Medical Policy

Subject:	Transcatheter Heart Valve Procedures		
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Description/Scope

This document addresses the transcatheter (percutaneous or catheter-based) approach for aortic or pulmonary heart valve replacement, transcatheter edge-to-edge repair (also referred to as transcatheter mitral valve repair using leaflet repair or percutaneous annuloplasty), and transcatheter tricuspid valve repair or replacement.

Position Statement

Medically Necessary:

Transcatheter Aortic Valve Replacement (TAVR):

TAVR using a U.S. Food and Drug Administration (FDA) approved device* is considered **medically necessary** when the following criteria have been met:

A. The individual has severe degenerative, native valve aortic stenosis demonstrated by **one** of the following:
   1. The aortic valve area (AVA) is equal to or less than 1.0 cm^2; **or**
   2. The AVA index is equal to or less than 0.6 cm^2/m^2; **or**
   3. A mean aortic valve gradient equal to or more than 40 mm Hg; **or**
   4. A peak aortic-jet velocity equal to or more than 4.0 m/sec; **and**
B. Heart failure symptoms of New York Heart Association (NYHA) class II or greater; **and**
C. The individual is in **one** of the following categories:
   1. *Age 65 years or older with* **any open surgical risk**; **or**
   2. *Age younger than 65 with* **intermediate or greater open surgical risk** (predicted risk of surgical mortality at 30 days greater than or equal to 3%) as determined by at least two physicians.

Valve-in-valve TAVR implantation using an FDA approved device* is considered **medically necessary** for treatment when the following criteria are met:

A. The individual has failure (that is, stenosed, insufficient, or both) of previous open surgical bioprosthetic *aortic* valve; **and**
B. The individual is at high or greater risk for open surgical therapy (that is, Society of Thoracic Surgeons operative risk score greater than or equal to 8% or at a 15% or greater risk of operative mortality at 30 days) as determined by at least two physicians.

***Note:** Please refer to background section of document for list of FDA approved transcatheter heart valve (THV) devices used for TAVR

Transcatheter Mitral Edge-to-Edge Repair:
Transcatheter mitral edge-to-edge repair/transcatheter mitral valve repair using an FDA approved device** is considered **medically necessary** when individual has **one** of the following conditions:

A. ***Chronic degenerative (primary) mitral regurgitation*** (***MR)*** and meets **all** the following criteria;
   1. Graded as moderate-to severe (3+ to 4+) MR; **and**
   2. Severely symptomatic heart failure (NYHA class III or IV); **and**
   3. Echocardiogram demonstrates that the primary regurgitant jet results from malcoaptation of the A2 and P2 scallops of the mitral valve; **and**
   4. Prohibitive surgical risk for open surgical therapy (predicted risk of surgical mortality greater than or equal to 8% at 30 days) as determined by at least two physicians (Multidisciplinary Heart valve team); **or**

B. ***Functional (secondary) MR*** and meets **all** the following criteria:
   1. Graded as moderate-severe (3+ to 4+) MR; **and**
   2. Severely symptomatic heart failure (NYHA class III or IV); **and**
   3. Echocardiogram demonstrates that the primary regurgitant jet results from malcoaptation of the A2 and P2 scallops of the mitral valve; **and**
   4. MR severity persist despite maximally tolerated guideline-directed medical therapy as determined by at least two physicians (Multidisciplinary Heart Team).

****Note:** Please refer to background section of document for list of FDA approved transcatheter mitral valve repair devices.

Transcatheter Pulmonary Valve (TPV):

TPV implantation with an FDA approved device*** is considered **medically necessary** when the following criteria are met:

A. Dysfunctional right ventricular outflow tract (RVOT) tract (native, patched or implanted conduit) with **one** of the following clinical indications for intervention:
   1. moderate or greater pulmonic regurgitation; **or**
   2. pulmonic stenosis with a mean RVOT gradient greater or equal to 35 mm Hg.

****Note:** Please refer to background section of document for list of FDA approved TPVs.

Not Medically Necessary:

Transcatheter (aortic, pulmonic, or valve-in-valve) valve replacement is considered **not medically necessary** when the criteria above are not met.

Transcatheter mitral edge-to-edge repair/transcatheter mitral valve repair is considered **not medically necessary** for the treatment of primary or secondary (functional) MR when the criteria above are not met.

Investigational and Not Medically Necessary:

TAVR cerebral protection devices (for example, Sentinel™ Cerebral Protection System) are considered **investigational and not medically necessary** for all indications.

Transcatheter mitral edge-to-edge repair/transcatheter mitral valve repair is considered **investigational and not medically necessary** for all other indications.

Valve-in-valve transcatheter mitral valve replacement is considered **investigational and not medically necessary** for all indications.

Transcatheter mitral valve repair using percutaneous annuloplasty (for example, CARILLON Mitral Contour System) is considered **investigational and not medically necessary** for all indications.

Transcatheter tricuspid valve repair or replacement is considered **investigational and not medically necessary** for all indications.

Rationale

The Centers for Disease Control and Prevention (CDC) estimates that about 2.5% of the U.S. population has valvular heart disease. The prevalence of valvular heart disease increases with age and affects about 13% of people born before 1943, when penicillin became widely available to treat streptococcal infection and thereby prevent development of rheumatic heart disease. There are about 23,000 deaths due to valvular heart disease each year in the U.S.; approximately 61% of these deaths are due to aortic valve disease, 15% from mitral valve disease, and 24% to dysfunction in the pulmonary or tricuspid valves (CDC, 2024).

The 2020 American College of Cardiology (ACC)/ American Heart Association (AHA) Guideline for the Management of individuals with valvular heart disease notes that the severity of valvular heart disease is characterized based on symptoms, valve anatomy, the severity of valve dysfunction, and the response of the ventricle and pulmonary circulation.

Prior to the 1980s, the only surgical options for individuals with severe symptomatic valvular heart disease who received inadequate benefits from medical therapy were open heart procedures. Many of the candidates for these procedures had prohibitive surgical risk due to the severity of their disease. Beginning with percutaneous pulmonary valvuloplasty in 1982, a variety of transcatheter valve interventions have been developed for each of the heart valves.

Transcatheter Aortic Valve Replacement (TAVR):

Techniques and technologies for TAVR have evolved significantly since the original proof of concept reported by Cribner in 2002. TAVR was initially considered an option only for individuals considered inoperable for conventional surgical aortic valve replacement (SAVR). Proposed indications for transcatheter aortic valve replacement have expanded for selected individuals with lower surgical risk as more experience has been gained with this procedure. TAVR is sometimes labeled as transcatheter aortic valve implantation (TAVI). In this document we consider TAVR and TAVI to be equivalent terms and will refer to the procedure as TAVR.

The design and major outcomes of major clinical trials investigating TAVR are summarized below:

Study	Rode's-Cabau 2010/2012	PARTNER B 2010/2015	PARTNER A 2011	CoreValve 2014/2018	PARTNER 2 2016/2020	SURTAVI 2017/2022	PARTNER 3 2019/2021	EVOLUT 2019
Lead Author	Rodes-Cabau	Leon Kapadia	Smith	Adams Gleason	Mack Makkar	Reardon Van Mieghem	Mack Leon	Popma
Design	Case series	RCT **TAVR vs Standard Care**	RCT **TAVR vs SAVR**	RCT **TAVR vs SAVR**	RCT **TAVR vs SAVR**	RCT **TAVR vs SAVR**	RCT **TAVR vs SAVR**	RCT **TAVR vs SAVR**
Device	SAPIEN or SAPIEN XT	SAPIEN	SAPIEN	CoreValve	SAPIEN XT or SAPIEN 3	CoreValve	SAPIEN 3	CoreValve, Evolut R, or Evolut Pro
Risk Level	High or prohibitive	Inoperable	High	High	Intermediate	Intermediate	Low	Low
N	345	358	699	795	2032	1746	1000	1403
Duration (# completing)	42 ± 15 months	1year (358) 5year (55)	1 year (699)	1 year (747) 5 year (158)	2 year (2032) 5 year (1751)	24 months (1660) 5 year (929)	1 year (984) 5 year (870)	24 months (921)
Mortality (%):								
• 30 day	10.4	5.0 vs 2.8	3.4 vs 6.5	3.3 vs 4.5	3.9 vs 4.1	2.2 vs 1.7	0.4 vs 1.1	0.5 vs 1.3
• 1 year	26	24.3 vs 26.8	24.2 vs 26.8	14.2 vs 19.1	12.3 vs 12.9	6.7 vs 6.8	1.0 vs 2.5	2.4 vs 3.0
• 2 year					16.7 vs 18.0	11.4 vs 11.6	2.5 vs 3.2	4.5 vs 4.5
• 5 year	55 at 42±15 months	33.9 TAVR		55.3 vs 55.4	47.9 vs 43.4	30 vs 28.7	10.0 vs 9.0	
Repeat hospitalization								
• 30 day		5.6 vs 10.6	4.4 vs 3.7			2.9 vs 4.2	3.4 vs 6.5	1.2 vs 2.5
• 1 year		22.3 vs 44.1	18.2 vs 15.5			8.5 vs 7.6	7.3 vs 11.0	3.2 vs 6.5
• 2 year					19.9 vs 17.5	13.2 vs 9.7	8.5 vs 12.5	
• 5 year						23.9 vs 20.8	13.7 vs 17.4	
Stroke or TIA								
• 30 day		6.7 vs 1.7	5.5 vs 2.4	4.9 vs 6.2	5.5 vs 4.3	4.5 vs 6.5	0.6 vs 2.4	3.4* vs 3.4*

Study	Rode's-Cabau 2010/2012	PARTNER B 2010/2015	PARTNER A 2011	CoreValve 2014/2018	PARTNER 2 2016/2020	SURTAVI 2017/2022	PARTNER 3 2019/2021	EVOLUT 2019
• 1 year		10.6 vs 4.5	8.3 vs 4.3	8.8 vs 12.6	8.0 vs 5.8	8.2 vs 8.6	1.2 vs 3.3	4.1 vs 4.3
• 2 year					9.5 vs 6.4	10.0 vs 11.0	2.5 vs 3.6	
• 5 year				17.5 vs 21.0		11.6 vs 13.6	5.8 vs 6.4	
Major Vascular Complications								
• 30 day		30.7 vs 5.0	11.0 vs 3.2	5.9 vs 1.7	7.9 vs 5.0	6.0 vs 1.1	2.2 vs 1.5	3.8 vs 3.2
• 1 year		32.4 vs 7.3	11.3 vs 3.5	6.2 vs 2.0	8.4 vs 5.3		2.8 vs 1.5	3.8 vs 3.5
• 2 year					8.6 vs 5.5			
Major Bleeding								
• 30 day		16.8 vs 3.9	16.8 vs 19.5	28.1 vs 34.5	10.4 vs 43.4	12.2 vs 9.3	3.6 vs 24.5	2.4 vs 7.5
• 1 year		22.3 vs 11.2	17.7 vs 25.7	29.5 vs 36.7	15.2 vs 45.5		7.7 vs 25.9	3.2 vs 8.9
• 2 year					17.3 vs 47.0			
New AF								
• 30 day		0.6 vs 1.1	8.6 vs 16.0	11.7 vs 30.5	9.1 vs 26.4	12.9 vs 43.4	5.0 vs 39.5	7.7 vs 35.4
• 1 year		0.6 vs 1.7	12.1 vs 17.1	15.9 vs 32.7	10.1 vs 27.2		7.0 vs 40.9	9.8 vs 38.3
• 2 year					11.3 vs 27.3			

Outcomes are reported as TAVR vs. SAVR, respectively; RCT = Randomized Clinical Trial

A multicenter case series evaluated the outcomes of 345 TAVR procedures in 339 participants who presented with severe symptomatic aortic stenosis (AS) at very high or prohibitive surgical risk (Rodés-Cabau, 2010). The transfemoral [TF] approach was used in 168 and a transapical [TA] approach was used for 177. Outcome results were reported in 332 cases. These results showed a 30-day procedural success rate of 93.3% and 10.4% mortality (TF: 9.5%, TA: 11.3%). A survival rate of 76% was reported at 1-year follow-up, with most deaths resulting from non-cardiac conditions. This study demonstrated the feasibility of transcatheter valve replacement for individuals with extremely high risk of death from an open surgical replacement. It did not, however, compare TAVR to optimal medical management.

Leon and colleagues reported results of the PARTNER clinical trial in 2010. Cohort B of this study evaluated the safety and effectiveness of Edwards SAPIEN THV in a population of inoperable participants. Participants in Cohort B were randomized to treatment with TF TAVR or to standard therapy. There were 179 participants in each group. Individuals who did not have suitable femoral access were not enrolled. All enrolled participants had severe

symptomatic AS with a functional NYHA class II or greater. Severe AS was defined by aortic-valve area of less than 0.8 cm^2, a mean aortic-valve gradient of 40 mm Hg or more, or a peak aortic-jet velocity of 4.0 m per second or more. At least two cardiovascular surgeon investigators had to agree that the individual was not a suitable candidate for surgery due to a predicted probability of 50% or more of either death within 30 days after surgery or a serious irreversible complication. Researchers categorized most participants as high risk based on Society of Thoracic Surgeons (STS) score (average 11 ± 6%). Some participants had lower STS scores but had pre-existing conditions that contributed to the surgeon's rationale for deeming a participant ineligible for surgery.

There were 9 deaths (5.0%) in the TAVR group within 30 days of their procedure. In the standard care cohort, there were 5 deaths (2.8%) in the first 30 days after randomization. After 12 months, there were 55 deaths (30.7%) in the TAVR group compared to 89 deaths (49.7%) in the standard care group. After 1 year, participants treated with TAVR were more likely than those in standard care to have experienced a stroke (10.6% TAVR vs 4.5% standard care), vascular complication (32.4% vs 7.3%), or major bleeding episode (22.3% vs 11.2%). Participants receiving standard care were more likely than those who received TAVR to have required repeat hospitalization (70.4% in standard care vs 42.5% in TAVR), balloon aortic valvuloplasty (36.9 % vs 0.6%), or open aortic valve replacement (9.5% vs 1.1%).

The PARTNER trial provided more evidence of the feasibility of TAVR for severe symptomatic aortic stenosis. While showing significantly lower 12-month rates of death or need for rehospitalization, TAVR resulted in a markedly higher rate of stroke. The authors proposed that this could be due to the large diameter devices then in use and with the fact that TAVR was a new procedure with which many of the investigators needed to gain experience. An important limitation of the trial was its exclusion of individuals with significant coronary or peripheral vascular disease (PAD). Many individuals with severe symptomatic AS also have those conditions; estimates indicate 20-30% of the TAVR population have comorbid PAD (Mazzolai, 2024). In 2024, the European Society of Cardiology (ESC) published guidelines for the management of peripheral arterial and aortic disease which endorse a Class 1 Level B recommendation for screening of ilio-femoral PAD prior to TAVR.

In 2011, based in part on the results of PARTNER, the Food and Drug Administration (FDA) approved use of the Edwards Sapien Valve for individuals with severe calcific AS who were considered to be non-operable for conventional SAVR.

Smith and colleagues (2011) reported results from cohort A of the PARTNER trial in 2011. Cohort A included 699 individuals considered to be at high risk for mortality or a severe event following SAVR. Participants were randomized to receive TAVR or SAVR. The mortality rate (24.2% for TAVR vs. 26.8% for SAVR) and the rate of rehospitalization (18.2% TAVR vs 15.5% SAVR) were comparable 1 year after the procedure. As observed for cohort B, the TAVR arm had higher rates of stroke (8.3% TAVR vs 4.3% SAVR) and vascular complications (18.0% TAVR vs 4.8% SAVR).

The FDA expanded its indications for TAVR in 2012 to include individuals with operative risk of greater than or equal to 8% or a risk of mortality greater than or equal to 15% with surgical valve replacement.

In 2016, the FDA expanded indications for the SAPIEN XT and SAPIEN 3 transcatheter heart valves to treatment of individuals with symptomatic severe calcific AS at intermediate or greater risk for open surgical therapy. This

level of risk was defined as predicted risk of surgical mortality greater than or equal to 3% at 30 days as determined by at least two physicians.

The FDA approval for the SAPIEN XT and SAPIEN 3 devices was based on results from the PARTNER 2 trials (Leon, 2016). These were two parallel, prospective, multicenter, randomized trials that enrolled 2,032 individuals with severe AS at intermediate surgical risk. Participants that met enrollment criteria were stratified in cohorts according to access route (transfemoral or transthoracic) then randomized at a 1:1 ratio to undergo TAVR or SAVR. In contrast to the PARTNER trials, PARTNER 2 allowed enrolment of individuals with noncomplex coronary artery disease requiring revascularization. In the SAVR arm, 77 of 1021 participants (7.5%) declined to undergo their assigned procedure. This compares to 17 of 1011 participants (1.7%) declining their procedure in the TAVR arm.

PARTNER 2 found comparable outcomes for TAVR and SAVR. After 2 years, the composite outcome of death from any cause or disabling stroke was 19.3% for TAVR and 21.1% for SAVR. TAVR resulted in larger aortic-valve areas and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation. SAVR resulted in fewer major vascular complications and less paravalvular aortic regurgitation. Major vascular complications occurred in 8.6% of those receiving TAVR as compared to 5.5% of those receiving SAVR. SAVR was more likely to result in life-threatening or disabling bleeding (47.0% vs 17.3%). The SAVR group also had a higher rate of new atrial fibrillation (27.3% vs 11.3%).

The authors of the PARTNER 2 trial concluded that TAVR, when performed by experienced centers using newer valve systems, was shown to be non-inferior to SAVR with regard to mortality or stroke. They also remarked that longer-term study was needed to evaluate the durability of outcomes for this procedure.

In 2020, Makkar and colleagues reported longer-term clinical outcomes after TAVR versus SAVR in the intermediate-risk population (PARTNER 2). At 5-year follow-up, at least mild paravalvular aortic regurgitation was more common in the TAVR group than the SAVR group (33.3% vs. 6.3%), as were repeat hospitalizations (33.3% vs 25.2%) and aortic-valve interventions (3.2% vs. 0.8%). At 5 years, the improvement in health status was similar for the TAVR and SAVR groups. The authors concluded, “Among patients with aortic stenosis who were at intermediate surgical risk, there was no difference in the incidence of death or disabling stroke at 5 years after TAVR as compared with surgical aortic-valve replacement.” A post-hoc study of registry data determined that 12.5% of participants in the trial required a permanent pacemaker implanted within 30 days of TAVR. The 5-year clinical outcomes data suggests that pacemaker implantation was not associated with worse clinical outcomes including mortality. Modifiable risk factors for pacemaker implantation included bioprosthetic valve oversizing, prostheses size and implantation depth (Chen, 2024).

Mack and colleagues reported preliminary results from the PARTNER 3 trial in 2019. This was a prospective, randomized, controlled, multicenter study evaluating the safety and effectiveness of the SAPIEN 3 transcatheter valve. The study compared TAVR to SAVR in individuals with severe symptomatic AS who were at low risk (STS < 4%) for surgery. The mean age of participants was 73. The mean STS score was 1.9. Investigators randomized 1000 participants into two groups: 496 received TAVR and 465 received SAVR. After 1 year, the composite rate of death, stroke, or hospitalization was 8.5% for the TAVR group and 15.1% in the SAVR group ($p<0.0001$ for non-

inferiority). As in PARTNER 2, a much larger number of participants in the SAVR arm declined their procedure (43 of 497 [8.7%] in the SAVR group vs 7 of 503 [1.4%] in the TAVR group).

Popma and colleagues (2019) reported results from a pre-market, multicenter, international, prospective study evaluating TAVR with the Medtronic CoreValve Evolut THV systems to SAVR in individuals with severe AS (AVA of 1.0 cm^2 or less; AVA index of ≤ 0.6 cm^2 per square meter; mean gradient of 40 mm Hg or more; or maximal aortic-valve velocity of 4.0 m or more per second) and who were at low surgical risk (STS score ≤ 3%). The as-treated cohort included 1403 assigned participants, 725 in the TAVR group and 678 in the surgery group. At 24 months, the estimated incidence of death from any cause and disabling stroke were 4.5% and 1.1% in the TAVR group versus 4.5% and 3.5% in the surgery group. The authors concluded that TAVR was noninferior to SAVR with respect to death from any cause or disabling stroke at 2 years for participants in this trial. They also stated that "longer-term follow-up will be necessary to understand the implications of these various valve characteristics on structural valve deterioration and long-term outcomes."

In December 2020, the ACC and AHA published an updated guideline for the management of valvular heart disease in adults (Otto, 2020). The panel offered recommendations for the choice between SAVR or TAVR for individuals for whom a bioprosthetic AVR is appropriate and for whom estimated risk is not high or prohibitive. In the guidelines, individuals with severe AS were defined by any of the following, (1) an AVA of equal to or less than 1.0 cm2, or (2) an AVA index equal to or less than 0.6cm2/m2, or (3) a mean aortic valve gradient of at least 40 mm Hg, or (4) a peak aortic-jet velocity of more than 4.0 m/second. The guidelines were based on the enrollment criteria in the PARTNER 3 (low risk), SURTAVI (intermediate risk) and EVOLUT (low risk) clinical trials. The authors new recommendations include treatment:

- For symptomatic patients with severe AS who are 65 to 80 years of age and have no anatomic contraindication to transfemoral TAVR, either SAVR or transfemoral TAVR is recommended after shared decision making about the balance between patient longevity and valve durability (*Category 1A*)

- For symptomatic patients with severe AS who are > 80 years of age or for younger patients with a life expectancy < 10 years and no anatomic contraindication to transfemoral TAVR, transfemoral TAVR is recommended in preference to SAVR (*Category 1A*)

The ACC/AHA recommendations are based on results from the PARTNER 3 study and the Medtronic Evolut Transcatheter Aortic Valve Replacement trials in low-risk individuals discussed above. (Mack, 2019; Popma, 2019)

In 2021, Leon and colleagues reported follow-up results from the PARTNER 3 (Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low-risk Patients with Aortic Stenosis) in individuals with symptomatic AS, comparing TAVR to SAVR. At 2 years, the primary composite endpoint was reached in 11.5% of participants in the TAVR group vs. 17.4% in the SAVR group. Mortality, strokes, TIAs, and rehospitalizations each occurred less frequently in the TAVR group than in the SAVR group. In 2023, 5-year data from the PARTNER 3 trial showed a TAVR vs SAVR mortality rate of 10.0 vs 9.0 and a rehospitalization rate 13.7 vs 17.4 (Mack, 2023).

The PARTNER 3 trial provides reassuring evidence that TAVR results in health outcomes comparable to SAVR 2 years after the procedure. The 2020 ACC/AHA guideline (Otto, 2020) notes that TAVR:

has a slightly lower mortality risk and is associated with a shorter hospital length of stay, more rapid return to normal activities, lower risk of transient or permanent atrial fibrillation, less bleeding, and less pain than SAVR. On the other hand, SAVR is associated with a lower risk of paravalvular leak, less need for valve reintervention, and less need for a permanent pacemaker.

These considerations form the basis for the ACC/AHA guideline 1A recommendation for either SAVR or transfemoral TAVR for individuals at low open surgical risk between the ages of 65-80 based on shared decision making about the balance between patient longevity and valve durability.

A prospective multicenter registry trial (NCT02628899) was conducted to assess the safety and feasibility of TAVR in individuals with symptomatic, severe AS who are at low risk (STS score ≤ 3%) for SAVR with either bicuspid or tricuspid aortic native valves (Rogers, 2017). This study was designed to have an estimated enrollment of 300 participants, 200 low-risk participants (up to 100 TAVR in bicuspid AS). While 30-day and 1-year outcome data are published, as of November, 2024, the ClinicalTrials.gov site for the study indicated that it was completed in January, 2023, but long-term, peer-reviewed published results are not yet available (Waksman, 2018 & 2019). The mean age of individuals currently enrolled in this clinical trial is 74 and the final study will include outcomes at 2, 3, 4 and 5 year follow-up.

In 2024, Kowalowka and colleagues published 2-year data from a registry study, Aortic Valve Multicenter Registry (AVALON) which compared elective transfemoral TAVR to SAVR in low-risk individuals. A total of 922 (SAVR n=593; TAVR n=329) individuals were enrolled and included in the final analysis. A total of 88% of the sample was over 70 years of age. At 30-days post-procedure mortality was 3.32% (n=11 of 329) in the TAVR group and 3.03% (18 of 593) in the SAVR group (p=0.801). At 2-years, the mortality rates began to diverge in favor the SAVR group with a 30% lower mortality (HR=0.70; 95% CI, 0.496-0.777); p=0.048).

In 2024, Thyregod and colleagues published 10-year results from the NordicAortic Valve Intervention (NOTION) clinical trial, the first to randomized low surgical risk participants to TAVR or SAVR. A total of 280 study participants were randomized to TAVR (n=145) with CoreValve bioprosthesis or SAVR (n=135) with a bioprosthesis. Eligible participants were all 70 years old or older. Individuals could participate if they had suitable anatomy regardless of their estimated surgical risk. The mean STS risk score, 3.0 ± 1.7 %, showed the cohort to be at low surgical risk. The baseline characteristics of the study arms were well balanced, with a mean age of 79 and 53-54% male. After 10-year follow-up, the composite outcome of all-cause mortality, stroke, myocardial infarction, bioprosthetic valve failure and endocarditis were not significantly different between the two groups. Both structural (HR=0.2, 95% CI, 0.04-0.7; p=0.02) and nonstructural valve dysfunction (p<0.001) significantly favored the TAVR arm. The SAVR arm experienced an increased risk of new-onset atrial fibrillation relative to the TAVR arm (74.1% vs 52.0%; p<0.01, respectively) and a significantly reduced risk of new permanent pacemaker placement (14.0 vs 44.7; p<0.01, respectively).

In 2024, Blankenberg published 1-year results from a randomized noninferiority trial conducted across 38 sites in Germany which enrolled low and intermediate risk individuals, 65 or older, and randomized them to receive TAVR (n=701) or SAVR (n=713). Enrolled study participants had a mean age of 74 years and 57% identified as male. The median Society of Thoracic Surgeons risk score was 1.8% (low surgical risk). Of note, 13.4% of the participants

assigned to this study's SAVR group either crossed over to the TAVR group (9.8%) or withdrew from the trial (3.6%) after randomization, a proportion that may have been driven by the participant's desire to avoid open surgery. These numbers compare with only 2.3% of participants in the TAVR group who either crossed over to the SAVR group (1.7%) or withdrew from the trial (0.6%) The primary outcome was a composite of death from any cause or stroke at 1 year and was reported for 5.4% in the TAVR group and 10.0% in the SAVR group (HR=0.53; 95% CI, 0.35 to 0.79; p<0.001 for noninferiority). The incidence of death from any cause was 2.6% in the TAVR group and 6.2% in the SAVR group (HR=0.43; 95% CI, 0.24 to 0.73); the incidence of stroke was 2.9% and 4.7%, respectively (HR=0.61; 95% CI, 0.35 to 1.06). Peri-procedural complications occurred in 1.5% and 1.0% of participants in the TAVR and SAVR groups, respectively and were not significantly different. The study authors noted that the incidence of primary and secondary outcomes were higher than expected and exceeded rates reported in other trials. They proposed that this could be a potential confounding effect from the COVID-19 pandemic which occurred during the clinical trial period. In summary, this trial met its primary endpoint demonstrating noninferiority of TAVR compared to SAVR at 1 year for low surgical risk individuals who are 65 years or older.

Requirement for Multidisciplinary Evaluation:
All of the major trials assessing the effects of TAVR required multi-physician confirmation of eligibility for the procedure. An informed decision to pursue an intervention may be optimized when a multidisciplinary team with primary care physicians, cardiologists, interventional cardiologists, cardiac surgeons, individuals, and family members communicate and proceed in a coordinated, interdisciplinary manner. Depending on the individual's unique circumstance, additional multidisciplinary team members may include other subspecialty consultants (e.g., hematology, oncology, pulmonology). Care may be optimized by leveraging the expertise and experience of subspecialists, each of whom can weigh in on the nuances of an individual's disease state relevant to their presenting illness.

TAVR Valve-in-Valve:

In a study published by Dvir and colleagues in 2014, the authors noted that increasing use of bioprosthetic rather than mechanical aortic valves was leading to an increasing prevalence of issues with degeneration of these bioprostheses. They reported results from a multinational (55 centers) valve-in-valve (ViV) registry that included 459 participants (mean age 77.6 years) with a degenerated aortic valve bioprosthesis who underwent ViV implantation using balloon or self-expandable THV. At 30 days post procedure, 35 (7.6%) deaths were reported. A higher mortality rate was reported for the stenosis group (10.5%) when compared to the regurgitation group (4.3%) and to the combined group (7.2%) (p=0.04). There was no difference between the self-expandable and balloon expandable ViV device groups in terms of mortality or stroke rates. There were more major or life-threatening bleeding events and more acute kidney injury events reported in the balloon-expandable device in terms of mortality or stroke rates, the self-expanding population had more permanent pacemaker implantation. The authors concluded, "In this registry of patients who underwent transcatheter ViV implantation for degenerated bioprosthetic aortic valves, overall 1-year survival was 83.2%. Survival was lower among patients with small bioprosthetic valves and in those with predominant surgical valve stenosis." Since this study did not compare ViV to open treatment of bioprosthetic valve degeneration, it does not permit conclusions to be drawn about the relative effectiveness of transcatheter and open procedures.

In March 2015, the FDA expanded approval of the CoreValve System TAVR as a ViV treatment of individuals with failure (either stenosed, insufficient, or combined) of a bioprosthetic aortic valve identified by a heart team including an interventional cardiologist to have high or greater risk for open surgical therapy. They specified high or greater surgical risk as Society of Thoracic Surgeons operative risk score greater than or equal to 8% or at a 15% or greater risk of operative mortality at 30 days. The FDA indication is based on preliminary data collected from 143 participants in registry 6 of the "TAV-in-SAV" observational study (NCT01675440).

In October 2015, Edwards Lifesciences received expanded approval for use of the SAPIEN XT THV for ViV implantation in individuals with failure (either stenosed, insufficient, or combined) of a bioprosthetic aortic valve, identified by a heart team including a cardiac surgeon to have high or greater risk for open surgical therapy. FDA specified high or greater surgical risk as Society of Thoracic Surgeons operative risk score greater than or equal to 8% or at a 15% or greater risk of operative mortality at 30 days. The FDA approval was based on cohort B of the PARTNER II trial (NCT01314313) with 197 ViV participants treated and the SOURCE XT registry including 57 participants who had a SAPIEN XT valve inserted into a failing bioprosthetic valve.

In 2024, Tran and colleagues published data from a retrospective registry cohort study that identified 375 matched pairs of individuals who underwent ViV TAVR or redo SAVR after a previous SAVR performed between 1995 and 2014. Records for review were obtained from registries maintained by state health officials in California, New York, and New Jersey. In order to focus more on individuals whose indication for reintervention was structural valve degeneration or failure, the authors excluded individuals who had their reintervention within 5 years of their initial SAVR procedure. The matched pairs were identified through propensity matching based on available demographic information. The authors did not have access to STS risk scores, so they computed frailty index scores using claims information. This study's primary outcome was all-cause mortality that was confirmed using public vital records sources. The study reported the following outcomes:

Outcome	ViV TAVR (95% CI)	Redo SAVR (95% CI)	p-value
Mortality within 30 days of procedure	Rate difference 1.1% (-1.0 – 3.3%)		0.28
Stroke within 30 days of procedure	Rate difference 0.3% CI not reported		0.74
Heart failure hospitalization within 30 days of procedure	2.7% (1.0 – 4.3%)	2.4% (0.8 – 4.0%)	0.81
2-year all cause mortality	Hazard ratio 2.97 (1.18 – 7.47)		0.86
5-year all cause mortality	23.4% (15.7 - 34.1%)	13.3% (9.2 – 18.9%)	0.02
5-year incidence of heart failure hospitalization	24.1% (13.9 – 35.9%)	10.1% (6.6 – 14.4%)	<0.001
Rate of new pacemaker implantation	3.5% (1.6 – 5.3%)	10.9% (7.7 – 14.1%)	<0.001
Rate of major bleeding	2.4% (0.8 – 3.9%)	5.1% (2.8 – 7.3%)	0.049

Rate of acute kidney failure	1.3% (0.2 – 2.5%)	7.2% (4.5 – 9.8%)	<0.001
% discharged to home	75.6%	34.7%	<0.001

There were no significant differences in the 5-year incidence of stroke, reoperation, major bleeding, or infective endocarditis. This retrospective registry study found similar mortality rates for ViV TAVR and re-do SAVR through approximately 2 years post-procedure; however, long-term follow-up showed significantly greater mortality in the ViV TAVR group beginning 2 years after the procedure and increasing through 5 years after the procedure. The authors note significant limitations related to this study's reliance on administrative data that may not have reported potential confounding factors. A prospective randomized trial comparing ViV TAVR to redo SAVR is needed to better understand the relative effectiveness of these 2 treatments.

To date, none of the TAVR systems have received FDA approval for use in the treatment as a repeat TAVR over a prior TAV.

TAVR Embolic Protection Device

In 2020, the FDA provided 510(k) premarket clearance for the Sentinel Cerebral Protection System (Boston Scientific Corporation) for use in individuals with aortic stenosis undergoing TAVR. The device consists of two filters placed percutaneously from the right radial or brachial artery in the brachiocephalic artery (proximal filter) and the left common carotid artery (distal filter) before TAVR. The device is removed once TAVR is complete.

In 2022, Kapadia and colleagues conducted an RCT to assess the safety and efficacy of the Sentinel Cerebral Protection device during TAVR procedures. The study's primary outcome was stroke within 72 hours of TAVR or prior to discharge. Secondary outcomes included disabling stroke, all-cause mortality, TIA, delirium, and acute kidney injury. In total, 3000 participants were randomized 1:1 to receive the embolic protection device (n=1406, successfully implanted [94% of those attempted]) and 1499 to the control group. The incidence of stroke during the follow-up period did not differ significantly between the intervention and control arms (2.3% vs. 2.9%; p=0.30). The study did not demonstrate a significant difference between the intervention arm and the control arm in mortality, stroke, TIA, delirium, or acute kidney injury. One vascular complication was reported at the cerebral embolic protection device access site. This RCT did not demonstrate added clinical benefit from implantation of a cerebral embolic protection device in the first 72 hours following TAVR.

In 2023, Wolfrum and colleagues published results of a prospective real-world registry of individuals undergoing TAVR with the Sentinel Cerebral Protection System. Participants with severe aortic stenosis undergoing TAVR were enrolled. The Sentinel Cerebral Protection System was successfully deployed in 330 participants (85%, Group 1) and was either not attempted, unsuccessful or only partially successful in 59 participants (15%, Group 2). Debris was captured in 98% of Group 1. The amount of debris was graded moderate or extensive for 40% of this group. The risk of stroke was numerically lower in participants who underwent TAVR with the Sentinel Cerebral Protection System but this reduction did not meet statistical significance (2.1 vs. 5.1%, respectively, p=0.15). No strokes occurred during Cerebral Protection System indwelling, but one participant experienced a stroke immediately after device retrieval. This registry study did not demonstrate an added clinical benefit from implantation of a cerebral embolic protection device.

Large registry studies (n=416) continue to demonstrate little effect on stroke distribution, severity, and outcomes with the use of cerebral protection devices during TAVR (Levi, 2024). On October 24, 2024 the BHF-PROECT-TAVI trial (target sample, n=7730) was halted early, the Data Monitoring Committee determined, "there is little prospect of demonstrating a benefit in the primary endpoint" and furthermore, "could not rule out the potential for harm" (Kharbanda, 2023). Other cerebral protection devices are being evaluated in on-going clinical trials, such as the TriGUARD 3 cerebral embolic protection device CEPD (Daal, 2023; Heuts, 2024).

Transcatheter Pulmonary Valve (TPV):

McElhinney and colleagues (2010) reported on 124 individuals with dysfunctional right ventricular outflow tract (RVOT) obstruction who underwent pulmonary valve placement. This feasibility study looked at the procedural success, safety and short-term effectiveness of the Medtronic Melody transcatheter pulmonary valve in individuals with dysfunctional RVOT conduits as defined by either moderate (3+) or severe (4+) pulmonary regurgitation or mean RVOT gradient greater than or equal to 35 mm Hg. The authors concluded that:

> In this updated report from the first prospective multicenter TPV trial; we demonstrated an ongoing high rate of procedural success and encouraging short-term function of the Melody valve. The addition of two sites to the original trial protocol supports the conclusion that this technology can be adopted safely and effectively by properly trained, experienced interventional pediatric/congenital cardiologists. The fact that all reinterventions in the series were for RVOT obstruction highlights the importance of appropriate patient selection, adequate relief of obstruction at the time of Melody valve placement, and measures to prevent and manage stent fracture.

In January 2010, the Melody TPV and Ensemble Delivery System was approved for marketing by the FDA through the Humanitarian Device Exemption (HDE) process. In January of 2015, the FDA granted PMA stating that the Melody TPV and Ensemble Delivery System provides a less invasive treatment option without open heart surgery for individuals with RVOT conduit regurgitation or stenosis. The approval was based on clinical studies including 99 individuals treated in the United States and 68 treated in Europe demonstrating that the device improved heart function and improved clinical symptoms in a majority of valve recipients. FDA's approved clinical indications in 2010 were as follows:
The Melody TPV is indicated for use as an adjunct to surgery in the management of pediatric and adult patients with the following clinical conditions:

- Existence of a full (circumferential) RVOT conduit that was equal to or greater than 16 mm in diameter when originally implanted and
- Dysfunctional RVOT conduits with a clinical indication for intervention, and either:
  - regurgitation: ≥ moderate regurgitation, or
  - stenosis: mean RVOT gradient ≥ 35 mm Hg

Individuals with severe regurgitation or stenosis related to a bioprosthetic pulmonic valve should be considered to have a dysfunctional RVOT.

Native or Patched RVOT

The initial FDA approval was for treatment of dysfunctional RVOT conduits. Since then, there has been interest in expanding transcatheter treatment to include native or patched RVOTs. A native RVOT is one that has never been surgically treated. There are currently three FDA approved valves for implantation in a native or patched RVOT: SAPIEN 3 with the Alterra adaptive prestent, Melody TPV (in a bioprosthetic valve), and the Harmony TPV System.

The 2020 ESC Guidelines support the use of transcatheter pulmonary valve implantation (TPVI) for native valves with the following statements:

> TPVI techniques have become an alternative to open heart surgery primarily in patients with RVOT conduit stenosis/regurgitation, but also in selected patients with native RVOT regurgitation/stenosis. TPVI, when technically feasible, provides outcomes comparable to surgical PVRep [pulmonary valve replacement] and is intended to extend the lifetime of a conduit, hence reducing the number of reoperations during a patient's lifetime.

The 2020 ESC guidelines include the following statements regarding pulmonary valve replacement (PVRep):

> PVRep and/or relief of RVOTO (RVOT obstruction) can be performed with low mortality risk in patients without heart failure and/or advanced ventricular dysfunction.
> A recent meta-analysis demonstrated that PVRep can improve symptoms and reduce RV volume, but a survival benefit still needs to be shown.

Currently there are no randomized controlled trials that compare TPVI to PVRep. The VenusP-Valve for transcatheter pulmonary valve replacement has been granted investigational device exemption (IDE) by the FDA with anticipated approval in 2026. There are ongoing post approval studies to assess long-term clinical performance and durability of the Melody TPV and the SAPIEN XT Transcatheter Heart Valve – Pulmonic after transcatheter implantation in participants with dysfunctional RVOT conduits.

Transcatheter Mitral Edge-to Edge Repair:

An open surgical technique introduced in the early 1990s to treat mitral regurgitation (MR) involves approximating the middle scallops of the mitral leaflets to create a double orifice with improved leaflet coaptation. The MitraClip Delivery System (Abbott Vascular Inc., Santa Clara, CA) was developed as a percutaneous method to accomplish a similar repair. Using a trans-septal approach, general anesthesia, fluoroscopy, and echo guidance, the clip device is centered over the mitral orifice, passed into the left ventricle, and then pulled back to grasp the mitral leaflets creating a double orifice. The MitraClip System consists of implant catheters and the MitraClip permanent implant device.

A prospective, multi-center, single-arm feasibility, safety, and efficacy trial of the MitraClip system was reported by Feldman and colleagues in 2009. A total of 107 participants with 3 to 4+ MR meeting ACC/AHA guidelines for intervention were treated with the device. Ten (9%) had a major adverse event, including 1 death assessed to be unrelated to the procedure. Overall, 79 participants (74%) achieved acute success, and 51 (64%) of those achieving acute success were discharged with MR of 1+ or less. Thirty-two (30%) individuals required open mitral valve surgery within 3 years. At 12 months, 50 of 76 (66%) individuals with acute procedural success remained free from

death, mitral valve surgery, or MR >2+ (primary efficacy endpoint). Within this cohort, 23 participants with functional (not degenerative) MR had similar acute results and durability.

Feldman and colleagues (2011) reported on the EVEREST II trial in which 279 operable participants with moderately severe (3+) or severe (4+) MR were enrolled in a 2:1 ratio to undergo either percutaneous mitral valve repair (n=184) or conventional surgery to repair or replace the mitral valve (n=95). The overall rates of achieving a composite efficacy endpoint were 55% in the percutaneous repair group and 73% in the conventional surgery group at 12 months. The rates of the components of the primary end points for the percutaneous repair versus conventional surgery were reported as follows: death rate of 6% for both groups; surgery for mitral-valve dysfunction, 20% versus 2%; and MR grade (3+) to (4+), 21% versus 20% at 12 months. The primary safety endpoint was a composite of major adverse events (MAEs) within 30 days. MAEs occurred in 15% of participants in the percutaneous-repair group and 48% of participants in the surgery group at 30 days. At 12 months, both groups had improved left ventricular size, New York Heart Association functional class and quality-of-life measures, as compared with baseline. Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery at 12 months, the procedure was associated with a lower adverse event rate.

Mauri and colleagues (2013) reported 4-year results from the EVEREST II trial. At 48 months, the composite end point of freedom from death, surgery for mitral valve dysfunction, and 3+ or 4+ MR was 39.8% in the transcatheter mitral valve repair arm versus 53.4% in the surgical arm (p=0.070). Participants in the transcatheter mitral valve repair group required surgery to treat residual MR more often compared to the conventional mitral valve surgery group with a rate of 20.4% versus 2.2% (p<0.0001) at 1 year and 24.8% versus 5.5% (p<0.001) at 4 years. The authors concluded:

> At 4 years, surgery remains the standard of care for treatment of MR among eligible patients. Percutaneous repair is associated with similar mortality and symptomatic improvement but a higher rate of MR requiring repeat procedures, and less improvement in left ventricular dimensions than surgery. Although percutaneous repair of the mitral valve to treat MR was associated with a higher rate of residual MR at 1 year, there was no difference in later occurrence of MR or mitral valve intervention between 1-year and 4-year follow-up.

The MitraClip System obtained European CE Mark approval in March 2008. Maisano and colleagues (2013) reported results from the ACCESS-EU registry study. ACCESS-EU was a prospective, nonrandomized, post-approval study conducted at 14 sites in Europe. The study enrolled a total of 567 participants with significant MR (77.1% functional; 22.9% degenerative) treated with MitraClip therapy. A total of 85% of participants were in NYHA functional class III or IV, and 53% had an ejection fraction ≤ 40%. Participants in this registry were older and at higher surgical risk than those studied in the EVEREST II comparison trial. There were 19 deaths within 30 days after the procedure in participants who underwent MitraClip implantation. The Kaplan-Meier freedom from mortality at 1 year was 81.8%. Among participants undergoing the MitraClip implantation, a total of 98 (17.3%) deaths were reported within 12 months. There were no device embolizations. Thirty-six participants (6.3%) required MV surgery within 12 months of the procedure. The severity of MR improved at twelve months compared to baseline (p<0.001), with 78.9% of participants with MR 2+ or less. At 12 months, 71.4% of participants were in NYHA Class I or II.

Whitlow and colleagues (2012) reported acute and 12-month results from a study of a cohort at high operative risk for open mitral valve surgery (EVEREST II High Risk Study (HRS)). All participants had congestive heart failure (89% NYHA Class III or IV), and the majority had a history of coronary artery disease. More than half of the participants had had prior cardiac surgery. Individuals were required to have symptomatic MR (3+ to 4+) and an estimated surgical mortality rate of greater than or equal to 12% according to the Society of Thoracic Surgeons [STS] operative risk calculator. The study enrolled 78 participants (46 functional MR; 32 degenerative MR) for percutaneous mitral valve repair with the MitraClip device. The participants' mean age was 77 years. Outcomes of those treated with MitraClip repair were contrasted with a comparator group of 58 participants screened concurrently. Twenty-two of the screened comparator group participants were not included due to lack of institutional review board approval, lack of informed consent, or inability to contact the participant. Of the remaining 36 participants, 8 met HRS eligibility criteria but were not enrolled in the HRS because enrollment had closed or they elected to not enroll. Seven participants in the comparator group were judged eligible based on echo assessment of MR severity, but anatomic eligibility based on transthoracic echo was not confirmed. The remaining 21 participants in the comparator group met all eligibility criteria for HRS except for 1 or more anatomic criteria related to MitraClip placement. The comparison group either received standard medical management (86%) or open mitral valve surgery (14%). STS predicted surgical mortality in the MitraClip group was 14.2% and 14.9% in the comparator group.

The major effectiveness end points at 12 months for the HRS cohort were survival, survival and MR ≤ 2+, NYHA functional class, LV measurements, SF-36 Health Survey quality of life, and rehospitalizations for CHF. The 30-day procedure-related mortality rate was 7.7% in the HRS and 8.3% in the comparator group (p=NS). The 12-month survival rate was 76% in the HRS and 55% in the concurrent comparator group (p=0.047). At 12 months, 78% of the surviving HRS cohort had MR grade of ≤ 2+ and both LV end-diastolic and end-systolic volume improved along with NYHA functional class (74% NYHA class I/II versus 89% class III/IV at baseline; p<0.0001). SF-36 quality of life measures at 12 months were improved (32.1 at baseline vs 36.1 12 months after the procedure; p=0.014) and the annual rate of hospitalization for CHF in surviving HRS cohort participants decreased from baseline for those participants with available matched data.

There are several limitations to the EVEREST II HRS study. The comparator group was recruited retrospectively and was limited in size. A randomized comparison of treatment arms was not performed. Follow-up was limited to 12 months. A portion of the individuals in the comparator group did not meet anatomic criteria for MitraClip placement and, therefore, was not directly comparable. In addition, the functional and echocardiographic data at 12 months may overestimate the benefit of the procedure since measures prior to death of non-surviving participants were not included. The early results 1 year after the EVEREST II HRS study suggests the MitraClip device may reduce MR in a subset of individuals deemed at high-risk for mitral valve surgery and result in improvement in clinical symptoms and left ventricular function.

The FDA granted PMA approval for the MitraClip device in October of 2013. Its labeled indication is for percutaneous reduction of symptomatic mitral regurgitation (MR greater than or equal to 3+) due to a *primary* abnormality of the mitral valve (degenerative MR) in individuals who have been determined to be at prohibitive risk for mitral valve surgery. The FDA Approval of the MitraClip Clip Delivery System was granted based on unpublished trial results for 127 individuals with symptomatic mitral regurgitation due to degenerative MR included in the EVEREST II HRR and REALISM HR registries. The outcomes of this combined cohort were

compared with 65 individuals with degenerative MR in a Duke University Medical Center database (Duke High Risk Cohort) who were managed non-surgically. Kaplan-Meier curves showed mortality in the MitraClip cohort was 6.4% at 30 days and 24.8% at 12 months compared to 10.9% at 30 days and 30.6% at 12 months in the Duke High Risk DMR cohort. The analysis cohort was developed post-hoc which limits the interpretation of the data, and the results were described as "only descriptive". Currently there are ongoing post-approval studies evaluating the long-term effectiveness of transcatheter mitral valve leaflet repair in this population.

Obadia and colleagues (2018) reported results from the MITRA-FR trial (NCT01920698) describing off-label use of the MitraClip for *secondary* MR. This multicenter, randomized, open-label, controlled phase 3 trial was conducted in France and enrolled participants with severe *secondary* MR. Severe MR was defined as a regurgitant volume of greater than 30 ml per beat or effective regurgitant orifice area of greater than 20 mm^2. Participants were randomized in a 1:1 ratio to undergo percutaneous mitral valve repair in addition to receiving medical therapy (intervention group; n=152) or to receive medical therapy alone (control group; n=152). Additional inclusion criteria for the study included participants with EF between 15-40% and chronic heart failure symptoms (NYHA functional class II, III or IV). Individuals who had prior mitral valve surgery were excluded from the study. The primary efficacy outcome was a composite of death from any cause and unplanned hospitalization for HF. At 12 months, the rate of the primary outcome was 54.6% (n=83) in the intervention group and 51.3% (n=78) in the control group (odds ratio, 1.16; 95% confidence interval [CI], 0.73 to 1.84; p=0.53). The rate of death from any cause was 24.3% (n=37) in the intervention group and 22.4% (n=34) in the control group (hazard ratio, 1.11; 95% CI, 0.69 to 1.77). A total of 74 participants in the intervention group (48.7%) and 72 participants in the control group (47.4%) had unplanned hospitalizations for heart failure (hazard ratio, 1.13; 95% CI, 0.81 to 1.56). The authors concluded that "the rate of the composite primary outcome of death or unplanned hospitalization for heart failure at 12 months did not differ significantly between the intervention group and the control group."

Stone and colleagues (2018) reported findings from the COAPT trial (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) (NCT01626079). This was a multicenter randomized, controlled, open-label trial that evaluated the use of the MitraClip device in symptomatic individuals with HF and moderate-to severe or severe *secondary* MR who remained symptomatic despite maximal guideline directed medical therapy. Participants were randomly assigned to receive transcatheter mitral valve repair with MitraClip plus medical therapy (device group; n=302) or medical therapy alone (control group; n=312). The primary efficacy outcome was all hospitalizations from HF up to a 24-month follow-up period. The annualized rate of hospitalization was 35.8% per patient-year in the device group compared to 67.9% in the control group (HR, 0.53; 95% CI, 0.40 to 0.71; p<0.001). The authors stated that "The rate of freedom from device-related complications at 12 months was 96.6% (lower 95% confidence limit, 94.8%), a rate that exceeded the objective performance goal of 88.0% for the primary safety endpoint (p<0.001)." In the device group the rate of death from any cause within 24 months was 29.1% as compared with 46.1% in the control group (hazard ratio, 0.62; 95% CI, 0.46 to 0.82; p<0.001). There was lower mortality (HR, 0.65, 95% CI, 0.49 to 0.86; p=0.003) after adjusting for differences in medical management for HF between trial groups. In participants with HF and moderate-to-severe or severe MR who continued to have symptoms despite maximum medical therapy, the authors concluded that "transcatheter mitral-valve repair resulted in a lower rate of hospitalization for heart failure and lower all-cause mortality within 24 months of follow-up than medical therapy alone. The rate of freedom from device-related complications exceeded a prespecified safety threshold." Five-year follow-up data from this trial were published in 2023. At that time, the annualized rate of hospitalization for heart failure narrowed slightly but

continued to show significant between-group differences: 33.1% per year in the device group and 57.2% per year in the control group (HR, 0.53; 95% CI= 0.41 to 0.68). All-cause mortality remained significantly lower at 57.3% in the device group and 67.2% in the control group (HR, 0.72; 95% CI, 0.58 to 0.89). Death or hospitalization for heart failure within 5 years occurred in 73.6% of the device group and in 91.5% of those in the control group (HR, 0.53; 95% CI, 0.44 to 0.64). During the 5-year study, device-specific safety events occurred in 1.4% of study participants (n=4 out of 293); all 4 events occurred within 30 days of the procedure. The COAPT authors used several methods to control for potential biases due to lack of blinding in this industry-sponsored trial. These included rigorous protocols for guideline-directed care and use of centralized resources to confirm events and echocardiographic findings. The authors also noted that "long-term follow-up, which is to be ongoing through 5 years, is necessary to fully characterize the safety and effectiveness of the device." (Stone, 2023).

On March 14, 2019 the FDA approved the MitraClip™ NTR/XTR Clip Delivery System for the treatment of *secondary/functional mitral regurgitation* in select individuals with heart failure who remain symptomatic despite guideline-directed medical therapy (GDMT). This FDA approval was based on evidence reported in the COAPT trial.

In 2019, Arnold and colleagues reported findings from a prospective sub-study of the COAPT trial to better understand the health status outcomes of individuals with HF and 3-4+ secondary MR treated with transcatheter mitral valve repair (TMVr, also known as transcatheter edge-to-edge repair or TEER) compared to standard care. At baseline, individuals had substantially impaired health status (mean Kansas City Cardiomyopathy Questionnaire (KCCQ) and SF-36 health status survey [KCCQ-0S] 52.4 ± 23.0). The health status was unchanged over time in the standard care group, participants in the TMVr group demonstrated substantial improvement in the KCCQ-OS at 1 month as measured by a mean between-group difference of 15.9 points (95% CI 12.9 to 19.5). Most of this improvement was maintained through 24 months when the mean between-group difference was 12.8 points (95% CI 7.5 to 18.2). The authors concluded that individuals with symptomatic HF and 3-4+ secondary MR who underwent TMVr with the edge-to-edge device experienced substantial health status improvement compared with standard care. "This benefit emerged early, was consistent across key subgroups, and was sustained through 24 months follow-up."

In December 2020, ACC/AHA guideline for the management of valvular heart disease (Otto, 2020), the authors provide recommendations for transcatheter edge-to-edge repair intervention *for chronic primary MR and secondary MR:*

Chronic Primary MR

- In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral value anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year (*Category 2a*)

Secondary MR

- In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), TEER is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF

between 20% and 50%, LVESD ≤70 mm, and pulmonary artery systolic pressure ≤70 mm Hg (*Category 2a*)

The committee recommendations for TMVr with the MitraClip are based on results from the EVEREST II, MITRA-FR trial and COAPT trials.

In April 2022, AHA/ACC/Heart Failure Society of America (HFSA) guideline for the management of heart failure: a report of the ACC/American Heart Association Joint Committee on clinical practice guidelines (Heidenreich, 2022), authors included 2a recommendation for management of heart failure and secondary MR for transcatheter mitral edge -to-edge. The procedure:

> Has been shown to be beneficial in patients with persistent symptoms despite GDMT, appropriate anatomy on transesophageal echocardiography and with LVEF between 20% and 50%, LVESD ≤ 70 mm, and pulmonary artery systolic pressure ≤ 70 mm Hg.
>
> A cardiologist with expertise in the management of HF is integral to shared decision-making for valve intervention and should guide optimization of GDMT to ensure that medical options for HF and secondary MR have been effectively applied for an appropriate time period and exhausted before considering intervention.

In 2024, Anker and colleagues published results of the international RESHAPE-HF2 RCT which enrolled individuals diagnosed with heart failure and moderate to severe functional mitral regurgitation. Study participants were randomized 1:1 in a blinded fashion to either mitral valve transcatheter edge-to-edge repair and guideline-recommended medical therapy (TEER+GDMT)(device group; n=250) or GDMT alone (control group; n=255). Study participants had grade 3-4+ functional MR, LVEF between 20 and 50%, and elevated B-type natriuretic peptide (BNP) levels. Eligibility was confirmed by a multidisciplinary heart team using centrally monitored standards. The study's primary endpoints were reported via unblinded follow-up and were as follows: (1) the rate of the composite of first or recurrent hospitalization for heart failure or cardiovascular death during 24 months; (2) the rate of first or recurrent hospitalization for heart failure during 24 months; and (3) the change from baseline to 12 months in the score on the KCCQ-OS. Study authors reported the following results:

Outcome	TEER + GDMT	GDMT	Difference 95% CI p value
24 month rate of first or recurrent hospitalization for heart failure or cardiovascular death (per 100 patient-years)	37.0	58.9	Rate ratio = 0.64 0.48 to 0.85 p=0.002
24 month rate of first or recurrent hospitalization for heart failure	26.9	46.6	Rate ratio = 0.59 0.42 to 0.82 p=0.002
24 month increase in KCCQ-OS score points in the device group and points in the control group (mean difference=10.9 points; 95% CI)	21.6±26.9	8.0±24.5	Mean difference = 10.9

			6.8 to 15.0 p<0.001

TEER = transcatheter edge-to-edge repair; GDMT = guideline-directed medical therapy

The rate of meeting the combined death and rehospitalization outcome was not significantly different for individuals who entered the study with a NYSHA score of I or II. Device-specific safety events occurred in 4 TEER+GDMT group participants (1.6%). These included 2 hematomas, 1 pericardial effusion, and 1 right atrial perforation requiring thoracotomy. The study's original statistical plan called for enrollment of 650 participants who would be followed for 24 months to produce 80% power to detect a difference between the treatment arms for the composite endpoint. Both enrollment and follow-up were hampered by the COVID-19 pandemic resulting in significant attrition at 24 months. While the ethics committees would not permit altering the follow-up schedule the steering committee accepted lower enrollment and the 2 additional primary endpoints. Study limitations include the lack of blinding during follow-up which may have influenced decisions to re-hospitalize and subjective responses in KCCQ-OS scoring. RESHAPE-HF2 demonstrates a potential benefit of TEER in selected individuals with moderate or severe functional MR who have persistent symptoms despite GDMT.

In 2024, Baldus and colleagues published results from the German, open-label, randomized MATERHORN study. MATERHORN enrolled individuals diagnosed with secondary MR and symptomatic heart failure (NYHA class II or higher) despite GDMT to undergo either TEER (n=102) or open mitral valve surgery (repair or replacement; n=94). The primary efficacy endpoint was a composite measure of death, hospitalization for heart failure, mitral-valve reintervention, implantation of an assist device, or stroke within 1 year after the procedure. The primary safety endpoint was a composite of major adverse events within 30 days following the interventional procedure. The mean age of the participants was 71, 40% were women, and the mean LVEF was 43% (an LVEF of 20-50% was an inclusion criteria). Participants were required to be at high open surgical risk as determined by a multidisciplinary team and have at least 2 of the following: effective regurgitant orifice area of at least 20 mm^2, biplane vena contracta width of more than 8 mm, a regurgitant volume of at least 30 ml, a regurgitant fraction of at least 50%, or at least two hospitalizations for acute heart failure during the 12 months prior to enrollment. Within 1 year, at least 1 of the components of the primary efficacy endpoint occurred in 16 (16.7%) of the 96 intervention group participants with available data and in 20 (22.5%) of the 89 open surgery group participants with available data (estimated mean difference, -6%; 95% CI, -17 to 6; p<0.001 for noninferiority). A primary safety endpoint event occurred in 15 (14.9%) of the 101 TEER group participants with available data and in 51 (54.8%) of the 93 open surgery group participants with available data (estimated mean difference, -40 percentage points; 95% CI, -51 to -27; p<0.001). There was no significant difference in mortality. As seen with other major transcatheter studies, significantly more individuals in the open surgery arm declined their assigned procedure. Only 94 of the 102 open surgery group participants underwent an open procedure whereas 102 of the 104 TEER group participants received TEER. The study's original statistical plan projected 80% power assuming 210 participants with a 5% dropout rate; however, only 172 of the 208 participants (83%) were available for evaluation at the 1-year follow up. The majority of attrition (24 of the 36 participants lost to follow up) occurred in the open surgery arm.

Other Transcatheter Mitral Valve Procedures

The CARILLON Mitral Contour System, an implantable device with a percutaneous catheter delivery system, is intended to reduce mitral annulus dilatation upon deployment, thereby significantly reducing functional mitral

regurgitation (FMR). CARILLON has been proposed to treat heart failure individuals in a minimally invasive fashion. There is an ongoing clinical trial evaluating the use of the CARILLON system to treat individuals with heart failure caused by FMR. At the time of this policy's update, the CARILLON system had not been granted final approval by the FDA for this indication.

In September 2020, Edwards Lifesciences, the manufacturer of the SAPIEN 3 THV System and SAPIEN 3 Ultra THV System received FDA approval, for ViV implantation in individuals with symptomatic heart disease due to failure of a surgical bioprosthetic mitral valve (either stenosed, insufficient, or combined) who are judged by a heart team, including a cardiac surgeon, to be at high risk or greater for open surgical therapy. The FDA approval for ViV transcatheter mitral valve replacement was based on extracted data from the multicenter STS/ACC Transcatheter Valve Therapy Registry (TVT registry) Analysis. This registry defined high surgical risk as a predicted risk of surgical mortality ≥ 3% at 30 days based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator. At the time of the FDA's approval, the registry had enrolled 311 participants (SAPIEN XT group, n=241; SAPIEN 3, n=70). Registry data showed a mortality rate at discharge of 5.1% (n=16) and a mortality rate at 30 days after discharge of 6.8% (n=20). For the 30-day follow-up, 84.1% of the participants (n=244) completed their follow-up visit while 15.9% (n=46) missed their visit. The FDA product label states that the long-term durability of the THV system has not been established (Product Label Information, 2020).

In 2020, Whisenant and colleagues published 1-year outcomes of implantation with the Sapien 3 valve for mitral ViV replacement as reported to the TVT registry. The average STS risk score of registry participants who had received mitral ViV surgery was 11%. This indicates severe surgical risk. The primary efficacy endpoint was all-cause mortality at 1-year. The primary safety endpoint was procedural technical success. A total of 1529 participants who underwent mitral ViV replacement were enrolled and 1480 (96.8%) achieved procedural technical success. All-cause mortality at 30 days was 5.4% and at 1 year, 16.7%. At baseline, 87.1% of the cohort was classified as NYHA Class III/IV heart failure, whereas at 1 year just 9.7% still met that classification. In this industry-sponsored study, authors conclude that mitral ViV with the Sapien 3 transcatheter heart valve is associated with high technical success, low 30- and 1-year mortality along with improvement in heart failure symptoms. Limitations include the observational design and lack of a standard definition of left ventricular outflow tract obstruction. The authors note that there may have been underreporting of prosthetic dysfunction.

In 2023, Zhou and colleagues published results from a systematic review and meta-analysis of 9 retrospective cohort studies comprised of 3038 study participants. The analysis compared redo surgical mitral valve replacement (SMVR) with TMVR. In this study, TMVR was associated with better results than SMVR for the following outcomes:

Results Favoring TMVR			
Outcome	**Odds Ratio (OR)**	**95% CI**	**p-value**
In-hospital mortality	0.44	0.30 – 0.64	< 0.001
Stroke	0.44	0.29 – 0.67	0.0003
Renal dysfunction	0.52	0.37 – 0.75	0.0003
Vascular complications	0.58	0.43 – 0.78	0.004
Pacemaker implantation	0.23	0.15 – 0.36	< 0.00001

Exploration for bleeding (OR=0.24; 95% CI, 0.06-0 to 96; p= 0.04)	0.24	0.06 – 0.96	0.04

Results were either better for SMVR or showed no significant difference for the following outcomes:

Result Favoring TMVR			
Outcome	**Odds Ratio (OR)**	**95% CI**	**p-value**
Paravalvular leak	22.12	2.81 – 174.16	0.003
No significant difference			
Mean difference mitral valve gradient	0.04	-0.47 – 0.55	0.87
30-day mortality	0.65	0.36 – 1.17	0.15
1-year mortality (OR=0.96; 95% CI, 0.63 to 1.45; p=0.84)	0.96	0.63 – 1.45	0.84

In May of 2024, the Edwards SAPIEN 3, SAPIEN 3 Ultra, and SAPIEN 3 Ultra RESILIA Transcatheter Heart Valve received expanded FDA approvals for mitral ViV implantation in individuals with symptomatic heart disease due to a failing surgical bioprosthetic mitral valve (stenosed, insufficient, or combined) who are judged by a heart team, including a cardiac surgeon, to be at *intermediate* or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 4% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator). The FDA approval was supported by unpublished analysis of data from 2 sources. The first source was real-world off-label use data recorded in the STS/ACC TVT registry for individuals at intermediate STS open surgical risk who received an Edwards SAPIEN 3 or Edwards SAPIEN 3 Ultra THV over a previously implanted bioprosthetic valve. The second source was unpublished investigational use data reported to FDA as the PARTNER 3 Mitral ViV study (P3 MViV; NCT03193801). P3 MViV included individuals who had a failing surgically implanted bioprosthetic valve in the mitral position demonstrating moderate or greater stenosis and/or moderate or greater insufficiency.

The FDA's analysis combined data for 452 TVT registry participants with data for 50 individuals who received implants in the P3 MViV study and evaluated 2 primary endpoints for the combined cohort of 502 individuals. The first endpoint was a composite score of death and stroke at 30 days. The second endpoint was the rate of death at 1 year. These outcomes were compared to predetermined performance benchmarks (10.4% at 30 days and 19.6% at 1 year) based on the STS risk calculator "plus a clinical margin to incorporate data uncertainty". Baseline characteristics showed the cohort's mean age to be 72 years. The majority were female (57%) and white (82%). The mean STS risk score was 5.0 ± 2.21.

Of the 502 individuals in the combined cohort, 9 had died and 10 were lost to follow up in the first 30 postoperative days. This left 483 available for evaluation 30-days after their procedure. Of these 483 remaining participants, 425 (88%) completed a visit within the 30-day allotted timeframe. At 1 year after their procedure, 29 individuals had died and 35 were lost to follow up, leaving 439 participants eligible for reevaluation. Of these 439, 308 (70%) completed their 1-year follow up visit.

The observed primary outcomes were as follows:

Outcome	**Result**	**95% CI**	**Benchmark**

All-cause death or all stroke at 30 days	2.5%	1.41 – 4.32	10.4%
All-cause death at 1 year	6.9%	4.81 – 9.90	19.6%

Noting that only 88% of eligible participants completed their 30-day follow up, and that only 70% of the eligible participants completed their 1-year follow up, the FDA performed a sensitivity analysis that determined the missing data was unlikely to have affected the primary outcomes. This analysis showed that, among the 195 individuals with missing data, death would have needed to occur in 26.7% to cause the 1-year mortality for the entire cohort to have exceeded the calculated benchmark threshold. That would have been 3.7 times the risk of death observed in those without missing data, a scenario that the FDA thought was unlikely.

The FDA's efficacy analysis showed the following:

Outcome	Baseline	30 days	1 year
% with moderate or greater mitral regurgitation	53.5%	0.8%	1.0%
% with moderate or greater paravalvular leak	9.9%	0.3%	1.2%
Mean mitral gradient	12.5 mmHg	7.6 mmHg	7.5 mmHg
Mitral valve area	1.31 cm^2	1.72 cm^2	1.69 cm^2
Left Ventricular Ejection Fraction (LVEF)	56.5 ± 0.49 %	55.4 ± 0.58 %	55.3 ± 0.80 %
6 minute walk test distance	221.5 m	332.9 m	331.5 m
% in NYHA functional class III or IV	70.6%	11.2%	10.7%
KCCQ overall summary score	42.6	77.3	78.6

As a condition for this expanded approval, the FDA has required Edwards Lifesciences to maintain a registry tracking outcomes for intermediate risk individuals who receive a mitral ViV implant over a 3-year period or until 1,000 treated individuals are tracked, whichever is greater. This tracking requirement will remain in effect until specified numbers of individuals from currently underrepresented racial and ethnic groups are enrolled.

Although the data compiled by FDA to support their expanded indication for mitral ViV implantation to include individuals at intermediate open surgical risk are promising, their analysis has several limitations; these include, the lack of peer review, combining data from unrelated studies, lack of comparison groups, and significant attrition. These results need to be confirmed in a prospective clinical trial comparing results to currently accepted therapies.

Additional data on ViV replacement of mitral valves that are stenosed, insufficient, or bioprosthetic are currently limited to uncontrolled prospective cohorts, registry studies and systematic reviews/meta-analyses with mixed findings (Guerrero, 2023; Ismayl 2023; Mack, 2021; Takagi, 2018; Yoon, 2019; Zahid, 2022; Zhou, 2023; Zia, 2021; Zogg, 2023).

Transcatheter Tricuspid Valve Repair or Replacement:

Transcatheter tricuspid valve repair or replacement (TTVR) for the treatment of tricuspid regurgitation, and associated devices, are in early stages of development. Studies have evaluated the use of three devices, the TriClip Delivery System, essentially the same clip delivery used for the mitral valve transcatheter edge-to-edge repair

(TEER, for example MitraClip), the Cardioband Valve System delivery via transfemoral approach (TRI-REPAIR Study), and the Evoque TTVR system.

In 2023, Sorajja and colleagues conducted a multi-center, prospective RCT of percutaneous tricuspid TEER (TriClip) for individuals with severe, symptomatic tricuspid valve regurgitation (Trial to Evaluate Cardiovascular Outcomes in Patients Treated with the Tricuspid Valve Repair System Pivotal [TRILUMINATE Pivotal]). The primary end point was a composite score of death from any cause or tricuspid-valve surgery, hospitalization for heart failure, and an improvement in quality of life as measured with the KCCQ. The study defined KCCQ improvement as an increase of at least 15 points in the KCCQ score (range, 0 to 100, with higher scores indicating better quality of life) at the 1-year follow-up. The severity of tricuspid regurgitation and safety were also assessed. A total of 350 participants were enrolled (175 were randomly assigned to the device group and 175 to the control group, ultimately 170 were successfully implanted with the device). The primary end point marginally favored the tricuspid TEER group (win ratio, 1.48; 95% CI, 1.06 to 2.13; p=0.02). No difference was detected between groups in the incidence of death or the rate of hospitalization for heart failure. The KCCQ quality-of-life score changed by a mean (± SD) of 12.3 ± 1.8 points in the tricuspid TEER group, as compared with 0.6 ± 1.8 points in the control group (p<0.001). At 30 days, 87.0% of the tricuspid TEER group and 4.8% of those in the control group had tricuspid regurgitation of no greater than moderate severity (p<0.001). While TEER demonstrated an improvement in self-reported quality of life, the difference did not reach the pre-specified 15-point improvement. Furthermore, there was only marginally significant clinically meaningful benefit demonstrated in the study's primary composite outcome measure. The authors noted that death and hospitalization occurred less frequently than expected for participants in both arms of this RCT. They propose that this may have been a result of their rigorous screening and enrollment of individuals with fewer coexisting conditions compared to previous trials. Further long-term study will be needed to confirm this study's findings.

In a 2023 analysis of use of the win ratio statistical method in cardiovascular trials, Ajufo and colleagues (2023) acknowledged that the TRILUMINATE Pivotal trial met its primary end point with a win ratio of 1.48 but point out that this was the result of an improvement in the subjective KCCQ score and that there was no significant improvement in the objective measures of mortality or HF rehospitalization. They also noted that TRILUMINATE Pivotal did not find significant between-group differences in diuretic use or 6-minute walk distance at the 1-year follow-up. The authors suggest "that the large patient-reported outcome measure benefit may have had a strong placebo component." This reinforces the need for further study to understand the clinical outcomes of treatment with the TriClip device.

In 2024, based on the TRILUMINATE Pivotal trial, the FDA granted Abbott approval for their tricuspid TEER system (TriClip G4 for TTVR). The FDA stated that the TriClip G4 System is indicated for the improvement of health status in individuals diagnosed with symptomatic severe tricuspid regurgitation despite being treated optimally with medical therapy who are at intermediate or greater risk for surgery, and in whom tricuspid valve edge-to-edge repair is appropriate as determined by a heart team.

In the same year (2024), the FDA granted Edward's Lifesciences approval for their Evoque TTVR system for individuals with tricuspid valve regurgitation. The system's approved indication is for individuals with symptomatic severe tricuspid regurgitation despite optimal medical therapy and for whom tricuspid valve replacement is deemed appropriate by a heart team (FDA, 2024). The approval was based on results of

the TRISCEND II pivotal trial, an unblinded, multinational, prospective RCT comparing TTVR using the EVOQUE TTR system with concomitant medical therapy to medical therapy alone. A total of 392 participants with severe symptomatic tricuspid regurgitation were randomized in a 2:1 manner to TTVR plus medical treatment or to medical treatment alone; crossover was permitted at 1 year. While baseline demographic characteristics of the two cohorts were well matched, the medical treatment group had higher rates of key comorbidities including chronic kidney disease, chronic obstruct pulmonary disease (COPD), prior coronary artery bypass graft (CABG), and previous myocardial infarct (MI). The primary endpoint was a composite score the authors have coined, the win-ratio. The win-ratio is a hierarchical composite (in rank order) of death from any cause, durable implantation of a right ventricular assist device or heart transplantation, tricuspid-valve surgery or percutaneous tricuspid intervention after any index intervention, annualized rate of hospitalization for heart failure, an improvement of at least 10 points in the score on the KCCQ-OS, an improvement of at least one NYHA functional class, and an increase in the 6-minute walk distance of at least 30 minutes. Authors report a win-ratio favoring the TTVR arm of 2.02 (95% CI, 1.56–2.62; p<0.001), which was considered significant; however, data for individual components of the composite win-ratio did not show significant differences and the authors note the study was not powered to detect such differences. There was significant attrition in the medical treatment arm – only 104 (78%) of the original 133 participants in this arm were available for follow-up at 1 year (16 withdrew and 13 died). The study excluded results for 8 individuals assigned to the TTVR group who did not have their procedure.

In 2024, Luz and colleagues published results of the bRIGHT trial. bRIGHT is a post approval, prospective, single-arm open-label multicenter post market TriClip registry study conducted at 26 sites across Europe. A total of 511 individuals with significant comorbidities and an average age of 79 years were enrolled. At baseline, 88% of the study population had baseline massive or torrential tricuspid regurgitation and 80% were in NYHA functional class III/IV. At 1-year, tricuspid regurgitation was reduced to moderate or less in 81% of participants. The percentage of enrollees in NYHA functional class I or II significantly increased (from 21% to 75%; p< 0.0001) as did KCCQ score (19-point improvement, p<0.0001; OR: 0.636; 95% CI, 0.42-0.97; p=0.038). This study did not report or analyze medical therapies provided to the enrollees. Within 1 year after their tricuspid TEER procedure, 8.8% of the registry enrollees had died, 15.3% required hospitalization to treat heart failure, 5.5% had new onset renal failure, 0.8% had a cardiac pacemaker inserted, and 3.5% required a tricuspid valve reintervention. Univariate analysis showed several demographic factors to be associated with mortality. These included the baseline KCCQ score, baseline right ventricular tricuspid annular plane systolic excursion, baseline aspartate transaminase (AST), TR grade at 30 days, sex, baseline serum creatinine, and baseline LVEF. The study authors concluded that "tricuspid TEER using the TriClip system was safe and effective through 1 year for subjects with significant TR [tricuspid regurgitation] and advanced disease in a diverse real-world population." The bRIGHT study plans to continue to report results through 5 years. The design of this study does not allow conclusions to be drawn regarding the relative effectiveness of tricuspid TEER compared to medical treatments. Prospective studies are needed to confirm the associations observed in this report.

There are currently no published RCTs evaluating the relative risks and benefits of TTVR or T-TEER compared to open surgical valve repair/replacement, largely due to the suboptimal risk-benefit ratio when performed as an isolated procedure.

Background/Overview

Transcatheter heart valve replacement is a less invasive alternative to conventional open-heart surgery that does not require heart-lung bypass. A catheter inserted using a TF, TA, or transaortic approach allows the introduction of an expandable prosthetic heart valve which is then delivered to the diseased native valve. The TF vascular access approach has been associated with reduced vascular complications (Carrol, 2020). The 2020 ACC/AHA guideline (Otto, 2020) recommendations for TAVR in moderate or lower STS risk patients specify that the TF vascular access approach should be used. Registry data shows that more than 90% of TAVR in the U.S. is now performed with the TF approach.

Two minimally invasive alternatives to surgical mitral valve repair include transcatheter leaflet repair and percutaneous annuloplasty. The purpose of transcatheter mitral valve leaflet repair is to keep the two valve leaflets more closely fitted together, thereby reducing regurgitation. Percutaneous annuloplasty attempts to reshape the mitral annulus using catheters guided through the vasculature to reach the heart to reduce regurgitation.

The FDA has approved marketing of the following THV devices:

Manufacturer, Device and Indication	Date Approved	PMA
Abbott, Abbott Park, IL		
MitraClip Delivery System • Indicated for the percutaneous reduction of significant symptomatic MR ≥ 3+ due to primary abnormality of the mitral apparatus (degenerative MR) in individuals who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the benefit from reduction of the MR	October 2013	P100009
MitraClip NTR/XTR Delivery System • Indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) MR (≥ Grade 3+) in individuals with left ventricular ejection fraction ≥ 20% and ≤ 50%. And a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of HF and mitral valve disease	February 2021	P100009/S038

PORTICO™ with FLEXNAV™ Transcatheter Aortic Valve Implantation System • Symptomatic, severe aortic stenosis at high or extreme risk for open surgical therapy Navitor™ TAVI System; next generation of Portico™ TAVI System • Severe aortic stenosis in individuals at high or extreme risk for open-heart surgery	September 2021 October 2022	P190023 P190023/S002
TriClip™ G4 Transcather Edge-to-Edge Repair (TEER) System • Symptomatic, severe tricuspid regurgitation in individuals whom despite being treated optimally with medical therapy, are at intermediate or greater risk for surgery, and in whom tricuspid valve edge-to-edge repair is appropriate as determined by a heart team	April 2024	P230007
Edwards Lifesciences, Inc. Irvine, CA		
Evoque Transcatheter Tricuspid Valve Replacement (TTVR) system • Symptomatic severe tricuspid regurgitation despite optimal medical therapy, for whom tricuspid valve replacement is deemed appropriate by a heart team	February 2024	P230013
PASCAL Precision Transcatheter Valve Repair System • Indicated for the percutaneous reduction of significant symptomatic MR ≥ 3+ due to primary abnormality of the mitral apparatus (degenerative MR) in individuals who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the benefit from reduction of the MR.	September 2022	P220003
SAPIEN XT™ Transcatheter Heart Valve (model 9300TFX) and accessories • Severe native aortic valve stenosis at high or greater risk for open surgical therapy	July 2014	P13000
SAPIEN XT™ Transcatheter Heart Valve and accessories • Expanded to include failure (stenosed, insufficient, or combined) of surgical bioprosthetic valve in high or greater risk for open surgical therapy, with native anatomy appropriate for the 23, 26, or 29 mm valve system, who	October 2015	P130009/034

are judged by a heart team including a cardiac surgeon, to be at high or greater risk for open surgical therapy (that is, Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days		
SAPIEN XT Transcatheter Heart Valve • Expanded to include severe aortic stenosis with intermediate surgical risk	August 2016	P130009/S057
SAPIEN 3 Transcatheter Heart Valve • Severe aortic stenosis inoperable or at high risk for open surgical therapy • Expanded to include severe aortic stenosis with intermediate risk	June 2015 August 2016	P140031 P140031/S010
SAPIEN 3 Ultra Transcatheter Heart Valve • Severe aortic stenosis at intermediate or greater risk for open surgical therapy • Symptomatic heart disease due to failure (stenosed, insufficient, or combined) of surgical bioprosthetic valve who are judged by a heart team, including a cardiac surgeon, to be at high risk or greater for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 3% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator)	June 2017	P140031/S028
SAPIEN 3 Transcatheter Heart Valve and SAPIEN 3 Ultra Transcatheter Heart Valve • Expanded to include severe aortic stenosis with low surgical risk	August 2019	P140031/S085
SAPIEN 3 Transcatheter Heart Valve and SAPIEN 3 Ultra Transcatheter Heart Valve • Expanded to include the replacement of failing (stenosed, insufficient or combined) previously implanted transcatheter aortic or mitral valve in individuals at high risk for open surgical therapy	September 2020	P140031/S112
SAPIEN 3, SAPIEN 3 Ultra, and SAPIEN 3 Ultra RESILIA • Expanded to include replacement of a failed (stenosed, insufficient or combined) surgical bioprosthetic mitral valve in individuals at intermediate risk for open surgical therapy	May 2024	P140031/S162
Medtronics, Inc., Santa Ana, CA		

Medtronic CoreValve System		
• Severe native aortic stenosis at extreme risk or inoperable for open surgical therapy	January 2014	P130021
• Expanded to include high-risk for open surgical therapy	June 2016	P130021/S002
• Expanded to include intermediate risk for open surgical therapy	July 2017	P130021/S033
• Medtronic CoreValve Evolut R System™ (design iteration for valve and accessories)	June 2015	P130021/S014
• Expanded to include intermediate risk for open surgical therapy • Expanded to include intermediate risk for open surgical therapy	July 2017	P130021/S033
• Expanded to include intermediate risk for open surgical therapy	September 2017	P130021/S029
• Expanded to include severe aortic stenosis with low surgical risk	August 2019	P130021/S058
• Medtronic CoreValve Evolut PRO+ System™ (design iteration)	August 2019	P130021/S059
Boston Scientific, Marlborough, MA		
LOTUS Edge Aortic Valve System • Severe native aortic stenosis at high or greater risk for open surgical therapy* ***Note:** In November 2020, Boston Scientific announced a voluntary recall of all unused inventory of the LOTUS edge Aortic Valve System due to complexities associated with product delivery.	April 2019	P1800029
SENTINEL™ Cerebral Protection System • An embolic protection device to capture and remove thrombus/debris while performing TAVR procedures	January 2020	K192460

*****The FDA has approved the following mitral valve TEER devices used for marketing which include the following:***

MitraClip NT Clip Delivery System and MitraClip NTR/XTR (Abbott Vascular, Menlo Park, CA)

- The MitraClip Delivery System is indicated for the percutaneous reduction of significant symptomatic MR ≥ 3+ due to primary abnormality of the mitral apparatus (degenerative MR) in individuals who have been

determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the benefit from reduction of the MR.

The MitraClip NTR/XTR System, when used with maximally tolerated GDMT, is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) MR (MR ≥ Grade III per American Society of Echocardiography criteria) in individuals with left ventricular ejection fraction ≥ 20% and ≤ 50%. And a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of HF and mitral valve disease.

PASCAL Precision Transcatheter Valve Repair System

- The PASCAL Precision Transcatheter Valve Repair System is indicated for the percutaneous reduction of significant symptomatic MR ≥ 3+ due to primary abnormality of the mitral apparatus (degenerative MR) in individuals who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the benefit from reduction of the MR.

******The FDA has approved the following TPV for marketing:***

Medtronic Melody® TPV (Medtronic, Inc., Minneapolis, MN)

- The Melody Transcatheter Pulmonary Valve (TPV) has an HDE approval from the FDA (2015) and is authorized by Federal law (USA) for use in pediatric and adult candidates with a regurgitant or stenotic RVOT conduit (greater than or equal to 16 mm in diameter when originally implanted). The effectiveness of this device for this use has not been demonstrated. FDA approval has been granted for devices for specific indications, through the HDE process. The HDE approval process is applicable to devices intended to benefit individuals in the treatment or diagnosis of conditions or diseases that affect fewer than 4000 individuals in the U.S. per year. An HDE application does not require submission of the results of scientifically valid clinical investigations demonstrating the effectiveness of the device for its intended use. However, the application must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury and that the probable health benefit outweighs the risks from its use. In 2017, this approval was expanded to include surgical bioprosthetic pulmonary valves (ViV) that have ≥ moderate regurgitation and/or a mean RVOT gradient ≥ 35 mmHg.

Medtronic Harmony™ TPV System (Medtronic, Inc., Minneapolis, MN)

- In the beginning of 2021, Medtronic, Inc. received FDA premarket approval the Harmony TPV System for use in the management of pediatric and adult candidates with severe pulmonary regurgitation (that is, severe pulmonary regurgitation as determined by echocardiography and/or pulmonary regurgitation fraction greater than or equal to 30% as determined by cardiac magnetic resonance imaging) who have a

native or surgically-repaired right ventricular outflow tract and are clinically indicated for surgical valve replacement.

SAPIEN THV Devices (Edwards Lifesciences, Inc., Irvine, CA Edward Lifesciences)

- In 2016, the SAPIEN XT THV and delivery system (previously approved for TAVR) received expanded approval by the FDA for use in children and adults with a dysfunctional, non-compliant RVOT conduit with a clinical indication for intervention and moderate or greater pulmonary regurgitation and/or mean RVOT gradient greater than or equal to 35 mmHg. The procedure is contraindicated in individuals with an inability to tolerate anticoagulation/antiplatelet regimen and present with active bacterial endocarditis.
- In 2020, the Edwards SAPIEN 3 Valve System was approved for pulmonary valve replacement when a pulmonary valve conduit or artificial pulmonary valve stopped working properly.
- In 2021, the Edwards SAPIEN 3 Valve System approval was expanded for use in combination with the Alterra Adaptive Prestent in children and adults with severe pulmonary regurgitation who have a native or surgically-repaired (patched) RVOT.

Definitions

Aortic valve stenosis: Also known as aortic stenosis, this form of valvular heart disease is characterized by narrowing of the aortic valve opening.

Congenital heart disease (CHD): Heart problems present at birth.

Humanitarian Device Exemption (HDE): Similar to a PMA application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose and does not pose an unreasonable or significant risk of illness or injury. The use of the device is limited to 4000 or less individuals per year.

Mitral regurgitation (also known as mitral insufficiency): A disorder in which the heart valve that separates the upper and lower chambers on the left side of the heart does not close properly, resulting in leakage of blood backward through the mitral valve each time the left ventricle contracts and increased pressure and congestion in the lungs.

PrePremarket Approval (PMA): The most stringent type of device marketing application required by the FDA. A PMA is an application submitted to the FDA to request clearance to market or to continue marketing of a Class III medical device. Class III medical devices are those devices that present significant risk to the individual and/or require significant scientific review of the safety and effectiveness of the medical device prior to commercial introduction. Frequently the FDA requires follow-up studies for these devices.

Win Ratio: a method of reporting composite endpoints in clinical trials. The win ratio method begins with ranking each component of a composite endpoint according to its clinical importance. For example, mortality would be ranked as more important than rehospitalization which, in turn, may be ranked as more important than changes in

serum biomarkers or quality of life measures. In this method, each individual in the active treatment group is matched to all individuals with similar clinical characteristics in the control group. Outcomes are compared for each matched pair beginning with the outcomes ranked most clinically important. The individual within each pair is declared a "winner" or "loser" depending on who had the outcome of interest first. If there is no winner for the outcome ranked most important, the method compares the next most important, and so on. The win ratio is the total number of winners in the treatment group divided by the number of losers. Because the win ratio does not include the results for pairs that have no winner or loser (ties), it can overestimate the treatment effect. Furthermore, differences could be driven by quality of life alone.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
33361	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; percutaneous femoral artery approach
33362	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open femoral artery approach
33363	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open axillary artery approach
33364	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open iliac artery approach
33365	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transaortic approach (eg, median sternotomy, mediastinotomy)
33366	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transapical exposure (eg, left thoracotomy)
33367	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with percutaneous peripheral arterial and venous cannulation (eg, femoral vessels) [add-on]
33368	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with open peripheral arterial and venous cannulation (eg, femoral, iliac, axillary vessels) [add-on]
33369	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with central arterial and venous cannulation (eg, aorta, right atrium, pulmonary artery) [add-on]
33418	Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; initial prosthesis
33419	Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed; additional prosthesis(es) during same session

33477	Transcatheter pulmonary valve implantation, percutaneous approach, including pre-stenting of the valve delivery site, when performed

ICD-10 Procedure

02RF3JH	Replacement of aortic valve with synthetic substitute, transapical, percutaneous approach
02RF3JZ	Replacement of aortic valve with synthetic substitute, percutaneous approach
02RF4JZ	Replacement of aortic valve with synthetic substitute, percutaneous endoscopic approach
02RH3JH	Replacement of pulmonary valve with synthetic substitute, transapical, percutaneous approach
02RH3JZ	Replacement of pulmonary valve with synthetic substitute, percutaneous approach
02RH4JZ	Replacement of pulmonary valve with synthetic substitute, percutaneous endoscopic approach
02UG3JZ	Supplement mitral valve with synthetic substitute, percutaneous approach

ICD-10 Diagnosis

	All diagnoses

When services are Not Medically Necessary:
For the codes listed above when criteria are not met.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

33370	Transcatheter placement and subsequent removal of cerebral embolic protection device(s), including arterial access, catheterization, imaging, and radiological supervision and interpretation, percutaneous [add-on]
33999	Unlisted procedure, cardiac surgery [when specified as transcatheter replacement of tricuspid heart valve]
0345T	Transcatheter mitral valve repair percutaneous approach via the coronary sinus
0483T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; percutaneous approach, including transseptal puncture, when performed
0484T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; transthoracic exposure (eg, thoracotomy, transapical)
0544T	Transcatheter mitral valve annulus reconstruction, with implantation of adjustable annulus reconstruction device, percutaneous approach including transseptal puncture
0545T	Transcatheter tricuspid valve annulus reconstruction with implantation of adjustable annulus reconstruction device, percutaneous approach
0569T	Transcatheter tricuspid valve repair, percutaneous approach; initial prosthesis
0570T	Transcatheter tricuspid valve repair, percutaneous approach; each additional prosthesis during same session

0646T	Transcatheter tricuspid valve implantation (TTVI)/replacement with prosthetic valve, percutaneous approach, including right heart catheterization, temporary pacemaker insertion, and selective right ventricular or right atrial angiography, when performed

ICD-10 Procedure

02RG3JH	Replacement of mitral valve with synthetic substitute, transapical, percutaneous approach
02RG3JZ	Replacement of mitral valve with synthetic substitute, percutaneous approach
02RG4JZ	Replacement of mitral valve with synthetic substitute, percutaneous endoscopic approach
02RJ4JZ	Replacement of tricuspid valve with synthetic substitute, percutaneous endoscopic approach
X2RJ3RA	Replacement of tricuspid valve with multi-plane flex technology bioprosthetic valve, percutaneous approach, new technology group 10

ICD-10 Diagnosis

All diagnoses

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Index

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/14/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Rationale, Background/Overview, References, and Websites sections.
	10/01/2024	Updated Coding section with 10/01/2024 ICD-10-PCS changes, added X2RJ3RA.

Revised	05/09/2024	MPTAC review. Revised MN statement for TAVR. Updated Rationale, Background/Overview, Coding, References, and Websites sections.
Revised	05/11/2023	MPTAC review. Revised text and formatting in the MN statement for TAVR. Revised MN statement for TPVs to remove RVOT conduit diameter criteria and added criteria for native and patched RVOT. Added a new INV and NMN statement addressing TAVR cerebral protection devices. Revised the INV and NMN statement regarding valve-in-valve repair to address replacement instead of repair. Updated Rationale, Background/Overview, Coding, References, and Websites sections.
Revised	08/11/2022	MPTAC review. Clarified TAVR MN clinical indications. Added MN statement for transcatheter Mitral Edge-to-Edge Repair/transcatheter mitral valve repair using an FDA approved device when criteria met. Added NMN statement for transcatheter mitral edge-to-edge repair/TMVr when the criteria above are not met. Revised INV/NMN statement for TMVr to address transcatheter mitral edge-to-edge repair for all "other" indications. Updated Rationale, Background/Overview, References, Websites and Index sections. Updated Coding section and added ICD-10 procedure 02UG3JZ.
	12/29/2021	Updated Coding section with 01/01/2022 CPT changes; added 33370 effective 01/01/2022.
	11/22/2021	Updated Background, References and Index sections, adding information for PORTICO Transcatheter Aortic Valve Implantation System and updated the "Manufacturer, TAVR (TAVI) device and indication table".
Revised	08/12/2021	MPTAC review. Clarified TAVR MN clinical criteria defining acronym for AVA. Revised MN criteria for TAVR in low open surgical risk to include individuals 65 years of age or older. Updated Rationale, Background, References, Websites and Index sections.
Revised	02/11/2021	MPTAC review. Revised MN medically necessary statement for TAVR to include criteria for low open surgical risk in individuals 80 years of age or older. Updated Rationale, Background, References, and Websites sections. Updated Coding section with 07/01/2021 CPT changes; added 0646T.
	01/25/2021	Updated first TAVR MN statement using a U.S Food and Drug Administration (FDA) approved device, the change is to correct a typographical error in the criteria hierarchy formatting and involves correcting criteria 'B' to appear as criteria 'A.4.'
Revised	05/14/2020	MPTAC review. Added INV/NMN statement for valve-in-valve transcatheter mitral valve repair for all indications. Updated Rationale, Background, References, and Websites sections.
Reviewed	11/07/2019	MPTAC review. Updated Rationale, Background, References and Websites sections. Updated Coding section with 01/01/2020 CPT changes; added 0569T, 0570T.
Revised	06/06/2019	MPTAC review. Added INV/NMN statement for use of transcatheter tricuspid valve repair or replacement for all indications. Updated Description, Rationale,

		References and Websites sections. Updated Coding section with 07/01/2019 CPT changes; added 0544T, 0545T.
Revised	03/21/2019	MPTAC review. Reformatted MN section, removing device names from position statements and list of comorbid conditions and contraindications. Added "Note" to refer to background section of document for list of FDA approved THV devices used for TAVR and TPVs. Revised Transcatheter (aortic, pulmonic, valve-in-valve) INV/NMN statements to NMN. Removed INV/NMN statement for TAVR with any device other than those listed above. Removed INV/NMN statement for transcatheter valve implantation in other valve locations. Updated Description, Rationale, Background, References, Websites and Index sections.
Revised	11/08/2018	MPTAC review. Revised MN statements for TAVR, removing "end stage renal disease requiring chronic dialysis or creatinine clearance" from list of comorbid conditions or contraindications that would preclude the expected benefit from aortic stenosis correction. Updated Rationale, Background, References and Websites sections.
Revised	03/22/2018	MPTAC review. Updated MN statement for TAVR devices removing "individual was offered surgery but refused" as contraindication to TAVR. Updated Rationale, References and Websites sections.
	01/01/2018	The document header wording updated from "Current Effective Date" to "Publish Date." Updated Coding section with 01/01/2018 CPT changes; added codes 0483T and 0484T.
Revised	08/03/2017	MPTAC review. Revised MN statement for TAVR with the CoreValve System, CoreValve Evolut R System and CoreValve Evolut PRO System to include coverage for individuals at intermediate or greater risk when criteria met. Updated Background, References and Websites sections.
Revised	05/04/2017	MPTAC review. Revised MN statement for TAVR with CoreValve System to include the CoreValve Evolut R System and CoreValve Evolut PRO System. Updated Description, Rationale, Background, Index, References and Websites sections.
Reviewed	02/02/2017	MPTAC review. Updated Rationale, Background, References and Websites sections.
Revised	11/03/2016	MPTAC review. Updated formatting in Position Statement section. Revised MN statement for TAVR with the Edwards SAPIEN, SAPIEN XT or SAPIEN 3 Transcatheter Heart Valve to include coverage for individuals at intermediate or greater risk when criteria met. Updated Rationale, Background, References, Websites, and Index sections.
Revised	08/04/2016	MPTAC review. Added MN statement for TAVR with an FDA-approved transcatheter heart valve system (SAPIEN XT or CoreValve System) for the treatment of individuals with a previous open surgical bioprosthetic aortic valve (valve-in-valve) when criteria met. Clarified contraindications for TAVR performed with the Edwards SAPIEN, SAPIEN XT, SAPIEN 3 or CoreValve

		system. Reformatted MN criteria. Updated Rationale, References and Websites sections.
	01/01/2016	Updated Coding section with 01/01/2016 CPT changes; removed 0262T deleted 12/31/2015.
Revised	11/05/2015	MPTAC review. Defined abbreviation in TAVR medically necessary criteria. Added SAPIEN 3 to TAVR medically necessary statement. Updated Description, Rationale, Background, References and Websites. Removed ICD-9 codes from Coding section.
Revised	11/13/2014	MPTAC review. Added the Edwards SAPIEN XT THV as medically necessary when criteria met. Clarified TAVR medically necessary criteria for CoreValve System. Updated Description, Rationale, Background and Index sections. Updated Coding section with 01/01/2015 CPT changes; removed 0343T, 0344T deleted 12/31/2014.
Reviewed	08/14/2014	MPTAC review. Updated Description, Rationale, Background, References, Websites.
Revised	05/15/2014	MPTAC review. Changed title to: *Transcatheter Heart Valve Procedures.* Added medically necessary statement for transcatheter aortic valve replacement with the CoreValve system. Revised investigational and not medically necessary statement transcatheter aortic valve replacement with any device other than those listed above as medically necessary. Added investigational and not medically necessary statements addressing transcatheter mitral valve repair using leaflet repair (e.g. MitraClip Clip Delivery System) and transcatheter mitral valve repair using percutaneous annuloplasty (e.g. Carillon Mitral Contour System). Updated Description, Rationale, Background, Index, Definitions, References and Websites.
Revised	02/13/2014	MPTAC review. Medically necessary criteria updated, removed requirement that the delivery of the TAVR be through a transfemoral approach. Added TAVR with any device other than the Edwards SAPIEN transcatheter heart valve as investigational and not medically necessary. Removed alternate approaches from investigational and not medically necessary statement. Updated Rationale, Background, Coding, Index, References and Websites.
	01/01/2014	Updated Coding section with 01/01/2014 CPT changes; removed 0318T deleted 12/31/2013.
Revised	02/14/2013	MPTAC review. Added medically necessary criteria for transcatheter pulmonary valve and revised investigational and not medically necessary statement for transcatheter pulmonary valve. Updated Rationale, Coding, References and Websites.
	01/01/2013	Updated Coding section with 01/01/2013 CPT changes; removed 0256T, 0257T, 0258T, 0259T deleted 12/31/2012.
Revised	02/16/2012	MPTAC review. Added medically necessary criteria and investigational and not medically necessary statement for transcatheter aortic heart valve. Added additional investigational and not medically necessary statement to address other valves and other methods of implantation. Revised investigational and not

		medically necessary statement addressing transcatheter pulmonary valve Updated Rationale, Background, Coding, Index, Websites and References.
Reviewed	11/17/2011	MPTAC review. Updated Rationale, Background, Websites and References.
	10/01/2011	Updated Coding section with 10/01/2011 ICD-9 changes.
	07/01/2011	Updated Coding section with 07/01/2011 CPT changes.
New	11/18/2010	MPTAC review. Initial document development.