Medtronic Evolut R System

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Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF LivaNova: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Millipede: SB, C, AB Kona: AB, E Abbott Vascular: AB InSeal Medical: AB, E, Valtech: E, SB, Claret: SB Keystone: AB Shockwave: E, AB

Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker' s Bureau O – Ownership OF – Other Financial Benefits '

Evolut R

Evolut R follows on a foundation provided by *almost 10 years* of clinical experience with CoreValve. The goals of this presentation are to:

- ✓ Highlight the design features of Evolut R
- ✓ Demonstrate how they translate into improved patient outcomes in several clinical settings
- ✓ Show the current clinical Evolut R portfolio

The CoreValve Foundation

CoreValve US Pivotal Trial | High Risk Study

3-Year follow-up is now complete for the High Risk Study, which randomized TAVR with CoreValve to SAVR

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

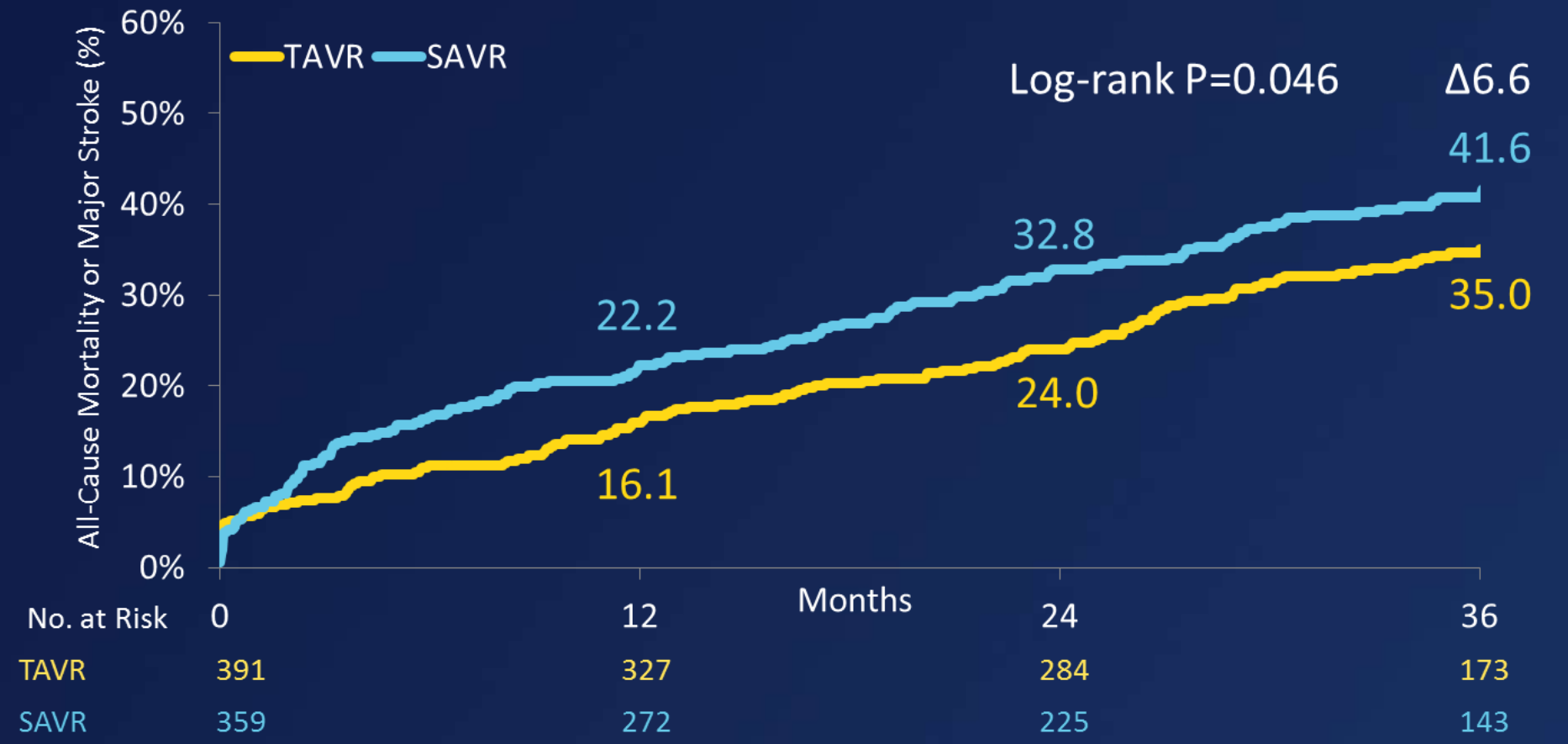
David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

CoreValve, N=390, STS 7.3% vs. SAVR, N=357, STS 7.5%

CoreValve US Pivotal Trial | High Risk

3-Year Follow-Up

TAVR superior to SAVR for All-Cause Mortality or Major Stroke

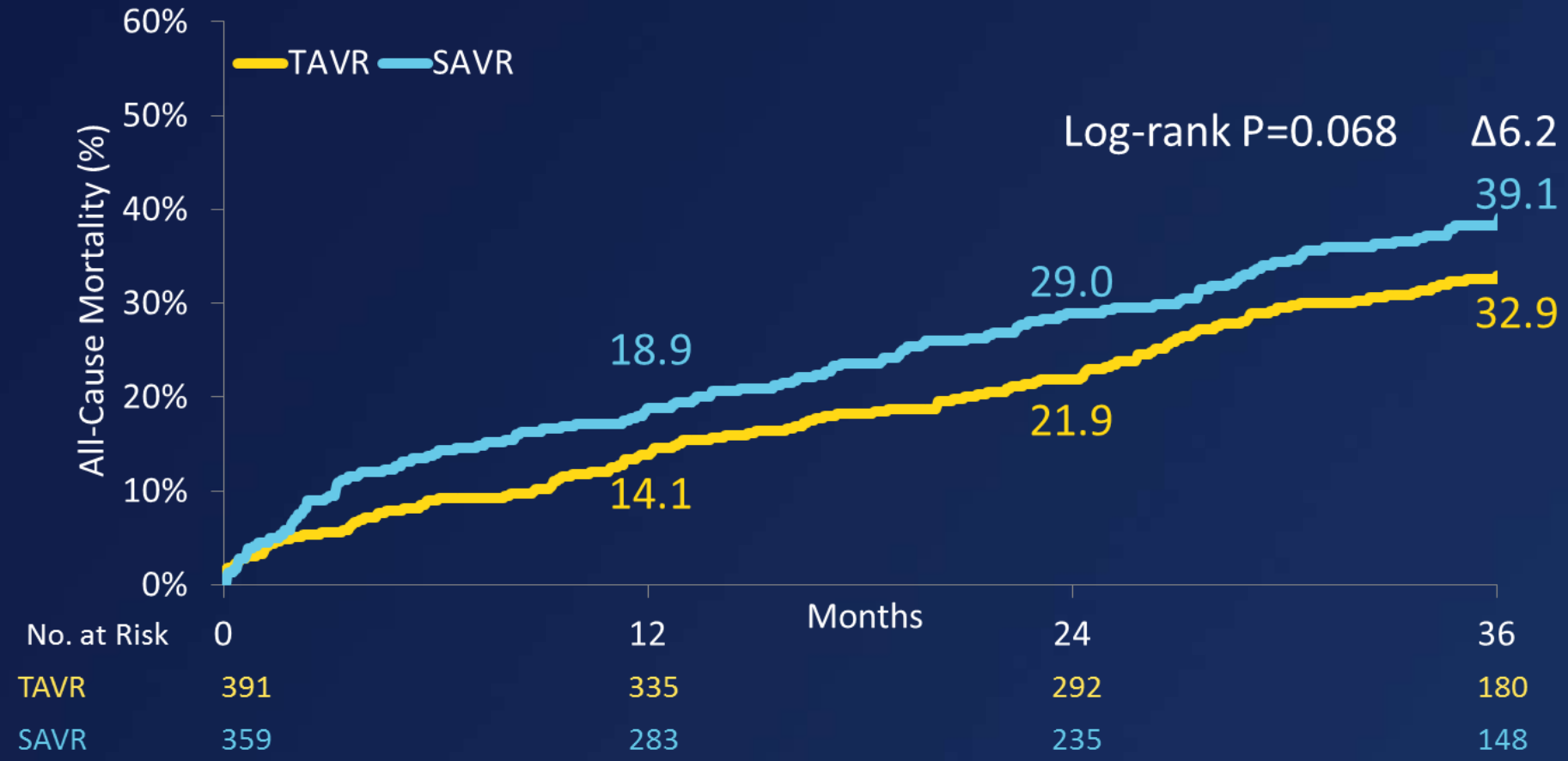


[1]Deeb, et al., *J Am Coll Cardiol* 2016 Mar 22; doi: 10.1016/j.jacc.2016.03.506

CoreValve US Pivotal Trial | High Risk

3-Year Follow-Up

Survival in TAVR patients in the CoreValve Pivotal Trial was superior to surgery to 2 years (p=0.04), with continued separation of the curves to 3 years

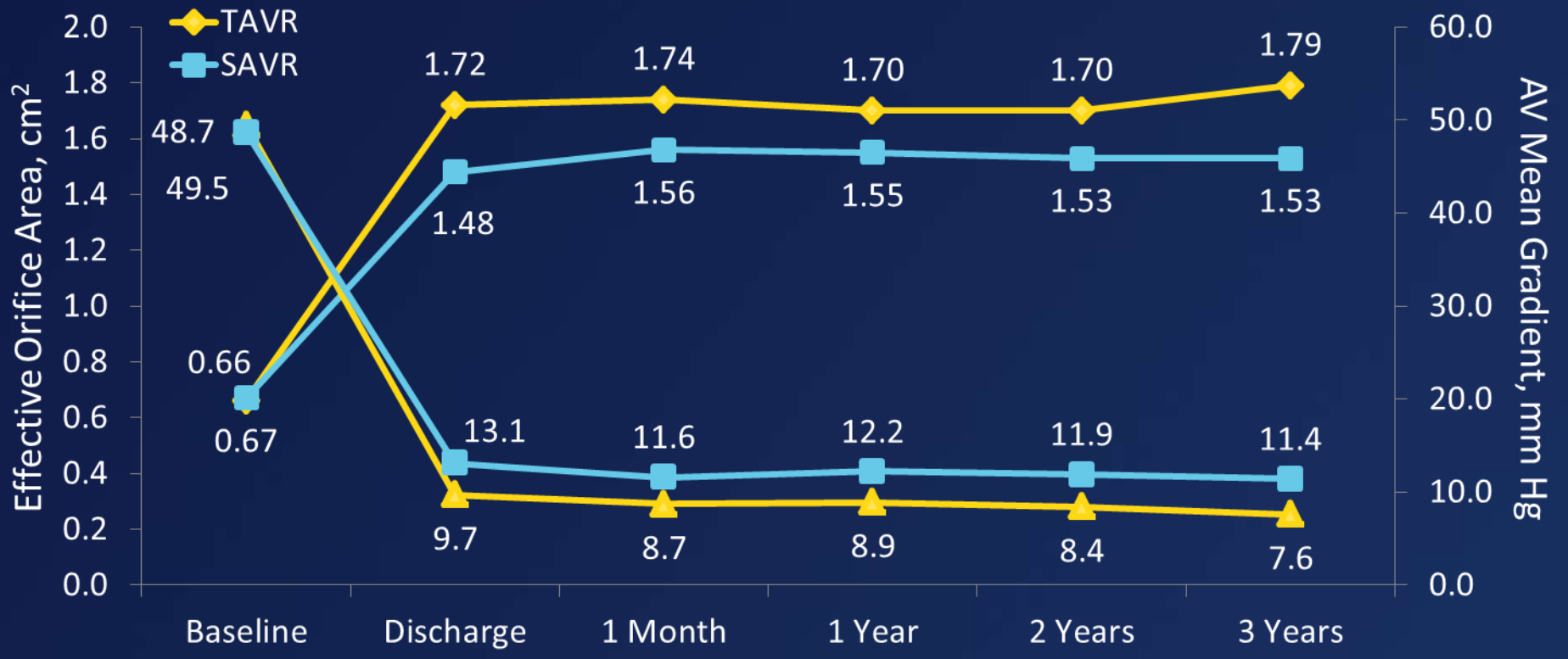


[1]Deeb, et al., *J Am Coll Cardiol* 2016 Mar 22; doi: 10.1016/j.jacc.2016.03.506

CoreValve US Pivotal Trial | High Risk

3-Year Follow-Up

Significantly better hemodynamics with TAVR vs. SAVR at all follow-ups (P<0.001)



[1]Deeb, et al., *J Am Coll Cardiol* 2016 Mar 22; doi: 10.1016/j.jacc.2016.03.506

Evolut R | Design Features and Special Attributes

Medtronic Transcatheter Valve Design

Evolut R Builds on the Proven Foundation CoreValve Platform

Supra-Annular Valve
Porcine Pericardial Tissue

Self-Expanding Frame
Pericardial Skirt
Cell Size Enables Coronary Access

CoreValve

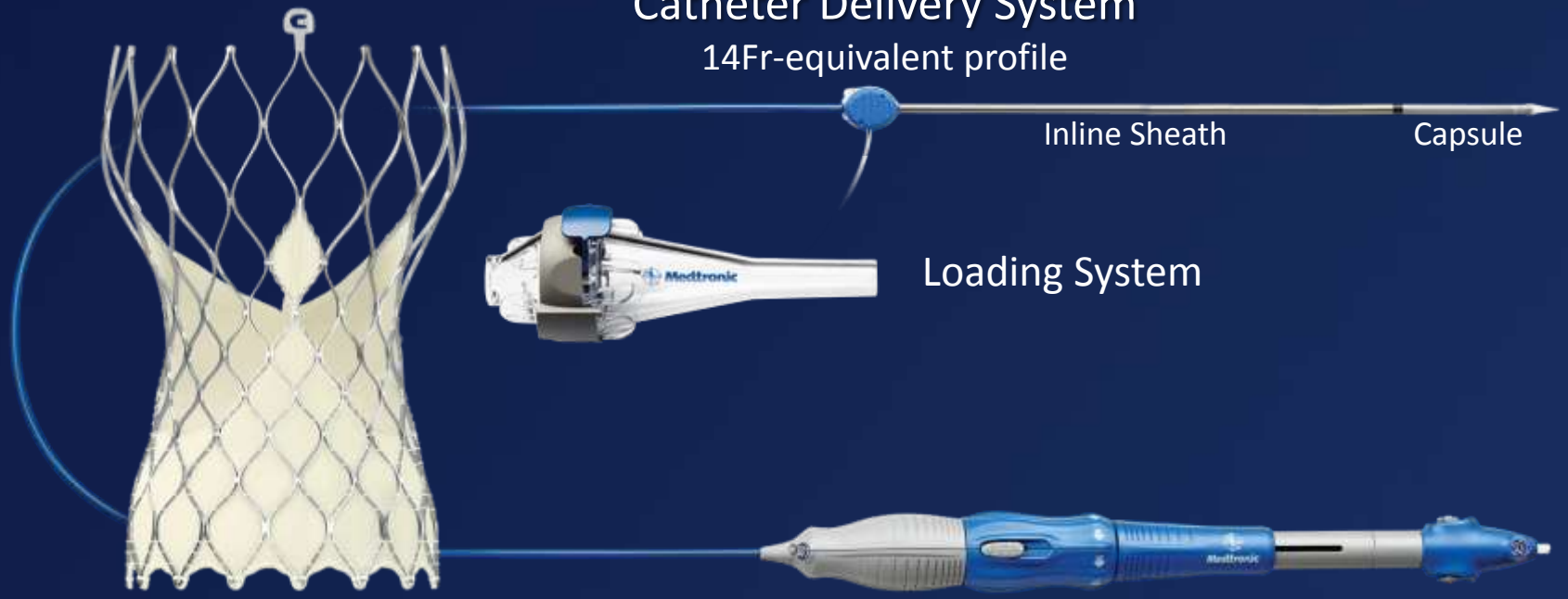
Evolut R

Evolut R Design Goals

1. Low Delivery Profile
2. Unsurpassed Hemodynamics
3. Enhanced Sealing with More Conformable Frame
   - More Consistent Radial Force
   - Optimized Oversizing
   - Extended Skirt

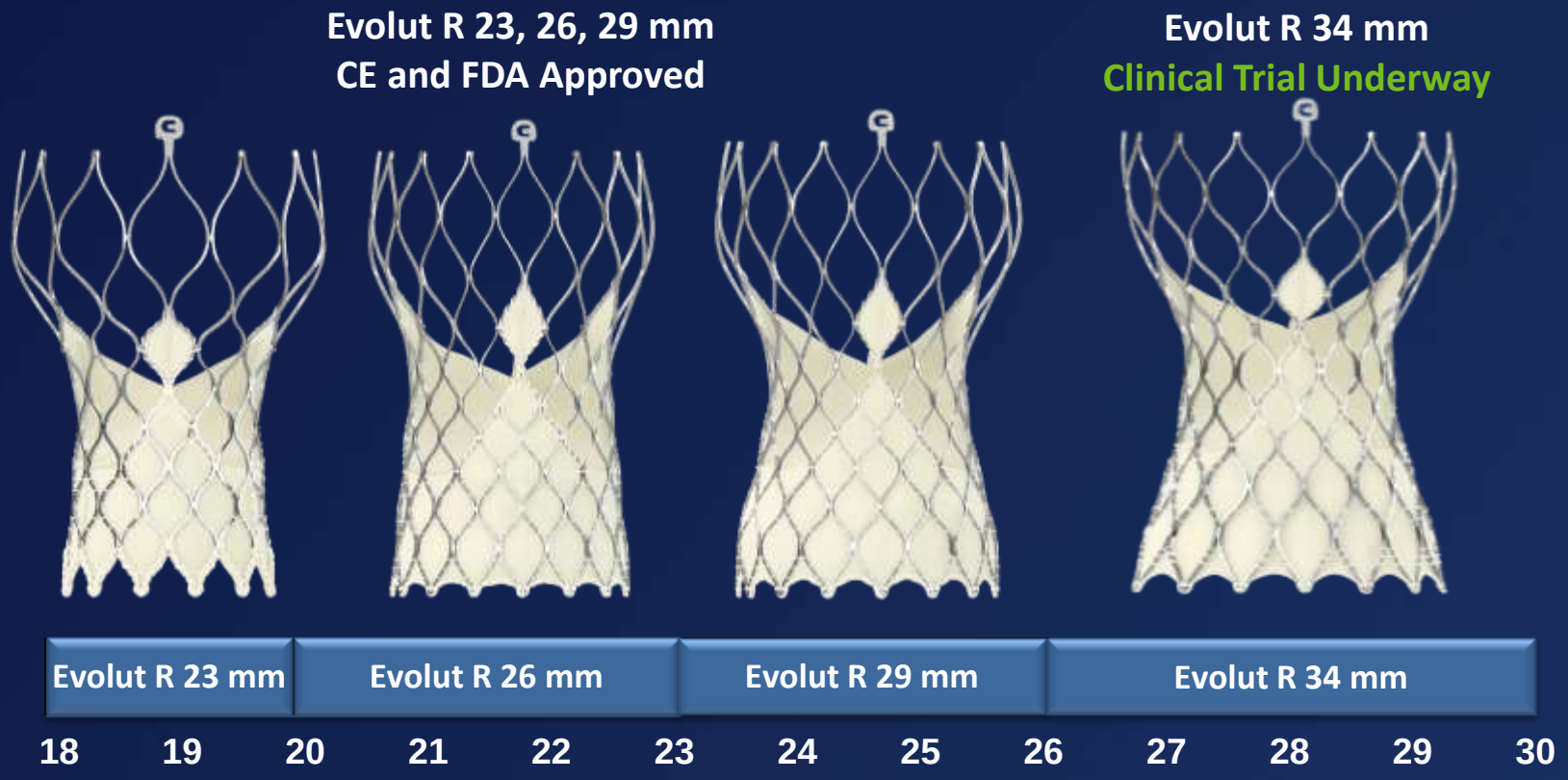
Evolut R

The System



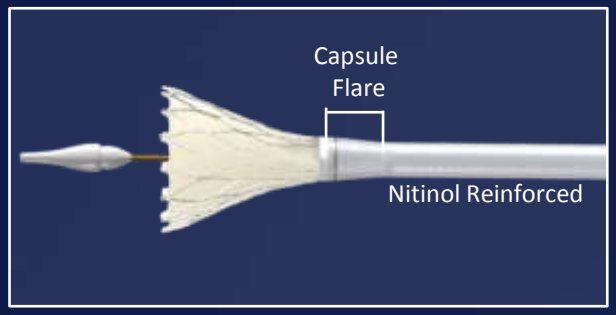
Evolut R

Indicated Size Range



EnVeo R Delivery Catheter System

Control During Deployment, Ability to Recapture and Reposition

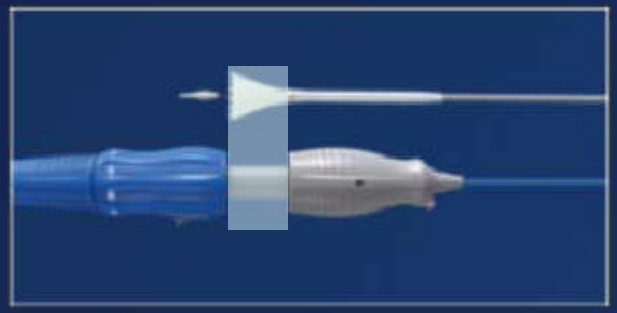


Capsule Flare

Enable uniform and controlled valve expansion and self-centering

Low Delivery Profile

14Fr-equivalent
Vessel Access ≥ 5.0 mm



1:1 Response

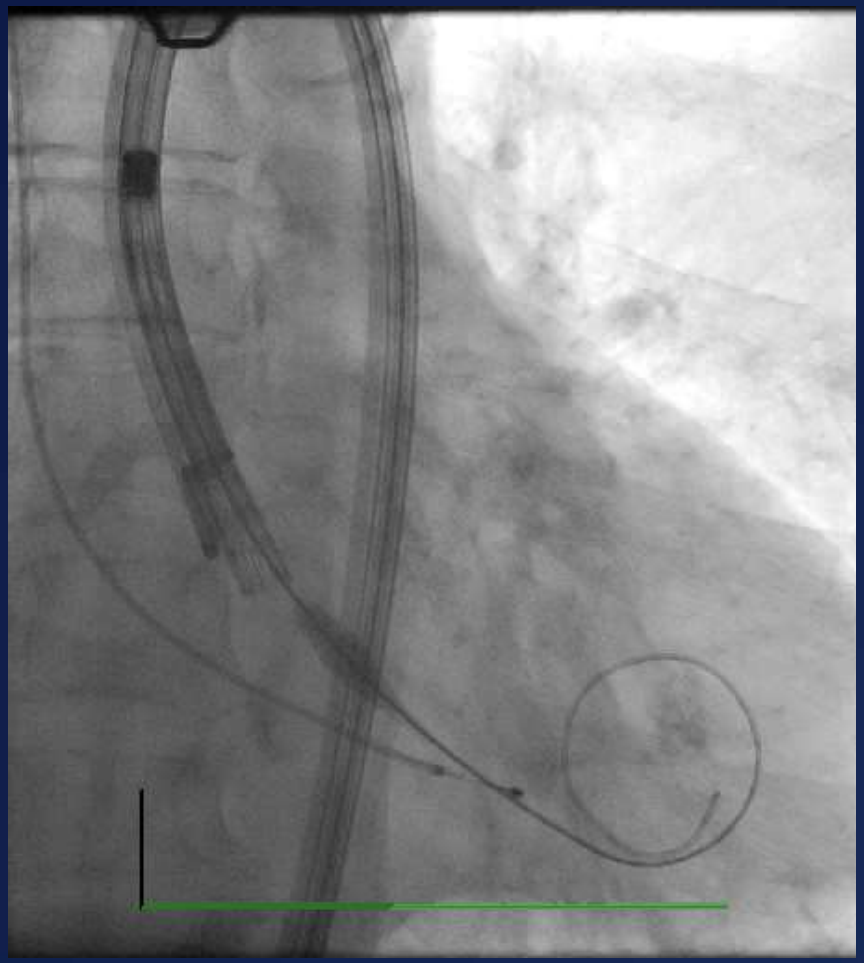
Direct correlation between movement of the deployment knob and movement of the capsule

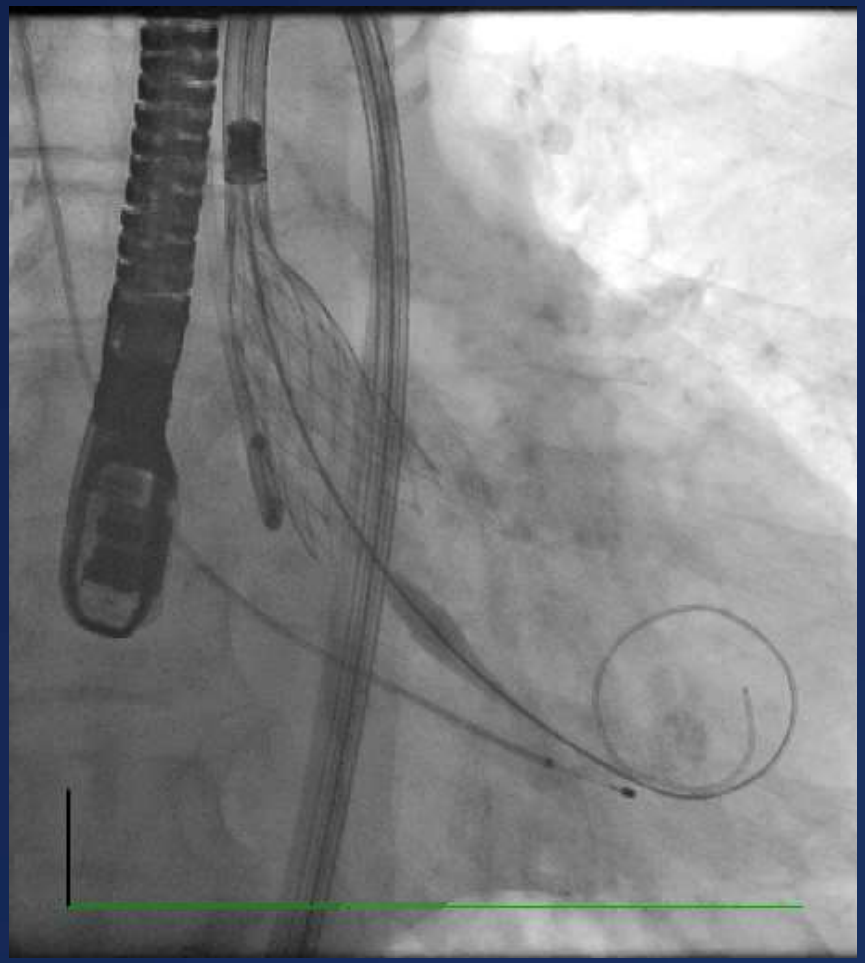
*Up to ~ 80% deployment. Medtronic Data on File.

Case Examples

Case Example | Recapture

Valve #1: 23 mm

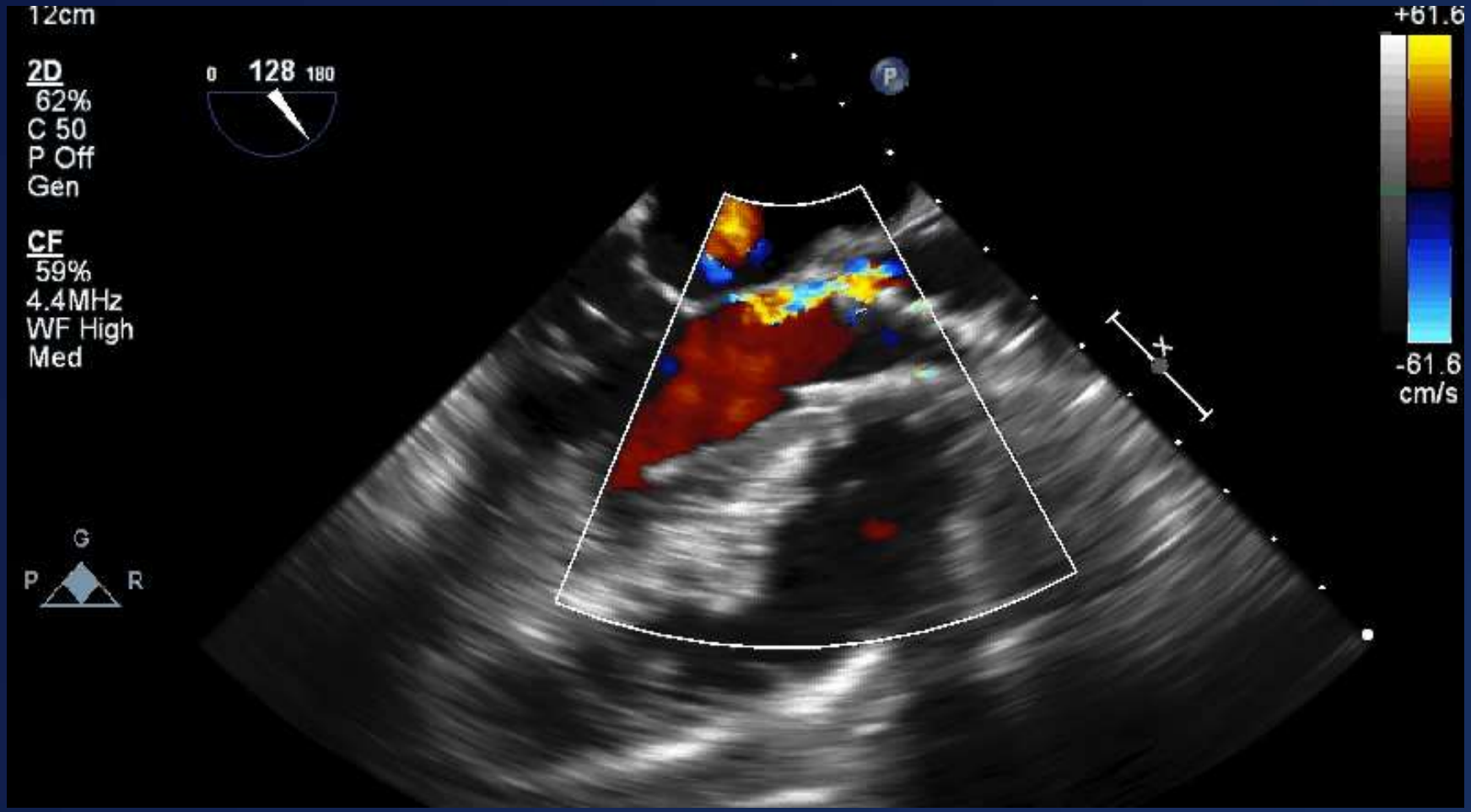




Mathew Williams, MD, NYU Langone Medical Center

Case Example | Recapture

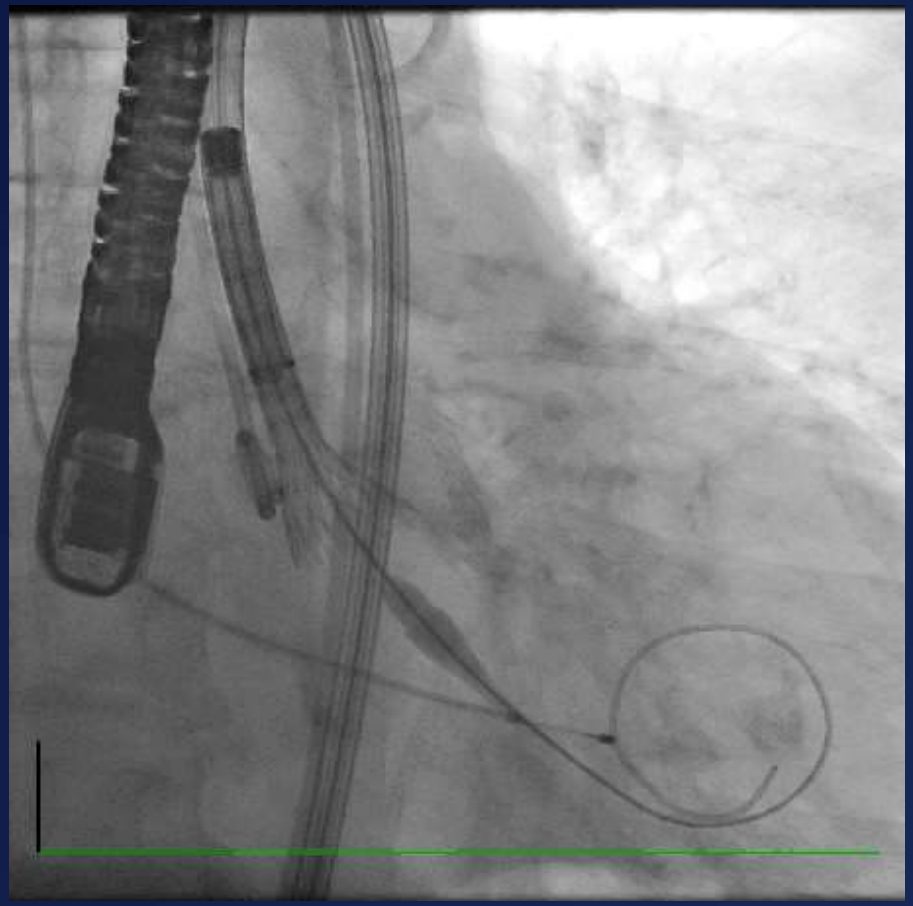
Valve #1: 23 mm, post-deployment TEE

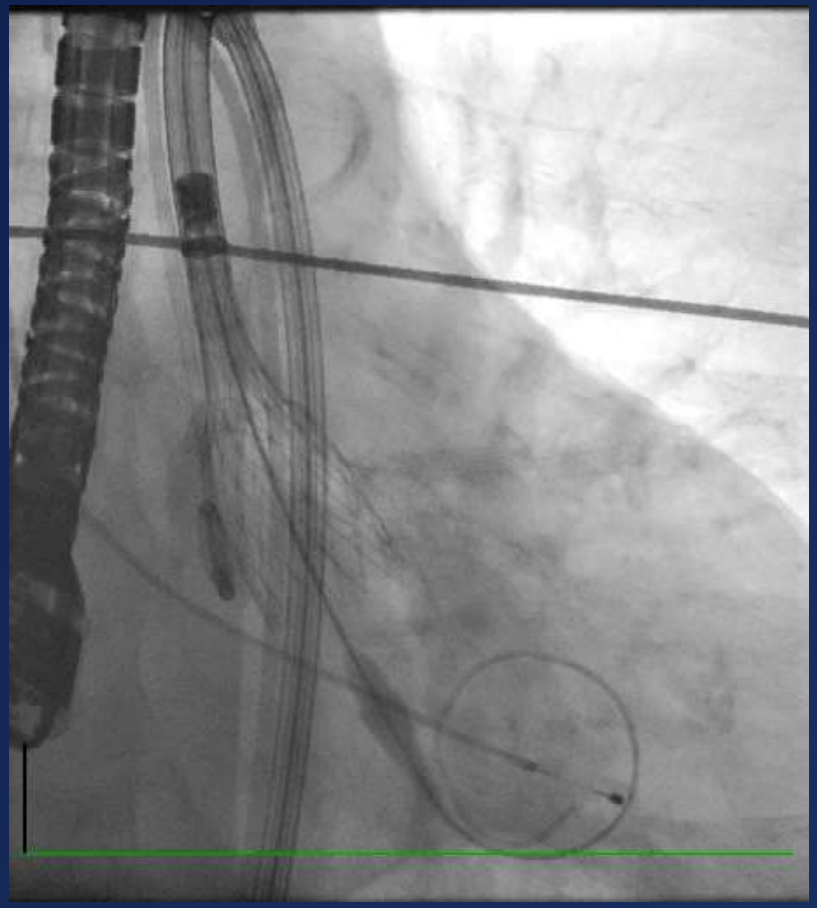


Mathew Williams, MD, NYU Langone Medical Center

Case Example | Recapture

Valve #2: 26 mm





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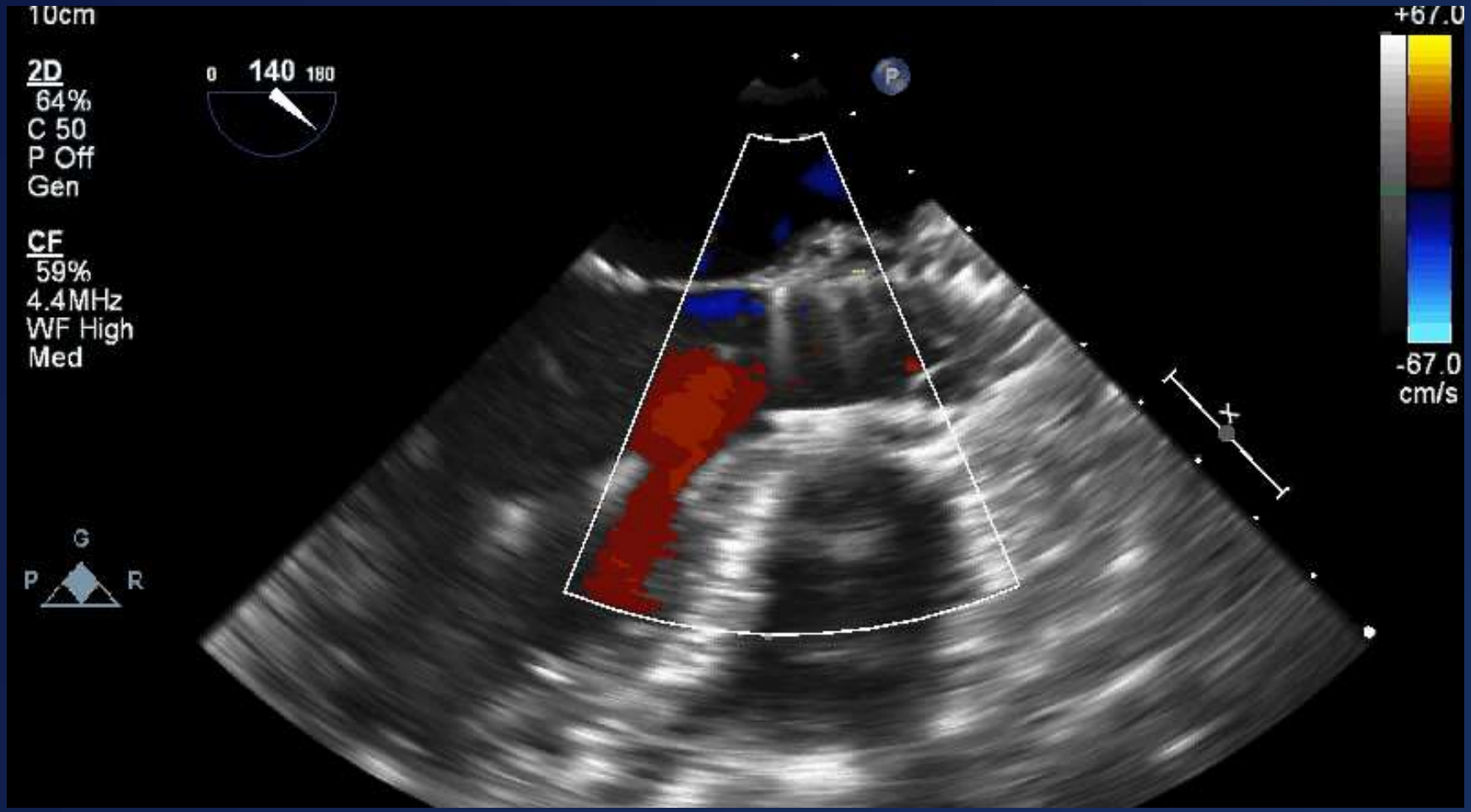
Case Example | Recapture

Valve #2: 26 mm, post-deployment TEE



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The Evidence for Evolut R

Evolut R Clinical Evidence

Medtronic-Sponsored Studies

Evolut R CE Study[1,2]

N = 60
Oct 2013 – July 2014
STS: 7.0 ± 3.7%
Age: 82.8 ± 6.1 years
Female: 66.7%
Diabetes: 26.7%
COPD: 43.3%
PVD: 16.7%
Follow-up through 1 yr

Evolut R US Study[3]

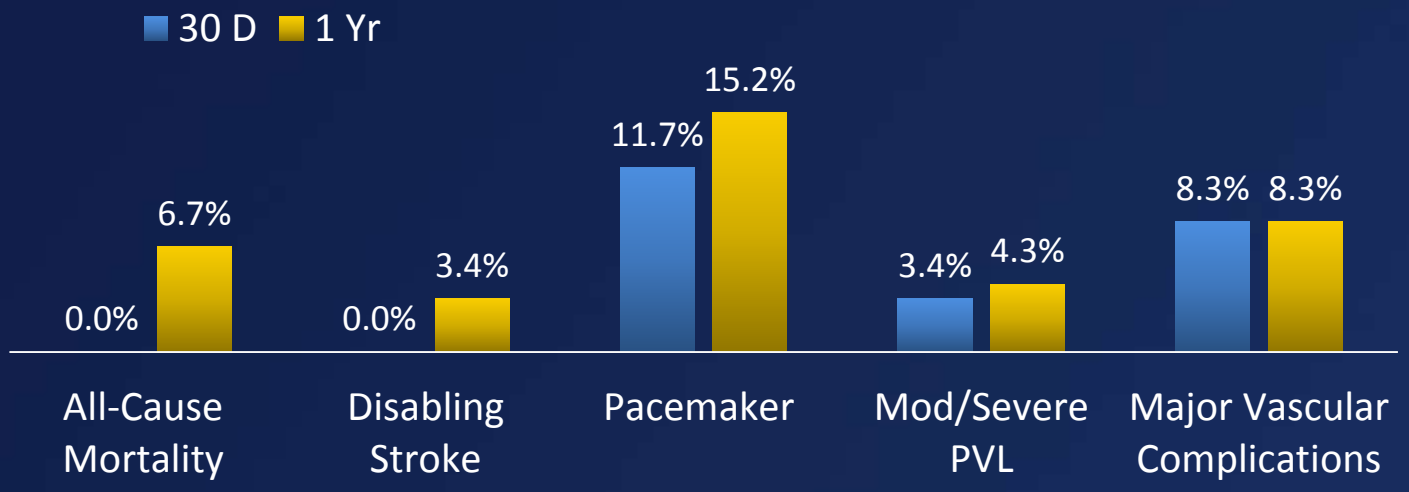
N = 241
Sept 2014 – July 2015
STS: 7.4 ± 3.4%
Age: 83.3 ± 7.2 years
Female: 68.5%
Diabetes: 32.4%
COPD: 54.0%
PVD: 34.9%
Follow-up through 30 d

[1]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67;[2]Manoharan, et al., presented at TCT 2015; [3]Williams, et al., presented at ACC 2016

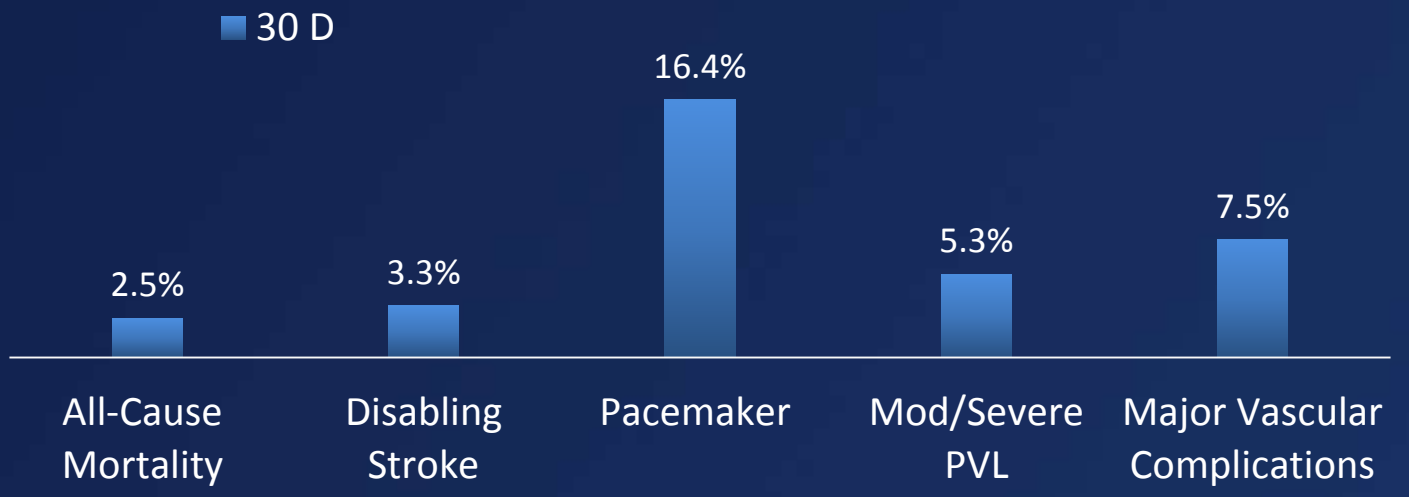
Evolut R Clinical Evidence

Medtronic-Sponsored Studies

Evolut R CE Study
N=60



Evolut R US Study
N=241



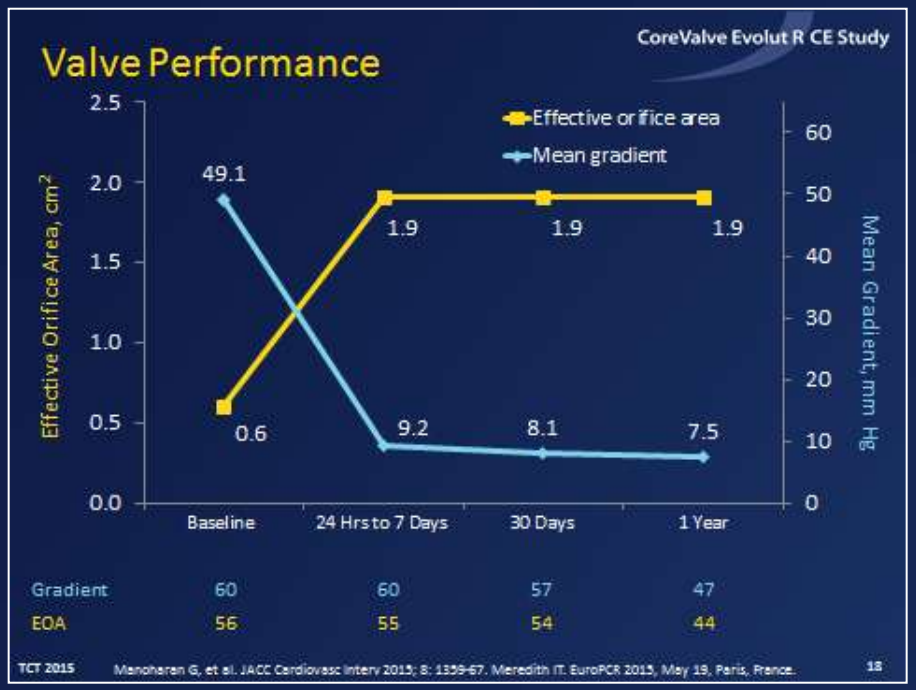
[1]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67;[2]Manoharan, et al., presented at TCT 2015; [3]Williams, et al., presented at ACC 2016;

Evolut R Clinical Evidence

Medtronic-Sponsored Studies

Exceptional forward-flow hemodynamics in both studies

Evolut R CE Study
N=60



Evolut R US Study
N=241

[1]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67;[2]Manoharan, et al., presented at TCT 2015; [3]Williams, et al., presented at ACC 2016;

Evolut R Clinical Evidence

Real-World Experience

REPLACE Registry[1]

N = 103
STS: 5.0 ± 3.7%
Age: 82
Female: 63%

UK and Ireland Evolut R Implanters Registry[2]

N = 240
STS: 6.0 ± 5.6%
Age: 81.2 years
Female: 61.6%

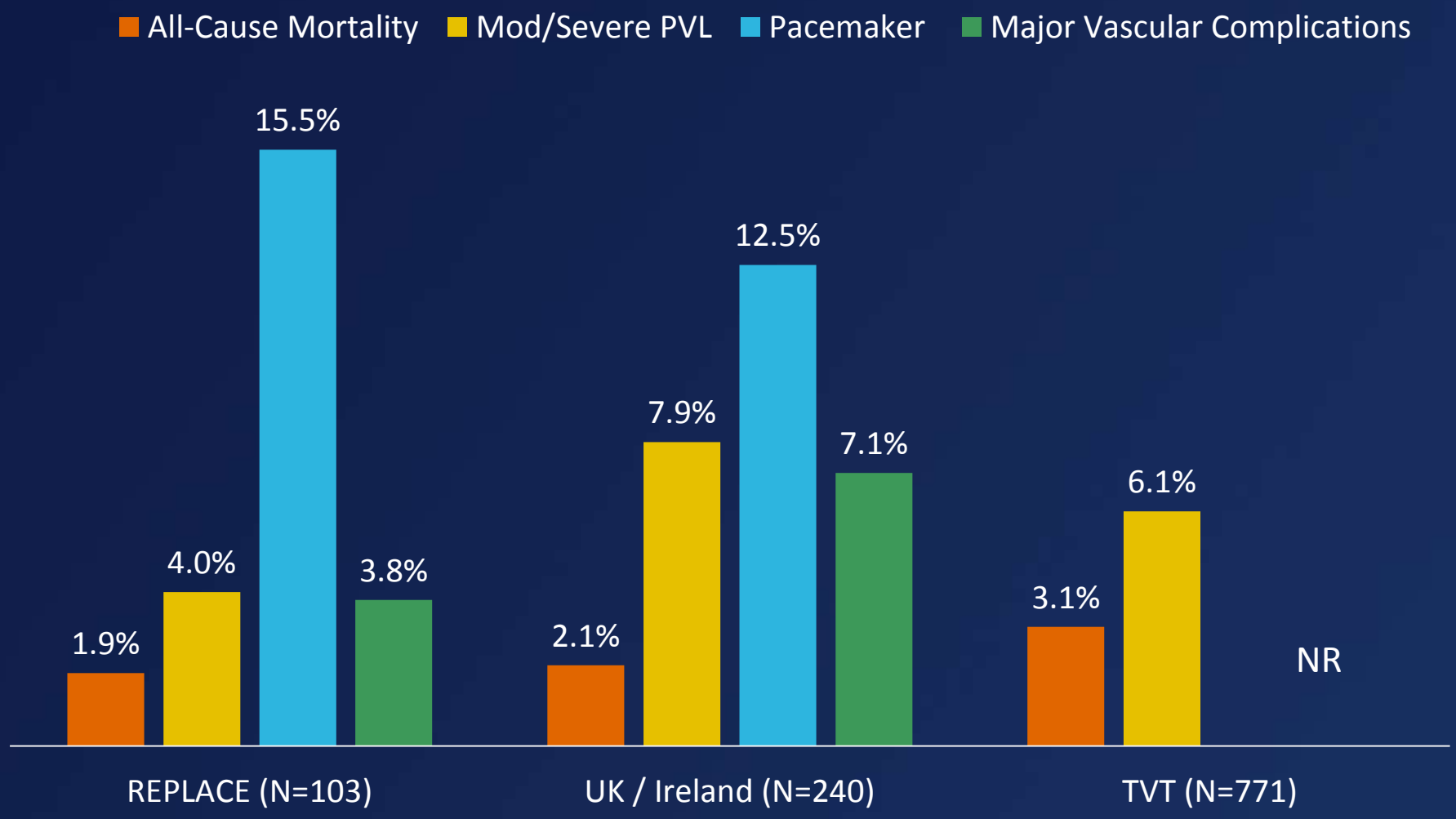
TVT Registry[3]

N = 771
STS: 8.0 ± 4.8%
Age: 81.2
Female: 63.7%

[1]Barbanti, et al., presented at EuroPCR 2016; [2]Kalra, et al., presented at EuroPCR 2016; [3]Williams, et al., presented at ACC 2016

Evolut R Clinical Evidence

Real-World Experience | 30-Day Outcomes



[1]Barbanti, et al., presented at EuroPCR 2016; [2]Kalra, et al., presented at EuroPCR 2016; [3]Williams, et al., presented at ACC 2016

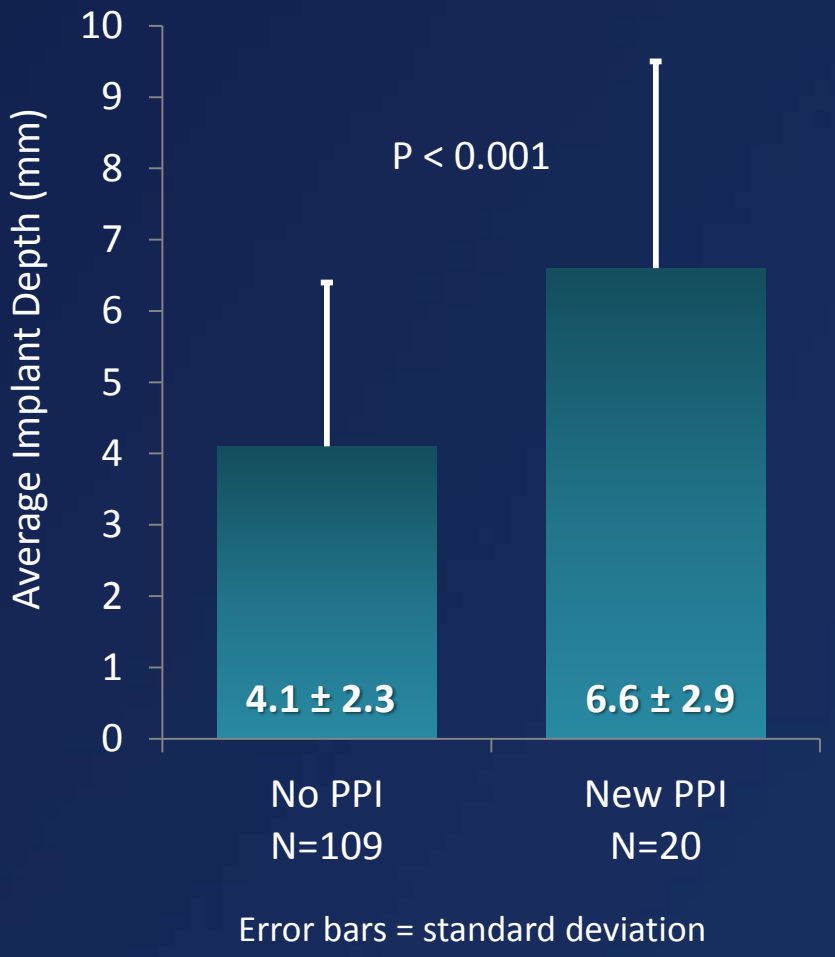
Utility of Repositioning | Importance of Controlling Implant Depth

Predictors of Permanent Pacemakers

Evolut R Sub-Analysis

- A Medtronic-sponsored sub-analysis was performed to find predictors of permanent pacemakers in a cohort of 151 Evolut R patients
- 22 patients with a pacemaker at baseline were excluded
- Of the remaining 129 patients, 20 required a new pacemaker
- The implants were significantly deeper in these patients

New Permanent Pacemaker Rate at 30 Days: 15.6% (n=20)

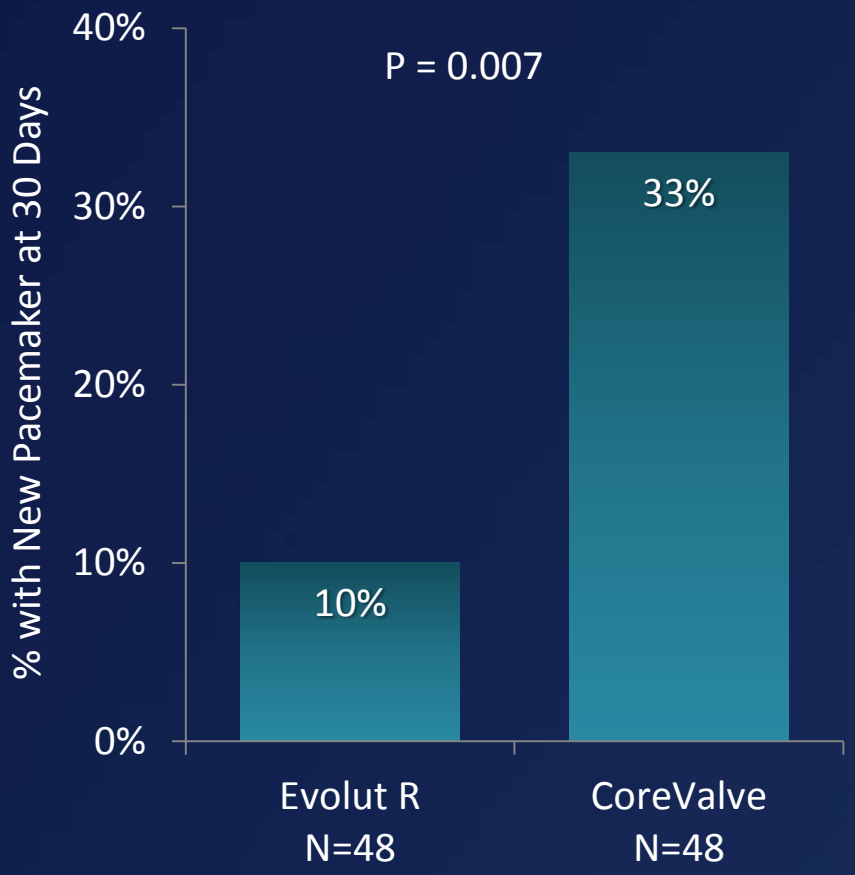


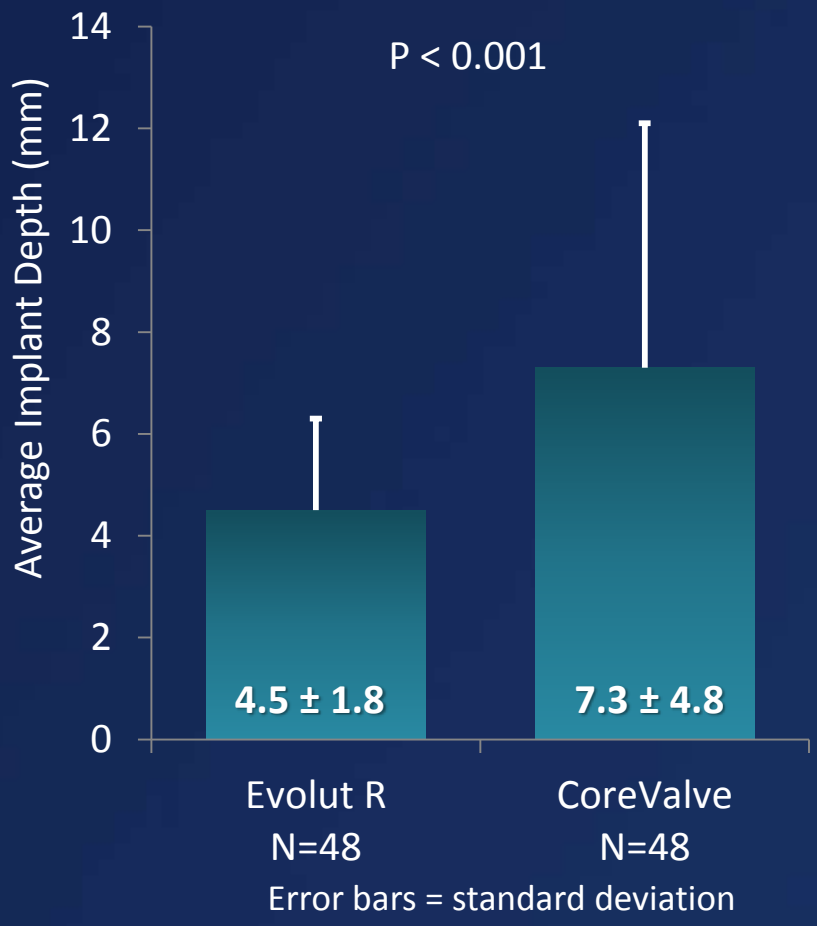
[1]Meredith, et al., presented at EuroPCR 2016

Predictors of Permanent Pacemakers

Real-World Experience with Evolut R

- Fiorina, et al., from Brescia, Italy, showed similar results
- In a propensity-matched comparison of CoreValve to Evolut R, the pacemaker rate was significantly less with Evolut R, driven by a shallower implant depth





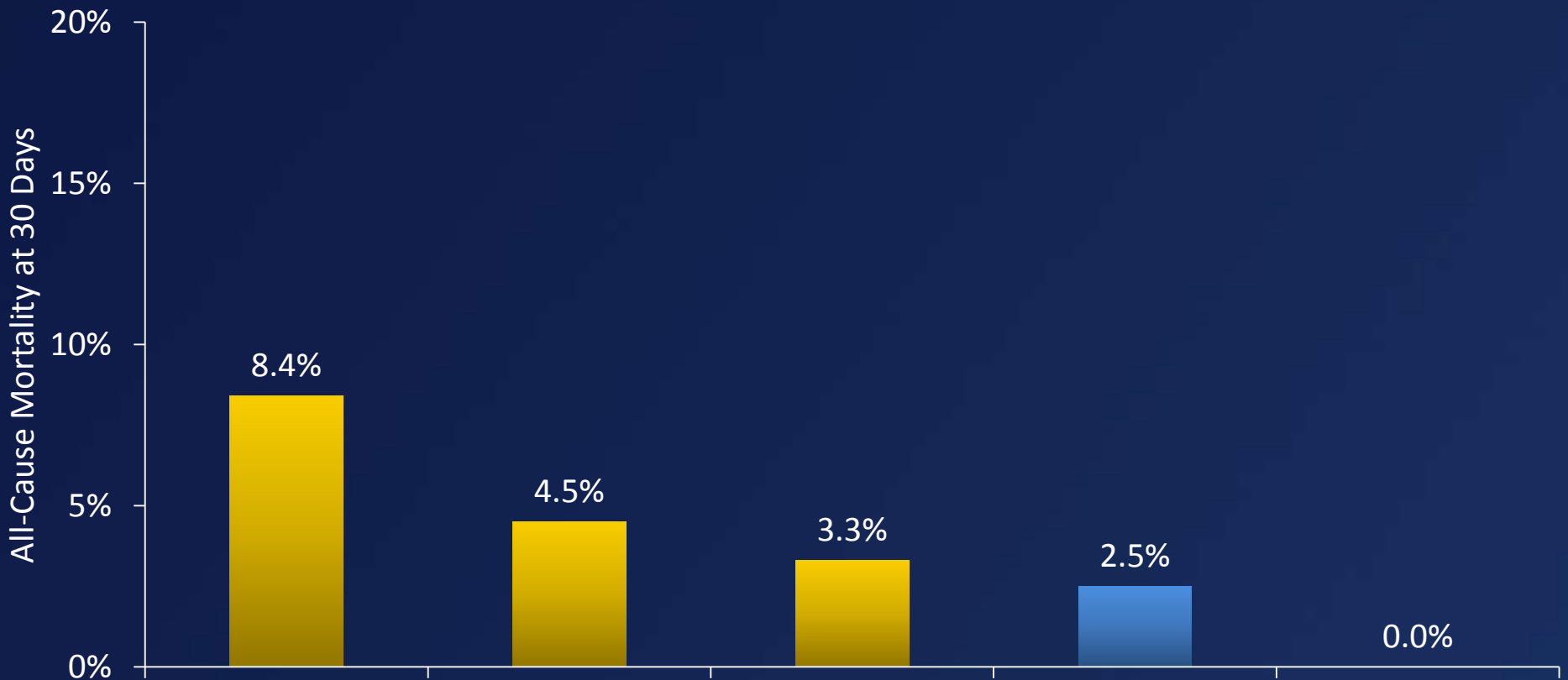
[1]Fiorina, et al., presented at EuroPCR 2016

Clinical Evidence for Evolut R

Clinical trial and real-world data shows that Evolut R produces excellent clinical outcomes.

How does it compare to CoreValve results from Medtronic-sponsored studies?

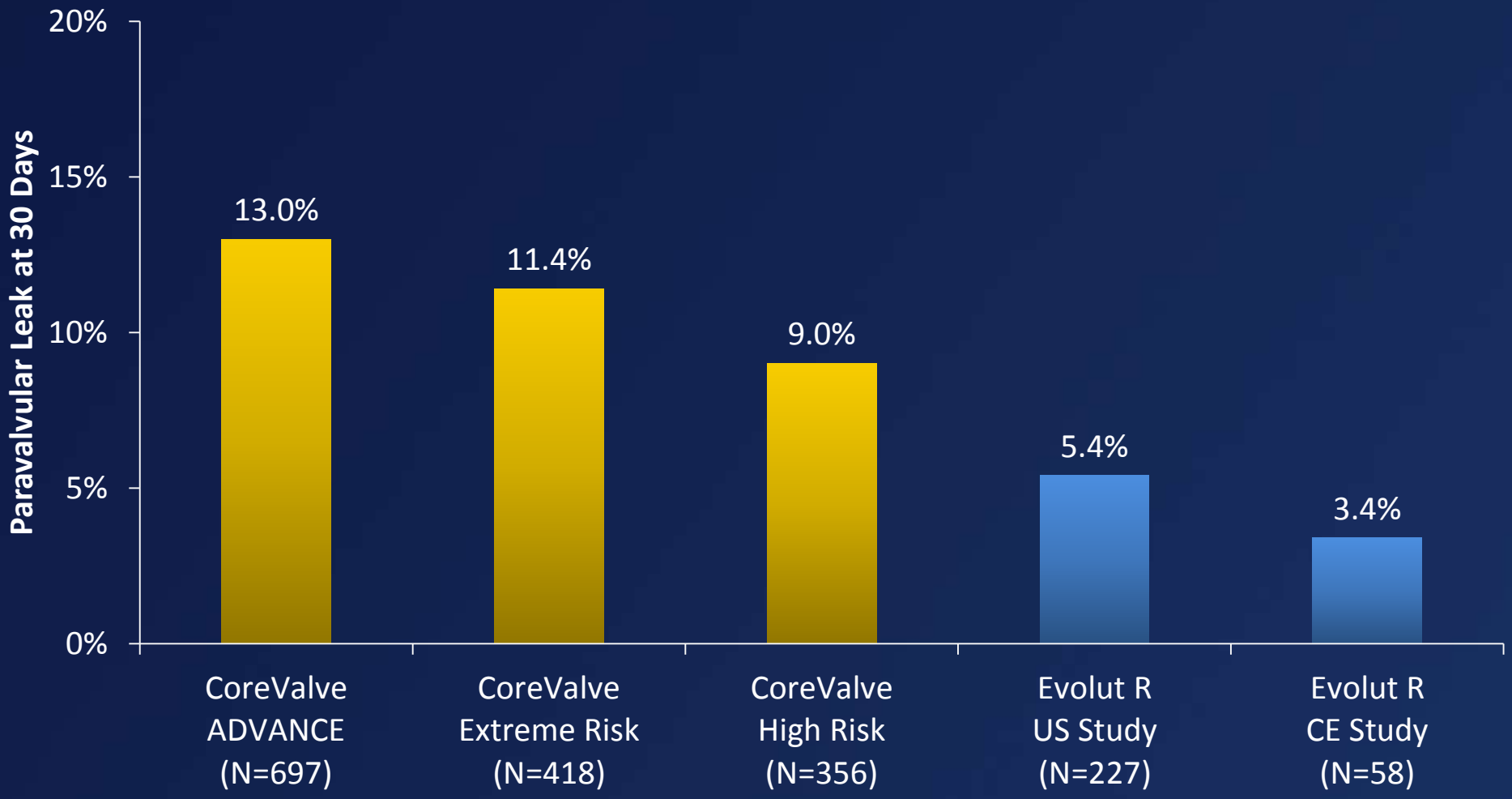
All-Cause Mortality at 30 Days



STS (%)	10.3	6.4	7.3	7.4	7.0

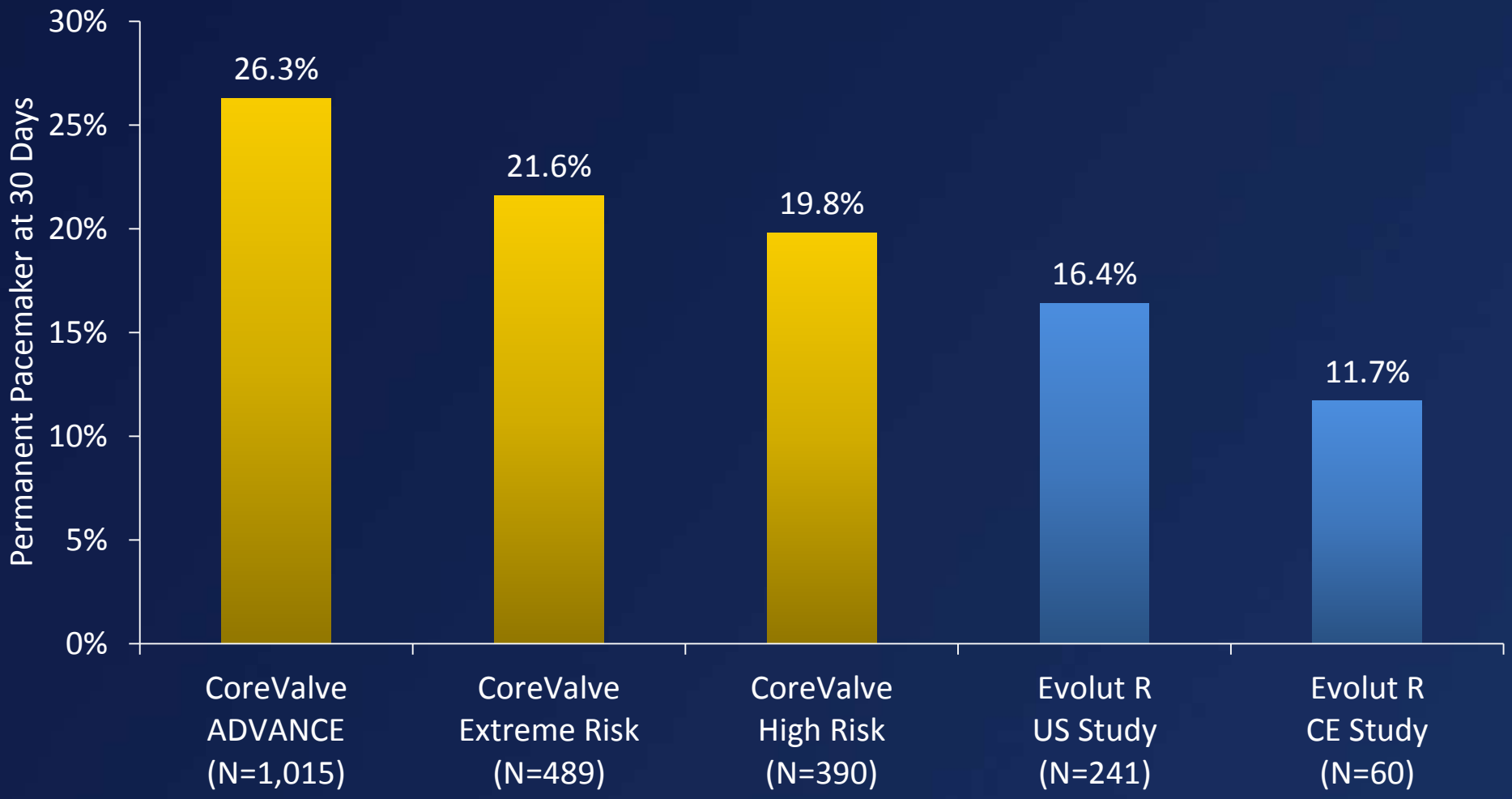
[1]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [2]Linke, et al. , *Eur Heart J* 2014; 35: 2672-84; [3]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [4]Williams, et al., presented at ACC 2016; [5]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67;

Paravalvular Leak at 30 Days



[1]Linke, et al. , *Eur Heart J* 2014; 35: 2672-84; [2]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [3]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [4]Williams, et al., presented at ACC 2016; [5]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67

Permanent Pacemaker Rate at 30 Days



[1]Linke, et al. , *Eur Heart J* 2014; 35: 2672-84; [2]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [3]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [4]Williams, et al., presented at ACC 2016; [5]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67

Summary

- Evolut R is built on the foundational self-expanding CoreValve platform, with a reduced delivery profile and the ability to recapture and reposition the valve.

- Data is now available on over 1,000 patients treated with this system.

- In both the clinical trial and real-world settings, Evolut R brings:
  - Low 30-day all-cause mortality
  - Reduced paravalvular leak and permanent pacemaker rate
  - Exceptional forward-flow hemodynamics

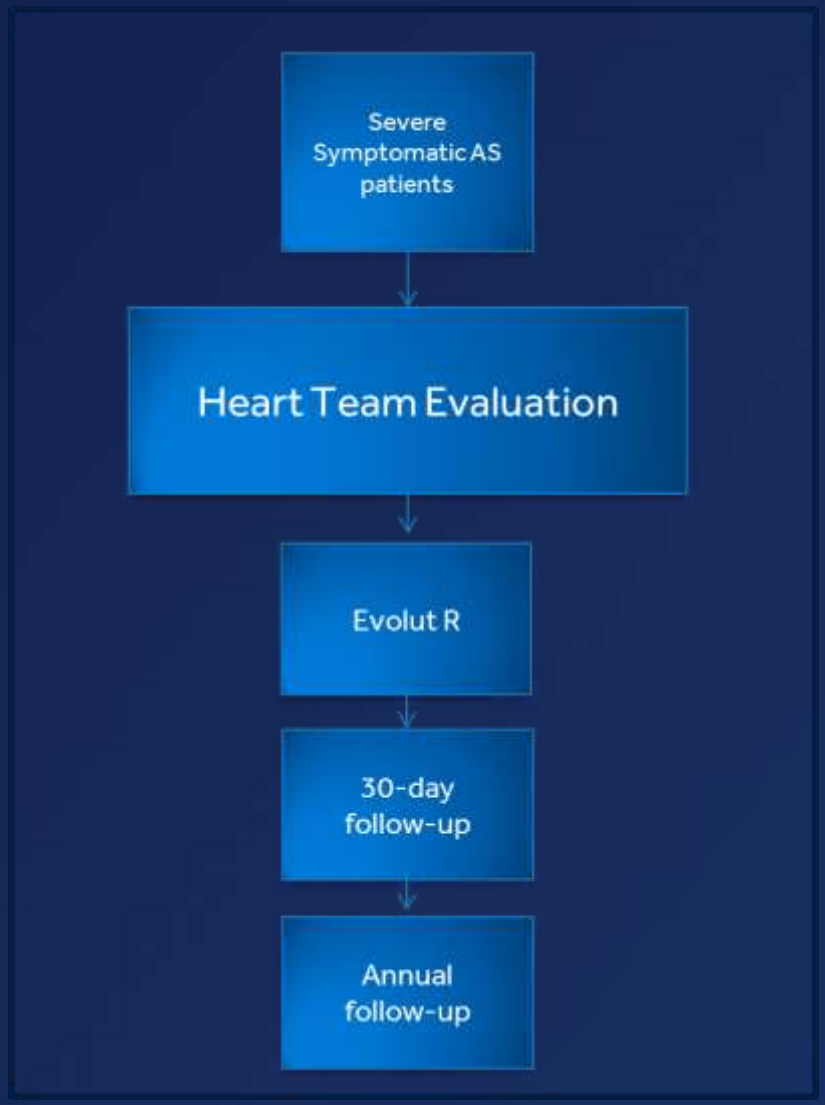
- Most importantly, iterative design changes have led to incremental improvement in all safety outcomes.

Medtronic Evolut R
Current Clinical Trials

Evolut R FORWARD Study

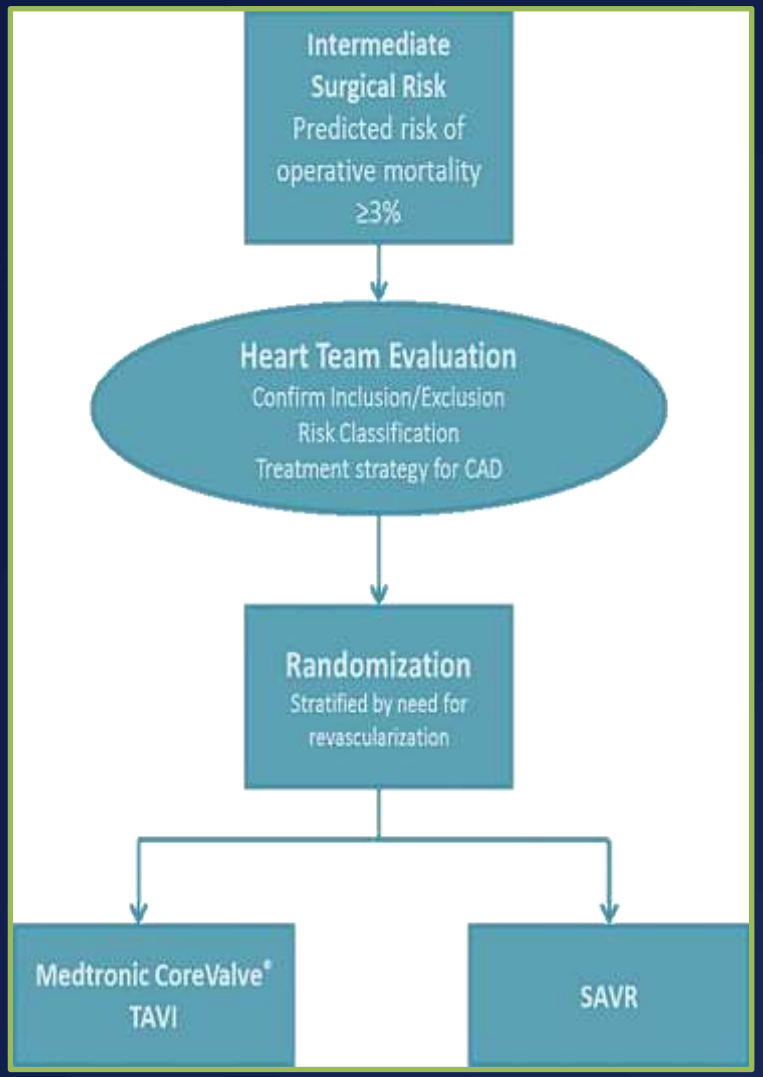
Global Post-Market Study

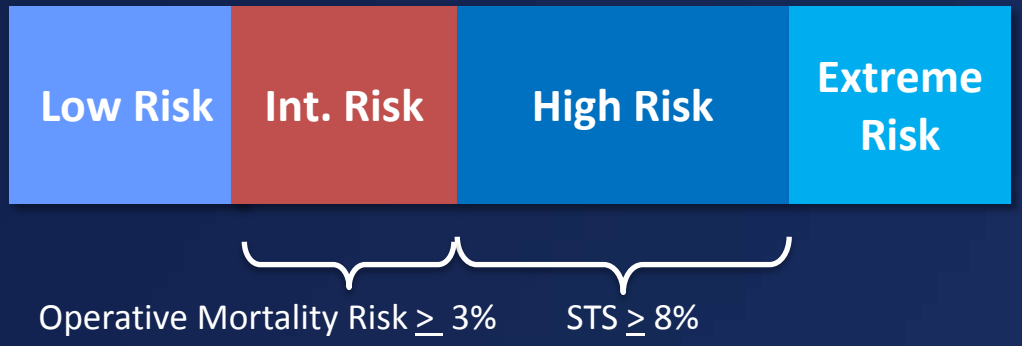
- **Patient Population:**
  - IFU indicated - severe symptomatic AS patients
  - Determined by Heart Team
- **Primary Objective:**
  - Develop safety and efficacy of TAVI evidence with Evolut R
- **Follow-up Evaluations:**
  - 30-days and annual follow-up
- **Sample Size: 1000 Subjects**
- **Number of Sites: 60**



SURTAVI

Randomized Trial for Intermediate Risk Patients





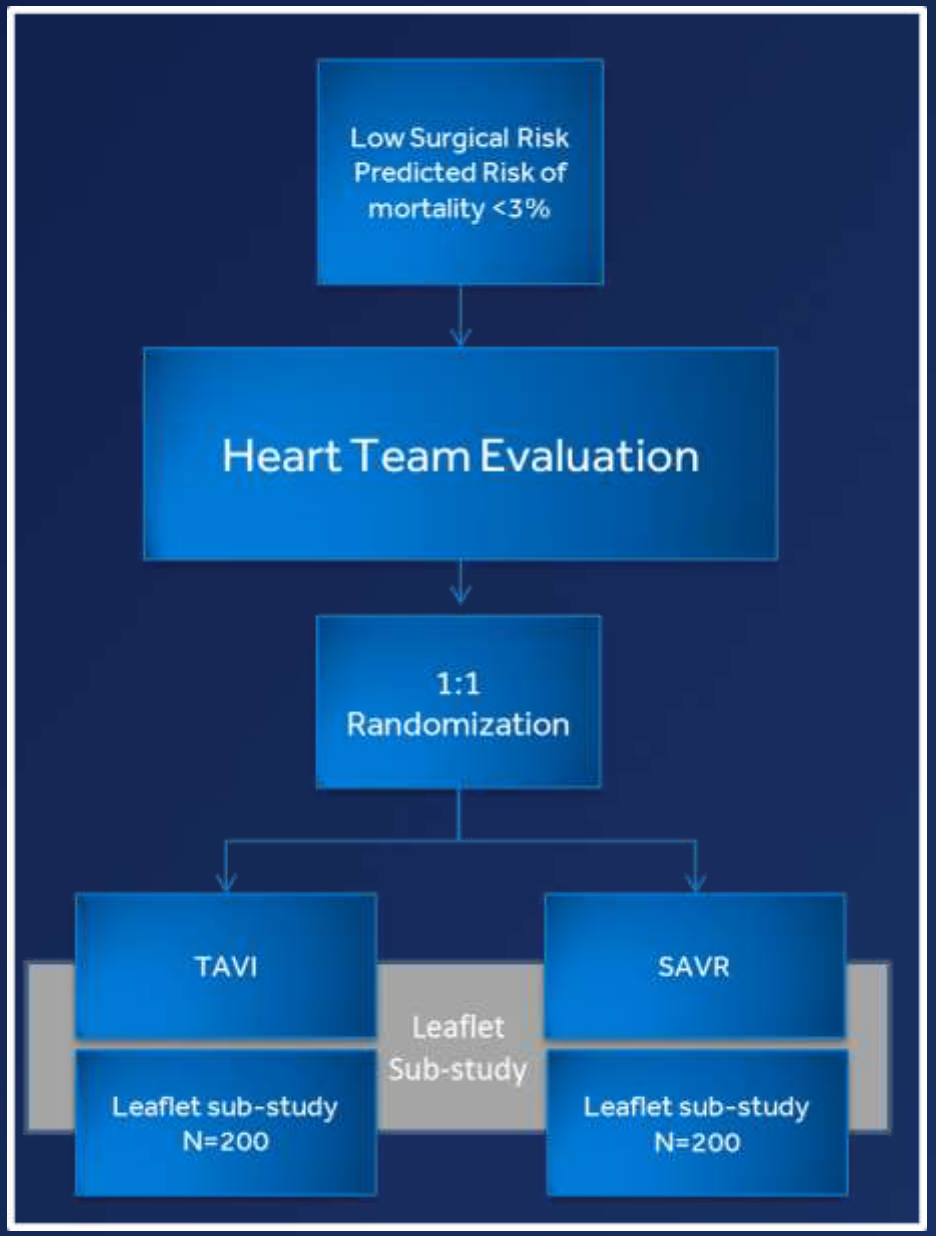
SURTAVI Study Status

- Study includes CoreValve and Evolut R
- Randomization completed in May 2016
- Plan to present at ACC 2017
- Submit for approval 1H CY17

Medtronic TAVR in Low Risk Patients

Trial Design

- **Patient Population: Low Risk Cohort**
  - Determined by Heart Team to be low surgical risk
- **Primary Endpoint:**
  - Safety: Death, all stroke, life-threatening bleeding, major vascular complications, or AKI at 30 days
  - Efficacy: Death or major stroke at 2 years
  - (One year analysis for early FDA submission)
- **Sample Size: ~1200 Subjects**
- **Follow-up Evaluations:**
  - 30-days, 6-month , 18-month, and 1 Through 5 years
- **Number of Sites: Up to 80**



Medtronic Evolut R 34mm

Extending Unsurpassed Hemodynamic Performance to All Patients

Evolut R 34mm

26 27 28 29 30

Patient Annulus Diameter Range (mm)

Evolut 34R Clinical Study

Indication	ER / HR Patients
Clinical Design	Single-arm, N=60 30-day Endpoint
Study Start/ Duration	**NOW ENROLLING** 6-8 months

Medtronic Evolut PRO

Innovating to Improve PVL Performance

Pericardial Tissue Wrap to Continue to Improve PVL Performance

Medtronic TAVR 2.0 Clinical Study

Indication	ER / HR Patients
Clinical Design	Single-arm, N=60 30-day Endpoint
Study Start/ Duration	NOW ENROLLING 6-8 months

Thank you for your kind attention!