease – no. (%)	595	86 (42.8)	79 (39.1)	83 (42.1)	0.74
Prior stroke – no. (%)	599	33 (16.4)	26 (12.9)	20 (10.2)	0.19
Immunosuppressive therapy - no. (%)	598	27 (13.4)	14 (6.9)	13 (6.6)	0.03
Prior transient ischemic attack – no. (%)	599	29 (14.4)	26 (12.9)	25 (12.7)	0.86
Cardiac risk factors – no. (%)					
Coronary artery disease	600	158 (78.6)	158 (78.2)	133 (67.5)	0.02
Prior CABG	600	98 (48.8)	63 (31.2)	27 (13.7)	< 0.001
Prior PCI	600	70 (34.8)	78 (38.6)	73 (37.1)	0.73
Pacemaker or Implantable Defibrillator	600	40 (19.9)	48 (23.8)	39 (19.8)	0.54
Prior myocardial infarction	600	71 (35.3)	41 (20.3)	47 (23.9)	0.002
Congestive Heart Failure	600	103 (51.2)	153 (75.7)	176 (89.3)	< 0.001
Atrial flutter or fibrillation	600	77 (38.3)	88 (43.8)	89 (45.2)	0.34
Procedural Variables					
Treatment assignment - no. (%)	600				
TAVR		106 (52.7)	111 (55.0)	97 (49.2)	0.52
SAVR		95 (47.3)	91 (45.1)	100 (50.8)	
Presence of a calcified aorta – no. (%)	600				
No calcification		22 (11.0)	23 (11.4)	20 (10.2)	0.65
Mild calcification		96 (47.8)	88 (43.6)	98 (50.0)	
Moderate calcification		61 (30.4)	58 (28.7)	58 (29.4)	
Severe calcification		22 (11.0)	33 (16.3)	21 (10.7)	
Arterial access site – no. (%)	313				0.70
Femoral		83 (41.3)	91 (45.0)	78 (39.6)	
Non-Femoral		23 (11.4)	19 (9.4)	19 (9.6)	

Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a PFI ≤ 0.22, those in tertile 2 had a PFI 0.23-0.34, and those in tertile 3 had a PFI ≥ 0.35. CABG = coronary artery bypass grafting, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, PFI = phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XI: Baseline demographic, procedural, risk score, and comorbidity characteristics of linked SURTAVI study participants across PFI tertiles

Characteristic	N obs	Tertile 1 (N = 281)	Tertile 2 (N = 281)	Tertile 3 (N = 280)	p-value
Demographics					
Age (years)	842	75.9 ± 5.3	81.5 ± 4.1	84.4 ± 3.7	< 0.001
Female sex – no. (%)	842	83 (29.5)	117 (41.6)	152 (54.3)	< 0.001
Risk Scores					
Society of Thoracic Surgeons Risk Score	842	4.2 ± 1.7	4.7 ± 1.3	5.4 ± 1.5	< 0.001
Logistic EuroSCORE	841	10.6 ± 7.3	12.4 ± 7.7	14.7 ± 9.3	< 0.001
Comorbidities					
Diabetes mellitus – no. (%)					
Total	842	125 (44.5)	101 (35.9)	91 (32.5)	0.01
Controlled by insulin	842	48 (17.1)	25 (8.9)	17 (6.1)	< 0.001
History of hypertension – no. (%)	842	266 (94.7)	269 (95.7)	260 (92.9)	0.33
Peripheral vascular disease – no. (%)	842	119 (42.4)	102 (36.3)	92 (32.9)	0.06
Prior stroke – no. (%)	842	23 (8.2)	15 (5.3)	21 (7.5)	0.37
Immunosuppressive therapy - no. (%)	842	23 (8.2)	22 (7.8)	21 (7.5)	0.96
Prior transient ischemic attack – no. (%)	842	15 (5.3)	20 (7.1)	20 (7.1)	0.60
Cardiac risk factors – no. (%)					
Coronary artery disease	842	203 (72.2)	188 (66.90)	173 (61.8)	0.03
Prior CABG	842	85 (30.3)	49 (17.4)	31 (11.1)	< 0.001
Prior PCI	842	69 (24.6)	70 (24.9)	52 (18.6)	0.13
Pacemaker or Implantable Defibrillator	842	33 (11.7)	26 (9.3)	33 (11.8)	0.54
Prior myocardial infarction	842	60 (17.8)	32 (11.4)	35 (12.5)	0.07
Congestive Heart Failure	842	123 (43.8)	197 (70.1)	235 (83.9)	< 0.001
Atrial flutter or fibrillation	842	79 (28.1)	95 (33.8)	81 (28.9)	0.29
Procedural Variables					
Treatment assignment - no. (%)					
TAVR	842	129 (45.9)	159 (56.6)	139 (49.6)	0.37
SAVR		152 (54.1)	122 (43.4)	141 (50.4)	
Presence of a calcified aorta – no. (%)	839				0.08
No calcification		52 (18.5)	49 (17.4)	30 (10.7)	
Mild calcification		151 (53.7)	139 (49.5)	160 (57.1)	
Moderate calcification		58 (20.6)	76 (27.0)	69 (24.6)	
Severe calcification		20 (7.1)	16 (5.7)	19 (6.8)	
Arterial access site – no. (%)	427				0.35
Femoral		121 (43.1)	150 (53.4)	126 (45.0)	
Non-Femoral		< 11	< 11	13	

Values are listed as means ± standard deviations unless otherwise specified. Individuals in tertile 1 had a PFI ≤ 0.15, those in tertile 2 had a PFI 0.16-0.24, and those in tertile 3 had a PFI ≥ 0.25. CABG = coronary artery bypass grafting, N obs = number of observations, no. = number, PCI = percutaneous coronary intervention, PFI = phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XII: Number of Individuals Experiencing Each Outcome by CoreValve Trial Subset, Treatment Group, and DFI Tertile

Outcome	DFI Tertile	Treatment Group	N (%) with Event in Overall Dataset	N (%) with Event in High Risk Trial	N (%) with Event in SURTAVI Trial
Death	1	SAVR	24 (10.2%)	30 (32.3%)	< 11
		TAVR	40 (16.5%)	37 (33.3%)	13 (9.8%)
	2	SAVR	55 (24.9%)	36 (38.7%)	17 (12.1%)
		TAVR	48 (19.4%)	30 (29.7%)	20 (14.4%)
	3	SAVR	83 (35.9%)	45 (46.4%)	27 (21.8%)
		TAVR	87 (37.5%)	45 (46.9%)	30 (21.1%)
MACCE	1	SAVR	41 (17.4%)	39 (41.9%)	17 (12.1%)
		TAVR	64 (26.3%)	48 (43.2%)	26 (19.6%)
	2	SAVR	77 (34.8%)	50 (53.8%)	30 (21.3%)
		TAVR	70 (28.3%)	37 (36.6%)	32 (23.0%)
	3	SAVR	103 (44.6%)	49 (50.5%)	36 (29.0%)
		TAVR	102 (44.0%)	46 (47.9%)	47 (33.1%)
AKI	1	SAVR	41 (17.4%)	15 (16.1%)	19 (13.6%)
		TAVR	< 11	< 11	< 11
	2	SAVR	37 (16.7%)	17 (18.3%)	30 (21.3%)
		TAVR	23 (9.3%)	< 11	12 (8.6%)
	3	SAVR	41 (17.8%)	17 (17.5%)	21 (16.9%)
		TAVR	15 (6.5%)	< 11	15 (9.9%)
Bleeding	1	SAVR	53 (22.5%)	48 (51.6%)	22 (15.7%)
		TAVR	65 (26.8%)	48 (43.2%)	25 (18.8%)
	2	SAVR	67 (30.3%)	45 (48.4%)	22 (15.6%)
		TAVR	82 (33.2%)	50 (49.5%)	34 (24.5%)
	3	SAVR	89 (38.5%)	43 (44.3%)	29 (23.4%)
		TAVR	83 (35.8%)	42 (43.8%)	31 (21.8%)
Stroke/TIA	1	SAVR	25 (10.6%)	16 (17.2%)	15 (10.7%)
		TAVR	30 (12.4%)	20 (18.0%)	14 (10.5%)
	2	SAVR	38 (17.2%)	21 (22.6%)	18 (12.8%)
		TAVR	29 (11.7%)	< 11	14 (10.1%)
	3	SAVR	41 (17.8%)	17 (17.5%)	17 (13.7%)
		TAVR	31 (13.4%)	16 (16.7%)	16 (11.3%)
MI	1	SAVR	< 11	< 11	< 11
		TAVR	< 11	< 11	< 11
	2	SAVR	< 11	< 11	< 11
		TAVR	< 11	< 11	< 11
	3	SAVR	< 11	< 11	< 11
		TAVR	< 11	0 (0.0%)	< 11
Hospitalization	1	SAVR	24 (10.2%)	11 (11.8%)	< 11
		TAVR	27 (11.1%)	19 (17.1%)	13 (9.8%)
	2	SAVR	36 (16.3%)	18 (19.4%)	22 (15.6%)
		TAVR	57 (23.1%)	30 (29.7%)	23 (16.6%)
	3	SAVR	52 (22.5%)	23 (23.7%)	32 (25.8%)
		TAVR	59 (25.4%)	27 (28.1%)	31 (21.8%)
Poor Function	1	SAVR	27 (11.4%)	21 (22.6%)	11 (7.9%)
		TAVR	27 (11.1%)	20 (18.0%)	16 (12.0%)
	2	SAVR	33 (14.9%)	15 (16.1%)	14 (9.9%)
		TAVR	33 (13.4%)	20 (19.8%)	< 11

	3	SAVR	48 (20.8%)	29 (29.9%)	18 (14.5%)
		TAVR	45 (19.4%)	21 (21.9%)	18 (12.7%)

Listed are the number of individuals who experienced each outcome stratified by randomly assigned treatment group (TAVR vs. SAVR) and DFI tertile. A poor functional outcome was defined as death, KCCQ-OS < 45 or a ≥ 10-point drop in KCCQ-OS at 6 months. All other event rates are provided at 1-year after the initial procedure and determined using Kaplan-Meier estimates. Non-death outcome rates are adjusted for the competing risk of death using Fine-Gray techniques. AKI = acute kidney injury, DFI = deficit-based frailty index, KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Summary score, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, N = number of individuals, TIA = transient ischemic attack. Cell values < 11 are suppressed per Medicare policy.

Supplemental Table XIII: Number of Individuals Experiencing Each Outcome by CoreValve Trial Subset, Treatment Group, and PFI Tertile

Outcome	PFI Tertile	Treatment Group	N (%) with Event in Overall Dataset	N (%) with Event in High Risk Trial	N (%) with Event in SURTAVI Trial
Death	1	SAVR	41 (16.8%)	31 (32.6%)	13 (8.9%)
		TAVR	45 (19.0%)	33 (31.1%)	17 (13.2%)
	2	SAVR	49 (23.1%)	31 (34.1%)	22 (18.0%)
		TAVR	52 (19.3%)	37 (33.3%)	23 (14.5%)
	3	SAVR	75 (30.6%)	52 (52.0%)	16 (11.4%)
		TAVR	87 (37.0%)	46 (47.4%)	28 (20.1%)
MACCE	1	SAVR	63 (25.8%)	44 (46.3%)	26 (17.1%)
		TAVR	64 (27.0%)	43 (40.6%)	28 (21.7%)
	2	SAVR	73 (34.4%)	38 (41.8%)	32 (26.2%)
		TAVR	89 (33.1%)	45 (40.5%)	44 (27.7%)
	3	SAVR	90 (36.7%)	59 (59.0%)	27 (19.2%)
		TAVR	95 (40.4%)	47 (48.5%)	41 (29.5%)
AKI	1	SAVR	45 (18.4%)	17 (17.9%)	28 (18.4%)
		TAVR	19 (8.0%)	< 11	13 (10.1%)
	2	SAVR	38 (17.9%)	14 (15.4%)	23 (18.9%)
		TAVR	18 (6.7%)	< 11	12 (7.8%)
	3	SAVR	39 (15.9%)	19 (19.0%)	21 (14.9%)
		TAVR	15 (6.4%)	< 11	< 11
Bleeding	1	SAVR	61 (25.0%)	43 (45.3%)	29 (19.1%)
		TAVR	63 (26.6%)	40 (37.7%)	25 (19.4%)
	2	SAVR	67 (31.6%)	43 (47.3%)	19 (15.6%)
		TAVR	74 (27.5%)	44 (39.6%)	39 (24.5%)
	3	SAVR	84 (34.3%)	51 (51.0%)	27 (19.2%)
		TAVR	98 (41.7%)	58 (59.8%)	29 (20.9%)
Stroke/TIA	1	SAVR	36 (14.8%)	21 (22.1%)	19 (12.5%)
		TAVR	23 (9.7%)	18 (17.0%)	< 11
	2	SAVR	29 (13.7%)	< 11	13 (10.7%)
		TAVR	43 (16.0%)	15 (13.5%)	19 (12.0%)
	3	SAVR	41 (16.7%)	23 (23.0%)	20 (14.2%)
		TAVR	28 (11.9%)	13 (13.4%)	19 (13.7%)
MI	1	SAVR	< 11	< 11	< 11
		TAVR	< 11	< 11	< 11
	2	SAVR	< 11	< 11	< 11
		TAVR	< 11	< 11	< 11
	3	SAVR	< 11	< 11	< 11
		TAVR	< 11	0 (0.0%)	< 11
Hospitalization	1	SAVR	34 (13.9%)	18 (19.0%)	14 (9.2%)
		TAVR	48 (20.3%)	29 (27.4%)	24 (18.6%)
	2	SAVR	39 (18.4%)	22 (24.2%	24 (19.7%)
		TAVR	48 (17.8%)	24 (21.6%)	23 (14.5%)
	3	SAVR	40 (16.3%)	13 (13.0%)	22 (15.6%)
		TAVR	52 (22.1%)	24 (24.7%)	24 (17.3%)
Poor Function	1	SAVR	27 (12.6%)	18 (25.7%)	12 (8.6%)
		TAVR	25 (11.9%)	16 (21.3%)	10 (8.1%)
	2	SAVR	29 (17.9%)	13 (20.0%)	16 (15.2%)
		TAVR	31 (13.2%)	20 (22.0%)	14 (9.4%)
	3	SAVR	53 (28.3%)	34 (50.0%)	16 (13.9%)
		TAVR	54 (27.7%)	28 (37.3%)	22 (17.3%)

Listed are the number of individuals who experienced each outcome stratified by randomly assigned treatment group (TAVR vs. SAVR) and PFI tertile. A poor functional outcome was defined as death, KCCQ-OS < 45 or a ≥ 10-point drop in KCCQ-OS at 6 months. All other event rates are provided at 1-year after the initial procedure and determined using Kaplan-Meier estimates. Non-death outcome rates are adjusted for the competing risk of death using Fine-Gray techniques. AKI = acute kidney injury, KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Summary score, MACCE = major adverse cardiovascular and cerebrovascular event, MI = myocardial infarction, N = number of individuals, PFI = phenotype-based frailty index, TIA = transient ischemic attack. Cell values < 11 are suppressed per Medicare policy.

Supplemental Table XIV: Characteristics of Individuals with Missing and Non-missing Functional Outcome Data

Characteristic	Missing functional data (N = 239)	Nonmissing functional data (N = 1118)	p-value
Age (years)	82.3 ± 6.2	81.5 ± 5.9	0.07
Female sex — no. (%)	120 (50.2)	477 (42.7)	0.04
Body Mass Index (kg/m^2)	28.2 ± 5.7	29.3 ± 6.0	0.007
New York Heart Association class — no. (%)			0.05
Class II	54 (22.6)	335 (30.0)	
Class III	161 (67.4)	674 (60.3)	
Class IV	19 (8.0)	99 (8.9)	
Society of Thoracic Surgeons Risk Score (%)	6.4 ± 2.9	5.6 ± 2.6	0.0003
Logistic EuroSCORE (%)	15.4 ± 10.0	14.6 ± 10.8	0.28
Diabetes mellitus — no. (%)			
All	72 (46.2)	158 (40.6)	0.25
Controlled by insulin	29 (12.1)	125 (11.2)	0.65
History of hypertension — no. (%)	228 (95.4)	1059 (94.7)	0.75
Peripheral vascular disease — no. (%)	97 (40.8)	430 (38.5)	0.56
Prior stroke — no. (%)	33 (21.2)	74 (19.0)	0.63
Prior transient ischemic attack — no. (%)	20 (8,4)	110 (9.8)	0.55
Cardiac risk factors— no. (%)			
Coronary artery disease	153 (64.0)	799 (71.5)	0.02
Prior coronary-artery bypass surgery	56 (23.4)	281 (25.1)	0.62
Prior percutaneous coronary intervention	47 (30.1)	169 (43.4)	0.005
Balloon Valvuloplasty	13 (5.4)	38 (3.4)	0.14
Pre-Existing Pacemaker of Implantable Cardioverter-Defibrillator	47 (19.7)	151 (13.5)	0.02
Prior myocardial infarction	51 (21.3)	200 (17.9)	0.23
Congestive heart failure	164 (68.6)	758 (67.8)	0.88
Prior atrial fibrillation or atrial flutter	90 (37.7)	380 (34.0)	0.29

Listed is a comparison of baseline characteristics of individuals with missing and non-missing functional status data. Values are listed as means ± standard deviations unless otherwise specified. N obs = number of observations, no. = number, PCI = percutaneous coronary intervention.

Supplemental eTable XV: Relative Treatment effect for TAVR vs. SAVR for Functional Impairment or Death by 6 Months Post-Procedure in the linked CoreValve Trials by DFI Tertile

Cohort	DFI Tertile	Adjusted OR (95% CI) for SAVR vs. TAVR (reference)	p-value	p-value for interaction
Overall	1	3.21 (0.84-12.26)	0.09	0.50
	2	0.96 (0.43-2.15)	0.93	
	3	1.40 (0.76-2.56)	0.28	
High Risk trial	1	1.56 (0.72-3.37)	0.26	0.50
	2	0.71 (0.31-1.63)	0.42	
	3	1.70 (0.81-3.56)	0.16	
SURTAVI trial	1	0.93 (0.38-2.30)	0.88	0.67
	2	1.58 (0.63-3.93)	0.33	
	3	1.00 (0.47-2.15)	0.99	

Shown are the adjusted odds ratios for functional impairment or death at 6 months in the CoreValve trials, stratified by cohort, and DFI tertile. A poor functional outcome was defined as death, a KCCQ-OS < 45 or a decrease ≥ 10 points in the KCCQ-OS at 6 months post-procedure. Adjusted odds ratios, 95% confidence intervals, and p-values for the effect of SAVR vs. TAVR (reference group) were estimated using multivariable logistic regression. Additionally, a pre-specified interaction between treatment group and DFI tertile was evaluated. In the overall cohort, estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, immunosuppressive therapy, prior transient ischemic attack or stroke, coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, prior myocardial infarction, atrial fibrillation or flutter, congestive heart failure, and presence of aortic calcification. In the HiR trial, estimates are adjusted for age, Society of Thoracic Surgeons Risk score, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, myocardial infarction, coronary artery bypass grafting, congestive heart failure, presence of pacemaker or implantable defibrillator, aortic calcification, and presence of atrial fibrillation or flutter. In the SURTAVI trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, diabetes, hypertension, peripheral vascular disease, coronary artery disease, pacemaker or implantable defibrillator, congestive heart failure, myocardial infarction, prior stroke, prior transient ischemic attack, receipt of percutaneous coronary intervention, aortic calcification, and atrial fibrillation or flutter. DFI = deficit-based frailty index, CI = confidence interval, OR = odds ratio, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XVI: Relative Treatment effect for TAVR vs. SAVR for Functional Impairment or Death by 6 Months Post-Procedure in the linked CoreValve Trials by PFI Tertile

Cohort	PFI Tertile	Adjusted OR (95% CI) for SAVR vs. TAVR (reference)	p-value	p-value for interaction
Overall	1	1.13 (0.61-2.07)	0.70	0.75
	2	1.33 (0.74-2.39)	0.34	
	3	1.00 (0.62-1.61)	> 0.99	
High Risk trial	1	1.46 (0.62-3.41)	0.39	0.54
	2	0.70 (0.29-1.67)	0.42	
	3	1.36 (0.65-2.87)	0.41	
SURTAVI trial	1	1.03 (0.41-2.56)	0.96	0.40
	2	1.69 (0.76-3.73)	0.20	
	3	0.87 (0.41-1.85)	0.73	

Shown are the adjusted odds ratios for functional impairment or death at 6 months in the CoreValve trials, stratified by cohort, and PFI tertile. A poor functional outcome was defined as death, a KCCQ-OS < 45 or a decrease ≥ 10 points in the KCCQ-OS at 6 months post-procedure. Adjusted odds ratios, 95% confidence intervals, and p-values for the effect of SAVR vs. TAVR (reference group) were estimated using multivariable logistic regression. Additionally, a pre-specified interaction between treatment group and PFI tertile was evaluated. In the overall cohort, estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery bypass grafting, congestive heart failure, and presence of aortic calcification. In the HiR trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, history of diabetes mellitus, hypertension, immunotherapy, myocardial infarction, coronary artery bypass grafting, and congestive heart failure. In the SURTAVI trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery disease, coronary artery bypass grafting, and congestive heart failure. CI = confidence interval, OR = odds ratio, PFI = phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XVII: Results of a Sensitivity Analysis Examining Relative Treatment Effects of TAVR vs. SAVR for Death Within 30-days of the Aortic Valve Procedure

Overall Cohort				
FI type	**FI tertile**	**Hazard Ratio (95% CI) for SAVR vs. TAVR (reference) comparison**	**Log-rank p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	1.96 (0.40-9.60)	0.41	0.16
	2	2.65 (0.66-10.69)	0.17	
	3	0.46 (0.14-1.48)	0.19	
PFI	1	0.59 (0.14-2.46)	0.47	0.34
	2	6.24 (0.95-40.92)	0.06	
	3	0.67 (0.24-1.83)	0.43	
High Risk Trial Cohort				
FI type	**FI tertile**	**Hazard Ratio (95% CI) for SAVR vs. TAVR (reference) comparison**	**Log-rank p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	3.18 (0.77-13.21)	0.11	0.31
	2	4.26 (0.33-55.54)	0.27	
	3	0.77 (0.17-3.49)	0.73	
PFI	1	1.17 (0.16-8.55)	0.88	0.92
	2	2.64 (0.18-38.69)	0.48	
	3	1.30 (0.42-3.98)	0.65	
SURTAVI Trial Cohort				
FI type	**FI tertile**	**Hazard Ratio (95% CI) for SAVR vs. TAVR (reference) comparison**	**Log-rank p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	N/A	N/A	0.73
	2	1.50 (0.13-17.53)	0.75	
	3	0.53 (0.09-2.97)	0.47	
PFI	1	0.32 (0.03-3.35)	0.34	0.28
	2	5.49 (0.36-83.44)	0.22	
	3	N/A	N/A	

Shown are the adjusted hazard ratios for death at 30 days in the CoreValve trials, stratified by cohort, and FI tertile. Adjusted hazard ratios, 95% confidence intervals, and p-values for the effect of SAVR vs. TAVR were estimated using multivariable Cox proportional hazards regression. N/A indicates that there were insufficient numbers of deaths in a tertile to estimate a hazard ratio and confidence interval. Additionally, a pre-specified interaction between treatment group and FI tertile was evaluated. In the overall cohort, estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery bypass grafting, congestive heart failure, and presence of aortic calcification. In the HiR trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, history of diabetes mellitus, hypertension, immunotherapy, myocardial infarction, coronary artery bypass grafting, and congestive heart failure. In the SURTAVI trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery disease, coronary artery bypass grafting, and congestive heart failure. CI = confidence interval, DFI = deficit-based frailty index, PFI = phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XVIII: Results of a Sensitivity Analysis Examining Absolute Treatment Effects of TAVR vs. SAVR for Death Within 30-days of the Aortic Valve Procedure

Overall Cohort				
FI type	**FI tertile**	**Risk Difference (95% CI) for SAVR vs. TAVR (reference) comparison**	**p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	0.5% (-1.7%, 2.6%)	0.68	0.41
	2	2.0% (-0.7%, 4.6%)	0.15	
	3	-1.7% (-4.8%, 1.4%)	0.28	
PFI	1	-0.5% (-2.9%, 2.0%)	0.70	0.91
	2	1.6% (-0.7%, 3.9%)	0.14	
	3	-1.4% (-4.7%, 1.9%)	0.40	
High Risk Trial Cohort				
FI type	**FI tertile**	**Risk Difference (95% CI) for SAVR vs. TAVR (reference) comparison**	**p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	4.8% (-1.4%, 11.0%)	0.12	0.10
	2	1.2% (-2.4%, 4.7%)	0.51	
	3	-2.1% (-7.8%, 3.5%)	0.46	
PFI	1	1.7% (-5.5%, 8.9%)	0.66	0.75
	2	1.3% (-2.4%, 5.0%)	0.47	
	3	0.4% (-4.6%, 5.4%)	0.89	
SURTAVI Trial Cohort				
FI type	**FI tertile**	**Risk Difference (95% CI) for SAVR vs. TAVR (reference) comparison**	**p-value for SAVR vs. TAVR comparison**	**p-value for interaction**
DFI	1	-0.8% (-2.2%, 0.7%)	0.30	0.80
	2	0.7% (-1.7%, 3.1%)	0.57	
	3	-1.2% (-4.7%, 2.3%)	0.51	
PFI	1	-1.2% (-3.3%, 1.0%)	0.29	0.74
	2	1.8% (-1.1%, 4.7%)	0.19	
	3	-3.6% (-7.6%, 0.4%)	0.05	

Shown are the adjusted risk differences for death at 30 days in the CoreValve trials, stratified by cohort, and FI tertile. Adjusted risk differences, 95% confidence intervals, and p-values for the effect of SAVR vs. TAVR were estimated using multivariable Cox proportional hazards regression. Additionally, a pre-specified interaction between treatment group and FI tertile was evaluated. In the overall cohort, estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery bypass grafting, congestive heart failure, and presence of aortic calcification. In the HiR trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, history of diabetes mellitus, hypertension, immunotherapy, myocardial infarction, coronary artery bypass grafting, and congestive heart failure. In the SURTAVI trial, estimates are adjusted for age, sex, Society of Thoracic Surgeons Risk score, Logistic EuroSCORE, history of diabetes mellitus, coronary artery disease, coronary artery bypass grafting, and congestive heart failure. CI = confidence interval, DFI = deficit-based frailty index, PFI = phenotype-based frailty index, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.

Supplemental Table XIX: Relative Treatment effect for TAVR vs. SAVR for Functional Impairment or Death by 6 Months Post-Procedure in the Unlinked Combined CoreValve Trials by DFI Tertile

DFI Tertile	Adjusted OR (95% CI) for SAVR vs. TAVR (reference)	p-value	p-value for interaction
1	0.91 (0.59-1.39)	0.66	0.14
2	1.63 (1.06-2.49)	0.02	
3	1.21 (0.84-1.74)	0.31	

Shown are the adjusted odds ratios for functional impairment or death at 6 months in the combined, non-linked CoreValve trials stratified by DFI tertile. A poor functional outcome was defined as death, a KCCQ-OS < 45 or a decrease ≥ 10 points in the KCCQ-OS at 6 months post-procedure. Adjusted odds ratios, 95% confidence intervals, and p-values for the effect of SAVR vs. TAVR (reference group) were estimated using multivariable logistic regression. Additionally, a pre-specified interaction between treatment group and DFI tertile was evaluated. Estimates are adjusted for age, sex, Society of Thoracic Surgeons risk score, Logistic EuroSCORE, Charlson comorbidity index, history of diabetes mellitus, hypertension, peripheral vascular disease, immunosuppressive therapy, prior transient ischemic attack or stroke, coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, prior myocardial infarction, atrial fibrillation or flutter, congestive heart failure, and presence of aortic calcification. DFI = deficit-based frailty index, CI = confidence interval, OR = odds ratio, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.