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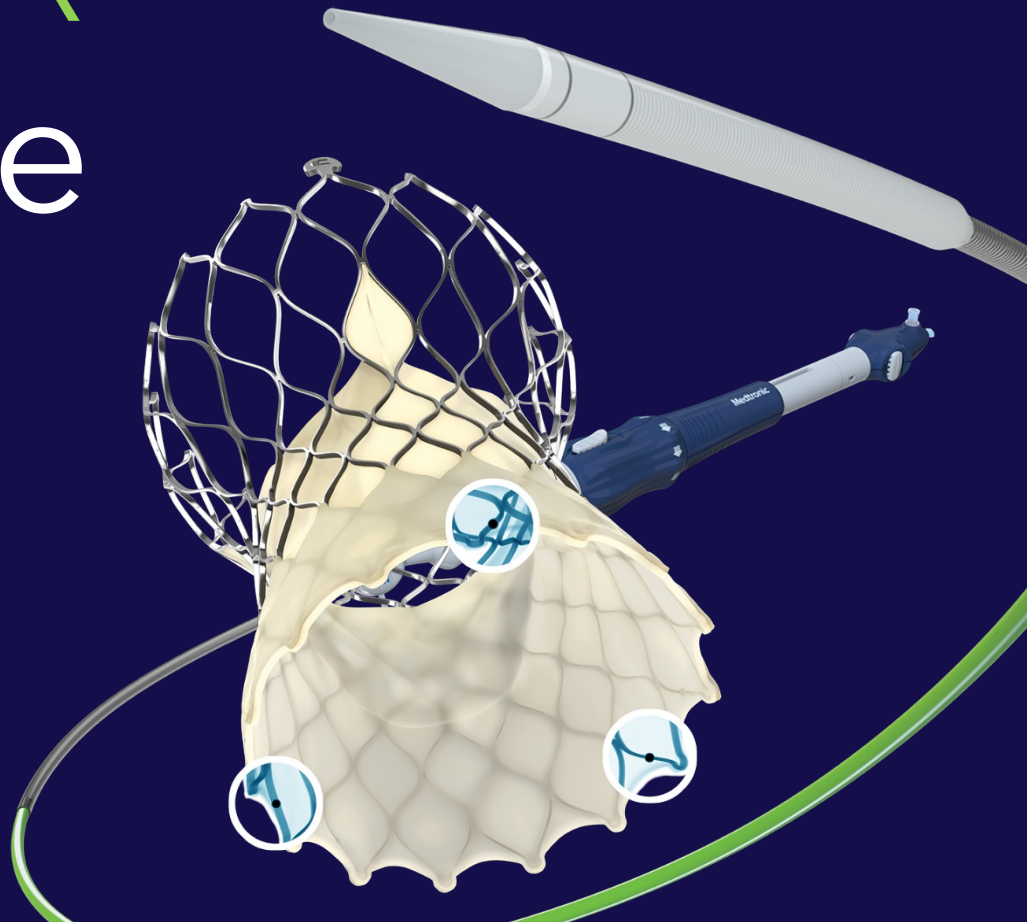
Evolut™ TAVR
Valve Performance & Durability Data



Thursday, February 29, 2024 | 7:00 pm ET
Medtronic Structural Heart

Agenda

1. Introduction & Overview
   Dr. O'Hair
2. TAVR Landscape
   Dr. Parwani
3. Evolut Design, Clinical impact of Valve Performance, and 4 YR LR data
   Dr. Byrne
4. Panel discussions with Q&A
   Dr. O'Hair & Panelists

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Featuring

Moderator:
Daniel O'Hair, M.D.

Cardiothoracic Surgeon,
Boulder Community Hospital

Faculty:
Purvi Parwani, M.D.

General Cardiology – Advanced Cardiac Imaging Specialist

Faculty:
Timothy Byrne, D.O.

Interventional Cardiologist,
Abrazo Arizona Heart Hospital

General Cardiology perspective on Durability and Valve Performance.

Dr. Purvi Parwani
Associate Prof. of Medicine
Director, Echocardiography lab
Advanced cardiovascular Imaging
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Loma Linda, CA, USA
Twitter: @purviparwani

LOMA LINDA UNIVERSITY HEALTH

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Disclosures

Medtronic
AstraZeneca

Objectives

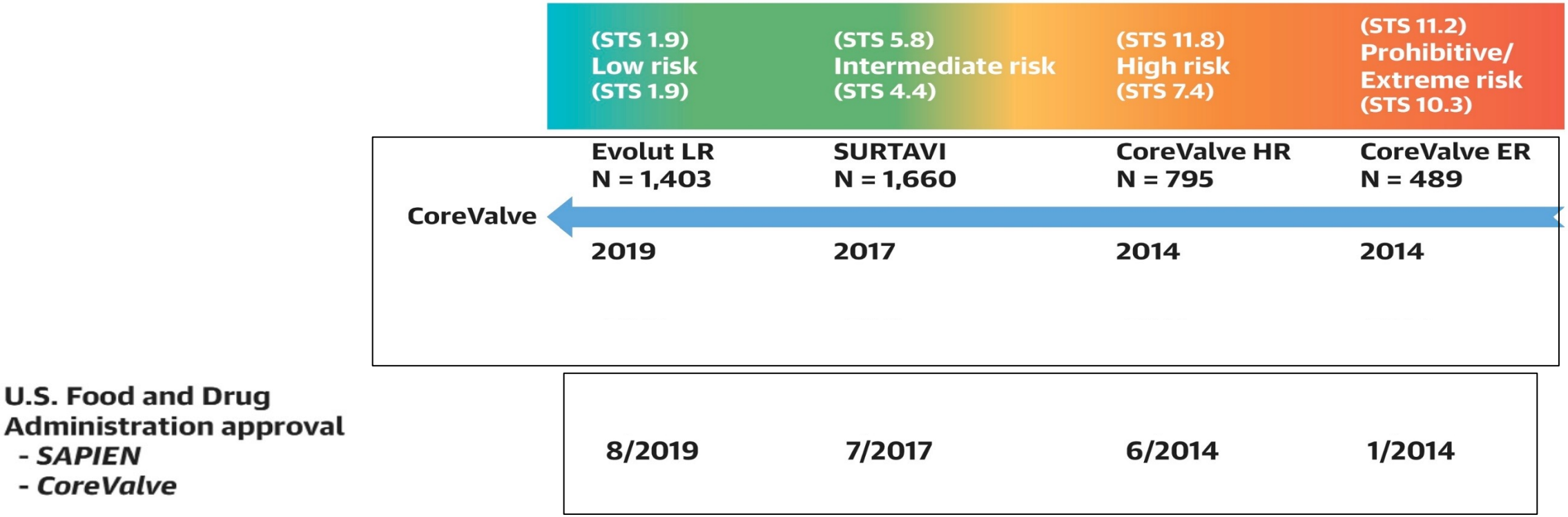
Evolution of TAVR and Aortic Stenosis management over the last decade

Review the need of ACC/AHA guidelines

Review the bioprosthetic valve dysfunction definitions

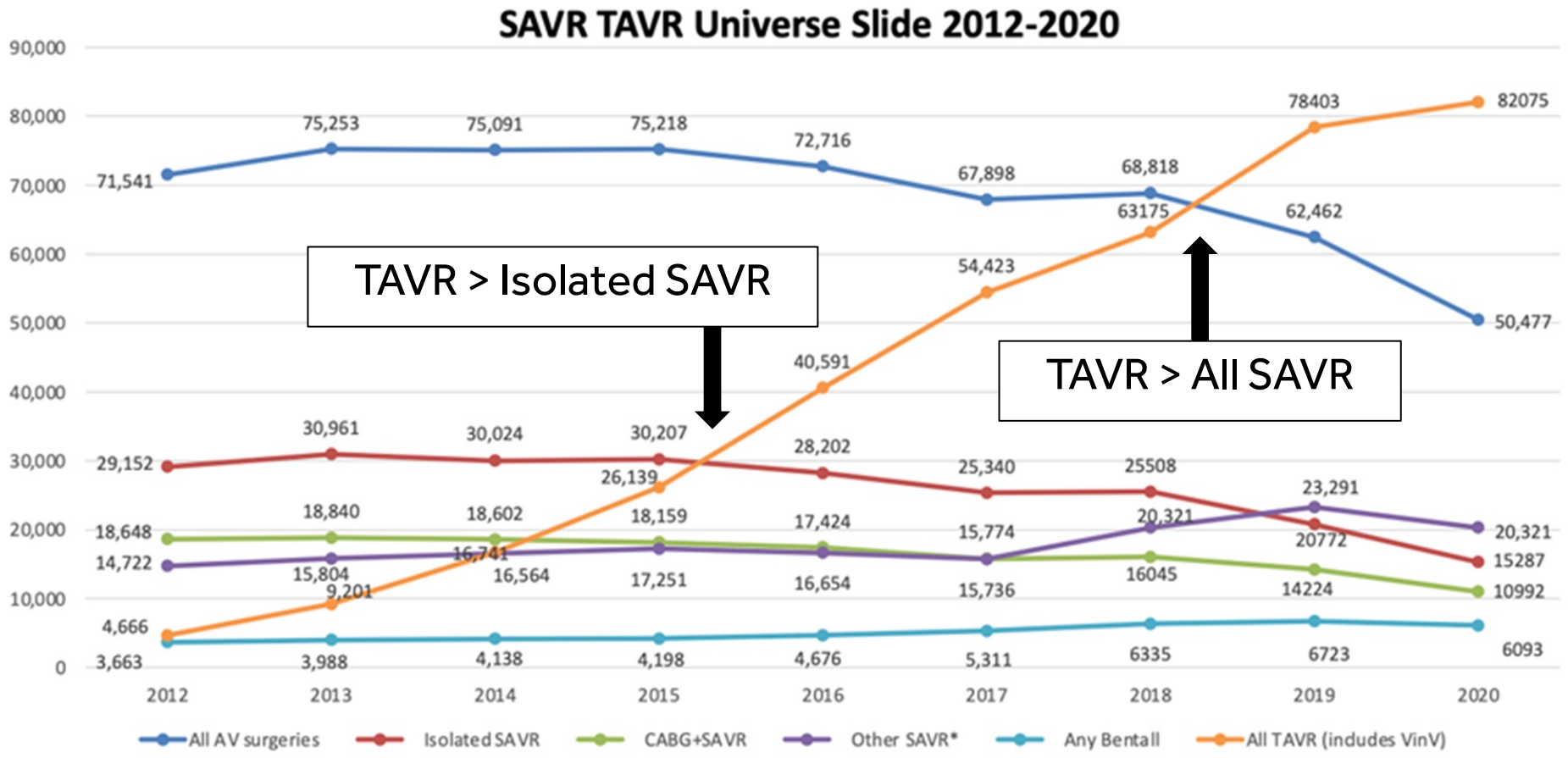
Review factor responsible for lifetime management of patients with TAVR

Evolution of TAVR and Aortic Stenosis management over the last decade



Kaul et al JACC 2020

- 2016-2017 TAVR and surgical AVR Volumes
- Fewer TAVRs than Surgeries



STS National Database
Trusted. Transformed. Real-Time.

NCDR
NATIONAL CARDIOVASCULAR DATA REGISTRY

Bavaria EACTS 2021

ACC/AHA recommendations for AS management

COR	LOE	RECOMMENDATIONS
1	A	1. For symptomatic and asymptomatic patients with severe AS and any indication for AVR who are <65 years of age or have a life expectancy >20 years, SAVR is recommended (123-125).
1	A	2. For symptomatic patients with severe AS who are 65 to 80 years of age and have no anatomic contraindication to transfemoral TAVI, either SAVR or transfemoral TAVI is recommended after shared decision-making about the balance between expected patient longevity and valve durability (123,126-130).
1	A	3. For symptomatic patients with severe AS who are >80 years of age or for younger patients with a life expectancy <10 years and no anatomic contraindication to transfemoral TAVI, transfemoral TAVI is recommended in preference to SAVR (123,126-132).

Otto et al Circulation 2020

ACC/AHA recommendations for AS management

Post-procedure TTE

With symptoms TTE

SAVR TTE at 5,10 yrs., then annually

TAVR annually

Recommendations for Diagnosis and Follow-Up of Prosthetic Valves
Referenced studies that support the recommendations are summarized in Online Data Supplement 34.

COR	LOE	Recommendations
1	B-NR	1. In patients with a surgical or transcatheter prosthetic valve and in patients who have had valve repair, an initial postprocedural TTE study is recommended for evaluation of valve hemodynamics and ventricular function.[1–4]
1	C-EO	2. In patients with a prosthetic valve or prior valve repair and a change in clinical symptoms or signs suggesting valve dysfunction, repeat TTE is recommended.
1	C-LD	3. In patients with a prosthetic valve replacement or prior valve repair and clinical symptoms or signs that suggest prosthetic valve dysfunction, additional imaging with TEE, gated cardiac CT, or fluoroscopy is recommended, even if TTE does not show valve dysfunction.
2a	C-LD	4. In patients with a bioprosthetic surgical valve, TTE at 5 and 10 years and then annually after implantation is reasonable, even in the absence of a change in clinical status.
2a	C-LD	5. In patients with a bioprosthetic TAVI, TTE annually is reasonable.

Otto et al Circulation 2020

FOCUS ON VALVE PERFORMANCE

CENTRAL PARADIGMS OF BIOPROSTHETIC VALVE SELECTION

Heart Team

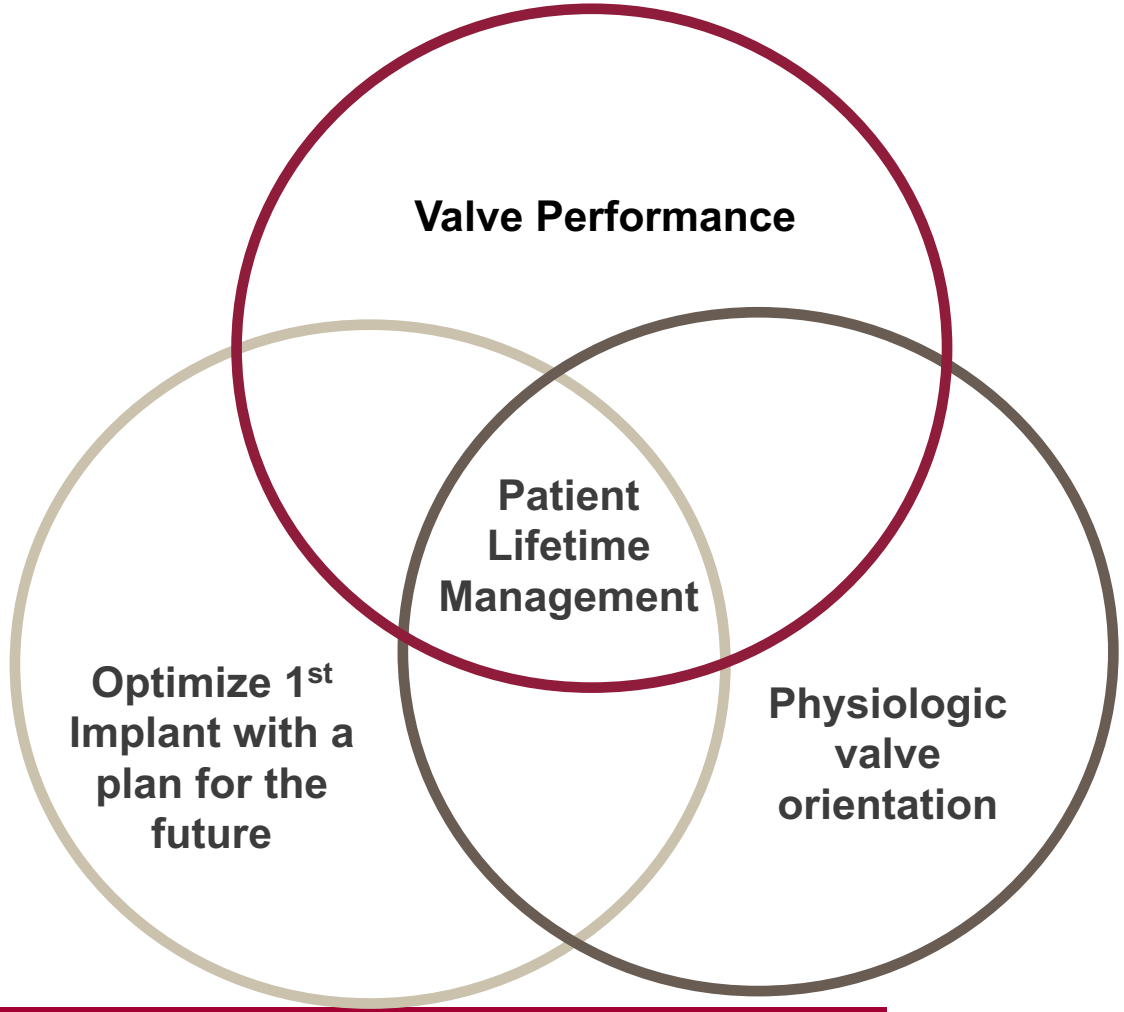
Structural Cardiologists
Heart Surgeon
Primary Provider
Patient Values and Preferences

COR	LOE
1	C-EO
2a	C-LD

Patients with severe VHD should be evaluated by a Multidisciplinary Heart Valve Team (MDT) when intervention is considered

Consultation with or referral to a Primary or Comprehensive Heart Valve Center is reasonable when treatment options are being discussed for 1) asymptomatic patients with severe VHD, 2) patients who may benefit from valve repair versus valve replacement, or 3) patients with multiple comorbidities for whom valve intervention is considered

Initial Bioprosthetic Valve Choice



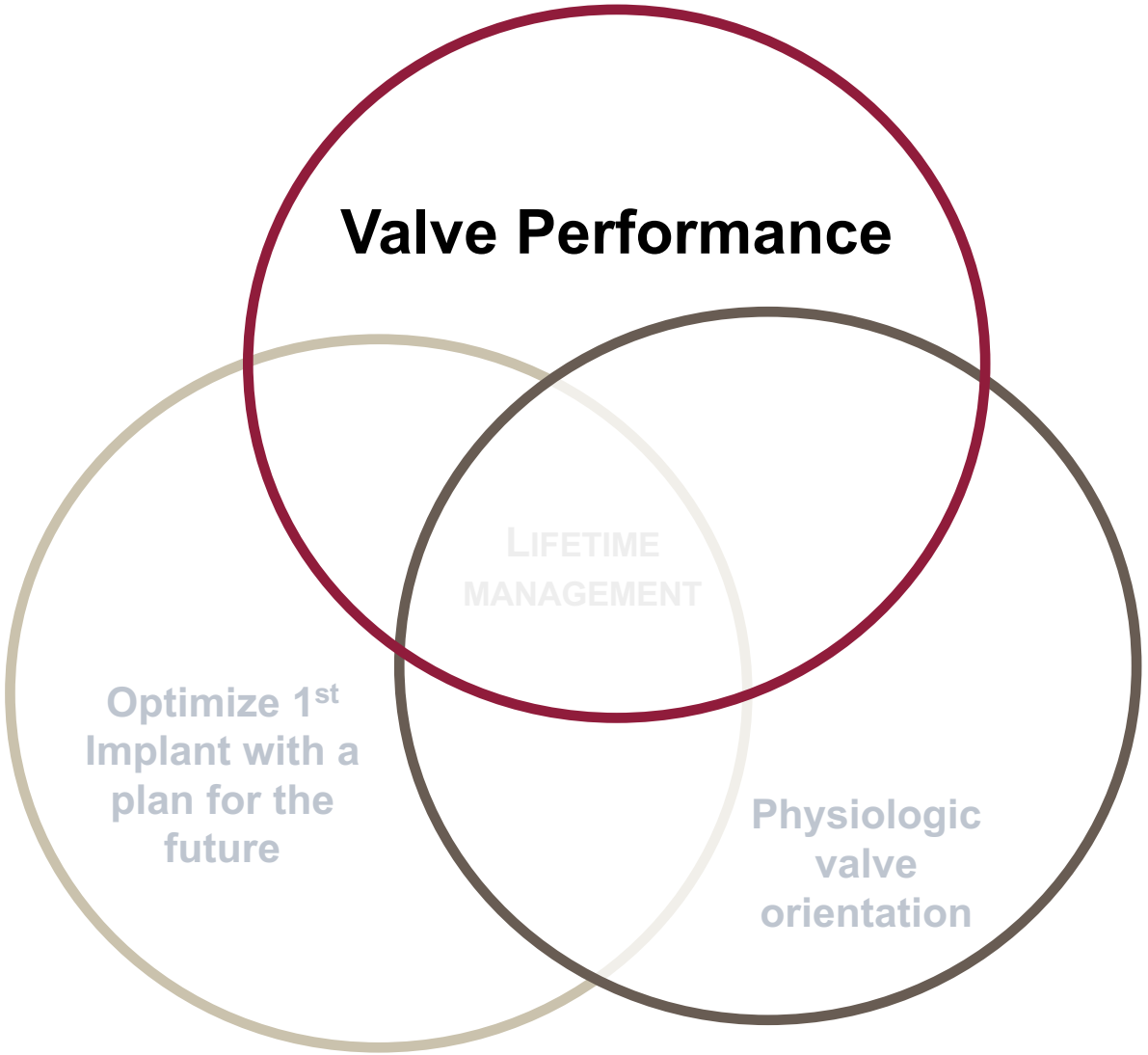
Otto JACC 2021 243; 50: e72-e227

FOCUS ON VALVE PERFORMANCE

CENTRAL PARADIGMS OF BIOPROSTHETIC VALVE SELECTION

How well does the THV perform – how long does it last?

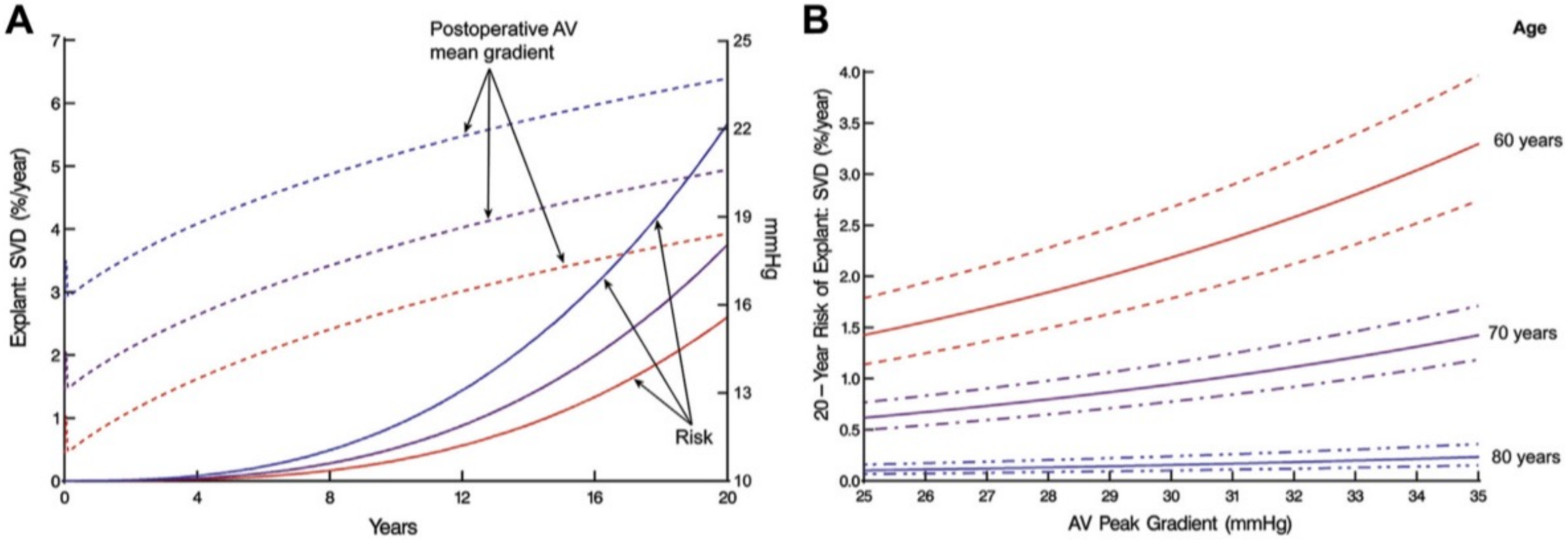
What about in younger (< 75 years) lower risk patients



» Clinical Impact of Bioprosthetic Valve Performance

» 354 Surgical Explants in 12,569 Patients after Surgical AVR

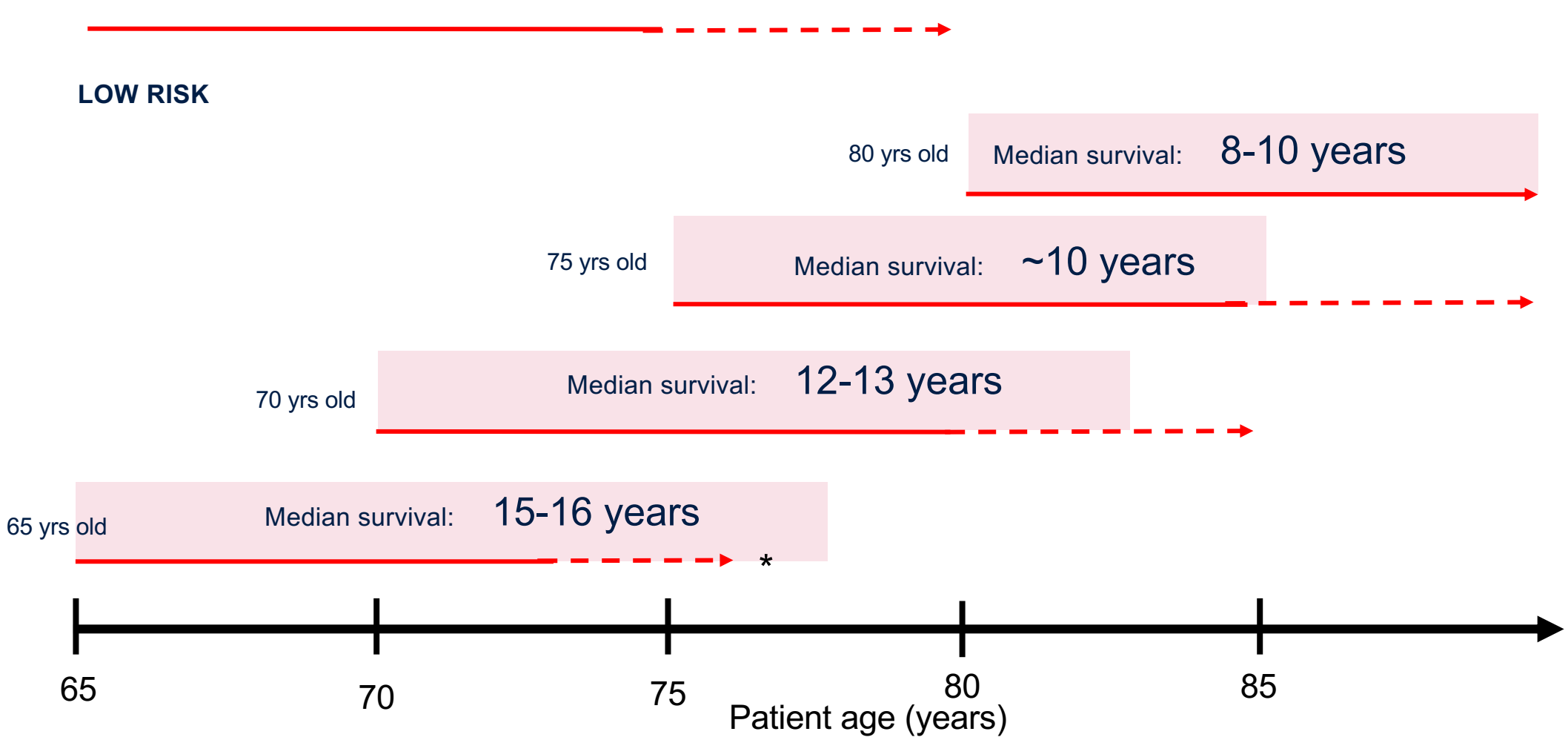
Higher residual gradients → increased risk for explant



Johnston DR, et al. Ann Thorac Surg 2015: 99(4): 1239-1247.

LIFETIME MANAGEMENT OF AORTIC STENOSIS PATIENT

LIFE EXPECTANCY WITH VALVE PERFORMANCE



Data from Martinsson, A., et al. JACC 2021;78(22):2147–57

VALVE PERFORMANCE AND DURABILITY

BACKGROUND

- Transcatheter aortic valve implantation (TAVR) is an established treatment for severe aortic stenosis (AS) in patients of all risk levels.
- Younger, low risk patients with increasingly long expected survivals are being offered TAVR.
- The lifetime management of these patients requires an understanding of bioprosthetic valve durability and failure.
- The VARC-3 and EAPCI consensus documents define four modes of bioprosthetic valve dysfunction: Structural valve deterioration (SVD), non-structural valve dysfunction, thrombosis, and endocarditis.[1,2]

1. VARC-3 Writing Committee, et al. European Heart Journal 42.19 (2021): 1825-1857
2. Capodanno D., et al. European Heart Journal 38.45 (2017): 3382-3390

Types of Bioprosthetic Valve Dysfunction

Structural Valve Deterioration

1. Wear and tear
2. Leaflet disruption
3. Flail Leaflet
4. Leaflet Thrombosis and calcification
5. Strut fracture of deformation

Non-Structural Valve Deterioration

1. PVL
2. PPM

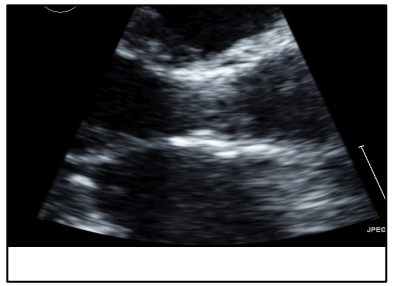
Thrombosis/Endocarditis

Thrombosis
= Subclinical
= Clinical

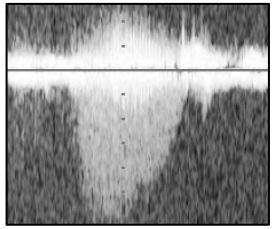
Endocarditis

Généreux et al. VARC 3 JACC 2021

Prosthesis Patient Mismatch



PPM -> Prosthesis with normal function but too small for patient's BSA
High residual gradient post AVR, small indexed EOA



Prosthesis Patient Mismatch

If BMI < 30 kg/m²

Severity	Indexed EOA (cm²/m²)
Insignificant	>0.85
Moderate	0.85-0.66
Severe	≤0.65

If BMI ≥ 30kg/m²

Severity	Indexed EOA (cm²/m²)
Insignificant	>0.70
Moderate	0.70-0.56
Severe	≤0.55

Généreux et al. VARC 3 JACC 2021

Bioprosthetic valve dysfunction

Stages of Deterioration

STAGE 1
Morphological valve deterioration

Evidence of structural valve deterioration, non-structural valve dysfunction (other than Paravalvular regurgitation or prothesis-patient mismatch), thrombosis, or endocarditis without significant hemodynamic changes.

STAGE 2
Moderate hemodynamic deterioration

Increase in mean transvalvular gradient ≥ 10 mmHg resulting in mean gradient ≥ 20mmHg with concomitant decrease in EOA ≥0.3 cm² or ≥ 25% and/or decrease in Doppler velocity index > 0.1 or ≥ 20% compared to echo assessment performed 1 to 3 months post-procedure.

Or

New occurrence or increase of ≥1 grade of intraprosthetic AR resulting in ≥ moderate AR

STAGE 3
Severe hemodynamic deterioration

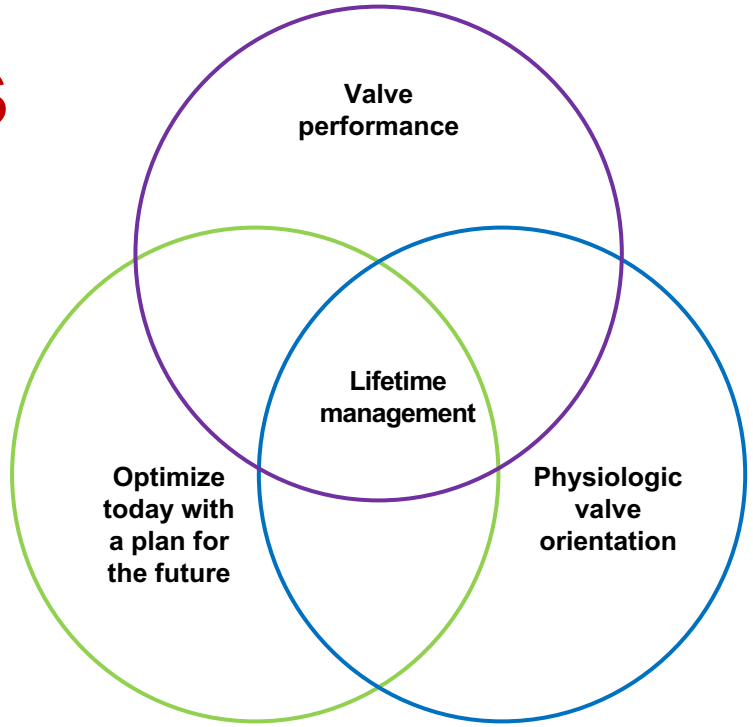
Increase in mean transvalvular gradient ≥ 20 mmHg resulting in mean gradient ≥ 30mmHg with concomitant decrease in EOA ≥0.6 cm² or ≥ 50% and/or decrease in Doppler velocity index > 0.2 or ≥ 40% compared to echo assessment performed 1 to 3 months post-procedure.

Or

New occurrence or increase of ≥2 grade of intraprosthetic AR resulting in ≥ moderate AR

Généreux et al. VARC 3 JACC 2021

Valve performance starts the day of the procedure and **continues for a lifetime.**



Patients without severe PPM have higher survival versus those with ≥ moderate PPM[1]

Early performance markers inform late outcomes.

0–30 days	Low gradients/large EOA Freedom from: • Markers of BVD – PVL – Patient prosthesis mismatch
30 days–1 year	Freedom from: • PVL • Thrombosis • Endocarditis
1–5 years	Freedom from: • SVD
5 years	Freedom from: • BVD/Bioprosthetic valve failure (BVF) • Valve reinterventions

» Kornyeva A, et al. *Front Cardiovasc Med.* 2023;10:1175246.

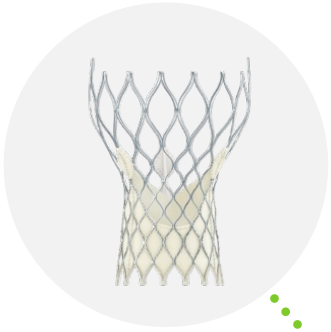
Evolut Design, Valve Performance & Evolut Low Risk

Disclosers

1. Medtronic Proctor Fees and Honoraria
2. Abbott Proctor Fees and Honoraria
3. ABIOMED/Johnson and Johnson Proctor Fees and Honoraria

Evolut Valve Design

The evolution of Evolut™

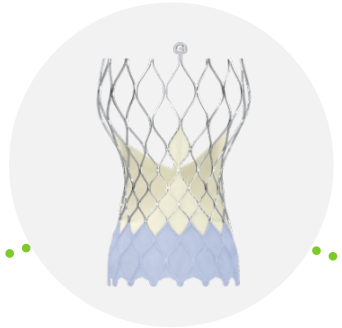


CoreValve™
2014

First self-expanding TAVR valve

Evolut™ R
2015

Recapturability, lower profile, and more consistent radial force across annulus range

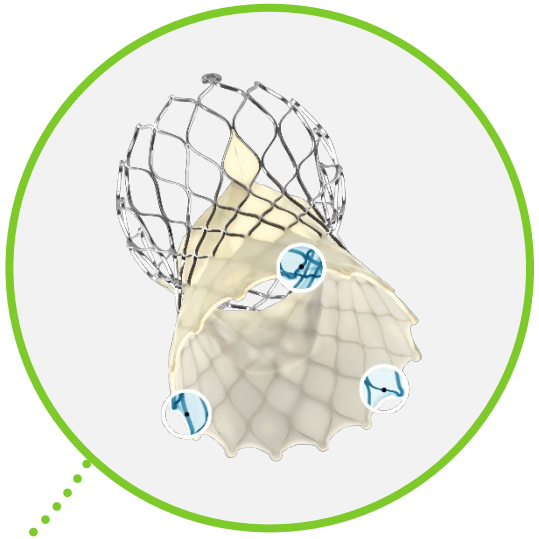


Evolut™ PRO
2017

PVL performance

Evolut™ PRO+
2019

Lower delivery profile and **large valve PVL performance**



Evolut™ FX
2022

- Delivery system re-engineered for greater **precision and control**
- Radiopaque markers provide a reference for deployment depth and commissure location
- **Ease of use**

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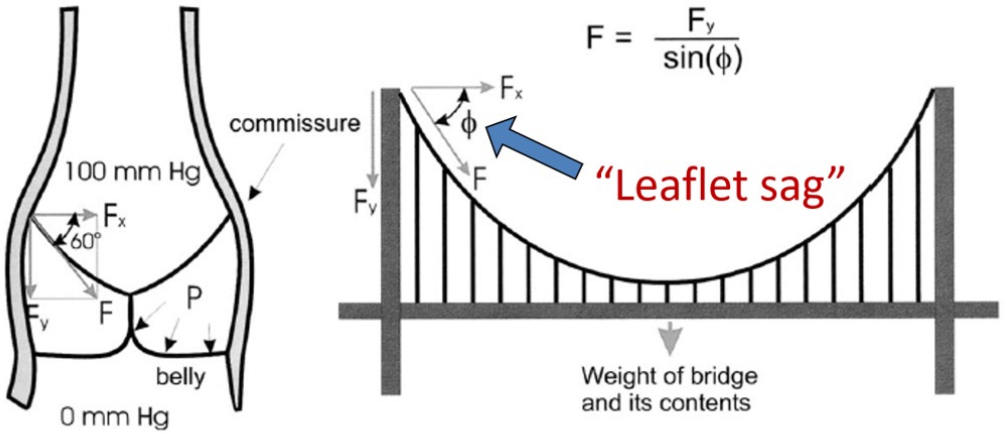
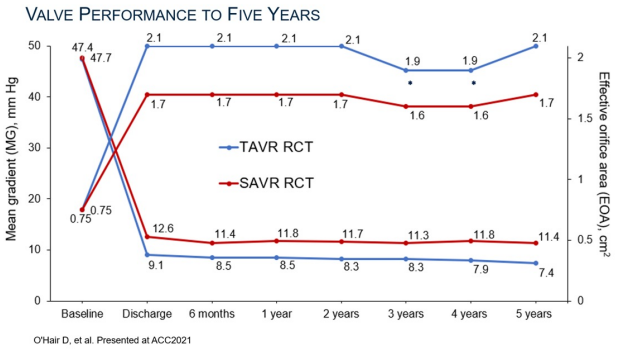
VALVE PERFORMANCE STARTS WITH DESIGN

EVOLUT FRAME DESIGN – BUILT ON A PROVEN DESIGN

Greater "sag" (ϕ) lowers the loaded leaflet stress
Influenced by frame height, leaflet length, frame angle



Piazza N London Valve 2022 Presentation



O'Hair D, et al. Presented at ACC2021

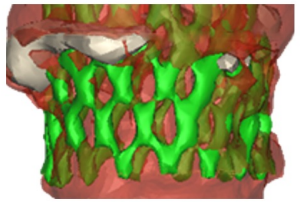
FOCUS ON THE INFLOW

- Nitinol yields strong outward radial force
- Multiple cells: Conformability for eccentricity
- Effective for LVOT calcium

NAVITOR

ACURATE NEO-2

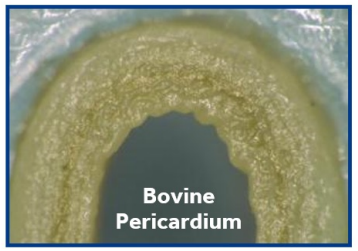
Conforming Frame Seals at **Multiple Levels***



Bright Green = Contact with Native Anatomy

External Wrap **Increases Surface Contact** to help **Reduce Gaps**

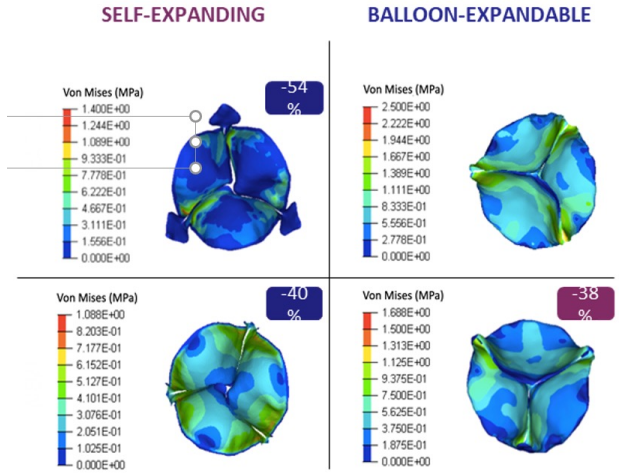
PORCINE PERICARDIUM



- Approximately half the thickness of bovine pericardium to enable low delivery profiles[1]
- Significantly stronger ultimate tensile strength than peak physiologic stresses for durable performance[1]

1. Sacks MS. 2008. Data on File
2. Li, K and Sun, W. Ann Biomed Eng. 2010 Aug;

New generation devices had 30% lower peak mechanical stress
Self-expanding valve had 40% lower peak mechanical stress



V. Stanova, P. Pibarot. EuroPCR 2021

Supra-annular design benefits

With its supra-annular, self-expanding valve frame, Evolut™ TAVR is built on the original CoreValve™ platform, which has consistently shown strong EOAs and low gradients over time.

Less restriction leads to low gradients (mean systolic gradient).

Large EOAs have been correlated to less patient-prosthesis mismatch (PPM).

Less PPM and low gradients after aortic valve replacement have been linked to:

- Better survival[1,2]
- Less heart failure rehospitalization[2,3]
- Better valve durability[4,5]

[1] Playford D, et al. *J Am Soc Echocardiogr.* 2020;33:1077–1086.e1.
[2] Herrmann HC, et al. *J Am Coll Cardiol.* 2018;72:2701–2711.
[3] Anand V, et al. *Am J Cardiol.* 2020;125:941–947.
[4] O'Hair D. Presented at American College of Cardiology 70th Annual Scientific Session & Expo. May 2021.
[5] Søndergaard L, et al. *J Am Coll Cardiol.* 2019;73:546–553.

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CLINICAL IMPACT OF VALVE PERFORMANCE

Clinical Impact of Valve Performance

Objectives

- To outline the differences in structural valve performance between surgical and transcatheter therapy, and the impact of SVD on clinical outcomes
- To discuss the impact of severe PPM on clinical outcomes after TAVR
- To discuss the early subclinical impact of leaflet thrombosis and SVD and its associations with stroke.
- To discuss the NOTION RCT and review the 10-year data.
- To highlight there is continued clinical focus on valve performance

STRUCTURAL VALVE DETERIORATION

POOLED RCT COREVALVE/EVOLUT TAVR V. SURGERY

OBJECTIVE: To evaluate the 5-year incidence, clinical outcomes, and predictors of hemodynamic SVD in patients undergoing self-expanding TAVI or surgery.

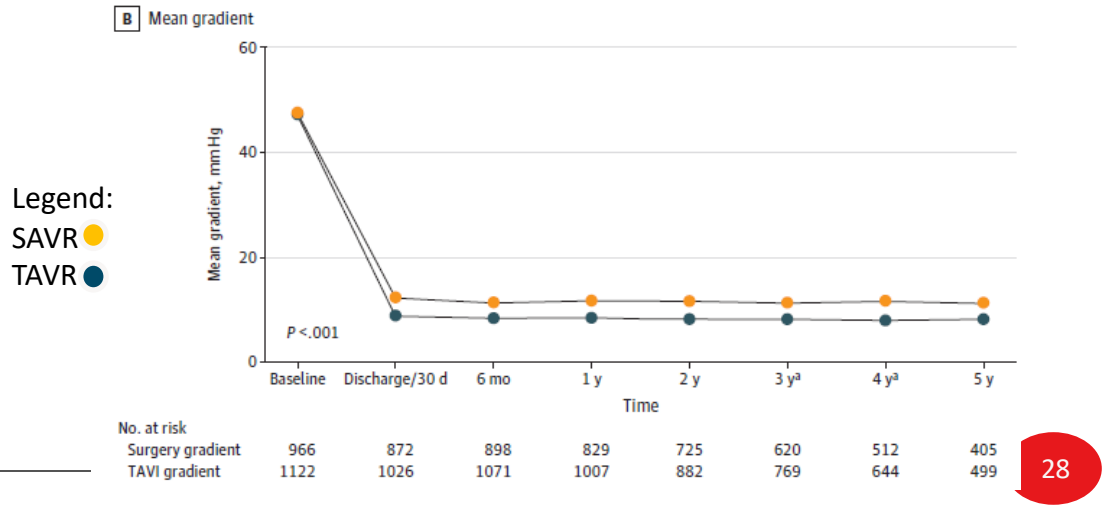
DESIGN: Post hoc analysis pooled data from the CoreValve US High Risk Pivotal (n = 615) and SURTAVI (n = 1484) randomized clinical trials (RCTs); it was supplemented by the CoreValve Extreme Risk Pivotal trial (n = 485) and CoreValve Continued Access Study (n = 2178).

DEFINITION: **SVD was defined as (1) an increase in mean gradient of 10mmHg or greater from discharge or at 30 days to last echocardiography with a final mean gradient of 20mmHg or greater** or (2) **new-onset moderate or severe intraprosthetic aortic regurgitation** or an increase of 1 grade or more.

Table. Baseline Clinical Characteristics

Characteristic	Patients, No. (%)[a]	
	Surgery RCT (n = 971)	TAVI RCT (n = 1128)
Age, mean (SD), y	80.6 (6.3)	80.9 (6.5)
Sex		
Female	444 (45.7)	496 (44.0)
Male	527 (54.3)	632 (56.0)
Body surface area, mean (SD), m^2	1.9 (0.2)	1.9 (0.2)
STS-PROM, mean (SD)[d]	5.3 (2.5)	5.2 (2.4)
NYHA HF class III/IV	639 (65.8)	757 (67.1)
Prior percutaneous coronary intervention	253 (26.1)	280 (24.8)
Prior coronary artery bypass surgery	213 (21.9)	229 (20.3)
Hypertension	889 (91.6)	1056 (93.6)
Creatinine >2.0 mg/dL	24 (2.5)	24 (2.1)
Prior atrial fibrillation/flutter	305 (31.4)	348 (30.9)
Baseline anticoagulation therapy	236 (24.3)	236 (20.9)

Sustained Reduction in Gradients to 5 years



Legend:
SAVR
TAVR

O'Hair, et al. JAMA Cardiol 2023;8(2):111-119

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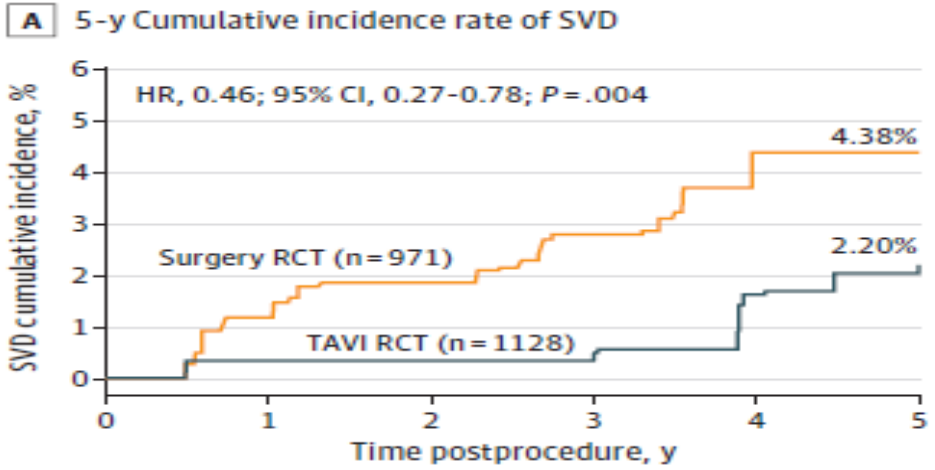
28

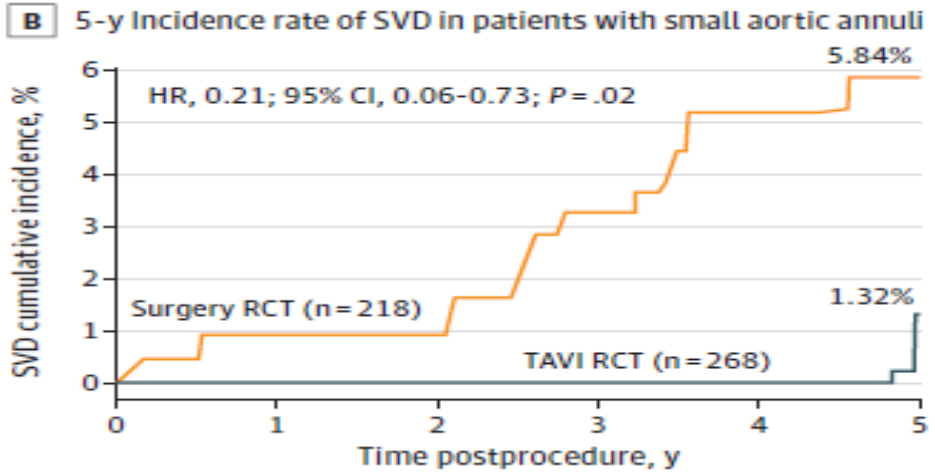
STRUCTURAL VALVE DETERIORATION

RANDOMIZED CLINICAL EVIDENCE: COREVALVE/EVOLUT TAVR V. SURGERY

SVD: All TAVI v SAVR



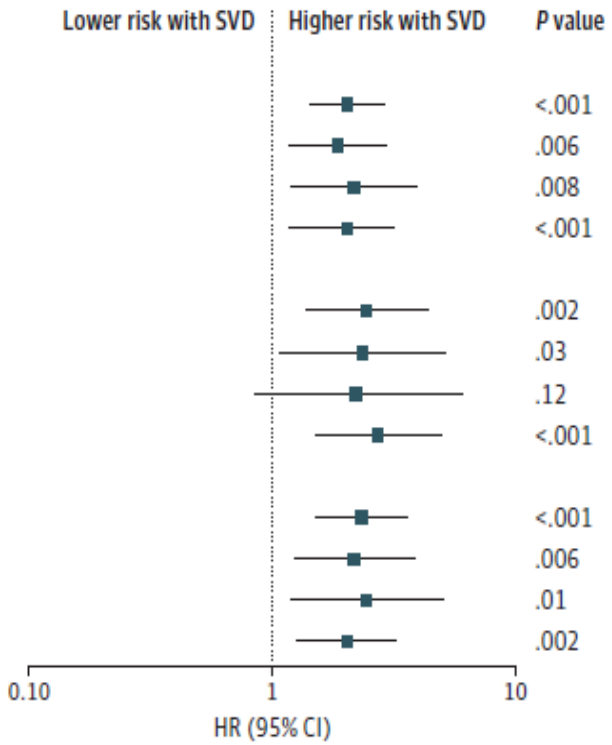
Small Annulus ≤ 23 mm



SVD Correlates with 5 Year Mortality

Figure 3. Association Between Clinical Outcomes and Structural Valve Deterioration (SVD)

Outcome	HR (95% CI)	P value
Pooled surgery RCT and all TAVI[a] (n = 4762)		
All-cause mortality	2.03 (1.46-2.82)	<.001
Cardiovascular mortality	1.86 (1.20-2.90)	.006
Hospitalization for AV disease/worsening HF	2.17 (1.23-3.84)	.008
Composite[b]	2.02 (1.42-2.88)	<.001
Surgery RCT (n = 971)		
All-cause mortality	2.45 (1.40-4.30)	.002
Cardiovascular mortality	2.37 (1.10-5.08)	.03
Hospitalization for AV disease/worsening HF	2.20 (0.81-5.98)	.12
Composite[b]	2.73 (1.53-4.88)	<.001
All TAVI[a] (n = 3791)		
All-cause mortality	2.34 (1.55-3.53)	<.001
Cardiovascular mortality	2.17 (1.26-3.76)	.006
Hospitalization for AV disease/worsening HF	2.45 (1.22-4.93)	.01
Composite[b]	2.03 (1.29-3.19)	.002



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O'Hair, et al. JAMA Cardiol 2023;8(2):111-119

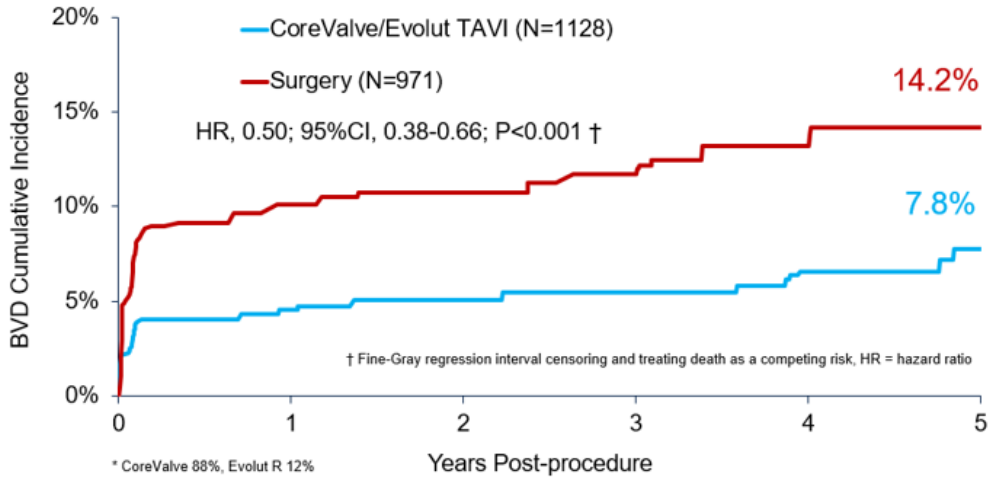
29

OVERALL BIOPROSTHETIC VALVE PERFORMANCE

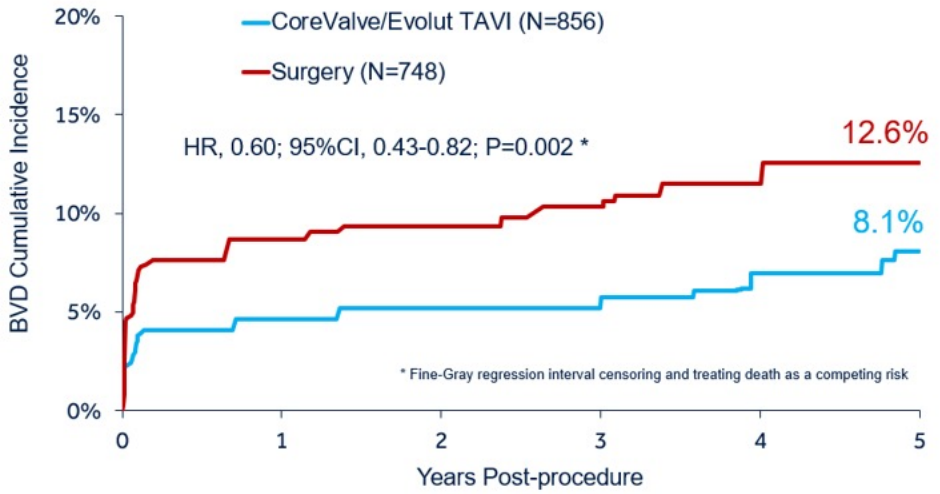
EVIDENCE FROM RCT COREVALVE/EVOLUT TAVR V SURGERY

- 2099 Patients Enrolled in High Risk and SURTAVI RCTs
- Valve performance measured by absence of bioprosthetic valve dysfunction
- CV/EV TAVR significantly better than surgery starting at 30 days and continuing to 5 years

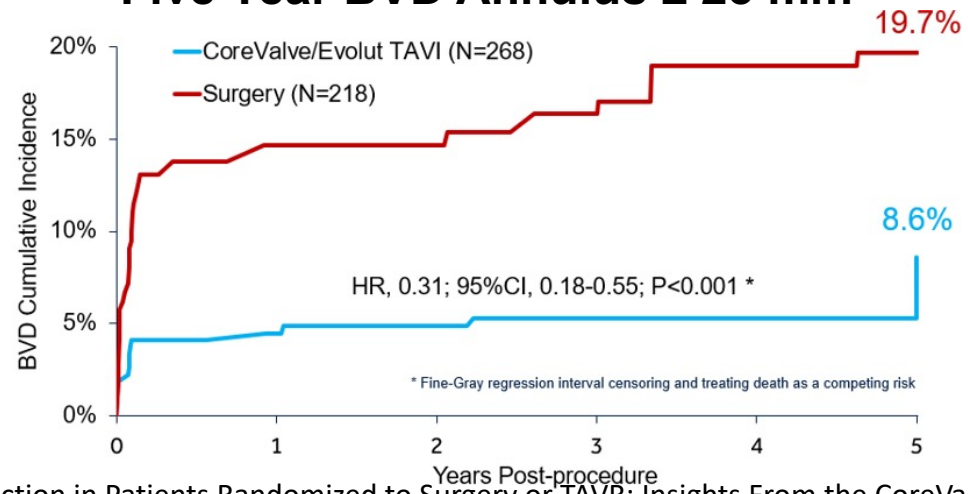
Five Year Bioprosthetic Valve Dysfunction (BVD)



Five Year BVD Annulus > 23 mm



Five Year BVD Annulus ≤ 23 mm



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Yakubov S, et al. Five-Year Incidence of Bioprosthetic Valve Dysfunction in Patients Randomized to Surgery or TAVR: Insights From the CoreValve US Pivotal and SURTAVI Trials. Presented at CRT; February 2023.

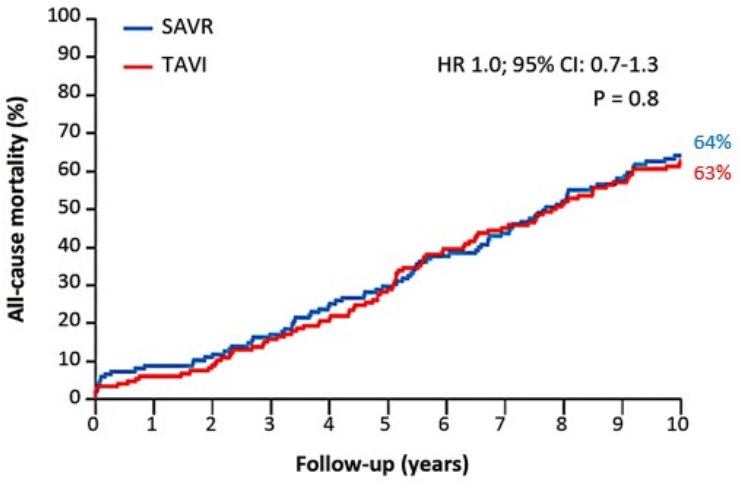
30

- 10-Year Data with 1st Generation COREVALVE vs Surgery

NOTION "ALL COMERS" TRIAL | 10 YEAR RESULTS

- Long-term data are limited in "all comer" lower risk patients. In the NOTION 10-year with an average age of ~79, 37% of TAVI patients survived 10 years – the rates of valve degeneration, as assessed by various measures of severe structural valve deterioration (SVD) and severe bioprosthetic valve dysfunction (BVD), were significantly lower in the patients treated with the 1st generation CoreValve compared with surgery[1]

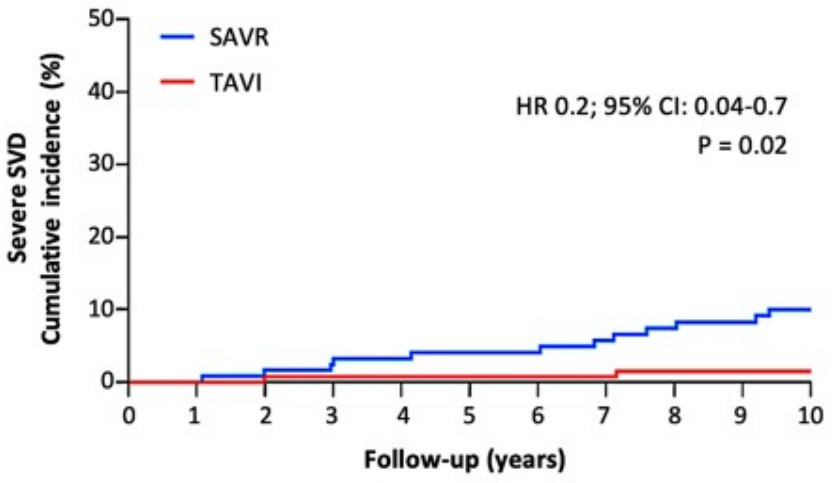
All-cause mortality



Patients at risk

TAVI	145	136	132	122	115	101	86	78	69	61	53
SAVR	135	123	120	112	102	95	83	75	64	56	48

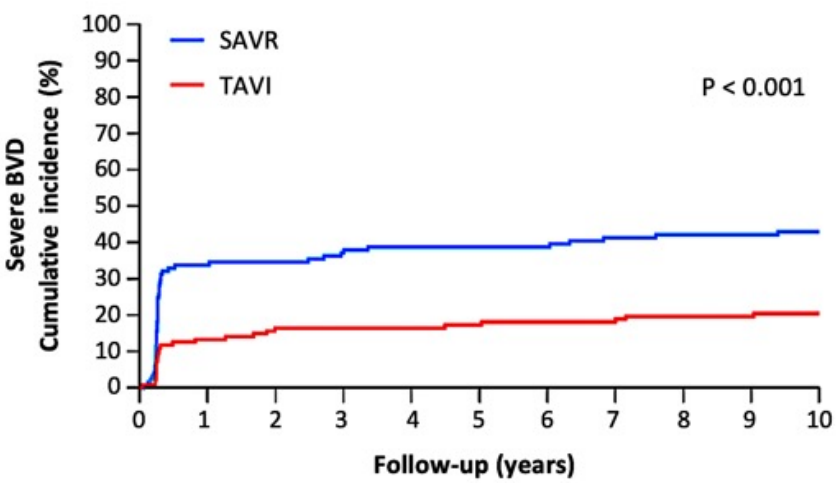
Severe SVD



Patients at risk

TAVI	134	132	129	118	109	96	82	73	62	51	40
SAVR	123	122	119	110	100	91	79	70	58	50	39

Severe BVD



Patients at risk

TAVI	127	108	102	95	91	79	69	62	53	46	40
SAVR	121	80	79	74	68	65	58	50	42	37	33

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[1]de Backer et al The Notion Trial London Valves 2023, London, with permission.

31

Subclinical Leaflet Thrombosis After TAVR
and Association with Stroke Rate

STATE-OF-THE-ART REVIEW

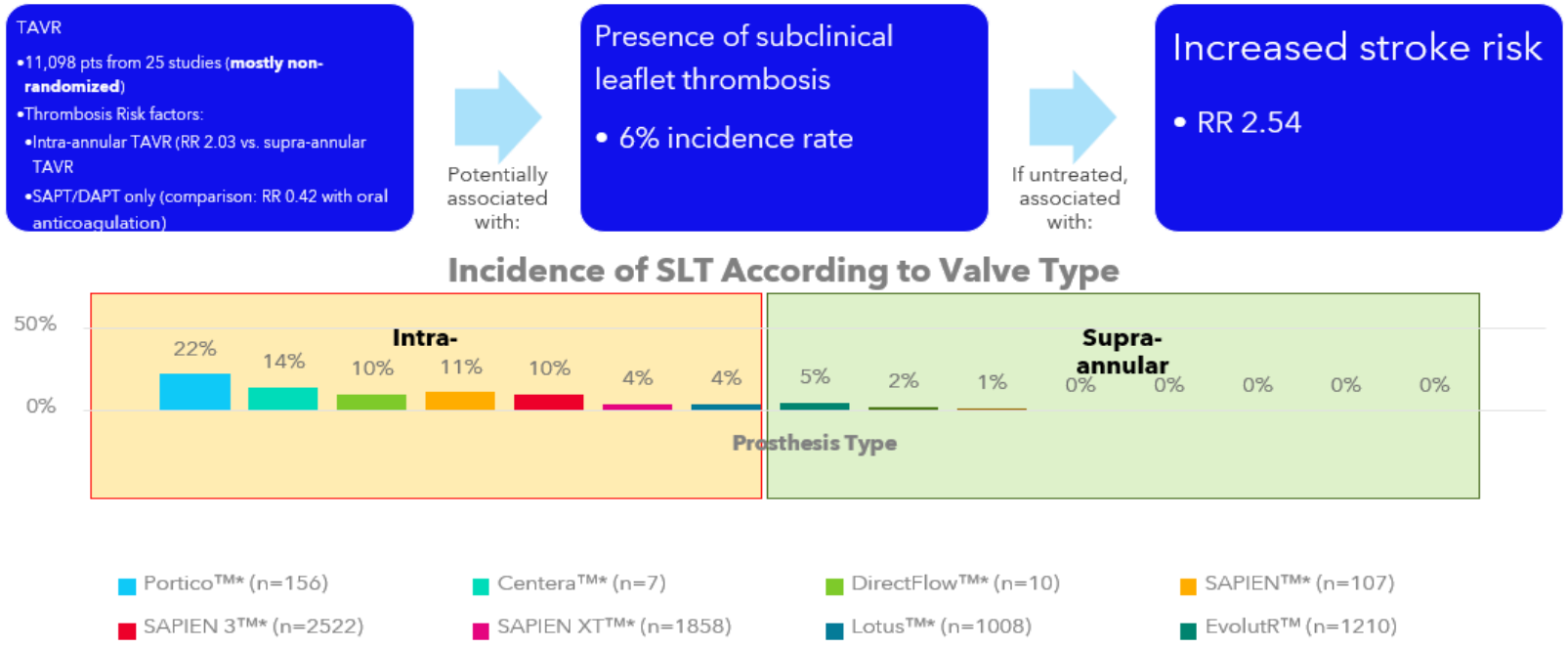
Subclinical Leaflet Thrombosis After Transcatheter Aortic Valve Replacement

A Meta-Analysis

Matthias Bogyi, MD,[a] Rüdiger E. Schernthaner, MD, PhD,[b] Christian Loewe, MD,[b] Gloria M. Gager, MD,[a,c] Al Medina Dizdarevic, MD,[a] Christina Kronberger, MD,[a] Marek Postula, MD, PhD,[d] Jacek Legutko, MD, PhD,[e] Poonam Velagapudi, MD,[f] Christian Hengstenberg, MD,[a] Jolanta M. Siller-Matula, MD, PhD[a,d]

HIGHLIGHTS

- Intra-annular TAVR increases risk for SLT formation compared with supra-annular TAVR.
- SLT after TAVR is associated with increased risk for stroke or TIA.
- OAC reduces risk for SLT and leads to SLT resolution compared with DAPT/SAPT.



Bogyi, M. et al. Subclinical Leaflet Thrombosis After Transcatheter Aortic Valve Replacement: A Meta-Analysis. JACC. 2021;14(24):2643-2656.

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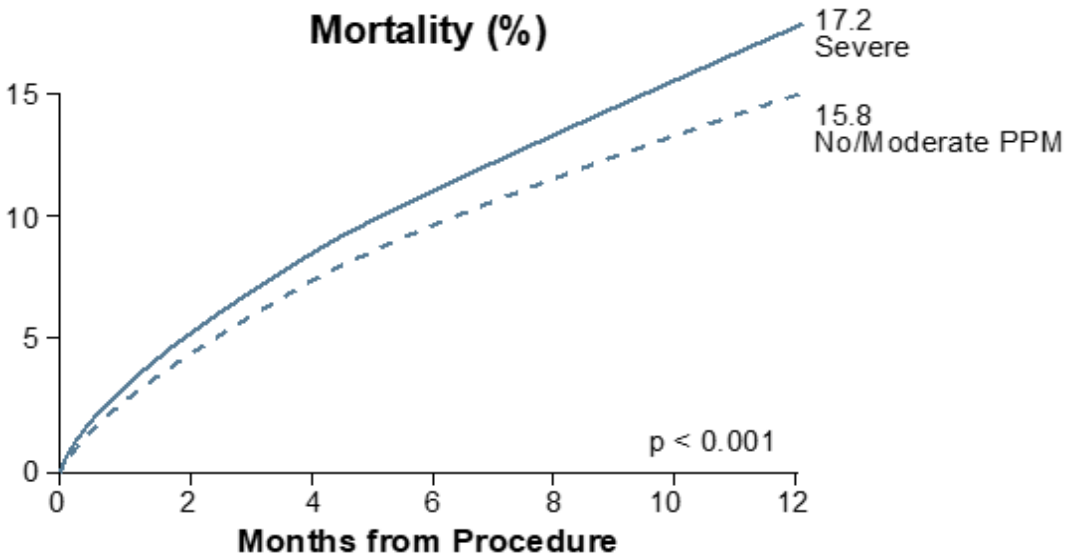
Bogyi, M. et al. Subclinical Leaflet Thrombosis After Transcatheter Aortic Valve Replacement: A Meta-Analysis. JACC. 2021;14(24):2643-2656.

Impact of Severe Prothesis patient mismatch after TAVR

- 62,125 patient enrolled in TVT Registry between 2014-2017
- PPM predictors: Small (≤23-mm diameter) valve prosthesis, valve-in-valve procedure, larger BSA, female sex, younger patients

Severe PPM was associated with higher 1-year mortality[1]



Herrmann HC, et al. *JACC.* 2018;72:2701-2711.

Severe PPM leads to a 12% increase in HF rehospitalization

Association of PPM with HF Hospitalization at One-Year				
	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio (95% CI)	p-value
Severe vs. Not Severe	1.22 (1.11–1.33)	< 0.001	1.12 (1.02–1.24)	0.017
Moderate vs. None	1.08 (1.00–1.15)	0.036	1.02 (0.95–1.10)	0.567
Severe vs. None	1.24 (1.13–1.37)	< 0.001	1.13 (1.03–1.25)	0.014

- Upcoming Clinical Trials

New Data from Low-Risk patients & SMART Randomized Trial

Clinical Trials to Be Presented at TCT 2023

Witness First-Time Presentations of Major Clinical Trials and Impactful Research

Get a front-row seat to the latest breakthroughs that will change your practice and revolutionize patient care around the world!

Don't miss these 12 presentations of late-breaking clinical trials at TCT 2023.

PARTNER 3 Low-Risk
Five-Year Clinical and Echocardiographic Outcomes from The **PARTNER 3 Low-Risk** Randomized Trial
Martin B. Leon

EVOLUT Low Risk
Four-Year Outcomes from the **EVOLUT Low Risk** Trial
Michael J. Reardon

Valve Performance ACC2024

SMART Annulus Diameter < 430 mm²
Sapien 20 mm, 23 mm v Evolut 23 mm, 26 mm (or 29mm)

TRIAL UPDATES: SMART (SMall Annuli Randomized To evolut or sapien)

Severe native aortic valve stenosis with a small annulus
(≤ 430 mm² by MDCT)

Randomization
1:1 Stratified by Sex
(~700 patients)

Prospective, multi-center, international, randomized controlled, post-market study at 90 sites in Canada, EMEA and the United States

Medtronic Evolut PRO/PRO+/FX

Edwards SAPIEN 3/ SAPIEN 3 Ultra

Co-primary endpoints at 12 mos:
1. Death, disabling stroke, HF re-hosp
2. Bioprosthetic valve dysfunction

30-Day and annual 5-Year follow-ups for all patients

Enrollment Completed

Clinical Impact of Valve Performance

Take Home Messages

- The development of bioprosthetic valve dysfunction and SVD have both been associated with higher rates of all cause mortality, cardiovascular mortality, and re-hospitalization
- Better bioprosthetic valve performance of CoreValve compared with surgery at 5 years
- Significantly lower structural valve degeneration at 10 years with CoreValve compared with surgery in NOTION RCT
- Severe PPM is associated with higher 1- year mortality and leads to 12% increase in HF hospitalization – More clinical evidence with SMART Trial
- Subclinical Leaflet Thrombosis associated with stroke if untreated. Evolut design has shown lower incidence of SLT.

Results of the Evolut Low Risk Randomized Clinical Trial

Evolut Low Risk 4 Year Data

Objectives

- To describe the patients who were enrolled in the Evolut Low Risk Study
- To describe key differences between PARTNER-3 and Evolut Low-Risk Trial design.
- To review the 4-year primary endpoint of all-cause mortality or disabling stroke, and its components in patients treated with Evolut or surgery
- To compare the hemodynamic results and valve performance in patients treated with Evolut TAV or surgery, including the occurrence of paravalvular regurgitation
- To discuss the clinical implications of the Evolut Low Risk Trial

EVOLUT LOW RISK 4-YEAR DATA

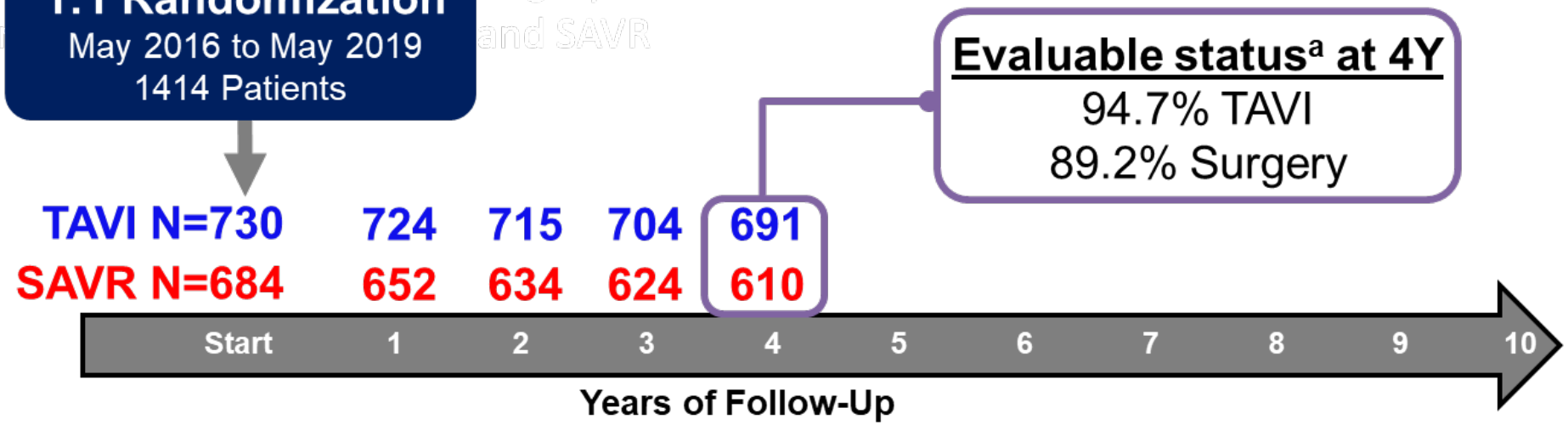
EVOLUT LOW RISK TRIAL | 4-YEAR RESULTS

Patients with Severe AS
Low risk of death (<3%) from surgery
Anatomy suitable for both TAVI and SAVR

Screening Committee

1:1 Randomization
May 2016 to May 2019
1414 Patients

Demographic	Evolut TAVR (N = 730)	SAVR (N = 684)
Age, years	74.1 ± 5.8	73.7 ± 5.9
< 70 years, %	21.4	24.0
Female, %	36.4	34.1
STS-PROM	2.0 ± 0.7	1.9 ± 0.7



[a]Evaluable status was calculated as the number of patients expected after withdrawal and loss to follow-up and included death as known status for each time point.

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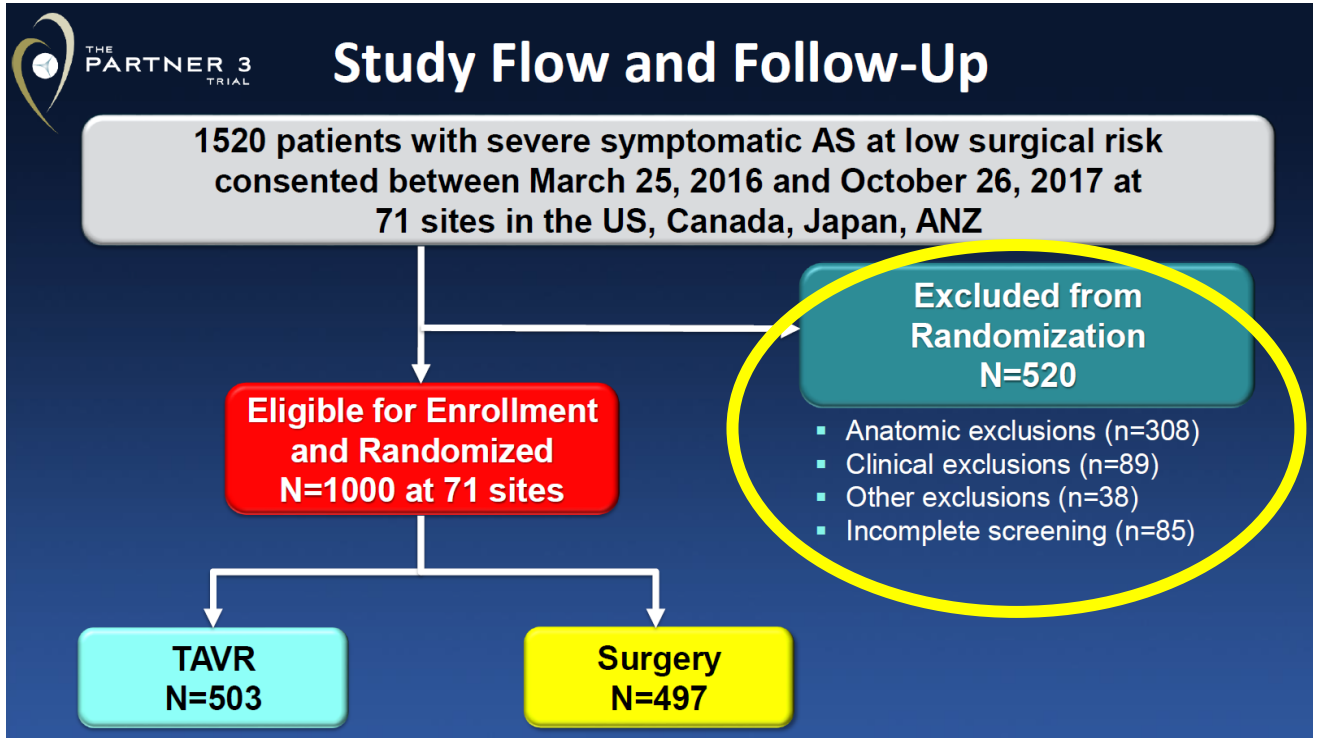
38

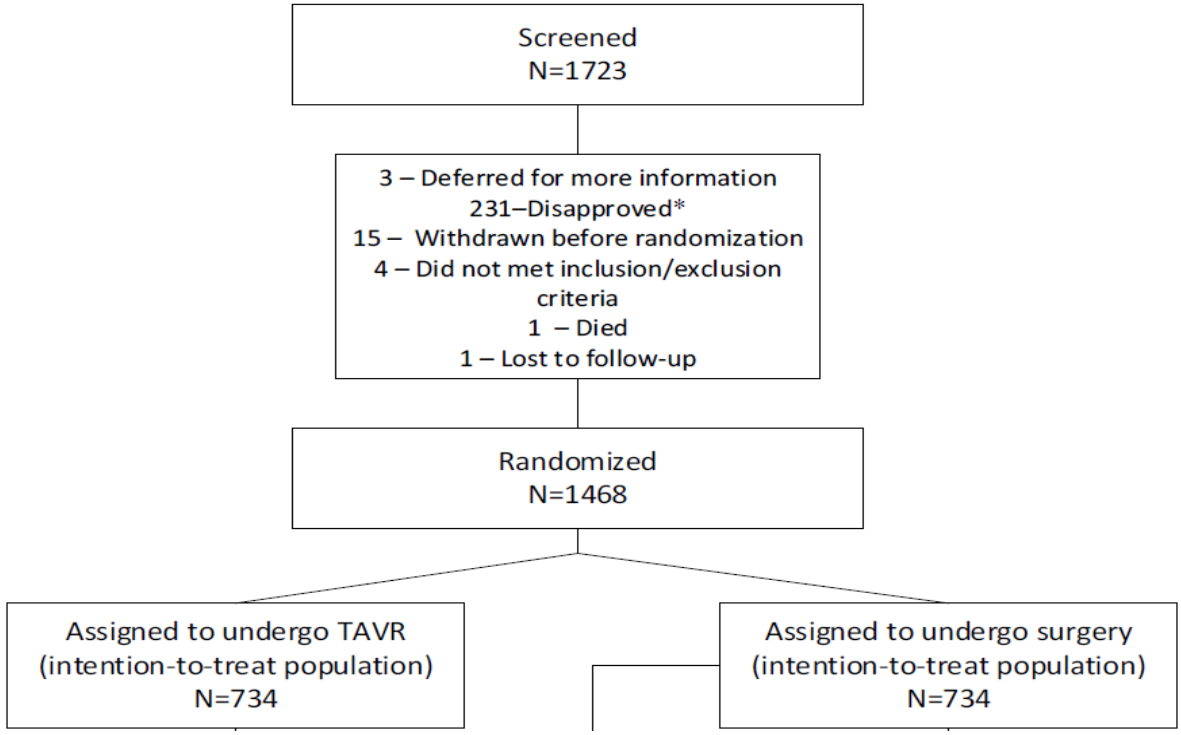
Difference between PARTNER 3 and Evolut Low Risk Trials

PARTNER 3



~34% of Patients Excluded from Trial

EVOLUT LOW RISK

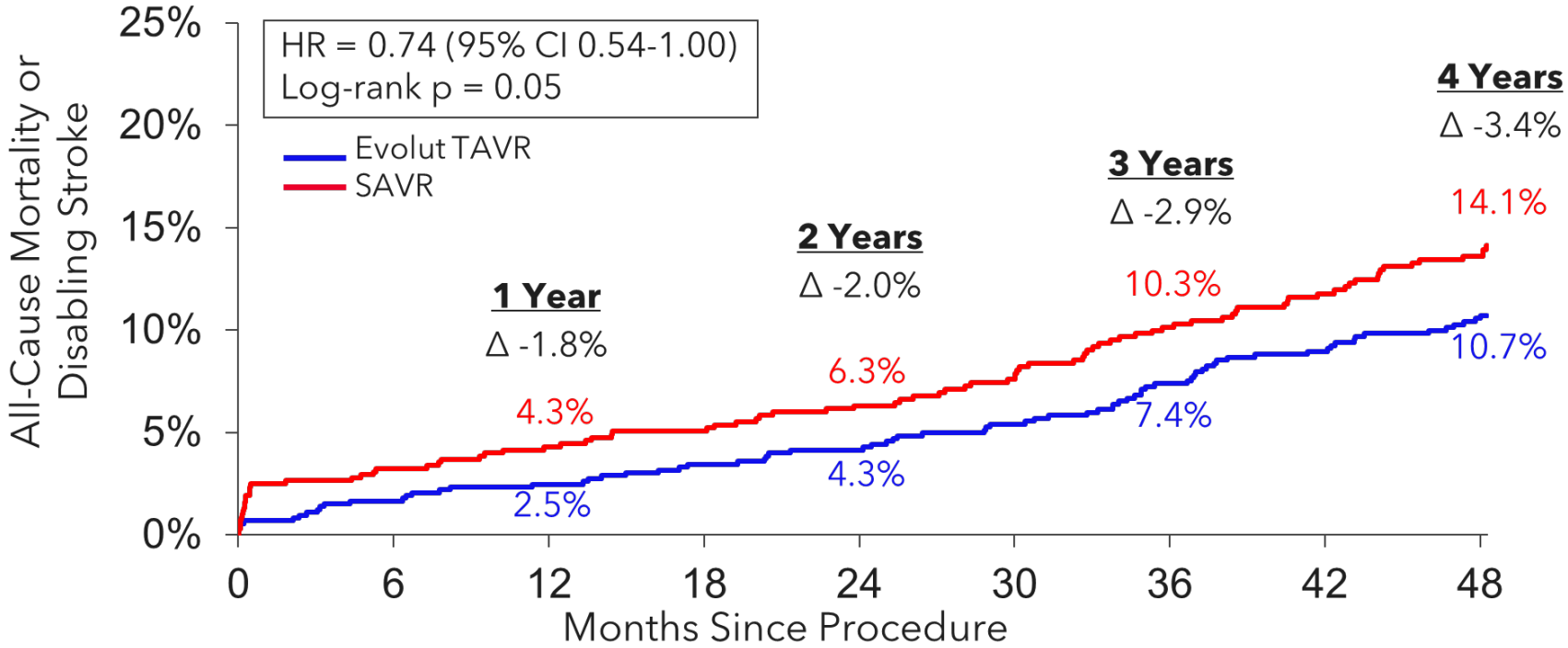


~15% of Patients Excluded from Trial

EVOLUT LOW RISK 4-YEAR DATA

- Primary Endpoint: All-Cause Mortality or Disabling Stroke

26% Relative Reduction in Hazard for Death or Disabling Stroke (p = 0.05) with Evolut TAVR vs SAVR and the Curves Continue to Separate Over Time



Evolut TAVR	730	715	706	695	685	671	651	627	592
SAVR	684	648	627	616	595	574	556	533	505

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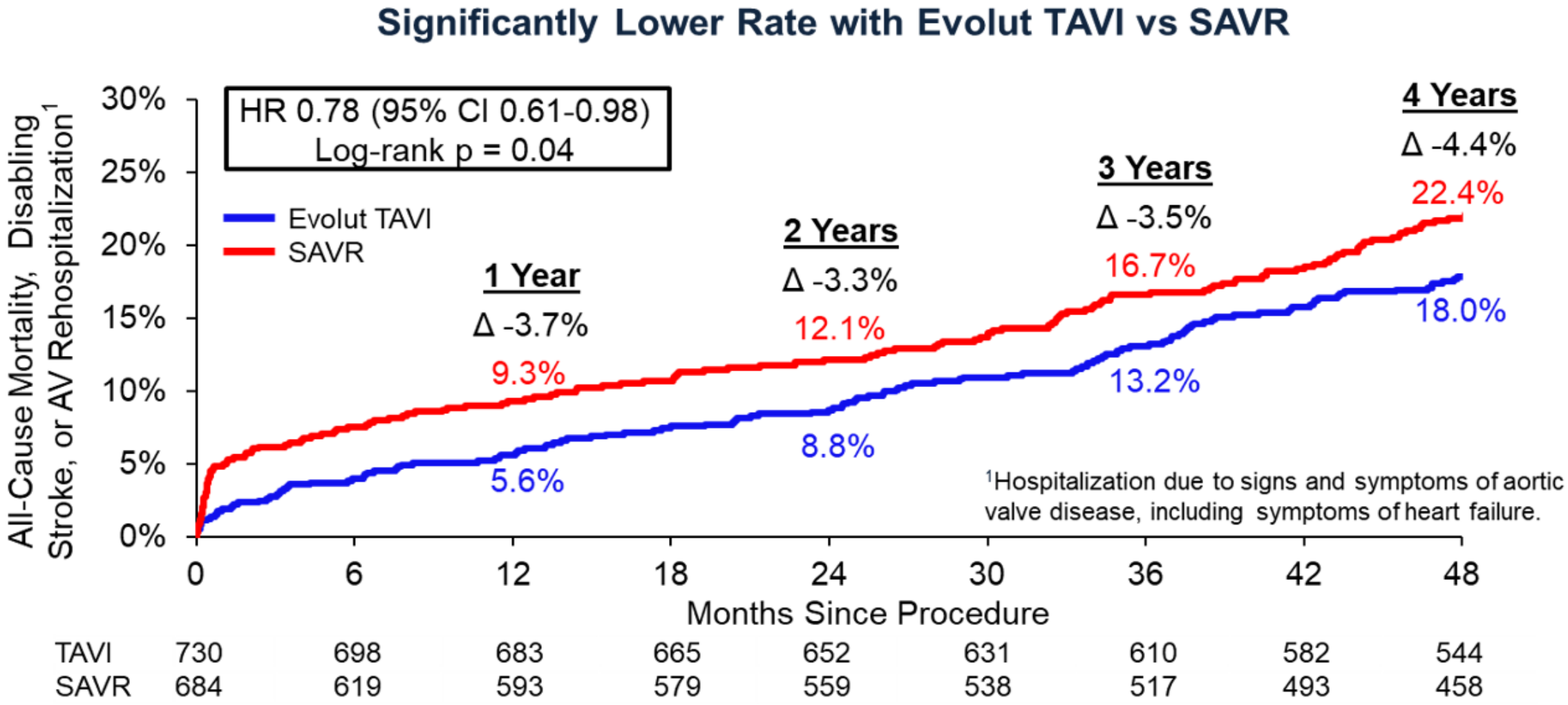
40

EVOLUT LOW RISK 4-YEAR DATA

PRIMARY ENDPOINT: ALL-CAUSE MORTALITY, DISABLING STROKE, OR AV REHOSPITALIZATION



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41

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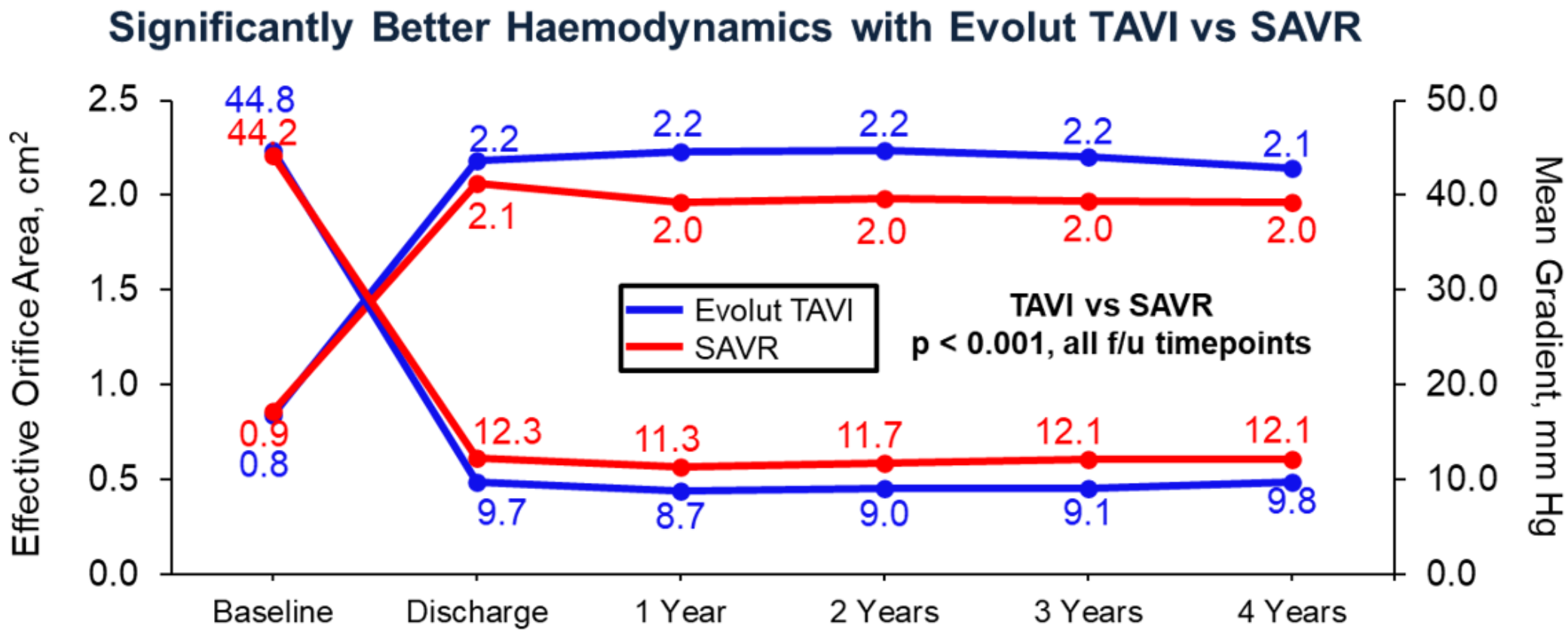
EVOLUT LOW RISK 4-YEAR DATA

COMPARATIVE HEMODYNAMICS



No. of Patients	Visit Post Procedure					
TAVI EOA	637	576	565	535	493	438
SAVR EOA	596	406	525	434	397	372
TAVI MG	717	703	662	607	547	497
SAVR MG	679	632	597	514	457	438

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42

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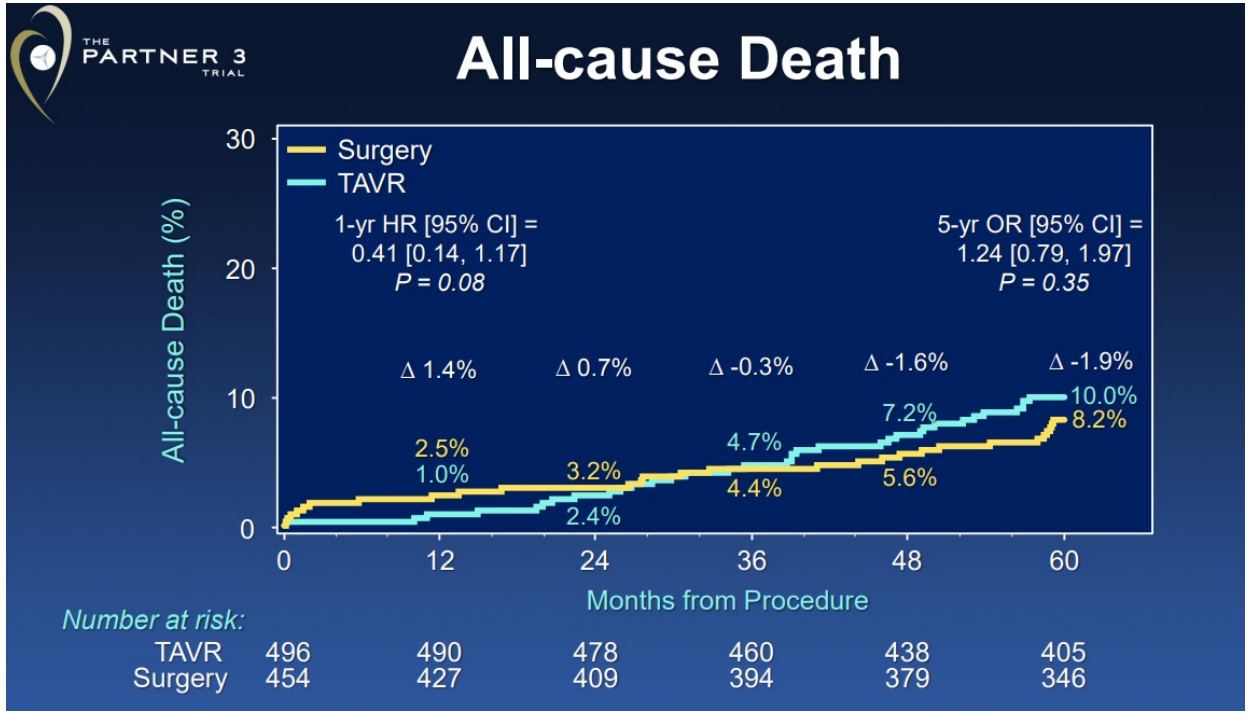
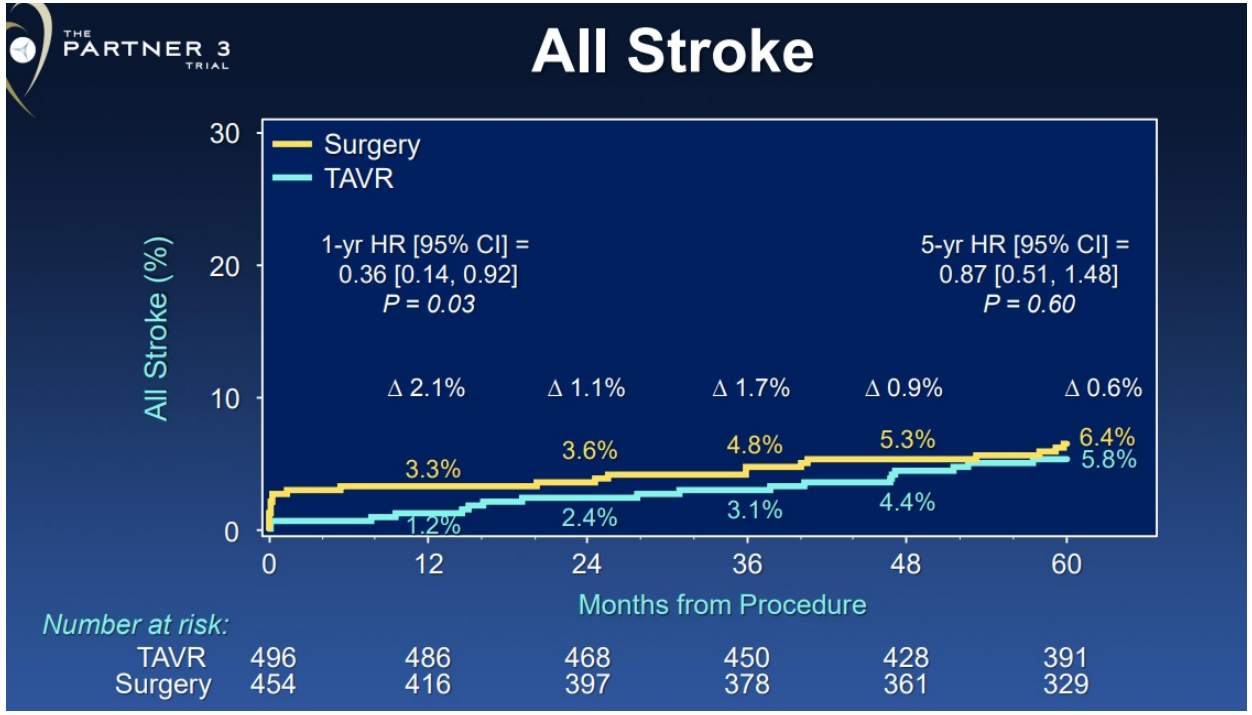
PARTNER-3

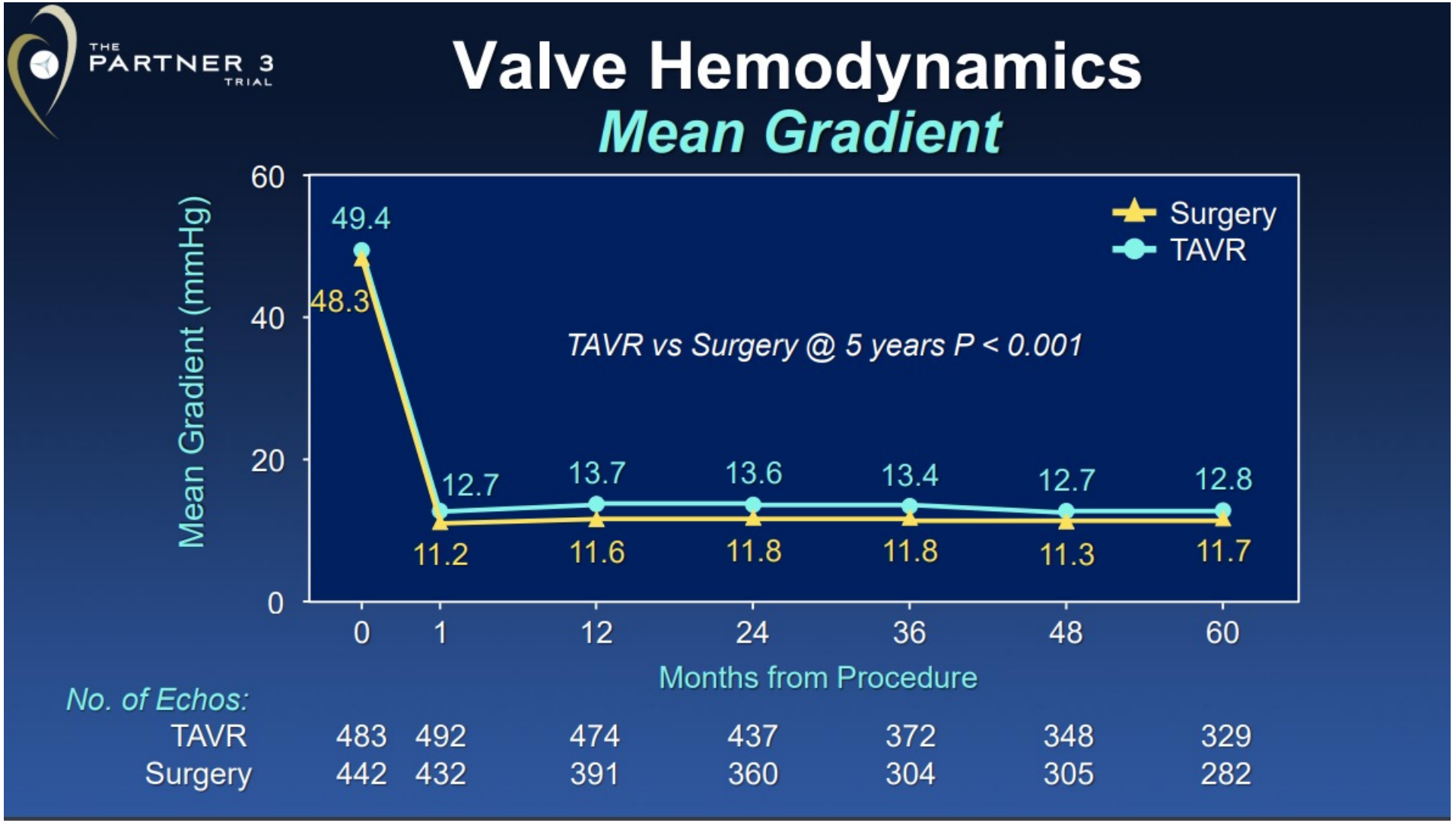
Primary Endpoints





PARTNER 3 TRIAL

VALVE HEMODYNAMICS



EVOLUT LOW RISK 4-YEAR DATA

- BIOPROSTHETIC VALVE PERFORMANCE AT 4 YEARS
  - Significantly Less Mean Gradient ≥ 20 mmHg and Severe PPM With Evolut TAVR vs Surgery

Parameter	Evolut TAVI	SAVR	P Value
Mean gradient ≥ 20 mm Hg[a]	**4.0 (20/497)**	**8.9 (39/438)**	**0.002**
Severe PVR[a], %	0.0 (0/496)	0.0 (0/426)	N/A
Severe PPM (VARC-3)[a], %	**1.1 (7/611)**	**3.5 (19/549)**	**0.008**
Valve endocarditis[b], %	0.9 (6)	2.2 (13)	0.06
Clinical or subclinical valve thrombosis[b], %	0.7 (5)	0.6 (4)	0.84
Clinical thrombosis, %	0.3 (2)	0.2 (1)	0.61
Subclinical thrombosis, %	0.4 (3)	0.5 (3)	0.91

[a]Non-cumulative data based on the 4-year (MG, PVR) or 30-day (PPM) echo, reported as proportion % (n), and compared by chi-square test. [b]Cumulative rates reported as Kaplan-Meier estimates % (n) and compared by log-rank test.
MG = mean gradient; PPM = patient-prosthesis mismatch; PVR = paravalvular regurgitation

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EVOLUT LOW RISK 4-YEAR DATA

CONSIDERATIONS

The Evolut Low Risk Trial has several important considerations

- Patients enrolled in the Evolut Low Risk study were on the higher end of the spectrum of “low risk” patients owing to the minimal number of exclusions by the national Screening Committee
- Patients enrolled in Evolut LR had an average age of 74 years – and approximately 23% of patients were under 70 years of age – comparative outcomes in much younger patients will require additional study
- The surgical operator proficiency and surgical valve selection and sizing were “best in class” surgery – but annular enlargement was performed in < 5% of patients. The effect of larger surgical valve sizing with annular enlargement will require additional study
- This report provides an analysis of hard clinical endpoints 4 years after AVR. Patients will be followed for 10 years to determine whether there is additional divergence of the clinical outcome curves

EVOLUT LOW RISK 4-YEAR DATA

SUMMARY

- TAVR patients in the Evolut Low Risk trial continue to show durable outcomes for the primary endpoint and significantly better hemodynamics than SAVR through 4 years
- 26% relative reduction in hazard for death or disabling stroke (p = 0.05) with Evolut TAVR compared to SAVR at 4 years and the curves continue to diverge over time
- Significantly lower mean gradients and higher EOAs with Evolut TAVR vs SAVR at all follow-up timepoints
- Indicators of valve performance, including high gradients at 4 years, severe PPM, and endocarditis overall favored TAVR, with similarly low thrombosis rates in both groups

Thank you!!!

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Take Home Message:

- TAVR landscape has changed in recent years since low-risk approval to have more focus on valve performance and durability.
- The lifetime management of these patients requires an understanding of bioprosthetic valve durability and failure.
- The development of bioprosthetic valve dysfunction and SVD have both been associated with higher rates of all cause mortality, cardiovascular mortality, and re-hospitalization
- **There is evidence of better bioprosthetic valve performance with CoreValve/Evolut compared with surgery at 5 years**.
- In Evolut Low Risk RCT - Indicators of valve performance, including high gradients at 4 years, severe PPM, and endocarditis overall favored TAVR, with similarly low thrombosis rates in both groups.
- **Important to track valve performance with yearly ECHO to evaluate gradients and EOA's.**

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Panel Discussion

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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 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 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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