

# Essentials of Lifetime Management in Aortic Disease

## Updated and Novel Points in 2024

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# Financial Disclosure

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I, Eberhard Grube have the following financial interest/arrangement that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

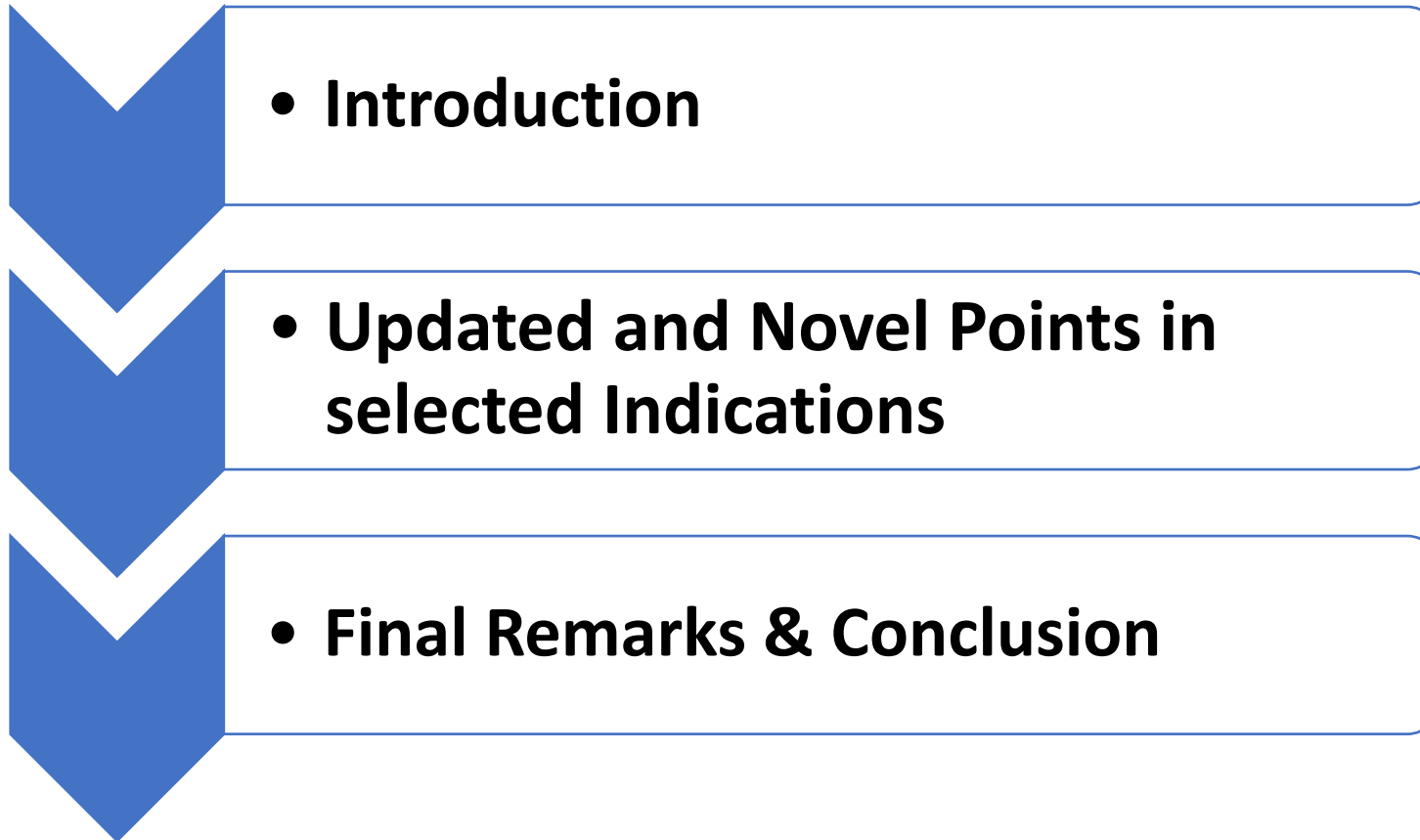
**Speaker Bureau/ SAB:** Medtronic, Boston Scientific, HighLife, Jena Valve, Protembis, Alta Valve, Valve Medical

**Equity Interest:** Cardiovalve, Claret, Shockwave, Valve medical, CardioMech, Millipede, Imperative Care, Pi-Cardia, Ancora, Laminar, ReNiva Medical

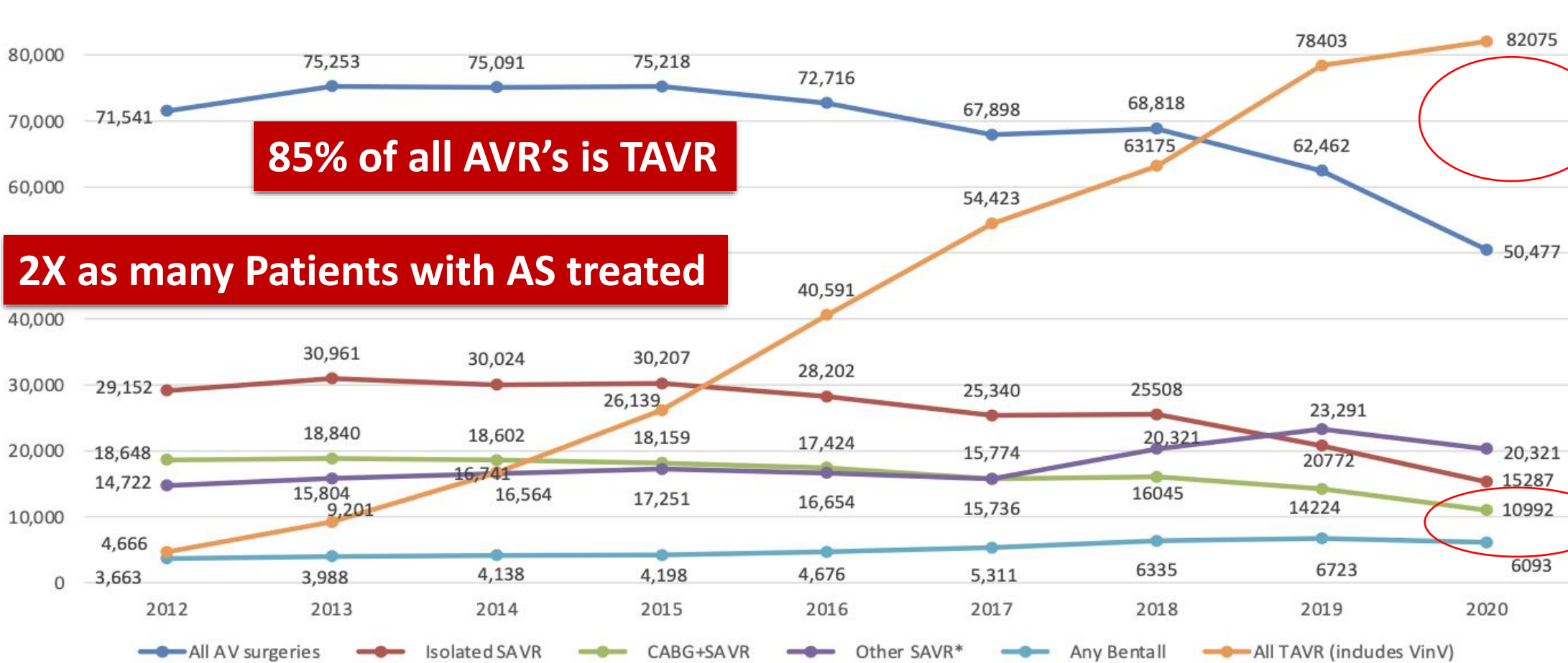
# Lifetime Management of Aortic Disease in 2024

## *Roadmap of my Presentation*

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# Latest TAVR-SAVR Data



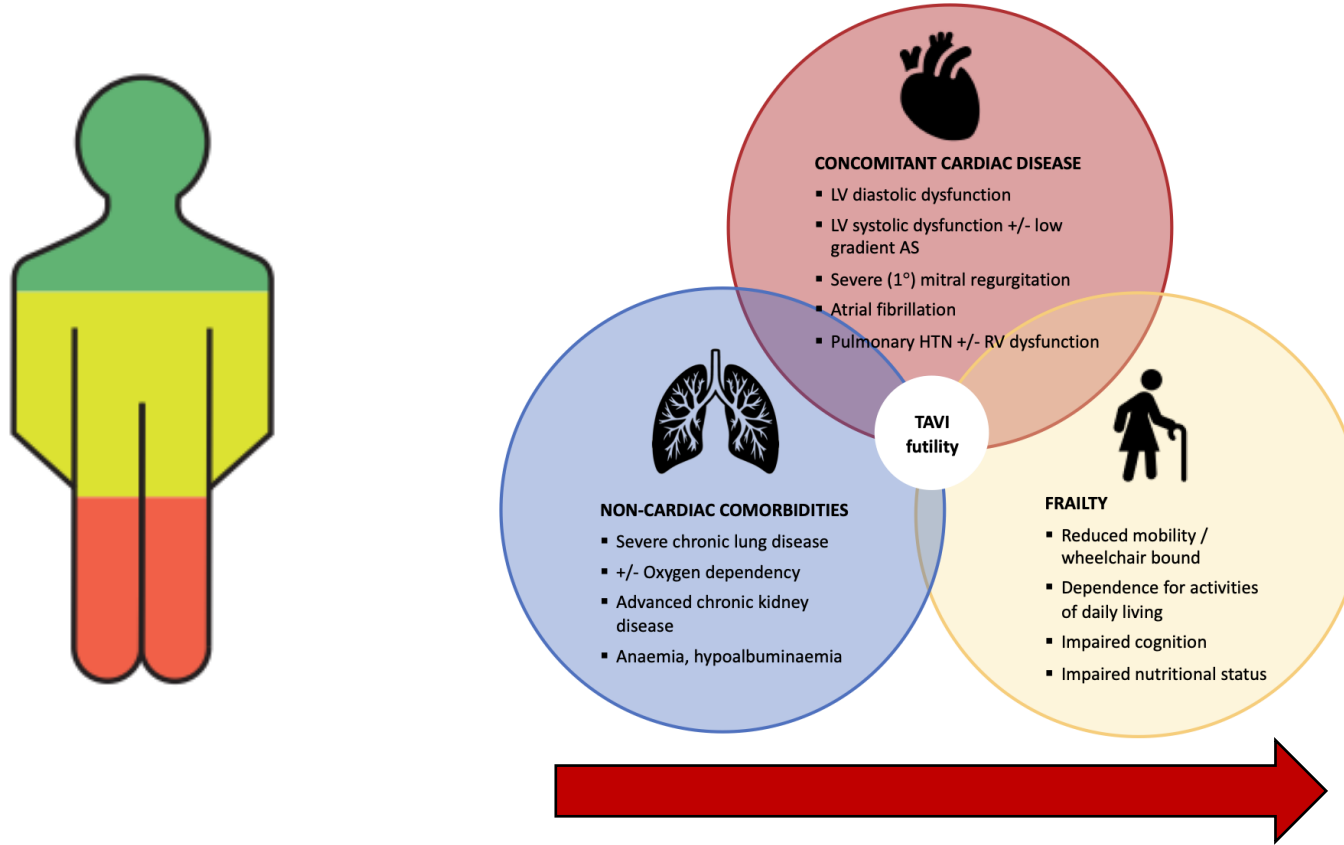
**STS National Database™**  
Trusted. Transformed. Real-Time.



**NCDR®**  
NATIONAL CARDIOVASCULAR DATA REGISTRY

# Improved Patient Selection and Disease Awareness

## Mean Treatment Difference



## Individual patient outcomes

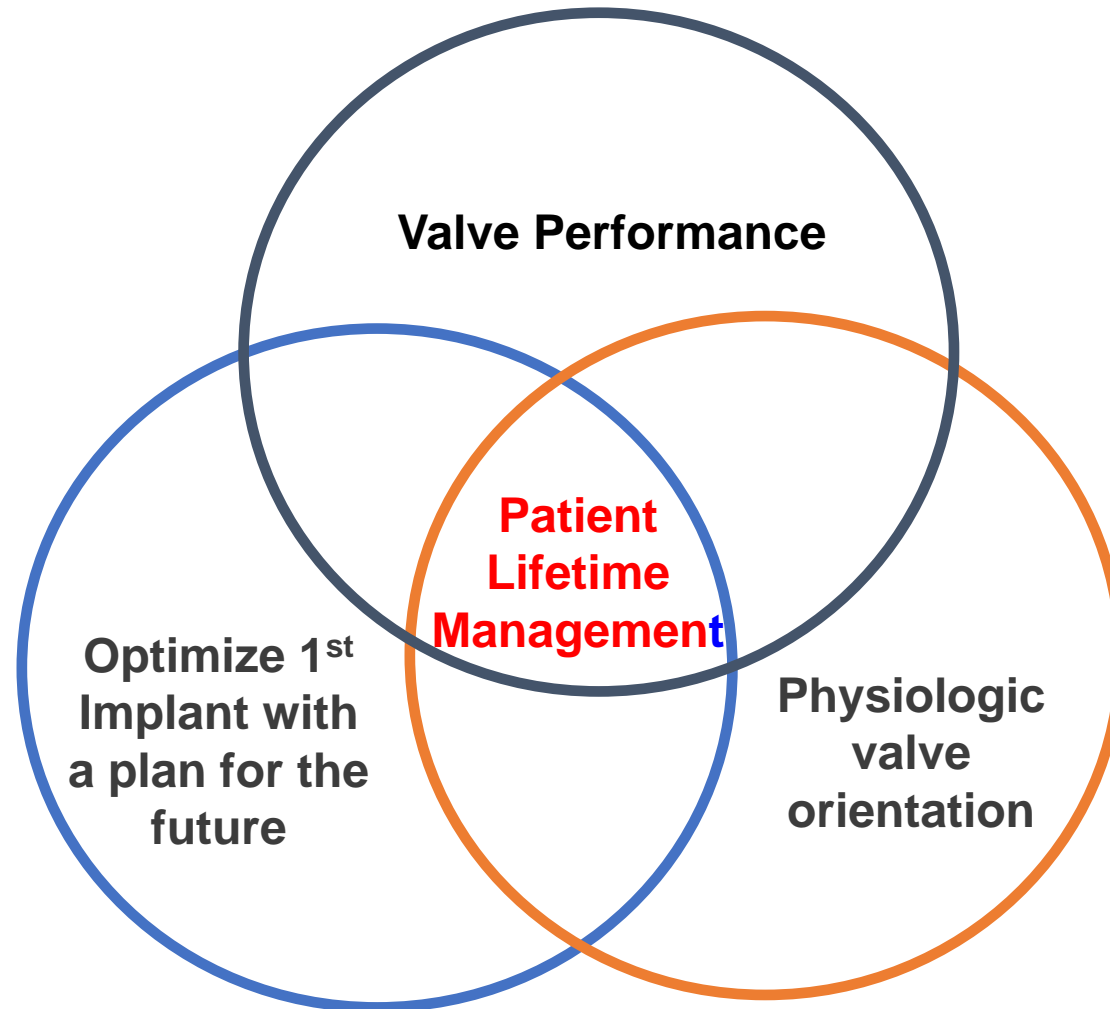


***30% of patients undergoing TAVR derive only minimal symptom benefit or die within 1 year. Therefore earlier interventions are most likely needed!***

# Lifetime Management of Aortic Disease in 2024

*Discussion focusing on initial Bioprosthetic Valve Choice?*

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# Lifetime Management of Aortic Disease in 2024

## *Discussion focusing on Patient oriented Aspects*

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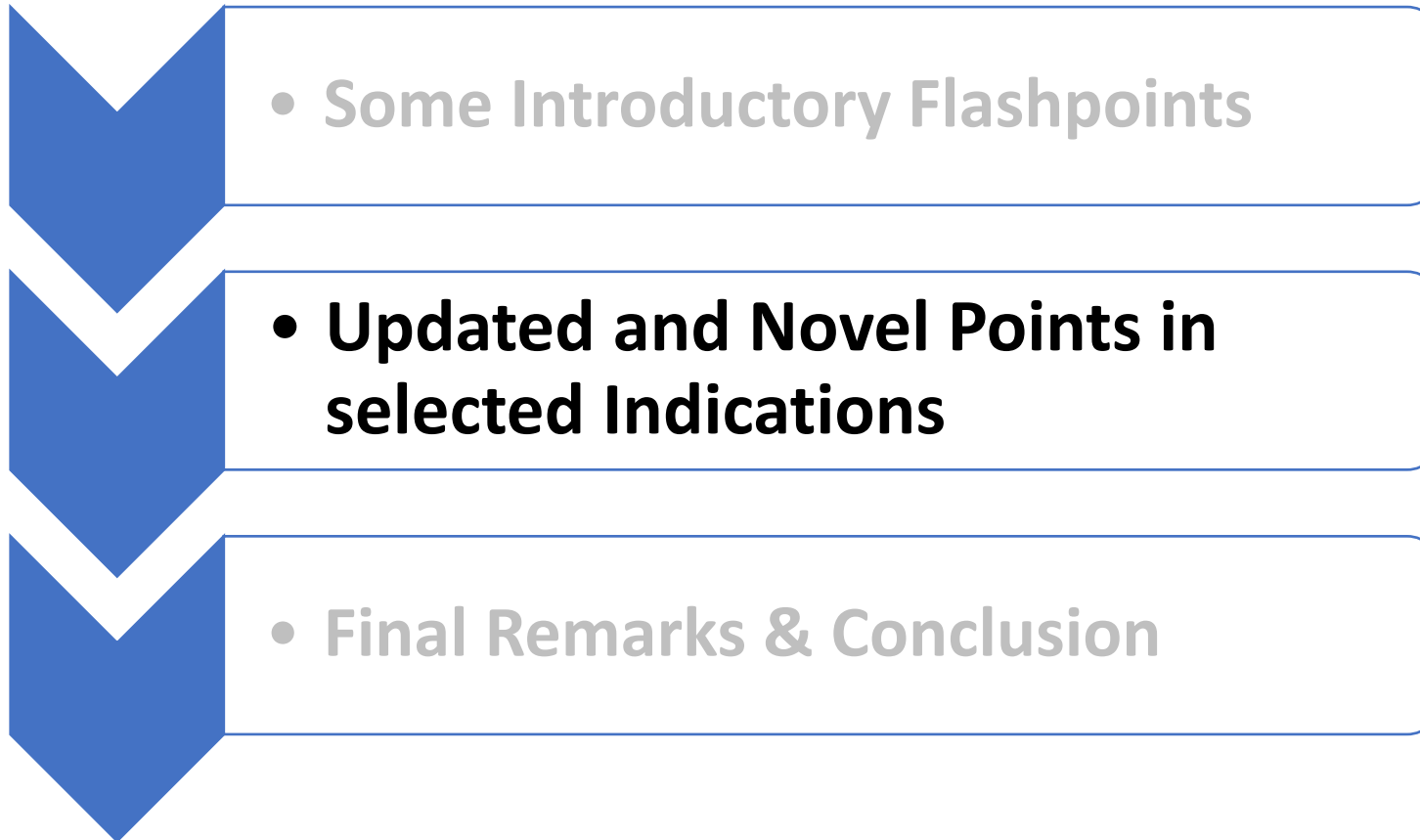
- ***Patient needs to be a part of the discussion***
- Clear explanation of risks and benefits as well as consequences of any decision must be provided
- ***Patient choice may not be the same as physician choice but must be respected***



# Lifetime Management of Aortic Disease in 2024

## *Roadmap of my Presentation*

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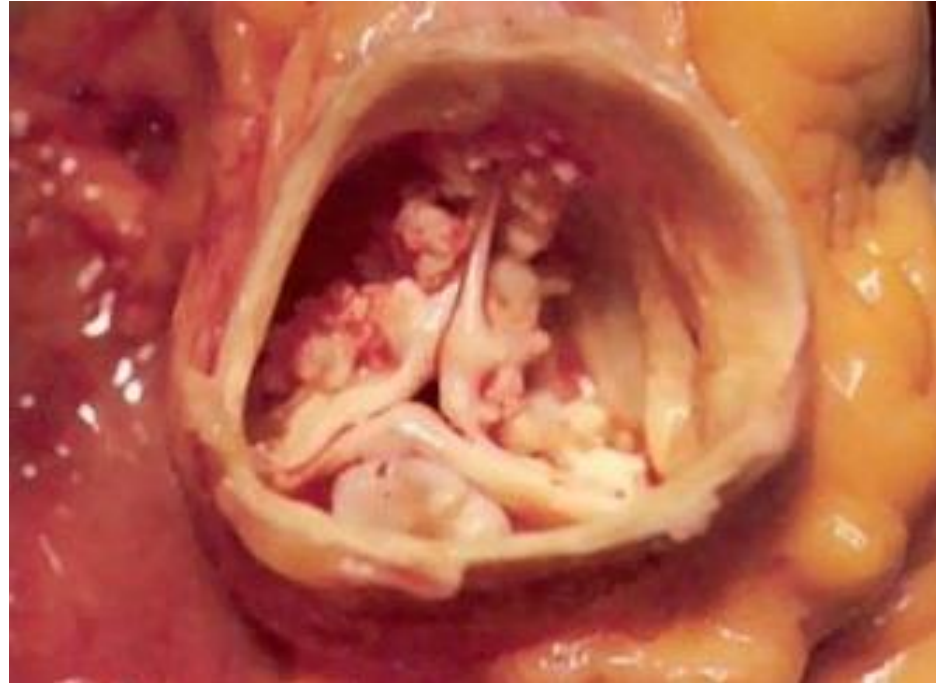




# TAVR NEXT STEPS | Asymptomatic/Mod AS

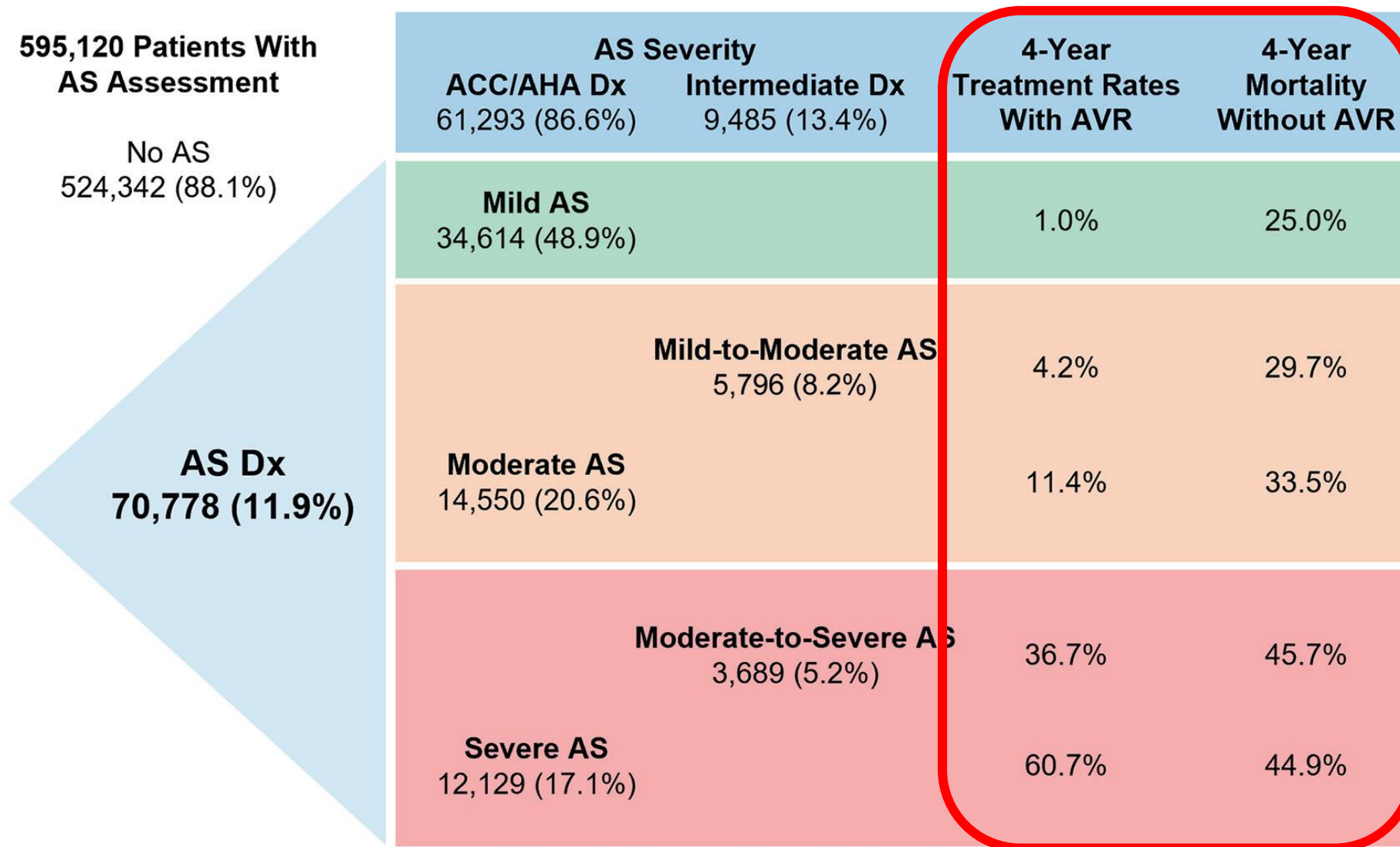
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## Asymptomatic/Moderate AS



# **Why are We Targeting Asymptomatic & Moderate Aortic Stenosis?**

# TAVR NEXT STEPS I Mortality in Untreated AS

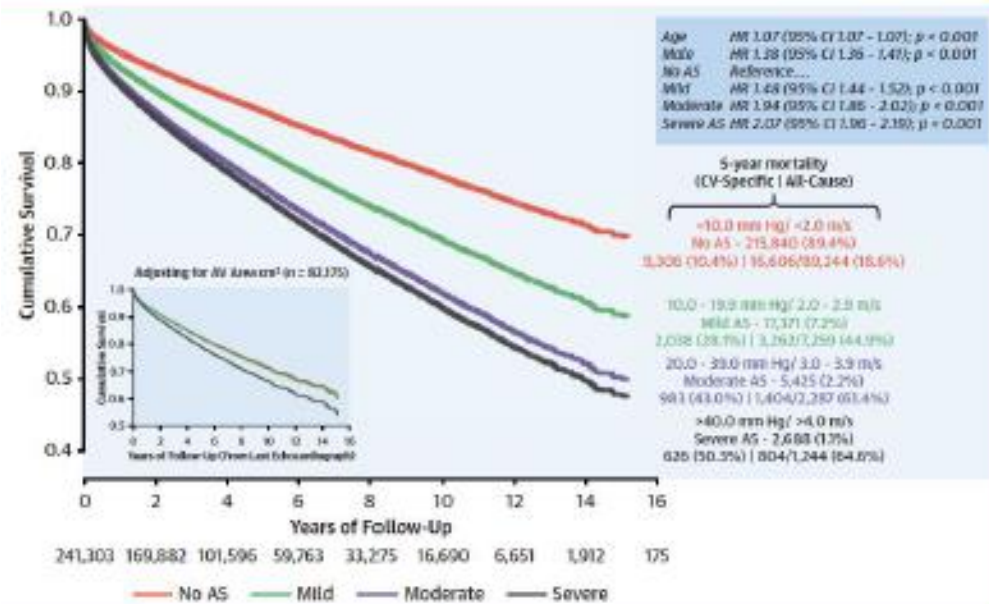


# Moderate AS as Bad as Severe AS?

*Watchful waiting is ingrained in clinical practice*

## Poor Long-Term Survival in Patients With Moderate Aortic Stenosis

Geoff Strange, PhD,<sup>a</sup> Simon Stewart, PhD,<sup>b</sup> David Celermajer, MD, PhD,<sup>c</sup> David Prior, MBBS, PhD,<sup>d</sup> Gregory M. Scalia, MBBS (Hons), MMEDSc,<sup>c</sup> Thomas Marwick, MBBS, PhD,<sup>e</sup> Marcus Ilton, MD,<sup>f</sup> Majo Joseph, MBBS,<sup>h</sup> Jim Codde, PhD,<sup>g</sup> David Playford, MBBS, PhD,<sup>g</sup> on behalf of the National Echocardiography Database of Australia contributing sites



### Why?

-Misclassification

-Challenges

-Rapid

-To

**Moderate AS is NOT a Benign Disease!**

# Transcatheter AVR Trials in Moderate Aortic Stenosis

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**TAVR-UNLOAD (n=300)**

**PROGRESS (n=450-750)**

**EXPAND II (n=650)**



*Enrollment  
complete  
Presented at  
ESC/TCT 2024*



**FPI  
Q4 '21**



**FPI  
Q1 '22**

**TAVR vs. no TAVR**

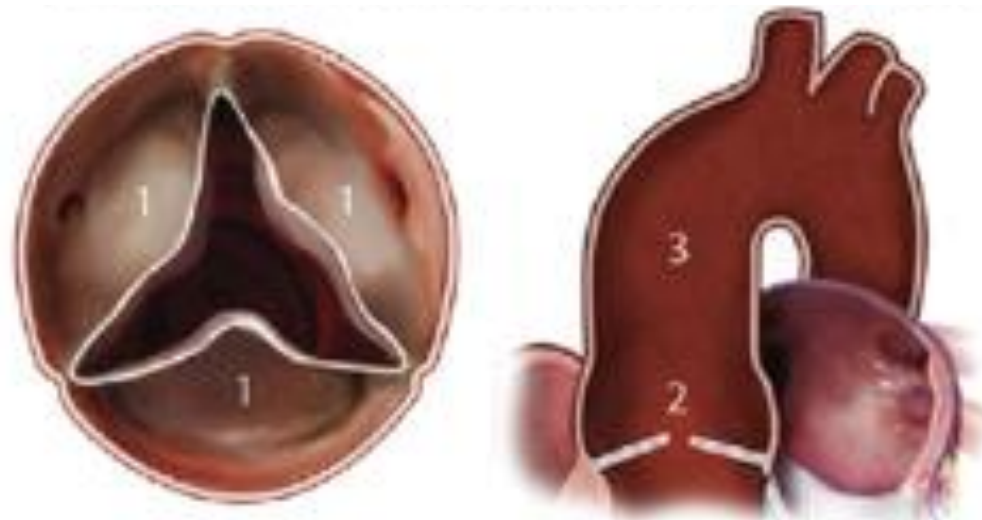
**Mortality, adverse heart failure endpoints**

**Potential new treatment pathways**

# TAVR NEXT STEPS | Aortic Regurgitation

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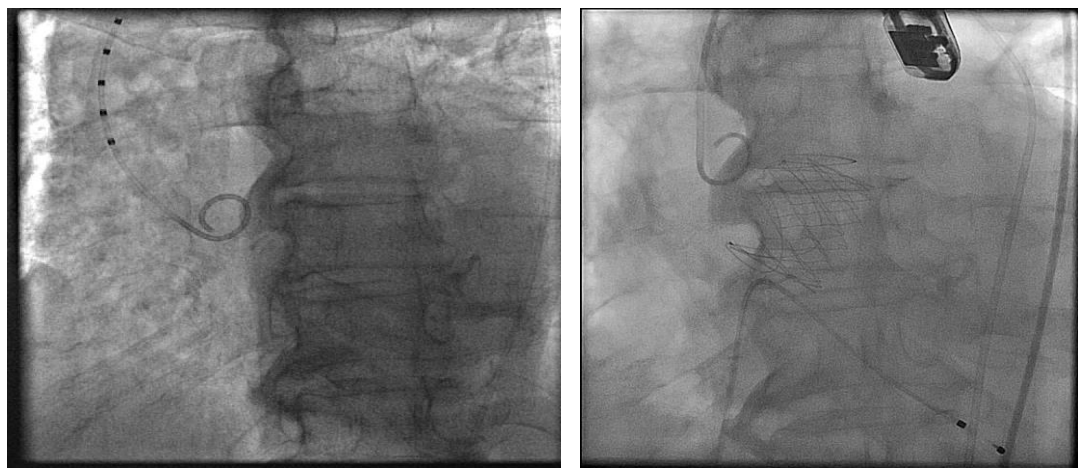
## Aortic Regurgitation



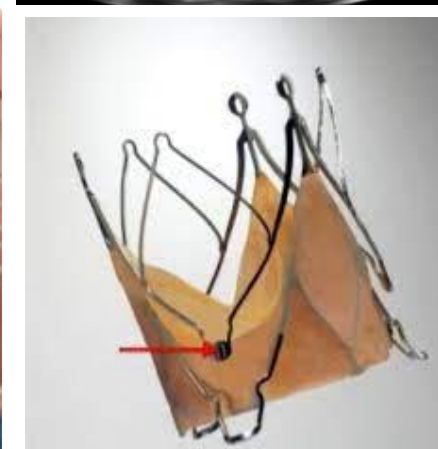
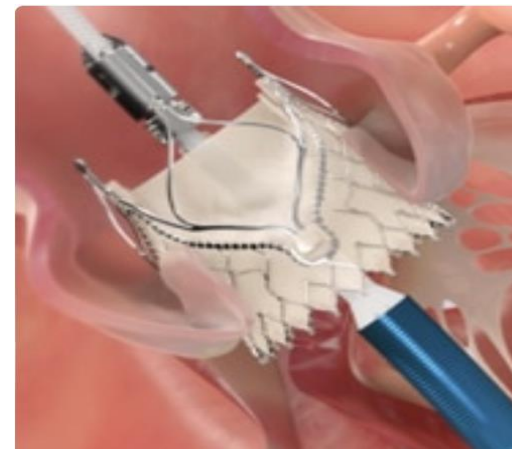
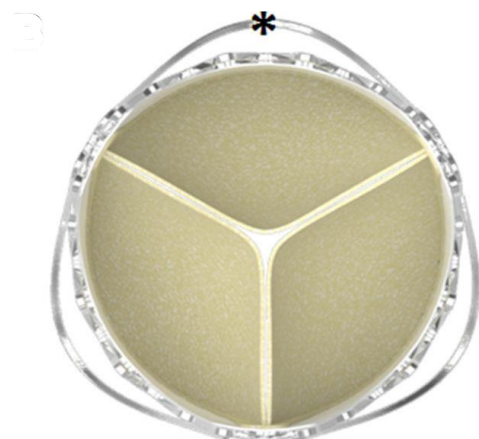
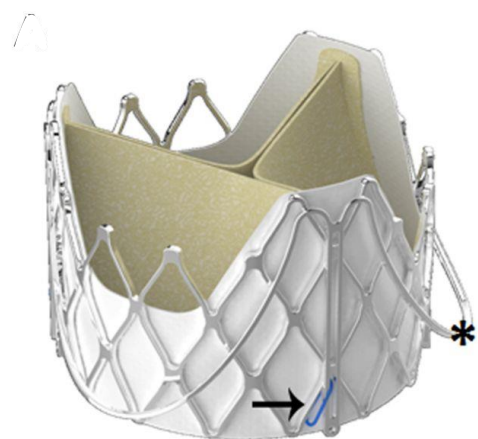
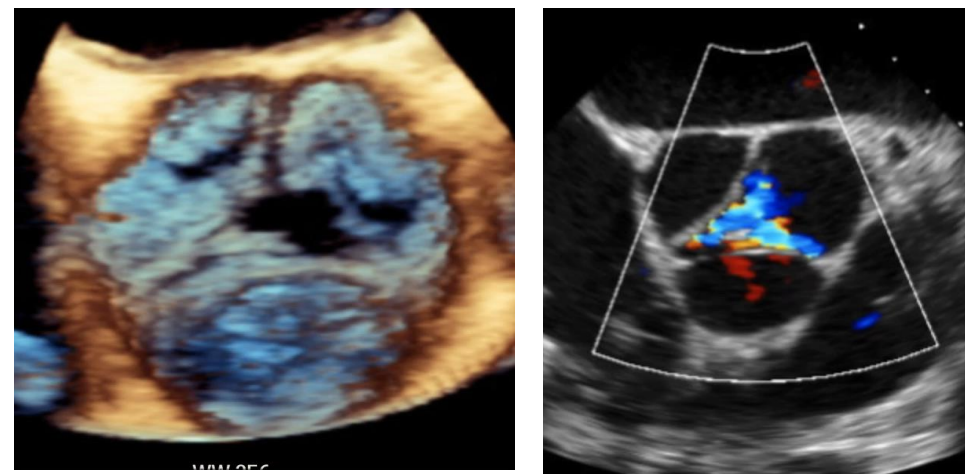


# Transfemoral THV's for Aortic Regurgitation

*JC Medicals J Valve*

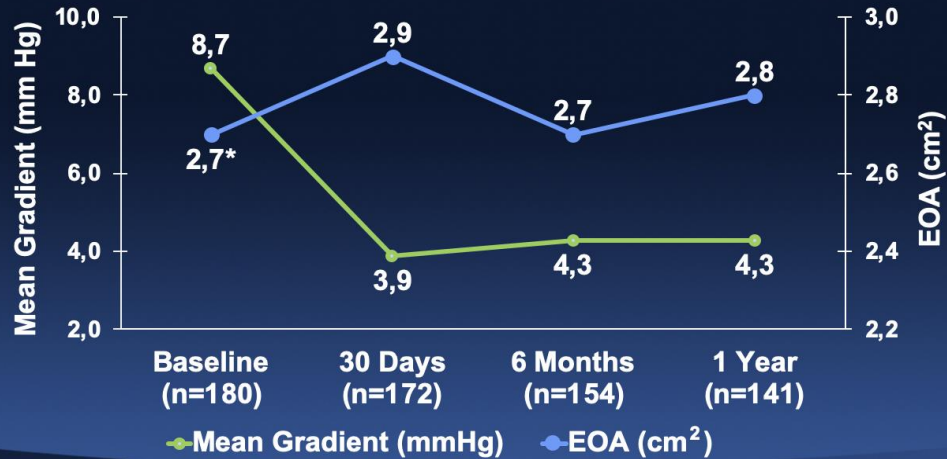


*Jena Trilogy Valve*

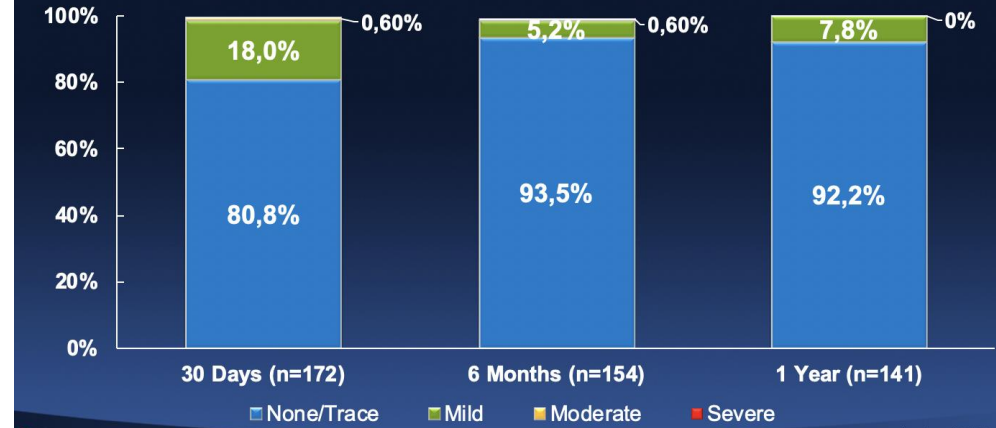


# Align AR Trial (Jena Trilogy Valve)

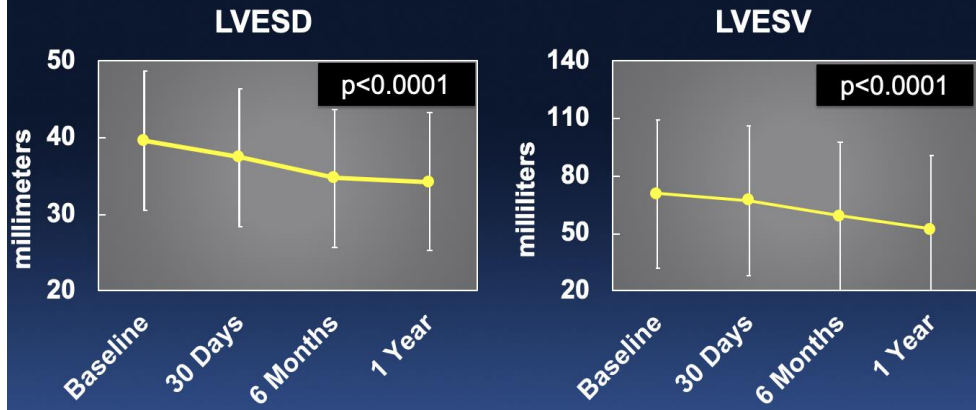
## Hemodynamic Valve Performance



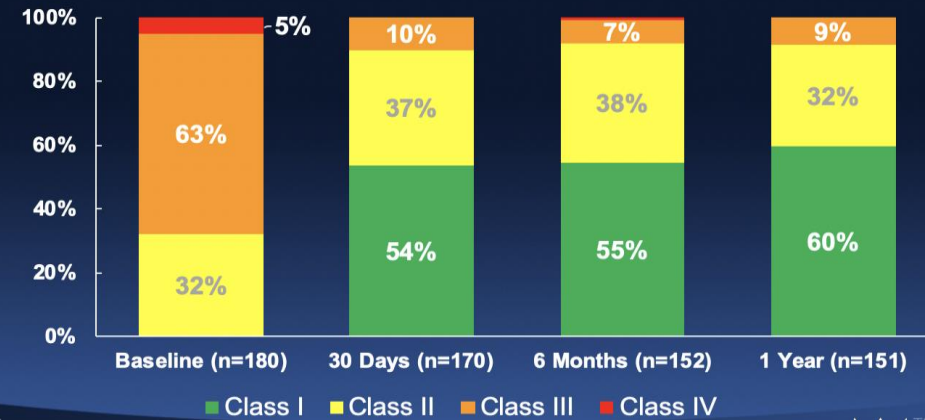
## Paravalvular Regurgitation



## LV Remodeling



## NYHA Functional Class





# The Case for Redefining “Moderate” AR

- **Growing data suggest that VHD guidelines are outdated and they are recommending treatment too late**

## ORIGINAL RESEARCH

### Do Guideline-Based Indications Result in an Outcome Penalty for Patients With Severe Aortic Regurgitation?

Christophe de Meester, PhD, Bernhard L. Gerber, MD, PhD, David Vancaeynest, MD, PhD, Anne-Catherine Pouleur, MD, PhD, Philippe Noirhomme, MD, Agnès Pasquet, MD, PhD, Laurent de Kerchove, MD, Gébrine El Khoury, MD, Jean-Louis Vanovershelde, MD, PhD

## ORIGINAL INVESTIGATIONS

### Outcomes in Chronic Hemodynamically Significant Aortic Regurgitation and Limitations of Current Guidelines



Li-Tan Yang, MD,<sup>a</sup> Hector I. Michelena, MD,<sup>a</sup> Christopher G. Scott, MS,<sup>b</sup> Maurice Enriquez-Sarano, MD,<sup>a</sup> Sorin V. Pislaru, MD,<sup>a</sup> Hartzell V. Schaff, MD,<sup>c</sup> Patricia A. Pellikka, MD<sup>a</sup>

## EDITORIAL COMMENT

### Aortic Regurgitation: Time to Reassess Timing of Valve Replacement?\*

Robert O. Bonow, MD  
*Chicago, Illinois*

## EDITORIAL COMMENT

### In the Eye of the Beholder

Defining Severe Aortic Regurgitation and the Timing of Intervention\*

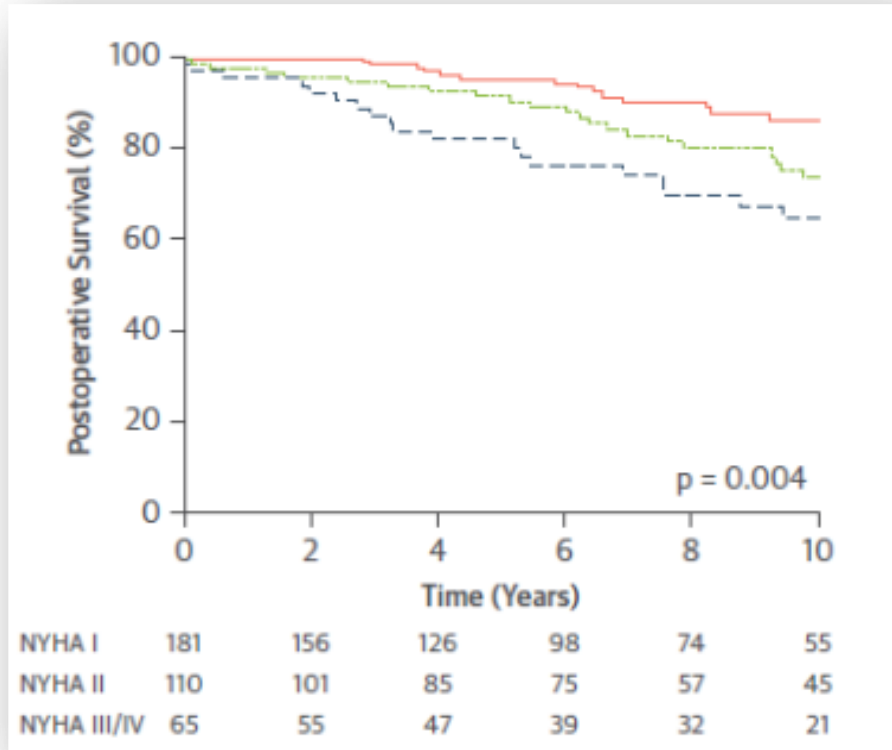


Sheldon E. Litwin, MD

# Aortic Regurgitation: Under Treatment

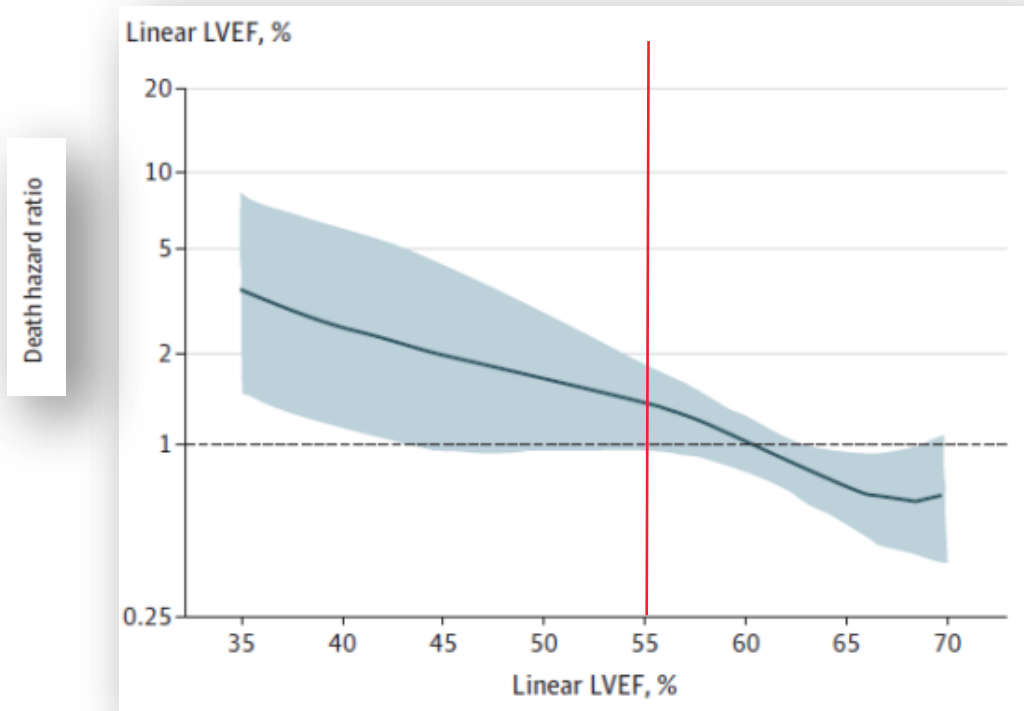
ACC/AHA Guidelines: Should We Wait For Class I Indications??

**Should We Wait for Symptoms?**



*Meester, et al. JACC. 2019*

**Should We Wait for an LVEF of  $\leq 55\%$ ?**



*Yang et al. JAMA Cardiol. 2021;6(2):189-198*

# The 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

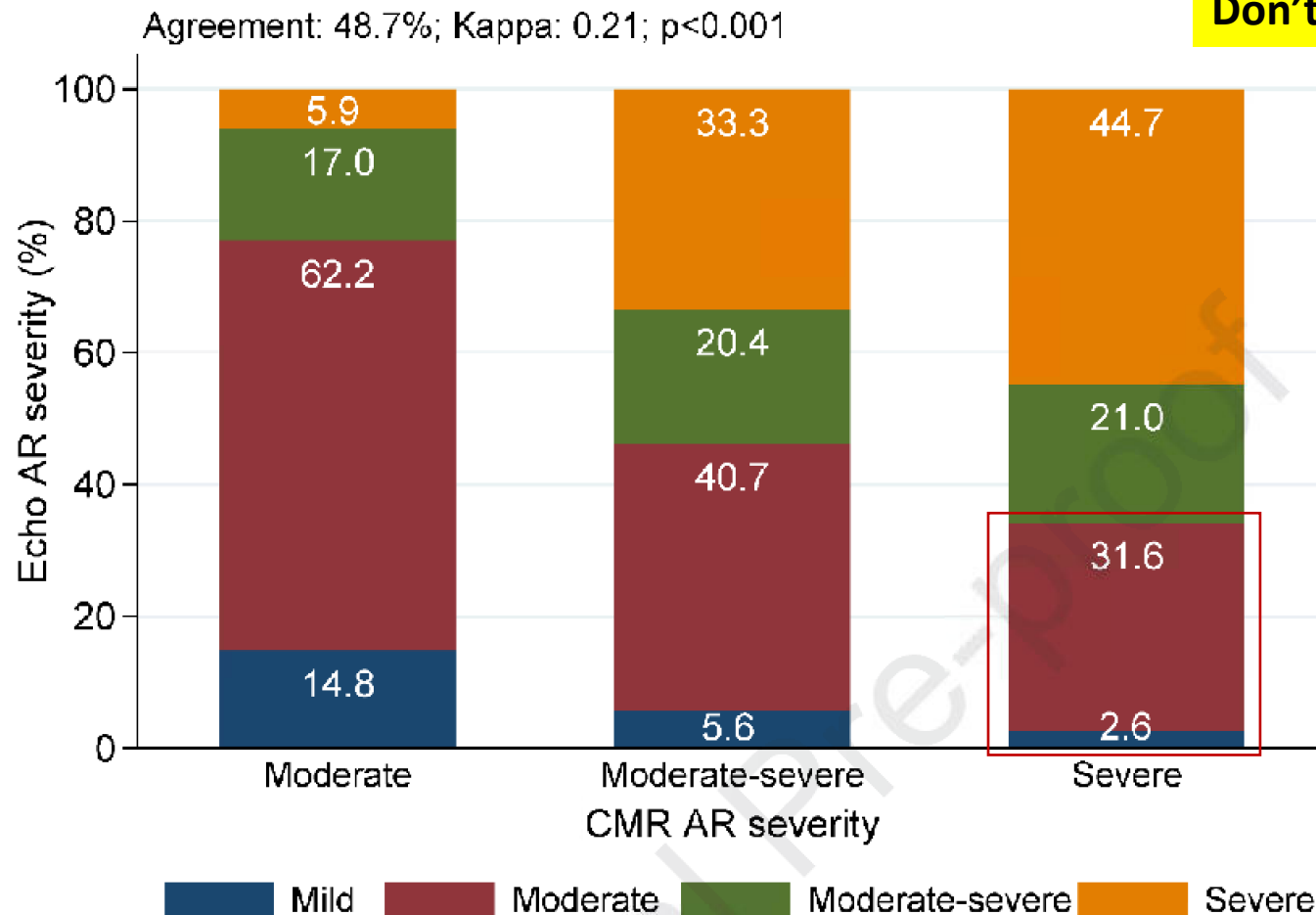
NCT01475047



**It took > 3 years to complete the study:**

- 1<sup>st</sup> reason for screen failure → Anatomical (annulus, LV-Ao angle)**
- 2<sup>nd</sup> reason for screen failure Non-Severe AR by Echocardiography**

# Poor Agreement between Echo vs. CMR AR Severity



Malahfji et al. JACC 2023 May 16;81(19):1885-1898.

# Aortic Regurgitation.

Disease Awareness has to be increased and Grading has to be re-defined

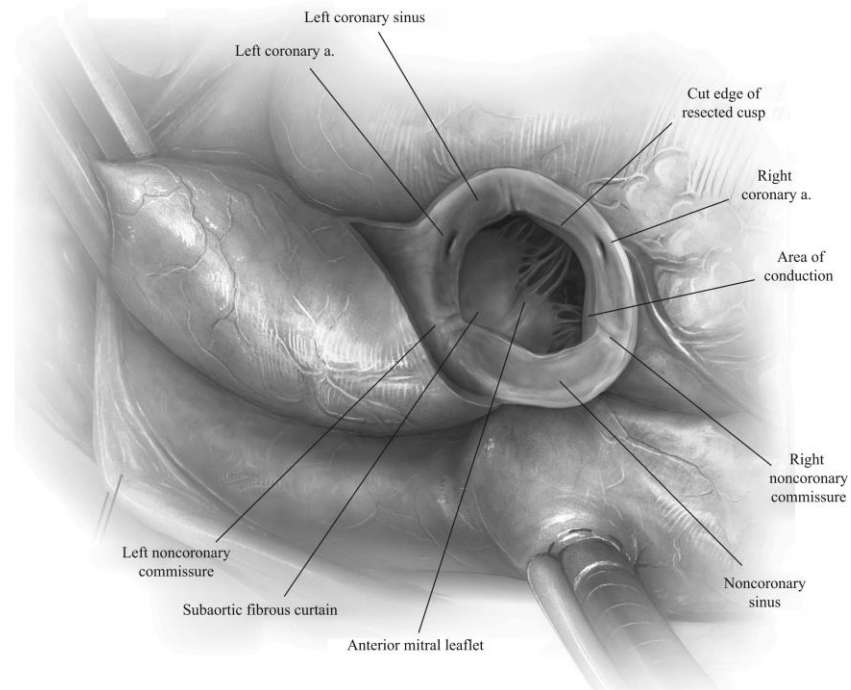
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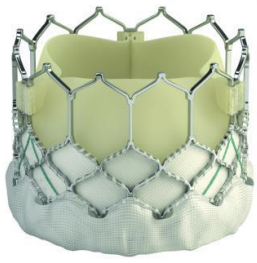
- Significant AR is NOT uncommon, but terribly underdiagnosed (remember when TR was the forgotten valve?!)
- 2D Echo is inadequate for quantification of AR severity and of LV remodeling. Forget linear dimensions → Guidelines are outdated!
  - Despite patients having a long asymptomatic clinical course, the LV is feeling it!
  - ***Don't stop at moderate AR in Echo, use CMR to confirm***
- While the current goal is to address the immediate need in HR/inoperable patients, true success will be measured by transforming diagnosis, selection and treatment of AR patients to an earlier stage.

# TAVR Next Steps I Small Annulus

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## Small Annulus





# SMART Trial Design

Prospective, randomized controlled, post-market trial conducted at 83 international sites

All-comer trial with all surgical risk categories including bicuspid patients

## Key eligibility

- ⌚ Symptomatic severe AS\*
- ⌚ Small aortic annulus ( $< 430 \text{ mm}^2$  by MDCT)

## Randomization

1:1 stratified by site & sex

716 patients treated

**SEV (N=355)**

Medtronic Evolut PRO/PRO+/FX

**BEV (N=361)**

Edwards SAPIEN 3/SAPIEN 3 Ultra

## Co-Primary Endpoints at 1 year with planned 5-year follow-up

Co-Primary Endpoint 1: Composite of mortality, disabling stroke, or heart failure rehospitalization through 12 months

Co-Primary Endpoint 2: Bioprosthetic valve dysfunction (BVD) through 12 months

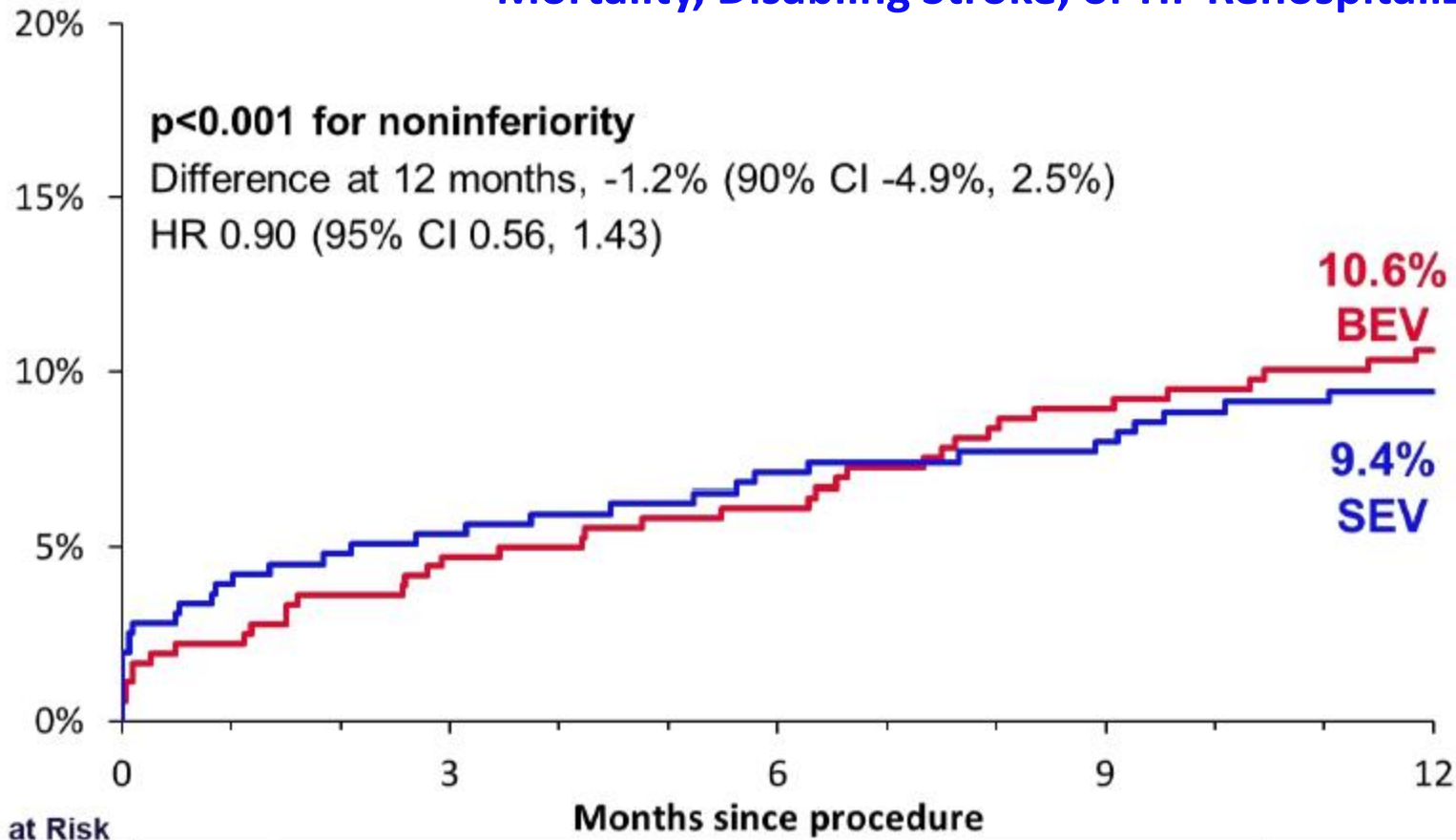
\*AVA  $\leq 1.0 \text{ cm}^2$  (AVA<sub>i</sub>  $\leq 0.6 \text{ cm}^2/\text{m}^2$ ) or mean gradient  $\geq 40 \text{ mmHg}$  or max velocity  $\geq 4.0 \text{ m/s}$ ; 30-day predicted risk of surgical mortality  $< 15\%$  by heart team assessment.



# Co-Primary Endpoint 1:

## Clinical Outcome Composite through 12 Months powered for Non-Inferiority

### Mortality, Disabling Stroke, or HF Rehospitalization



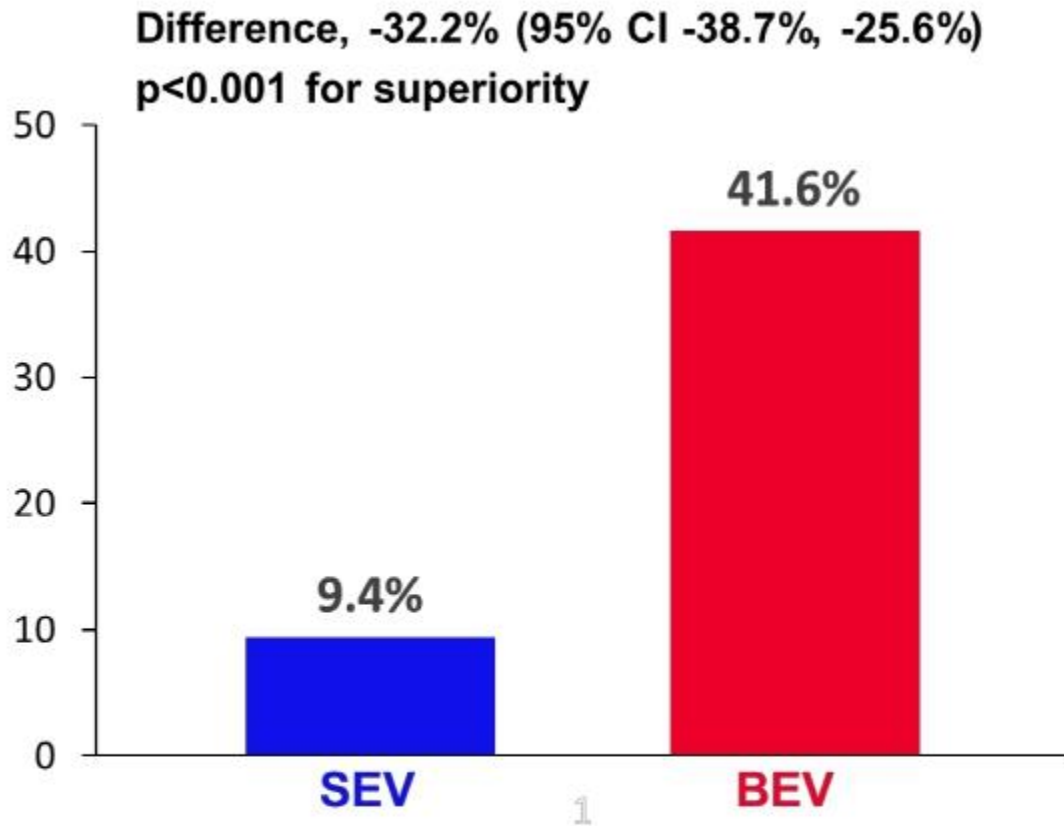
12 Months	SEV (N=355)	BEV (N=361)	HR (95% CI)
All-cause mortality	5.1%	5.9%	0.88 (0.47, 1.65)
Disabling stroke	3.1%	2.6%	1.26 (0.52, 3.03)
HF rehos	3.8%	3.5%	1.11 (0.51, 2.44)



# Co-primary endpoint 2:

## BVD through 12 months powered for superiority

### Bioprosthetic Valve Dysfunction through 12 months



	SEV (N=350)	BEV (N=365)	P Value
<b>BVD composite</b>	<b>9.4%</b>	<b>41.6%</b>	<b>&lt;0.001</b>
⊙ HSVD	3.2%	32.2%	
⊙ NSVD	5.9%	18.2%	
⊙ Thrombosis (clinical)	0.3%	0.3%	
⊙ Endocarditis	0.6%	2.3%	
⊙ AV Reintervention	0.9%	0.6%	

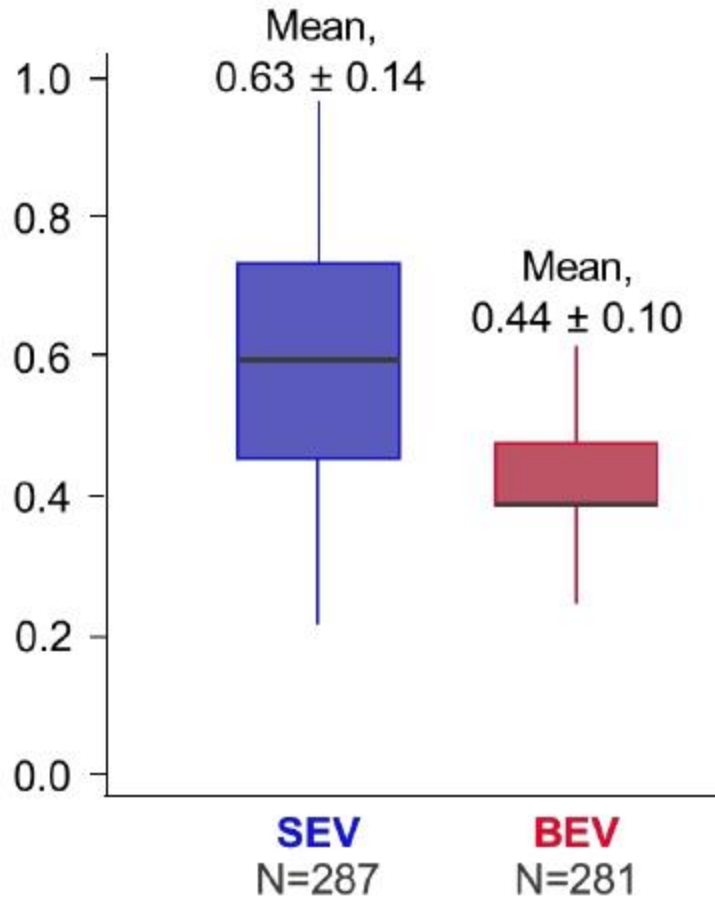
HSVD = Mean gradient  $\geq$  20 mmHg

NSVD = Severe PPM per VARC-3 or  $\geq$  moderate total AR

# Other hemodynamic Outcomes at 12 Months

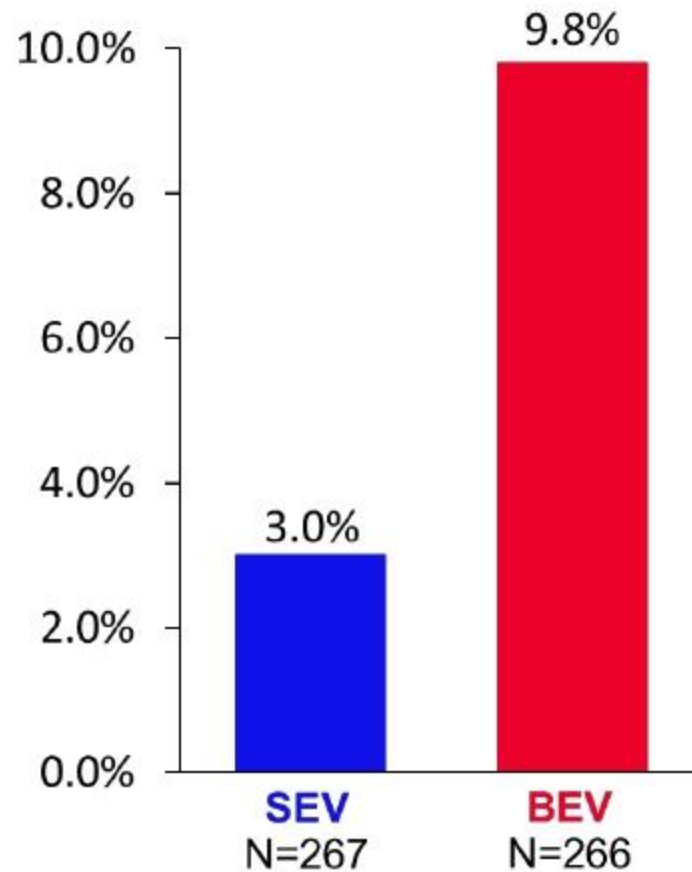
## Doppler velocity index

Difference, 0.19 (95% CI 0.17, 0.21)  
 $p < 0.001$



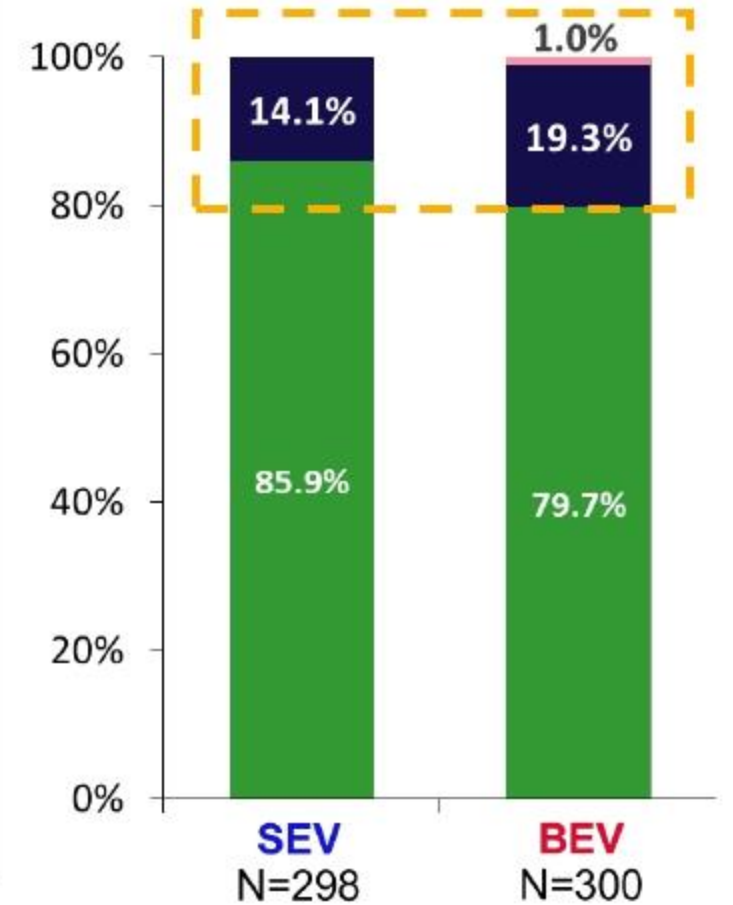
## Severe Prosthesis-Patient Mismatch (VARC-3)

Difference, -6.8% (95% CI -10.9, -2.7)  
 $p = 0.001$



## Total Aortic Regurgitation

$\geq$ Mild total AR at 12 months:  
14.1% SEV vs 20.3% BEV,  $p = 0.043$



# Summary

The SMART trial is the largest, most rigorous trial to date, to randomize patients to the 2 most widely used TAVR devices, and the largest TAVR trial to enroll mostly women.

The SMART trial met both primary and all 5 prespecified secondary endpoints.

Compared with BEV, the supra-annular SEV demonstrated:

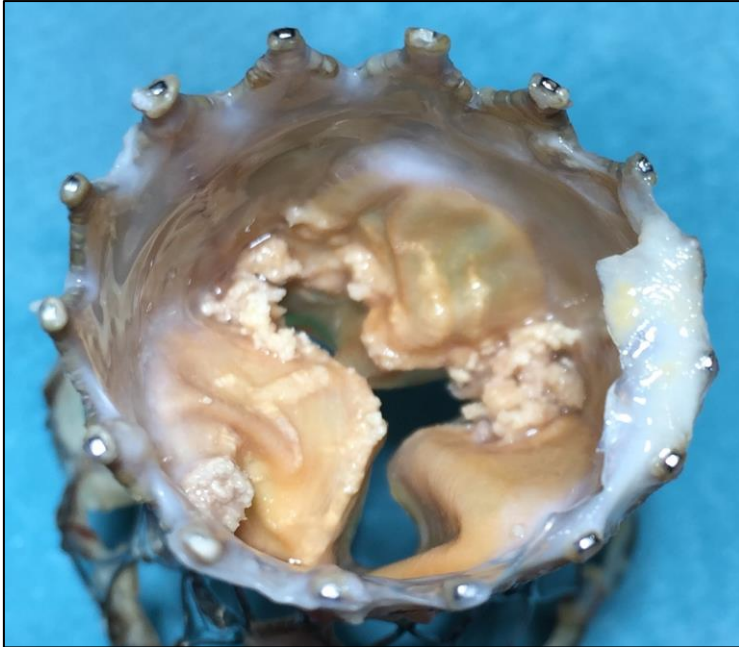
- **Noninferior clinical outcomes at 1 year**
- **Superior valve performance at 1 year:**
  - 32.2% lower incidence of BVD
  - 8 mmHg lower mean gradient
  - 0.5 cm<sup>2</sup> greater effective orifice area
  - 0.19 larger Doppler velocity index
  - 6.8% lower incidence of severe PPM
- **Improvements in other secondary outcomes at 1 year:**
  - Less total AR and better QOL per the KCCQ ordinal outcome

*Based on the large differences observed in valve performance, we expect that the SEV will demonstrate improved valve durability and outcomes during longer follow-up*

# TAVR NEXT STEPS | Lifetime Management

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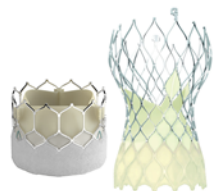
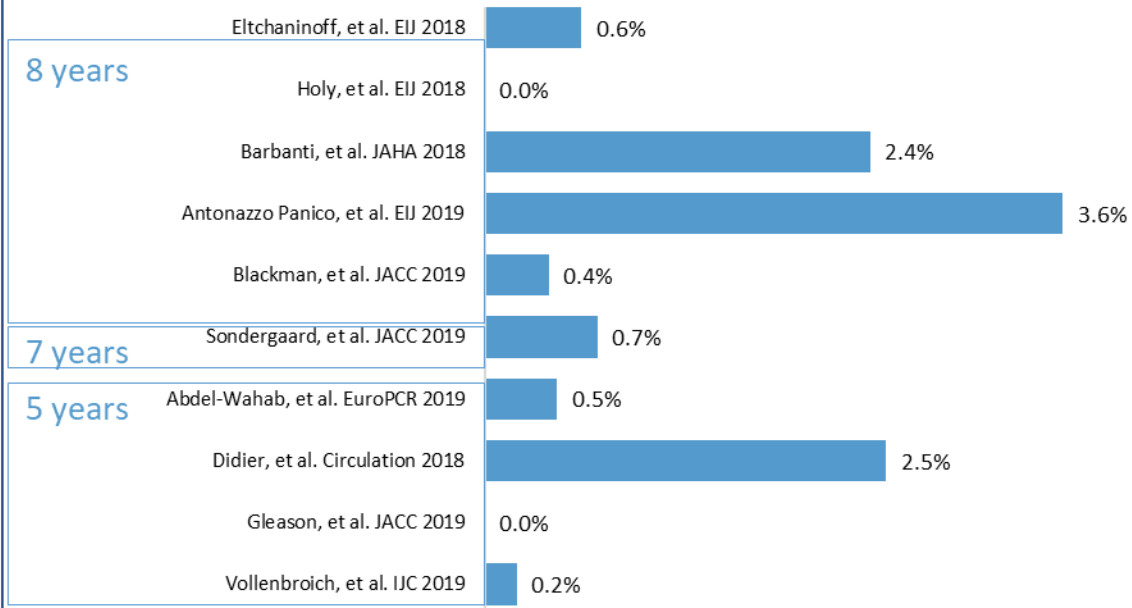
## Durability and Valve in Valve



# Lifetime Management of Aortic Disease in 2024

## *Durability of THVs – So far so good!*

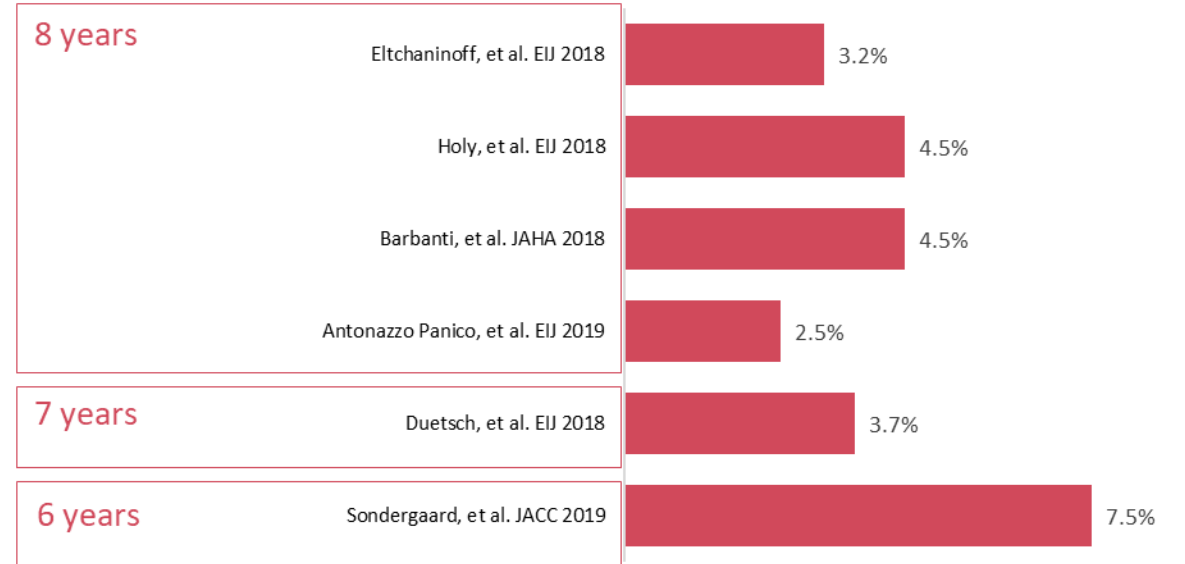
### Severe SVD



SVD at 5 to 8 years  
Weighted incidence

**1.3%**  
(95% CI 0.7-1.9)

### Bioprosthetic valve failure (BVF)



BVF at 6 to 8 years  
Weighted incidence

**3.7%**  
(95% CI 2.7-4.6)

# TAVR NEXT STEPS | Lifetime Management

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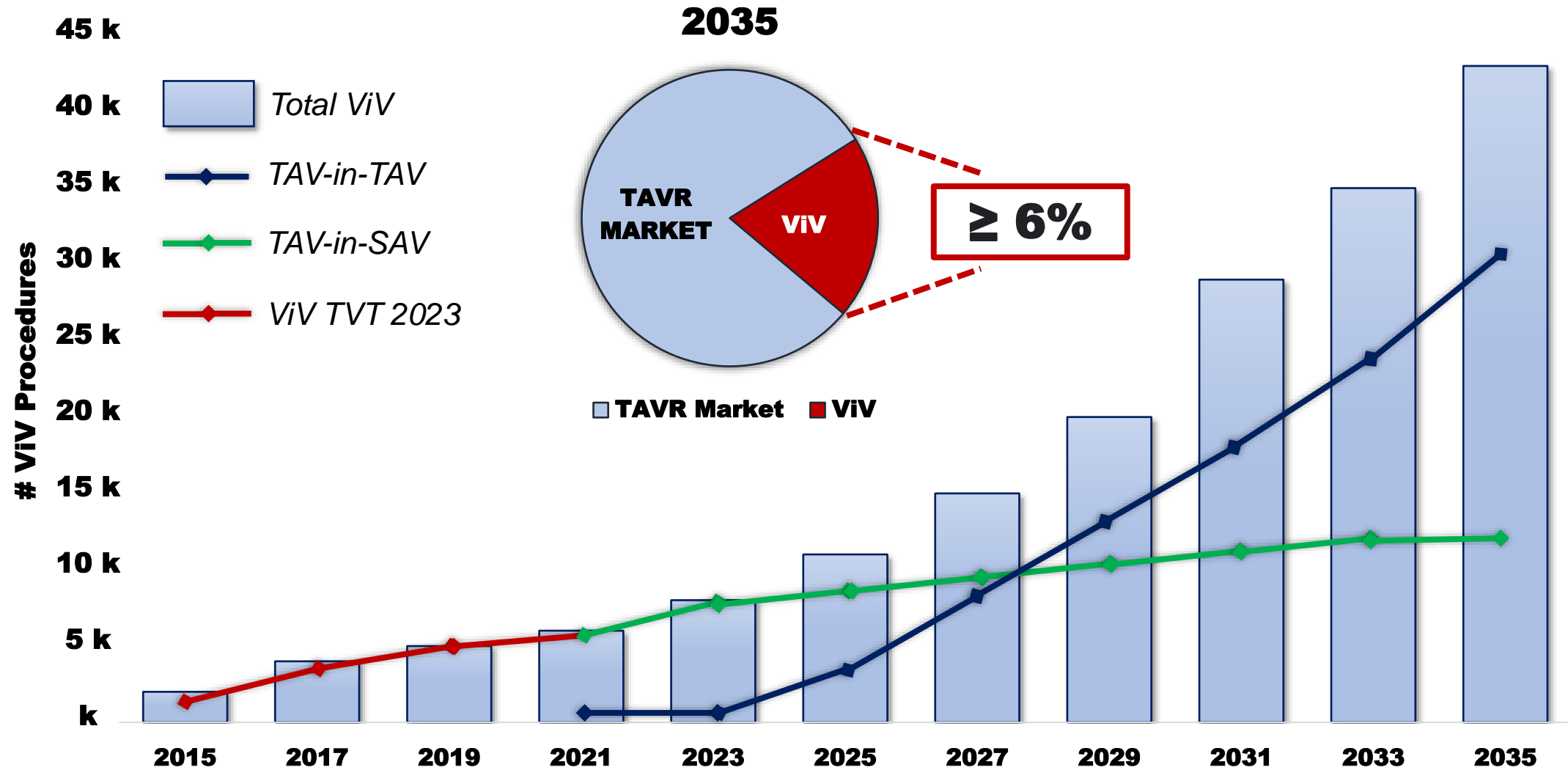
## Valve in Valve







# US ViV Market Forecast until 2035



Adapted from: Généreux P et al.



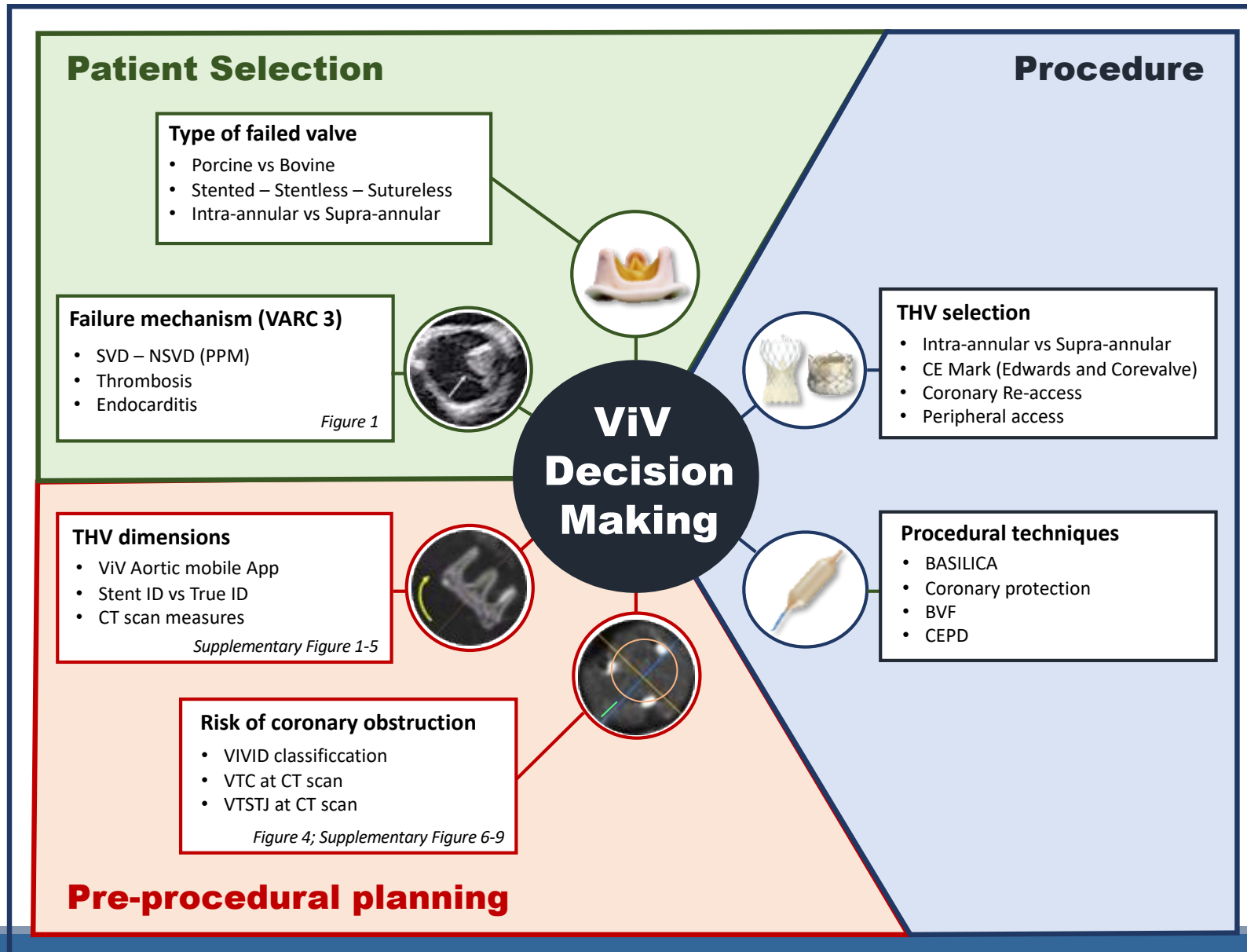
# ViV Decision Making Process

Type of Failed Valve

Mechanism of Failure

THV Dimensions

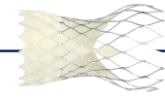
Risk of Coronary Obstruction



# Lifetime Management of Aortic Disease



**First Intervention  
SAVR**



**First Intervention  
TAVR**



*«The first Cut is the Deepest»*

*TAVR will likely be the most frequent 2nd intervention in a lifetime management and «TAVR repeatability» might be as important as leaflet durability»*

365

10-11%

JACC 2020; 4;76(5):489-499.  
EuroIntervention 2022;17:1227-1237.

365

5-6%

JACC Intv. 2021;14(2):211-20  
EuroIntervention 2022;17:1227-1237.

365

21-29%

Percy ED et al., JACC Intv 2021, Vol 14 N 15

365

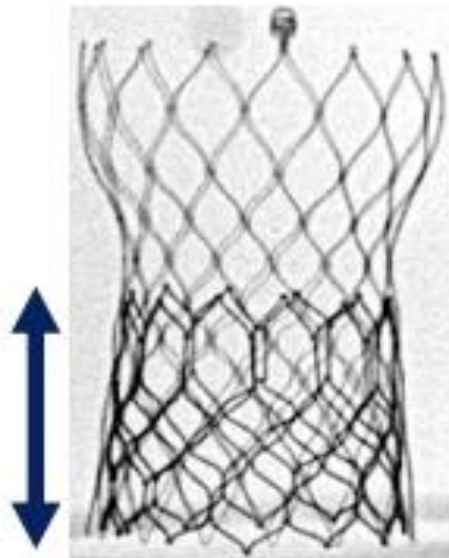
20%

Percy ED et al., JACC Intv 2021, Vol 14 N 15

# What else is important in RE-Do TAVR?

## NEOSKIRT

S3 Outflow at Node 5



23.0 mm

## LEAFLET OVERHANG

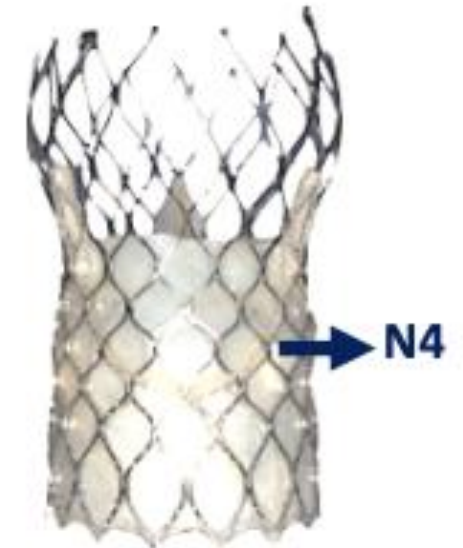
S3 Outflow at Node 5



59% leaflet  
overhang

## INDEX THV EXPANSION

S3 Outflow at Node 5



+2.0 mm

# What's important in RE-Do TAVR?

## • Leaflet Modification Methods

### Basilica Techniques

#### Leaflet "splitting" - Three Unmet Needs

1

Degenerated valves that require reintervention present a risk of coronary obstruction and coronary access impairment



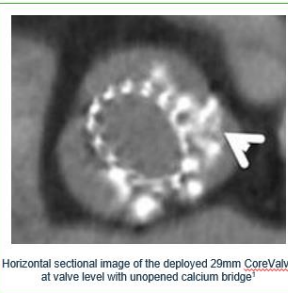
2

TAVI in Native Valves that present a risk of coronary impairment in certain anatomies



3

TAVI in Bicuspid is suboptimal



1. Hayashida et al, Circulation: Cardiovascular Interventions. 2013;6:284–291

#### Leaflet Splitting: potential use

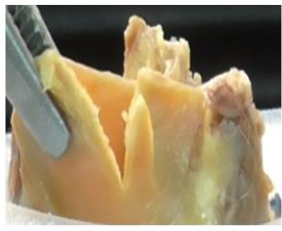
1

Splitting leaflets to enable a safe valve-in-valve



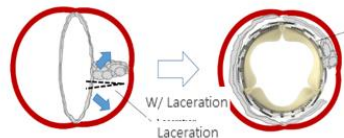
2

Splitting of native valve leaflets to avoid coronary impairment

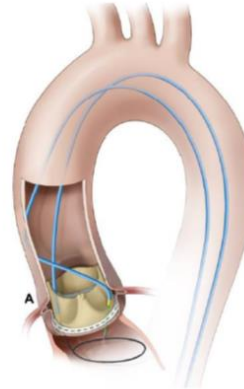


3

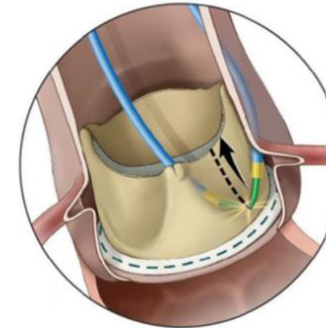
"Tricuspidization" of Bicuspids pre-TAVI



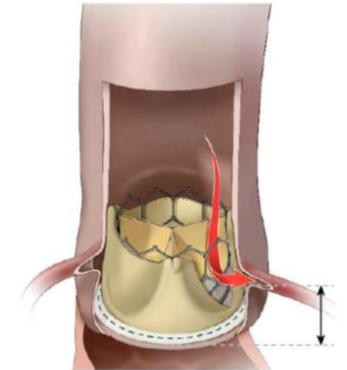
Leaflet wire transversal and snaring



Leaflet slicing

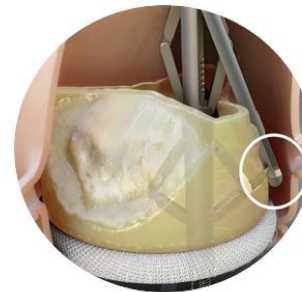


Preserved coronary flow

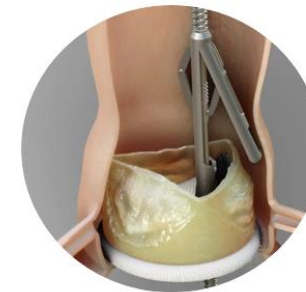


### ShortCut™ Catheter

First dedicated transcatheter leaflet splitting device



Designed to **enable coronary access & prevent coronary obstruction** during TAVI



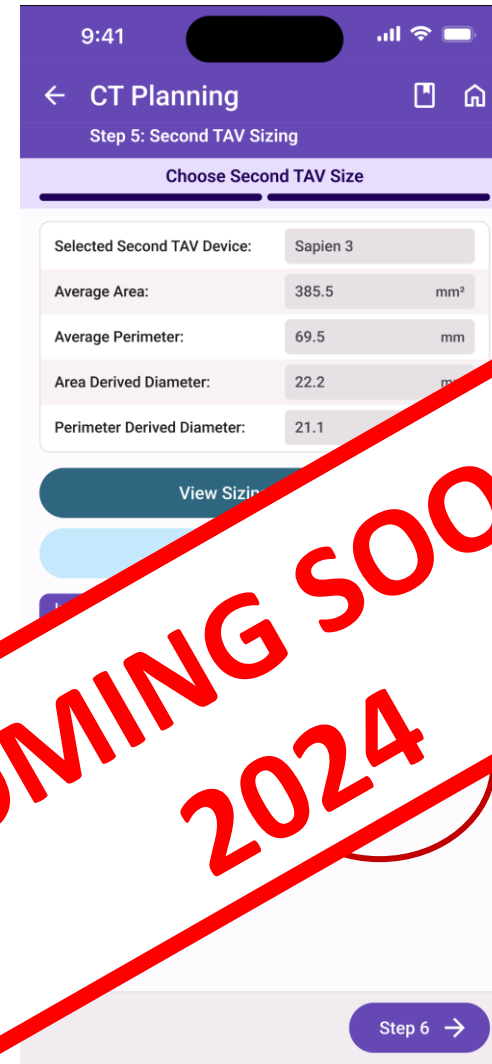
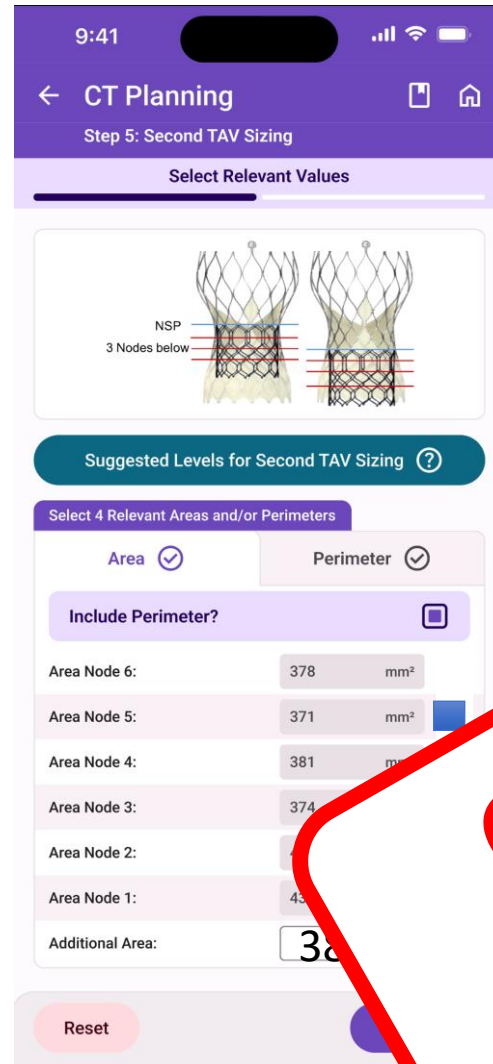
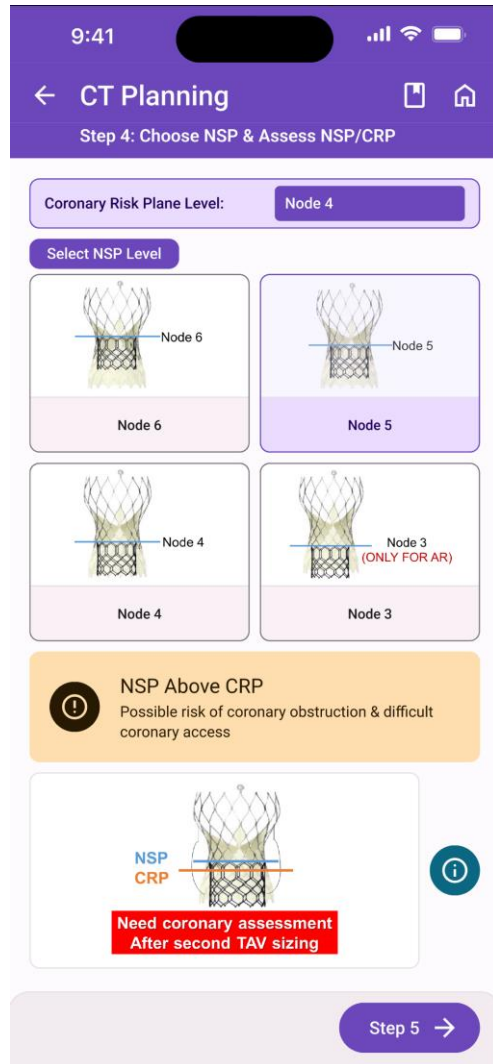
Complete **control over positioning & leaflet splitting location**



Allows for **safe, simple splitting of single or double leaflets using same device**



# iPhone APP for THV-in-THV



COMING SOON  
2024

# TAVR Projection - Final Thoughts

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- ❑ Older (than 75 yrs by ESC guidelines) regardless of pt's risk - *TAVR is the first line therapy*
- ❑ Younger *AND* low risk Surgery - in 2022 guidelines, SAVR as first line

***BUT ..... Many aspects need to be discussed for final decision:***

- ❑ ***Friality/futility***
- ❑ ***Adequate Informed consent*** of the patients (that must be part of the final decision)
- ❑ ***Life expectancy*** of the patients
- ❑ ***Re-do permutations : SAVR-TAVR, TAVR-TAVR***  
***(eg. surgical prostheses - TAVR Friendly )***
- ❑ ***TAVR repeatability (eg. Coronary access)***
- ❑ ***Not all TAVR centers are created equal!!***