# Three-Year Outcomes for Women in the SMART Trial

SMART

Small Annuli Randomized to Evolut or SAPIEN

Niki Procopi, MD; on behalf of the SMART Trial Investigators

Roxana Mehran, MD, Didier Tchétché, MD, & Howard C. Herrmann, MD

Presented at AHA Scientific Sessions 2026, Nov 7, 2026, Chicago, IL

# Potential conflicts of interest

**Speaker's name:** Niki Procopi

**Trial Registration**: NCT04722250. **Funding**: Medtronic (Minneapolis, MN)

**Disclosures:** Dr. Procopi reports nothing to disclose.

**Acknowledgments**: Linda Wires, MA, MS, an employee of Medtronic, prepared tables and figures and assisted in preparation of this poster.

## Background and Rationale

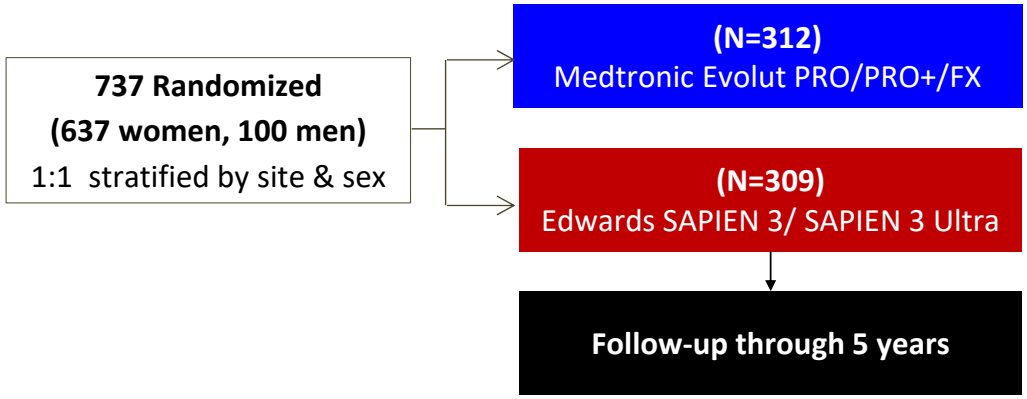
- Women frequently (70-80%) have a small aortic annulus (SAA), increasing their risk for adverse hemodynamics after aortic valve replacement.
- In patients with SAA treated with transcatheter aortic valve replacement (TAVR), studies have shown better hemodynamics using Evolut self-expanding valves (SEV) versus SAPIEN balloon-expandable valves (BEV).[1]
- The Small Annuli Randomized To Evolut or SAPIEN Trial (SMART) compares performance of these valves in predominantly women (87%) with SAA.[2]
- Through 12 months, women in SMART had similar clinical outcomes with both devices but lower bioprosthetic valve dysfunction (BVD) with Evolut.[3]



[1]Hahn et al. *JACC Imaging* 2019; 12:25-34; [2]Herrmann et al. *N Engl J Med*. 2024;390(21):1959-1971; [3]Tchétché et al. *JAMA Cardiol*. 2024;9:1106-1114.

# Study Design and Patient Characteristics

- Prospective, randomized controlled, post-market trial
- 621 Women treated (312 with Medtronic Evolut PRO/PRO+/FX; 309 with Edwards SAPIEN 3/SAPIEN 3 Ultra) at 81 sites in 13 countries
- Key eligibility: symptomatic severe aortic stenosis; SAA ≤430 $mm^2$ by MDCT
- Mean age 80.2±6.2 years, mean STS score 3.4±1.8%, mean aortic annulus area 378.7±34.2 $mm^2$




**Key eligibility**

- Symptomatic severe aortic stenosis
- Small aortic annulus (≤430 $mm^2$ by MDCT)

**Co-primary endpoints**

- Composite of mortality, disabling stroke, or heart failure (HF) rehospitalization through 12 months (as-treated population)
- Bioprosthetic valve dysfunction through 12 months (implanted population)

**Primary analyses published[1]**

**Objective: Report 3-year outcomes for women from the SMART Trial**

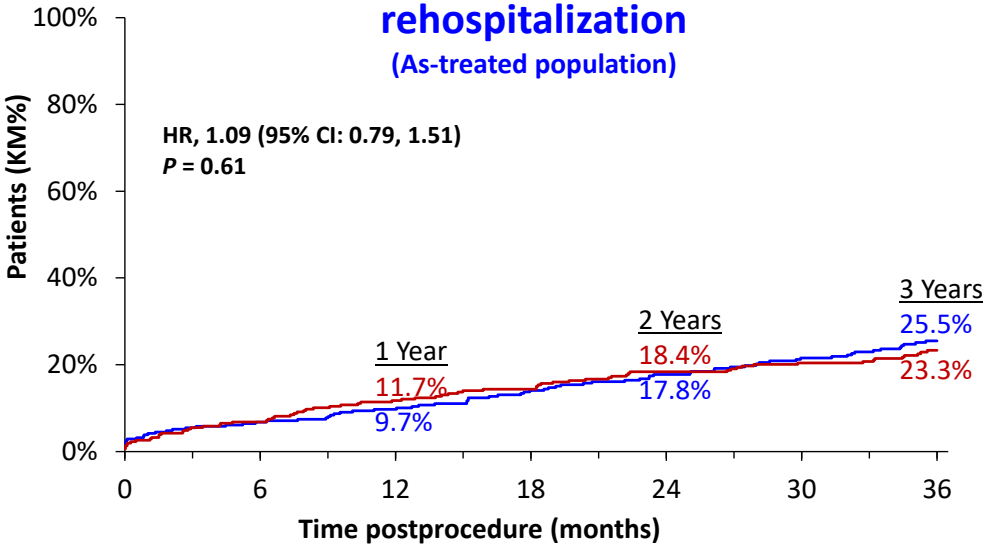


[1] Herrmann et al. *N Engl J Med*. 2024;390(21):1959-1971.

# Co-Primary Endpoints: Annual Follow-Up

## Mortality, disabling stroke, or HF rehospitalization

(As-treated population)




**No. at Risk**

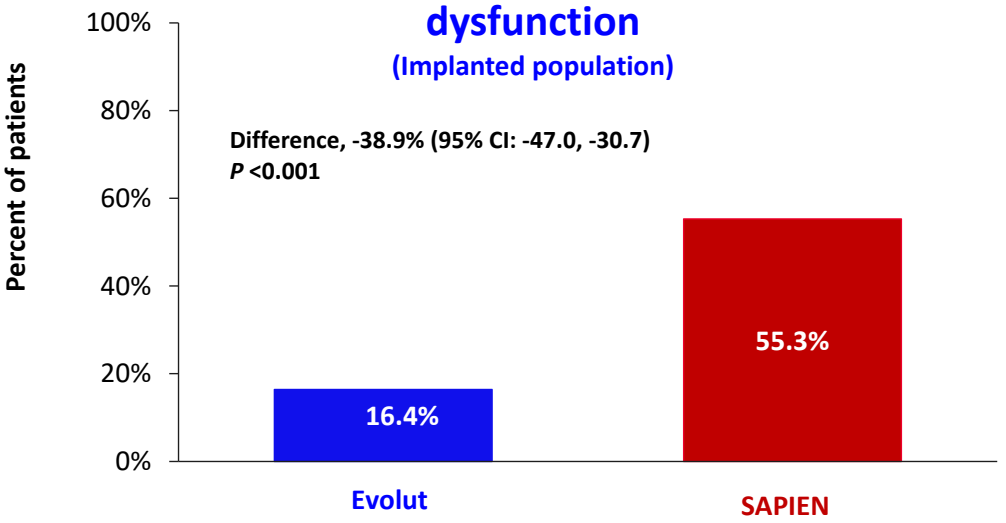
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Evolut | 312 | 286 | 272 | 256 | 243 | 226 | 168 |
| SAPIEN | 309 | 285 | 268 | 258 | 243 | 234 | 170 |

Clinical outcome composite reported as Kaplan Meier estimates; HF=heart failure

***Clinical composite similar between groups***

## Bioprosthetic valve dysfunction

(Implanted population)




| Composite events through 3 years | Evolut (N=307) | SAPIEN (N=313) | *P* value |
|---|---|---|---|
| HSVD | 6.1% | 47.7% | <0.001 |
| NSVD | 6.9% | 19.7% | <0.001 |
| Thrombosis (clinical) | 0.3% | 1.4% | 0.17 |
| Endocarditis | 3.4% | 5.1% | 0.32 |
| AV reintervention | 0.7% | 1.1% | 0.60 |

AV=aortic valve, HSVD=hemodynamic structural valve dysfunction, NSVD=nonstructural valve dysfunction (severe PPM, or ≥ moderate total aortic regurgitation)

***BVD composite significantly lower with Evolut***

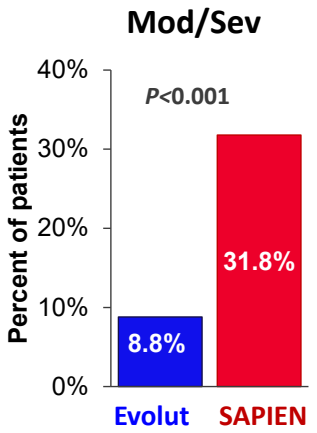
# Secondary Endpoints

| Endpoints | Evolut (N=312) | SAPIEN (N=309) | *P* Value* |
|---|---|---|---|
| **CEC Adjudicated Events, KM%** | | | |
| All-cause mortality | 18.7% | 15.7% | 0.39 |
| Cardiovascular mortality | 10.5% | 7.8% | 0.32 |
| Heart failure rehospitalization | 9.0% | 8.7% | 0.88 |
| Aortic valve reintervention | 0.7% | 1.1% | 0.66 |
| New pacemaker implant[a] | 15.9% | 12.1% | 0.13 |
| All stroke | 8.5% | 8.6% | 0.86 |
| Disabling stroke | 5.1% | 4.2% | 0.56 |
| Transient ischemic attack | 2.6% | 4.7% | 0.17 |
| Endocarditis | 3.4% | 5.2% | 0.31 |
| Definite | **1.0%** | **3.6%** | **0.05** |
| Prosthetic valve thrombosis (VARC-2) | **1.5%** | **5.8%** | **0.007** |
| Clinical valve thrombosis | 0.3% | 1.4% | 0.18 |
| Subclinical valve thrombosis | **1.1%** | **4.4%** | **0.02** |
| **Echocardiographic outcomes % (n/N)** | | | |
| Mild or greater total aortic regurgitation | 16.2% (32/197) | 23.5% (48/204) | 0.07 |
| **Quality of life outcomes, mean ± SD or % (n/N)** | | | |
| KCCQ Overall Summary Score | 78.5±21.3 | 79.3±19.6 | 0.66 |
| VARC-3 favorable binary outcome[b], % | 62.4% (169/271) | 65.9% (180/273) | 0.39 |

[a]Site reported data; patients with pacemaker/ICD at baseline excluded; [b]patient is alive with KCCQ Overall Score ≥60 and has not had decline >10 in KCCQ Overall Summary from baseline *P values for KM estimates used log-rank test
CEC=Clinical Events Committee; KM=Kaplan-Meier

# Effects of Prosthesis-Patient Mismatch

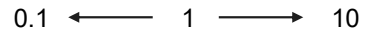
## PPM at reference echo[a] (VARC-3)




[a]Reference echo = 30-day echo if available, otherwise discharge echo used

## Impact of mod/severe vs no PPM[a] on mortality[b] Adjusted analysis[c]

| Mortality | Decreased mortality / Increased mortality | Hazard Ratio (95% CI) | Wald *P*-Value |
|---|---|---|---|
| **Evolut + SAPIEN** | | | |
| All-cause | | 1.64 (0.99, 2.71) | 0.06 |
| Cardiovascular | | 2.20 (1.12, 4.32) | **0.02** |
| **Evolut** | | | |
| All-cause | | 1.61 (0.61, 4.21) | 0.34 |
| Cardiovascular | | 1.72 (0.43, 6.88) | 0.44 |
| **SAPIEN** | | | |
| All-cause | | 2.17 (1.07, 4.39) | **0.03** |
| Cardiovascular | | 2.89 (1.10, 7.59) | **0.03** |



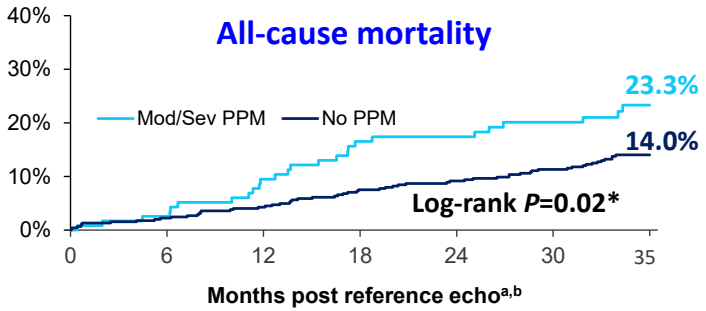

**Mod/Sev vs No PPM, HR (95% CI)**

[b]Mortality was landmarked at the reference echo

[c]Adjusted for age, COPD status, renal function (GFR <60 mL/min/1.73 m²), LVEF, and stroke volume index (SVI)

## KM%: Evolut + SAPIEN

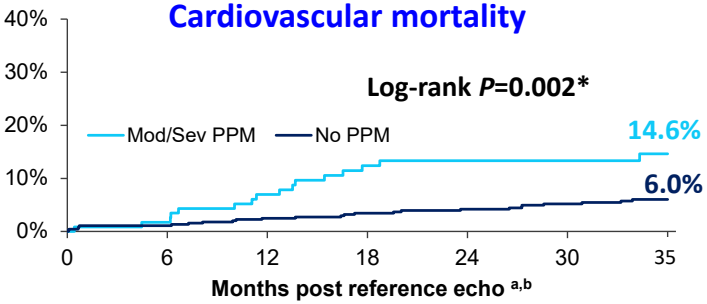
### All-cause mortality




**Number at risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| 117 | 113 | 104 | 95 | 92 | 88 | 11 |
| 448 | 433 | 415 | 396 | 383 | 371 | 72 |

### Cardiovascular mortality

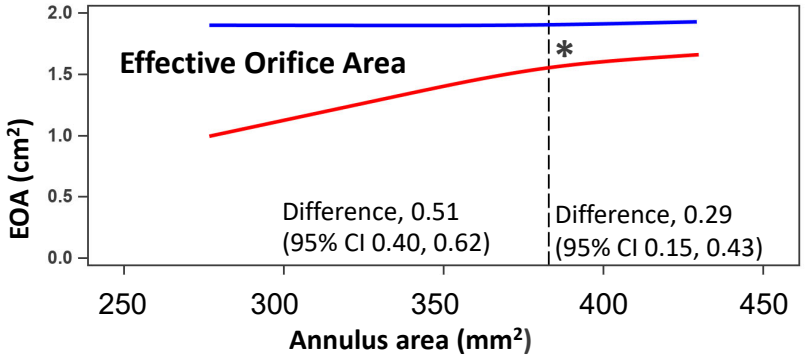



**Number at risk**

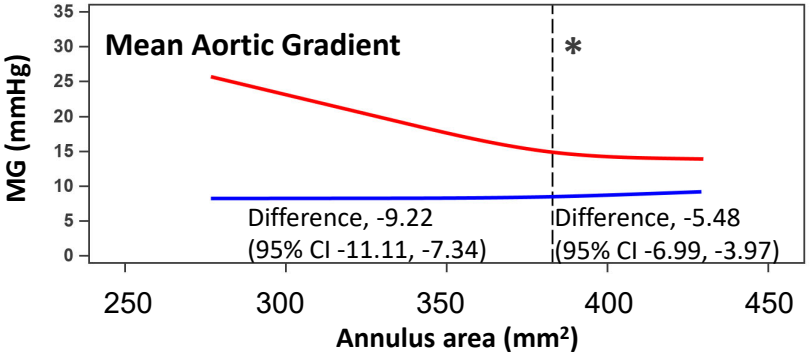
| | | | | | | |
|---|---|---|---|---|---|---|
| 117 | 113 | 104 | 95 | 92 | 88 | 11 |
| 448 | 433 | 415 | 396 | 383 | 371 | 72 |

*Log-rank P-value is unadjusted

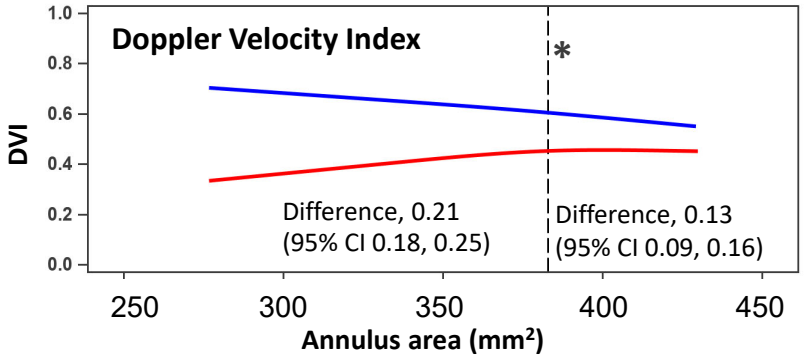
# Valve Performance Throughout Range of Annulus Area




| Annulus area | Evolut | SAPIEN | *P*-value |
|---|---|---|---|
| <383.45 mm² | 1.89±0.44 | 1.38±0.33 | <0.001 |
| ≥383.45 mm² | 1.92±0.52 | 1.63±0.38 | <0.001 |




| Annulus area | Evolut | SAPIEN | *P*-value |
|---|---|---|---|
| <383.45 mm² | 8.21±5.10 | 17.44±8.24 | <0.001 |
| ≥383.45 mm² | 8.85±5.13 | 14.33±5.60 | <0.001 |




| Annulus area | Evolut | SAPIEN | *P*-value |
|---|---|---|---|
| <383.45 mm² | 0.63±0.15 | 0.42±0.10 | <0.001 |
| ≥383.45 mm² | 0.58±0.15 | 0.46±0.09 | <0.001 |

- Restricted cubic spline regression analysis
- Inclusion criterion: Annulus area ≤430 mm²
- Median annulus area = 383.45mm²

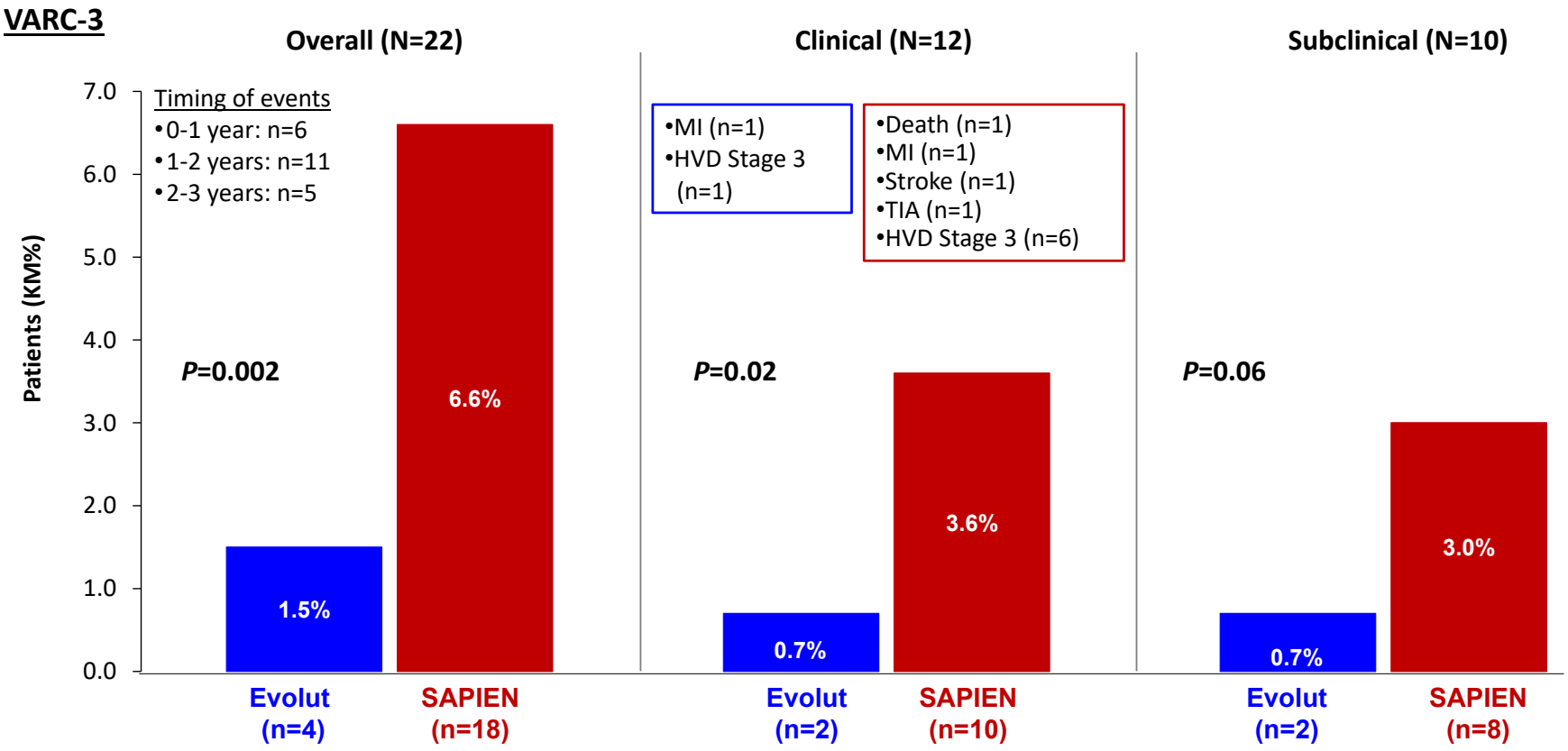
*Differences for regions below & above median

***Evolut:***
***larger EOA, lower MG, and greater DVI throughout range of annulus area***



Data presented as mean ± SD

# VARC-3 Prosthetic Valve Thrombosis (CEC adjudicated)




HVD Stage 3 = Severe hemodynamic valve deterioration: increase in MG ≥ 20 mmHg for final MG ≥30 mmHg and any of: decrease in EOA ≥0.6 $cm^2$ or ≥50%; decrease in DVI ≥0.2 or ≥40%; new occurrence or increase of ≥2 grades of intraprosthetic AR resulting in severe AR.

## Conclusions

- At 3 years of follow-up for women in the SMART Trial:
  - Evolut and SAPIEN have similar rates for the composite of death, disabling stroke, or HF rehospitalization.
  - Evolut had a significantly lower rate of BVD.
  - Evolut had significantly less VARC-3 clinical thrombosis.
  - All individual and composite hemodynamic measures remained superior with Evolut, including a markedly lower risk for prosthesis-patient mismatch (PPM).
  - In an exploratory analysis, moderate/severe PPM at 30 days was associated with higher risk of cardiovascular mortality.
- These findings support the importance of minimizing PPM when feasible and the planned comparison through 5 years of follow-up.

**Indications**
The Medtronic Evolut™ PRO+, Evolut™ FX, and Evolut™ FX+ Systems are 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+, Evolut FX, and Evolut FX+ Systems are 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).

**Contraindications**
The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ Systems are contraindicated in patients who cannot tolerate Nitinol (titanium or nickel), gold (for Evolut FX and Evolut FX+ Systems alone), an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

**Warnings**
*General* Implantation of the Evolut PRO+, Evolut FX, and Evolut FX+ Systems should be performed only by physicians who have received Medtronic Evolut PRO+, Evolut FX, or Evolut FX+ training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. *Transcatheter aortic valve (bioprosthesis)* Accelerated deterioration due to calcific degeneration of the bioprostheses may occur in: children, adolescents, or young adults; patients with altered calcium metabolism (e.g., chronic renal failure or hyperthyroidism).

**Precautions**
*General* 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 Evolut PRO+, Evolut FX, and Evolut FX+ Systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprostheses 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: (1) 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 mm Hg, or a peak aortic-jet velocity ≥ 4.0 m/s; (2) 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 mm Hg, 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 an Evolut PRO+, Evolut FX, or 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 (e.g., wire form frame fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer-labeled inner diameter < 17 mm. Implanting the Evolut PRO+, Evolut FX, or Evolut FX+ bioprosthesis in a degenerated transcatheter bioprosthetic valve (transcatheter aortic valve in transcatheter aortic valve [TAV in TAV]) 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+, Evolut FX, or Evolut FX+ implantation is high. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in patient populations presenting with the following: Blood dyscrasias as defined as leukopenia (WBC < 1,000 cells/$mm^3$), thrombocytopenia (platelet count < 50,000 cells/$mm^3$), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital unicuspid valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+]); moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation; hypertrophic obstructive cardiomyopathy; new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation; native aortic annulus size < 18 mm or > 30 mm per the baseline diagnostic imaging or a surgical bioprosthetic or failed transcatheter aortic annulus size < 17 mm or > 30 mm; transarterial access unable to accommodate an 18 Fr introducer sheath or the 14 Fr equivalent Evolut PRO+ inline sheath when using model D-EVPROP2329US or Evolut FX Delivery Catheter System with inline sheath when using model D-EVOLUTFX-2329 or transarterial access unable to accommodate a 22 Fr introducer sheath or the 18 Fr equivalent Evolut PRO+ inline sheath when using model D-EVPROP34US or Evolut FX Delivery Catheter System with inline sheath when using model D-EVOLUTFX-34; 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; and severe basal septal hypertrophy with an outflow gradient.

*Before Use* Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging. The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the devices is the responsibility of the physician. Refer to the Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with transarterial access vessel diameters of ≥ 5 mm when using models D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6 mm when using models D-EVPROP34US/D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥ 60 mm from the basal plane for both systems. Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of > 30° for right subclavian/axillary access or > 70° for femoral and left subclavian/axillary access. 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 models D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6.5 mm when using models D-EVPROP34US/D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft. 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.

*During Use* If a misload is detected during fluoroscopic inspection, do not attempt to reload the bioprosthesis. Discard the entire system. 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. After the procedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. After the procedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Prior to the procedure, 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. For TAV in TAV procedures, failed valve size and patient anatomy must be considered before implantation of the Evolut PRO+, Evolut FX, or Evolut FX+ bioprosthesis to ensure patient safety (for example, to avoid coronary obstruction).

**Potential adverse events**
Potential risks associated with the implantation of the Evolut PRO+, Evolut FX, or Evolut FX+ transcatheter aortic valve may include, but are not limited to, the following: • death • myocardial infarction, cardiac arrest, cardiogenic shock, or 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 (e.g., 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 recrossing 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 (e.g., 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 (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, or stenosis) • mitral valve regurgitation or injury • conduction system disturbances (e.g., atrioventricular node block, left bundle-branch block, asystole), which may require a permanent pacemaker • infection (including septicemia) • hypotension or hypertension • hemolysis • peripheral ischemia • General surgical risks applicable to transcatheter aortic valve implantation: • bowel ischemia • abnormal lab values (including electrolyte imbalance) • allergic reaction to antiplatelet agents, contrast medium, or anesthesia • exposure to radiation through fluoroscopy and angiography • permanent disability.

Please reference the Evolut PRO+, Evolut FX, and Evolut FX+ Instructions for Use for more information regarding indications, warnings, precautions, and potential adverse events.

**Caution:** Federal Law (USA) restricts these devices to the sale by or on the order of a physician.

The commercial name of the Evolut™ PRO+ device is Medtronic Evolut™ PRO+ System, the commercial name of the Evolut™ FX device is Medtronic Evolut™ FX System, and the commercial name of the Evolut™ FX+ device is Medtronic Evolut™ FX+ System.

©2026 Medtronic. All rights reserved. Medtronic, Medtronic logo, and Engineering the extraordinary are trademarks of Medtronic. All other brands are trademarks of a Medtronic company.

US-CV-2602725
11/2026