Final Global Results from the Optimize PRO Study

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on behalf of the Optimize PRO Investigators

Disclosure of relevant financial relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Financial Relationship	Company
Institutional grants/research support	Boston Scientific, Medtronic

Medtronic funded the Optimize PRO study (NCT04091048)

Background

- The Optimize PRO study collected clinical evidence on valve performance and procedural outcomes associated with an “optimized” TAVR care pathway, post-TAVR conduction disturbance pathway and cusp overlap technique (COT).
- The Optimize PRO study 30-day results[1-2]
  - Low rates of adverse events
  - 6.4% new permanent pacemaker implantation rate with COT compliance and 11.1% overall
  - No moderate to severe aortic regurgitation at discharge

Objective

Report final results from the Optimize PRO study, including 1-year safety events and hemodynamics, and an evaluation of how procedural technique impacts these outcomes.

[1]Grubb K, Gada H, Mittal S, et al. JACC Cardiovasc Interv. March 13, 2023;16(5):558-570
[2]Grubb K, Gada H, Fraser, et al. JSCAI. May 1 2025;4(5):103515

Study administration

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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

Statistical Analyses: Medtronic

Sponsor: Medtronic

Study design

Prospective, nonrandomized, post-market, multicenter study conducted at 50 global centers in 653 patients[1]

Valve deployment was performed with cusp overlap technique (COT) and the standard procedures of the "optimized" TAVR care pathway protocol requirements.

Key eligibility

- Symptomatic severe aortic stenosis (NYHA Class ≥ II)
- Anatomically suitable for transfemoral TAVR with the Medtronic system
- Excluded: bicuspid anatomy, previous aortic valve replacement, existing permanent pacemaker, and LVEF <35%

September 2019 to November 2023
Evolut PRO and PRO+ devices

Final 1-Year Results

Endpoints

Primary: 30-day rate of all-cause mortality or all stroke

[1]Attempted implants

Evolution of Evolut transcatheter aortic valves

Optimize PRO

Optimize PRO Study Valves

Earlier Generations

CoreValve™
2014

- First self-expanding TAVR valve

*0.2%

Evolut™ R
2015

- Recapturability
- Lower delivery profile
- Consistent radial force

21.5%

Evolut™ PRO
2017

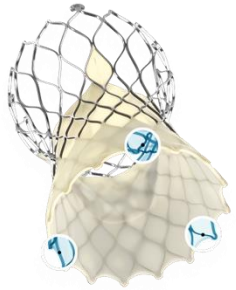
- Reduction in paravalvular leak

78.4%

Evolut™ PRO+
2019

- Lower delivery profile
- Large valve PVL performance

Subsequent Generations



Evolut™ FX
2022

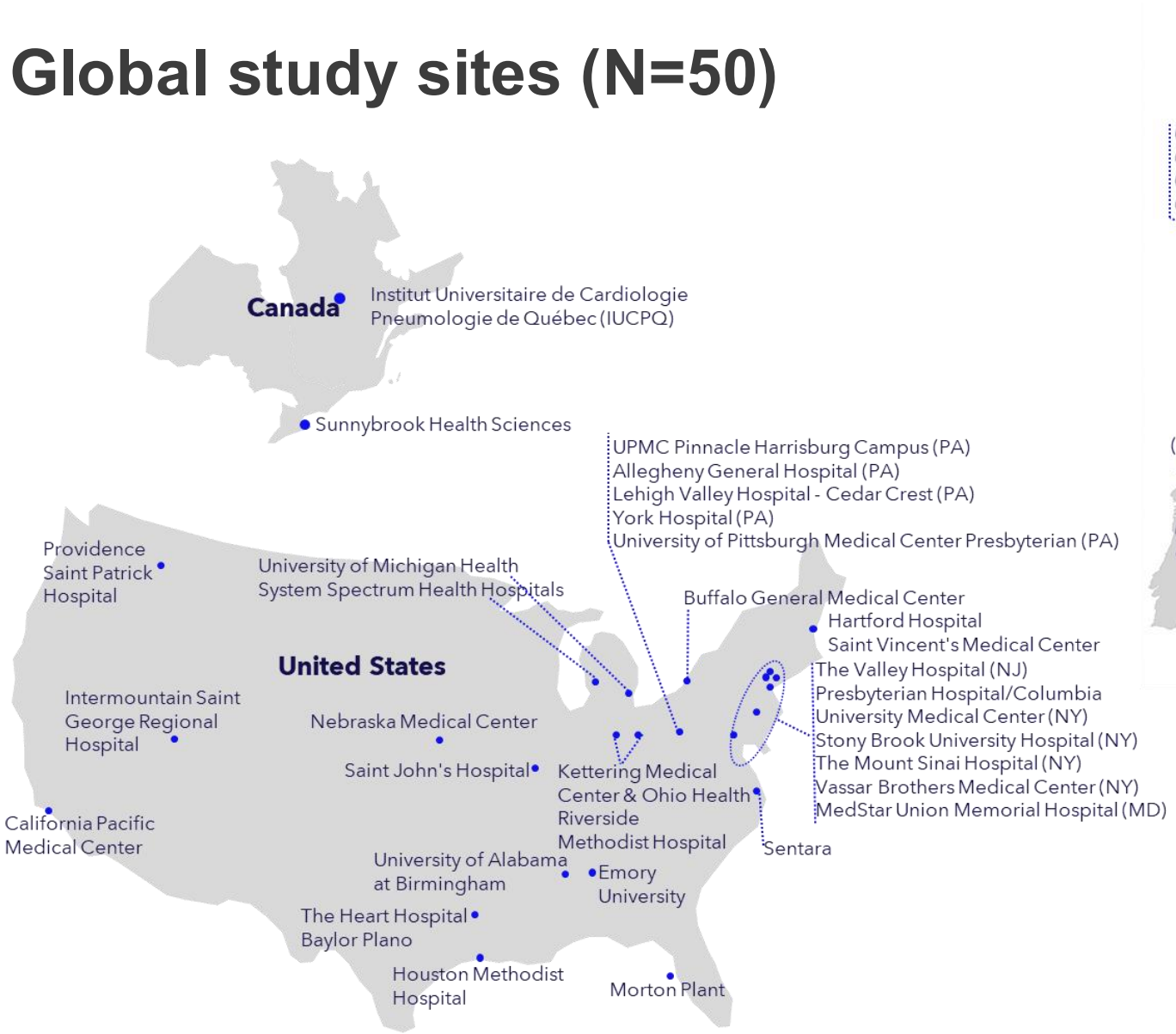
- Greater precision and control
- Radiopaque markers deployment depth and commissure location
- Ease of use

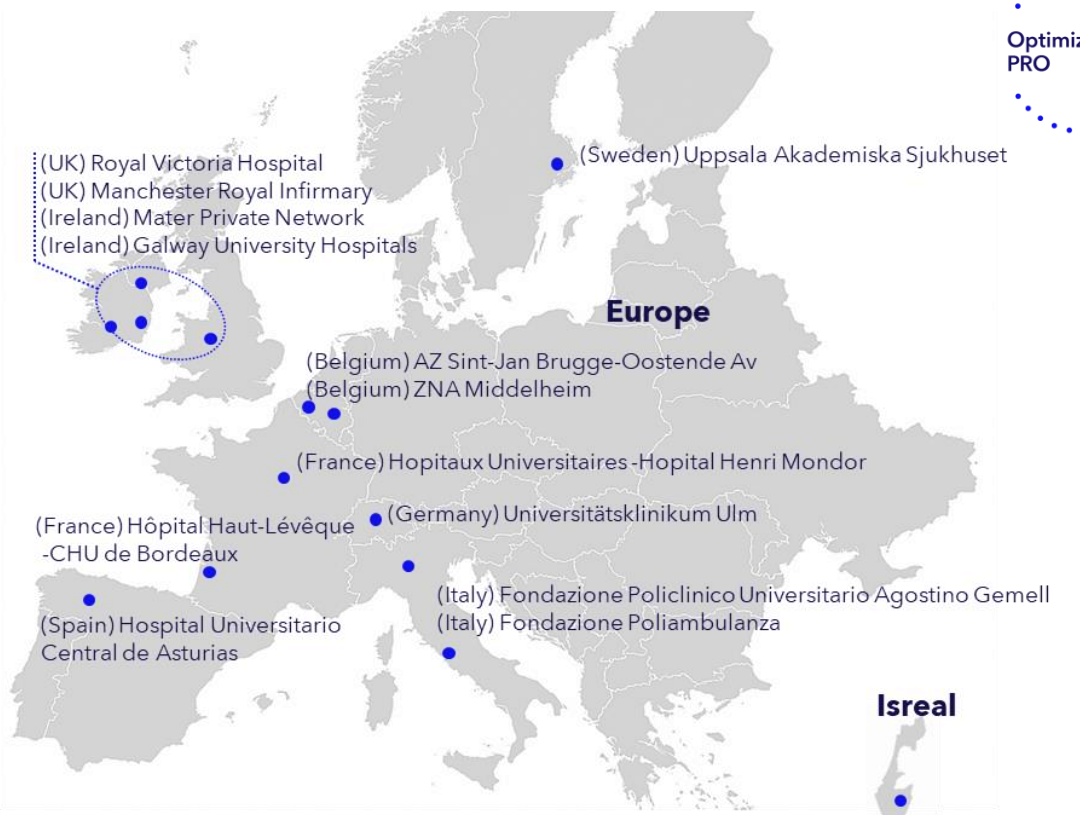
Evolut™ FX+
2024

- Larger window for enhanced coronary access
- Same valve performance as the CoreValve/Evolut platform

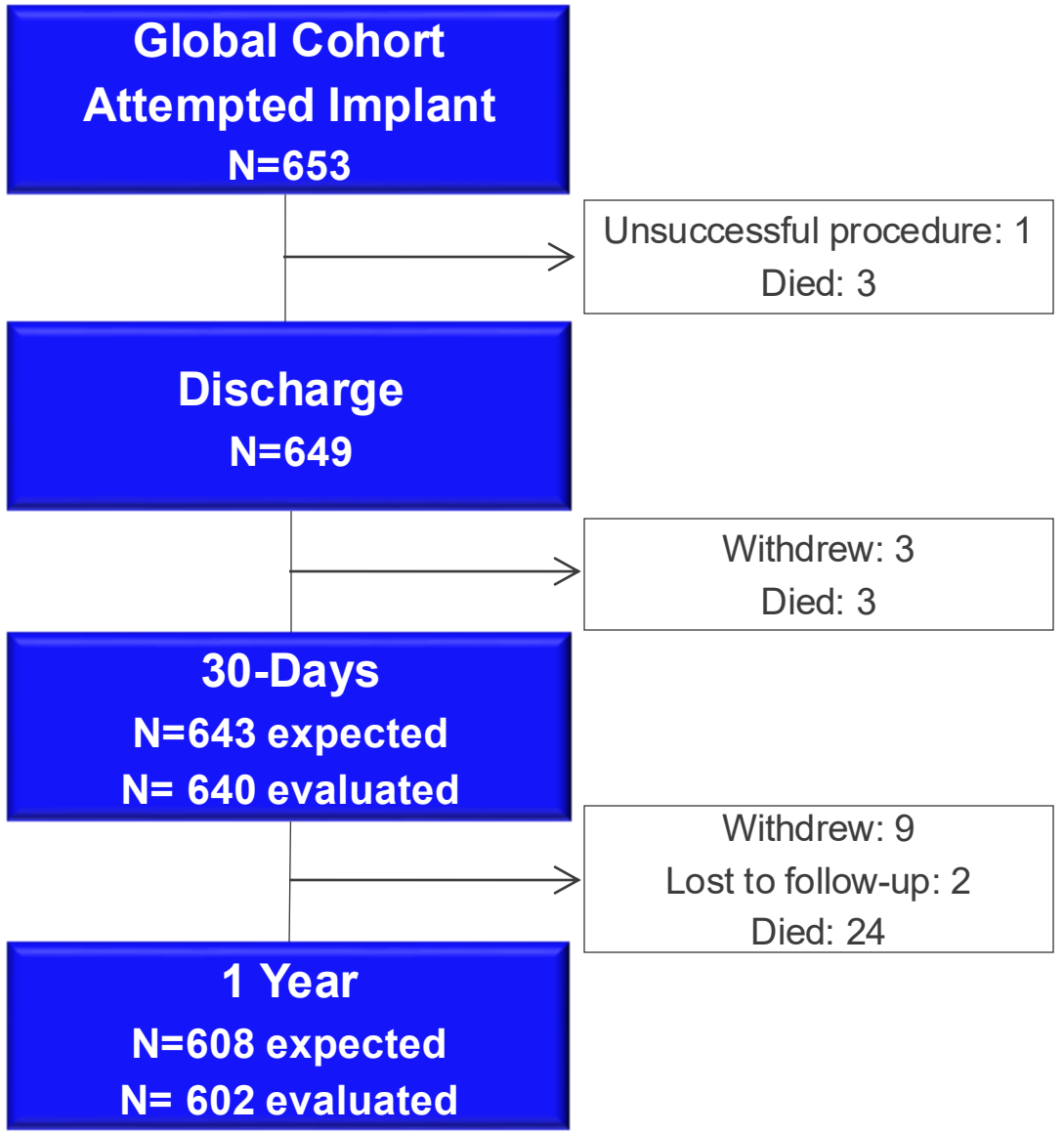
*Evolut R implanted in one subject as Evolut PRO or PRO+ were not available at study site on the index procedure date.

Global study sites (N=50)





Patient flow



1-year analysis:
Data evaluated for 92.2% (602/653) of patients

Baseline characteristics

Characteristic	Optimize PRO Global Cohort (N=653)
Age – yr	**79.1 ± 6.5**
Female sex	**47.0%**
STS-PROM score – %	**3.2 ± 2.5**
Body mass index, kg/m^2	29.6 ± 5.9
NYHA functional class III/IV	42.7%
Diabetes	32.2%
Hypertension	78.9%
COPD or chronic lung disease	19.6%
Cerebrovascular disease	14.5%
Previous coronary artery bypass graft	10.0%
Previous percutaneous coronary intervention	21.9%
Previous myocardial infarction	9.1%
History of right bundle branch block	6.9%
Atrial fibrillation/flutter	19.4%
Left ventricular ejection fraction	59.7 ± 7.8

Data presented as mean ± SD or %; COPD=Chronic Obstructive Pulmonary Disease; NYHA=New York Heart Association; STS-PROM=Society of Thoracic Surgeons Predicted Risk of Mortality

Key procedural data

Outcome / Assessment	Optimize PRO Global Cohort (N=652[1])
4-step cusp overlap technique (COT) compliance[2]	
Yes	**50.3%**
No	**39.7%**
Length of stay (days)	2 (1-3)
Femoral access site	100%
Lunderquist extra stiff guidewire	**80.7%**
Resheathing or recapture	41.3%
NCC implant depth, mm, core lab[3]	3.9 ± 3.2
Length of membranous septum, mm, core lab[3]	2.9 ± 2.2
Discharge prosthesis-patient mismatch (PPM) VARC-3[3]	
No PPM	91.6%
Moderate PPM	6.8%
Severe PPM	1.6%

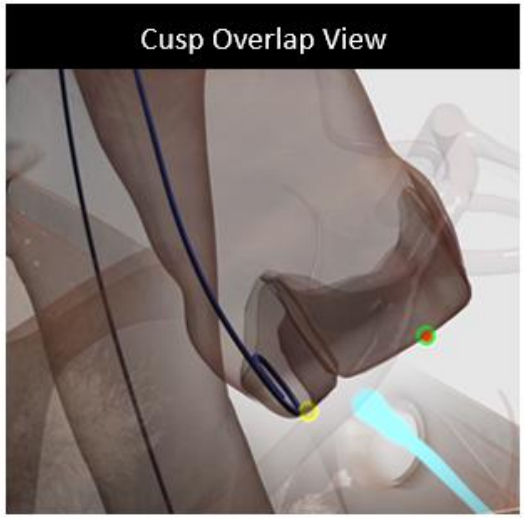
Values are mean ± SD, n (%), n/N (%) or median (Q1-Q3)
[1]Subjects in which the delivery system was introduced. [2]Unable to assess in 10%.[3]Sample size n=606, n=649, n=429, respectively.

Clinical outcomes at 1 year

Outcome	Optimize PRO Global Cohort (N=653)
All-cause mortality or all stroke	**9.7%**
All-cause mortality	**4.6%**
Cardiovascular mortality	**2.4%**
All stroke	6.0%
Disabling stroke	2.7%
Reintervention	0.3%
Myocardial infarction	2.9%
Clinical valve thrombosis	0.3%
Endocarditis	0.3%
Major vascular complication	3.2%
Cardiovascular hospitalizations	15.2%
Heart failure hospitalization	3.5%
Left bundle branch block	27.8%

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

Cusp Overlap Technique with Evolut PRO/PRO+ and FX



4-Step COT PRO/PRO+

1. **Initial positioning**: Start deployment in cusp overlap view and estimate implant depth at NCC.
2. **Guidewire**: Confirm left ventricle placement, use of Lunderquist guidewire is highly recommended.
3. **Depth Control**: Do not exceed 3mm depth prior to full annular contact.
4. **Final assessment**: Assess final implant depth at NCC in cusp overlap view.

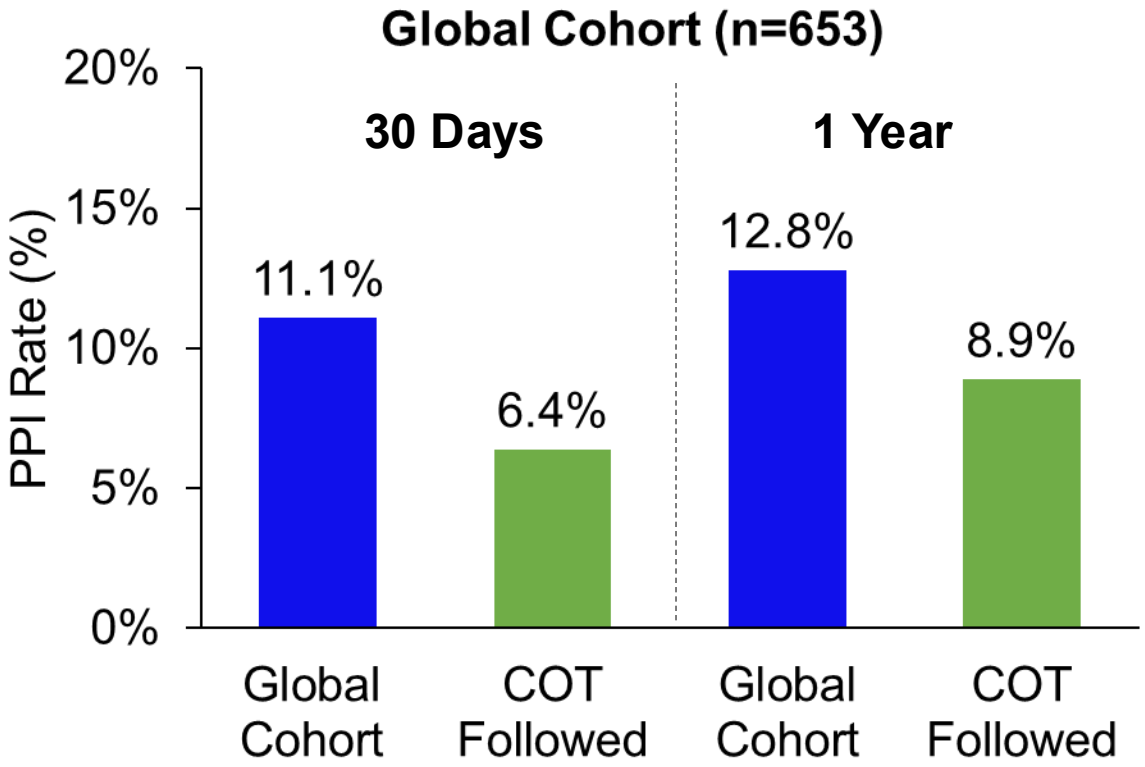
3-Step COT FX

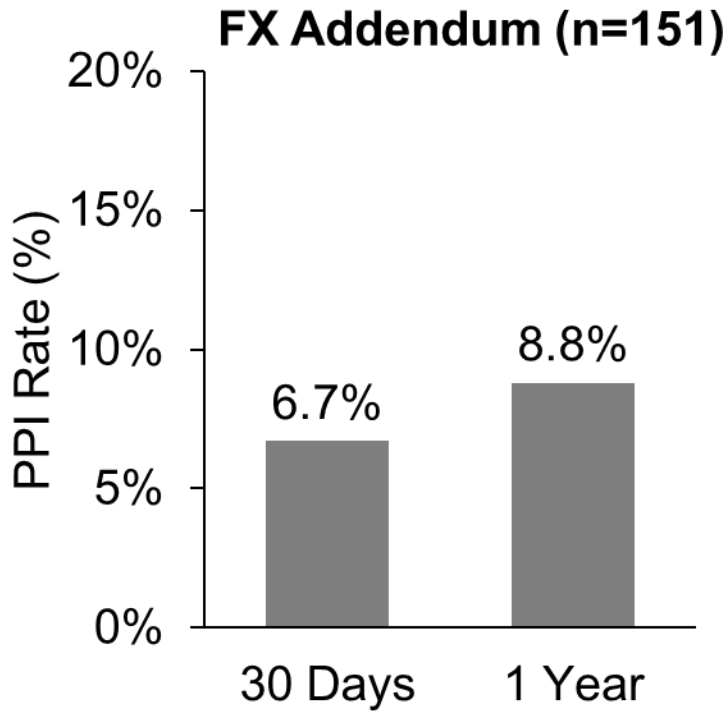
1. **Initial positioning**: Start deployment in cusp overlap view and estimate implant depth at NCC.
2. **Deployment start:** Begin with marker band at mid-pigtail or higher.
3. **Depth Check**: At 80% deployment, assess final depth at NCC in cusp overlap view.

NCC=non-coronary cusp

Pacemaker implantation

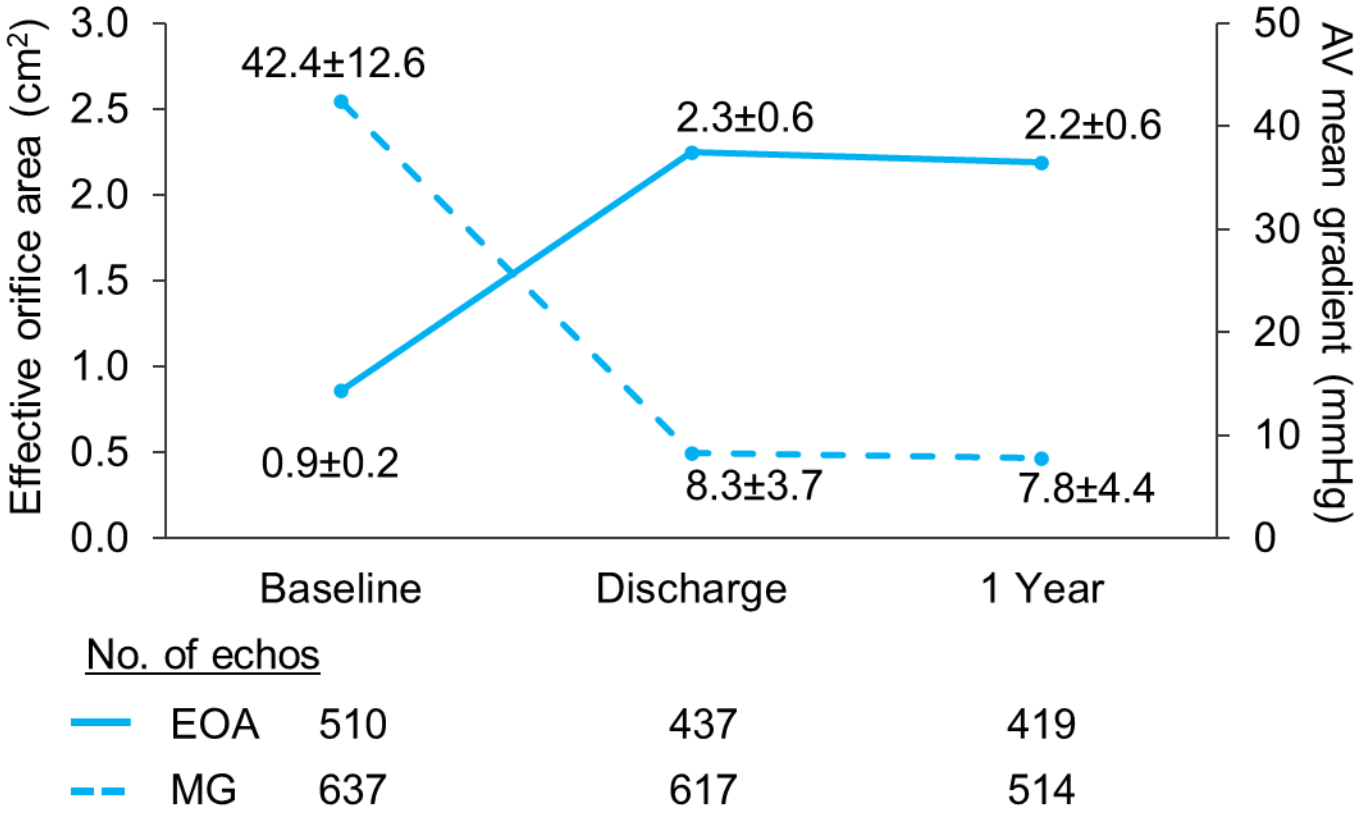
- The 30-day PPI rate was 11.1% overall and 6.4% with 4-step COT compliance.
- The new 1-year PPI rate was 12.8% overall and 8.9% with 4-step COT compliance.
- For reference, the 1-year PPI rate was 8.8% in the FX Addendum Study.





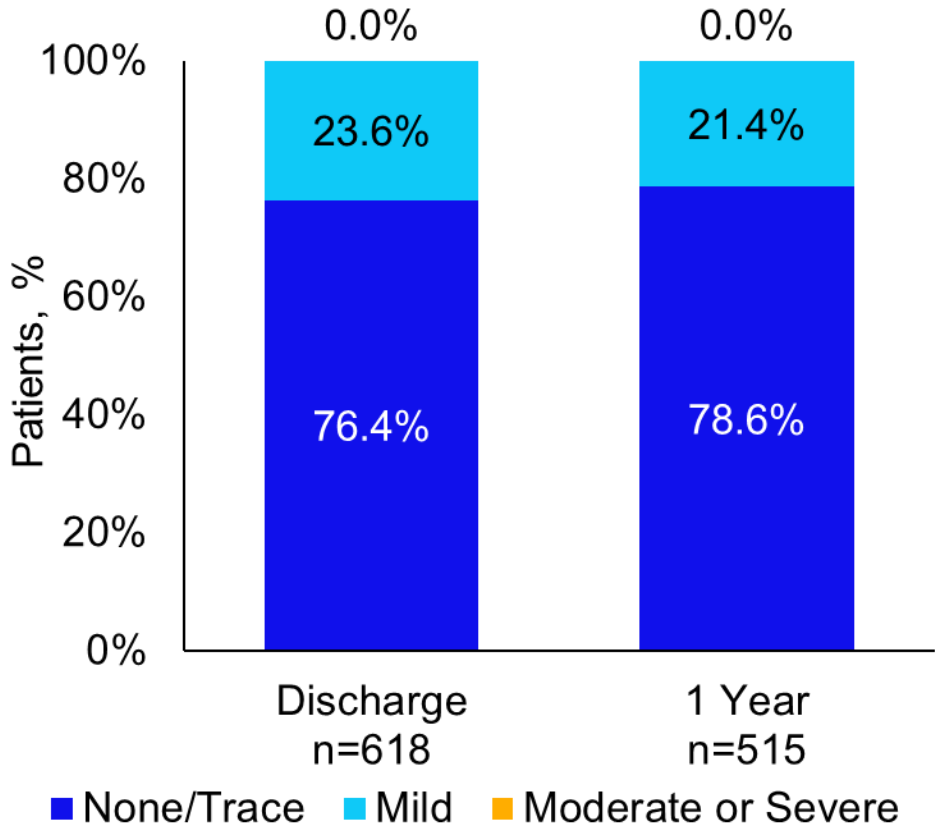
COT followed n=328; COT followed vs not followed *P* <.001 at 30 days and 1 year.
COT not followed or unable to access is not shown here

Valve hemodynamics through 1 year



Excellent hemodynamics through 1 year

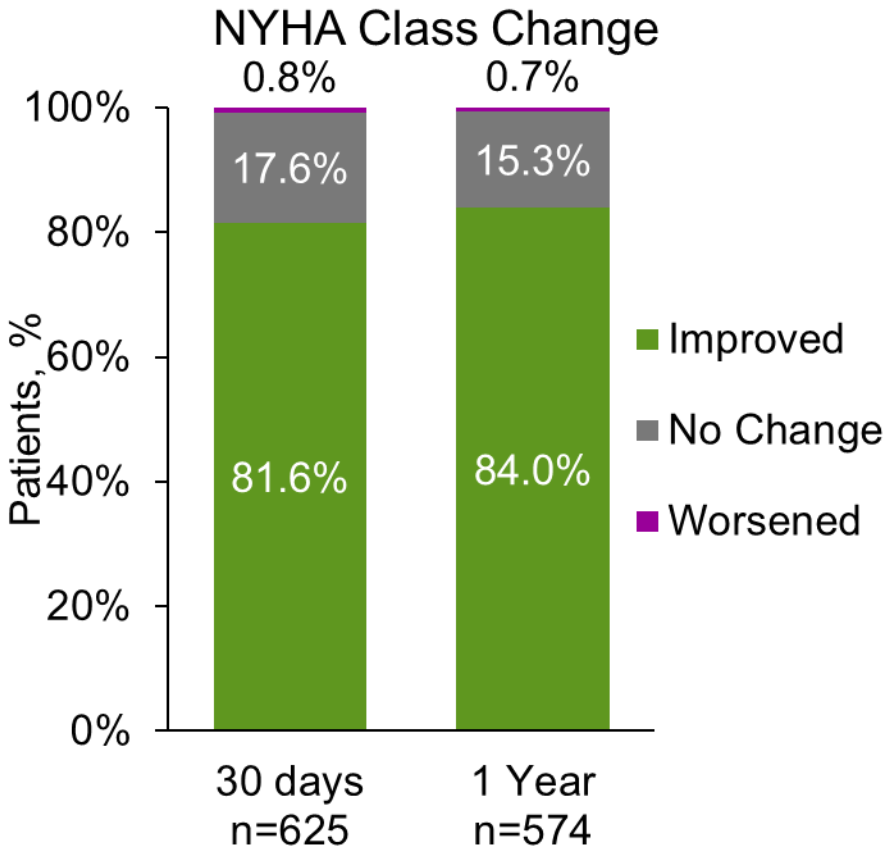
Paravalvular regurgitation through 1 year



No patients had moderate or severe paravalvular regurgitation at 1 year

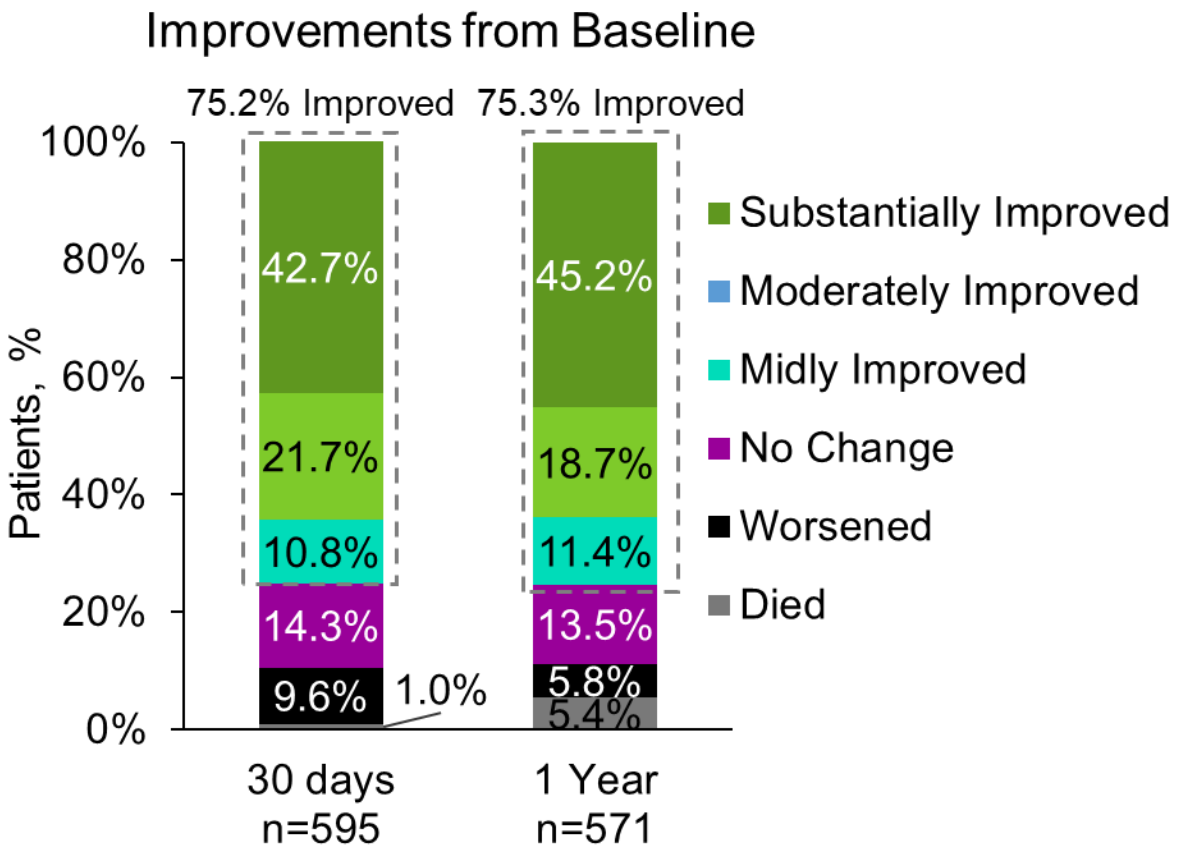
Core lab data

New York Heart Association through 1 year



Improvement in NYHA score by at least 1 functional class from baseline to 1 year occurred in 84% of patients

Quality of life through 1 year



>75% of patients had improved quality of life at 1-year post-procedure

VARC-3 ordinal outcome:
(i) death; (ii) worsened: decrease from baseline >5 points; (iii) no change:
change between -5 and <5 points; (iv) mildly improved: increase between 5 and <10 points; (v) moderately improved: increase between 10 and <20 points; (vi) substantially improved: increase ≥20 points

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.

Conclusions

- Evolut TAVR platform continues to demonstrate a *strong safety profile* (2.4% cardiovascular mortality)
- *Procedural technique drives lower PPI rates with COT compliance* (6.4% at 30 days and 8.9% at 1 year)
- Hemodynamic performance is sustained with Evolut TAVR with no moderate or severe paravalvular regurgitation
- **Evolut TAVR improves quality of life**

Thank You to All of Our Patients, Study Investigators, Research Coordinators, and Top Implanting Sites!

- University of Pittsburgh Medical Center (UPMC) Pinnacle Hospitals, Harrisburg, PA, USA
- Shaare Zedek Medical Center, Jerusalem, Israel
- Hôpitaux Universitaires - Hôpital Henri Mondor, Créteil, France
- Morton Plant Hospital - BayCare Health System, Clearwater, FL, USA
- Allegheny General Hospital - Allegheny Health Network Research Institute, Pittsburgh, PA, USA
- University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA, USA
- Austin Hospital, Melbourne, VIC, Australia
- Intermountain Saint George Regional Hospital, St. George, UT, USA
- Saint Vincent's Medical Center, Bridgeport, CT, USA
- University of Michigan Health System - University Hospital, Ann Arbor, MI, USA
- Lehigh Valley Hospital - Cedar Crest, Allentown, PA, USA
- York Hospital, York, PA, USA
- Manchester Royal Infirmary, Manchester, United Kingdom
- Sentara Hospitals, Norfolk, VA, USA
- Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy
- Galway University Hospitals-University Hospital Galway (UHG), Galway, Ireland
- Kettering Medical Center, Kettering, OH, USA
- Vassar Brothers Medical Center, Poughkeepsie, NY, USA
- AZ Sint-Jan Brugge-Oostende av, Brugge, Belgium
- OhioHealth Riverside Methodist Hospital-OhioHealth Research Institute, Columbus, OH, USA
- Fondazione Poliambulanza, Brescia, Italy
- Fiona Stanley Hospital, Perth, WA, Australia
- Emory University Hospital Midtown, Atlanta, GA, USA
- Hospital Universitario Central de Asturias, Oviedo, Spain
- MedStar Union Memorial Hospital, Baltimore, MD, USA
- Monash Medical Centre Clayton, Melbourne, Victoria, Australia

Backup

Optimized TAVI Care Pathway with Evolut PRO/PRO+

Optimize PRO

Pre-Procedure

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

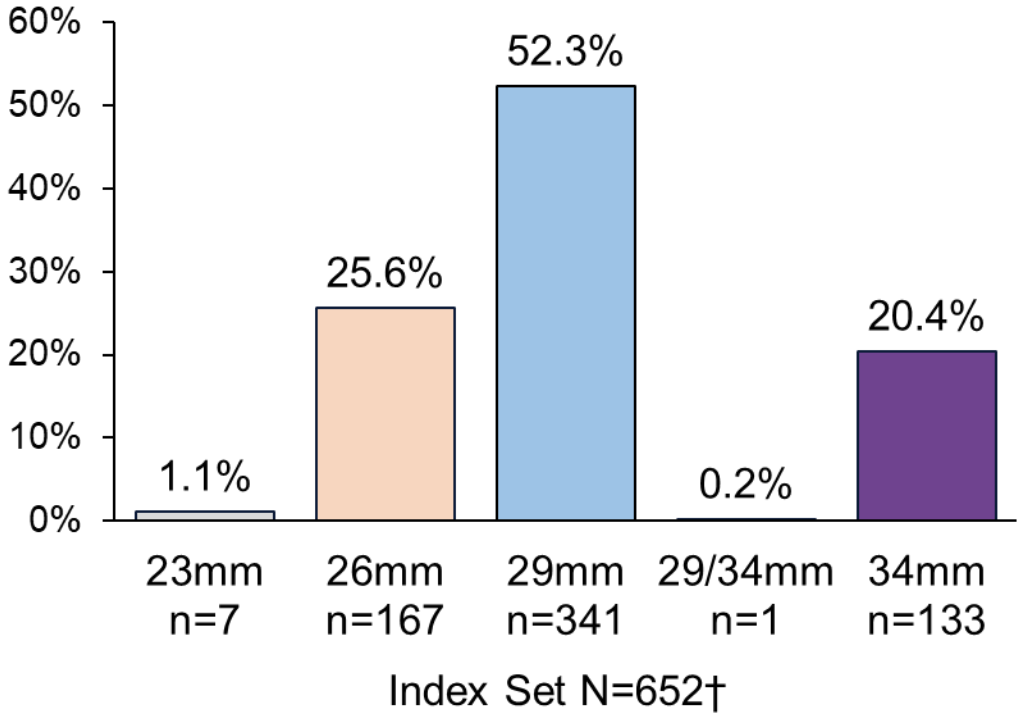
Peri-Procedure

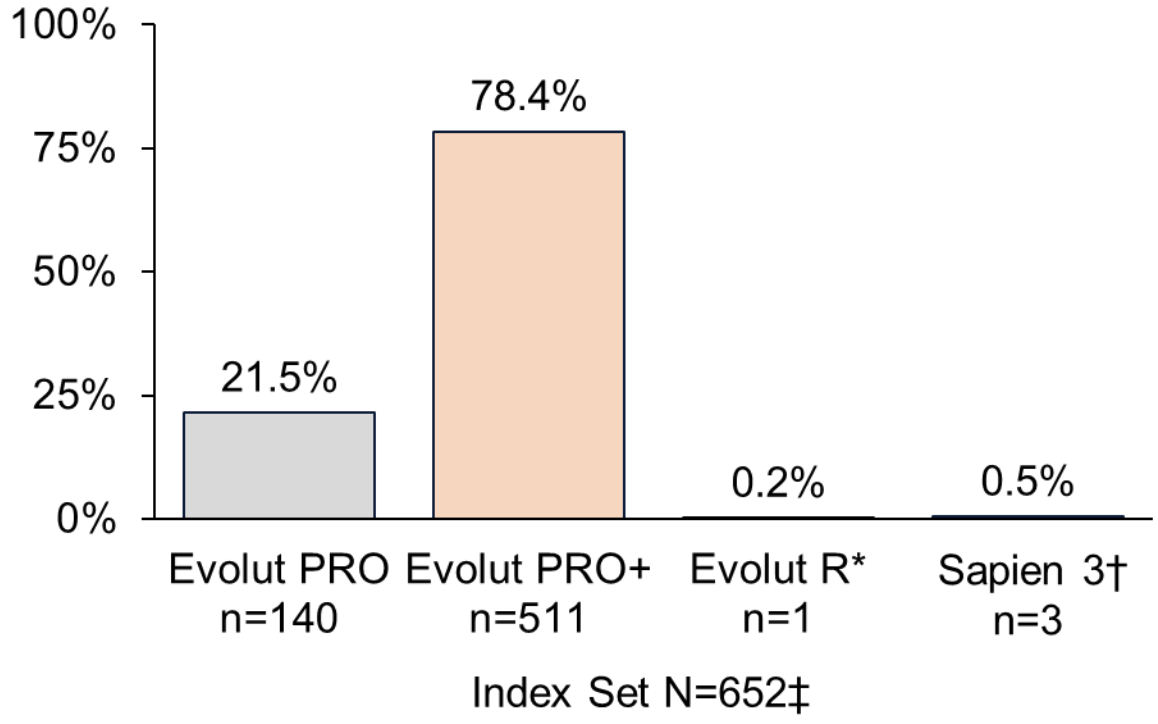
- Valve deployment using the cusp overlap technique
- Pre-BAV not required
- Avoid general anesthesia
- Use transfemoral access only
- Minimize central lines

Post-Procedure

- 12-lead ECG within 2 hours
- If no pre-existing 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

Valve size and type





Index Set N=652 is the first procedure that the Medtronic Evolut PRO/PRO+ System delivery catheter is introduced.

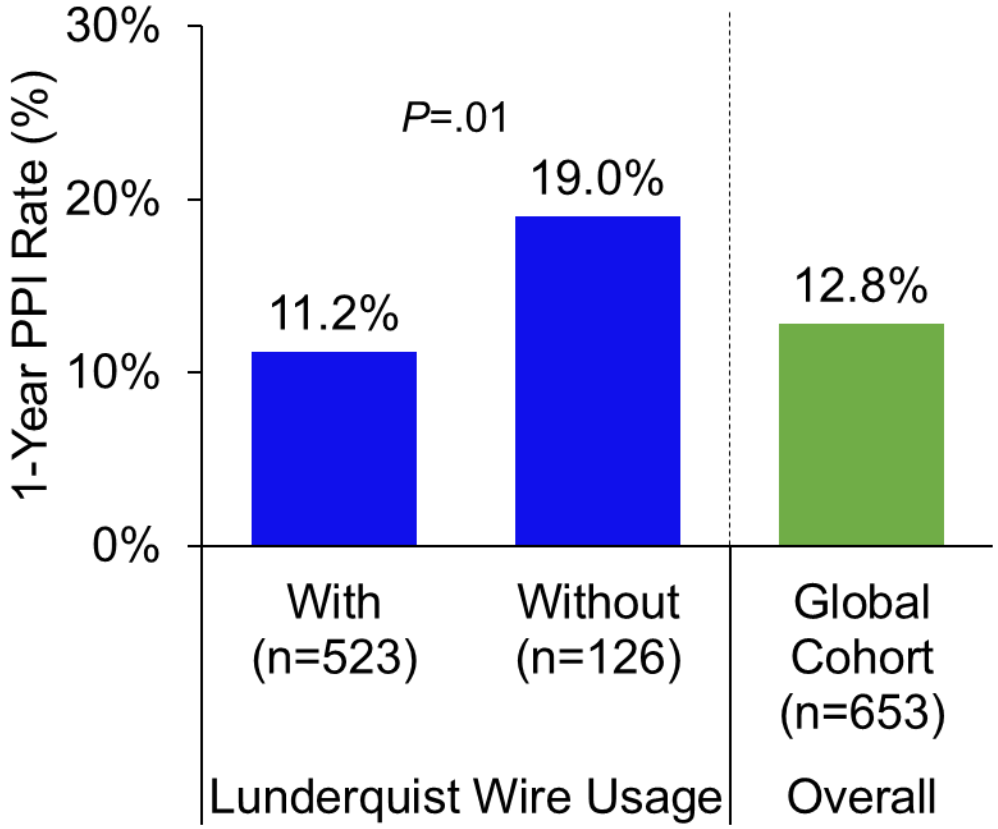
*Evolut R implanted in one subject as Evolut PRO or PRO+ were not available at study site on the index procedure date.

†Sapien transcatheter aortic valve implanted after attempted implant with Evolut PRO+ or after implant with Evolut PRO or Evolut PRO+ TAV (valve-in-valve).

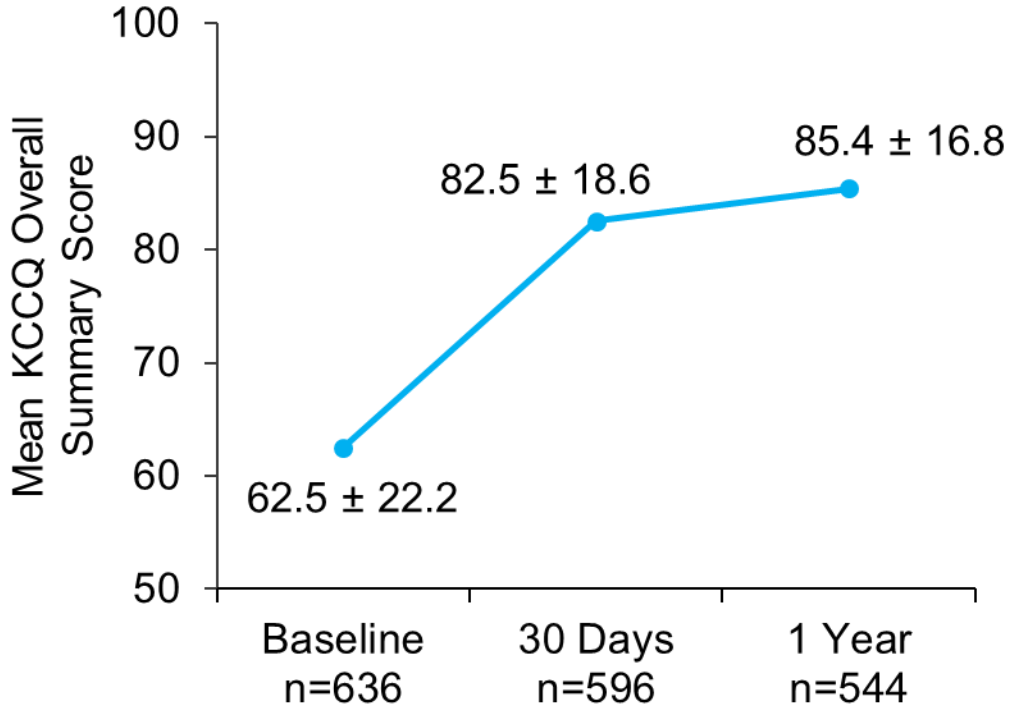
‡If more than one valve was implanted, it is possible that more than one model of valve was implanted.

Pacemaker implantation based on Lunderquist wire usage

- A Lunderquist Extra-Stiff guide wire was used in 80.7% of implants.
- Failure to use a Lunderquist guide wire resulted in a higher 1-year PPI rate.

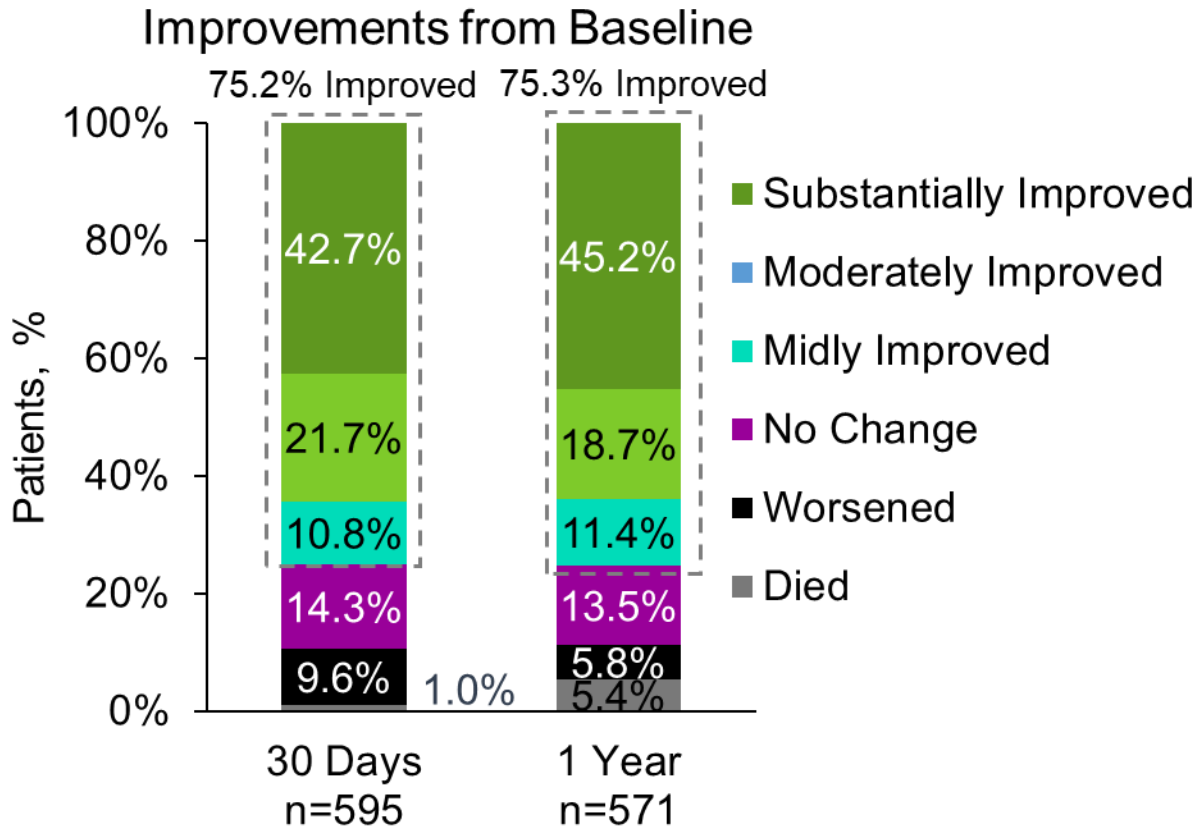


KCCQ outcomes through 1 year



Change from Baseline

n	589	540
Mean ± SD	19.8±21.6	22.1±21.3
P value	<0.001	<0.001



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New York Heart Association score through 1 year