# Transcatheter vs. Surgical Aortic Valve Replacement in Low Risk Patients: 3-Year Outcomes from the Evolut Low Risk Trial

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*For the CoreValve – Evolut Clinical Investigators*

# 3-Year Outcomes from the Evolut Low Risk Trial

## Disclosures

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below

| Financial Relationship | Company |
| --- | --- |
| Research grants, consulting fees, honoraria, speakers bureau fees | Medtronic, Edwards Lifesciences |



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# 3-Year Outcomes from the Evolut Low Risk Trial

## Study Administration

**Principal Investigators:** John Forrest, Michael Reardon

**Executive Committee:** G. Michael Deeb, Michael Reardon, Steven Yakubov

**Steering Committee:** David Adams, Stanley Chetcuti, G. Michael Deeb, John Forrest, John Heiser, William Merhi, Mubashir Mumtaz, Daniel O'Hair, Jon Resar, Joshua Rovin, Michael Reardon, Paul Teirstein, Steven Yakubov, George Zorn

**Screening Committee:** Michael Reardon, G. Michael Deeb, Steven Yakubov, Robert Stoler, Thomas Gleason

**Echo Core Laboratory:** Jae Oh, Mayo Clinic, Rochester, MN

**Statistical Analyses:** Jian Huang, Medtronic

**Sponsor:** Medtronic



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# 3-Year Outcomes from the Evolut Low Risk Trial

Evolut™ Low Risk Trial

## Background

- Now approved for all patients with severe symptomatic aortic stenosis regardless of surgical risk, TAVR has become the dominant form of AVR in the US.
- Current ACC/AHA guidelines recommend that heart teams utilize a shared decision-making process when discussing AVR with patients aged 65-80 years.[1]
- Randomized data of TAVR vs. surgery in intermediate and high-risk patients demonstrate similar survival outcomes at 5 years.[2-5]


[1]Otto CM, et al. 2020 ACC/AHA Guidelines.JACC 2021;77:e25-e197.
[2]Gleason TG, et al. JACC 2018;72:2687-2696.
[3]Mack MJ, et al. Lancet 2015;385:2477-2484.
[4]Van Mieghem NM, et al. JAMA Cardiol 2022;7:1000-1008.
[5]Makkar RR, et al. NEJM 2020;382:799-809.




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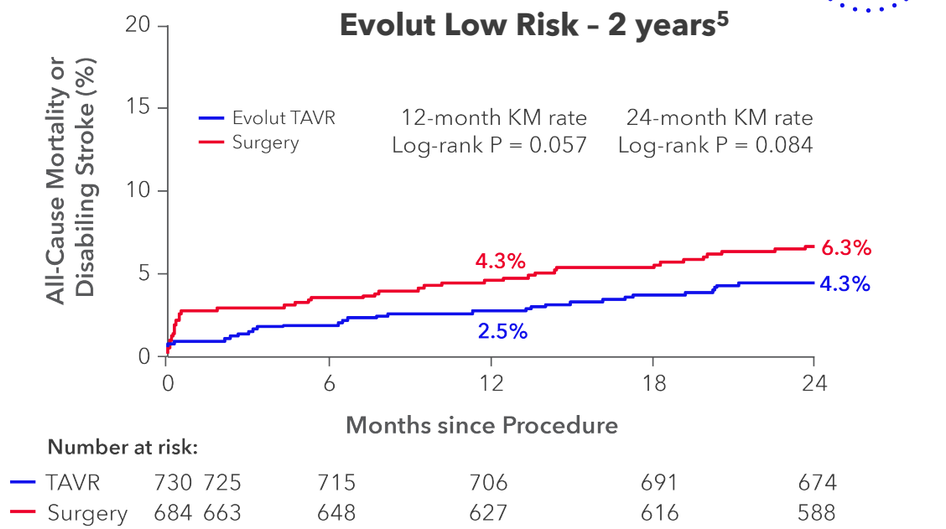
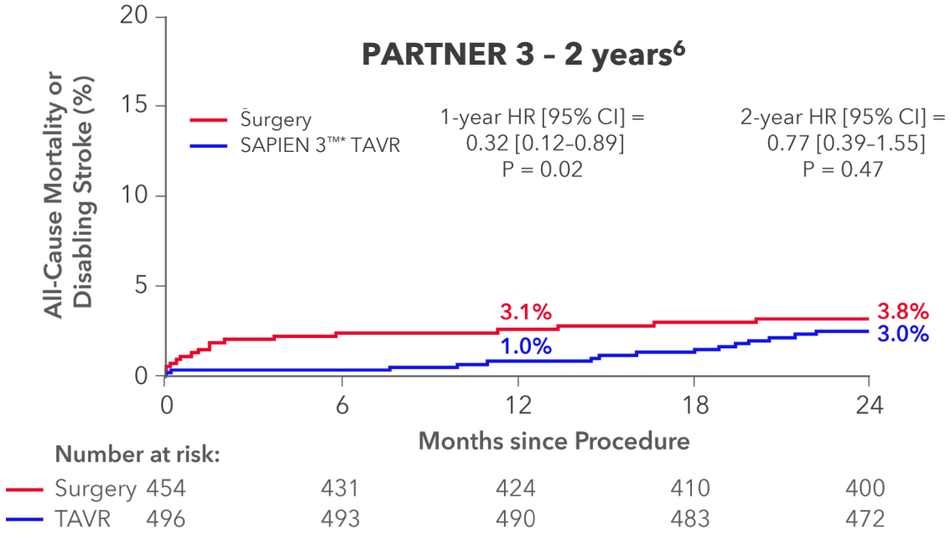
# 3-Year Outcomes from the Evolut Low Risk Trial

Evolut™ Low Risk Trial

## Background

- Data in low-risk patients have shown promising short-term mortality, stroke, and recovery benefits, and understanding how durable these results are will help to guide the shared decision-making process.




[5]Forrest JK, et al. JACC 2022;79:882-896. [6]Leon MB, et al. JACC 2021;77:1149-1161.



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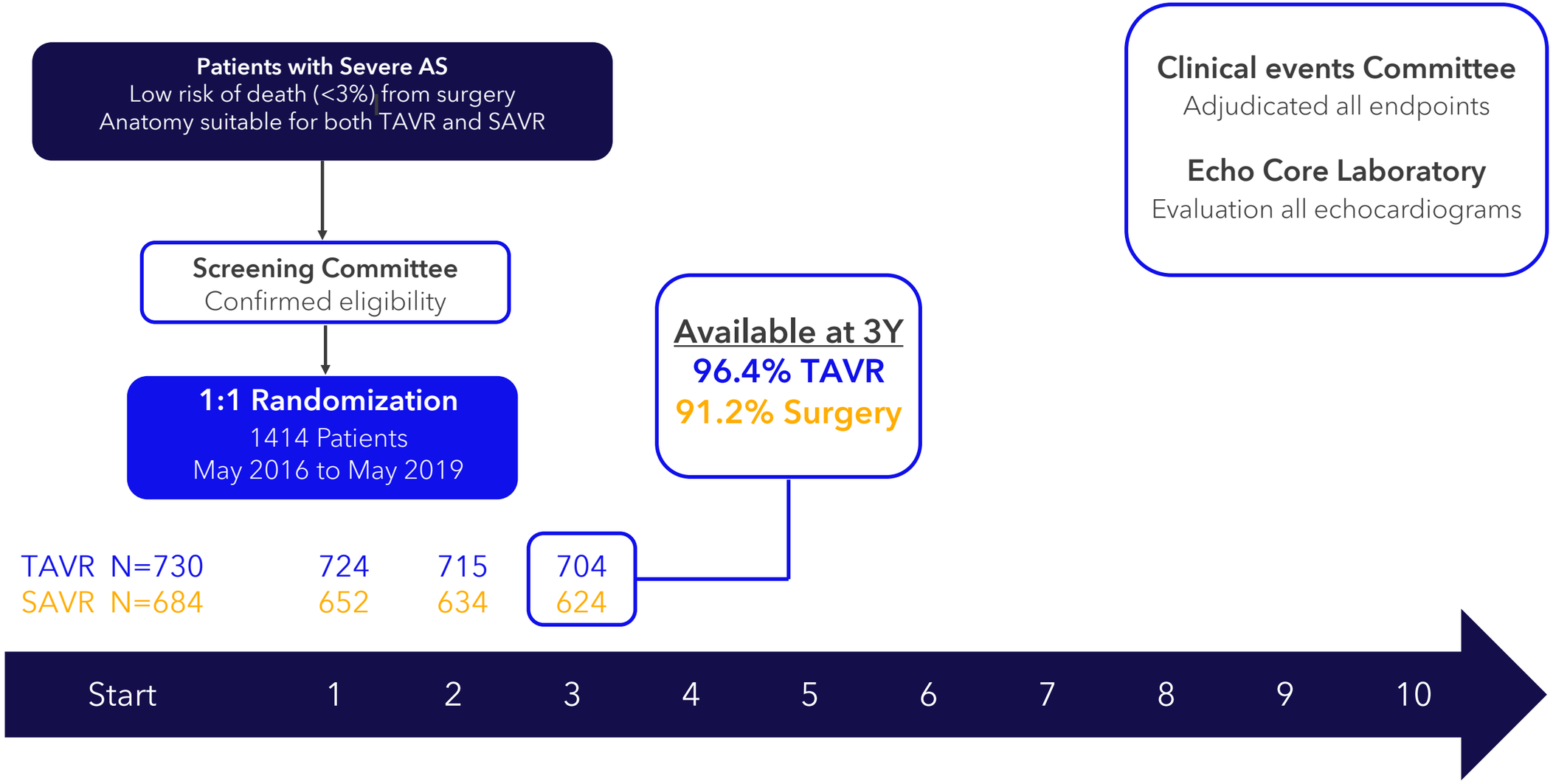
# 3-Year Outcomes from the Evolut Low Risk Trial

## Study Design



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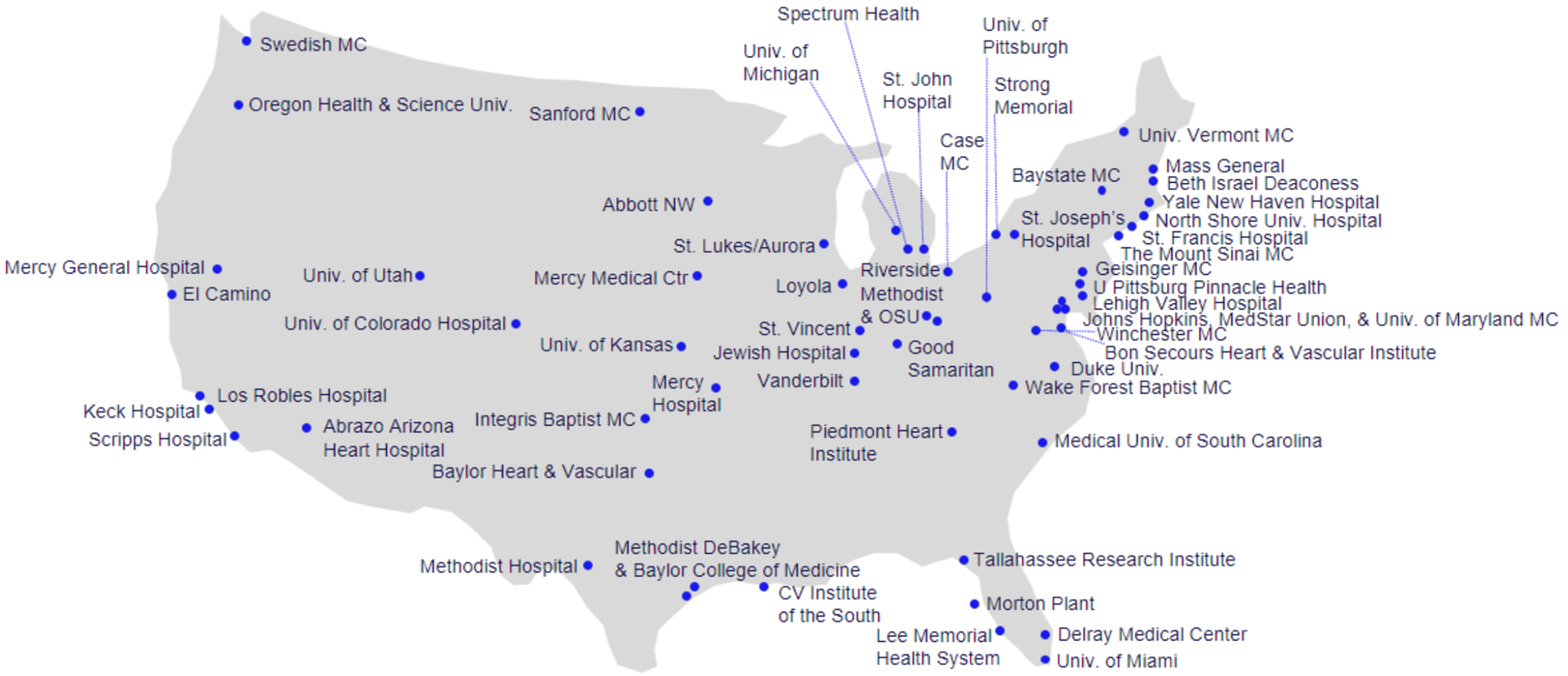
# 3-Year Outcomes from the Evolut Low Risk Trial

## Participating Sites in the United States (61)



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# 3-Year Outcomes from the Evolut Low Risk Trial

## Participating Sites in Australia, Canada, Europe, Japan and New Zealand (25)




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# 3-Year Outcomes from the Evolut Low Risk Trial

Evolut™ Low Risk Trial

## Baseline Characteristics

| Mean ± SD or % | Evolut TAVR (N=730) | Surgery (N=684) |
|---|---|---|
| Age | 74.1 ± 5.8 | 73.7 ± 5.9 |
| Female | 36.4 | 34.1 |
| Left ventricular ejection fraction, % | 61.7 ± 7.9 | 61.9 ± 7.7 |
| STS-PROM score, % | 2.0 ± 0.7 | 1.9 ± 0.7 |
| NYHA class III/IV | 24.9 | 28.2 |
| Hypertension | 84.8 | 82.6 |
| Chronic lung disease, COPD | 15.1 | 18.0 |
| Previous CABG | 2.5 | 2.0 |
| Previous PCI | 14.1 | 12.9 |
| Atrial fibrillation/atrial flutter | 15.4 | 14.4 |
| Pre-existing permanent pacemaker or defibrillator | 3.3 | 3.8 |

No significant differences between treatment groups



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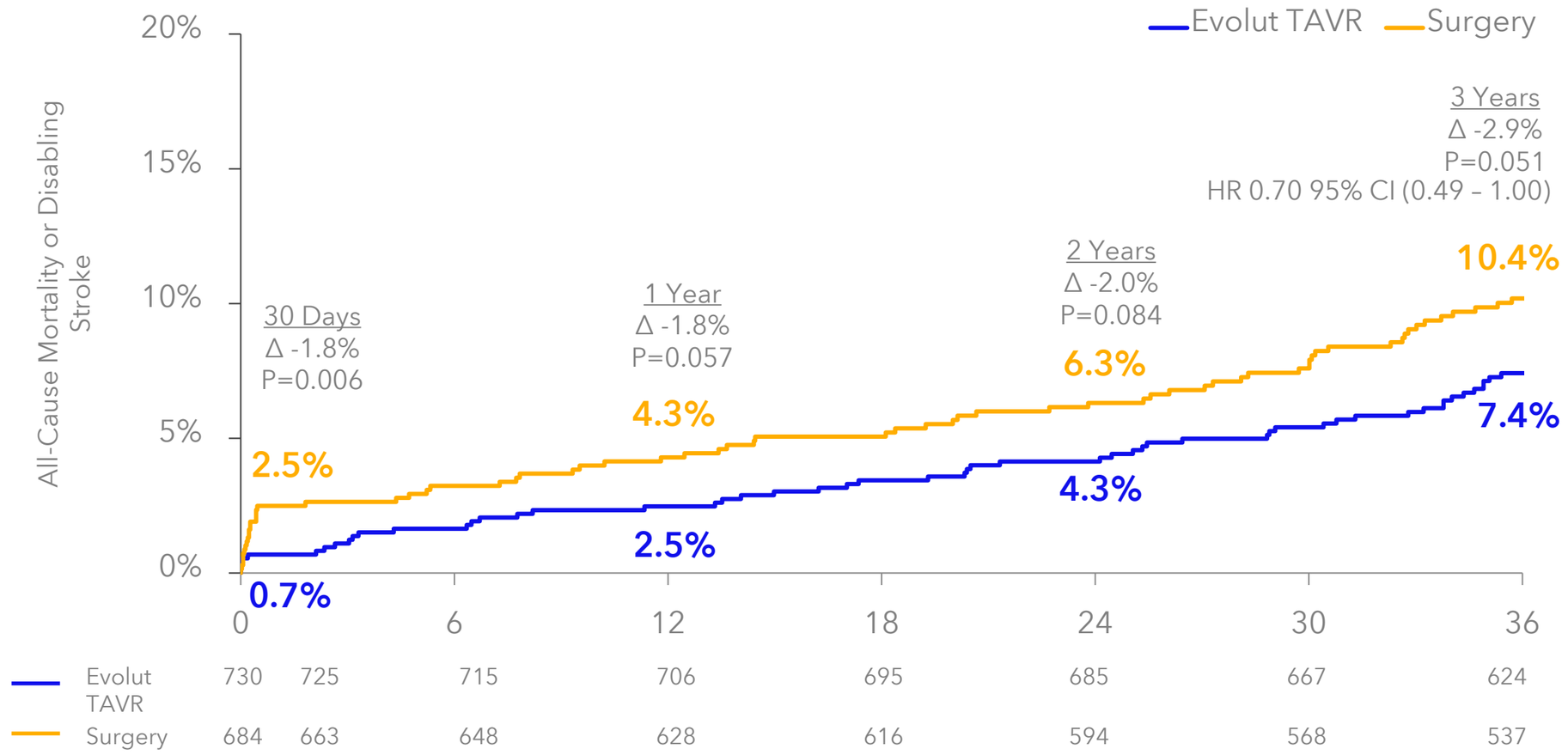
# 3-Year Outcomes from the Evolut Low Risk Trial

## Primary Endpoint: All-Cause Mortality or Disabling Stroke



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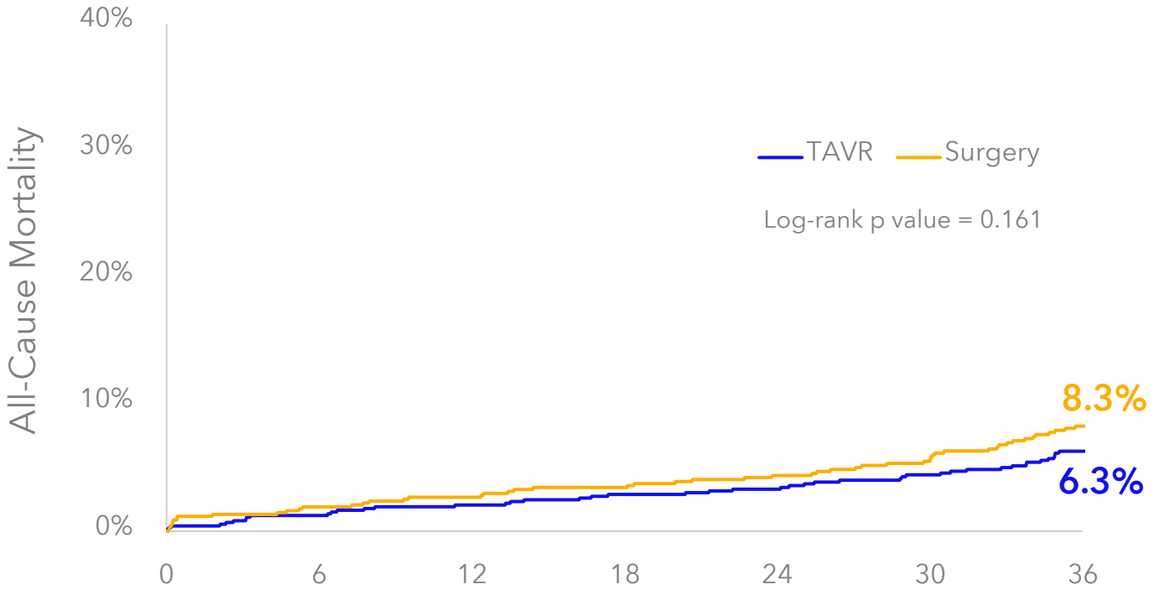
# 3-Year Outcomes from the Evolut Low Risk Trial

## All-Cause Mortality and Disabling Stroke

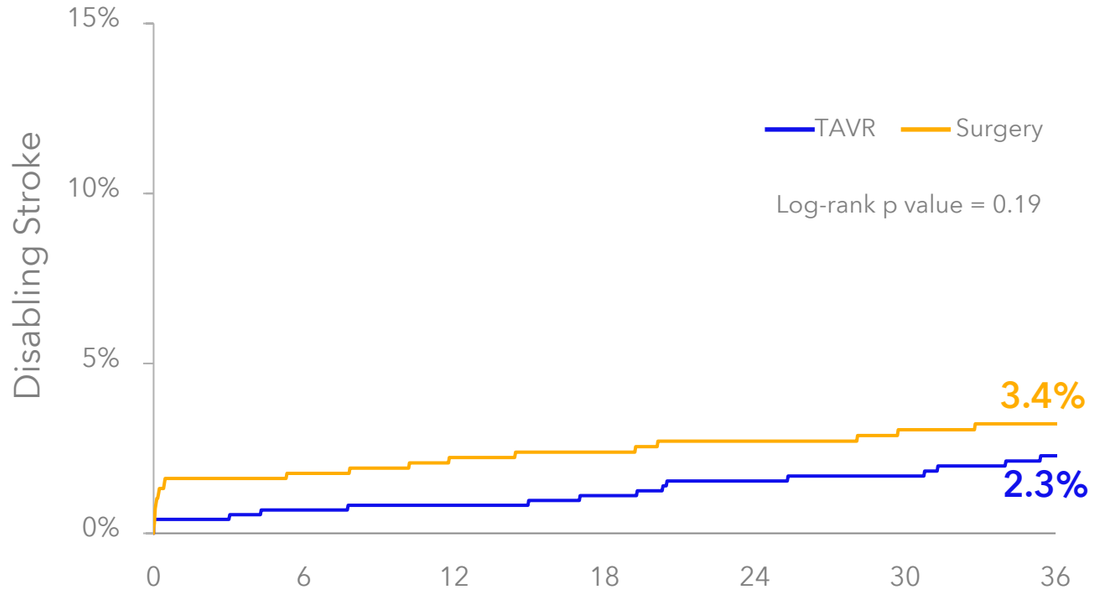
Evolut™ Low Risk Trial

### All-Cause Mortality




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Evolut TAVR | 730 | 727 | 718 | 709 | 699 | 691 | 674 | 632 |
| Surgery | 684 | 672 | 656 | 637 | 624 | 604 | 579 | 548 |

### Disabling Stroke




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Evolut TAVR | 730 | 725 | 715 | 706 | 695 | 685 | 667 | 624 |
| Surgery | 684 | 663 | 648 | 628 | 616 | 594 | 568 | 537 |



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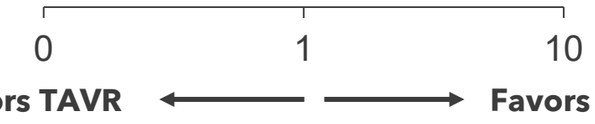
# 3-Year Outcomes from the Evolut Low Risk Trial

## 3-Year Death or Disabling Stroke by Baseline Demographics

| Variable | KM rate at 3 years | | HR (95% CI) | P value for Interaction |
|---|---|---|---|---|
| | Evolut TAVR | Surgery | | |
| Age, years | | | | 0.95 |
| < 75 | 5.7 | 8.0 | 0.71 (0.40-1.26) | |
| ≥ 75 | 9.1 | 13.0 | 0.68 (0.43-1.07) | |
| Sex | | | | 0.41 |
| Male | 7.8 | 11.7 | 0.64 (0.41-0.98) | |
| Female | 6.8 | 7.8 | 0.89 (0.46-1.73) | |
| BMI, kg/m$^2$ | | | | 0.71 |
| ≤ 30 | 6.6 | 9.9 | 0.65 (0.39-1.10) | |
| > 30 | 8.2 | 10.8 | 0.75 (0.45-1.23) | |
| STS Score, % | | | | 0.55 |
| < 2 | 5.8 | 9.0 | 0.62 (0.37-1.06) | |
| ≥ 2 | 9.4 | 12.0 | 0.77 (0.47-1.26) | |
| NYHA | | | | 0.71 |
| I/II | 6.7 | 9.7 | 0.78 (0.41-1.47) | |
| III/IV | 9.7 | 11.9 | 0.77 (0.47-1.26) | |
| Baseline KCCQ | | | | 0.43 |
| ≤ 72 | 8.1 | 12.7 | 0.62 (0.38-0.99) | |
| > 72 | 6.5 | 7.8 | 0.83 (0.47-1.45) | |
| COPD | | | | 0.63 |
| No | 7.8 | 10.9 | 0.89 (0.35-2.25) | |
| Yes | 7.6 | 8.8 | 0.83 (0.47-1.45) | |



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# 3-Year Outcomes from the Evolut Low Risk Trial

Evolut™ Low Risk Trial

## Clinical Outcomes Through 3-Years

| Kaplan-Meier estimate, % | Evolut TAVR (N=730) | Surgery (N=684) | Log-rank P Value |
|---|---|---|---|
| All-cause mortality, disabling stroke, or AV hospitalization | 13.2 | 16.8 | 0.050 |
| AV hospitalization[a] | 7.4 | 9.2 | 0.20 |
| Myocardial infarction | 3.4 | 2.3 | 0.25 |
| Permanent pacemaker implant[b] | 23.2 | 9.1 | <0.001 |
| Atrial fibrillation | 13.1 | 40.0 | <0.001 |
| Valve endocarditis | 0.7 | 1.3 | 0.30 |
| Total valve thrombosis | 0.7 | 0.6 | 0.84 |
| Clinical valve thrombosis | 0.3 | 0.2 | 0.61 |
| Subclinical valve thrombosis | 0.4 | 0.5 | 0.91 |

[a]Hospitalization due to signs and symptoms of aortic valve disease, including symptoms of heart failure. [b]Patients with pacemaker or ICD at baseline are not included.



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# 3-Year Outcomes from the Evolut Low Risk Trial

## Valve Performance at 3 Years

| % (n)[a] | Evolut TAVR | Surgery | Log-rank P Value |
|---|---|---|---|
| Paravalvular Regurgitation | **N=541** | **N=447** | |
| None/trace | 78.7 | 97.3 | |
| ≥ Mild | 21.3 | 2.7 | <0.001 |
| ≥ Moderate | 0.9 | 0.2 | 0.16 |
| Prosthesis-Patient Mismatch (VARC-3) | **N=489** | **N=394** | |
| None | 89.4 | 74.9 | |
| Moderate | 9.2 | 20.3 | |
| Severe | 1.4 | 4.8 | 0.003 |
| ≥ Moderate | 10.6 | 25.1 | <0.001 |
| Reintervention | 1.0 | 0.9 | 0.92 |

[a]PVR and PPM are reported as proportion % (n) and compared by chi-square test, with number of patients with echos at 3 years shown in the top row for each. Reintervention is reported as a Kaplan-Meier estimate % (n) and compared by log-rank test.

Most TAVs in the study were Evolut R (73%) and did not have an external pericardial wrap. PVR and PPM were based on Echo Core Laboratory assessment.



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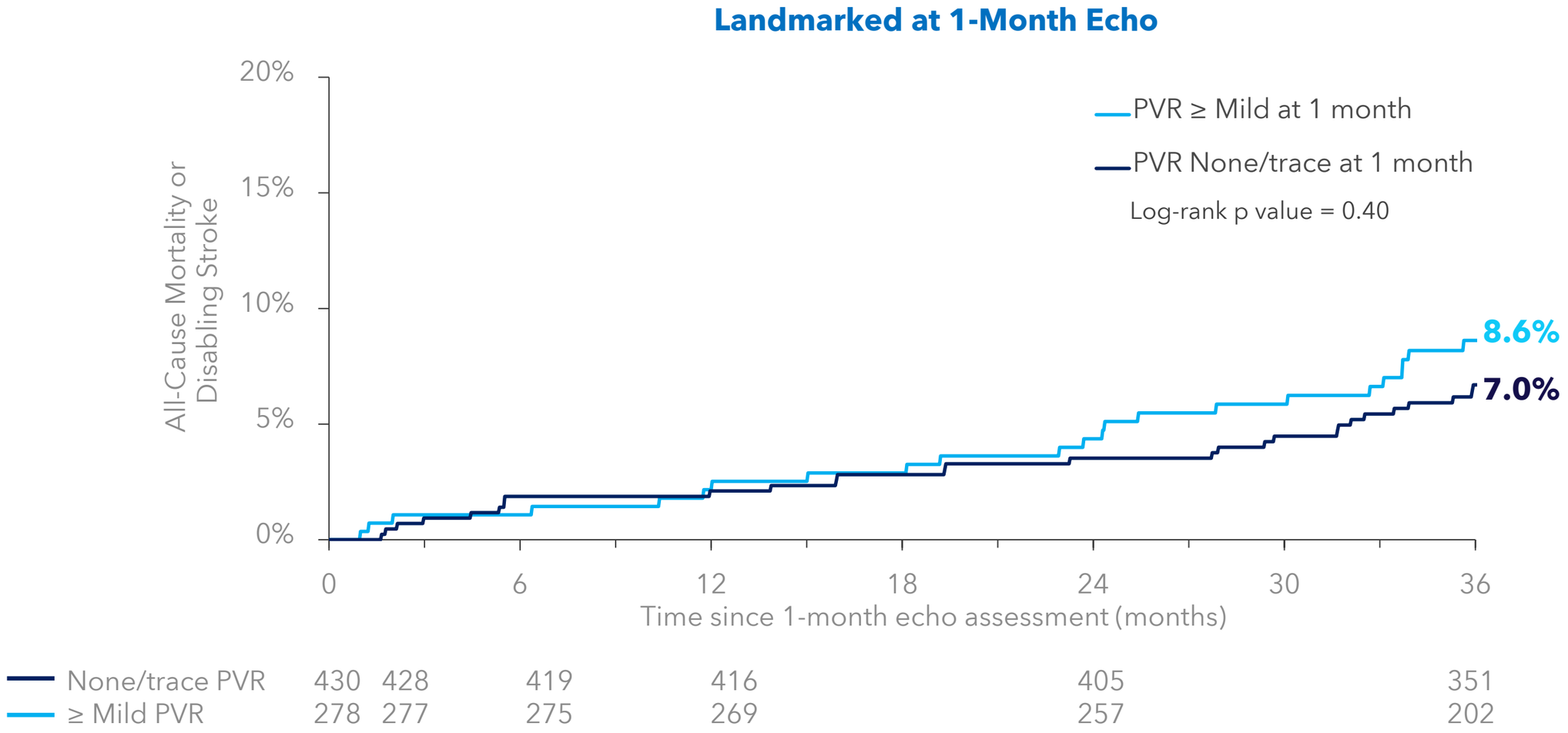
# 3-Year Outcomes from the Evolut Low Risk Trial

## 3-Year All-Cause Mortality or Disabling Stroke in the TAVR Cohort by PVR




PVR = paravalvular regurgitation
PVR was based on Echo Core Laboratory assessment.



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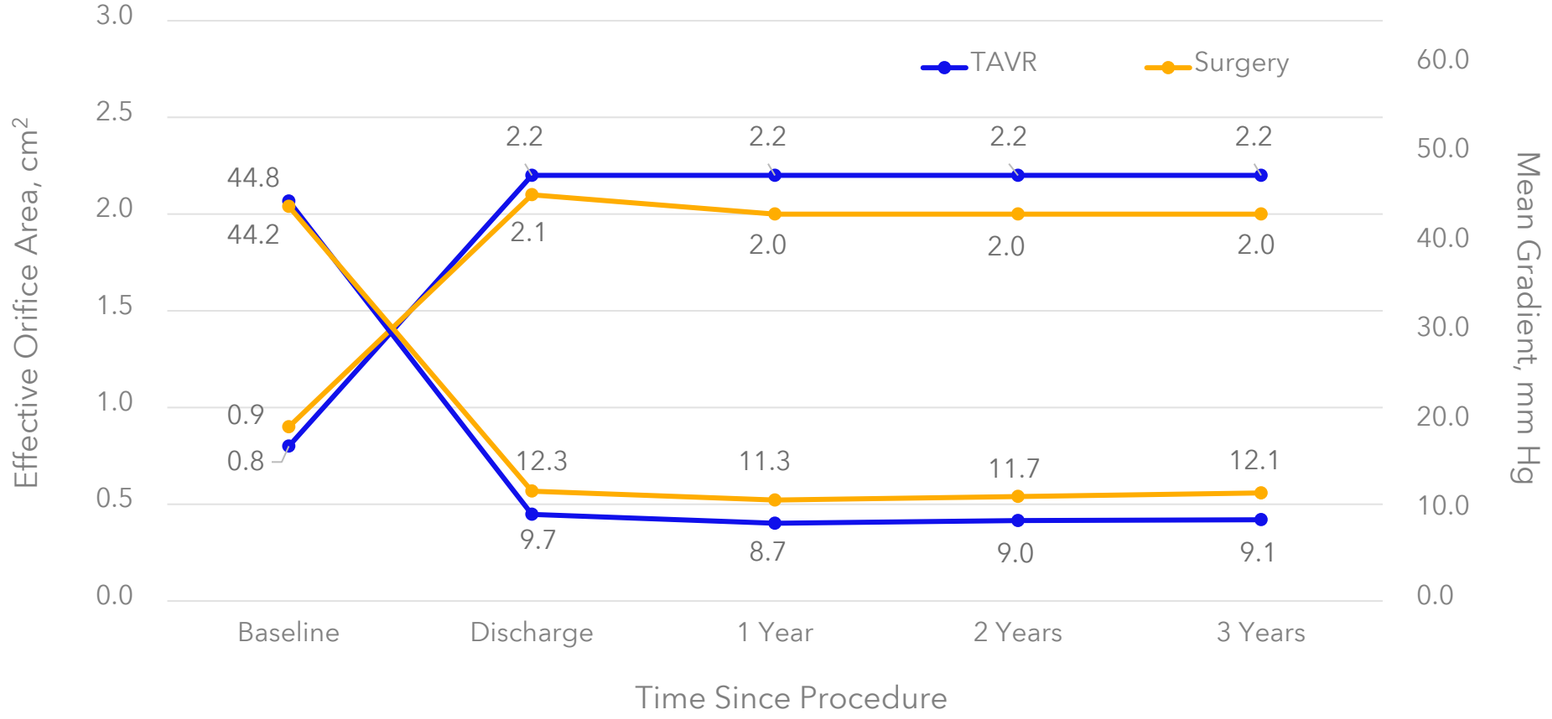
# 3-Year Outcomes from the Evolut Low Risk Trial

## Valve Hemodynamics to 3-Years

Significantly better MG and EOA with TAVR at all follow-up timepoints ($p < 0.01$)




**No. of patients**

| | | | | | |
|---|---|---|---|---|---|
| TAVR EOA | 637 | 576 | 565 | 535 | 493 |
| Surgery EOA | 596 | 406 | 525 | 434 | 396 |
| TAVR MG | 717 | 703 | 662 | 607 | 547 |
| Surgery MG | 679 | 632 | 597 | 514 | 456 |



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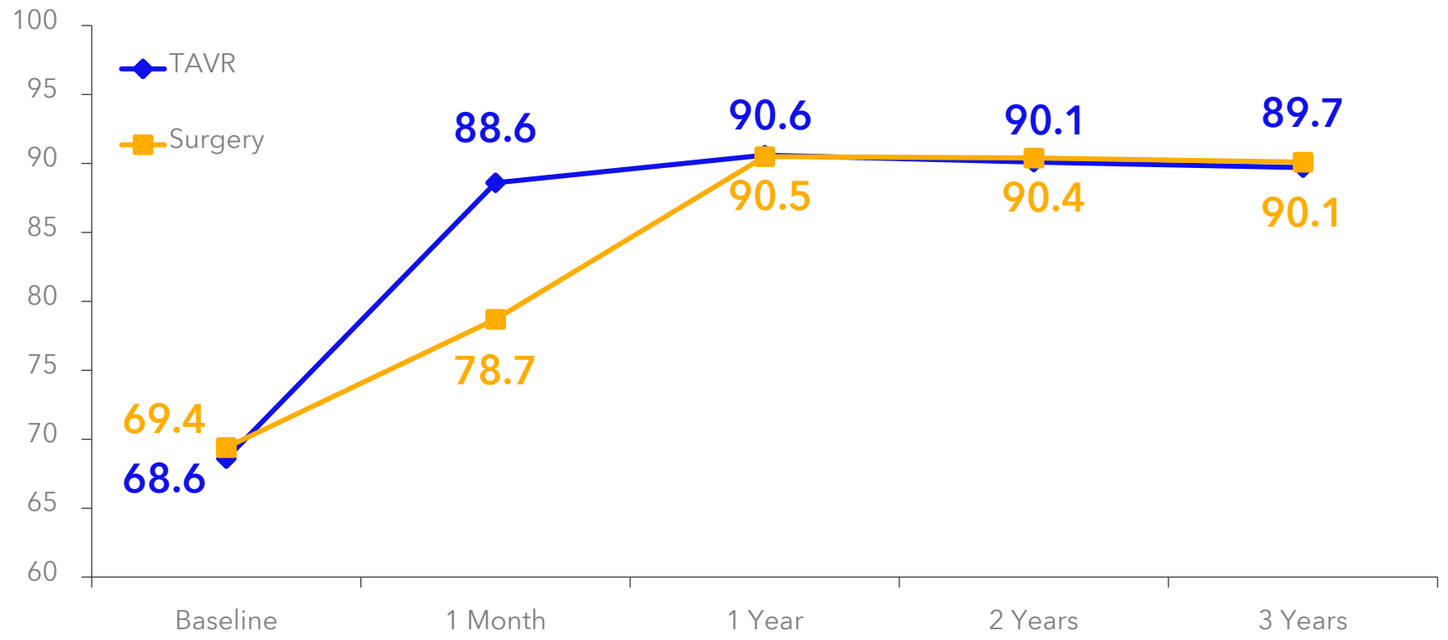
# 3-Year Outcomes from the Evolut Low Risk Trial

## KCCQ Overall Summary Score




| Change from Baseline | | | | |
|---|---|---|---|---|
| Evolut TAVR | 20.0 ± 21.1 | 21.6 ± 20.6 | 20.9 ± 20.8 | 20.1 ± 20.6 |
| Surgery | 9.2 ± 22.3 | 20.7 ± 20.3 | 20.0 ± 20.0 | 19.3 ± 21.1 |
| P value | <0.001 | 0.42 | 0.44 | 0.53 |



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# 3-Year Outcomes from the Evolut Low Risk Trial

**Summary**

Evolut™ Low Risk Trial

- At 3 years, the rate of all-cause mortality or disabling stroke after TAVR with the Evolut Valve compared favorably to surgery.
    - The absolute difference between treatment arms remained consistent with a 30% relative reduction in hazard ($p = 0.051$) for death or disabling stroke.
- TAVR patients continued to have better valve hemodynamics at 3 years with very low rates of valve thrombosis.
- Residual paravalvular regurgitation 3 years after TAVR was none/trace in nearly 80% of patients and there was no difference in >mild PVL.



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# 3-Year Outcomes from the Evolut Low Risk Trial

**Limitations**

Evolut™ Low Risk Trial

- Patients with bicuspid aortic valves were excluded
- Patients had to have anatomy suitable for both TAVR and SAVR
- These are 3-year results and longer-term data are needed to evaluate the impact that valve design, hemodynamics, new pacemakers, and other secondary endpoints may have on longer-term outcomes in low-risk patients.



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# 3-Year Outcomes from the Evolut Low Risk Trial

## Clinical Implications

Evolut™ Low Risk Trial

- These results provide physicians, patients and heart teams important data to aid in the shared decision-making process.
- The excellent valve performance and durable outcomes out to 3 years in low-risk patients affirms the role of TAVR with the Evolut valve in this population.



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**Indications**
The Medtronic CoreValve™ Evolut™ R, Evolut™ PRO+, 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 CoreValve Evolut R, Evolut PRO+, 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 ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

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

**Warnings**
*General* Implantation of the CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems should be performed only by physicians who have received Medtronic CoreValve Evolut R, Evolut PRO+, 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 CoreValve Evolut R, Evolut PRO+, 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. The safety and effectiveness of a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis have not been demonstrated. Implanting a CoreValve Evolut R, Evolut PRO+, 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/$mm^3$), 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 surgical bioprosthetic aortic annulus size < 17 mm or > 30 mm; transarterial access unable to accommodate an 18 Fr introducer sheath or the 14 Fr equivalent EnVeo InLine™ Sheath when using models ENVEOR-US/D-EVPROP2329US or Evolut FX Delivery Catheter System with InLine™ Sheath when using model D-EVOLUTFX-2329 or transarterial access unable to accommodate a 20 Fr introducer sheath or the 16 Fr equivalent EnVeo InLine Sheath when using model ENVEOR-N-US 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 ENVEOR-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 5.5 mm when using model ENVEOR-N-US 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 ENVEOR-L-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6 mm when using model ENVEOR-N-US 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* 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 a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis implanted within a transcatheter bioprosthesis have not been demonstrated.

**Potential adverse events**
Potential risks associated with the implantation of the CoreValve Evolut R, Evolut PRO+, 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 CoreValve Evolut R, Evolut PRO+, 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™ R device is Medtronic CoreValve™ Evolut™ R System, the commercial name of the Evolut™ PRO+ device is Medtronic Evolut™ PRO+ System, and the commercial name of the Evolut™ FX device is Medtronic Evolut™ FX System.

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