Long-Term Valve Durability Issues and Optimal Decision-Making:

TAVR *vs.* SAVR, Mechanical *vs*. Bioprosthetic?

"I am a protagonist "TAVR in Young Age"

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University of Ulsan College of Medicine, Seoul, Korea

Disclosure Statement

- I am an Interventional Cardiologist > 20 yrs.
- Up to 2022, our team performs ~1,500 TAVRs and ~300 TAVR/yr and ~300 SAVR/yr.
- I work in a collaborative environment with 4 cardiac surgeons in Heart-Team involved in TAVR.
- All decision-making was taken by consensus in weekly Heart-Team Meeting on the basis of clinical/anatomical data and patient preferences.

Current SAVR Status

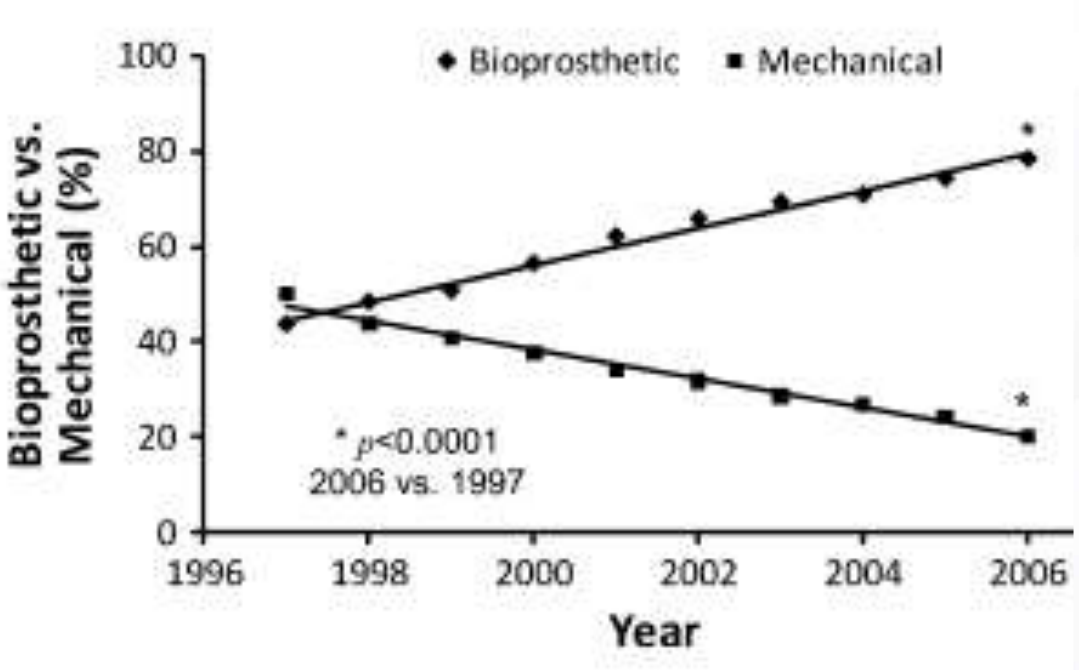
Mechanical Valves

Tissue Valves

Currently, need to weigh risks and benefits of both in an individual patient

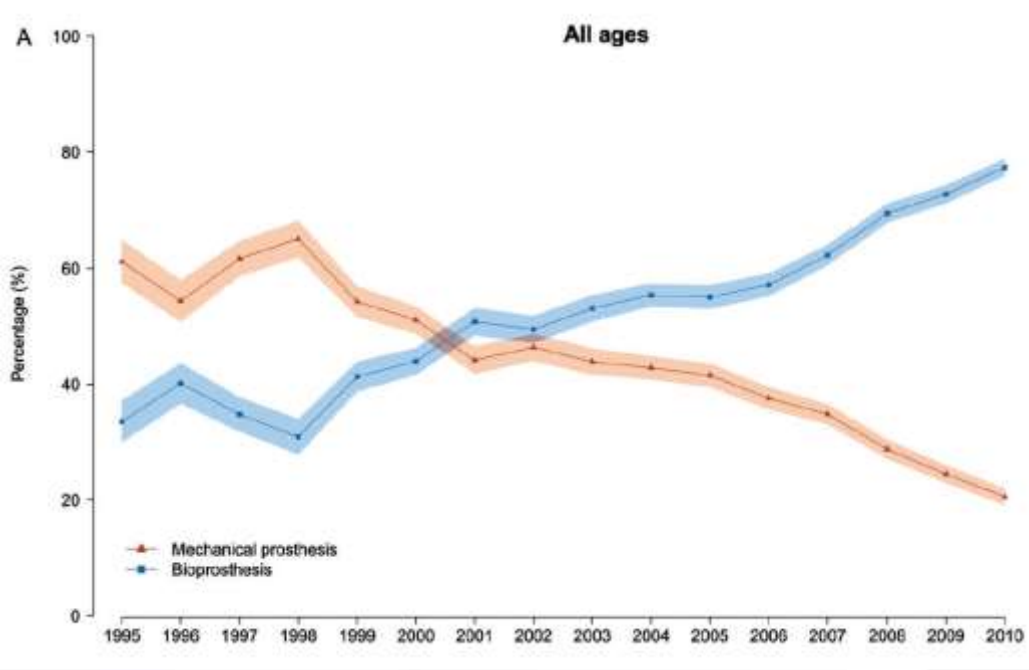
Trends in SAVR
Bioprosthetic vs Mechanical choice over time

STS Database



Brown JM et al. J Thorac Cardiovasc Surg 137:82, 2009

NVT Database (Netherlands)



Siregar et al. EJCTS 2014

Current SAVR Status

Original Investigation

Survival and Long-term Outcomes Following Bioprosthetic vs Mechanical Aortic Valve Replacement in Patients Aged 50 to 69 Years

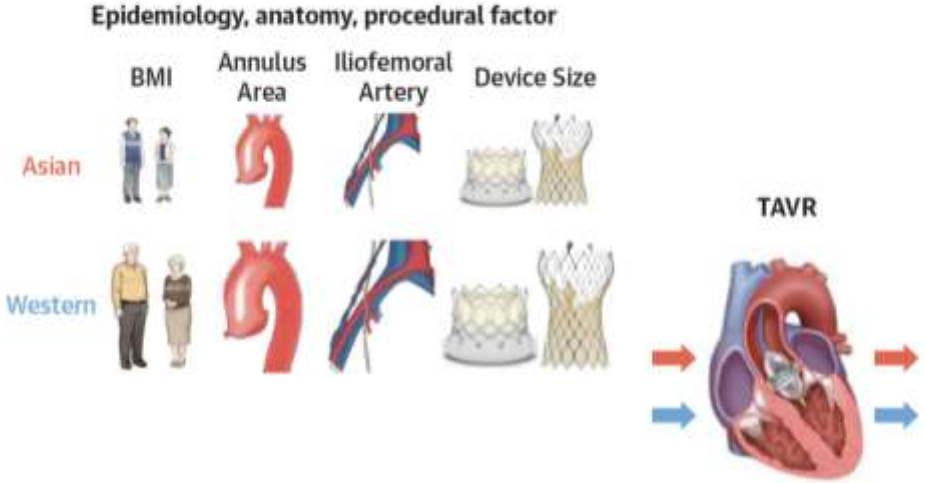
Yuting P. Chiang, BA; Joanna Chikwe, MD; Alan J. Moskowitz, MD; Shinobu Itagaki, MD; David H. Adams, MD; Natalia N. Egorova, PhD

CONCLUSIONS AND RELEVANCE Among propensity-matched patients aged 50 to 69 years who underwent aortic valve replacement with bioprosthetic compared with mechanical valves, there was no significant difference in 15-year survival or stroke. Patients in the bioprosthetic valve group had a greater likelihood of reoperation but a lower likelihood of major bleeding. These findings suggest that bioprosthetic valves may be a reasonable choice in patients aged 50 to 69 years.

JAMA. 2014;312(13):1323-1329

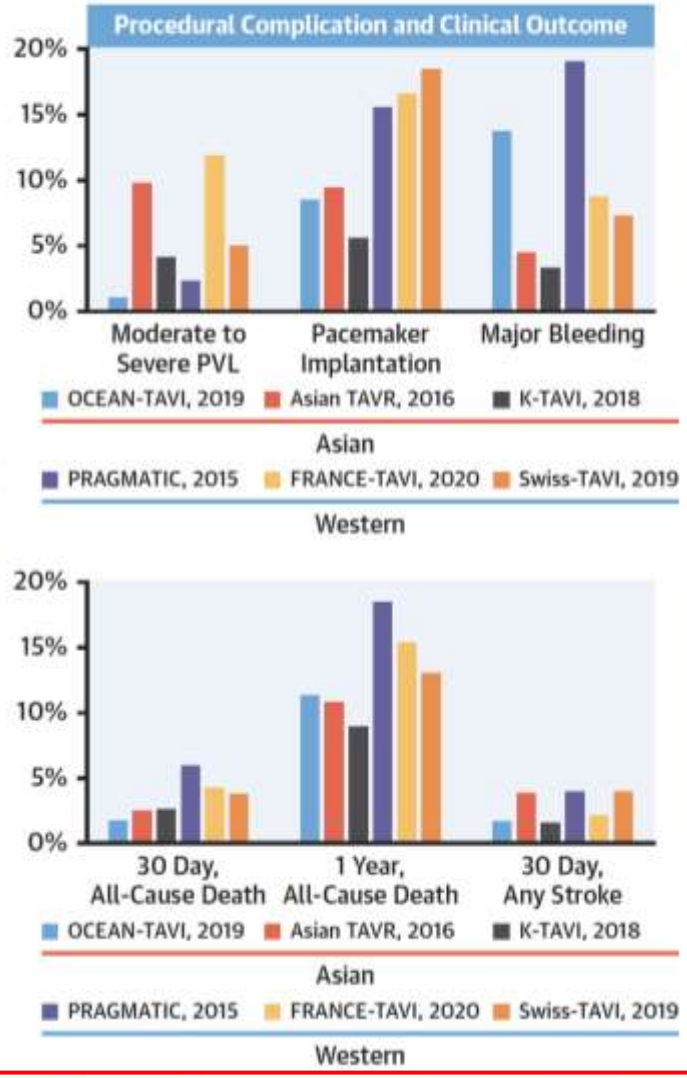
TAVR in Asia

CENTRAL ILLUSTRATION Specific Clinical and Anatomic Features and Outcomes of Transcatheter Aortic Valve Replacement in Asian Populations



	Age	Male	BMI	LVEF	STS score
Asian	◄►	◄►		◄►	◄►
Western	◄►	◄►	▲	◄►	◄►

	Valve area	Annulus area	Bicuspid	Device size	Transfemoral
Asian	◄►		▲		◄►
Western	◄►	▲		▲	◄►



CH Lee, T. Inohara, K. Hayashida, DW Park, JACC Asia: 2021 Dec, 1 (3) 279–293


Current Score
UNITED STATES
65:75
EUROPE

Why 65 Years Old?

Following the Evidence

- **Most patients enrolled in PARTNER 3 trial were ≥65 yo**
  - Mean age 73.4 ± 5.95 yr
  - ~93% > 65 yr and ~7% < 65 yr
- **Most patients enrolled in PARTNER 3 trial were <75 yo**
  - ~55% of pts in P3 were <75 yr
- No interaction with age with regards to primary endpoints
- No signal so far of lesser durability of TAVR compared to bioprosthesis SAVR

Mack. et al. N Engl J Med 2019; 380:1695-1705

Considerations for SAVR vs. TAVR

TABLE 14 A Simplified Framework With Examples of Factors Favoring SAVR, TAVI, or Palliation Instead of Aortic Valve Intervention

	Favors SAVR	Favors TAVI	Favors Palliation
Age/life expectancy*	■ Younger age/longer life expectancy	■ Older age/fewer expected remaining years of life	■ Limited life expectancy
Valve anatomy	■ BAV ■ Subaortic (LV outflow tract) calcification ■ Rheumatic valve disease ■ Small or large aortic annulus †	■ Calcific AS of a trileaflet valve	
Prosthetic valve preference	■ Mechanical or surgical bioprosthetic valve preferred ■ Concern for patient-prosthesis mismatch (annular enlargement might be considered)	■ Bioprosthetic valve preferred ■ Favorable ratio of life expectancy to valve durability ■ TAVI provides larger valve area than same size SAVR	
Concurrent cardiac conditions	■ Aortic dilation ‡ ■ Severe primary MR ■ Severe CAD requiring bypass grafting ■ Septal hypertrophy requiring myectomy ■ AF	■ Severe calcification of the ascending aorta ("porcelain" aorta)	■ Irreversible severe LV systolic dysfunction ■ Severe MR attributable to annular calcification

Otto CM et al, J Am Coll Cardiol 2021;77:450-500

SAVR vs. TAVR: Age Category
in "Real-World" Practice of Korea or Other Countries

- **>80: Both Surgeon and Interventionist Agree**
- **70-80: Arguable & Negotiable - Consider Pt's Selection**
- **<70: Surgeon Strongly Disagree - "SAVR-is-always-better concept"**
  - ✓**Aged 50 to 69 yrs: SAVR, Bioprosthetic use >>> Mechanical use**
  - ✓ **Prerequisite 1: Bioprosthetic SAVR >> Bioprosthetic TAVR**
  - ✓ **Prerequisite 2: Sutureless bioprosthetic >> TAVR bioprosthetic**
  - ✓ **Prerequisite 3: different bioprosthetic materials for SAVR or TAVR from same company (i.e., Edwards or Medtronic)**

Hypothetical Reasons for Reduced TAVR Durability

Device characteristics

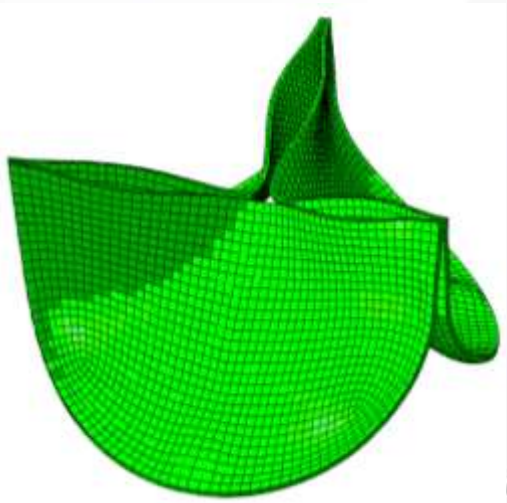
- Lack of advanced anti-calcification treatment
- Lack of multiple iterative design enhancements d/t limited years of clinical practice
- Leaflet morphology and design

Device deployment

- Valve crimping
- Valve damage during small sheath delivery / balloon inflation / unsheathing

Device-anatomy interaction

- Lack of native leaflet decalcification
- Device under expansion
- Paravalvular regurgitation
- Asymmetric expansion
- Lack of stent tip deflection
- Leaflet thrombosis



* May apply for specific TAVR devices only

Li and Sun. *Ann Biomed Eng.* 2010
Sun, Li and Sirois. *J Biomech.* 2010
Martin C and Sun W, *J Biomech*, 2015
Kiefer P. Ann Thorac Surg. 2011

Surgeon's Most Common Concerns for TAVR If Applied in Young Age (<65 or <70 years)

- **No surgical resection of diseased valve: thrombosis =>** cerebral embolism or durability?
- **Cramping: durability**

Rationale for "SAVR-Is-Always-Better Concept" ??

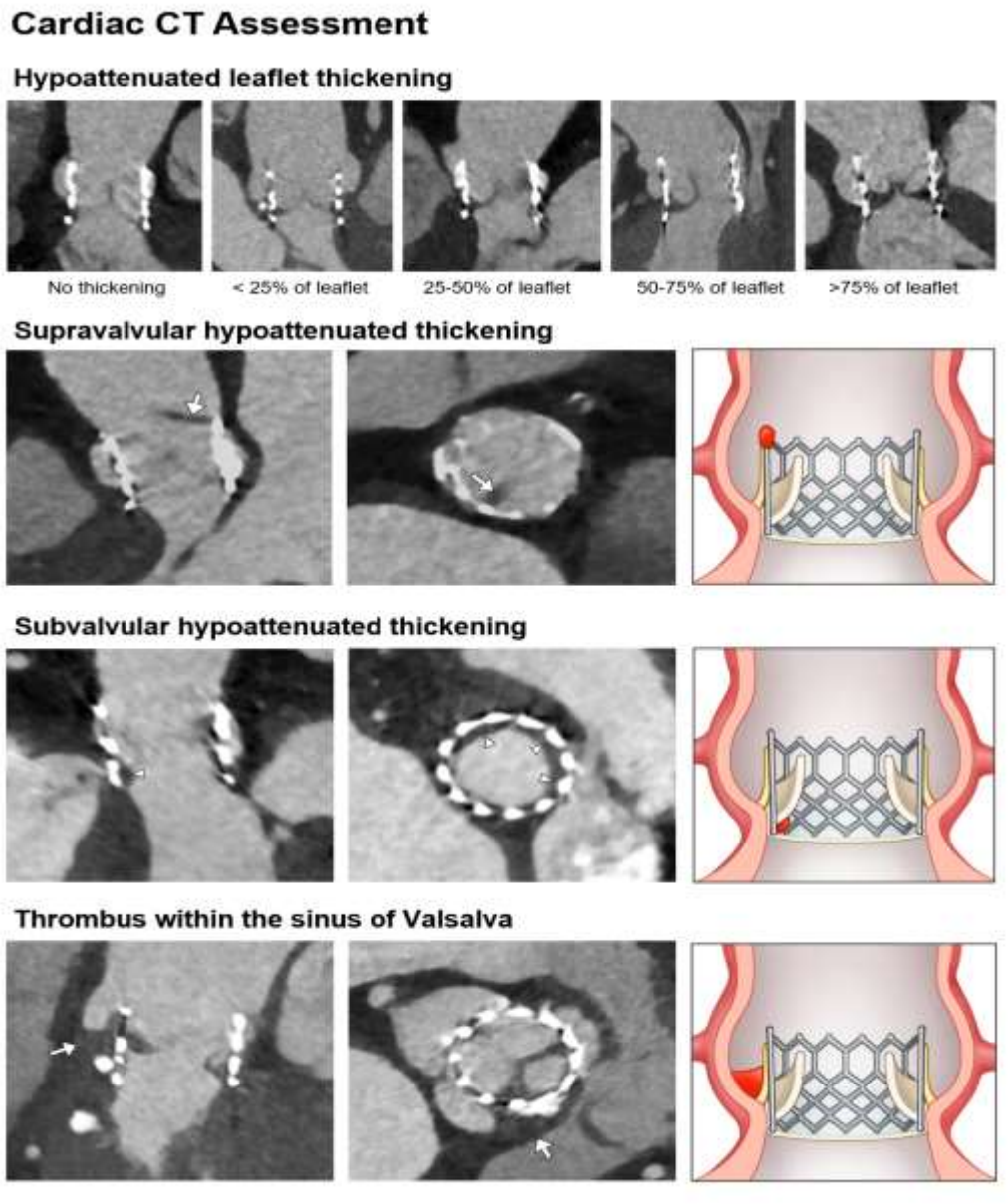
Perivalvular Thrombosis

Valve

Supravalvular

Subvalvular

Sinus of Valsalva



DW Park et al. Circulation 2022

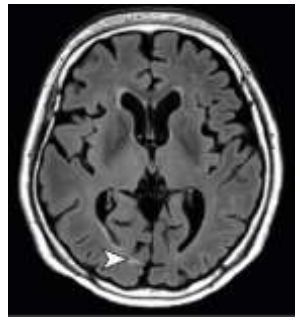
No surgical resection of diseased valve: Valve or Paravalvular thrombosis

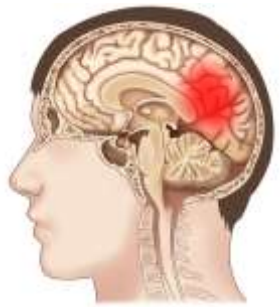
>75% of leaflet

SLT

Unknown

Causal relationship of SLT with cerebral embolism





Cerebral thromboembolism
Stroke or TIA

Known

OAC can reduce SLT

OAC therapy

Unknown

OAC can reduce SLT-related cerebral embolism

SLT, subclinical leaflet thrombosis; OAC, oral anticoagulation; TAVR, transcatheter aortic valve replacement; TIA, transient ischemic attack.

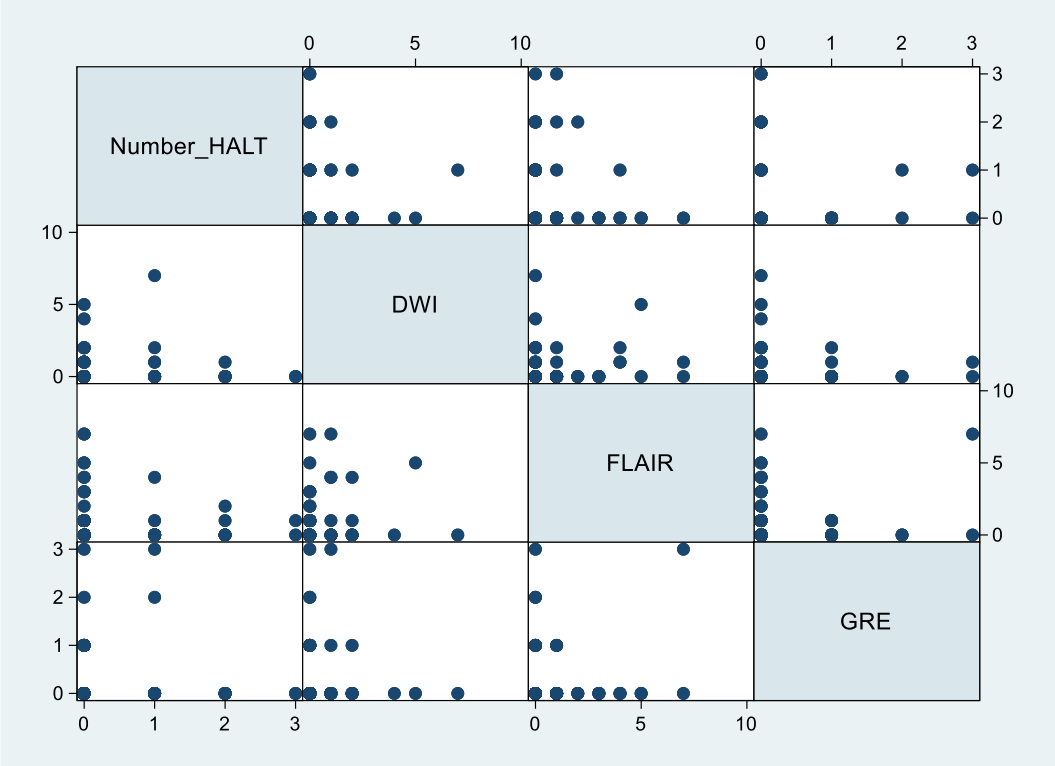
[1]Makkar RR, et al. *NEJM*. 2015;373:2015-2024. [2]Chakravarty T, et al. *Lancet* 2017;389:2383-2392. [3]Makkar RR, et al. *JACC* 2020;75:3003-3015. [4]Bogyi M, et al. *JACC: Cardiovascular Interventions* 2021;14:2643-2656.

Perivalvular Thrombosis – Analysis at patient Level

	Edoxaban	DAPT
Leaflet thrombosis	9.8%	18.4%
Subvalvular thrombosis	27.5%	26.6%
Supravalvular thrombosis	0%	1%
Sinus of Valsalva thrombosis	12.8%	22.0%
Any thrombosis at aortic valve complex dimension	37.3%	48.6%

DW Park et al. Circulation 2022

Association of Severity of HALT with Extent of New Lesions on Brain MRI

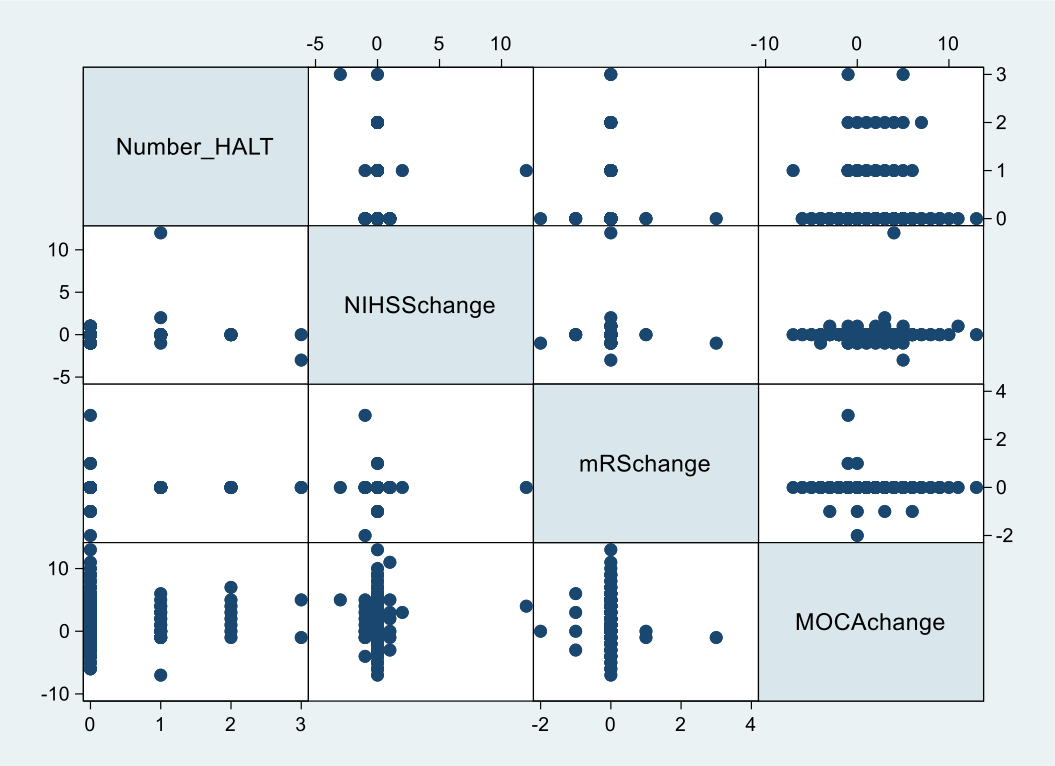


		Number of New Lesions on DWI-MRI	Number of New Lesions on FLAIR-MRI	Number of New Lesions on GRE-MRI
Number of HALT Per-Patient	N	209	209	209
	Spearman Rho	**0.09**	**-0.04**	**-0.02**
	P-Value	**0.19**	**0.60**	**0.81**

HALT, hypoattenuated leaflet thickening; DWI, diffusion weighted image; FLAIR, fluid attenuated inversion recovery; GRE, gradient echo; MRI, magnetic resonance imaging

DW Park et al. Circulation 2022

Association of Severity of HALT with Neurological Dysfunction



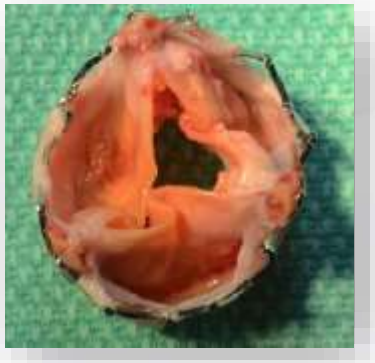
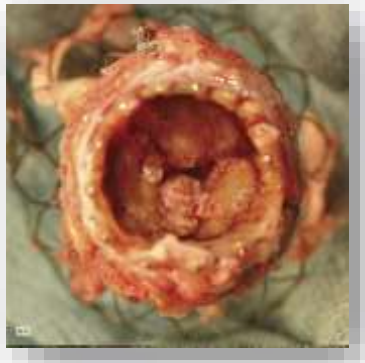
		Serial Change of NIHSS Score	Serial Change of mRS Score	Serial Change of MOCA Score
Number of HALT Per-Patient	N	204	204	204
	Spearman Rho	**0.01**	**0.02**	**0.03**
	P-Value	**0.94**	**0.77**	**0.68**

HALT, hypoattenuated leaflet thickening; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; MoCA, Montreal Cognitive Assessment

DW Park et al. Circulation 2022

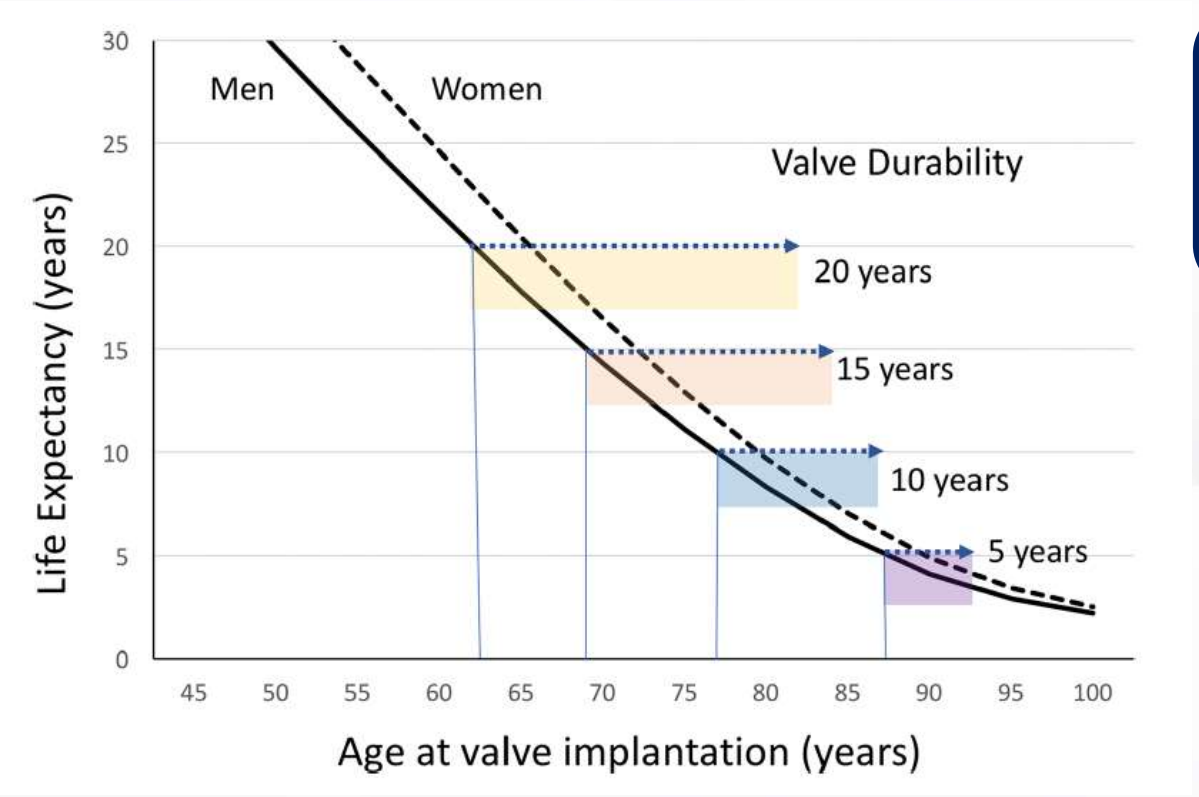
Cramping:
Valve durability

Long-Term Durability Matters
The Latest Chapter in the Story


Matching Valve Durability with Life Expectancy

- **DURABILITY TO LIFE EXPECTANCY RATIO**



The vertical lines show the age (for men) at which the valve durability equals life expectancy (US Statistics 2014)

Valve durability to life expectancy ratio (for men) is 1:

- at **age 62** for a valve durable for **20 years**
- at **age 69** for a valve durable for **15 years**
- at **age 77** for a valve durable for **10 years**
- at **age 87** for a valve durable for **5 years**

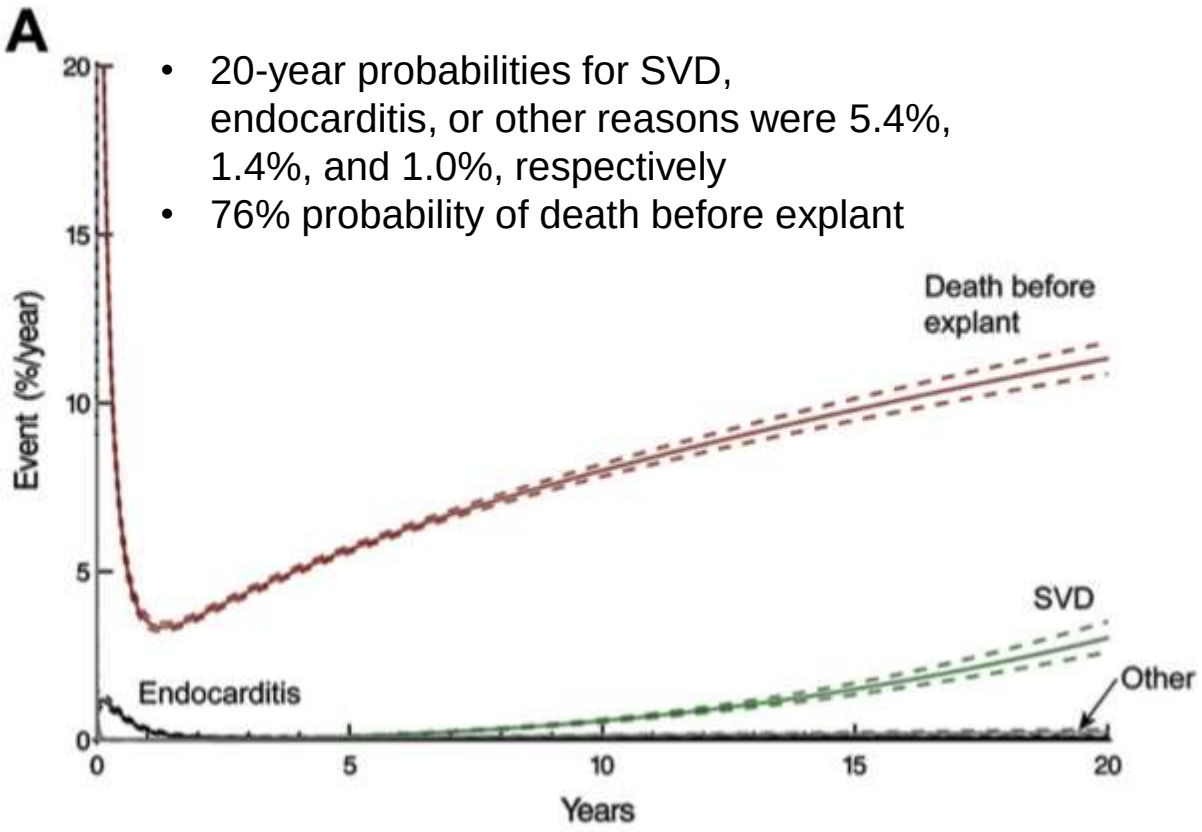
Bagur R, et al. Heart. 2017;103:1756-1759

SAVR Bioprosthesis Durability

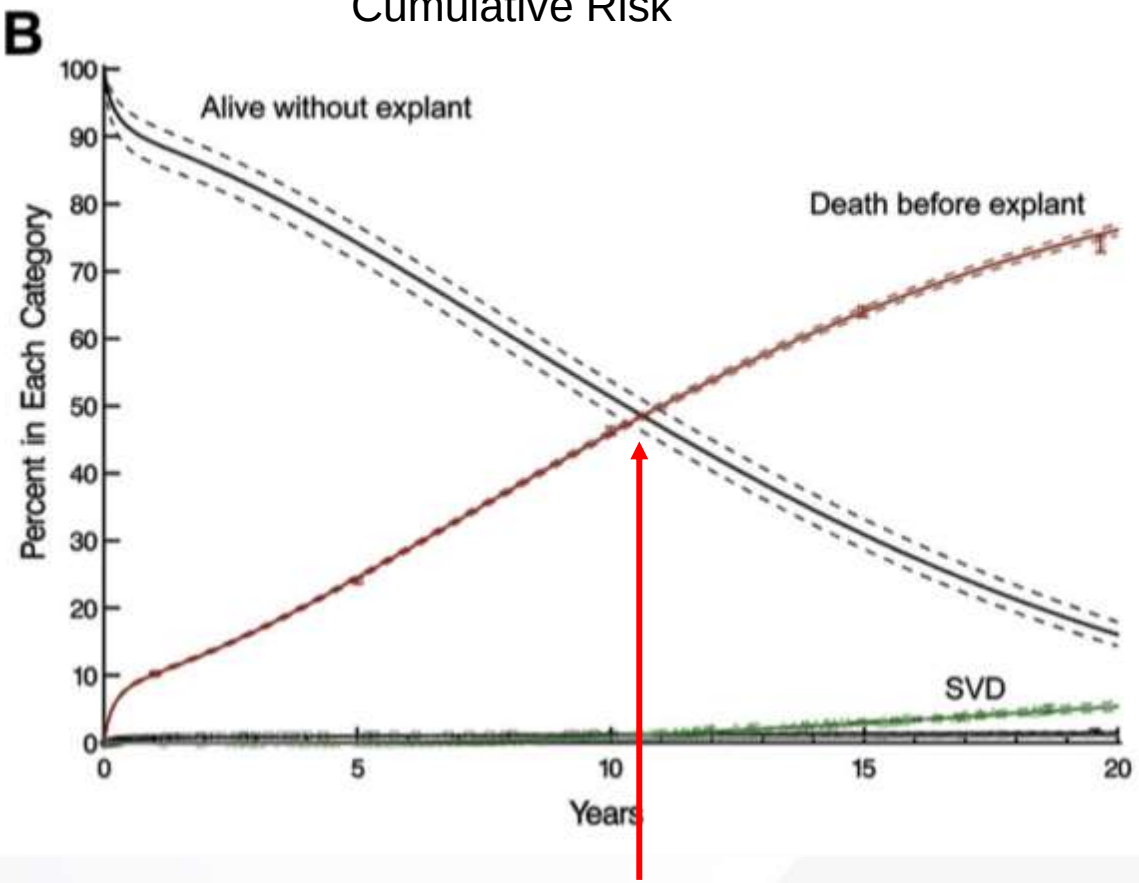
Surgical Explants in 12,569 Patients after Surgical AVR

Instantaneous Risk

- 20-year probabilities for SVD, endocarditis, or other reasons were 5.4%, 1.4%, and 1.0%, respectively
- 76% probability of death before explant



Cumulative Risk

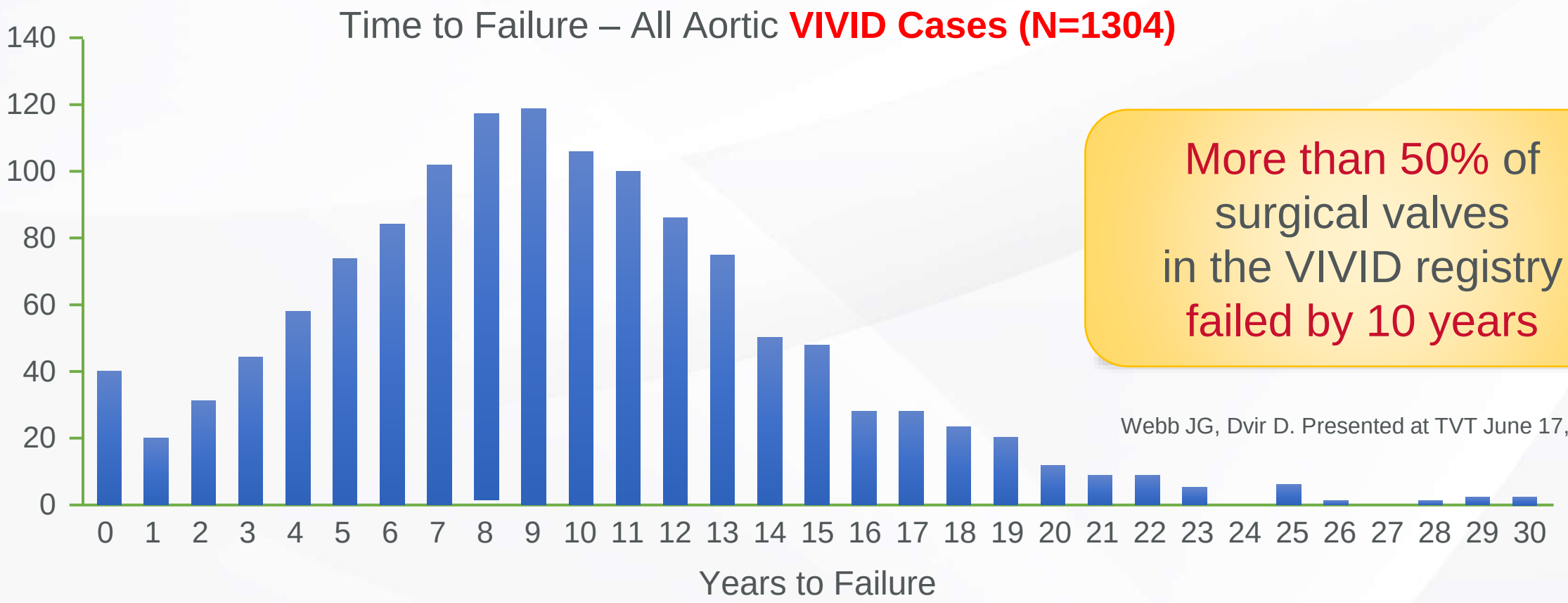


12-13 yrs

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

Real-World SAVR Durability: VIVID Registry

: Surgical valves failure for valve-in-valve TAVI in a median time of only 9 years



More than 50% of surgical valves in the VIVID registry failed by 10 years

Webb JG, Dvir D. Presented at TVT June 17, 2016.

NOTION 8-YEAR ALL COMERS

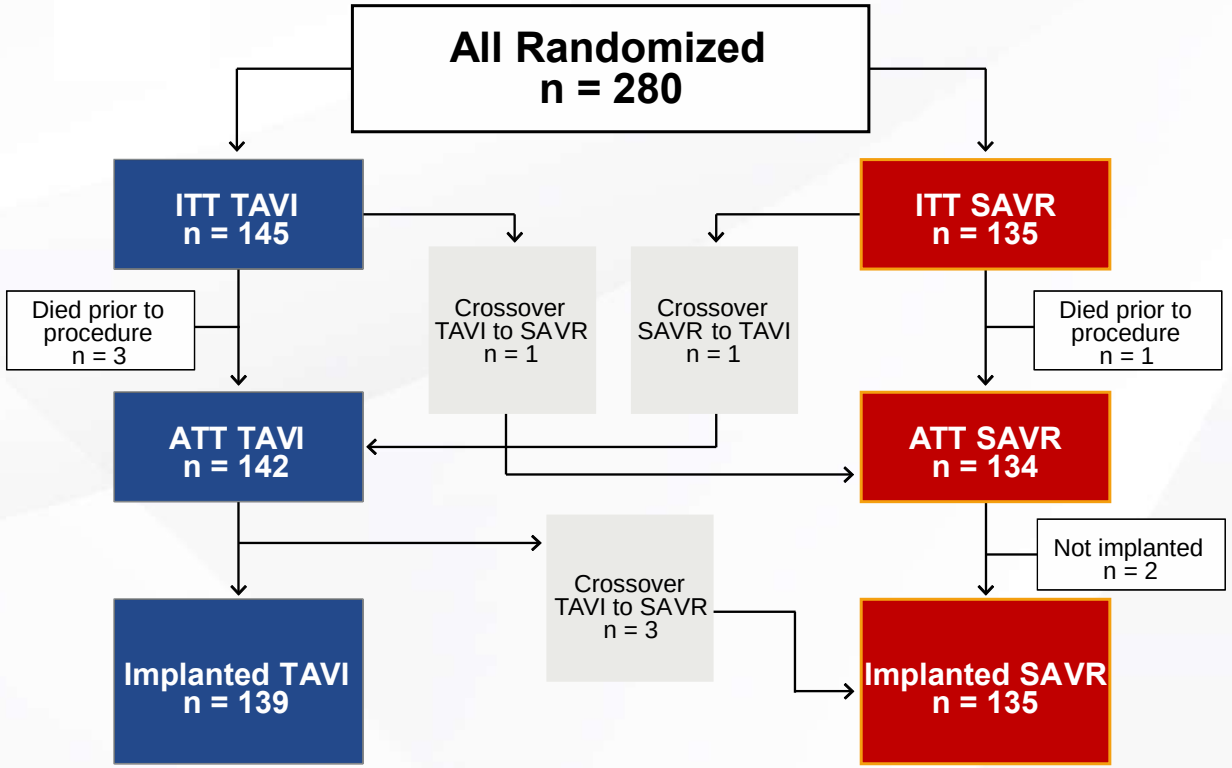
RANDOMIZED TRIAL IN LOWER RISK PATIENTS

TAVR Durability Data

Nordic Aortic Valve Intervention CoreValve NOTION Trial

Objective:	To compare TAVI vs. SAVR in lower risk patients ≥ 70 years eligible for surgery (all-comers population)
Primary Outcome:	Composite rate of all-cause mortality, stroke, or myocardial infarction at 1 year (VARC II-defined)
Secondary Outcomes:	Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)
Design:	Prospective, multicenter, non-blinded, randomized trial
Enrollment Period:	December 2009–April 2013

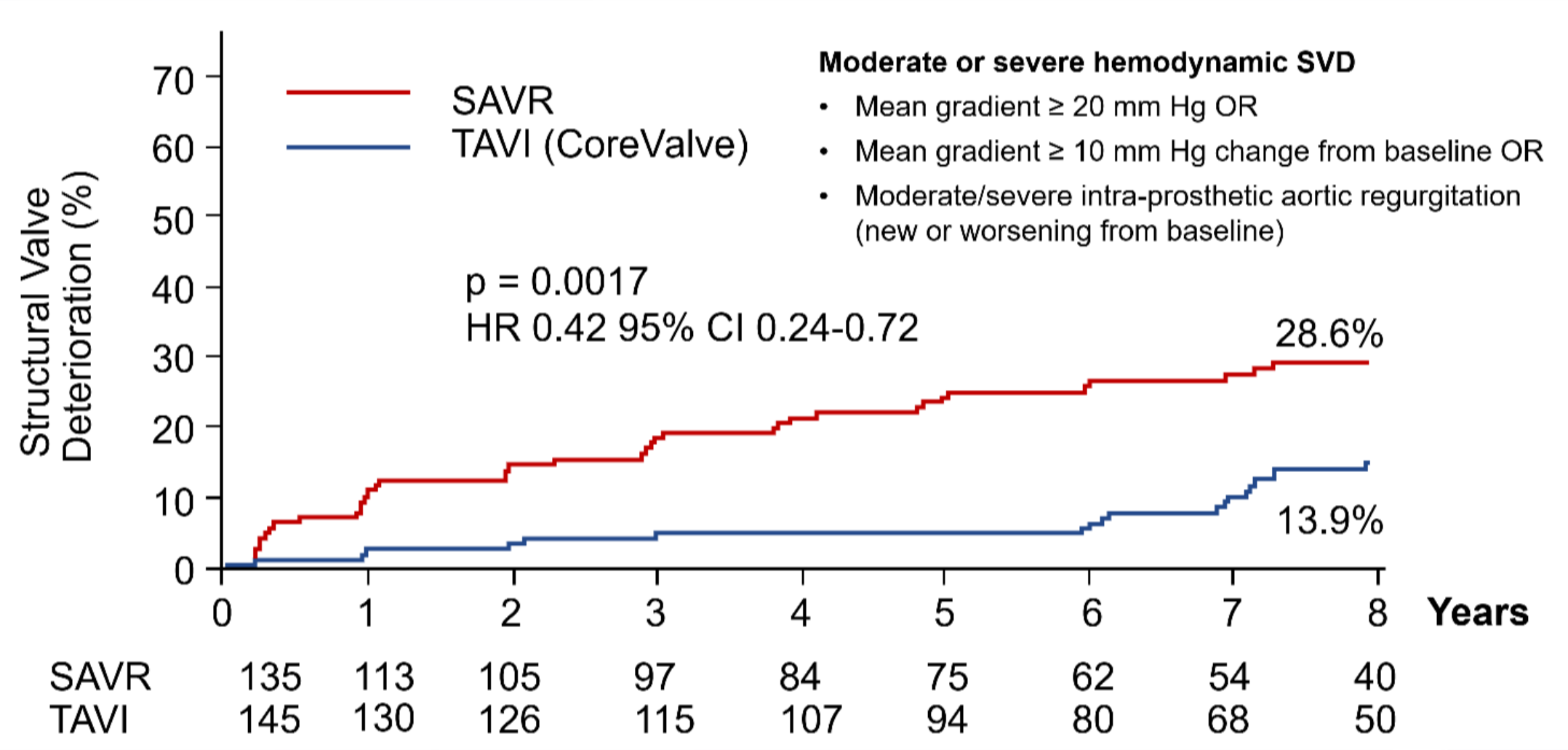
Trial Flow



Søndergaard L, et al. Presented at PCR Valves Conference 2020.

NOTION 8 YEAR OUTCOMES TAVI VERSUS SURGERY

STRUCTURAL VALVE DETERIORATION



Jorgensen, et al. Eur Heart J. 2021;42:2912-9

5-Year Incidence, Outcomes and Predictors of Structural Valve Deterioration of Transcatheter and Surgical Aortic Bioprostheses: *Insights from the CoreValve US Pivotal and SURTAVI Trials*

Michael J. Reardon, MD
Houston Methodist, Houston, TX, USA
For the CoreValve – Evolut Clinical Investigators

UPDATED 23May2022 MDT Data on File

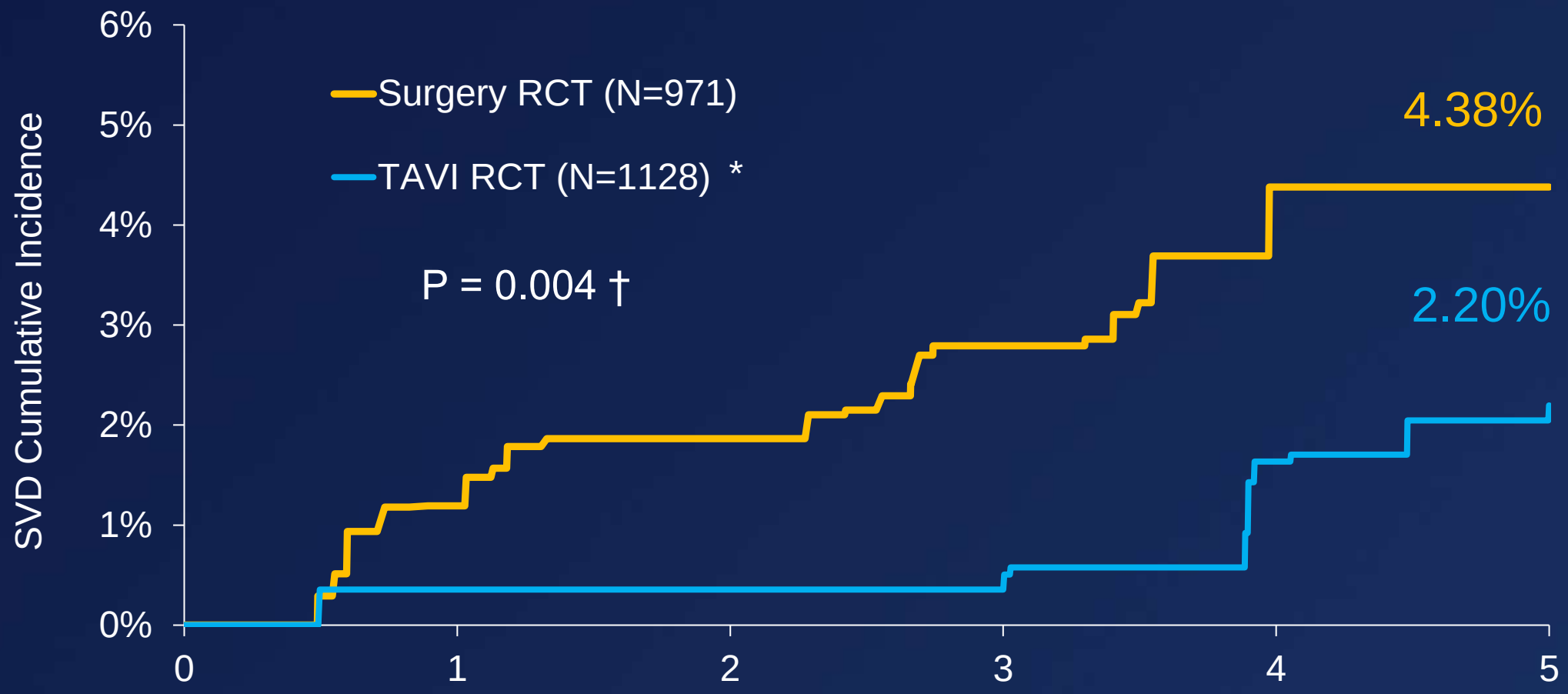
CoreValve Evolut Pooled Analysis

5-Year SVD Adjusted for Competing Risk of Mortality

TAVR Durability Data

CoreValve Evolut Clinical Program

Significantly lower rate of **SVD** with TAVI vs. Surgery through 5 years



* CoreValve 88%, Evolut R 12%

† Fine-Gray P value

UPDATED 23May2022 MDT Data on File

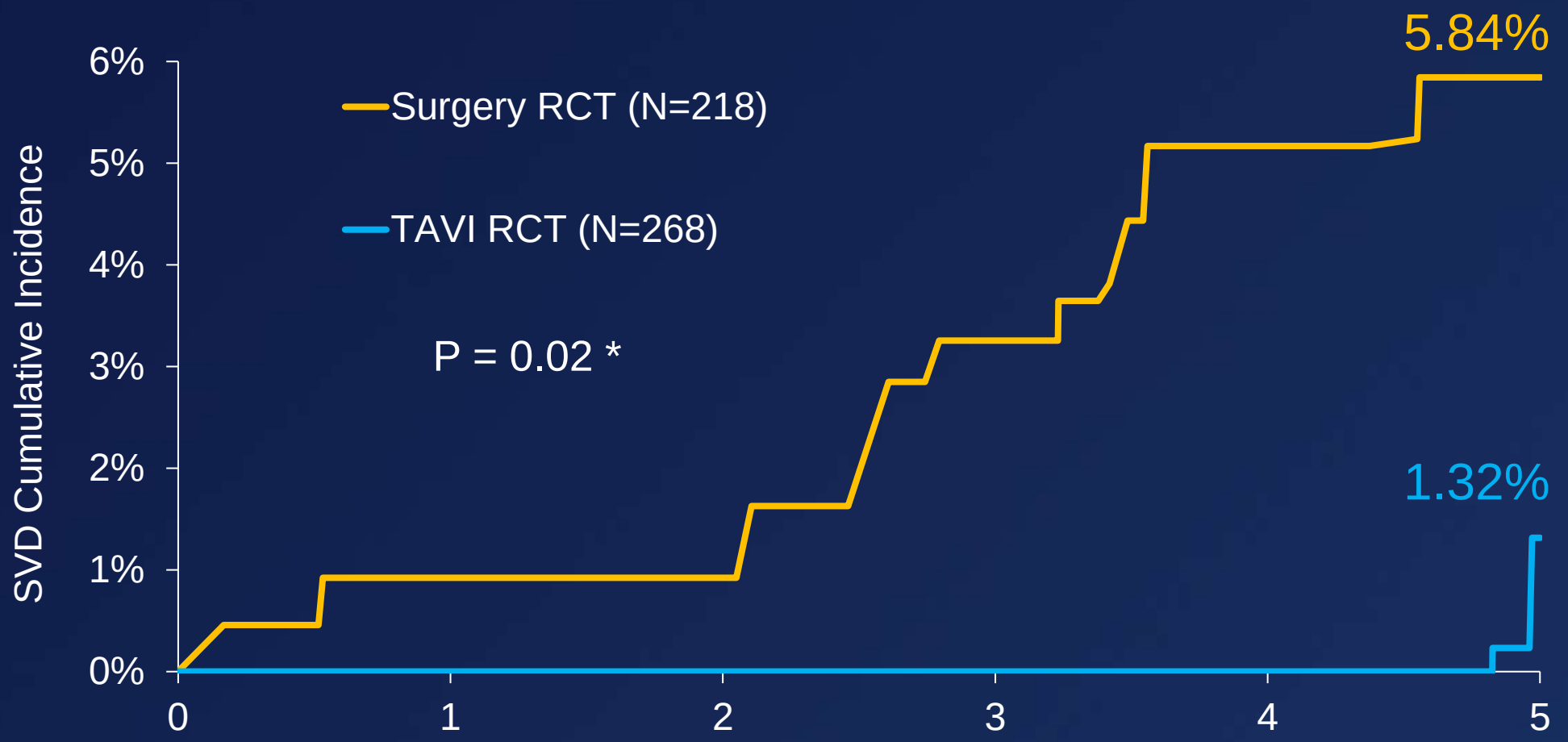
CoreValve Evolut Pooled Analysis

5-Year SVD In Smaller (≤23 mm) Annular Diameters

TAVR Durability Data

CoreValve™ Evolut™ Clinical Program

Significantly lower rate of **SVD** with TAVI vs. Surgery through 5 years in small annuli



* Fine-Gray P value

UPDATED 23May2022 MDT Data on File

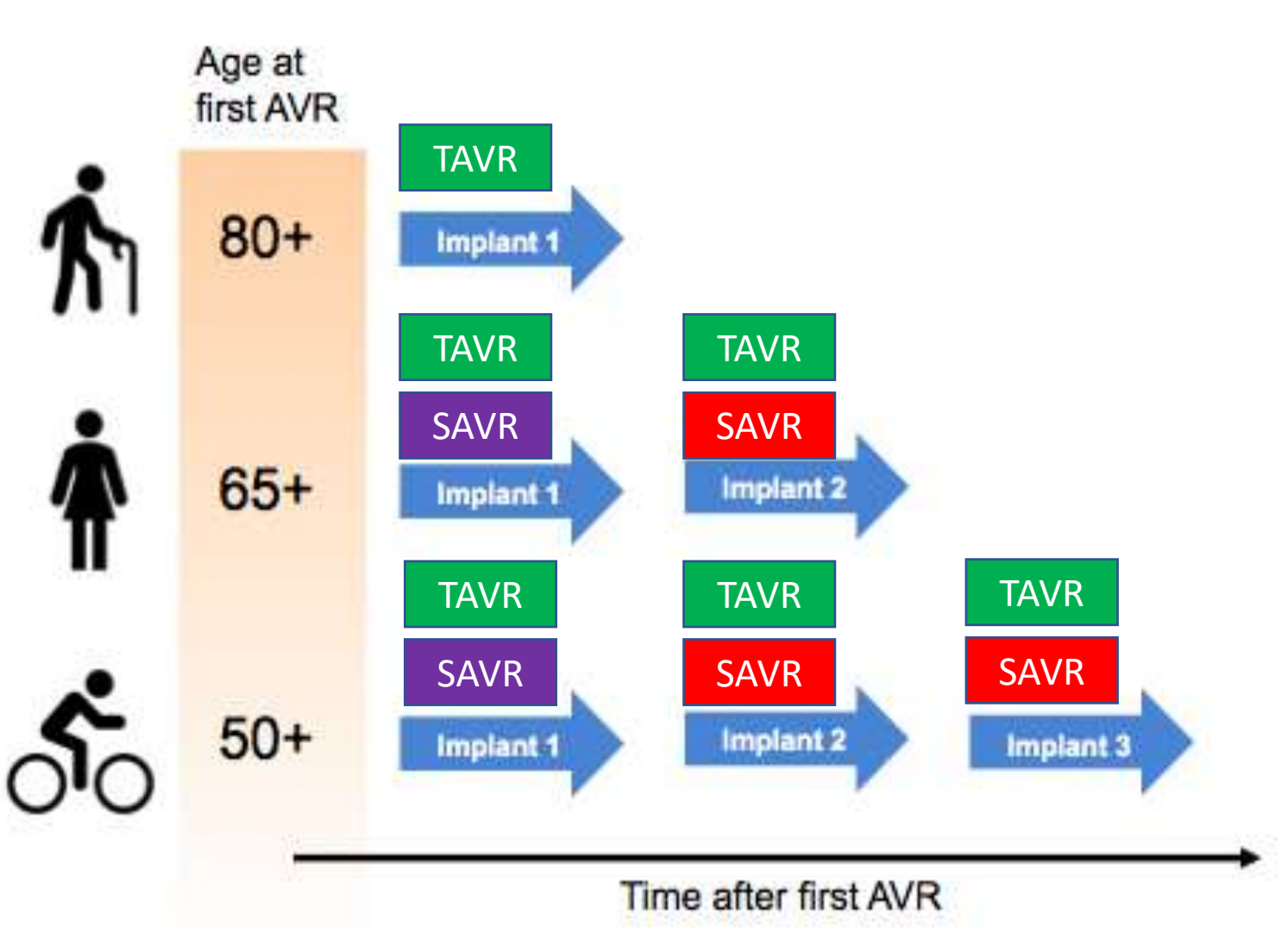
Current available data for TAVR for Young Age (>65yo ~ <70yo)

IF…Yes

- CTA anatomy is suitable and favorable for TF-TAVR
- No other significant valve, aortopathy, or coronaries issues co-exist
- The patient strongly opposed to SAVR
- Ensure that first TAVR will allow for:
  - Future coronary access
  - Future TAVR in TAVR
  - Future SAVR after TAVR

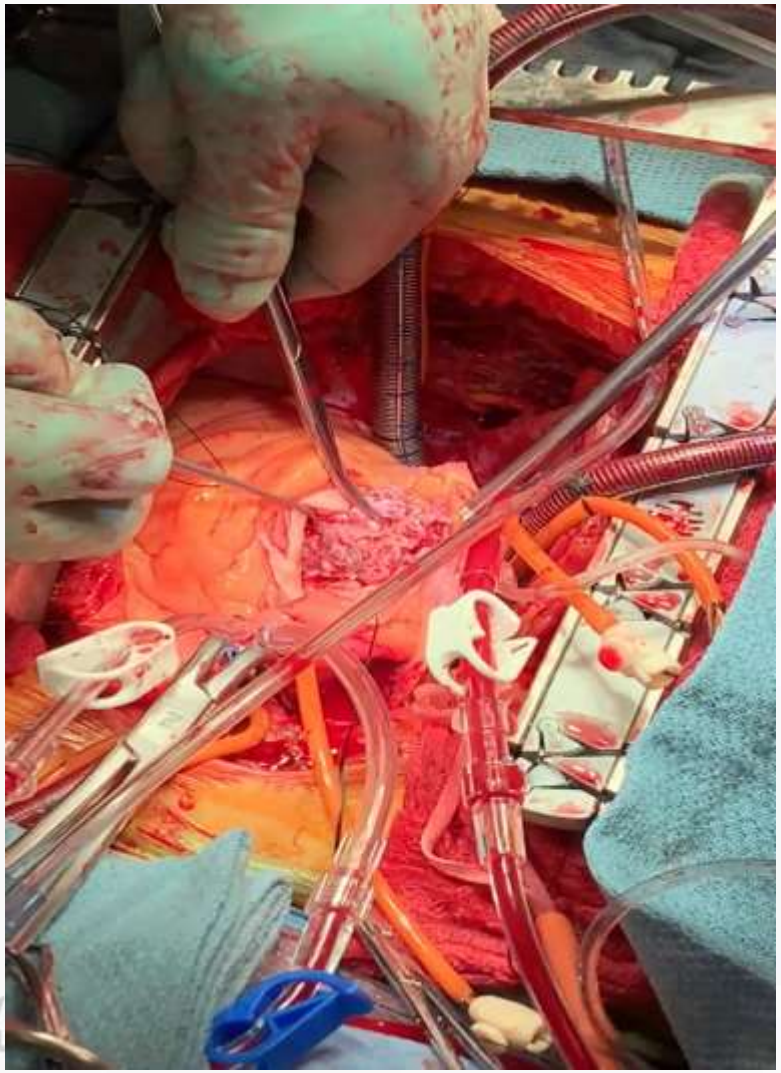
“AS Life-Time Management”

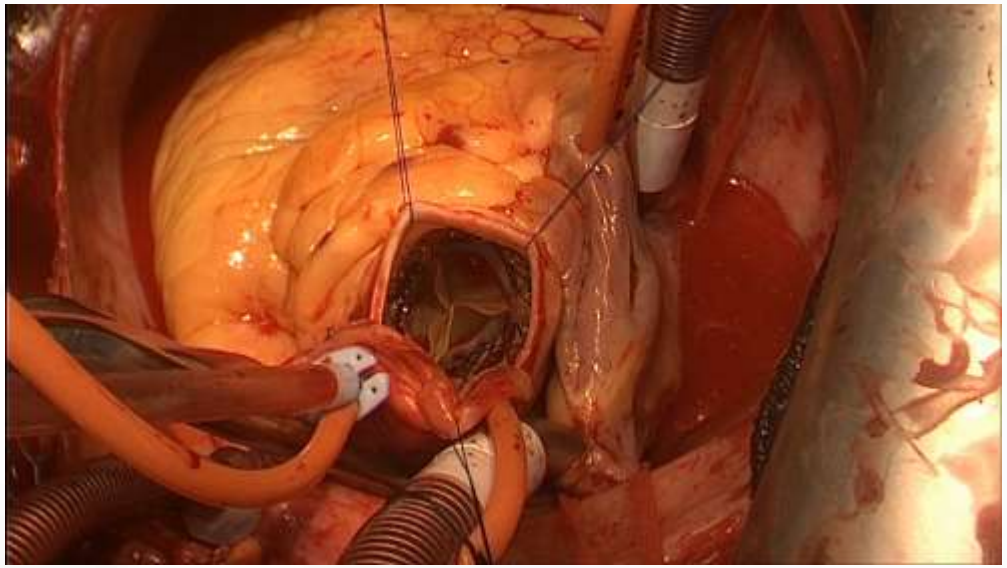
AS Lifetime Management:
Why is TAVI Explant so important?



Developing Surgical Techniques for TAVI Explant

TAVI Explant is Technically Challenging





1. Stent Frames Can be Adherent
2. Difficulty CrossClamping (SEV)
3. Very Sick at Baseline

Courtesy of Vinnie Bapat

Take Home Messages

- Long-term valve durability has become a most important issue for decision-making btw TAVR and SAVR, particularly for younger patients with few comorbidities.
- TAVI durability data between 5 and 10 years using standardized definitions do not show safety concerns compared to SAVR; RCT data from the NOTION, CoreValve US Pivotal, and SURTAVI trials .
- Because what really matters is durability beyond 10 years, meaningful long-term (>10 years) durability data for TAVI are expected no sooner than 2025.
- Lifetime management strategy should be considered in younger patients undergoing TAVR given potential benefits with SAVR / Ross procedure