Transcatheter Heart Valve Procedures (for Louisiana Only)

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➲ Instructions for Use

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Application

This Medical Policy only applies to the state of Louisiana.

Coverage Rationale

Aortic

Transcatheter aortic heart valve replacement is proven and medically necessary when performed according to U.S. Food and Drug Administration (FDA) labeled indications, contraindications, warnings, and precautions, and all of the following criteria are met:

- Diagnosis of severe calcific native aortic valve stenosis as indicated by **one** of the following:
  - Mean aortic valve gradient ≥ 40 mmHg; or
  - Peak aortic jet velocity ≥ 4.0 m/s; or
  - Aortic valve area of ≤ 1.0 cm^2
- Individual is symptomatic [New York Heart Association (NYHA) class II or greater] and symptoms are due to aortic valve stenosis
- An interventional cardiologist and an experienced cardiothoracic surgeon have determined that the procedure is appropriate
- Individual has engaged in a Shared Decision Making conversation with an interventional cardiologist and an experienced cardiothoracic surgeon
- Procedure is performed in a center that meets **all** of the following criteria:
  - On-site heart valve surgery and interventional cardiology programs; and
  - Post-procedure intensive care unit with personnel experienced in managing individuals who have undergone open-heart valve procedures; and
  - Volume Requirements consistent with the Centers for Medicare and Medicaid Services (CMS); for additional information, refer to the corresponding CMS National Coverage Determination and the Society of Thoracic Surgeons/American College of Cardiology (STS/ACC) Transcatheter Valve Therapy (TVT) Registry.

Transcatheter valve-in-valve (ViV) replacement within a failed bioprosthetic aortic valve is proven and medically necessary for individuals at high or prohibitive surgical risk [Predicted Risk of Mortality (PROM) score of ≥ 8%] when performed according to FDA labeled indications, contraindications, warnings, and precautions.

Note: Requests for transcatheter aortic heart valve replacement for low-flow/low-gradient aortic stenosis in individuals who do not meet the peak velocity, mean gradient and valve area criteria listed above will be considered on a case-by-case basis. These requests will be evaluated using recommendations from the American College of Cardiology/American Heart Association Guideline for the Management of Patients With Valvular Heart Disease (Otto et al., 2021) when all the clinical evaluation has been facilitated by a transcatheter aortic heart valve replacement expert and after appropriate additional testing has been conducted.

Mitral

Transcatheter edge-to-edge repair of the mitral heart valve is proven and medically necessary when used according to FDA labeled indications, contraindications, warnings, and precautions in individuals with one of the following clinical indications for intervention:

- Primary (degenerative) mitral regurgitation (MR) when **all** of the following criteria are met:
  - Moderate-to-severe or severe MR (grade ≥ 3); and
  - Symptomatic NYHA class III or IV; and
  - Prohibitive surgical risk as defined by **one** of the following:
    - PROM score of ≥ 8% for individuals deemed likely to undergo mitral valve replacement; or
    - PROM score of ≥ 6% for individuals deemed likely to undergo mitral valve repair; or
    - Predicted risk of death or major morbidity at 1 year of over 50%

    and
  - Care directed by a multidisciplinary heart team which includes a heart failure specialist, interventional cardiologist and cardiothoracic surgeon experienced in the evaluation and treatment of heart failure and mitral valve disease
- Secondary (functional) MR when **all** of the following criteria are met:
  - Moderate-to-severe or severe MR (grade ≥ 3) with left ventricular ejection fraction (LVEF) ≥ 20 and ≤ 50; and
  - Symptomatic NYHA class II–IV (ambulatory); and
  - Optimal evidence-based management which includes pharmacologic therapy plus cardiac resynchronization therapy as indicated; and
  - High surgical risk (PROM score of ≥ 8%); and
  - Care directed by a multidisciplinary heart team which includes a heart failure specialist, interventional cardiologist and cardiothoracic surgeon experienced in the evaluation and treatment of heart failure and mitral valve disease

Transcatheter mitral heart valve repair (e.g., annuloplasty), except where noted above, is unproven and not medically necessary due to insufficient evidence of efficacy.

Transcatheter mitral heart valve reconstruction or replacement is unproven and not medically necessary due to insufficient evidence of efficacy.

Pulmonary

Transcatheter pulmonary heart valve replacement and related devices (e.g., Alterra are proven and medically necessary, when used according to FDA labeled indications, contraindications, warnings, and precautions, in individuals with right ventricular outflow tract (RVOT) dysfunction with one of the following clinical indications for intervention:

- Moderate or greater pulmonary regurgitation; and/or
- Pulmonary stenosis with a mean RVOT gradient ≥ 35 mmHg

Tricuspid

Transcatheter tricuspid heart valve repair, reconstruction, or replacement is unproven and not medically necessary due to insufficient evidence of efficacy.

The following transcatheter heart valve devices and/or procedures are unproven and not medically necessary due to insufficient evidence of efficacy:

- Cerebral protection devices (e.g., Sentinel™)
- Valve-in-Valve (ViV) replacement within a failed bioprosthesis for mitral, pulmonary, or tricuspid valves
- Transcatheter superior and inferior vena cava prosthetic valve implantation (CAVI)

Definitions

CMS Volume Requirements for Transcatheter Aortic Heart Valve Replacement (TAVR):
To begin a TAVR program for hospitals without TAVR experience, the hospital program must have the following:

- ≥ 50 open heart surgeries in the previous year prior to TAVR program initiation; and
- ≥ 20 aortic valve related procedures in the 2 years prior to TAVR program initiation; and
- ≥ 2 physicians with cardiac surgery privileges; and
- ≥ 1 physician with interventional cardiology privileges; and
- ≥ 300 percutaneous coronary interventions per year.

To begin a TAVR program for heart teams without TAVR experience, the heart team must include:
- Cardiovascular surgeon with ≥ 100 career open heart surgeries of which ≥ 25 are aortic valve related; and
- Interventional cardiologist with:
  - Professional experience of ≥ 100 career structural heart disease procedures; or, ≥ 30 left-sided structural procedures per year; and
  - Device-specific training as required by the manufacturer.

For hospital programs with TAVR experience, the hospital program must maintain the following:
- ≥ 50 aortic valve replacements [TAVR or surgical aortic valve replacement (SAVR)] per year including ≥ 20 TAVR procedures in the prior year; or
- ≥ 100 aortic valve replacements (TAVR or SAVR) every 2 years, including ≥ 40 TAVR procedures in the prior 2 years; and
- ≥ 2 physicians with cardiac surgery privileges; and
- ≥ 1 physician with interventional cardiology privileges; and
- ≥ 300 percutaneous coronary interventions per year.

CMS National Coverage Determination (NCD) for TAVR Accessed October 27, 2023.

New York Heart Association (NYHA) Heart Failure Classification (NYHA, 1994):
- I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
- II: Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
- III: Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
- IV: Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Predicted Risk of Mortality (PROM): The Society of Thoracic Surgeons (STS) PROM score is a predictor of 30-day mortality after cardiac procedures (Otto et al., 2020).

Shared Decision-Making (SDM): SDM is a process by which physicians and individuals work together to choose the treatment option that best reflects the clinical evidence and the individual's values and preferences (Coylewright et al., 2020).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
*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 (e.g., thoracotomy, transapical)
*0543T	Transapical mitral valve repair, including transthoracic echocardiography, when performed, with placement of artificial chordae tendineae

CPT Code	Description
*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 (List separately in addition to code for primary procedure)
*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
*0805T	Transcatheter superior and inferior vena cava prosthetic valve implantation (i.e., caval valve implantation [CAVI]); percutaneous femoral vein approach
*0806T	Transcatheter superior and inferior vena cava prosthetic valve implantation (i.e., caval valve implantation [CAVI]); open femoral vein approach
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 (e.g., median sternotomy, mediastinotomy)
33366	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transapical exposure (e.g., left thoracotomy)
33367	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with percutaneous peripheral arterial and venous cannulation (e.g., femoral vessels) (List separately in addition to code for primary procedure)
33368	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with open peripheral arterial and venous cannulation (e.g., femoral, iliac, axillary vessels) (List separately in addition to code for primary procedure)
33369	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with central arterial and venous cannulation (e.g., aorta, right atrium, pulmonary artery) (List separately in addition to code for primary procedure)
33370	Transcatheter placement and subsequent removal of cerebral embolic protection device(s), including arterial access, catheterization, imaging, and radiological supervision and interpretation, percutaneous (List separately in addition to code for primary procedure)
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 (List separately in addition to code for primary procedure)
33477	Transcatheter pulmonary valve implantation, percutaneous approach, including pre-stenting of the valve delivery site, when performed
33999	Unlisted procedure, cardiac surgery
93799	Unlisted cardiovascular service or procedure

Codes labeled with an asterisk (*) are not on the State of Louisiana Medicaid Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program.

Description of Services

The four natural valves of the heart (aortic, pulmonary, mitral, and tricuspid) act as one-way valves to direct the flow of blood to the lungs and aorta. Heart valves with congenital defects or those that become diseased over time can result in either a leaky valve (regurgitation/incompetence/insufficiency) or a valve that does not open wide enough (stenosis).

Conventional treatment of structural heart valve disorders is surgical repair or replacement requiring open-heart surgery using cardiopulmonary bypass. Transcatheter (percutaneous or catheter-based) valve procedures use catheter technology to access the heart and manage heart valve disorders without the need for open-heart surgery and cardiopulmonary bypass. During the procedure, a compressed artificial heart valve or other device is attached to a wire frame and guided by a catheter to the heart. Once in position, the wire frame expands, allowing the device to fully open.

Aortic Valve

The aortic valve directs blood flow from the left ventricle into the aorta. Flaps of tissue (cusps) on the valve open and close with each heartbeat and make sure blood flows in the right direction. The aortic valve typically has three cusps. When only two cusps are present, the valve is referred to as bicuspid.

Aortic valve stenosis, a common valvular disorder in older adults, is a narrowing or obstruction of the aortic valve that prevents the valve leaflets from opening normally. When the aortic valve does not open properly, the left ventricle has to work harder to pump enough blood through the narrowed opening to the rest of the body. Reduced blood flow can cause chest pain, shortness of breath, excess fluid retention and other symptoms. Left untreated, severe aortic stenosis can lead to left ventricular hypertrophy and heart failure. The various stages of valvular aortic stenosis are addressed by Otto et al. (2020).

The standard for treating severe, symptomatic aortic stenosis is surgical replacement with a prosthetic valve. Transcatheter aortic valve replacement (TAVR) is a minimally invasive alternative to surgical valve replacement. Transcatheter aortic valves feature a metal, stent-like scaffold that contains a bioprosthetic valve. Depending on individual anatomy, possible access routes to the aortic valve include transfemoral (percutaneous or endovascular approach), transapical, subaxillary or transaortic approaches. The procedure is done without removing the diseased native valve.

Mitral Valve

The mitral valve directs blood flow from the left atrium into the left ventricle. Mitral regurgitation (MR) occurs when the mitral valve does not close properly, allowing blood to flow backwards from the ventricle to the atrium. MR is sometimes referred to as mitral incompetence or mitral insufficiency. Primary, or degenerative, MR is usually caused by damage to the valve components (e.g., leaflets, attached chords or adjacent supporting tissue). Secondary, or functional, MR is typically due to changes in the shape of the left ventricle that pull the leaflets apart, preventing complete closure. Left untreated, moderate to severe MR can lead to congestive heart failure. MR that cannot be managed conservatively may require surgical valve repair or replacement.

Transcatheter mitral valve replacement (TMVR) is a minimally invasive alternative to surgical valve replacement. Transcatheter mitral valves feature a metal, stent-like scaffold that contains a bioprosthetic valve. Depending on individual anatomy, possible access routes to the mitral valve include transfemoral (percutaneous or endovascular approach), transseptal, transapical or transthoracic approaches. The procedure is done without removing the diseased native valve.

Transcatheter leaflet repair, percutaneous annuloplasty, artificial chordae tendineae and annulus reconstruction are minimally invasive approaches to repair damaged mitral valves. Transcatheter leaflet repair keeps the two valve leaflets more closely fitted together, thereby reducing regurgitation. The procedure, based on the surgical edge-to-edge technique, creates a double orifice using a clip instead of a suture to secure the leaflets. The device consists of a steerable guide catheter, including a clip delivery device and a two-armed, flexible metal clip covered in polyester fabric. A transseptal puncture is required to implant the device in the left side of the heart. Access to the mitral valve is achieved via the femoral vein.

Percutaneous transcatheter annuloplasty attempts to replicate the functional effects of open surgical annuloplasty by reshaping the mitral annulus from within the coronary sinus. The coronary sinus is a large vein located along the heart's outer wall, between the left atrium and left ventricle, adjacent to the mitral valve.

Various artificial chordae tendineae and annulus reconstruction devices are in the early stages of development.

Pulmonary Valve

The pulmonary valve directs blood flow from the right ventricle into the lungs. Disorders of the pulmonary valve are often due to congenital heart disease such as tetralogy of Fallot, pulmonary atresia, transposition of the great arteries and double-outlet right ventricle. Surgery to replace the valve with a bioprosthesis may also include a conduit (graft) to open the RVOT. Over time, the valved conduit may fail, leading to pulmonary valve stenosis (narrowing), pulmonary valve regurgitation (incompetence/insufficiency) or a combination of the two. Because individuals undergoing this procedure are typically children or adolescents, the bioprosthetic valve will require revisions as the individual grows.

Transcatheter pulmonary valve implantation, a minimally invasive alternative to surgical valve repair or replacement, is designed to reduce the number of surgeries needed throughout an individual's lifetime. Transcatheter pulmonary valves feature a metal, stent-like scaffold that contains a bioprosthetic valve. Access to the pulmonary valve is most often achieved via the femoral vein. Depending on the device, the replacement valve can be positioned in a native or surgically repaired RVOT.

Tricuspid Valve

The tricuspid valve directs blood flow from the right atrium into the right ventricle. Tricuspid regurgitation (TR) occurs when the tricuspid valve does not close properly, allowing blood to flow backwards from the ventricle to the atrium. TR is sometimes referred to as tricuspid incompetence or tricuspid insufficiency. The standard for treating tricuspid valve disease is surgical annuloplasty. Devices for transcatheter tricuspid valve repair, reconstruction and replacement are in development. Caval valve implantation (CAVI) is an emerging technology for treating TR. In this procedure, a valve is placed in the inferior vena cava alone or in combination with a second valve in the superior vena cava to redirect regurgitant flow away from the tricuspid valve.

Valve-in-Valve Procedures

Transcatheter heart valve implantation within an existing bioprosthetic valve, also called a valve-in-valve procedure, replaces a previously implanted bioprosthetic heart valve that has failed or degenerated over time.

Cerebral Protection

Transcatheter cerebral embolic protection devices are designed to filter and collect debris released during TAVR procedures. These devices are intended to reduce the risk of stroke and decline in cognitive function following surgery.

Clinical Evidence

Aortic Valve

Koch et al. (2022) performed a single-center, retrospective cohort study of patients undergoing transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) for native aortic insufficiency (AI) between 2014 and 2020, to compare in-hospital and 30-day outcomes. Data were obtained from the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database, Transcatheter Valve Therapy (TVT) registry, and chart review. In-hospital and 30-day outcomes were reported. Of 125 total patients, 91 underwent SAVR and 34 underwent TAVR. The TAVR group had a higher STS predictive risk of mortality (PROM) (TAVR = 3.96%, SAVR = 1.25%, $p < 0.0001$). In the postoperative period, the SAVR group had higher rates of new-onset atrial fibrillation (20.9% vs. 0%, $p < 0.001$), while the TAVR group had higher rates of complete heart block requiring permanent pacemaker implantation (20.6% vs. 2.2%, $p < 0.001$). There was no difference in in-hospital or 30-day mortality, stroke, myocardial infarction, residual AI, or repeat valve intervention. The authors concluded that despite higher STS PROM and more comorbidities, patients who underwent TAVR for AI had similar in-hospital and 30-day outcomes as patients who underwent SAVR for AI. They also concluded that these results support TAVR in selected high-risk patients with AI, with the knowledge that pacemaker needs may be higher than patients undergoing SAVR. This study is limited by its retrospective observations, non-randomization, and small sample size (n = 125). Long-term evaluations of the results and prospective randomized studies are needed to validate these findings.

Saito et al. (2022) completed a retrospective cohort study to compare the short-term outcomes of TAVR and SAVR in high-, intermediate-, and low-preoperative risk patients. A total of 454 patients who underwent TAVR or SAVR were included. Patients were categorized into high-, intermediate-, and low-risk according to the Society of Thoracic Surgery-Predicted Risk of Mortality score and clinical outcomes were compared between TAVR and SAVR groups. TAVR was less invasive, with less bleeding and transfusion ($p < 0.001$), less frequent new-onset atrial fibrillation ($p < 0.001$), and shorter intensive care unit stay ($p < 0.001$). Furthermore, transcatheter valves performed better than surgical valves, with lower peak velocity ($p = 0.003$) and pressure gradient ($p < 0.001$) and higher effective orifice area index ($p < 0.001$). The clinical outcomes of TAVR were comparable to or even superior to those of SAVR in high- and intermediate-risk patients. In low-

risk patients, the 1- and 2-year mortality rates were 6.3% and 12.1%, respectively, in the TAVR group and 0% and 0.9%, respectively, in the SAVR group ($p < 0.001$). Mild or greater paravalvular leakage was a risk factor for mortality (hazard ratio 35.78; $p < 0.001$). The authors concluded that TAVR was superior to SAVR in the sense of less invasiveness and valvular function. However, the indication of TAVR in low-risk patients should be carefully discussed, because paravalvular leakage was a risk factor for short-term mortality. This study is limited by its retrospective observational design, and short-term follow-up did not allow for assessment of intermediate and long-term outcomes.

In a meta-analysis of seven landmark randomized controlled trials (RCTs), Siontis et al. (2019) compared the safety and efficacy of TAVR versus SAVR across the entire spectrum of surgical risk patients. Across the seven trials, 8,020 participants with severe, symptomatic aortic stenosis were enrolled: TAVR (n = 4,014) and SAVR (n = 4,006). The primary endpoint was all-cause mortality up to 2 years. The authors reported a lower risk of all-cause mortality (12% relative risk reduction) and stroke (19% relative risk reduction), regardless of underlying surgical risk, up to two years of follow-up. TAVR was linked to a higher risk of permanent pacemaker implantation and major vascular complications, but a reduced risk of major bleeding, new onset atrial fibrillation and acute kidney injury.

Several systematic reviews and/or meta-analyses comparing TAVR and SAVR in intermediate-risk patients with severe aortic stenosis reported similar clinical efficacy in the two groups (Lazkani et al., 2019; Singh et al., 2018; Sardar et al., 2017).

Witberg et al. (2018) conducted a systematic review and meta-analysis of RCTs and observational studies of TAVR versus SAVR in patients at low surgical risk. The primary outcome was all-cause mortality. The secondary outcomes included stroke, myocardial infarction, bleeding and various procedural complications. Six studies including 3,484 patients were included. The short-term mortality was similar with either TAVR or SAVR; however, TAVR was associated with increased risk for intermediate-term mortality. TAVR was associated with reduced risk for bleeding and renal failure but an increased risk for vascular complications and pacemaker implantation. The authors noted that until more data is available, SAVR should remain the treatment of choice for low-risk patients.

Using registry data, Ribeiro et al. (2018) evaluated clinical outcomes and changes in LVEF following TAVR in patients with classic low-flow, low-gradient aortic stenosis (LFLG-AS). A total of 287 patients were included in the analysis. Clinical follow-up was obtained at 1 and 12 months, and yearly thereafter. TAVR was associated with good periprocedural outcomes among patients with LFLG-AS and reduced LVEF. However, approximately one third of patients with LFLG AS who underwent TAVR had died by 2-year follow-up; with pulmonary disease, anemia and residual paravalvular leak associated with worse outcomes. LVEF improved following TAVR, but dobutamine stress echocardiography (DSE) did not predict clinical outcomes or LVEF changes over time. Data from this multicenter registry supports an expanding role for TAVR among patients with LFLG severe AS and reduced LVEF. NCT01835028

Arora et al. (2017) performed a systematic review and meta-analysis comparing the 30-day risk of clinical outcomes between TAVR and SAVR in the lower surgical risk population. Four studies were included. Compared to SAVR, TAVR had a significantly lower risk of bleeding complications and acute kidney injury. However, a higher risk of vascular complications, moderate or severe paravalvular leak and permanent pacemaker implantations was noted for TAVR. The authors noted that additional high-quality studies are needed to further explore the feasibility and long-term durability of TAVR in low-risk patients.

In a large, multicenter registry of inoperable, high-risk and intermediate-risk patients, Kodali et al. (2016) reported early outcomes following TAVR with the next-generation SAPIEN 3 valve. Patients with severe, symptomatic aortic stenosis (583 high surgical risk or inoperable and 1078 intermediate risk) were enrolled. All patients received the SAPIEN 3 valve via transfemoral (n = 1443) and transapical or transaortic (n = 218) access routes. The rate of 30-day all-cause mortality was 2.2% in high-risk/inoperable patients (mean STS score 8.7%) and 1.1% in intermediate-risk patients (mean STS score 5.3%). In high-risk/inoperable patients, the 30-day rate of major/disabling stroke was 0.9%, major bleeding 14.0%, major vascular complications 5.1% and requirement for permanent pacemaker 13.3%. In intermediate-risk patients, the 30-day rate of major/disabling stroke was 1.0%, major bleeding 10.6%, major vascular complications 6.1% and requirement for permanent pacemaker 10.1%. Overall, paravalvular regurgitation at 30 days was none/trace in 55.9% of patients, mild in 40.7%, moderate in 3.4% and severe in 0.0%. Mean gradients among patients with paired baseline and 30-day or discharge echocardiograms decreased from 45.8 mmHg at baseline to 11.4 mmHg at 30 days, while aortic valve area increased from 0.69 to 1.67 cm2.

PARTNER (Placement of AoRtic TraNscathetER) Valves Study

The PARTNER trial is a two-part, multicenter, RCT funded by Edwards Lifesciences. Cohort A compared TAVR to SVR. Cohort B compared TAVR to medical therapy in patients with severe aortic stenosis who were unable to undergo surgery. NCT00530894.

Cohort A

In a multicenter, noninferiority, open-label, RCT, Smith et al. (2011) randomly assigned 699 high-risk patients with severe aortic stenosis to undergo either TAVR with a balloon-expandable bovine pericardial valve (n = 348; transfemoral n = 244; transapical n = 104) or surgical replacement (n = 351). The primary end point was death from any cause at 1 year. The rates of death from any cause were 3.4% in the transcatheter group and 6.5% in the surgical group at 30 days and 24.2% and 26.8%, respectively, at 1 year. The rates of major stroke were 3.8% in the transcatheter group and 2.1% in the surgical group at 30 days and 5.1% and 2.4%, respectively, at 1 year. At 30 days, major vascular complications were significantly more frequent with transcatheter replacement (11.0% vs. 3.2%). Adverse events that were more frequent after surgical replacement included major bleeding (9.3% vs. 19.5%) and new-onset atrial fibrillation (8.6% vs. 16.0%). The authors concluded that in high-risk patients with severe aortic stenosis, transcatheter and surgical procedures for aortic-valve replacement were associated with similar rates of survival at 1 year, although there were important differences in periprocedural risks.

A 2-year follow-up of patients in Cohort A did not report significantly different outcomes in the two groups with respect to mortality, reduction in cardiac symptoms and improved valve hemodynamics. Paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality. An early increase in the risk of stroke with TAVR was attenuated over time. The authors concluded that these results support TAVR as an alternative to surgery in high-risk patients (Kodali et al., 2012).

At 5 years, the risk of death was 67.8% in the TAVR group compared with 62.4% in the surgical group. There were no structural valve deteriorations requiring surgical valve replacement in either group. Moderate or severe aortic regurgitation occurred in 40 (14%) of 280 patients in the TAVR group and two (1%) of 228 in the surgical group and was associated with increased 5-year risk of mortality in the TAVR group (72.4% for moderate or severe aortic regurgitation versus 56.6% for those with mild aortic regurgitation or less) (Mack et al., 2015).

Cohort B

In the same multicenter, open label, RCT, Leon et al. (2010) evaluated TAVR in patients with severe aortic stenosis who were not candidates for surgery. A total of 358 patients were randomized to standard therapy (including balloon aortic valvuloplasty) (n = 179) or transfemoral transcatheter implantation of a balloon-expandable bovine pericardial valve (n = 179). At 1 year, the rate of death from any cause was 30.7% with TAVR, as compared with 50.7% with standard therapy [hazard ratio with transcatheter aortic valve implantation (TAVI), 0.55; 95% confidence interval (CI), 0.40 to 0.74; $p < 0.001$]. The rate of the composite end point of death from any cause or repeat hospitalization was 42.5% with TAVR as compared with 71.6% with standard therapy. Among survivors at 1 year, the rate of cardiac symptoms (NYHA class III or IV) was lower among patients who had undergone TAVR than among those who had received standard therapy (25.2% vs. 58.0%). At 30 days, TAVR, as compared with standard therapy, was associated with a higher incidence of major strokes (5.0% vs. 1.1%) and major vascular complications (16.2% vs. 1.1%). In the year after TAVR, there was no deterioration in the functioning of the bioprosthetic valve. The authors concluded that in patients with severe aortic stenosis who were not suitable candidates for surgery, TAVR, as compared with standard therapy, significantly reduced the rates of death from any cause, the composite end point of death from any cause or repeat hospitalization and cardiac symptoms, despite the higher incidence of major strokes and major vascular events.

At 2 years, the mortality rates in Cohort B were 43.3% in the TAVR group and 68.0% in the standard therapy group ($p < 0.001$). The corresponding rates of cardiac death were 31.0% and 62.4% ($p < 0.001$). The survival advantage associated with TAVR at 1 year remained significant among patients who survived beyond the first year. The rate of stroke was higher after TAVR than with standard therapy (13.8% vs. 5.5%). There was an increased frequency of early ischemic strokes (≤ 30 days) but little change in the rate of late ischemic strokes (> 30 days). At 2 years, the rate of rehospitalization was 35.0% in the TAVR group and 72.5% in the standard-therapy group. TAVR, as compared with standard therapy, was also associated with improved functional status. The data suggest that the mortality benefit after TAVR may be limited to patients who do not have extensive coexisting conditions. The authors concluded that among appropriately selected patients with severe aortic stenosis who were not suitable candidates for surgery, TAVR reduced the rates of death and hospitalization, with a decrease in symptoms and an improvement in valve hemodynamics that were sustained at 2 years of follow-up (Makkar et al., 2012).

Using a longitudinal echocardiographic analysis of patients in the PARTNER trial, Daubert et al. (2016) reported that valve performance and cardiac hemodynamics were stable 5 years after implantation of both the SAPIEN TAVR and SAVR valves. Eighty-six TAVR and 48 SAVR patients with paired first post-implant and 5-year echocardiograms were analyzed.

PARTNER II Study

The PARTNER II study is a two-part, multicenter, RCT, also funded by Edwards Lifesciences, evaluating a second-generation transcatheter valve system in intermediate-risk patients. The newer, low-profile SAPIEN XT system was developed to reduce adverse events noted in the PARTNER study. Cohort A compared TAVR to conventional surgery in patients with severe aortic stenosis and intermediate surgical risk. Cohort B compared the SAPIEN XT valve with the first-generation SAPIEN valve in patients with severe aortic stenosis who were unable to undergo surgery. NCT01314313.

Cohort A

Leon et al. (2016) evaluated TAVR and SAVR in a multicenter, noninferiority, open-label, RCT involving intermediate-risk patients. A total of 2,032 intermediate-risk patients with severe aortic stenosis were randomly assigned to undergo either TAVR with the SAPIEN XT valve (n = 1,011) or SAVR (n = 1,021). The primary end point was death from any cause or disabling stroke at 2 years. The primary hypothesis was that TAVR would not be inferior to surgical replacement. Before randomization, patients were entered into one of two cohorts on the basis of clinical and imaging findings: transfemoral access (76.3%) and transthoracic access (23.7%). The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group. At 2 years, the event rates were 19.3% in the TAVR group and 21.1% in the surgery group. In the transfemoral access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery, whereas in the transthoracic access cohort, outcomes were similar in the two groups. TAVR resulted in larger aortic-valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding and new-onset atrial fibrillation. Surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.

At 5 years, there was no significant difference in the incidence of death from any cause or disabling stroke between the TAVR and SAVR groups. More patients in the TAVR group had at least mild paravalvular aortic regurgitation (33.3% vs. 6.3%). Repeat hospitalizations were more frequent after TAVR than after SAVR (33.3% vs. 25.2%), as were aortic valve reinterventions (3.2% vs. 0.8%) (Makkar et al., 2020).

Cohort B

Webb et al. (2015) evaluated the safety and effectiveness of the SAPIEN XT versus SAPIEN valve systems in patients with symptomatic, severe aortic stenosis who were not candidates for surgery. The primary endpoint was a composite of all-cause mortality, major stroke and rehospitalization. Secondary endpoints included cardiovascular death, NYHA functional class, myocardial infarction, stroke, acute kidney injury, vascular complications, bleeding, 6-min walk distance and valve performance. A total of 560 patients were randomized to receive the SAPIEN (n = 276) or SAPIEN XT (n = 284) systems. At 1-year follow-up, there was no difference in all-cause mortality, major stroke or rehospitalization between SAPIEN and SAPIEN XT, but the SAPIEN XT was associated with less vascular complications and bleeding requiring transfusion. No differences in the secondary endpoints were found. The authors concluded that in inoperable patients with severe, symptomatic aortic stenosis, the lower-profile SAPIEN XT system provided an incremental improvement from the prior generation of TAVR technology.

PARTNER 3 Low Risk Study

The PARTNER 3 study, a multicenter, noninferiority, open label, RCT, also funded by Edwards Lifesciences, evaluated the third generation SAPIEN 3 transcatheter valve system. The study compared outcomes of TAVR with those of SAVR in patients with severe aortic stenosis and a low risk of death with surgery. NCT02675114.

Mack et al. (2019) randomly assigned patients with severe aortic stenosis and low surgical risk to undergo either TAVR with a third-generation balloon-expandable valve (n = 503) or standard SAVR with a bioprosthetic valve (n = 497). The assigned procedure was performed in 950 patients (496 in the TAVR group and 454 in the SAVR group). The primary end point was a composite of death from any cause, stroke, or rehospitalization at one year after the procedure. At one year, TAVR using the SAPIEN 3 system was superior to surgery with regard to the primary composite end point of death, stroke, or rehospitalization (hazard ratio: 0.54; 95% CI, 0.37 to 0.79; p = 0.001). At 30 days, TAVR was associated with a significantly lower rate of new-onset atrial fibrillation, a shorter index hospitalization and a lower risk of a poor treatment outcome. There were no significant differences in major vascular complications, new permanent pacemaker insertions or moderate or severe paravalvular regurgitation.

The 2-year follow-up showed continued superiority of the composite outcome primary endpoint favoring TAVR versus surgery, but more frequent deaths, strokes, and valve thrombosis events in the TAVR group between 1 and 2 years. Disease-specific health status at 2 years was better after TAVR than surgery. Echocardiographic findings through 2 years indicated stable valve hemodynamics and no differences in valve durability parameters (Leon et al., 2021).

At the 5-year follow-up, Mack et al. (2023) reported the incidence of the two primary composite end points appeared to be not different between the two groups. The restricted mean event-free survival time was longer in the TAVR group than in

the surgery group. Valve durability appeared to be similar in the two groups. Among the secondary end points, atrial fibrillation and bleeding appeared to be less frequent in the TAVR group than in the surgery group, whereas paravalvular aortic regurgitation, valve thrombosis, and pacemaker implantation appeared to be less frequent in the surgery group. Functional and health-status outcomes appeared to be similar in the two groups.

EVOLUT Low Risk Study

The EVOLUT study, a multicenter, randomized noninferiority trial funded by Medtronic, evaluated the safety and efficacy of TAVR with a self-expanding bio-prosthesis compared with SAVR in patients at low risk of death with surgery. NCT02701283.

Popma et al. (2019) performed a randomized noninferiority, open-label trial comparing TAVR with a self-expanding supra-annular bioprosthesis with SAVR in patients with severe aortic stenosis who were at low surgical risk. Of the 1,468 patients who underwent randomization, an attempted TAVR (n = 725) or SAVR (n = 678) was performed in 1,403. When 850 patients reached the 12-month follow-up, data was analyzed regarding the primary end point, a composite of death or disabling stroke at 24 months. The authors reported no significant differences between the two treatment groups. In low-risk patients, TAVR was noninferior to surgery with respect to the risk of death or disabling stroke at 24 months. At 30 days, TAVR was associated with a lower incidence of disabling stroke, acute kidney injury, bleeding events and atrial fibrillation than surgery but with a higher incidence of aortic regurgitation and permanent pacemaker use. At 12 months, patients in the TAVR group had lower aortic-valve gradients than those in the surgery group and larger effective orifice areas. Patients were evaluated at baseline, at discharge and at 1, 6, 12, 18 and 24 months after the procedure. At the 12-month follow-up, data was available for 432 patients in the TAVR group and 352 in the surgery group. At the 24-month follow-up, data was available for 72 patients in the TAVR group and 65 patients in the surgery group. The median follow-up time in each group was 12.2 months. Long-term clinical and echocardiographic follow-up will continue through 10 years for all patients.

At two years, Forrest et al. (2022) evaluated clinical and echocardiographic outcomes and found that TAVR was noninferior to surgery for the primary endpoint of all-cause mortality or disabling stroke, with event rates that were slightly better than predictions. At three years, Forrest et al. (2023) reported that TAVR showed durable benefits compared with surgery for all-cause mortality or disabling stroke.

Nordic Aortic Valve Intervention Trial (NOTION)

The NOTION study, a multicenter, RCT compared TAVR with a self-expanding bioprosthesis with SAVR in patients with severe aortic stenosis from all risk categories. NCT01057173.

In the NOTION trial, 280 patients ≥ 70 years old with severe aortic valve stenosis and no significant coronary artery disease were randomized 1:1 to TAVR versus SAVR. The primary outcome was the composite rate of death from any cause, stroke or myocardial infarction. Results of the NOTION study at five years demonstrated no statistical difference for major clinical outcomes after TAVR with a self-expanding prosthesis compared to SAVR. However, higher rates of prosthetic regurgitation and pacemaker implantation were reported after TAVR (Thyregod et al., 2019). Earlier publications reported similar results (Thyregod et al., 2015; Søndergaard et al., 2016). At 6 years, the rates of all-cause mortality were not statistically different between patients undergoing TAVR (42.5%) and SAVR (37.7%). The rate of structural valve deterioration was higher for SAVR than TAVR (24.0% vs. 4.8%), whereas there were no differences in nonstructural valve deterioration (57.8% vs. 54.0%) or endocarditis (5.9% vs. 5.8%). Bioprosthetic valve failure rates were low and similar for both groups (Søndergaard et al., 2019). At 8 years, there were no significant differences in the risk for all-cause mortality, stroke, or myocardial infarction, as well as the risk of bioprosthetic valve failure. The risk of structural valve deterioration was lower after TAVR than after SAVR (13.9% vs. 28.3) (Jørgensen et al., 2021).

Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI) Study

The SURTAVI study is a multicenter, RCT, funded by Medtronic, to compare the safety and efficacy of TAVR performed with the use of a self-expanding bioprosthesis with SAVR in patients at intermediate risk for surgery. NCT01586910.

In this randomized trial comparing TAVR with SAVR, Reardon et al. (2017) evaluated the clinical outcomes in intermediate-risk patients with severe, symptomatic aortic stenosis. The primary end point was a composite of death from any cause or disabling stroke. A total of 1,746 patients underwent randomization at 87 centers. Of these patients, 1,660 underwent an attempted TAVR or surgical procedure. The authors reported a large number of unplanned withdrawals in the surgery group, primarily due to the withdrawal of patient consent after randomization. At 24 months, the risk of death or disabling stroke ranged from 12.6% in the TAVR group to 14.0% in the surgery group. Surgery was associated with higher rates of acute kidney injury, atrial fibrillation and transfusion requirements, whereas TAVR had higher rates of residual aortic regurgitation and need for pacemaker implantation. TAVR resulted in lower mean gradients and larger

aortic-valve areas than surgery. Structural valve deterioration at 24 months did not occur in either group. The authors concluded that TAVR was a noninferior alternative to surgery in patients at intermediate surgical risk.

CoreValve US Pivotal Trial

In a multicenter, randomized, noninferiority trial, Adams et al. (2014) reported that TAVR, using a self-expanding bioprosthesis (CoreValve), had a significantly higher rate of survival at one year than SAVR in patients with severe aortic stenosis and an increased surgical risk. A total of 795 patients were randomly assigned in a 1:1 ratio to TAVR with the CoreValve (TAVR group) or to SAVR (surgical group). The rate of death from any cause at one year was significantly lower in the TAVR group than in the surgical group (14.2% vs. 19.1%) with an absolute reduction in risk of 4.9 percent. Results were similar in the intention-to-treat analysis where the event rate was 13.9 percent in the TAVR group compared to 18.7 percent in the surgical group. The survival benefit with TAVR was consistent across clinical subgroups. NCT01240902.

At 2 years, all-cause mortality was significantly lower in the TAVR group (22.2%) than in the surgical group (28.6%) in the as-treated cohort, with an absolute reduction in risk of 6.5 percentage points. Similar results were found in the intention-to-treat cohort. The rate of 2-year death or major stroke was significantly lower in the TAVR group (24.2%) than in the surgical group (32.5%) (Reardon et al., 2015).

At 3 years, all-cause mortality or stroke was significantly lower in TAVR patients (37.3% vs. 46.7% in SAVR). Adverse clinical outcome components were also reduced in TAVR patients compared with SAVR patients, including all-cause mortality (32.9% vs. 39.1%, respectively), all stroke (12.6% vs. 19.0%, respectively) and major adverse cardiovascular or cerebrovascular events (40.2% vs. 47.9%, respectively). Hemodynamics were better with TAVR patients (mean aortic valve gradient 7.62 ±3.57 mmHg vs. 11.40 ±6.81 mmHg in SAVR), although moderate or severe residual aortic regurgitation was higher in TAVR patients (6.8% vs. 0.0% in SAVR). There was no clinical evidence of valve thrombosis in either group (Deeb et al., 2016).

In a prospective, multicenter, nonrandomized study, Popma et al. (2014) evaluated the safety and efficacy of the CoreValve transcatheter heart valve for the treatment of severe aortic stenosis in patients at extreme risk for surgery. Forty-one sites recruited 506 patients, of whom 489 underwent treatment with the CoreValve device. The rate of all-cause mortality or major stroke at 12 months was 26.0% vs. 43.0%. Individual 30-day and 12-month events included all-cause mortality (8.4% and 24.3%, respectively) and major stroke (2.3% and 4.3%, respectively). Procedural events at 30 days included, life threatening/disabling bleeding (12.7%), major vascular complications (8.2%) and need for permanent pacemaker placement (21.6%). The frequency of moderate or severe paravalvular aortic regurgitation was lower 12-months after self-expanding TAVR (4.2%) than at discharge (9.7%).

Several national TAVR registries were identified in the literature. Published results indicate that use of the SAPIEN and CoreValve devices was fairly equal, and the transfemoral approach was used approximately 3 times as often as the transapical approach. Conversion to surgical valve replacement occurred in 0.4% to 4% of procedures. Procedural success was very high and ranged from 91% to 99%. Procedural mortality was low and ranged from 0.4% to 3%. Survival at 30 days ranged from 87% to 95% and at 1 year from 63% to 100%, depending on the device and approach used (Walther et al., 2015; Gilard et al., 2012; Ussia et al., 2012; Bosmans et al., 2011; Thomas et al., 2011; Eltchaninoff et al., 2011; Zahn et al., 2011; Moat et al., 2011; Rodés-Cabau et al., 2010).

A meta-analysis of the adverse effects associated with TAVR included over 16,000 patients in 49 studies. Khatri et al. (2013) found that the need for a permanent pacemaker was the most common adverse outcome (13.1%) and was 5 times more common with the CoreValve than the Edwards SAPIEN valve. Vascular complications were also common (10.4%) and was highest with the trans arterial implantation of the Edwards SAPIEN valve (22.3%). Acute renal failure was the third most common complication, occurring in 4.9% of patients. Overall, 30-day and 1-year survival after TAVR were 91.9% and 79.2%, respectively.

Bicuspid Aortic Valve (BAV)

Several systematic reviews and meta-analyses have been conducted to evaluate outcomes of TAVR in patients with BAV. While RCTs are lacking, evidence from observational or registry studies show comparable outcomes of TAVR in BAV and tricuspid aortic valve stenosis. Further trials are needed to define which anatomic features of BAV are most suitable for TAVR and which implantation techniques offer optimal outcomes. While surgery remains the first-line treatment for the majority of BAV patients, TAVR using the latest devices may be a safe and reasonable alternative in patients with increased risk for surgery (Saeed Al-Asad et al., 2023; Chan et al., 2022; Chen et al., 2022; Zhang et al., 2022; Du et al., 2021; Quintana et al., 2020; Quintana et al., 2019; Kanjanahattakij et al., 2018).

Mitral Valve

Transcatheter Mitral Valve Replacement (TMVR)

There is insufficient quality evidence in the clinical literature demonstrating the long-term efficacy of catheter-delivered mitral valve prostheses for treating mitral disease. Further results from prospective, RCTs are needed to determine device durability and the ideal candidates for the procedure. Several clinical trials are in progress.

The multicenter CHOICE-MI registry performed a retrospective study of outcomes following TMVR for MR. Primary endpoints included mortality, heart failure hospitalization rates, procedural complications, residual MR, and functional status. Ludwig et al. (2023a) reported 2-year results on all 400 patients with symptomatic MR treated with TMVR. Technical success was achieved in 95.2% of patients. MR reduction to ≤1+ was observed in 95.2% at discharge with durable results at 1 and 2 years. NYHA functional class had improved significantly at 1 and 2 years. All-cause mortality was 9.2% at 30 days, 27.9% at 1 year and 38.1% at 2 years after TMVR. The authors noted that optimized patient selection and improved access site management are mandatory to improve outcomes. The findings are limited by lack of comparison group and large loss to follow up.

Using propensity matched scoring, Ludwig et al. (2023b) compared outcomes after TMVR and transcatheter edge-to-edge repair (TEER) for the treatment of secondary MR. A total of 235 TMVR patients were compared to 411 TEER patients. All-cause mortality was 6.8% after TMVR and 3.8% after TEER at 30 days and 25.8% after TMVR and 18.9% after TEER at 1 year. While post-procedural mortality tended to be higher after TMVR, no significant differences in mortality were found beyond 30 days.

Ludwig et al. (2023c) compared outcomes after TMVR and guideline-directed medical therapy (GDMT) for the treatment of secondary MR. After propensity score matching, 97 patient pairs undergoing TMVR versus GDMT were compared. At 1 and 2 years, residual MR was ≤1+ in all patients of the TMVR group compared with 6.9% and 7.7%, respectively, in those receiving GDMT alone. Over a 2-year follow-up period, TMVR in patients with secondary MR was associated with significant reduction of MR, symptomatic improvement, less frequent hospitalizations for heart failure, and similar mortality compared with GDMT. Inherent limitations of registry data include lack of randomization and control, incomplete follow-up and missing or incomplete data. NCT04688190.

A single-center, retrospective cohort study by Taha et al. (2022) was performed to evaluate the feasibility and safety of transcatheter mitral valve replacement (TMVR) in patients with high surgical risk with degenerated mitral bio-prostheses (TMViV), failed surgical rings (TMViR), and mitral annular calcification (TMViMAC). Patients with high surgical risk who underwent TMVR from February 2017 to September 2020, were enrolled in this study. The TMVR procedure was performed using Edwards SAPIEN-3 valves through the transseptal approach. Sixty-four patients aged 62.7 ±16.1 years with an STS score of 9.2 ±3.7% underwent TMVR [35 (55%) TMViV, 16 (25%) TMViR, and 13 (20%) TMViMAC]. Mitral stenosis was more frequent in TMViV, mitral regurgitation was more frequent in TMViR, and combined mitral stenosis and regurgitation were more frequent in TMViMAC ($p < 0.05$). The MV gradient was 14.3 ±5.3 mmHg and the MV area was 1.5 ±0.6 cm^2. The 29 mm valve was frequently used in TMViV and TMViMAC, while the 23 mm valve was frequently used in TMViR ($p = 0.003$). The procedural and fluoroscopy times were 58.7 ±8.9 and 41.1 ±8.2 minutes, respectively. Technical success was reported in 62 (98.4%) patients; 1 TMViR patient experienced valve embolization and salvage surgery, and 1 TMViMAC patient experienced slight valve malposition. At 3 months, 2 (3.1%) patients showed valve thrombosis (treated with anticoagulation), and 1 (1.6%) patient developed a paravalvular leak (underwent surgical MV replacement). At 6 months, 3 (4.7%) patients showed valve degeneration (underwent surgical MV replacement). Throughout follow-up, no patient exhibited mortality. The authors concluded that TMVR is a feasible and safe approach in patients with high surgical risk. TMViV and TMViR are reasonable as the first treatment approaches, and TMViMAC seems encouraging. Limitations include lack of comparison with other therapeutic approaches, small sample size (n = 64), short duration of follow-up (6 months), and single-center design. Further research is needed to determine the clinical relevance of these findings.

A Hayes report concluded that there is insufficient evidence to draw conclusions regarding the effectiveness and safety of TMVR for treating patients with MR. Substantial uncertainty remains due to a small body of evidence and lack of studies comparing TMVR with clinical alternatives (Hayes, 2021; updated 2023).

In a multicenter global registry, Guerrero et al. (2016) evaluated the outcomes of TMVR in patients with severe mitral annular calcification. Sixty-four patients in 32 centers underwent TMVR with compassionate use of balloon-expandable valves. Mean age was 73 ±13 years, 66% were female and mean STS score was 14.4 ±9.5%. The mean mitral gradient was 11.45 ±4.4 mmHg, and the mean mitral area was 1.18 ±0.5 cm^2. SAPIEN valves were used in 7.8%, SAPIEN XT in 59.4%, SAPIEN 3 in 28.1% and Inovare in 4.7%. Access was transatrial in 15.6%, transapical in 43.8% and transseptal in 40.6%. Technical success was achieved in 46 (72%) patients, primarily limited by the need for a second valve in 11

(17.2%). Six (9.3%) had left ventricular outflow tract obstruction with hemodynamic compromise. Mean mitral gradient post-procedure was 4 ±2.2 mmHg, and paravalvular regurgitation was mild or absent in all. Thirty-day all-cause mortality was 29.7%. Eighty-four percent of the survivors with follow-up data available were in NYHA functional class I or II at 30 days (n = 25). The authors concluded that TMVR with balloon-expandable valves in patients with severe mitral annular calcification is feasible but may be associated with significant adverse events. This study is limited by retrospective design, lack of comparison group, short-term follow-up and small sample size.

Puri et al. (2016) conducted a systematic review of TMVR for inoperable severely calcified native mitral valve disease. Nine publications describing 11 patients (82% severe mitral stenosis; 18% severe mitral regurgitation) were identified. The procedural success rate was 73%, without residual paravalvular leaks. Successful immediate re-deployment of a 2nd valve was needed in 2 instances, following significant paravalvular leak detection. All patients survived the procedure, with 2 non-cardiac-related deaths reported on days 10 and 41 post-TMVR. Mid-term follow-up, reported in 8 patients, revealed 6 patients were alive at 3-months with much improved functional status. Further studies with a larger number of patients and longer follow-up are warranted.

Transcatheter Edge-to-Edge Mitral Valve Leaflet Repair

In a registry-based cohort study of 19,088 patients with isolated moderate to severe or severe degenerative MR, Makkar et al. (2023) evaluated the outcomes of transcatheter edge-to-edge mitral valve repair using the MitraClip device. The primary end point was defined as moderate or less residual MR and a mean mitral gradient of less than 10 mm Hg. The authors reported the procedure was safe and resulted in successful repair in 88.9% of patients. The lowest mortality was observed in patients with mild or less residual MR and low mitral gradients. Compared to unsuccessful repair, successful valve repair was associated with lower mortality and heart failure hospitalization over one year. The findings are limited by the observational nature of the study.

Lim et al. (2022) conducted a prospective, multicenter, randomized controlled pivotal trial (CLASP IID) to evaluate the safety and effectiveness of the PASCAL system compared with the MitraClip system in patients with degenerative MR. Patients with 3+ or 4+ degenerative MR at prohibitive surgical risk were assessed and randomized 2:1 (PASCAL:MitraClip). The primary safety endpoint was the composite major adverse event rate at 30 days. The primary effectiveness endpoint was the proportion of patients with MR ≤2+ at 6 months. A prespecified interim analysis in 180 patients demonstrated noninferiority of the PASCAL system versus the MitraClip system for the primary safety and effectiveness endpoints of major adverse event rate (3.4% vs 4.8%) and MR ≤2+ (96.5% vs 96.8%), respectively. Functional and quality-of-life outcomes significantly improved in both groups. The proportion of patients with MR ≤1+ was durable in the PASCAL group from discharge to 6 months. The CLASP IID trial demonstrated safety and effectiveness of the PASCAL system and met noninferiority endpoints. NCT03706833

Marmagkiolis et al. (2019) performed a meta-analysis to evaluate the safety and efficacy of percutaneous mitral valve repair for the management of functional MR. Seven studies (two RCTs and 5 observational studies) comparing percutaneous mitral valve repair using the MitraClip device (n = 1,174) against conservative therapy (n = 1,015) for the management of functional MR were included. The 12-month mortality rate in the MitraClip group was 18.4% compared with 25.9% in the medical therapy group. The rate of readmission at 12 months was 29.9% in the MitraClip group compared with 54.1% in the medical therapy group.

The multicenter randomized controlled COAPT study enrolled patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy. Patients were randomly assigned to transcatheter mitral valve repair plus medical therapy (device group) or medical therapy alone (control group). Of the 614 patients who were enrolled in the trial, 302 were assigned to the device group and 312 to the control group. The primary effectiveness end point was all hospitalizations for heart failure within 24 months of follow-up. The primary safety end point was freedom from device-related complications at 12 months. Transcatheter mitral valve repair resulted in a lower rate of hospitalization for heart failure [hazard ratio, 0.53; 95% confidence interval (CI), 0.40 to 0.70; $p < 0.001$] and lower all-cause mortality (hazard ratio, 0.62; 95% CI, 0.46 to 0.82; $p < 0.001$) within 24 months of follow-up than medical therapy alone. The rate of freedom from device-related complications (96.6%) exceeded a prespecified safety threshold (Stone et al., 2018). With extended follow-up through 36 months, there was no loss of effectiveness with MitraClip treatment nor did new safety concerns emerge. Additionally, among 58 patients assigned to medical therapy alone who crossed over and were treated with MitraClip, the subsequent composite rate of mortality or hospitalizations for heart failure was reduced compared with those who continued on medical therapy alone (Mack et al., 2021). Stone et al. (2023) reported transcatheter edge-to-edge repair of the mitral valve was safe, led to a lower rate of hospitalization for heart failure than medical therapy alone, and prolonged survival during five years of follow-up. NCT01626079.

In the MITRA-FR study, patients with severe secondary MR were randomly assigned to undergo percutaneous mitral valve repair plus medical therapy (n = 152) or medical therapy alone (n = 152). Severe secondary MR was defined as an effective regurgitant orifice area of > 20 mm^2 or a regurgitant volume of > 30 ml per beat, a LVEF between 15 and 40% and symptomatic heart failure. Among patients with severe secondary MR, the rate of death or unplanned hospitalization for heart failure at 1 year did not differ significantly between the two groups. The rate of death from any cause was 24.3% (37 of 152 patients) in the intervention group and 22.4% (34 of 152 patients) in the control group. The rate of unplanned hospitalization for heart failure was 48.7% (74 of 152 patients) in the intervention group and 47.4% (72 of 152 patients) in the control group (Obadia et al., 2018). NCT01920698.

Bail (2015) performed a meta-analysis of the safety and efficacy of the MitraClip device. Twenty-six observational studies (n = 3,821) were included in the analysis. Based on the analysis, the authors reported that treatment with MitraClip was associated with good short-term success and low mortality and that the procedure was safe and effective for patients with limited surgical options. The results were comparable with open mitral valve repair, but patients were markedly older and had a higher risk profile than patients who undergo open mitral valve repair. These findings are limited by the lack of randomization of the included studies.

EVEREST II (Endovascular Valve Edge-to-Edge Repair Study)

EVEREST II is a two-part multicenter, RCT and registry to evaluate the safety and efficacy of endovascular mitral valve repair using the MitraClip device compared with conventional mitral valve surgery in patients with moderate to severe mitral regurgitation (MR). The study is funded by Abbott Vascular. EVEREST II consists of a randomized arm and a high-risk registry arm. NCT00209274.

EVEREST II Randomized Arm

Feldman et al. (2011) randomly assigned 279 patients with moderately severe or severe (grade 3-4+) MR in a 2:1 ratio to undergo either percutaneous repair (n = 184) or conventional surgery (n = 95) for repair or replacement of the mitral valve. The patients enrolled in this trial had a normal surgical risk and mainly degenerative MR with preserved left ventricular function. The primary end point for efficacy was freedom from death, from surgery for mitral-valve dysfunction and from grade 3-4+ MR at 12 months. The primary safety end point was a composite of major adverse events within 30 days. At 12 months, the rates of the primary end point for efficacy were 55% in the percutaneous-repair group and 73% in the surgery group. The respective rates of the components of the primary end point were as follows: death, 6% in each group; surgery for mitral-valve dysfunction, 20% versus 2%; and grade 3-4+ MR, 21% versus 20%. Major adverse events occurred in 15% of patients in the percutaneous-repair group and 48% of patients in the surgery group at 30 days. At 12 months, both groups had improved left ventricular size, NYHA functional class and quality-of-life measures, as compared with baseline. Although percutaneous repair was less effective at reducing MR than conventional surgery at 12 and 24 months, the procedure was associated with a lower adverse event rate and similar improvements in clinical outcomes.

At 4 years follow-up, Mauri et al. (2013) reported no significant differences between the MitraClip and conventional surgery treatment groups in all-cause mortality, presence of moderate or severe MR or event-free survival. However, at 4 years follow-up, additional mitral valve surgery was needed for 25% of MitraClip patients versus 6% of conventional surgery patients.

At 5 years follow-up, Feldman et al. (2015) reported that, although mitral valve repair surgery is superior to percutaneous mitral valve intervention using the MitraClip device in reducing the severity of MR, the device reduces symptoms, produces durable reduction of MR and promotes favorable reverse remodeling of the left ventricle 5 years after intervention.

EVEREST II High Risk Registry Arm

Using registry data from the EVEREST II High-Risk registry and the REALISM Continued Access Study High-Risk Arm registry, Glower et al. (2014) reported 12-month outcomes in high-risk patients treated with the MitraClip device for MR. Patients with grades 3 to 4+ MR and a surgical mortality risk of ≥ 12% were enrolled. In the studies, 327 of 351 patients completed 12 months of follow-up. Patients were elderly (76 ±11 years of age), with 70% having functional MR and 60% having prior cardiac surgery. The mitral valve device reduced MR to ≤ 2+ in 86% of patients at discharge (n = 325). Major adverse events at 30 days included death in 4.8%, myocardial infarction in 1.1% and stroke in 2.6%. At 12 months, MR was ≤ 2+ in 84% of patients (n = 225). From baseline to 12 months, left ventricular (LV) end-diastolic volume improved from 161 ±56 ml to 143 ±53 ml (n = 203) and LV end-systolic volume improved from 87 ±47 ml to 79 ±44 ml (n = 202). NYHA functional class improved from 82% in class III/IV at baseline to 83% in class I/II at 12 months (n = 234). Survival estimate at 12 months was 77.2%.

Whitlow et al. (2012) evaluated 78 high-risk symptomatic patients with severe (Grade 3 or 4+) MR and an estimated surgical mortality rate of ≥ 12%. Percutaneous mitral valve leaflet repair, using the MitraClip device, was compared with 36 patients with similar degrees of MR, risks and comorbidities who were screened for the study but were not enrolled for various reasons. The devices were successfully placed in 96% of patients. Procedure-related mortality rate at 30 days was similar in the patients who underwent MitraClip placement and the comparator group (7.7% versus 8.3%), but the MitraClip patients appeared to have a better 1-year survival (76% versus 55%). In surviving patients with matched baseline and 12-month data, 78% had an MR grade of ≤ 2+. Left ventricular end-diastolic volume improved from 172 ml to 140 ml, and end-systolic volume improved from 82 ml to 73 ml. NYHA functional class improved from III/IV at baseline in 89% to class I/II in 74%. Quality of life improved (Short Form-36 physical component score increased from 32.1 to 36.1), and the mental component score increased from 45.5 to 48.7 at 12 months. The annual rate of hospitalization for congestive heart failure in surviving patients with matched data decreased from 0.59 to 0.32. The authors concluded that the MitraClip device reduced MR in a majority of patients deemed at high risk of surgery, resulting in improvement in clinical symptoms and significant left ventricular reverse remodeling over 12 months. The findings are however limited by lack of randomization.

At 5 years, clinical follow-up was achieved in 90% of 78 enrolled patients. The rate of post-procedural adverse events declined from 30 days to 1-year follow-up and was stable thereafter through 5 years. Two patients developed mitral stenosis. Two patients underwent mitral valve surgery. A total of 42 deaths were reported through 5 years most likely a consequence of the advanced age and comorbidity profile of the enrolled patients. Effectiveness measures at 5 years showed reductions in MR severity to ≤ 2+ in 75% of patients, left ventricular end-diastolic volume and left ventricular end-systolic volume compared with baseline. NYHA functional class improved from baseline to 5 years, and septal-lateral annular dimensions remained stable with no indication of mitral annular dilation through 5 years (Kar et al., 2019).

EVEREST (Endovascular Valve Edge-to-Edge Repair Study)

EVEREST is a multicenter, prospective single-arm study to evaluate the feasibility, safety and efficacy of a percutaneous mitral valve repair system (MitraClip) for treating MR. Patients will undergo 30-day, 6-month, 12-month, and 5-year clinical follow-up. The study is funded by Abbott Vascular. NCT00209339.

Feldman et al. (2009) conducted an analysis of this prospective, multicenter single-arm study to evaluate the feasibility, safety and efficacy of the MitraClip system. A total of 107 patients with moderate to severe (grade 3-4+) MR or compromised left ventricular function (if asymptomatic) underwent percutaneous valve repair with the MitraClip device. Ten (9%) had a major adverse event, including 1 nonprocedural death. Freedom from clip embolization was 100%. Partial clip detachment occurred in 10 (9%) patients. Overall, 74% of patients achieved acute success and 64% were discharged with MR of ≤ 1+. Thirty-two patients (30%) had mitral valve surgery during the 3.2 years after clip procedures. When repair was planned, 84% (21 of 25) were successful. Thus, surgical options were preserved. A total of 50 of 76 (66%) successfully treated patients were free from death, mitral valve surgery or MR > 2+ at 12 months (primary efficacy end point). Kaplan-Meier freedom from death was 95.9%, 94.0% and 90.1%, and Kaplan-Meier freedom from surgery was 88.5%, 83.2% and 76.3% at 1, 2 and 3 years, respectively. The findings are limited by lack of comparison group.

Maisano et al. (2013) and Reichenspurner et al. (2013) reported early outcomes from the ACCESS-EU trial. The prospective, multicenter, single-arm post-approval study enrolled 567 patients with MR. Maisano et al. reported an implant success rate of 99.6%. Nineteen patients (3.4%) died within 30 days after the MitraClip procedure. Survival at 1 year was 81.8%. Thirty-six patients (6.3%) required mitral valve surgery within 12 months after the implant procedure. There was improvement in the severity of MR at 12 months, compared with baseline. In a subset of 117 patients with severe degenerative MR, Reichenspurner et al. reported that the MitraClip procedure resulted in significant reductions in MR and improvements in clinical outcomes at 12 months. Limitations of this study include lack of randomization, absence of a control group and short-term follow-up. Additionally, patient selection criteria varied at participating centers.

Cohort studies have compared the MitraClip procedure in high-risk patients with conventional surgery in patients at normal risk. A study by Conradi et al. (2013), enrolled 171 patients with secondary MR and found that after 6 months, the MitraClip procedure was associated with lower survival (87% versus 96% of patients) and lower freedom from moderate or severe MR (88% versus 97% of patients). These differences may have been due to the poorer health status of patients who underwent the MitraClip procedure. Adjustment for these differences eliminated the statistically significant difference in survival. Similar results were obtained by Taramasso et al. (2012) in a cohort study that enrolled 143 patients and preferentially assigned higher-risk patients to the MitraClip procedure. At 1-year follow-up, there were no significant differences between the treatment groups in patient survival, but the MitraClip group was more likely to have moderate or severe MR (21% versus 6% of patients). Again, these differences may have been due to the poorer health status of patients who underwent the MitraClip procedure.

Percutaneous Annuloplasty

There is insufficient quality evidence in the clinical literature demonstrating the long-term efficacy of coronary sinus annuloplasty devices for treating mitral regurgitation. Further results from prospective, RCTs are needed to determine safety, efficacy, durability and the ideal candidates for the procedure.

An ECRI Clinical Evidence Assessment concluded that Carillon is a safe procedure that may provide clinical benefits in some patients with functional MR; however, the evidence is too limited in quality to support conclusions. The studies reported moderate improvements in physical function and quality of life and modest cardiovascular risk reduction after one year in Carillon recipients; however, the findings are at high risk of bias from high attrition in the RCT and lack of randomization and small sample or single-center focus in other studies. How Carillon placement compares with medical therapy and other TMVR systems is unclear because relevant studies assessed too few patients. Large multicenter RCTs comparing Carillon with conventional mitral repair surgery (in eligible patients), optimal medical therapy (in patients ineligible for surgery), transcatheter edge-to-edge repair, and other transcatheter annuloplasty devices are needed to validate available data and determine Carillon's optimal place in MR treatment (ECRI, 2023).

Giallauria et al. (2020) performed a meta-analysis of individual patient data from the TITAN, TITAN II, and REDUCE-FMR studies (n=209). The studies compared transcatheter mitral valve repair with the Carillon device to optimal medical therapy alone in patients with functional MR. Measured outcomes included MR severity/grade, left ventricular remodeling, functional status, and heart failure-related outcomes in heart failure patients with reduced ejection fraction. At one-year follow-up, the authors reported that the Carillon device was more effective than optimal medical therapy alone for improving MR grade in patients with functional MR; however, left ventricular ejection fraction improvement did not differ significantly between the two groups. NYHA functional status improved more with Carillon than with medical therapy alone. Heart failure-related hospitalizations occurred less frequently among Carillon recipients than among control group patients. Two of the three trials were small and lacked randomization and control; the third was randomized but had high patient attrition. Furthermore, Carillion was not compared to other proven transcatheter or surgical approaches to MR. The study by Siminiak et al. (2012) previously discussed in this policy was included in this meta-analysis.

In the REDUCE FMR trial, Witte et al. (2019) evaluated the effects of the Carillon device on MR severity and left ventricular remodeling. In this blinded, randomized, proof-of-concept, sham-controlled trial, patients receiving optimal heart failure medical therapy were assigned to a coronary sinus-based mitral annular reduction approach for functional MR or sham. The primary endpoint was change in mitral regurgitant volume at 12 months, measured by echocardiography. Patients (n = 120) were randomized to either the treatment (n = 87) or the sham-controlled (n = 33) arm. There were no significant differences in baseline characteristics between the groups. In the treatment group, 73 of 87 (84%) had the device implanted. The primary endpoint was met with a statistically significant reduction in mitral regurgitant volume in the treatment group compared to the control group. Additionally, there was a significant reduction in left ventricular volumes in patients receiving the device versus those in the control group. This study was not powered to evaluate clinical endpoints. Carillion was not compared to other proven transcatheter or surgical approaches to MR. Studies are underway to assess the effect of this approach on mortality and hospitalization in patients with FMR. NCT02325830.

Schofer et al. (2009) evaluated patients with moderate heart disease who were enrolled in the CARILLON Mitral Annuloplasty Device European Union Study (AMADEUS). Percutaneous mitral annuloplasty was achieved through the coronary sinus with the CARILLON Mitral Contour System. Of the 48 patients enrolled in the trial, 30 received the CARILLON device. Eighteen patients did not receive a device because of access issues, insufficient acute FMR reduction, or coronary artery compromise. Echocardiographic FMR grade, exercise tolerance, NYHA class, and quality of life were assessed at baseline and 1 and 6 months. The major adverse event rate was 13% at 30 days. At 6 months, the degree of FMR reduction among 5 different quantitative echocardiographic measures ranged from 22% to 32%. Six-minute walk distance improved from 307 ±87 m at baseline to 403 ±137 m at 6 months. Quality of life, measured by the Kansas City Cardiomyopathy Questionnaire, improved from 47 ±16 points at baseline to 69 ±15 points at 6 months. The authors concluded that percutaneous reduction in FMR with a novel coronary sinus-based mitral annuloplasty device is feasible in patients with heart failure, is associated with a low rate of major adverse events, and is associated with improvement in quality of life and exercise tolerance. Study limitations include the lack of a randomized, blinded control group with whom to compare safety and efficacy results.

Several other minimally invasive mitral valve repair devices are in the early stages of development. Large, prospective studies with long-term follow-up are needed to establish their clinical role.

Small case series from a single research group reported early results with the Harpoon expanded polytetrafluoroethylene (ePTFE) chordal implantation system. The results were promising; however, larger prospective studies with long-term follow-up are needed to establish their clinical role (Gammie et al., 2021; Gammie et al., 2016; Gammie et al., 2018).

Messika-Zeitoun et al. (2019) reported the 1-year outcomes of 60 consecutive patients with moderate or severe secondary MR who underwent the Cardioband procedure. At 1 year, most patients had moderate or less MR and experienced significant functional improvements. There were two in-hospital deaths (none device-related), one stroke, two coronary artery complications and one tamponade. Anchor disengagement, observed in 10 patients, resulted in device inefficacy in five patients and led to device modification halfway through the study to mitigate this issue. Study limitations include lack of randomization and control and short-term follow-up.

Colli et al. (2018) reported early results of the NeoChord mitral valve repair system for treating degenerative MR. In a consecutive case series of patients, 213 participants were enrolled in the NeoChord Independent International Registry. All participants presented with severe MR. The primary end points were procedural success, freedom from mortality, stroke, reintervention, recurrence of severe MR, rehospitalization and decrease of at least 1 NYHA functional class at 1-year follow-up. Procedural success was achieved in 206 (96.7%) patients. At 1-year follow-up, overall survival was 98 ±1%. Composite end point was achieved in 84 ±2.5% for the overall population. Study limitations include lack of randomization and control and short-term follow-up.

Pulmonary Valve

Gillespie et al. (2023) presented one-year outcomes in a pooled cohort of clinical trial participants from three earlier studies of the Harmony transcatheter pulmonary heart valve. The Harmony device continued to demonstrate favorable clinical and hemodynamic outcomes across studies and valve types through one year. Continued follow-up of this patient cohort through 10 years will allow long-term evaluation of valve performance and durability.

In the prospective, single-arm, multicenter COMPASSION S3 study (n = 58), Lim et al. (2023) evaluated the safety and effectiveness of the SAPIEN 3 transcatheter heart valve for treating patients with a dysfunctional RVOT conduit or surgical valve in the pulmonary position. The primary end point was a composite of valve dysfunction at one year comprising RVOT reintervention, ≥ moderate total pulmonary regurgitation, and mean RVOT gradient > 40 mm Hg. Prestenting was performed 53% of the time. At discharge, the device success was 98%. At 30 days, there were no major adverse clinical events. At one year, the composite primary end point of valve dysfunction occurred in 4.3% of participants. No mortality, endocarditis, thrombosis, or stent fractures were reported at one year. Long-term follow-up to determine the durability of these results will continue.

A Hayes report concluded that there is insufficient evidence to draw conclusions regarding the effectiveness and safety of percutaneous pulmonary valve implantation (PPVI) using SAPIEN 3 and SAPIEN XT valves for the treatment of right ventricular outflow tract (RVOT). Substantial uncertainty exists regarding the long-term durability and efficacy compared with open heart surgery (Hayes, 2022; updated 2023).

McElhinney et al. (2022) evaluated mid- and long-term outcomes after transcatheter pulmonary valve replacement in a large, multicenter cohort using international registry data on 2476 patients. The analysis found that survival and freedom from reintervention or surgery after transcatheter pulmonary valve replacement are generally comparable to outcomes of surgical conduit/valve replacement across a wide range of patient ages.

Ribeiro et al. (2020) performed a systematic review and meta-analysis of 18 studies comparing transcatheter with surgical pulmonary valve replacement. The primary endpoint was early mortality after replacement. Secondary endpoints included procedure-related complications, length of hospital stay, mortality during follow-up, infective endocarditis, need for reintervention, post-replacement transpulmonary peak systolic gradient, and significant pulmonary regurgitation. No significant difference was observed in the primary endpoint of early mortality between the groups. At midterm follow-up the transcatheter technique was comparable with the surgical procedure in terms of repeat intervention but was associated with an increased risk of infective endocarditis. In selected patients, the transcatheter technique was found to have a shorter length of hospital stay and fewer procedure-related complications.

Benson et al. (2020) reported 3-year clinical and hemodynamic outcomes in a follow-up to the Bergersen et al. (2017) feasibility study. Of the original 20 implanted patients, 17 completed 3-year follow-up. Results showed good valve function in most, and the absence of moderate/severe paravalvular leak and significant late frame fractures. Two patients developed significant neointimal tissue ingrowth requiring ViV treatment, while all others had no clinically significant RVOT obstruction. The authors noted that these results are encouraging, but further follow-up is required. At 5 years, Gillespie et al. (2021) reported in a letter to the editor sustained valve function with freedom from moderate-to-severe valve or perivalvular leak and no reports of endocarditis. Two patients underwent surgical explant. There were 3 catheter-based reinterventions performed in 2 patients who both ultimately underwent Melody ViV procedures. One patient passed away shortly after the 3-year follow-up assessment. These and the original publication described below are limited by lack of a comparison group undergoing a different therapeutic approach.

Kenny et al. (2018) reported 3-year follow-up results of the COMPASSION (Congenital Multicenter Trial of Pulmonic Valve Regurgitation Studying the SAPIEN Transcatheter Heart Valve) trial. Patients with moderate to severe pulmonary regurgitation and/or RVOT conduit obstruction were implanted with the SAPIEN transcatheter heart valve. Fifty-seven of the 63 eligible patients were accounted for at the 3-year follow-up visit from a total of 69 implantations in 81 enrolled patients. Indications for implantation were pulmonary stenosis (7.6%), regurgitation (12.7%) or both (79.7%). Functional improvement in NYHA functional class was observed in 93.5% of patients. Mean peak conduit gradient decreased from 37.5 ±25.4 to 17.8 ±12.4 mmHg, and mean right ventricular systolic pressure decreased from 59.6 ±17.7 to 42.9 ±13.4 mmHg. Pulmonary regurgitation was mild or less in 91.1% of patients. When implanted in patients with moderate to severe pulmonary regurgitation and/or RVOT conduit obstruction, the SAPIEN valve was associated with favorable outcomes at 3 years, with low rates of all-cause mortality, reintervention and endocarditis and no stent fractures.

Chatterjee et al. (2017) performed a systematic review and meta-analyses of observational studies evaluating transcatheter pulmonary valve implantation. Nineteen studies (n = 1,044) with 5 or more patients and at least 6 months of follow-up were included. Thirteen studies used the Melody valve, three used the Edwards SAPIEN or SAPIEN XT valves and three used both Melody and Edwards valve systems. Procedural success rate was 96.2% with a conduit rupture rate of 4.1% and coronary complication rate of 1.3%. The authors reported favorable updated estimates of procedural and follow-up outcomes after transcatheter pulmonary valve implantation. They also noted that widespread adoption of pre-stenting has improved long-term outcomes in these patients. (This systematic review includes Cheatham et al. 2015, Armstrong et al. 2014, Butera et al. 2013 and Eicken et al. 2011 which were previously cited in this policy.) Note: These versions of the SAPIEN valve are no longer commercialized.

Bergersen et al. (2017) reported clinical outcomes from an early feasibility study to assess the self-expanding Harmony transcatheter pulmonary valve. Of sixty-six enrolled participants, 21 patients were approved for implant and 20 received the Harmony device. Most patients had been diagnosed with tetralogy of Fallot and had augmented RVOTs or transannular patch repairs. Clinical assessments were collected at baseline and after 1-month, 3-month and 6-month follow-ups. In the 20 implanted patients, the device was implanted in the intended location; however, proximal migration occurred in one participant during delivery system removal. Two devices were surgically explanted. Premature ventricular contractions related to the procedure were reported in three patients; two were resolved without treatment. One patient had ventricular arrhythmias that required treatment and were later resolved. Eighteen patients returned for the 3- and 6-month follow-up assessments. Echocardiographic data remained consistent with those observed at the 1-month visit. Compared with baseline, patients had significant improvements in pulmonary regurgitation. By the 6-month follow-up, there were minimal changes in incidence of paravalvular leak, mean RVOT gradient or tricuspid regurgitation. Study limitations include lack of randomization, control group and small sample size. Additionally, enrollment was limited to three sites, each with an experienced catheterization cardiologist performing the procedure. The authors noted that further studies with larger patient populations are needed to assess long-term durability, function and safety of the Harmony device.

McElhinney et al. (2010) conducted a single-arm multicenter trial of 136 patients (median age, 19 years) who underwent catheterization for intended Melody valve implantation. Implantation was attempted in 124 patients. In the other 12, transcatheter pulmonary valve placement was not attempted because of the risk of coronary artery compression (n = 6) or other clinical or protocol contraindications. There was 1 death and 1 explanted valve after conduit rupture. The median peak RVOT gradient was 37 mmHg before implantation and 12 mmHg immediately after implantation. Before implantation, pulmonary regurgitation was moderate or severe in 92 patients. No patient had more than mild pulmonary regurgitation early after implantation or during follow-up. Freedom from stent fracture was 77.8 ±4.3% at 14 months. Freedom from valve dysfunction or reintervention was 93.5 ±2.4% at 1 year. A higher RVOT gradient at discharge and younger age were associated with shorter freedom from dysfunction. The results demonstrated an ongoing high rate of procedural success and encouraging short-term valve function. All re-interventions in this series were for RVOT obstruction, highlighting the importance of patient selection, adequate relief of obstruction, and measures to prevent and manage stent fracture. Jones et al. (2022) reported on 58 patients at 10 years. The estimated freedom from mortality was 90%, from reoperation 79%, and from any reintervention 60%. Ten-year freedom from TPV dysfunction was 53% and was significantly shorter in children than in adults. Estimated freedom from TPV-related endocarditis was 81% at 10 years, with an annualized rate of 2.0% per patient-year. NCT00740870.

Tricuspid Valve

There is insufficient quality evidence in the clinical literature demonstrating the long-term safety and efficacy of transcatheter procedures for treating tricuspid valve disease. Further results from prospective, RCTs are needed to determine safety, efficacy, durability and the ideal candidates for the procedure.

Badwan et al. (2023) performed a meta-analysis of studies evaluating clinical outcomes after caval valve implantation (CAVI) for severe symptomatic tricuspid regurgitation. Fifteen studies (n = 142) were included, 8 of which were case

reports or case series. The median follow-up duration ranged from 61 to 350 days. The authors found that CAVI was associated with a high procedural success rate and significant reductions in NYHA functional class and TR severity but noted several limitations, including small sample size, short-term follow-up, and dissimilar definitions of procedural success. Also, multiple CAVI systems are incorporated into the pooled analysis. While hemodynamic and functional improvements are encouraging, larger-scale prospective studies with longer follow-up are needed.

In the TRICAVAL prospective, open-label, single-center, randomized trial, Dreger et al. (2020) compared the impact of a balloon-expandable transcatheter valve into the inferior vena cava (CAVI) on exercise capacity with optimal medical therapy in patients with severe TR and high surgical risk. Twenty-eight patients were randomized to optimal medical therapy (n = 14) or CAVI (n = 14). The primary endpoint was maximal oxygen uptake at three months. Secondary endpoints included the six-minute walk test, NYHA functional class, NT-proBNP levels, right heart function, unscheduled heart failure hospitalization, and quality of life. Patients underwent follow-up examinations one, three, six, and twelve months after randomization. Maximal oxygen uptake did not change significantly in either group after three months and there was no difference between the medical therapy and CAVI groups. Compared to baseline, CAVI improved NYHA class, dyspnea, and quality of life after three months. However, there were no statistically significant differences in the secondary endpoints between the groups. CAVI did not result in a superior functional outcome compared to medical therapy. Due to an unexpectedly high rate of valve dislocations, the study was stopped for safety reasons resulting in a low number of enrolled patients.

Bugan et al. (2022) completed a systematic review and meta-analysis to evaluate the feasibility of orthotopic transcatheter tricuspid valve replacement (TTVR) devices, echocardiographic, functional improvements, and mortality rates following replacement in patients with significant tricuspid valve regurgitation. The authors systematically searched for the studies evaluating the efficacy and safety of transcatheter tricuspid valve replacement for significant tricuspid valve regurgitation. The efficacy and safety outcomes were the improvements in New York Heart Association functional class, 6-minute walking distance, all-cause death, and periprocedural and long-term complications. In addition, a random-effect meta-analysis was performed comparing outcomes before and after transcatheter tricuspid valve replacement. Nine studies with 321 patients were included in this study. The mean age was 75.8 years, and the mean European System for Cardiac Operative Risk Evaluation II score was 8.2% (95% CI: 6.1 to 10.3). Severe, massive, and torrential tricuspid valve regurgitation was diagnosed in 95% of patients (95% CI: 89% to 98%), and 83% (95% CI: 73% to 90%) of patients were in New York Heart Association functional class III or IV. At a weighted mean follow-up of 122 days, New York Heart Association functional class (risk ratio = 0.20; 95% CI: 0.11 to 0.35; p < .001) and 6-minute walking distance (mean difference = 91.1 m; 95% CI: 37.3 to 144.9 m; p < .001) improved. The prevalence of severe or greater tricuspid valve regurgitation was reduced after transcatheter tricuspid valve replacement (baseline risk ratio = 0.19; 95% CI: 0.10 to 0.36; p < .001). In total, 28 patients (10%; 95% CI: 6% to 17%) died. Pooled analyses demonstrated non-significant differences in hospital and 30-day mortality and > 30-day mortality than predicted operative mortality (risk ratio = 1.03; 95% CI: 0.41 to 2.59; p = .95, risk ratio = 1.39; 95% CI: 0.69 to 2.81; p = .35, respectively). The authors concluded that transcatheter tricuspid valve replacement could be an emerging treatment option for patients with severe tricuspid regurgitation who are not eligible for transcatheter repair or surgical replacement because of high surgical risk. Limitations include a potential for bias as the analysis only included single-arm interventional studies case series, and no RCTs. Moderate heterogeneity was found in the consistency of results. In addition, there are no specific guideline recommendations for patient selection for TTVR, therefore, this meta-analysis is limited by the lack of uniformity in the definition of procedural success. Further research with RCTs is needed to validate these findings.

An ECRI Clinical Evidence Assessment found very low quality evidence on percutaneous tricuspid valve repair for treating TR in patients who are ineligible for surgery. Study results were at high risk of bias due to small sample size and lack of controls and randomization (ECRI, 2022).

Bocchino et al. (2021) performed a meta-analysis to assess the pooled clinical and echocardiographic outcomes of different isolated transcatheter tricuspid valve repair strategies for moderate or greater TR in patients who were ineligible for surgery. Fourteen observational studies (n = 771) were included. At a mean follow-up of 212 days, 209 patients (35%) were in NYHA functional class III or IV compared with 586 patients (84%) at baseline. Six-minute walking distance significantly improved by a mean 50 meters. One hundred forty-seven patients (24%) showed severe or greater TR after isolated transcatheter tricuspid valve repair compared with 616 (96%) at baseline. The included studies are at a high risk of bias due to several factors: small sample size, single-center focus, retrospective design, and/or lack of controls, randomization and blinding. Further results from prospective, RCTs are needed to confirm these findings.

The international TriValve Registry (n = 312) was developed to evaluate several transcatheter tricuspid valve interventions in high-risk patients with severe TR (predominantly functional). Interventions included leaflet repair, annulus repair, coaptation and replacement. Implanted devices included MitraClip (n = 210), Trialign (n = 18), TriCinch first generation (n = 14), caval valve implantation (n = 30), FORMA (n = 24), Cardioband (n = 13), NaviGate (n = 6) and PASCAL (n = 1).

Preliminary results of transcatheter tricuspid valve interventions were promising in terms of safety and feasibility. Mid-term survival was favorable in this high-risk population. However, long-term outcomes and better patient selection are needed to better understand the clinical role of these procedures for treating TR (Taramasso et al., 2019).

In an observational study of 64 consecutive patients, Nickenig et al. (2017) evaluated the safety and feasibility of transcatheter repair of chronic severe TR using edge-to-edge clipping. The procedure was successfully performed in 97% of the patients. After the procedure, TR was reduced by at least 1 grade in 91% of the patients, with significant improvements in NYHA class and 6-minute walk test. In 13% of patients, TR remained severe after the procedure. Significant reductions in effective regurgitant orifice area, vena contracta width and regurgitant volume were observed. This study is limited by small sample size, lack of randomization and control, and limited follow-up.

Valve-in-Valve (ViV) Procedures

There is insufficient quality evidence in the clinical literature demonstrating the long-term efficacy of ViV procedures for mitral, pulmonary, or tricuspid valves. The evidence for these procedures is still evolving. Evidence supporting ViV procedures for aortic valves is stronger.

Ismayl et al. (2023) conducted a systematic review and meta-analysis of observational studies comparing ViV transcatheter mitral valve replacement versus redo surgical mitral valve replacement in a degenerated bioprosthetic mitral valve. Outcomes included in-hospital, 30-day, 1-year, and 2-year mortality, stroke, bleeding, acute kidney injury, arrhythmias, permanent pacemaker insertion, and hospital length of stay. A total of six observational studies (n = 707) were included. ViV transcatheter mitral valve replacement was associated with better outcomes than redo surgical mitral valve replacement, including lower complication rates and shorter hospital LOS, with no significant difference in mortality rates. The findings are limited by the observational nature of the included studies, which could have led to biased estimates. Large-scale randomized trials are needed to confirm these findings.

Eleid et al. (2021) conducted a systematic review of observational studies to evaluate outcomes after transcatheter mitral valve-in-valve ViV implantation for treatment of a degenerated mitral bioprostheses. Five studies (n = 2684) were included in the review. Procedural technical success ranged from 94-98%, with 1-3% rates of periprocedural death, 0-2% stroke and 1-5% risk of left ventricular outflow tract (LVOT) obstruction. Thirty-day post-procedure mean mitral prosthetic gradient ranged from 6-7 mmHg and residual mitral regurgitation was mild or less in 96-100% of patients. Thirty-day survival and one-year survival ranged from 93-97% and 83-89% respectively. Further longitudinal studies are needed to assess long-term outcomes. The findings are limited by lack of comparison groups.

Al-Abcha et al. (2021) performed a meta-analysis to compare clinical outcomes of ViV TAVR versus redo SAVR in failed bioprosthetic aortic valves. Twelve observational studies were included (n = 8,430). Compared to redo SAVR, ViV TAVR was associated with a similar risk of all-cause mortality, cardiovascular mortality, myocardial infarction, permanent pacemaker implantation, and the rate of moderate to severe paravalvular leakage. However, the rates of major bleeding, stroke, procedural mortality and 30-day mortality were significantly lower in the ViV group. Randomized clinical trials are needed to confirm the safety and efficacy of ViV TAVR in patients with failed bioprosthetic aortic valves.

Gozdek et al. (2018) performed a systematic review and meta-analysis to compare redo SAVR with ViV TAVR for patients with failed aortic bioprostheses. Five observational studies (n = 342) were included in the analysis. Although there was no statistical difference in procedural mortality, 30-day mortality, and cardiovascular mortality at a mean follow-up period of 18 months, cumulative survival analysis favored surgery. ViV procedures were associated with a significantly lower rate of permanent pacemaker implantations and shorter intensive care unit and hospital stays. Redo SAVR offered superior echocardiographic outcomes, lower incidence of patient-prosthesis mismatch, fewer paravalvular leaks, and lower mean postoperative aortic valve gradients. The authors concluded that ViV approach is a safe, feasible alternative to conventional surgery that may offer an effective, less invasive treatment for patients with failed surgical aortic bioprostheses who are inoperable or at high risk , but that SAVR should remain the standard of care, particularly in the low-risk population, because it offers superior hemodynamic outcomes with low mortality rates.

Tam et al. (2018) performed a systematic review and meta-analysis to determine the safety and efficacy of ViV TAVR versus redo SAVR for the treatment of previously failed aortic bioprostheses. Four unadjusted (n = 298) and two propensity-matched
(n = 200) observational studies were included. Despite higher predicted surgical risk of ViV patients, there was no difference in perioperative mortality (4.4% versus 5.7%) or late mortality, reported at median one-year follow-up. The incidence of permanent pacemaker implantation (8.3% versus 14.6%) and dialysis (3.2% versus 10.3%) were lower in ViV. There was a reduction in the incidence of severe patient-prosthesis mismatch (3.3% versus 13.5%) and mild or greater paravalvular leak (5.5% versus 21.1%) in the redo SAVR group compared to ViV.

Using patient data from the STS/American College of Cardiology Transcatheter Valve Therapy Registry, Tuzcu et al. (2018) evaluated the safety and effectiveness of ViV TAVR for failed surgically implanted bioprostheses by comparing it with the benchmark of native valve (NV) TAVR. Patients who underwent ViV TAVR (n = 1,150) were matched 1:2 to patients undergoing NV TAVR (n = 2,259). Unadjusted analysis revealed lower 30-day mortality (2.9% vs. 4.8%), stroke (1.7% vs. 3.0%) and heart failure hospitalizations (2.4% vs. 4.6%) in the ViV TAVR compared with the NV TAVR group. Adjusted analysis revealed lower 30-day mortality, lower 1-year mortality and hospitalization for heart failure in the ViV TAVR group. Patients in the ViV TAVR group had higher post-TAVR mean gradient (16 vs. 9 mmHg), but less moderate or severe aortic regurgitation (3.5% vs. 6.6%). Post-TAVR gradients were highest in small SAVRs and stenotic SAVRs.

Eleid et al. (2017) reported 1-year outcomes of percutaneous balloon-expandable transcatheter heart valve implantation in a failed mitral bioprosthesis (n = 60), previous ring annuloplasty (n = 15) and severe mitral annular calcification (n = 12). Acute procedural success was achieved in 97% of the ViV group and 74% in the valve in ring/valve in mitral annular calcification (MAC) group. Thirty-day survival free of death and cardiovascular surgery was 95% in the ViV subgroup and 78% in the valve in ring/valve in MAC group. One-year survival free of death and cardiovascular surgery was 86% in the ViV group compared with 68%. At 1 year, 90% had NYHA functional class I or II symptoms, no patients had more than mild residual mitral prosthetic or periprosthetic regurgitation and the mean transvalvular gradient was 7 ±3 mmHg. The procedure for failed annuloplasty rings and severe MAC was feasible but associated with significant rates of left ventricular outflow tract obstruction, need for a second valve and/or cardiac surgery. This study reflects very early results with the procedure and is limited by small sample size and lack of randomization. Further studies of a larger number of patients treated using similar techniques and with longer follow-up duration will be necessary to continually assess outcomes of this novel therapy.

In an observational study, Yoon et al. (2017) evaluated the outcomes of TMVR in 248 patients with failed mitral bioprosthetic valves (ViV) and annuloplasty rings. The TMVR procedure provided acceptable outcomes in high-risk patients with degenerated bioprostheses or failed annuloplasty rings, but mitral valve-in-ring was associated with higher rates of procedural complications and mid-term mortality compared with mitral ViV. This study is limited by lack of randomization and control. Further studies evaluating the long-term outcomes of patients undergoing TMVR for degenerated bioprostheses or failed annuloplasty rings are needed.

Deeb et al. (2017) evaluated the safety and effectiveness of the CoreValve in patients with failed surgical aortic bioprostheses. The CoreValve U.S. Expanded Use Study was a prospective, nonrandomized study that enrolled 233 patients with symptomatic surgical valve failure who were deemed unsuitable for reoperation. Patients were treated with the CoreValve and evaluated for 30-day and 1-year outcomes after the procedure. Surgical valve failure occurred through stenosis (56.4%), regurgitation (22.0%) or a combination (21.6%). A total of 227 patients underwent attempted TAVR and successful TAVR was achieved in 225 (99.1%) patients. Patients were elderly (76.7 ±10.8 years), had an STS PROM score of 9.0 ±6.7% and were severely symptomatic (86.8% NYHA functional class III or IV). The all-cause mortality rate was 2.2% at 30 days and 14.6% at 1 year; major stroke rate was 0.4% at 30 days and 1.8% at 1 year. Moderate aortic regurgitation occurred in 3.5% of patients at 30 days and 7.4% of patients at 1 year, with no severe aortic regurgitation. The rate of new permanent pacemaker implantation was 8.1% at 30 days and 11.0% at 1 year. The mean valve gradient was 17.0 ±8.8 mmHg at 30 days and 16.6 ±8.9 mmHg at 1 year.

Webb et al. (2017) evaluated 30-day and 1-year outcomes in high-risk patients undergoing ViV TAVR using the SAPIEN XT valve. Patients with symptomatic degeneration of surgical aortic bioprostheses at high risk (≥ 50% major morbidity or mortality) for reoperative surgery were prospectively enrolled in the multicenter PARTNER 2 ViV trial and continued access registries. ViV procedures were performed in 365 patients (96 initial registry, 269 continued access patients). Mean age was 78.9 ±10.2 years, and mean STS score was 9.1 ±4.7%. At 30 days, all-cause mortality was 2.7%, stroke was 2.7%, major vascular complication was 4.1%, conversion to surgery was 0.6%, coronary occlusion was 0.8% and new pacemaker insertion was 1.9%. One-year all-cause mortality was 12.4%. Mortality fell from the initial registry to the subsequent continued access registry, both at 30 days (8.2% vs. 0.7%, respectively) and at 1 year (19.7% vs. 9.8%, respectively). At 1-year, mean gradient was 17.6 mmHg, and effective orifice area was 1.16 cm^2, with greater than mild paravalvular regurgitation of 1.9%. LVEF increased (50.6% to 54.2%), and mass index decreased (135.7 to 117.6 g/m^2), with reductions in both mitral (34.9% vs. 12.7%) and tricuspid (31.8% vs. 21.2%) moderate or severe regurgitation.

Phan et al. (2016) conducted a systematic review to compare outcomes and safety of transcatheter ViV implantation with reoperative conventional aortic valve replacement. A total of 18 relevant observational studies (823 patients) were included. Pooled analysis suggested that transcatheter ViV implantation achieved similar hemodynamic outcomes, with lower risk of strokes and bleeding, but higher rates of paravalvular leaks compared to reoperative conventional aortic valve replacement. The authors noted that future randomized studies and prospective registries are essential to compare the effectiveness of these procedures.

Using VIVID registry data, Dvir et al. (2014) determined the survival of patients after transcatheter aortic ViV implantation inside failed surgical bioprosthetic valves. Correlates for survival were evaluated using a multinational registry that included 459 patients with degenerated bioprosthetic valves undergoing ViV implantation. Modes of bioprosthesis failure were stenosis (n = 181), regurgitation (n = 139) and combined (n = 139). The stenosis group had a higher percentage of small valves (37% vs. 20.9% and 26.6% in the regurgitation and combined groups, respectively). Within 1 month following ViV implantation, 35 (7.6%) patients died, 8 (1.7%) had major stroke and 313 (92.6%) of surviving patients had good functional status (NYHA class I/II). The overall 1-year survival rate was 83.2%; 62 death events; 228 survivors). Patients in the stenosis group had worse 1-year survival (76.6%; 34 deaths; 86 survivors) in comparison with the regurgitation group (91.2%; 10 deaths; 76 survivors) and the combined group (83.9%; 18 deaths; 66 survivors). Similarly, patients with small valves had worse 1-year survival (74.8%; 27 deaths; 57 survivors) versus with intermediate-sized valves (81.8%; 26 deaths; 92 survivors) and with large valves (93.3%; 7 deaths; 73 survivors). Factors associated with mortality within 1 year included having small surgical bioprosthesis (≤ 21 mm) and baseline stenosis (vs. regurgitation). In a follow-up study, Bleiziffer et al. (2020) assessed long-term survival and reintervention outcomes after transcatheter aortic ViV procedures. A total of 1,006 aortic ViV procedures were included in the analysis. The primary endpoint was patient survival, and the main secondary endpoint was all-cause reintervention. Results showed that the size of the original failed valve may influence long-term mortality, and the type of transcatheter valve may influence the need for reintervention after aortic ViV procedures.

Cerebral Protection

There is insufficient quality evidence in the clinical literature demonstrating the long-term efficacy of transcatheter cerebral protection devices in improving neurological and cognitive function following transcatheter aortic valve replacement.

A prospective, post-market, multi-center, RCT was conducted by Kapadia et al. (2022) to evaluate the Sentinel cerebral embolic protection (CEP) device in patients with aortic stenosis undergoing transfemoral transcatheter TAVR. A total of 3,000 patients with aortic stenosis across North America, Europe, and Australia underwent randomization in a 1:1 ratio to undergo transfemoral TAVR with CEP (CEP group) or without CEP (control group); 1,501 were assigned to the CEP group and 1,499 to the control group. The primary end point was stroke within 72 hours after TAVR or before discharge (whichever came first) in the intention-to-treat population. Disabling stroke, death, transient ischemic attack, delirium, major or minor vascular complications at the CEP access site, and acute kidney injury were also assessed. A neurology professional examined all enrolled study patients at baseline and again after TAVR. A CEP device was successfully deployed in 1,406 of the 1,489 patients (94.4%) in whom an attempt was made. The incidence of stroke within 72 hours after TAVR or before discharge did not differ between the CEP group and the control group (2.3% vs. 2.9%; difference, −0.6 percentage points; 95% confidence interval, −1.7 to 0.5; p = 0.30). Disabling stroke occurred in 0.5% of the patients in the CEP group and in 1.3% of those in the control group. There were no sizeable differences between the CEP group and the control group in the percentage of patients who died (0.5% vs. 0.3%); had a stroke, a transient ischemic attack, or delirium (3.1% vs. 3.7%); or had acute kidney injury (0.5% vs. 0.5%). One patient (0.1%) had a vascular complication at the CEP access site. The authors concluded among patients with aortic stenosis undergoing transfemoral TAVR, the use of CEP did not influence the incidence of periprocedural stroke but based on the 95% confidence interval around this outcome, the results may not rule out a benefit of CEP during TAVR. Limitations include a greater percentage of female patients in the CEP group despite randomization and large number of enrolled patients. Female sex has been reported to be a risk factor for stroke with TAVR. Granular data on clinical outcomes were restricted to a small number of endpoints, with only short-term follow-up. In addition, the trial results apply only to the Sentinel CEP device and cannot be generalized to other CEP devices. There are additional ongoing clinical trials including the BHF PROTECT-TAVI (British Heart Foundation Randomized Trial of Routine Cerebral Embolic Protection in Transcatheter Aortic Valve Implantation; ISRCTN Registry number, ISRCTN16665769) in which additional data on the effectiveness of CEP during TAVR are forthcoming.

In a letter to the editor, Radwan et al. (2021) performed a meta-analysis of studies evaluating the safety and efficacy of the Sentinel cerebral protection system during TAVR. Three RCTs and four observational studies were included (n = 117,329). The Sentinel group was associated with lower risk of 30-day stroke, mortality and major bleeding. These short-term results were mainly driven from observational data as subgroup analysis from the RCTs showed a trend toward benefit without statistical significance. The rate of major vascular complications was similar between the 2 groups. Results from large RCTs are needed to confirm these results.

Ndunda et al. (2019) performed a systematic review and meta-analysis to compare the clinical outcomes following TAVR with and without the use of the Sentinel Cerebral Protection System (Sentinel CPS). Four studies (three RCTs and one propensity score-matched cohort study) comparing patients undergoing TAVR with Sentinel CPS (n = 606) to those without any embolic protection device (n = 724) were included. Sentinel CPS use was associated with lower rates of 30-day mortality, 30-day symptomatic stroke and major or life-threatening bleeding. There was no significant difference between the two arms in the incidence of acute kidney injury and major vascular complications. The authors noted

limitations for the analyzed studies including lack of a control group for some studies, small sample sizes, lack of patient-level data and missing outcomes data. Furthermore, not all included studies were randomized.

An ECRI product brief on the Sentinel device reported that the evidence suggests that device placement is relatively safe, but whether it benefits patients undergoing TAVR is unclear. Studies reported inconsistent findings on the device's impact on reducing stroke risk and too few data are available on the long-term neurocognitive burden of brain microinfarction in patients treated with the device. Additional controlled studies that report on these outcomes are needed to assess the device's effectiveness (ECRI, 2017b; updated 2022).

Bagur et al. (2017) performed a systematic review and meta-analysis evaluating the impact of embolic protection devices on cerebrovascular events during TAVR. Sixteen studies (5 RCTs and 11 observational studies) involving 1,170 patients (865/305 with/without embolic protection devices) were included. The embolic protection device delivery success rate was reported in all studies and was achieved in 94.5% of patients. Meta-analyses comparing the two methods showed no significant differences between patients undergoing TAVR with or without embolic protection devices with respect to clinically evident stroke and 30-day mortality. Embolic protection during TAVR may be associated with smaller volume of silent ischemic lesions and smaller total volume of silent ischemic lesions. However, it may not reduce the number of new-single, multiple or total number of lesions.

In an observational cohort study, Seeger et al. (2017) evaluated the impact of cerebral embolic protection on stroke-free survival in 802 consecutive patients undergoing TAVR for severe aortic stenosis. The Sentinel cerebral embolic protection device was used in 34.9% (n = 280) of patients. In the remaining group of patients, TAVR was performed without cerebral embolic protection. In patients undergoing TAVR, use of a cerebral embolic protection device demonstrated a significantly higher rate of stroke-free survival compared with unprotected TAVR. This study is limited by lack of randomization.

In two randomized, controlled trials (Kapadia et al., 2017; Van Mieghem et al., 2016), the primary efficacy endpoint was reduction in volume of new cerebral lesions on diffusion-weighted magnetic resonance imaging (DW-evaluation) up to 7 days post-TAVR, a surrogate endpoint for cerebral damage. This endpoint was not met in either trial, although both trials demonstrated a nonsignificant numerical reduction in new cerebral lesions favoring the Sentinel device over no transcatheter cerebral embolic protection. In addition, both trials were limited by small sample sizes and poor compliance with DW-MRI follow-up, which was missing for 21% of SENTINEL trial patients (Kapadia et al., 2017) and 43% of MISTRAL-C trial patients (Van Mieghem et al., 2016).

In the Claret Embolic Protection and TAVI (CLEAN-TAVI) trial, Haussig et al. (2016) evaluated the effect of a cerebral protection device on the number and volume of cerebral lesions in patients undergoing TAVR. One hundred patients were randomly assigned to undergo TAVR with a cerebral protection device (filter group; n = 50) or without a cerebral protection device (control group; n = 50). Brain MRI was performed at baseline, 2 days and 7 days after TAVR. The use of a cerebral protection device reduced the frequency of ischemic cerebral lesions in potentially protected regions. The number of new lesions was 4.00 in the filter group and 10.00 in the control group. New lesion volume after TAVR was 242 mm^3 in the filter group and 527 mm^3 in the control group. One patient in the control group died prior to the 30-day visit. Life-threatening hemorrhages occurred in 1 patient in the filter group and 1 in the control group. Major vascular complications occurred in 5 patients in the filter group and 6 patients in the control group. One patient in the filter group and 5 in the control group had acute kidney injury, and 3 patients in the filter group had a thoracotomy. Larger studies, with longer follow-up are needed to assess the effect of cerebral protection device use on neurological and cognitive function after TAVR. NCT01833052.

Giustino et al. (2016) conducted a systematic review and meta-analysis of four RCTs (n = 252) that tested the safety and efficacy of embolic protection during TAVR. Use of embolic protection was associated with lower total lesion volume and smaller number of new ischemic lesions. Embolic protection was associated with a trend toward lower risk for deterioration in National Institutes of Health Stroke Scale score at discharge and higher Montreal Cognitive Assessment score. Risk for overt stroke and all-cause mortality were not significantly lower in the embolic protection group. The authors noted that the findings are subject to the inherent limitations of the included trials due to study design, length of follow-up, imaging and neurocognitive assessment dropout. Some of the endpoints were not available in all of the included trials. Most of the valves used were first-generation TAVR devices. Given the substantial limitations of the included studies, the results are only hypothesis generating. Further prospective, adequately powered RCTs are needed to establish the role of embolic protection during TAVR.

Clinical Practice Guidelines

American College of Cardiology (ACC)/American Heart Association (AHA)

ACC/AHA guidelines for the management of patients with valvular heart disease (Otto et al., 2020) make the following recommendations regarding transcatheter valve therapies:

Aortic

In patients with an indication for aortic valve replacement, the choice of prosthetic valve should be based on a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for and risks of anticoagulant therapy and the potential need for and risks associated with valve reintervention.

In patients with BAV and symptomatic, severe aortic stenosis, TAVR may be considered as an alternative to SAVR after consideration of patient-specific procedural risks, values, trade-offs, and preferences, and when the surgery is performed at a Comprehensive Valve Center. RCTs are needed to obtain full clarity on the optimal use of TAVR in this population, as well as long-term outcomes.

Mitral

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

In patients with chronic severe secondary MR related to left ventricular systolic dysfunction (LVEF < 50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal guideline-directed management and therapy for heart failure, transcatheter edge-to-edge repair is reasonable in patients with appropriate anatomy as defined on transesophageal echocardiography and with LVEF between 20% and 50%, left ventricular end-systolic dimension ≤ 70 mm, and pulmonary artery systolic pressure ≤ 70 mmHg.

Pulmonary

Transcatheter pulmonary valve replacement is outside the scope of these guidelines. See Stout et al., 2019.

Tricuspid

The guideline does not address the transcatheter approach for tricuspid valve replacement.

ViV

For severely symptomatic patients with bioprosthetic aortic valve stenosis and high or prohibitive surgical risk, a transcatheter ViV procedure is reasonable when performed at a Comprehensive Valve Center.

For patients with severe heart failure symptoms caused by bioprosthetic valve regurgitation who are at high to prohibitive surgical risk, a transcatheter ViV procedure is reasonable when performed at a Comprehensive Valve Center.

The ACC and STS, along with the Society for Cardiovascular Angiography and Interventions (SCAI) and the American Association for Thoracic Surgery (AATS), released an expert consensus statement outlining operator and institutional recommendations and requirements for creating and maintaining transcatheter aortic valve replacement programs. The recommendations are aimed at ensuring optimal patient care (Bavaria et al., 2018). The same organizations released similar statements addressing transcatheter therapies for mitral valve procedures (Bonow et al., 2020) and pulmonary valve procedures (Hijazi et al., 2015).

ACC guidelines on the management of adults with congenital heart disease address interventions for patients with RVOT dysfunction. Interventions include surgical replacement or percutaneous stenting and/or transcatheter valve placement. Patients with moderate or greater conduit stenosis and/or regurgitation who have reduced exercise capacity or arrhythmias can benefit from surgical or transcatheter conduit intervention to relieve stenosis and/or regurgitation. Transcatheter stenting and pulmonary valve replacement may be performed with high procedural success and low mortality rates, and result in improved hemodynamics and improved exercise capacity. Surgical conduit replacement carries a higher risk of periprocedural complications with good long-term outcomes. Predictors of conduit dysfunction and reoperation include placement of small diameter conduits; therefore, insertion of conduits with the largest possible diameter should be attempted, anticipating that subsequent valve replacement may be via a transcatheter approach (Stout et al., 2019).

ACC appropriate use criteria for the treatment of severe aortic stenosis include criteria for patients with LFLG-AS (Bonow et al., 2017).

European Society of Cardiology (ESC)

ESC guidelines for the management of adult congenital heart disease state that transcatheter pulmonary valve implantation techniques are an alternative to open heart surgery in patients with RVOT conduit stenosis/regurgitation. Transcatheter replacement, when technically feasible, provides outcomes comparable to surgical pulmonary valve replacement and is intended to extend the lifetime of a conduit, reducing the number of reoperations during a patient's lifetime (Baumgartner et al., 2020).

European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS)

In a joint guideline for the management of valvular heart disease, the ESC and the EACTS (Vahanian, 2022) recommend the following with regard to transcatheter heart valve procedures:

Aortic

The guideline recommends that the choice between surgical and transcatheter intervention for aortic stenosis be based upon careful evaluation of clinical, anatomical and procedural factors by the cardiac treatment team, weighing the risks and benefits of each approach for the individual patient.

The guideline recommends SAVR in younger patients who are at low risk for surgery (< 75 years and STSPROM/ EuroSCORE II < 4%) or in patients who are operable and unsuitable for transfemoral TAVI; however, they recommend TAVI for older patients (≥75 years), or for those who are high-risk (STS-PROM/EuroSCORE II > 8%) or unsuitable for surgery. SAVR or TAVI are recommended for remaining patients according to individual clinical, anatomical and procedural characteristics.

Tricuspid

The guideline indicates that transcatheter treatment of symptomatic secondary severe tricuspid regurgitation has a IIb recommendation which indicates the procedure may be considered in inoperable patients at a heart valve center with expertise in the treatment of tricuspid valve disease. This level of recommendation indicates that the usefulness or efficacy of this approach is less well established by evidence/opinion.

National Institute for Health and Care Excellence (NICE)

NICE published an interventional procedures guidance (IPG) for transcatheter tricuspid valve annuloplasty for tricuspid regurgitation in which they state that the evidence on efficacy of transcatheter tricuspid valve annuloplasty is limited in quantity and quality and that the evidence on safety shows there are serious but well-recognized complications when this procedure is done on people with severe and symptomatic tricuspid regurgitation. For people with mild or moderate tricuspid regurgitation, the evidence is inadequate in quantity and quality on the safety and efficacy of this procedure (NICE, 2022a).

In another IPG published by NICE that addresses transcatheter tricuspid valve leaflet repair for tricuspid regurgitation, NICE states that the evidence on efficacy of transcatheter valve leaflet repair is limited in quantity and quality for people with severe and symptomatic tricuspid regurgitation. The IPG also states that the evidence on its safety shows there are serious but well-recognized complications. For people with mild or moderate tricuspid regurgitation, the IPG states that the evidence is inadequate in quantity and quality for the safety and efficacy of transcatheter tricuspid valve leaflet repair (NICE, 2022b).

NICE published an overarching guideline for heart valve disease presenting in adults. In the evidence review supporting documentation for the guideline, NICE states that transcatheter valve interventions may allow for quicker recovery if the procedure is uncomplicated and notes that the abnormal valve is not removed using the transcatheter approach, rather, the abnormal valve is pushed aside to allow for the prosthetic valve to be implanted.

For aortic valve disease, this guideline states that TAVI is clinically effective but not currently cost effective for patients defined as intermediate or low risk for cardiac surgery for aortic valve disease. For aortic stenosis, the guideline states that transcatheter interventions are currently only indicated for symptomatic patients; however, for aortic regurgitation, there is no current accepted transcatheter intervention. The guideline also stated that there is no evidence for TAVI valve durability beyond 6-7 years and that there is evidence of valve leaflet deterioration due to crimping which cannot be avoided when a valve is implanted through a catheter.

With regard to mitral stenosis, this guideline on heart valve disease in adults recommends transcatheter valvotomy for adults with rheumatic severe mitral stenosis if the valve is suitable for the procedure or surgical mitral valve replacement when the transcatheter valvotomy is not suitable. Transcatheter edge-to-edge repair is recommended, if suitable, for adults with severe primary mitral regurgitation and symptoms when surgery is unsuitable and for adults with heart failure and severe secondary mitral regurgitation if surgery is unsuitable and the patient remains symptomatic on medical management.

The guideline does not include any guidance for transcatheter tricuspid valve repair for tricuspid regurgitation (NICE, 2021a).

A NICE guidance document states that the current evidence on the safety of transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis shows some serious but well-recognized complications. Evidence on its efficacy is limited in quality. This procedure should only be used with special arrangements for clinical governance, consent and audit or research (NICE, 2021b).

A NICE IPG on the transapical transcatheter mitral valve-in-ring implantation procedure states that the evidence on the safety of this procedure after failed mitral valve repair surgery is adequate and shows some serious but well recognized complications. It also states that the evidence on this procedure's efficacy is limited in quality and that the procedure should only be used with special arrangements for clinical governance, consent, and audit or research (NICE, 2021c).

A NICE guidance document states that the evidence on the safety and efficacy of ViV TAVR for aortic bioprosthetic dysfunction is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. The report also notes that long-term evidence for ViV TAVR is from earlier-generation devices. The technology is evolving, and longer-term evidence is needed (NICE, 2019a).

A NICE guidance document states that transcatheter insertion of a cerebral protection device to prevent cerebral embolism during TAVR raises no major safety concerns other than those associated with the TAVR procedure. However, the evidence on efficacy for preventing TAVR-related stroke is inconclusive. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research (NICE, 2019b).

A NICE guidance document states that evidence on the safety and efficacy of percutaneous mitral valve leaflet repair for mitral regurgitation is adequate to support the use of this procedure, in patients for whom open surgery is contraindicated following risk assessment, provided that standard arrangements are in place for clinical governance, consent and audit (NICE, 2019c).

A NICE guidance document states that the evidence on the safety and efficacy of TAVR for aortic stenosis is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Patient details should be entered into the national registry and adverse events should be reported. Patient selection should be carried out by an experienced multidisciplinary team, which must include interventional cardiologists experienced in the procedure, cardiac surgeons, an expert in cardiac imaging and, when appropriate, a cardiac anesthetist and a specialist in elderly medicine. The multidisciplinary team should determine the risk level for each patient and the TAVR device most suitable for them (NICE, 2017).

A NICE guidance document states that the evidence on percutaneous pulmonary valve implantation (PPVI) for RVOT dysfunction shows good short-term efficacy. There is little evidence on long-term efficacy, but it is well documented that these valves may need to be replaced in the longer term. With regard to safety there are well-recognized complications, particularly stent fractures in the longer term, which may or may not have clinical effects. Patients having this procedure are often very unwell and might otherwise need open heart surgery (typically reoperative) with its associated risks (NICE, 2013).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Aortic

FDA approval status for transcatheter aortic valve prostheses can be found by searching the FDA's Premarket Approval (PMA) database using Product Code NPT: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm. Accessed October 30, 2023

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P130021. Accessed October 30, 2023
- Evolut™ FX (Medtronic)
- Evolut™ PRO (Medtronic)
- Evolut™ R (Medtronic)

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P190023. Accessed October 30, 2023
- Navitor™ (Abbott)

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140031. Accessed October 30, 2023
- SAPIEN 3 Ultra RESILIA (Edwards Lifesciences)
- SAPIEN 3 Ultra (Edwards Lifesciences)
- SAPIEN 3 (Edwards Lifesciences)

Mitral

FDA approval status for transcatheter mitral valve repair devices can be found by searching the FDA's Premarket Approval (PMA) database using Product Code NKM: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm. Accessed October 30, 2023

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100009. Accessed October 30, 2023
- MitraClip™ (Abbott)

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P220003. Accessed October 30, 2023
- PASCAL (Edwards Lifesciences)

Pulmonary

FDA approval status for transcatheter pulmonary valve prostheses and related devices can be found by searching the FDA's Premarket Approval (PMA) database using Product Code NPV:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm. Accessed October 30, 2023

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P200046. Accessed October 30, 2023
- Harmony™ (Medtronic)

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140017. Accessed October 30, 2023
- Melody™ (Medtronic)

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P200015. Accessed October 30, 2023
- SAPIEN 3 (Edwards Lifesciences)
- SAPIEN 3 with Alterra Adaptive Prestent (Edwards Lifesciences)

Cerebral Protection

FDA approval status for cerebral embolic protection devices used during transcatheter intracardiac procedures can be found by searching the FDA's De Novo or 510(k) Premarket Notification database using Product Code PUM:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm or
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. Accessed October 30, 2023

- SENTINEL™ (Boston Scientific)

Additional Products

The following products may not have full FDA approval:
- Cardioband™
- Carillon® Mitral Contour System™
- EVOQUE (Edwards Lifesciences)
- Harpoon
- Intrepid™ (Medtronic)
- NeoChord
- Tendyne™ (Abbott)
- Tiara™ (Neovasc, Inc.)

- TriClip
- TricValve®
- TriGUARD 3™ (Keystone Heart)

References

Adams DH, Popma JJ, Reardon MJ, et al.; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014 May 8;370(19):1790-8.

Al-Abcha A, Saleh Y, Boumegouas M, et al. Meta-analysis of valve-in-valve transcatheter aortic valve implantation versus redo-surgical aortic valve replacement in failed bioprosthetic aortic valve. Am J Cardiol. 2021 Jan 30:S0002-9149(21)00099-0.

Armstrong AK, Balzer DT, Cabalka AK, et al. One-year follow-up of the Melody transcatheter pulmonary valve multicenter post-approval study. JACC Cardiovasc Interv. 2014 Nov;7(11):1254-62.

Arora S, Strassle PD, Ramm CJ, et al. Transcatheter versus surgical aortic valve replacement in patients with lower surgical risk scores: a systematic review and meta-analysis of early outcomes. Heart Lung Circ. 2017 Aug;26(8):840-845.

Badwan OZ, Skoza W, Mirzai S, et al. Clinical outcomes after caval valve implantation for severe symptomatic tricuspid regurgitation: a meta-analysis. Am J Cardiol. 2023 Oct 15;205:84-86.

Bagur R, Solo K, Alghofaili S, et al. Cerebral embolic protection devices during transcatheter aortic valve implantation: systematic review and meta-analysis. Stroke. 2017 May;48(5):1306-1315.

Bail DH. Meta-analysis of safety and efficacy following edge-to-edge mitral valve repair using the MitraClip system. J Interv Cardiol. 2015 Feb;28(1):69-75.

Baumgartner H, De Backer J, Babu-Narayan SV, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. Eur Heart J. 2020 Aug 29:ehaa554.

Baumgartner H, Falk V, Bax JJ, et al.; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017 Sep 21;38(36):2739-2791.

Bavaria JE, Tommaso CL, Brindis RG, et al. 2018 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document: Operator and institutional recommendations and requirements for transcatheter aortic valve replacement. J Am Coll Cardiol. 2018 Jul 18. pii: S0735-1097(18)35377-4.

Benson LN, Gillespie MJ, Bergersen L, et al. Three-year outcomes from the Harmony Native Outflow Tract Early Feasibility Study. Circ Cardiovasc Interv. 2020 Jan;13(1):e008320.

Bergersen L, Benson LN, Gillespie MJ, et al. Harmony feasibility trial: acute and short-term outcomes with a self-expanding transcatheter pulmonary valve. JACC Cardiovasc Interv. 2017 Sep 11;10(17):1763-1773.

Bleiziffer S, Simonato M, Webb JG, et al. Long-term outcomes after transcatheter aortic valve implantation in failed bioprosthetic valves. Eur Heart J. 2020 Aug 1;41(29):2731-2742.

Bocchino PP, Angelini F, Vairo A, et al. Clinical outcomes following isolated transcatheter tricuspid valve repair: a meta-analysis and meta-regression study. JACC Cardiovasc Interv. 2021 Oct 25;14(20):2285-2295.

Bonow RO, O'Gara PT, Adams DH, et al. 2019 AATS/ACC/SCAI/STS Expert consensus systems of care document: operator and institutional recommendations and requirements for transcatheter mitral valve intervention: a joint report of the American Association for Thoracic Surgery, the American College of Cardiology, the Society for Cardiovascular Angiography and Interventions, and The Society of Thoracic Surgeons Endorsed by the Heart Failure Society of America. J Thorac Cardiovasc Surg. 2020 Jul;160(1):72-92.

Bonow RO, Brown AS, Gillam LD, et al. ACC/AATS/AHA/ASE/EACTS/HVS/SCA/SCAI/SCCT/SCMR/STS 2017 Appropriate Use Criteria for the Treatment of Patients With Severe Aortic Stenosis: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, European Association for Cardio-Thoracic Surgery, Heart Valve Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2017 Nov 14;70(20):2566-2598.

Bosmans JM, Kefer J, De Bruyne B, et al.; Belgian TAVI Registry Participants. Procedural, 30-day and one year outcome following CoreValve or Edwards transcatheter aortic valve implantation: results of the Belgian national registry. Interact Cardiovasc Thorac Surg. 2011;12(5):762-767.

Buğan B, Çekirdekçi Eİ, Onar LÇ, et al. Transcatheter tricuspid valve replacement for tricuspid regurgitation: a systematic review and meta-analysis. Anatol J Cardiol. 2022 Jul;26(7):505-519. doi: 10.5152/AnatolJCardiol.2022.1440.

Butera G, Milanesi O, Spadoni I, et al. Melody transcatheter pulmonary valve implantation. Results from the registry of the Italian Society of Pediatric Cardiology. Catheter Cardiovasc Interv. 2013 Feb;81(2):310-6.

Chan JSK, Singh S, Eriksen P, et al. Transcatheter aortic valve implantation in bicuspid aortic valve with aortic stenosis: a meta-analysis and trial sequential analysis. Braz J Cardiovasc Surg. 2022 Mar 10;37(1):88-98.

Chatterjee A, Bajaj NS, McMahon WS, et al. Transcatheter pulmonary valve implantation: a comprehensive systematic review and meta-analyses of observational studies. J Am Heart Assoc. 2017 Aug 4;6(8):e006432.

Cheatham JP, Hellenbrand WE, Zahn EM, et al. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. Circulation. 2015 Jun 2;131(22):1960-70.

Chen CJ, Jiang H, Martin O, et al. Procedural and clinical outcomes of transcatheter aortic valve replacement in bicuspid aortic valve patients: a systematic review and meta-analysis. Ann Cardiothorac Surg. 2022 Jul;11(4):351-362.

CMS National Coverage Determination (NCD) for Transcatheter Aortic Valve Replacement (TAVR) (20.32). Available at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=355&ncdver=2&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=All&KeyWord=transcatheter+aortic+valve+replacement&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=EAAAABAAAAAA&. Accessed October 30, 2023.

Colli A, Manzan E, Aidietis A, et al. An early European experience with transapical off-pump mitral valve repair with NeoChord implantation. Eur J Cardiothorac Surg. 2018 Sep 1;54(3):460-466.

Conradi L, Treede H, Rudolph V, et al. Surgical or percutaneous mitral valve repair for secondary mitral regurgitation: comparison of patient characteristics and clinical outcomes. Eur J Cardiothorac Surg. 2013 Sep;44(3):490-6; discussion 496.

Coylewright M, Forrest JK, McCabe JM, Nazif TM. TAVR in low-risk patients: FDA approval, the new NCD, and shared decision-making. J Am Coll Cardiol. 2020 Mar 17;75(10):1208-1211.

Daubert MA, Weissman NJ, Hahn RT, et al. Long-term valve performance of TAVR and SAVR: a report from the PARTNER I trial. JACC Cardiovasc Imaging. 2016 Dec 8. pii: S1936-878X(16)30895-6.

Deeb GM, Chetcuti SJ, Reardon MJ, et al. 1-Year results in patients undergoing transcatheter aortic valve replacement with failed surgical bioprostheses. JACC Cardiovasc Interv. 2017 May 22;10(10):1034-1044.

Deeb GM, Reardon MJ, Chetcuti S, et al.; CoreValve US Clinical Investigators. 3-year outcomes in high-risk patients who underwent surgical or transcatheter aortic valve replacement. J Am Coll Cardiol. 2016 Jun 7;67(22):2565-74.

Dreger H, Mattig I, Hewing B, et al. Treatment of severe tricuspid regurgitation in patients with advanced heart failure with caval vein implantation of the Edwards Sapien XT valve (TRICAVAL): a randomised controlled trial. EuroIntervention. 2020 Apr 17;15(17):1506-1513.

Dreyfus J, Dreyfus GD, Taramasso M. Tricuspid valve replacement: The old and the new. Prog Cardiovasc Dis. 2022 May-Jun;72:102-113.

Du Y, Wang Z, Liu W, et al. Transcatheter aortic valve implantation in Sievers type 0 vs. type 1 bicuspid aortic valve morphology: systematic review and meta-analysis. Front Cardiovasc Med. 2021 Nov 5;8:771789.

Dvir D, Webb JG, Bleiziffer S, et al. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. JAMA. 2014 Jul;312(2):162-70.

ECRI Institute. Clinical Evidence Assessment. Carillon Mitral Contour System (Cardiac Dimensions) for treating mitral regurgitation. May 2023.

ECRI Institute. Clinical Evidence Assessment. Percutaneous tricuspid valve repair for treating tricuspid regurgitation. January 2022.

ECRI Institute. Clinical Evidence Assessment. MitraClip clip delivery system (Abbott Vascular) for treating functional mitral regurgitation. December 2017a; updated August 2020.

ECRI Institute. Clinical Evidence Assessment. Sentinel Cerebral Protection System (Boston Scientific Corp.) for preventing stroke during transcatheter aortic valve implantation. December 2017b. Updated October 2022.

Eicken A, Ewert P, Hager A, et al. Percutaneous pulmonary valve implantation: two-centre experience with more than 100 patients. Eur Heart J. 2011 May;32(10):1260-5.

Eleid MF, Rihal CS, Guerrero ME. Transcatheter mitral valve replacement for degenerated mitral bioprostheses: a systematic review. Ann Cardiothorac Surg. 2021 Sep;10(5):558-563.

Eleid MF, Whisenant BK, Cabalka AK, et al. Early outcomes of percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty, and severe mitral annular calcification. JACC Cardiovasc Interv. 2017 Oct 9;10(19):1932-1942.

Eltchaninoff H, Prat A, Gilard M, et al.; FRANCE Registry Investigators. Transcatheter aortic valve implantation: early results of the FRANCE (French Aortic National CoreValve and Edwards) registry. Eur Heart J. 2011;32(2):191-197.

Feldman T, Foster E, Glower DD, et al.; EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med. 2011 Apr 14;364(15):1395-406.

Feldman T, Kar S, Elmariah S, et al.; EVEREST II Investigators. Randomized comparison of percutaneous repair and surgery for mitral regurgitation: 5-year results of EVEREST II. J Am Coll Cardiol. 2015 Dec 29;66(25):2844-54.

Feldman T, Kar S, Rinaldi M, et al.; EVEREST Investigators. Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge Repair Study) cohort. J Am Coll Cardiol. 2009 Aug 18;54(8):686-94.

Forrest JK, Deeb GM, Yakubov SJ, et al.; Low Risk Trial Investigators. 3-year outcomes after transcatheter or surgical aortic valve replacement in low-risk patients with aortic stenosis. J Am Coll Cardiol. 2023 May 2;81(17):1663-1674.

Forrest JK, Deeb GM, Yakubov SJ, et al. 2-year outcomes after transcatheter versus surgical aortic valve replacement in low-risk patients. J Am Coll Cardiol. 2022 Mar 8;79(9):882-896.

Gammie JS, Wilson P, Bartus K, et al. Transapical beating-heart mitral valve repair with an expanded polytetrafluoroethylene cordal implantation device: initial clinical experience. Circulation. 2016 Jul 19;134(3):189-97.

Gammie JS, Bartus K, Gackowski A, et al. Beating-heart mitral valve repair using a novel ePTFE cordal implantation device: a prospective trial. J Am Coll Cardiol. 2018 Jan 2;71(1):25-36.

Gammie JS, Bartus K, Gackowski A, et al. Safety and performance of a novel transventricular beating heart mitral valve repair system: 1-year outcomes. Eur J Cardiothorac Surg. 2021 Jan 4;59(1):199-206.

Giallauria F, Di Lorenzo A, Parlato A, et al.. Individual patient data meta-analysis of the effects of the CARILLON® mitral contour system. ESC Heart Fail. 2020 Dec;7(6):3383-3391.

Gilard M, Eltchaninoff H, Iung B, et al.; FRANCE 2 Investigators. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med. 2012 May 3;366(18):1705-15.

Gillespie MJ, McElhinney DB, Jones TK, et al. 1-year outcomes in a pooled cohort of Harmony transcatheter pulmonary valve clinical trial participants. JACC Cardiovasc Interv. 2023 Aug 14;16(15):1917-1928.

Gillespie MJ, Bergersen L, Benson LN, et al. 5-Year outcomes from the Harmony Native Outflow Tract early feasibility study. JACC Cardiovasc Interv. 2021 Apr 12;14(7):816-817.

Giustino G, Mehran R, Veltkamp R, et al. Neurological outcomes with embolic protection devices in patients undergoing transcatheter aortic valve replacement: a systematic review and meta-analysis of randomized controlled trials. JACC Cardiovasc Interv. 2016 Oct 24;9(20):2124-2133.

Glower DD, Kar S, Trento A, et al. Percutaneous mitral valve repair for mitral regurgitation in high-risk patients: results of the EVEREST II study. J Am Coll Cardiol. 2014 Jul 15;64(2):172-81.

Gozdek M, Raffa GM, Suwalski P, et al.; SIRIO-TAVI group. Comparative performance of transcatheter aortic valve-in-valve implantation versus conventional surgical redo aortic valve replacement in patients with degenerated aortic valve bioprostheses: systematic review and meta-analysis. Eur J Cardiothorac Surg. 2018 Mar 1;53(3):495-504.

Guerrero M, Dvir D, Himbert D, et al. Transcatheter mitral valve replacement in native mitral valve disease with severe mitral annular calcification: results from the first multicenter global registry. JACC Cardiovasc Interv. 2016 Jul 11;9(13):1361-71.

Haussig S, Mangner N, Dwyer MG, et al. Effect of a cerebral protection device on brain lesions following transcatheter aortic valve implantation in patients with severe aortic stenosis: the CLEAN-TAVI randomized clinical trial. JAMA. 2016 Aug 9;316(6):592-601.

Hayes, Inc. Hayes Medical Technology Directory. Comparative effectiveness review of percutaneous mitral valve repair. Lansdale, PA: Hayes, Inc.; April 2018. Archived May 2023.

Hayes, Inc. Health Technology Assessment. Comparative effectiveness review of transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR) for aortic stenosis in lower risk patients. Lansdale, PA: Hayes, Inc.; September 2018. Updated November 2022. Archived October 2023.

Hayes, Inc. Comparative Effectiveness Review. Percutaneous mitral valve repair for secondary (functional) mitral valve regurgitation in high-risk adults. Lansdale, PA: Hayes, Inc.; December 2020. Updated March 2023.

Hayes, Inc. Health Technology Assessment. Transcatheter mitral valve replacement for mitral regurgitation. Lansdale, PA: Hayes, Inc.; January 2021. Updated May 2023.

Hayes, Inc. Health Technology Assessment. Percutaneous pulmonary valve implantation with the Edwards SAPIEN 3 and SAPIEN XT valves (Edwards Lifesciences Corp.) for right ventricular outflow. Lansdale, PA: Hayes, Inc.; June 2022. Updated June 2023.

Hijazi ZM, Ruiz CE, Zahn E, et al. SCAI/AATS/ACC/STS Operator and institutional requirements for transcatheter valve repair and replacement. Part III: Pulmonic valve. J Am Coll Cardiol. 2015 Mar 17. pii: S0735-1097(15)00652-X.

Ismayl M, Abbasi MA, Mostafa MR, et al. Meta-analysis comparing valve-in-valve transcatheter mitral valve replacement versus redo surgical mitral valve replacement in degenerated bioprosthetic mitral valve. Am J Cardiol. 2023 Feb 15;189:98-107.

Jones TK, McElhinney DB, Vincent JA, et al. Long-term outcomes after Melody transcatheter pulmonary valve replacement in the US Investigational Device Exemption Trial. Circ Cardiovasc Interv. 2022 Jan;15(1):e010852.

Jørgensen TH, Thyregod HGH, Ihlemann N, et al. Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement. Eur Heart J. 2021 Aug 7;42(30):2912-2919.

Kanjanahattakij N, Horn B, Vutthikraivit W, et al. Comparing outcomes after transcatheter aortic valve replacement in patients with stenotic bicuspid and tricuspid aortic valve: a systematic review and meta-analysis. Clin Cardiol. 2018 Jul;41(7):896-902.

Kapadia SR, Kodali S, Makkar R, et al.; SENTINEL Trial Investigators. Protection against cerebral embolism during transcatheter aortic valve replacement. J Am Coll Cardiol. 2017 Jan 31;69(4):367-377.

Kapadia SR, Makkar R, Leon M, et al.; PROTECTED TAVR Investigators. Cerebral embolic protection during transcatheter aortic-valve replacement. N Engl J Med. 2022 Sep 17.

Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: The Valve Academic Research Consortium-2 consensus document. Eur Heart J. 2012 Oct;33(19):2403-18.

Kar S, Feldman T, Qasim A, et al.; EVEREST II Investigators. Five-year outcomes of transcatheter reduction of significant mitral regurgitation in high-surgical-risk patients. Heart. 2019 Nov;105(21):1622-1628.

Kenny D, Rhodes JF, Fleming GA, et al. 3-year outcomes of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position from the COMPASSION multicenter clinical trial. JACC Cardiovasc Interv. 2018 Oct 8;11(19):1920-1929.

Khatri PJ, Webb JG, Rodés-Cabau J, et al. Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies. Ann Intern Med. 2013 Jan 1;158(1):35-46.

Koch R, Inci E, Grubb K, et al. A comparison of thirty-day clinical and echocardiographic outcomes of patients undergoing transcatheter vs. surgical aortic valve replacement for native aortic insufficiency. Cardiovasc Revasc Med. 2022 Aug 11:S1553-8389(22)00708-4.

Kodali S, Thourani VH, White J, et al. Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. Eur Heart J. 2016 Jul 21;37(28):2252-62.

Kodali SK, Williams MR, Smith CR, et al.; PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med. 2012 May 3;366(18):1686-95.

Lazkani M, Singh N, Howe C, et al. An updated meta-analysis of TAVR in patients at intermediate risk for SAVR. Cardiovasc Revasc Med. 2019 Jan;20(1):57-69.

Leon MB, Mack MJ, Hahn RT, et al.; PARTNER 3 Investigators. Outcomes 2 years after transcatheter aortic valve replacement in patients at low surgical risk. J Am Coll Cardiol. 2021 Mar 9;77(9):1149-1161.

Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. Eur Heart J. 2011 Jan;32(2):205-17.

Leon MB, Smith CR, Mack M, et al.; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010 Oct 21;363(17):1597-607.

Leon MB, Smith CR, Mack MJ, et al.; PARTNER 2 Investigators. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med. 2016 Apr 28;374(17):1609-20.

Lim DS, Kim D, Aboulhosn J, et al. Congenital pulmonic valve dysfunction treated with SAPIEN 3 transcatheter heart valve (from the COMPASSION S3 Trial). Am J Cardiol. 2023 Mar 1;190:102-109.

Lim DS, Smith RL, Gillam LD, et al.; CLASP IID Pivotal Trial Investigators. Randomized comparison of transcatheter edge-to-edge repair for degenerative mitral regurgitation in prohibitive surgical risk patients. JACC Cardiovasc Interv. 2022 Dec 26;15(24):2523-2536.

Lim DS, Reynolds MR, Feldman T, et al. Improved functional status and quality of life in prohibitive surgical risk patients with degenerative mitral regurgitation after transcatheter mitral valve repair. J Am Coll Cardiol. 2014 Jul 15;64(2):182-92.

Ludwig S, Perrin N, Coisne A, et al. Clinical outcomes of transcatheter mitral valve replacement: two-year results of the CHOICE-MI Registry. EuroIntervention. 2023a Aug 21;19(6):512-525.

Ludwig S, Kalbacher D, Ali WB, et al.; the CHOICE-MI and the EuroSMR Investigators. Transcatheter mitral valve replacement or repair for secondary mitral regurgitation: a propensity score-matched analysis. Eur J Heart Fail. 2023b Mar;25(3):399-410.

Ludwig S, Conradi L, Cohen DJ, et al.; CHOICE-MI and the COAPT Trial Investigators. Transcatheter mitral valve replacement versus medical therapy for secondary mitral regurgitation: a propensity score-matched comparison. Circ Cardiovasc Interv. 2023c Jun;16(6):e013045.

Mack MJ, Leon MB, Thourani VH, et al.; PARTNER 3 Investigators. Transcatheter aortic-valve replacement in low-risk patients at five years. N Engl J Med. 2023 Oct 24.

Mack MJ, Lindenfeld J, Abraham WT, et al.; COAPT Investigators. 3-year outcomes of transcatheter mitral valve repair in patients with heart failure. J Am Coll Cardiol. 2021 Mar 2;77(8):1029-1040.

Mack MJ, Leon MB, Smith CR, et al.; PARTNER 1 trial investigators. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomized controlled trial. Lancet. 2015 Jun 20;385(9986):2477-84.

Mack MJ, Leon MB, Thourani VH, et al.; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019 May 2;380(18):1695-1705.

Maisano F, Franzen O, Baldus S, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. J Am Coll Cardiol. 2013;62(12):1052-1061.

Makkar RR, Chikwe J, Chakravarty T, et al. Transcatheter mitral valve repair for degenerative mitral regurgitation. JAMA. 2023 May 23;329(20):1778-1788.

Makkar RR, Fontana GP, Jilaihawi H, et al.; PARTNER Trial Investigators. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med. 2012 May 3;366(18):1696-704. Erratum in N Engl J Med. 2012 Aug 30;367(9):881.

Makkar RR, Thourani VH, Mack MJ, et al.; PARTNER 2 Investigators. Five-year outcomes of transcatheter or surgical aortic-valve replacement. N Engl J Med. 2020 Jan 29;382(9):799-809.

Marmagkiolis K, Hakeem A, Ebersole DG, et al. Clinical outcomes of percutaneous mitral valve repair with MitraClip for the management of functional mitral regurgitation. Catheter Cardiovasc Interv. 2019 Nov 15;94(6):820-826.

Mauri L, Foster E, Glower DD, et al.; EVEREST II Investigators. 4-year results of a randomized controlled trial of percutaneous repair versus surgery for mitral regurgitation. J Am Coll Cardiol. 2013 Jul 23;62(4):317-28.

McElhinney DB, Zhang Y, Levi DS, et al. Reintervention and survival after transcatheter pulmonary valve replacement. J Am Coll Cardiol. 2022 Jan 4;79(1):18-32.

McElhinney DB, Hellenbrand WE, Zahn EM, Jones TK, Cheatham JP, Lock JE, Vincent JA. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US melody valve trial. Circulation. 2010 Aug 3;122(5):507-16.

Messika-Zeitoun D, Nickenig G, Latib A, et al. Transcatheter mitral valve repair for functional mitral regurgitation using the Cardioband system: 1 year outcomes. Eur Heart J. 2019 Feb 1;40(5):466-472.

Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. J Am Coll Cardiol. 2011 Nov 8;58(20):2130-8.

National Institute for Health and Care Excellence (NICE). IPG436. Percutaneous pulmonary valve implantation for right ventricular outflow tract dysfunction. January 2013.

National Institute for Health and Care Excellence (NICE). IPG586. Transcatheter aortic valve implantation for aortic stenosis. July 2017.

National Institute for Health and Care Excellence (NICE). IPG649. Percutaneous mitral valve leaflet repair for mitral regurgitation. May 2019c.

National Institute for Health and Care Excellence (NICE). IPG650. Percutaneous insertion of a cerebral protection device to prevent cerebral embolism during TAVI. June 2019b.

National Institute for Health and Care Excellence (NICE). IPG653. Valve-in-valve TAVI for aortic bioprosthetic valve dysfunction. June 2019a.

National Institute for Health and Care Excellence (NICE). IPG706. Transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis. September 2021b.

National Institute for Health and Care Excellence (NICE). IPG707. Transapical transcatheter mitral valve-in-ring implantation after failed annuloplasty for mitral valve repair. September 2021c.

National Institute for Health and Care Excellence (NICE). IPG730. Transcatheter tricuspid valve annuloplasty for tricuspid regurgitation. July 2022a.

National Institute for Health and Care Excellence (NICE). IPG731. Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation. July 2022b.

National Institute for Health and Care Excellence (NICE). NG208. Heart valve disease presenting in adults: investigation and management. November 2021a.

Ndunda PM, Vindhyal MR, Muutu TM, Fanari Z. Clinical outcomes of sentinel cerebral protection system use during transcatheter aortic valve replacement: a systematic review and meta-analysis. Cardiovasc Revasc Med. 2019 Apr 25. pii:S1553-8389(19)30257-X.

New York Heart Association. Criteria Committee. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston, MA: Little, Brown & Co.; 1994: 253–256.

Nickenig G, Kowalski M, Hausleiter J, et al. Transcatheter treatment of severe tricuspid regurgitation with the edge-to-edge MitraClip technique. Circulation. 2017 May 9;135(19):1802-1814.

Obadia JF, Messika-Zeitoun D, Leurent G, et al.; MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. N Engl J Med. 2018 Dec 13;379(24):2297-2306.

O'Gara PT, Calhoon JH, Moon MR, Tommaso CL. Transcatheter therapies for mitral regurgitation: a professional society overview from the American College of Cardiology, the American Association for Thoracic Surgery, Society for Cardiovascular Angiography and Interventions Foundation and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2014 Mar 4;63(8):840-52.

Otto CM, Kumbhani DJ, Alexander KP, et al. 2017 ACC Expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol. 2017 Mar 14;69(10):1313-1346.

Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2021 Feb 2;77(4):e25-e197. Erratum in: J Am Coll Cardiol. 2021 Feb 2;77(4):509.

Phan K, Zhao DF, Wang N, et al. Transcatheter valve-in-valve implantation versus reoperative conventional aortic valve replacement: a systematic review. J Thorac Dis. 2016 Jan;8(1):E83-93.

Popma JJ, Deeb GM, Yakubov SJ, et al.; Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med. 2019 May 2;380(18):1706-1715.

Popma JJ, Adams DH, Reardon MJ, et al.; CoreValve United States Clinical Investigators. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. J Am Coll Cardiol. 2014 Mar 13. pii: S0735-1097(14)01396-5.

Puri R, Abdul-Jawad Altisent O, del Trigo M, et al. Transcatheter mitral valve implantation for inoperable severely calcified native mitral valve disease: a systematic review. Catheter Cardiovasc Interv. 2016 Feb 15;87(3):540-8.

Quintana RA, Monlezun D, Davogustto G, et al. Network analysis of outcomes in patients undergoing transcatheter aortic valve replacement for stenotic bicuspid aortic valves according to valve type. Cardiovasc Revasc Med. 2020 Sep;21(9):1076-1085.

Quintana RA, Monlezun DJ, DaSilva-DeAbreu A, et al. One-year mortality in patients undergoing transcatheter aortic valve replacement for stenotic bicuspid versus tricuspid aortic valves: a meta-analysis and meta-regression. J Interv Cardiol. 2019 Jan 2;2019:8947204.

Radwan Y, Al-Abcha A, Salam MF, et al. Meta-analysis of the safety and efficacy of the Sentinel cerebral protection system in transcatheter aortic valve implantation. Am J Cardiol. 2021 Aug 1;152:169-170.

Reardon MJ, Feldman TE, Meduri CU, et al.; Reprise III Investigators. Two-year outcomes after transcatheter aortic valve replacement with mechanical vs self-expanding valves: the REPRISE III randomized clinical trial. JAMA Cardiol. 2019 Mar 1;4(3):223-229.

Reardon MJ, Van Mieghem NM, Popma JJ, et al.; SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2017 Apr 6;376(14):1321-1331.

Reardon MJ, Adams DH, Kleiman NS, et al. 2-year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. J Am Coll Cardiol. 2015 Jul 14;66(2):113-21.

Regueiro A, Ye J, Fam N, et al. 2-year outcomes after transcatheter mitral valve replacement. JACC Cardiovasc Interv. 2017 Aug 28;10(16):1671-1678.

Reichenspurner H, Schillinger W, Baldus S, et al. Clinical outcomes through 12 months in patients with degenerative mitral regurgitation treated with the MitraClip® device in the ACCESS-Europe Phase I trial. Eur J Cardiothorac Surg. 2013;44(4):e280-288.

Ribeiro JM, Teixeira R, Lopes J, et al. Transcatheter versus surgical pulmonary valve replacement: a systemic review and meta-analysis. Ann Thorac Surg. 2020 Nov;110(5):1751-1761.

Ribeiro HB, Lerakis S, Gilard M, et al. Transcatheter aortic valve replacement in patients with low-flow, low-gradient aortic stenosis: the TOPAS-TAVI registry. J Am Coll Cardiol. 2018 Mar 27;71(12):1297-1308.

Rodés-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. J Am Coll Cardiol. 2010 Mar 16;55(11):1080-90.

Saeed Al-Asad K, Martinez Salazar A, Radwan Y, et al. Transcatheter aortic valve replacement in bicuspid versus tricuspid aortic valve stenosis: meta-analysis and systemic review. Am J Cardiol. 2023 Sep 15;203:105-112.

Saito S, Sairenchi T, Tezuka M, et al. Contemporary short-term outcomes of surgery for aortic stenosis: transcatheter vs. surgical aortic valve replacement. Gen Thorac Cardiovasc Surg. 2022 Feb;70(2):124-131.

Sardar P, Kundu A, Chatterjee S, et al. Transcatheter versus surgical aortic valve replacement in intermediate-risk patients: evidence from a meta-analysis. Catheter Cardiovasc Interv. 2017 Sep 1;90(3):504-515.

Schofer J, Siminiak T, Haude M, et al. Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the CARILLON Mitral Annuloplasty Device European Union Study. Circulation 2009 Jul 28;120(4):326-33. PMID: 19597051.

Seeger J, Gonska B, Otto M, et al. Cerebral embolic protection during transcatheter aortic valve replacement significantly reduces death and stroke compared with unprotected procedures. JACC Cardiovasc Interv. 2017 Nov 27;10(22):2297-2303.

Siminiak T, Wu JC, Haude M, et al. Treatment of functional mitral regurgitation by percutaneous annuloplasty: results of the TITAN Trial. Eur J Heart Fail 2012 Aug;14(8):931-8.

Singh K, Carson K, Rashid MK, et al. Transcatheter aortic valve implantation in intermediate surgical risk patients with severe aortic stenosis: a systematic review and meta-analysis. Heart Lung Circ. 2018 Feb;27(2):227-234.

Siontis GCM, Overtchouk P, Cahill TJ, et al. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. Eur Heart J. 2019 Oct 7;40(38):3143-3153.

Smith CR, Leon MB, Mack MJ, et al.; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011 Jun 9;364(23):2187-98.

Søndergaard L, Ihlemann N, Capodanno D, et al. Durability of transcatheter and surgical bioprosthetic aortic valves in patients at lower surgical risk. J Am Coll Cardiol. 2019 Feb 12;73(5):546-553.

Søndergaard L, Steinbrüchel DA, Ihlemann N, et al. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement: the all-comers Nordic Aortic Valve Intervention randomized clinical trial. Circ Cardiovasc Interv. 2016 Jun;9(6). pii: e003665.

Stone GW, Abraham WT, Lindenfeld J, et al.; COAPT Investigators. Five-year follow-up after transcatheter repair of secondary mitral regurgitation. N Engl J Med. 2023 Jun 1;388(22):2037-2048.

Stone GW, Lindenfeld J, Abraham WT, et al.; COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med. 2018 Dec 13;379(24):2307-2318.

Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019 Apr 2;73(12):e81-e192.

Taha FA, Naeim H, Alnozha F, et al. Transcatheter mitral valve replacement in high-surgical risk patients: a single-center experience and outcome. J Interv Cardiol. 2022 Jun 22;2022:6587036.

Tam DY, Vo TX, Wijeysundera HC, et al. Transcatheter valve-in-valve versus redo surgical aortic valve replacement for the treatment of degenerated bioprosthetic aortic valve: a systematic review and meta-analysis. Catheter Cardiovasc Interv. 2018 Dec 1;92(7):1404-1411.

Taramasso M, Alessandrini H, Latib A, et al. Outcomes after current transcatheter tricuspid valve intervention: mid-term results from the international TriValve registry. JACC Cardiovasc Interv. 2019 Jan 28;12(2):155-165.

Taramasso M, Denti P, Buzzatti N, et al. Mitraclip therapy and surgical mitral repair in patients with moderate to severe left ventricular failure causing functional mitral regurgitation: a single-centre experience. Eur J Cardiothorac Surg. 2012 Dec;42(6):920-6.

Thomas M, Schymik G, Walther T, et al. One-year outcomes of cohort 1 in the Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) registry: the European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. Circulation. 2011;124(4):425-433.

Thyregod HGH, Ihlemann N, Jørgensen TH, et al. Five-year clinical and echocardiographic outcomes from the Nordic Aortic Valve Intervention (NOTION) randomized clinical trial in lower surgical risk patients. Circulation. 2019;139:2714–2723.

Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers NOTION randomized clinical trial. J Am Coll Cardiol. 2015 May 26;65(20):2184-94.

Tuzcu EM, Kapadia SR, Vemulapalli S, et al. Transcatheter aortic valve replacement of failed surgically implanted bioprostheses: the STS/ACC Registry. J Am Coll Cardiol. 2018 Jul 24;72(4):370-382.

Ussia GP, Barbanti M, Petronio AS, et al.; CoreValve Italian Registry Investigators. Transcatheter aortic valve implantation: 3-year outcomes of self-expanding CoreValve prosthesis. Eur Heart J. 2012;33(8):969-976.

Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2022 Feb 12;43(7):561-632.

Van Mieghem NM, van Gils L, Ahmad H, et al. Filter-based cerebral embolic protection with transcatheter aortic valve implantation: the randomized MISTRAL-C trial. EuroIntervention. 2016 Jul 20;12(4):499-507.

Walther T, Hamm CW, Schuler G, et al.; GARY Executive Board. Perioperative results and complications in 15,964 transcatheter aortic valve replacements: prospective data from the GARY Registry. J Am Coll Cardiol. 2015 May 26;65(20):2173-80.

Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults with Congenital Heart Disease). J Am Coll Cardiol. 2008 Dec 2;52(23):e143-263.

Webb JG, Mack MJ, White JM, et al. Transcatheter aortic valve implantation within degenerated aortic surgical bioprostheses: PARTNER 2 Valve-in-Valve Registry. J Am Coll Cardiol. 2017 May 9;69(18):2253-2262.

Webb JG, Doshi D, Mack MJ, et al. A randomized evaluation of the SAPIEN XT transcatheter heart valve system in patients with aortic stenosis who are not candidates for surgery. JACC Cardiovasc Interv. 2015 Dec 21;8(14):1797-806.

Webb JG, Wood DA. Current status of transcatheter aortic valve replacement. J Am Coll Cardiol. 2012 Aug 7;60(6):483-92.

Whitlow PL, Feldman T, Pedersen WR, et al.; EVEREST II Investigators. Acute and 12-month results with catheter-based mitral valve leaflet repair: the EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study. J Am Coll Cardiol. 2012 Jan 10;59(2):130-9.

Witberg G, Lador A, Yahav D, Kornowski R. Transcatheter versus surgical aortic valve replacement in patients at low surgical risk: a meta-analysis of randomized trials and propensity score matched observational studies. Catheter Cardiovasc Interv. 2018 Aug 1;92(2):408-416.

Witte KK, Lipiecki J, Siminiak T, et al. The REDUCE FMR Trial: a randomized sham-controlled study of percutaneous mitral annuloplasty in functional mitral regurgitation. JACC Heart Fail. 2019 Nov;7(11):945-955.

Writing Committee Members, Otto CM, Nishimura RA, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. J Thorac Cardiovasc Surg. 2021 Aug;162(2):e183-e353.

Yoon SH, Whisenant BK, Bleiziffer S, et al. Transcatheter mitral valve replacement for degenerated bioprosthetic valves and failed annuloplasty rings. J Am Coll Cardiol. 2017 Aug 29;70(9):1121-1131.

Zahn R, Gerckens U, Grube E, et al.; German Transcatheter Aortic Valve Interventions Registry Investigators. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. Eur Heart J. 2011;32(2):198-204.

Zhang Y, Xiong TY, Li YM, et al. Patients with bicuspid aortic stenosis undergoing transcatheter aortic valve replacement: a systematic review and meta-analysis. Front Cardiovasc Med. 2022 Mar 16;9:794850.

Policy History/Revision Information

Date	Summary of Changes

06/01/2024	**Coverage Rationale**
	• Revised list of unproven and not medically necessary devices/procedures:
	  ○ Added "transcatheter superior and inferior vena cava prosthetic valve implantation (CAVI)"
	  ○ Removed "transcatheter pulmonary heart valve replacement using the Harmony™ valve"
	Aortic
	• Revised coverage criteria for transcatheter aortic heart valve replacement due to diagnosis of severe calcific native aortic valve stenosis; replaced criterion requiring "aortic valve area of ≤ ***0.8*** cm^2" with "aortic valve area of ≤ ***1.0*** cm^2"
	• Revised notation to indicate requests for transcatheter aortic heart valve replacement for low-flow/low-gradient aortic stenosis *in individuals who do not meet the peak velocity, mean gradient, and valve area criteria listed [in the policy]* will be *considered* on a case-by-case basis; *these requests will be evaluated using recommendations from the American College of Cardiology/American Heart Association Guideline for the Management of Patients With Valvular Heart Disease when all the clinical evaluation has been facilitated by a transcatheter aortic heart valve replacement expert and after appropriate additional testing has been conducted*
	Mitral
	• Replaced language indicating:
	  ○ "Transcatheter mitral valve *repair* is proven and medically necessary when used according to FDA labeled indications, contraindications, warnings, and precautions in individuals with one of the [listed] clinical indications for intervention" with "transcatheter *edge-to-edge repair of the* mitral *heart* valve is proven and medically necessary when used according to FDA labeled indications, contraindications, warnings, and precautions in individuals with one of the [listed] clinical indications for intervention"
	  ○ "Transcatheter mitral heart valve repair, except where noted [in the policy as proven and medically necessary], is unproven and not medically necessary due to insufficient evidence of efficacy" with "transcatheter mitral heart valve repair *(e.g., annuloplasty)*, except where noted [in the policy as proven and medically necessary], is unproven and not medically necessary due to insufficient evidence of efficacy"
	Pulmonary
	• Replaced language indicating "transcatheter pulmonary heart valve replacement *using the Melody™ or Sapien valves* is proven and medically necessary when used according to FDA labeled indications, contraindications, warnings, and precautions in individuals with right ventricular outflow tract (RVOT) dysfunction with one of the [listed] clinical indications for intervention" with "transcatheter pulmonary heart valve replacement *and related devices (e.g., Alterra)* are proven and medically necessary when used according to FDA labeled indications, contraindications, warnings, and precautions in individuals with right ventricular outflow tract (RVOT) dysfunction with one of the [listed] clinical indications for intervention"
	Applicable Codes
	• Added CPT codes 0805T and 0806T

Date	Summary of Changes
	• Added notation to indicate CPT codes 0805T and 0806T are not on the State of Louisiana Medicaid Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program **Supporting Information** • Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version CS123LA.O

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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