



# Where will TAVR be in 2030? Who will we be treating?

---

**Eberhard Grube MD, FACC, MSCAI**

University Hospital Bonn, Heart Center, Germany

INCOR Heart Institute, São Paulo, Brazil

Stanford University, Palo Alto, California, USA

# Financial Disclosure

---

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

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



# TAVR: Future Projections & Expectations

---

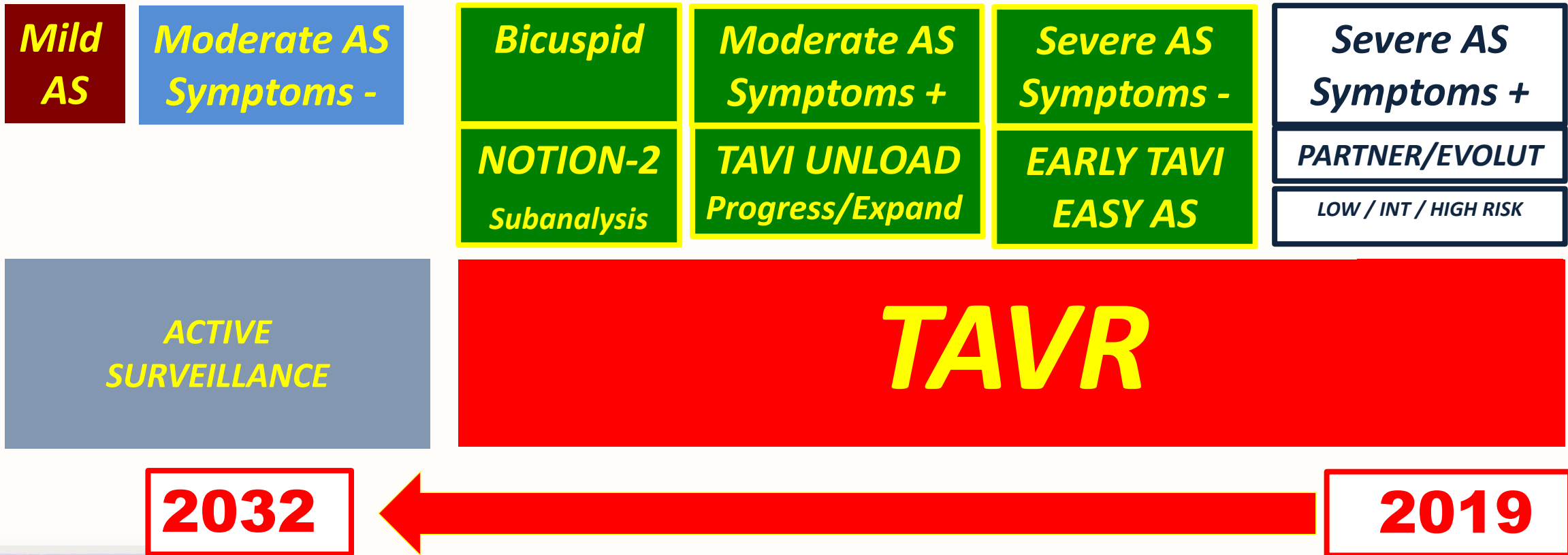


- ❑ improved disease *awareness* and *access* to TAVR
- ❑ *Explosive growth* in TAVR worldwide
- ❑ Accelerated *innovation* of TAVR platforms and evolving accessory devices (eg , balloon, pm, closure devices, cv protection)
- ❑ *Aortic valve remodeling* technologies (eg scoring, lithotripsy)
- ❑ Re-defining disease state and «*timing/trigger points*» for therapy
- ❑ Realization of *new clinical extended indications*

# Aortic Stenosis Redefined:

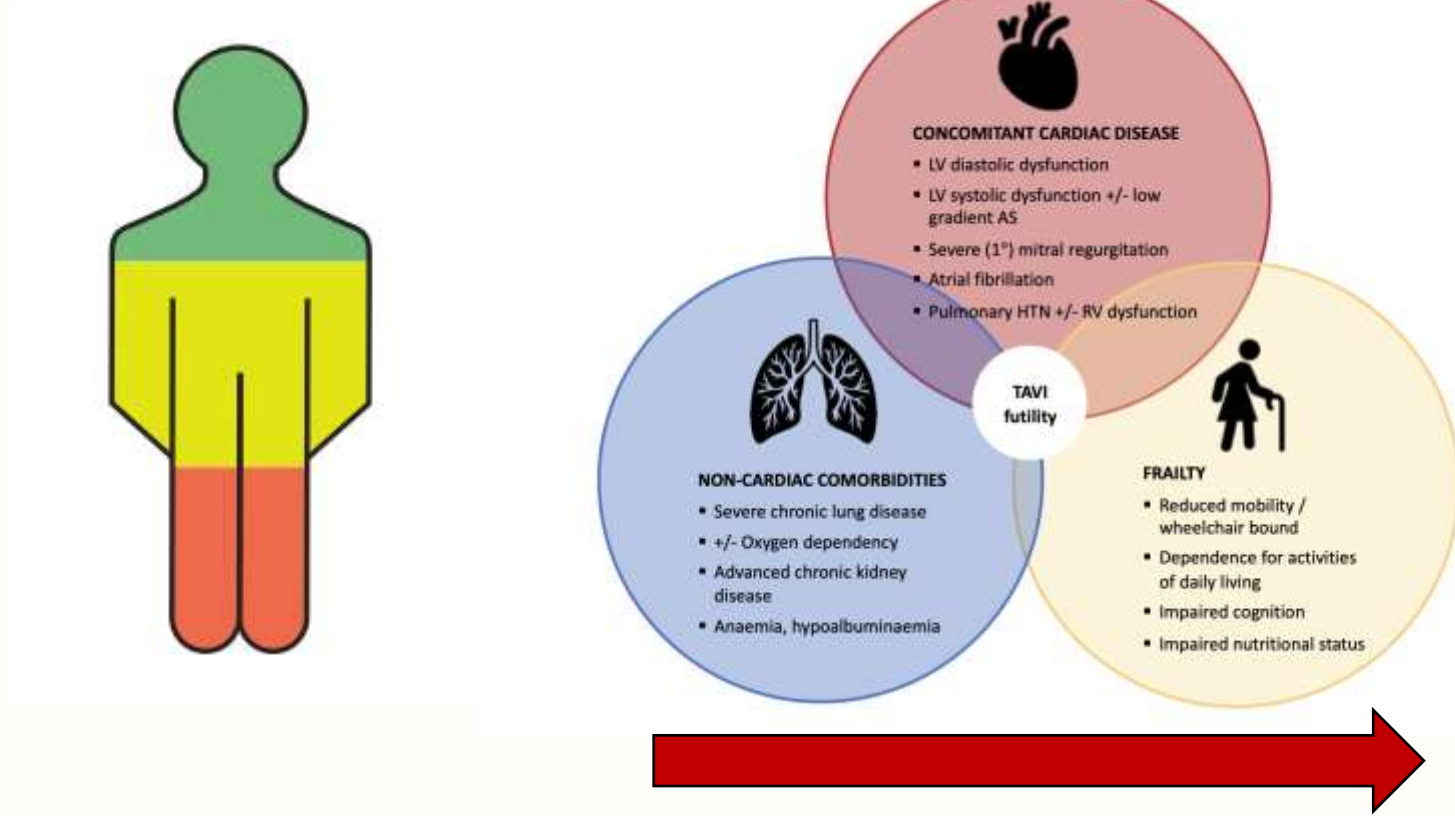
## *Functional classification / New trigger points*

---



# Improved Patient Selection and Disease Awareness

## Mean Treatment Difference



## Individual patient outcomes



**30% of patients undergoing TAVR derive minimal symptom benefit or die within one year**

# TAVR Lifetime Management of Aortic Disease

## *Who will we be treating in the Future?*

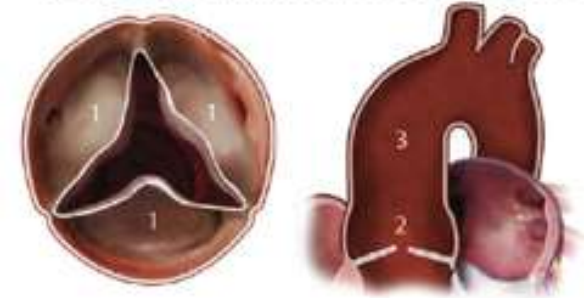
Low Risk



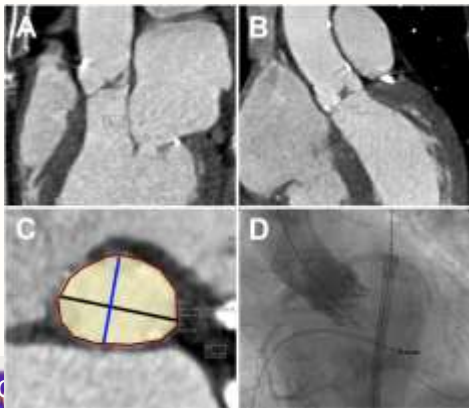
Bicuspid AS



Aortic Regurgitation



Small Annulus



Valve in Valve



Asymptomatic/Moderate AS

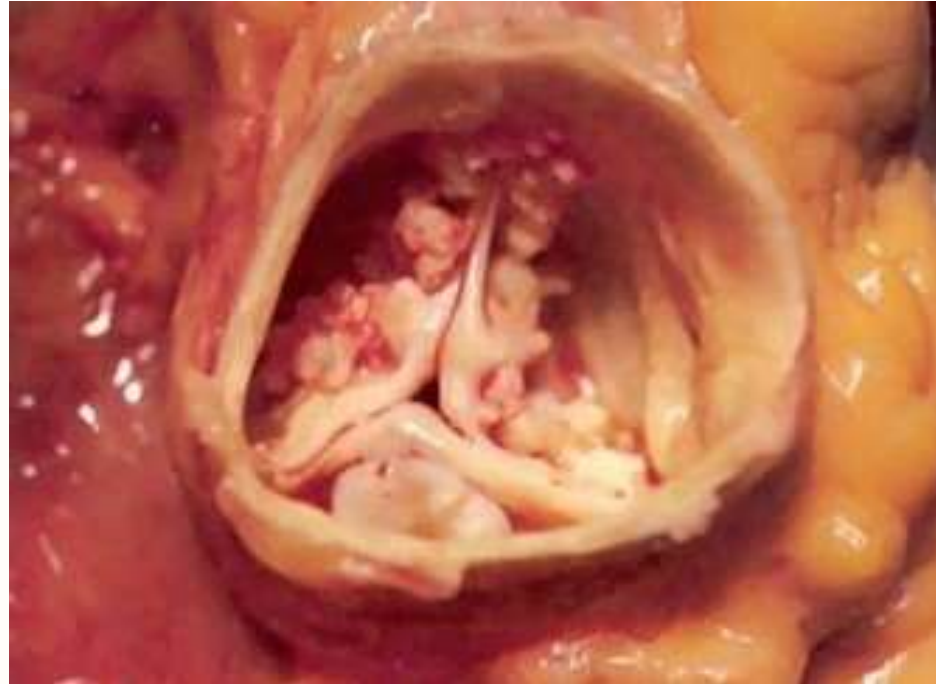




# TAVR NEXT STEPS | Asymptomatic/Mod AS

---

## Asymptomatic/Moderate AS



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



# TAVR NEXT STEPS | Mortality in Untreated AS

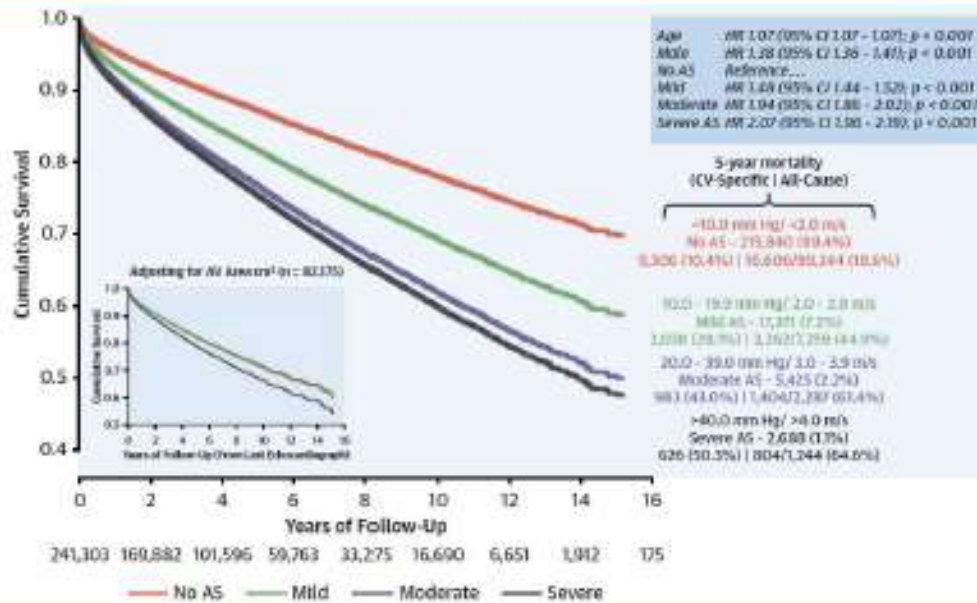
| 595,120 Patients With AS Assessment | AS Severity                           |                 | 4-Year Treatment Rates With AVR | 4-Year Mortality Without AVR |
|-------------------------------------|---------------------------------------|-----------------|---------------------------------|------------------------------|
|                                     | ACC/AHA Dx                            | Intermediate Dx |                                 |                              |
| No AS<br>524,342 (88.1%)            | 61,293 (86.6%)                        | 9,485 (13.4%)   |                                 |                              |
| AS Dx<br>70,778 (11.9%)             | Mild AS<br>34,614 (48.9%)             |                 | 1.0%                            | 25.0%                        |
|                                     | Mild-to-Moderate AS<br>5,796 (8.2%)   |                 | 4.2%                            | 29.7%                        |
|                                     | Moderate AS<br>14,550 (20.6%)         |                 | 11.4%                           | 33.5%                        |
|                                     | Moderate-to-Severe AS<br>3,689 (5.2%) |                 | 36.7%                           | 45.7%                        |
|                                     | Severe AS<br>12,129 (17.1%)           |                 | 60.7%                           | 44.9%                        |

# 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>e</sup> Thomas Marwick, MBBS, PhD,<sup>f</sup> Marcus Ilton, MD,<sup>g</sup> Majo Joseph, MBBS,<sup>h</sup> Jim Codde, PhD,<sup>i</sup> David Playford, MBBS, PhD,<sup>j</sup> on behalf of the National Echocardiography Database of Australia contributing sites



Why?

-Misclassification

-Challenges

-Rapid

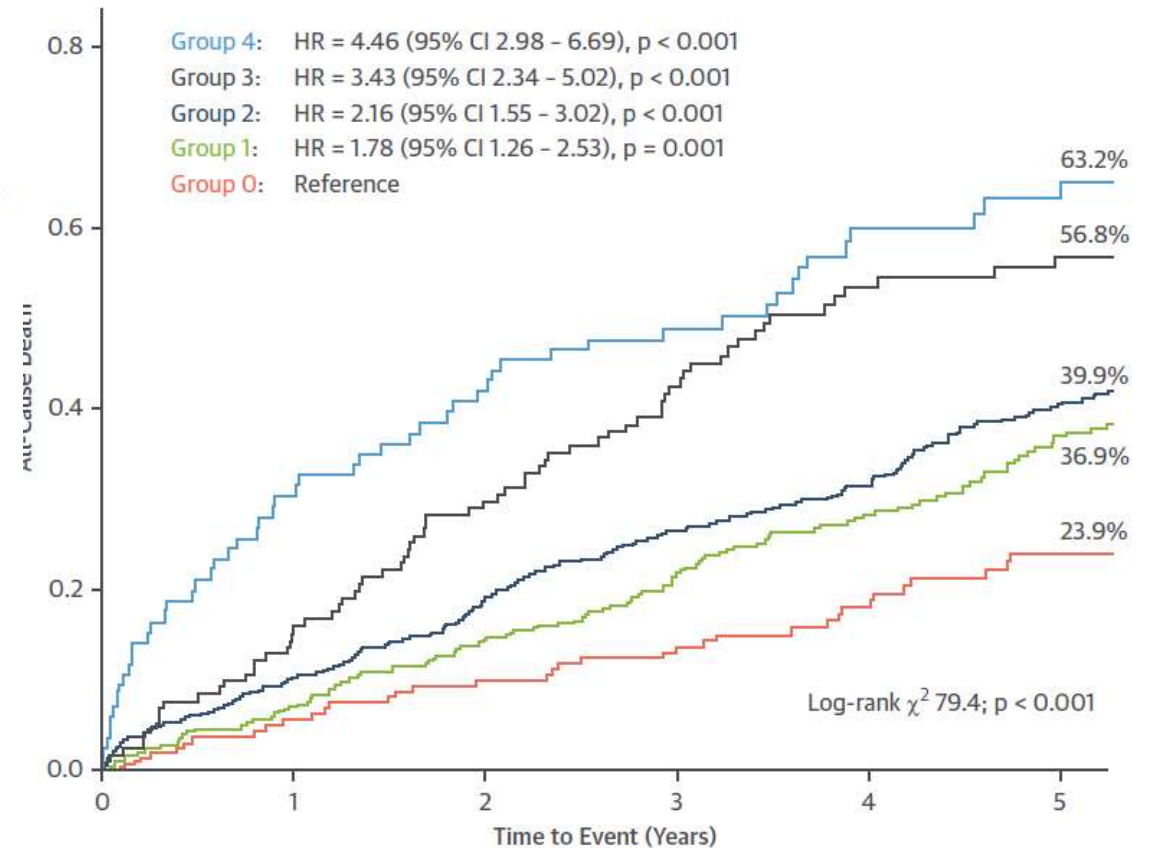
-To

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

# Extent of Cardiac Damage among Moderate AS 5-Year Death; N=1,245 pts.



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

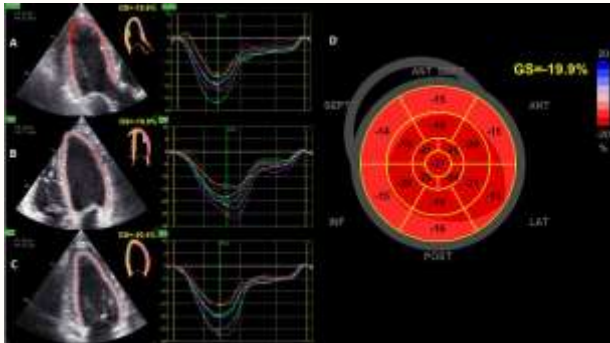




# Earlier Intervention | Challenges in Evaluating Cardiac Function

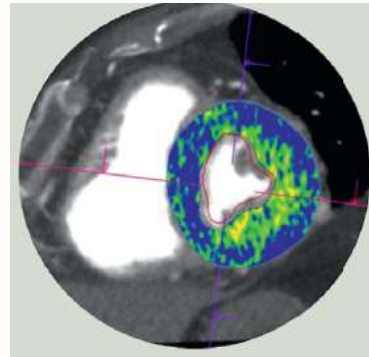
*Multi-modalities to evaluate impact of intervention and enhance prognostic risk stratification*

## Echocardiography (Baseline and follow-up)



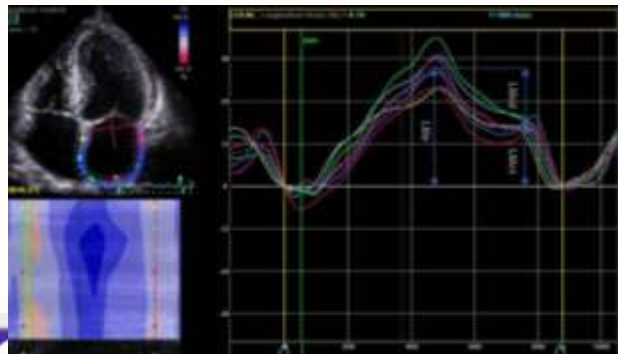
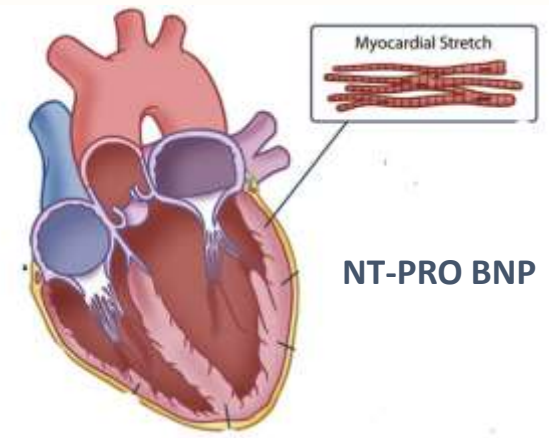
Left Ventricular Global Longitudinal Strain

## Cardia CT/ MRI (Baseline and Follow Up))

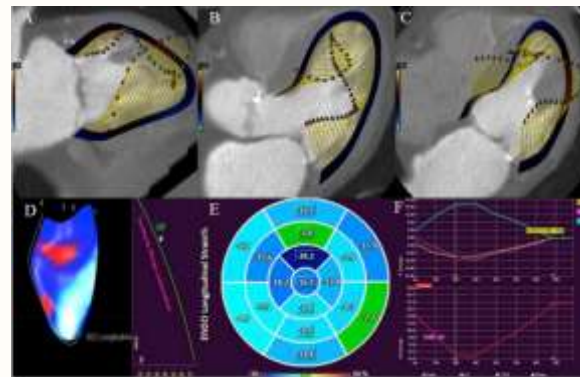


Extra-Cellular Volume

## Bio-markers (Baseline and follow-up)



Left Atrial Strain



Left Ventricular Global Longitudinal Strain

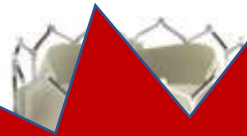
# Transcatheter AVR Trials in Moderate Aortic Stenosis

---

**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**

# Prediction #1

---

**TAVR will be the treatment of choice for all patients with Severe Asymptomatic severe AS and Moderate Aortic Stenosis**

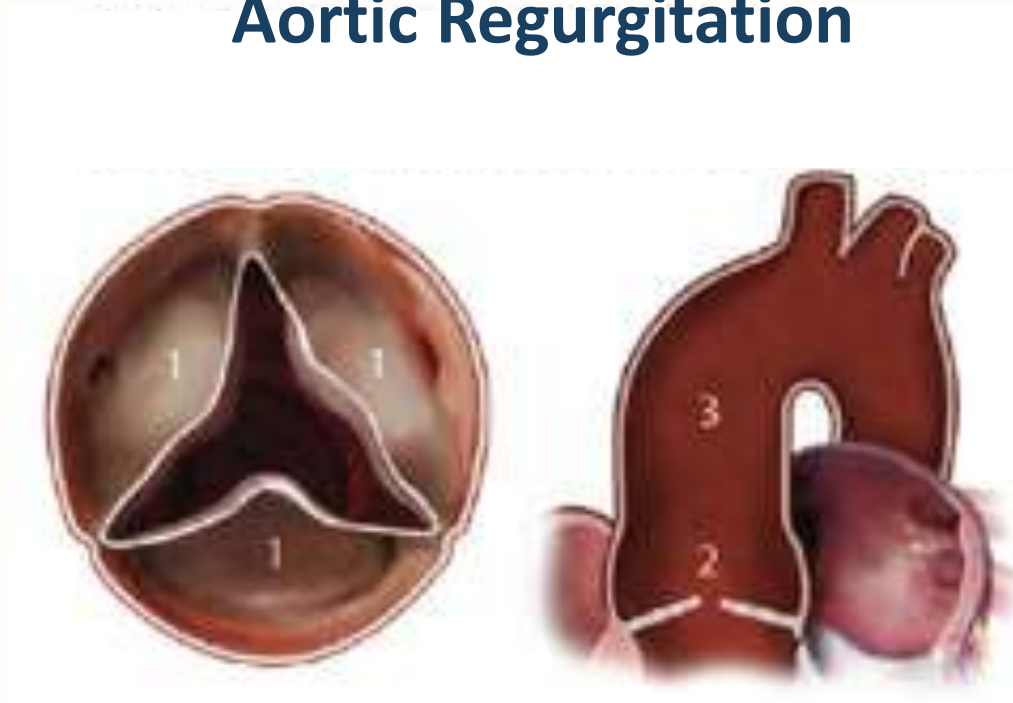




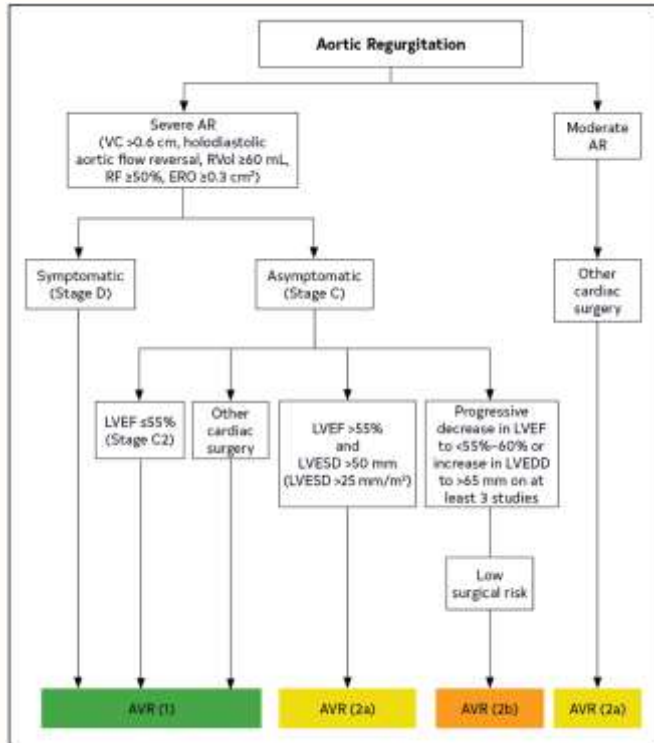
# TAVR NEXT STEPS I Aortic Regurgitation

---

## Aortic Regurgitation



# Guidelines for AVR Have Not Changed In Decades



Wait for symptoms...  
wait for LV dysfunction (EF ≤ 50%)... or wait for severe LV remodeling...

| Indications for surgery   | Class <sup>a</sup> | Level <sup>b</sup> |
|---|--------------------|--------------------|
| <b>A. Severe aortic regurgitation</b>   |                    |                    |
| Surgery is indicated in symptomatic patients. <sup>57,58,66,67</sup>  | I                  | B                  |
| Surgery is indicated in asymptomatic patients with resting LVEF ≤ 50%. <sup>57,58</sup>   | I                  | B                  |
| Surgery is indicated in patients undergoing CABG or surgery of the ascending aorta or of another valve.   | I                  | C                  |
| Heart Team discussion is recommended in selected patients <sup>c</sup> in whom aortic valve repair may be a feasible alternative to valve replacement.  | I                  | C                  |
| Surgery should be considered in asymptomatic patients with resting ejection fraction > 50% with severe LV dilatation: LVESD > 70 mm or LVESD > 50 mm (or LVESD > 25 mm/m <sup>2</sup> BSA in patients with small body size). <sup>58,66</sup> | IIa                | B                  |

# The Case for Redefining “Moderate” AR

---

- *Growing data suggesting VHD guidelines also may recommend 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 Vancraeynest, MD, PhD, Anne-Catherine Pouleur, MD, PhD, Philippe Noirhomme, MD, Agnès Pasquet, MD, PhD, Laurent de Kerchove, MD, Gébrine El Khoury, MD, Jean-Louis Vanoverschelde, MD, PhD

## ORIGINAL INVESTIGATIONS

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



Li-Tan Yang, MD,<sup>†</sup> Hector I. Michelena, MD,<sup>‡</sup> Christopher G. Scott, MS,<sup>§</sup> Maurice Enriquez-Sarano, MD,<sup>§</sup> Sorin V. Pislaru, MD,<sup>‡</sup> Hartzell V. Schaff, MD,<sup>†</sup> Patricia A. Pellikka, MD<sup>§</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\*



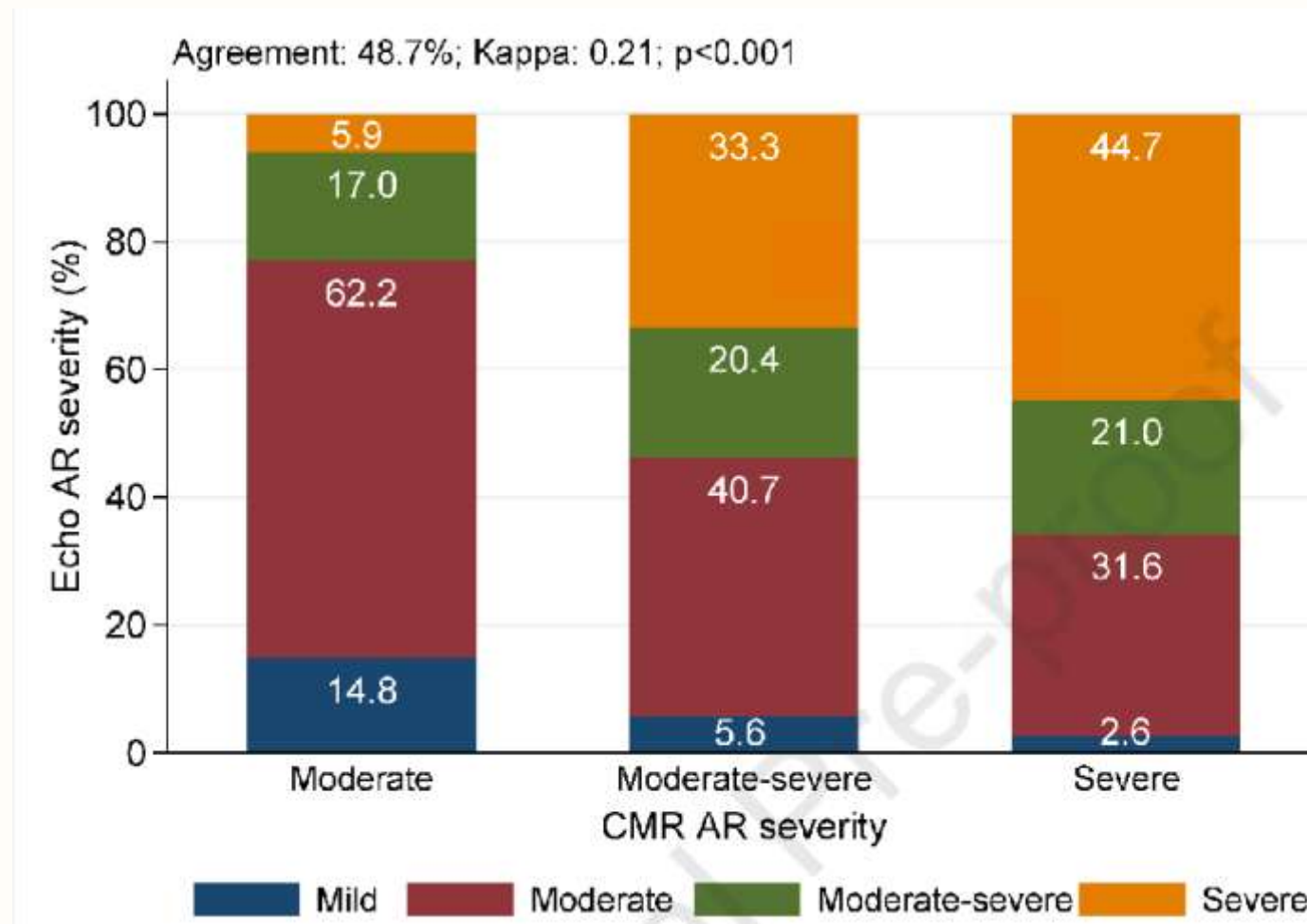
Sheldon E. Litwin, MD

# The Case for Redefining “Moderate” AR

---

- 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 → Beware guidelines are outdated!
  - Despite patients having a long asymptomatic clinical course, the LV is feeling it!
  - Don't stop at moderate AR, use CMR to confirm
- .While the current goal is to address the immediate need in HR/inoperable patients, true success will be measured by transformation of the diagnosis, selection and treatment of AR patients.

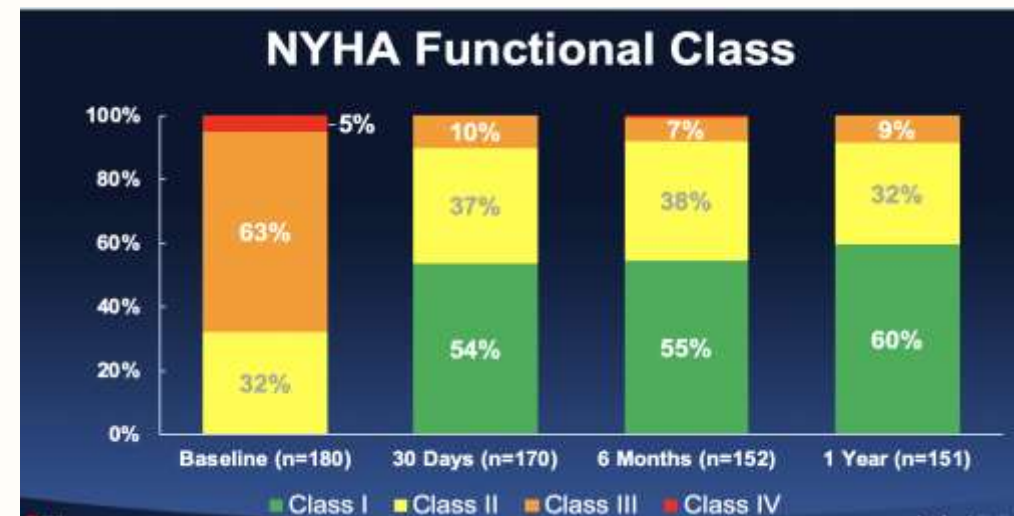
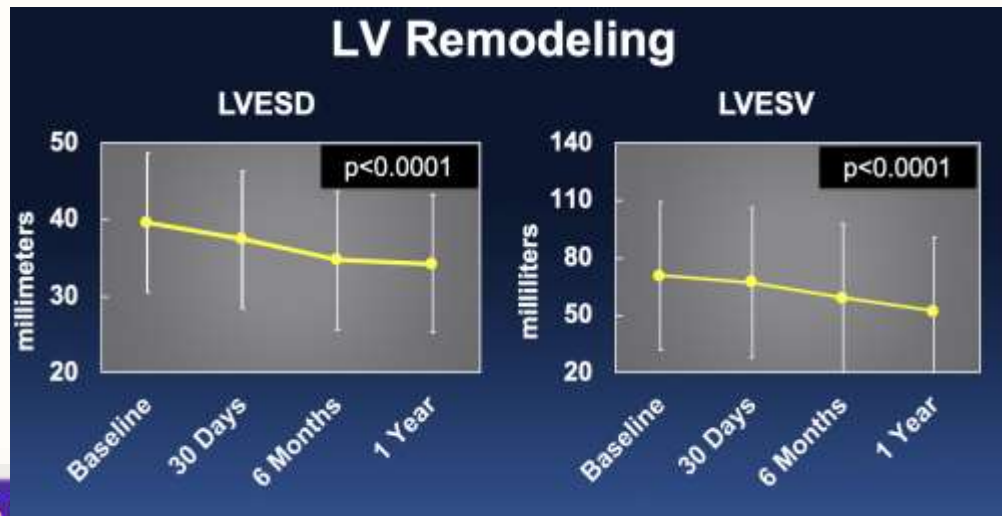
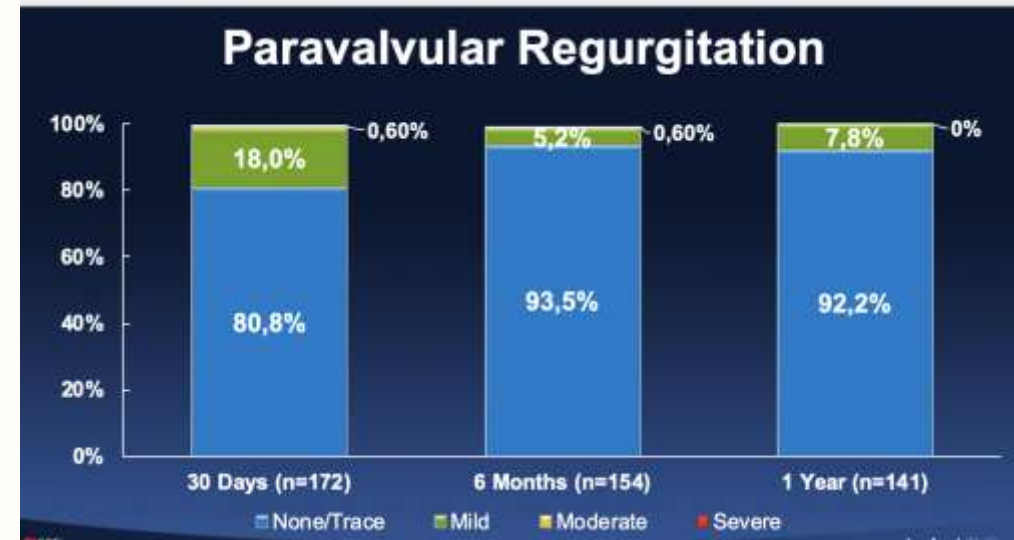
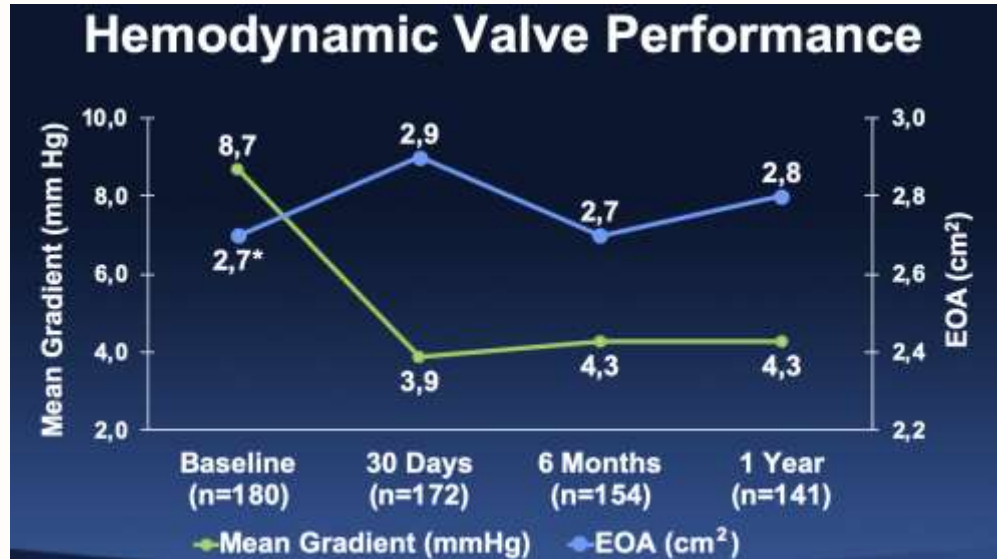
# Poor Agreement between Echo vs. CMR AR Severity



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



# Align AR Trial





# Prediction #2

---

**Aortic Regurgitation Grading will be redefined; Patients will be treated earlier and more effectively via transcatheter approach with dedicated devices**



# TAVR NEXT STEPS I Bicuspid Aortic Valve Disease

---

## Bicuspid Aortic Stenosis

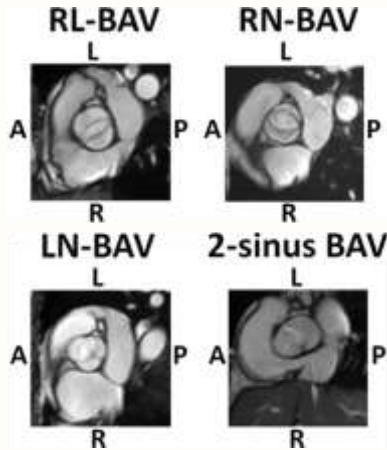


# BICUSPID AORTIC STENOSIS

Windecker et al. Eur Heart J 2022 ;43(29):2729-2750; Elbadawi et al. JACC Cardiovasc Interv 2019;12(18):1811-1822; Rodríguez-Palomares. et al. J Am Coll Cardiol 2023 ;82(5):448-464.

## Anatomical Considerations

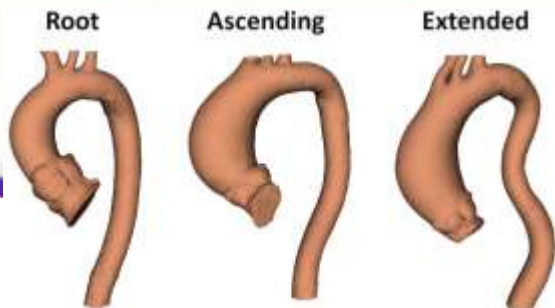
Aortic valve fusion morphotypes



Severity and distribution of leaflet calcification

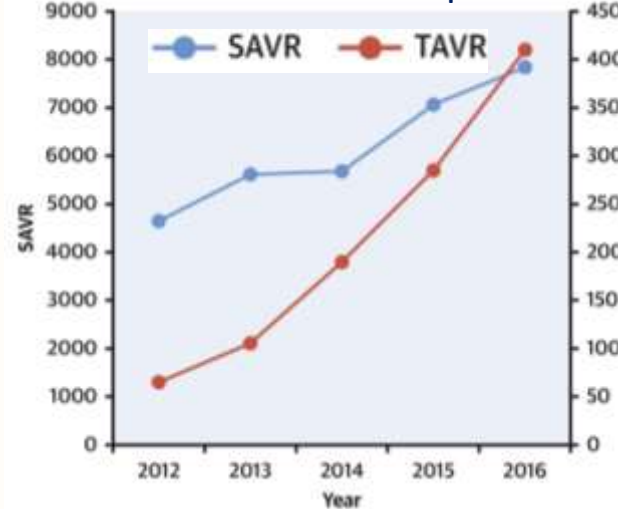


Dilatation

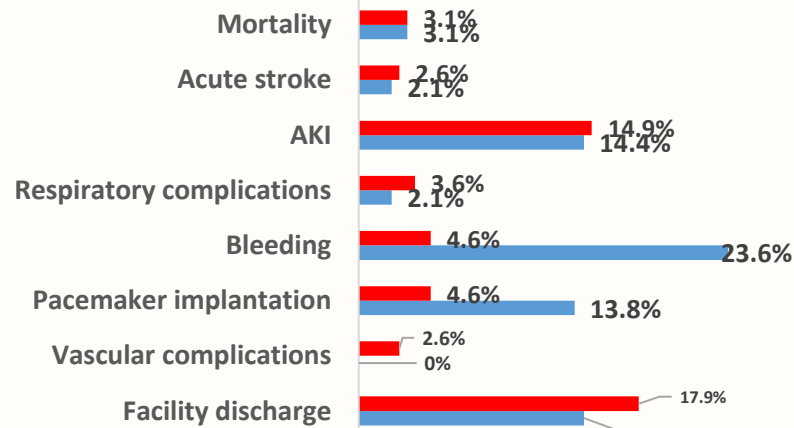


## Treatment Choice

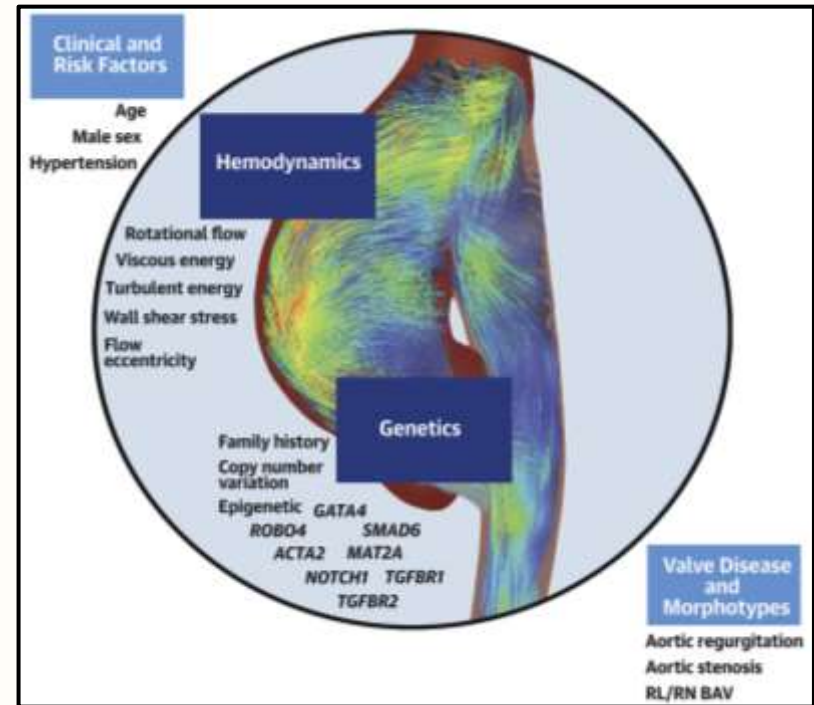
Trend of AVR in Bicuspid AS



## In-hospital outcomes



## Future Progression of Aortopathy



## Bicuspid Aortic Stenosis

- Younger patients
- More complex, non-circular anatomy
- Prosthetic hemodynamic outcomes
- Risk of stroke, annulus rupture

**No randomized clinical trial compared TAVI and SAVR to date**

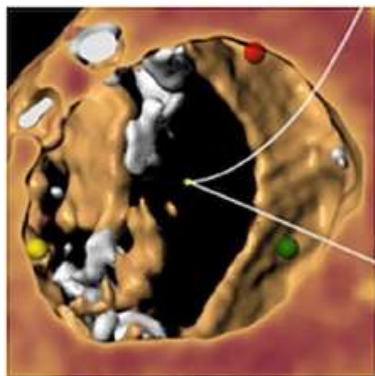


# Anatomical Considerations in Patients with Bicuspid Valve

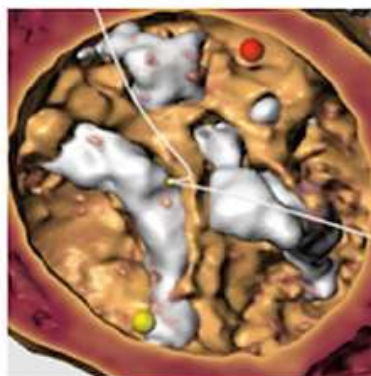
Suitable for TAVR

NOT Suitable for SAVR

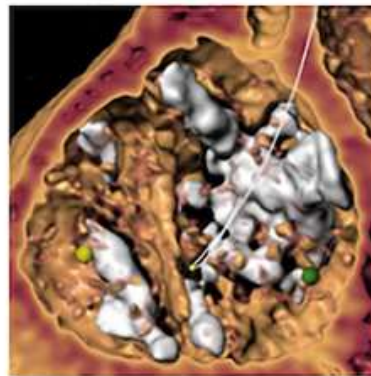
No Calcified Raphe or Excess Leaflet Calcification



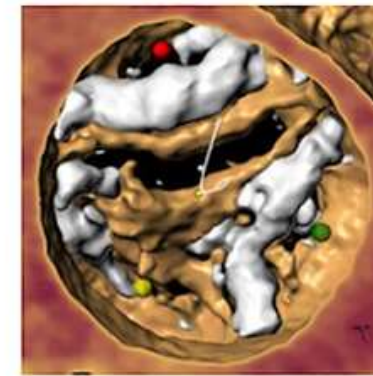
Excess Leaflet Calcification



Calcified Raphe



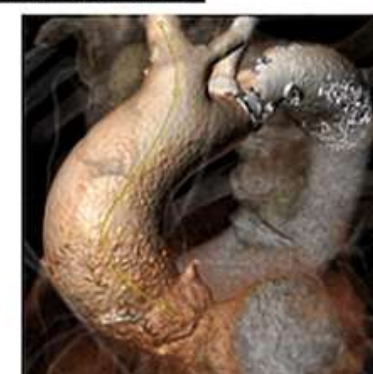
Calcified Raphe Plus Excess Leaflet Calcification & Calcified raphe



No dilation of ascending aorta



Dilated ascending aorta (>45mm, >50mm, >55mm)



# TAVR in Bicuspid Aortic Valve



## What we know

- Better results with newest generation of THV
- A CT scan is mandatory for procedure planning
- Calcified raphe + highly calcified leaflets associated with poor outcomes



## Warning

- Low but higher risk of annular rupture than TAV (BEV)
- Higher risk of  $\geq$ mild PVR than TAV or surgery



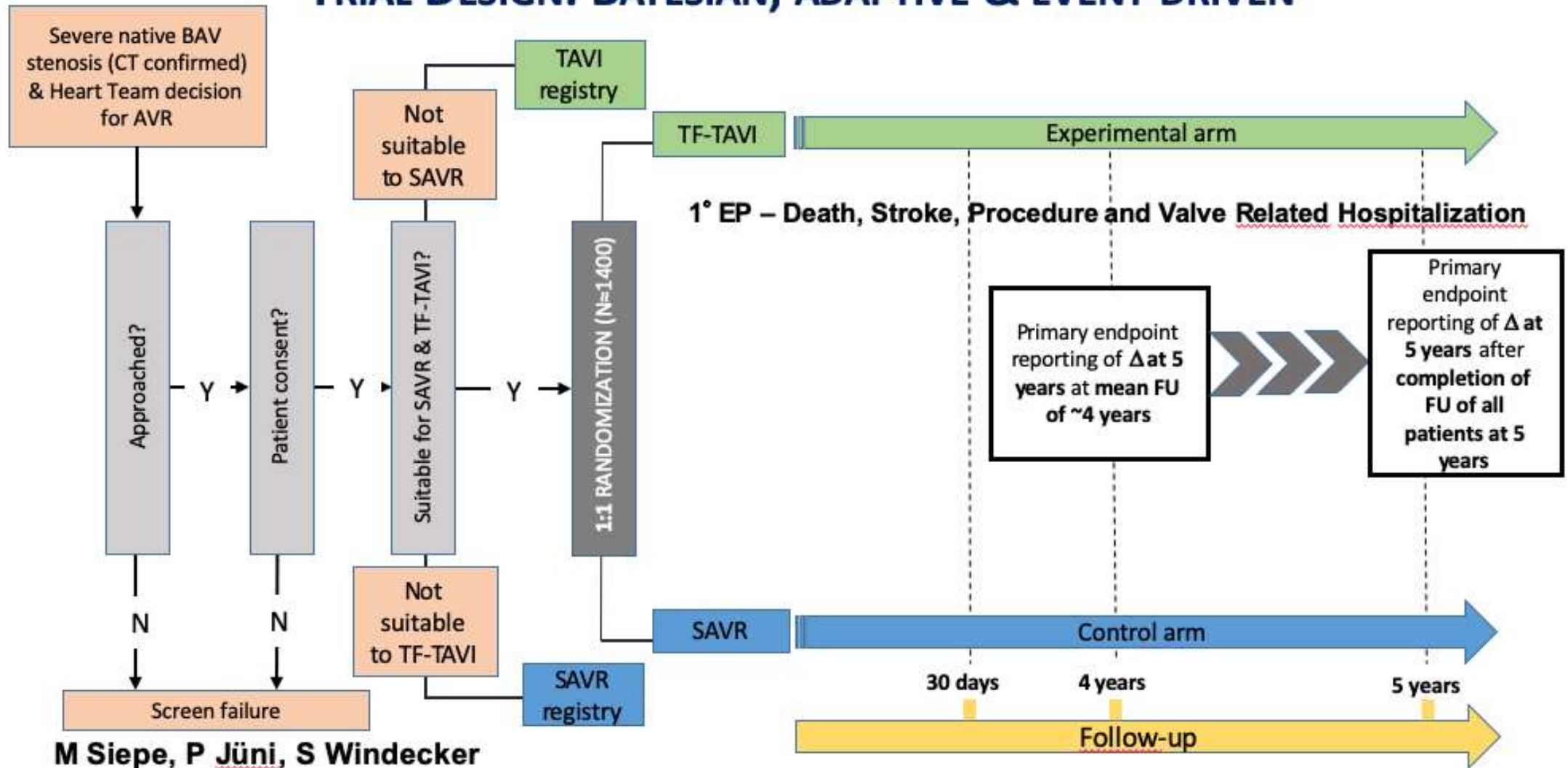
## Remaining questions

- Methods for THV selection
- Type of valve based on anatomy
- Prosthetic valve durability
- Prosthetic valve thrombosis
- Evolution of the aortopathy after TAVR

*Need for randomized trial of TAVI vs. SAVR and larger cohorts with long-term follow-up in patients with BAV after TAVR*

# NAVIGATE BICUSPID TRIAL

## TRIAL DESIGN: BAYESIAN, ADAPTIVE & EVENT-DRIVEN



M Siepe, P Jüni, S Windecker



# Prediction #3

---

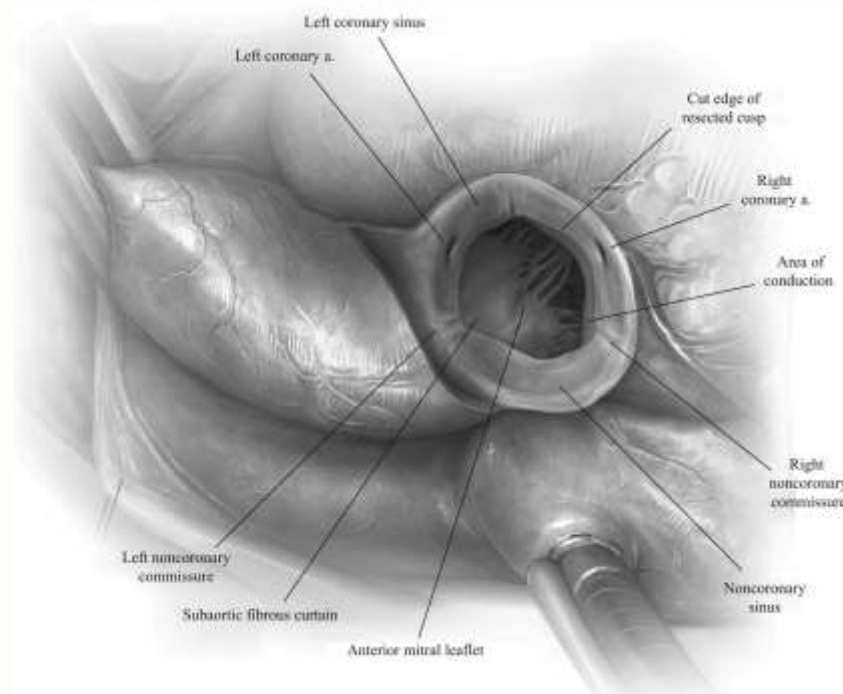
**Bicuspid aortic valve is an anatomical factor that favours SAVR. However, patients will continue to be treated with TAVR (given the excellent results so far) after considering specific risks and preferences in a joint decision making process and until results of a RCT.**



# TAVR Next Steps I Small Annulus

---

## Small Annulus



# TAVR Next Steps I Small Annulus

- Small Annuli Are Common:

SAVR prostheses  $\leq 21$  mm <sup>1</sup> = **22-44%**

- Use of small TAVR prostheses:

|   | Area $\leq 430$ mm <sup>2</sup><br>(IFU 20/23 mm BE)<br>PARTNER Trials | Perimeter-derived diam $\leq 23.4$ mm<br>(IFU 23/26 SE)<br>Corevalve/EVOLUT Trials |
|---|--|--|
| Intermediate Risk Trials <sup>2,3</sup> | <b>36%</b>   | <b>22%</b>   |
| Low Risk Trials <sup>4,5</sup>          | <b>31%</b>   | <b>21%</b>   |

- **Higher in Southern Europe and Asia** <sup>1</sup>
- **TAV in SAV = 70-80%** <sup>6,7</sup>
- **Several fold higher in women who make up ~90% of small annulus population**  
<sub>1</sub>

<sup>1</sup> Freitas-Ferraz et al, Circ 2017;139:2685

<sup>2</sup> Reardon et al, NEJM 2017;376:1321

<sup>3</sup> Kodali et al, European Heart J 2016;37:2252

<sup>4</sup> Popma et al, NEJM 2019;380:1706

<sup>5</sup> Mack et al, NEJM 2019;380:1695

<sup>6</sup> Dvir et al, JAMA 2014;312:162

<sup>7</sup> Webb et al, JACC 2017;69:2253



# SMART Trial

Severe native aortic valve stenosis with a small annulus  
( $\leq 430 \text{ mm}^2$  by MDCT)

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

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

Edwards SAPIEN 3/  
SAPIEN 3 Ultra

Primary endpoints at 12 mos:

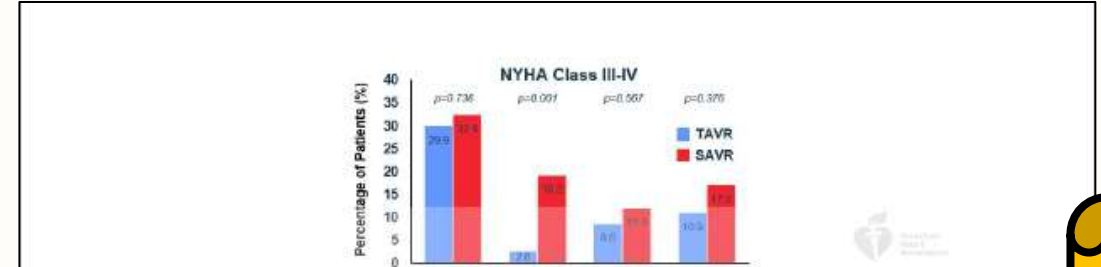
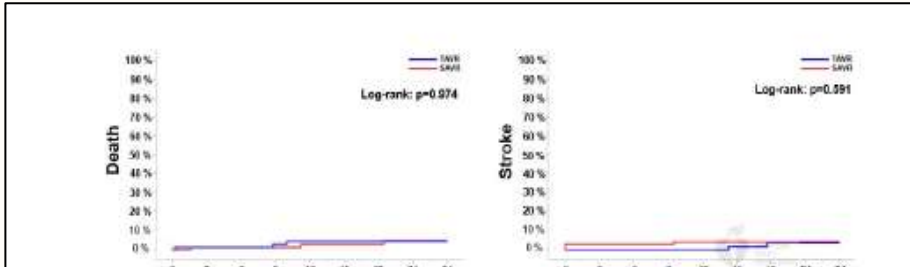
1. Death, disabling stroke, re-hosp HF
2. Bioprosthetic valve dysfunction

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

**FULLY ENROLLED!**  
Submitted for LBCT at  
ACC 2024

|   |   |
|---|---|
| <b>Study Organization</b>                 | Chair/PI: Howard C. Herrmann, MD    Co-PIs: Roxana Mehran, MD and Didier Tchetché MD  |
| <b>Major inclusion/exclusion criteria</b> | <ul style="list-style-type: none"> <li>• Small annulus with all risk groups (low to high)</li> <li>• An "all-comers" trial (including bicuspid valves)</li> <li>• Patient's anatomy must be suitable for TF TAVR treatment with both devices</li> </ul> |
| <b>External Support (Medtronic)</b>       | Echocardiographic Core Laboratory, Clinical Events Committee (CEC), Data Safety Monitoring Board (DSMB), Subject Confirmation of Qualification/Case Planning Committee (screening phase)  |

# TAVR Next Steps | Small Annulus | VIVA Trial



**«...findings suggest that the 2 therapies (SAVR/TAVR) represent a valid alternative for treating patients with AS and SAA. Treatment selection should likely be individualized...»**



# Prediction #4

---

**Pending results of the SMART trial and based on the results of the VIVA trial, TAVR represents a safe and effective alternative to surgery after careful consideration of patients age, preferences and anatomical conditions**





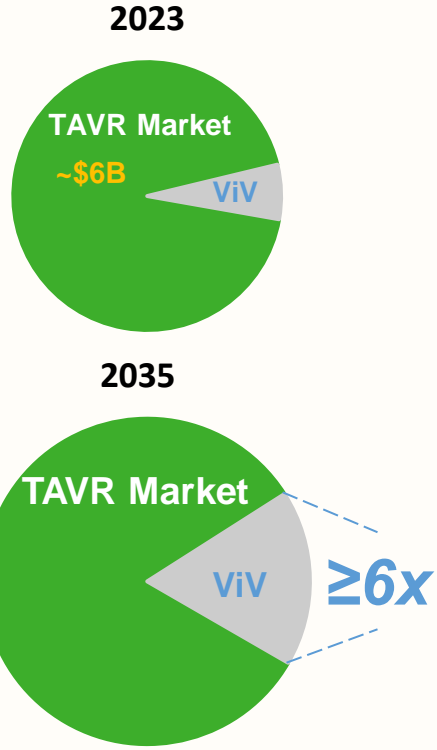
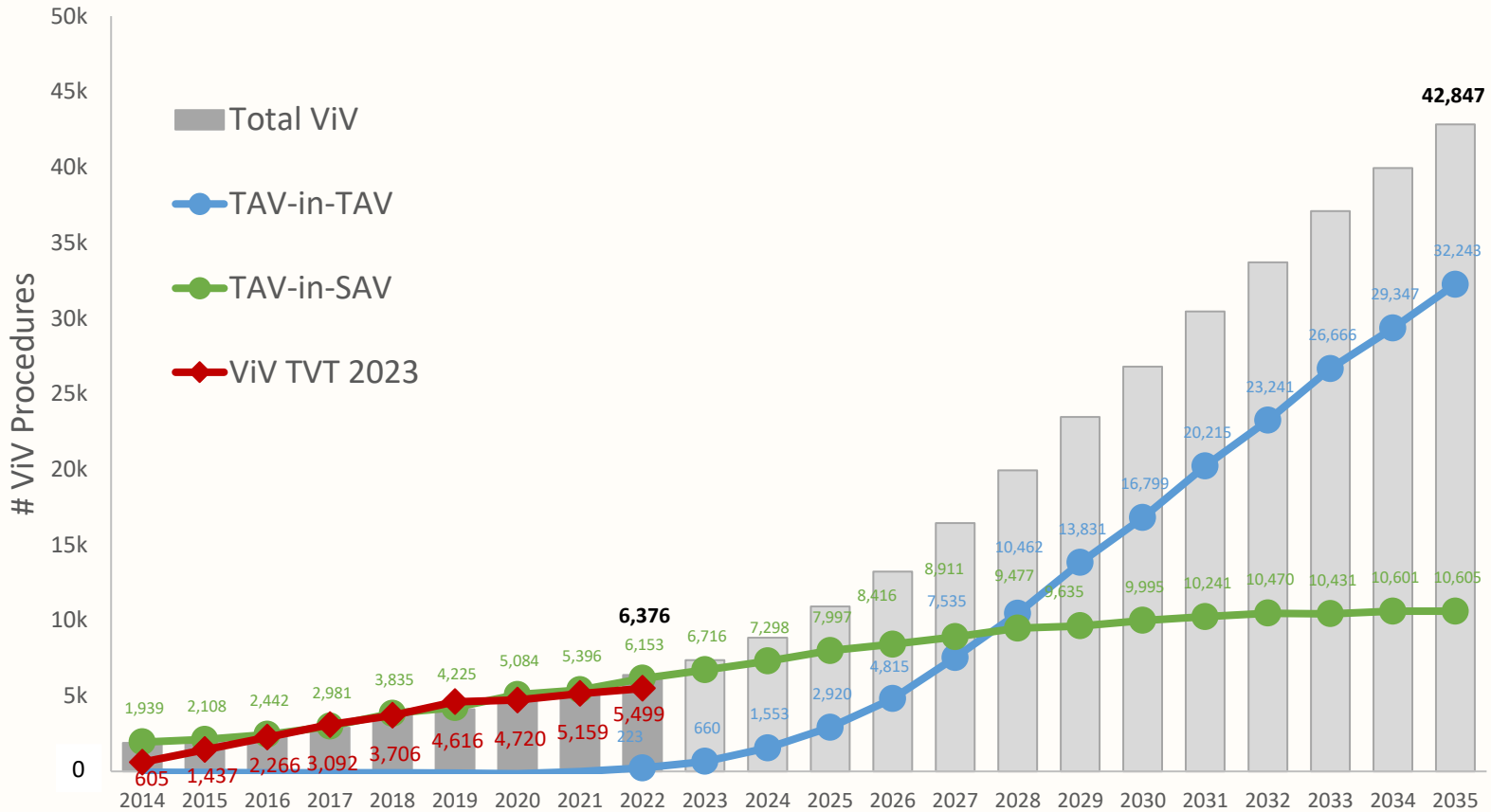
# TAVR NEXT STEPS | Lifetime Management

---

## Valve in Valve



# US ViV Market Forecast until 2035



# Longest Follow-up of Landmark Trials of TAVR versus SAVR



10 years

5 years

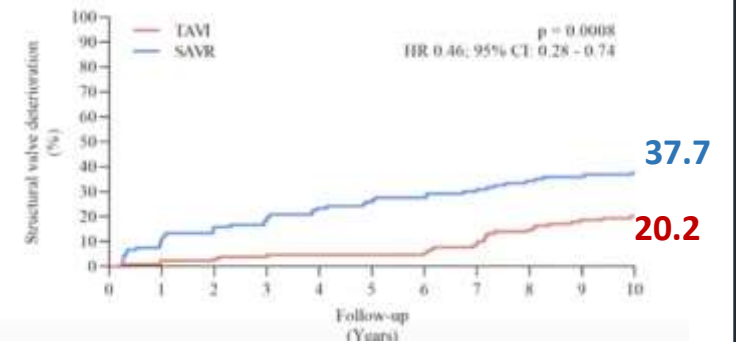
4 years

1 year

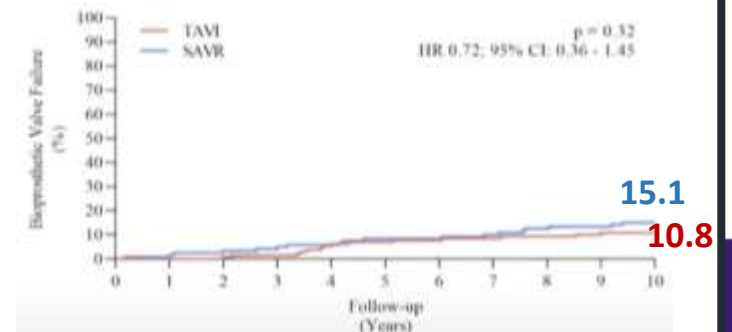
- **Notion** *ESC Congress 2023*
- **PARTNER 1A**
- **Corevalve High risk**
- **PARTNER 2A**
- **SURTAVI**
- **PARTNER 3**
- **Evolut Low-Risk**
- **UK-TAVI (all THVs)**

Notion Trial – 10y

**SVD -  $p < 0.001$**



**BVF -  $p = \text{NS}$**



## Patient Selection

### Type of failed valve

- Porcine vs Bovine
- Stented – Stentless – Sutureless
- Intra-annular vs Supra-annular

### Failure mechanism (VARC 3)

- SVD – NSVD (PPM)
- Thrombosis
- Endocarditis

Figure 1

### THV dimensions

- ViV Aortic mobile App
- Stent ID vs True ID
- CT scan measures

Supplementary Figure 1-5

### Risk of coronary obstruction

- VIVID classification
- VTC at CT scan
- VTSTJ at CT scan

Figure 4; Supplementary Figure 6-9

## Pre-procedural planning

## Procedure

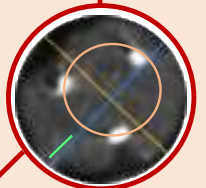
### THV selection

- Intra-annular vs Supra-annular
- CE Mark (Edwards and Corevalve)
- Coronary Re-access
- Peripheral access

### Procedural techniques

- BASILICA
- Coronary protection
- BVF
- CEPD

# ViV Decision Making



# Lifetime Management of Aortic Disease (Concept #1)



**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 of a patient**

30 7-8%  
 365 10-11%

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

30 2-3%  
 365 5-6%

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

with Ao. Root replacement)

30 12-13%  
 365 21-29%

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

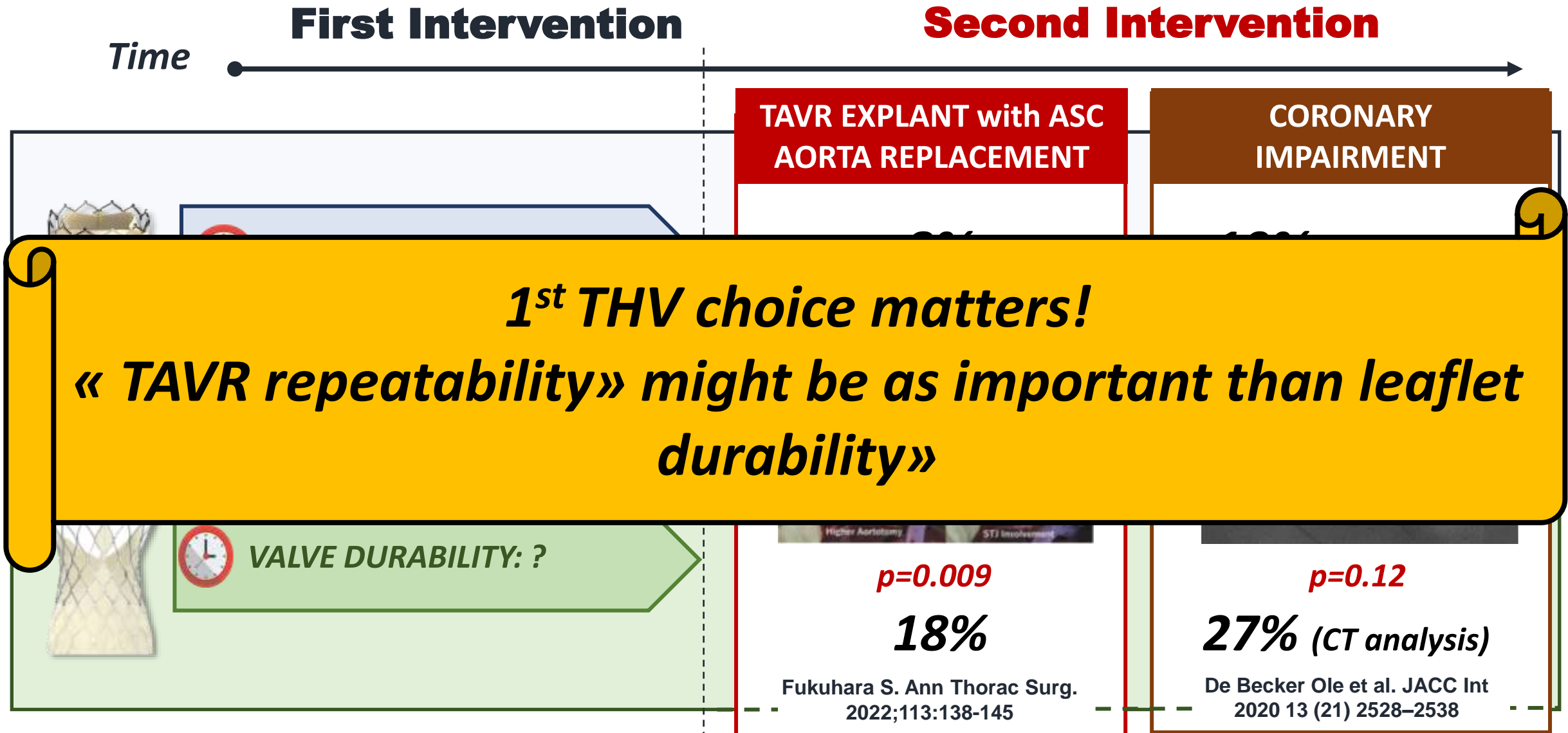
30 6%  
 365 20%

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





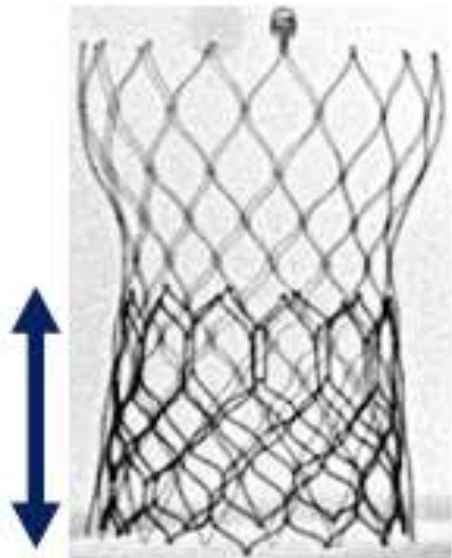
# Lifetime Management of Aortic Disease (Concept #2)



# What's important in RE-do TAVR?

## NEOSKIRT

S3 Outflow at Node 5



23.0 mm

## LEAFLET OVERHANG

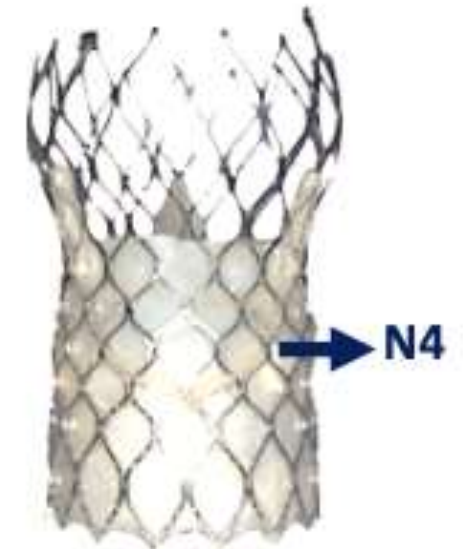
S3 Outflow at Node 5



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

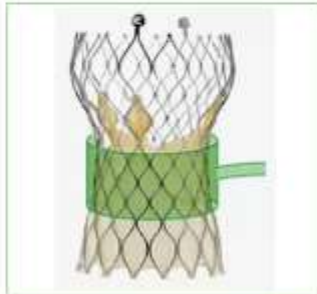
1

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

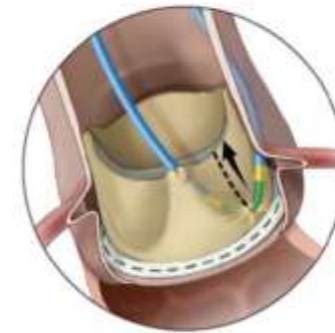


1. Hayashida et al, Circulation: Cardiovascular Interventions. 2013;6:284-291

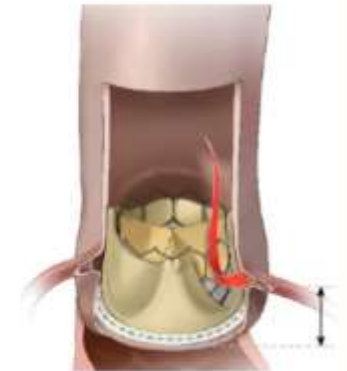
#### Leaflet wire transversal and snaring



#### Leaflet slicing



#### Preserved coronary flow



#### 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



#### 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

# Prediction #5

---

Valve in Valve and leaflet modification procedures will increase!

***Which is the first procedure?*** (NOT all THVs and SHVs are created equal (coronary access, fracturability, neoskirt, index expansion, leaflet overhang etc)

***Second procedure*** most likely THV (consider THV type, size & positioning)

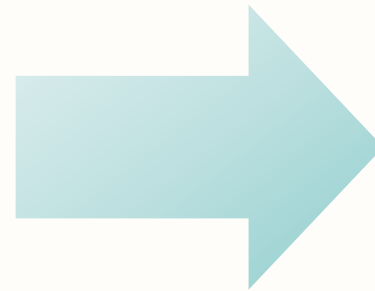




# TAVR Projection 2030

---

*Longer-term management of TAVR patients will improve with the ability to monitor patients from home with minimal disruption to their daily lives. This technology, along with improved home care pathways, will allow a greater number of patients to discharge to home.*





***THANK YOU AND  
BE SAFE!***

