

Medtronic

Transcatheter aortic valve

Clinical trial summary



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EXPAND II – Enrollment closed

Objective
The EXPAND TAVR II Trial is a multicenter, international, prospective, randomized clinical trial to obtain safety and effectiveness data to support indication expansion for the Medtronic Evolut™ PRO+ and Evolut™ FX transcatheter aortic valve replacement (TAVR) systems to include patients with moderate, symptomatic aortic stenosis. The primary objective of this trial is to demonstrate that the Medtronic TAVR system administered in conjunction with guideline-directed management and therapy (GDMT) is superior to GDMT alone in terms of safety and effectiveness.
Specifics
Study status/duration 1-year and 2-year outcomes to be reported/10-year follow-up
Sample size 650 subjects, up to 100 sites
Primary outcomes to be measured 1. Safety: Composite of all-cause mortality, all stroke, life-threatening or fatal bleeding, acute kidney injury, hospitalization due to device or procedure-related complication, or valve dysfunction requiring reintervention at 30 days (life-threatening or fatal bleeding is defined as BARC Type 3 or 4 and acute kidney injury is defined as VARC-3 Stage IV). 2. Effectiveness: Non-hierarchical composite of all-cause mortality, heart failure hospitalization or event, or medical instability leading to aortic valve replacement or re-intervention at two years.
Device Evolut™ PRO+, Evolut™ FX and Evolut™ FX+
Key takeaways
The study will evaluate the safety and effectiveness of the Evolut™ PRO+ TAVR and Evolut™ FX TAVR systems combined with GDMT compared to GDMT alone in the patient population with moderate, symptomatic aortic stenosis. The data may be used to support future regulatory submissions to expand the current indications for the Evolut TAVR platform.

Optimize PRO Study¹

Objective		
The primary objective of the Optimize PRO study is to collect clinical evidence on valve performance and procedural outcomes associated with an “optimized” pre- and post-procedural TAVR care pathway, including the cusp overlap technique (COT) to deploy the Evolut™ TAVR system.		
Specifics		
Study status/duration 30-day outcomes reported/1-year follow-up		
Sample size N = 653		
30-day outcomes Results from the full global cohort		
0% Mod/Severe AR	1.7% Disabling stroke 6.4% PPI (with 4-step COT compliance)	0.8% All-cause mortality
Devices Evolut™ PRO+ 78.4%, Evolut™ PRO 21.5%, Evolut™ R 0.2%, SAPIEN™ 3 0.5%		
Key takeaways		
Results from the Optimize PRO full global cohort reveal excellent outcomes at 30 days. The study showed minimal all-cause mortality and stroke occurrences, with a new pacemaker implantation rate of 6.4% with 4-step COT compliance, and 11.1% overall. Aortic regurgitation (AR) rates were exceptionally low, with no instances of moderate or severe AR observed upon discharge. Patients had a median length of stay of two days and excellent post-procedure hemodynamics.		

Key: primary device used

● CoreValve™ TAV
 ● Evolut™ PRO TAV
 ● Evolut™ R TAV
 ● Evolut™ PRO+ TAV
 ● Evolut™ FX

Optimize PRO FX Addendum²

Objective
The Optimize PRO FX study evaluates valve performance and procedural outcomes using an optimized TAVR care pathway and cusp overlap technique in patients receiving the Evolut™ FX TAVR platform.
Specifics
Study status/duration 30-day outcomes reported/1-year follow-up
Sample size 151 patients
30-day outcomes 1.3% all-cause mortality, 1.3% disabling stroke, 6.7% PPI
Devices Evolut™ FX 100%
Key takeaways
At 30 days, the use of standardized optimized care pathways and cusp overlap technique with the next generation Evolut™ FX TAVR system is associated with low PPI rates and no moderate/severe aortic regurgitation. The Evolut™ FX TAVR platform demonstrated favorable clinical and hemodynamic outcomes with low 30-day all-cause mortality or stroke (2.7%), large EOAs and mean gradients (at discharge), and a median length of stay of 1 day. Continued excellent clinical outcomes are anticipated as procedural techniques continue to be refined.

SMART Trial³

Objective		
The SMAll Annuli Randomized to Evolut™ or SAPIEN™ (SMART) trial is a prospective, multicenter, international, randomized, controlled, post-market study comparing the Medtronic Evolut self-expanding valve (SEV) to the Edwards SAPIEN™ balloon-expanding valve (BEV). This study focuses on patients with symptomatic severe aortic stenosis (AS) and a small annulus size of 430 mm ² or less.		
Specifics		
Study status/duration 2-year outcomes reported/5-year follow-up		
Sample size N = 716 patients		
<table border="0" style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;"> 1-year outcomes Clinical outcome co-primary endpoint†: Evolut™ SEV 9.7%, SAPIEN™ BEV 10.6% Valve function co-primary endpoint‡: Evolut™ SEV 9.4%, SAPIEN™ BEV 42.3% </td> <td style="width: 50%; vertical-align: top;"> 2-year outcomes Clinical outcomes co-primary endpoint†: Evolut™ SEV 17.8%, SAPIEN™ BEV 17.6% Valve function co-primary endpoint‡: Evolut™ SEV 12.5%, SAPIEN™ BEV 48.4% </td> </tr> </table>	1-year outcomes Clinical outcome co-primary endpoint†: Evolut™ SEV 9.7%, SAPIEN™ BEV 10.6% Valve function co-primary endpoint‡: Evolut™ SEV 9.4%, SAPIEN™ BEV 42.3%	2-year outcomes Clinical outcomes co-primary endpoint†: Evolut™ SEV 17.8%, SAPIEN™ BEV 17.6% Valve function co-primary endpoint‡: Evolut™ SEV 12.5%, SAPIEN™ BEV 48.4%
1-year outcomes Clinical outcome co-primary endpoint†: Evolut™ SEV 9.7%, SAPIEN™ BEV 10.6% Valve function co-primary endpoint‡: Evolut™ SEV 9.4%, SAPIEN™ BEV 42.3%	2-year outcomes Clinical outcomes co-primary endpoint†: Evolut™ SEV 17.8%, SAPIEN™ BEV 17.6% Valve function co-primary endpoint‡: Evolut™ SEV 12.5%, SAPIEN™ BEV 48.4%	
Devices Evolut™ PRO/Evolut™ PRO+/Evolut™ FX and SAPIEN™ 3/SAPIEN™ 3 Ultra		
Key takeaways		
The purpose of this trial is to generate randomized clinical evidence on valve safety and performance of Evolut™ SEV versus SAPIEN™ BEV in patients with symptomatic severe native aortic valve stenosis. At 2-year follow-up, patients with symptomatic severe aortic stenosis and small aortic annuli undergoing Evolut™ SEV implantation were associated with similar clinical outcomes and superior valve function outcomes compared with SAPIEN™ BEV.		

† Composite of all-cause mortality, disabling stroke, or heart failure hospitalization.

‡ Bioprosthetic valve dysfunction (BVD) is a composite including any of the following: hemodynamic structural valve dysfunction (mean gradient ≥ 20 mmHg), non-structural valve dysfunction (severe prosthesis patient mismatch [PPM] or ≥ moderate aortic regurgitation), thrombosis, endocarditis, and aortic valve reintervention.

FORWARD PRO Study⁴

Objective	
The objective of the FORWARD PRO Study was to evaluate the acute and long-term clinical performance and safety of the Evolut™ PRO system in patients with symptomatic severe aortic stenosis or failed bioprosthesis in routine practice.	
Specifics	
Study status/duration 3-year outcomes/5-year follow-up	
Sample size N = 629	
30-day outcomes 3.2% All-cause mortality 2.9% Disabling stroke 18.9% New PPI	3-year outcomes 25.0% All-cause mortality 6.5% Disabling stroke 24.7% New PPI
Device Evolut PRO	
Key takeaways	
The results of the FORWARD PRO Study highlighted the exceptional safety profile of the Evolut™ PRO valve. The Evolut™ PRO valve demonstrated outstanding hemodynamics and favorable sealing around the annulus, as evidenced by a 0% occurrence of moderate/severe paravalvular leakage (PVL) after three years, among patients with complete echocardiographic follow-up.	

Evolut™ PRO Study⁵

Objective	
The Evolut™ PRO Study was a prospective, multicenter, nonrandomized, single-arm study. Primary safety endpoints were all-cause mortality and disabling stroke at 30 days, and the primary efficacy endpoint was percentage of patients with no or trace aortic regurgitation at 30 days.	
Specifics	
Study status/duration 3-year outcomes reported/5-year follow-up	
Sample size N = 60	
30-day outcomes 1.7% All-cause mortality 1.7% Disabling stroke 11.8% New PPI	3-year outcomes 25.8% All-cause mortality 10.7% Disabling stroke 15.9% New PPI
Device Evolut™ PRO	
Key takeaways	
Three-year outcomes from the Evolut™ PRO Study demonstrated consistent and excellent performance of the Evolut™ PRO TAVR system. The primary safety and efficacy endpoints were achieved, maintaining a 0% occurrence of moderate/severe paravalvular leak (PVL) at 30 days and sustaining this outcome over a span of three years in a small patient population.	

Key: primary device used

● CoreValve™ TAV
 ● Evolut™ PRO TAV
 ● Evolut™ R TAV
 ● Evolut™ PRO+ TAV
 ● Evolut™ FX

Evolut™ Low Risk Bicuspid Trial⁶

Objective	
The objective of this multicenter, international, prospective, randomized, interventional, premarket trial was to evaluate the procedural safety and efficacy of the Medtronic TAVR system in patients with bicuspid aortic anatomy and severe aortic stenosis at low risk.	
Specifics	
Study status/duration 3-year outcomes reported/10-year follow-up	
Sample size N = 150	
30-day outcomes 1.3% All-cause mortality or disabling stroke 15.1% New PPI 0.0% ≥ Moderate PVL	3-year outcomes 4.1% All-cause mortality or disabling stroke 19.4% New PPI 0.0% ≥ Moderate PVL
Devices Evolut™ R 43%/Evolut™ PRO 57% (The Evolut™ Platform is not CE marked for the Bicuspid Low Risk indication)	
Key takeaways	
Transcatheter aortic valve replacement in low-surgical risk patients with bicuspid aortic valve stenosis achieved excellent 3-year clinical outcomes, with low rates of death and stroke. The mean AV gradient at 3 years was 9.1 mmHg and effective orifice area was 2.2 cm ² . TAVR patients with bicuspid aortic valves had sustained improvement in NYHA and KCCQ scores at 3 years with low reintervention rates (1.4%). These results are comparable to the 3-year results of the Evolut™ valve in low surgical risk patients with tricuspid aortic valve stenosis.	

Evolut™ Low Risk Trial⁷

Objective	
The Evolut™ Low Risk Trial was a prospective, randomized, multicenter, noninferiority study to assess the safety and efficacy of the Evolut™ TAVR system compared with surgical aortic valve replacement (SAVR) in patients with a low predictive risk of 30-day surgical mortality.	
Specifics	
Study status/duration 5-year outcomes reported/10-year follow-up	
Sample size TAVR = 730 and SAVR = 684	
30-day outcomes 0.5% All-cause mortality 0.5% Disabling stroke 0.1% Clinical valve thrombosis	5-year outcomes 13.5% All-cause mortality 3.6% Disabling stroke 0.3% Clinical valve thrombosis
Devices Evolut™ R 73%/Evolut™ PRO 23.4%/CoreValve™ 3.6%	
Key takeaways	
The Low Risk trial's five-year findings highlighted the impressive performance of the Evolut TAVR system among patients with severe aortic stenosis at a low surgical risk. The primary endpoint of all-cause mortality or disabling stroke at 5 years was 15.5% TAVR vs. 16.4% SAVR; p = 0.47. The Evolut™ TAVR system continues to showcase a statistically better hemodynamic performance compared to SAVR at the five year milestone. Notably, both TAVR and SAVR exhibited similarly low rates of reintervention and clinical valve thrombosis, with 3.3% and 0.3% for TAVR and 2.5% and 0.2% for TAVR and SAVR, respectively. These results continue to support that Evolut™ TAVR may be a preferred strategy to surgery in the appropriate patients with severe AS at low surgical risk.	

Evolut™ R FORWARD Study⁸

Objective	
The FORWARD Study was a prospective, single-arm, multicenter, observational study that assessed the safety and clinical performance of the Medtronic Evolut™ R system in patients with symptomatic native aortic stenosis or failed bioprosthesis in routine practice.	
Specifics	
Study status/duration 3-year outcomes reported/3-year follow-up	
Sample size N = 1038	
30-day outcomes 1.9% All-cause mortality 1.8% Disabling stroke 17.5% New PPI	3-year outcomes 24.8% All-cause mortality 4.8% Disabling stroke 24.7% New PPI
Device Evolut™ R	
Key takeaways	
The FORWARD Study demonstrated excellent and reproducible results in real-world clinical practice. The high survival rate, low stroke rate, low permanent pacemaker rates, unsurpassed hemodynamics, and low rates of moderate/severe PVL confirmed the advantages of the Evolut™ R system.	

Evolut™ R U.S. Study⁹

Objective	
The Evolut™ R U.S. Clinical Study was a prospective, multicenter, controlled, nonrandomized, single-arm clinical study that evaluated the repositionable Evolut™ R system in patients deemed high risk or greater for surgery.	
Specifics	
Study status/duration 3-year outcomes reported/5-year follow-up	
Sample size N = 241	
30-day outcomes 2.5% All-cause mortality 3.3% Disabling stroke 16.4% New PPI	3-year outcomes 25% All-cause mortality 6.1% Disabling stroke 79.2% None/trace PVL
Device Evolut™ R	
Key takeaways	
Results from the Evolut™ R U.S. Study highlighted the safety and effectiveness of the Evolut™ R TAVR system. The 34 mm Appendix Study confirmed the performance of the Evolut™ R 34 mm valve in line with the Evolut™ platform.	

Key: primary device used

● CoreValve™ TAV
 ● Evolut™ PRO TAV
 ● Evolut™ R TAV
 ● Evolut™ PRO+ TAV
 ● Evolut™ FX

Evolut™ R CE Mark Study¹⁰

Objective	
The Evolut™ R CE Mark Clinical Study was a prospective, multicenter, controlled, nonrandomized, single-arm clinical study to evaluate the repositionable Evolut™ R system in patients with symptomatic aortic stenosis and heart team-assessed risk of operative mortality.	
Specifics	
Study status/duration 2-year outcomes reported/2-year follow-up	
Sample size N = 60	
30-day outcomes 0.0% All-cause mortality 0.0% Disabling stroke 11.7% New PPI	2-year outcomes 23.6% All-cause mortality 5.3% Disabling stroke 80% None/trace PVL
Device Evolut™ R	
Key takeaways	
The Evolut™ R CE Mark Study confirmed the safety and effectiveness of the Evolut™ R transcatheter aortic valve, a self-expanding bioprosthesis that provides a low-profile delivery system, conformable annular sealing, and the ability to reposition during deployment.	

VIVA Study¹¹

Objective	
The VIVA study was a prospective, observational, single-arm, post-market, multicenter study to collect data regarding use of TAVR with the CoreValve™ and Evolut™ R devices in patients with failing surgical aortic bioprostheses at high risk for redo open-heart surgery.	
Specifics	
Study status/duration 2-year outcomes reported/2-year follow-up	
Sample size N = 202	
30-day outcomes 2.5% All-cause mortality 0.0% Disabling stroke 8.0% New PPI	2-year outcomes 16.5% All-cause mortality 1.7% Disabling stroke 12.0% PPI
Devices Evolut™ R 91%/CoreValve™ 9%	
Key takeaways	
Results from the VIVA Study confirmed the feasibility, safety, and effectiveness of the TAV-in-SAV intervention using the CoreValve/Evolut™ R devices in high-risk patients with failing surgical aortic bioprostheses.	

SURTA VI Continued Access Study¹²

Objective	
Prior to intermediate risk approval, the SURTA VI Continued Access Study (CAS) enrolled patients in the U.S. who underwent attempted TAV implant under the same inclusion and exclusion criteria and trial procedures as the SURTA VI Trial with no randomization to surgery.	
Specifics	
Study status/duration 5-year outcomes reported/5-year follow-up	
Sample size N = 275	
30-day outcomes 0.0% All-cause mortality 0.4% Disabling stroke 17.2% PPI	5-year outcomes 29.2% All-cause mortality 3.4% Disabling stroke 27.6% PPI
Devices Evolut™ R 93%/CoreValve 7%	
Key takeaways	
For patients with severe symptomatic AS at intermediate surgical risk treated with TAVR, five-year data from SURTA VI CAS showed favorable clinical outcomes, with excellent valve hemodynamics, low reintervention rates (1.1%), and no clinical valve thrombosis. These data demonstrated the longer-term safety and effectiveness of TAVR in this risk population.	

SURTA VI Trial¹³

Objective	
The SURTA VI Trial was a prospective, randomized, multicenter, noninferiority study to assess the safety and efficacy of the Medtronic TAVR system to SAVR in patients with symptomatic severe aortic stenosis at intermediate surgical risk.	
Specifics	
Study status/duration 5-year outcomes reported/10-year follow-up	
Sample size N = 864 TAVR, N = 796 SAVR	
30-day outcomes 2.2% All-cause mortality 3.4% All stroke 0.9% Aortic valve reintervention	5-year outcomes 31.3% All-cause mortality or disabling stroke 3.5% Aortic valve reintervention 3.0% ≥ Mild PVL
Devices CoreValve™ 84%/Evolut™ R 16%	
Key takeaways	
Among intermediate-risk patients with symptomatic severe aortic stenosis, major clinical outcomes at five years were similar for TAVR and surgery. Bioprosthetic valve performance was consistent through five years. TAVR was associated with superior hemodynamic valve performance at five years and had significantly better hemodynamics than surgery at each follow-up. Clinical valve thrombosis and endocarditis were infrequent through five years with both TAVR and SAVR. Rates of heart failure or valve-related rehospitalization were similar as well. Reintervention rates between two and five years were equally low for TAVR and surgery. Health status improved similarly after TAVR or surgery, and was maintained at five years.	

Key: primary device used

● CoreValve™ TAV
 ● Evolut™ PRO TAV
 ● Evolut™ R TAV
 ● Evolut™ PRO+ TAV
 ● Evolut™ FX

Objective	
The Nordic Aortic Valve Intervention (NOTION) Trial randomized all-comers with severe native aortic valve stenosis to either TAVR or SAVR, including a lower-risk patient population from three centers in Denmark and Sweden.	
Specifics	
Study status/duration 10-year outcomes reported/10-year follow-up	
Sample size N = 145 TAVR, N = 135, as-treated SAVR	
30-day outcomes 2.1% All-cause mortality 1.4% All stroke 34.1% New PPI	10-year outcomes 62.7% All-cause mortality 9.7% All stroke SVD [§] : 20.2% (TAVR), 37.7% (SAVR); p = 0.0008 Severe SVD: 1.5% (TAVR), 10.0% (SAVR); P = 0.02
Device CoreValve™	
Key takeaways	
The NOTION trial 10-year results constitute the longest follow-up data from a prospective, randomized trial between TAVR and SAVR available to date. The NOTION Trial results demonstrate the strong clinical performance of CoreValve™ in lower risk patients (80% of patients had an STS < 3%) versus surgery. After 10 years of follow up, there was no difference between CoreValve™ TAVR and SAVR with regards to all-cause mortality, stroke, or myocardial infarction. At 10 years follow-up, the TAVR arm had less severe SVD, defined according a modified VARC-3 endpoint, [§] compared to SAVR, whereas there was no difference in bioprosthetic valve failure between arms (9.7% TAVR and 13.8% SAVR {HR 0.7; 95% CI 0.4-1.5; P = 0.4}).	

§ Modified VARC-3 definition: Mean gradient ≥ 30 mmHg; AND increase in mean gradient ≥ 20 mmHg, Severe intraprosthetic AR.

BVD Pooled analysis

from the CoreValve™ U.S. Pivotal trial, SURTAVI trial, and CoreValve™ CAS¹⁵

Objective				
The purpose of the BVD pooled analysis was to evaluate the five-year incidence, outcomes, and predictors of BVD in patients undergoing supra-annular, self-expanding TAVR or surgery from the CoreValve™ U.S. High-Risk and SURTAVI randomized clinical trials, and the CoreValve™ Extreme Risk and CoreValve™ CAS non-randomized trials.				
Specifics				
Study status/duration 5-year BVD rate and outcomes reported	5-year incidence			
		CoreValve™/ Evolut™ TAVR	SAVR	P value
Sample size N = 5485 (TAVR RCT = 1209, TAVR non-RCT = 3190, SAVR RCT = 1086)	BVD, %[‡]	9.6	15.4	< 0.001
	SVD [‡]	2.1	4.5	0.007
	NSVD [‡]	5.5	9.6	< 0.001
Devices CoreValve™ 89.0%, Evolut™ R 11.0%	Thrombosis	0.3	0.2	0.80
	Endocarditis	1.6	1.8	0.67
Key takeaways				
The CoreValve™/Evolut™ supra-annular, self-expanding bioprosthesis is the first and only transcatheter valve to demonstrate lower rates of BVD and significantly better five-year valve performance compared with surgery in randomized clinical trials. This difference in valve performance was driven by a two-fold lower SVD and three-fold lower severe PPM, and was more profound in patients with smaller (≤ 23 mm) annuli (8.7% TAVR vs. 19.5% SAVR, p < 0001). Development of BVD, regardless of aortic valve replacement therapy, is associated with a significantly increased risk for worsened clinical outcomes including a 58% relative increase in 5-year hazard of death, 85% relative increase in 5-year hazard of cardiovascular death, and 50% relative increase in 5-year hazard of hospitalization. This was the first analysis to validate clinical criteria for valve performance (BVD) and its association with clinical outcomes, as evaluated by a comprehensive, contemporary BVD definition and > 5000 patient analysis.				

‡ BVD was defined as: SVD (mean gradient ≥ 10 mmHg increase from discharge/30 days AND ≥ 20 mmHg at last echo or new onset/increase of ≥ moderate intraprosthetic aortic regurgitation), NSVD (30-day severe PPM at 30-day/discharge or severe PVR through five years), clinical valve thrombosis, or endocarditis.

‡ Adapted from VARC-3 Writing Committee; Généreux P, et al. *Eur Heart J.* 2021;42:1825-1857. Capodanno D, et al. *Eur Heart J.* 2017;38:3382-3390.

CoreValve™ U.S. Pivotal Extreme Risk Trial¹⁶

Objective	
The CoreValve™ U.S. Pivotal Extreme Risk Trial evaluated the safety and efficacy of the Medtronic CoreValve™ system for the treatment of patients with symptomatic severe aortic stenosis in whom the predicted risk of operative mortality or serious, irreversible morbidity was 50% or greater at 30 days.	
Specifics	
Study status/duration 5-year outcomes reported/5-year follow-up	
Sample size N = 489	
30-day outcomes 8.4% All-cause mortality 2.3% Major stroke 21.6% New PPI	5-year outcomes 71% All-cause mortality 10.7% Major stroke
Device CoreValve™	
Key takeaways	
Results from the CoreValve™ U.S. Pivotal Extreme Risk Trial achieved the primary endpoint, confirming the safety and efficacy of the CoreValve™ system in patients with symptomatic severe aortic stenosis at prohibitive risk for surgical valve replacement. The five-year results showed sustained hemodynamics with low gradients and large EOAs.	

CoreValve™ U.S. Pivotal High Risk Trial¹⁷

Objective	
The CoreValve™ U.S. Pivotal High Risk Trial was a prospective, randomized, multicenter, noninferiority study that compared the safety and efficacy of the Medtronic CoreValve™ system to SAVR in patients with symptomatic severe aortic stenosis at increased surgical risk.	
Specifics	
Study status/duration 5-year outcomes reported/5-year follow-up	
Sample size N = 795 (TAVR = 390, SAVR = 357, as treated)	
30-day outcomes 3.3% All-cause mortality 3.9% Major stroke 19.8% New PPI	5-year outcomes 55.3% All-cause mortality 12.3% Major stroke 3% Reintervention
Device CoreValve™	
Key takeaways	
Study achieved one-year all-cause mortality primary endpoint showing the CoreValve™ system is superior to SAVR for patients with an increased surgical risk. The CoreValve™ system is the only TAVR valve to show patient survival superiority versus SAVR in a randomized controlled study at one year. At the five-year mark, all-cause mortality was similar for TAVR and SAVR. The significantly better hemodynamic performance was sustained for TAVR over SAVR. Additionally, TAVR showed less moderate structural valve deterioration [#] (SVD) than SAVR.	

[#]SVD definition reference: Capodanno D, et al. *Eur Heart J.* 2017;38:3382-3390.

Key: primary device used

● CoreValve™ TAV
 ● Evolut™ PRO TAV
 ● Evolut™ R TAV
 ● Evolut™ PRO+ TAV
 ● Evolut™ FX

CoreValve™ Expanded Use Study¹⁸

Objective	
<p>The purpose was to evaluate the safety and effectiveness of the CoreValve™ system in a subset of subjects excluded from the U.S. Extreme Risk Pivotal Trial population due to one or more additional comorbidities:</p> <ul style="list-style-type: none"> • Severe mitral valve regurgitation (MR) • Severe tricuspid valve regurgitation (TR) • End stage renal disease (ESRD) • Low gradient low output (LGLO) • Failed bioprosthetic surgical aortic valve (TAV-in-SAV) • Two or more conditions (listed above) 	
Specifics	
<p>Study status/duration 5-year outcomes reported/5-year follow-up</p>	
<p>Sample size N = 782 (53 = severe MR, 54 = severe TR, 215 = LGLO, 133 = ESRD, 232 = TAV-in-SAV, 95 = 2 or more conditions)</p>	
<p>30-day outcomes for TAV-in-SAV 2.2% All-cause mortality 0.4% Major stroke 8.1% New PPI</p>	<p>5-year outcomes for TAV-in-SAV All-cause mortality: 46.8% Reintervention: 5.9% Major stroke: 6.7%</p>
<p>Device CoreValve™</p>	
Key takeaways	
<p>Primary endpoint results confirmed the safety and effectiveness of the CoreValve™ system in the EUS TAV-in-SAV, LGLO, severe MR, severe TR, and ESRD cohorts. The safety outcomes within each of the cohorts, to the extent which they differ from each other and previous trials in inoperable patients, were reasonable given the underlying disease states in these extreme-risk cohorts and the additional morbidity they introduced. Similarly, treatment with CoreValve™ was efficacious through the follow-up with improvements in QoL and hemodynamic performance being substantial, especially when considered within the context of the baseline characteristics of the cohorts (e.g., limitations in flow area with the TAV-in-SAV cohort and a very serious comorbidity limiting the potential to improve QoL in the ESRD cohort).</p>	

CoreValve™ ADVANCE Study¹⁹

Objective	
<p>The ADVANCE study was a multicenter, prospective, single-arm, observational study to evaluate safety and performance of the CoreValve™ system in a routine hospital setting.</p>	
Specifics	
<p>Study status/duration 5-year outcomes reported/5-year follow-up</p>	
<p>Sample size N = 1015</p>	
<p>30-day outcomes 4.5% All-cause mortality 1.2% Major stroke 26.3% New PPI</p>	<p>5-year outcomes 50.7% All-cause mortality 5.4% Major stroke 0.9% SVD</p>
<p>Device CoreValve™</p>	
Key takeaways	
<p>Five-year results in real-world, elderly, high-risk patients undergoing TAVR with a self-expanding bioprosthesis provided evidence for continued valve durability and sustained unsurpassed hemodynamics.</p>	

1. OPTIMIZE PRO

Grubb K, Gada H, Mittal S, et al. Clinical Impact of Standardized TAVR Technique and Care Pathway: Insights from the Optimize PRO Study. *JACC Cardiovasc Interv.* March 13, 2023;16(5):558-570.

Yakubov, S. Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results. Presented at PCR LV 2024; November 26, 2024, London UK.

2. Optimize PRO FX Addendum

Gada H, et al. Early Outcomes from the Optimize PRO TAVR Pathway Evolut™ FX System addendum study. SCAI 2024; May 2024.

3. SMART Trial

Herrmann HC, Mehran R, Blackman DJ, et al. Self-Expanding or Balloon-Expandable TAVR in Patients with a Small Aortic Annulus. *N Engl J Med.* June 6, 2024;390(21):1959-1971.

Herrmann, HC. SMART 2-Year Data Update. Presented at CRT 2025; March 9, 2025, Washington D.C.

4. FORWARD PRO STUDY

Manoharan G, Grube E, Van Mieghem NM, et al. Thirty-day clinical outcomes of the Evolut™ PRO self-expanding transcatheter aortic valve: the international FORWARD PRO study. *EuroIntervention.* November 20, 2020;16(10):850-857.

Van Mieghem NM, Windecker S, Manoharan G, et al. Three-Year Outcomes With a Supra-Annular, Self-Expanding Bioprosthesis and a Pericardial Wrap-The FORWARD PRO Study. *Cath Cardiovasc Interv.* 2025;105(3):577-587.

5. EVOLUT™ PRO STUDY

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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 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 (e.g., STS predicted risk of operative mortality score $\geq 8\%$ or at $\geq 15\%$ risk of mortality at 30 days).

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 cm² or aortic valve area index ≤ 0.6 cm²/m², 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 cm² or aortic valve area index ≤ 0.6 cm²/m², 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. The safety and effectiveness of an Evolut™ PRO+, Evolut™ FX, or Evolut™ FX+ bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis have not been demonstrated. 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. 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/mm³), thrombocytopenia (platelet count $< 50,000$ cells/mm³), 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 surgical bioprosthetic aortic annulus size ≤ 17 mm or > 30 mm; transarterial access unable to accommodate a 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-EVOLUT™ FX-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-EVOLUT™ FX-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 $> 30^\circ$ for right subclavian/axillary access or $> 70^\circ$ 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. The safety and efficacy of an Evolut™ PRO+, Evolut™ FX, or Evolut™ FX+ bioprosthesis implanted within a transcatheter bioprosthesis have not been demonstrated.

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 migration/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.

This material should not be considered the exclusive source of information, it does not replace or supersede information contained in the device manual(s).

Please note that the intended use of a product may vary depending on geographical approvals.

See the device manual(s) for detailed information regarding the intended use, the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events.

For a MRI compatible device(s), consult the MRI information in the device manual(s) before performing a MRI. If a device is eligible for eIFU usage, instructions for use can be found at Medtronic's website manuals.medtronic.com. Manuals can be viewed using a current version of any major internet browser. For best results, use Adobe Acrobat® Reader with the browser.

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Medtronic

Medtronic International Trading Sàrl
Route du Molliau 31
Case postale
1131 Tolochenaz
Switzerland
Tel: +41 (0) 21 802 70 00
Fax: +41 (0) 21 802 79 00

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