What's New In TAVR?

Matthew Saybolt MD, FACC
Medical Director, Structural Heart Disease Program
Hackensack Meridian Jersey Shore University Medical Center

Cors at the Shore 2023

Disclosures

- Advisory board: Medtronic
- Speakers Bureau/Consulting: Abbott, Edwards, Medtronic
- Grant/Research Support: Infraredx

What's New In TAVR

- **Lifetime Management**
- **Durability**
- **Device Improvements**
- **Unique populations, expanding indications, redefining "severe" aortic stenosis**
- **Stroke Prevention**

2023 Cors at the Shore

HOT TOPICS in Lifetime Management Of Aortic Stenosis

1) Understand the durability of valves as well as patient's life expectancy

2) Post-op Pacemakers, conduction delay, PVL, stroke, patient prosthesis mismatch (PPM), structural valve deterioration (SVD), annular/LVOT disruption are bad things

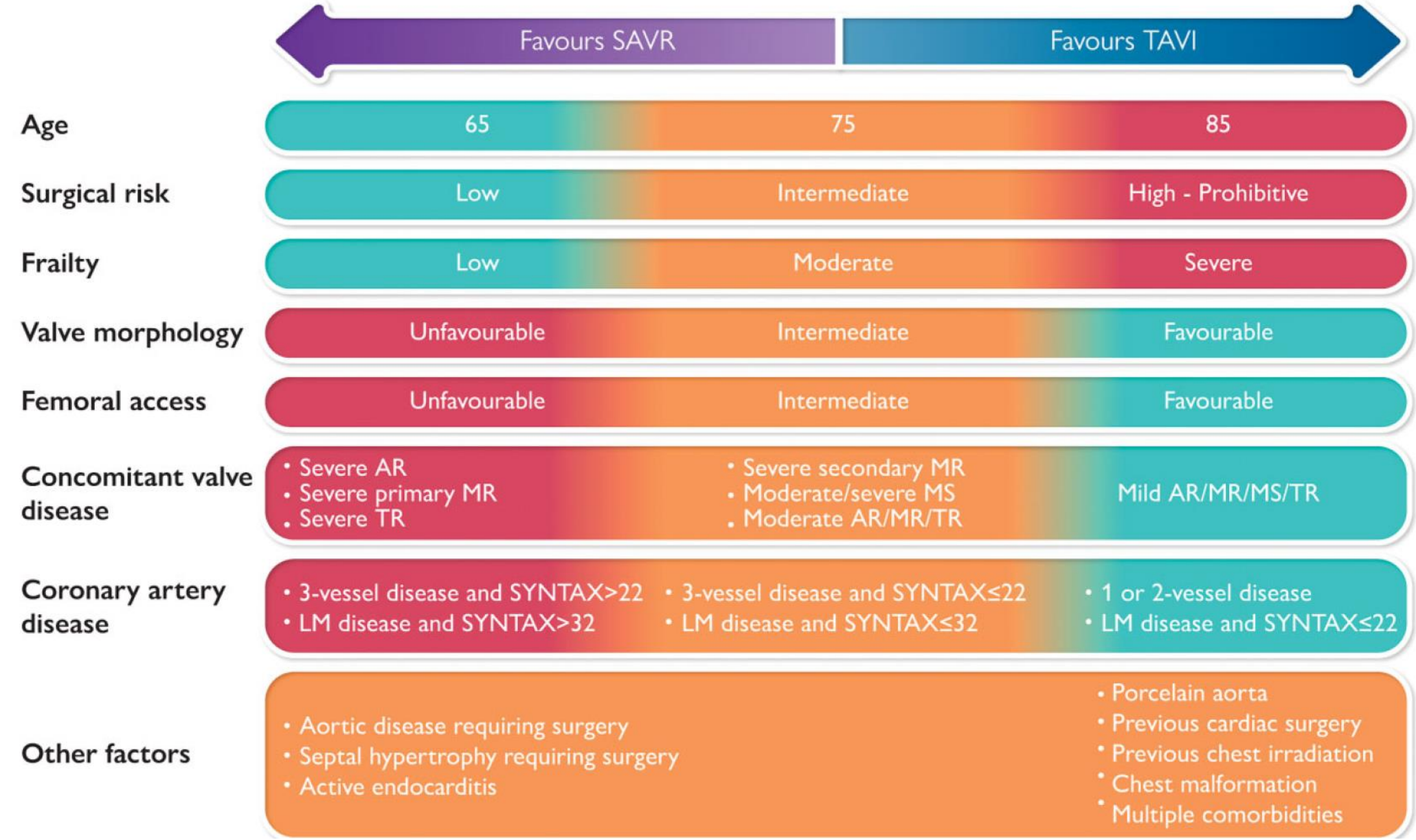
3) CAD is not benign… and it might get worse in the future…

4) The way we treat CAD with PCI or CABG can be dangerous and is not a sure thing
-The additive risk of high-risk PCI to pre-TAVR need to be considered
-Preserving coronary re-access is important (and predicable)
-Achieving commissural alignment is important
-Honesty about longer term patency and what is going to be achieved with PCI or CABG

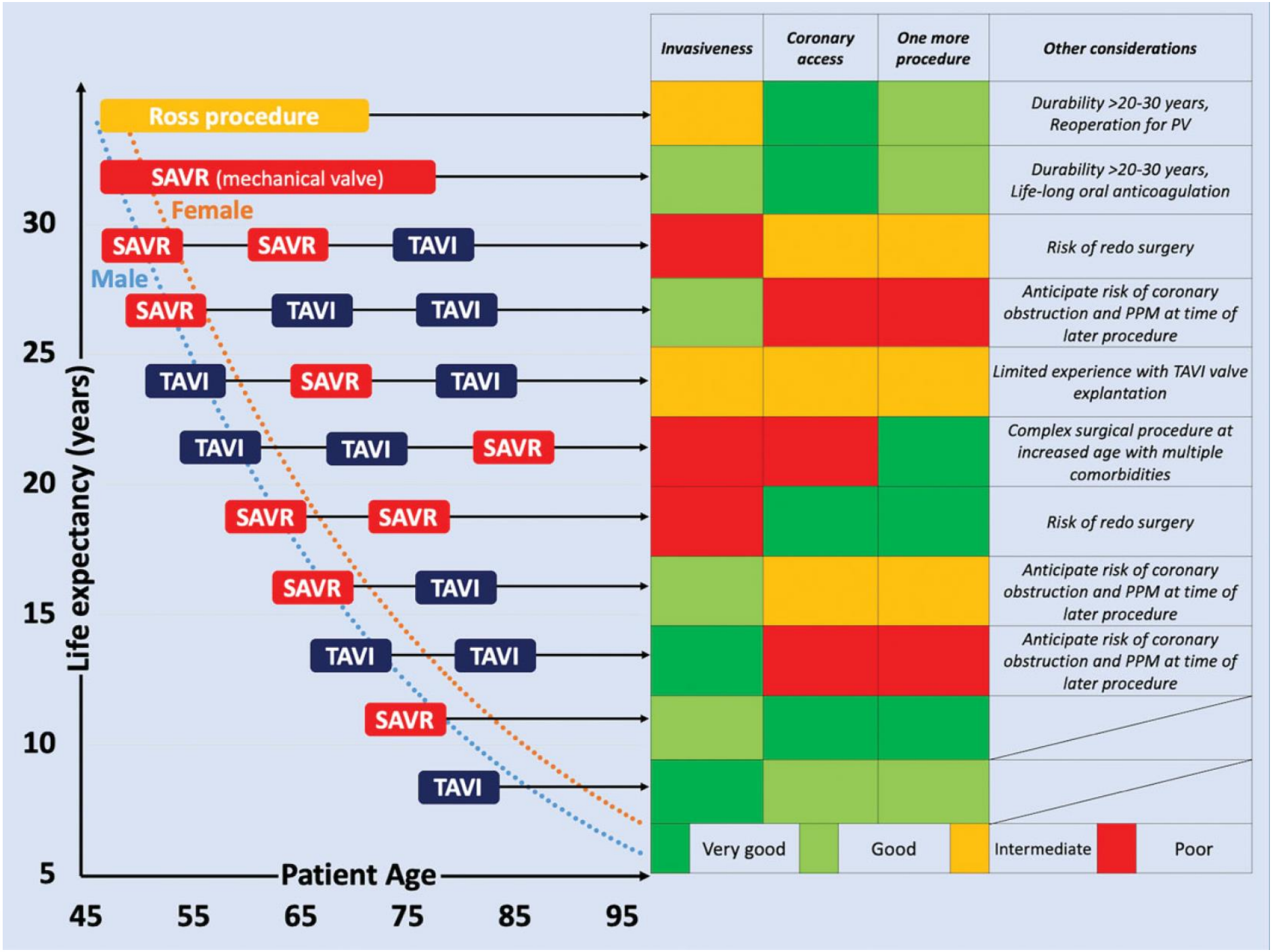
5) Plan and predict NOW for future TAVR in TAVR –vs- TAVR in SAVR –vs- reoperation

6) Avoid high-risk TAVR in low-risk patients…..DON'T discover that SAVR is a bad idea while in the OR

7) ANATOMIC CRITERIA by CT SCAN = Gold Standard



Falk V, et al. European Heart Journal. 2022



Cors at the Shore 2023

Define Durability: Structural Valve Deterioration (SVD)

<u>Pre TAVR era, Surgical Series:</u>

-Define SVD at the time point when surgeon performs a reoperation

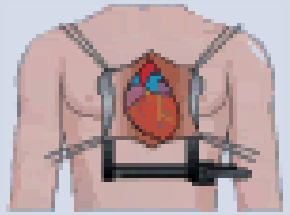
-Given that reoperation does not necessary imply SVD, one would expect a systematic underestimation of the true incidence of SVD, which can be subclinical

-Incomplete echo data, retrospective

2023 Cors at the Shore

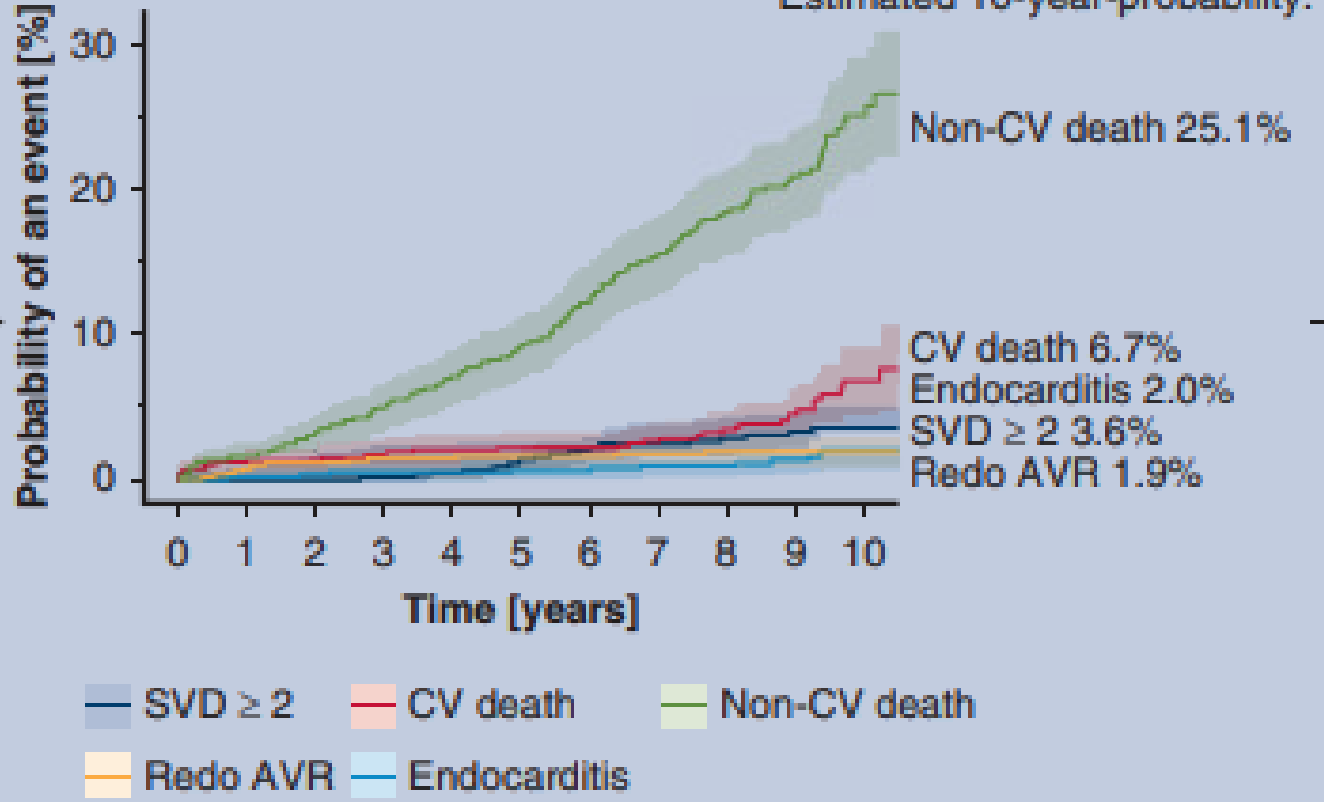
Ten-year Clinical and Echocardiographic Follow-up of Third-Generation Biological Prosthesis in Aortic Position

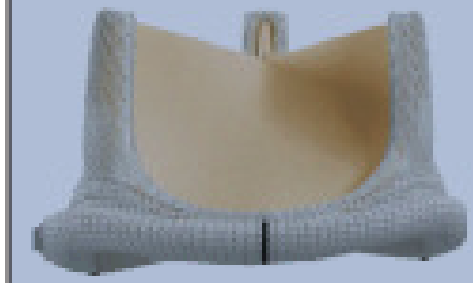
2010-2012:
689 Patients underwent isolated or combined AVR using PME valve



Outcomes after 10 years from implantation were estimated

PME showed a low cumulative incidence of SVD ≥ 2, reoperation, and endocarditis at long-term follow-up





PME prosthesis shows good clinical and echocardiographic long-term outcome

Cors at the Shore 2023

Francica A, et al. The Journal Of Thoracic and Cardiovascular Surgery.2022.

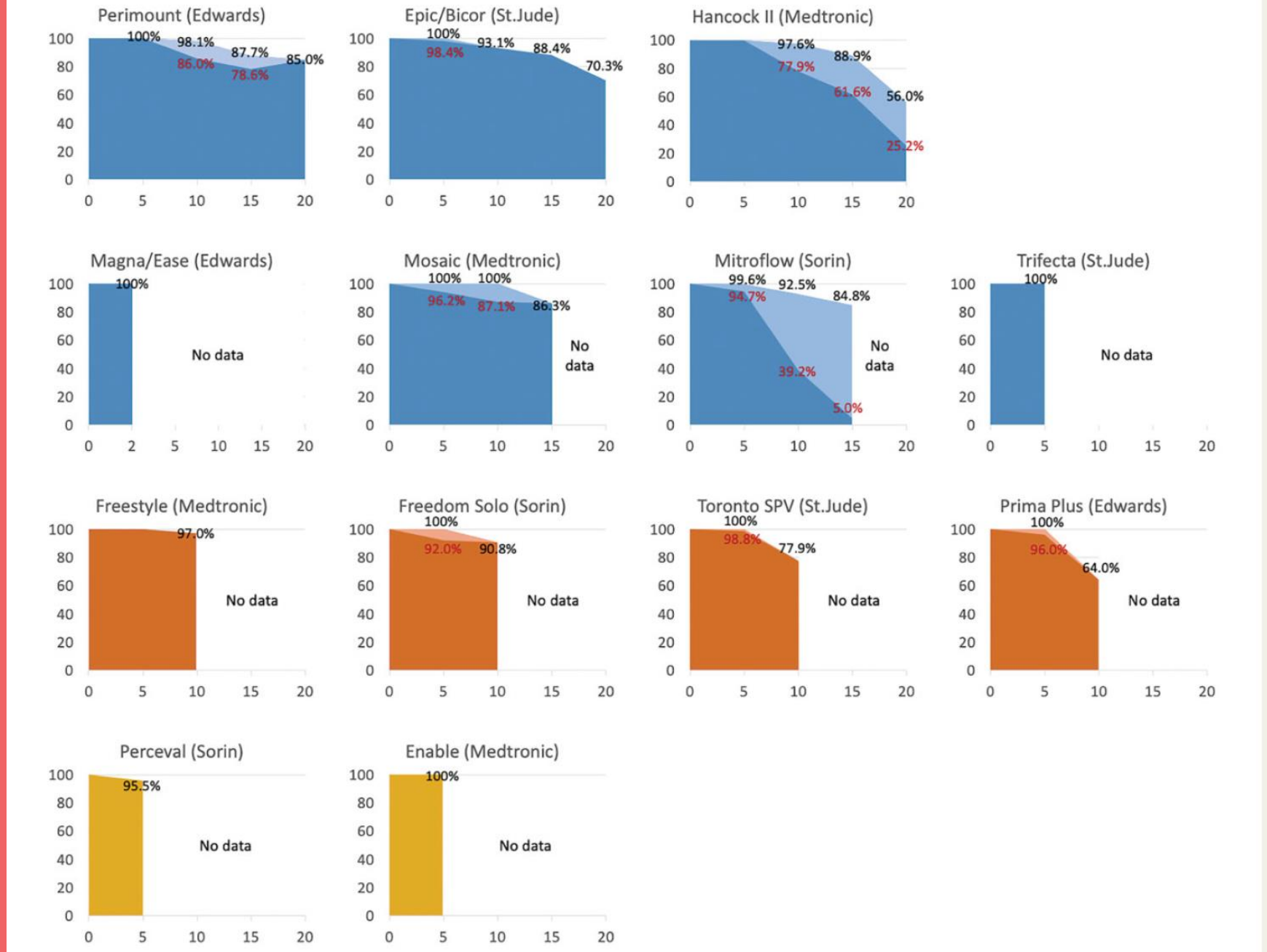


Figure 10 Durability data of surgical aortic bioprostheses. A range of actuarial freedom from SVD for each surgical bioprosthesis, obtained from studies in which these data were available for the whole cohort, is provided.[177]

SVD is unusual (<15%) in 1st decade post SAVR

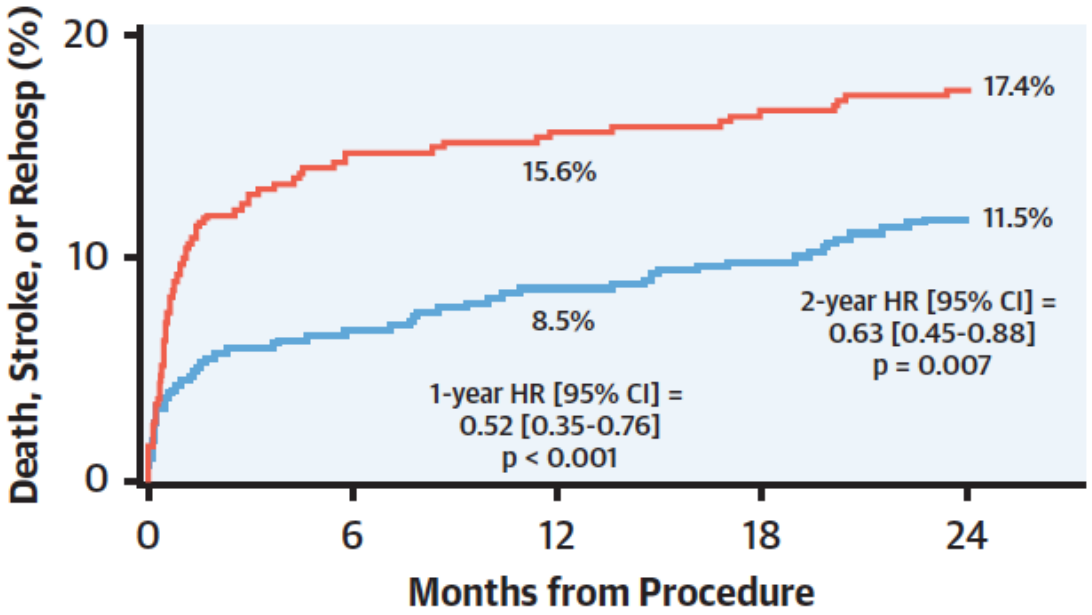
Incidence progressively increases thereafter

No systemic surveillance studies and true incidence of SVD is camouflaged

Falk V, et al. European Heart Journal. 2022

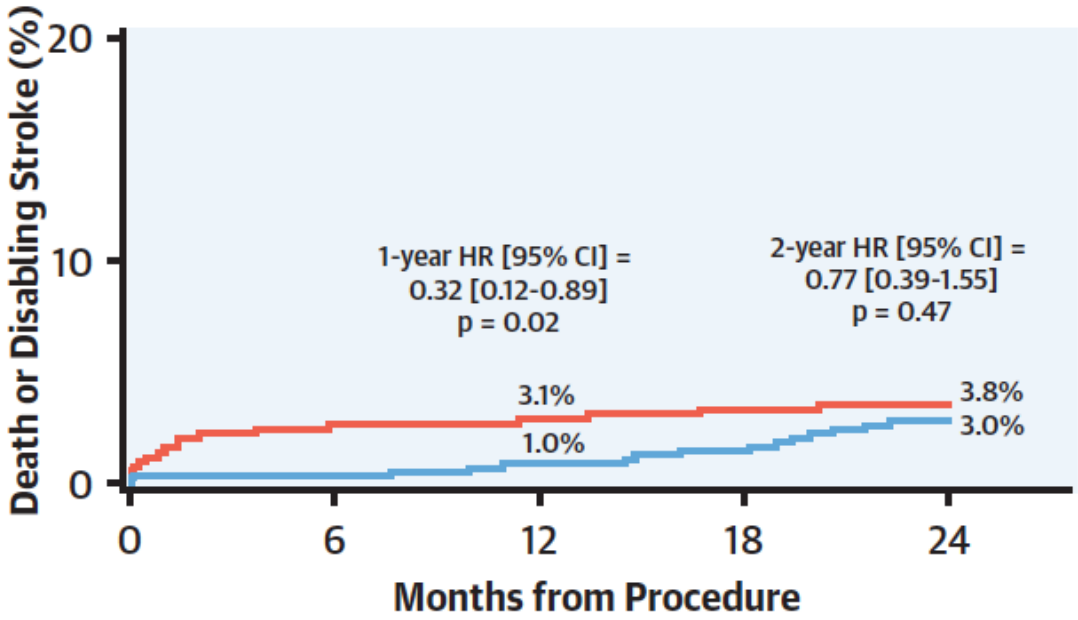
PARTNER 3: 2-year outcomes SAPIEN S3 TAVR vs. SAVR

A



Number at risk:					
Surgery	454	379	371	357	345
TAVR	496	462	453	444	431

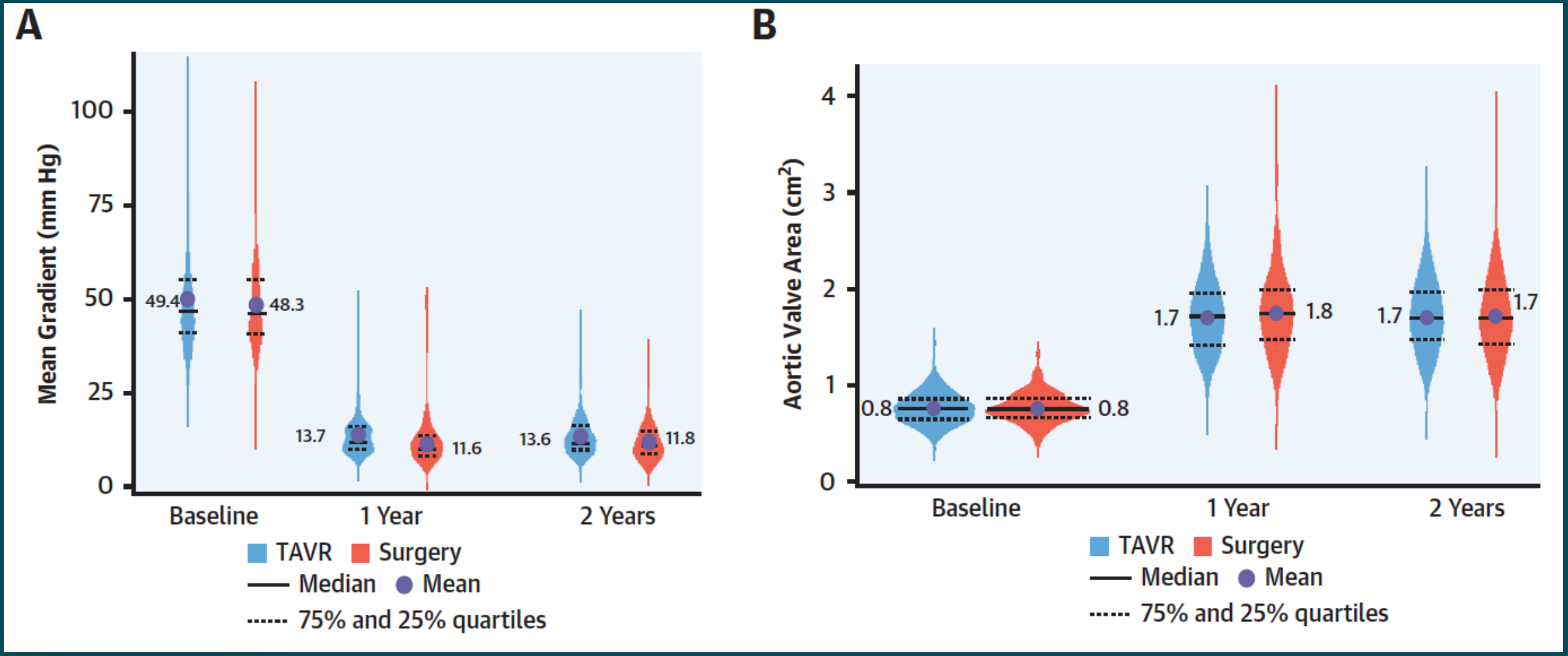
B



Number at risk:					
Surgery	454	431	424	410	400
TAVR	496	493	490	483	472

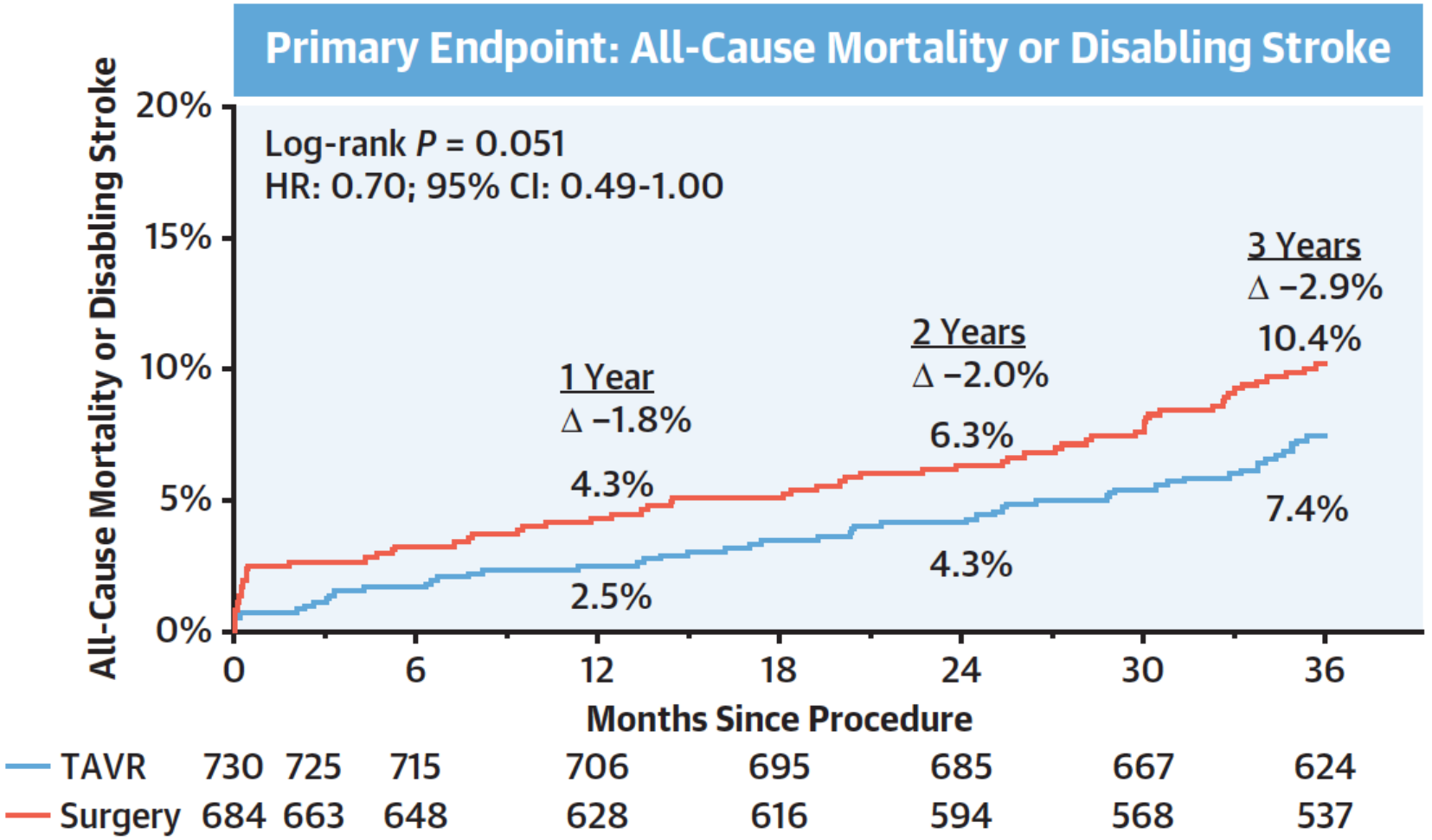
Cors at the Shore 2023

Leon MB, et al. JACC 2021



Cors at the Shore 2023

CENTRAL ILLUSTRATION 3-Year Outcomes From the Evolut Low Risk Trial

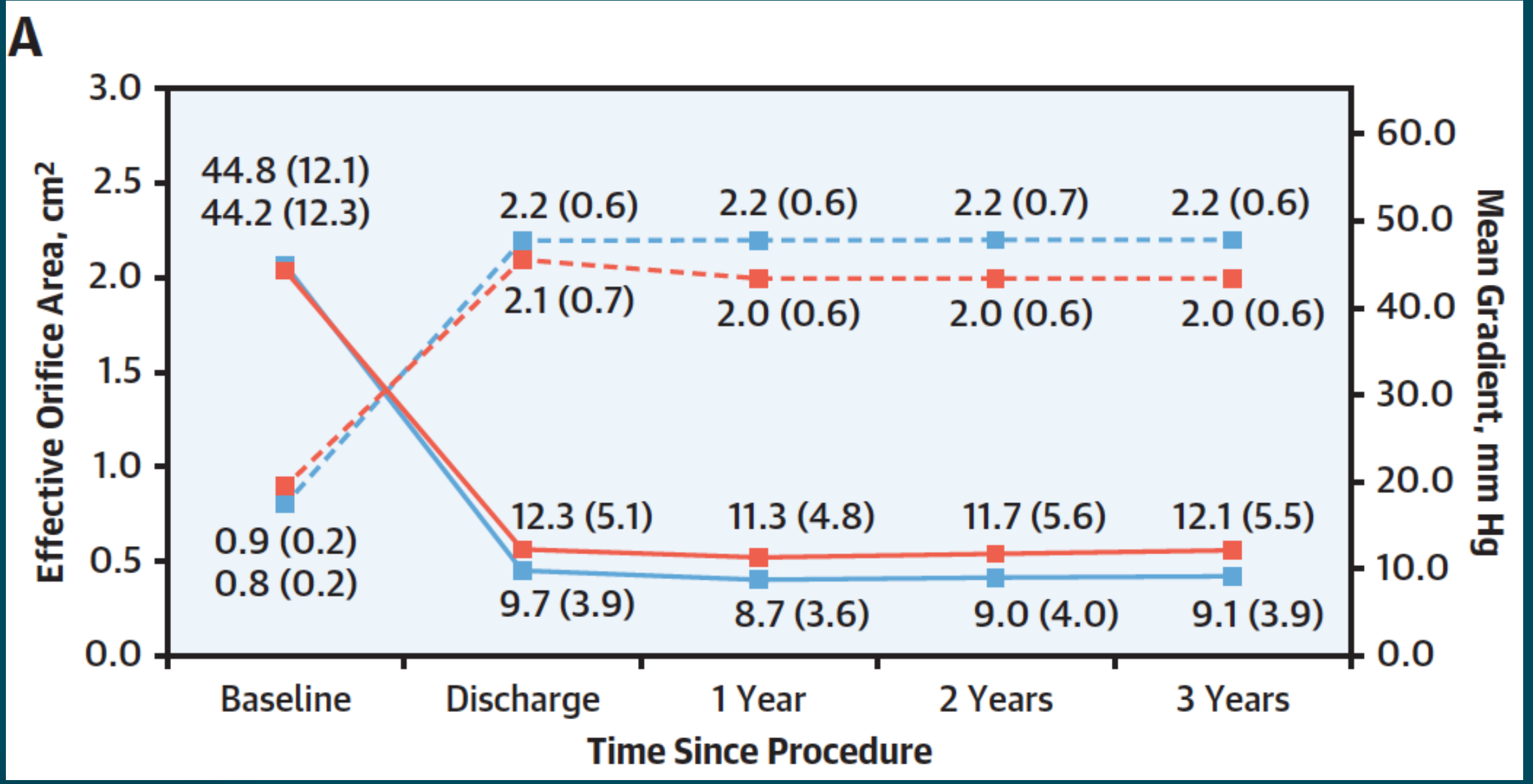


All-cause mortality or disabling stroke was lower with self-expanding TAVR vs surgery at 3 years

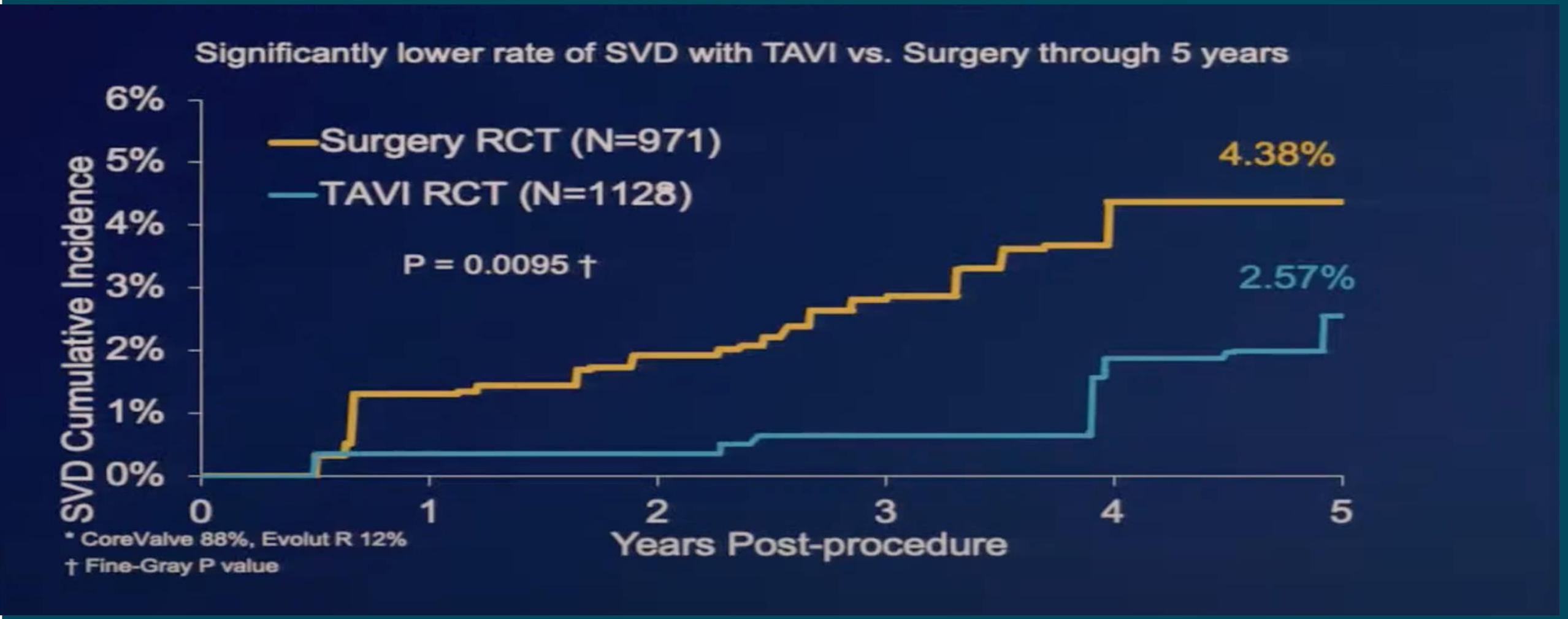
Difference in KM rates for TAVR vs surgery remained broadly consistent over time

Forrest JK, et al. J Am Coll Cardiol. 2023;81(17):1663-1674.

Cors at the Shore 2023



Cors at the Shore 2023



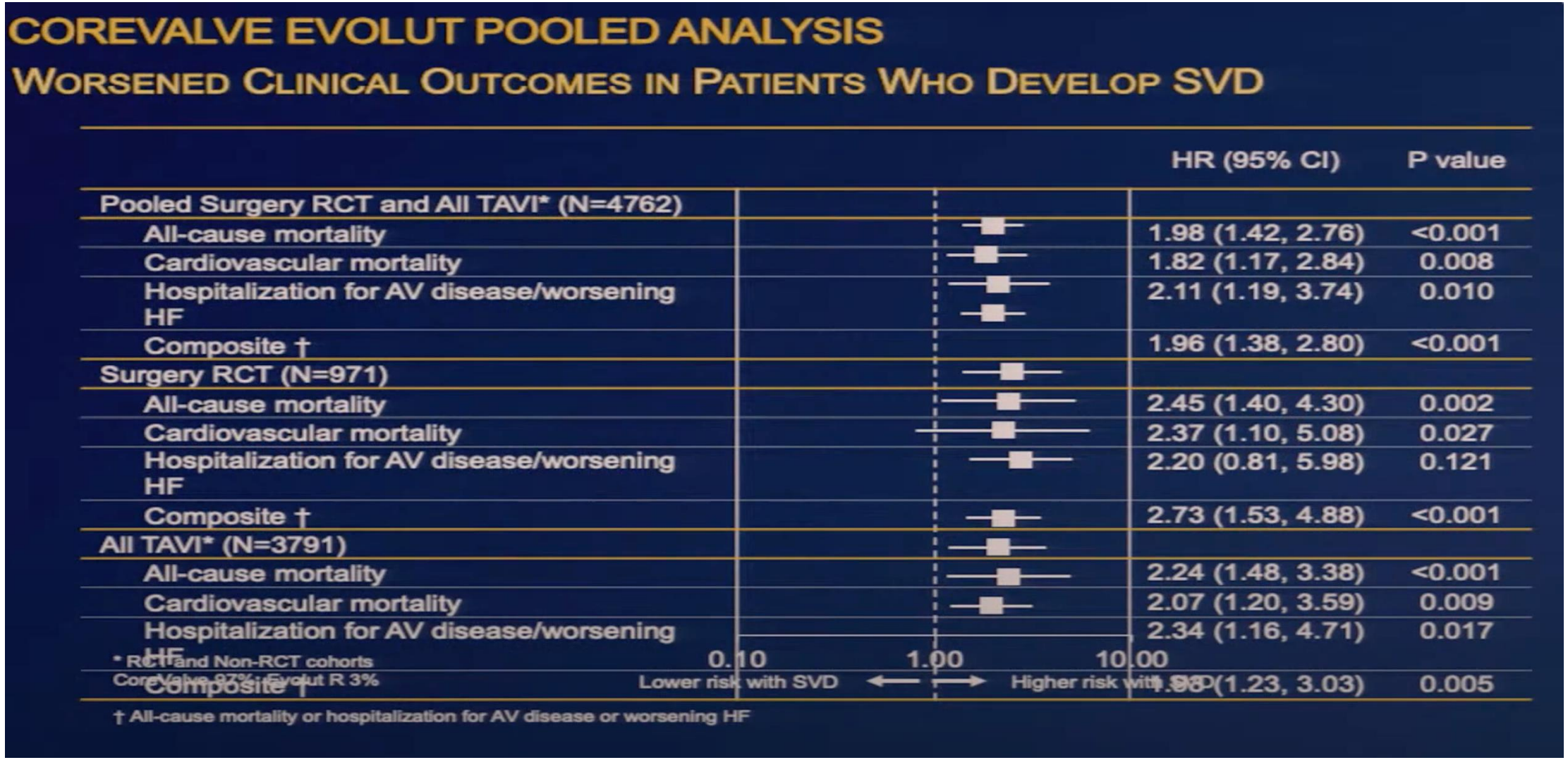
-Pooled data from the CoreValve US High Risk and SURTAVI clinical trials
-at 5 years, there was a 2-fold increase in SVD for patients who had surgery compared with TAVR

Cors at the Shore 2023

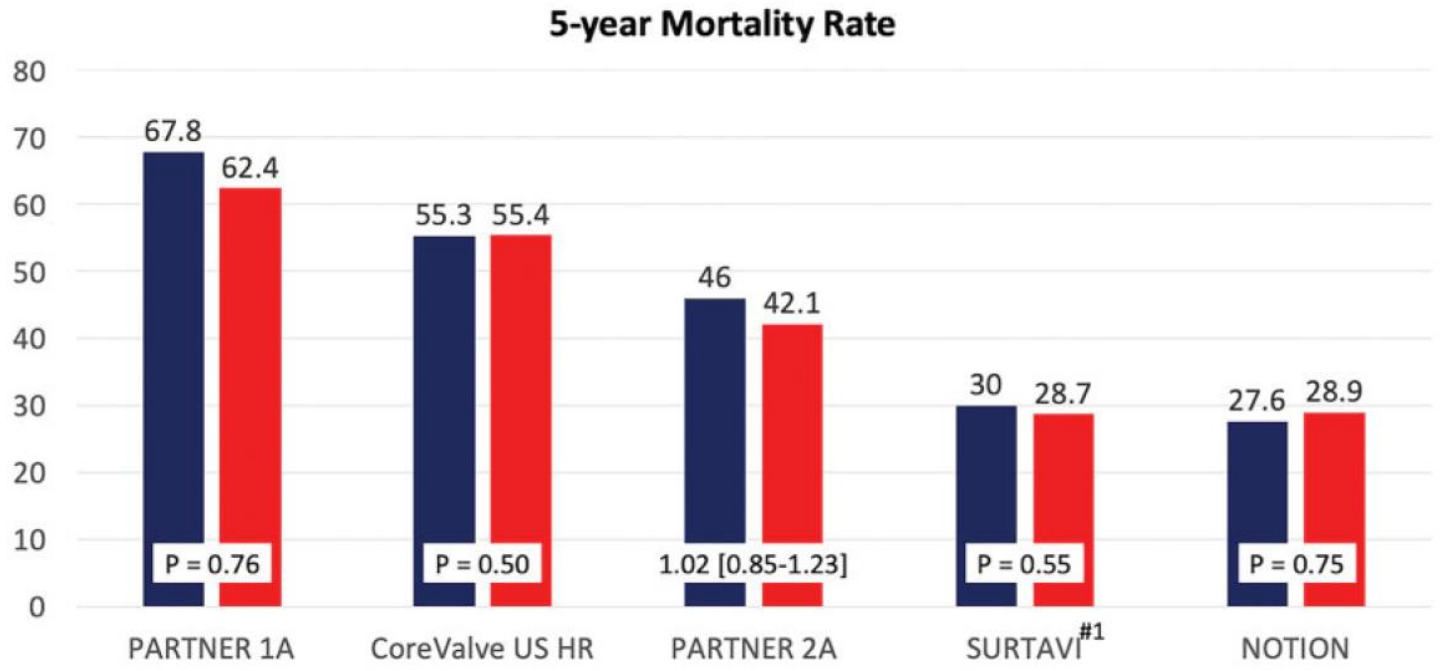
O'Hair D, et al. JAMA Cardiology. 2022

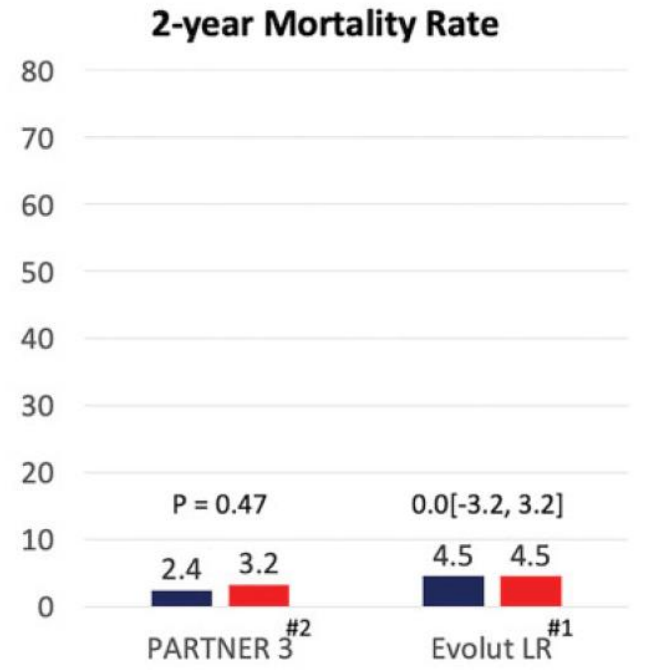
COREVALVE EVOLUT POOLED ANALYSIS

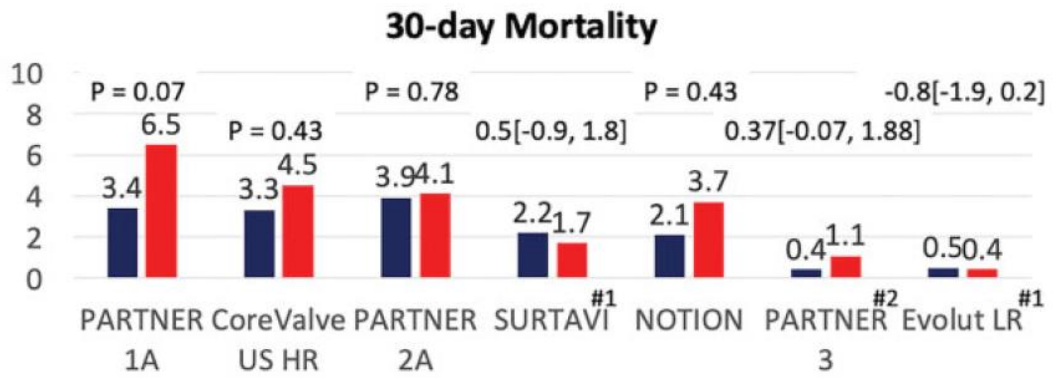
WORSENED CLINICAL OUTCOMES IN PATIENTS WHO DEVELOP SVD

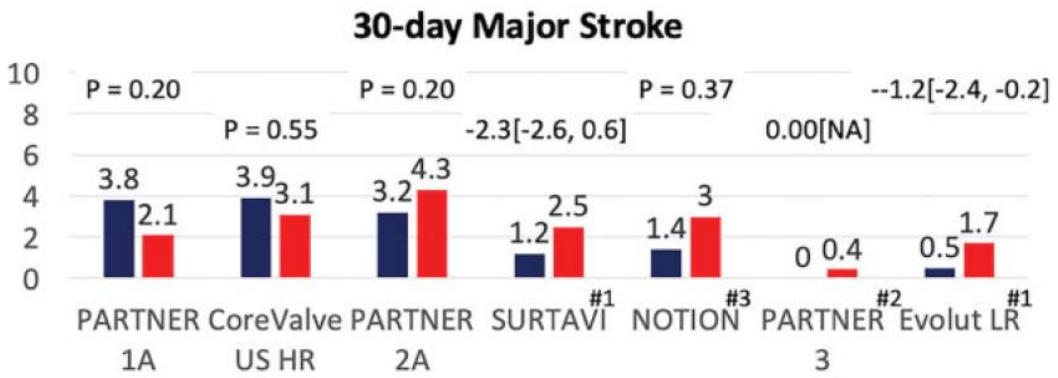


Cors at the Shore 2023


5-year Mortality Rate
80
70
60
50
40
30
20
10
0
67.8
62.4
55.3
55.4
46
42.1
30
28.7
27.6
28.9
P = 0.76
P = 0.50
1.02 [0.85-1.23]
P = 0.55
P = 0.75
PARTNER 1A
CoreValve US HR
PARTNER 2A
SURTAVI#1
NOTION


2-year Mortality Rate
80
70
60
50
40
30
20
10
0
P = 0.47
0.0[-3.2, 3.2]
2.4
3.2
4.5
4.5
PARTNER 3#2
Evolut LR#1


30-day Mortality
10
8
6
4
2
0
P = 0.07
P = 0.43
P = 0.78
0.5[-0.9, 1.8]
P = 0.43
0.37[-0.07, 1.88]
-0.8[-1.9, 0.2]
3.4
6.5
3.3
4.5
3.9
4.1
2.2
1.7
2.1
3.7
0.4
1.1
0.5
0.4
PARTNER 1A
CoreValve US HR
PARTNER 2A
SURTAVI#1
NOTION
PARTNER 3#2
Evolut LR#1


30-day Major Stroke
10
8
6
4
2
0
P = 0.20
P = 0.55
P = 0.20
-2.3[-2.6, 0.6]
P = 0.37
0.00[NA]
--1.2[-2.4, -0.2]
3.8
2.1
3.9
3.1
3.2
4.3
1.2
2.5
1.4
3
0
0.4
0.5
1.7
PARTNER 1A
CoreValve US HR
PARTNER 2A
SURTAVI#1
NOTION#3
PARTNER 3#2
Evolut LR#1

TAVI SAVR

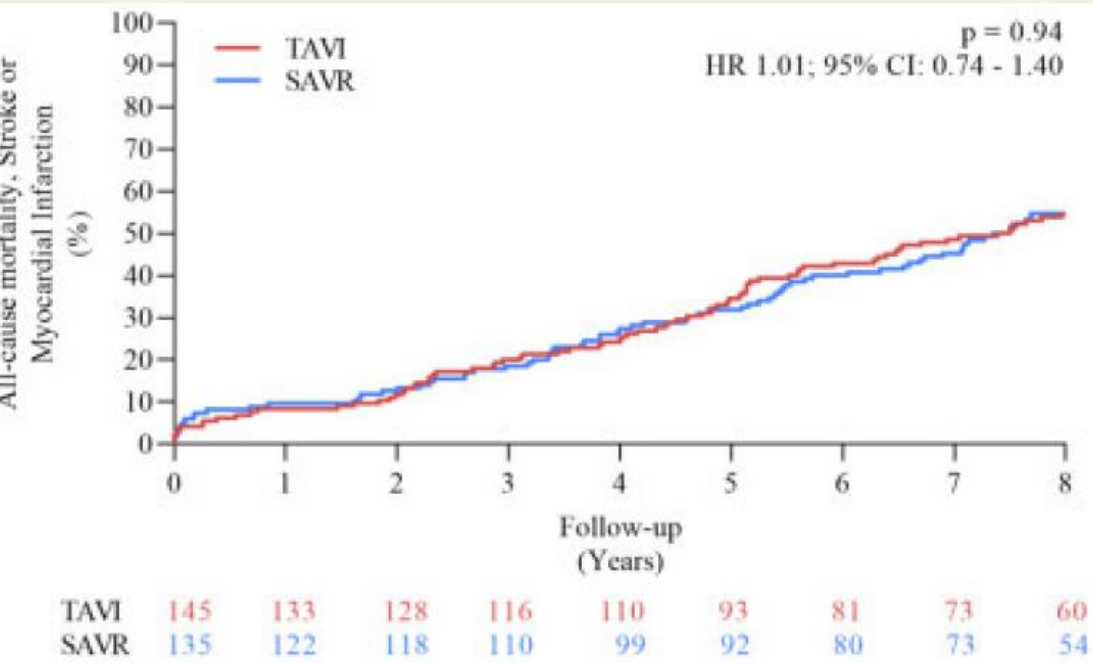
There is no question that TAVR has an up-front advantage compared to surgery, but do we lose that advantage…and when… and by how much?

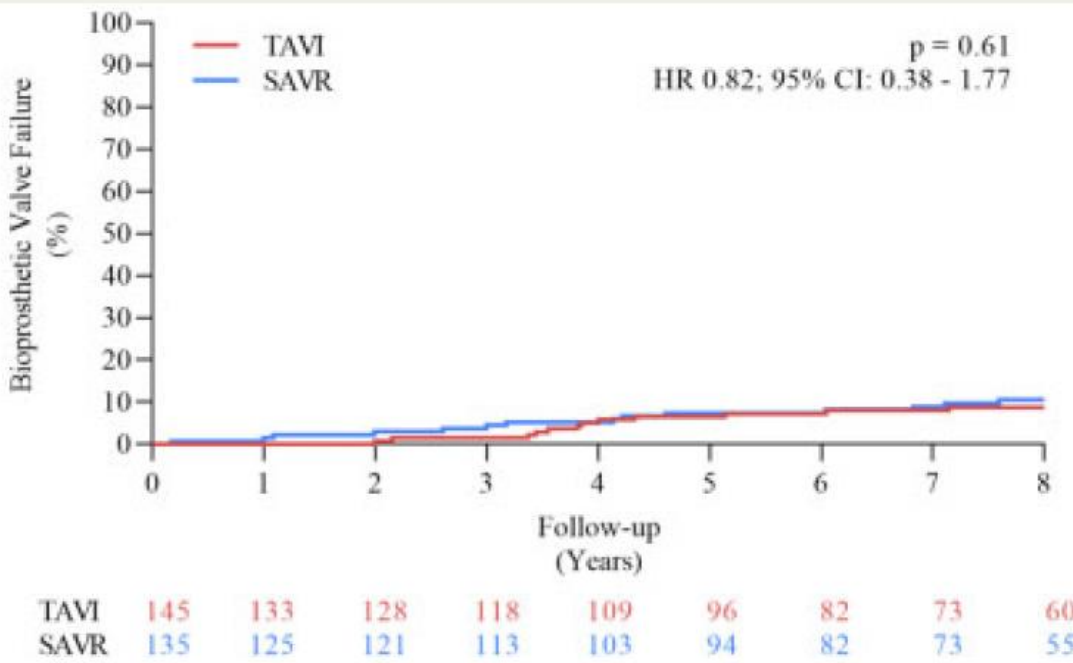
Are TAVR valves durable?

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 2912–2919
doi:10.1093/eurheartj/ehab375

Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement

NOTION TRIAL





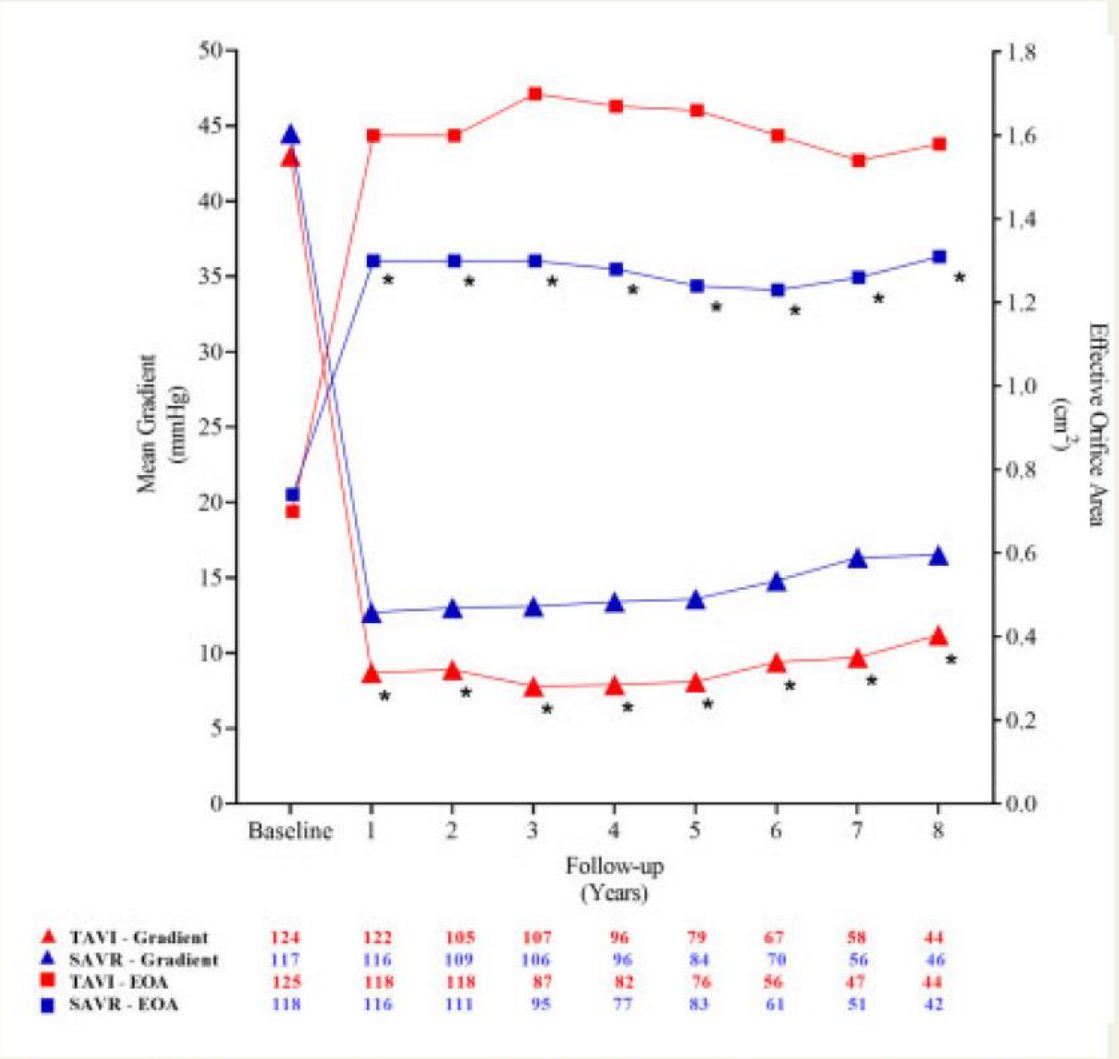


Figure 3 Mean gradient and effective orifice area during follow-up. EOA, effective orifice area; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation. *$P < 0.05$.

TAVR: Lower gradients, larger EROA

TAVR: Lower incidence of SVD

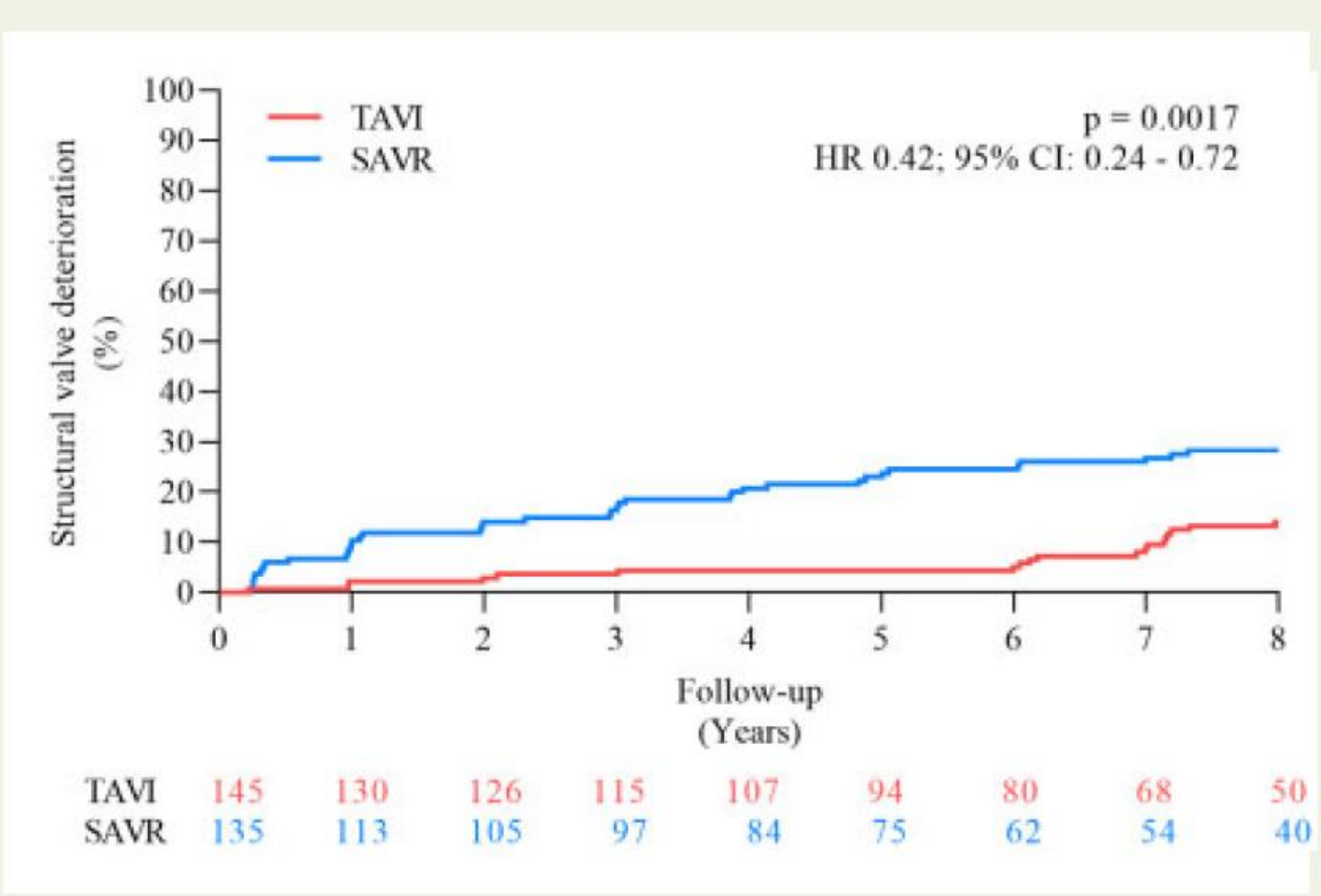


Figure 4 Structural valve deterioration. CI, confidence interval; HR, hazard ratio; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

Long-term durability of self-expanding and balloon-expandable transcatheter aortic valve prostheses: UK TAVI registry

Number of UK centres
11

Total number of TAVI patients
1185

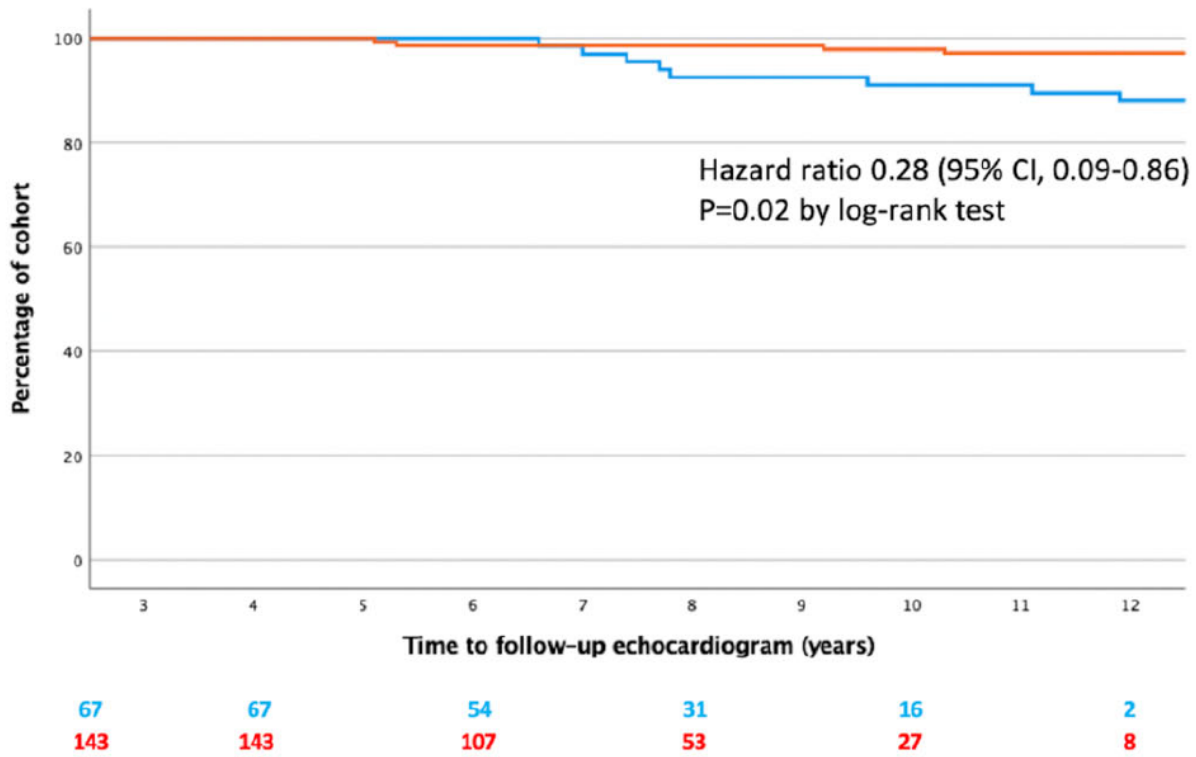
Patients alive at 5 years
371

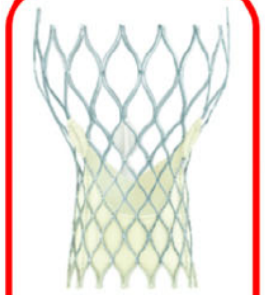
Patients with paired echocardiograms
221

Severe SVD

- Mean gradient ≥40mm Hg and/or ≥20mm Hg increase from baseline
- Peak velocity ≥4 m/s and/or ≥2 m/s increase from baseline
- Severe new or worsening intra-prosthetic aortic regurgitation

KM curves comparing balloon-expandable (SAPIEN; blue) and self-expanding (CoreValve; red) valves with respect to freedom from severe SVD over time





SEV
CoreValve

BEV
SAPIEN

Ali N, et al. Catheter Cardiovasc Interv. 2023

	All (*n* = 221)	BEV (*n* = 67)	SEV (*n* = 143)	*p* Value
SVD	30 (13.6)	15 (22.4)	14 (9.8)	0.01
Moderate SVD	17 (56.7)	7 (10.4)	9 (6.3)	0.29
Severe SVD	13 (5.9)	8 (11.9)	5 (3.5)	0.02
Mean gradient ≥ 40 mmHg[a]	2 (0.9)	0 (0)	2 (1.4)	1.00
Mean gradient increase ≥ 20 mmHg	8 (3.6)	6 (9.0)	2 (1.4)	0.01
Severe intravalvular AR	3 (1.4)	2 (3.0)	1 (0.7)	0.19
Valve-related death/reintervention	5 (2.3)	3 (4.5)	2 (1.4)	0.17

SVD More common in smaller Balloon expandable valves

TAVR (and SAVR) Evidence Gaps

- Valve Durability
- Important of valve leaflet thickening/thrombosis
- TAV in TAV safety
- Coronary Access
- Echo gradients -vs- hemodynamic gradients
- Post AVR conduction disturbances
- Optimal medical therapy post AVR
- Concomitant CV Dz/CAD/Valve dz management
- Bicuspid
- Asymptomatic severe AS and moderate symptomatic AS
- Aortic regurgitation
- Cerebral embolic protection

When is the above data not as applicable?

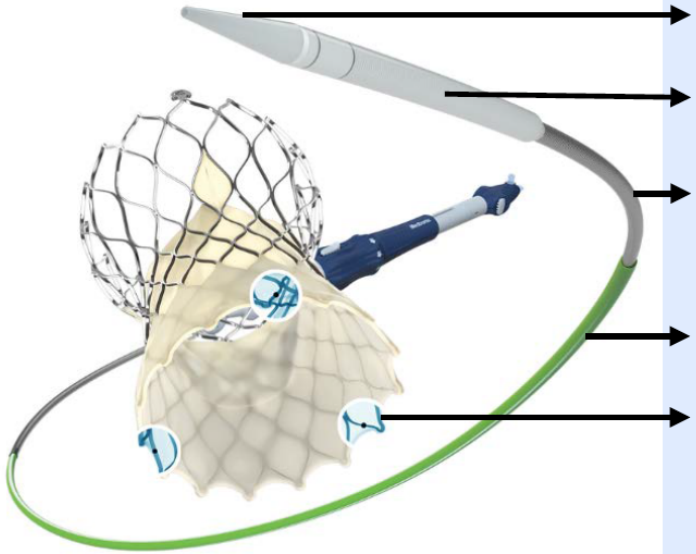
HIGH RISK TAVR in “LOW RISK” PATIENTS

Anatomic Factors Associated with Hazard in TAVR (anatomic risk stratification)

-Horizontal Aorta
-Low take off of left main coronary artery with small sinus of Valsalva
-Poor femoral/peripheral access
-Non calcified Aortic valve
-Severe calcified AV leaflets, annulus or LVOT
-Extreme Annulus Dimensions
-Risk of conduction disturbances
-Concomitant HOCM
-Unicuspid or Bicuspid AV
-Mixed Valve disease
-Concommitant ischemic heart disease/CAD

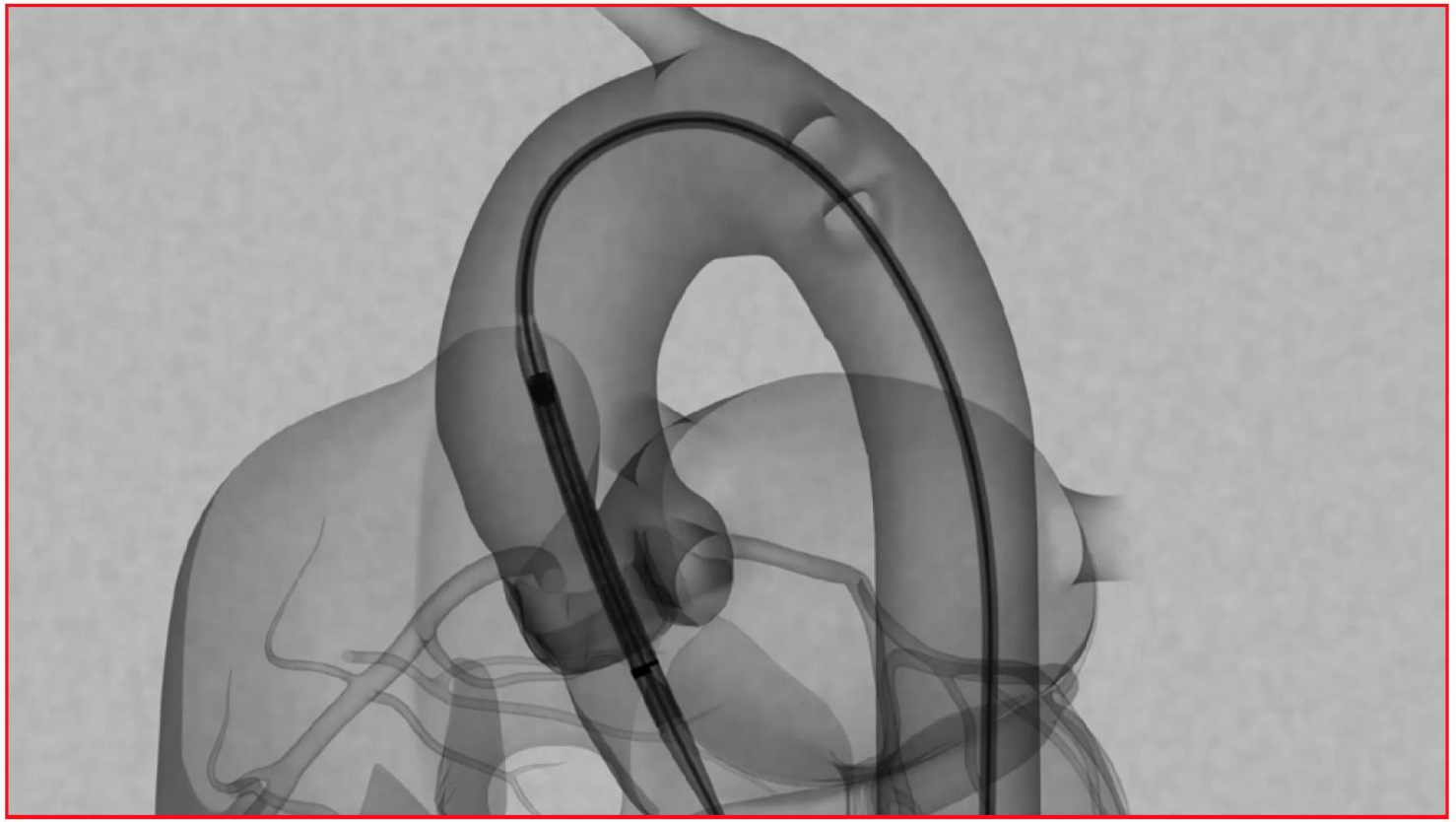
Device Improvements

Evolut FX System Modifications from PRO+

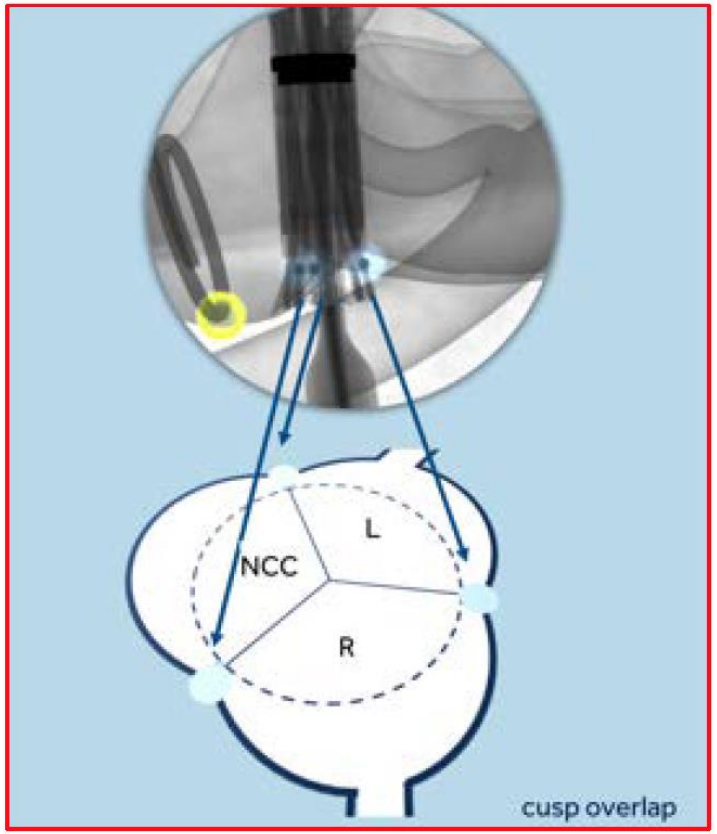
SHARED FEATURES		KEY REFINEMENTS
EVOLUT PRO+	EVOLUT FX	
	Self-expanding Nitinol Frame Supra-annular Design Porcine Pericardium Pericardial Skirt with External Pericardial Wrap	 Redesigned Nose Cone Redesigned Capsule Single Spine Shaft Optimized Stability Layer Radiopaque Dot Markers at 3 mm from inflow

Evolut FX System Modifications from PRO+

Deployment Symmetry



Commissural Alignment



Cors at the Shore 2023

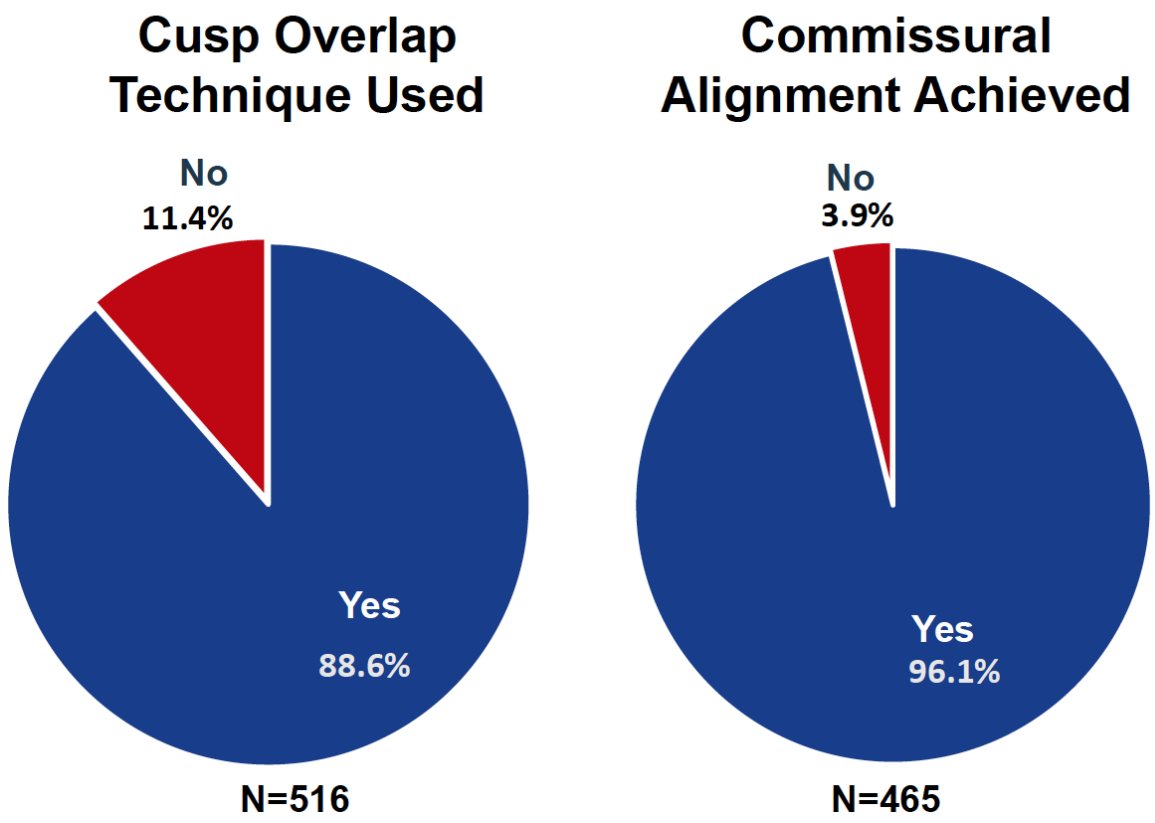
Real-World Early Outcomes of Evolut FX Versus PRO+ Transcatheter Aortic Valve Replacement

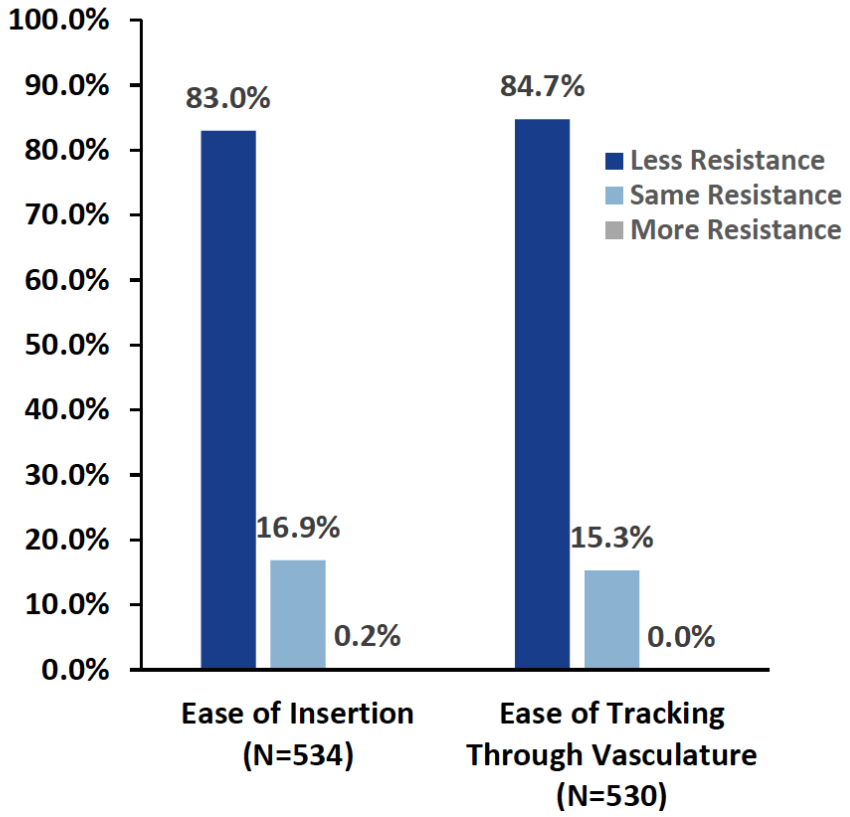
Wah Wah Htun, MD; Mustafa Ahmed, MD; Guilherme F. Attizzani, MD; Tanvir Bajwa, MD; Stanley J. Chetcuti, MD; Hemal Gada, MD; Puja B. Parikh, MPH; George Petrossian, MD; Matthew D. Saybolt, MD; Sampoornima Setty, MD; Nishtha Sodhi, MD; Yu Jung Yeh, MS; Gilbert H.L. Tang, MD, MSc, MBA

CRF TVT

Cors at the Shore 2023

Recent Findings From the Evolut FX Limited Market Release Survey*





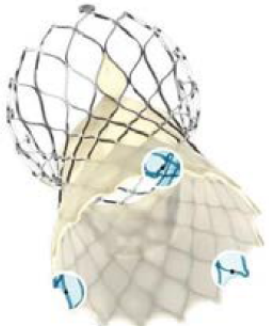
Cors at the Shore 2023

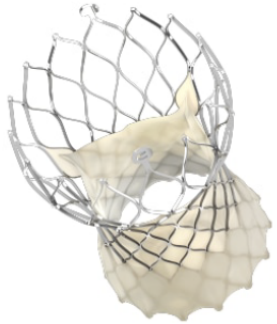
Methods

- The first implant of Evolut FX in the US occurred June 24, 2022. For this analysis, the STS/ACC TVT registry was utilized to identify all patients who underwent TAVR with an Evolut FX or PRO+ valve between July 1, 2022 through September 30, 2022.
- Procedural, in-hospital and 30-day clinical and echocardiographic outcomes are reported for both groups of patients and compared between groups.

701 Centers

Evolut FX
1700
procedures





Evolut PRO+
4058
procedures

Cors at the Shore 2023

Baseline Demographics

Mean ± SD or %	Evolut FX (N=1700)	Evolut PRO+ (N=4058)	P-Value
Age (years)	79.2 ± 8.5 (1699)	78.8 ± 8.3 (4057)	0.11
Body surface area (m^2)	1.9 ± 0.2 (1694)	1.9 ± 0.3 (4048)	0.36
BMI < 21 kg/m^2	7.8 (132/1694)	7.0 (283/4044)	0.29
Male	51.1	46.7	0.002
NYHA Class III/IV	57.0 (964/1692)	62.7 (2521/4022)	<0.001
STS Score (Risk of Mortality, %)	3.9 ± 3.4 (1677)	4.3 ± 3.6 (3976)	<0.001
Diabetes Mellitus	38.0	36.9	0.42
Creatinine level >2 mg/dl	6.0 (101/1684)	6.0 (242/4039)	0.99
History of hypertension	89.5	89.9	0.65
Peripheral vascular disease	15.5	15.0	0.58
Prior stroke	10.2	9.7	0.59
Prior TIA	7.1	6.4	0.34
Chronic lung disease/COPD	25.5	24.5	0.45
Coronary artery bypass surgery	14.9	14.2	0.46
Percutaneous coronary intervention	25.2	26.6	0.30
Pre-Existing IPG/ICD	12.5	13.7	0.20
Conduction defect	36.8	31.5	<0.001
Previous MI	13.5	14.9	0.19
Atrial fibrillation / Atrial flutter	36.5	34.2	0.10

Procedural Data

Assessment	Evolut FX (N=1700)	Evolut PRO+ (N=4058)	P-Value
General anesthesia	28.2 (480)	36.0 (1461/4057)	<0.001
Ilio-femoral access	96.1 (1633)	96.1 (3898/4056)	0.93
Device capture & repositioning	12.6 (184/1461)	18.7 (601/3206)	<0.001
More than 1 valve used	1.9 (32)	1.4 (57)	0.18
Device implanted successfully	99.7 (1694/1699)	99.8 (4048/4056)	0.48
Valve size implanted			
23 mm	6.5 (110/1693)	9.2 (371/4048)	<0.001
26 mm	29.9 (506/1693)	31.7 (1283/4048)	0.18
29 mm	43.3 (733/1693)	40.7 (1647/4048)	0.07
34 mm	20.3 (344/1693)	18.5 (747/4048)	0.10
Median procedure time (minutes)	62.0 [44.0, 84.0]	66.0 [49.0, 87.0]	<0.001
Median length of stay (days)	1.0 [1.0, 2.0]	1.0 [1.0, 2.0]	0.14
Discharged - home	94.1 (1579/1678)	92.8 (3728/4017)	0.08

Data are presented as % (n/N) or median [q1, q3].

30-Day Patient Outcomes

Events[1]	Evolut FX (n=1700)	Evolut PRO+ (n=4058)	P-value
All-cause mortality	2.3 (36)	2.2 (79)	0.78
Cardiovascular mortality	1.2 (19)	1.4 (50)	0.65
Stroke	3.2 (52)	2.7 (105)	0.35
Myocardial infarction	0.3 (4)	0.4 (15)	0.39
Major or life-threatening bleeding	4.2 (69)	5.6 (220)	0.03
Major vascular complication	1.8 (30)	1.7 (66)	0.74
Permanent pacemaker implant[2]	9.8 (159)	10.3 (396)	0.50
Permanent pacemaker implant[3]	11.1 (157)	12.0 (395)	0.35
Aortic valve re-intervention	0.4 (6)	0.2 (8)	0.29
Valve related readmission	0.8 (13)	0.5 (19)	0.20
Non-valve related readmission	7.9 (121)	8.0 (281)	0.94

Values are reported as Kaplan Meier event rates, %(n).

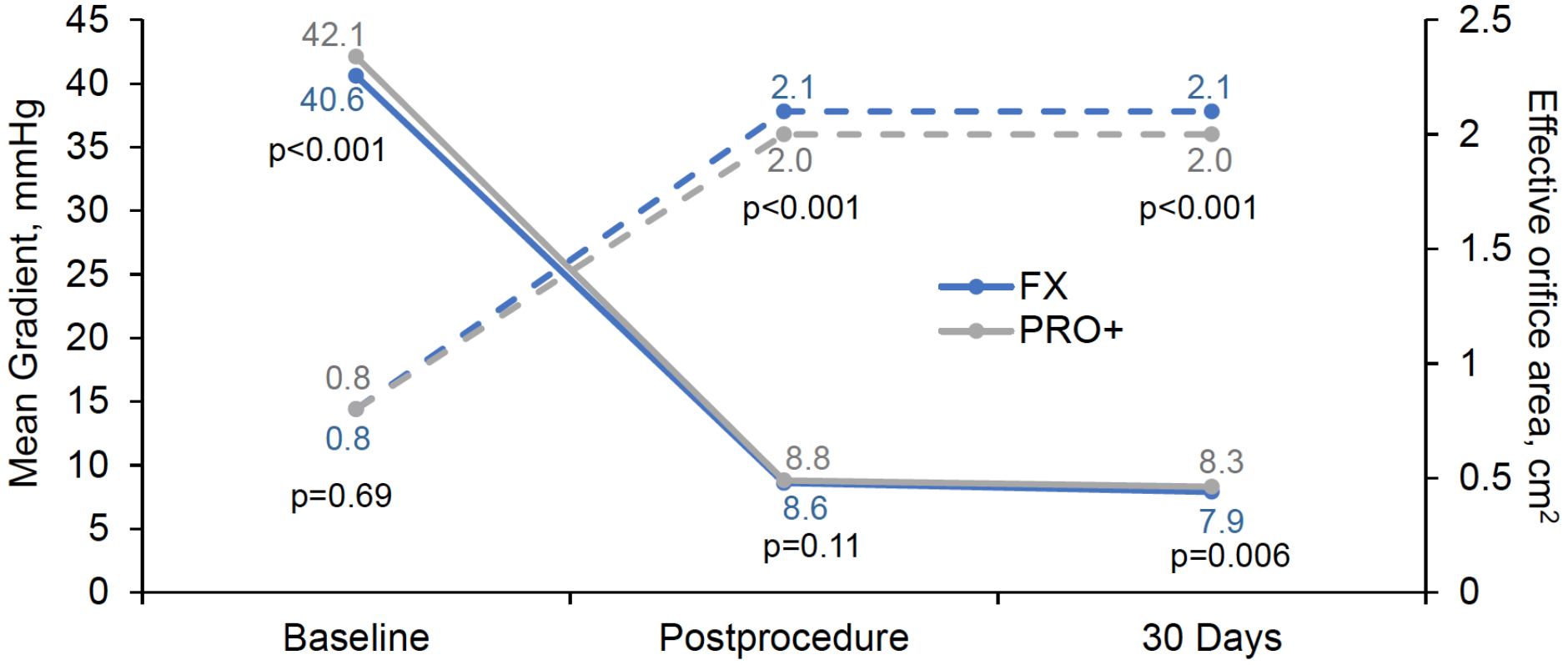
[1]Event rates include in-hospital reported events and events reported at follow-up.

[2]Subjects with pacemaker or ICD at baseline are included.

[3]Subjects with pacemaker or ICD at baseline are not included.

2023 Cors at the Shore

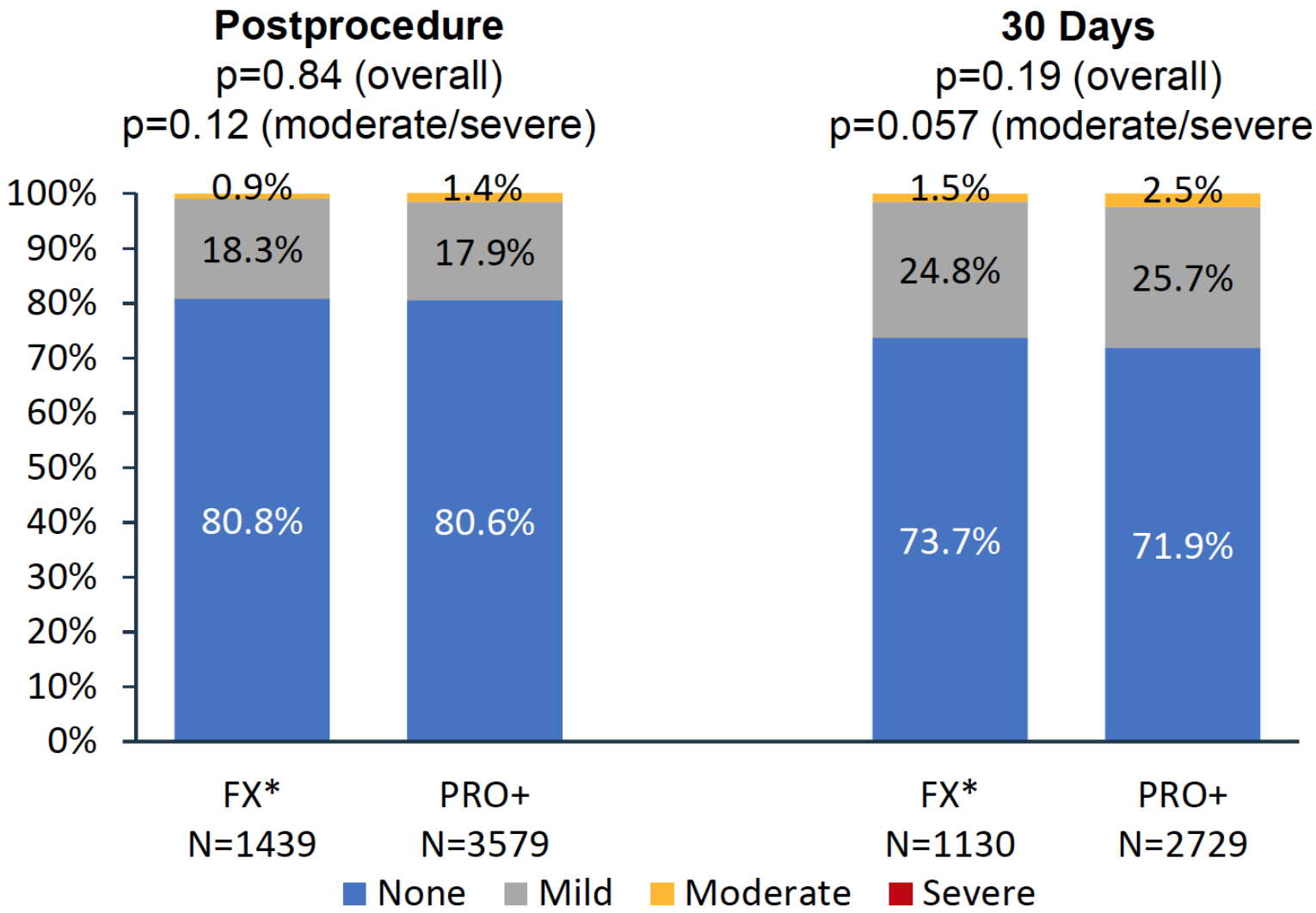
Valve Hemodynamics to 30 Days



FX MG (N)	1667	1550	1213
PRO+ MG (N)	3972	3801	2976
FX EOA (N)	1642	1275	953
PRO+ EOA (N)	3897	2892	2240

Cors at the Shore 2023

Paravalvular Regurgitation



***No severe PVR with FX**

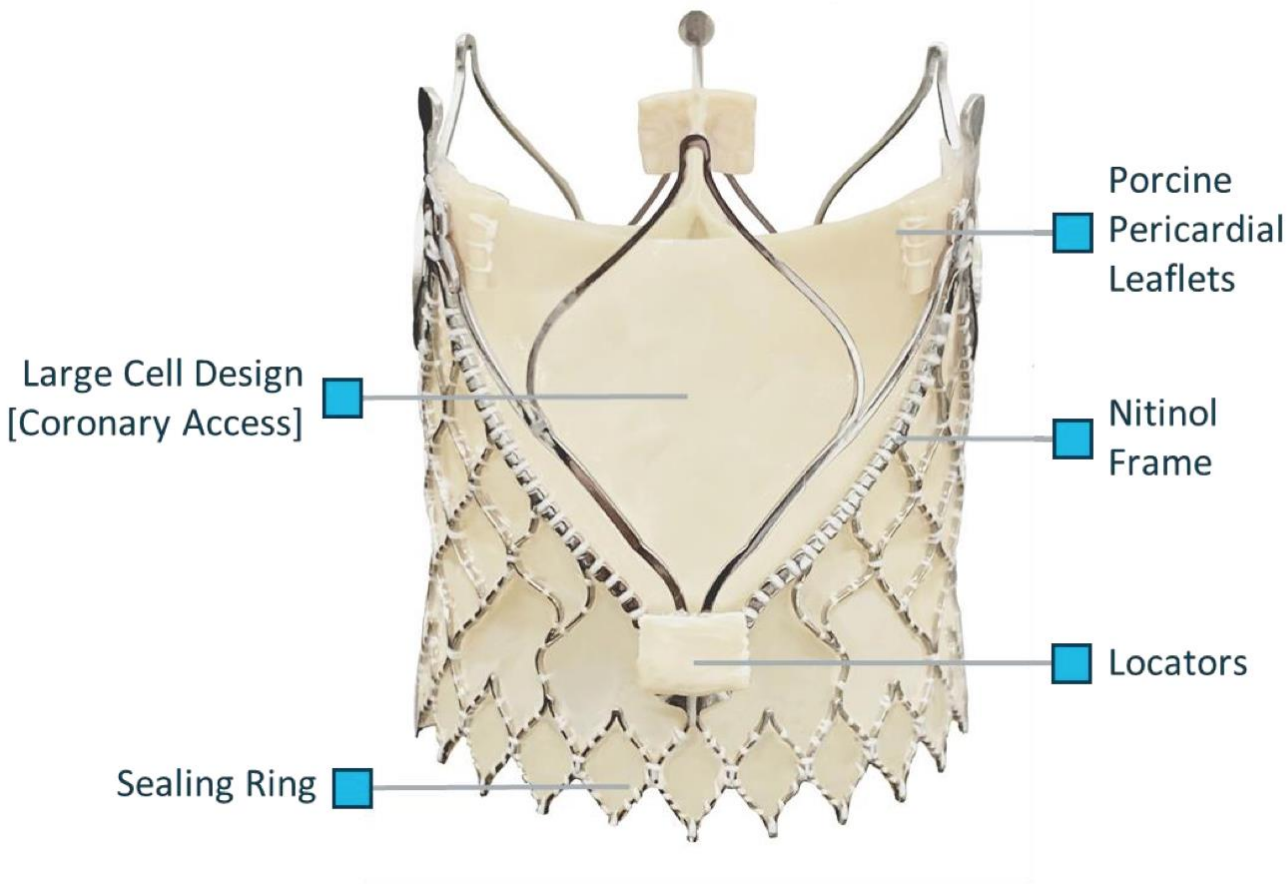
Cors at the Shore 2023

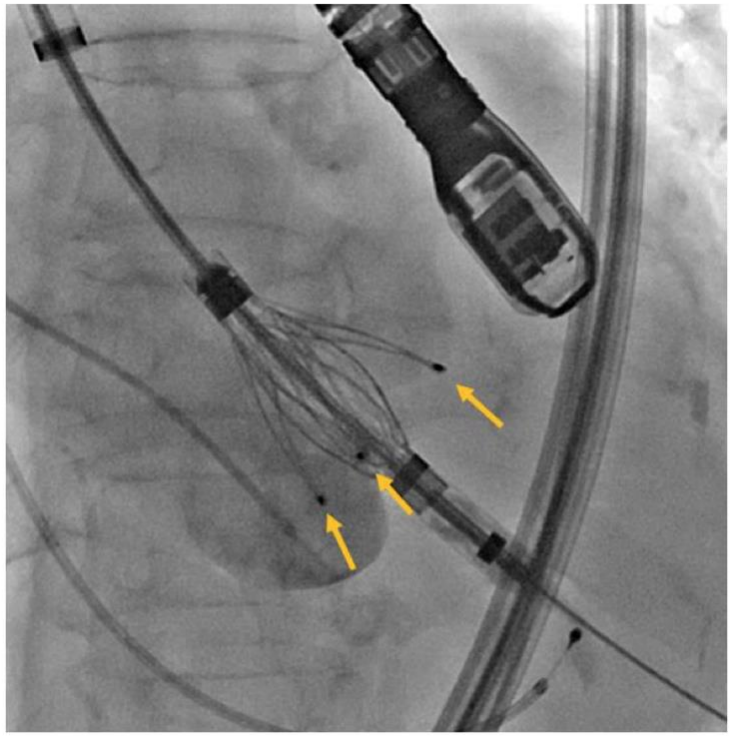
Summary: Patients Implanted with Evolut FX vs PRO+

- Need for device repositioning, procedure time, and major/life-threatening bleeding were significantly less with Evolut FX
- Moderate/severe PVR at 30 days was numerically less with Evolut FX ($p = 0.057$)
- High rates of successful device implantation in both groups
- Clinical outcomes were favorably low in both groups, including mortality, stroke reintervention, and new PPI
- Preserved 30-day valve hemodynamics in both groups

Unique populations, expanding indications, redefining “severe” aortic stenosis

TAVR for Aortic Regurgitation: JenaValve Trilogy

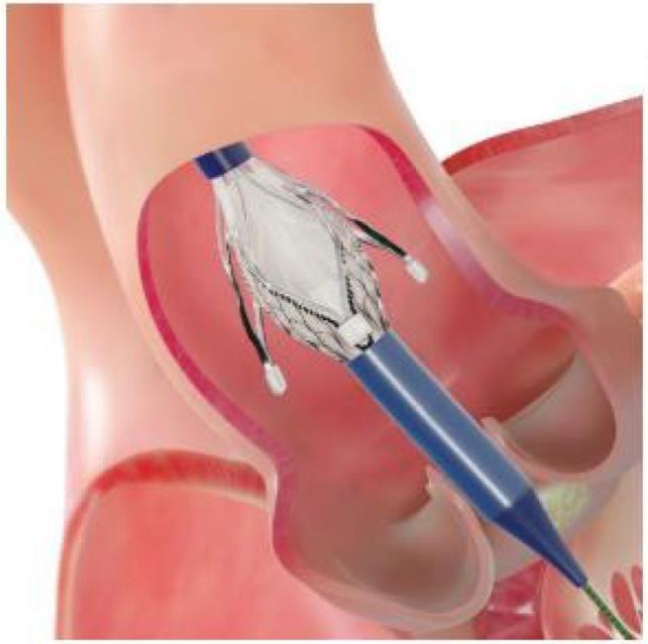




Three Locators on Fluoroscopy

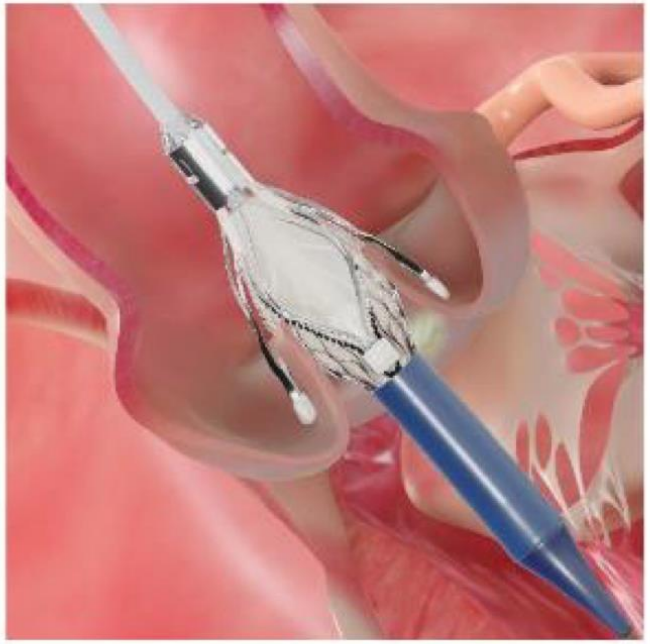
Cors at the Shore 2023

Technology Overview - JenaValve Trilogy with Locator Technology



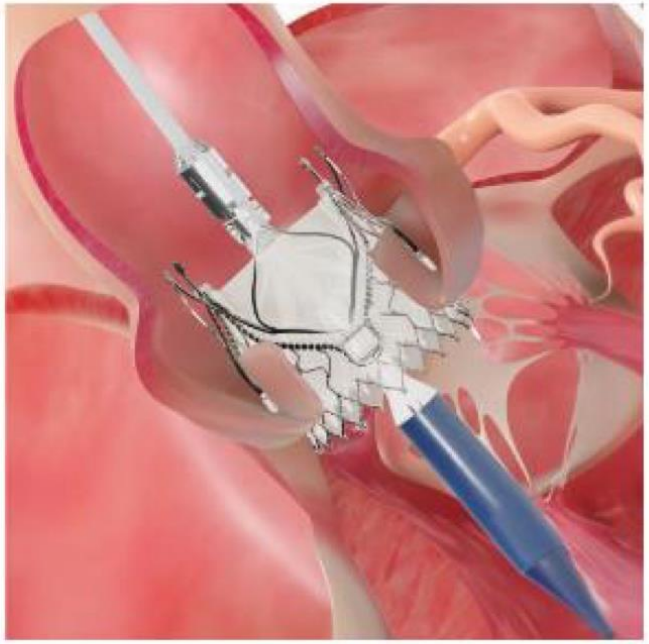
Alignment

- Aligns THV with native cusps



Positioning/Anchoring

- Locators "clip" onto native leaflets forming a natural seal and stable securement



Deployment

- Large open cells provide access to low coronaries
- 24 diamond-shaped cells provide annular conformability and sealing

Cors at the Shore 2023

Baldas S, TVT. 2023

Align-AR Study

A Study to Assess Safety and Effectiveness of the JenaValve Trilogy™ Heart Valve System in the Treatment of High Surgical Risk Patients with Symptomatic, Severe Aortic Regurgitation (AR)

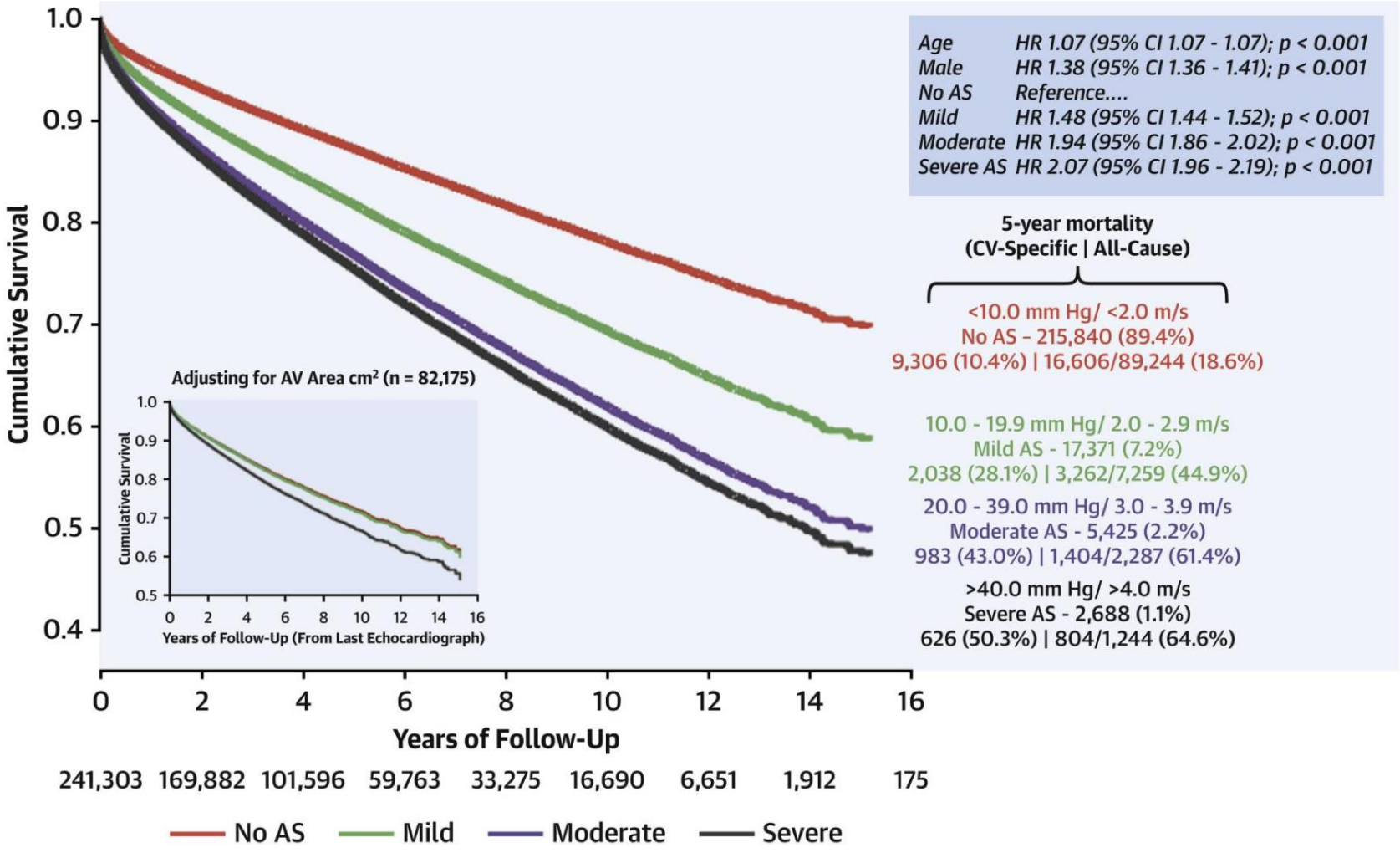
Study Design	Prospective, Multi-Center, Single-Arm
Indication	Symptomatic Severe AR w/ High Surgical Risk
Sample Size	N = 180 **[enrollment complete]**
Primary Endpoint	All-Cause Mortality at 1 Year
Additional 30-Day Evaluations	All Stroke, Major Bleeding, AKI, Major Vascular Complications, PPMI, Total Aortic Regurgitation
Regions	United States
Clinicaltrials.gov NCT	#04415047

2023 Cors at the Shore

Poor Long-Term Survival in Patients with Moderate AS*

Strange et al found that the 5-year mortality rate of patients with moderate AS approaches that of severe AS:

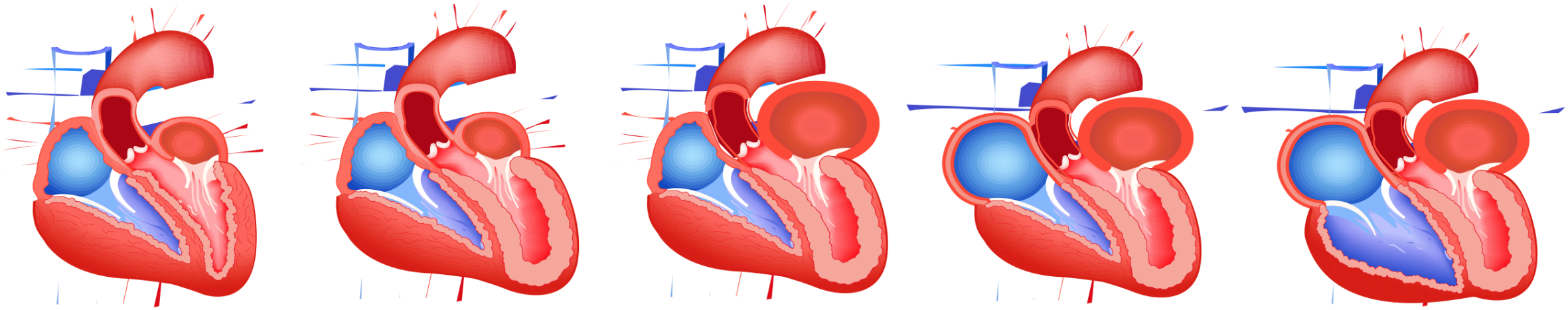
- High risk of death
- Potential risk of fast progression to severe AS



*Strange G, Stewart S, Celermajer D, et al. Poor long-term survival in patients with moderate aortic stenosis. Journal of the American College of Cardiology. 2019;74 (15):1851-1863.

Staging Classification of Patients with AS:

Specific Criteria



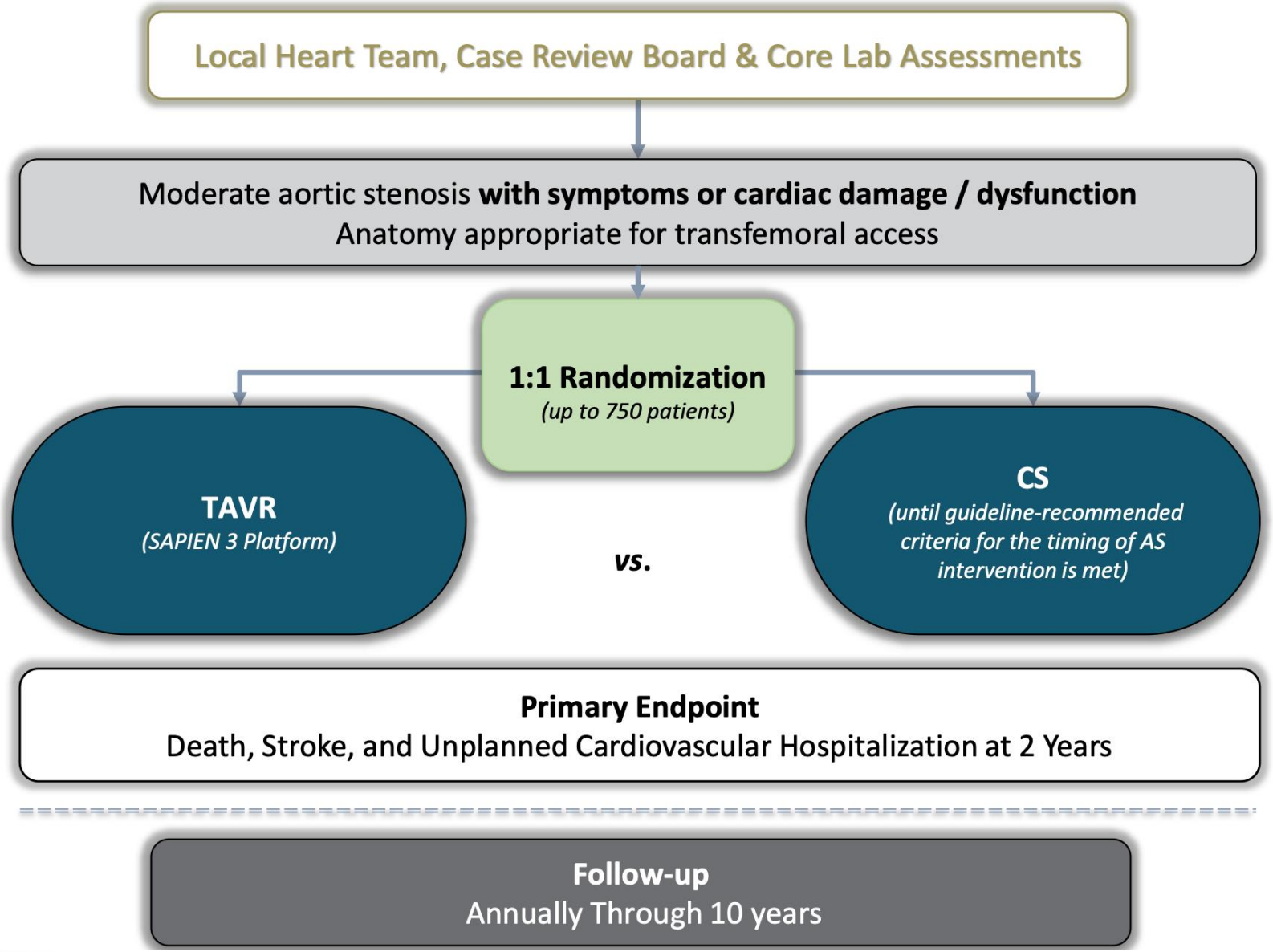
Stage 0 No damage	Stage 1 LV damage	Stage 2 LA/Mitral damage	Stage 3 PA/Tricuspid damage	Stage 4 RV damage
	Increased LV Mass Index >115 g/m^2 Male >95 g/m^2 Female	Indexed left atrial volume >34mL/m^2	PAS ≥60mmhg	Moderate-Severe RV dysfunction
	E/e' >14	Moderate-Severe MR	Moderate-Severe TR	
	EF <50%	Atrial Fibrillation		

Cors at the Shore 2023

Genereuex et al. Eur Heart J 2017

Study Design

THE PROGRESS TRIAL



Key Inclusion Criteria

1

≥65 Years

2

Moderate AS

1. Moderate AVA/i

- AVA 1.0 – 1.5 cm^2 OR
- AVA < 1.0 with AVAi > 0.6 cm^2/m^2 if BMI <30 kg/m^2 OR
- AVA < 1.0 with AVAi > 0.5 cm^2/m^2 if BMI ≥30 kg/m^2

AND

2. Moderate peak aortic velocity or gradient:

- Peak velocity 3.0 – < 4.0 m/s **OR** mean gradient 20 – < 40 mmHg

Note: Subjects who only meet one of the above criteria on resting echo due to low flow state are eligible if both criteria are met following dobutamine stress echo (DSE).

3

At-Risk Factors

1. Evidence of Symptoms

(NYHA 2-3-4 or valve-related symptoms)

OR

2. Evidence of Cardiac Damage or Dysfunction

- LVEF < 60%
- Diastolic dysfunction ≥ Grade 2
- Stroke volume index < 35 mL/m^2
- Persistent atrial fibrillation or any paroxysmal episode within 6 months
- NT-Pro BNP > 3x normal
- Elevated calcium score (> 1200 AU for female and > 2000 AU for male)

Shore

The NEW ENGLAND JOURNAL of MEDICINE

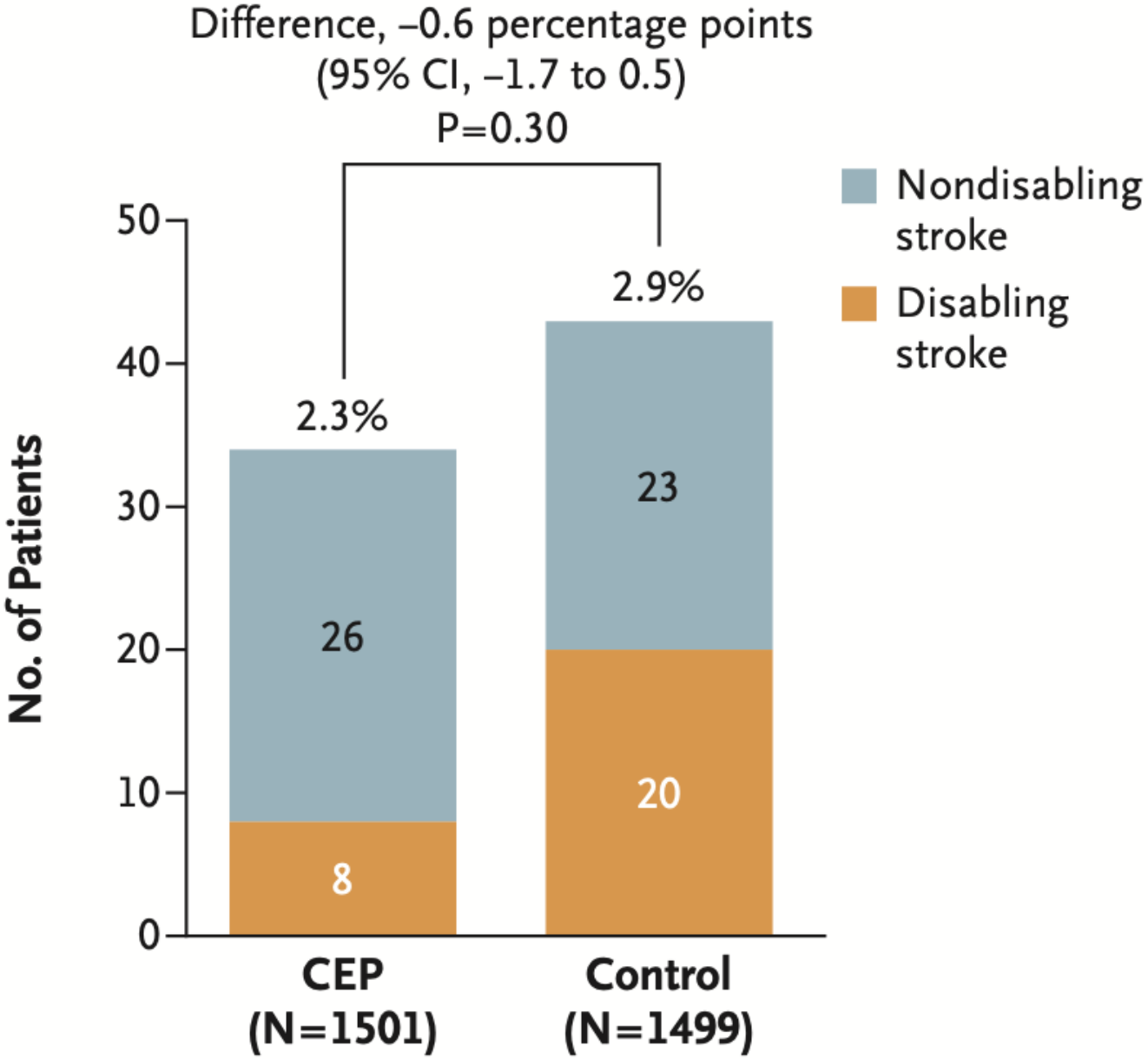
ESTABLISHED IN 1812 OCTOBER 6, 2022 VOL. 387 NO. 14

Cerebral Embolic Protection during Transcatheter Aortic-Valve Replacement

Samir R. Kapadia, M.D., Raj Makkar, M.D., Martin Leon, M.D., Mohamed Abdel-Wahab, M.D., Thomas Waggoner, D.O., Steffen Massberg, M.D., Wolfgang Rottbauer, M.D., Ph.D., Samuel Horr, M.D., Lars Sondergaard, M.D., Juhana Karha, M.D., Robert Gooley, M.B., B.S., Ph.D., Lowell Satler, M.D., Robert C. Stoler, M.D., Steven R. Messé, M.D., Suzanne J. Baron, M.D., Julia Seeger, M.D., Susheel Kodali, M.D., Amar Krishnaswamy, M.D., Vinod H. Thourani, M.D., Katherine Harrington, M.D., Stuart Pocock, Ph.D., Rodrigo Modolo, M.D., Ph.D., Dominic J. Allocco, M.D., Ian T. Meredith, M.D., Ph.D., and Axel Linke, M.D., for the PROTECTED TAVR Investigators*

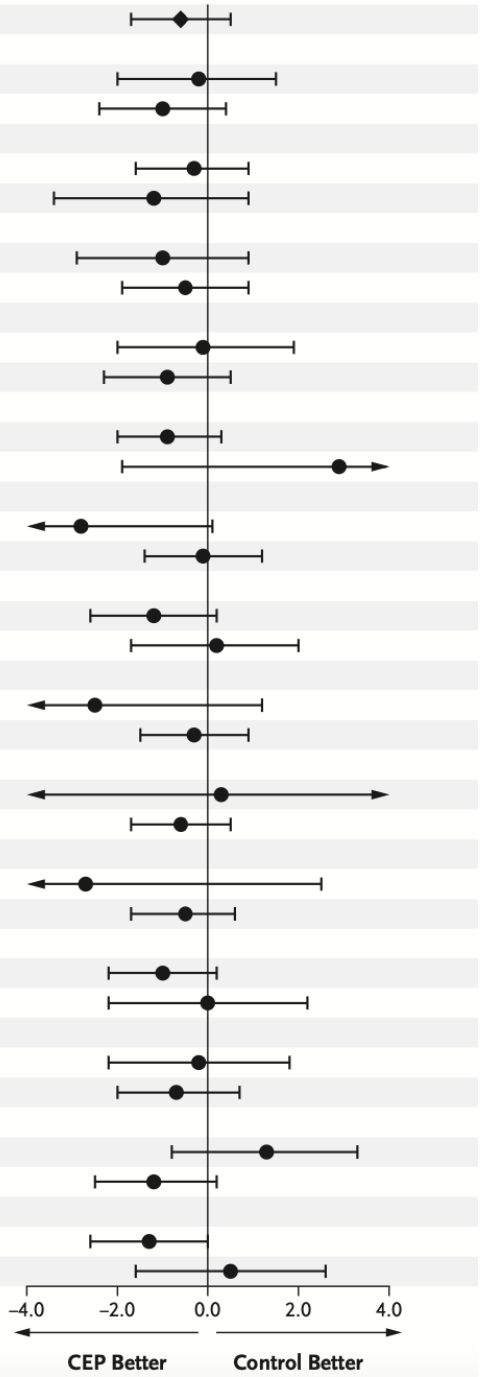
3000 Patients randomized 1:1 to cerebral embolic protection vs. control

Primary Endpoint: stroke w/in 72 hours after TAVR or before discharge (ITT)



Cors at the Shore 2023

Subgroup	CEP	Control	Difference (95% CI)
	no. of patients with event/total no. of patients (%)		
All patients	34/1501 (2.3)	43/1499 (2.9)	
Age			
≥80 yr	23/760 (3.0)	25/771 (3.2)	
<80 yr	11/741 (1.5)	18/728 (2.5)	
Sex			
Male	15/870 (1.7)	19/933 (2.0)	
Female	19/631 (3.0)	24/566 (4.2)	
STS surgical risk score			
≥3%	17/658 (2.6)	22/620 (3.5)	
<3%	16/823 (1.9)	21/862 (2.4)	
Operative risk (according to heart team)			
Low	15/545 (2.8)	15/351 (2.8)	
Intermediate or higher	19/956 (2.0)	28/968 (2.9)	
Valve morphology			
Tricuspid	27/1313 (2.1)	39/1341 (2.9)	
Bicuspid	7/131 (5.3)	3/121 (2.5)	
Aortic-valve calcification			
None or mild	3/241 (1.2)	9/223 (4.0)	
Moderate or greater	30/1192 (2.5)	32/1218 (2.6)	
History of coronary artery disease			
Yes	15/850 (1.8)	26/880 (3.0)	
No	19/643 (3.0)	17/613 (2.8)	
History of peripheral vascular disease			
Yes	3/165 (1.8)	7/162 (4.3)	
No	31/1319 (2.4)	35/1319 (2.7)	
Previous cerebrovascular event			
Yes	5/114 (4.4)	5/122 (4.1)	
No	29/1382 (2.1)	37/1369 (2.7)	
Use of valve-in-valve procedure			
Yes	0/56	1/37 (3.0)	
No	34/1445 (2.4)	42/1462 (2.9)	
Use of balloon-expandable valve			
Yes	11/913 (1.2)	20/914 (2.2)	
No	23/588 (3.9)	23/585 (3.9)	
Balloon dilation before valve implant			
Yes	18/573 (3.1)	21/624 (3.4)	
No	16/916 (1.7)	21/866 (2.4)	
Balloon dilation after valve implant			
Yes	11/390 (2.8)	6/383 (1.6)	
No	23/1099 (2.1)	36/1107 (3.3)	
Geographic region			
United States	12/914 (1.3)	24/929 (2.6)	
Other	22/587 (3.7)	19/580 (3.3)	



2023 Cors at the Shore

Questions?

Matthew.Saybolt@HMHN.org

jsumc.structuralheart.HMHN.org

JSUMC Structural Heart Hot Line: 732-776-4073

twitter @MatthewSaybolt

Cors at the Shore 2023