Medtronic

Evolut™ PRO+ System

MR Evolut™ PRO+ Transcatheter Aortic Valve

Evolut™ PRO+ Delivery Catheter System

Evolut™ PRO+ Loading System

Instructions for Use

! USA **Caution:** Federal law (USA) restricts this device to sale by or on the order of a physician.

Explanation of symbols on package labeling

	Use by
	Consult instructions for use at this website
	Do not reuse
	Do not resterilize
	Size
SN	Serial number
STERILE LC	Sterile LC: Device has been sterilized using liquid chemical sterilants according to EN/ISO 14160
REF	Catalog number
	Lower limit of temperature
	Quantity
LOT	Lot number
STERILE EO	Sterilized using ethylene oxide
	Nonpyrogenic
MR	MR Conditional
	Do not use if package is damaged
	Manufacturer
	Date of manufacture
Model	Model
! USA	For US audiences only
	Keep dry
	Keep away from sunlight
	Manufactured in
	Maximum guidewire diameter
BIO	Contains biological material of animal origin
	Single sterile barrier system
	Double sterile barrier system

UDI	Unique Device Identifier

1 Device description

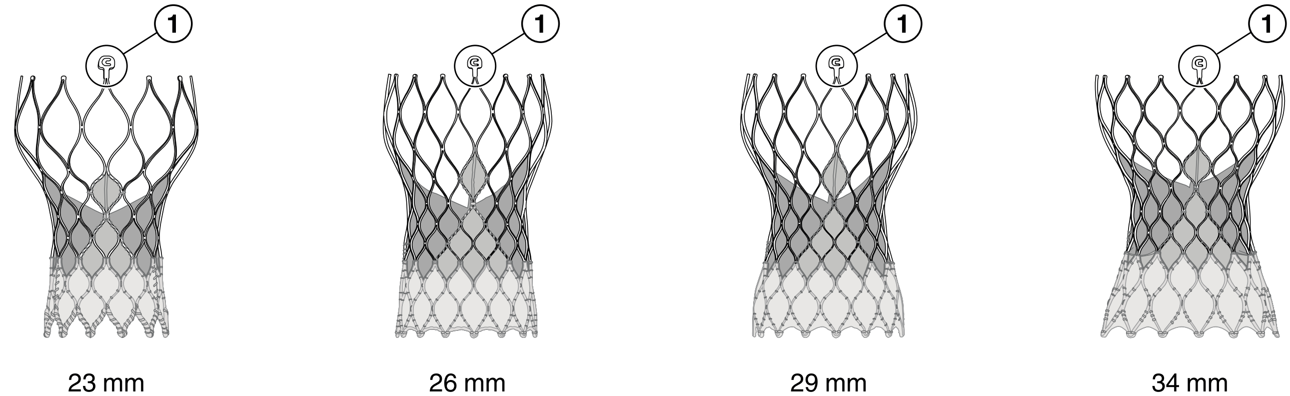
Caution: Implantation of the Medtronic Evolut PRO+ system should be performed only by physicians who have received Medtronic Evolut PRO+ training.

These devices are supplied sterile for single use only. After use, dispose of the delivery catheter system and the loading system in accordance with local regulations and hospital procedures. Do not resterilize.

The Medtronic Evolut PRO+ system is a recapturable transcatheter aortic valve replacement system, which includes the Evolut PRO+ transcatheter aortic valve (bioprosthesis)[1], the delivery catheter system (catheter), and the loading system (LS).

1.1 Evolut PRO+ transcatheter aortic valve (bioprosthesis)

Figure 1. Evolut PRO+ transcatheter aortic valve (bioprosthesis)



1 "C" paddle

The bioprosthesis is manufactured by suturing 3 valve leaflets and an inner skirt, made from a single layer of porcine pericardium, onto a self-expanding, multi-level, radiopaque frame made of Nitinol. The bioprosthesis has a porcine pericardial tissue outer skirt (wrap), which is 1.5 cells in height and is sutured to the inflow section of the bioprosthesis. It is designed to replace the native, surgical bioprosthetic, or transcatheter bioprosthetic aortic heart valve without open heart surgery and without concomitant surgical removal of the failed valve.

Table 1. Heart valve materials

Component	Materials
Tissue	Processed porcine pericardium
Frame	Nitinol (a nickel titanium alloy)
Suture	Polyethylene[a]

[a] The Evolut PRO+ 23 mm valve also uses expanded polytetrafluoroethylene (ePTFE).

The bioprosthesis is processed with alpha-amino oleic acid (AOA™), which is a compound derived from oleic acid, a naturally occurring long-chain fatty acid. The bioprosthesis is available for a range of aortic annulus diameters (*Table 2*).

Table 2. Patient anatomical criteria

Bioprosthesis model	Size	Aortic annulus diameter[a]	Aortic annulus perimeter (π × aortic annulus diameter)[a]
EVPROPLUS-23US	23 mm	17[b]/18 mm to 20 mm	53.4[b]/56.5 mm to 62.8 mm
EVPROPLUS-26US	26 mm	20 mm to 23 mm	62.8 mm to 72.3 mm
EVPROPLUS-29US	29 mm	23 mm to 26 mm	72.3 mm to 81.7 mm
EVPROPLUS-34US	34 mm	26 mm to 30 mm	81.7 mm to 94.2 mm

[a] For TAV in SAV and TAV in TAV, diameter and perimeter criteria are applicable to the failed SAV or TAV measured inner diameter.
[b] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only.

[1] The terms "bioprosthesis" and "transcatheter aortic valve" are synonymous terms and are used interchangeably throughout the document to refer to the Evolut PRO+ device.

1.2 Delivery catheter system (catheter)

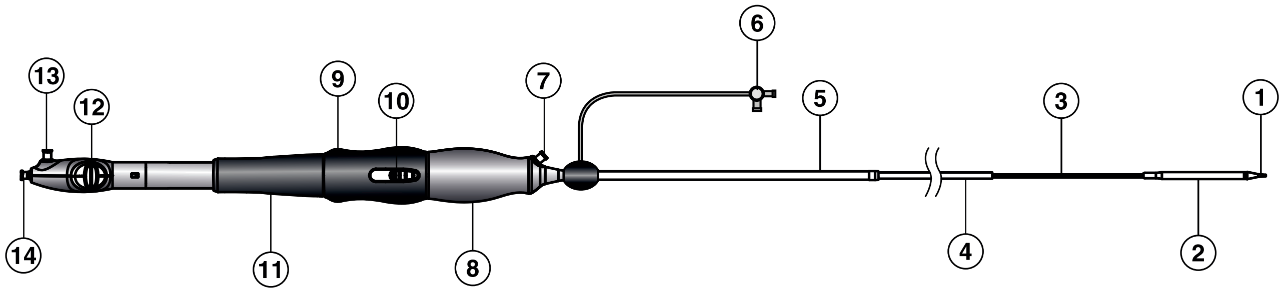
The catheter comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 2* and *Figure 3* for catheter components.

The catheter facilitates the placement of the bioprosthesis within the annulus of the aortic valve. The catheter assembly is flexible and compatible with a 0.035 in (0.889 mm) guidewire. The distal (deployment) end of the system features an atraumatic, radiopaque catheter tip and a capsule that covers and maintains the bioprosthesis in a crimped position. The capsule includes a distal flare to enable the bioprosthesis to be partially or fully recaptured after partial deployment. A stability layer is fixed at the handle and extends down the outside of the catheter shaft. It provides a barrier between the retractable catheter and the introducer sheath and vessel walls, thus enabling the catheter to retract freely. An Evolut PRO+ inline sheath is assembled over the stability layer, which functions as a hemostatic introducer sheath and minimizes the access site size to the capsule diameter. The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

The delivery catheter system consists of a catheter with an integrated handle to provide the user with accurate and controlled deployment. The handle is on the proximal end of the catheter and is used to load, deploy, recapture, and reposition the bioprosthesis. The handle features a gray front grip used to stabilize the system. The deployment knob turns to deploy the bioprosthesis precisely. Arrows on the deployment knob indicate the direction of rotation required to deploy the bioprosthesis. If desired, the deployment knob can be turned in the opposite direction to partially or fully recapture the bioprosthesis if the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture. The deployment knob also features a trigger, which can be engaged to make macro adjustments to the capsule position. A blue hand rest connects to the deployment knob. The end of the handle features a tip-retrieval mechanism, which can be used to withdraw the catheter tip to meet the capsule after the device has been fully deployed.

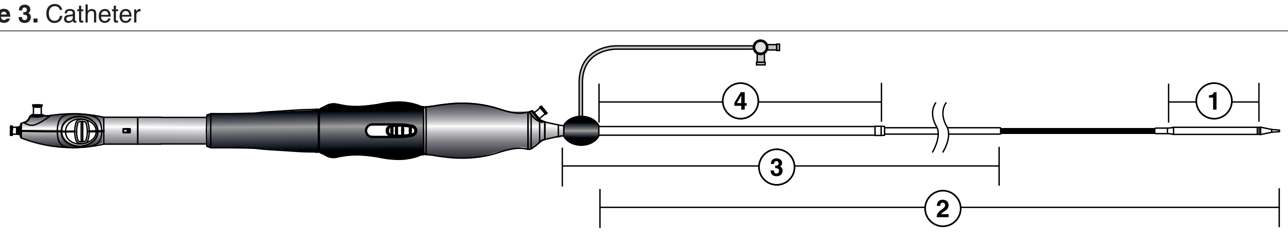
The catheter packaging contains an integrated loading bath and a removable tray with 3 rinsing bowls for loading and rinsing the bioprosthesis. The integrated loading bath features a mirror, which aids in accurate placement of the bioprosthesis frame paddles during loading. In addition to these features, the device packaging is swiveled and secured to facilitate the bioprosthesis loading procedure.

Figure 2. Catheter



1 Catheter tip
2 Capsule (Model D-EVPROP2329US: 18 Fr [6.0 mm] outer diameter [OD]; Model D-EVPROP34US: 22 Fr [7.33 mm] OD)
3 Catheter shaft
4 Stability layer
5 Model D-EVPROP2329US: 14 Fr equivalent Evolut PRO+ inline sheath (18 Fr [6.0 mm] OD); Model D-EVPROP34US: 18 Fr equivalent Evolut PRO+ inline sheath (22 Fr [7.33 mm] OD)
6 Evolut PRO+ inline sheath flush port
7 Stability layer flush port
8 Gray front grip
9 Deployment knob
10 Trigger
11 Blue hand rest
12 Tip-retrieval mechanism
13 Capsule flush port
14 Wire lumen flush port

Figure 3. Catheter



1 7.6 cm (Model D-EVPROP2329US); 7.7 cm (Model D-EVPROP34US)
2 107 cm
3 88.6 cm
4 30 cm

Figure 4. Catheter distal tray

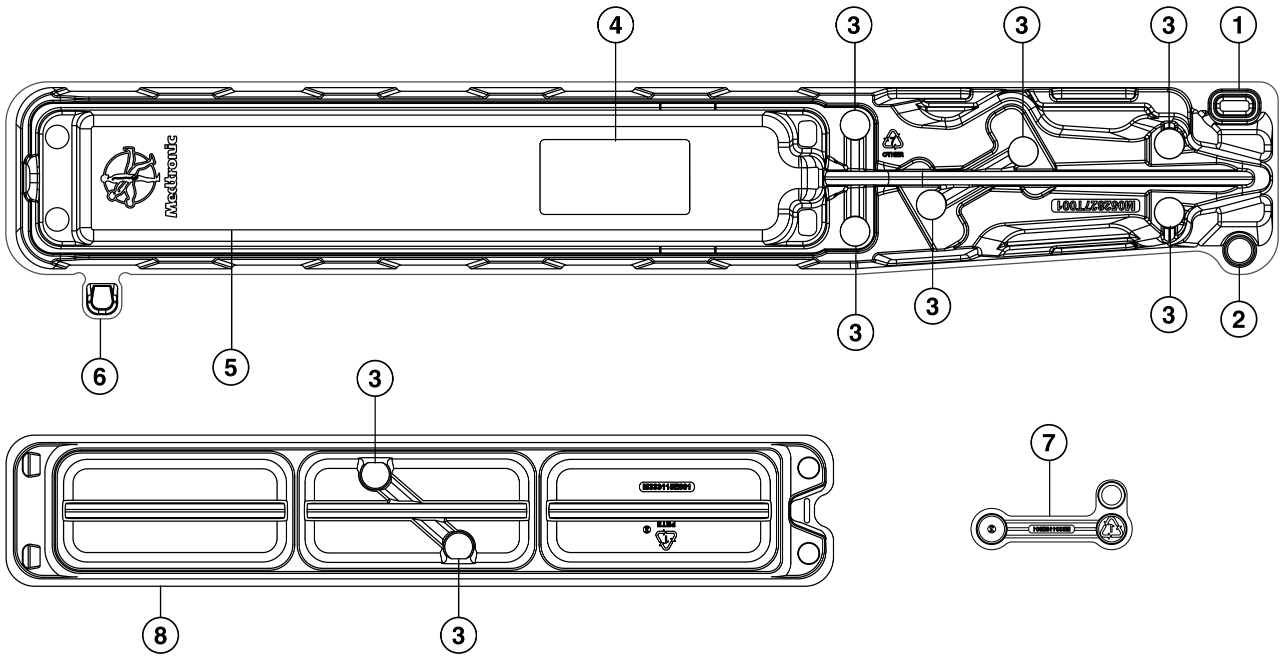
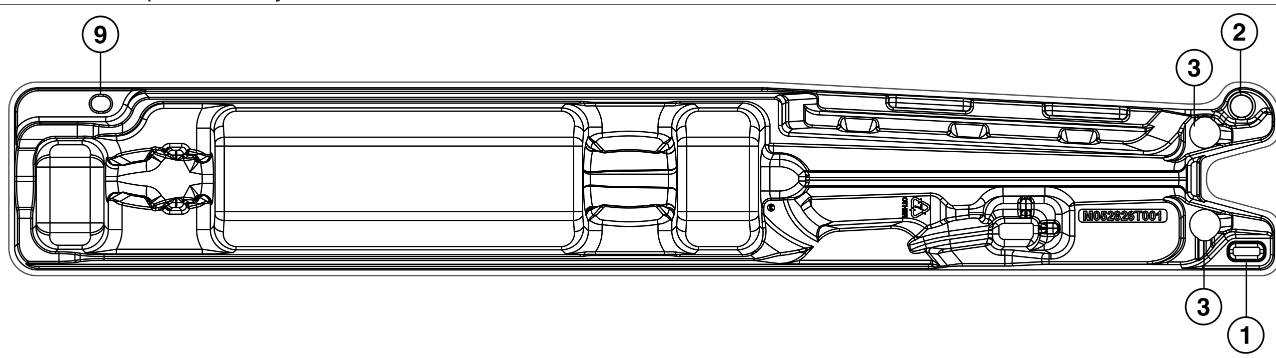


Figure 5. Catheter proximal tray

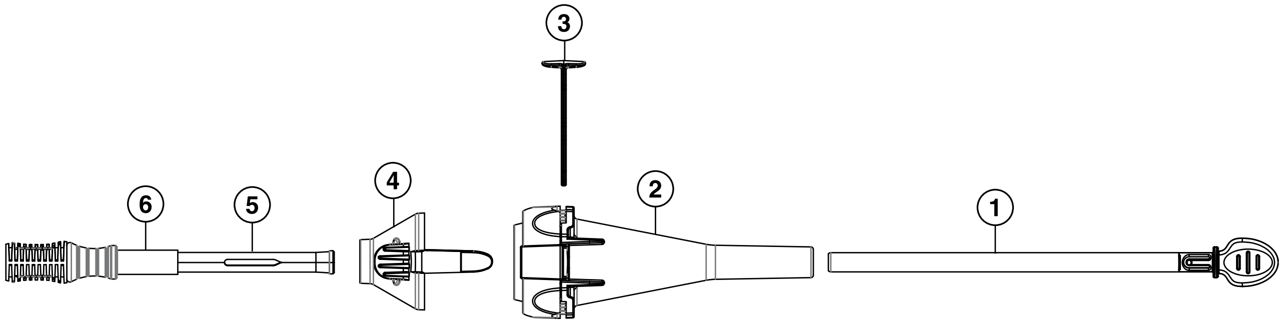


1 Tray connector
2 Swivel hinge
3 Clip holder
4 Mirror
5 Integrated loading bath
6 Tray tab
7 Locking clip
8 Rinsing bowls
9 Tray tab holder

1.3 Loading system (LS)

The LS compresses the bioprosthesis into the catheter. The LS comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 6* for components.

Figure 6. Evolut PRO+ LS



1 Catheter tip guide tube
2 Inflow cone
3 Backplate
4 Outflow cone
5 Capsule guide tube
6 Locking collar

Table 3. System compatibility

Bioprosthesis model	Compatible LS models	Compatible catheter models
EVPROPLUS-23US	L-EVPROP2329US	D-EVPROP2329US
EVPROPLUS-26US		
EVPROPLUS-29US		
EVPROPLUS-34US	L-EVPROP34US	D-EVPROP34US

2 Indications

The Medtronic Evolut PRO+ system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic Evolut PRO+ system is indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical or transcatheter 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 (i.e., predicted risk of surgical mortality ≥8% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

3 Contraindications

The Evolut PRO+ system is contraindicated in patients who cannot tolerate the device materials listed in *Table 1*, an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

4 Warnings and precautions

Carefully read all warnings, precautions, and instructions for use for all components of the system before use. Failure to read and follow all instructions or failure to observe all stated warnings could cause serious injury or death to the patient.

4.1 Warnings

General

- Implantation of the Medtronic Evolut PRO+ system should be performed only by physicians who have received Medtronic Evolut PRO+ training.
- The transcatheter aortic valve is to be used only in conjunction with the delivery catheter system and the loading system.
- System failure could occur if an incorrect combination of devices is used. Refer to *Table 3* for system compatibility.
- This procedure should only be performed where emergency aortic valve surgery can be performed promptly.
- **Do not** use any of the Medtronic Evolut PRO+ system components if any of the following has occurred:
  - It has been dropped, damaged, or mishandled in any way
  - The Use By date has elapsed
- Mechanical failure of the delivery catheter system and/or accessories may result in patient complications.

Transcatheter aortic valve (bioprosthesis)

- **Do not** use the bioprosthesis if any of the following conditions is observed:
  - There is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket)
  - The serial number tag does not match the container label
  - The freeze indicator in the secondary package has activated
  - The storage solution does not completely cover the bioprosthesis
- Accelerated deterioration of the bioprosthesis due to calcific degeneration may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)

4.2 Precautions

General

- **Do not** contact any of the Medtronic Evolut PRO+ system components with cotton or cotton swabs.
- **Do not** expose any of the Medtronic Evolut PRO+ system components to organic solvents, such as alcohol.
- **Do not** introduce air into the catheter.
- **Do not** expose the bioprosthesis to solutions other than the storage and rinse solutions.
- **Do not** add antibiotics or any other substance to either the storage or rinse solutions. **Do not** apply antibiotics or any other substance to the bioprosthesis.
- **Do not** allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.
- **Do not** attempt to repair a damaged bioprosthesis.
- **Do not** handle or use forceps to manipulate the bioprosthesis leaflet tissue.
- **Do not** deform the bioprosthesis in excess of what is experienced during crimping, loading, and implantation.
- Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up.
- The safety and effectiveness of the Medtronic Evolut PRO+ system 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:
  - Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined below:

    - **Symptomatic severe high-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2, a mean aortic valve gradient ≥40 mmHg, or a peak aortic-jet velocity ≥4.0 m/s

    - **Symptomatic severe low-flow/low-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2; a mean aortic valve gradient <40 mmHg; and a peak aortic-jet velocity <4.0 m/s
  - 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
  - Patients with liver failure (Child-Pugh Class C)
  - With cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
  - Patients who are pregnant or breastfeeding
- Implanting the Evolut PRO+ bioprosthesis in a degenerated surgical bioprosthetic valve (transcatheter aortic valve in surgical aortic valve [TAV in SAV]) should be avoided in the following conditions. The degenerated surgical bioprosthetic valve presents with a:
  - Significant concomitant paravalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (for example, 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
- Before implanting the Evolut PRO+ bioprosthesis in a degenerated transcatheter bioprosthetic valve (transcatheter aortic valve in transcatheter aortic valve [TAV in TAV]), additional factors regarding failed valve size and patient anatomy must be considered in order to ensure patient safety (for example, to avoid coronary obstruction). The potential need for future coronary access should be considered. TAV in TAV implantation should be avoided in the following conditions:
  - The degenerated TAV presents with a significant concomitant paravalvular leak (between the prosthesis and the native annulus),
  - The degenerated TAV is not securely fixed in the native annulus, or is not structurally intact (for example, frame fracture) or
  - The risk of coronary obstruction or sinus sequestration after Evolut PRO+ bioprosthesis implantation is high

- 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/mm^3), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
  - Congenital unicuspid valve
  - Mixed native 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 >30 mm per the baseline diagnostic imaging or a surgical or transcatheter bioprosthetic aortic annulus size <17 mm or >30 mm
  - Transarterial access not able to accommodate the following:
    - 22 Fr introducer sheath or the 18 Fr equivalent Evolut PRO+ inline sheath
    - 18 Fr introducer sheath or the 14 Fr equivalent Evolut PRO+ inline sheath
  - Prohibitive left ventricular outflow tract calcification
  - Sinus of Valsalva anatomy that would prevent adequate coronary perfusion
  - Significant aortopathy requiring ascending aortic replacement
  - Moderate to severe mitral stenosis
  - Severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20%
  - Symptomatic carotid or vertebral artery disease
  - Severe basal septal hypertrophy with an outflow gradient
  - A known hypersensitivity or contraindication to any of the following that cannot be adequately pre-medicated:
    - Aspirin or heparin (HIT/HITTS) and bivalirudin
    - Ticlopidine and clopidogrel
    - Nitinol (titanium or nickel)
    - Contrast media

Before use

- Accelerated deterioration due to calcific degeneration of bioprostheses may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)
- 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 *Table 2* for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed in *Chapter 5*.
- Patients must present with transarterial access vessels with diameters that are ≥5.0 mm when using Model D-EVPROP2329US or ≥6.0 mm when using Model D-EVPROP34US, or patients must present with an ascending aortic (direct aortic) access site ≥60 mm from the basal plane.
- 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.
- For subclavian access, patients with a patent Left Internal Mammary Artery (LIMA) graft must present with access vessel diameters that are either ≥5.5 mm when using Model D-EVPROP2329US or ≥6.5 mm when using Model D-EVPROP34US. Use caution when using the subclavian/axillary approach in patients with a patent Left Internal Mammary Artery (LIMA) graft (for left subclavian/axillary approach only) or patent Right Internal Mammary Artery (RIMA) graft (for right subclavian/axillary approach only).
- For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft.
- For transfemoral access, use caution in patients who present with multiplanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥2 of these factors are present, consider an alternative access route to prevent vascular complications.
- Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.
- Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water (minimum of 15 minutes). In the event of eye contact, flush with water for a minimum of 15 minutes and seek medical attention immediately.

- The bioprosthesis and the glutaraldehyde storage solution are **sterile**. The outside of the bioprosthesis container is **nonsterile** and must not be placed in the sterile field.
- 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.
- Before catheter insertion, remove the loading stylet.

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 Evolut PRO+ inline sheath. Maintain the Evolut PRO+ inline sheath at the proximal end of the catheter throughout the procedure.
- Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. No other solutions, drugs, chemicals, or antibiotics should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.
- During rinsing, do not touch the leaflets or squeeze the bioprosthesis.
- If a misload is detected during fluoroscopic (cine mode) inspection, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components. A misload is defined as one or more of the following:
  - Inflow crown overlap (non-uniform shadow starting at the inflow) that has not ended before the 4th node from the inflow.
  - Outflow crown misalignment and/or not parallel to the paddle attachment.
  - Curved or bent capsule.
  - Direct load as detailed in *Section 9.1.4*, *Step 17*.
  - Shadow or outline in outflow indicating a bent strut.
- Inflow crown overlap that has not ended before the 4th node within the capsule, increases the risk of an infold upon deployment in constrained anatomies, particularly with moderate-severe levels of calcification and/or bicuspid condition.
  - Do not attempt to direct load the valve (for example, loading the valve without completing *Step 17* in *Section 9.1.4* and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. If a valve has been direct loaded, discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
- Prevent contamination of the bioprosthesis, its storage solution, the catheter, and the LS with glove powder.
- If a bioprosthesis and catheter have been removed from a patient, dispose of both the bioprosthesis and catheter; do not attempt to reuse either component. Both the bioprosthesis and catheter must be replaced with new sterile components.
- While the catheter is in the patient, ensure the guidewire is extending from the proximal end of the catheter. Do not remove the guidewire from the catheter while the catheter is inserted in the patient.
- There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).
- 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.
- From annular contact (or contact with the failed valve, for valve-in-valve procedures) to just before the point of no recapture, the bioprosthesis will occlude cardiac output. Promptly deploy or recapture the valve during this occlusive phase as prolonged obstruction or occlusion of blood flow may lead to hypotension, bradycardia, conduction disturbance, congestive heart failure, pulmonary edema, or death.
- If the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment, the bioprosthesis can be recaptured or repositioned. During deployment, the deployment knob provides a tactile indication as a notification before the point of no recapture.
- Infold detection steps are outlined in *Section 9.2.4*. An observation of any inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopic (cine mode) inspection, may indicate an infold. If identified, and if the patient's condition allows, do not proceed and do not release the valve.
  - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
  - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
  - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.

- If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.

- Implanting a valve with an unresolved infold increases the risk of PVL and need for post implant dilatation, which is associated with higher rates of adverse events such as dislodgement and dissection.

  Note: Predilatation may confer some risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient. For TAV in TAV procedures, the characteristics of the failed TAV (for example, under-expansion, depth of index implant) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and the treatment plan for each patient.
- 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 (for example, use of the catheter) 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.
- During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact (or contact with the failed valve, for valve-in-valve procedures) 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.

  Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

  Caution: Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath.
- Physicians should use judgment when considering repositioning a fully deployed bioprosthesis (for example, using a snare, balloon, and/or forceps). Repositioning the bioprosthesis is not recommended, except in cases where imminent serious harm or death is possible (for example, coronary occlusion). 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 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.
- 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. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term.

Post-implant balloon dilatation considerations

If valve function or sealing is impaired due to excessive calcification or incomplete expansion, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing. If the heart team determines that balloon dilatation is appropriate, consider all of the following factors when selecting the dilatation parameters to ensure patient safety:

- Balloon model
- Balloon size
- Balloon position
- Inflation pressure
- Patient anatomy

To mitigate trauma to the annulus or the Evolut PRO+ TAV bioprosthetic leaflets, the maximum balloon size chosen for dilatation using a compliant, semi-compliant, or non-compliant balloon should not exceed the level set forth in *Table 4*, and the applied inflation pressure should be no greater than 2 atm.

Table 4. Post-implant balloon dilatation sizing

Evolut PRO+ size	23 mm			26 mm				29 mm				34 mm				
Native annulus (failed SAV or TAV inner) diameter (in mm)	17[a]/18	19	20	20	21	22	23	23	24	25	26	26	27	28	29	30
TAV waist diameter (in mm)	20	20	20	22	22	22	22	23	23	23	23	24	24	24	24	24
Maximum balloon diameter (in mm) for compliant and semi-compliant balloons @ 2 atm	17[a]/18	19	20	20	21	22	23	23	24	25	26	26	27	28	28	28
Maximum balloon diameter (in mm) for non-compliant balloons @ 2 atm	16[a]/17	18	19	19	20	21	22	22	23	24	24	25	25	25	25	25

[a] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only

Caution: Overexpansion of the narrowest portion (waist) of the Evolut PRO+ TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up.

It is important to note that the mechanical compliance properties of the selected balloon influence the dilatation dynamics.

Balloons should not be inflated beyond 2 atm of applied pressure.

The maximum balloon sizes in *Table 4* are derived from bench testing based on a single Evolut PRO+ TAV dilation to 2 atm. Multiple dilations of the Evolut PRO+ TAV increases the risk of damage to the bioprosthetic leaflets.

Compliant and semi-compliant (softer) balloons will more readily conform to the hourglass profile of the TAV bioprosthesis at lower pressures, but must be inflated at pressures that preserve the hourglass profile of the TAV.

Conversely, non-compliant (stiffer) balloons will achieve the nominal diameter during inflation irrespective of the underlying annulus or TAV resistance and should be downsized (see *Table 4*).

For additional instructions on the use of balloon catheter devices refer to the specific balloon catheter manufacturer's labeling.

In the event that larger balloon diameters than those listed in *Table 4* are required to expand the Evolut PRO+ TAV due to clinically important residual aortic regurgitation or stenosis, using "bailout" intraventricular balloon positioning when performing PID avoids expansion of the narrowest portion (waist) of the Evolut PRO+ TAV. This can mitigate the risk of leaflet damage. Dilatation with intraventricular balloon positioning should be performed with caution in the setting of a smaller ventricle cavity, presence of LVOT calcification, or wire positioning that interferes with mitral valve function, in order to avoid any unintended balloon interaction with anatomy. The balloon's length and diameter, along with the individual patient anatomy, must be considered. Care should also be taken not to exceed the annular diameters when performing PID with intraventricular balloon positioning (see *Table 4*).

In the event that a bailout PID with intraventricular balloon positioning is performed, the nominal diameter of the balloon should not exceed the annular diameter when using compliant or semi-compliant balloons; the nominal diameter of the balloon should be at least 1 mm smaller than the annular diameter when using non-compliant balloons.

4.3 Magnetic resonance imaging (MRI)

MRI may be used on the bioprosthesis only under specific conditions. See *Section 6.2*: MRI Safety Information for more information.

5 Potential adverse events

Potential risks associated with the implantation of the Evolut PRO+ bioprosthesis 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 embolization
- Stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits
- 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 (for example, 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

General surgical risks applicable to transcatheter aortic valve implantation:

- Abnormal lab values (including electrolyte imbalance)
- Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- Exposure to radiation through fluoroscopy and angiography
- Permanent disability

6 Patient information

6.1 Registration information

! USA A patient registration form is included in each bioprosthesis package. After implantation, please complete all requested information. The serial number is located on both the package and the identification tag attached to the bioprosthesis. Return the original form to the Medtronic address indicated on the form and provide the temporary identification card to the patient prior to discharge.

! USA Medtronic will provide an Implanted Device Identification Card to the patient. The card contains the name and telephone number of the patient's physician as well as information that medical personnel would require in the event of an emergency. Patients should be encouraged to carry this card with them at all times.

6.2 MRI safety information

The MRI safety information for the Medtronic Evolut PRO+ bioprosthesis is presented in *Table 5*.

Table 5. MRI safety information

MR	A patient with the Medtronic Evolut PRO+ bioprosthesis may be safely scanned under the following conditions, including immediately after placement of this device. Failure to follow these conditions may result in injury to the patient.
Name/Identification of the device	Evolut PRO+ bioprosthesis
Nominal value of static magnetic field [T]	1.5 T or 3.0 T
Maximum spatial field gradient [T/m and gauss/cm]	30 T/m (3000 gauss/cm)
RF excitation	Circularly polarized (CP)
RF transmit coil type	Whole body transmit coil

Table 5. MRI safety information (continued)

Maximum whole body SAR [W/kg]	2 W/kg (Normal Operating Mode)
Maximum head SAR [W/kg]	3.2 W/kg (Normal Operating Mode)
Limits on scan duration	2 W/kg whole body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scan without breaks)
MR image artifact	The presence of this implant may produce an image artifact. Some manipulation of scan parameters may be needed to compensate for the artifact.
If information about a specific parameter is not included, there are no conditions associated with that parameter. The presence of other implants or medical circumstances of the patient may require lower limits on some or all of the above parameters. For deployment of a Medtronic Evolut PRO+ bioprosthesis inside of a failed surgical or transcatheter bioprosthetic valve, consult the MRI labeling pertaining to the failed valve for additional artifact information.	

7 How supplied

7.1 Packaging

The bioprosthesis is supplied **sterile** and **nonpyrogenic** in a glass container and a screw cap with a liner. The outside of the container is **nonsterile** and must not be placed in the sterile field. A freeze indicator is placed inside the labeled carton. If the freeze indicator has been activated, do not use the bioprosthesis.

The catheter is packaged in a single-pouch configuration and sterilized with ethylene oxide gas. The catheter is sterile if the package is undamaged and unopened. The outer surfaces of the pouch are **nonsterile** and must not be placed in the sterile field.

The LS is packaged in a double-pouch configuration. The LS is sterile if the pouches are undamaged and unopened. The outer surfaces of the outer pouch are **nonsterile** and must not be placed in the sterile field. The LS is sterilized with ethylene oxide gas.

7.2 Storage

Store the bioprosthesis at room temperature (5 °C to 25 °C [41 °F to 77 °F]). Avoid exposing to extreme fluctuations of temperature. Do not freeze. Appropriate inventory control should be maintained so that bioprostheses with earlier Use By dates are implanted preferentially.

Caution: Do not use the bioprosthesis if the freeze indicator in the secondary package has activated. If the freeze indicator has activated, dispose of the bioprosthesis in accordance with applicable laws, regulations, and hospital procedures.

Store the catheter and loading system at room temperature in a dry environment.

8 Additional equipment

Note: While extensive, this equipment list is not meant to cover all possible scenarios.

Transesophogeal echocardiogram (TEE) or transthoracic echocardiography (TTE) on standby

Temporary pacer insertion

- Temporary pacemaker lead
- Sterile sleeve for pacemaker lead
- Hemostatic vessel introducer sheath
- Temporary pacemaker generator
- Sterile temporary pacemaker-to-generator cable

If indicated, pulmonary artery catheter insertion

- Standard pulmonary artery catheter
- Hemostatic vessel introducer sheath
- Saline flush line connected to pressure transducer

Baseline aortography via radial, brachial, or femoral approach

- 5 Fr or 6 Fr pigtail angiographic catheter
- 6 Fr hemostatic vessel introducer sheath
- 2-port manifold with saline flush line and pressure tubing or transducer
- Power injector syringe
- Contrast media
- High-pressure power injector tubing

Predilatation of implant site

- 2-port manifold with saline flush and transducer
- 9 Fr hemostatic vessel introducer sheath and a 14 Fr, 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.
- Standard length 0.035 in (0.889 mm) straight guidewire
- Appropriate suture-mediated closure system, if applicable
- Angiographic catheter
- 0.035 in (0.889 mm) × 260 cm standard high support guidewire to be shaped with a pigtail loop
- Balloon valvuloplasty catheters, ≤4 cm length × 18 mm, 20 mm, 22 mm or 23 mm, and 25 mm, 28 mm, and 30 mm diameters
- Inflation device or syringe and diluted 1:5 contrast media

Bioprosthesis implantation

- 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

  Note: A separate introducer sheath is optional for transfemoral and subclavian access procedures.

Standby supplies (must be available in the room)

- Pericardiocentesis tray
- 35 mm × 120 cm single loop snare
- Standard percutaneous coronary intervention (PCI) equipment
- 14 Fr and 18 Fr hemostatic vessel introducer sheaths
- Standard cardiac catheterization lab equipment
- Intra-aortic balloon pump (IABP)

9 Instructions for use

9.1 Inspection and bioprosthesis loading procedure

Caution: Once the bioprosthesis is removed from its container and the catheter and LS are removed from their packaging, ensure all subsequent procedures are performed in a sterile field.

Caution: Do not allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.

9.1.1 Inspection before use and swivel tray setup

1. Before removing the bioprosthesis, catheter, or loading system from its primary packaging, carefully inspect the packaging for any evidence of damage that could compromise the sterility or integrity of the device (for example, cracked jar or lid, leakage, broken or missing seals, torn or punctured pouch).

   Caution: Do not use after the Use By date or if there is evidence of damage.

   Caution: Do not use the bioprosthesis if the freeze indicator has been activated.
2. Remove the product from the protective package.
3. Visually check that the product is free of defects. Do not use if any defects are noted.
4. Remove the locking clip attached to the rinsing bowls.
5. Remove the rinsing bowls from the integrated loading bath.
6. Remove the locking clips that connect the distal and proximal trays.
7. Lift the tray connector from the distal tray, and swivel the distal tray 180° counterclockwise.
8. Clip the tray tab on the distal tray to the tray tab holder on the proximal tray.
9. Fill the integrated loading bath with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]).

9.1.2 Preparation of the catheter and LS

1. Attach a 10 mL syringe filled with sterile saline to the capsule flush port on the proximal end of the handle. Leave the syringe in place until loading is complete.
2. Carefully lift the distal end of the catheter to a near vertical orientation. To prevent kinking, do not bend the catheter severely.
3. Open the capsule and expose the paddle attachment.

   Note: Use the deployment knob to open the capsule completely until the paddle attachment is fully exposed.
4. With the capsule held vertically, flush the capsule flush port. Verify that no catheter leakage is observed during any of the flushing steps. If leakage is observed, use a new system.

5. Submerge the capsule completely in the cold saline bath while flushing the capsule flush port. Continue flushing the capsule until it is completely submerged in the bath to prevent air from entering the catheter (*Figure 7*).

   Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.

   Figure 7.

   Note: The bioprosthesis, catheter, and LS may look slightly different from the figures in *Chapter 9*. The functionality of the system is the same.
6. Secure a locking clip in the clip holder to angle the catheter tip into the integrated loading bath.
7. Place the LS components in the integrated loading bath.

9.1.3 Bioprosthesis rinsing procedure

1. Fill each of the 3 rinsing bowls (provided within the packaging) with approximately 500 mL of fresh, sterile saline at ambient temperature (15 °C to 25 °C [59 °F to 77 °F]).

   Caution: Do not handle or manipulate the bioprosthesis with sharp or pointed objects. Use atraumatic forceps only.
2. Confirm the integrity of the primary bioprosthesis container. Do not use the bioprosthesis if there is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket).
3. Remove the bioprosthesis from its container by carefully grasping one of the bioprosthesis frame paddles with a pair of blunt tipped forceps. Do not use the forceps to grasp the tissue portion of the bioprosthesis. Let any remaining solution drain from the bioprosthesis completely.

   Note: Retain the container with the original solution. It may be needed to store and return a rejected bioprosthesis.
4. Compare the serial number on the container with the serial number on the tag attached to the bioprosthesis.

   Caution: If the serial numbers do not match, do not use the bioprosthesis.
5. Carefully remove the serial number tag from the bioprosthesis and retain the tag.
6. Immerse the entire bioprosthesis in a sterile rinsing bowl.
7. Gently agitate the bioprosthesis by hand for 15 seconds to remove the glutaraldehyde from the bioprosthesis.
8. Repeat *Step 6* and *Step 7* in one of the remaining rinsing bowls.
9. Leave the bioprosthesis submerged in sterile saline in the third rinsing bowl until it is ready to be loaded.

9.1.4 Bioprosthesis loading procedure

Perform the bioprosthesis loading procedure while the distal end of the catheter is immersed in the integrated loading bath filled with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]). The bioprosthesis should remain immersed in saline during the loading process to minimize the introduction of air into the loaded system.

Note: Confirm the LS and catheter sizes are compatible with the bioprosthesis size (*Table 3*).

Note: Refer to *Figure 6* for Evolut PRO+ LS components.

Caution: Rapid capsule advancement can contribute to difficulties with loading the valve. Slowly advancing the capsule helps facilitate successful loading.

1. Submerge and cool the bioprosthesis in the integrated loading bath filled with cold, sterile saline.
2. Ensure that the capsule guide tube is fully open (unlocked) with the locking collar at the proximal end of the capsule guide tube (*Figure 8*).

   Figure 8.

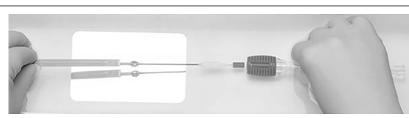
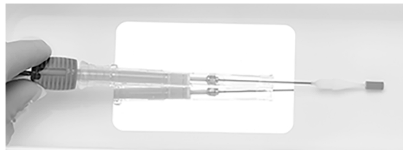
   
3. Advance the capsule guide tube over the catheter shaft toward the handle and across the catheter tip (*Figure 9*).

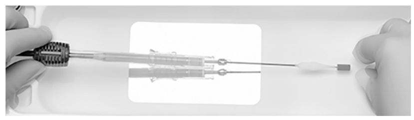
Figure 9.



4. Once the catheter tip has been crossed, fully advance the locking collar to the distal end of the capsule guide tube until it is closed (locked).
5. Continue to advance the capsule guide tube over the catheter shaft towards the handle until it contacts the distal end of the capsule (*Figure 10*).

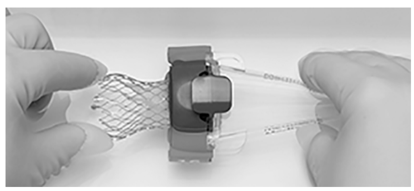
   Caution: Do not attempt to advance the capsule guide tube over the capsule; this will prevent the capsule flare from expanding fully and prevent proper loading.

   Figure 10.



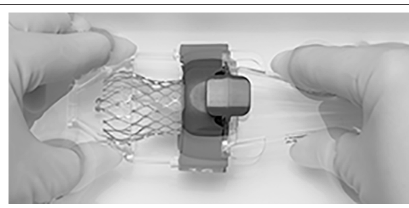
6. Ensure that the backplate has been inserted into the inflow cone and the exposed part of the backplate is facing up.
7. Insert the inflow portion of the bioprosthesis frame into the inflow cone. Ensure that the bioprosthesis frame paddle marked with a "C" is facing up and that the paddles are aligned with the paddle attachment pockets (*Figure 11*).

   Figure 11.



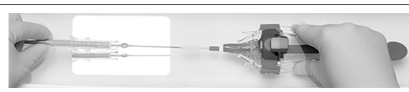
8. Secure the outflow cone onto the inflow cone (*Figure 12*) until it locks.

   Figure 12.



9. Insert the catheter tip guide tube completely into the distal end of the inflow cone (*Figure 13*). Inspect the outflow struts of the bioprosthesis and, if needed, manually manipulate so that they are evenly spaced and the bioprosthesis frame paddles are approximately 180° apart.

   Figure 13.



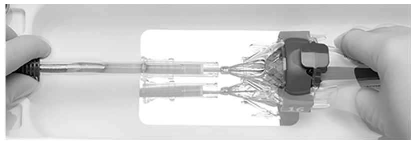
10. Insert the distal catheter tip into the catheter tip guide tube.

    Note: Allow the loading tool to rest on the loading bath floor to ensure coaxial alignment with the catheter to assist in seating the bioprosthesis frame paddles within the paddle attachment pockets.
11. Retract the catheter tip guide tube to set the bioprosthesis frame paddles into the paddle attachment pockets (*Figure 14*).

    Note: If the bioprosthesis frame paddles do not seat properly within the paddle attachment pockets upon retracting the catheter tip guide tube, slightly manipulate the position of the loading tool until paddle seating is achieved.

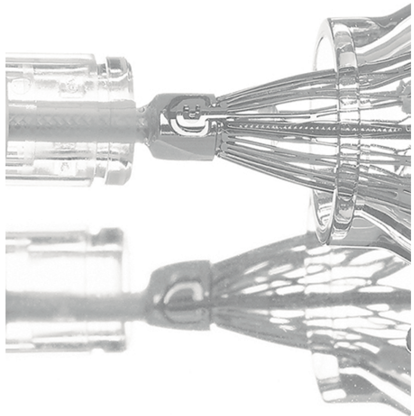
    Note: If necessary, it is acceptable to manually compress the bioprosthesis frame paddles with fingertips to help seat the paddles within the paddle attachment pockets.

Figure 14.



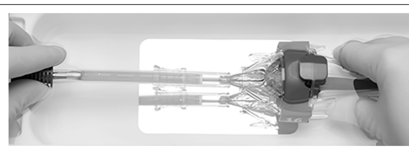
Note: Ensure both bioprosthesis frame paddles are completely seated within the paddle attachment pockets (*Figure 15*) before continuing to the next step.

Figure 15.



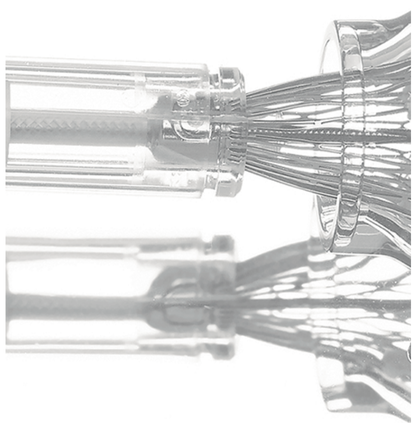
12. Hold the loading tool stationary with one hand, and with the other hand manually advance the capsule guide tube so that the distal section covers the paddle attachment pockets and the top portion of the outflow struts (*Figure 16*).

    Figure 16.

    Use the mirror to ensure that both bioprosthesis frame paddles are positioned correctly in the paddle attachment pockets and the outflow struts are within the distal tip of the capsule guide tube (*Figure 17*).

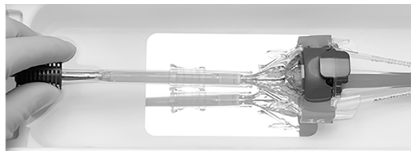
    Figure 17.

13. Advance the capsule to cover the bioprosthesis frame paddles (*Figure 18*), pausing when the capsule covers the proximal half of the paddles to confirm the paddles are both still properly seated before advancing further.

    Use the mirror to ensure that both paddles are captured in the capsule.

Figure 18.

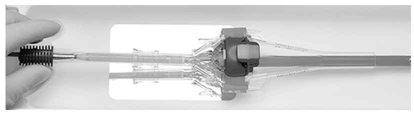


Caution: Do not advance the capsule over the bioprosthesis frame paddles unless they are fully seated in the center of the paddle attachment pockets. Advancing the capsule before the paddles are fully seated could damage the capsule and result in emboli.

14. Advance the capsule to capture the bioprosthesis outflow struts (*Figure 19*).

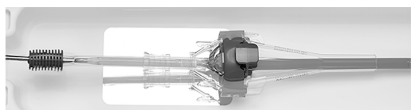
    Use the mirror to ensure that all bioprosthesis outflow struts are symmetrical and captured in the capsule.

Figure 19.



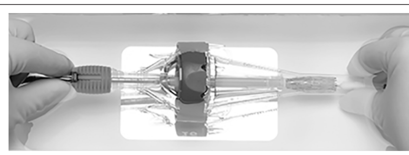
15. Continue to advance the capsule until the distal end of the capsule guide tube covers the distal end of the commissure pad of the bioprosthesis (*Figure 20*). The capsule guide tube should completely cover the commissure pad.

Figure 20.



16. Remove the backplate and the catheter tip guide tube from the outflow cone.
17. While holding the capsule guide tube stationary, advance the inflow cone to crimp the inflow portion of the bioprosthesis frame until the outflow cone contacts the capsule guide tube (*Figure 21*). During this step, the outflow cone contacts the locking collar component and moves the locking collar to the proximal end of the capsule guide tube.

Figure 21.



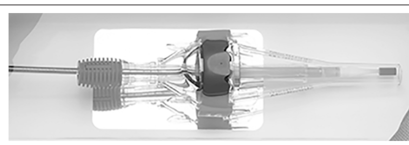
Note: The capsule guide tube will be in the unlocked configuration after this step.

Note: Ensure the bioprosthesis frame axis is visually aligned (coaxial) with the inflow cone axis during the insertion of the bioprosthesis into the inflow cone. Complete the insertion of the bioprosthesis into the inflow cone in one uninterrupted movement.

Caution: Do not attempt to direct load the valve (for example, loading the valve without completing Step 17 and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. **If a valve has been direct loaded, discard the entire system.** The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.

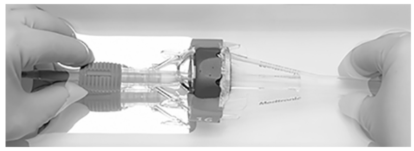
18. Advance the capsule over the bioprosthesis until the capsule comes within 5 mm of the catheter tip (*Figure 22*).

Figure 22.



19. Remove the capsule guide tube together with the outflow cone and inflow cone from the catheter (*Figure 23*).

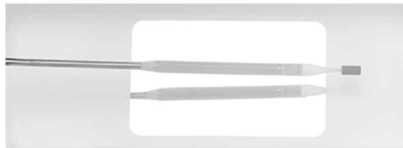
Figure 23.



20. Advance the capsule to close the gap between the capsule and catheter tip completely (*Figure 24*).

    Caution: Stop advancing the capsule once the gap to the catheter tip is closed. Advancing the capsule farther could damage the capsule.

    Figure 24.



21. Slightly rotate the deployment knob in the direction of the arrows to relieve stress. Ensure that the capsule does not separate from the catheter tip.

    Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.
22. Visually and tactilely inspect the capsule for a misloaded bioprosthesis. The capsule should be straight, smooth, and free of any bends, protrusions, or discolorations. If any of these conditions are felt or observed, the bioprosthesis is likely to be misloaded.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
23. Attach a 10 mL syringe filled with sterile saline to the stability layer flush port on the distal end of the handle and flush.
24. Remove the loading stylet from the guidewire lumen at the capsule.
25. Attach a 10 mL syringe filled with sterile saline to the wire lumen flush port on the proximal end of the handle and flush.
26. Attach a 10 mL syringe filled with sterile saline to the Evolut PRO+ inline sheath flush port and flush.
27. Before inserting into a patient, visually inspect the loaded bioprosthesis under fluoroscopy.

    Note: Complete fluoroscopy check under a magnified, high-resolution view over an area selected to not impede the clarity of the device.

    Note: Ensure the capsule is slowly rotated 360° during the fluoroscopy check.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
28. Leave the bioprosthesis submerged in sterile saline until implantation.

9.2 Bioprosthesis implantation

Note: Use systemic anticoagulation during the implantation procedure based on physician/clinical judgment. If heparin is contraindicated, consider an alternative anticoagulant.

9.2.1 Vascular access

Note: Vascular access should be achieved per standard practice (either percutaneously or via surgical cutdown).

Note: The primary access artery will be used to introduce the Evolut PRO+ device and, if predilatation is performed, the balloon catheter; the secondary access artery will be used to introduce the reference pigtail.

1. Establish a central venous line. Insert a temporary pacemaker lead via the right internal jugular vein (or other appropriate access vessel) per physician/clinical judgment.
2. Insert an introducer sheath into the secondary access artery.
3. Insert an introducer sheath into the primary access artery.
4. Administer anticoagulant according to physician/clinical judgment. If heparin is administered as an anticoagulant, check activated clotting time (ACT) and monitor every 30 minutes after initial bolus of heparin. Maintain ACT ≥250 seconds.

   Note: Anticoagulant may be administered at any time prior to this point, but avoid delaying beyond this point.

9.2.2 Crossing the valve

1. Advance the graduated pigtail catheter to the ascending aorta and position the distal tip in the noncoronary cusp of the aortic valve.
2. Identify the ideal annular viewing plane using contrast injections at various angiographic angles.

Note: It is recommended that a dedicated individual prepare and operate the contrast injector.

3. Insert an angiographic catheter over a standard J-tip guidewire into the primary access sheath and advance to the ascending aorta.
4. Exchange the J-tip guidewire for a 0.035 in (0.889 mm) straight-tip guidewire. Advance the straight-tip guidewire across the aortic valve into the left ventricle (LV).
5. After crossing the aortic valve with the guidewire, advance the angiographic catheter into the LV.
6. Exchange the straight-tip guidewire for an exchange length J-tip guidewire.
7. Exchange the angiographic catheter for a 6 Fr pigtail catheter.
8. Remove the guidewire and connect the catheter to the transducer. Using both catheters, record the aortic pressure gradient.
9. Using a right anterior oblique (RAO) projection, advance the previously pigtail-shaped, 0.035 in (0.889 mm) high support guidewire through the pigtail catheter and position in the apex of the LV.
10. Remove the pigtail catheter while maintaining guidewire position in the LV.

9.2.3 Predilatation of the implant site

Adequate predilatation can help reduce the need for post dilatation and may mitigate the occurrence of infolding.

Predilatation may also be useful to prepare the valve for crossing by the delivery catheter system and implantation of the transcatheter valve but may also confer some additional risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient.

The size and model of the predilatation BAV balloon should be selected such that it results in effective expansion and relief of the stenosis in the context of BAV to allow full expansion of the TAV upon implantation. Avoid balloon under sizing to ensure effective predilatation, therefore minimizing the risk of under expansion and infolding.

Notes:

- Predilatation is specifically recommended prior to implantation in the following situations:
  - Moderate-severe calcification
  - Bicuspid anatomy
  - Size 34 mm valve
- Utilize an adequate size balloon for effective predilatation, avoid under dilatation.

Information for failed surgical or transcatheter bioprosthetic valve: Balloon predilatation of a stenotic surgical or transcatheter aortic bioprosthetic valve has not been evaluated. In cases where there is severe stenosis, predilatation of the surgical or transcatheter aortic bioprosthetic valve may be done at the discretion of the heart team, and the steps used are identical to native valve predilatation.

1. Insert the valvuloplasty balloon through the introducer sheath in the primary access artery and advance it to the ascending aorta.
2. Reposition the angiographic equipment to the ideal viewing plane. Position the valvuloplasty balloon across the valve, while maintaining strict fluoroscopic surveillance of the distal tip of the guidewire in the LV.
3. Perform balloon valvuloplasty per standard practice and remove the valvuloplasty balloon while maintaining guidewire position across the aortic valve.

9.2.4 Deployment

1. Insert the device over the 0.035 in (0.889 mm) guidewire with the delivery catheter flush ports oriented at 3 o'clock (toward the left side of the patient) to better facilitate commissure alignment (flush ports shown in *Figure 2*, callouts 7 and 13). Insert the catheter tip and capsule through the access site, while maintaining the Evolut PRO+ inline sheath tip against the proximal end of the capsule. Then, insert the Evolut PRO+ inline sheath through the access site, maintaining contact with the capsule. When advancing the delivery system, allow the catheter handle to rotate freely after insertion of the system. Maintain strict fluoroscopic surveillance of the guidewire in the LV.

   Note: The 23-29 mm catheter model is compatible with introducer sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with introducer sheaths that can accommodate a 22 Fr (7.33 mm) device.

   Note: For transfemoral and subclavian access procedures, a separate introducer sheath is optional. For direct aortic access procedures, use a separate introducer sheath; do not use the Evolut PRO+ inline sheath. Maintain the Evolut PRO+ inline sheath at the proximal end of the catheter throughout the procedure.
2. Under fluoroscopic guidance, advance the catheter over the guidewire to the aortic annulus. To assist capsule advancement, the capsule orientation may be adjusted by rotating the handle a quarter turn before the capsule crosses into the arch. If adjustment to capsule orientation is required after crossing the arch, withdraw the system until the capsule is in the descending aorta and rotate the handle a quarter turn before readvancing.

Caution: Stop handle rotation if resistance is encountered or the capsule does not respond to rotation under fluoroscopic visualization. Do not rotate the handle when the capsule is at or beyond the arch. Continued attempts to rotate the capsule during resistance may result in product failure and/or patient harm.

Caution: There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).

Caution: Persistent force on the catheter can cause the catheter to kink, which could increase the risk of vascular complications (for example, vessel dissection or rupture).

Note: When crossing the aortic arch, it is critical that the guidewire is controlled to prevent it from moving forward. Without proper management of the distal tip of the guidewire, the guidewire could move forward and cause trauma to the LV.

3. Advance the device through the valve. Perform an angiogram to confirm that the pigtail catheter is in position within the noncoronary cusp of the aortic root. Fluoroscopically identify the appropriate landmarks.
4. Position the catheter so that the bioprosthesis is at the recommended target depth of 3 mm relative to the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture (*Section 9.2.5*).

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.
5. To deploy the bioprosthesis, rotate the deployment knob in the direction of the arrows. The capsule retracts and exposes the bioprosthesis. Continue deploying the bioprosthesis in a controlled manner, adjusting valve position as necessary and noting the position of the radiopaque capsule marker band and paddle attachment.

   Warning: 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.

   Note: Consider pacing to increase valve stability during deployment, especially in patients with larger anatomies. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.

   Note: Slight antegrade repositioning of a partially deployed bioprosthesis (before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment) can be achieved by carefully withdrawing the catheter.

   Caution: Use the catheter handle to reposition the bioprosthesis. **Do not** use the outer catheter shaft.
6. Before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, evaluate the bioprosthesis position.

   Note: When the bioprosthesis is approximately 2/3 deployed, the deployment knob provides a tactile indication as a notification before the point of no recapture. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture.
7. A right and left cusp overlap projection prior to deployment with a second radiographic view without parallax, may be useful to detect infolding, particularly in the presence of complex anatomies (bicuspid nature, severe calcification). An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.
   - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.
8. Either complete bioprosthesis deployment or initiate bioprosthesis recapture.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.5 Bioprosthesis recapture (optional)

The bioprosthesis is recapturable during deployment before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment. Deployment of the bioprosthesis can be attempted 3 times. If the bioprosthesis is recaptured a third time, it must be removed from the patient.

1. Rotate the deployment knob in the opposite direction of the arrows to recapture the bioprosthesis. A partially recaptured bioprosthesis can be repositioned or fully recaptured.

Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce the risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

Warning: 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.

2. To fully recapture the bioprosthesis, continue rotating the deployment knob until the gap between the capsule and catheter tip is closed.

   Caution: Stop advancing the capsule once the gap between the capsule and the catheter tip is closed. Advancing the capsule farther could damage the capsule.

3. Reposition the recaptured bioprosthesis at the recommended target depth of 3 mm relative to the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture.

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.

4. Redeploy the bioprosthesis (*Section 9.2.4*, *Step 5* and *Step 6*).
5. Monitor frame during recapture to detect any presence of infolding. An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.
   - Fully complete the recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.
6. Either complete bioprosthesis redeployment or initiate bioprosthesis recapture. If the bioprosthesis has been recaptured 3 times, withdraw the recaptured bioprosthesis.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.6 Postdeployment

1. Perform an angiogram to assess the location of the bioprosthesis.
2. Under fluoroscopic guidance, confirm that the catheter tip is coaxial with the inflow portion of the bioprosthesis.
3. Withdraw the catheter to the aorta while maintaining guidewire position.

   Note: For transfemoral access, withdraw the catheter until the catheter tip is positioned in the descending aorta. For direct aortic access and subclavian access, withdraw the catheter until the catheter tip is close to the distal tip of the introducer sheath.

4. Under fluoroscopic guidance, close the catheter capsule.

   Caution: Close the capsule until it is aligned with the catheter tip. Do not overcapture the catheter tip, because it could interfere with catheter withdrawal through the introducer sheath or cause vessel trauma upon removal.

   Caution: Ensure the capsule is closed before catheter removal.

   Caution: 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.

5. Withdraw the catheter until the capsule meets the distal end of the Evolut PRO+ inline sheath.

   Note: For direct aortic access procedures, maintain the Evolut PRO+ inline sheath at the proximal end of the catheter.

6. Withdraw the catheter and Evolut PRO+ inline sheath together. Dispose of the catheter and loading system in accordance with the applicable laws, regulations, and hospital procedures, including those regarding biohazards, microbial biohazards, and infectious substances.
7. Advance a 6 Fr pigtail catheter over the guidewire into the LV.
8. Remove the guidewire and connect the pigtail catheter to the transducer.
9. Using both pigtail catheters, record aortic pressure gradient.
10. Remove the 6 Fr pigtail over a standard, J-tip guidewire.
11. Perform a post-implant aortogram with the reference pigtail to ensure coronary patency and assess aortic regurgitations.
12. Remove the introducer sheath (if used) and complete the puncture site closure per standard practice.

13. Perform contrast angiography to verify the absence of any vascular complications.
14. Remove the reference pigtail catheter over a standard guidewire. Remove the 6 Fr introducer sheath and close the access site per standard practice.
15. Administer anticoagulation and/or antiplatelet therapy as required according to physician/clinical judgment.

9.2.7 Post implant dilatation

If valve function or sealing is impaired due to excessive calcification, bicuspid nature, incomplete expansion or infolding, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing.

1. **Cautions:**
   - Use caution when considering post dilatation in the presence of an infold to minimize dislodgement risk, particularly in the case of shallow implant depth. Consider pacing to increase valve stability, especially in patients with 34 mm valves. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.
   - Overexpansion of the narrowest portion (waist) of the Evolut PRO+ TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up. Multiple dilatations of the Evolut PRO+ TAV increases the risk of damage to the bioprosthetic leaflets.
   - Snares should be available to stabilize the bioprosthesis in the event of dislodgement following post implant dilatation.
2. Consider the precautions outlined in *Chapter 4* Warnings and Precautions when selecting the post implant dilatation balloon model, size, and applied inflation pressure.

10 Return of explanted bioprostheses

Medtronic is interested in obtaining recovered bioprostheses. Specific pathological studies of the explanted bioprosthesis will be conducted under the direction of a consulting pathologist. A written summary of the findings will be returned to the physician. To obtain a product return kit, contact a Medtronic distribution center or a Medtronic Representative. If a kit is not available, place the explanted bioprosthesis in a container of glutaraldehyde or 10% buffered formalin immediately after excision. For further instructions on the return of an explanted device, contact a Medtronic Representative.

11 Clinical studies

Information regarding clinical studies and post-approval studies that are applicable to Evolut PRO+ are available on the Medtronic Manual Library website:

1. Point your browser to www.medtronic.com/manuals.
2. Select the geography and language, and then search by product name for Evolut PRO+. The instructions for use and premarket and post-approval study summaries are listed. The clinical study summaries include the following: study name, applicable device, patient population and indication, sample size, and follow-up duration.

If you do not have web access, you can order printed copies of the clinical study summaries from your Medtronic representative or by calling the toll-free number located on the back cover.

12 Disclaimer of warranty

The following disclaimer of warranty applies to United States customers only:

DISCLAIMER OF WARRANTY

ALTHOUGH THE MEDTRONIC EVOLUT™ PRO+ TRANSCATHETER AORTIC VALVE (MODELS EVPROPLUS-23US, EVPROPLUS-26US, EVPROPLUS-29US, AND EVPROPLUS-34US), EVOLUT PRO+ DELIVERY CATHETER SYSTEM (MODEL D-EVPROP2329US AND D-EVPROP34US), EVOLUT PRO+ LOADING SYSTEM (MODELS L-EVPROP2329US AND L-EVPROP34US), HEREAFTER REFERRED TO AS “PRODUCT”, HAVE BEEN MANUFACTURED UNDER CAREFULLY CONTROLLED CONDITIONS, MEDTRONIC HAS NO CONTROL OVER THE CONDITIONS UNDER WHICH THIS PRODUCT IS USED. MEDTRONIC THEREFORE DISCLAIMS ALL WARRANTIES, BOTH EXPRESS AND IMPLIED, WITH RESPECT TO THE PRODUCT, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. MEDTRONIC SHALL NOT BE LIABLE TO ANY PERSON OR ENTITY FOR ANY MEDICAL EXPENSES OR ANY DIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES CAUSED BY ANY USE, DEFECT, FAILURE OR MALFUNCTION OF THE PRODUCT, WHETHER A CLAIM FOR SUCH DAMAGES IS BASED UPON WARRANTY, CONTRACT, TORT OR OTHERWISE. NO PERSON HAS ANY AUTHORITY TO BIND MEDTRONIC TO ANY REPRESENTATION OR WARRANTY WITH RESPECT TO THE PRODUCT.

The exclusions and limitations set out above are not intended to, and should not be construed so as to, contravene mandatory provisions of applicable law. If any part or term of this DISCLAIMER OF WARRANTY is held by any court of competent jurisdiction to be illegal, unenforceable or in conflict with applicable law, the validity of the remaining portion of the DISCLAIMER OF WARRANTY shall not be affected, and all rights and obligations shall be construed and enforced as if this DISCLAIMER OF WARRANTY did not contain the particular part or term held to be invalid.

13 Patents

Protected by one or more of the following United States Patents: 8,226,710 and 7,914,569.

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M987524A001

Medtronic

Evolut™ FX System

MR Evolut™ FX Transcatheter Aortic Valve

Evolut™ FX Delivery Catheter System

Evolut™ FX Loading System

Instructions for Use

! USA **Caution:** Federal law (USA) restricts this device to sale by or on the order of a physician.

Explanation of symbols on package labeling

	Use by
www.medtronic.com/manuals	Consult instructions for use at this website
	Do not reuse
STERILIZE	Do not resterilize
	Size
SN	Serial number
STERILE LC	Sterile LC: Device has been sterilized using liquid chemical sterilants according to EN/ISO 14160
REF	Catalog number
	Lower limit of temperature
	Quantity
LOT	Lot number
STERILE EO	Sterilized using ethylene oxide
	Nonpyrogenic
MR	MR Conditional
	Do not use if package is damaged
	Manufacturer
	Date of manufacture
Model	Model
! USA	For US audiences only
	Keep dry
	Keep away from sunlight
	Manufactured in
	Maximum guidewire diameter
BIO	Contains biological material of animal origin
	Single sterile barrier system
	Double sterile barrier system

UDI Unique Device Identifier

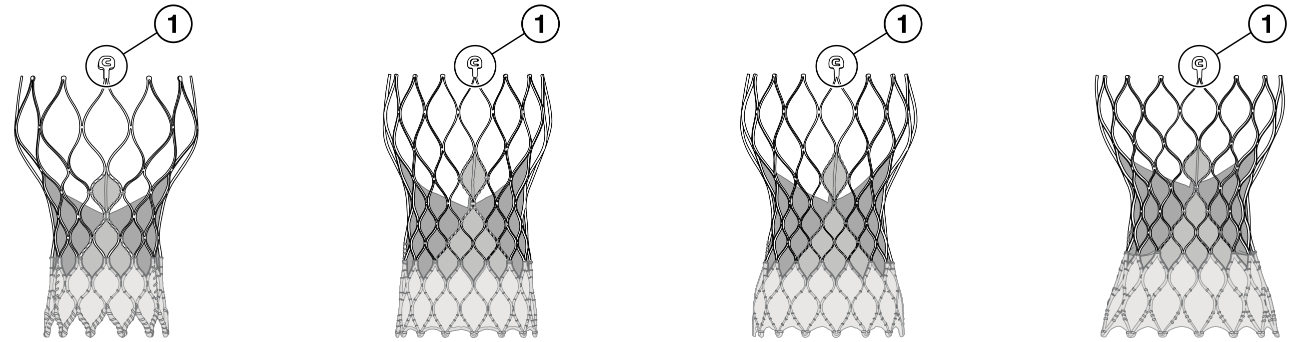
1 Device description

Caution: Implantation of the Medtronic Evolut FX system should be performed only by physicians who have received Medtronic Evolut FX training. These devices are supplied sterile for single use only. After use, dispose of the delivery catheter system and the loading system in accordance with local regulations and hospital procedures. Do not resterilize.

The Medtronic Evolut FX system is a recapturable transcatheter aortic valve replacement system, which includes the Evolut FX transcatheter aortic valve (bioprosthesis)[1], the delivery catheter system (catheter), and the loading system (LS).

1.1 Evolut FX transcatheter aortic valve (bioprosthesis)

Figure 1. Evolut FX transcatheter aortic valve (bioprosthesis)



23 mm 26 mm 29 mm 34 mm

1 "C" paddle

The bioprosthesis is manufactured by suturing 3 valve leaflets and an inner skirt, made from a single layer of porcine pericardium, onto a self-expanding, multi-level, radiopaque frame made of nitinol. The support frame includes three gold radiopaque markers approximately 3 mm from the inflow portion of the TAV frame, below the 3 tissue commissure pads. The bioprosthesis has a porcine pericardial tissue outer skirt (wrap), which is 1.5 cells in height and is sutured to the inflow section of the bioprosthesis. It is designed to replace the native, surgical bioprosthetic, or transcatheter bioprosthetic aortic heart valve without open heart surgery and without concomitant surgical removal of the failed valve.

Table 1. Heart valve materials

Component	Materials
Tissue	Processed porcine pericardium
Frame	Nitinol (a nickel titanium alloy)
Suture	Polyethylene[a]
Radiopaque markers	Gold

[a] The Evolut FX 23 mm valve also uses expanded polytetrafluoroethylene (ePTFE).

The bioprosthesis is processed with alpha-amino oleic acid (AOA™), which is a compound derived from oleic acid, a naturally occurring long-chain fatty acid. The bioprosthesis is available for a range of aortic annulus diameters (*Table 2*).

Table 2. Patient anatomical criteria

Bioprosthesis model	Size	Aortic annulus diameter[a]	Aortic annulus perimeter (π × aortic annulus diameter)[a]
EVOLUTFX-23	23 mm	17[b]/18 mm to 20 mm	53.4[b]/56.5 mm to 62.8 mm
EVOLUTFX-26	26 mm	20 mm to 23 mm	62.8 mm to 72.3 mm
EVOLUTFX-29	29 mm	23 mm to 26 mm	72.3 mm to 81.7 mm
EVOLUTFX-34	34 mm	26 mm to 30 mm	81.7 mm to 94.2 mm

[a] For TAV in SAV and TAV in TAV, diameter and perimeter criteria are applicable to the failed SAV or TAV measured inner diameter.
[b] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only.

[1] The terms "bioprosthesis" and "transcatheter aortic valve" are synonymous terms and are used interchangeably throughout the document to refer to the Evolut FX device.

1.2 Delivery catheter system (catheter)

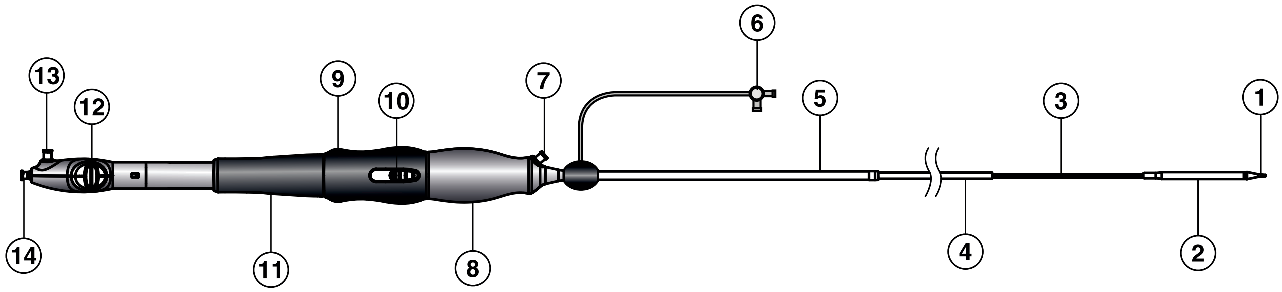
The catheter comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 2* and *Figure 3* for catheter components.

The catheter facilitates the placement of the bioprosthesis within the annulus of the aortic valve. The catheter assembly is flexible and compatible with a 0.035 in (0.889 mm) guidewire. The distal (deployment) end of the system features an atraumatic, radiopaque catheter tip and a capsule that covers and maintains the bioprosthesis in a crimped position. The capsule includes a distal flare to enable the bioprosthesis to be partially or fully recaptured after partial deployment. A green stability layer is fixed at the handle and extends down the outside of the catheter shaft. It provides a barrier between the retractable catheter and the introducer sheath and vessel walls, thus enabling the catheter to retract freely. An Evolut FX inline sheath is assembled over the stability layer, which functions as a hemostatic introducer sheath and minimizes the access site size to the capsule diameter. The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

The delivery catheter system consists of a catheter with an integrated handle to provide the user with accurate and controlled deployment. The handle is on the proximal end of the catheter and is used to load, deploy, recapture, and reposition the bioprosthesis. The handle features a gray front grip used to stabilize the system. The deployment knob turns to deploy the bioprosthesis precisely. Arrows on the deployment knob indicate the direction of rotation required to deploy the bioprosthesis. If desired, the deployment knob can be turned in the opposite direction to partially or fully recapture the bioprosthesis if the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture. The deployment knob also features a trigger, which can be engaged to make macro adjustments to the capsule position. A dark blue hand rest connects to the deployment knob. The end of the handle features a tip-retrieval mechanism, which can be used to withdraw the catheter tip to meet the capsule after the device has been fully deployed.

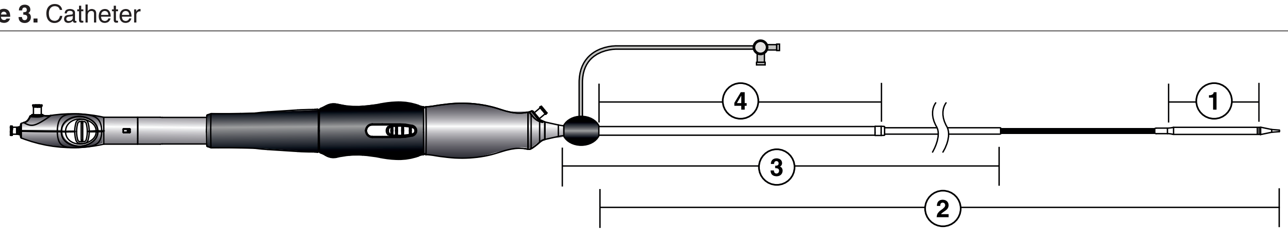
The catheter packaging contains an integrated loading bath and a removable tray with 3 rinsing bowls for loading and rinsing the bioprosthesis. The integrated loading bath features a mirror, which aids in accurate placement of the bioprosthesis frame paddles during loading. In addition to these features, the device packaging is swiveled and secured to facilitate the bioprosthesis loading procedure.

Figure 2. Catheter



1 Catheter tip
2 Capsule (Model D-EVOLUTFX-2329: 18 Fr [6.0 mm] outer diameter [OD]; Model D-EVOLUTFX-34: 22 Fr [7.33 mm] OD)
3 Catheter shaft
4 Stability layer
5 Model D-EVOLUTFX-2329: 14 Fr equivalent Evolut FX inline sheath (18 Fr [6.0 mm] OD); Model D-EVOLUTFX-34: 18 Fr equivalent Evolut FX inline sheath (22 Fr [7.33 mm] OD)
6 Evolut FX inline sheath flush port
7 Stability layer flush port
8 Gray front grip
9 Deployment knob
10 Trigger
11 Dark blue hand rest
12 Tip-retrieval mechanism
13 Capsule flush port
14 Wire lumen flush port

Figure 3. Catheter



1 7.6 cm (Model D-EVOLUTFX-2329); 7.7 cm (Model D-EVOLUTFX-34)
2 108 cm
3 90 cm
4 30 cm

Figure 4. Catheter distal tray

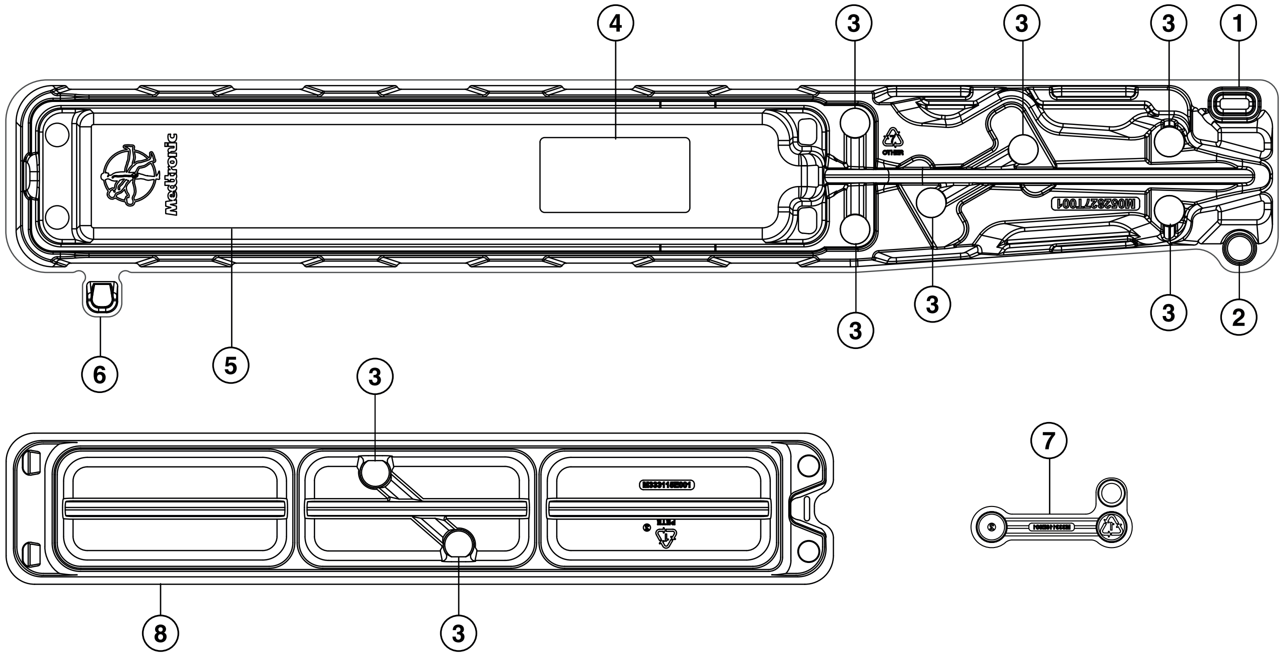
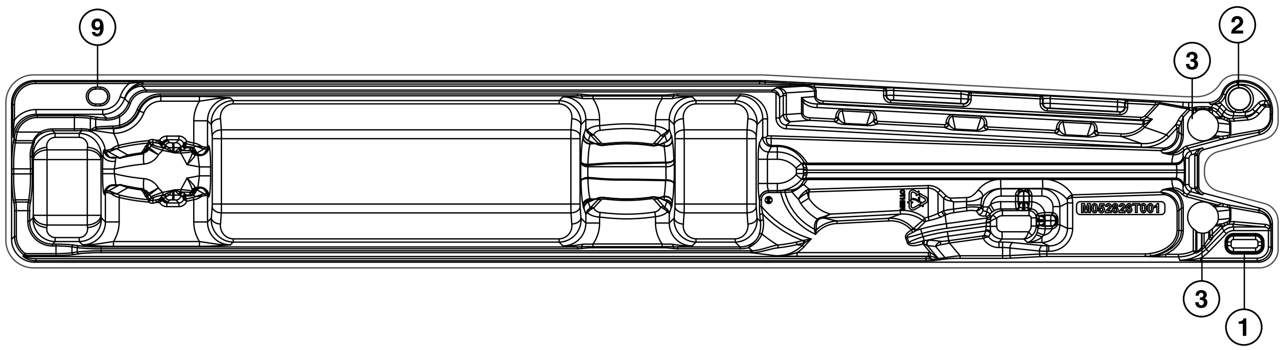


Figure 5. Catheter proximal tray

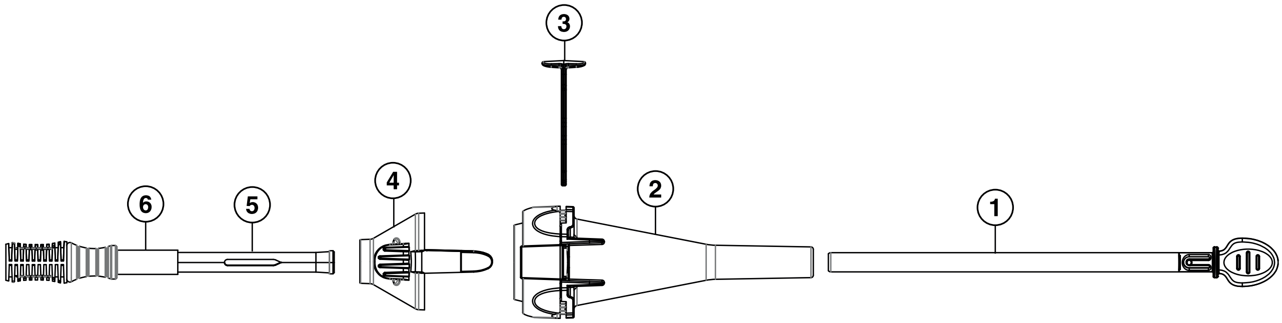


1 Tray connector
2 Swivel hinge
3 Clip holder
4 Mirror
5 Integrated loading bath
6 Tray tab
7 Locking clip
8 Rinsing bowls
9 Tray tab holder

1.3 Loading system (LS)

The loading system compresses the bioprosthesis into the catheter. The loading system comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 6* for components.

Figure 6. Evolut FX loading system



1 Catheter tip guide tube
2 Inflow cone
3 Backplate
4 Outflow cone
5 Capsule guide tube
6 Locking collar

Table 3. System compatibility

Bioprosthesis model	Compatible loading system models	Compatible catheter models
EVOLUTFX-23	L-EVOLUTFX-2329	D-EVOLUTFX-2329
EVOLUTFX-26		
EVOLUTFX-29		
EVOLUTFX-34	L-EVOLUTFX-34	D-EVOLUTFX-34

2 Indications

The Medtronic Evolut FX system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic Evolut FX system is indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical or transcatheter 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 (i.e., predicted risk of surgical mortality ≥8% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

3 Contraindications

The Evolut FX system is contraindicated in patients who cannot tolerate the device materials listed in *Table 1*, an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

4 Warnings and precautions

Carefully read all warnings, precautions, and instructions for use for all components of the system before use. Failure to read and follow all instructions or failure to observe all stated warnings could cause serious injury or death to the patient.

4.1 Warnings

General

- Implantation of the Medtronic Evolut FX system should be performed only by physicians who have received Medtronic Evolut FX training.
- The transcatheter aortic valve is to be used only in conjunction with the delivery catheter system and the loading system.
- System failure could occur if an incorrect combination of devices is used. Refer to *Table 3* for system compatibility.
- This procedure should only be performed where emergency aortic valve surgery can be performed promptly.
- **Do not** use any of the Medtronic Evolut FX system components if any of the following has occurred:
  - It has been dropped, damaged, or mishandled in any way
  - The Use By date has elapsed
- Mechanical failure of the delivery catheter system and/or accessories may result in patient complications.

Transcatheter aortic valve (bioprosthesis)

- **Do not** use the bioprosthesis if any of the following conditions is observed:
  - There is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket)
  - The serial number tag does not match the container label
  - The freeze indicator in the secondary package has activated
  - The storage solution does not completely cover the bioprosthesis
- Accelerated deterioration of the bioprosthesis due to calcific degeneration may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)

4.2 Precautions

General

- **Do not** contact any of the Medtronic Evolut FX system components with cotton or cotton swabs.
- **Do not** expose any of the Medtronic Evolut FX system components to organic solvents, such as alcohol.
- **Do not** introduce air into the catheter.
- **Do not** expose the bioprosthesis to solutions other than the storage and rinse solutions.
- **Do not** add antibiotics or any other substance to either the storage or rinse solutions. **Do not** apply antibiotics or any other substance to the bioprosthesis.
- **Do not** allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.
- **Do not** attempt to repair a damaged bioprosthesis.
- **Do not** handle or use forceps to manipulate the bioprosthesis leaflet tissue.
- **Do not** deform the bioprosthesis in excess of what is experienced during crimping, loading, and implantation.
- Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up.
- The safety and effectiveness of the Medtronic Evolut FX system 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:
  - Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined below:

    - **Symptomatic severe high-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2, a mean aortic valve gradient ≥40 mmHg, or a peak aortic-jet velocity ≥4.0 m/s

    - **Symptomatic severe low-flow/low-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2; a mean aortic valve gradient <40 mmHg; and a peak aortic-jet velocity <4.0 m/s
  - 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
  - Patients with liver failure (Child-Pugh Class C)
  - With cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
  - Patients who are pregnant or breastfeeding
- Implanting the Evolut FX bioprosthesis in a degenerated surgical bioprosthetic valve (transcatheter aortic valve in surgical aortic valve [TAV in SAV]) should be avoided in the following conditions. The degenerated surgical bioprosthetic valve presents with a:
  - Significant concomitant paravalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (for example, 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
- Before implanting the Evolut FX bioprosthesis in a degenerated transcatheter bioprosthetic valve (transcatheter aortic valve in transcatheter aortic valve [TAV in TAV]), additional factors regarding failed valve size and patient anatomy must be considered in order to ensure patient safety (for example, to avoid coronary obstruction). The potential need for future coronary access should be considered. TAV in TAV implantation should be avoided in the following conditions:
  - The degenerated TAV presents with a significant concomitant paravalvular leak (between the prosthesis and the native annulus),
  - The degenerated TAV is not securely fixed in the native annulus, or is not structurally intact (for example, frame fracture) or
  - The risk of coronary obstruction or sinus sequestration after Evolut FX bioprosthesis implantation is high

- 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/mm^3), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
  - Congenital unicuspid valve
  - Mixed native 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 >30 mm per the baseline diagnostic imaging or a surgical or transcatheter bioprosthetic aortic annulus size <17 mm or >30 mm
  - Transarterial access not able to accommodate the following:
    - 22 Fr introducer sheath or the 18 Fr equivalent Evolut FX inline sheath
    - 18 Fr introducer sheath or the 14 Fr equivalent Evolut FX inline sheath
  - Prohibitive left ventricular outflow tract calcification
  - Sinus of Valsalva anatomy that would prevent adequate coronary perfusion
  - Significant aortopathy requiring ascending aortic replacement
  - Moderate to severe mitral stenosis
  - Severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20%
  - Symptomatic carotid or vertebral artery disease
  - Severe basal septal hypertrophy with an outflow gradient
  - A known hypersensitivity or contraindication to any of the following that cannot be adequately pre-medicated:
    - Aspirin or heparin (HIT/HITTS) and bivalirudin
    - Ticlopidine and clopidogrel
    - Nitinol (titanium or nickel)
    - Gold
    - Contrast media

Before use

- Accelerated deterioration due to calcific degeneration of bioprostheses may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)
- 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 *Table 2* for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed in *Chapter 5*.
- Patients must present with transarterial access vessels with diameters that are ≥5.0 mm when using Model D-EVOLUTFX-2329 or ≥6.0 mm when using Model D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥60 mm from the basal plane.
- 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.
- For subclavian access, patients with a patent Left Internal Mammary Artery (LIMA) graft must present with access vessel diameters that are either ≥5.5 mm when using Model D-EVOLUTFX-2329 or ≥6.5 mm when using Model D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent Left Internal Mammary Artery (LIMA) graft (for left subclavian/axillary approach only) or patent Right Internal Mammary Artery (RIMA) graft (for right subclavian/axillary approach only).
- For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft.
- For transfemoral access, use caution in patients who present with multiplanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥2 of these factors are present, consider an alternative access route to prevent vascular complications.
- Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.
- Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water (minimum of 15 minutes). In the event of eye contact, flush with water for a minimum of 15 minutes and seek medical attention immediately.

- The bioprosthesis and the glutaraldehyde storage solution are **sterile**. The outside of the bioprosthesis container is **nonsterile** and must not be placed in the sterile field.
- 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.
- Before catheter insertion, remove the loading stylet.

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 Evolut FX inline sheath. Maintain the Evolut FX inline sheath at the proximal end of the catheter throughout the procedure.
- Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. No other solutions, drugs, chemicals, or antibiotics should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.
- During rinsing, do not touch the leaflets or squeeze the bioprosthesis.
- If a misload is detected during fluoroscopic (cine mode) inspection, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components. A misload is defined as one or more of the following:
  - Inflow crown overlap (non-uniform shadow starting at the inflow) that has not ended before the 4th node from the inflow.
  - Outflow crown misalignment and/or not parallel to the paddle attachment.
  - Curved or bent capsule.
  - Direct load as detailed in *Section 9.1.4*, *Step 17*.
  - Shadow or outline in outflow indicating a bent strut.
- Inflow crown overlap that has not ended before the 4th node within the capsule, increases the risk of an infold upon deployment in constrained anatomies, particularly with moderate-severe levels of calcification and/or bicuspid condition.
  - Do not attempt to direct load the valve (for example, loading the valve without completing *Step 17* in *Section 9.1.4* and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. If a valve has been direct loaded, discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
- Prevent contamination of the bioprosthesis, its storage solution, the catheter, and the loading system with glove powder.
- If a bioprosthesis and catheter have been removed from a patient, dispose of both the bioprosthesis and catheter; do not attempt to reuse either component. Both the bioprosthesis and catheter must be replaced with new sterile components.
- While the catheter is in the patient, ensure the guidewire is extending from the proximal end of the catheter. Do not remove the guidewire from the catheter while the catheter is inserted in the patient.
- There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).
- 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.
- From annular contact (or contact with the failed valve, for valve-in-valve procedures) to just before the point of no recapture, the bioprosthesis will occlude cardiac output. Promptly deploy or recapture the valve during this occlusive phase as prolonged obstruction or occlusion of blood flow may lead to hypotension, bradycardia, conduction disturbance, congestive heart failure, pulmonary edema, or death.
- If the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment, the bioprosthesis can be recaptured or repositioned. During deployment, the deployment knob provides a tactile indication as a notification before the point of no recapture.
- Infold detection steps are outlined in *Section 9.2.4*. An observation of any inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopic (cine mode) inspection, may indicate an infold. If identified, and if the patient's condition allows, do not proceed and do not release the valve.
  - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
  - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
  - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.

– If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.

- Implanting a valve with an unresolved infold increases the risk of PVL and need for post implant dilatation, which is associated with higher rates of adverse events such as dislodgement and dissection.

  Note: Predilatation may confer some risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient. For TAV in TAV procedures, the characteristics of the failed TAV (for example, under-expansion, depth of index implant) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and the treatment plan for each patient.
- 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 (for example, use of the catheter) 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.
- During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact (or contact with the failed valve, for valve-in-valve procedures) 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.

  Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

  Caution: Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath.
- Physicians should use judgment when considering repositioning a fully deployed bioprosthesis (for example, using a snare, balloon, and/or forceps). Repositioning the bioprosthesis is not recommended, except in cases where imminent serious harm or death is possible (for example, coronary occlusion). 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 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.
- 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. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term.

Post-implant balloon dilatation considerations

If valve function or sealing is impaired due to excessive calcification or incomplete expansion, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing. If the heart team determines that balloon dilatation is appropriate, consider all of the following factors when selecting the dilatation parameters to ensure patient safety:

- Balloon model
- Balloon size
- Balloon position
- Inflation pressure
- Patient anatomy

To mitigate trauma to the annulus or the Evolut FX TAV bioprosthetic leaflets, the maximum balloon size chosen for dilatation using a compliant, semi-compliant, or non-compliant balloon should not exceed the level set forth in *Table 4*, and the applied inflation pressure should be no greater than 2 atm.

Table 4. Post-implant balloon dilatation sizing

Evolut FX size	23 mm			26 mm				29 mm				34 mm				
Native annulus (failed SAV or TAV inner) diameter (in mm)	17[a]/18	19	20	20	21	22	23	23	24	25	26	26	27	28	29	30
TAV waist diameter (in mm)	20	20	20	22	22	22	22	23	23	23	23	24	24	24	24	24
Maximum balloon diameter (in mm) for compliant and semi-compliant balloons @ 2 atm	17[a]/18	19	20	20	21	22	23	23	24	25	26	26	27	28	28	28
Maximum balloon diameter (in mm) for non-compliant balloons @ 2 atm	16[a]/17	18	19	19	20	21	22	22	23	24	24	25	25	25	25	25

[a] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only

Caution: Overexpansion of the narrowest portion (waist) of the Evolut FX TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up.

It is important to note that the mechanical compliance properties of the selected balloon influence the dilatation dynamics.

Balloons should not be inflated beyond 2 atm of applied pressure.

The maximum balloon sizes in *Table 4* are derived from bench testing based on a single Evolut FX TAV dilation to 2 atm. Multiple dilations of the Evolut FX TAV increases the risk of damage to the bioprosthetic leaflets.

Compliant and semi-compliant (softer) balloons will more readily conform to the hourglass profile of the TAV bioprosthesis at lower pressures, but must be inflated at pressures that preserve the hourglass profile of the TAV.

Conversely, non-compliant (stiffer) balloons will achieve the nominal diameter during inflation irrespective of the underlying annulus or TAV resistance and should be downsized (see *Table 4*).

For additional instructions on the use of balloon catheter devices refer to the specific balloon catheter manufacturer's labeling.

In the event that larger balloon diameters than those listed in *Table 4* are required to expand the Evolut FX TAV due to clinically important residual aortic regurgitation or stenosis, using "bailout" intraventricular balloon positioning when performing PID avoids expansion of the narrowest portion (waist) of the Evolut FX TAV. This can mitigate the risk of leaflet damage. Dilatation with intraventricular balloon positioning should be performed with caution in the setting of a smaller ventricle cavity, presence of LVOT calcification, or wire positioning that interferes with mitral valve function, in order to avoid any unintended balloon interaction with anatomy. The balloon's length and diameter, along with the individual patient anatomy, must be considered. Care should also be taken not to exceed the annular diameters when performing PID with intraventricular balloon positioning (see *Table 4*).

In the event that a bailout PID with intraventricular balloon positioning is performed, the nominal diameter of the balloon should not exceed the annular diameter when using compliant or semi-compliant balloons; the nominal diameter of the balloon should be at least 1 mm smaller than the annular diameter when using non-compliant balloons.

4.3 Magnetic resonance imaging (MRI)

MRI may be used on the bioprosthesis only under specific conditions. See *Section 6.2*: MRI Safety Information for more information.

5 Potential adverse events

Potential risks associated with the implantation of the Evolut FX bioprosthesis 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 embolization
- Stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits
- 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 (for example, 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

General surgical risks applicable to transcatheter aortic valve implantation:

- Abnormal lab values (including electrolyte imbalance)
- Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- Exposure to radiation through fluoroscopy and angiography
- Permanent disability

6 Patient information

6.1 Registration information

! USA A patient registration form is included in each bioprosthesis package. After implantation, please complete all requested information. The serial number is located on both the package and the identification tag attached to the bioprosthesis. Return the original form to the Medtronic address indicated on the form and provide the temporary identification card to the patient prior to discharge.

! USA Medtronic will provide an Implanted Device Identification Card to the patient. The card contains the name and telephone number of the patient's physician as well as information that medical personnel would require in the event of an emergency. Patients should be encouraged to carry this card with them at all times.

6.2 MRI safety information

The MRI safety information for the Medtronic Evolut FX bioprosthesis is presented in *Table 5*.

Table 5. MRI safety information

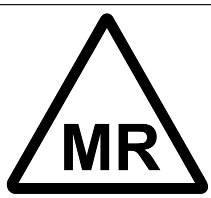
	A patient with the Medtronic Evolut FX bioprosthesis may be safely scanned under the following conditions, including immediately after placement of this device. Failure to follow these conditions may result in injury to the patient.
Name/Identification of the device	Evolut FX bioprosthesis
Nominal value of static magnetic field [T]	1.5 T or 3.0 T
Maximum spatial field gradient [T/m and gauss/cm]	30 T/m (3000 gauss/cm)
RF excitation	Circularly polarized (CP)
RF transmit coil type	Whole body transmit coil

Table 5. MRI safety information (continued)

Maximum whole body SAR [W/kg]	2 W/kg (Normal Operating Mode)
Maximum head SAR [W/kg]	3.2 W/kg (Normal Operating Mode)
Limits on scan duration	2 W/kg whole body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scan without breaks)
MR image artifact	The presence of this implant may produce an image artifact. Some manipulation of scan parameters may be needed to compensate for the artifact.
If information about a specific parameter is not included, there are no conditions associated with that parameter. The presence of other implants or medical circumstances of the patient may require lower limits on some or all of the above parameters. For deployment of a Medtronic Evolut FX bioprosthesis inside of a failed surgical or transcatheter bioprosthetic valve, consult the MRI labeling pertaining to the failed valve for additional artifact information.	

7 How supplied

7.1 Packaging

The bioprosthesis is supplied **sterile** and **nonpyrogenic** in a glass container and a screw cap with a liner. The outside of the container is **nonsterile** and must not be placed in the sterile field. A freeze indicator is placed inside the labeled carton. If the freeze indicator has been activated, do not use the bioprosthesis.

The catheter is packaged in a single-pouch configuration and sterilized with ethylene oxide gas. The catheter is sterile if the package is undamaged and unopened. The outer surfaces of the pouch are **nonsterile** and must not be placed in the sterile field.

The loading system is packaged in a double-pouch configuration. The loading system is sterile if the pouches are undamaged and unopened. The outer surfaces of the outer pouch are **nonsterile** and must not be placed in the sterile field. The loading system is sterilized with ethylene oxide gas.

7.2 Storage

Store the bioprosthesis at room temperature (5 °C to 25 °C [41 °F to 77 °F]). Avoid exposing to extreme fluctuations of temperature. Do not freeze. Appropriate inventory control should be maintained so that bioprostheses with earlier Use By dates are implanted preferentially.

Caution: Do not use the bioprosthesis if the freeze indicator in the secondary package has activated. If the freeze indicator has activated, dispose of the bioprosthesis in accordance with applicable laws, regulations, and hospital procedures.

Store the catheter and loading system at room temperature in a dry environment.

8 Additional equipment

Note: While extensive, this equipment list is not meant to cover all possible scenarios.

Transesophogeal echocardiogram (TEE) or transthoracic echocardiography (TTE) on standby

Temporary pacer insertion

- Temporary pacemaker lead
- Sterile sleeve for pacemaker lead
- Hemostatic vessel introducer sheath
- Temporary pacemaker generator
- Sterile temporary pacemaker-to-generator cable

If indicated, pulmonary artery catheter insertion

- Standard pulmonary artery catheter
- Hemostatic vessel introducer sheath
- Saline flush line connected to pressure transducer

Baseline aortography via radial, brachial, or femoral approach

- 5 Fr or 6 Fr pigtail angiographic catheter
- 6 Fr hemostatic vessel introducer sheath
- 2-port manifold with saline flush line and pressure tubing or transducer
- Power injector syringe
- Contrast media
- High-pressure power injector tubing

Predilatation of implant site

- 2-port manifold with saline flush and transducer
- 9 Fr hemostatic vessel introducer sheath and a 14 Fr, 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.
- Standard length 0.035 in (0.889 mm) straight guidewire
- Appropriate suture-mediated closure system, if applicable
- Angiographic catheter
- 0.035 in (0.889 mm) × 260 cm standard high support guidewire to be shaped with a pigtail loop
- Balloon valvuloplasty catheters, ≤4 cm length × 18 mm, 20 mm, 22 mm or 23 mm, and 25 mm, 28 mm, and 30 mm diameters
- Inflation device or syringe and diluted 1:5 contrast media

Bioprosthesis implantation

- 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

  Note: A separate introducer sheath is optional for transfemoral and subclavian access procedures.

Standby supplies (must be available in the room)

- Pericardiocentesis tray
- 35 mm × 120 cm single loop snare
- Standard percutaneous coronary intervention (PCI) equipment
- 14 Fr and 18 Fr hemostatic vessel introducer sheaths
- Standard cardiac catheterization lab equipment
- Intra-aortic balloon pump (IABP)

9 Instructions for use

9.1 Inspection and bioprosthesis loading procedure

Caution: Once the bioprosthesis is removed from its container and the catheter and loading system are removed from their packaging, ensure all subsequent procedures are performed in a sterile field.

Caution: Do not allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.

9.1.1 Inspection before use and swivel tray setup

1. Before removing the bioprosthesis, catheter, or loading system from its primary packaging, carefully inspect the packaging for any evidence of damage that could compromise the sterility or integrity of the device (for example, cracked jar or lid, leakage, broken or missing seals, torn or punctured pouch).

   Caution: Do not use after the Use By date or if there is evidence of damage.

   Caution: Do not use the bioprosthesis if the freeze indicator has been activated.
2. Remove the product from the protective package.
3. Visually check that the product is free of defects. Do not use if any defects are noted.
4. Remove the locking clip attached to the rinsing bowls.
5. Remove the rinsing bowls from the integrated loading bath.
6. Remove the locking clips that connect the distal and proximal trays.
7. Lift the tray connector from the distal tray, and swivel the distal tray 180° counterclockwise.
8. Clip the tray tab on the distal tray to the tray tab holder on the proximal tray.
9. Fill the integrated loading bath with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]).

9.1.2 Preparation of the catheter and loading system

1. Attach a 10 mL syringe filled with sterile saline to the capsule flush port on the proximal end of the handle. Leave the syringe in place until loading is complete.
2. Carefully lift the distal end of the catheter to a near vertical orientation. To prevent kinking, do not bend the catheter severely.
3. Open the capsule and expose the paddle attachment.

   Note: Use the deployment knob to open the capsule completely until the paddle attachment is fully exposed.

4. With the capsule held vertically, flush the capsule flush port. Verify that no catheter leakage is observed during any of the flushing steps. If leakage is observed, use a new system.
5. Submerge the capsule completely in the cold saline bath while flushing the capsule flush port. Continue flushing the capsule until it is completely submerged in the bath to prevent air from entering the catheter (*Figure 7*).

   Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.

   Figure 7.

   Note: The bioprosthesis, catheter, and LS may look slightly different from the figures in *Chapter 9*. The functionality of the system is the same.
6. Secure a locking clip in the clip holder to angle the catheter tip into the integrated loading bath.
7. Place the loading system components in the integrated loading bath.

9.1.3 Bioprosthesis rinsing procedure

1. Fill each of the 3 rinsing bowls (provided within the packaging) with approximately 500 mL of fresh, sterile saline at ambient temperature (15 °C to 25 °C [59 °F to 77 °F]).

   Caution: Do not handle or manipulate the bioprosthesis with sharp or pointed objects. Use atraumatic forceps only.
2. Confirm the integrity of the primary bioprosthesis container. Do not use the bioprosthesis if there is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket).
3. Remove the bioprosthesis from its container by carefully grasping one of the bioprosthesis frame paddles with a pair of blunt tipped forceps. Do not use the forceps to grasp the tissue portion of the bioprosthesis. Let any remaining solution drain from the bioprosthesis completely.

   Note: Retain the container with the original solution. It may be needed to store and return a rejected bioprosthesis.
4. Compare the serial number on the container with the serial number on the tag attached to the bioprosthesis.

   Caution: If the serial numbers do not match, do not use the bioprosthesis.
5. Carefully remove the serial number tag from the bioprosthesis and retain the tag.
6. Immerse the entire bioprosthesis in a sterile rinsing bowl.
7. Gently agitate the bioprosthesis by hand for 15 seconds to remove the glutaraldehyde from the bioprosthesis.
8. Repeat *Step 6* and *Step 7* in one of the remaining rinsing bowls.
9. Leave the bioprosthesis submerged in sterile saline in the third rinsing bowl until it is ready to be loaded.

9.1.4 Bioprosthesis loading procedure

Perform the bioprosthesis loading procedure while the distal end of the catheter is immersed in the integrated loading bath filled with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]). The bioprosthesis should remain immersed in saline during the loading process to minimize the introduction of air into the loaded system.

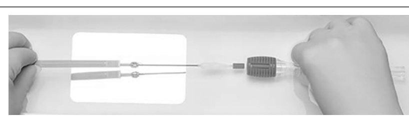
Note: Confirm the loading system and catheter sizes are compatible with the bioprosthesis size (*Table 3*).

Note: Refer to *Figure 6* for Evolut FX loading system components.

Caution: Rapid capsule advancement can contribute to difficulties with loading the valve and can increase the risk of damage to the catheter. Slowly advancing the capsule helps facilitate successful loading.

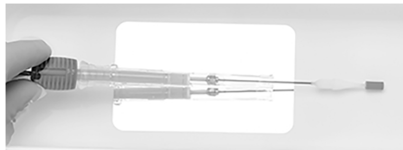
1. Submerge and cool the bioprosthesis in the integrated loading bath filled with cold, sterile saline.
2. Ensure that the capsule guide tube is fully open (unlocked) with the locking collar at the proximal end of the capsule guide tube (*Figure 8*).

   Figure 8.



3. Advance the capsule guide tube over the catheter shaft toward the handle and across the catheter tip (*Figure 9*).

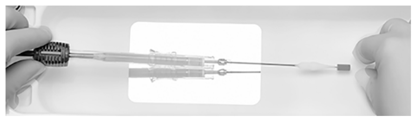
Figure 9.



4. Once the catheter tip has been crossed, fully advance the locking collar to the distal end of the capsule guide tube until it is closed (locked).
5. Continue to advance the capsule guide tube over the catheter shaft towards the handle until it contacts the distal end of the capsule (*Figure 10*).

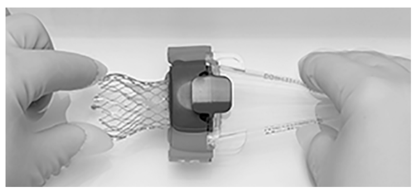
   Caution: Do not attempt to advance the capsule guide tube over the capsule; this will prevent the capsule flare from expanding fully and prevent proper loading.

   Figure 10.



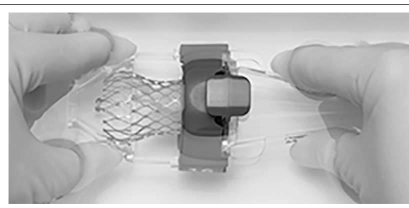
6. Ensure that the backplate has been inserted into the inflow cone and the exposed part of the backplate is facing up.
7. Insert the inflow portion of the bioprosthesis frame into the inflow cone. Ensure that the bioprosthesis frame paddle marked with a “C” is facing up and that the paddles are aligned with the paddle attachment pockets (*Figure 11*).

   Figure 11.



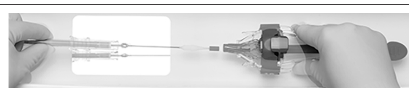
8. Secure the outflow cone onto the inflow cone (*Figure 12*) until it locks.

   Figure 12.



9. Insert the catheter tip guide tube completely into the distal end of the inflow cone (*Figure 13*). Inspect the outflow struts of the bioprosthesis and, if needed, manually manipulate so that they are evenly spaced and the bioprosthesis frame paddles are approximately 180° apart.

   Figure 13.



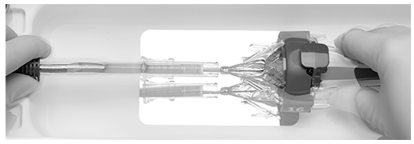
10. Insert the distal catheter tip into the catheter tip guide tube.

    Note: Allow the loading tool to rest on the loading bath floor to ensure coaxial alignment with the catheter to assist in seating the bioprosthesis frame paddles within the paddle attachment pockets.
11. Retract the catheter tip guide tube to set the bioprosthesis frame paddles into the paddle attachment pockets (*Figure 14*).

    Note: If the bioprosthesis frame paddles do not seat properly within the paddle attachment pockets upon retracting the catheter tip guide tube, slightly manipulate the position of the loading tool until paddle seating is achieved.

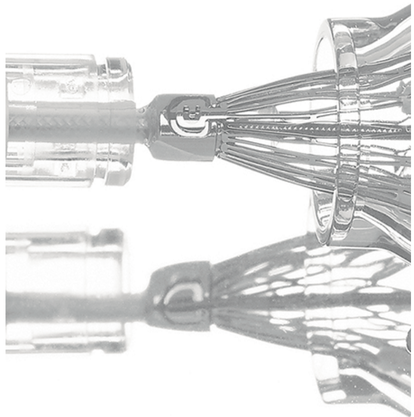
    Note: If necessary, it is acceptable to manually compress the bioprosthesis frame paddles with fingertips to help seat the paddles within the paddle attachment pockets.

Figure 14.



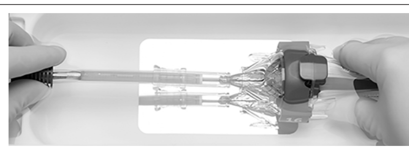
Note: Ensure both bioprosthesis frame paddles are completely seated within the paddle attachment pockets (*Figure 15*) before continuing to the next step.

Figure 15.



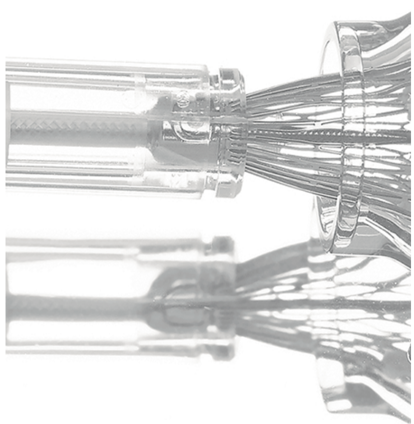
12. Hold the loading tool stationary with one hand, and with the other hand manually advance the capsule guide tube so that the distal section covers the paddle attachment pockets and the top portion of the outflow struts (*Figure 16*).

Figure 16.



Use the mirror to ensure that both bioprosthesis frame paddles are positioned correctly in the paddle attachment pockets and the outflow struts are within the distal tip of the capsule guide tube (*Figure 17*).

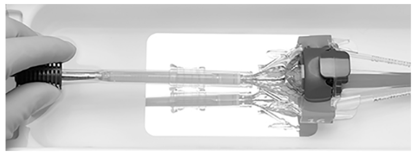
Figure 17.



13. Advance the capsule to cover the bioprosthesis frame paddles (*Figure 18*), pausing when the capsule covers the proximal half of the paddles to confirm the paddles are both still properly seated before advancing further.

    Use the mirror to ensure that both paddles are captured in the capsule.

Figure 18.

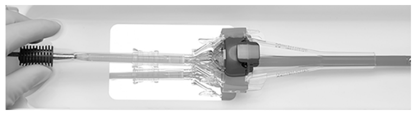


Caution: Do not advance the capsule over the bioprosthesis frame paddles unless they are fully seated in the center of the paddle attachment pockets. Advancing the capsule before the paddles are fully seated could damage the capsule and result in emboli.

14. Advance the capsule to capture the bioprosthesis outflow struts (*Figure 19*).

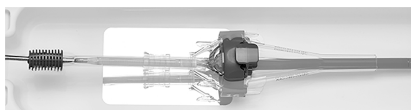
    Use the mirror to ensure that all bioprosthesis outflow struts are symmetrical and captured in the capsule.

    Figure 19.



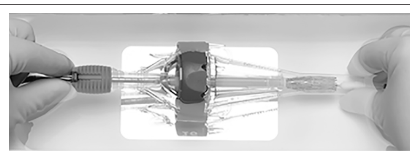
15. Continue to advance the capsule until the distal end of the capsule guide tube covers the distal end of the commissure pad of the bioprosthesis (*Figure 20*). The capsule guide tube should completely cover the commissure pad.

    Figure 20.



16. Remove the backplate and the catheter tip guide tube from the outflow cone.
17. While holding the capsule guide tube stationary, advance the inflow cone to crimp the inflow portion of the bioprosthesis frame until the outflow cone contacts the capsule guide tube (*Figure 21*). During this step, the outflow cone contacts the locking collar component and moves the locking collar to the proximal end of the capsule guide tube.

    Figure 21.



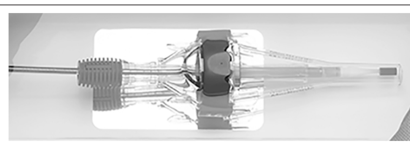
Note: The capsule guide tube will be in the unlocked configuration after this step.

Note: Ensure the bioprosthesis frame axis is visually aligned (coaxial) with the inflow cone axis during the insertion of the bioprosthesis into the inflow cone. Complete the insertion of the bioprosthesis into the inflow cone in one uninterrupted movement.

Caution: Do not attempt to direct load the valve (for example, loading the valve without completing Step 17 and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. **If a valve has been direct loaded, discard the entire system.** The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.

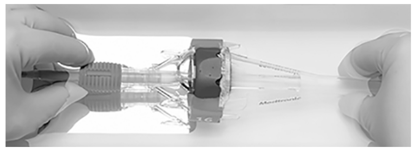
18. Advance the capsule over the bioprosthesis until the capsule comes within 5 mm of the catheter tip (*Figure 22*).

    Figure 22.



19. Remove the capsule guide tube together with the outflow cone and inflow cone from the catheter (*Figure 23*).

Figure 23.

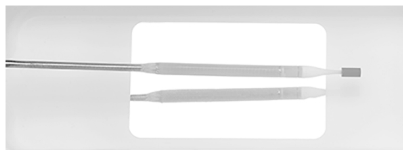


20. Slowly advance the capsule to close the gap between the capsule and catheter tip completely (*Figure 24*).

    Caution: Stop advancing the capsule once the gap to the catheter tip is closed. Advancing the capsule farther could damage the capsule.

    Note: If the deployment knob has reached the gray front grip and a gap exists between the capsule and the catheter tip, pause to allow any additional capsule movement to occur. If the gap remains, slowly continue rotating the deployment knob to advance the capsule one increment at a time, pausing between each increment.

    Figure 24.



21. Slightly rotate the deployment knob in the direction of the arrows to relieve stress. Ensure that the capsule does not separate from the catheter tip.

    Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.
22. Visually and tactilely inspect the capsule for a misloaded bioprosthesis. The capsule should be straight, smooth, and free of any bends, protrusions, or discolorations. If any of these conditions are felt or observed, the bioprosthesis is likely to be misloaded.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
23. Attach a 10 mL syringe filled with sterile saline to the stability layer flush port on the distal end of the handle and flush.
24. Remove the loading stylet from the guidewire lumen at the capsule.
25. Attach a 10 mL syringe filled with sterile saline to the wire lumen flush port on the proximal end of the handle and flush.
26. Attach a 10 mL syringe filled with sterile saline to the Evolut FX inline sheath flush port and flush.
27. Before inserting into a patient, visually inspect the loaded bioprosthesis under fluoroscopy.

    Note: Complete fluoroscopy check under a magnified, high-resolution view over an area selected to not impede the clarity of the device.

    Note: Ensure the capsule is slowly rotated 360° during the fluoroscopy check.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
28. Leave the bioprosthesis submerged in sterile saline until implantation.

9.2 Bioprosthesis implantation

Note: Use systemic anticoagulation during the implantation procedure based on physician/clinical judgment. If heparin is contraindicated, consider an alternative anticoagulant.

9.2.1 Vascular access

Note: Vascular access should be achieved per standard practice (either percutaneously or via surgical cutdown).

Note: The primary access artery will be used to introduce the Evolut FX device and, if predilatation is performed, the balloon catheter; the secondary access artery will be used to introduce the reference pigtail.

1. Establish a central venous line. Insert a temporary pacemaker lead via the right internal jugular vein (or other appropriate access vessel) per physician/clinical judgment.
2. Insert an introducer sheath into the secondary access artery.
3. Insert an introducer sheath into the primary access artery.
4. Administer anticoagulant according to physician/clinical judgment. If heparin is administered as an anticoagulant, check activated clotting time (ACT) and monitor every 30 minutes after initial bolus of heparin. Maintain ACT ≥250 seconds.

   Note: Anticoagulant may be administered at any time prior to this point, but avoid delaying beyond this point.

9.2.2 Crossing the valve

1. Advance the graduated pigtail catheter to the ascending aorta and position the distal tip in the noncoronary cusp of the aortic valve.
2. Identify the ideal annular viewing plane using contrast injections at various angiographic angles.

   Note: It is recommended that a dedicated individual prepare and operate the contrast injector.
3. Insert an angiographic catheter over a standard J-tip guidewire into the primary access sheath and advance to the ascending aorta.
4. Exchange the J-tip guidewire for a 0.035 in (0.889 mm) straight-tip guidewire. Advance the straight-tip guidewire across the aortic valve into the left ventricle (LV).
5. After crossing the aortic valve with the guidewire, advance the angiographic catheter into the LV.
6. Exchange the straight-tip guidewire for an exchange length J-tip guidewire.
7. Exchange the angiographic catheter for a 6 Fr pigtail catheter.
8. Remove the guidewire and connect the catheter to the transducer. Using both catheters, record the aortic pressure gradient.
9. Using a right anterior oblique (RAO) projection, advance the previously pigtail-shaped, 0.035 in (0.889 mm) high support guidewire through the pigtail catheter and position in the apex of the LV.
10. Remove the pigtail catheter while maintaining guidewire position in the LV.

9.2.3 Predilatation of the implant site

Adequate predilatation can help reduce the need for post dilatation and may mitigate the occurrence of infolding.

Predilatation may also be useful to prepare the valve for crossing by the delivery catheter system and implantation of the transcatheter valve but may also confer some additional risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient.

The size and model of the predilatation BAV balloon should be selected such that it results in effective expansion and relief of the stenosis in the context of BAV to allow full expansion of the TAV upon implantation. Avoid balloon under sizing to ensure effective predilatation, therefore minimizing the risk of under expansion and infolding.

Notes:

- Predilatation is specifically recommended prior to implantation in the following situations:
  - Moderate-severe calcification
  - Bicuspid anatomy
  - Size 34 mm valve
- Utilize an adequate size balloon for effective predilatation, avoid under dilatation.

Information for failed surgical or transcatheter bioprosthetic valve: Balloon predilatation of a stenotic surgical or transcatheter aortic bioprosthetic valve has not been evaluated. In cases where there is severe stenosis, predilatation of the surgical or transcatheter aortic bioprosthetic valve may be done at the discretion of the heart team, and the steps used are identical to native valve predilatation.

1. Insert the valvuloplasty balloon through the introducer sheath in the primary access artery and advance it to the ascending aorta.
2. Reposition the angiographic equipment to the ideal viewing plane. Position the valvuloplasty balloon across the valve, while maintaining strict fluoroscopic surveillance of the distal tip of the guidewire in the LV.
3. Perform balloon valvuloplasty per standard practice and remove the valvuloplasty balloon while maintaining guidewire position across the aortic valve.

9.2.4 Deployment

1. Insert the device over the 0.035 in (0.889 mm) guidewire with the delivery catheter flush ports oriented at 3 o'clock (toward the left side of the patient) to better facilitate commissure alignment (flush ports shown in *Figure 2*, callouts 7 and 13). Insert the catheter tip and capsule through the access site, while maintaining the Evolut FX inline sheath tip against the proximal end of the capsule. Then, insert the Evolut FX inline sheath through the access site, maintaining contact with the capsule. When advancing the delivery system, allow the catheter handle to rotate freely after insertion of the system. Maintain strict fluoroscopic surveillance of the guidewire in the LV.

   Note: The 23-29 mm catheter model is compatible with introducer sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with introducer sheaths that can accommodate a 22 Fr (7.33 mm) device.

   Note: For transfemoral and subclavian access procedures, a separate introducer sheath is optional. For direct aortic access procedures, use a separate introducer sheath; do not use the Evolut FX inline sheath. Maintain the Evolut FX inline sheath at the proximal end of the catheter throughout the procedure.

2. Under fluoroscopic guidance, advance the catheter over the guidewire to the aortic annulus. To assist capsule advancement or alignment, the capsule orientation may be adjusted by rotating the handle a quarter turn before the capsule crosses into the arch. If adjustment to capsule orientation is required after crossing the arch, withdraw the system until the capsule is in the descending aorta and rotate the handle a quarter turn before readvancing.

   Caution: Stop handle rotation if resistance is encountered or the capsule does not respond to rotation under fluoroscopic visualization. Do not rotate the handle when the capsule is at or beyond the arch. Continued attempts to rotate the capsule during resistance may result in product failure and/or patient harm.

   Caution: There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).

   Caution: Persistent force on the catheter can cause the catheter to kink, which could increase the risk of vascular complications (for example, vessel dissection or rupture).

   Note: When crossing the aortic arch, it is critical that the guidewire is controlled to prevent it from moving forward. Without proper management of the distal tip of the guidewire, the guidewire could move forward and cause trauma to the LV.

3. Advance the device through the valve. Perform an angiogram to confirm that the pigtail catheter is in position within the noncoronary cusp of the aortic root. Fluoroscopically identify the appropriate landmarks.

4. Position the catheter so that the bioprosthesis is at the recommended target depth of 3 mm relative to the valve annulus. Position the radiopaque markers at the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture (*Section 9.2.5*).

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.

5. To deploy the bioprosthesis, rotate the deployment knob in the direction of the arrows. The capsule retracts and exposes the bioprosthesis. Continue deploying the bioprosthesis in a controlled manner, adjusting valve position as necessary and noting the position of the radiopaque capsule marker band and paddle attachment. Position the bioprosthesis so that the radiopaque markers are at the level of the native valve annulus. Note that the radiopaque markers are 3 mm from the inflow tip of the bioprosthesis.

   Warning: 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.

   Note: Consider pacing to increase valve stability during deployment, especially in patients with larger anatomies. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.

   Note: Slight antegrade repositioning of a partially deployed bioprosthesis (before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment) can be achieved by carefully withdrawing the catheter.

   Caution: Use the catheter handle to reposition the bioprosthesis. **Do not** use the outer catheter shaft.

6. Before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, evaluate the bioprosthesis position by assessing the position of the radiopaque markers.

   Note: When the bioprosthesis is approximately 2/3 deployed, the deployment knob provides a tactile indication as a notification before the point of no recapture. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture.

7. A right and left cusp overlap projection prior to deployment with a second radiographic view without parallax, may be useful to detect infolding, particularly in the presence of complex anatomies (bicuspid nature, severe calcification). An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.
   - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.

8. Either complete bioprosthesis deployment or initiate bioprosthesis recapture.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.5 Bioprosthesis recapture (optional)

The bioprosthesis is recapturable during deployment before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment. Deployment of the bioprosthesis can be attempted 3 times. If the bioprosthesis is recaptured a third time, it must be removed from the patient.

1. Rotate the deployment knob in the opposite direction of the arrows to recapture the bioprosthesis. A partially recaptured bioprosthesis can be repositioned or fully recaptured.

   Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce the risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

   Warning: 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.
2. To fully recapture the bioprosthesis, continue rotating the deployment knob until the gap between the capsule and catheter tip is closed.

   Caution: Stop advancing the capsule once the gap between the capsule and the catheter tip is closed. Advancing the capsule farther could damage the capsule.
3. Reposition the recaptured bioprosthesis at the recommended target depth of 3 mm relative to the valve annulus. Position the radiopaque markers at the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture.

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.
4. Redeploy the bioprosthesis (*Section 9.2.4*, *Step 5* and *Step 6*).
5. Monitor frame during recapture to detect any presence of infolding. An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.
   - Fully complete the recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.
6. Either complete bioprosthesis redeployment or initiate bioprosthesis recapture. If the bioprosthesis has been recaptured 3 times, withdraw the recaptured bioprosthesis.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.6 Postdeployment

1. Perform an angiogram to assess the location of the bioprosthesis.
2. Under fluoroscopic guidance, confirm that the catheter tip is coaxial with the inflow portion of the bioprosthesis.
3. Withdraw the catheter to the aorta while maintaining guidewire position.

   Note: For transfemoral access, withdraw the catheter until the catheter tip is positioned in the descending aorta. For direct aortic access and subclavian access, withdraw the catheter until the catheter tip is close to the distal tip of the introducer sheath.
4. Under fluoroscopic guidance, close the catheter capsule.

   Caution: Close the capsule until it is aligned with the catheter tip. Do not overcapture the catheter tip, because it could interfere with catheter withdrawal through the introducer sheath or cause vessel trauma upon removal.

   Caution: Ensure the capsule is closed before catheter removal.

   Caution: 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.
5. Withdraw the catheter until the capsule meets the distal end of the Evolut FX inline sheath.

   Note: For direct aortic access procedures, maintain the Evolut FX inline sheath at the proximal end of the catheter.
6. Withdraw the catheter and Evolut FX inline sheath together. Dispose of the catheter and loading system in accordance with the applicable laws, regulations, and hospital procedures, including those regarding biohazards, microbial biohazards, and infectious substances.

7. Advance a 6 Fr pigtail catheter over the guidewire into the LV.
8. Remove the guidewire and connect the pigtail catheter to the transducer.
9. Using both pigtail catheters, record aortic pressure gradient.
10. Remove the 6 Fr pigtail over a standard, J-tip guidewire.
11. Perform a post-implant aortogram with the reference pigtail to ensure coronary patency and assess aortic regurgitations.
12. Remove the introducer sheath (if used) and complete the puncture site closure per standard practice.
13. Perform contrast angiography to verify the absence of any vascular complications.
14. Remove the reference pigtail catheter over a standard guidewire. Remove the 6 Fr introducer sheath and close the access site per standard practice.
15. Administer anticoagulation and/or antiplatelet therapy as required according to physician/clinical judgment.

9.2.7 Post implant dilatation

If valve function or sealing is impaired due to excessive calcification, bicuspid nature, incomplete expansion or infolding, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing.

1. **Cautions:**
   - Use caution when considering post dilatation in the presence of an infold to minimize dislodgement risk, particularly in the case of shallow implant depth. Consider pacing to increase valve stability, especially in patients with 34 mm valves. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.
   - Overexpansion of the narrowest portion (waist) of the Evolut FX TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up. Multiple dilatations of the Evolut FX TAV increases the risk of damage to the bioprosthetic leaflets.
   - Snares should be available to stabilize the bioprosthesis in the event of dislodgement following post implant dilatation.
2. Consider the precautions outlined in *Chapter 4* Warnings and Precautions when selecting the post implant dilatation balloon model, size, and applied inflation pressure.

10 Return of explanted bioprostheses

Medtronic is interested in obtaining recovered bioprostheses. Specific pathological studies of the explanted bioprosthesis will be conducted under the direction of a consulting pathologist. A written summary of the findings will be returned to the physician. To obtain a product return kit, contact a Medtronic distribution center or a Medtronic Representative. If a kit is not available, place the explanted bioprosthesis in a container of glutaraldehyde or 10% buffered formalin immediately after excision. For further instructions on the return of an explanted device, contact a Medtronic Representative.

11 Clinical studies

Information regarding clinical studies and post-approval studies that are applicable to Evolut FX are available on the Medtronic Manual Library website:

1. Point your browser to www.medtronic.com/manuals.
2. Select the geography and language, and then search by product name for Evolut FX. The instructions for use and premarket and post-approval study summaries are listed. The clinical study summaries include the following: study name, applicable device, patient population and indication, sample size, and follow-up duration.

If you do not have web access, you can order printed copies of the clinical study summaries from your Medtronic representative or by calling the toll-free number located on the back cover.

12 Disclaimer of warranty

The following disclaimer of warranty applies to United States customers only:

DISCLAIMER OF WARRANTY

ALTHOUGH THE MEDTRONIC EVOLUT™ FX TRANSCATHETER AORTIC VALVE (MODELS EVOLUTFX-23, EVOLUTFX-26, EVOLUTFX-29, AND EVOLUTFX-34), EVOLUT FX DELIVERY CATHETER SYSTEM (MODEL D-EVOLUTFX-2329 AND D-EVOLUTFX-34), EVOLUT FX LOADING SYSTEM (MODELS L-EVOLUTFX-2329 AND L-EVOLUTFX-34), HEREAFTER REFERRED TO AS "PRODUCT", HAVE BEEN MANUFACTURED UNDER CAREFULLY CONTROLLED CONDITIONS, MEDTRONIC HAS NO CONTROL OVER THE CONDITIONS UNDER WHICH THIS PRODUCT IS USED. MEDTRONIC THEREFORE DISCLAIMS ALL WARRANTIES, BOTH EXPRESS AND IMPLIED, WITH RESPECT TO THE PRODUCT, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR

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The exclusions and limitations set out above are not intended to, and should not be construed so as to, contravene mandatory provisions of applicable law. If any part or term of this DISCLAIMER OF WARRANTY is held by any court of competent jurisdiction to be illegal, unenforceable or in conflict with applicable law, the validity of the remaining portion of the DISCLAIMER OF WARRANTY shall not be affected, and all rights and obligations shall be construed and enforced as if this DISCLAIMER OF WARRANTY did not contain the particular part or term held to be invalid.

13 Patents

Protected by one or more of the following United States Patents: 8,226,710 and 7,914,569.

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Medtronic

Evolut™ FX+ System

MR Evolut™ FX+ Transcatheter Aortic Valve

Evolut™ FX Delivery Catheter System

Evolut™ FX Loading System

Instructions for Use

! USA **Caution:** Federal law (USA) restricts this device to sale by or on the order of a physician.

Explanation of symbols on package labeling

	Use-by date
	Consult instructions for use or consult electronic instructions for use
	Do not reuse
	Do not resterilize
	Size
SN	Serial number
STERILE LC	Sterile LC: Device has been sterilized using liquid chemical sterilants according to EN/ISO 14160
REF	Catalog number
	Lower limit of temperature
	Quantity
LOT	Lot number
STERILE EO	Sterilized using ethylene oxide
	Nonpyrogenic
	MR Conditional
	Do not use if package is damaged and consult instructions for use
	Manufacturer
	Date of manufacture
	Model
! USA	For US audiences only
	Keep dry
	Keep away from sunlight
	Manufactured in
	Maximum guidewire diameter
	Contains biological material of animal origin
	Single sterile barrier system
	Double sterile barrier system

UDI Unique Device Identifier

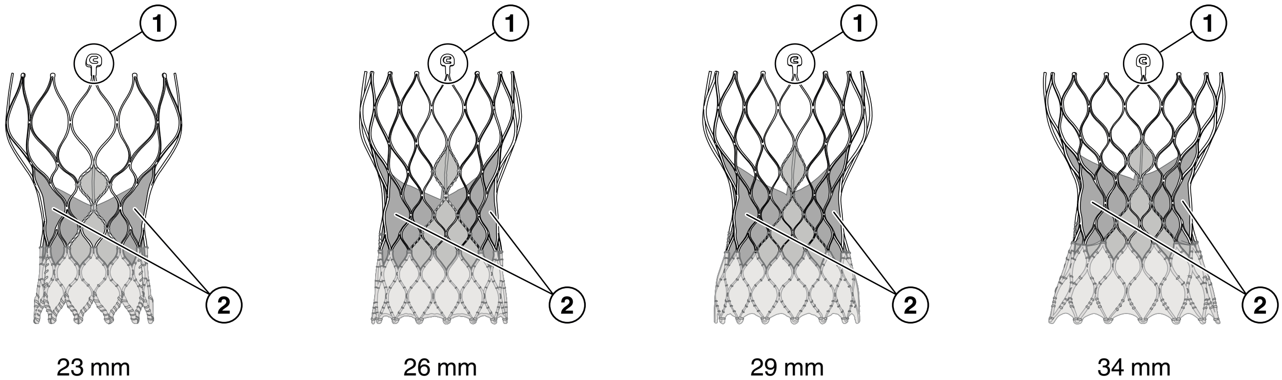
1 Device description

Caution: Implantation of the Medtronic Evolut FX+ system should be performed only by physicians who have received Medtronic Evolut FX+ training. These devices are supplied sterile for single use only. After use, dispose of the delivery catheter system and the loading system in accordance with local regulations and hospital procedures. Do not resterilize.

The Medtronic Evolut FX+ system is a recapturable transcatheter aortic valve replacement system, which includes the Evolut FX+ transcatheter aortic valve (bioprosthesis)[1], the delivery catheter system (catheter), and the loading system (LS).

1.1 Evolut FX+ transcatheter aortic valve (bioprosthesis)

Figure 1. Evolut FX+ transcatheter aortic valve (bioprosthesis)



1 “C” paddle
2 Windows

The bioprosthesis is manufactured by suturing 3 valve leaflets and an inner skirt, made from a single layer of porcine pericardium, onto a self-expanding, multi-level, radiopaque frame made of nitinol. The support frame includes three gold radiopaque markers approximately 3 mm from the inflow portion of the TAV frame, below the 3 tissue commissure pads. The support frame has expanded windows (*Figure 1*) behind each of the 3 valve leaflets for post implant access to the coronary ostia for potential future percutaneous coronary intervention (PCI). The bioprosthesis has a porcine pericardial tissue outer skirt (wrap), which is 1.5 cells in height and is sutured to the inflow section of the bioprosthesis. It is designed to replace the native, surgical bioprosthetic, or transcatheter bioprosthetic aortic heart valve without open heart surgery and without concomitant surgical removal of the failed valve.

Table 1. Heart valve materials

Component	Materials
Tissue	Processed porcine pericardium
Frame	Nitinol (a nickel titanium alloy)
Suture	Polyethylene[a]
Radiopaque markers	Gold

[a] The Evolut FX+ 23 mm valve also uses expanded polytetrafluoroethylene (ePTFE).

The bioprosthesis is processed with alpha-amino oleic acid (AOA™), which is a compound derived from oleic acid, a naturally occurring long-chain fatty acid. The bioprosthesis is available for a range of aortic annulus diameters (*Table 2*).

Table 2. Patient anatomical criteria

Bioprosthesis model	Size	Aortic annulus diameter[a]	Aortic annulus perimeter (π × aortic annulus diameter)[a]
EVFXPLUS-23	23 mm	17[b]/18 mm to 20 mm	53.4[b]/56.5 mm to 62.8 mm
EVFXPLUS-26	26 mm	20 mm to 23 mm	62.8 mm to 72.3 mm

[1] The terms “bioprosthesis” and “transcatheter aortic valve” are synonymous terms and are used interchangeably throughout the document to refer to the Evolut FX+ device.

Table 2. Patient anatomical criteria (continued)

Bioprosthesis model	Size	Aortic annulus diameter[a]	Aortic annulus perimeter (π × aortic annulus diameter)[a]
EVFXPLUS-29	29 mm	23 mm to 26 mm	72.3 mm to 81.7 mm
EVFXPLUS-34	34 mm	26 mm to 30 mm	81.7 mm to 94.2 mm

[a] For TAV in SAV and TAV in TAV, diameter and perimeter criteria are applicable to the failed SAV or TAV measured inner diameter.

[b] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only.

1.2 Delivery catheter system (catheter)

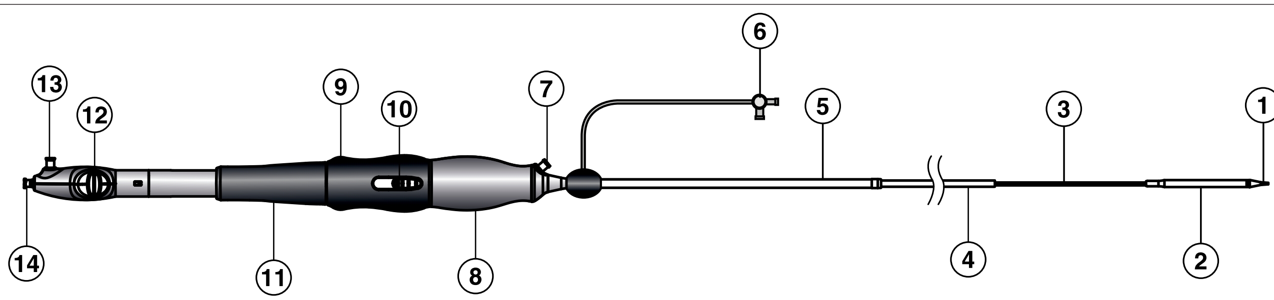
The catheter comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 2* and *Figure 3* for catheter components.

The catheter facilitates the placement of the bioprosthesis within the annulus of the aortic valve. The catheter assembly is flexible and compatible with a 0.035 in (0.889 mm) guidewire. The distal (deployment) end of the system features an atraumatic, radiopaque catheter tip and a capsule that covers and maintains the bioprosthesis in a crimped position. The capsule includes a distal flare to enable the bioprosthesis to be partially or fully recaptured after partial deployment. A green stability layer is fixed at the handle and extends down the outside of the catheter shaft. It provides a barrier between the retractable catheter and the introducer sheath and vessel walls, thus enabling the catheter to retract freely. An Evolut FX inline sheath is assembled over the stability layer, which functions as a hemostatic introducer sheath and minimizes the access site size to the capsule diameter. The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

The delivery catheter system consists of a catheter with an integrated handle to provide the user with accurate and controlled deployment. The handle is on the proximal end of the catheter and is used to load, deploy, recapture, and reposition the bioprosthesis. The handle features a gray front grip used to stabilize the system. The deployment knob turns to deploy the bioprosthesis precisely. Arrows on the deployment knob indicate the direction of rotation required to deploy the bioprosthesis. If desired, the deployment knob can be turned in the opposite direction to partially or fully recapture the bioprosthesis if the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture. The deployment knob also features a trigger, which can be engaged to make macro adjustments to the capsule position. A dark blue hand rest connects to the deployment knob. The end of the handle features a tip-retrieval mechanism, which can be used to withdraw the catheter tip to meet the capsule after the device has been fully deployed.

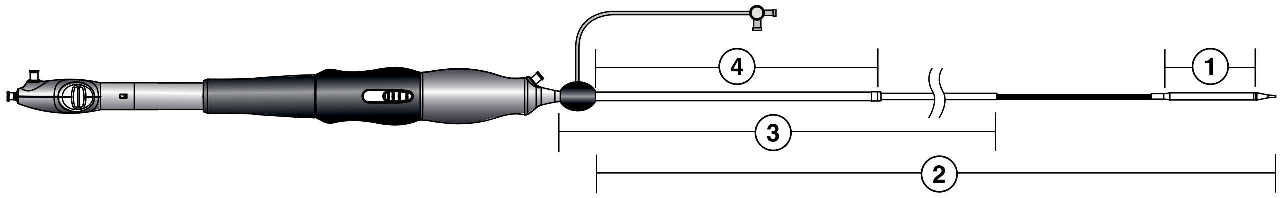
The catheter packaging contains an integrated loading bath and a removable tray with 3 rinsing bowls for loading and rinsing the bioprosthesis. The integrated loading bath features a mirror, which aids in accurate placement of the bioprosthesis frame paddles during loading. In addition to these features, the device packaging is swiveled and secured to facilitate the bioprosthesis loading procedure.

Figure 2. Catheter



1 Catheter tip
2 Capsule (Model D-EVOLUTFX-2329: 18 Fr [6.0 mm] outer diameter [OD]; Model D-EVOLUTFX-34: 22 Fr [7.33 mm] OD)
3 Catheter shaft
4 Stability layer
5 Model D-EVOLUTFX-2329: 14 Fr equivalent Evolut FX inline sheath (18 Fr [6.0 mm] OD); Model D-EVOLUTFX-34: 18 Fr equivalent Evolut FX inline sheath (22 Fr [7.33 mm] OD)
6 Evolut FX inline sheath flush port
7 Stability layer flush port
8 Gray front grip
9 Deployment knob
10 Trigger
11 Dark blue hand rest
12 Tip-retrieval mechanism
13 Capsule flush port
14 Wire lumen flush port

Figure 3. Catheter



1 7.6 cm (Model D-EVOLUTFX-2329); 7.7 cm (Model D-EVOLUTFX-34)
2 108 cm
3 90 cm
4 30 cm

Figure 4. Catheter distal tray

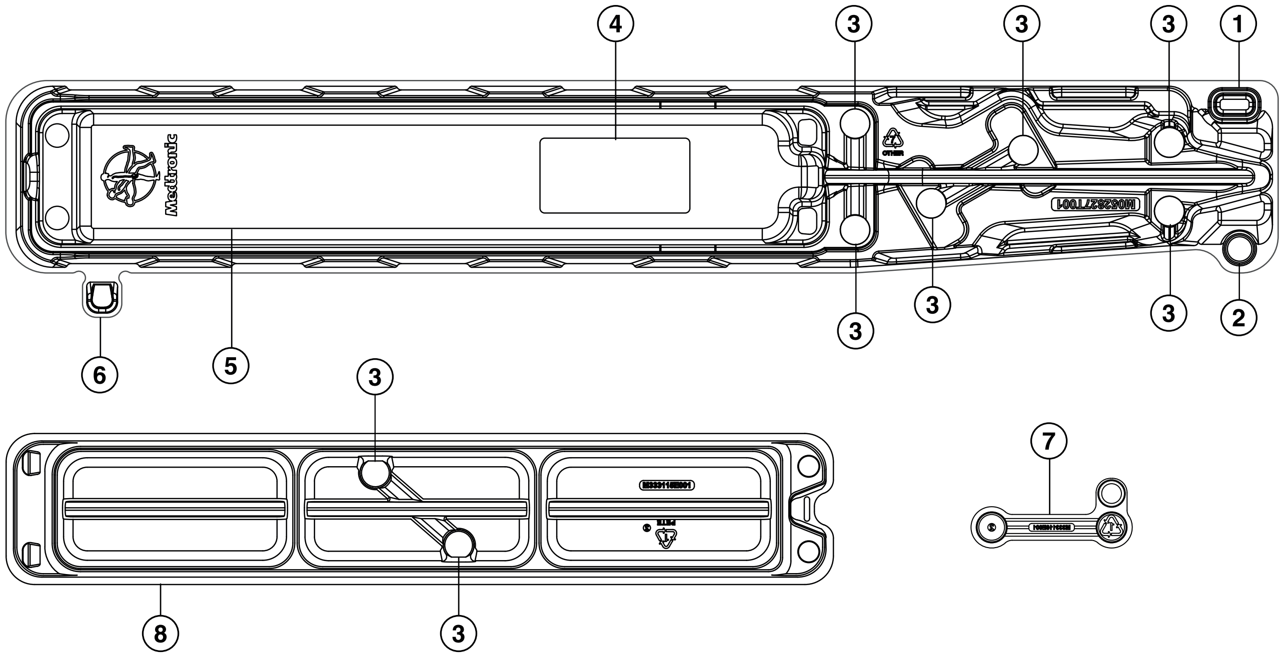
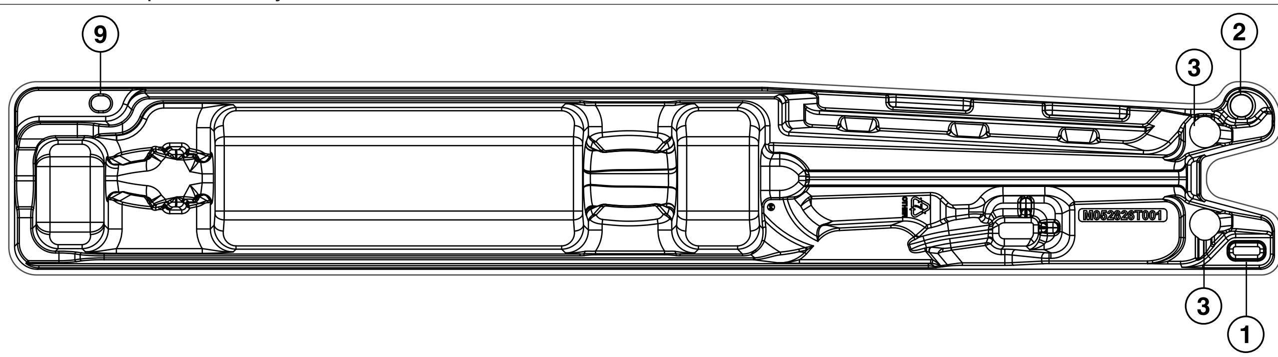


Figure 5. Catheter proximal tray

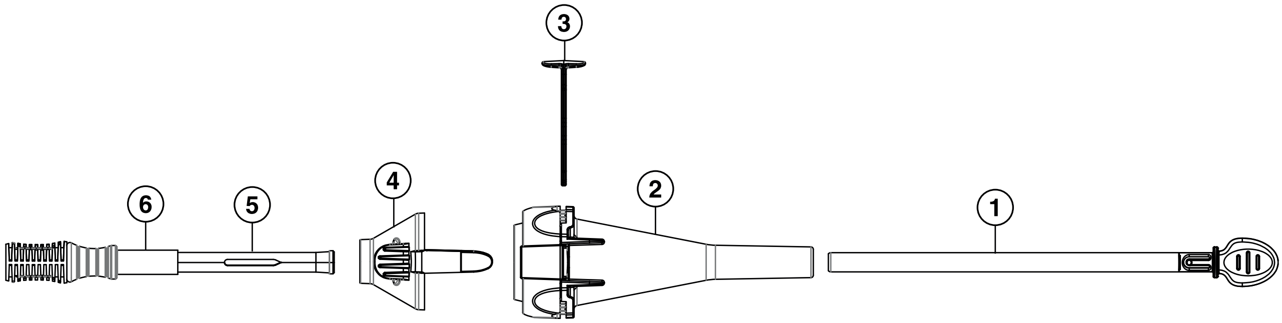


1 Tray connector
2 Swivel hinge
3 Clip holder
4 Mirror
5 Integrated loading bath
6 Tray tab
7 Locking clip
8 Rinsing bowls
9 Tray tab holder

1.3 Loading system (LS)

The loading system compresses the bioprosthesis into the catheter. The loading system comes in different sizes. Refer to *Table 3* for system compatibility. Refer to *Figure 6* for components.

Figure 6. Evolut FX loading system



1 Catheter tip guide tube
2 Inflow cone
3 Backplate
4 Outflow cone
5 Capsule guide tube
6 Locking collar

Table 3. System compatibility

Bioprosthesis model	Compatible loading system models	Compatible catheter models
EVFXPLUS-23	L-EVOLUTFX-2329	D-EVOLUTFX-2329
EVFXPLUS-26		
EVFXPLUS-29		
EVFXPLUS-34	L-EVOLUTFX-34	D-EVOLUTFX-34

2 Indications

The Medtronic Evolut FX+ system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic Evolut FX+ system is indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical or transcatheter 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 (i.e., predicted risk of surgical mortality ≥8% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

3 Contraindications

The Evolut FX+ system is contraindicated in patients who cannot tolerate the device materials listed in *Table 1*, an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

4 Warnings and precautions

Carefully read all warnings, precautions, and instructions for use for all components of the system before use. Failure to read and follow all instructions or failure to observe all stated warnings could cause serious injury or death to the patient.

4.1 Warnings

General

- Implantation of the Medtronic Evolut FX+ system should be performed only by physicians who have received Medtronic Evolut FX+ training.
- The transcatheter aortic valve is to be used only in conjunction with the delivery catheter system and the loading system.
- System failure could occur if an incorrect combination of devices is used. Refer to *Table 3* for system compatibility.
- This procedure should only be performed where emergency aortic valve surgery can be performed promptly.
- **Do not** use any of the Medtronic Evolut FX+ system components if any of the following has occurred:
  - It has been dropped, damaged, or mishandled in any way
  - The Use By date has elapsed
- Mechanical failure of the delivery catheter system and/or accessories may result in patient complications.

Transcatheter aortic valve (bioprosthesis)

- **Do not** use the bioprosthesis if any of the following conditions is observed:
  - There is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket)
  - The serial number tag does not match the container label
  - The freeze indicator in the secondary package has activated
  - The storage solution does not completely cover the bioprosthesis
- Accelerated deterioration of the bioprosthesis due to calcific degeneration may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)

4.2 Precautions

General

- **Do not** contact any of the Medtronic Evolut FX+ system components with cotton or cotton swabs.
- **Do not** expose any of the Medtronic Evolut FX+ system components to organic solvents, such as alcohol.
- **Do not** introduce air into the catheter.
- **Do not** expose the bioprosthesis to solutions other than the storage and rinse solutions.
- **Do not** add antibiotics or any other substance to either the storage or rinse solutions. **Do not** apply antibiotics or any other substance to the bioprosthesis.
- **Do not** allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.
- **Do not** attempt to repair a damaged bioprosthesis.
- **Do not** handle or use forceps to manipulate the bioprosthesis leaflet tissue.
- **Do not** deform the bioprosthesis in excess of what is experienced during crimping, loading, and implantation.
- Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up.
- The safety and effectiveness of the Medtronic Evolut FX+ system 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:
  - Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined below:
    - **Symptomatic severe high-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2, a mean aortic valve gradient ≥40 mmHg, or a peak aortic-jet velocity ≥4.0 m/s
    - **Symptomatic severe low-flow/low-gradient aortic stenosis:** aortic valve area ≤1.0 cm^2 or aortic valve area index ≤0.6 cm^2/m^2; a mean aortic valve gradient <40 mmHg; and a peak aortic-jet velocity <4.0 m/s
  - 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
  - Patients with liver failure (Child-Pugh Class C)
  - With cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
  - Patients who are pregnant or breastfeeding
- Implanting the Evolut FX+ bioprosthesis in a degenerated surgical bioprosthetic valve (transcatheter aortic valve in surgical aortic valve [TAV in SAV]) should be avoided in the following conditions. The degenerated surgical bioprosthetic valve presents with a:
  - Significant concomitant paravalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (for example, 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
- Before implanting the Evolut FX+ bioprosthesis in a degenerated transcatheter bioprosthetic valve (transcatheter aortic valve in transcatheter aortic valve [TAV in TAV]), additional factors regarding failed valve size and patient anatomy must be considered in order to ensure patient safety (for example, to avoid coronary obstruction). The potential need for future coronary access should be considered. TAV in TAV implantation should be avoided in the following conditions:
  - The degenerated TAV presents with a significant concomitant paravalvular leak (between the prosthesis and the native annulus),
  - The degenerated TAV is not securely fixed in the native annulus, or is not structurally intact (for example, frame fracture) or
  - The risk of coronary obstruction or sinus sequestration after Evolut FX+ bioprosthesis implantation is high

- 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/mm^3), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
  - Congenital unicuspid valve
  - Mixed native 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 >30 mm per the baseline diagnostic imaging or a surgical or transcatheter bioprosthetic aortic annulus size <17 mm or >30 mm
  - Transarterial access not able to accommodate the following:
    - 22 Fr introducer sheath or the 18 Fr equivalent Evolut FX inline sheath
    - 18 Fr introducer sheath or the 14 Fr equivalent Evolut FX inline sheath
  - Prohibitive left ventricular outflow tract calcification
  - Sinus of Valsalva anatomy that would prevent adequate coronary perfusion
  - Significant aortopathy requiring ascending aortic replacement
  - Moderate to severe mitral stenosis
  - Severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20%
  - Symptomatic carotid or vertebral artery disease
  - Severe basal septal hypertrophy with an outflow gradient
  - A known hypersensitivity or contraindication to any of the following that cannot be adequately pre-medicated:
    - Aspirin or heparin (HIT/HITTS) and bivalirudin
    - Ticlopidine and clopidogrel
    - Nitinol (titanium or nickel)
    - Gold
    - Contrast media

Before use

- Accelerated deterioration due to calcific degeneration of bioprostheses may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (for example, chronic renal failure, or hyperparathyroidism)
- 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 *Table 2* for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed in *Chapter 5*.
- Patients must present with transarterial access vessels with diameters that are ≥5.0 mm when using Model D-EVOLUTFX-2329 or ≥6.0 mm when using Model D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥60 mm from the basal plane.
- 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.
- For subclavian access, patients with a patent Left Internal Mammary Artery (LIMA) graft must present with access vessel diameters that are either ≥5.5 mm when using Model D-EVOLUTFX-2329 or ≥6.5 mm when using Model D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent Left Internal Mammary Artery (LIMA) graft (for left subclavian/axillary approach only) or patent Right Internal Mammary Artery (RIMA) graft (for right subclavian/axillary approach only).
- For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft.
- For transfemoral access, use caution in patients who present with multiplanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥2 of these factors are present, consider an alternative access route to prevent vascular complications.
- Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.
- Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water (minimum of 15 minutes). In the event of eye contact, flush with water for a minimum of 15 minutes and seek medical attention immediately.

- The bioprosthesis and the glutaraldehyde storage solution are **sterile**. The outside of the bioprosthesis container is **nonsterile** and must not be placed in the sterile field.
- 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.
- Before catheter insertion, remove the loading stylet.

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 Evolut FX inline sheath. Maintain the Evolut FX inline sheath at the proximal end of the catheter throughout the procedure.
- Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. No other solutions, drugs, chemicals, or antibiotics should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.
- During rinsing, do not touch the leaflets or squeeze the bioprosthesis.
- If a misload is detected during fluoroscopic (cine mode) inspection, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components. A misload is defined as one or more of the following:
  - Inflow crown overlap (non-uniform shadow starting at the inflow) that has not ended before the 4th node from the inflow.
  - Outflow crown misalignment and/or not parallel to the paddle attachment.
  - Curved or bent capsule.
  - Direct load as detailed in *Section 9.1.4*, *Step 17*.
  - Shadow or outline in outflow indicating a bent strut.
- Inflow crown overlap that has not ended before the 4th node within the capsule, increases the risk of an infold upon deployment in constrained anatomies, particularly with moderate-severe levels of calcification and/or bicuspid condition.
  - Do not attempt to direct load the valve (for example, loading the valve without completing *Step 17* in *Section 9.1.4* and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. If a valve has been direct loaded, discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
- Prevent contamination of the bioprosthesis, its storage solution, the catheter, and the loading system with glove powder.
- If a bioprosthesis and catheter have been removed from a patient, dispose of both the bioprosthesis and catheter; do not attempt to reuse either component. Both the bioprosthesis and catheter must be replaced with new sterile components.
- While the catheter is in the patient, ensure the guidewire is extending from the proximal end of the catheter. Do not remove the guidewire from the catheter while the catheter is inserted in the patient.
- There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).
- 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.
- From annular contact (or contact with the failed valve, for valve-in-valve procedures) to just before the point of no recapture, the bioprosthesis will occlude cardiac output. Promptly deploy or recapture the valve during this occlusive phase as prolonged obstruction or occlusion of blood flow may lead to hypotension, bradycardia, conduction disturbance, congestive heart failure, pulmonary edema, or death.
- If the radiopaque capsule marker band has not yet reached the distal end of the radiopaque paddle attachment, the bioprosthesis can be recaptured or repositioned. During deployment, the deployment knob provides a tactile indication as a notification before the point of no recapture.
- Infold detection steps are outlined in *Section 9.2.4*. An observation of any inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopic (cine mode) inspection, may indicate an infold. If identified, and if the patient's condition allows, do not proceed and do not release the valve.
  - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
  - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
  - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.

  - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.
- Implanting a valve with an unresolved infold increases the risk of PVL and need for post implant dilatation, which is associated with higher rates of adverse events such as dislodgement and dissection.

  Note: Predilatation may confer some risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient. For TAV in TAV procedures, the characteristics of the failed TAV (for example, under-expansion, depth of index implant) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and the treatment plan for each patient.
- 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 (for example, use of the catheter) 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.
- During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact (or contact with the failed valve, for valve-in-valve procedures) 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.

  Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

  Caution: Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath.
- Physicians should use judgment when considering repositioning a fully deployed bioprosthesis (for example, using a snare, balloon, and/or forceps). Repositioning the bioprosthesis is not recommended, except in cases where imminent serious harm or death is possible (for example, coronary occlusion). 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 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.
- 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. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term.

Post-implant balloon dilatation considerations

If valve function or sealing is impaired due to excessive calcification or incomplete expansion, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing. If the heart team determines that balloon dilatation is appropriate, consider all of the following factors when selecting the dilatation parameters to ensure patient safety:

- Balloon model
- Balloon size
- Balloon position
- Inflation pressure
- Patient anatomy

To mitigate trauma to the annulus or the Evolut FX+ TAV bioprosthetic leaflets, the maximum balloon size chosen for dilatation using a compliant, semi-compliant, or non-compliant balloon should not exceed the level set forth in *Table 4*, and the applied inflation pressure should be no greater than 2 atm.

Table 4. Post-implant balloon dilatation sizing

Evolut FX+ size	23 mm			26 mm				29 mm				34 mm				
Native annulus (failed SAV or TAV inner) diameter (in mm)	17[a]/18	19	20	20	21	22	23	23	24	25	26	26	27	28	29	30
TAV waist diameter (in mm)	20	20	20	22	22	22	22	23	23	23	23	24	24	24	24	24
Maximum balloon diameter (in mm) for compliant and semi-compliant balloons @ 2 atm	17[a]/18	19	20	20	21	22	23	23	24	25	25	26	27	28	28	28
Maximum balloon diameter (in mm) for non-compliant balloons @ 2 atm	16[a]/17	18	19	19	20	21	22	22	23	23	23	25	25	25	25	25

[a] Applicable to surgical aortic valves (SAV) and failed transcatheter aortic valves (TAV) only

Caution: Overexpansion of the narrowest portion (waist) of the Evolut FX+ TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up.

It is important to note that the mechanical compliance properties of the selected balloon influence the dilatation dynamics.

Balloons should not be inflated beyond 2 atm of applied pressure.

The maximum balloon sizes in *Table 4* are derived from bench testing based on a single Evolut FX+ TAV dilation to 2 atm. Multiple dilations of the Evolut FX+ TAV increases the risk of damage to the bioprosthetic leaflets.

Compliant and semi-compliant (softer) balloons will more readily conform to the hourglass profile of the TAV bioprosthesis at lower pressures, but must be inflated at pressures that preserve the hourglass profile of the TAV.

Conversely, non-compliant (stiffer) balloons will achieve the nominal diameter during inflation irrespective of the underlying annulus or TAV resistance and should be downsized (see *Table 4*).

For additional instructions on the use of balloon catheter devices refer to the specific balloon catheter manufacturer’s labeling.

In the event that larger balloon diameters than those listed in *Table 4* are required to expand the Evolut FX+ TAV due to clinically important residual aortic regurgitation or stenosis, using “bailout” intraventricular balloon positioning when performing PID avoids expansion of the narrowest portion (waist) of the Evolut FX+ TAV. This can mitigate the risk of leaflet damage. Dilatation with intraventricular balloon positioning should be performed with caution in the setting of a smaller ventricle cavity, presence of LVOT calcification, or wire positioning that interferes with mitral valve function, in order to avoid any unintended balloon interaction with anatomy. The balloon’s length and diameter, along with the individual patient anatomy, must be considered. Care should also be taken not to exceed the annular diameters when performing PID with intraventricular balloon positioning (see *Table 4*).

In the event that a bailout PID with intraventricular balloon positioning is performed, the nominal diameter of the balloon should not exceed the annular diameter when using compliant or semi-compliant balloons; the nominal diameter of the balloon should be at least 1 mm smaller than the annular diameter when using non-compliant balloons.

4.3 Magnetic resonance imaging (MRI)

MRI may be used on the bioprosthesis only under specific conditions. See *Section 6.2*: MRI Safety Information for more information.

5 Potential adverse events

Potential risks associated with the implantation of the Evolut FX+ bioprosthesis 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 embolization
- Stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits
- 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 (for example, 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

General surgical risks applicable to transcatheter aortic valve implantation:

- Abnormal lab values (including electrolyte imbalance)
- Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- Exposure to radiation through fluoroscopy and angiography
- Permanent disability

6 Patient information

6.1 Registration information

!USA A patient registration form is included in each bioprosthesis package. After implantation, please complete all requested information. The serial number is located on both the package and the identification tag attached to the bioprosthesis. Return the original form to the Medtronic address indicated on the form and provide the temporary identification card to the patient prior to discharge.

!USA Medtronic will provide an Implanted Device Identification Card to the patient. The card contains the name and telephone number of the patient's physician as well as information that medical personnel would require in the event of an emergency. Patients should be encouraged to carry this card with them at all times.

6.2 MRI safety information

The MRI safety information for the Medtronic Evolut FX+ bioprosthesis is presented in *Table 5*.

Table 5. MRI safety information

MR	A patient with the Medtronic Evolut FX+ bioprosthesis may be safely scanned under the following conditions, including immediately after placement of this device. Failure to follow these conditions may result in injury to the patient.
Name/Identification of the device	Evolut FX+ bioprosthesis
Nominal value of static magnetic field [T]	1.5 T or 3.0 T
Maximum spatial field gradient [T/m and gauss/cm]	30 T/m (3000 gauss/cm)
RF excitation	Circularly polarized (CP)
RF transmit coil type	Whole body transmit coil

Table 5. MRI safety information (continued)

Maximum whole body SAR [W/kg]	2 W/kg (Normal Operating Mode)
Maximum head SAR [W/kg]	3.2 W/kg (Normal Operating Mode)
Limits on scan duration	2 W/kg whole body average SAR for 60 minutes of continuous RF (a sequence or back-to-back series/scan without breaks)
MR image artifact	The presence of this implant may produce an image artifact. Some manipulation of scan parameters may be needed to compensate for the artifact.
If information about a specific parameter is not included, there are no conditions associated with that parameter. The presence of other implants or medical circumstances of the patient may require lower limits on some or all of the above parameters. For deployment of a Medtronic Evolut FX+ bioprosthesis inside of a failed surgical or transcatheter bioprosthetic valve, consult the MRI labeling pertaining to the failed valve for additional artifact information.	

7 How supplied

7.1 Packaging

The bioprosthesis is supplied **sterile** and **nonpyrogenic** in a glass container and a screw cap with a liner. The outside of the container is **nonsterile** and must not be placed in the sterile field. A freeze indicator is placed inside the labeled carton. If the freeze indicator has been activated, do not use the bioprosthesis.

The catheter is packaged in a single-pouch configuration and sterilized with ethylene oxide gas. The catheter is sterile if the package is undamaged and unopened. The outer surfaces of the pouch are **nonsterile** and must not be placed in the sterile field.

The loading system is packaged in a double-pouch configuration. The loading system is sterile if the pouches are undamaged and unopened. The outer surfaces of the outer pouch are **nonsterile** and must not be placed in the sterile field. The loading system is sterilized with ethylene oxide gas.

7.2 Storage

Store the bioprosthesis at room temperature (5 °C to 25 °C [41 °F to 77 °F]). Avoid exposing to extreme fluctuations of temperature. Do not freeze. Appropriate inventory control should be maintained so that bioprostheses with earlier Use By dates are implanted preferentially.

Caution: Do not use the bioprosthesis if the freeze indicator in the secondary package has activated. If the freeze indicator has activated, dispose of the bioprosthesis in accordance with applicable laws, regulations, and hospital procedures.

Store the catheter and loading system at room temperature in a dry environment.

8 Additional equipment

Note: While extensive, this equipment list is not meant to cover all possible scenarios.

Transesophogeal echocardiogram (TEE) or transthoracic echocardiography (TTE) on standby

Temporary pacer insertion

- Temporary pacemaker lead
- Sterile sleeve for pacemaker lead
- Hemostatic vessel introducer sheath
- Temporary pacemaker generator
- Sterile temporary pacemaker-to-generator cable

If indicated, pulmonary artery catheter insertion

- Standard pulmonary artery catheter
- Hemostatic vessel introducer sheath
- Saline flush line connected to pressure transducer

Baseline aortography via radial, brachial, or femoral approach

- 5 Fr or 6 Fr pigtail angiographic catheter
- 6 Fr hemostatic vessel introducer sheath
- 2-port manifold with saline flush line and pressure tubing or transducer
- Power injector syringe
- Contrast media
- High-pressure power injector tubing

Predilatation of implant site

- 2-port manifold with saline flush and transducer
- 9 Fr hemostatic vessel introducer sheath and a 14 Fr, 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.
- Standard length 0.035 in (0.889 mm) straight guidewire
- Appropriate suture-mediated closure system, if applicable
- Angiographic catheter
- 0.035 in (0.889 mm) × 260 cm standard high support guidewire to be shaped with a pigtail loop
- Balloon valvuloplasty catheters, ≤4 cm length × 18 mm, 20 mm, 22 mm or 23 mm, and 25 mm, 28 mm, and 30 mm diameters
- Inflation device or syringe and diluted 1:5 contrast media

Bioprosthesis implantation

- 18 Fr or 22 Fr hemostatic vessel introducer sheath

  Note: The 23-29 mm catheter model is compatible with sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with sheaths that can accommodate a 22 Fr (7.33 mm) device.

  Note: A separate introducer sheath is optional for transfemoral and subclavian access procedures.

Standby supplies (must be available in the room)

- Pericardiocentesis tray
- 35 mm × 120 cm single loop snare
- Standard percutaneous coronary intervention (PCI) equipment
- 14 Fr and 18 Fr hemostatic vessel introducer sheaths
- Standard cardiac catheterization lab equipment
- Intra-aortic balloon pump (IABP)

9 Instructions for use

9.1 Inspection and bioprosthesis loading procedure

Caution: Once the bioprosthesis is removed from its container and the catheter and loading system are removed from their packaging, ensure all subsequent procedures are performed in a sterile field.

Caution: Do not allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.

9.1.1 Inspection before use and swivel tray setup

1. Before removing the bioprosthesis, catheter, or loading system from its primary packaging, carefully inspect the packaging for any evidence of damage that could compromise the sterility or integrity of the device (for example, cracked jar or lid, leakage, broken or missing seals, torn or punctured pouch).

   Caution: Do not use after the Use By date or if there is evidence of damage.

   Caution: Do not use the bioprosthesis if the freeze indicator has been activated.
2. Remove the product from the protective package.
3. Visually check that the product is free of defects. Do not use if any defects are noted.
4. Remove the locking clip attached to the rinsing bowls.
5. Remove the rinsing bowls from the integrated loading bath.
6. Remove the locking clips that connect the distal and proximal trays.
7. Lift the tray connector from the distal tray, and swivel the distal tray 180° counterclockwise.
8. Clip the tray tab on the distal tray to the tray tab holder on the proximal tray.
9. Fill the integrated loading bath with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]).

9.1.2 Preparation of the catheter and loading system

1. Attach a 10 mL syringe filled with sterile saline to the capsule flush port on the proximal end of the handle. Leave the syringe in place until loading is complete.
2. Carefully lift the distal end of the catheter to a near vertical orientation. To prevent kinking, do not bend the catheter severely.
3. Open the capsule and expose the paddle attachment.

   Note: Use the deployment knob to open the capsule completely until the paddle attachment is fully exposed.

4. With the capsule held vertically, flush the capsule flush port. Verify that no catheter leakage is observed during any of the flushing steps. If leakage is observed, use a new system.
5. Submerge the capsule completely in the cold saline bath while flushing the capsule flush port. Continue flushing the capsule until it is completely submerged in the bath to prevent air from entering the catheter (*Figure 7*).

   Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.

   Figure 7.

   Note: The bioprosthesis, catheter, and LS may look slightly different from the figures in *Chapter 9*. The functionality of the system is the same.
6. Secure a locking clip in the clip holder to angle the catheter tip into the integrated loading bath.
7. Place the loading system components in the integrated loading bath.

9.1.3 Bioprosthesis rinsing procedure

1. Fill each of the 3 rinsing bowls (provided within the packaging) with approximately 500 mL of fresh, sterile saline at ambient temperature (15 °C to 25 °C [59 °F to 77 °F]).

   Caution: Do not handle or manipulate the bioprosthesis with sharp or pointed objects. Use atraumatic forceps only.
2. Confirm the integrity of the primary bioprosthesis container. Do not use the bioprosthesis if there is any damage to the container (for example, cracked jar or lid, leakage, particulate material, broken or missing seals or jar lid gasket).
3. Remove the bioprosthesis from its container by carefully grasping one of the bioprosthesis frame paddles with a pair of blunt tipped forceps. Do not use the forceps to grasp the tissue portion of the bioprosthesis. Let any remaining solution drain from the bioprosthesis completely.

   Note: Retain the container with the original solution. It may be needed to store and return a rejected bioprosthesis.
4. Compare the serial number on the container with the serial number on the tag attached to the bioprosthesis.

   Caution: If the serial numbers do not match, do not use the bioprosthesis.
5. Carefully remove the serial number tag from the bioprosthesis and retain the tag.
6. Immerse the entire bioprosthesis in a sterile rinsing bowl.
7. Gently agitate the bioprosthesis by hand for 15 seconds to remove the glutaraldehyde from the bioprosthesis.
8. Repeat *Step 6* and *Step 7* in one of the remaining rinsing bowls.
9. Leave the bioprosthesis submerged in sterile saline in the third rinsing bowl until it is ready to be loaded.

9.1.4 Bioprosthesis loading procedure

Perform the bioprosthesis loading procedure while the distal end of the catheter is immersed in the integrated loading bath filled with cold, sterile saline (0 °C to 8 °C [32 °F to 46 °F]). The bioprosthesis should remain immersed in saline during the loading process to minimize the introduction of air into the loaded system.

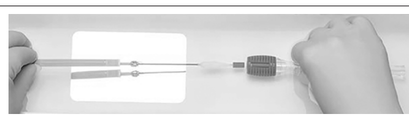
Note: Confirm the loading system and catheter sizes are compatible with the bioprosthesis size (*Table 3*).

Note: Refer to *Figure 6* for Evolut FX loading system components.

Caution: Rapid capsule advancement can contribute to difficulties with loading the valve and can increase the risk of damage to the catheter. Slowly advancing the capsule helps facilitate successful loading.

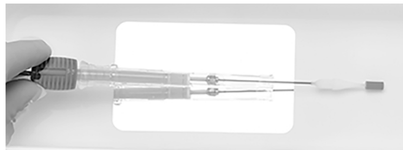
1. Submerge and cool the bioprosthesis in the integrated loading bath filled with cold, sterile saline.
2. Ensure that the capsule guide tube is fully open (unlocked) with the locking collar at the proximal end of the capsule guide tube (*Figure 8*).

   Figure 8.



3. Advance the capsule guide tube over the catheter shaft toward the handle and across the catheter tip (*Figure 9*).

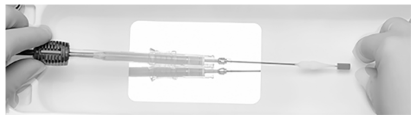
Figure 9.



4. Once the catheter tip has been crossed, fully advance the locking collar to the distal end of the capsule guide tube until it is closed (locked).
5. Continue to advance the capsule guide tube over the catheter shaft towards the handle until it contacts the distal end of the capsule (*Figure 10*).

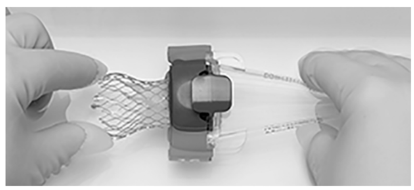
   Caution: Do not attempt to advance the capsule guide tube over the capsule; this will prevent the capsule flare from expanding fully and prevent proper loading.

   Figure 10.



6. Ensure that the backplate has been inserted into the inflow cone and the exposed part of the backplate is facing up.
7. Insert the inflow portion of the bioprosthesis frame into the inflow cone. Ensure that the bioprosthesis frame paddle marked with a "C" is facing up and that the paddles are aligned with the paddle attachment pockets (*Figure 11*). Ensure the paddles are presented straight and are not bent inwards prior to proceeding to the next step.

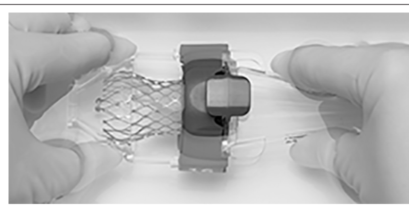
   Figure 11.



8. Secure the outflow cone onto the inflow cone (*Figure 12*) until it locks.

   Note: Ensure that the outflow cone is aligned with the inflow cone when attaching and crimping the valve.

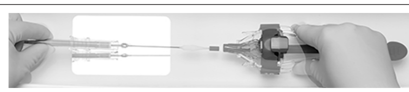
   Figure 12.



9. Insert the catheter tip guide tube completely into the distal end of the inflow cone (*Figure 13*). Inspect the outflow struts of the bioprosthesis and, if needed, manually manipulate so that they are evenly spaced and the bioprosthesis frame paddles are approximately 180° apart.

   Note: Do not apply excessive force when inserting the tip guide tube. If resistance is encountered, stop and observe the paddle presentation.

   Figure 13.



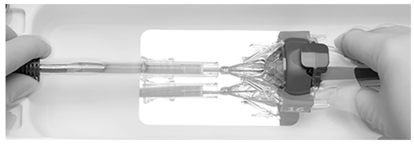
10. Insert the distal catheter tip into the catheter tip guide tube.

    Note: Allow the loading tool to rest on the loading bath floor to ensure coaxial alignment with the catheter to assist in seating the bioprosthesis frame paddles within the paddle attachment pockets.
11. Retract the catheter tip guide tube to set the bioprosthesis frame paddles into the paddle attachment pockets (*Figure 14*).

    Note: If the bioprosthesis frame paddles do not seat properly within the paddle attachment pockets upon retracting the catheter tip guide tube, slightly manipulate the position of the loading tool until paddle seating is achieved.

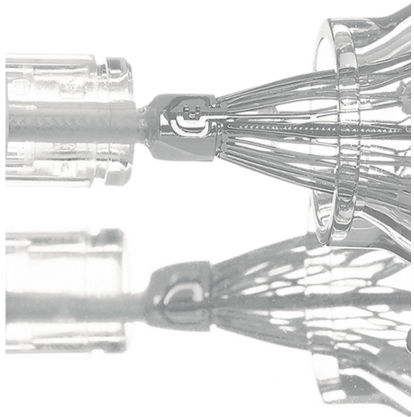
Note: If necessary, it is acceptable to manually compress the bioprosthesis frame paddles with fingertips to help seat the paddles within the paddle attachment pockets.

Figure 14.



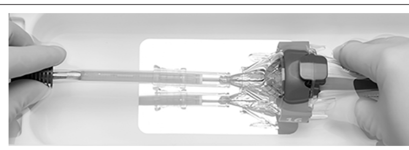
Note: Ensure both bioprosthesis frame paddles are completely seated within the paddle attachment pockets (*Figure 15*) before continuing to the next step.

Figure 15.



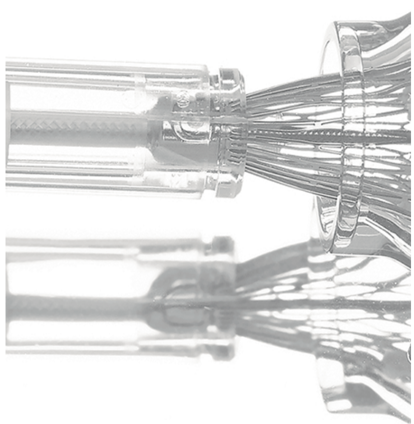
12. Hold the loading tool stationary with one hand, and with the other hand manually advance the capsule guide tube so that the distal section covers the paddle attachment pockets and the top portion of the outflow struts (*Figure 16*).

Figure 16.



Use the mirror to ensure that both bioprosthesis frame paddles are positioned correctly in the paddle attachment pockets and the outflow struts are within the distal tip of the capsule guide tube (*Figure 17*).

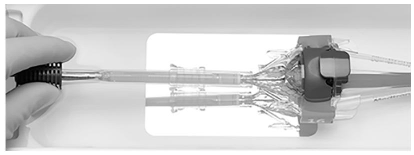
Figure 17.



13. Advance the capsule to cover the bioprosthesis frame paddles (*Figure 18*), pausing when the capsule covers the proximal half of the paddles to confirm the paddles are both still properly seated before advancing further.

Use the mirror to ensure that both paddles are captured in the capsule.

Figure 18.

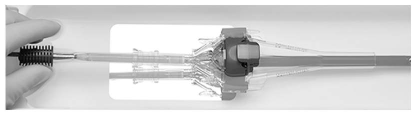


Caution: Do not advance the capsule over the bioprosthesis frame paddles unless they are fully seated in the center of the paddle attachment pockets. Advancing the capsule before the paddles are fully seated could damage the capsule and result in emboli.

14. Advance the capsule to capture the bioprosthesis outflow struts (*Figure 19*).

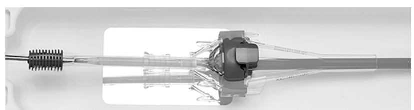
    Use the mirror to ensure that all bioprosthesis outflow struts are symmetrical and captured in the capsule.

    Figure 19.



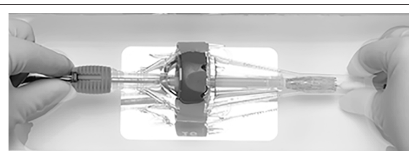
15. Continue to advance the capsule until the distal end of the capsule guide tube covers the distal end of the commissure pad of the bioprosthesis (*Figure 20*). The capsule guide tube should completely cover the commissure pad.

    Figure 20.



16. Remove the backplate and the catheter tip guide tube from the outflow cone.
17. While holding the capsule guide tube stationary, advance the inflow cone to crimp the inflow portion of the bioprosthesis frame until the outflow cone contacts the capsule guide tube (*Figure 21*). During this step, the outflow cone contacts the locking collar component and moves the locking collar to the proximal end of the capsule guide tube.

    Figure 21.



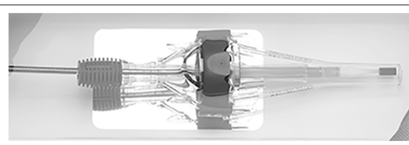
Note: The capsule guide tube will be in the unlocked configuration after this step.

Note: Ensure the bioprosthesis frame axis is visually aligned (coaxial) with the inflow cone axis during the insertion of the bioprosthesis into the inflow cone. Complete the insertion of the bioprosthesis into the inflow cone in one uninterrupted movement.

Caution: Do not attempt to direct load the valve (for example, loading the valve without completing Step 17 and simply advancing the capsule to load the valve). This increases the likelihood of excessive inflow crown overlap. **If a valve has been direct loaded, discard the entire system.** The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.

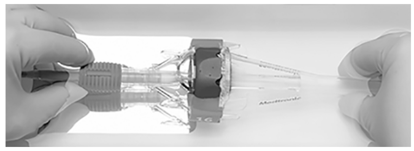
18. Advance the capsule over the bioprosthesis until the capsule comes within 5 mm of the catheter tip (*Figure 22*).

    Figure 22.



19. Remove the capsule guide tube together with the outflow cone and inflow cone from the catheter (*Figure 23*).

Figure 23.

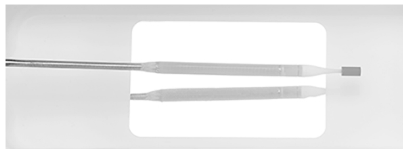


20. Slowly advance the capsule to close the gap between the capsule and catheter tip completely (*Figure 24*).

    Caution: Stop advancing the capsule once the gap to the catheter tip is closed. Advancing the capsule farther could damage the capsule.

    Note: If the deployment knob has reached the gray front grip and a gap exists between the capsule and the catheter tip, pause to allow any additional capsule movement to occur. If the gap remains, slowly continue rotating the deployment knob to advance the capsule one increment at a time, pausing between each increment.

    Figure 24.



21. Slightly rotate the deployment knob in the direction of the arrows to relieve stress. Ensure that the capsule does not separate from the catheter tip.

    Note: After the bioprosthesis has been loaded into the capsule, the capsule flush port can no longer be flushed.
22. Visually and tactilely inspect the capsule for a misloaded bioprosthesis. The capsule should be straight, smooth, and free of any bends, protrusions, or discolorations. If any of these conditions are felt or observed, the bioprosthesis is likely to be misloaded.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
23. Attach a 10 mL syringe filled with sterile saline to the stability layer flush port on the distal end of the handle and flush.
24. Remove the loading stylet from the guidewire lumen at the capsule.
25. Attach a 10 mL syringe filled with sterile saline to the wire lumen flush port on the proximal end of the handle and flush.
26. Attach a 10 mL syringe filled with sterile saline to the Evolut FX inline sheath flush port and flush.
27. Before inserting into a patient, visually inspect the loaded bioprosthesis under fluoroscopy.

    Note: Complete fluoroscopy check under a magnified, high-resolution view over an area selected to not impede the clarity of the device.

    Note: Ensure the capsule is slowly rotated 360° during the fluoroscopy check.

    Note: If a misload is detected, do not attempt to reload the bioprosthesis. Discard the entire system. The valve, catheter, loading system, loading tray, and saline must all be replaced with new sterile components.
28. Leave the bioprosthesis submerged in sterile saline until implantation.

9.2 Bioprosthesis implantation

Note: Use systemic anticoagulation during the implantation procedure based on physician/clinical judgment. If heparin is contraindicated, consider an alternative anticoagulant.

9.2.1 Vascular access

Note: Vascular access should be achieved per standard practice (either percutaneously or via surgical cutdown).

Note: The primary access artery will be used to introduce the Evolut FX+ device and, if predilatation is performed, the balloon catheter; the secondary access artery will be used to introduce the reference pigtail.

1. Establish a central venous line. Insert a temporary pacemaker lead via the right internal jugular vein (or other appropriate access vessel) per physician/clinical judgment.
2. Insert an introducer sheath into the secondary access artery.
3. Insert an introducer sheath into the primary access artery.
4. Administer anticoagulant according to physician/clinical judgment. If heparin is administered as an anticoagulant, check activated clotting time (ACT) and monitor every 30 minutes after initial bolus of heparin. Maintain ACT ≥250 seconds.

    Note: Anticoagulant may be administered at any time prior to this point, but avoid delaying beyond this point.

9.2.2 Crossing the valve

1. Advance the graduated pigtail catheter to the ascending aorta and position the distal tip in the noncoronary cusp of the aortic valve.
2. Identify the ideal annular viewing plane using contrast injections at various angiographic angles.

   Note: It is recommended that a dedicated individual prepare and operate the contrast injector.
3. Insert an angiographic catheter over a standard J-tip guidewire into the primary access sheath and advance to the ascending aorta.
4. Exchange the J-tip guidewire for a 0.035 in (0.889 mm) straight-tip guidewire. Advance the straight-tip guidewire across the aortic valve into the left ventricle (LV).
5. After crossing the aortic valve with the guidewire, advance the angiographic catheter into the LV.
6. Exchange the straight-tip guidewire for an exchange length J-tip guidewire.
7. Exchange the angiographic catheter for a 6 Fr pigtail catheter.
8. Remove the guidewire and connect the catheter to the transducer. Using both catheters, record the aortic pressure gradient.
9. Using a right anterior oblique (RAO) projection, advance the previously pigtail-shaped, 0.035 in (0.889 mm) high support guidewire through the pigtail catheter and position in the apex of the LV.
10. Remove the pigtail catheter while maintaining guidewire position in the LV.

9.2.3 Predilatation of the implant site

Adequate predilatation can help reduce the need for post dilatation and may mitigate the occurrence of infolding.

Predilatation may also be useful to prepare the valve for crossing by the delivery catheter system and implantation of the transcatheter valve but may also confer some additional risk to the patient (for example, liberation of embolic debris, damage to the tissue, or perforation of the aortic root). Patient anatomical characteristics (for example, bicuspid anatomy, excessive or asymmetric leaflet calcification, and possible leaflet fusion) should be considered by the heart team when evaluating and determining the risk/benefit of predilatation and treatment plan for each patient.

The size and model of the predilatation BAV balloon should be selected such that it results in effective expansion and relief of the stenosis in the context of BAV to allow full expansion of the TAV upon implantation. Avoid balloon under sizing to ensure effective predilatation, therefore minimizing the risk of under expansion and infolding.

Notes:

- Predilatation is specifically recommended prior to implantation in the following situations:
  - Moderate-severe calcification
  - Bicuspid anatomy
  - Size 34 mm valve
- Utilize an adequate size balloon for effective predilatation, avoid under dilatation.

Information for failed surgical or transcatheter bioprosthetic valve: Balloon predilatation of a stenotic surgical or transcatheter aortic bioprosthetic valve has not been evaluated. In cases where there is severe stenosis, predilatation of the surgical or transcatheter aortic bioprosthetic valve may be done at the discretion of the heart team, and the steps used are identical to native valve predilatation.

1. Insert the valvuloplasty balloon through the introducer sheath in the primary access artery and advance it to the ascending aorta.
2. Reposition the angiographic equipment to the ideal viewing plane. Position the valvuloplasty balloon across the valve, while maintaining strict fluoroscopic surveillance of the distal tip of the guidewire in the LV.
3. Perform balloon valvuloplasty per standard practice and remove the valvuloplasty balloon while maintaining guidewire position across the aortic valve.

9.2.4 Deployment

1. Insert the device over the 0.035 in (0.889 mm) guidewire with the delivery catheter flush ports oriented at 3 o'clock (toward the left side of the patient) to better facilitate commissure alignment (flush ports shown in *Figure 2*, callouts 7 and 13). Insert the catheter tip and capsule through the access site, while maintaining the Evolut FX inline sheath tip against the proximal end of the capsule. Then, insert the Evolut FX inline sheath through the access site, maintaining contact with the capsule. When advancing the delivery system, allow the catheter handle to rotate freely after insertion of the system. Maintain strict fluoroscopic surveillance of the guidewire in the LV.

   Note: The 23-29 mm catheter model is compatible with introducer sheaths that can accommodate an 18 Fr (6.0 mm) device. The 34 mm catheter model is compatible with introducer sheaths that can accommodate a 22 Fr (7.33 mm) device.

   Note: For transfemoral and subclavian access procedures, a separate introducer sheath is optional. For direct aortic access procedures, use a separate introducer sheath; do not use the Evolut FX inline sheath. Maintain the Evolut FX inline sheath at the proximal end of the catheter throughout the procedure.

2. Under fluoroscopic guidance, advance the catheter over the guidewire to the aortic annulus. To assist capsule advancement or alignment, the capsule orientation may be adjusted by rotating the handle a quarter turn before the capsule crosses into the arch. If adjustment to capsule orientation is required after crossing the arch, withdraw the system until the capsule is in the descending aorta and rotate the handle a quarter turn before readvancing.

   Caution: Stop handle rotation if resistance is encountered or the capsule does not respond to rotation under fluoroscopic visualization. Do not rotate the handle when the capsule is at or beyond the arch. Continued attempts to rotate the capsule during resistance may result in product failure and/or patient harm.

   Caution: There will be some resistance when the catheter is advanced through the vasculature. If there is a significant increase in resistance, stop advancement and investigate the cause of the resistance (for example, magnify the area of resistance) before proceeding. Do not force passage. Forcing passage could increase the risk of vascular complications (for example, vessel dissection or rupture).

   Caution: Persistent force on the catheter can cause the catheter to kink, which could increase the risk of vascular complications (for example, vessel dissection or rupture).

   Note: When crossing the aortic arch, it is critical that the guidewire is controlled to prevent it from moving forward. Without proper management of the distal tip of the guidewire, the guidewire could move forward and cause trauma to the LV.

3. Advance the device through the valve. Perform an angiogram to confirm that the pigtail catheter is in position within the noncoronary cusp of the aortic root. Fluoroscopically identify the appropriate landmarks.

4. Position the catheter so that the bioprosthesis is at the recommended target depth of 3 mm relative to the valve annulus. Position the radiopaque markers at the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture (*Section 9.2.5*).

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.

5. To deploy the bioprosthesis, rotate the deployment knob in the direction of the arrows. The capsule retracts and exposes the bioprosthesis. Continue deploying the bioprosthesis in a controlled manner, adjusting valve position as necessary and noting the position of the radiopaque capsule marker band and paddle attachment. Position the bioprosthesis so that the radiopaque markers are at the level of the native valve annulus. Note that the radiopaque markers are 3 mm from the inflow tip of the bioprosthesis.

   Warning: 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.

   Note: Consider pacing to increase valve stability during deployment, especially in patients with larger anatomies. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.

   Note: Slight antegrade repositioning of a partially deployed bioprosthesis (before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment) can be achieved by carefully withdrawing the catheter.

   Caution: Use the catheter handle to reposition the bioprosthesis. **Do not** use the outer catheter shaft.

6. Before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, evaluate the bioprosthesis position by assessing the position of the radiopaque markers.

   Note: When the bioprosthesis is approximately 2/3 deployed, the deployment knob provides a tactile indication as a notification before the point of no recapture. Once the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment, it is at the point of no recapture.

7. A right and left cusp overlap projection prior to deployment with a second radiographic view without parallax, may be useful to detect infolding, particularly in the presence of complex anatomies (bicuspid nature, severe calcification). An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.

   - Recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.

8. Either complete bioprosthesis deployment or initiate bioprosthesis recapture.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.5 Bioprosthesis recapture (optional)

The bioprosthesis is recapturable during deployment before the radiopaque capsule marker band reaches the distal end of the radiopaque paddle attachment. Deployment of the bioprosthesis can be attempted 3 times. If the bioprosthesis is recaptured a third time, it must be removed from the patient.

1. Rotate the deployment knob in the opposite direction of the arrows to recapture the bioprosthesis. A partially recaptured bioprosthesis can be repositioned or fully recaptured.

   Note: For TAV in SAV or TAV in TAV procedures, fully recapture the bioprosthesis before repositioning to reduce the risk of hang up or snagging on the failed bioprosthesis and to aid with positioning using the radiopaque capsule marker band.

   Warning: 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.
2. To fully recapture the bioprosthesis, continue rotating the deployment knob until the gap between the capsule and catheter tip is closed.

   Caution: Stop advancing the capsule once the gap between the capsule and the catheter tip is closed. Advancing the capsule farther could damage the capsule.
3. Reposition the recaptured bioprosthesis at the recommended target depth of 3 mm relative to the valve annulus. Position the radiopaque markers at the valve annulus. If the implant depth is ≤1 mm or >5 mm, consider recapture.

   Caution: Bioprosthesis implant depth ≤1 mm may contribute to an increased risk of prosthetic valve dislodgement during valve release, DCS retrieval, or post-implant dilatation. Bioprosthesis implant depth >5 mm may contribute to an increased risk of conduction disturbances, which may require a permanent pacemaker.

   Note: For surgical or transcatheter bioprosthetic valves, consider the features of the valve when determining the optimal placement of the bioprosthesis.

   Note: Physicians should consider patient anatomy when determining implant depth.
4. Redeploy the bioprosthesis (*Section 9.2.4*, *Step 5* and *Step 6*).
5. Monitor frame during recapture to detect any presence of infolding. An observation of **any** inward fold or crease in the valve, extending from the inflow, identified as a dark line under fluoroscopy inspection, may indicate an infold. If identified and if the patient's condition allows, do not proceed and do not release the valve.
   - Fully complete the recapture, remove and discard the entire system. The valve, catheter, loading system, loading tray, and saline all must be replaced with new sterile components.
   - Predilatation is strongly recommended prior to subsequent implantation attempts to minimize infold risk.
   - If initial predilatation does not prevent infolding, reassess valve sizing in the presence of complex anatomies.
   - If an infold is detected and the valve is removed, consider a slightly lower depth of implantation of the second valve to provide additional space for frame expansion.
6. Either complete bioprosthesis redeployment or initiate bioprosthesis recapture. If the bioprosthesis has been recaptured 3 times, withdraw the recaptured bioprosthesis.

   Note: Shortly after annular contact, the blood pressure will be reduced until approximately the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

9.2.6 Postdeployment

1. Perform an angiogram to assess the location of the bioprosthesis.
2. Under fluoroscopic guidance, confirm that the catheter tip is coaxial with the inflow portion of the bioprosthesis.
3. Withdraw the catheter to the aorta while maintaining guidewire position.

   Note: For transfemoral access, withdraw the catheter until the catheter tip is positioned in the descending aorta. For direct aortic access and subclavian access, withdraw the catheter until the catheter tip is close to the distal tip of the introducer sheath.
4. Under fluoroscopic guidance, close the catheter capsule.

   Caution: Close the capsule until it is aligned with the catheter tip. Do not overcapture the catheter tip, because it could interfere with catheter withdrawal through the introducer sheath or cause vessel trauma upon removal.

   Caution: Ensure the capsule is closed before catheter removal.

   Caution: 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.
5. Withdraw the catheter until the capsule meets the distal end of the Evolut FX inline sheath.

   Note: For direct aortic access procedures, maintain the Evolut FX inline sheath at the proximal end of the catheter.
6. Withdraw the catheter and Evolut FX inline sheath together. Dispose of the catheter and loading system in accordance with the applicable laws, regulations, and hospital procedures, including those regarding biohazards, microbial biohazards, and infectious substances.

7. Advance a 6 Fr pigtail catheter over the guidewire into the LV.
8. Remove the guidewire and connect the pigtail catheter to the transducer.
9. Using both pigtail catheters, record aortic pressure gradient.
10. Remove the 6 Fr pigtail over a standard, J-tip guidewire.
11. Perform a post-implant aortogram with the reference pigtail to ensure coronary patency and assess aortic regurgitations.
12. Remove the introducer sheath (if used) and complete the puncture site closure per standard practice.
13. Perform contrast angiography to verify the absence of any vascular complications.
14. Remove the reference pigtail catheter over a standard guidewire. Remove the 6 Fr introducer sheath and close the access site per standard practice.
15. Administer anticoagulation and/or antiplatelet therapy as required according to physician/clinical judgment.

9.2.7 Post implant dilatation

If valve function or sealing is impaired due to excessive calcification, bicuspid nature, incomplete expansion or infolding, a post-implant balloon dilatation (PID) of the bioprosthesis may improve valve function and sealing.

1. **Cautions:**
   - Use caution when considering post dilatation in the presence of an infold to minimize dislodgement risk, particularly in the case of shallow implant depth. Consider pacing to increase valve stability, especially in patients with 34 mm valves. Pace at a rate sufficient to achieve a desired decrease in systolic pressure. If pacing at a high rate, consider stepping the pacing rate down incrementally.
   - Overexpansion of the narrowest portion (waist) of the Evolut FX+ TAV beyond the levels set forth in *Table 4* has been demonstrated through bench data to cause damage to the bioprosthetic leaflets. Complaints of damage to the bioprosthetic leaflets during post-implant balloon dilatation have been reported in some clinical cases, resulting in moderate to severe aortic insufficiency, which may be detected acutely or during follow-up. Multiple dilatations of the Evolut FX+ TAV increases the risk of damage to the bioprosthetic leaflets.
   - Snares should be available to stabilize the bioprosthesis in the event of dislodgement following post implant dilatation.
2. Consider the precautions outlined in *Chapter 4* Warnings and Precautions when selecting the post implant dilatation balloon model, size, and applied inflation pressure.

10 Return of explanted bioprostheses

Medtronic is interested in obtaining recovered bioprostheses. Specific pathological studies of the explanted bioprosthesis will be conducted under the direction of a consulting pathologist. A written summary of the findings will be returned to the physician. To obtain a product return kit, contact a Medtronic distribution center or a Medtronic Representative. If a kit is not available, place the explanted bioprosthesis in a container of glutaraldehyde or 10% buffered formalin immediately after excision. For further instructions on the return of an explanted device, contact a Medtronic Representative.

11 Clinical studies

Information regarding clinical studies and post-approval studies that are applicable to Evolut FX+ are available on the Medtronic Manual Library website:

1. Point your browser to www.medtronic.com/manuals.
2. Select the geography and language, and then search by product name for Evolut FX+. The instructions for use and premarket and post-approval study summaries are listed. The clinical study summaries include the following: study name, applicable device, patient population and indication, sample size, and follow-up duration.

If you do not have web access, you can order printed copies of the clinical study summaries from your Medtronic representative or by calling the toll-free number located on the back cover.

12 Disclaimer of warranty

The following disclaimer of warranty applies to United States customers only:

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ALTHOUGH THE MEDTRONIC EVOLUT™ FX+ TRANSCATHETER AORTIC VALVE (MODELS EVFXPLUS-23, EVFXPLUS-26, EVFXPLUS-29, AND EVFXPLUS-34), EVOLUT FX DELIVERY CATHETER SYSTEM (MODEL D-EVOLUTFX-2329 AND D-EVOLUTFX-34), EVOLUT FX LOADING SYSTEM (MODELS L-EVOLUTFX-2329 AND L-EVOLUTFX-34), HEREAFTER REFERRED TO AS "PRODUCT", HAVE BEEN MANUFACTURED UNDER CAREFULLY CONTROLLED CONDITIONS, MEDTRONIC HAS NO CONTROL OVER THE CONDITIONS UNDER WHICH THIS PRODUCT IS USED. MEDTRONIC THEREFORE DISCLAIMS ALL WARRANTIES, BOTH EXPRESS AND IMPLIED, WITH RESPECT TO THE PRODUCT, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR

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13 Patents

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CoreValve™
CoreValve™ Evolut R
CoreValve™ Evolut PRO
Evolut™ PRO+
Evolut™ FX
Evolut™ FX+

Transcatheter Aortic Valve System

Clinical Study Summary

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

Contents

1.0 Summary of premarket approval clinical studies

A list of the applicable premarket approval clinical studies contained in this report are summarized in Table 1. The studies are organized by study name, study design, patient population and indication, applicable device name, sample size, and follow-up duration.

Table 1: Applicable Premarket Approval Clinical Studies

Study Name	Study Design	Patient Population and Indication	Applicable Device	Sample Size (Subjects)	Follow-Up Duration
Low Risk	Prospective, multi-center, multi-national, randomized (TAVR v SAVR) study	Subjects with severe aortic stenosis (AS) at low surgical risk	SAVR	678	24 Months
			TAVR (Evolut R, Evolut PRO, CoreValve (31mm))	725	
Intermediate Risk (SURTAVI)	Prospective, multi-center, multi-national, randomized (TAVR v SAVR) study	Subjects with severe, symptomatic aortic stenosis (AS) at intermediate surgical risk	SAVR	796	24 Months
			TAVR (CoreValve, Evolut R)	864	
Evolut R	Prospective, non-randomized, multi-center study	Subjects with severe, symptomatic aortic stenosis (AS) at high to extreme surgical risk	Evolut R	166	12 Months
Evolut PRO	Prospective, non-randomized, multi-center study	Subjects with severe, symptomatic aortic stenosis (AS) at high to extreme surgical risk	Evolut PRO	45	30 Days

Study Name	Study Design	Patient Population and Indication	Applicable Device	Sample Size (Subjects)	Follow-Up Duration
Bicuspid (Intermediate or Greater Surgical Risk)	Observational, non-randomized, registry-based data collected via the Society of Thoracic Surgeons/American College of Cardiology Foundation (STS/ACCF) Transcatheter Valve Therapy (TVT) Registry™	Subjects with bicuspid aortic valves and severe aortic stenosis (AS) at intermediate or greater surgical risk	Evolut R, Evolut PRO	545	12 Months
Bicuspid (Low Risk)	Prospective, non-randomized, multi-center study	Subjects with bicuspid aortic valves and severe aortic stenosis (AS) at low surgical risk	Evolut R, Evolut PRO	150	12 Months
Redo TAV patient population	Observational, non-randomized, registry-based data collected via STS/ACCF TVT Registry™	Subjects with failed (stenosed, insufficient, or combined) transcatheter bioprosthetic aortic valve at high or greater surgical risk	Evolut PRO+, FX, and FX+	744	12 Months

The Medtronic Low Risk Trial was designed and executed to evaluate the safety and efficacy of transcatheter aortic valve replacement (TAVR) in subjects with severe aortic stenosis (AS) at low surgical risk (heart team agreement of predicted risk of operative mortality is <3% at 30 days) by randomizing subjects to either surgical aortic valve replacement (SAVR) or TAVR.

Section 1.1 presents the results of the Low Risk trial.

The Medtronic CoreValve SURTAVI Trial was designed and executed to evaluate the safety and efficacy of transcatheter aortic valve replacement (TAVR) in subjects with severe, symptomatic aortic stenosis (AS) at intermediate surgical risk (heart team agreement of predicted risk of operative mortality is ≥3% and <15% at 30 days) by randomizing subjects to either surgical aortic valve replacement (SAVR) or TAVR. Section 1.2 presents the results of the SURTAVI Trial.

The Medtronic CoreValve Evolut R Global Clinical Studies are prospective, single-arm, historical-controlled, multi-center studies designed to evaluate the safety and efficacy of the Evolut R system (23 mm, 26 mm, and 29 mm valves) for the treatment of severe aortic stenosis in patients considered at high through extreme risk for surgical aortic valve replacement. The US IDE study addendum evaluated the safety and effectiveness of the 34 mm valve in a subset of the US study sites included in the CoreValve Evolut R Global Clinical Studies. The results of these studies are presented as a combined population in Section 1.3, with the exception of the Quality of Life data (Table 29), which were only collected at the US study sites.

Patients received the Evolut R bioprosthesis either through the iliofemoral access route [95.2% (158/166)] or through the non-iliofemoral—subclavian [0.6% (1/166)] and direct aortic [4.2% (7/166)]—access routes. The recapture/resheath feature, unique to the Evolut R system, was used in 38/166 subjects.

The data in Section 1.3 summarize the results from the Evolut R clinical studies.

The Society of Thoracic Surgeons/American College of Cardiology Foundation (STS/ACC) Transcatheter Valve Therapy (TVT) Registry (TVT Registry) is a tool developed to track patient safety and real-world outcomes related to TAVR. The data in Section 1.5 summarize data entered into the TVT Registry for patients identified to have bicuspid valve morphology who were implanted with either the Evolut R or Evolut PRO TAVR system between July 2015 and September 2017.

Section 1.6 summarizes procedural safety and efficacy data of the Medtronic TAVR systems in patients with bicuspid aortic anatomy and severe aortic stenosis at low risk for SAVR who were treated with either the Evolut R or Evolut PRO TAVR system.

The data in section 1.7 summarize data entered into the TVT Registry for patients who received commercially available Evolut TAVR (Evolut R, PRO, PRO+, FX, and FX+) as the redo TAV procedure through September 2023.

1.1 The Low Risk Trial

The Low Risk Trial was a prospective, randomized (1:1), multi-center investigational study. The purpose of this trial was to investigate the safety and efficacy of transcatheter aortic valve implantation (TAVR) in subjects with severe aortic stenosis (AS) at low surgical risk by randomizing subjects to either surgical aortic valve replacement (SAVR) or TAVR. A total of 1468 subjects were randomized in this study (734 subjects were randomized to TAVR, 734 subjects were randomized to SAVR) at 86 activated centers. A subset of patients were enrolled in a computed tomography (CT) substudy to investigate the prevalence of Hypoattenuated Leaflet Thickening (HALT) and reduced leaflet mobility.

The primary objective of the study was to demonstrate that the safety and effectiveness of Medtronic TAVR, as measured by all-cause mortality or disabling stroke at 24 months, is non-inferior to surgical aortic valve replacement (SAVR) in the treatment of severe aortic stenosis in subjects who have a predicted low risk for aortic valve surgery. The analysis for the primary and secondary endpoints was performed from the data received as of November 30, 2018, including all subjects randomized to TAVR or SAVR. Within the randomized cohort, 725 TAVR subjects received an attempted implant and comprise the primary analysis cohort (the As Treated [AT] cohort) TAVR set while 678 subjects randomized to SAVR received an attempted implant and comprise the AT SAVR set. The implanted population (722 TAVR and 680 SAVR) consists of all subjects who were implanted with a valve. Of the 722 patients in the implanted TAVR cohort, 534 patients were implanted with the Evolut R TAV, 162 patients with the Evolut PRO TAV, and 26 patients with the CoreValve 31 mm TAV.

Subsequently, a supplemental analysis was performed on an expanded dataset, which included additional follow-up data on the cohort collected through May 3, 2019. The data presented in this section reflect the results of the supplemental analysis unless noted otherwise. Specifically, all hypothesis testing was conducted on the original dataset.

There were four different analysis populations defined in the statistical analysis plan of the study: intention-to-treat (ITT), as treated (AT), implanted, and per protocol (PP), as summarized in Table 2. The primary analysis population at both the “early win” and the supplemental analysis was the AT analysis population.

Table 2: Analysis Populations

Analysis Population	Definition	Number of Patients	
		TAVR	SAVR
Intention-to-treat (ITT)	All randomized patients	734	734
As treated (AT)	All ITT patients with an attempted implant procedure*	725	678
Implanted	All AT patients who were actually implanted with a valve	722	680
Per protocol (PP)	Based on the International Council for Harmonisation (ICH) E9 Statistical Principals: – All implanted patients who were implanted according to their randomization; and – Patients without early exit (e.g., lost to follow-up) before 24 months (730 days), except those experiencing the primary endpoint (death or disabling stroke) prior to the early exit; and – Patients without crossover to a different type of procedure from their first attempted procedure type before their 24-month visits; and – Patients must satisfy all inclusion/exclusion criteria.	702	647

*Attempted implant procedure was defined as when the subject was brought into the procedure room and any of the following had occurred: anesthesia administered, vascular line placed, transesophageal echocardiography probe placed, or any monitoring line placed. Patients were analyzed according to their first attempted procedure (TAVR or SAVR).

1.1.1 Patient population

The demographics and baseline characteristics of the study population are summarized in Table 3. The treatment cohorts were generally well balanced with respect to age, gender, baseline NYHA classification, and STS risk score.

Table 3: Patient Demographics and Baseline Characteristics – AT Population

Demographics and Baseline Characteristics	Summary Statistics*		
	TAVR	SAVR	Difference (TAVR – SAVR) (95% BCI)
Age (years)	74.1 ± 5.8 (725)	73.6 ± 5.9 (678)	(-0.17, 1.07)
Gender female (%)	36.0% (261/725)	33.8% (229/678)	(-2.77%, 7.18%)
NYHA class			
I	10.5% (76/725)	9.3% (63/678)	(-1.95%, 4.30%)
II	64.4% (467/725)	62.2% (422/678)	(-2.85%, 7.21%)
III	25.0% (181/725)	28.0% (190/678)	(-7.64%, 1.57%)
IV	0.1% (1/725)	0.4% (3/678)	(-1.07%, 0.34%)
STS score, %	1.9 ± 0.7 (725)	1.9 ± 0.7 (678)	(-0.03, 0.11)
Peripheral arterial disease	7.5% (54/718)	8.3% (56/677)	(-3.62%, 2.09%)
Previous MI	6.6% (48/725)	4.9% (33/678)	(-0.70%, 4.20%)
Previous reintervention			
Coronary artery bypass Surgery	2.5% (18/725)	2.1% (14/678)	(-1.20%, 2.02%)
Percutaneous coronary intervention	14.2% (103/725)	12.8% (87/678)	(-2.21%, 4.94%)
Cerebrovascular disease	10.2% (74/725)	11.8% (80/678)	(-4.90%, 1.67%)
Immunosuppressive therapy	2.1% (15/725)	0.9% (6/678)	(-0.11%, 2.53%)
Chronic lung disease/COPD	15.0% (104/695)	18.0% (117/649)	(-7.04%, 0.90%)
Diabetes	31.4% (228/725)	30.5% (207/678)	(-3.91%, 5.73%)
Creatinine level > 2 mg/dl	0.4% (3/725)	0.1% (1/678)	(-0.41%, 0.98%)
Atrial fibrillation/atrial flutter	15.4% (111/722)	14.5% (98/676)	(-2.86%, 4.60%)
Pre-existing permanent pacemaker or defibrillator	3.2% (23/725)	3.8% (26/677)	(-2.66%, 1.28%)
Hypertension	84.8% (614/724)	82.6% (559/677)	(-1.63%, 6.11%)
Dialysis	0.0% (0/725)	0.1% (1/678)	(-0.72%, 0.31%)
Echocardiographic findings - Implanted Population			
Aortic valve area (cm^2)	0.8 ± 0.2 (716)	0.8 ± 0.2 (673)	(-0.02, 0.02)
Mean gradient (mmHg)	47.0 ± 12.1 (724)	46.6 ± 12.2 (678)	(-0.87, 1.69)

*Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.)

1.1.2 Procedure data

The procedure data of the TAVR and SAVR cohorts are summarized in Table 4 and Table 5, respectively.

Table 4: TAVR Procedure Data (AT Population)

Procedure Data	Summary Statistics* (N=725)
Number of index procedures	724
Total delivery catheter in the body time (min)	17.4 ± 19.4
Type of anesthesia	
General	56.9% (412/724)
Local	43.1% (312/724)
Access site	
Iliofemoral	99.0% (717/724)
Non-iliofemoral	1.0% (7/724)
Valve size	
23 mm	1.2% (9/721)
26 mm	19.6% (141/721)
29 mm	42.7% (308/721)
31 mm	3.6% (26/721)
34 mm	32.9% (237/721)
Total time in catheterization laboratory or operating room (min)	148.2 ± 55.1
Embolic protection device used	1.2% (9/722)
Pre-TAVR balloon valvuloplasty performed	34.9% (253/724)
Post-TAVR balloon valvuloplasty performed	31.3% (226/723)
Concomitant procedure (percutaneous coronary intervention; PCI)	6.9% (50/724)
Length of index hospitalization (days)	2.6 ± 2.1

*Continuous measures - Mean ± SD; categorical measures - % (no./total no.). Data included subjects with the index procedure defined as the first procedure in which the delivery catheter was introduced. If a patient had two implant procedures, the index procedure was used.

Table 5: SAVR Procedure Data (AT Population)

Procedure Data	Summary Statistics*
	SAVR (N=678)
Procedure aborted†	0.4% (3/678)
Valve size	
19 mm	3.6% (24/675)
21 mm	18.4% (124/675)
23 mm	31.3% (211/675)
25 mm	28.0% (189/675)
27 mm	7.3% (49/675)
29 mm	0.4% (3/675)
Other‡	11.1% (75/675)
Total aortic cross clamp time (min)	68.6 ± 28.9
Total time in catheterization laboratory or operating room (min)	276.6 ± 79.5
SAVR approach	
Full sternotomy	65.9% (446/677)
Mini sternotomy	14.5% (98/677)
Right anterior thoracotomy	19.4% (131/677)
Other	0.3% (2/677)
Concomitant procedures§	
Aortic root enlargement	1.6% (11/678)
Coronary artery bypass grafting (CABG)	13.6% (92/678)
Permanent pacemaker implantation	0.0% (0/678)
Surgical treatment of atrial fibrillation	3.5% (24/678)
Automatic implantable cardioverter-defibrillator (AICD) implantation	0.0% (0/678)
Left atrial appendage (LAA) closure	6.2% (42/678)
Patent foramen ovale (PFO) closure	0.7% (5/678)
Mitral valve repair	0.6% (4/678)
Mitral valve replacement	0.0% (0/678)
Other	5.0% (34/678)
Length of index hospitalization (days)	6.2 ± 3.3

*Continuous measures - mean ± SD (n); categorical measures - % (no./Total no.).
†Adjudicated by CEC: Aborted procedure or SAVR conversion to alternate procedure.
‡Others included sutureless valves categorized as "S," "M," or "L" for valve size.
§Subjects might have more than one concomitant procedure.

1.1.3 Safety and effectiveness results

1.1.3.1 Primary safety and effectiveness endpoint

The primary objective was to demonstrate that the safety and effectiveness of Evolut TAVR, as measured by the all-cause mortality or disabling stroke rate during a fixed follow-up of 24 months, is non-inferior to SAVR in the treatment of severe aortic stenosis in subjects who were determined by the heart team to be at low surgical risk.

The first "early win" assessment of the primary endpoint of all-cause mortality or disabling stroke rate at 24 months included all patients in the AT population (N=1403). The median of the posterior distribution for the primary endpoint event rate was 5.3% for the TAVR cohort and 6.7% for the SAVR cohort, with a median of the posterior distribution of the difference in the primary endpoint event rate of -1.4% (TAVR-SAVR) and a 95% Bayesian credible interval (BCI) of (-4.9%, 2.1%), as summarized in Table 6. The posterior probability of non-inferiority with a margin of 6% was >0.999, which is greater than the pre-specified threshold of 0.972, thus the primary endpoint non-inferiority could be concluded.

Similarly, the supplemental analysis showed that the median of the posterior distribution for the primary endpoint event rate was 4.4% for the TAVR cohort and 6.2% for the SAVR cohort, with a median of the posterior distribution of the difference in the primary event rate of -1.8% (TAVR – SAVR) and a 95% BCI of (-4.6%, 1.0%), as summarized in Table 6. The hypothesis testing was not repeated on the expanded dataset because it was not prespecified; the supplemental analysis for the posterior probability of non-inferiority with a margin of 6% is shown for context.

Table 6: All-Cause Mortality or Disabling Stroke at 24 Months - AT Population

	"Early Win" Analysis*		Supplemental Analysis†	
	TAVR (N=725)	**SAVR (N=678)**	**TAVR (N=725)**	**SAVR (N=678)**
Posterior median (95% BCI)	5.3% (3.3%, 8.0%)	6.7% (4.4%, 9.6%)	4.4% (2.9%, 6.4%)	6.2% (4.3%, 8.6%)
Difference (TAVR-SAVR) posterior median (95% BCI)	-1.4% (-4.9%, 2.1%)		-1.8% (-4.6%, 1.0%)	
Primary objective – Non-inferiority				
Posterior probability $P(H_{A,\delta=0.06} \mid \text{data})$	> 0.999		> 0.999	
Posterior threshold for non-inferiority	0.972			
Non-inferiority test	Passed			

*Conducted on the original dataset

†Conducted on the expanded dataset

Figure 1 shows the Kaplan-Meier (K-M) curve of all-cause mortality or disabling stroke in the AT population for both TAVR and SAVR through 24 months follow-up.

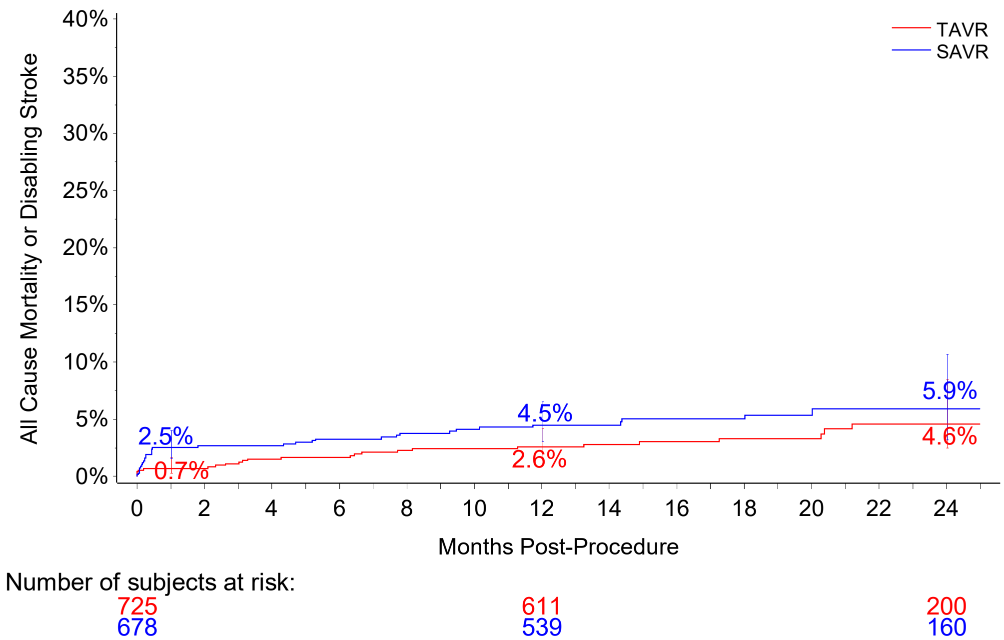

Figure 1: All-Cause Mortality or Disabling Stroke through 24 Months (AT Population)

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

1.1.3.2 Key secondary safety and effectiveness endpoints

Hierarchical testing of secondary endpoints

Hypothesis testing was performed hierarchically on pre-specified secondary endpoints based on the original dataset, as shown in Table 7. TAVR was found to be non-inferior to SAVR within the pre-specified non-inferiority margins in terms of mean gradient and effective orifice area (EOA) at 12 months, the NYHA functional classification change from baseline to 12 months, and the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall score change from baseline to 12 months. TAVR was found to be superior to SAVR with respect to mean gradient and EOA at 12 months and the KCCQ score change from baseline to 30 days (posterior probability > 0.999 for all).

Table 7: Secondary Endpoints Hierarchical Testing

Secondary Endpoint	TAVR Mean±SD (N)	SAVR Mean±SD (N)	Difference (TAVR – SAVR) (90% BCI)	Posterior Probability Prob (H_A | data)	Threshold	Test Result
Non-inferiority testing						
#1 Mean gradient at 12 months	8.6 ± 3.7 (409)	11.2 ± 4.9 (339)	-2.6 (-3.1, -2.1)	>0.999	0.95	Passed
#2 EOA at 12 months	2.3 ± 0.7 (341)	2.0 ± 0.6 (293)	0.3 (0.2, 0.4)	>0.999	0.95	Passed
#3 NYHA change (baseline – 12 months)	0.9 ± 0.7 (428)	1.0 ± 0.7 (342)	-0.1 (-0.2, 0.0)	>0.999	0.95	Passed
#3 KCCQ overall score change (12 months – baseline)	22.2 ± 20.3 (428)	20.9 ± 21.0 (347)	1.3 (-1.2, 3.8)	>0.999	0.95	Passed
Secondary Endpoint	**TAVR Mean±SD (N)**	**SAVR Mean±SD (N)**	**Difference (TAVR – SAVR) (95% BCI)**	**Posterior Probability Prob (H | data)**	**Threshold**	**Test Result**
Superiority testing						
#4 Mean gradient at 12 months	8.6 ± 3.7 (409)	11.2 ± 4.9 (339)	-2.6 (-3.2, -2.0)	>0.999	0.975	Passed
#5 EOA at 12 months	2.3 ± 0.7 (341)	2.0 ± 0.6 (293)	0.3 (0.2, 0.4)	>0.999	0.975	Passed
#6 KCCQ overall score change (30 day – baseline)	20.0 ± 21.1 (713)	9.1 ± 22.3 (636)	10.9 (8.6, 13.2)	>0.999	0.975	Passed

Note: The Implanted population was used for the mean gradient and EOA, and the AT population was used for the rest. All testing was conducted on the original dataset.

1.1.3.3 Additional effectiveness data

Valve performance

Effective orifice area (EOA) and mean gradient for TAVR and SAVR subjects are shown in Figure 2 and Figure 3.

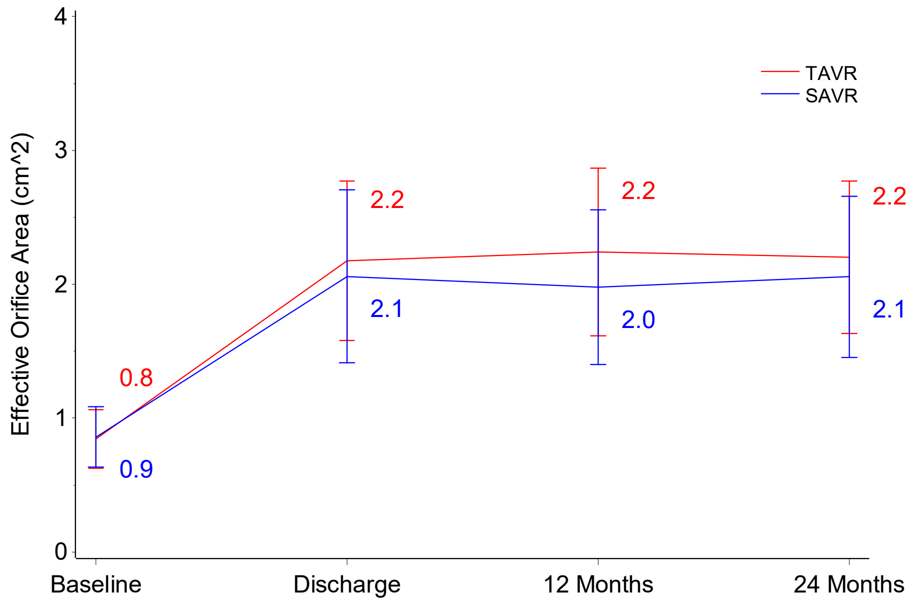

Figure 2: Effective Orifice Area through 24 Months (Implanted Population)

Note: Line plot with mean and standard deviation.

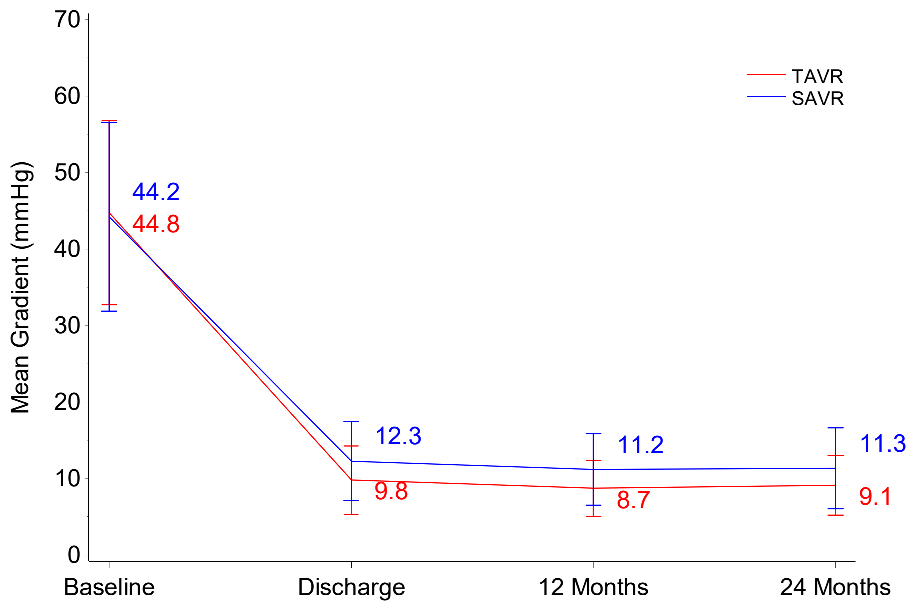

Figure 3: Mean Aortic Gradient through 24 Months (Implanted Population)

Note: Line plot with mean and standard deviation.

Figure 4 shows total aortic regurgitation (AR) severity over time for both TAVR and SAVR. Figure 5 shows paravalvular aortic regurgitation.

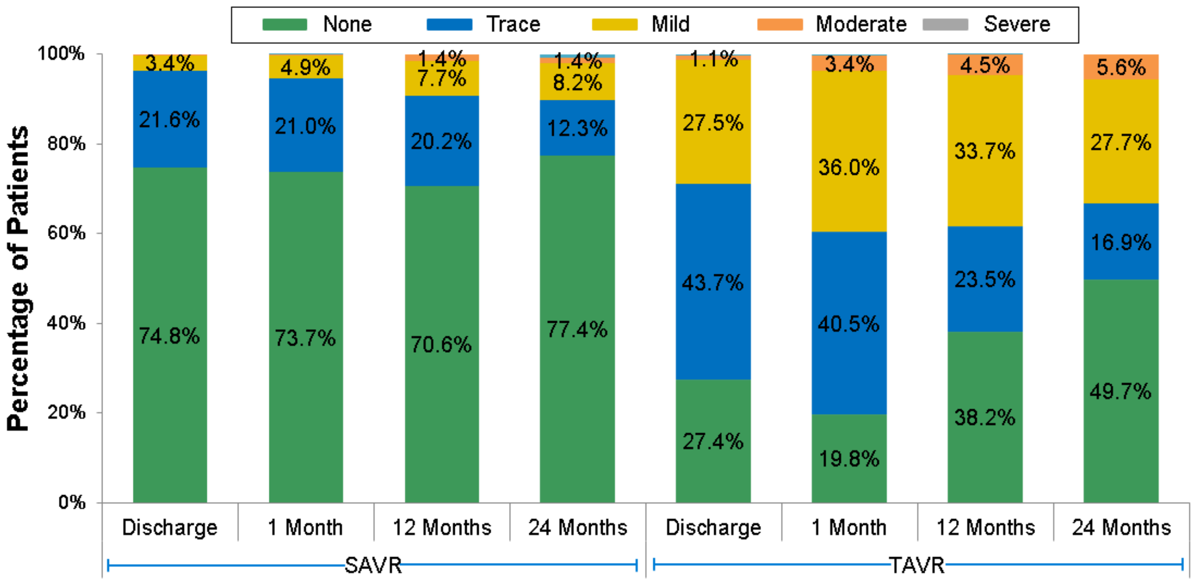

Figure 4: Total Aortic Regurgitation (Implanted Population)

Note: Values < 1.0% are not labeled.

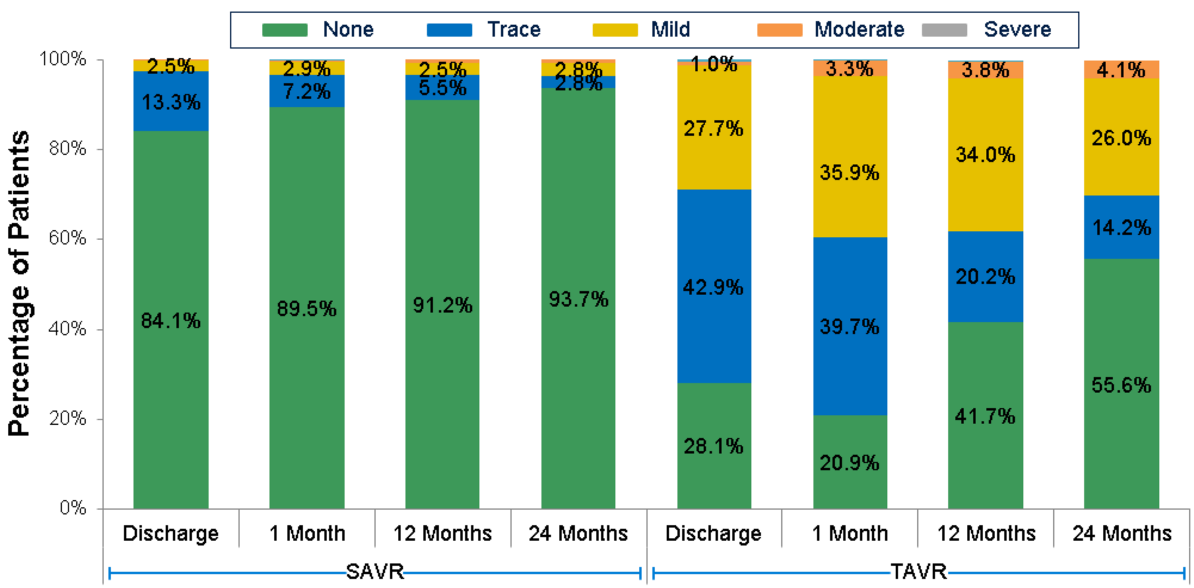

Figure 5: Paravalvular Aortic Regurgitation by Visit (Implanted Population)

Note: Values < 1.0% are not labeled.

NYHA functional class

The NYHA classifications by visit are presented in Figure 6.

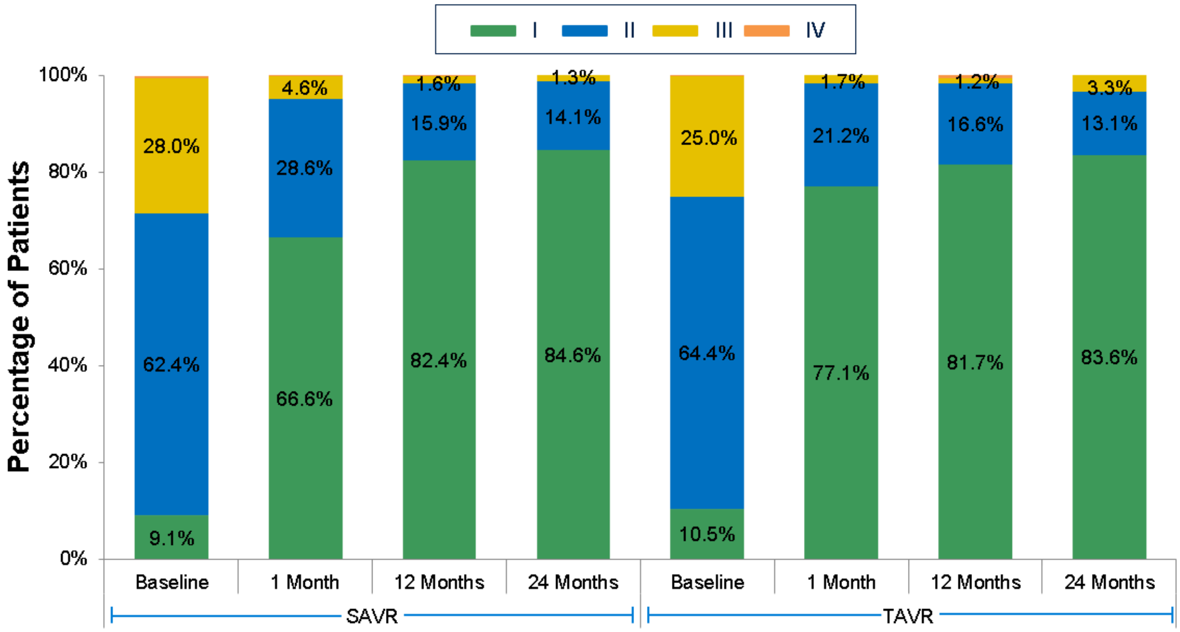

Figure 6: NYHA Classification by Visit (AT Population)

Note: Values < 1.0% are not labeled.

Quality of Life (QoL)

KCCQ

The KCCQ overall and clinical summary scores for the two treatment cohorts are shown in Figure 7 and Figure 8, respectively.

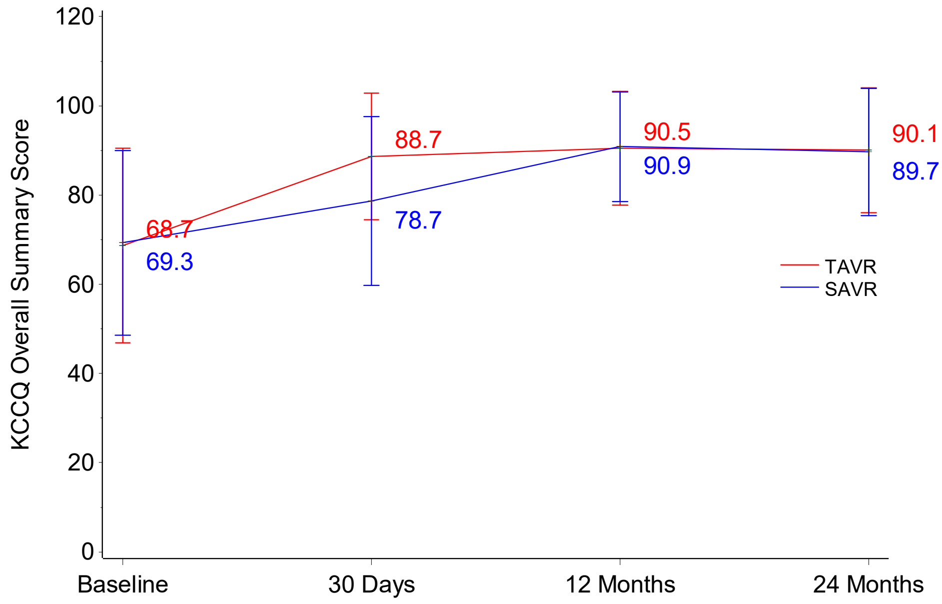

Figure 7: KCCQ Overall Summary Score (AT Population)

Note: Line plot with mean and standard deviation.

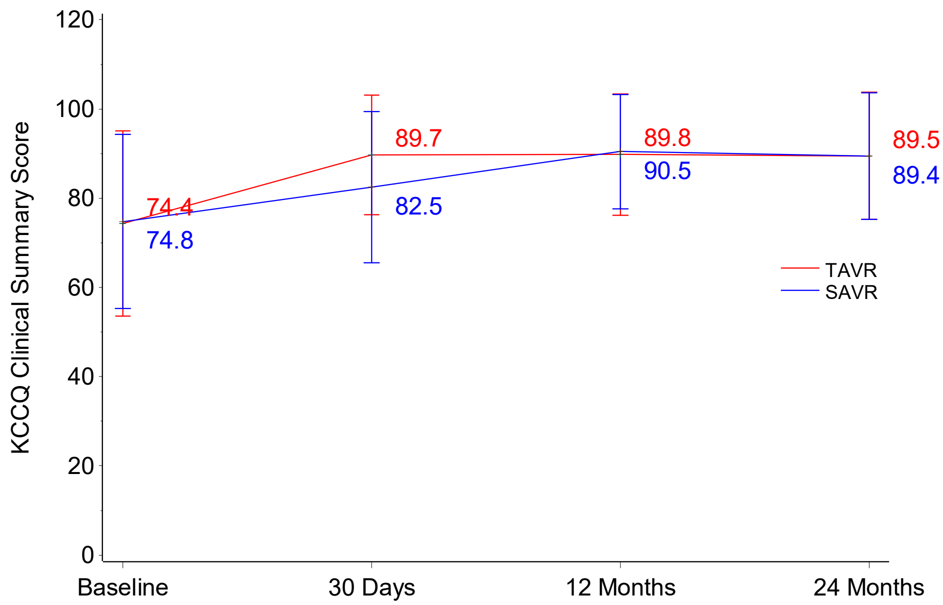

Figure 8: KCCQ Clinical Summary Score (AT Population)

Note: Line plot with mean and standard deviation.

EuroQoL (EQ-5D)

The EQ-5D index scores for the two treatment cohorts are shown in Figure 9.

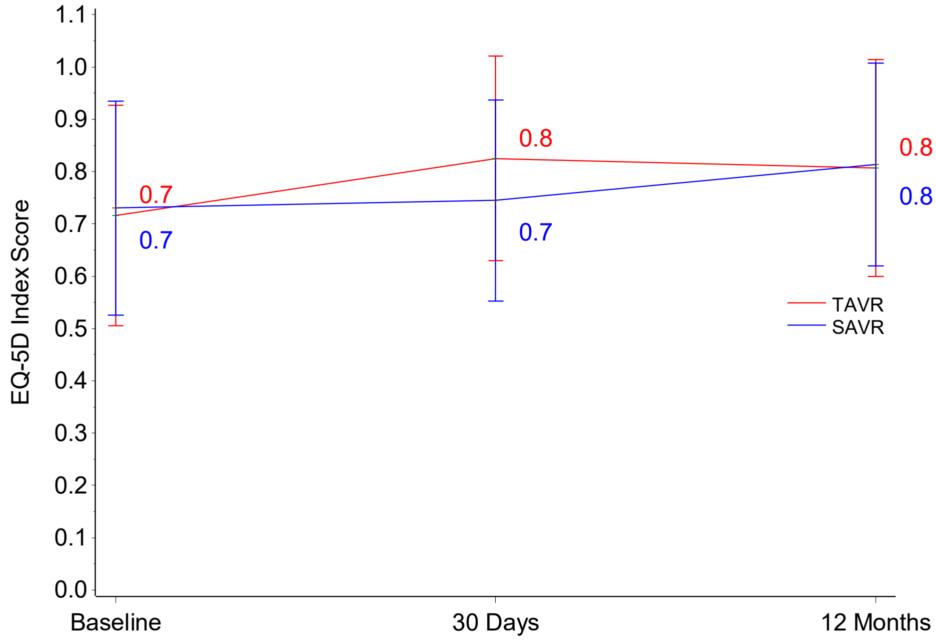

Figure 9: EQ-5D Index Score (AT Population)

Note: Line plot with mean and standard deviation.

1.1.3.4 Additional safety data

The key adverse events that occurred in the trial through 24 months are presented in Table 8.

Table 8: CEC Adjudicated Adverse Events through 24 months (AT Population)

Events	Kaplan-Meier Rate *					
	0-30 Days		0-12 Months		0-24 Months	
	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
All-cause mortality or disabling stroke	0.7% (5, 6)	2.5% (17, 20)	2.6% (18, 21)	4.5% (29, 34)	4.6% (24, 28)	5.9% (33, 39)
All-cause mortality	0.4% (3, 3)	1.2% (8, 8)	2.2% (15, 15)	2.8% (18, 18)	4.0% (20, 20)	3.6% (21, 21)
Cardiovascular	0.4% (3, 3)	1.2% (8, 8)	1.6% (11, 11)	2.5% (16, 16)	2.7% (14, 14)	2.8% (17, 17)
Non-cardiovascular	0.0% (0, 0)	0.0% (0, 0)	0.6% (4, 4)	0.3% (2, 2)	1.3% (6, 6)	0.8% (4, 4)
Reintervention	0.3% (2, 2)	0.3% (2 2)	0.6% (4, 4)	0.5% (3, 3)	0.8% (5, 5)	1.3% (5, 5)
All stroke	3.5% (25, 25)	3.3% (22, 23)	4.3% (31, 33)	4.4% (29, 31)	6.4% (37, 39)	6.4% (33, 35)
Disabling stroke	0.4% (3, 3)	1.6% (11, 12)	0.8% (6, 6)	2.3% (15, 16)	1.5% (8, 8)	3.1% (17, 18)
Non-disabling stroke	3.0% (22, 22)	1.6% (11, 11)	3.5% (25, 27)	2.2% (15, 15)	4.9% (29, 31)	3.4% (17, 17)
Life threatening/disabling bleeding	2.3% (17, 17)	7.5% (51, 51)	3.5% (25, 25)	8.7% (58, 59)	4.1% (28, 28)	8.7% (58, 59)
Major vascular complication	3.7% (27, 27)	3.1% (21, 21)	3.7% (27, 27)	3.4% (23, 23)	4.2% (28, 28)	3.7% (24, 24)
Acute kidney injury - Stage 3	0.4% (3, 3)	1.8% (12, 12)	0.4% (3, 3)	1.8% (12, 12)	0.4% (3, 3)	1.8% (12, 12)
Myocardial infarction	0.8% (6, 6)	1.3% (9, 9)	1.8% (13, 15)	1.6% (11, 12)	2.0% (14, 16)	1.6% (11, 12)
Aortic valve hospitalization†	1.1% (8, 8)	2.4% (16, 17)	3.3% (23, 29)	6.2% (40, 44)	5.0% (30, 39)	7.5% (44, 53)
New permanent pacemaker implantation‡	17.3% (125, 125)	6.1% (41, 41)	19.1% (138, 138)	6.7% (45, 45)	22.7% (150, 150)	7.6% (48, 48)

*Kaplan-Meier rate (# patients, # events).
†Not adjudicated by CEC.
‡ Patients with pacemaker or ICD at baseline were not counted as new events. Not adjudicated by CEC.

The patient prosthesis mismatch adjudicated by the core laboratory is summarized in Table 9.

Table 9: Patient Prosthesis Mismatch (Implanted Population)

Severity[†]	Summary Statistics[*]					
	30 Days		12 Months		24 Months	
	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
Severe	1.1% (7/610)	4.4% (24/545)	1.8% (9/489)	6.8% (30/438)	1.3% (2/154)	2.5% (3/120)
Moderate	10.0% (61/610)	16.0% (87/545)	5.5% (27/489)	16.7% (73/438)	7.1% (11/154)	14.2% (17/120)
None	88.9% (542/610)	79.6% (434/545)	92.6% (453/489)	76.5% (335/438)	91.6% (141/154)	83.3% (100/120)

[*]Observed rate - % (no./total no.)
[†]Severe: (Body mass index [BMI] < 30 and effective orifice area index [EOAI] < 0.65) OR (BMI ≥ 30 and EOAI < 0.60); moderate: (BMI < 30 and $0.65 \leq$ EOAI ≤ 0.85) OR (BMI ≥ 30 and $0.60 \leq$ EOAI ≤ 0.70); none: (BMI < 30 and EOAI > 0.85) OR (BMI ≥ 30 and EOAI > 0.70)

1.1.4 Additional study observations

1.1.4.1 Pre-specified analyses

The protocol specified subgroup analyses of the primary endpoint of all-cause mortality or disabling stroke at 24 months by randomization designation (TAVR vs. SAVR) for patients with and without revascularization and for patients of different genders.

***All-Cause Mortality or Disabling Stroke Stratified by Need for Revascularization*:**

The K-M curves of all-cause mortality or disabling stroke are shown in Figure 10 and Figure 11 for patients with and without the need for concomitant revascularization, respectively.

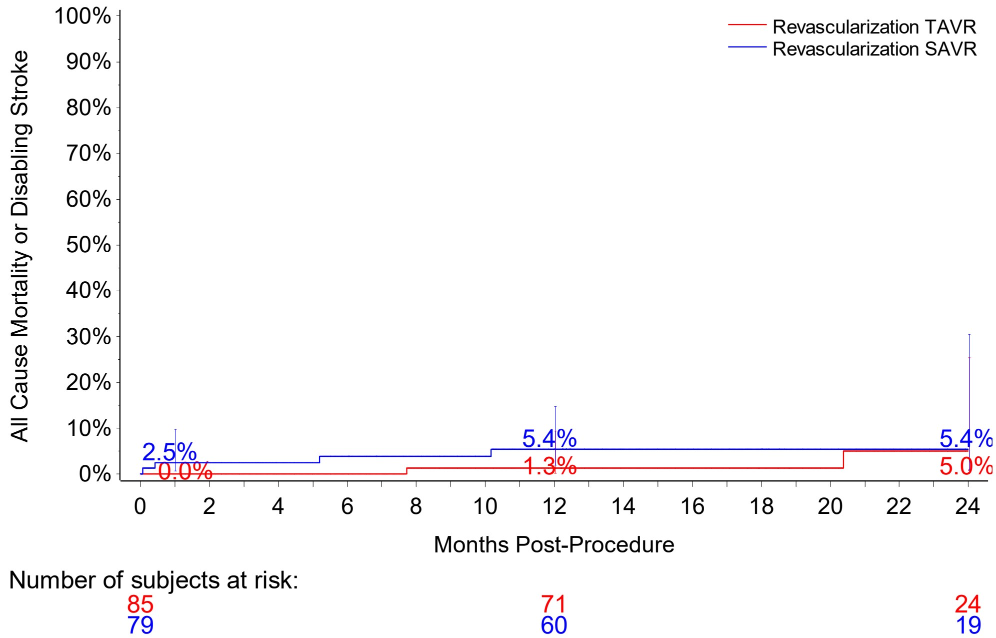

Figure 10: All-Cause Mortality or Disabling Stroke for Patients with Need for Revascularization – AT Population

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

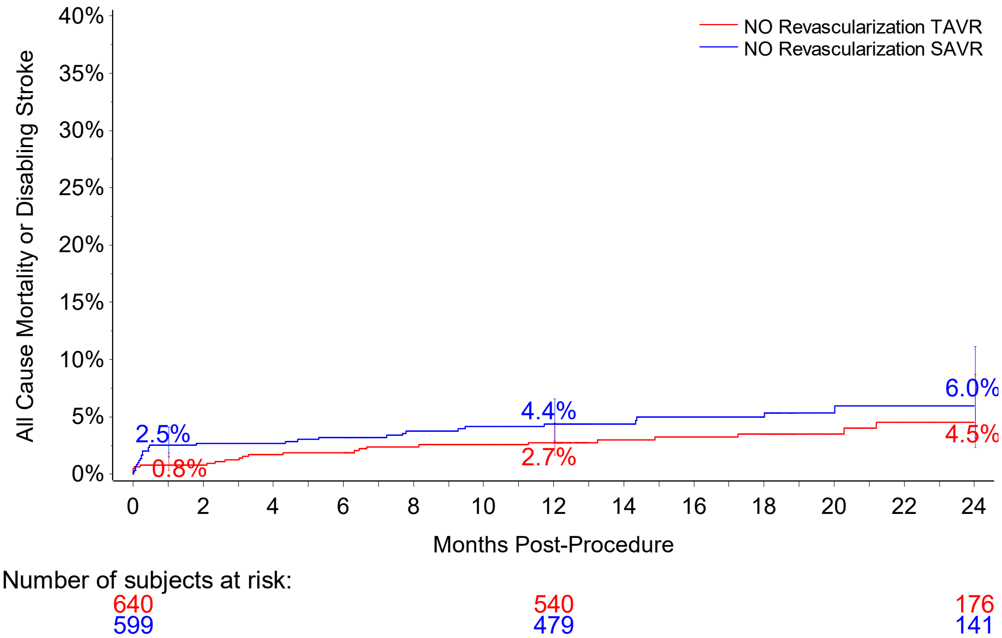

Figure 11: All-Cause Mortality or Disabling Stroke for Patients without Need for Revascularization – AT Population

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

All-cause mortality or disabling stroke analyzed by gender – AT Population

Figure 12 and Figure 13 present all-cause mortality or disabling stroke analyzed by gender for the AT population through 24 months.

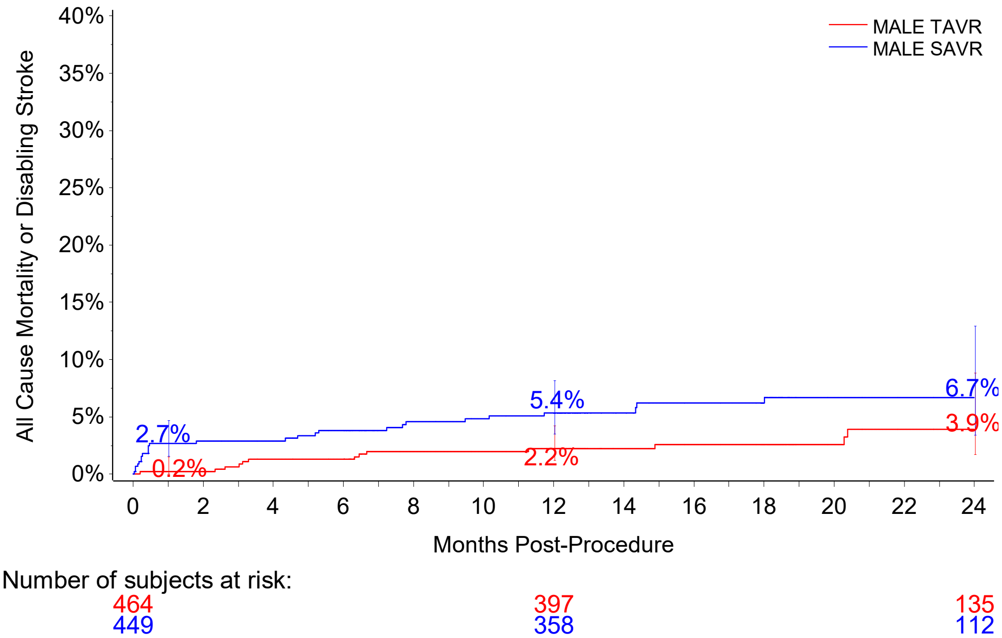

Figure 12: All-Cause Mortality or Disabling Stroke for Male Patients - AT Population

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

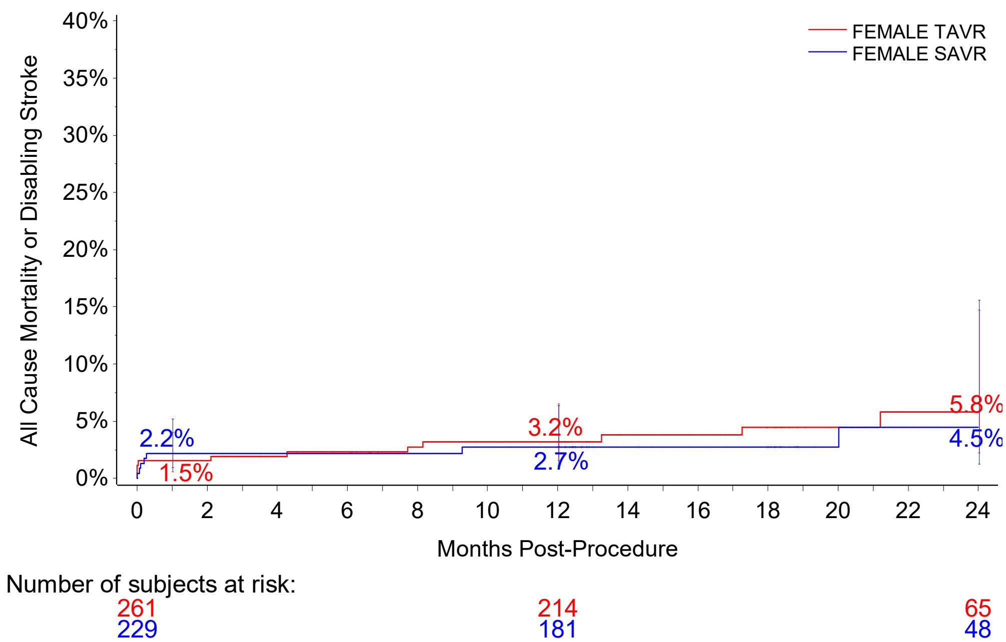

Figure 13: All-Cause Mortality or Disabling Stroke for Female Patients - AT Population

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

1.1.4.2 CT Sub-study

There were 197 TAVR and 178 SAVR patients at 30 days and 168 and 149 patients at 12 months, respectively, who had an adequate CT for leaflet assessments at both time points. The HALT and leaflet mobility imaging findings are summarized in Table 10 along with the associated mean aortic pressure gradients. The mean aortic pressure gradients at 12 months stratified by HALT and leaflet mobility at 30 days are summarized in Table 11 and Table 12, respectively. The rate of death, stroke or TIA at 1 year stratified by HALT and leaflet mobility at 30 days are summarized in Table 13 and Table 14, respectively. The CT substudy was not powered to compare the relative incidence or the severity of HALT or reduced leaflet mobility between the TAVR and SAVR cohorts, or to determine whether late clinical outcomes were affected by the presence of HALT or reduced leaflet mobility.

The information in Table 10 through Table 12 represents the data retrieved as of January 2020.

Table 10: HALT and Leaflet Mobility Findings and Associated Mean Gradients

Findings	Summary Statistics*			
	At 30 Days		At 12 Months	
	TAVR (N=197)	SAVR (N=178)	TAVR (N=168)	SAVR (N=149)
Proportion of patients on oral anticoagulants at time of scan†	9.1% (18/197)	21.9% (39/178)	11.3% (19/168)	18.1% (27/149)
HALT‡				
No HALT (no thickening)	82.2% (162/197)	87.1% (155/178)	70.2% (118/168)	77.2% (115/149)
Mean gradient (mmHg)	8.6 ± 3.6 (160)	10.5 ± 3.6 (153)	8.5 ± 3.2 (114)	11.2 ± 4.6 (114)
Presence of HALT	17.8% (35/197)	12.9% (23/178)	29.8% (50/168)	22.8% (34/149)
<25% leaflet length Thickened	10.7% (21/197)	2.8% (5/178)	17.3% (29/168)	4.7% (7/149)
Mean gradient (mmHg)	7.2 ± 3.0 (21)	9.4 ± 4.0 (5)	8.4 ± 2.8 (29)	9.7 ± 3.6 (7)
25%-50% leaflet length Thickened	3.0% (6/197)	5.1% (9/178)	6.0% (10/168)	8.1% (12/149)
Mean gradient (mmHg)	8.1 ± 1.6 (6)	10.8 ± 3.7 (9)	7.1 ± 2.3 (9)	11.4 ± 3.7 (12)
50%-75% leaflet length Thickened	2.0% (4/197)	3.4% (6/178)	5.4% (9/168)	4.7% (7/149)
Mean gradient (mmHg)	6.8 ± 3.0 (2)	12.2 ± 5.6 (6)	8.2 ± 4.0 (9)	11.5 ± 3.7 (7)
>75% leaflet length Thickened	2.0% (4/197)	1.7% (3/178)	1.2% (2/168)	5.4% (8/149)
Mean gradient (mmHg)	5.9 ± 1.4 (4)	6.9 ± 3.5 (3)	11.6 ± NA (1)	13.7 ± 11.2 (8)
Number of leaflets with HALT				
0 leaflet	82.2% (162/197)	87.1% (155/178)	70.2% (118/168)	77.2% (115/149)
1 leaflet thickening	11.7% (23/197)	5.1% (9/178)	16.1% (27/168)	12.8% (19/149)

Findings	Summary Statistics*			
	At 30 Days		At 12 Months	
	TAVR (N=197)	SAVR (N=178)	TAVR (N=168)	SAVR (N=149)
2 leaflets thickening	5.1% (10/197)	5.6% (10/178)	10.7% (18/168)	8.1% (12/149)
3 leaflets thickening	1.0% (2/197)	2.2% (4/178)	3.0% (5/168)	2.0% (3/149)
Leaflet mobility§				
Unrestricted	84.6% (148/175)	89.0% (153/172)	70.2% (113/161)	77.9% (109/140)
Mean gradient (mmHg)	8.6 ± 3.7 (146)	10.5 ± 3.6 (151)	8.4 ± 3.2 (111)	11.0 ± 4.5 (108)
Partially restricted (<25%)	9.7% (17/175)	5.2% (9/172)	19.9% (32/161)	5.7% (8/140)
Mean gradient (mmHg)	7.6 ± 3.2 (17)	9.6 ± 3.4 (9)	8.3 ± 2.9 (32)	8.8 ± 3.8 (8)
Partially restricted (25%-50%)	3.4% (6/175)	4.1% (7/172)	5.0% (8/161)	8.6% (12/140)
Mean gradient (mmHg)	7.0 ± 2.1 (5)	12.8 ± 5.5 (7)	8.0 ± 1.8 (7)	12.1 ± 3.3 (12)
Partially restricted (50%-75%)	1.7% (3/175)	1.2% (2/172)	3.7% (6/161)	4.3% (6/140)
Mean gradient (mmHg)	7.8 ± 1.6 (2)	10.6 ± 6.3 (2)	9.0 ± 4.5 (6)	12.3 ± 2.8 (6)
Largely immobile	0.6% (1/175)	0.6% (1/172)	1.2% (2/161)	3.6% (5/140)
Mean gradient (mmHg)	5.9 ± NA (1)	9.7 ± NA (1)	7.2 ± NA (1)	15.4 ± 14.3 (5)
Number of leaflets partially restricted or largely immobile				
0 leaflet	84.6% (148/175)	89.0% (153/172)	70.2% (113/161)	77.9% (109/140)
1 leaflet	10.3% (18/175)	4.1% (7/172)	16.1% (26/161)	12.1% (17/140)
2 leaflets	4.0% (7/175)	4.7% (8/172)	10.6% (17/161)	7.9% (11/140)

Findings	Summary Statistics*			
	At 30 Days		At 12 Months	
	TAVR (N=197)	SAVR (N=178)	TAVR (N=168)	SAVR (N=149)
3 leaflets	1.1% (2/175)	2.3% (4/172)	3.1% (5/161)	2.1% (3/140)

*Continuous measures - mean ± SD (n); categorical measures - % (no./total no.). The analysis population for the 30-day analysis included all the patients enrolled in the CT substudy and had an adequate CT for leaflet assessments at 30 days; the analysis population for the 12-month analysis had an adequate CT for leaflet assessments at both time points.

†During the course of the substudy enrollment, a protocol amendment removed the requirement for discontinuation of anticoagulation therapy prior to the CT scan at 30 days.

‡HALT was defined as: the presence of any hypoattenuated leaflet thickening in any singular leaflet as identified by an independent CT core laboratory. The extent of the hypoattenuated leaflet thickening was graded with regards to the entire leaflet as: none, <25%, 25-50%, 50-75%, >75%. If more than one leaflet had the appearance of HALT, the thickening measure of the most impacted leaflet was used.

§Leaflet mobility was determined by an independent CT core laboratory and included: unrestricted, partially restricted mobility limited to the base of a leaflet, partially restricted mobility involving more than the base of the leaflet but less than 50% of the leaflet, partially restricted mobility involving more than 50% of the leaflet but less than 75% of the leaflet, and/or a largely immobile leaflet. Presence of immobility any degree of restriction or immobility on any one leaflet rendered a finding.

Table 11: Mean Aortic Gradient at 1 Year Stratified by HALT at 30 Days

	Summary Statistics*			
	No HALT at 30 Days		HALT at 30 Days	
	TAVR (N=162)	SAVR (N=155)	TAVR (N=35)	SAVR (N=23)
Mean gradient	8.4 ± 3.0 (154)	11.5 ± 5.1 (145)	7.4 ± 3.5 (31)	10.6 ± 3.7 (21)

*Mean ± SD (n). The analysis population included all the patients enrolled in the CT substudy and had an adequate CT for leaflet assessments at 30 days.

Table 12: Mean Aortic Gradient at 1 Year Stratified by Leaflet Mobility at 30 Days

	Summary Statistics*			
	Unrestricted at 30 Days		Reduced Leaflet Mobility at 30 Days	
	TAVR (N=148)	SAVR (N=153)	TAVR (N=27)	SAVR (N=19)
Mean gradient	8.2 ± 2.9 (141)	11.4 ± 5.2 (142)	7.5 ± 3.6 (26)	11.1 ± 3.7 (18)

*Mean ± SD (n). The analysis population included all the patients enrolled in the CT substudy and had an adequate CT for leaflet assessments at 30 days.

Table 13: All-Cause Mortality, All Stroke or TIA at 1 Year Stratified by HALT

1-Year Endpoint	Kaplan-Meier Rate*			
	No HALT at 30 Days		HALT at 30 Days	
	TAVR (N=162)	SAVR (N=155)	TAVR (N=35)	SAVR (N=23)
All-cause mortality	0.0% (0, 0)	0.7% (1, 1)	0.0% (0, 0)	8.7% (2, 2)
All stroke	2.5% (4, 4)	1.9% (3, 3)	2.9% (1, 2)	4.5% (1, 2)
TIA	1.9% (3, 3)	0.0% (0, 0)	2.9% (1, 1)	0.0% (0, 0)
All-cause mortality or all stroke or TIA	4.3% (7, 7)	2.6% (4, 4)	5.7% (2, 3)	8.7% (2, 4)

*Kaplan-Meier rate (# patients, # events). The analysis population included all the patients enrolled in the CT substudy and had an adequate CT for leaflet assessments at 30 days. The Kaplan-Meier analysis used the procedure date as the start date in determining time to event. Presence of any degree of HALT on any one leaflet rendered a finding and inclusion in the HALT cohort.

Table 14: All-Cause Mortality, All Stroke or TIA at 1 Year Stratified by Leaflet Mobility at 30 Days

1-Year Endpoint	Kaplan-Meier Rate*			
	Unrestricted at 30 Days		Reduced Leaflet Mobility at 30 Days	
	TAVR (N=148)	SAVR (N=153)	TAVR (N=27)	SAVR (N=19)
All-cause mortality	0.0% (0, 0)	1.3% (2, 2)	0.0% (0, 0)	5.3% (1, 1)
All stroke	2.7% (4, 4)	2.6% (4, 5)	3.7% (1, 2)	0.0% (0, 0)
TIA	1.4% (2, 2)	0.0% (0, 0)	3.7% (1, 1)	0.0% (0, 0)

1-Year Endpoint	Kaplan-Meier Rate*			
	Unrestricted at 30 Days		Reduced Leaflet Mobility at 30 Days	
	TAVR (N=148)	SAVR (N=153)	TAVR (N=27)	SAVR (N=19)
All-cause mortality or all stroke or TIA	4.1% (6, 6)	3.3% (5, 7)	7.4% (2, 3)	5.3% (1, 1)

*Kaplan-Meier rate (# patients, # events). The analysis population included all the patients enrolled in the CT substudy and had an adequate CT for leaflet assessments at 30 days. The Kaplan-Meier analysis used the procedure date as the start date in determining time to event. The presence of any degree of restriction or immobility on any one leaflet rendered a finding and inclusion in the reduced leaflet mobility cohort.

1.2 Intermediate Risk trial (SURTAVI)

The Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI) trial is a prospective, randomized, unblinded, multi-center investigational study. The purpose of this trial is to investigate the safety and efficacy of transcatheter aortic valve implantation (TAVR) in subjects with severe, symptomatic aortic stenosis (AS) at intermediate surgical risk by randomizing subjects to either surgical aortic valve replacement (SAVR) or TAVR.

A total of 1746 subjects were randomized in this study (879 subjects were randomized to TAVR and 867 subjects were randomized to surgical aortic valve replacement [SAVR]) at 87 activated centers. Severe aortic stenosis was defined as an aortic valve area of ≤0.8 cm^2 or aortic valve area index ≤0.5 cm^2, a mean aortic valve gradient of >40 mmHg or jet velocity >4 m/sec. The primary objective of the study was to demonstrate that the safety and effectiveness of the Medtronic CoreValve system (TAVR), as measured by all-cause mortality or disabling stroke at 24 months, is non-inferior to surgical aortic valve replacement (SAVR) in the treatment of symptomatic severe aortic stenosis in subjects who have a predicted intermediate risk for aortic valve surgery.

Of the 879 subjects randomized to TAVR, 864 received an attempted implant and comprise the primary analysis cohort (the modified intention-to-treat [mITT] cohort) TAVR set, while 796 of the 867 randomized to SAVR received an attempted implant and comprise the mITT SAVR cohort. The implanted population (863 TAVR and 794 SAVR) consists of all subjects who were implanted with a valve. Of the 863 subjects in the Implanted TAVR group, 724 were attempted with the CoreValve system, 139 with the CoreValve Evolut R system. The following data summarize the results from the SURTAVI trial.

1.2.1 Patient population

The demographics of the study population are shown in Table 15. The treatment arms were generally well balanced (i.e., no statistically significant differences were identified between the treatment arms) with respect to age, gender, baseline NYHA classification, and aggregate indicators of surgical risk (STS score and EuroSCORE). Most the subjects were in NYHA class II and III.

Table 15: Subject Demographics and Clinical Characteristics – mITT Set

Demographics and Baseline Characteristics	Summary Statistics[1]		
	TAVR	SAVR	Difference (TAVR – SAVR) (95% BCI)[2]
Age (years)	79.9 ± 6.2 (864)	79.7 ± 6.1 (796)	(-0.37, 0.81)
Male	57.6% (498/864)	55.0% (438/796)	(-2.15%, 7.37%)
NYHA Class			
II	39.8% (344/864)	41.8% (333/796)	(-6.71%, 2.72%)
III	54.6% (472/864)	51.6% (411/796)	(-1.80%, 7.78%)
IV	5.6% (48/864)	6.5% (52/796)	(-3.30%, 1.31%)
STS Score (risk of mortality, %)	4.4 ± 1.5 (864)	4.5 ± 1.6 (796)	(-0.28, 0.03)
Logistic EuroScore (%)	11.9 ± 7.6 (864)	11.6 ± 8.0 (795)	(-0.44, 1.06)
Coronary artery disease	62.6% (541/864)	64.2% (511/796)	(-6.20%, 3.05%)
Previous MI	14.5% (125/864)	13.9% (111/796)	(-2.84%, 3.88%)
Previous reintervention			
Coronary artery bypass surgery	16.0% (138/864)	17.2% (137/796)	(-4.83%, 2.34%)
Percutaneous coronary intervention	21.3% (184/864)	21.2% (169/796)	(-3.88%, 3.99%)
Cerebrovascular disease	17.5% (151/864)	16.3% (130/796)	(-2.47%, 4.73%)
Peripheral vascular disease	30.8% (266/864)	29.9% (238/796)	(-3.54%, 5.29%)
Prior stroke	6.6% (57/864)	7.2% (57/796)	(-3.04%, 1.87%)
Chronic lung disease/COPD	35.4% (305/862)	33.5% (267/796)	(-2.74%, 6.39%)
Home oxygen	2.1% (18/864)	2.6% (21/795)	(-2.09%, 0.92%)
Creatinine level >2 mg/dl	1.6% (14/864)	2.1% (17/796)	(-1.90%, 0.81%)
Atrial fibrillation/atrial flutter	28.1% (243/864)	26.5% (211/796)	(-2.68%, 5.89%)
Permanent pacemaker implantation	9.7% (84/864)	9.0% (72/796)	(-2.14%, 3.47%)
History of hypertension	92.7% (801/864)	90.3% (719/796)	(-0.30%, 5.10%)
Cirrhosis of the liver	0.5% (4/863)	0.6% (5/795)	(-0.99%, 0.60%)
Echocardiographic findings—Implanted Population			
Effective orifice area (cm^2)	0.8 ± 0.2 (790)	0.8 ± 0.2 (727)	(-0.01, 0.03)
Mean gradient (mmHg)	47.2 ± 14.3 (856)	47.8 ± 13.8 (786)	(-2.03, 0.70)

[1] Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.)
[2] BCI: Bayesian credible interval

1.2.2 Procedure data

As shown in Table 16, total time the delivery catheter was in the body was approximately 15 minutes. A majority of TAVR subjects were administered general anesthesia while the remaining subjects underwent the procedure with conscious sedation. A substantial majority of the subjects (greater than 90%) has the valve delivered via iliofemoral access and percutaneous access was more common than surgical cut-down. Balloon predilatation was performed in approximately half of the subjects and postdilatation was performed in approximately 30%.

Table 16: Procedural Data Summary for TAVR Subjects – mITT Set

Assessment	Summary Statistics[1] N=864
Number of Index Procedures	863
Total delivery catheter in the body time (min)	15.0 ± 15.9
Type of Anesthesia	
General	75.7% (653/863)
Conscious Sedation	24.3% (210/863)
Respiratory Support Required	69.8% (602/863)
Access Site	
Femoral	93.2% (804/863)
Percutaneous	81.3% (654/804)
Surgical cut-down	18.7% (150/804)
Iliac	0.5% (4/863)
Percutaneous	75.0% (3/4)
Surgical cut-down	25.0% (1/4)
Subclavian axillary	2.3% (20/863)
Direct Aortic	4.1% (35/863)
Other	0.0% (0/863)
Total Time in Cath Lab or OR (min)	190.8 ± 61.3
Total Procedure Time (min)	52.3 ± 32.7
Pre-TAVR balloon valvuloplasty performed	47.2% (407/863)
Post-TAVR balloon valvuloplasty performed	29.0% (250/863)

[1] Continuous measures - Mean ± SD; categorical measures - % (no./Total no.). Data include subjects with the index procedure defined as the first procedure that the delivery catheter is introduced.

1.2.3 Safety and effectiveness results

1.2.3.1 Primary safety and effectiveness endpoint

The primary objective was to demonstrate that the safety and effectiveness of TAVR using the Medtronic CoreValve and CoreValve Evolut R systems, as measured by the all-cause mortality or disabling stroke rate during a fixed follow-up of 24 months, is non-inferior to SAVR in the treatment of symptomatic severe aortic stenosis in subjects who were determined by the heart team to be at intermediate surgical risk.

The "early win" assessment of the primary endpoint included all subjects in the mITT population (N = 1660). The median of the posterior distribution for the primary endpoint event rate was 12.6% for the TAVR arm and 14.0% for the SAVR arm, with a median of the posterior distribution of the difference in the primary endpoint event rate (TAVR – SAVR) of -1.4% and a 95% Bayesian credible interval (BCI) of (-5.2%, 2.3%), as summarized in Table 17. The posterior probability of non-inferiority with a margin of 7% was > 0.9999, which is greater than the pre-specified threshold of 0.971, thus the primary endpoint non-inferiority could be concluded.

Table 17: Primary Endpoint: All-Cause Mortality or Disabling Stroke at 24 Months - mITT Set

	TAVR N=864	SAVR N=796
Posterior Median (95% BCI)	12.6% (10.2%, 15.3%)	14.0% (11.4%, 17.0%)
Difference (TAVR-SAVR) Posterior Median (95% BCI)	-1.4% (-5.2%, 2.3%)	
Primary Objective – Non-Inferiority		
Posterior Probability $P(H_{A,\delta=0.07} \mid \text{data})$	> 0.9999	
Posterior Threshold for Non-Inferiority	0.971	
Non-inferiority test	Passed	

Figure 14 shows K-M rates of all-cause mortality or disabling stroke in the mITT set for both treatment arms up to 24 months follow-up.

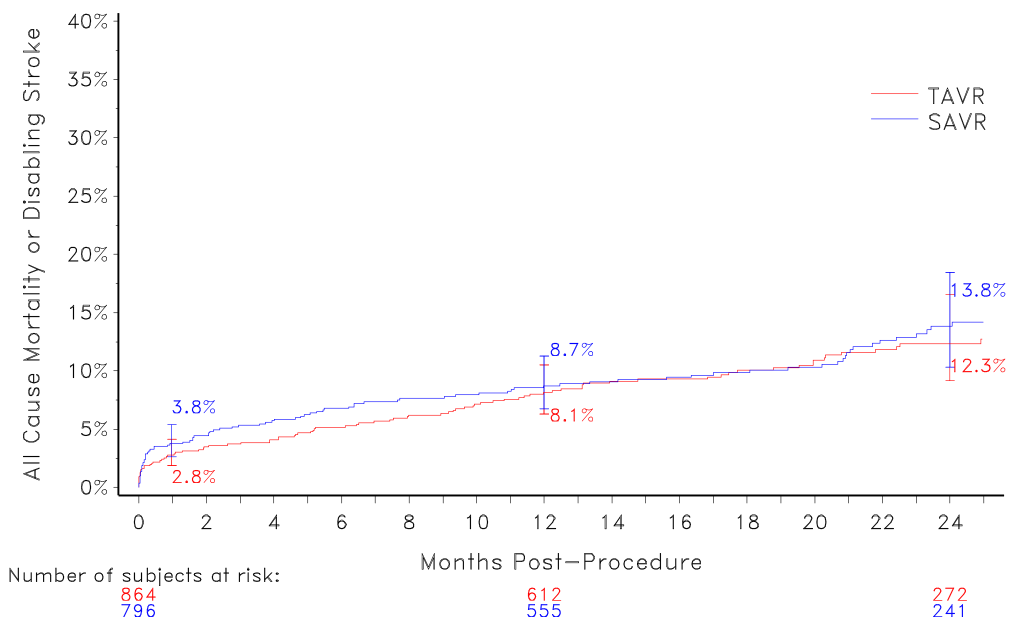

Figure 14: Primary Endpoint: All-Cause Mortality or Disabling Stroke Kaplan-Meier Event Rate – mITT Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

1.2.3.2 Key secondary safety and effectiveness endpoints

Hierarchical testing of secondary endpoints

Hypothesis testing was performed on pre-specified secondary endpoints using a hierarchical test procedure, as shown in Table 18. TAVR was found to be non-inferior to SAVR within the pre-specified non-inferiority margins in terms of mean gradient and EOA at 12 months, the NYHA functional classification change from baseline to 12 months, and the KCCQ score change from baseline to 30 days. TAVR was determined to be superior to SAVR with respect to length of index procedure hospital stay, the mean pressure gradient at 12 months, EOA at 12 months, and the KCCQ score change from baseline to 30-days.

TAVR was not found to be superior to SAVR with respect to days alive and out of hospital at 12 months. The remaining secondary endpoints were not tested.

Table 18: Secondary Endpoints: Hierarchical Testing

Secondary Endpoint	TAVR Mean ± SD (N)	SAVR Mean ± SD (N)	Difference (TAVR-SAVR) (95% BCI)	Posterior Probability $Pr(H_A \mid data)$	Threshold	Test Result
Non-inferiority testing						
#1 Mean gradient at 12 months	8.3 ± 4.0 (590)	11.7 ± 5.6 (500)	(-4.0, -2.8)	1.00	0.95	Passed
#2 EOA at 12 months	2.2 ± 0.6 (545)	1.8 ± 0.6 (455)	(0.3, 0.5)	1.00	0.95	Passed
#3 NYHA change (baseline – 12 months)	1.3 ± 0.8 (604)	1.3 ± 0.8 (508)	(-0.1, 0.1)	1.00	0.95	Passed
#4 KCCQ summary score change (30 day – baseline)	18.4 ± 22.8 (819)	5.9 ± 27.0 (700)	(10.0, 15.1)	1.00	0.95	Passed
Superiority testing						
#5 Length of index procedure hospital stay	5.8 ± 4.9 (863)	9.8 ± 8.0 (795)	(-4.7, -3.4)	1.00	0.975	Passed
#6 Mean gradient at 12 months	8.3 ± 4.0 (590)	11.7 ± 5.6 (500)	(-4.0, -2.8)	1.00	0.975	Passed
#7 EOA at 12 months	2.2 ± 0.6 (545)	1.8 ± 0.6 (455)	(0.3, 0.5)	1.00	0.975	Passed
#8 KCCQ summary score change (30 day – baseline)	18.4 ± 22.8 (819)	5.9 ± 27.0 (700)	(10.0, 15.1)	1.00	0.975	Passed

Note: The Implanted population was used for the mean gradient and EOA, and the mITT population for the rest.

1.2.3.3 Additional effectiveness data

Valve performance

Effective orifice area (EOA) and mean gradient for TAVR and SAVR subjects are shown in Figure 15 and Figure 16.

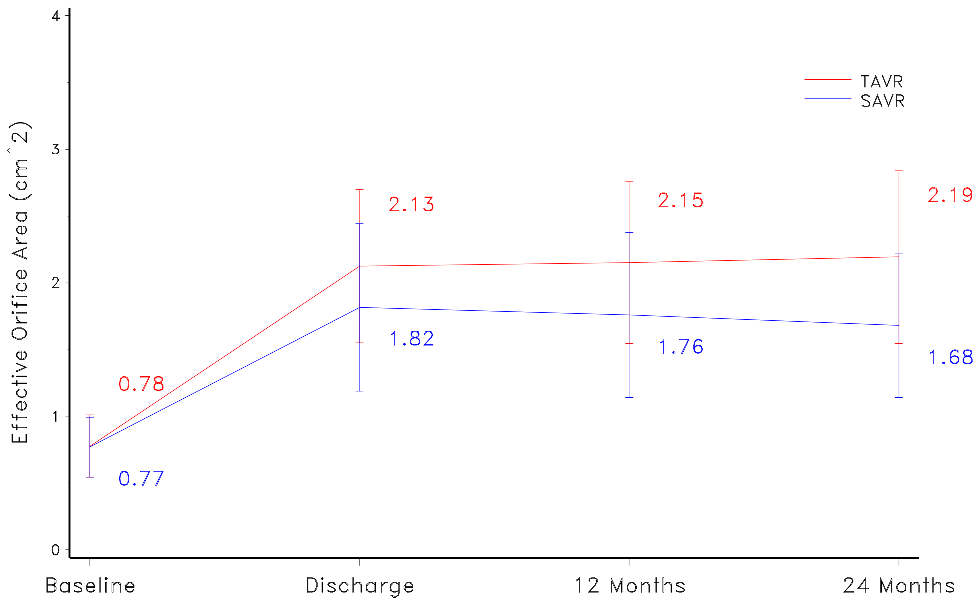

Figure 15: TAVR and SAVR EOA by Visit (Implanted Population)

Note: Line plot with mean and standard deviation.

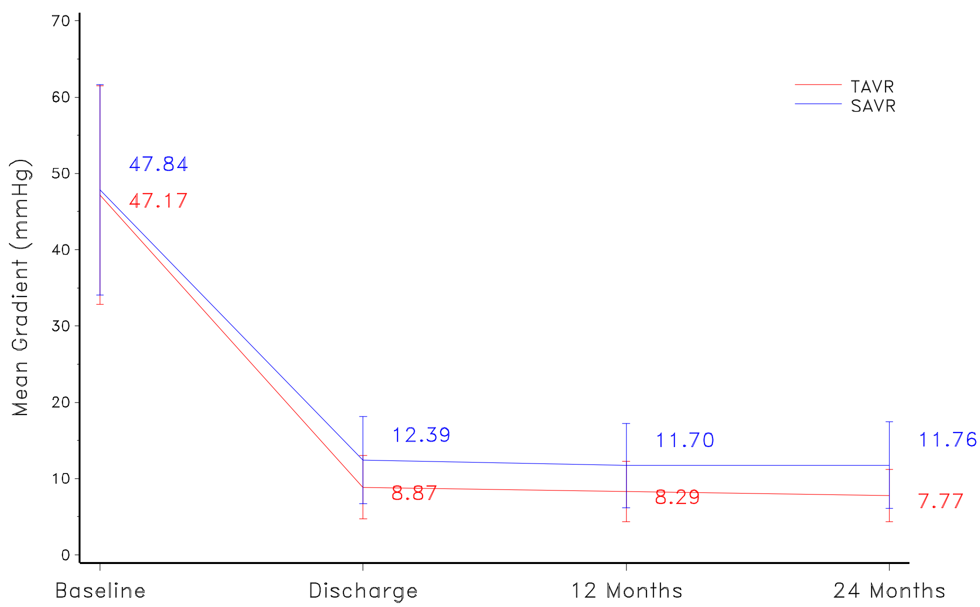

Figure 16: TAVR and SAVR Mean Gradient by Visit (Implanted Population)

Note: Line plot with mean and standard deviation.

Figure 17 shows total aortic regurgitation (AR) severity over time for both treatment arms. Figure 18 shows paravalvular aortic regurgitation.

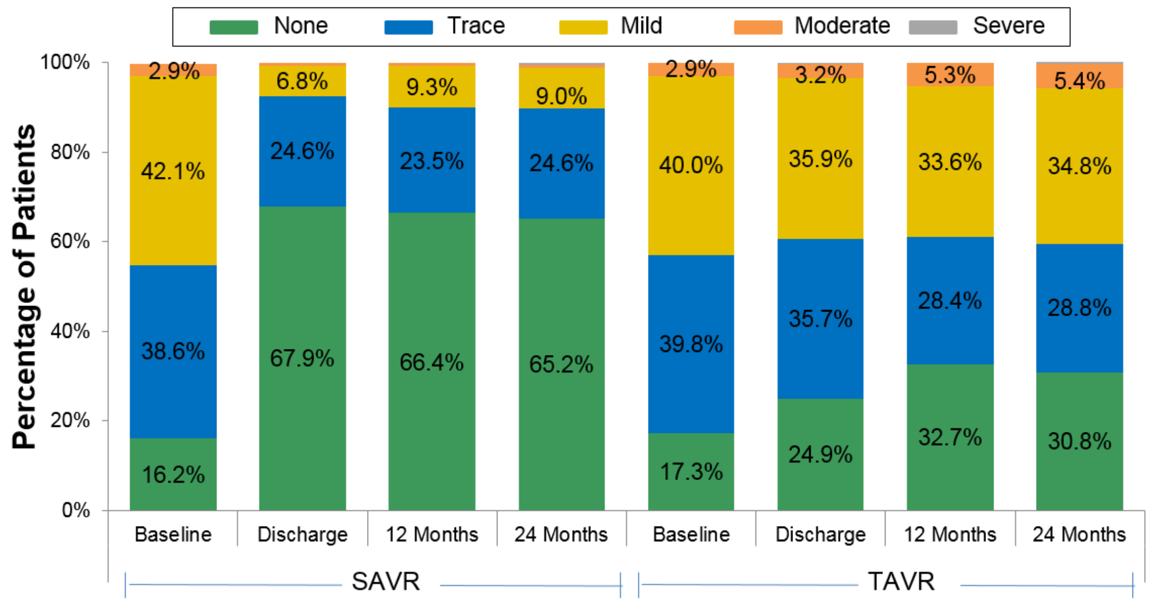

Figure 17: TAVR and SAVR Total Aortic Regurgitation by Visit (Implanted Population)

Note: Values < 1.0% are not labeled.

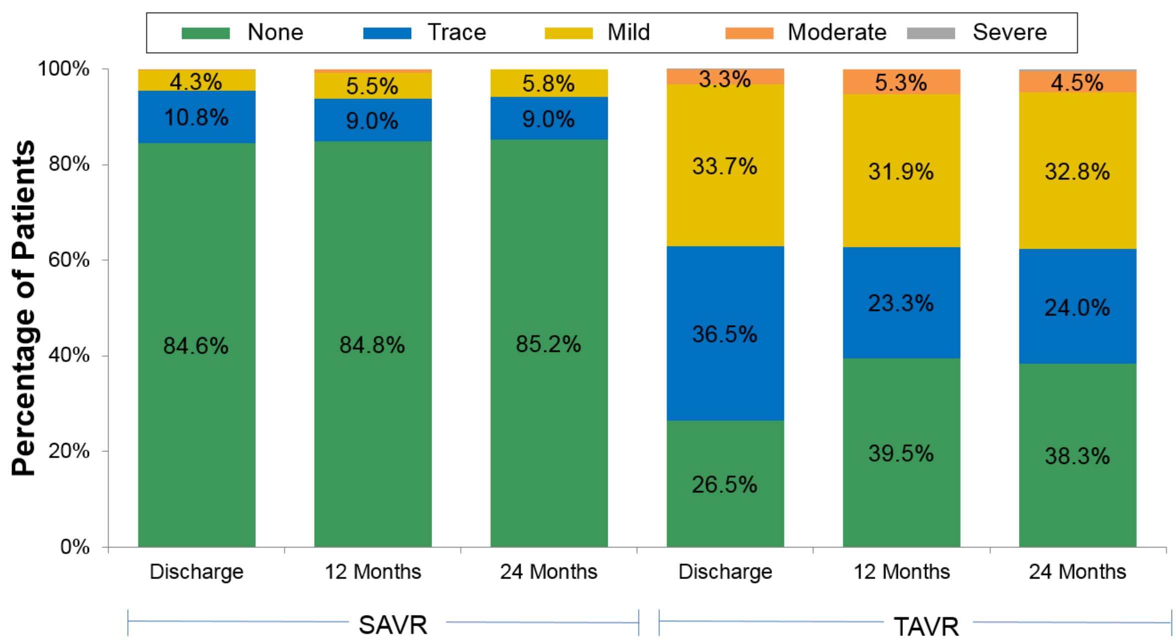

Figure 18: Paravalvular Aortic Regurgitation by Visit (Implanted Population)

Note: Values < 1.0% are not labeled.

NYHA functional class

NYHA functional classification was evaluated for subjects at each interval for the TAVR and SAVR treatment arms. NYHA classification data for subjects at each interval are shown in Figure 19.

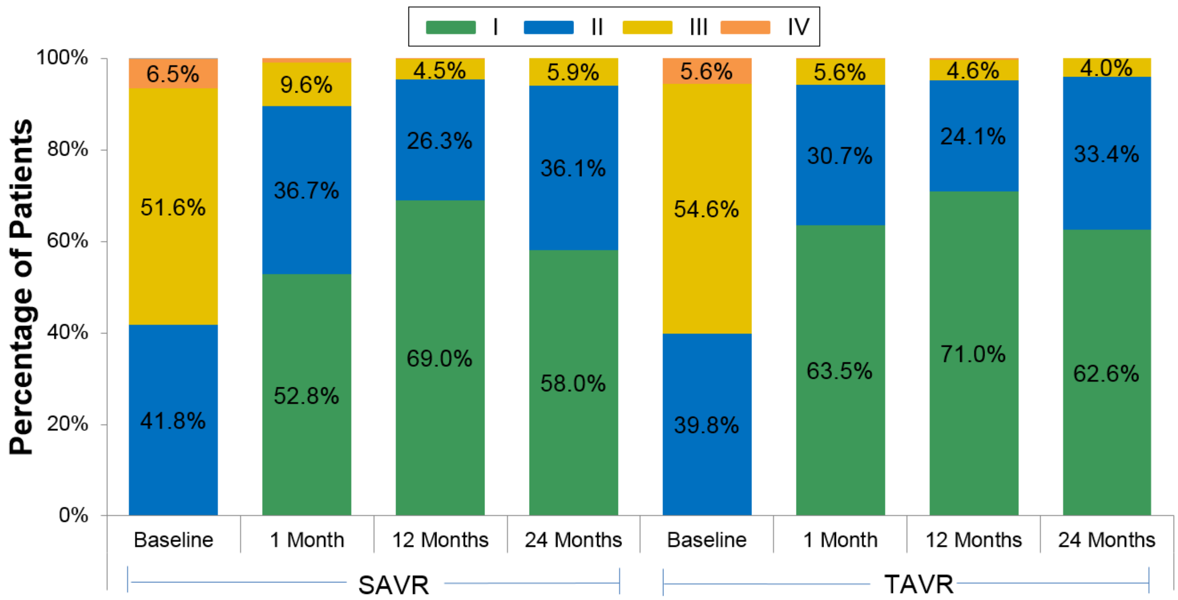

Figure 19: TAVR and SAVR NYHA Classification by Visit (mITT Population)

Note: Values < 1.0% are not labeled.

Health status/QoL change

QoL was measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ), the SF-36 Health Status Questionnaire, and the EuroQoL (EQ-5D) measure.

The KCCQ overall and clinical summary scores for the two treatment arms are shown in Figure 20 and Figure 21, respectively.

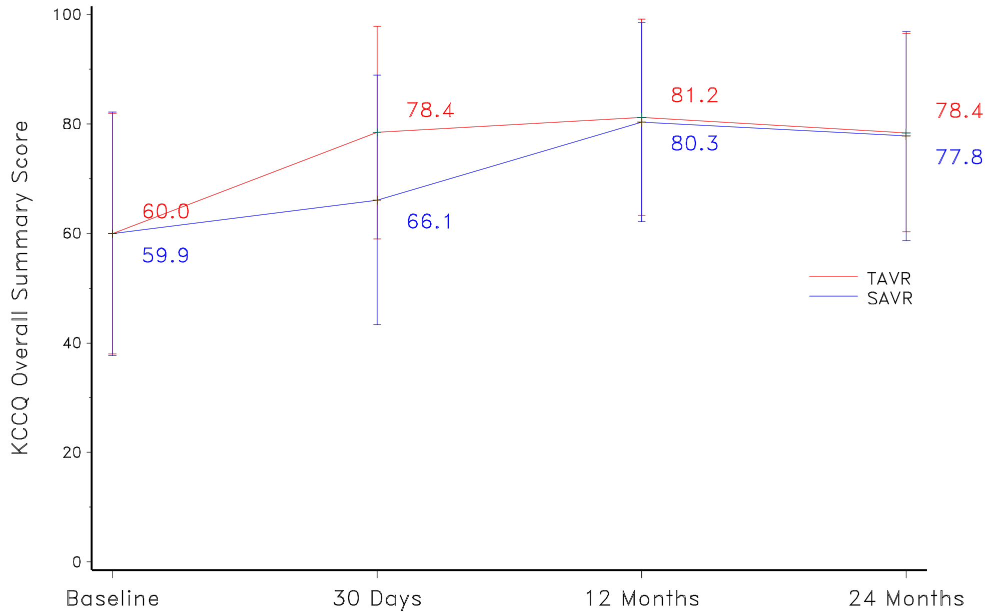

Figure 20: KCCQ Overall Summary Scores

Note: Line plot with mean and standard deviation.

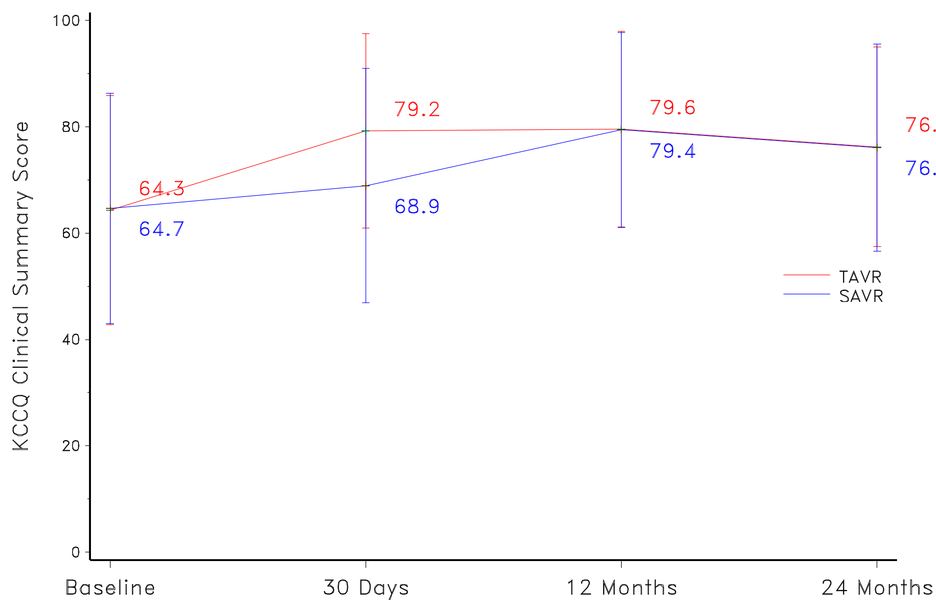

Figure 21: KCCQ Clinical Summary Scores

Note: Line plot with mean and standard deviation.

The SF-36 physical and mental component summary scores for the two treatment arms are shown in Figure 22 and Figure 23, respectively.

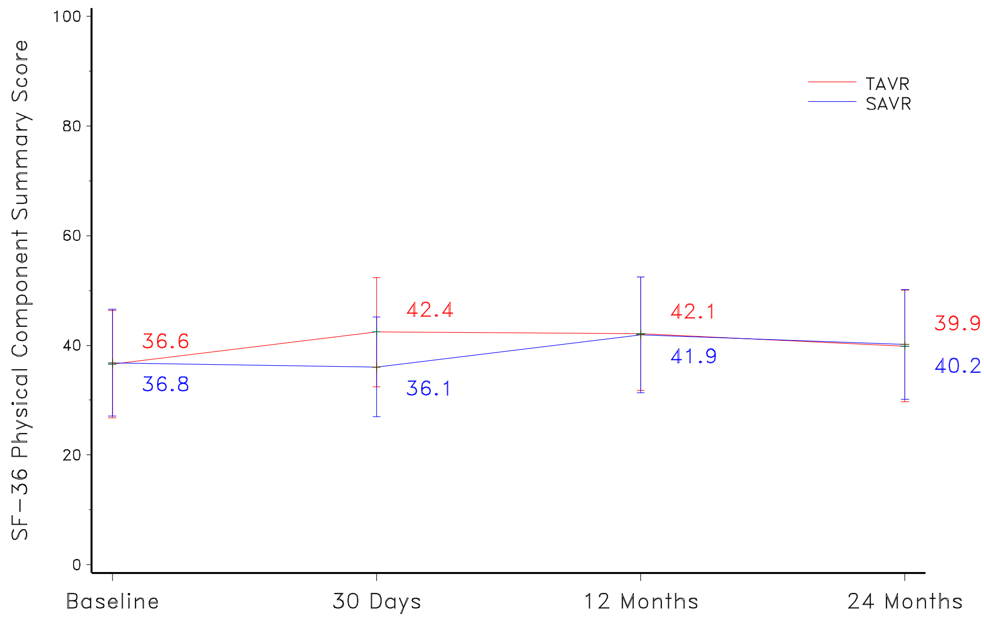

Figure 22: SF-36 Physical Component Summary Scores

Note: Line plot with mean and standard deviation.

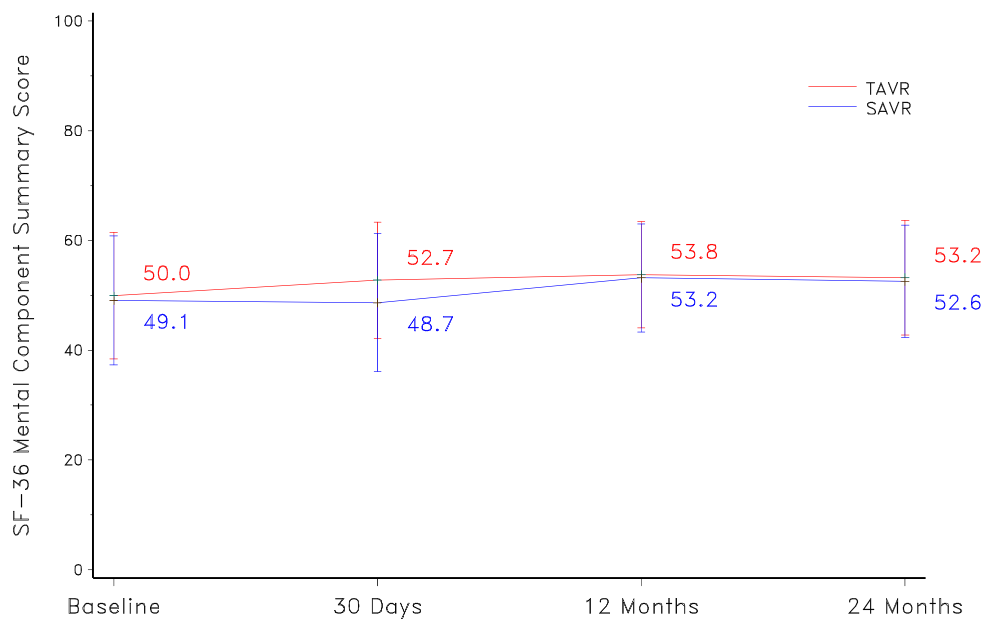

Figure 23: SF-36 Mental Component Summary Scores

Note: Line plot with mean and standard deviation.

The EQ-5D index scores for the two treatment arms are shown in Figure 24.

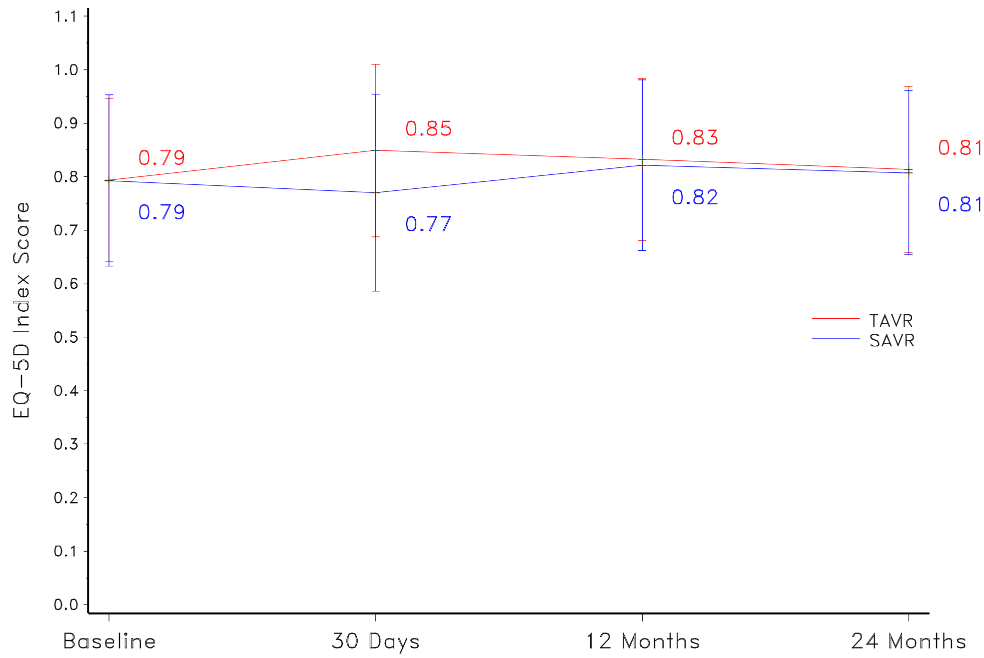

Figure 24: EQ5D Index Scores

Note: Line plot with mean and standard deviation.

1.2.3.4 Additional safety data

Adverse events that occurred in the PMA clinical study

Procedural safety and safety during follow-up were evaluated for both TAVR and SAVR within the SURTAVI trial. Kaplan-Meier (K-M) rates of some key CEC-adjudicated events are presented in Table 19.

Table 19: All Adverse Events (0-24 Months) -mITT Set

Events	Summary Statistics[1]					
	0-30 Days		0-12 Months		0-24 Months	
	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
All-cause mortality or disabling stroke	2.8% (24, 29)	3.8% (30, 33)	8.1% (66, 74)	8.7% (66, 79)	12.3% (87, 97)	13.8% (87, 101)
All-cause mortality	2.1% (18, 18)	1.6% (13, 13)	6.8% (55, 55)	6.9% (51, 51)	11.2% (77, 77)	11.5% (70, 70)
Cardiovascular	2.0% (17, 17)	1.6% (13, 13)	4.8% (39, 39)	5.5% (41, 41)	7.5% (52, 52)	7.8% (51, 51)
Valve-related[2]	0.0% (0, 0)	0.0% (0, 0)	0.0% (0, 0)	0.1% (1, 1)	0.0% (0, 0)	0.1% (1, 1)

Non-cardiovascular	0.1% (1, 1)	0.0% (0, 0)	2.1% (16, 16)	1.4% (10, 10)	4.0% (25, 25)	4.0% (19, 19)
Reintervention	0.8% (7, 7)	0.1% (1, 1)	2.1% (17, 19)	0.4% (3, 3)	2.6% (20, 22)	0.4% (3, 3)
All stroke	3.3% (28, 29)	5.4% (43, 45)	5.3% (44, 45)	6.7% (52, 55)	6.3% (48, 50)	8.0% (58, 61)
Disabling stroke	1.2% (10, 11)	2.4% (19, 20)	2.2% (18, 19)	3.4% (26, 28)	2.4% (19, 20)	4.1% (29, 31)
Non-disabling stroke	2.1% (18, 18)	3.0% (24, 25)	3.1% (26, 26)	3.3% (26, 27)	4.1% (30, 30)	4.0% (29, 30)
Life threatening/disabling bleeding	5.7% (49, 51)	5.9% (47, 47)	7.1% (60, 66)	7.8% (60, 61)	8.0% (64, 72)	8.4% (63, 65)
Major vascular complication	5.9% (51, 55)	1.0% (8, 8)	6.3% (54, 59)	1.0% (8, 8)	6.3% (54, 59)	1.0% (8, 8)
Acute kidney injury - Stage 3	0.7% (6, 6)	1.3% (10, 10)	0.7% (6, 6)	1.3% (10, 10)	0.7% (6, 6)	1.3% (10, 10)
MI	0.8% (7, 7)	0.9% (7, 7)	1.9% (15, 15)	1.4% (11, 11)	2.6% (18, 18)	1.9% (13, 13)
Aortic valve hospitalization	2.8% (24, 26)	4.1% (32, 34)	8.4% (68, 104)	7.4% (55, 68)	13.2% (90, 134)	9.0% (62, 85)
Permanent pacemaker implantation[3]	28.1% (217, 217)	6.8% (48, 48)	31.3% (239, 241)	9.0% (62, 64)	34.6% (253, 257)	10.3% (67, 70)
Permanent pacemaker implantation[4]	25.6% (220, 220)	6.5% (51, 51)	28.5% (242, 244)	8.6% (66, 68)	31.5% (256, 260)	9.8% (71, 74)

[1] Kaplan-Meier rate (# patients, # events).
[2] Valve-related death is any death caused by structural or non-structural valve dysfunction or aortic valve re-intervention.
[3] Subjects with pacemaker or ICD at baseline are not included. Not adjudicated by CEC.
[4] Subjects with pacemaker or ICD at baseline are included. Not adjudicated by CEC.

1.2.4 Additional study observations

1.2.4.1 Pre-specified analyses

The primary endpoint was examined for treatment arm differences in outcome between the stratified randomization designation (revascularization or no revascularization) and gender.

All-cause mortality or disabling stroke stratified by need for revascularization – mITT set

Figure 25 and Figure 26 present the all-cause mortality or disabling stroke analysis stratified by need for coronary revascularization for the mITT set.

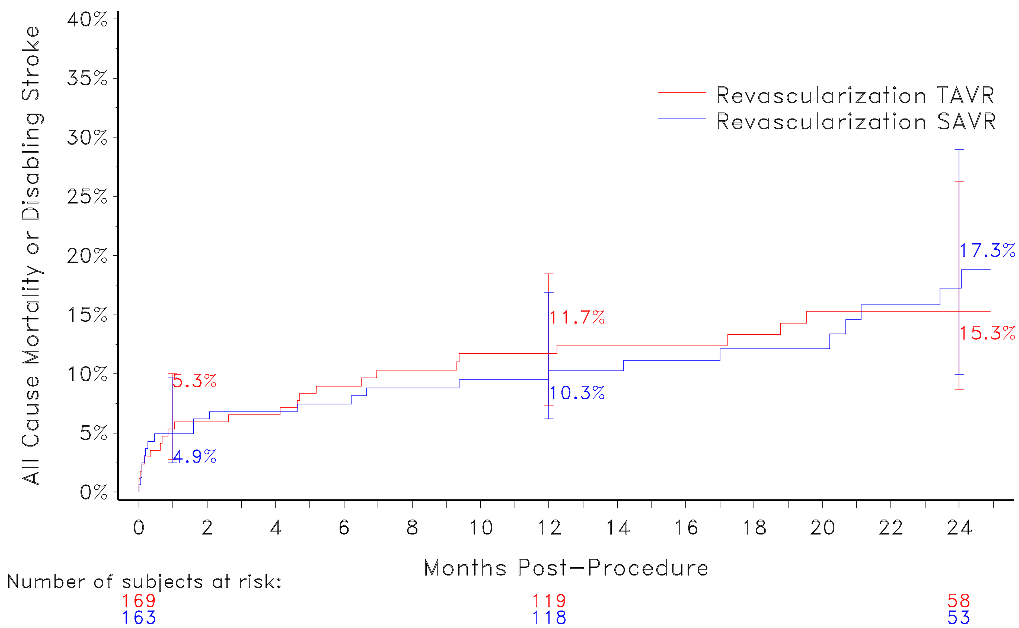

Figure 25: All-Cause Mortality or Disabling Stroke for Subjects with Need for Revascularization – mITT Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

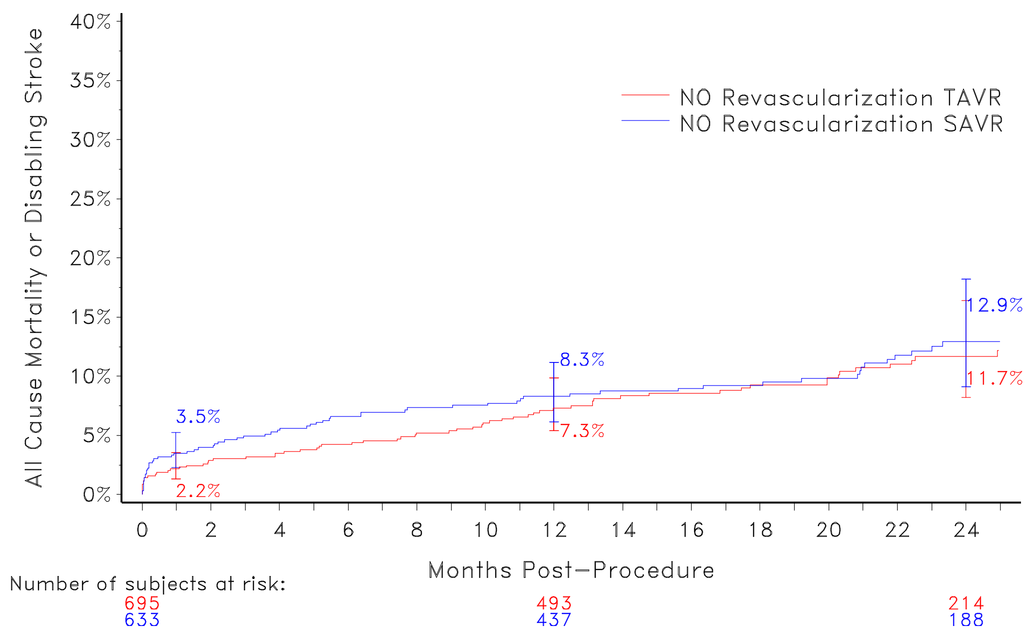

Figure 26: All-Cause Mortality or Disabling Stroke for Subjects without Need for Revascularization – mITT Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

All-cause mortality or disabling stroke analyzed by gender – mITT set

Figure 27 and Figure 28 present all-cause mortality or disabling stroke analyzed by gender for the mITT set.

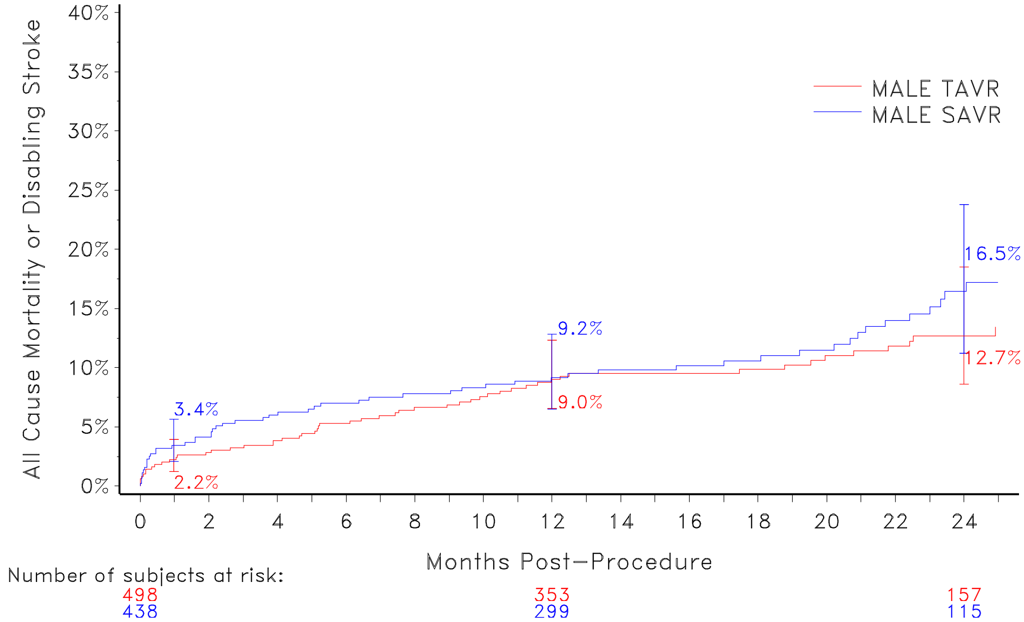

Figure 27: All-Cause Mortality or Disabling Stroke at 24 Months for Male Subjects - mITT Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

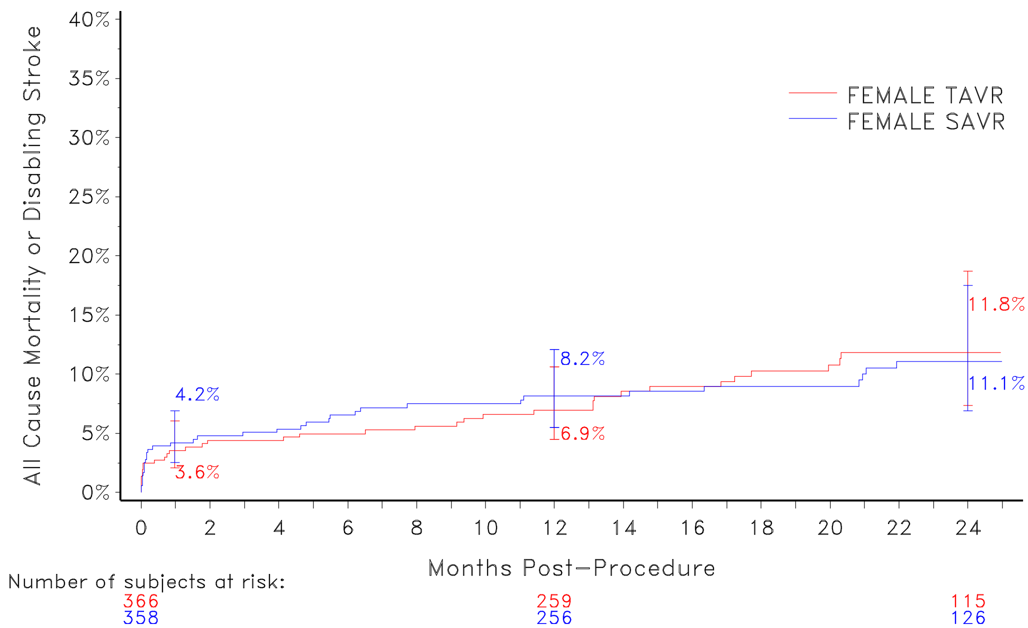

Figure 28: All-Cause Mortality or Disabling Stroke at 24 Months for Female Subjects – mITT Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

1.2.4.2 All-cause mortality by severity of aortic regurgitation

A sub-group analysis was performed to investigate the relationship between all-cause mortality and severity of aortic regurgitation at discharge. Two sub-groups of subjects with none/trace and mild/moderate/severe total AR as assessed at discharge were analyzed.

The results from the analysis with 2 subgroups are shown for the TAVR treatment arm in Figure 29.

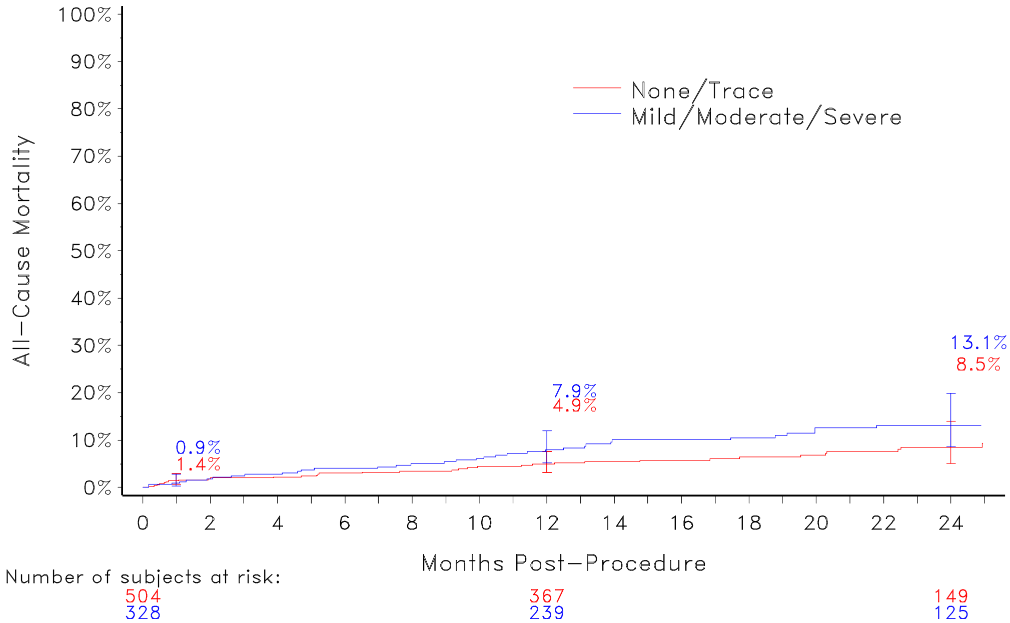

Figure 29: All-Cause Mortality by Severity of Aortic Regurgitation (2 Groups) – TAVR Implanted Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference between the two subgroups.

1.2.4.3 All-cause mortality by conduction disturbance requiring a permanent pacemaker post-TAVR

An analysis was performed for implanted TAVR subjects to investigate the relationship between all-cause mortality and permanent pacemaker implantation (PPI) through 30 days post TAVR (Figure 30). Similar rates between subjects without a PPI and subjects with a new PPI indicate that new-onset conduction disturbance and resultant PPI was not significantly associated with mortality in this study.

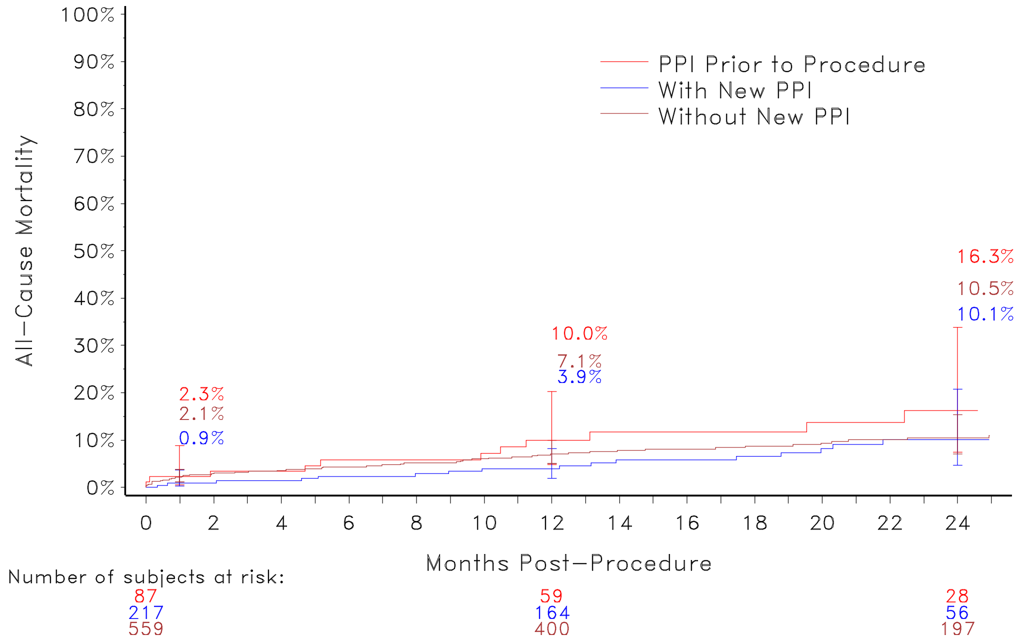

Figure 30: All-Cause Mortality by New Permanent Pacemaker – TAVR Implanted Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference among the three subgroups.

All-cause mortality by patient prosthesis mismatch

The site reported aortic annular perimeters were comparable between the two treatment arms (TAVR: 78.3 ± 7.2 mm vs. SAVR: 78.4 ± 7.1 mm). Patient prosthesis mismatch (PPM) is defined as an indexed EOA of 0.85-0.65 cm^2/m^2 (moderate) and <0.65 cm^2/m^2 (severe) for subjects with a BMI <30 kg/cm^2, or 0.70-0.60 cm^2/m^2 (moderate) and <0.60 cm^2/m^2 (severe) for subjects with a BMI ≥30 kg/cm^2. Figure 31 and Figure 32 present the prevalence of PPM at 12 months in the two treatment arms by valve size. The majority of SAVR patients received a labeled valve size of ≤23 mm, and smaller valve sizes generally had more prevalent PPM. In comparison, PPM was less prevalent in the TAVR arm.

The K-M curves for all-cause mortality by PPM grade (none, moderate, and severe) are shown in Figure 33 and Figure 34 for the TAVR and SAVR arm, respectively.

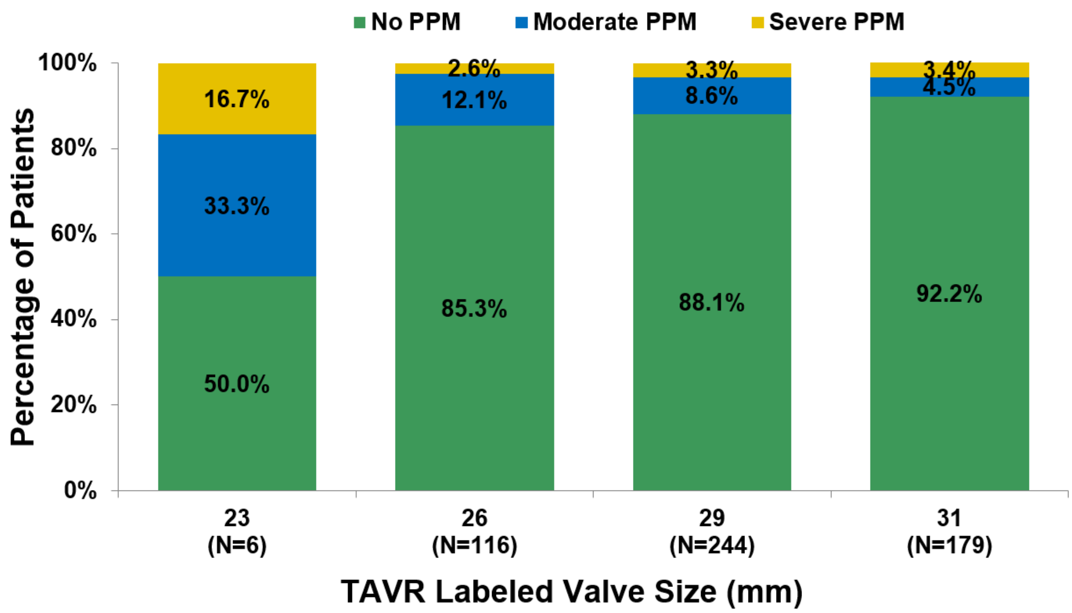

Figure 31: Prevalence of PPM at 12 Months in the TAVR Arm by Valve Size

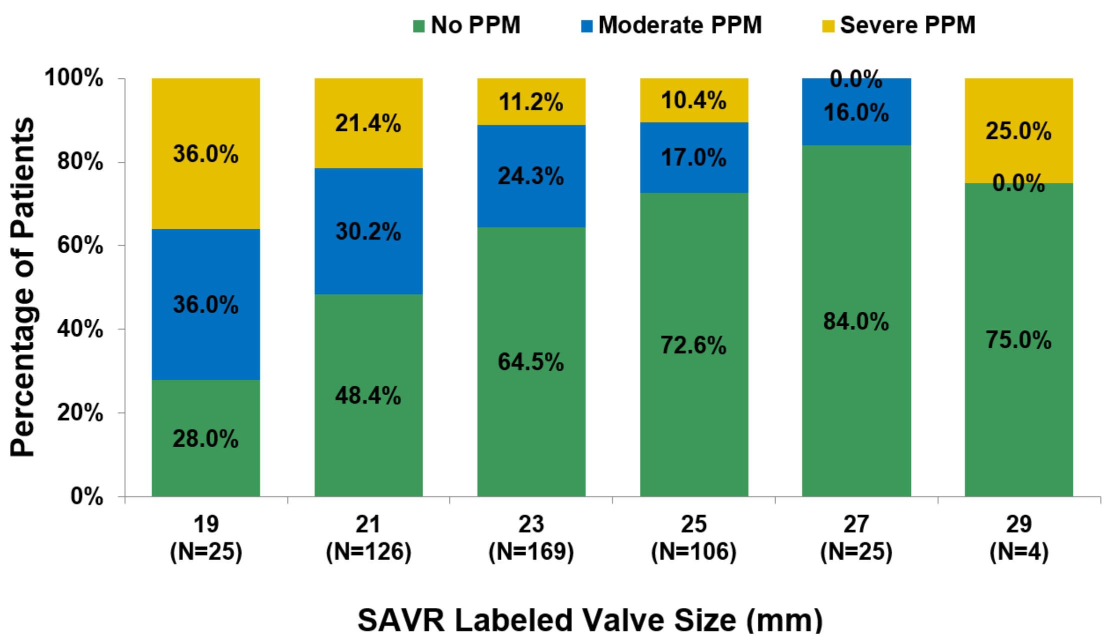

Figure 32: Prevalence of PPM at 12 Months in the SAVR Arm by Valve Size

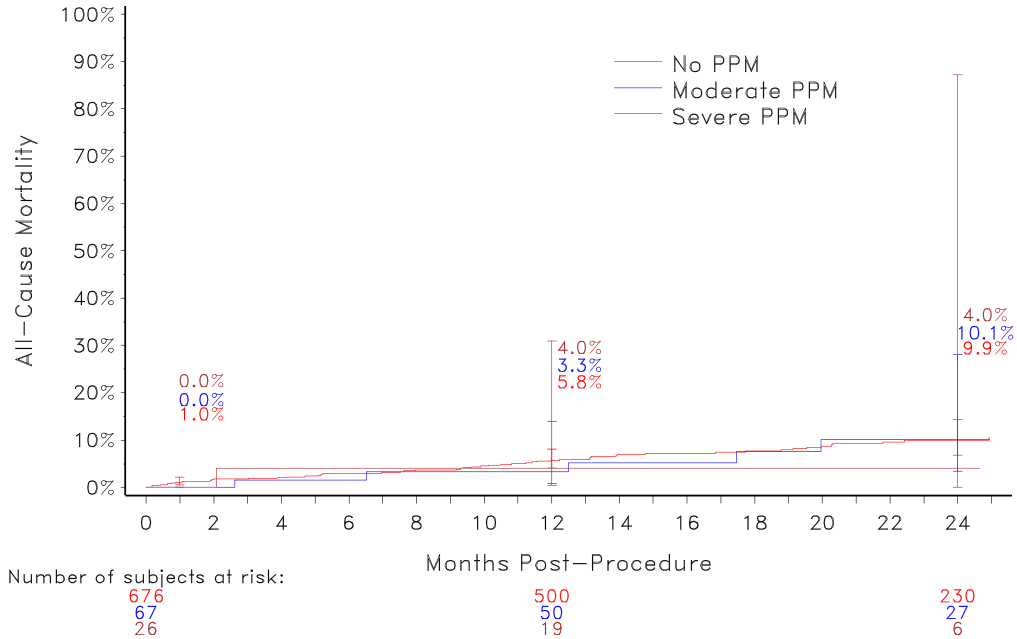

Figure 33: All-Cause Mortality by PPM - TAVR Implanted Population

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference among the three subgroups.

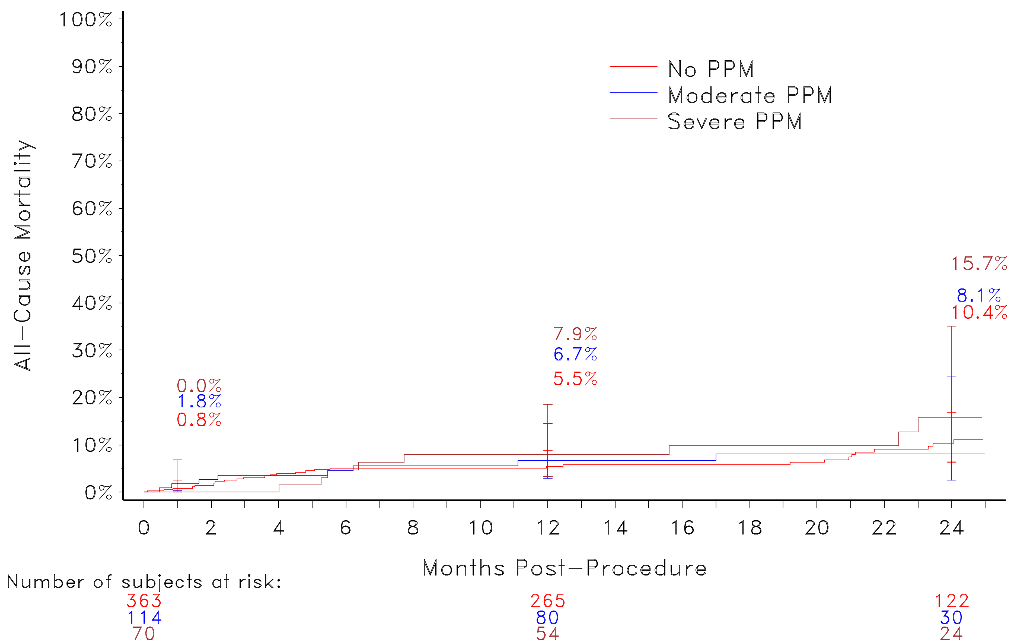

Figure 34: All-Cause Mortality by PPM - SAVR Implanted Set

Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. The trial was not powered to assess the difference among the three subgroups.

1.3 Evolut R study

1.3.1 Patient population

Eligible subjects presented with severe symptomatic aortic stenosis and significant co-morbidities in whom the risk of surgical aortic valve replacement was considered at high through extreme risk for surgical aortic valve replacement.

A total of 166 subjects were enrolled in the Global Evolut R Clinical Studies with 106 subjects from the United States and 60 subjects from Australia, New Zealand and the UK.

The patient characteristics analyzed include demographics, clinical characteristics, medical history, and potentially prohibitive anatomic factors for surgical aortic valve replacement (SAVR) and assessments for co-morbidity, frailty, and disability (Table 20).

The mean age for patients participating in the studies was 83.4 years old, and 62.7% of patients were female. The mean Society of Thoracic Surgeons (STS) score was 6.9%. A total of 74.7% of all patients were in NYHA class III or IV. Additionally, frailty was present in 67.5% of patients, COPD in 48.8%, atrial fibrillation/atrial flutter was present in 33.1% of the patients, and peripheral vascular disease was present in 30.1% of patients. Additional baseline information is provided in Table 20.

Table 20: Baseline Characteristics

Characteristic	Evolut R (N=166)
Age (years)	83.4±6.8
Gender Female (%)	62.7% (104/166)
STS PROM Score (%)	6.9±3.5
NYHA	
I/II	25.3% (42/166)
III/IV	74.7% (124/166)
STS Factors	
Serum Creatinine >2 mg/dl	2.4% (4/166)
Chronic Lung Disease (COPD)	48.8% (81/166)
Peripheral Vascular Disease	30.1% (50/166)
Cerebrovascular Disease	18.7% (31/166)
Previous CABG	23.5% (39/166)
Previous Other Cardiac - PCI	25.9% (43/166)
Previous MI	13.3% (22/166)
Atrial Fibrillation / Atrial Flutter	33.1% (55/166)
Other Co-Morbidities and Medical History	
Porcelain Aorta	1.8% (3/166)
Severely Atherosclerotic Aorta	4.2% (7/166)
Frailty	67.5% (112/166)
Abnormal Chest Wall Anatomy	1.8% (3/166)
Cirrhosis of the Liver	0.0% (0/166)
Pre-Existing Permanent Pacemaker or Defibrillator	15.1% (25/166)

1.3.2 Procedural results

Table 21 provides a summary of the transcatheter valve implantation procedures. Evolut R implantation was attempted in all 166 subjects. The majority of implantations (71.7%) were performed under general anesthesia and using the transfemoral approach (95.2%). There were no intra-procedural deaths, conversions to surgery, aortic annular ruptures, or coronary obstructions.

Table 21: Procedural Results

Assessment	Evolut R (N=166)
Anesthesia Type	
General	71.7% (119/166)
Local	28.3% (47/166)
Implanted Valve Size	
23 mm	1.2% (2/166)
26 mm	32.5% (54/166)
29 mm	57.2% (95/166)
34 mm	9.0% (15/166)
Pre-BAV	57.8% (96/166)
Post-Implant Dilatation	26.5% (44/166)
Access Route	
Transfemoral	95.2% (158/166)
Subclavian	0.6% (1/166)
Direct Aortic	4.2% (7/166)
Multiple Valve (≥ 2 Implanted)	1.2% (2/166)
Coronary Obstruction	0.0% (0/166)

1.3.3 Safety and efficacy results

1.3.3.1 Primary safety endpoints

The primary safety endpoints were all-cause mortality at 30 days and disabling stroke at 30 days.

The K-M estimate of all-cause mortality was 1.2% at 30 days, as shown in Figure 35 and Table 22.

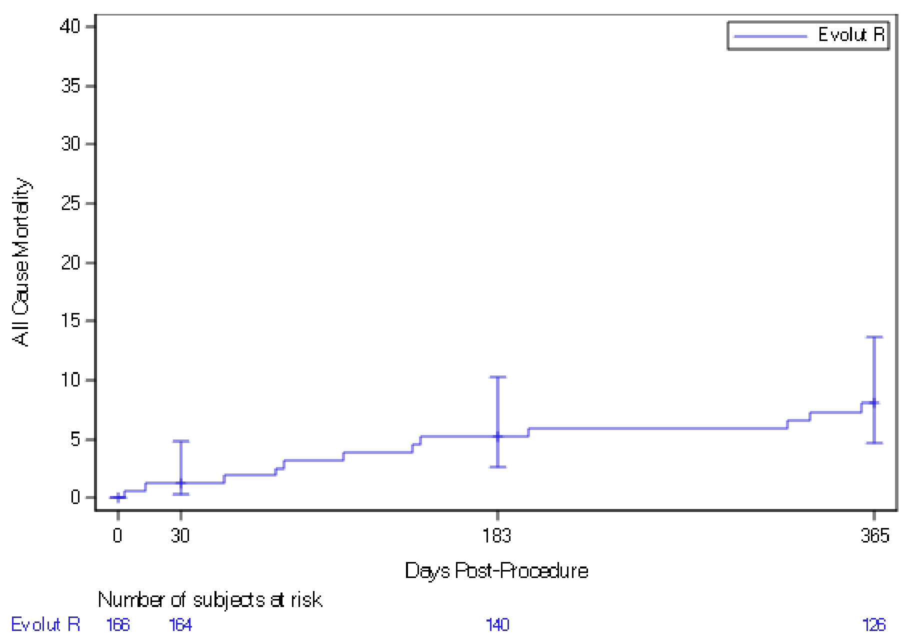

Figure 35: All-Cause Mortality

Note: The confidence intervals are calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. Note the 6-month and 12-month data are incomplete at this time and the data collection is ongoing.

Table 22: All-Cause Mortality

	Evolut R (N=166)		
	30 Days	6 Months	12 Months
Number at Risk	164	140	126
# Subjects (# Events)	2 (2)	8 (8)	12 (12)
K-M Rate (%)	1.2%	5.2%	8.0%
Two-Sided 95% CI	0.3% - 4.7%	2.6% - 10.3%	4.5% - 14.0%

The K-M estimate of disabling stroke was 3.0% at 30 days, as shown in Figure 36 and Table 23.

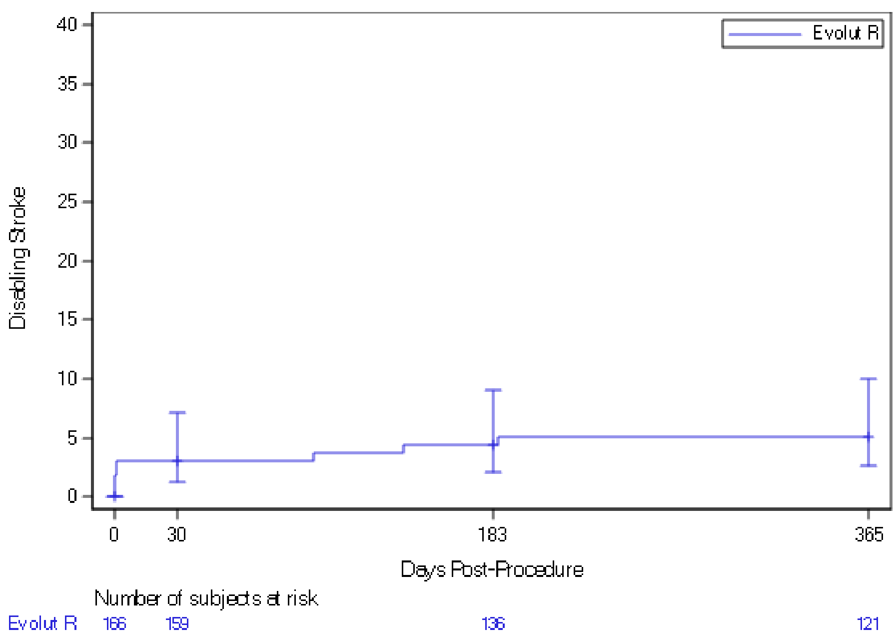

Figure 36: Disabling Stroke

Note: The confidence intervals are calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion. Note the 6-month and 12-month data are incomplete at this time and the data collection is ongoing.

Table 23: Stroke (Disabling)

	Evolut R (N=166)		
	30 Days	6 Months	12 Months
Number at Risk	159	136	121
# Subjects (# Events)	5 (5)	7 (7)	8 (9)
K-M Rate (%)	3.0%	4.4%	5.1%
Two-Sided 95% CI	1.3% - 7.1%	2.0% - 9.4%	2.4% - 10.7%

1.3.3.2 Primary efficacy endpoints

The primary clinical efficacy endpoint was device success at 24 hours to 7 days as defined by the Valve Academic Research Consortium (VARC II). The overall composite device success rate was 70.7%, as shown in Table 24.

Table 24: Device Success Rate – VARC II

	Device Success (24 hours to 7 days) (N=166)
Absence of Procedural Mortality	98.8% (164/166)
Correct Positioning of Single Valve in Proper Anatomical Location	98.8% (164/166)
Intended Performance of Prosthetic Heart Valve	71.8% (107/149)
Absence of Patient Prosthesis Mismatch	74.8% (110/147)
Mean Gradient < 20 mmHg or Peak Velocity < 3 m/sec	98.8% (161/163)
Absence of Moderate or Severe Prosthetic Regurgitation	94.5% (156/165)
Overall Device Success	70.7% (106/150)

The second primary clinical efficacy endpoint was the percentage of subjects with no more than mild aortic regurgitation at early post procedure echocardiogram (24 hours to 7 days). The result for this endpoint was 94.5% (refer to Table 27 for additional hemodynamic performance results).

1.3.3.3 Comparison of primary endpoints to historical control rates

The Evolut R study endpoints were intended to confirm the changes and features incorporated in the Evolut R system did not adversely affect safety and clinical performance characteristics of the predecessor CoreValve system. Table 25 summarizes the results for the primary endpoints, along with the corresponding historical control rates, which were established through data from the U.S. CoreValve Extreme and High Risk clinical studies, and a review of the contemporary published literature on the Medtronic CoreValve system. The results confirmed that the Evolut R system performed comparably with the CoreValve system.

Table 25: Primary Endpoints

Endpoint	Historical Control Rates	Evolut R Result
All-cause mortality at 30 days	7.3%	1.2%
Disabling stroke at 30 days	3.3%	3.0%
Device Success	73.2%	70.7%
% with ≤ mild AR at early post procedure echo	84.4%	94.5%

1.3.3.4 Additional safety endpoints

Table 26 provides a summary of the adverse events (AEs) that occurred in this study. Bleeding complications and major vascular access site and access-related complications were the most frequently observed early adverse events.

Table 26: Safety Endpoints at 30 Days, 6 Months, and 12 Months Post Procedure

	30 Days		6 Months		12 Months	
	# Subjects (# Events)	K-M Rate (%)	# Subjects (# Events)	K-M Rate (%)	# Subjects (# Events)	K-M Rate (%)
All-Cause Mortality	2 (2)	1.2%	8 (8)	5.2%	12 (12)	8.0%
Cardiovascular	2 (2)	1.2%	6 (6)	3.9%	10 (10)	6.7%
Myocardial Infarction	1 (1)	0.6%	1 (2)	0.6%	2 (3)	1.3%
Peri-Procedural	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
Spontaneous	1 (1)	0.6%	1 (2)	0.6%	2 (3)	1.3%
Stroke or TIA	6 (6)	3.6%	10 (11)	6.4%	13 (17)	8.5%
All Stroke	6 (6)	3.6%	8 (9)	5.0%	10 (13)	6.4%
Disabling Stroke	5 (5)	3.0%	7 (7)	4.4%	8 (9)	5.1%
TIA	0 (0)	0.0%	2 (2)	1.4%	4 (4)	2.9%
Vascular Access Site and Access-Related Complications	22 (23)	13.3%	22 (23)	13.3%	22 (23)	13.3%
Major	12 (12)	7.2%	12 (12)	7.2%	12 (12)	7.2%
Bleeding Complications	28 (30)	16.9%	30 (35)	18.3%	37 (43)	23.4%
Life Threatening or Disabling	10 (10)	6.0%	13 (14)	8.1%	15 (16)	9.6%
Major	13 (13)	7.9%	14 (14)	8.5%	19 (19)	12.2%
Acute Kidney Injury	8 (8)	4.8%	8 (8)	4.8%	8 (8)	4.8%
Stage 1	7 (7)	4.2%	7 (7)	4.2%	7 (7)	4.2%
Stage 2	1 (1)	0.6%	1 (1)	0.6%	1 (1)	0.6%
Stage 3	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
Prosthetic Valve Thrombosis	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
Prosthetic Valve Endocarditis	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
Late Valve Embolization or Migration	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
Valve-Related Dysfunction Requiring (Reintervention) Repeat Procedure	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
New Pacemaker*	22 (22)	15.7%	25 (25)	18.1%	26 (26)	19.0%
New Pacemaker	22 (22)	13.3%	25 (25)	15.3%	26 (26)	16.1%
Coronary Artery Obstruction	0 (0)	0.0%	0 (0)	0.0%	0 (0)	0.0%
*Subjects with pacemaker or ICD at baseline are not included in the denominator.						

1.3.3.5 Additional efficacy endpoints

Figure 37 shows the Mean Gradient and Effective Orifice Area (EOA) values obtained by visit for Evolut R subjects.

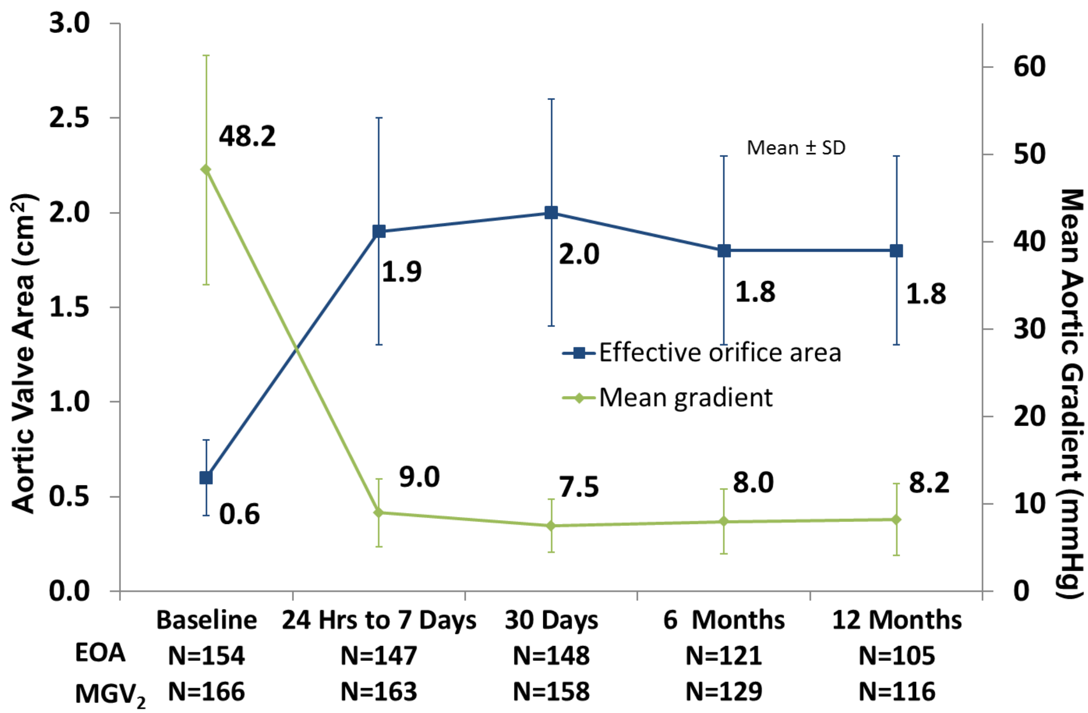

Figure 37: Evolut R Core Lab Echocardiographic Results: Mean Gradient and Aortic Valve Area

Table 27 shows prosthetic valve regurgitation results by visit interval.

Table 27: Core Lab Echocardiographic Results

Assessment	Device Success (24 hours to 7 days) (N=166)	30 Days (N=163)	6 Months (N=138)	12 Months (N=124)
Total Aortic Regurgitation				
None	18.8% (31/165)	18.9% (30/159)	36.8% (49/133)	38.5% (45/117)
Trace	38.2% (63/165)	30.8 (49/159)	32.3% (43/133)	33.3% (39/117)
Mild	37.6% (62/165)	42.1% (67/159)	22.6% (30/133)	23.1% (27/117)
Moderate	5.5% (9/165)	8.2% (13/159)	8.3% (11/133)	5.1% (6/117)
Severe	0.0% (0/165)	0.0% (0/159)	0.0% (0/133)	0.0% (0/117)
Paravalvular Aortic Regurgitation				
None	21.5% (35/163)	21.4% (34/159)	42.1% (56/133)	47.9% (56/117)
Trace	35.6% (58/163)	28.9% (46/159)	27.8% (37/133)	24.8% (29/117)
Mild	37.4% (61/163)	42.8% (68/159)	22.6% (30/133)	22.2% (26/117)
Moderate	5.5% (9/163)	6.9% (11/159)	7.5% (10/133)	5.1% (6/117)
Severe	0.0% (0/163)	0.0% (0/159)	0.0% (0/133)	0.0% (0/117)

Improvement in NYHA functional classification was evaluated for Evolut R patients. An evaluation of cardiac symptom severity based on NYHA classification was conducted at 30 days, 6 months, and 12 months post implant (Table 28).

Table 28: NYHA Classification Change from Baseline

Outcome	30 Days (N=162)	6 Months (N=144)	12 Months (N=134)
Improved	80.9% (131/162)	82.6% (119/144)	81.3% (109/134)
No Change	16.0% (26/162)	10.4% (15/144)	6.7% (9/134)
Worsened	1.9% (3/162)	0.7% (1/144)	1.5% (2/134)
Died	1.2% (2/162)	6.3% (9/144)	10.4% (14/134)

Quality of Life (QoL) was evaluated using the Kansas City Cardiomyopathy Questionnaire (KCCQ) as shown in Table 29. KCCQ was only collected at the US study sites.

Table 29: Quality of Life

	Baseline (N=106)	30 Days (N=104)	6 Months (N=82)	12 Months (N=72)
KCCQ				
Overall Summary Score	49.2 ± 23.4	71.6 ± 21.6	74.4 ± 23.6	75.4 ± 21.4
Clinical Summary Score	54.2 ± 22.6	73.2 ± 20.9	72.7 ± 23.8	73.7 ± 23.3

1.3.3.6 Resheath and recapture

Table 30 shows the resheath and/or recapture feature results. Resheathing or recapturing of the TAV was attempted 53 times among 38 subjects (22.9%). Successful resheath or recapture was achieved in 52/53 attempts (98.1%). In one attempt, the operator was unable to fully recapture the TAV to the desired intent; however, the TAV was successfully deployed without clinical consequence.

Table 30: Resheath and Recapture Feature Results

	All (N=166)
Resheath or Recapture	
# Attempts	53
% (# Subjects)	22.9% (38/166)
Success Rate	98.1% (52/53)

1.4 Evolut PRO study

1.4.1 Patient population

Eligible subjects were patients who presented with severe symptomatic aortic stenosis and significant comorbidities in whom the risk of surgical aortic valve replacement was considered at high to extreme risk.

A total of 45 subjects were enrolled in the CoreValve Evolut PRO US Clinical Study.

The patient characteristics analyzed include demographics, clinical characteristics, medical history, and potentially prohibitive anatomic factors for surgical aortic valve replacement (SAVR) and assessments for comorbidity, frailty, and disability (Table 31).

The mean age for patients participating in the study was 83.1 years old, and 68.9% of patients were female. The mean Society of Thoracic Surgeons (STS) score was 6.5%. A total of 71.1% of all patients were in NYHA class III or IV. Additionally, frailty was present in 77.8% of patients, COPD was present in 28.9% of patients, previous percutaneous coronary intervention (PCI) was present in 26.7% of patients, and peripheral vascular disease was present in 42.2% of patients. Additional baseline information is provided in Table 31.

Table 31: Baseline characteristics

Characteristic	Evolut PRO (N=45)
Age (years)	83.1 ± 7.4
Gender female (%)	68.9% (31/45)
STS PROM score (%)	6.5 ± 4.2
NYHA	
I/II	28.9% (13/45)
III/IV	71.1% (32/45)
STS factors	
Serum creatinine >2 mg/dl	2.2% (1/45)
Chronic lung disease (COPD)	28.9% (13/45)
Peripheral vascular disease	42.2% (19/45)
Cerebrovascular disease	17.8% (8/45)
Previous CABG	17.8% (8/45)
Previous other cardiac - PCI	26.7% (12/45)
Previous MI	11.1% (5/45)
Atrial fibrillation / atrial flutter	18.2% (8/44)
Other comorbidities and medical history	
Porcelain aorta	6.7% (3/45)
Severely atherosclerotic aorta	4.5% (2/44)
Frailty	77.8% (35/45)
Abnormal chest wall anatomy	2.2% (1/45)
Cirrhosis of the liver	0.0% (0/45)
Preexisting permanent pacemaker or defibrillator	6.7% (3/45)

1.4.2 Procedural results

Table 32 provides a summary of the transcatheter valve implantation procedures. Evolut PRO implantation was attempted in all 45 subjects. The majority of implantations (60.0%) were performed under general anesthesia and using the transfemoral approach (97.8%). There were no intraprocedural deaths, conversions to surgery, aortic annular ruptures, or coronary obstructions.

Table 32: Procedural results

Assessment	Evolut PRO (N=45)
Anesthesia type	
General	60.0% (27/45)
Local	40.0% (18/45)
Implanted valve size	
23 mm	0.0% (0/45)
26 mm	37.8% (17/45)
29 mm	62.2% (28/45)
Pre-BAV	53.3% (24/45)
Postimplant dilatation	24.4% (11/45)
Access route	
Transfemoral	97.8% (44/45)
Subclavian	2.2% (1/45)
Direct aortic	0.0% (0/45)
Multiple valve (≥2 implanted)	2.2% (1/45)
Coronary obstruction	0.0% (0/45)

1.4.3 Safety and efficacy results

1.4.3.1 Primary safety endpoints

The primary safety endpoints were all-cause mortality at 30 days and disabling stroke at 30 days.

The K-M estimate of all-cause mortality was 2.2% at 30 days, as shown in Figure 38 and Table 22: .

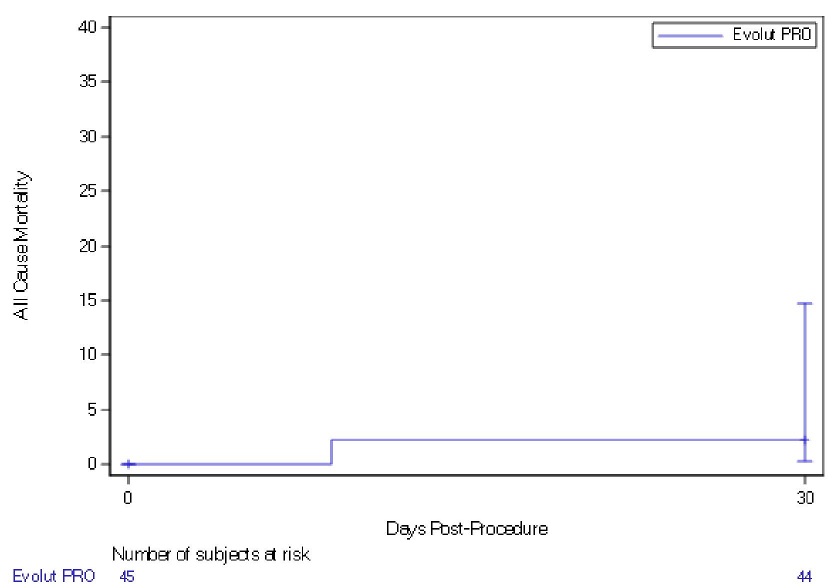

Figure 38: All-cause mortality

Note: The confidence intervals are calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

Table 33: All-cause mortality

	Evolut PRO 30 days (N=45)
Number at risk	44
# subjects (# events)	1 (1)
K-M rate (%)	2.2%
Two-sided 95% CI	0.3% - 14.7%

The K-M estimate of disabling stroke was 0.0% at 30 days, as shown in Figure 39Figure 36: and Table 34.

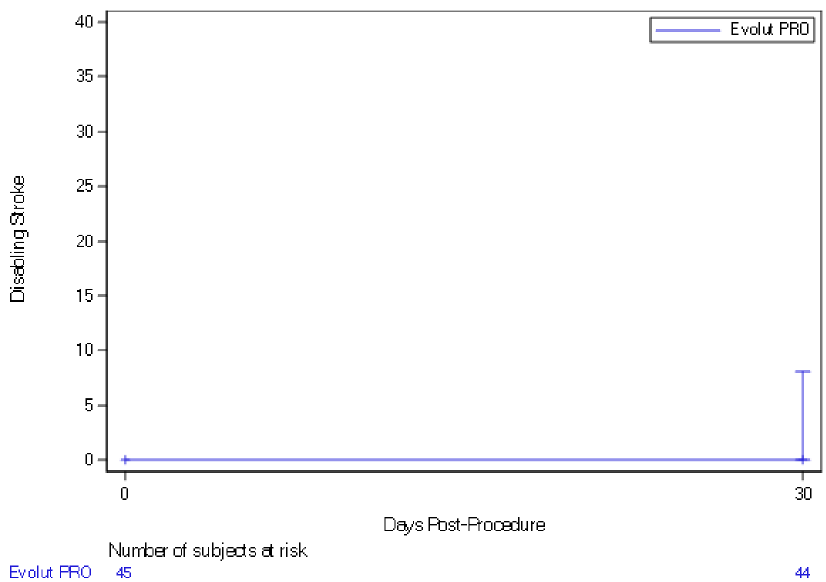

Figure 39: Disabling stroke

Note: The confidence intervals are calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

Table 34: Disabling stroke

	Evolut PRO 30 days (N=45)
Number at risk	44
# subjects (# events)	0 (0)

	Evolut PRO 30 days (N=45)
K-M rate (%)	0.0%
Two-sided 95% CI	0.0% - 8.0%

1.4.3.2 Primary efficacy endpoint

The primary clinical efficacy endpoint was the percentage of subjects with either none or trace prosthetic regurgitation at 30 days. Table 35 shows prosthetic valve regurgitation results by visit interval.

Table 35: Core lab echocardiographic results

Assessment	Evolut PRO device success (24 hours to 7 days) (N=45)	Evolut PRO 30 days (N=44)
Total aortic regurgitation		
None	44.4% (20/45)	43.2% (19/44)
Trace	35.6% (16/45)	22.7% (10/44)
Mild	17.8% (8/45)	34.1% (15/44)
Mild to moderate	0.0% (0/45)	0.0% (0/44)
Moderate	2.2% (1/45)	0.0% (0/44)
Moderate to severe	0.0% (0/45)	0.0% (0/44)
Severe	0.0% (0/45)	0.0% (0/44)
Paravalvular aortic regurgitation		
None	46.7% (21/45)	43.2% (19/44)
Trace	33.3% (15/45)	22.7% (10/44)
Mild	17.8% (8/45)	34.1% (15/44)
Mild to moderate	0.0% (0/45)	0.0% (0/44)
Moderate	2.2% (1/45)	0.0% (0/44)
Moderate to severe	0.0% (0/45)	0.0% (0/44)
Severe	0.0% (0/45)	0.0% (0/44)

1.4.3.3 Additional safety endpoints

An additional endpoint was safety at 30 days as defined by the Valve Academic Research Consortium (VARC II). Device safety information is shown in Table 36.

Table 36: Device safety – VARC II

	Evolut PRO 30 days (N=45)
All-cause mortality	2.2%
All stroke (disabling and non-disabling)	0.0%
Life-threatening bleeding	13.3%
Acute kidney injury: stage 2 or 3 (including renal replacement therapy)	2.2%
Coronary artery obstruction	0.0%
Major vascular complication	8.9%
Valve-related dysfunction requiring repeat procedure (BAV, TAVR, or SAVR)	0.0%

Table 37 provides a summary of the adverse events (AEs) that occurred in this study. Bleeding complications and major vascular access site and access-related complications were the most frequently observed early adverse events.

Table 37: Safety endpoints at 30 days post procedure

	Evolut PRO 30 days (N=45)	
	# subjects (# events)	K-M rate (%)
All-cause mortality	1 (1)	2.2%
Cardiovascular	1 (1)	2.2%
Myocardial infarction	0 (0)	0.0%
Periprocedural	0 (0)	0.0%
Spontaneous	0 (0)	0.0%
Stroke or TIA	0 (0)	0.0%
All stroke	0 (0)	0.0%
Disabling stroke	0 (0)	0.0%
TIA	0 (0)	0.0%
Vascular access site and access-related complications	5 (6)	11.1%
Major	4 (5)	8.9%
Bleeding complications	10 (10)	22.2%
Life threatening or disabling	6 (6)	13.3%
Major	2 (2)	4.4%
Acute kidney injury	3 (3)	6.7%
Stage 1	2 (2)	4.4%
Stage 2	1 (1)	2.2%
Stage 3	0 (0)	0.0%
Prosthetic valve thrombosis	0 (0)	0.0%
Prosthetic valve endocarditis	0 (0)	0.0%
Valve embolization or migration	1 (1)	2.2%
Valve-related dysfunction requiring (reintervention) repeat procedure	0 (0)	0.0%
New pacemaker*	5 (5)	11.9%
New pacemaker	5 (5)	11.1%
Coronary artery obstruction	0 (0)	0.0%
*Subjects with pacemaker or ICD at baseline are not included in the denominator.		

1.4.3.4 Additional efficacy endpoints

Figure 40 shows the mean gradient and effective orifice area (EOA) values obtained by visit for Evolut PRO subjects.

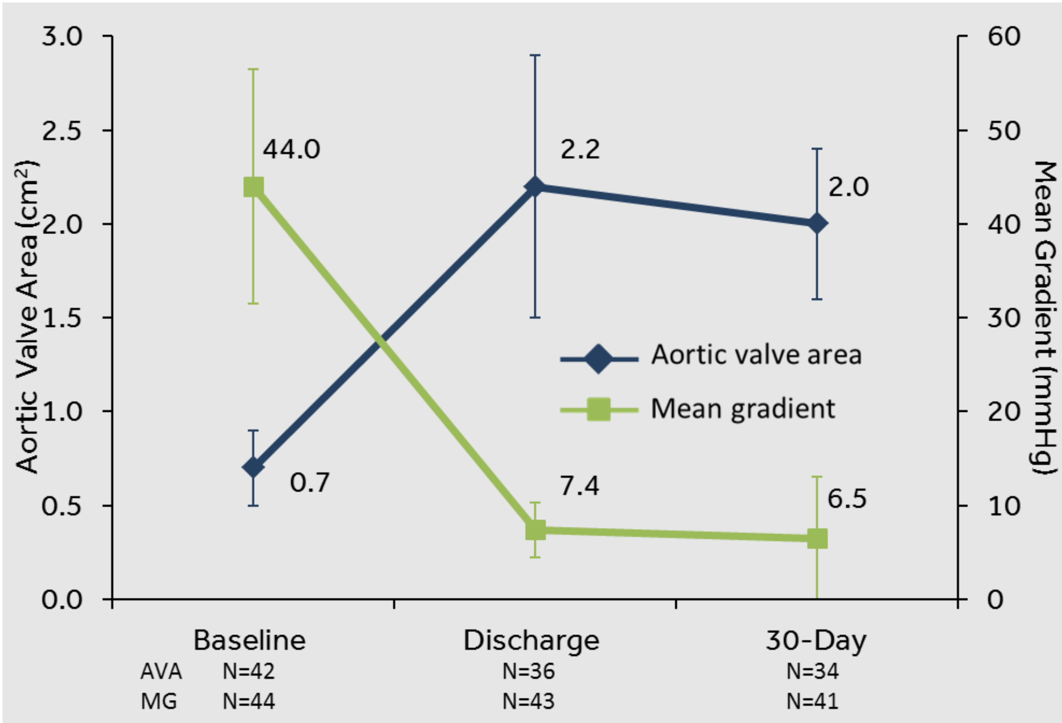

Figure 40: Evolut PRO core lab echocardiographic results: mean gradient and aortic valve area

An additional efficacy endpoint was device success at 24 hours to 7 days as defined by the Valve Academic Research Consortium (VARC II). The overall composite device success rate was 82.1%, as shown in Table 38.

Table 38: Device success rate – VARC II

	Evolut PRO device success (24 hours to 7 days) (N=45)
Absence of procedural mortality	97.8% (44/45)
Correct positioning of single valve in proper anatomical location	97.8% (44/45)
Intended performance of prosthetic heart valve	86.5% (32/37)
Absence of patient prosthesis mismatch	88.9% (32/36)
Mean gradient <20 mmHg or peak velocity <3 m/sec	100.0% (43/43)
Absence of moderate or severe prosthetic regurgitation	97.8% (44/45)
Overall device success	82.1% (32/39)

Improvement in NYHA functional classification was evaluated for Evolut PRO patients. An evaluation of cardiac symptom severity based on NYHA classification was conducted at 30 days post implant (Table 39).

Table 39: NYHA classification change from baseline

Outcome	Evolut PRO 30 days (N=44)
Improved	86.4% (38/44)
No change	13.6% (6/44)
Worsened	0.0% (0/44)

Quality of life (QoL) was evaluated using the Kansas City Cardiomyopathy Questionnaire (KCCQ) as shown in Table 40.

Table 40: Quality of life

	Baseline (N=45)	Evolut PRO 30 days (N=44)
KCCQ		
Overall summary score	52.8 ± 23.8	72.7 ± 23.2
Clinical summary score	57.0 ± 20.6	72.7 ± 21.6

1.5 Bicuspid patient population (intermediate or greater surgical risk)

The following analysis is inclusive of data entered into the TVT Registry for patients identified to have bicuspid valve morphology, who were judged by a heart team, including a cardiac surgeon, to be at intermediate or greater risk for open surgical therapy, and who were implanted with either the Evolut R or Evolut PRO TAVR system between July 2015 and September 2017. A total of 545 patients were included in this analysis.

1.5.1 Patient population

Baseline clinical characteristics and demographics are shown in Table 41. The mean age of subjects implanted with Evolut R was 72.8 ± 10.7 and 70.6 ± 10.8 in patients implanted with Evolut PRO. The majority of subjects presented as NYHA Class II–IV (98.1% in patients implanted with Evolut R and 97.2% in patients implanted with Evolut PRO), and mean STS score was slightly lower in patients implanted with Evolut PRO (4.7 ± 3.6%) than in patients implanted with Evolut R (5.6 ± 3.9%).

Table 41: Patient Demographics and Clinical Characteristics

Demographics	Evolut R (N=474)	Evolut PRO (N=71)
Age[1] (yrs)	72.8 ± 10.7 (n=474)	70.6 ± 10.8 (n=71)
Male	56.1% (266/474)	43.7% (31/71)
Non-Hispanic/Latino	94.1% (433/460)	91.5% (65/71)
NYHA Class		

Demographics	Evolut R (N=474)	Evolut PRO (N=71)
I	1.9% (9/469)	2.8% (2/71)
II	17.3% (81/469)	28.2% (20/71)
III	66.1% (310/469)	53.5% (38/71)
IV	14.7% (69/469)	15.5% (11/71)
STS Score (Risk of Mortality, %)	5.6 ± 3.9 (n=461)	4.7 ± 3.6 (n=70)
Peripheral Vascular Disease	25.5% (121/474)	21.1% (15/71)
Prior Stroke	9.1% (43/474)	8.5% (6/71)
Chronic Lung Disease/COPD	49.0% (232/473)	45.1% (32/71)
Coronary Artery Disease	48.9% (232/474)	53.5% (38/71)
Coronary Artery Bypass Surgery	17.1% (81/474)	16.9% (12/71)
Percutaneous Coronary Intervention	26.8% (127/474)	33.8% (24/71)
Pre-Existing IPG/ICD	14.8% (70/472)	8.5% (6/71)
Previous MI	19.9% (94/473)	29.6% (21/71)
Atrial Fibrillation/Atrial Flutter	31.3% (148/473)	25.4% (18/71)
[1]Subjects with age >90 are reported as "90 plus" in the database and for calculation are set to 90		

1.5.2 Procedural data

Procedural information is summarized in Table 42. The majority of subjects were implanted using left/right femoral access (90.9% with Evolut R and 93.0% with Evolut PRO) and the device was implanted successfully in 98.5% of subjects implanted with Evolut R and 95.8% of subjects implanted with Evolut PRO.

Table 42: Procedural Data Summary

Assessment	Evolut R (N=474)	Evolut PRO (N=71)
Left/Right Femoral Access	90.9% (431/474)	93.0% (66/71)
Valve-in-Valve Procedure[1]	1.5% (7/473)	2.8% (2/71)
Procedure Aborted	0.0% (0/473)	1.4% (1/71)
Conversion to Open Heart Surgery	0.4% (2/473)	2.8% (2/71)
Device Implanted Successfully	98.5% (466/473)	95.8% (68/71)
Device Success	95.8% (451/471)	95.7% (67/70)
Procedure Time (mins)	119.5 ± 58.9 (n=472)	112.9 ± 63.7 (n=71)
[1]Valve-in-Valve Procedure is defined by TVT-R as a case in which the patient has a previously implanted bioprosthetic valve, and the procedure being documented is now an additional bioprosthetic valve replacement.		

1.5.3 Safety data

Thirty-Day and 1-Year safety data are shown in Table 43. Safety data are presented as Kaplan-Meier rates.

Table 43: Safety Data Summary

Events[1]	30-Day Evolut R (N=474)	30-Day Evolut PRO (N=71)	1-Year[2,3] Evolut R (N=194)
All-Cause Mortality	1.7% (8)	5.9% (4)	8.0% (13)
Any Stroke	2.8% (13)	4.2% (3)	3.3% (6)
Life Threatening/Major Bleed	7.7% (36)	5.6% (4)	8.5% (16)
Life Threatening Bleeding[4]	0.0% (0)	0.0% (0)	0.0% (0)
Major Bleeding Event[4]	0.7% (3)	0.0% (0)	1.8% (3)
Major Vascular Complication	1.3% (6)	1.4% (1)	0.5% (1)
Conduction/Native Pacer Disturbance Req Pacer/ICD[5]	14.6% (68)	16.5% (11)	13.7% (26)
Conduction/Native Pacer Disturbance Req Pacer/ICD[6]	16.9% (67)	18.0% (11)	16.0% (26)
Device Thrombosis	0.0% (0)	0.0% (0)	0.0% (0)
Aortic Valve Re-intervention	0.7% (3)	0.0% (0)	2.3% (4)

[1]Event rates include in-hospital reported events and events reported at follow-up.
[2]1-Year Evolut PRO data not available at time of data analysis.
[3]1-Year Evolut R data includes procedures through September 2016.
[4]In-hospital bleeds are either life-threatening or major but were not reported as the categories life-threatening event or major event; therefore, rates only include bleeds reported after index hospitalization.
[5]Subjects with pacemaker or ICD at baseline are included.
[6]Subjects with pacemaker or ICD at baseline are not included.

1.5.4 Efficacy data

Thirty-Day and 1-Year efficacy data are shown in Table 44. At 30 days post-implant, the incidence of moderate or severe total aortic regurgitation was 9.4% in patients implanted with Evolut R and 2.0% in patients implanted with Evolut PRO. In patients implanted with Evolut R, the LVEF demonstrated consistency from 30 days post-implant (54.1 ± 12.6%) to 1 year post-implant (53.7 ± 14.0%) as did the mean gradient across the aortic valve (9.0 ± 5.1 mmHg and 9.3 ± 6.4 mmHg respectively).

Table 44: Hemodynamic Data Summary

Measurement	30-Day Evolut R (N=470)	30-Day Evolut PRO (N=69)	1-Year[1,2] Evolut R (N=191)
LVEF (%)	54.1 ± 12.6 (n=336)	56.8 ± 12.0 (n=51)	53.7 ± 14.0 (n=96)
Mean Gradient across Aortic Valve (mmHg)	9.0 ± 5.1 (n=337)	8.9 ± 4.0 (n=50)	9.3 ± 6.4 (n=97)
Total Aortic Regurgitation Grade			
None	36.2% (123/340)	39.2% (20/51)	53.6% (52/97)
Trace/Trivial	25.9% (88/340)	25.5% (13/51)	15.5% (15/97)
Mild	28.5% (97/340)	33.3% (17/51)	25.8% (25/97)
Moderate	9.1% (31/340)	2.0% (1/51)	5.2% (5/97)
Severe	0.3% (1/340)	0.0% (0/51)	0.0% (0/97)

Measurement	30-Day		1-Year[1,2]
	Evolut R (N=470)	Evolut PRO (N=69)	Evolut R (N=191)
Paravalvular Regurgitation Grade			
None	59.7% (181/303)	60.5% (26/43)	72.4% (63/87)
Mild	30.7% (93/303)	37.2% (16/43)	24.1% (21/87)
Moderate	9.2% (28/303)	2.3% (1/43)	3.4% (3/87)
Severe	0.3% (1/303)	0.0% (0/43)	0.0% (0/87)
Central Aortic Regurgitation Grade			
None	97.3% (254/261)	97.4% (38/39)	97.5% (77/79)
Mild	2.3% (6/261)	2.6% (1/39)	2.5% (2/79)
Moderate	0.4% (1/261)	0.0% (0/39)	0.0% (0/79)
Severe	0.0% (0/261)	0.0% (0/39)	0.0% (0/79)

[1] 1-Year Evolut PRO data not available at time of data analysis.
[2] 1-Year Evolut R data includes procedures through September 2016.

1.6 Bicuspid patient population (low risk)

The Low Risk Bicuspid Study was a multi-center, prospective, single-arm clinical study. The purpose of this study was to assess the safety and efficacy of the Medtronic transcatheter aortic valve (TAVR) system in patients with bicuspid aortic valves and severe aortic stenosis (AS) at low surgical risk for surgical aortic valve replacement (SAVR) as measured by the rate of all-cause mortality or disabling stroke at 30 days and the rate of device success, defined as absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical location, and absence of moderate to severe total prosthetic valve regurgitation (at 18 hours to 7 days).

A total of 150 subjects received an attempted implant and comprise the primary analysis population for the Low Risk Bicuspid Study. Of the 150 subjects with an attempted implant, 64 received an Evolut R system and 85 received an Evolut PRO system; the TAVR procedure for one subject was aborted. The implanted population (148 subjects) consists of all subjects who were implanted with a valve. Patients will be followed through 10 years. The following data summarize the 30-day and the 12-month results from the Bicuspid Low Risk Study.

1.6.1 Patient population

The demographics and baseline characteristics of the study population are summarized in Table 45.

Table 45: Baseline Clinical Characteristics – Attempted Implant

Baseline Clinical Characteristics	Summary Statistics*
	TAVR
Age (years)	70.3 ± 5.5 (150)
Gender female (%)	48.0% (72/150)
NYHA class	

Baseline Clinical Characteristics	Summary Statistics*
	TAVR
I	2.0% (3/150)
II	70.7% (106/150)
III	26.7% (40/150)
IV	0.7% (1/150)
STS score, %	1.4 ± 0.6 (150)
Peripheral arterial disease	9.3% (14/150)
Previous MI	3.3% (5/150)
Previous reintervention	
Coronary artery bypass surgery	1.3% (2/150)
Percutaneous coronary intervention	7.3% (11/150)
Cerebrovascular disease	6.7% (10/150)
Immunosuppressive therapy	1.3% (2/150)
Chronic lung disease/COPD	17.7% (26/147)
Diabetes	24.7% (37/150)
Atrial fibrillation/atrial flutter	7.3% (11/150)
Pre-existing permanent pacemaker or defibrillator	2.7% (4/150)
Hypertension	74.7% (112/150)
Dialysis	0.0% (0/150)
Echocardiographic findings	
Aortic valve area (cm^2)	0.8 ± 0.2
Mean gradient (mmHg)	49.9 ± 15.5

*Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.)

1.6.2 Procedure data

The procedure data is summarized in Table 46.

Table 46: Procedural Information – Attempted Implant

Assessment	Summary Statistics* (N=150)
Number of index procedures	150
Total delivery catheter in the body time (min)	21.1 ± 20.5
Type of anesthesia	
General	63.3% (95/150)
Local	36.7% (55/150)
Access site	

Assessment	Summary Statistics* (N=150)
Iliofemoral	98.7% (147/149)
Non-iliofemoral	1.3% (2/149)
Valve size	
23 mm	0.0% (0/149)
26 mm	21.5% (32/149)
29 mm	36.9% (55/149)
34 mm	41.6% (62/149)
Total time in catheterization laboratory or operating room (min)	140.0 ± 43.6
Embolic protection device used	30.0% (45/150)
Pre-TAVR balloon valvuloplasty performed	91.3% (137/150)
Post-TAVR balloon valvuloplasty performed	36.9% (55/149)
Concomitant procedure (percutaneous coronary intervention; PCI)	2.7% (4/150)
Length of index procedure hospital stay (days)	2.0 ± 4.0

*Continuous measures - Mean ± SD; categorical measures - % (no./total no.).
Data included subjects with the index procedure defined as the first procedure in which the delivery catheter was introduced. If a patient had two implant procedures, the index procedure was used.

1.6.3 Safety and effectiveness results

1.6.3.1 Primary safety endpoint

The primary safety endpoint was the rate of all-cause mortality or disabling stroke at 30 days.

The K-M estimate of all-cause mortality or disabling stroke rate was 1.3 % at 30 days and 12 months, as shown in Table 47 and Figure 41.

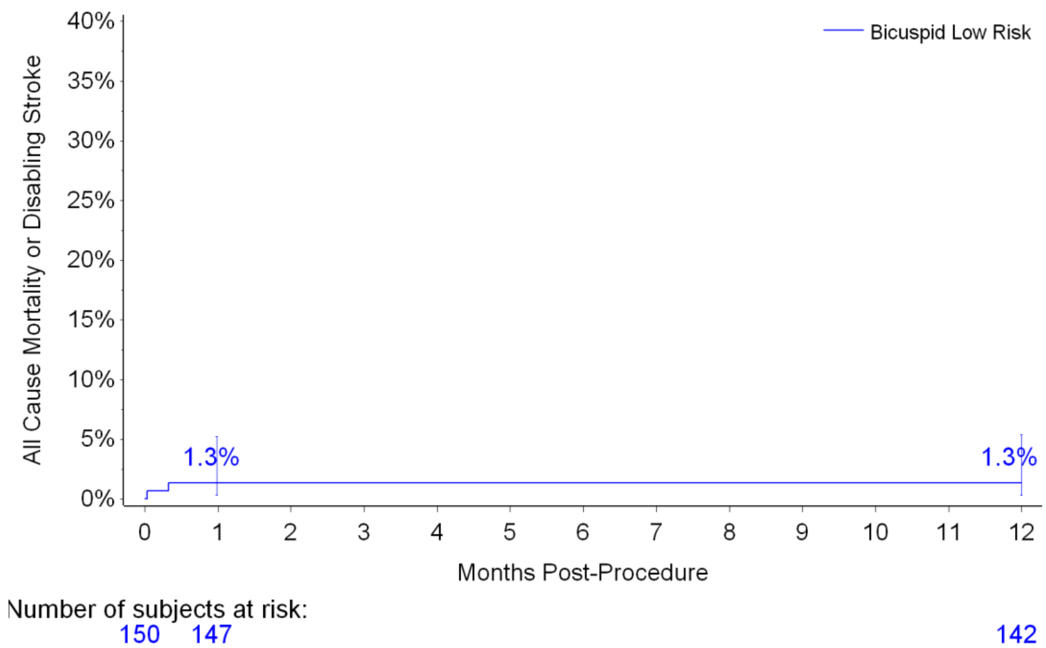

Figure 41: All-Cause Mortality or Disabling Stroke Kaplan-Meier Event Rate - Attempted Implant

Table 47: All-Cause Mortality or Disabling Stroke – Attempted Implant

	TAVR 30 days (N=150)	TAVR 12 months (N=150)
Number at risk	147	142
# subjects (# events)	2 (2)	2 (2)
K-M rate (%)	1.3%	1.3%
Two-sided 95% CI	0.3% - 5.2%	0.3% - 5.4%

1.6.3.2 Primary effectiveness endpoint

The primary effectiveness endpoint was device success rate, defined as:

- Absence of procedural mortality, AND
- Correct positioning of a single prosthetic heart valve into the proper anatomical location, AND
- Absence of moderate or severe total prosthetic valve regurgitation (at 18 hours to 7 days)

Table 48 shows the results from the pre-specified device success analysis for the implanted set. The overall device success rate for the implanted set was 95.9%.

An additional sensitivity analysis was performed on a modified implanted analysis set which included a subject converted to SAVR. This subject required intraprocedural conversion to aortic valve replacement, and as a result, was not included in the implanted set. Results from this analysis were presented in Table 48 as the modified implanted set. The overall device success rate for the modified implanted set was 95.3%.

Table 48: Device Success Rate – Implanted and Modified Implanted

	Implanted (N=148)	**Modified Implanted[1] (N=149)**
Absence of procedural mortality	99.3% (147/148)	99.3% (148/149)
Correct positioning of single valve in proper anatomical location	96.6% (143/148)	96.0% (143/149)
Absence of moderate or severe prosthetic regurgitation (at 18 hours to 7 days)	100.0% (147/147)	100.0% (148/148)
Overall device success	95.9% (141/147)	95.3% (141/148)

[1.] Included 1 subject who was initially implanted with TAVR and was converted to a surgical valve on the same day.

1.6.3.3 Additional outcome measures

Valve performance

Rates of moderate and severe PPM were reported at 30 days (7.6% and 5.3%, respectively) and 12 months (7.0% and 3.5%, respectively) as defined by VARC II.

Effective orifice area (EOA) and mean gradient for TAVR subjects are shown in Figure 42 and Figure 43.

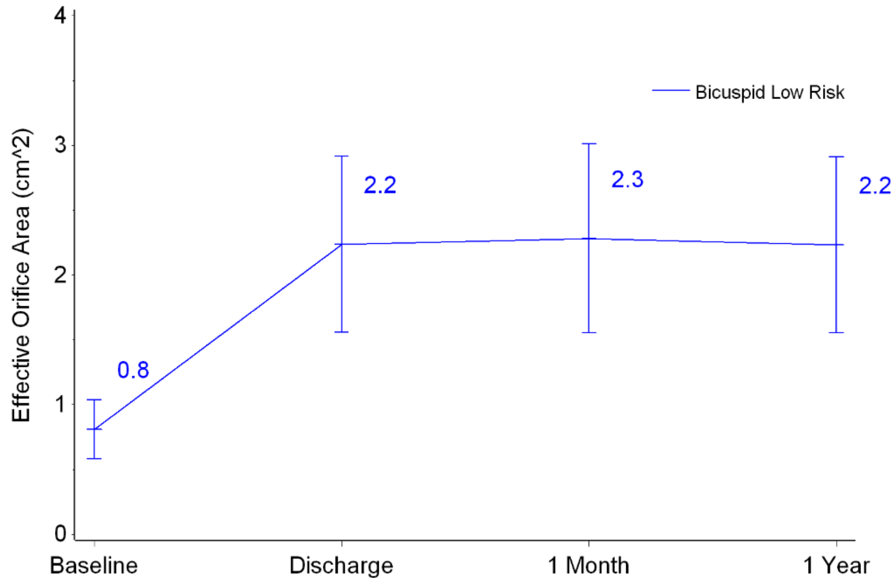

Figure 42: Effective Orifice Area through 12 Months (Implanted)

Note: Line plot with mean and standard deviation.

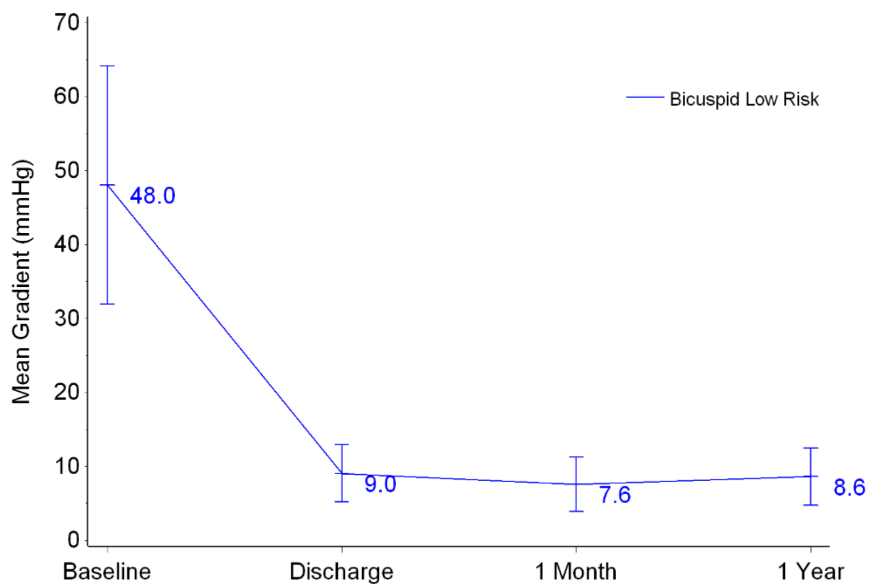

Figure 43: Mean Aortic Gradient through 12 Months (Implanted)

Note: Line plot with mean and standard deviation.

Figure 44 shows total aortic regurgitation (AR) severity over time for TAVR subjects. Figure 45 shows paravalvular aortic regurgitation.

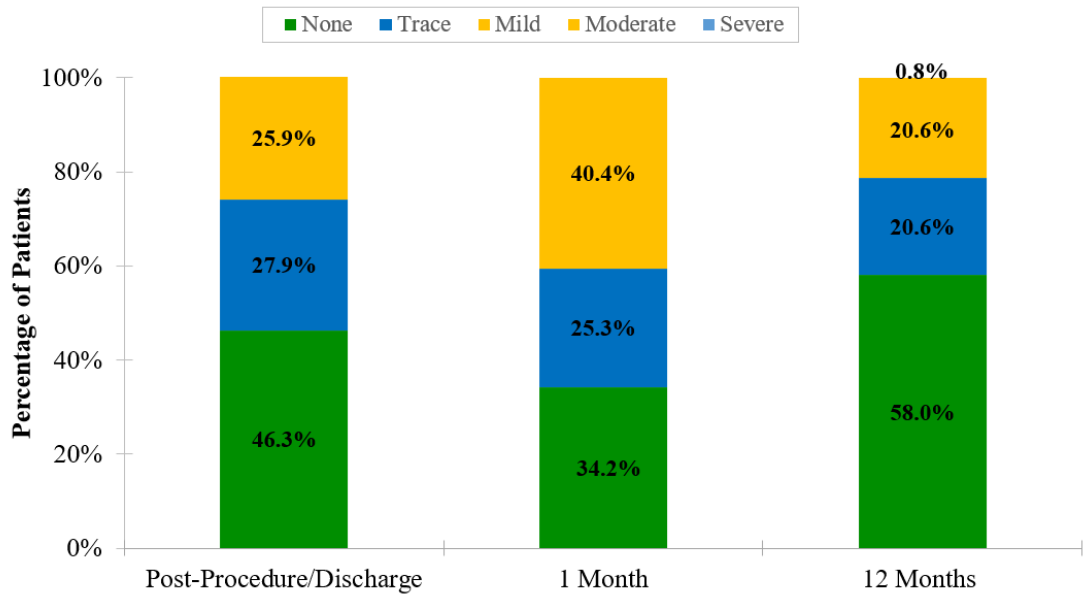

Figure 44: Total Aortic Regurgitation (Implanted)

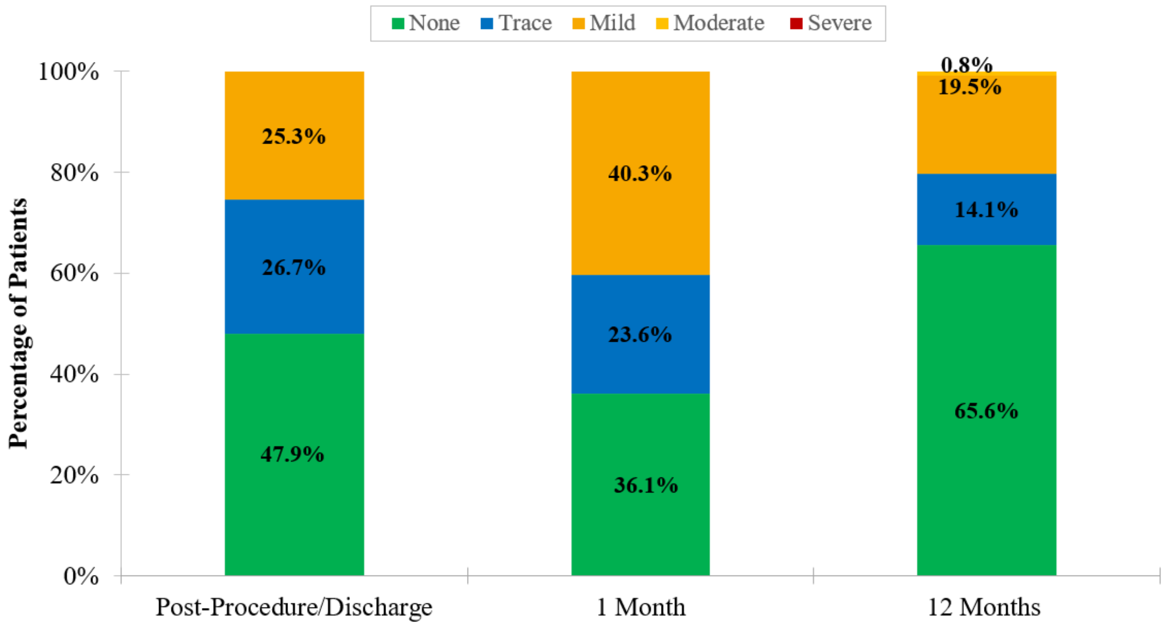

Figure 45: Paravalvular Aortic Regurgitation by Visit (Implanted)

NYHA functional class

The NYHA classifications by visit are presented in Figure 46.

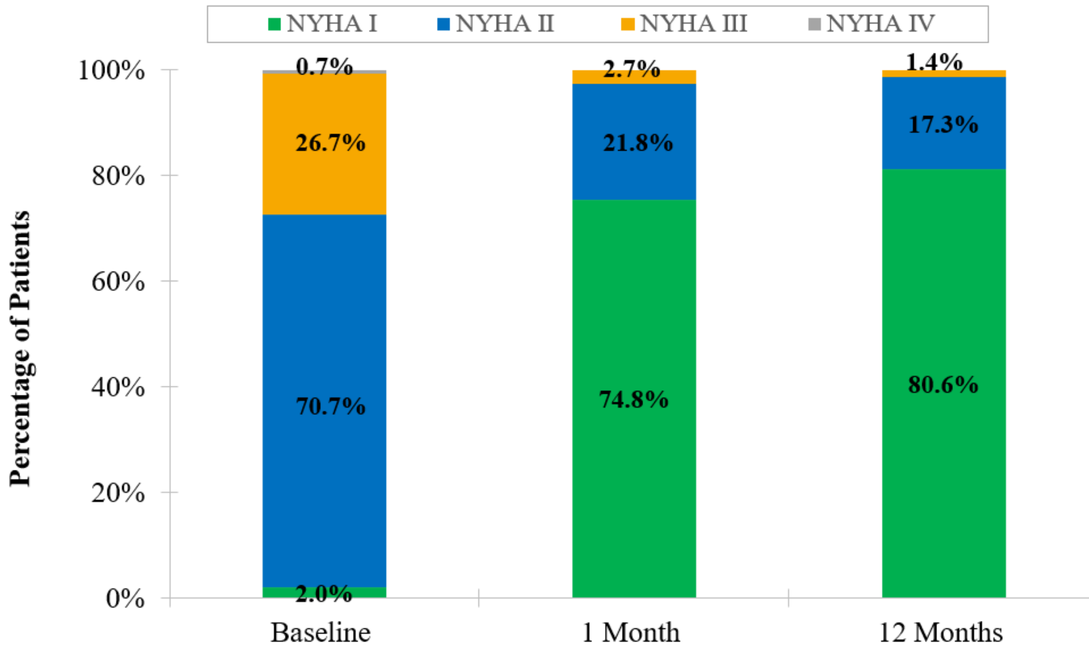

Figure 46. NYHA Classification Change from Baseline - Attempted Implants

Quality of Life (QoL)

KCCQ

The KCCQ overall and clinical summary scores for the treatment group are shown in Figure 47 and Figure 48, respectively.

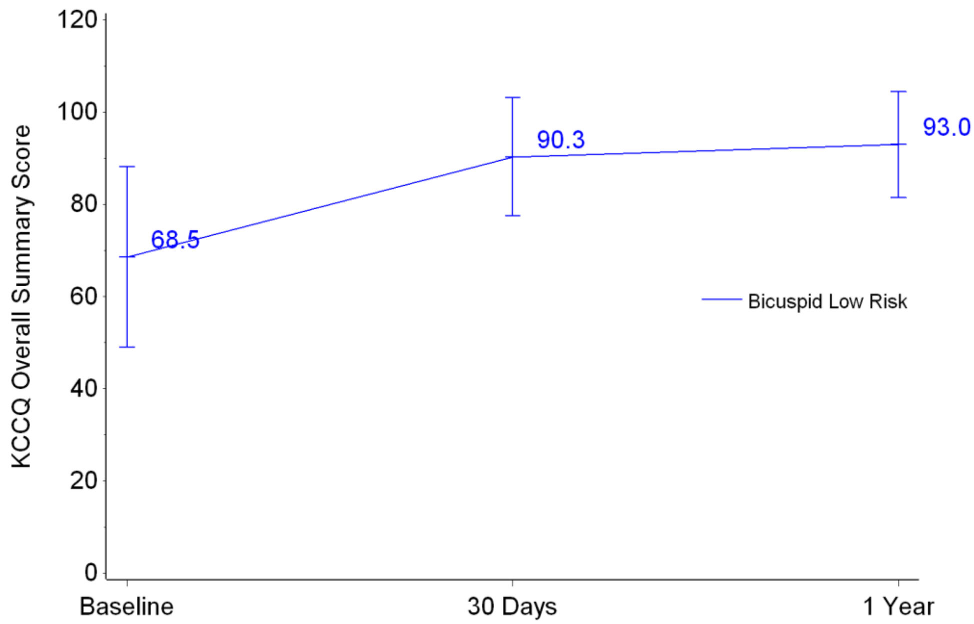

Figure 47: KCCQ Overall Summary Score (Attempted Implant)

Note: Line plot with mean and standard deviation.

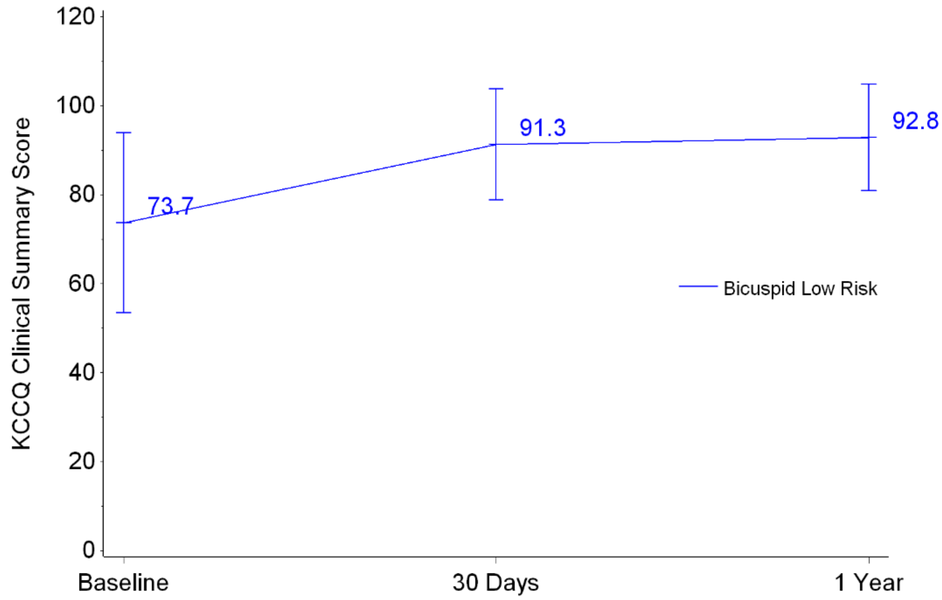

Figure 48: KCCQ Clinical Summary Score (Attempted Implant)

Note: Line plot with mean and standard deviation.

EuroQoL (EQ-5D)

The EQ-5D index scores for the treatment group are shown in Figure 49.

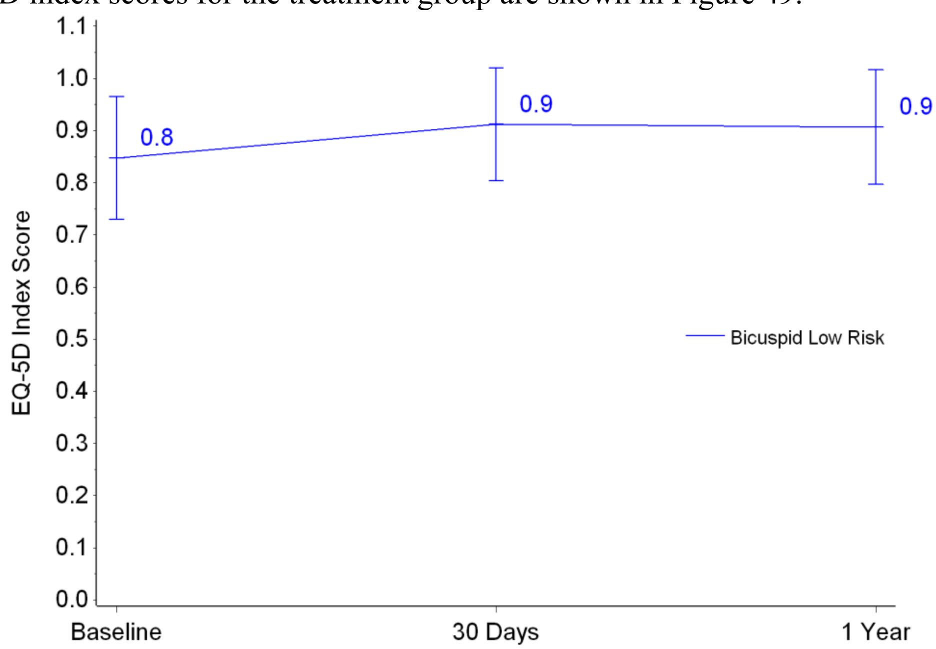

Figure 49: EQ-5D Index Score (Attempted Implant)

Note: Line plot with mean and standard deviation.

1.6.3.4 Additional safety data

The key adverse events that occurred in the study through 12 months are presented in Table 49.

Table 49: CEC Adjudicated Adverse Events Through 12 Months - Attempted Implant

Events	Kaplan-Meier Rate*	
	0-30 Days	12 Months
All-cause mortality or disabling stroke	1.3% (2, 2)	1.3% (2, 2)
All-cause mortality	0.7% (1, 1)	0.7% (1, 1)
Cardiovascular	0.7% (1, 1)	0.7% (1, 1)
Non-cardiovascular	0.0% (0, 0)	0.0% (0, 0)
Valve-related dysfunction requiring repeat procedure	0.0% (0, 0)	0.7% (1, 1)
All stroke	4.0.% (6, 6)	4.7% (7, 7)
Disabling stroke	0.7% (1, 1)	0.7% (1, 1)
Non-disabling stroke	3.3% (5, 5)	4.0% (6, 6)
Life threatening or disabling bleeding	4.0% (6, 6)	4.7% (7, 7)
Major vascular complications	1.3% (2, 2)	1.3% (2, 2)
Acute kidney injury - Stage 3	0.0% (0, 0)	0.0% (0, 0)
Myocardial infarction	0.7% (1, 1)	1.3% (2, 2)
Repeat hospitalization for ascending aorta disease†	0.0% (0, 0)	0.0% (0, 0)
Repeat hospitalization for aortic valve disease†	2.0% (3, 3)	3.4% (5, 5)
New permanent pacemaker implantation‡	14.7% (22, 22)	16.7% (25, 25)
Prosthetic valve thrombosis	0.7% (1, 1)	1.3% (2, 2)
Prosthetic valve endocarditis	0.0% (0, 0)	0.7% (1, 1)
Valve embolization or migration	1.3% (2, 2)	1.3% (2, 2)

*Kaplan-Meier rate (# patients, # events).

†Not adjudicated by CEC.

‡ Patients with pacemaker or ICD at baseline were not counted as new events. Not adjudicated by CEC.

1.7 Redo TAV patient population

The following analysis is inclusive of data entered into the TVT Registry for Redo TAV patients that were treated through September 2023 and eligible for 1-year follow-up who received a commercially available Medtronic TAVR (Evolut R, PRO, PRO+, FX or FX+) as the redo TAV[1]. A total of 744 patients with an attempted implant were included in this analysis. To increase available follow-up data for 1-year all-cause mortality, linkage to Centers for Medicare & Medicaid Services (CMS) administrative claims and encounter data was performed. As available, CMS data were combined with data entered in TVT-R to report all-cause mortality through 1 year (365 days). All-cause mortality rates, inclusive of CMS linkage data, are presented separately in Section 1.7.3.2 below.

1.7.1 TVT-R Patient population

Subject demographics and baseline clinical characteristics are provided in Table 50. The mean age of subjects treated with Redo TAV was 78.9 ± 9.1 years. The majority of subjects presented as NYHA Class III/IV (80.4%) and the mean STS score was 8.6 ± 7.6% consistent with the high or greater risk for open surgery therapy population.

Table 50. Demographics and Baseline Characteristics (Attempted Implant)

Demographics and Baseline Characteristics	Redo TAV (N=744)
Age (years)	78.9 ± 9.1 (744)
Male sex	39.9% (297/744)
Society of Thoracic Surgeons (STS) score (Risk of Mortality, %)	8.6 ± 7.6 (712)
New York Heart Association (NYHA) Class	
I/II	19.6% (144/734)
III/IV	80.4% (590/734)
Previous myocardial infarction	23.4% (174/744)
Previous intervention	
Coronary artery bypass grafting (CABG)	21.9% (163/744)
Percutaneous coronary intervention (PCI)	34.9% (260/744)
Aortic balloon valvuloplasty	9.3% (69/738)
Prior Stroke or Cerebrovascular accident (CVA)	13.8% (103/744)
Peripheral vascular disease (PVD)	24.3% (181/744)
Atrial fibrillation / Atrial Flutter	46.2% (344/744)
Permanent pacemaker or ICD	28.0% (208/744)

[1] The indication is applicable for Evolut PRO+, FX, and FX+. The Medtronic Evolut portfolio of TAVs in this Redo TAV dataset is comprised of Evolut R, PRO, PRO+, and FX TAVR systems. No changes have been made to the valve housing or leaflets as the design progressed from Evolut R TAVs through Evolut FX TAVs. Therefore, clinical data from these systems were pooled to evaluate the safety and performance of the Evolut redo TAVs for the Redo TAV indication. Evolut FX+ Redo TAV procedures were not available in the TVT-R data download given the timing of Evolut FX+ commercial approval in the US. Equivalence between FX and FX+ in the Redo TAV boundary condition has been established through pre-clinical testing.

Demographics and Baseline Characteristics	Redo TAV (N=744)
Porcelain Aorta	3.0% (22/744)
Hostile chest	7.3% (54/744)
Echocardiographic findings (Implanted Population)	
Aortic valve area (cm^2)	0.8 ± 0.3 (576)
Mean gradient across aortic valve (mmHg)	42.3 ± 16.5 (622)
Left ventricular ejection fraction (LVEF) (%)	52.5 ± 13.9 (732)
Moderate or severe aortic regurgitation	49.5% (365/737)
Moderate or severe mitral regurgitation	41.2% (263/638)
*Continuous measures - Mean ± SD (Total no.); Categorical measures – % (no./Total no.)	

1.7.2 TVT-R Procedural data

Redo TAV procedural information is provided in Table 51. The percentage of patients classified as inoperable / extreme or high risk for open surgery were 17.3% and 60.4%, respectively. The majority of procedures utilized transfemoral or iliac approach (94.5%). The two most common types of anesthesia were general anesthesia (48.3%) and moderate sedation (47.3%). The most common valve models implanted were the Evolut R and Evolut PRO+ (33.8% and 31.8%, respectively) and the most common valve size was 26 mm valve size (46.3%). Successful device implantation was achieved in 99.3% of procedures with no reports of aborted procedures and 0.4% converted to open heart surgery.

Table 51. Procedural Data Summary (Attempted Implant)

Procedural Data	Redo TAV (N=744)
Operator reason for procedure	
Inoperable/extreme risk	17.3% (127/734)
High risk	60.4% (443/734)
Intermediate risk	19.2% (141/734)
Low risk	3.1% (23/734)
Failed index transcatheter valve model	
Evolut/CoreValve	9.3% (69/744)
Unknown	90.7% (675/744)
Implant approach	
Femoral & Iliac	94.5% (702/743)
Subclavian/Axillary	3.0% (22/743)
Transcarotid	1.6% (12/743)
Direct Aortic	0.5% (4/743)

Procedural Data	Redo TAV (N=744)
Other	0.4% (3/743)
Implanted bioprosthesis model	
Evolut R	33.8% (250/740)
Evolut PRO	13.1% (97/740)
Evolut PRO+	31.8% (235/740)
Evolut FX	21.4% (158/740)
Evolut FX+	0.0% (0/740)
Valve size implanted (Implanted Population)	
23 mm	24.0% (177/739)
26 mm	46.3% (342/739)
29 mm	23.4% (173/739)
34 mm	6.4% (47/739)
Cardiopulmonary bypass used	0.4% (3/699)
Cardiopulmonary bypass status	
Emergent	66.7% (2/3)
Cardiopulmonary bypass time, minutes	115.0 ± 39.9 (3)
	129.0 (70.0, 146.0)
Type of Anesthesia	
General anesthesia	48.3% (359/744)
Deep sedation[1]	3.6% (27/744)
Moderate sedation	47.3% (352/744)
Minimal sedation[1]	0.7% (5/744)
Epidural[2]	0.0% (0/744)
Combination[2]	0.1% (1/744)
Total procedure time, minutes	94.9 ± 54.8 (744)
	81.0 (62.0, 113.0)
Device implanted successfully	99.3% (738/743)
Procedure aborted	0.0% (0/744)
Conversion to open heart surgery	0.4% (3/744)
Conversion to open heart surgery reason	
Ventricular rupture	0.1% (1/744)
Annulus rupture	0.0% (0/744)
Other	0.3% (2/744)

Procedural Data	Redo TAV (N=744)
Mechanical assist device in place at start of procedure	1.1% (8/744)

Continuous measures - Mean ± SD (Total no.), Median (Q1, Q3); Categorical measures – % (no./Total no.)
[1]Only collected in procedures during or after 2021 (Version 3.0 TAVR Data Collection Form)
[2]Only collected in procedures through 2020 (Version 2.1 TAVR Data Collection Form)

1.7.3 Safety data

1.7.3.1 Reported Safety Data

The 30-day and 1-year K-M rates of site reported adverse events are summarized in Table 52.

The rate of all-cause mortality was 3.1% and 16.2% at 30 days and 1 year, respectively. The rate of all stroke was 3.7% and 4.3% at 30 days and 1 year follow-up, respectively, and the rate of new PPI was 6.8% and 8.0% at 30 days and 1 year, respectively. At 1 year, the rate of aortic valve reintervention and thrombosis was 0.8% and 0.1%, respectively.

Table 52. Site Reported 30 Day and 1 Year Adverse Events (Redo TAV, Attempted Implant)

	Redo TAV (N=744)	
	Kaplan-Meier Rate (# Subjects, # Events)	
Adverse Event	**30 Days**	**1 Year**
All-Cause Mortality[1]	3.1% (23, 23)	16.2% (114, 114)
Cardiovascular Mortality	2.1% (15, 15)	5.4% (34, 34)
Any Stroke	3.7% (27, 28)	4.3% (31, 32)
Ischemic Stroke	3.5% (26, 26)	4.2% (30, 30)
Hemorrhagic Stroke	0.3% (2, 2)	0.3% (2, 2)
Undetermined Stroke	0.0% (0, 0)	0.0% (0, 0)
Transient Ischemic Attack	0.1% (1, 1)	0.9% (5, 5)
Major Vascular Complication	2.0% (15, 15)	2.2% (16, 16)
Life Threatening/Major Bleeding	7.6% (56, 58)	9.0% (64, 69)
Myocardial Infarction	0.3% (2, 2)	1.3% (8, 8)
New Requirement for Dialysis	1.2% (9, 9)	1.7% (12, 12)
Conduction/Native Pacer Disturbance Req Pacer/ICD[2]	5.0% (37, 37)	6.1% (43, 44)
Conduction/Native Pacer Disturbance Req Pacer/ICD[3]	6.8% (36, 36)	8.0% (41, 42)
Aortic Valve Re-intervention	0.7% (5, 5)	0.8% (6, 6)
Unplanned Other Cardiac Surgery or Intervention	1.5% (11, 11)	2.2% (15, 15)
Unplanned Vascular Surgery or Intervention	5.1% (38, 42)	5.5% (40, 45)
Device Thrombosis	0.1% (1, 1)	0.1% (1, 1)

	Redo TAV (N=744)	
	Kaplan-Meier Rate (# Subjects, # Events)	
Adverse Event	**30 Days**	**1 Year**
Valve Related Readmission	0.3% (2, 2)	1.6% (10, 10)
Endocarditis	0.3% (2, 2)	0.7% (4, 4)

%=Kaplan-Meier event rate (no. of subjects with event, no. of events)
[1] All-Cause Mortality rate from TVT-R and CMS data.
[2]Subjects with pacemaker or ICD at baseline are included.
[3]Subjects with pacemaker or ICD at baseline are not included.

1.7.3.2 All-Cause Mortality – TVT-R with CMS Claims and Encounter Data

To increase data availability for 1-year all-cause mortality, TVT-R data were linked with CMS claims and encounter data, where available. Of the 744 patients with an attempted implant included in the analysis, 588 patients were linked to CMS claims data via a one-to-one match with their corresponding TVT-R record. Details on the available matching are provided in Table 53 below.

Table 53. CMS Linked Data – Match Information

	Redo TAV (N=744)	
	One-to-one Match	**No Match**
N	588	156
Medicare Fee-For-Service (%)	71.4%	N/A
Medicare Advantage (%)	28.6%	N/A

1.7.4 Efficacy data

Echocardiographic results are presented at baseline through 1 year follow-up as assessed by sites in Table 54. The mean aortic gradient decreased from 42.3 ± 16.5 mmHg at baseline to 11.8 ± 6.2 at 30 days and was similar at 1 year with 11.9 ± 7.1 mmHg.

At 30 days and 1 year, 97.0% and 97.0% of echocardiograms, respectively, demonstrated no more than mild total aortic regurgitation in the Redo TAV cohort. Similar results were seen with paravalvular regurgitation with 97.7% and 96.7% of echocardiograms at 30 days and 1 year, respectively, demonstrating no more than mild regurgitation.

Table 54.Table 54. Hemodynamic Data Summary (Redo TAV, Implanted)

	Redo TAV (N=740)			
Measurement	**Baseline**	**Post-Procedure**	**30 Days**	**1 Year**
Mean Gradient across Aortic Valve (mmHg)	42.3 ± 16.5 (622)	12.6 ± 7.1 (665)	11.8 ± 6.2 (521)	11.9 ± 7.1 (299)
Total Aortic Regurgitation Grade				
None	15.3% (113/737)	60.1% (406/675)	56.2% (295/525)	58.6% (177/302)
Trace/Trivial	10.9% (80/737)	21.9% (148/675)	21.3% (112/525)	17.5% (53/302)
Mild	24.3% (179/737)	16.9% (114/675)	19.4% (102/525)	20.9% (63/302)
Moderate	28.4% (209/737)	0.9% (6/675)	3.0% (16/525)	2.3% (7/302)
Severe	21.2% (156/737)	0.1% (1/675)	0.0% (0/525)	0.7% (2/302)
Paravalvular Regurgitation Grade				
None	NA	81.5% (503/617)	77.2% (372/482)	80.7% (222/275)
Mild	NA	17.3% (107/617)	20.5% (99/482)	16.0% (44/275)
Moderate	NA	0.8% (5/617)	2.3% (11/482)	2.5% (7/275)
Severe	NA	0.3% (2/617)	0.0% (0/482)	0.7% (2/275)

Continuous measures - Mean ± SD (Total no.); Categorical measures – % (no./Total no.)

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