COREVALVE® EVOLUT® R &
COREVALVE®
TAVR PLATFORMS

VALVE-IN-VALVE IN FAILED SURGICAL BIOPROSTHESIS

MEDICAL EDUCATION **ACADEMIA**

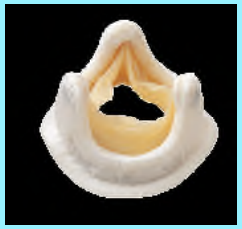
CAUTION Federal law (USA) restricts this device to sale by or on the order of a physician.

UC201602622b EN

SURGICAL AORTIC VALVE BACKGROUND

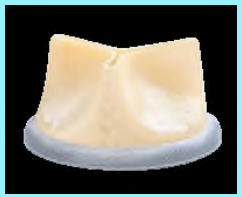
EXAMPLES OF SURGICAL AORTIC BIOPROSTHESES

Stented



Medtronic Mosaic®

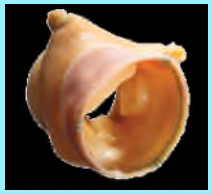
Carpentier-Edwards®
Perimount® Magna



Sorin Mitroflow®
LX Valve

St. Jude Medical Epic™
Supra Valve

Stentless



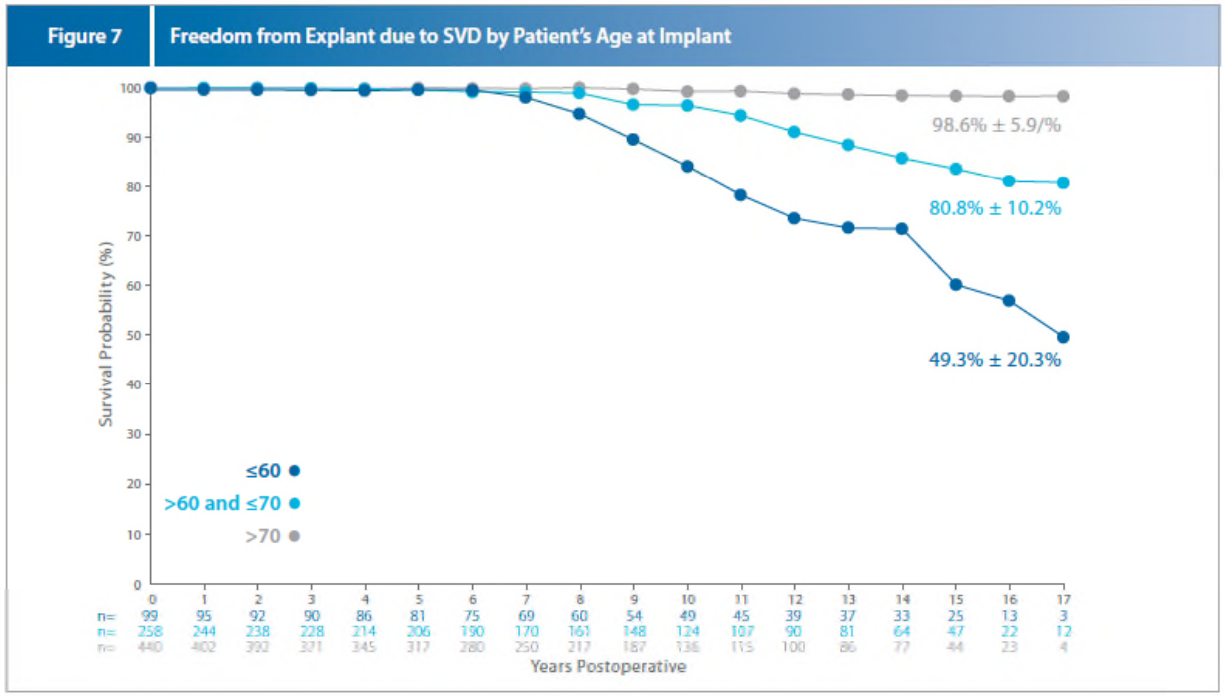
Medtronic
Freestyle® Valve

Medtronic 3f®
Valve

With permission from the following paper: Piazza N, et al. Transcatheter Aortic Valve Implantation for Failing Surgical Aortic Bioprosthetic Valve. JACC Cardiovascular Interventions. Vol. 4, No. 7, 2011:733-42.
We would like to thank Vinayak Bapat, FRCS. CTh, from Guy's and St. Thomas' Hospital in London for providing us with many of the images.

SAV DURABILITY

SAV durability is age dependent with the risk of failure decreasing with increasing patient age.[1] Durability may vary by valve model with fewer than 10% of patients ≥ 65 years requiring reoperation at 15 years.[2]



An example of contemporary aortic valve durability by age group[3]

1. *Rahimtoola S. Choice of Prosthetic Heart Valve In Adults An Update. J Am Coll Caridiol 2010;55:2413-26.*
2. *Bonow R, Carabello B, Chatterjee K, et al. ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease J Am Coll Cardiol 2006;48:1-148.*
3. *Mosaic® Aortic Bioprosthesis. Medtronic, Inc. 2014 UC201503587EN*

PRESENTATION OF FAILED SURGICAL BIOPROSTHESIS

- Failed bioprosthetic valves will present with 1 of 3 failure modes; stenosis, insufficiency or “combined” where the valve exhibits both lesions.
- In the TAV in SAV expanded use clinical study for CoreValve ®, SAV failure presentation was1

Failure Presentation	Percentage
Regurgitation	23.8%
Stenosis	59.4%
Combined	16.8%

1. CoreValve US Expanded Use Study, Failed Bioprosthetic Surgical Valve Failure (TAV in SAV) Cohort.

COREVALVE® EXPANDED USE STUDY

MEDICAL EDUCATION **ACADEMIA**

PROCEDURAL DATA

	N=143
Total Procedure Time (mins), mean ± SD	52.1 ± 32.2
General Anesthesia, %	87.9
Emergent Operation Due to Device or Procedure, %	0.0
Number of Devices Implanted, %	
0	1.4
1	93.0
2	5.6
VARC-1 Device Success, %	92.2

Source: Medtronic Data on File

TAV IN SAV EXPANDED USE OBSERVATIONS

Most SAV's were stented

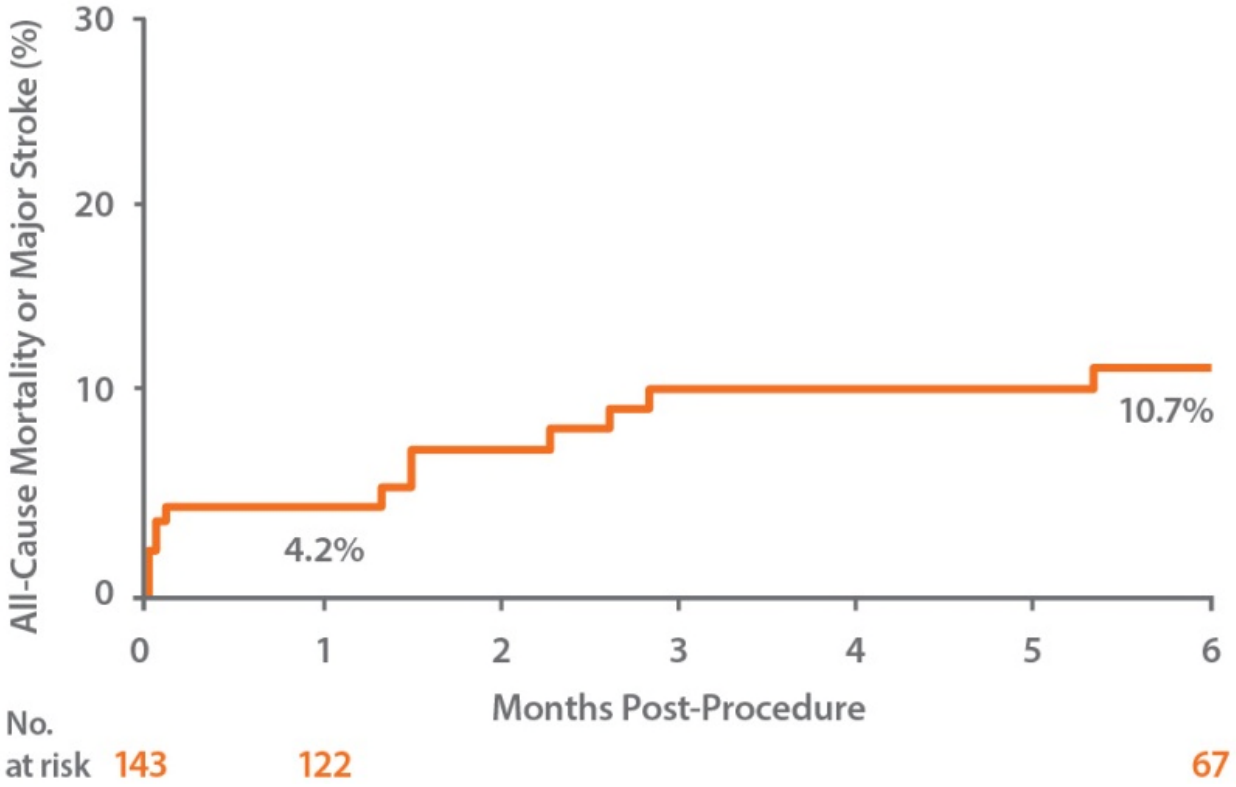
Bioprosthesis Type	Percentage
Stented	83.2
Stentless	10.5
Homograft	6.3

Most common CoreValve Size = 23

Expanded Use TAV in SAV	23 mm	26 mm	29 mm	31 mm
	55.3%	28.4%	12.1%	4.3%

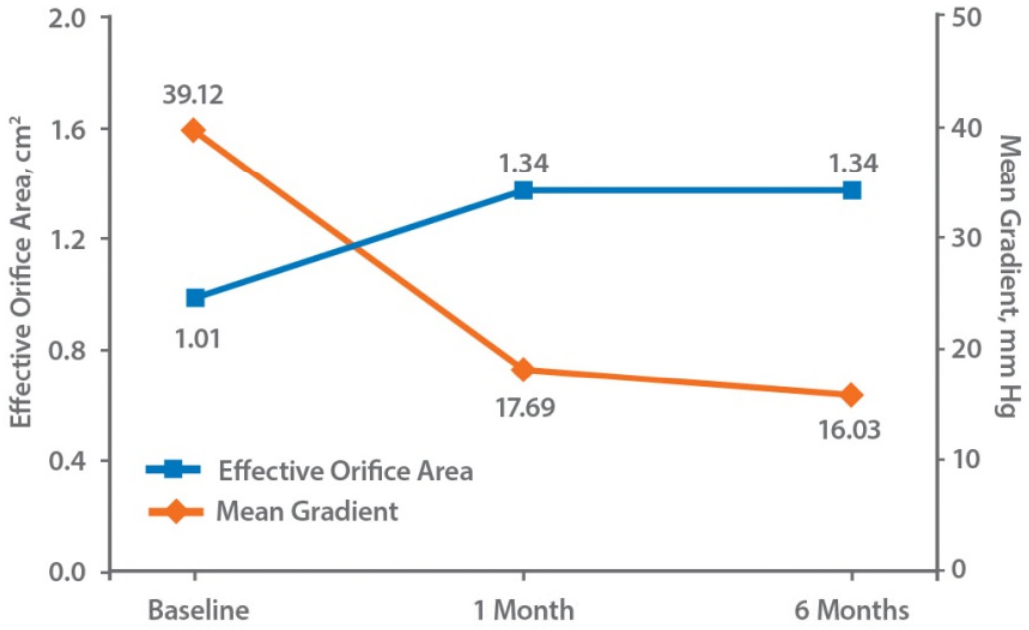
Source: Medtronic Data on File

OUTCOMES: HIGH SURVIVAL & LOW STROKE



Source: Medtronic Data on File

OUTCOMES: HEMODYNAMIC IMPROVEMENT

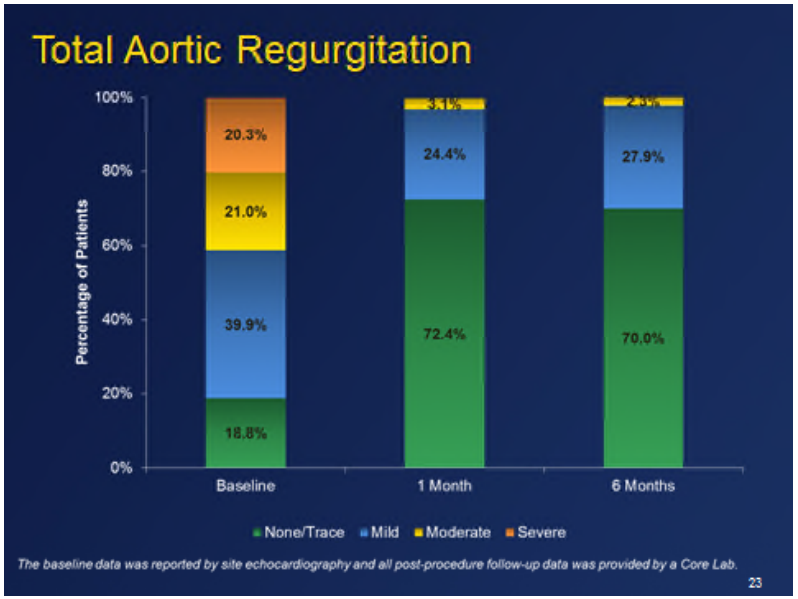


Gradients		
Valve	**19 mm**	**21 mm**
Mosaic (*n* = 14, 189)	15.3 ± 5.3	14.5 ± 5
Hancock II (n = 9)	NA	12.9 ± 4.2
Perimount† (*n* = 9, 16)	15	15
Magna (*n* = 16, 34)	16.7 ± 4	13.8 ± 5
Mitroflow (*n* = 34, 143)	13.4 ± 5.0	11.4 ± 4
Biocor & Supra (*n* = 40)	NA	18.8 ± 6
Epic & Supra (*n* = 49)	NA	19.1 ± 8

(Consider surgical valve results)

Source: Medtronic Data on File

OUTCOMES: TOTAL AORTIC REGURGITATION & PERMANENT PACEMAKER



New Permanent Pacemaker	
0 – 30 days	0 – 60 days
9.2%	10.5%

Source: Medtronic Data on File

NOMENCLATURE AND VIV STEPS CHART

NOMENCLATURE:

TAV:
Transcatheter Aortic Valve

SAV:
Surgical Aortic Valve

ViV:
Valve-in-Valve

Stented SAV

Stented SAV:
Valve composed of xenograft material suspended on a man made stent or frame

Stentless SAV:
Valve composed of xenograft material
without a stent or frame, includes homografts

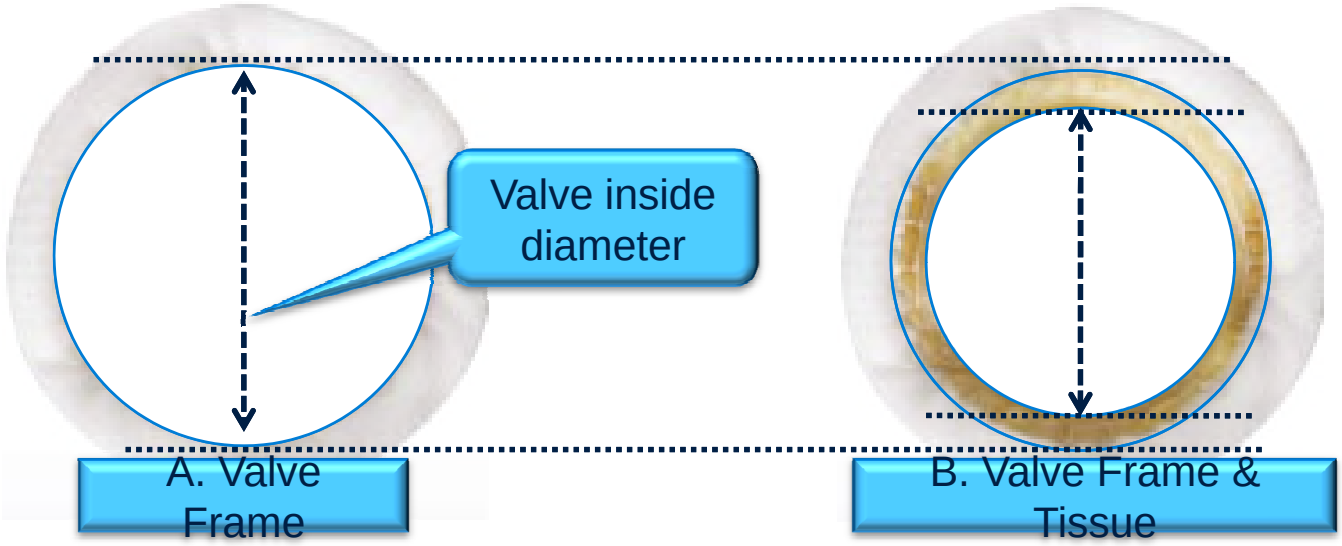
Stentless SAV

Generally, references in this document to “annulus” or “annular contact” apply to the inner diameter of the surgical aortic bioprosthesis for TAV in SAV procedures.

WHY THE "BEST PRACTICE" IS TO MEASURE ID? MEASURED ID IS ALMOST ALWAYS SMALLER…

Consideration:

When using the bioprosthesis manufacturer's stated inside diameter it is important to know that "inside diameter" is only the space within the valve's stent or frame (A). Thus, "inside diameter" does not consider the space taken by the bioprosthetic tissue (B).



Exceptions are the Sorin Mitroflow and St. Jude Medical Trifecta valves as these have the bioprosthetic tissue mounted outside of the frame.

STEPS FOR VALVE-IN-VALVE:

1

- Identify failed SAV

2

- Measure SAV and Size accordingly

3

- Implant

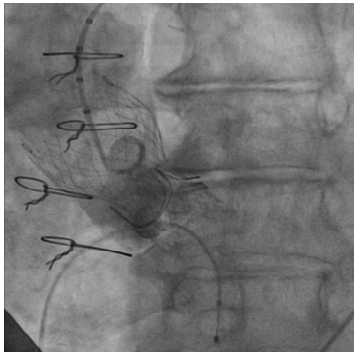


Image from: Fariley SL, Jeganathan R, Manoharan G, et al. Early Experience of Implantation of the New CoreValve Evolut in Degenerated Bioprosthetic Aortic Valves. Catherization and Cardiovascular Interventions 00:00-00 (2013)

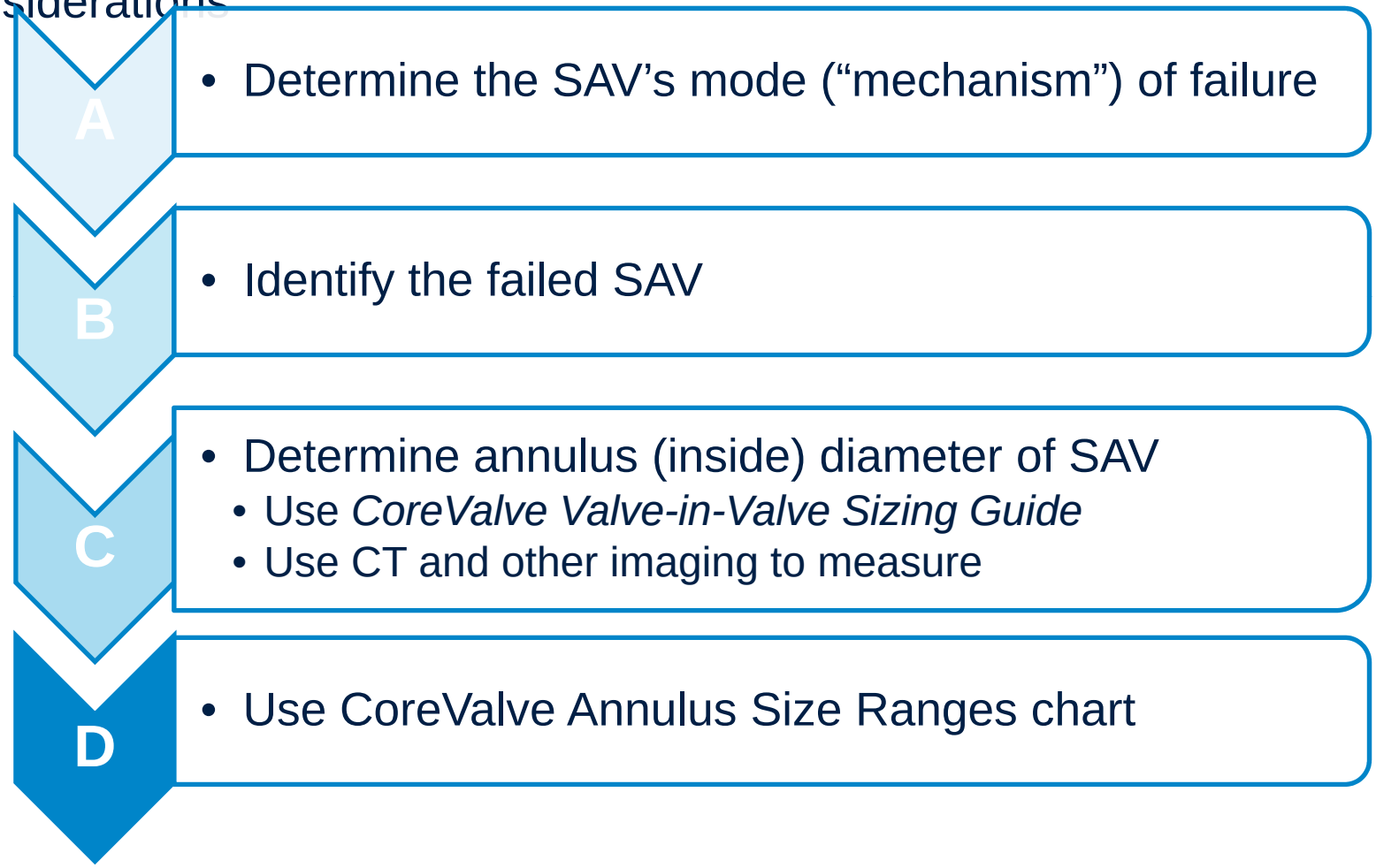
BEST PRACTICE OVERVIEW

IMPORTANT DISCLAIMERS

- The content in this presentation was created with detailed input, review and approval from Medtronic proctors. It is intended to be a resource to support heart teams in their training, planning for, and performing procedures and is in no way intended to constitute medical advice or in any way replace the independent medical judgment of a licensed and trained physician with respect to any patient needs or circumstances.
- The physician is solely responsible for all decision and medical judgments relating to the treatment of their patients.
- Please see the complete Instructions for Use, including all product indications, contraindications, precautions, warnings, and adverse events.

PRE-PROCEDURE

Summary of pre-procedure Steps for Sizing and Orientation Considerations



A. DETERMINE THE SAV'S MECHANISM OF FAILURE

Best Practice:

Determine whether the failure mode of the SAV is:

- Stenosis
- Insufficiency
- Combined stenotic/Insufficient lesions

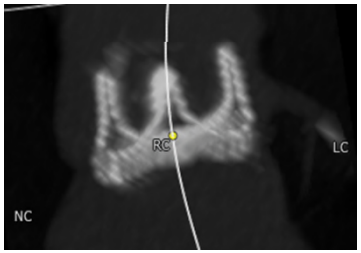
Considerations:

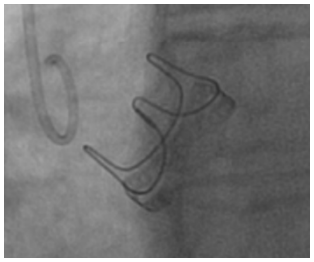
- Implanting a CoreValve bioprosthesis in a degenerated SAV should be avoided if the there is significant concomitant perivalvular leak (between the prosthesis and the native annulus)
- The procedural impact of aortic regurgitation should be appreciated

B. IDENTIFY THE FAILED SAV

Methods for identifying the SAV include:

- Obtain the operative report from the patient's SAV surgery (including implant technique) and other relevant details regarding the patient's medical history
- Secure manufacturer, model and size information for the patient's SAV. Information may be in:
  - The operative notes and/or
  - Valve identification card supplied to patient by manufacturer





OPERATIVE REPORT

Surgeon: Slick Hands, MD
Assistant: John Smith, PA-C

PREOPETATIVE DIAGNOSIS: Severe AI

PROCEDURE: Re-do AVR

PROCEDURE IN DETAIL:

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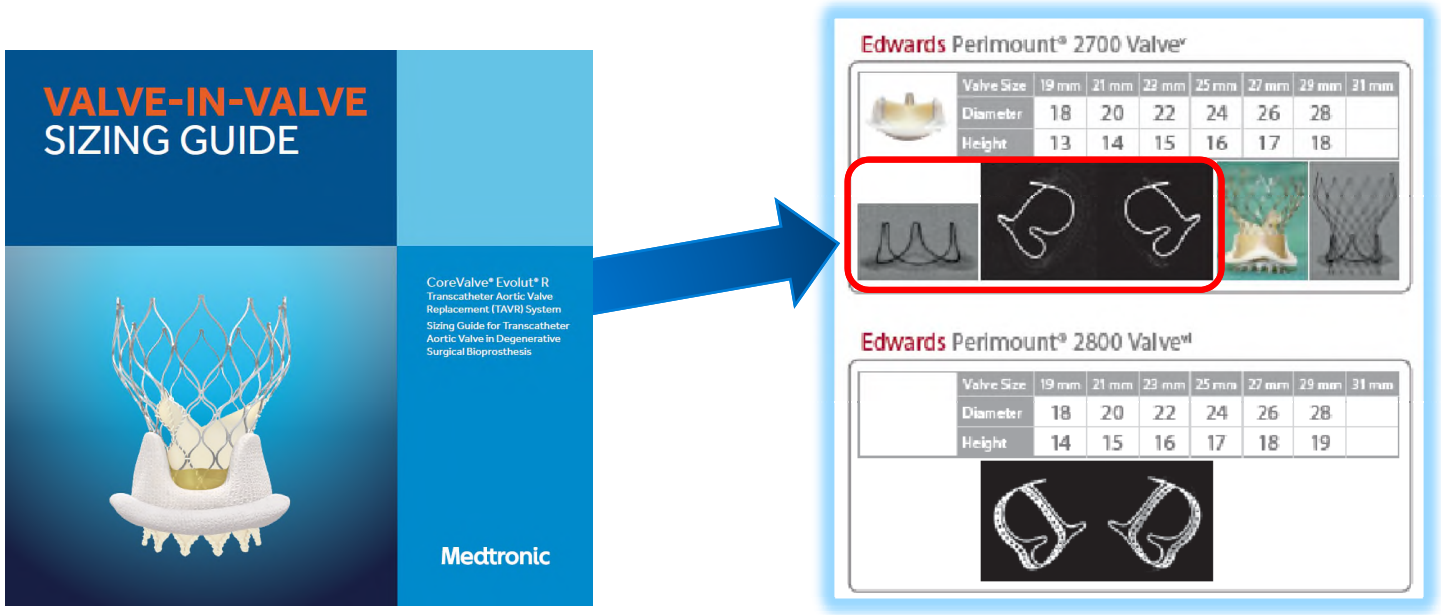
B. IDENTIFY THE FAILED SAV

Failed stented SAVs may also be identified by radiopaque structures unique to a given device

- Use the CoreValve *Valve-in-Valve Sizing Guide* to compare radiographic images of the SAV to the Guide's library of images.
- Lack of radiopaque structures likely indicates a *stentless* SAV



C. DETERMINE ANNULUS DIAMETER OF SAV

Best Practice:

- To determine the annulus (internal diameter) of the SAV:
- Cross reference valve model and size to SAV specifications in the Valve-in-Valve Sizing Guides (see next slide)
- Image the failed SAV to measure its annulus diameter
- Compare internal diameter specification to measured diameter to confirm the annulus diameter
- Use the smaller of the manufacturer's and measured diameters[1]

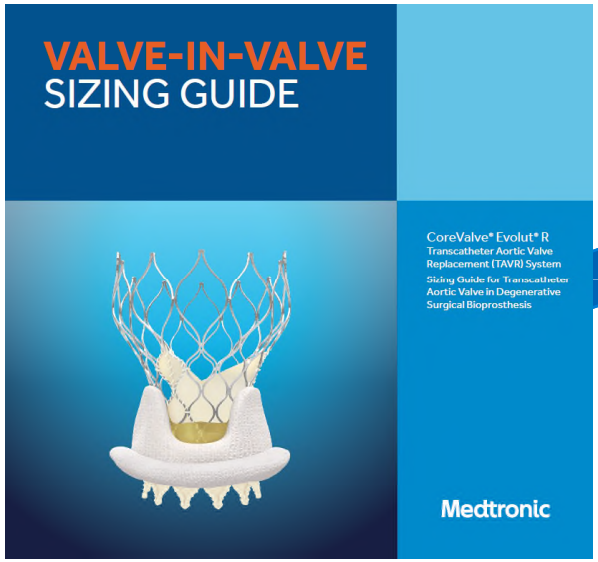
Considerations:

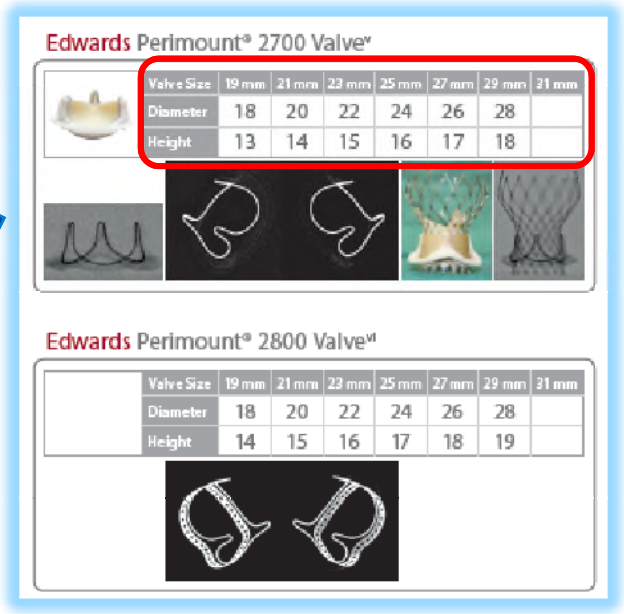
- For pre-procedural screening:
- It is possible that the recorded size or even model of the failed prosthesis is incorrect so this should be verified
- Pannus, etc., may have restricted the inflow orifice of the failed valve1

1. This is the recommendation of experienced proctors and is not intended to replace independent medical judgment
2. Bapat V. Valve-in-valve app: Why And How They Were Developed And How To Use Them. EuroIntervention 2014;10:U44-U51

C. DETERMINE ANNULUS DIAMETER OF SAV

Cross reference valve model and size to SAV specifications in the Valve-in-Valve Sizing Guide

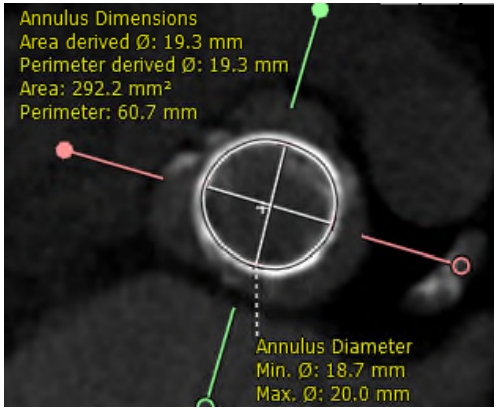


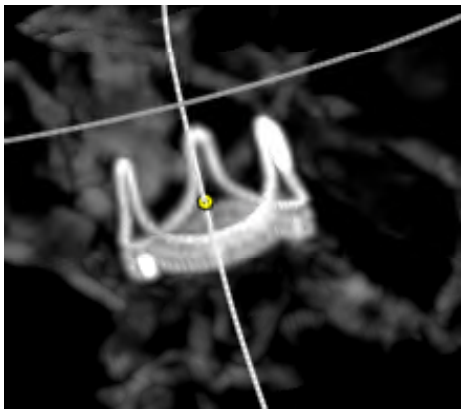


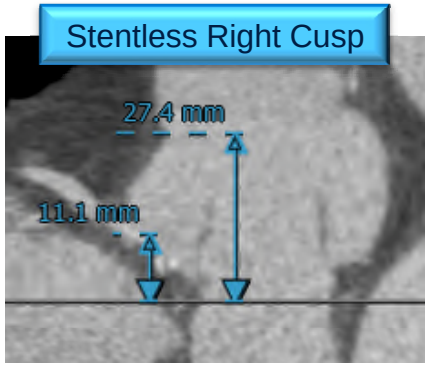
C. DETERMINE ANNULUS DIAMETER OF SAV

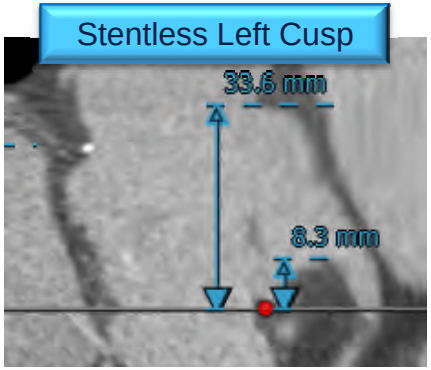
Best Practice:

- Imaging techniques consistent with native valve transcatheter replacement implant methodology should be used.
- Computed tomography (CT) is required. Instead of measuring the native annulus, measure the:
  - Inside diameter of SAV inflow (at the annulus)
  - Inside diameter of stentless SAV outflow
  - Distance between left and right ostia and the valve









C. STENTLESS SAVS & HOMOGRAFTS

Considerations:

- Stentless xenografts typically present with less calcification than homografts (Figs 1-2)
- With stented SAVs the geometry of the device are generally maintained after implantation. With stentless SAVs the final dimension will vary depending on the native root geometries and implant technique
- Homograft sizing is not standardized
- Homograft geometries can change after implantation1
  - There can be marked variability of homograft LVOT and annular dimensions.

Fig. 1 Toronto SPV

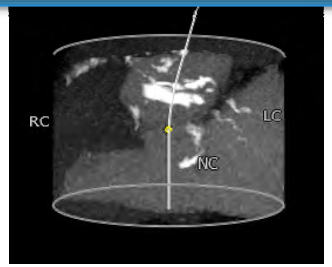
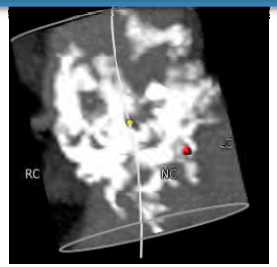


Fig. 2 Homograft



1. Bapat V, Davies W, Attia R, et al. Use of Balloon Expandable Transcatheter Valves for Valve-in-Valve Implantation in Patients with Degenerative Stentless Aortic Bioprostheses; Technical Considerations and Results. J Thorac Cardiovasc Surg 2014;148:917-24.

D. DETERMINE COREVALVE AND COREVALVE EVOLUT R SIZE

Best Practice:

- Refer to Annulus Size Ranges for TAV in SAV and
  - If the measured internal diameter dimension of the SAV is smaller than the manufacturer's stated internal diameter then use the measured size to determine the CoreValve device size
  - If measurements are "in between" choose the smaller CoreValve device†

Annulus Size Ranges Chart for *TAV in SAV*		
Valve Size	**Aortic Annulus Diameter**	**Perimeter Ranges**
23	**17***/18 mm – 20 mm	**53.4***/56.5 mm – 62.8 mm
26	20 mm – 23 mm	62.8 mm – 72.3 mm
29	23 mm – 26 mm	72.3 mm – 81.7 mm
31	26 mm – 29 mm	81.7 mm – 91.1 mm

***Consideration: ViV Only** - The aortic annulus diameter for CoreValve size determination applies **only** to prosthetic valves and is not indicated for TAV in native valves. U.S. only.

†This is the recommendation of experienced proctors and is not intended to replace independent medical judgment

PROCEDURE HIGHLIGHTS

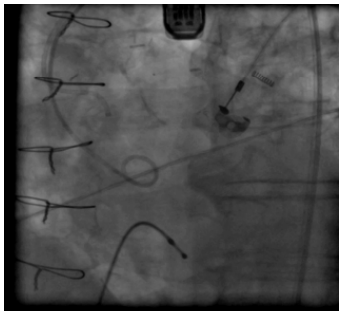
- In most cases predilatation (BAV) is not necessary
- Considerations for ViV include differences between SAV's and native valves. Stented SAV's:
  - Present a stiffer non-expandable landing zone
  - Have less ellipticity than native anatomy
  - The contact between TAV and SAV is different than between TAV and native valve during deployment.
    - Anticipate movement towards the ventricle
- Implant depth below the SAV annulus:
  - CoreValve: Target 4 mm
  - CoreValve Evolut R 3-5 mm

PROCEDURAL CONSIDERATIONS – UNIQUE TO STENTLESS

- Surgical implant technique varies for stentless SAVs and may impact the relationship of the prosthetic annulus to the coronary ostia.

Different Stentless Valve Surgical Techniques

- Radiolucency of stentless SAVs present imaging challenges. These may be addressed by use of additional catheters, e.g., placement of a pigtail catheter in both the non- and left coronary sinuses



Example: 25 mm Freestyle®

BEST PRACTICES: POST-PROCEDURE

- Confirm gradient across the valve with invasive measurement.
- Perform a post-implant aortogram with the reference pigtail to ensure coronary patency and assess aortic regurgitations.

POST-PROCEDURE (POST DILATATION)

- Note: In the event that valve function or sealing is impaired due to excessive calcification or incomplete expansion, a postimplant balloon dilatation of the bioprosthesis may improve valve function and sealing. To ensure patient safety, valve size and patient anatomy must be considered when selecting the size of the balloon. The balloon size chosen for dilatation should not exceed the diameter of the native aortic annulus or, for surgical bioprosthetic valves, the manufacturer's labeled inner diameter.
- Note: Bench testing has only been conducted to confirm compatibility with NuMED Z-MED II™ Balloon Aortic Valvuloplasty catheters where CoreValve Evolut R and CoreValve bioprosthesis device performance was maintained after dilatation.

IMAGING/MEASURING REQUIREMENTS

TAV IN SAV IMAGING REQUIREMENTS

Chest CT:

- Contrast ECG gated chest CT images with 0.6 mm slice thickness (submillimeter)
- 2 systolic phase (20 – 35% cardiac phase) and 2 diastolic phase (60-75% cardiac phase) image sets
- From Asc Ao to diaphragm

Iliofemoral / Subclavian CT:

- Contrast images < 1 mm slice thickness
- From above renal arteries to mid thigh
- Or from above the clavicles to mid thigh (depending if chest CT excludes subclavian arteries)

Echo:

- If AI present evaluate for central vs. PVL

Optional, but helpful:

- Full comprehensive echocardiogram
- Angiogram
- Op Notes, SAV data

INDICATIONS The Medtronic CoreValve and CoreValve Evolut R systems are indicated for use in patients with symptomatic heart disease due to either severe native calcific aortic stenosis or failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (ie, Society of Thoracic Surgeons predicted risk of operative mortality score ≥8% or at a ≥15% risk of mortality at 30 days).

CONTRAINDICATIONS The CoreValve and CoreValve Evolut R systems are contraindicated for patients presenting with any of the following conditions: known hypersensitivity or contraindication to aspirin, heparin (HIT/HITTS) and bivalirudin, ticlopidine, clopidogrel, Nitinol (Titanium or Nickel), or sensitivity to contrast media, which cannot be adequately premedicated; ongoing sepsis, including active endocarditis; preexisting mechanical heart valve in aortic position.

WARNINGS *General* Implantation of the CoreValve and CoreValve Evolut R systems should be performed only by physicians who have received Medtronic CoreValve training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. *Transcatheter Aortic Valve (Bioprosthesis)* Accelerated deterioration of the bioprosthesis may occur in patients presenting with an altered calcium metabolism.

Precautions *General* The safety and effectiveness of the CoreValve and CoreValve Evolut R systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in the following patient populations: with a native valve lesion which does not meet the criteria for severe aortic stenosis (aortic valve area ≤1.0 cm2 or aortic valve area index ≤0.6 cm2/m2, a mean aortic valve gradient of ≥40 mm Hg, or a peak aortic-jet velocity ≥4.0 m/s); who are at moderate or low surgical risk (predicted perioperative mortality risk of <15%); with untreated, clinically significant coronary artery disease requiring revascularization; with a preexisting prosthetic heart valve with a rigid support structure in either the mitral or pulmonic position if either the preexisting prosthetic heart valve could affect the implantation or function of the bioprosthesis or the implantation of the bioprosthesis could affect the function of the preexisting prosthetic heart valve; with cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support. The safety and effectiveness of a CoreValve or CoreValve Evolut R bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis has not been demonstrated. Implanting a CoreValve or CoreValve Evolut R bioprosthesis in a degenerated surgical bioprosthesis [transcatheter aortic valve in surgical aortic valve (TAV in SAV)] should be avoided in the following conditions. The degenerated surgical bioprosthesis presents with a: significant concomitant perivalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (eg, wireform frame fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer's labeled inner diameter <17 mm. The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in patient populations presenting with the following: blood dyscrasias as defined: leukopenia (WBC <1000 cells/mm3), thrombocytopenia (platelet count <50,000 cells/mm3), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital bicuspid or unicuspid valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+]); moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation; hypertrophic obstructive cardiomyopathy; new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation; native aortic annulus size <18 mm or >29 mm for CoreValve and <18 mm or >26 mm for CoreValve Evolut R per the baseline diagnostic imaging or surgical bioprosthetic aortic annulus size <17 mm or >29 mm for CoreVavle and <17 mm or >26 mm for CoreValve Evolut R; transarterial access not able to accommodate an 18-Fr sheath or the 14-Fr equivalent EnVeo R InLine sheath; sinus of valsalva anatomy that would prevent adequate coronary perfusion; moderate to severe mitral stenosis; severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20%; end-stage renal disease requiring chronic dialysis or creatinine clearance <20 cc/min; symptomatic carotid or vertebral artery disease; severe basal septal hypertrophy with an outflow gradient.

Prior to Use Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging.This device was designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the device is the responsibility of the physician. Refer to Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with access vessel diameters of ≥6 mm for the CoreValve system and ≥5 mm for the CoreValve Evolut R system or an ascending aortic (direct aortic) access site ≥60 mm from the basal plane for both systems. Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of >30° for right subclavian/axillary access or >70° for femoral and left subclavian/axillary access. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft.

During Use For direct aortic and subclavian access procedures, care must be exercised when using the tip-retrieval mechanism to ensure adequate clearance to avoid advancement of the catheter tip through the bioprosthesis leaflets during device closure. For direct aortic access procedures, use a separate introducer sheath; do not use the EnVeo R InLine sheath. Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. During rinsing, do not touch the leaflets or squeeze the bioprosthesis. If a capsule becomes damaged during loading or the capsule fails to close, replace the entire system (bioprosthesis, catheter, and CLS). Do not use a catheter with a damaged capsule. After a bioprosthesis has been inserted into a patient, do not attempt to reload that bioprosthesis on the same or any other catheter. AccuTrak DCS Only: During implantation, if resistance to deployment is encountered (e.g., the micro knob starts clicking or is tight or stuck), apply upward pressure to the macro slider while turning the micro knob. If the bioprosthesis still does not deploy, remove it from the patient and use another system. AccuTrak DCS Only: Once deployment is initiated, retrieval of the bioprosthesis from the patient (e.g., use of the catheter) is not recommended. Retrieval of a partially deployed valve using the catheter may cause mechanical failure of the delivery catheter system, aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. AccuTrak DCS Only: During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact has not been made. Once annular contact is made, the bioprosthesis cannot be advanced in the retrograde direction; if necessary, and the frame has only been deployed ≤2/3 of its length, the bioprosthesis can be withdrawn (repositioned) in the antegrade direction. However, use caution when moving the bioprosthesis in the antegrade direction. EnVeo R DCS Only: If a misload is detected, unsheath the bioprosthesis and examine the bioprosthesis for damage (for example, permanent frame deformation, frayed sutures, or valve damage). Do not attempt to reload a damaged bioprosthesis. Do not load the bioprosthesis onto the catheter more than 2 times or after it has been inserted into a patient. EnVeo R DCS Only: Use the deployment knob to deploy and recapture the bioprosthesis. Do not use the trigger for deploying or recapturing because it could cause inaccurate placement of the bioprosthesis. EnVeo R DCS Only: Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment (point of no recapture), retrieval of the bioprosthesis from the patient is not recommended. Retrieval after the point of no recapture may cause mechanical failure of the delivery catheter system, aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. EnVeo R DCS Only: During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact has not been made. Once annular contact is made, the bioprosthesis cannot be advanced in the retrograde direction; recapture until the bioprosthesis is free from annular contact, and then reposition in the retrograde direction. If necessary, and the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment, the bioprosthesis can be withdrawn (repositioned) in the antegrade direction. However, use caution when moving the bioprosthesis in the antegrade direction. While the catheter is in the patient, ensure the guidewire is extending from the tip. Do not remove the guidewire from the catheter while the catheter is inserted in the patient. Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath. Once deployment is complete, repositioning of the bioprosthesis (e.g., use of a snare and/or forceps) is not recommended. Repositioning of a deployed valve may cause aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery. Do not attempt to retrieve or to recapture (EnVeo DCS only) a bioprosthesis if any one of the outflow struts is protruding from the capsule. If any one of the outflow struts has deployed from the capsule, the bioprosthesis must be released from the catheter before the catheter can be withdrawn. Ensure the capsule is closed before catheter removal. When using a separate introducer sheath, if increased resistance is encountered when removing the catheter through the introducer sheath, do not force passage. Increased resistance may indicate a problem and forced passage may result in damage to the device and/or harm to the patient. If the cause of resistance cannot be determined or corrected, remove the catheter and introducer sheath as a single unit over the guidewire, and inspect the catheter and confirm that it is complete. Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up. Postprocedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. Postprocedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Preprocedure, measure the patient's creatinine level. During the procedure, monitor contrast media usage. Conduct the procedure under fluoroscopy. The safety and efficacy of a CoreValve or CoreValve Evolut R bioprosthesis implanted within the initial transcatheter bioprosthesis have not been demonstrated. However, in the event that a CoreValve or CoreValve Evolut R bioprosthesis must be implanted within the initial transcatheter bioprosthesis to improve valve function, valve size and patient anatomy must be considered before implantation of the bioprosthesis to ensure patient safety (for example, to avoid coronary obstruction). In the event that valve function or sealing is impaired due to excessive calcification or incomplete expansion, a postimplant balloon dilatation of the bioprosthesis may improve valve function and sealing. To ensure patient safety, valve size and patient anatomy must be considered when selecting the size of the balloon used for dilatation. The balloon size chosen for dilatation should not exceed the diameter of the native aortic annulus or, for surgical bioprosthetic valves, the manufacturer's labeled inner diameter. Refer to the specific balloon catheter manufacturer's labeling for proper instruction on the use of balloon catheter devices. Note: Bench testing has only been conducted to confirm compatibility with NuMED Z-MED IITM Balloon Aortic Valvuloplasty catheters where CoreValve or CoreValve Evolut R bioprosthesis device performance was maintained after dilation. Data on File..

POTENTIAL ADVERSE EVENTS Potential risks associated with the implantation of the CoreValve or CoreValve Evolut R transcatheter aortic valve may include, but are not limited to, the following: • death • myocardial infarction, cardiac arrest, cardiogenic shock, cardiac tamponade • coronary occlusion, obstruction, or vessel spasm (including acute coronary closure) • cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention) • emergent surgical or transcatheter intervention (for example, coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty) • prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement • prosthetic valve migration/embolization • prosthetic valve endocarditis • prosthetic valve thrombosis • delivery catheter system malfunction resulting in the need for additional re-crossing of the aortic valve and prolonged procedural time • delivery catheter system component migration/embolization • stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits • heart failure • cardiac failure or low cardiac output • ancillary device embolization • individual organ (for example, cardiac, respiratory, renal [including acute kidney failure]) or multi-organ insufficiency or failure • major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding) • vascular access-related complications (eg, dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, stenosis) • mitral valve regurgitation or injury • conduction system disturbances (for example, atrioventricular node block, left-bundle branch block, asystole), which may require a permanent pacemaker • infection (including septicemia) • hypotension or hypertension • hemolysis • peripheral ischemia • bowel ischemia • abnormal lab values (including electrolyte imbalance) • allergic reaction to antiplatelet agents, contrast medium, or anesthesia • exposure to radiation through fluoroscopy and angiography • permanent disability.

CAUTION Federal law (USA) restricts this device to sale by or on the order of a physician.