

# Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results

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## Potential conflicts of interest

Speaker's name: Steven J. Yakubov

I have the following potential conflicts of interest to declare:  
Grants from Boston Scientific and Medtronic (paid to institution) and personal fees from Medtronic during the conduct of the study.

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## Background and Objective

- TAVI with the Evolut PRO & PRO+ valves has been proven safe and effective for treating severe aortic stenosis in patients with varying surgical risk.<sup>1-2</sup>
- However, variability in prevalence of conduction disturbances and rates of new permanent pacemaker implant persist due to non-uniform protocols for TAVI and post-implant management.

The Optimize PRO clinical study was designed to collect clinical evidence on valve performance and procedural outcomes associated with an “optimized” TAVI care pathway, post-TAVI conduction disturbance pathway and cusp overlap technique (COT).

Forrest JK, Mangi AA, Popma JJ, et al. JACC Cardiovasc Interv. January 22, 2018;11(2):160-168.

Grubb K, Gada H, Mittal S, et al. JACC Cardiovasc Interv. March 13, 2023;16(5):558-570.

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## Methods

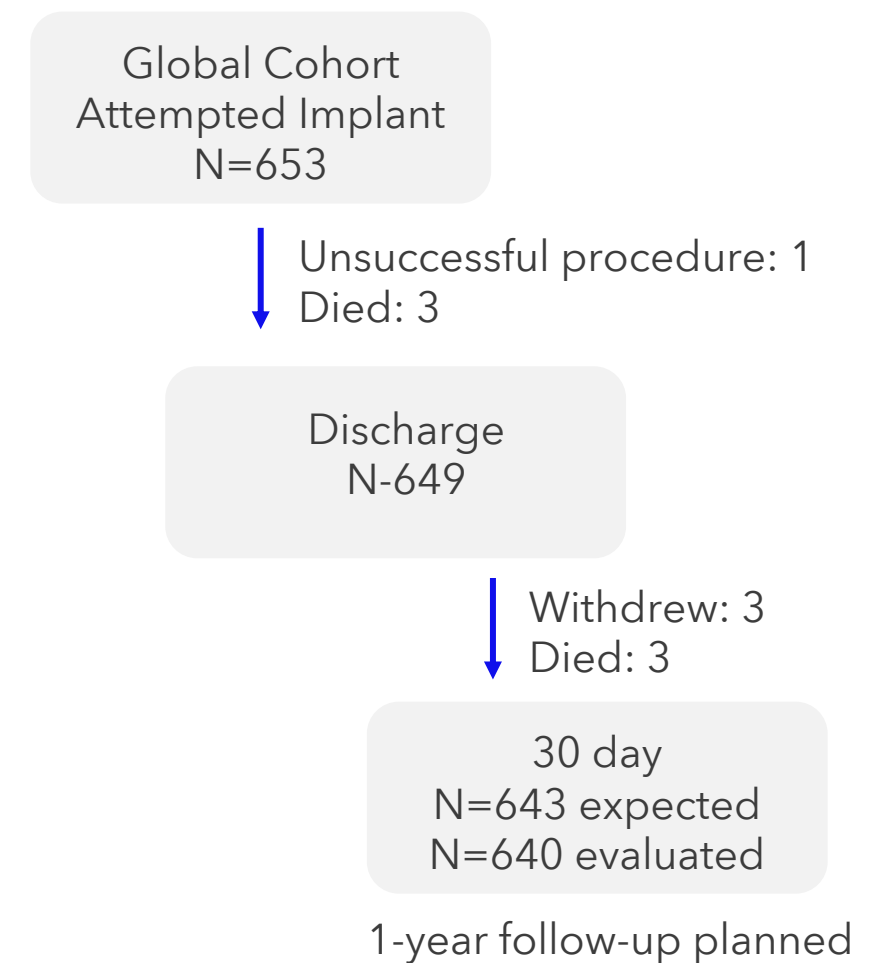
### Study Design

- The Optimize PRO study is a multi-center, post-market, prospective study conducted in 50 centers in the United States, Canada, Europe, Middle East, and Australia.
- Valve deployment was performed with COT and the standard procedures of the “optimized” TAVI care pathway protocol requirements.
- Primary Endpoint: Rate of all-cause mortality or all stroke at 30 days

### Patient Selection Criteria

- Patients with symptomatic severe aortic stenosis (NYHA Class  $\geq$  II)
- Anatomically suitable for transfemoral TAVI with the Medtronic system
- Exclusion criteria include bicuspid anatomy, previous aortic valve replacement, existing permanent pacemaker, and LVEF  $<$  35%

### Patient Flowchart



# Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results

## Baseline Characteristics

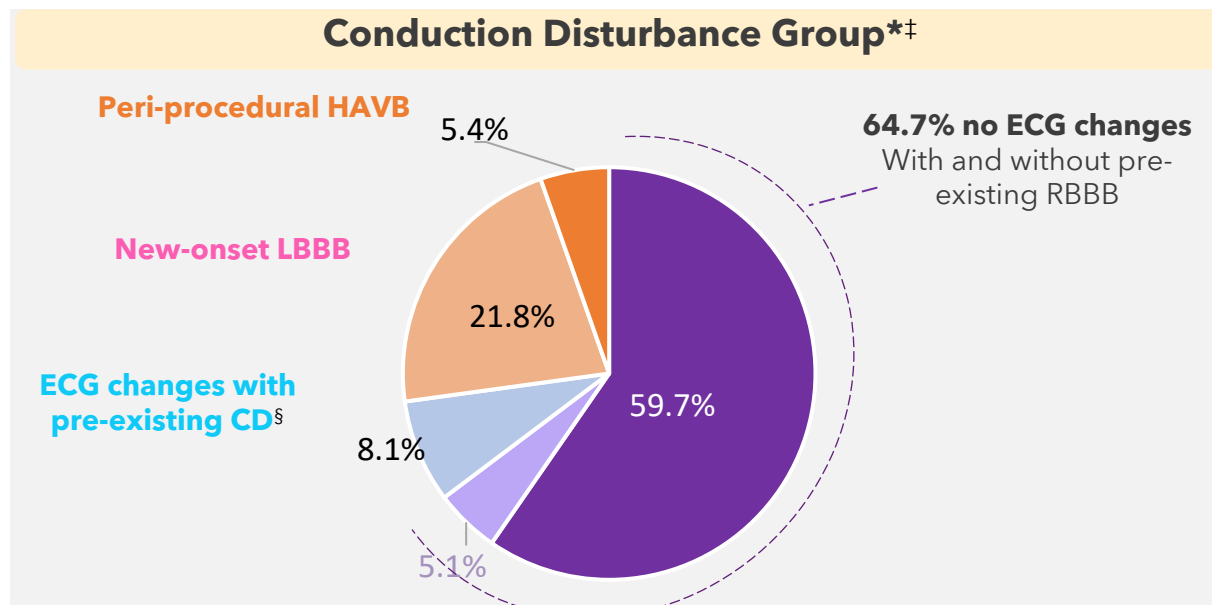
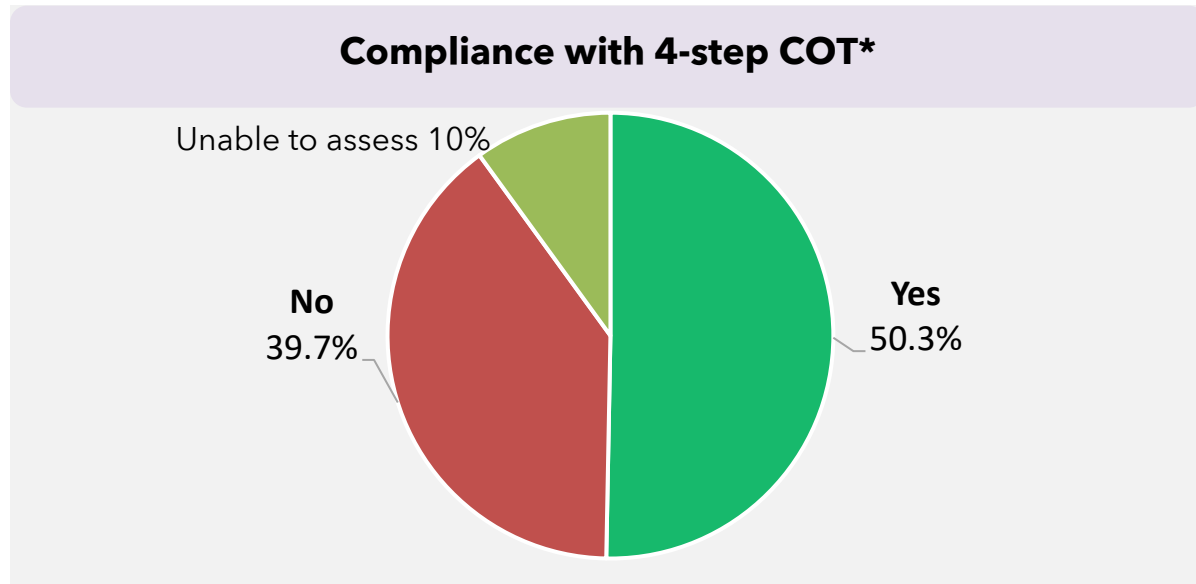
Demographic	Global Cohort (N=653)
Age, years	79.1 ± 6.5
Body mass index, kg/m <sup>2</sup>	29.6 ± 5.9
Female sex	47.0
STS PROM, %	3.2 ± 2.5
NYHA III/IV	42.7
Diabetes	32.2
Hypertension	78.9
Peripheral arterial disease	6.5
Previous MI	9.1
Previous CABG	10.0
Previous PCI	21.9
Arrhythmia history	22.5
Atrial fibrillation/flutter	19.4
History of RBBB	6.9
LVEF, %	59.7 ± 7.8

Values presented as mean ± SD or %

CABG=coronary artery bypass graft; LVEF=left ventricular ejection fraction; MI=myocardial infarction; NYHA=New York Heart Association; PCI=percutaneous coronary intervention; RBBB=right bundle branch block; STS-PROM=Society of Thoracic Surgeons Predicted Risk of Mortality

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## Results - Procedural Outcomes



\*Index procedure set N = 652. †Based on 2-hour site ECG. §Pre-existing RBBB, LBBB, IVCD, or 1st degree AV Block

Procedural Outcome	Global Cohort (N=652*)
Lunderquist Guidewire	80.7
Pre-balloon valvuloplasty	55.8
Post-implant dilatation	14.1
NCC implant depth, mm <sup>†, ‡</sup>	3.9 ± 3.2
Resheathing or recapture	41.3
Discharged with Holter device	17.0
EP study prior to discharge	1.5
Length of stay, median days	2 [1-3]

Values presented as %, mean ± SD or median [Q1-Q3]. \*Index procedure set. †Sample size n=606. ‡Core lab

CD= conduction disturbance; COT=cusp overlap technique; ECG=electrocardiogram; EP=Electrophysiology; HAVB=high-degree atrioventricular block; IVCD=Intraventricular conduction delays; LBBB = left bundle branch block; NCC = noncoronary cusp; RBBB = right bundle branch block

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## Results - 30-Day Clinical Outcomes

Outcomes	Global Cohort (N=653)
All-cause mortality or all stroke	5.1
All-cause mortality	0.8
All stroke	4.4
Disabling stroke	1.7
Reintervention	0.3
Myocardial infarction	1.1
Clinical valve thrombosis	0.3
Definite valve endocarditis	0.0
Valve migration	0.8
Valve embolization	0.6
Major vascular complication	2.8
CV hospitalizations	5.7
Hospital re-admission	9.1
PPI	11.1

Percentages are Kaplan-Meier estimates (%). Clinical events were defined according to VARC-2.

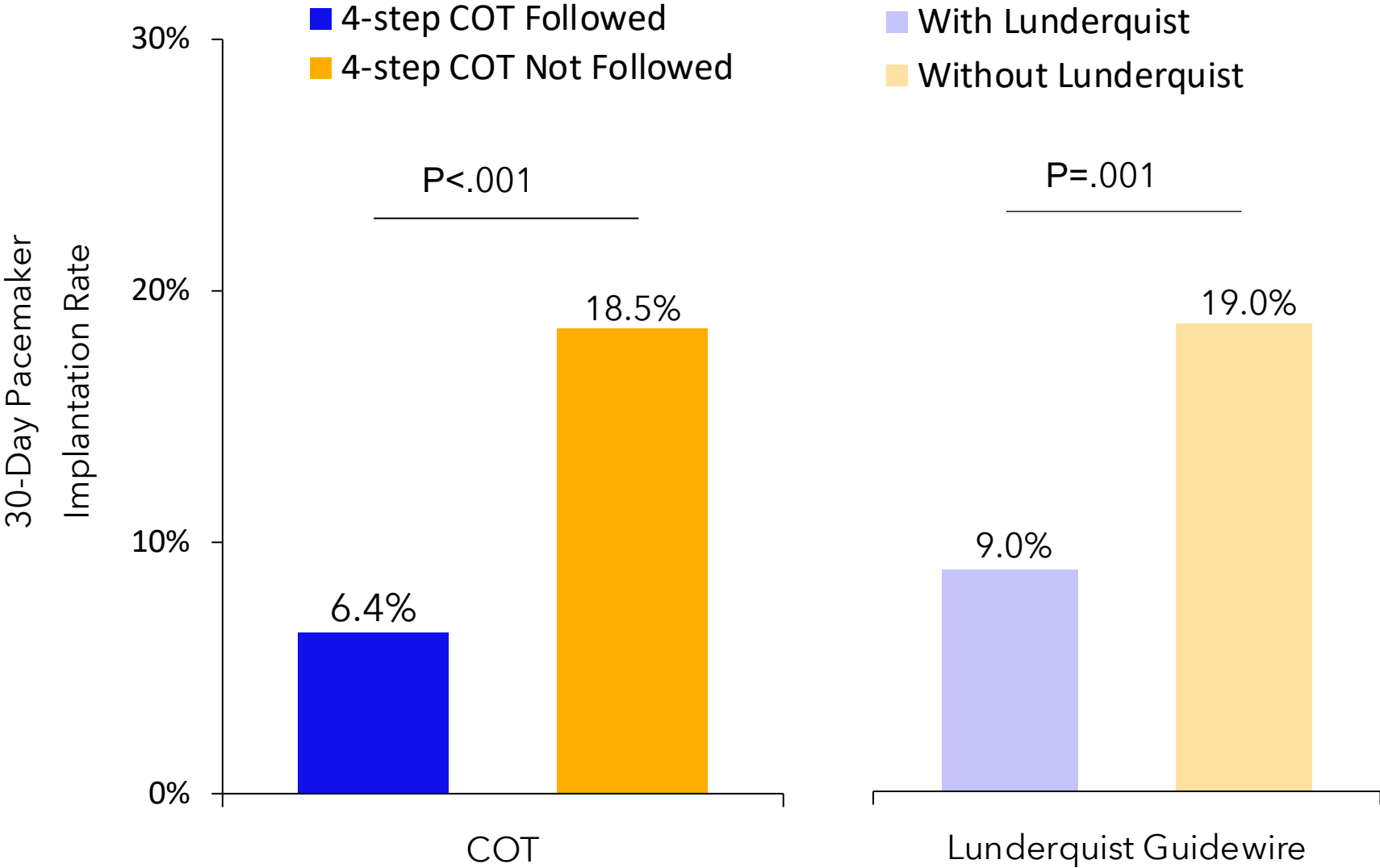
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## Results - PPI

### Key 4-step COT<sup>1</sup>

1. Reconstructed computed tomography angiography overlay of the cusp overlap view
2. Fluoroscopic image of the wire appropriately positioned in the left ventricle
3. Fluoroscopic image demonstrating 3mm depth in the cusp overlap view after full annular contact below the noncoronary cusp
4. Final aortography performed in the cusp overlap view

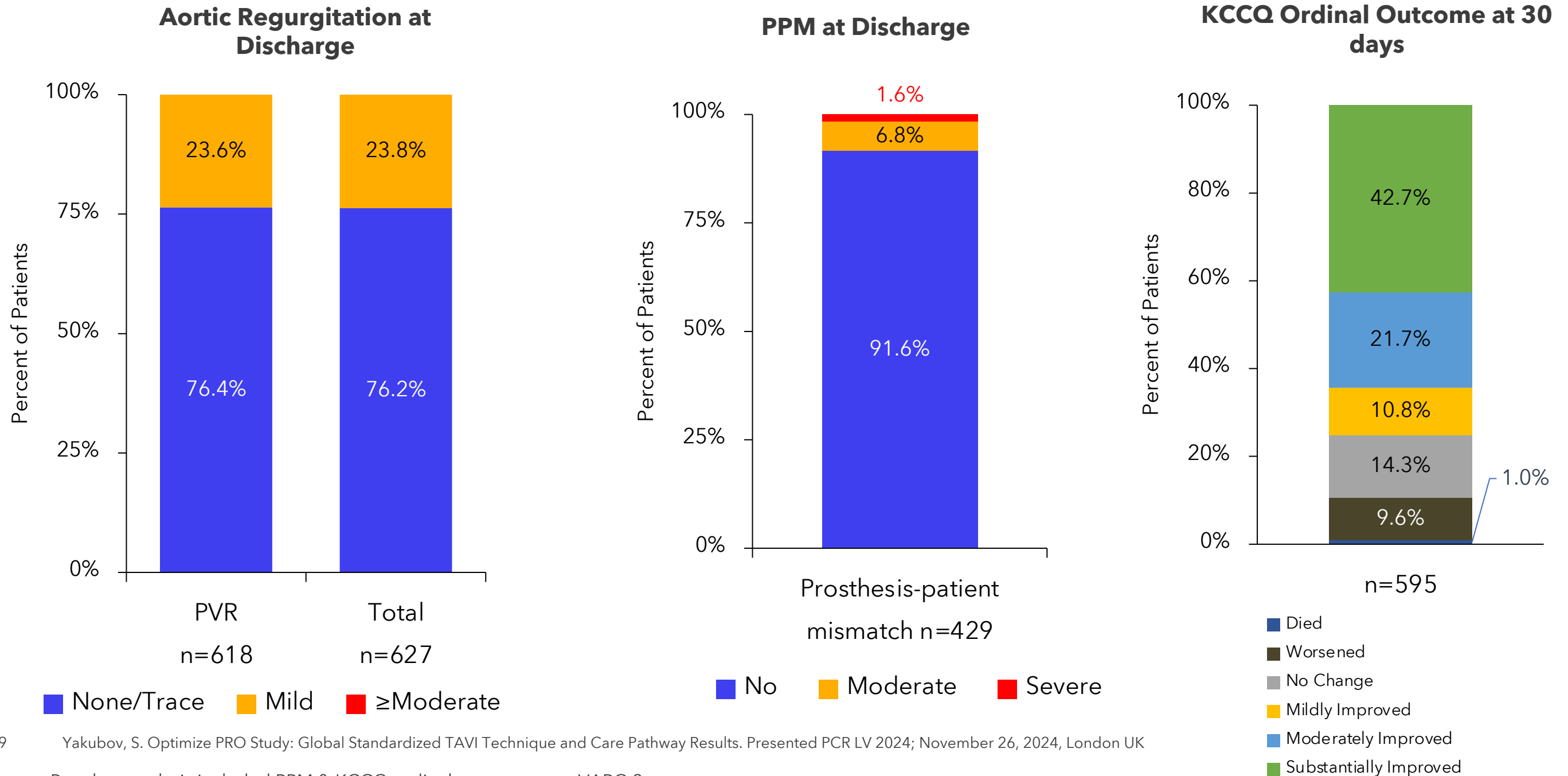
\*Use of Lunderquist guidewire is highly recommended.



Grubb K, Gada H, Mittal S, et al. *JACC Cardiovasc Interv.* March 13, 2023;16(5):558-570.

# Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results

## Results - AR, PPM and Quality of Life



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## Conclusions

The Optimize PRO study was the first investigation of a standardized TAVI protocol with Evolut PRO/PRO+ using COT and perioperative protocols in a global cohort of patients with symptomatic severe aortic stenosis.

Favorable clinical outcomes:

- Median length of stay = 2 days
- Primary endpoint: **5.1%** all-cause mortality or all stroke rate
- Low all-cause mortality: **0.8%**
- Low disabling stroke: **1.7%**

### Summary

New 30-day permanent pacemaker implantation rate was **6.4% with 4-step COT compliance and 11.1% overall**

**0% of patients** had moderate/severe aortic regurgitation at discharge

**Back-Up Slides**

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## Limitations

1. Not all sites had access to the Evolut PRO+ valve or recommended Lunderquist wire, making protocol adherence less consistent.
2. Potential confounders could have been introduced as data was site-reported, and some variables (pre-existing RBBB, wire use, and COT compliance) may not have been correctly documented.
3. The study excluded bicuspid patients, those with heavy calcification extending into the left ventricular outflow tract, requiring alternative access, prior aortic valve replacement, and left ventricular ejection fraction <35%.
4. The 4-step COT assessment was post hoc, and in 10% of cases, there was inadequate imaging capture to confirm compliance.

# Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results

## Study Oversight

**Principal Investigators:** Kendra Grubb, MD, MHA; Steven Yakubov, MD

**Steering Committee:** Douglas Fraser, MD; Hemal Gada, MD; Kendra Grubb, MD, MHA, Suneet Mittal, MD; Tamim Nazif, MD; Josep Rodes-Cabau, MD, Steven Yakubov, MD

**Clinical Events Committee:** Baim Institute for Clinical Research, Boston, MA

**Procedural Angiogram Core Laboratory:** BIDMC (acquired by Baim in 2023), Boston, MA

**ECG Core Laboratory:** HeartcoR , Algonquin, IL

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

**Membranous Septum Measurements:** New York University, New York, NY

**External ECG Monitoring Core Laboratory:** Houston, TX

# Participating Sites

Site name	# AT
UPMC Pinnacle Harrisburg Campus	50
Shaare Zedek Medical Center	48
Hopitaux Universitaires -Hopital Henri Mondor	44
Morton Plant Hospital	38
Allegheny General Hospital	35
University of Pittsburgh Medical Center UPMC Presbyterian	32
Austin Hospital	26
Intermountain Saint George Regional Hospital	24
Saint Vincent's Medical Center	23
University of Michigan Health System - University Hospital	22
Lehigh Valley Hospital - Cedar Crest	22
York Hospital	22
Manchester Royal Infirmary	20
Sentara Norfolk General Hospital	18

Site name	# AT
Fondazione Policlinico Universitario Agostino Gemell	18
Galway University Hospitals-University Hospital Galway (UHG)	17
Kettering Medical Center	13
Vassar Brothers Medical Center	13
AZ Sint-Jan Brugge-Oostende av	11
OhioHealth Riverside Methodist Hospital	11
Fondazione Poliambulanza	11
Fiona Stanley Hospital	11
Emory University Hospital Midtown	10
Hospital Universitario Central de Asturias	10
MedStar Union Memorial Hospital	9
Monash Medical Centre Clayton	9
The Heart Hospital Baylor Plano	8
Institut Universitaire de Cardiologie et de Pneumologie de Québec	7
Fondazione Policlinico Universitario Agostino Gemell	18

**AT= Attempted Implant (N=653)**

# Participating Sites

Site name	# AT
University of Alabama at Birmingham Hospital	6
The Mount Sinai Hospital	6
Hôpital Haut-Lévêque -CHU de Bordeaux	6
Stony Brook University Hospital	6
Royal Victoria Hospital - Belfast Health and Social Care Tru	6
Hartford Hospital	5
Mater Private Network	5
Spectrum Health Hospitals	5
John Hunter Hospital	4
Providence Saint Patrick Hospital	3
Sunnybrook Health Sciences Centre	3
Nebraska Medical Center	3
ZNA Middelheim	3
Saint John's Hospital	2

Site name	# AT
Universitätsklinikum Ulm	2
The Valley Hospital	1
Buffalo General Medical Center	1
New York-Presbyterian Hospital/Columbia University Medical Center	1
The Prince Charles Hospital	1
Uppsala Akademiska Sjukhuset	1
California Pacific Medical Center	1
Houston Methodist Hospital	0*

**AT= Attempted Implant (N=653)**

**\*Houston had 1 enrolled patient but did not have attempted implant**

# Optimized TAVI Care Pathway with Evolut PRO/PRO+

## Pre-procedure

- 12-lead ECG
- Early discharge plan with multi-disciplinary team
- Screening checklist

## Peri-procedure

- Valve deployment using the cusp overlap technique
- Pre-BAV not required
- Avoid general anesthesia
- Use transfemoral access only
- Minimize central lines

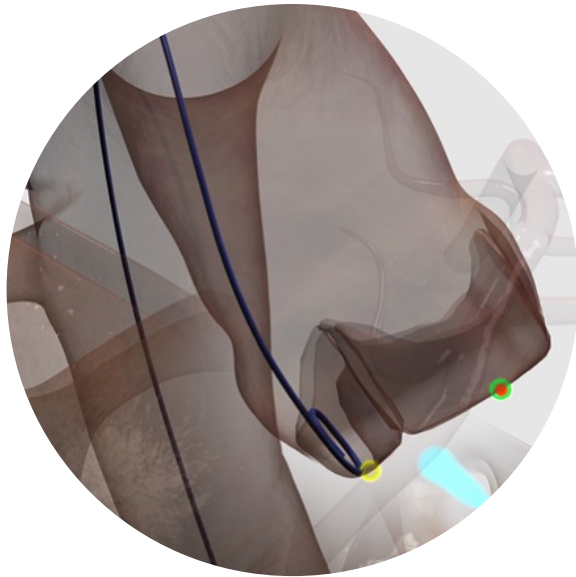
## Post-procedure

- 12-lead ECG within 2 hours
- If no preexisting RBBB or ECG changes remove all lines\*
- Mobilize within 4-6 hours
- Consider PACU or stepdown unit vs. ICU
- TTE and ECG prior to discharge

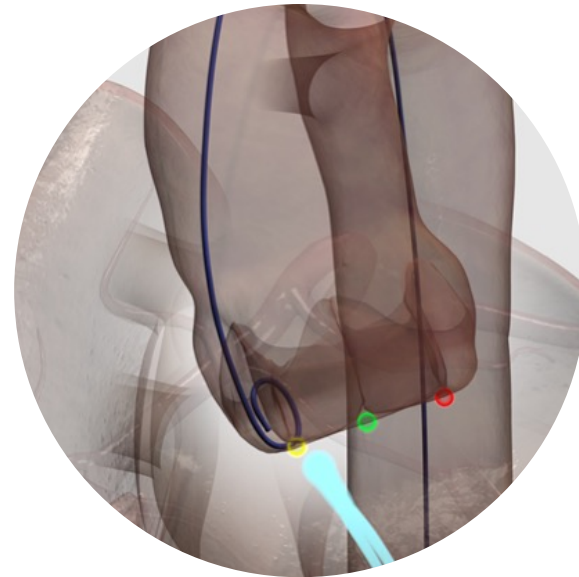
\* Follow to conduction disturbance pathway if patient has preexisting RBBB or ECG changes (PR and QRS increase  $\geq 20$  ms).

# Cusp Overlap Technique with Evolut PRO/PRO+

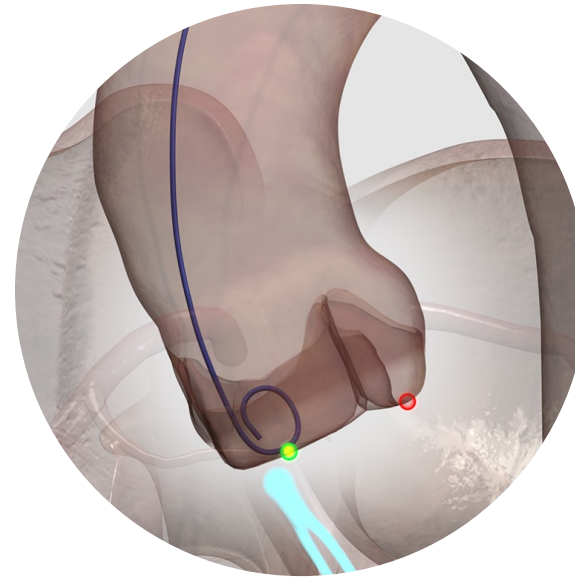
Cusp overlap view



3-cusp coplanar view



LAO view



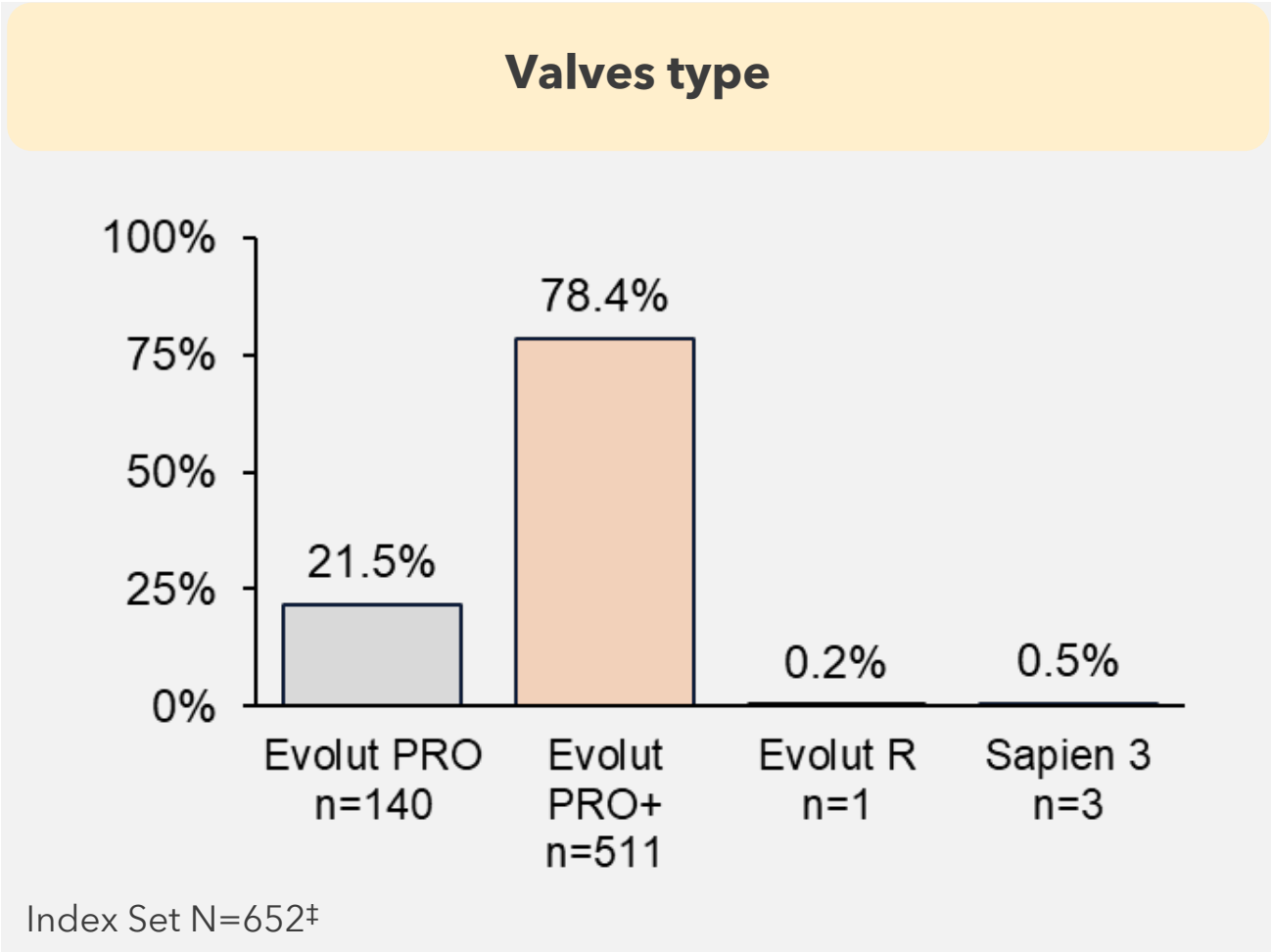
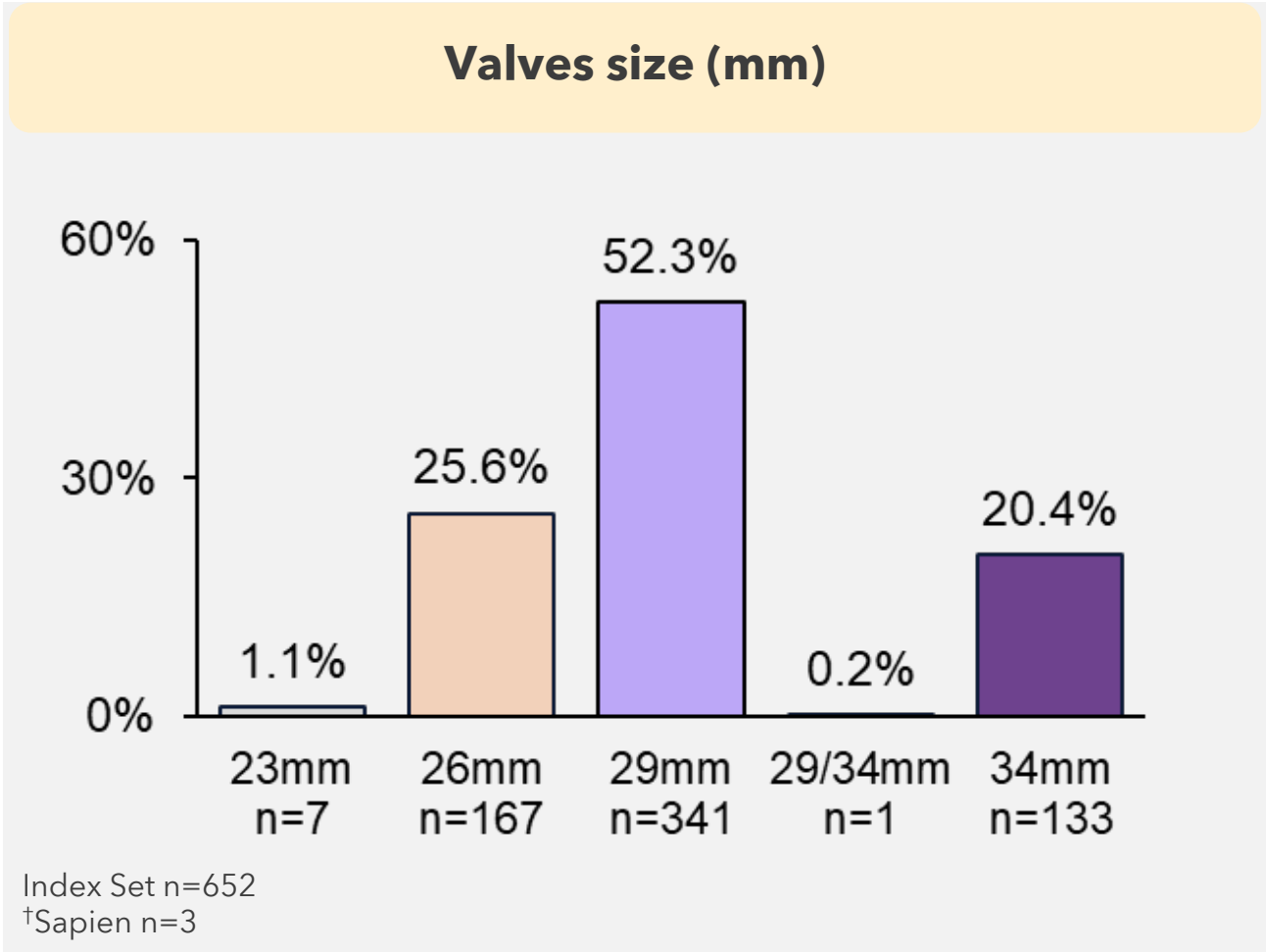
## **Key steps\***

1. Initial deployment in the cusp overlap projection to estimate implant depth at the NCC.
2. Deploy with the marker band positioned at mid-pigtail or higher.
3. Assess depth in cusp overlap view.
4. Roll LAO. Remove any remaining parallax. Estimated depth at the LCC.
5. Redeployment in cusp overlap view, if applicable.
6. Assess final implant depth on the NCC.

\* Use of Lunderquist® guidewire is highly recommended.

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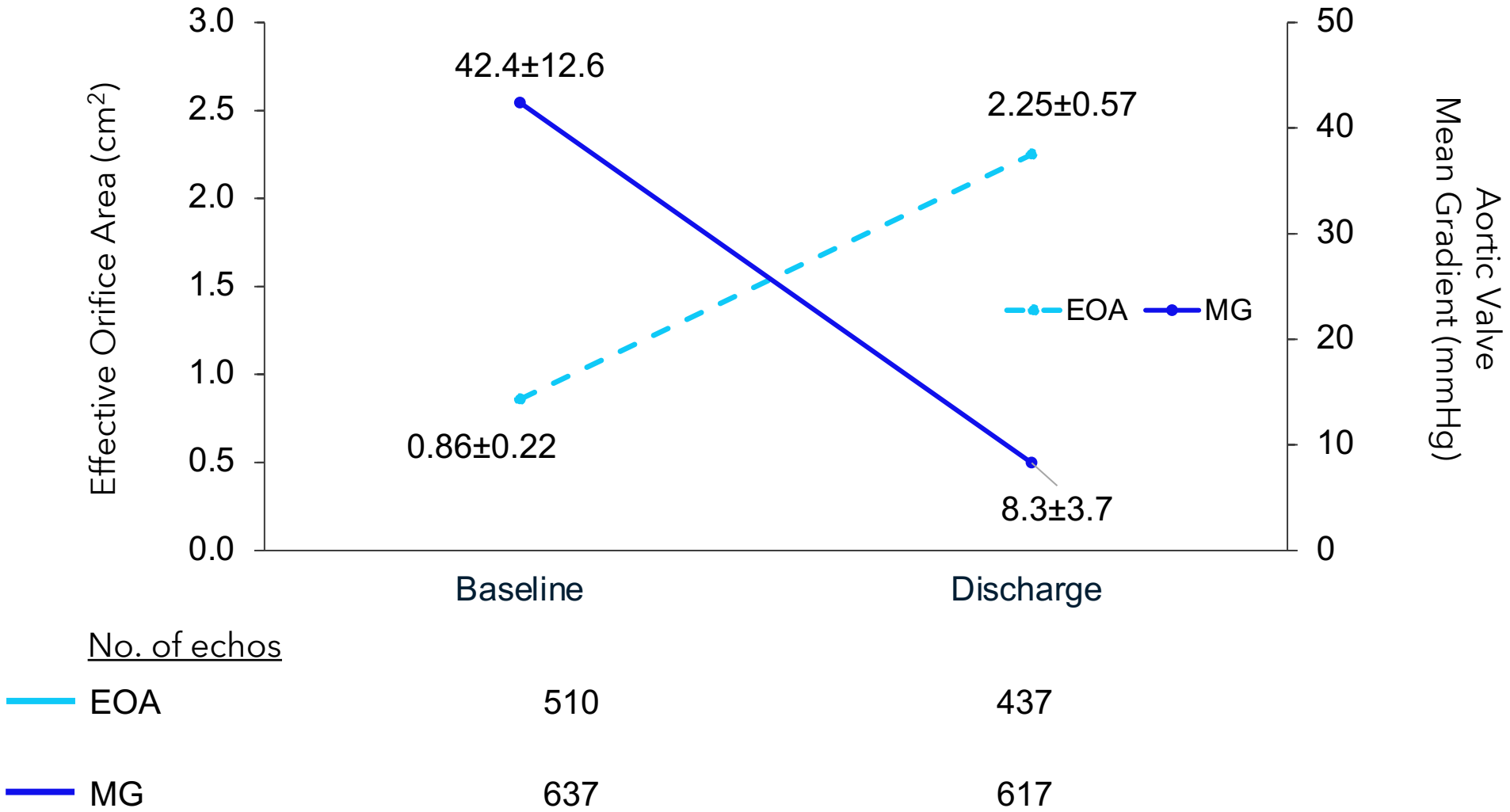
## Results



\*Evolut R implanted in one subject as Evolut PRO or PRO+ were not available at study site on the index procedure date.  
 †Sapien transcatheter aortic valve (TAV) implanted after attempted implant with Evolut PRO+ or after implant with Evolut PRO or Evolut PRO+ TAV (Valve-in-Valve).  
 ‡If more than one valve was implanted, it is possible that more than one model of valve was implanted.

# Optimize PRO Study: Global Standardized TAVI Technique and Care Pathway Results

## Results - Hemodynamics



## 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 ≥ 8% or at a ≥ 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 cm<sup>2</sup> or aortic valve area index ≤ 0.6 cm<sup>2</sup>/m<sup>2</sup>, 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<sup>2</sup> or aortic valve area index ≤ 0.6 cm<sup>2</sup>/m<sup>2</sup>, 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/mm<sup>3</sup>), thrombocytopenia (platelet count < 50,000 cells/mm<sup>3</sup>), 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 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.

# Medtronic

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**medtronic.com**

*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. 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.

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