TAVR 2024
What do we know, what is missing and what do we need to know?

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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, Valve Medical, Anteris

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

GENERAL REMARKS

RUMSFELDIAN THINKING

”There are “***known knowns”***; things we know we know. We also know there are “***known unknowns”***; that is to say we know there are some things we do not know. But there are also “***unknown unknowns”***—the ones we don't know we don't know… “

RUMSFELDIAN THINKING → TAVR 2024

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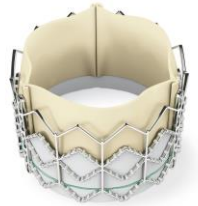
TODAY, TAVR IS BECOMING MAINSTREAM THERAPY, SAVING LIFES AND IMPROVING NON-SURGICAL QOL

- More than 1 Mio cases done globally to date
- $4.5B market (2023) will grow to $17B in 2030
- TAVR is expanding into lower risk and younger patients
- Advance THV versions, better tissue treatment to increase durability
- Drive the creation of “Heart Team” concept forward.
- Surgeons are migrating to experience interventional procedures.

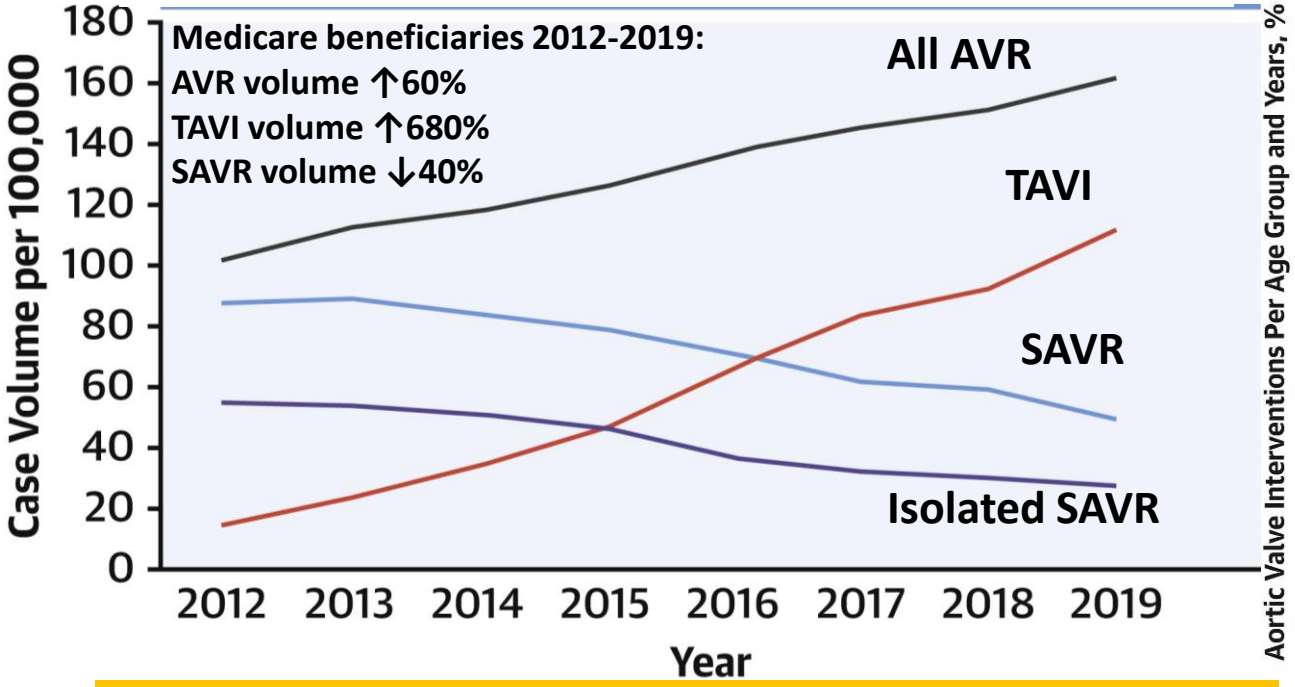
TAVR gave birth to Structural Heart Interventions



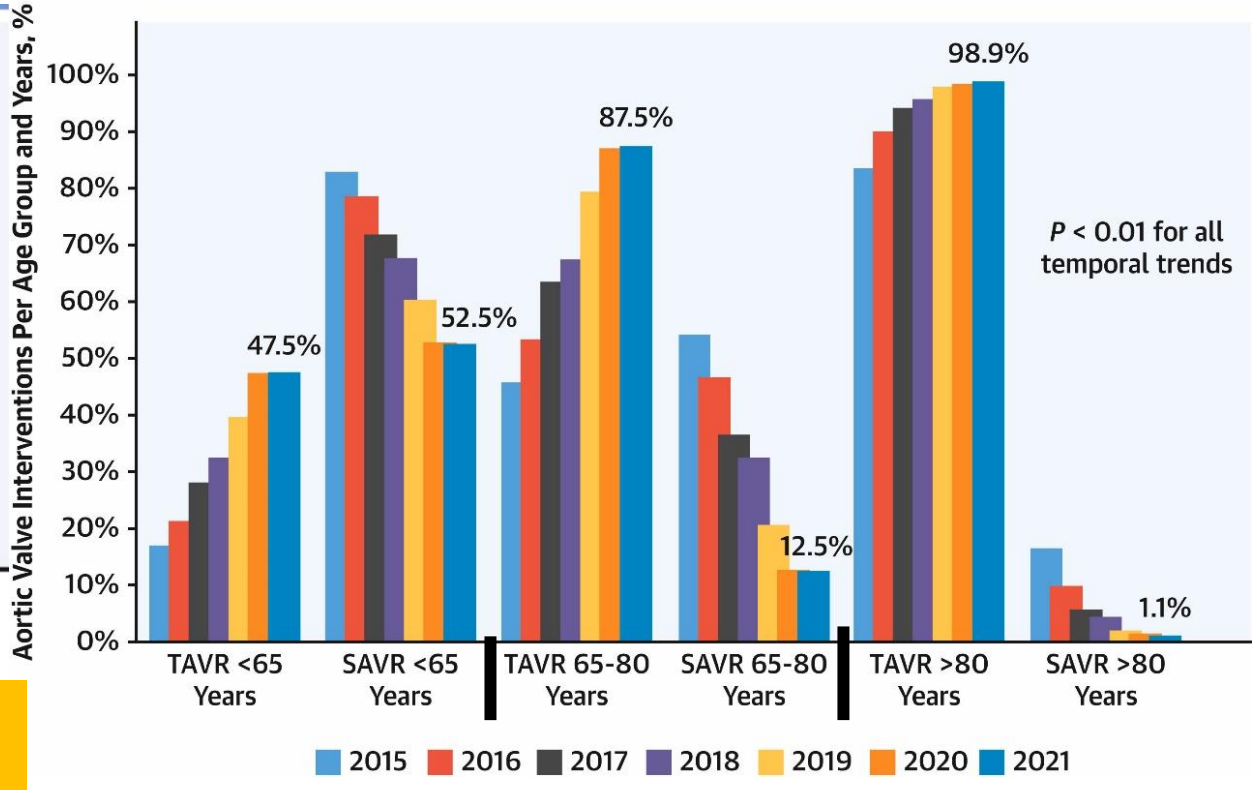
TRENDS OF AVR IN THE US

- ✓ **402,671 AVR hospitalizations** (181,359 TAVI; 221,312 SAVR) from Medicare inpatient claims data.
- ✓ The **median age decreased** from 84 to 81 years for TAVR and from 76 to 72 years for SAVR.

- ✓ In 142,953 AVR patients from the Vizient Clinical Data Base, **temporal trends in AVR** were compared **according to the 3 guideline-recommended age groups that influence strategy: <65 years, 65 to 80 years, and >80 years.**



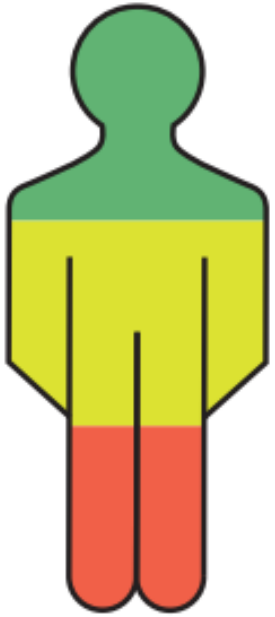
Expected Growth until 2030: 300% !!

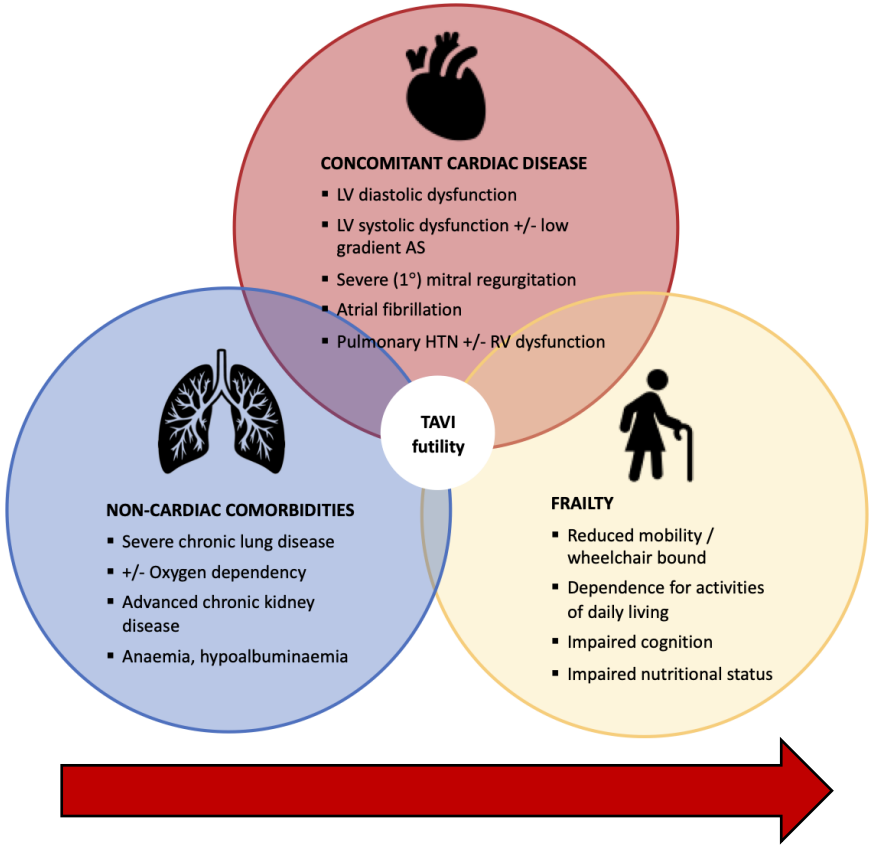


Mori M et al. J Am Coll Cardiol 2021;78:2161-2172; Sharma et al. J Am Coll Cardiol 2022; 80(21):2054-2056.

IMPROVED PATIENT SELECTION AND DISEASE AWARENESS

Mean Treatment Difference

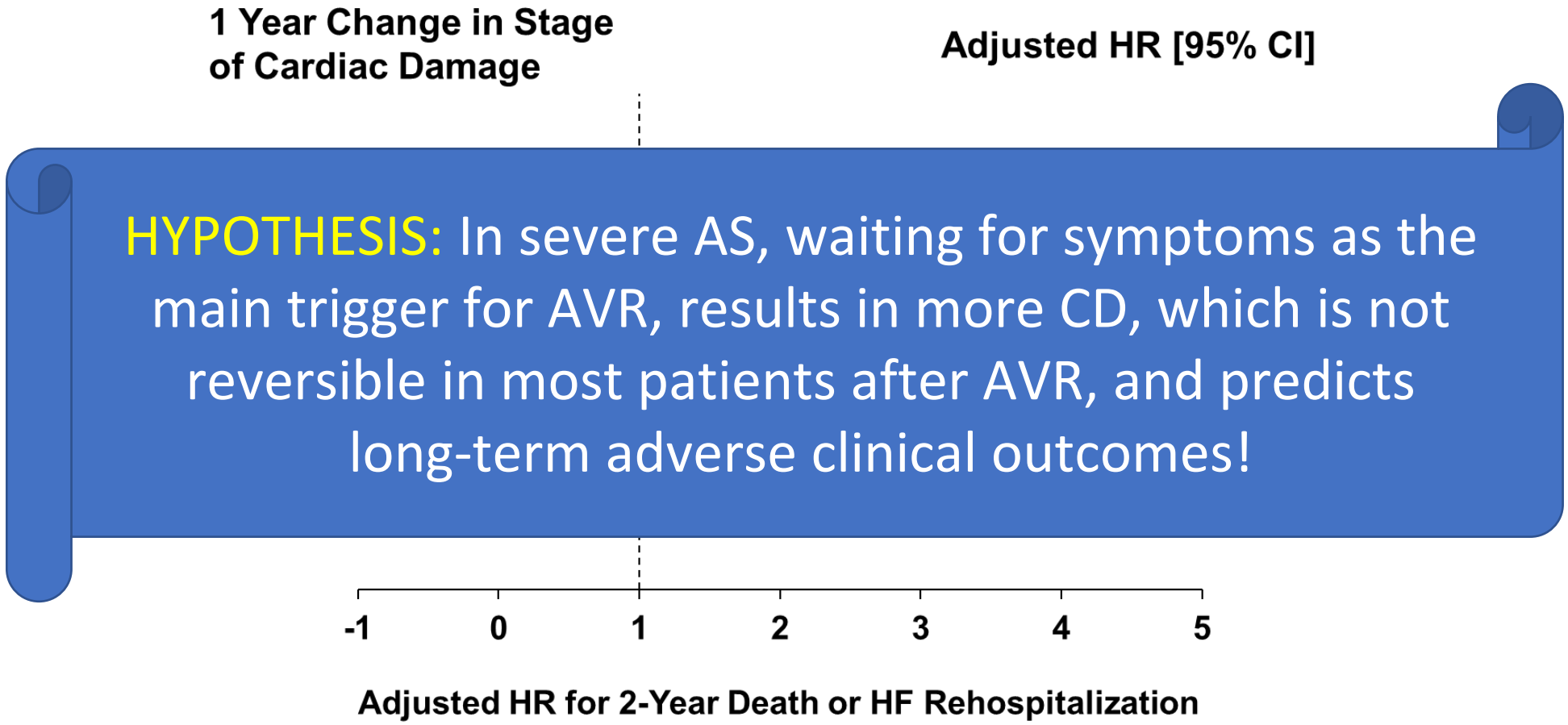




Individual patient outcomes

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

IMPACT OF 1-YR CHANGES IN CARDIAC DAMAGE ON CLINICAL COURSE (2-YR DEATH OR HF REHOSP)



Généreux et al. JACC 2022

TAVR VS SURGERY

WHAT HAVE WE LEARNED?

Similar Late Clinical Outcomes

- All cause Mortality
- Disabling Stroke

Higher Rates with SAVR

- New Atrial Fibrillation
- Bleeding complications
- Renal Injury

Higher Rates with TAVR

- Permanent Pacemaker
- Paravalvular Regurgitation

Competing Risks

Shared Decision Making

Heart Team

RUMSFELDIAN THINKING → TAVR 2024

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AORTIC VALVE THERAPIES IN 2024

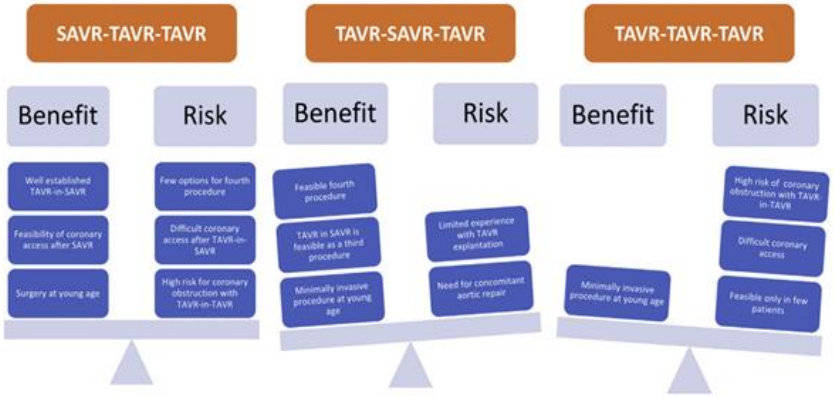
TAVR: EVIDENCE GAPS

- ***Bioprosthetic valve durability (BVF)***
- ***Importance of valve leaflet thickening and valve thrombosis (HALT/RELM)***
- ***Use of cerebral protection devices***
- ***TAV-in-TAV procedures and safety of failed TAVR surgical explants***
- ***Coronary access (esp. younger patients)***
- ***Echo-derived gradients – concordance with clinical events and invasive hemodynamics***
- ***PPM and small annulus patients***
- ***Optimal anti-thrombotic pharmacology***
- ***Bicuspid aortic valve disea***se
- ***Asymptomatic severe AS and 'at risk' moderate AS cohorts (e.g. low EF)***
- ***Aortic regurgitation (predominant lesion)***
- ***Life journey of AS in younger patients (multiple sequential procedures)***
- Post-TAVR conduction disturbances (new pacemakers and new LBBB)
- Concomitant CV diseases – multi-valve, CAD, AF, others

TAVR – 2023/4 YEARS IN REVIEW

CENTRAL THEMES

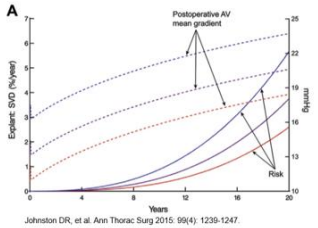
Lifetime Management



Yerasi, C. et al. J Am Coll Cardiol Intv. 2021;14(11):1169–80.

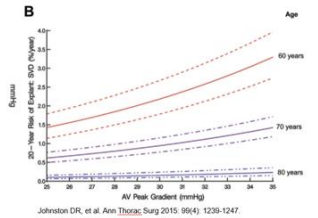
Hemodynamics/ Gradients

12,569 Patients after Surgical AVR



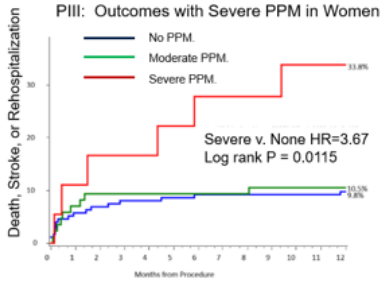
Johnston DR, et al. Ann Thorac Surg 2015; 99(4): 1239-1247.

Residual Gradients and Age



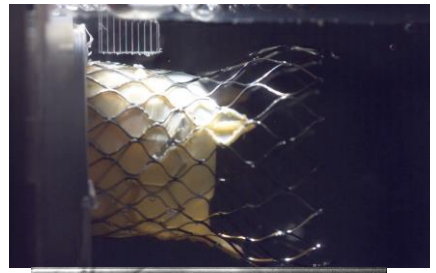
Johnston DR, et al. Ann Thorac Surg 2015; 99(4): 1239-1247.

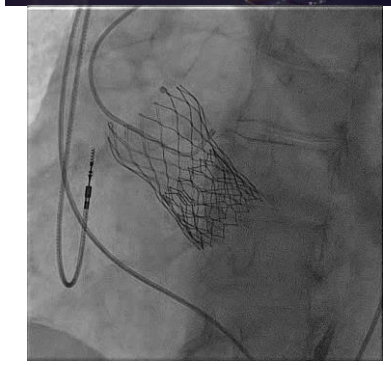
TAVR & PPM



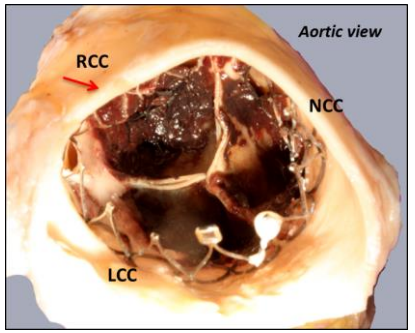
Pibarot P, et al. *Circulation*. 2020;141:1527-1537.

Redo TAVR

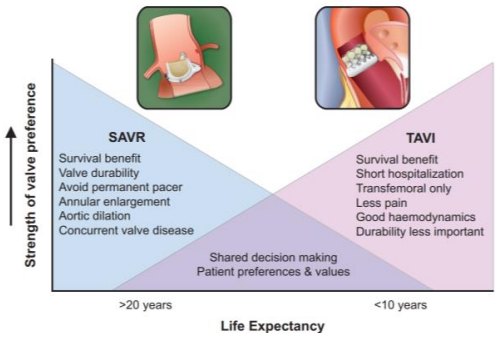


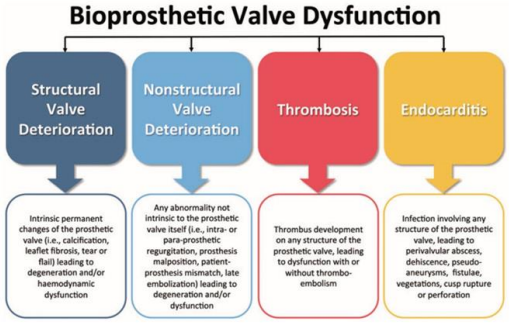


Valve Thrombosis (HALT/RELM)



Durability

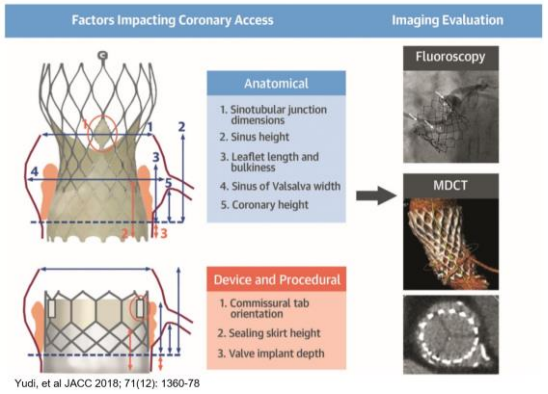




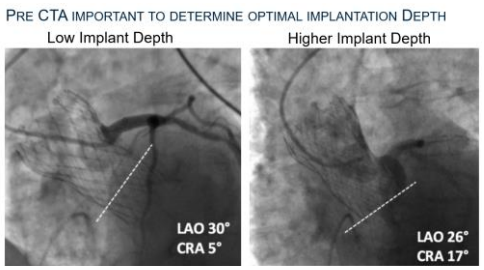
TAVR – 2023/4 YEARS IN REVIEW

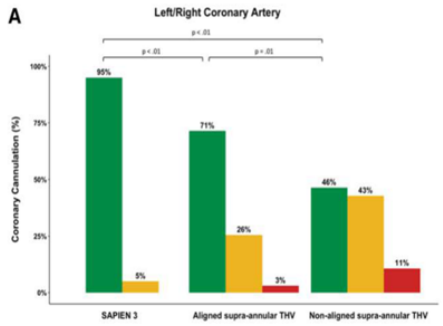
CENTRAL THEMES

Coronary Access



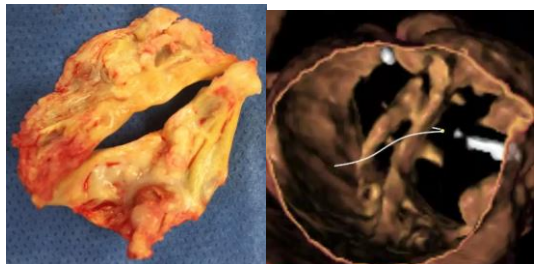
Yudi, et al JACC 2018; 71(12): 1360-78

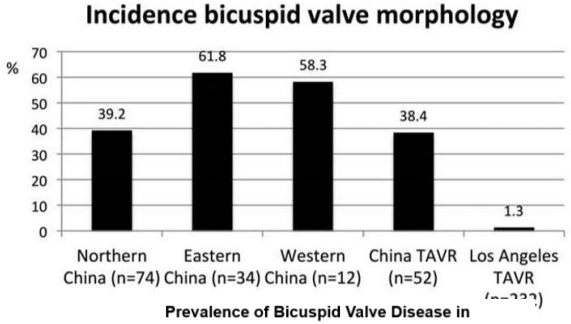


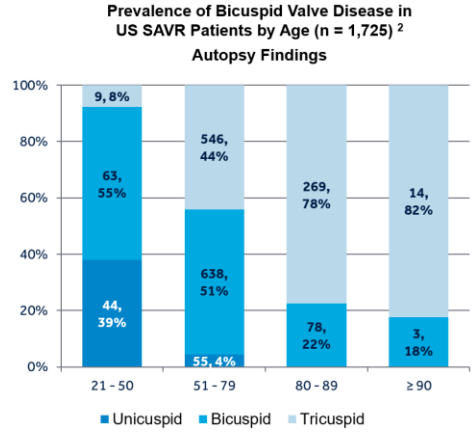


Tarantini et a l CCI. 2022;15:e011045

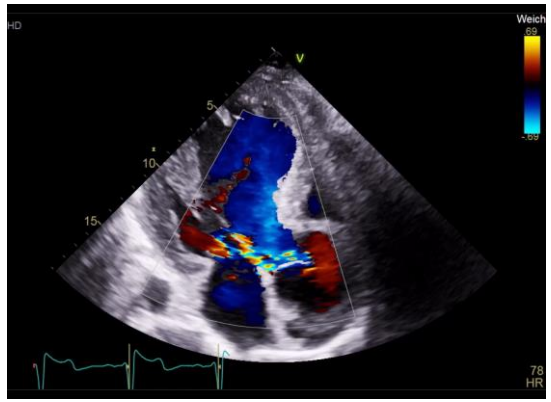
Bicuspid Valve Disease

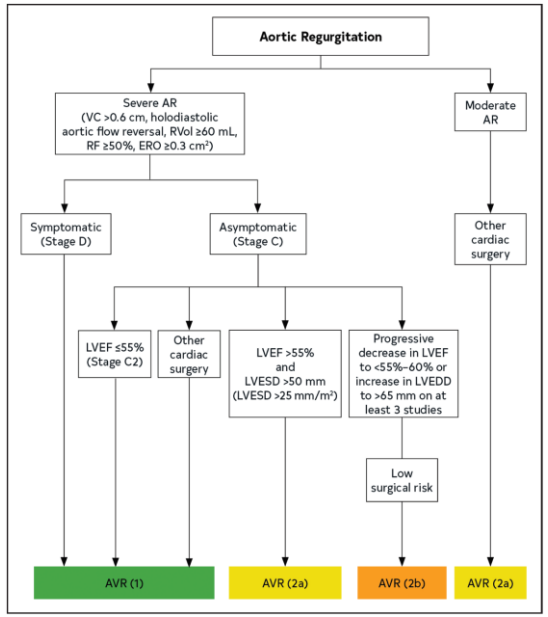




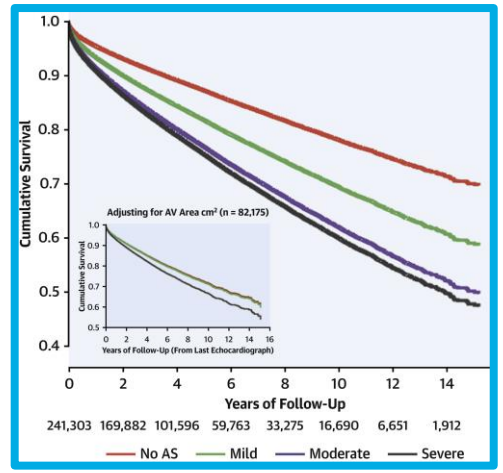


Aortic Insufficiency





Moderate Aortic Stenosis

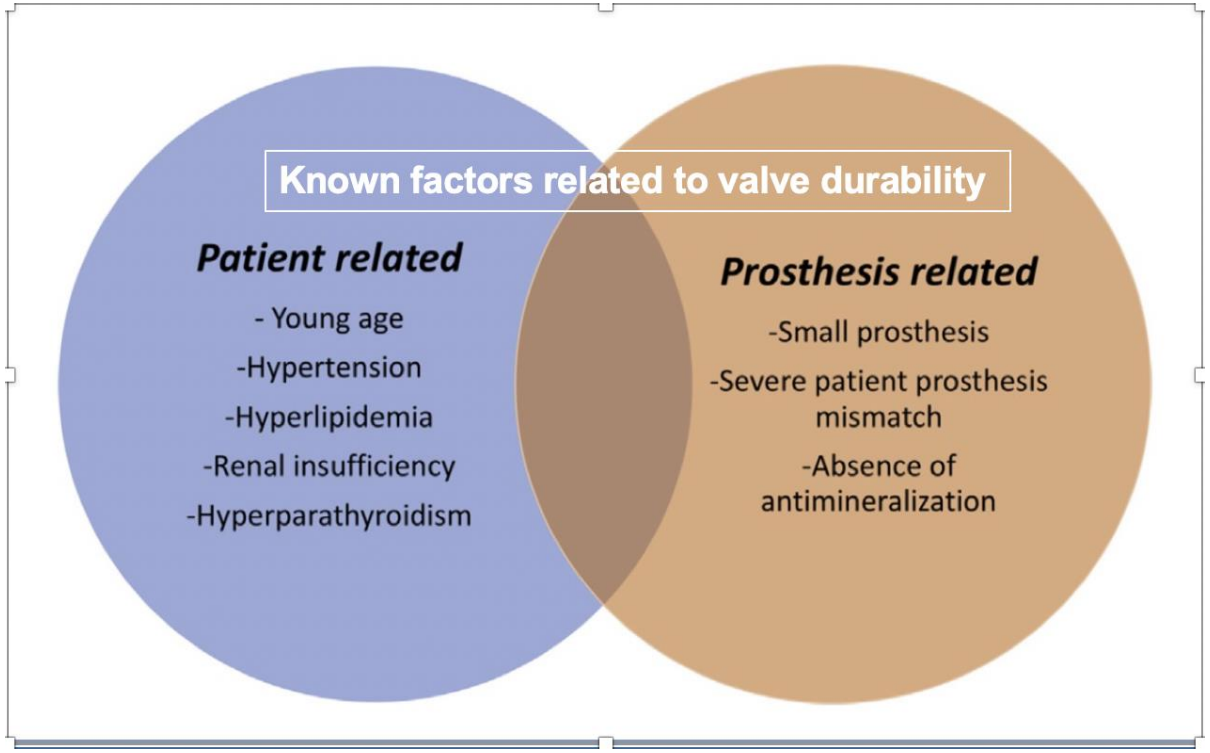


Stages/Criteria	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Cardiac Damage	LV Damage	LA or Mitral Damage	Pulmonary Vasculature or Tricuspid Damage	RV Damage
Echocardiogram		Increased LV Mass Index >115 g/m² (Male) >95 g/m² (Female)	Indexed left atrial volume >34mL/m²	Systolic Pulmonary hypertension ≥60 mmHg	Moderate-Severe right ventricular dysfunction
		E/e' >14	Moderate-Severe mitral regurgitation	Moderate-Severe tricuspid regurgitation	
		LV Ejection Fraction <50%	Atrial Fibrillation		

WHAT MEANS “DURABILITY”?
HOW IS IT DEFINED?

LIFETIME MANAGEMENT OF AORTIC DISEASE IN 2024

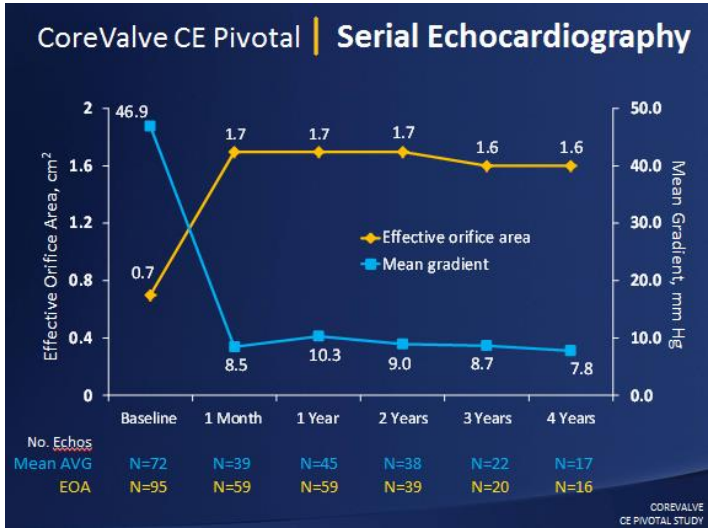
MULTI-FACTORIAL IMPACTS ON EXPECTED VALVE DURABILITY

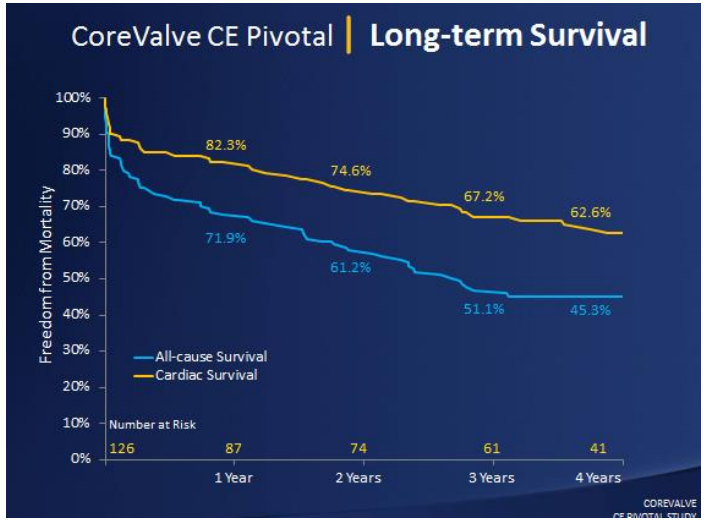


An ideal THV should replicate a healthy aortic valve going through 40 million cycles per year with unfaltering function.

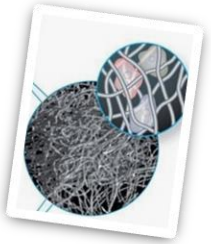
ENSURING DURABILITY

Continued Trial Follow-up

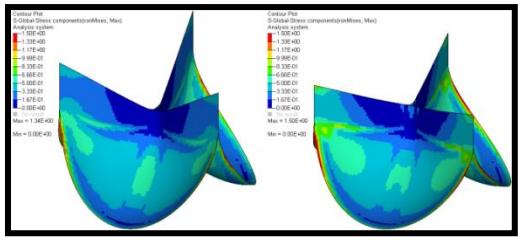




Engineering and Bench Testing



Tissue engineering

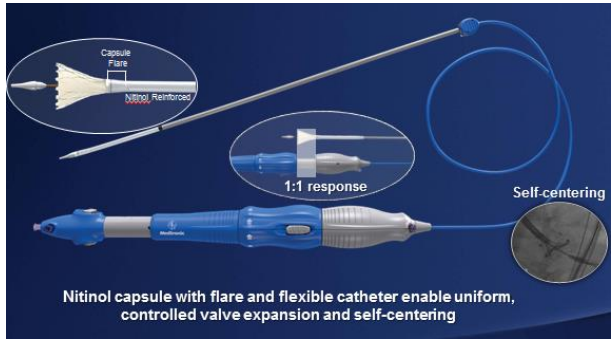


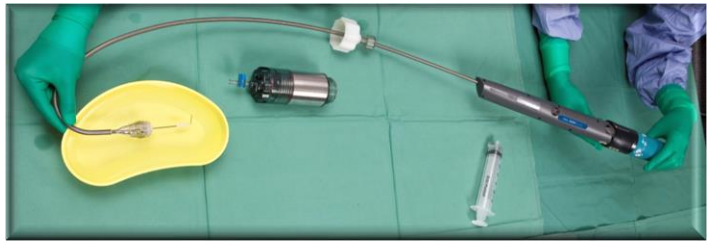
FEA Modeling

Animal Testing

ENSURING DURABILITY: IMPROVE DEPLOYMENT ACCURACY, EASE OF USE

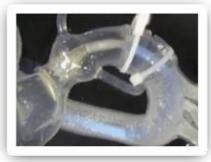
New Repositionable Systems



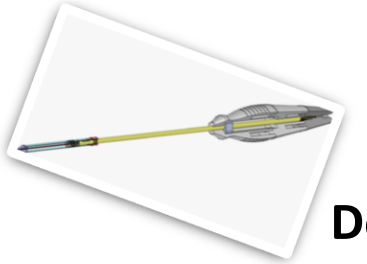


Continued Advancements

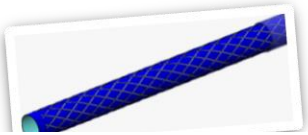
Advanced steering



Torqueability



Depth control



Low Profile Materials

Questions to be asked today:

1. Results of SAVR vs TAVR trials; long term results?

2. Are all THVs created equal? Does THV design matter?

3. Is there a “THV Class Effect” in TAVR?

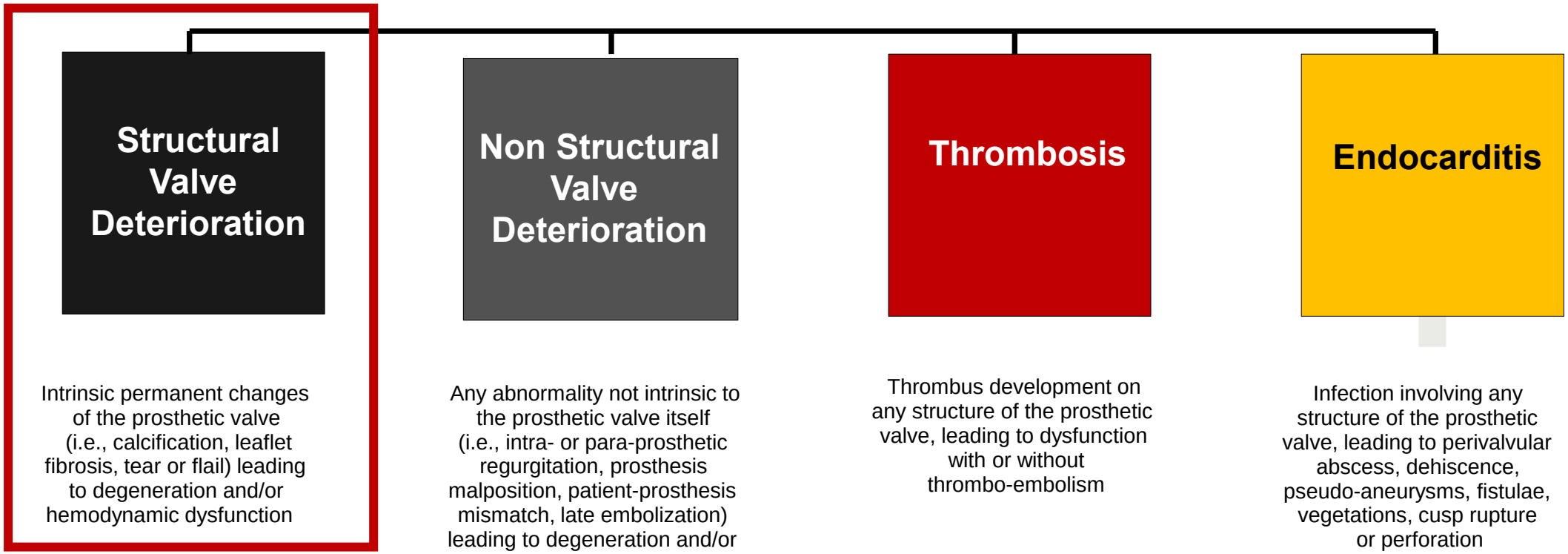
4. What is the significance of PPM? Does only severe PPM matter?

5. Should we look for and treat valve thrombosis and if YES how and does SLT triggers SVD/BVF?

EAPCI-ESC-EACTS CONSENSUS DOCUMENT

BIOPROSTHETIC VALVE DYSFUNCTION

Bioprosthetic Valve Dysfunction[1]



1. Capodanno D, et al. *Eur J Cardiothorac Surg*. 2017;52:408-417.

TAVR vs SAVR: short- and long-term results

DEDICATE Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Treatment of Aortic-Valve Stenosis

S. Blankenberg, M. Seiffert, R. Vonthein, H. Baumgartner, S. Bleiziffer, M.A. Borger, Y.-H. Choi, P. Clemmensen, J. Cremer, M. Czerny, N. Diercks, I. Eitel, S. Ensminger, D. Frank, N. Frey, A. Hagendorff, C. Hagl, C. Hamm, U. Kappert, M. Karck, W.-K. Kim, I.R. König, M. Krane, U. Landmesser, A. Linke, L.S. Maier, S. Massberg, F.-J. Neumann, H. Reichenspurner, T.K. Rudolph, C. Schmid, H. Thiele, R. Twerenbold, T. Walther, D. Westermann, E. Xhepa, A. Ziegler, and V. Falk, for the DEDICATE-DZHK6 Trial Investigators*

DEDICATE Trial

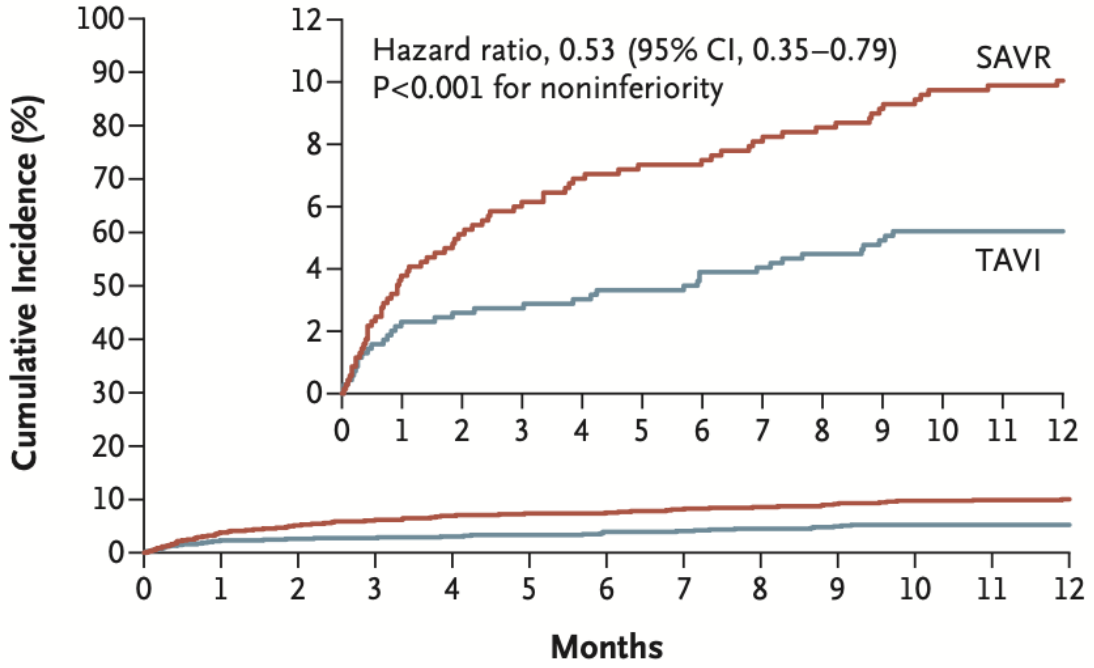
not sponsored by industry

real-world setting

unrestricted access to several contemporary transcatheter heart-valve devices

CONTINUOUSLY INCREASING GAP IN KAPLAN-MEIER CURVES

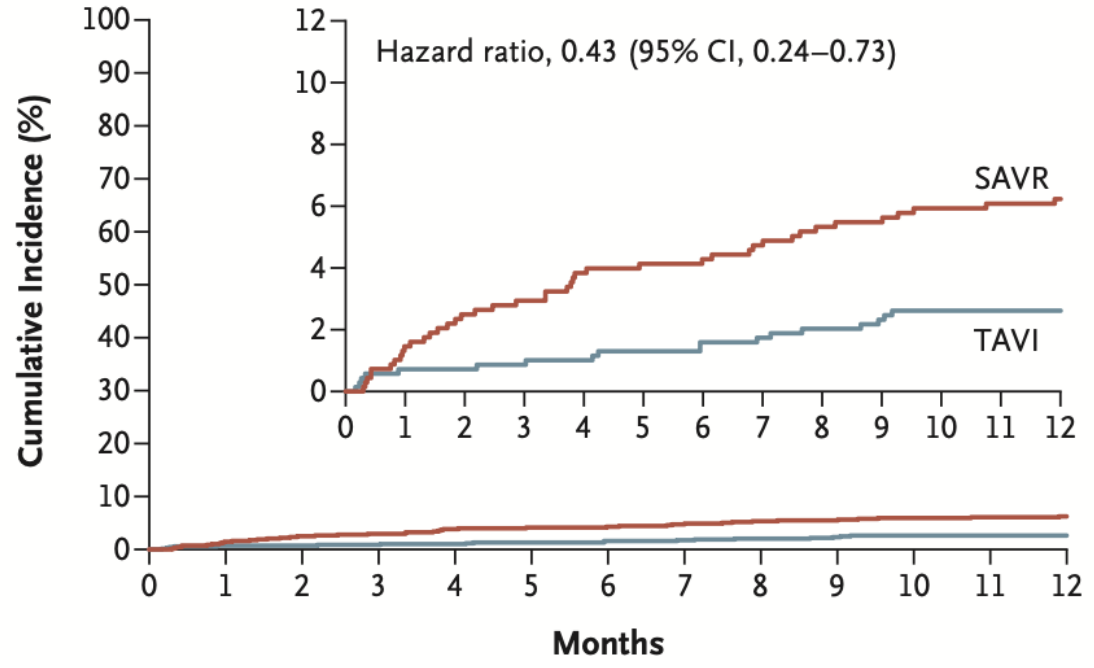
A **Stroke or Death from Any Cause**



No. at Risk

SAVR	697	658	641	631	625	622	619	615	612	608	602	600	591
TAVI	696	680	674	670	668	666	663	661	656	653	651	651	639

B **Death from Any Cause**

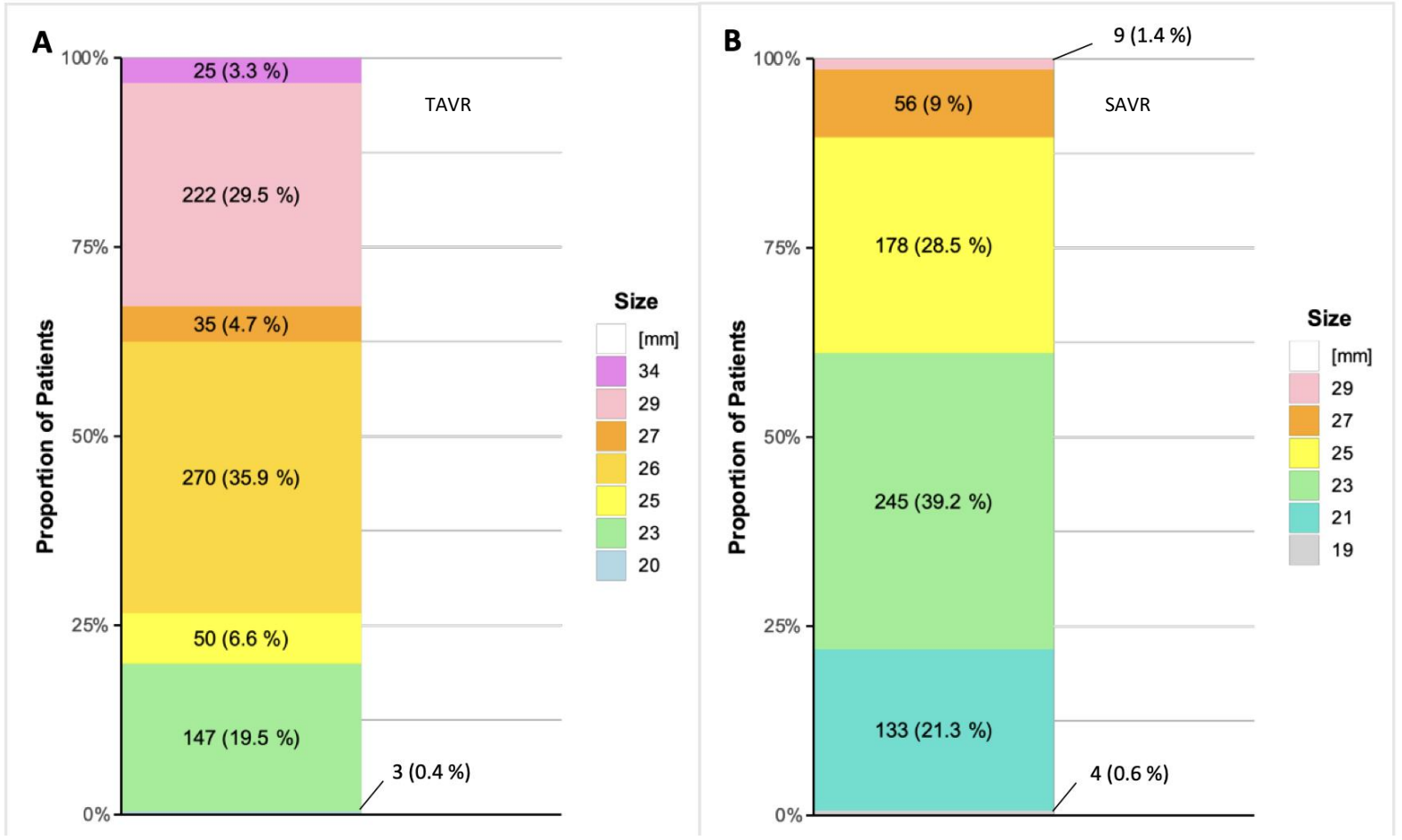


No. at Risk

SAVR	697	674	659	652	645	643	640	637	633	632	627	625	616
TAVI	696	691	685	681	680	678	677	675	671	669	667	667	655

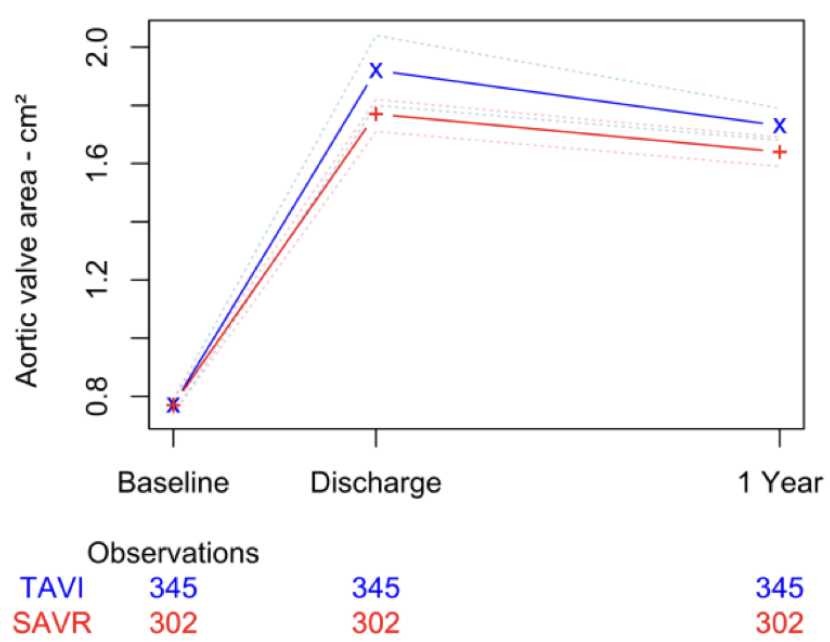
LARGER VALVES IN TAVR COHORT

Figure S2. Distribution of Prosthetic-valve Implant Sizes.



IMPROVED VALVE AREA AND DYSPNEA IN TAVR COHORT

B



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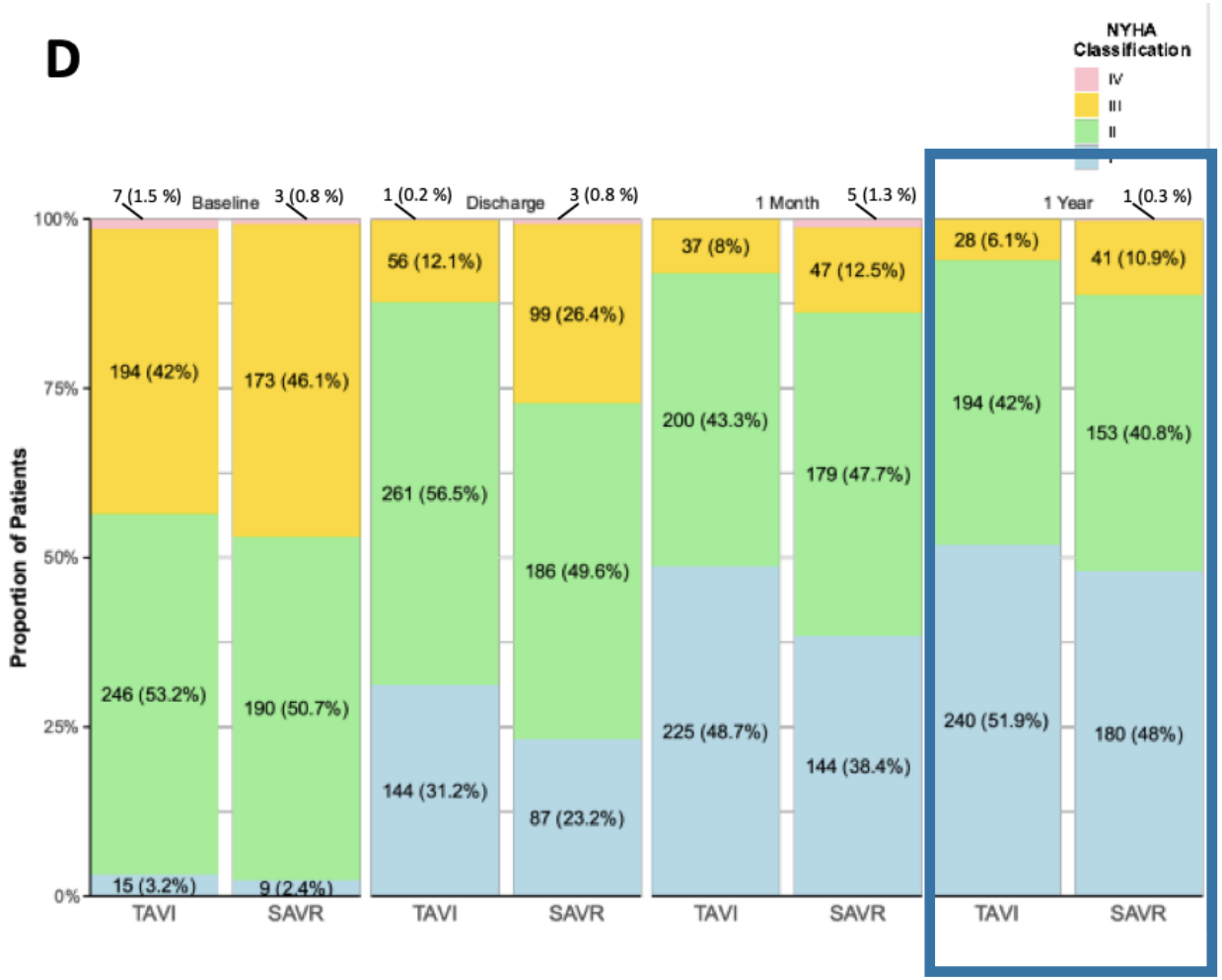
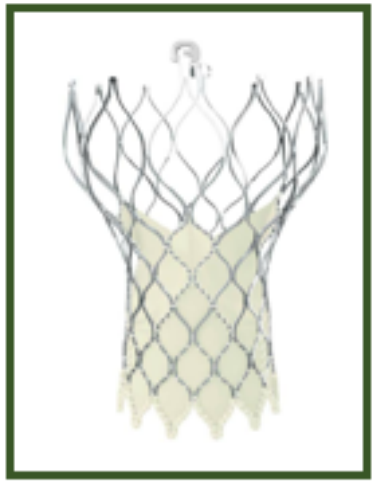


Longest Follow-up of Landmark Trials of TAVR vs SAVR



10 years

- **Notion** *ESC Congress 2023*

5 years

- PARTNER 1A
- Corevalve High risk
- PARTNER 2A
- SURTAVI

4 years

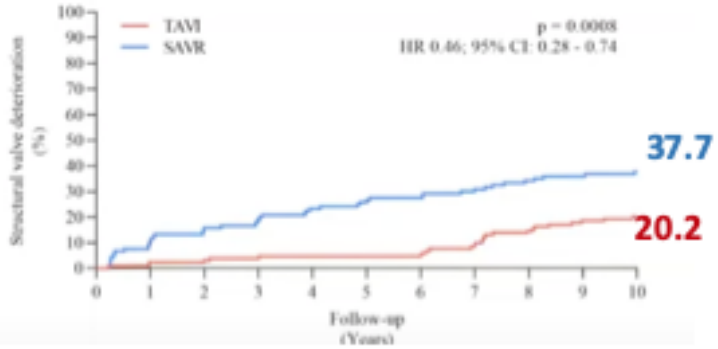
- PARTNER 3
- Evolut Low-Risk

1 year

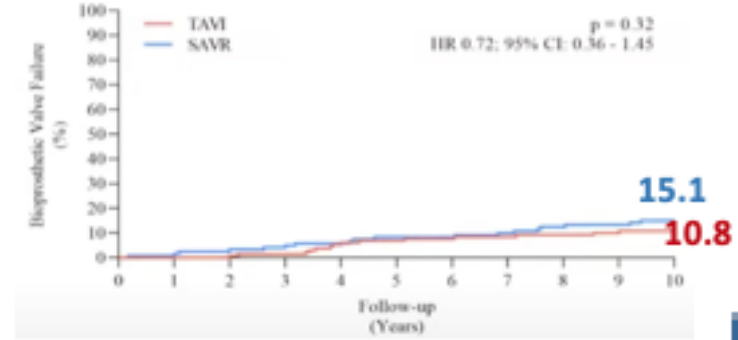
- UK-TAVI (all THVs)

Notion Trial – 10y

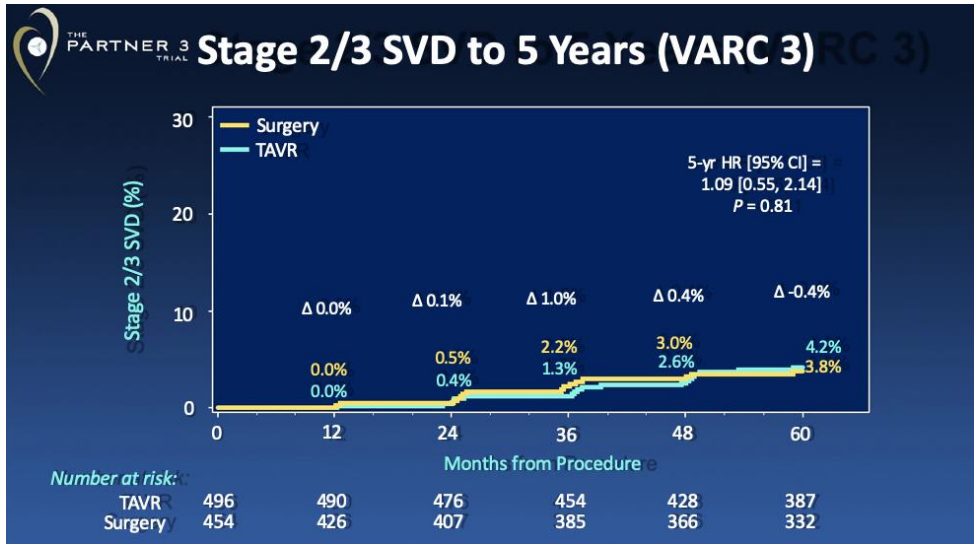
SVD - p<0.001

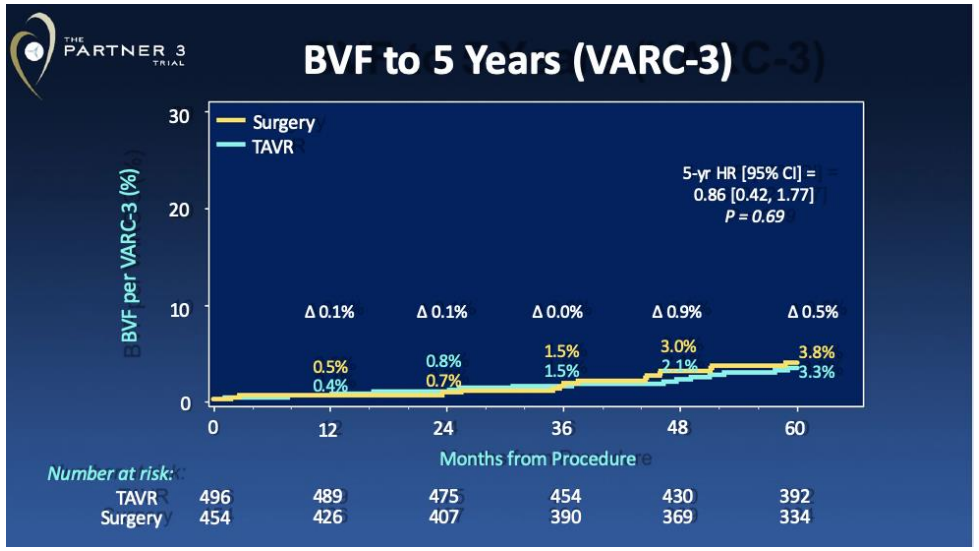


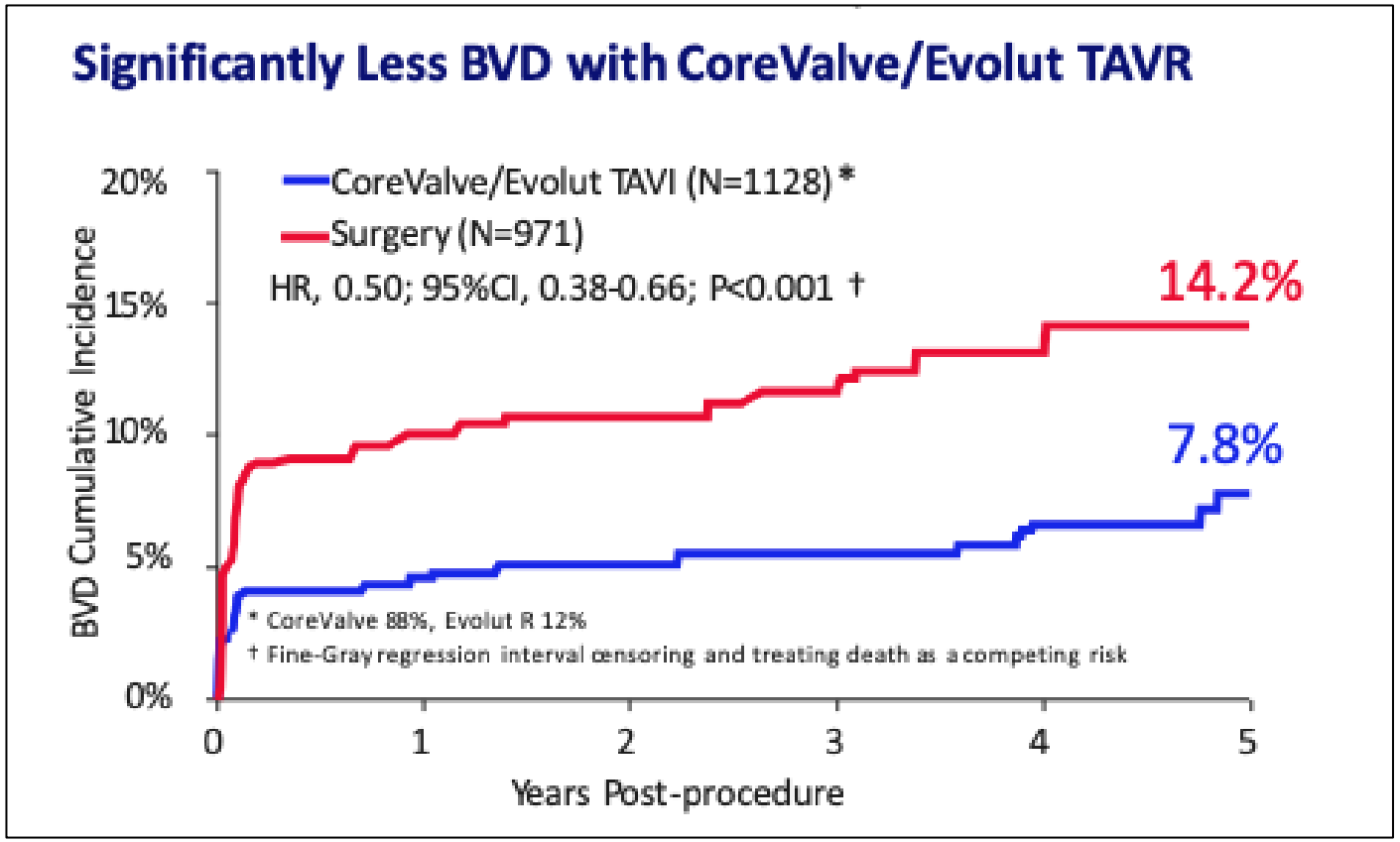
BVF - p= NS



Low risk trials showed non-inferiority (PARTNER3) or superiority (EVOLUT LR) for TAVR compared to SAVR (SVD and BVF)



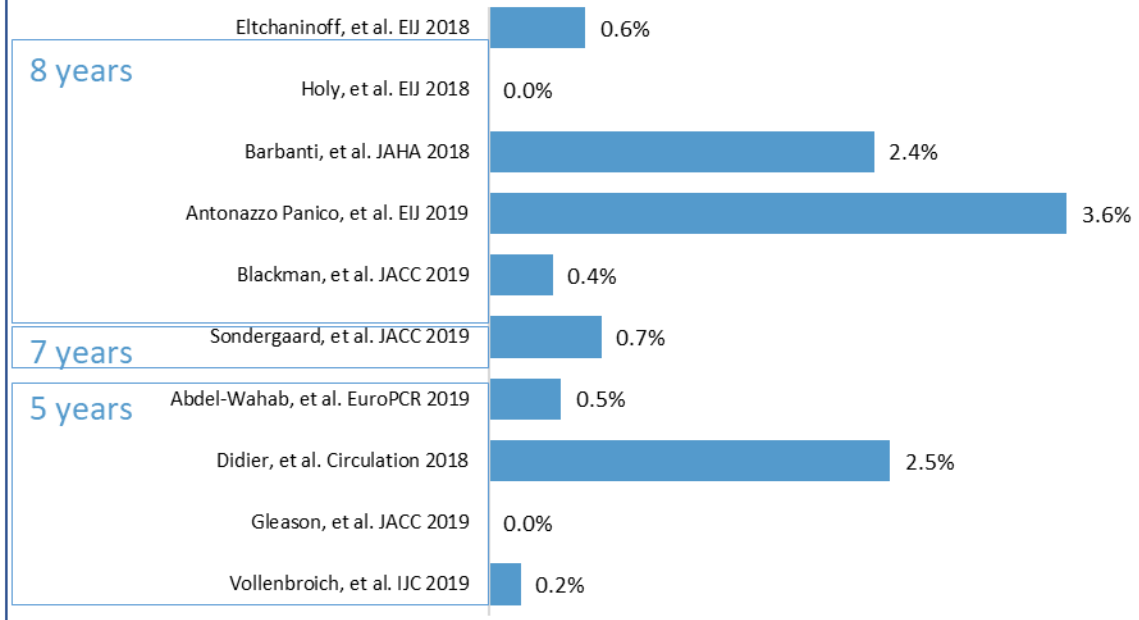




LIFETIME MANAGEMENT OF AORTIC DISEASE IN 2024

DURABILITY OF THVs – SO FAR SO GOOD!

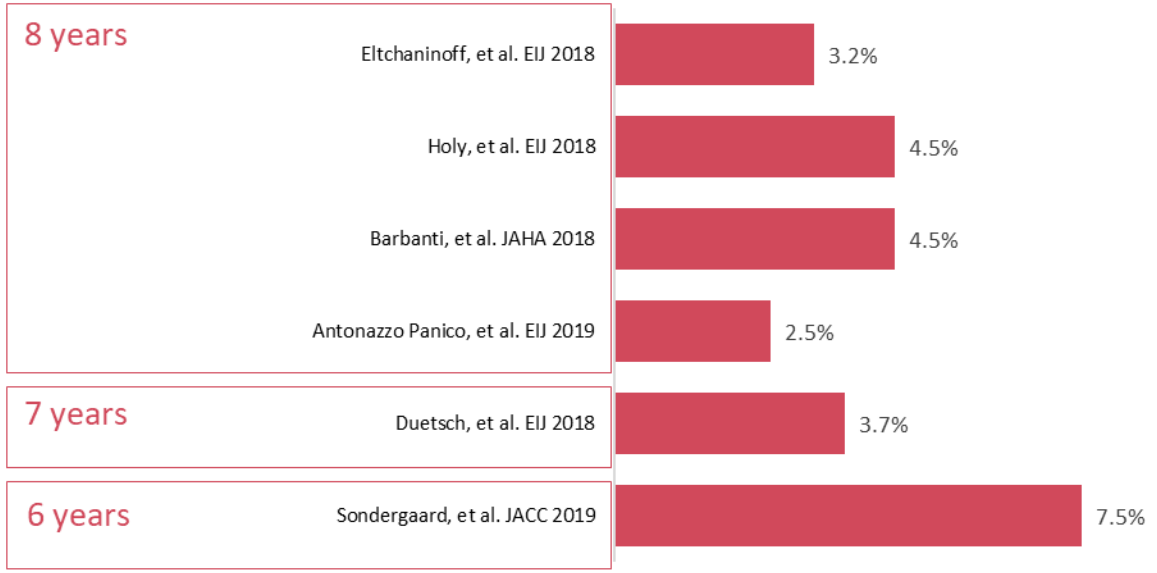
Severe SVD



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)

Are all THVs created equal?
Does THV design matter?
Is there a “Class Effect”?

COMPONENTS OF LATE VALVE PERFORMANCE

Bioprosthetic Valve Dysfunction[1]

Structural Valve Deterioration

Intrinsic permanent changes of the prosthetic valve (i.e., calcification, leaflet fibrosis, tear or flail) leading to degeneration and/or hemodynamic dysfunction

Non Structural Valve Deterioration

Any abnormality not intrinsic to the prosthetic valve itself (i.e., intra- or para-prosthetic regurgitation, prosthesis malposition, patient-prosthesis mismatch, late embolization) leading to degeneration and/or dysfunction

Thrombosis

Thrombus development on any structure of the prosthetic valve, leading to dysfunction with or without thrombo-embolism

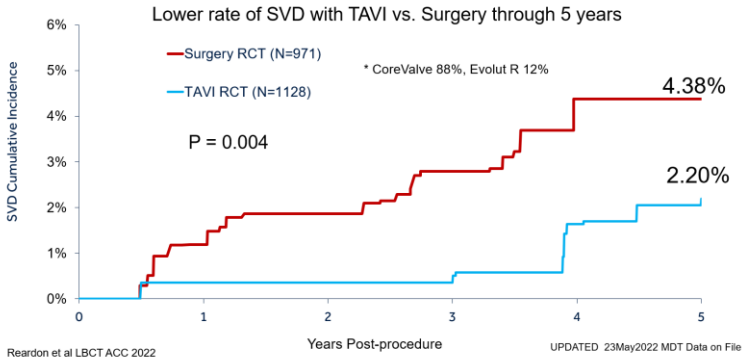
Endocarditis

Infection involving any structure of the prosthetic valve, leading to perivalvular abscess, dehiscence, pseudo-aneurysms, fistulae, vegetations, cusp rupture or perforation

Capodanno D, et al. *Eur J Cardiothorac Surg*. 2017;52:408-417.

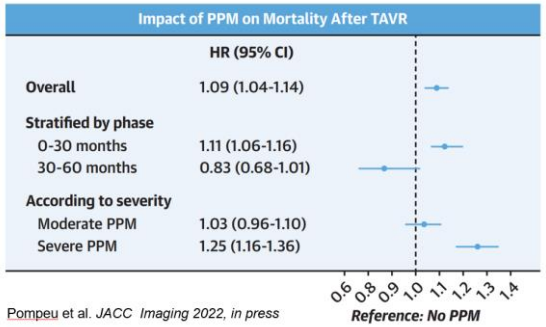
Low Rates of SVD

5-YEAR SVD ADJUSTED FOR COMPETING RISK OF MORTALITY



Low Rates of PPM

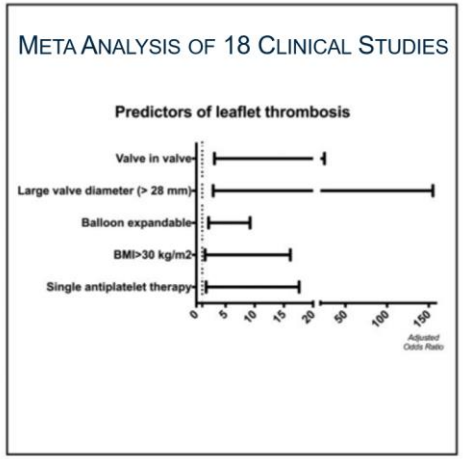
Only Severe Prosthesis-Patient Mismatch Is Associated With Higher Risk of Mortality Following TAVR



Pompeu et al. *JACC Imaging 2022, in press*

Low Rates of Thrombosis

META ANALYSIS OF 18 CLINICAL STUDIES

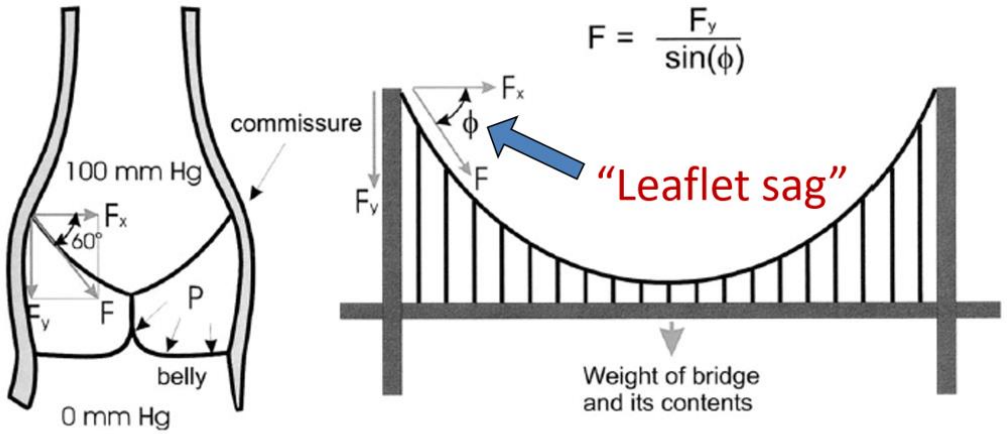


D'Ascenzoa, et al. EJCVS 56 (2019) 488–494

EVOLUT TRANSCATHETER DESIGN

EVOLUT FRAME DESIGN – HEMODYNAMICS AND DURABILITY

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



Piazza N London Valve 2022 Presentation

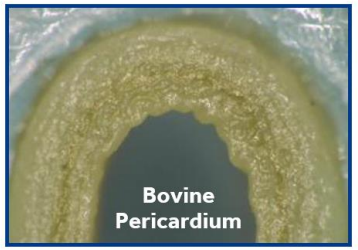
FOCUS ON THE INFLOW

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

NAVITOR

ACURATE NEO-2

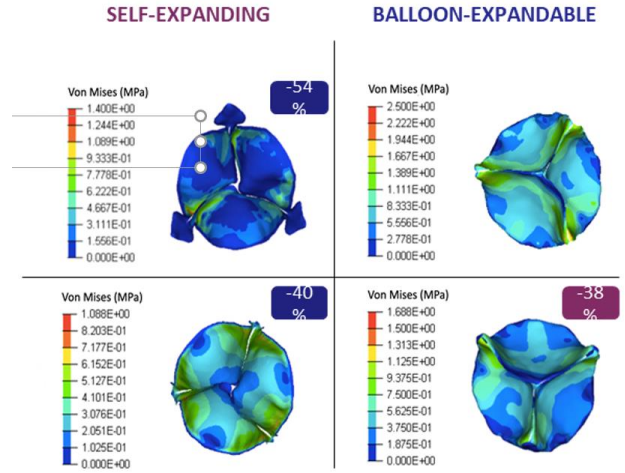
PORCINE PERICARDIUM



- 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

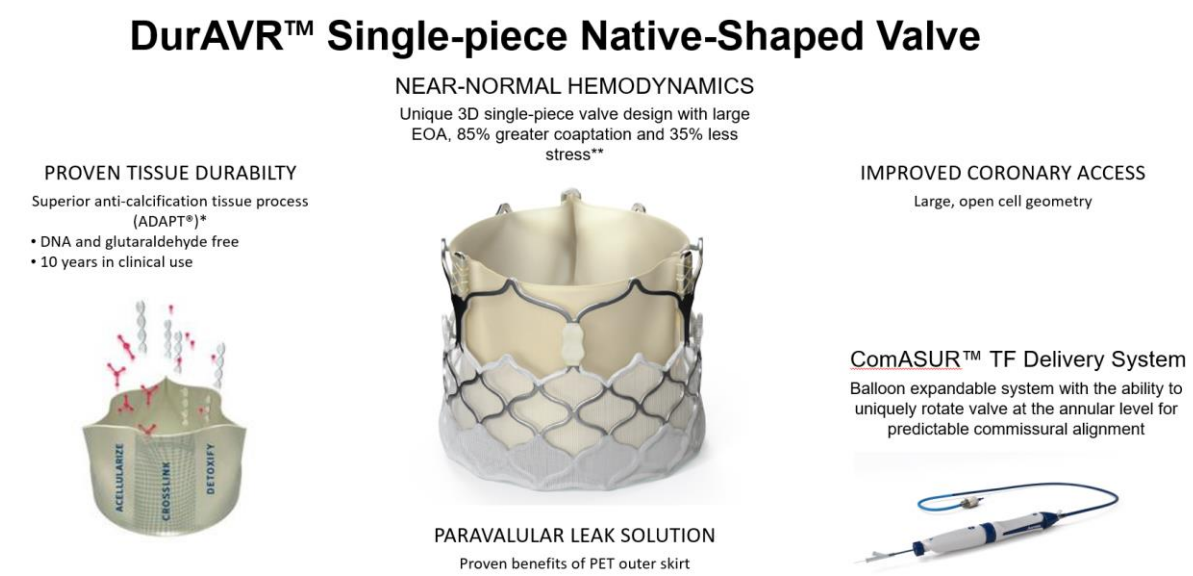
THV design matters and may account for differences in hemodynamics/gradients as well as early/late outcomes and durability.

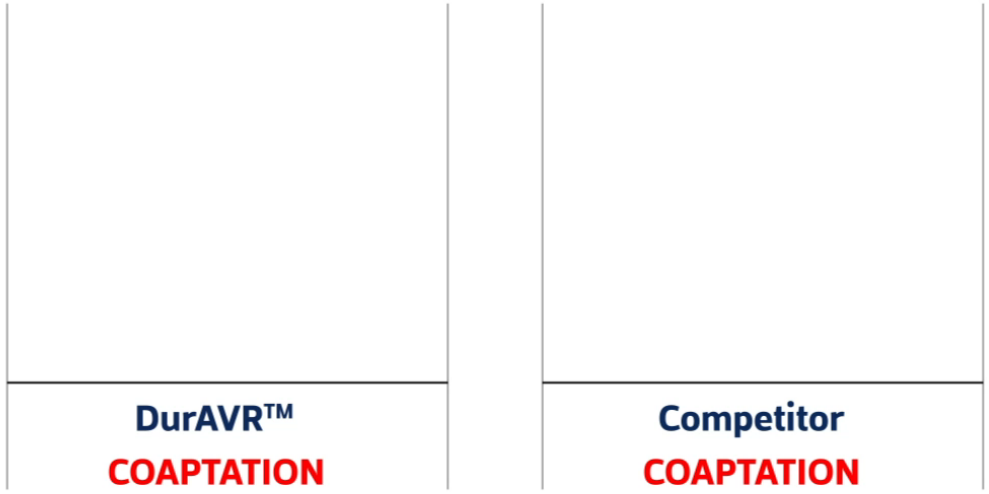
- **TAVR has revolutionized the treatment of patients with severe aortic stenosis, which has become the *dominant therapy in all patients except the very young (< 65 years)***
- **Similar to surgical valves, TAVR valves have varying designs and performance metrics – *we can no longer consider TAVR a "Class Effect"***
- **Linking THV performance to late clinical outcomes is essential to understand the value of THV in younger patients (< 65 years)**

DO NEW VALVE DESIGNS IMPROVE DURABILITY & OUTCOMES?

ALTERNATIVE VALVE DESIGNS

ANTERIS DURAVR™ BIOPROSTETHIC





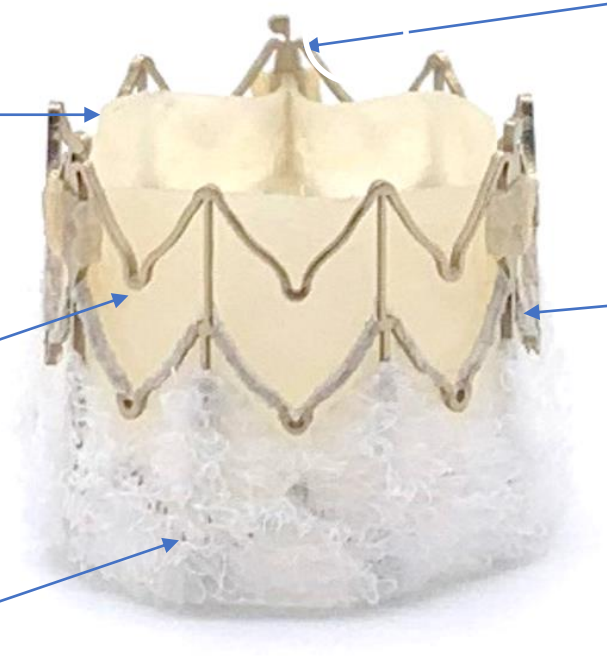
Meduri et al TCT2022 presentation

SIEGEL THV SYSTEM

Rhenium Frame
Nickel Free

Nitride Oxide
Coating

Conformable PVL skirt



Commissural
Alignment Flags

Leaflets
- Dry Porcine
- Anti-calcification
- Leaflet Folding

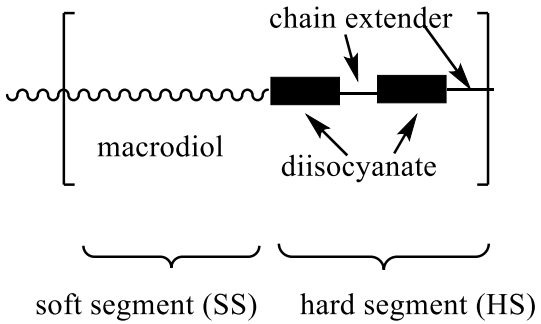
Delivered Crimped On Balloon Through 8 Fr Expandable Sheath

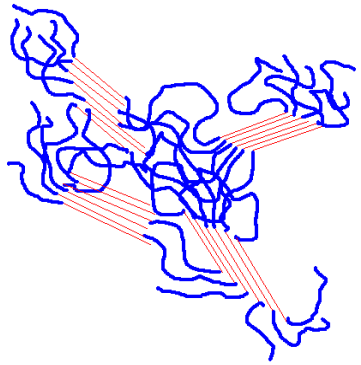
Courtesy Pradeep Numar Yadav

NEW LEAFLET DESIGNS

TRIA POLYMER VALVE + ROBOTIC MANUFACTURING (FOLDAX)

Polyurethane





Siloxane polyurethane

Similar structure used in pacing leads for over 15 years

TRIA™ Mitral Surgical Valve

TRIA™ TAVR Systems

NEW LEAFLET DESIGNS

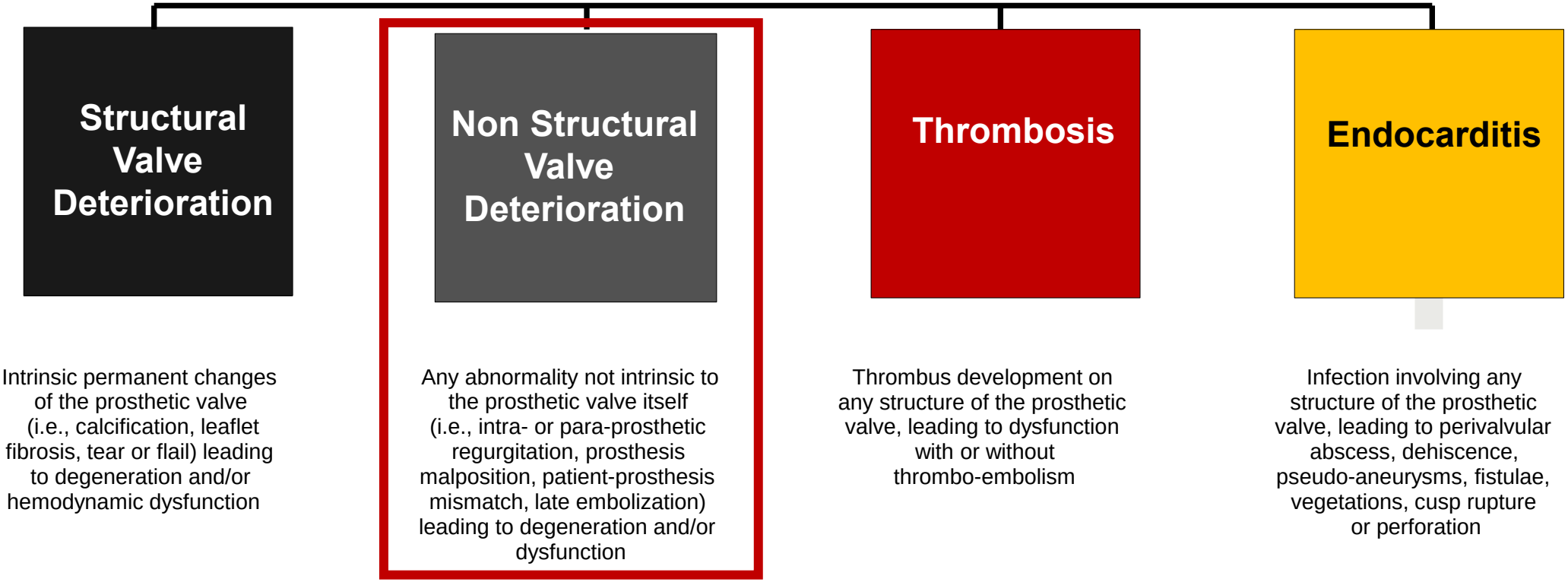
TRIA POLYMER VALVE + ROBOTIC MANUFACTURING (FOLDAX)

- Highly precise, reproducible processes with minimal human handling required
- No labor-intensive hand sewing
- Small, efficient robotic pods can produce valves in-geography

EAPCI-ESC-EACTS CONSENSUS DOCUMENT

BIOPROSTHETIC VALVE DYSFUNCTION

Bioprosthetic Valve Dysfunction[1]



1. Capodanno D, et al. *Eur J Cardiothorac Surg*. 2017;52:408-417.

CONCEPT CHECK: PROSTHESIS PATIENT MISMATCH (PPM)

THE CONUNDRUM OF PPM IN TAVR CLINICAL STUDIES

- **Severe prosthesis patient mismatch (PPM): the prosthetic valve is relatively small compared with the patient's body size.**
- **Severe PPM (TVT registry) has also been a predictor for late mortality for BE and SE valves.**

However:

- **An analysis of the same TVT Registry, *Tang et al did not identify that severe PPM was a predictor of mortality,* and that other factors related to patient co-morbidity were predictive of mortality.**
- **In the *Partner III study however, severe PPM was an important predictor of death, stroke, or rehospitalization.***

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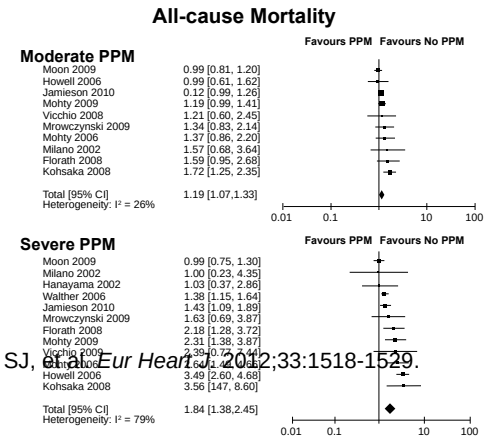
PROSTHESIS PATIENT MISMATCH

THE CONUNDRUM OF PPM IN TAVR CLINICAL STUDIES

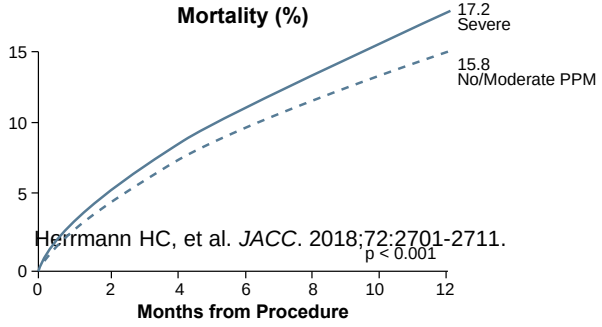
Severe PPM → Mortality

SAVR



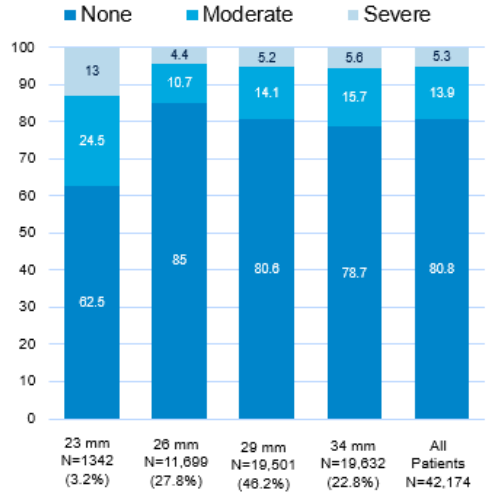
Head SJ, et al. *Eur Heart J*. 2012;33:1518-1529.

TAVR



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

Severe PPM ≠ Mortality



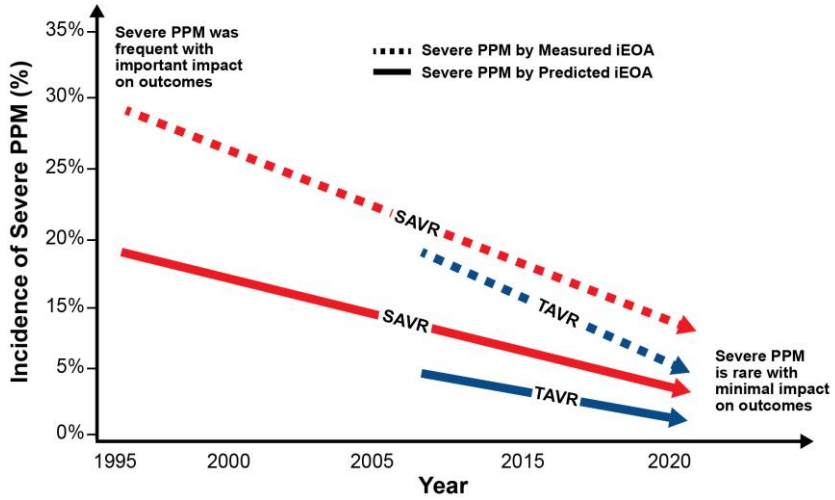
Tang GL et al JACC CV Interv 2021;14:964–76

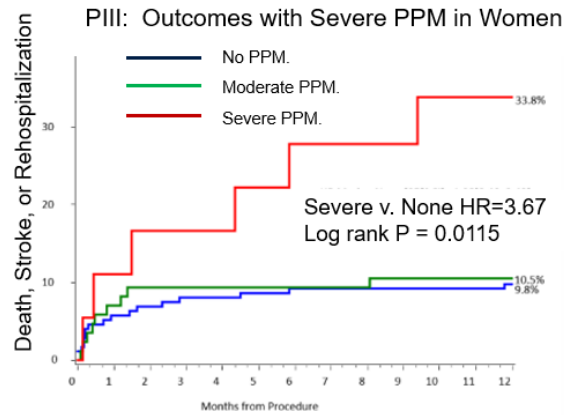
TABLE 4 Multivariable Predictors of 1-Year Valve-Related Readmission

	De Novo TAVR		TAV-in-SAV	
	Adjusted Hazard Ratio (95% CI)	p Value	Adjusted Hazard Ratio (95% CI)	p Value
Pre-procedural variables				
New York Heart Association functional class III or IV	1.50 (1.18-1.91)	<0.001		
Atrial fibrillation or flutter	1.48 (1.24-1.77)	<0.001		
Peripheral vascular disease	1.40 (1.17-1.69)	<0.001		
Creatinine >2.0 mg/dl	1.29 (0.97-1.71)	0.085		
Coronary artery bypass surgery	1.27 (1.04-1.56)	0.022		
5-m gait speed average >6 s or unable to walk	1.36 (1.09-1.71)	0.008	2.18 (1.14-4.17)	0.019
Diabetes mellitus	1.27 (1.06-1.52)	0.009		
Post-procedural variables				
Severe vs. nonsevere PPM	1.01 (0.69-1.48)	0.954	0.76 (0.43-1.35)	0.353
Major vascular complication	2.26 (1.30-3.92)	0.004		
Post-procedural moderate or severe aortic regurgitation	3.50 (2.54-4.82)	<0.001	2.86 (1.04-7.87)	0.042

Tang GL et al JACC CV Interv 2021;14:964–76

Severe PPM → Clinical Events





Pibarot P, et al. *Circulation*. 2020;141:1527-1537.

PROSTHESIS PATIENT MISMATCH

CONTROVERSES IN ESTABLISHING APPROPRIATE PPM CRITERIA

TABLE 3 Definitions for Prosthesis-Patient Mismatch

ch Consortium.

TABLE 4 Summary of Reasons for Discrepancy in Effects of Severe PPM on Outcomes

Reasons why the reported incidence of PPM varies after

cting

me

Older patients or other survival limitations

Underpowered analyses

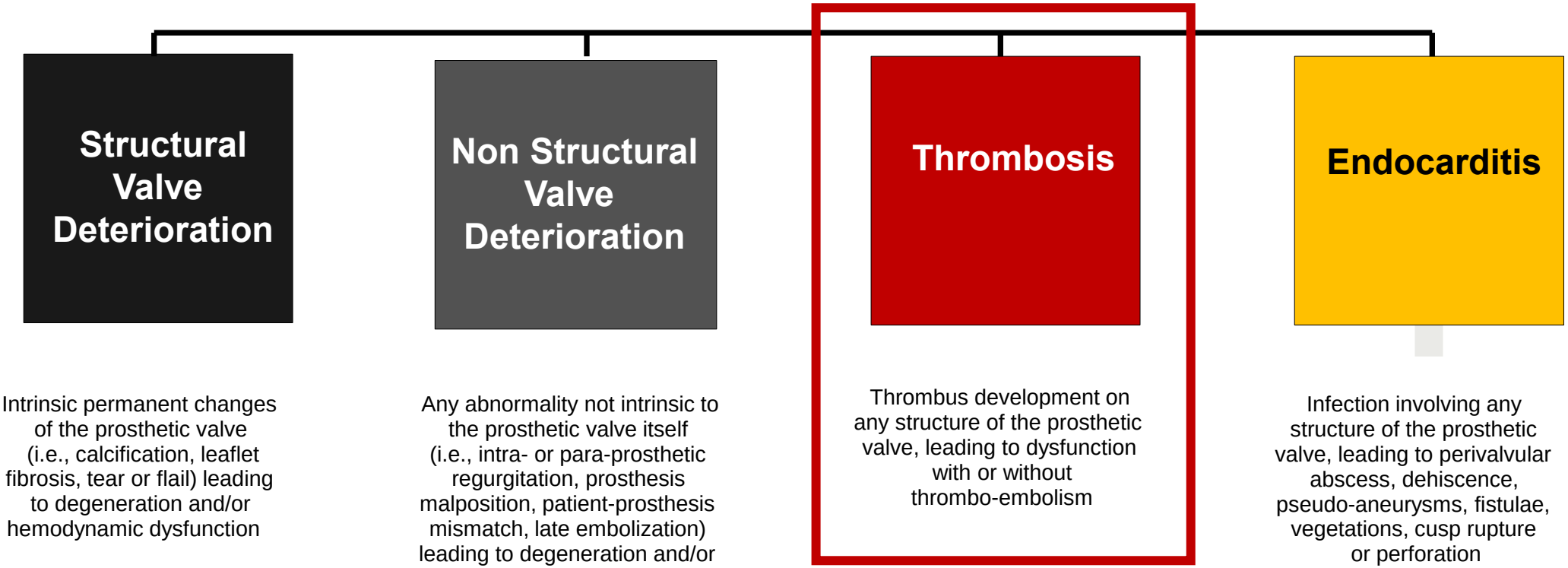
Limited follow-up (1 year may not be sufficient)

«There are reasons why reported incidence of PPM varies after TAVR and why the effects of severe PPM on outcomes are conflicting»

EAPCI-ESC-EACTS CONSENSUS DOCUMENT

BIOPROSTHETIC VALVE DYSFUNCTION

Bioprosthetic Valve Dysfunction[1]



1. Capodanno D, et al. *Eur J Cardiothorac Surg*. 2017;52:408-417.

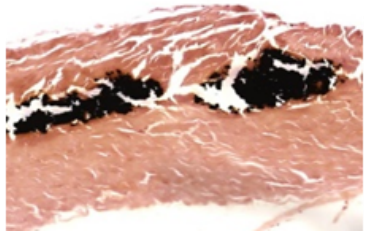
PATHOLOGIC CHANGES LEADING TO VALVE DETERIORATION

THROMBUS FORMATION MAY LEAD TO BASAL LEAFLET CALCIFICATION

N=115

Extrinsic calcification

Intrinsic calcification



Case	Duration of implantation	Score of Calcification (per leaflet)	Number of leaflets with calcification	Score of thrombus (per leaflet)	CKD*
No.1	180 days	Moderate	3	Severe	+
No.2	199 days	Minimum	2	Mild	+
No.3	581 days	Minimum	1	Minimum	+
No.4	876 days	Minimum	1	Minimum	-
No.5	1238 days	Minimum	1	Moderate	+
No.6	1764 days	Minimum	1	Severe	+
No.1	976 days	Mild	2	Severe	HD*
No.2	1470 days	Minimum	1	Minimum	-

- ✓ Any duration
- ✓ CKD
- ✓ With thrombus

- ✓ Later phase

Sato, et al. TCT2020 Abstract Presentation.

VALVE THROMBOSIS

WHAT IS KNOWN, WHAT IS NEW AND WHAT IS STILL UNKNOWN

What's known about subclinical leaflet thrombosis		New information about subclinical leaflet thrombosis	What remians unknown about subclinical leaflet thrombosis
Incidence Subclinical leaflet thrombosis is reported in 10-15% of patients after TAVR	**Natural history** Subclinical leaflet thrombosis is a dynamic finding, with spontaneous appearance and spontaneous resolution in a significant proportion of patients, even in the absence of anticoagulation	**Procedural predictors** 1. Valve deformation index for balloon-expandable valves 2. Valve inflow eccentricity for self-expanding valves 3. Asymmetric leaflet adaptation 4. Smaller neo-sinus volume	• Impact on valve durability • Impact on clinical outcomes: Conflicting data in multiple studies • Role of routine CT screening for subclinical leaflet thrombosis • Differences in the rate of subclinical leaflet thrombosis amongst different valve types • Role of routine anticoagulation after TAVR in young low risk patients undergoing TAVR • Impact of subclinical leaflet thrombosis on new cerebral lesions and neurocognitive function • Predictors of progression, resolution, persistence or recurrence of subclinical leaflet thrombosis • Impact of hypercoagulability on subclinical leaflet thrombosis
Impact on hemodynamics Subclinical leaflet thrombosis is associated with relatively normal aortic valve gradients	**Role of DOACs** DOACs (rivaroxaban or apixaban) are effective in the prevention of subclinical leaflet thrombosis	**Edoxaban for routine anticoagulation after TAVR** Edoxaban, compared with DAPT, was associated with decreased incidence of sublinical leaflet thrombosis	
Anticoagulation Subclinical leaflet thrombosis is less prevalent in patients on anticoagulation	**Routine anticoagulation after TAVR and clinical outcomes** Routine anticoagulation with rivaroxaban 10mg daily or apixaban 5mg twice a day after TAVR, compared with DAPT, is associated with increased death and thromboembolic events	**Routine anticoagulation after TAVR and new cerebral lesions** Routine anticoagulation with edoxaban, compared with DAPT, after TAVR did not impact new cerebral lesions or change in neurocognative function after TAVR	

Impact on valve durability

Impact on clinical outcomes

Role of routine CT screening

Differece of SLT in different valve types

Role of routine anticoagulation in young and low risk patients

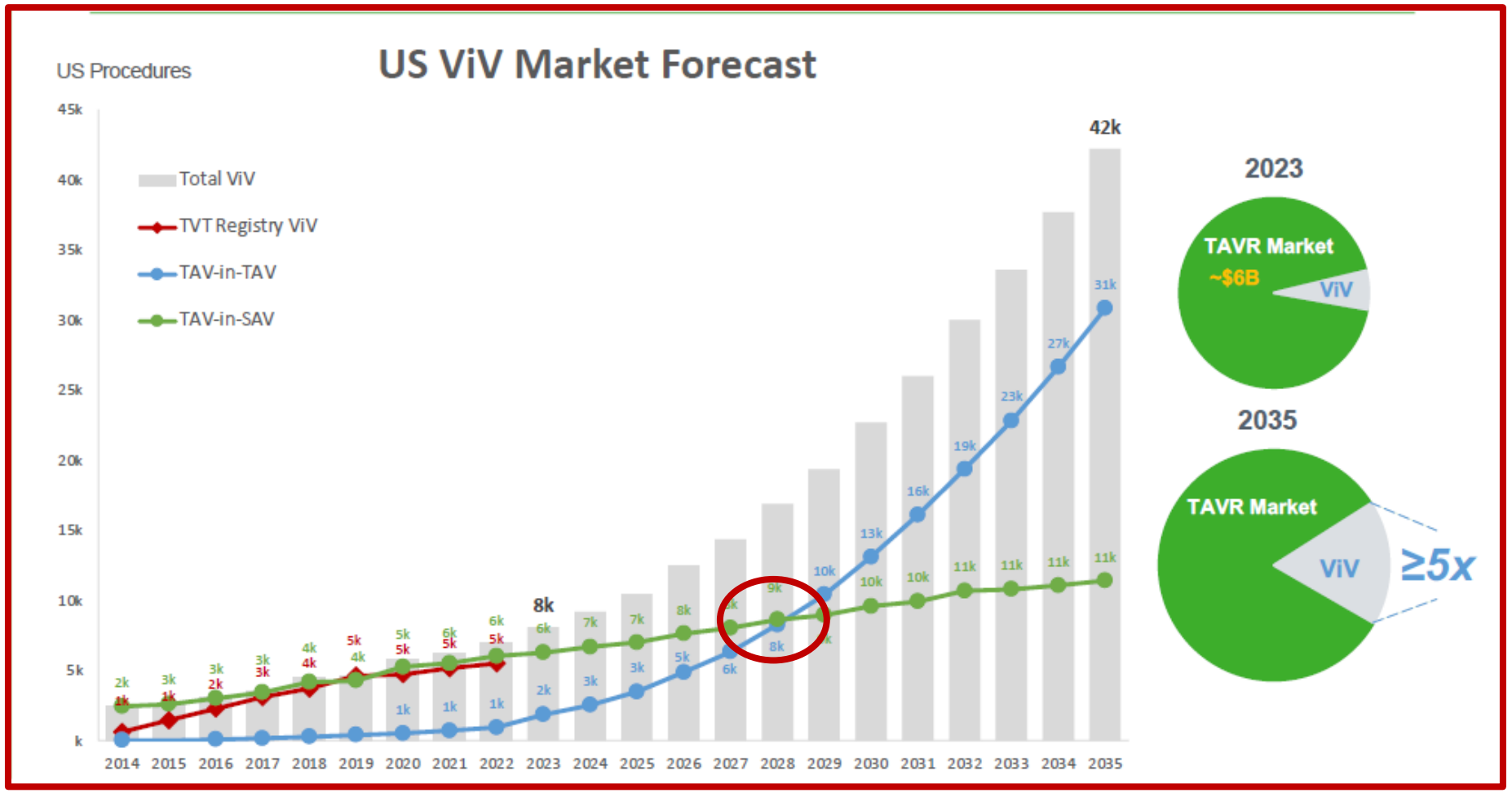
Cerebral events with SLT?

Predictors of progression, resolution, persistence or recurrence

Impact of Hypercoagulability

THV in THV - Redo TAVR

BIOPROSTHETIC VALVE DURABILITY (TAV-IN-TAV 'WAVE')



P Genereux, R Puri, MB Leon, D Dvir – SH Journal 2024

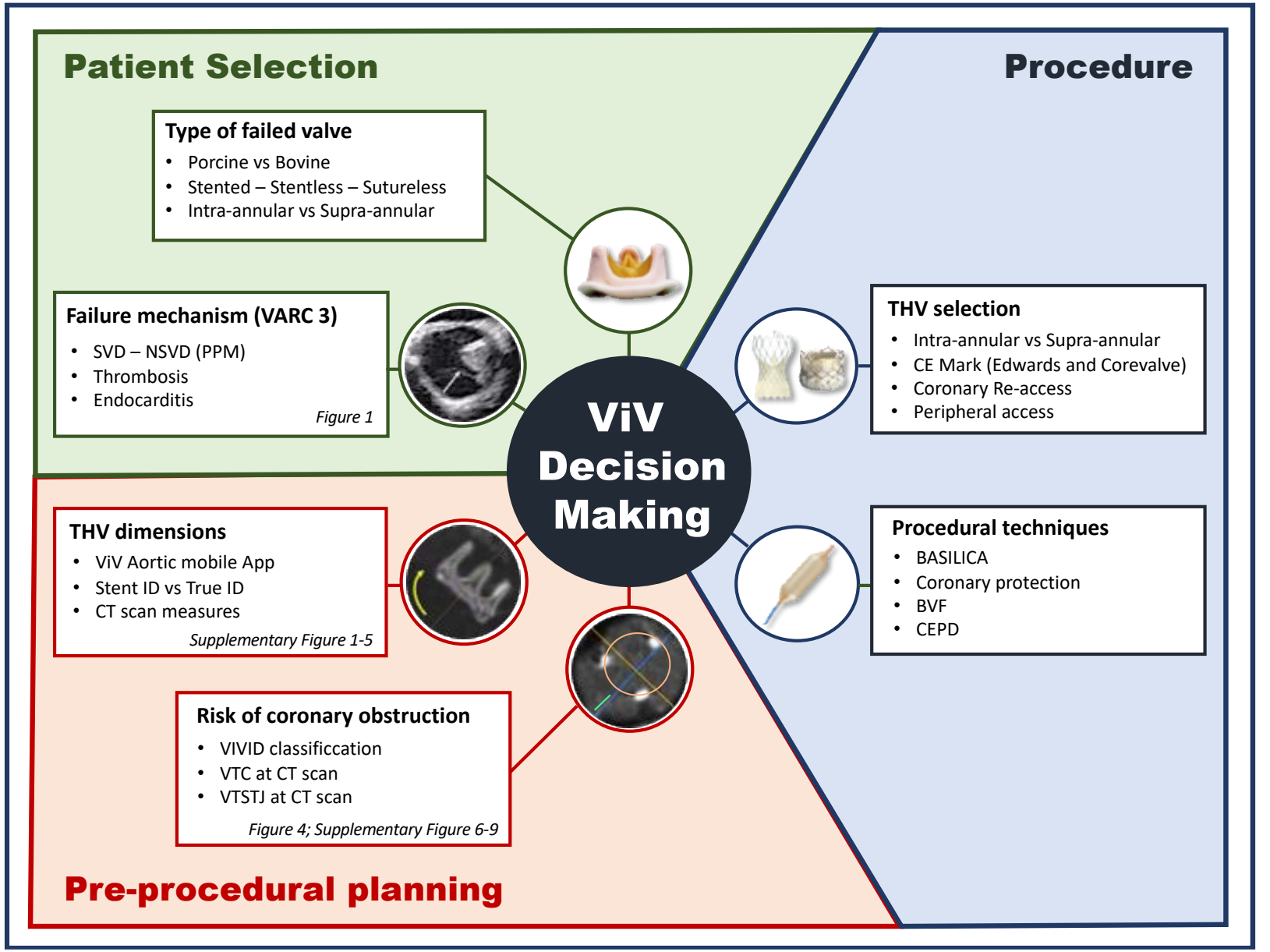
VIV DECISION MAKING PROCESS

Type of Failed Valve

Mechanism of Failure

THV Dimensions

Risk of Coronary Obstruction



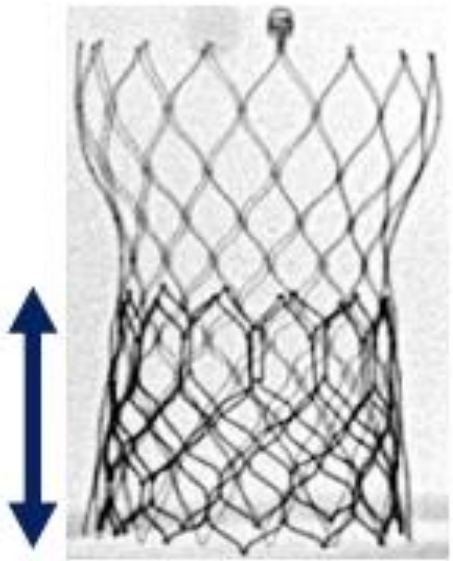
THV Selection

Procedural Planning

WHAT ELSE IS IMPORTANT IN RE-DO TAVR?

NEOSKIRT

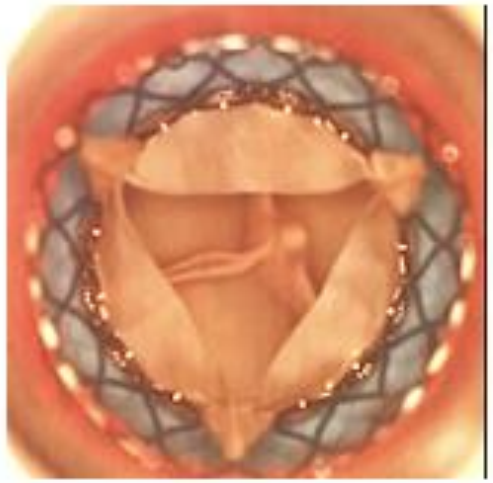
S3 Outflow at Node 5



23.0 mm

LEAFLET OVERHANG

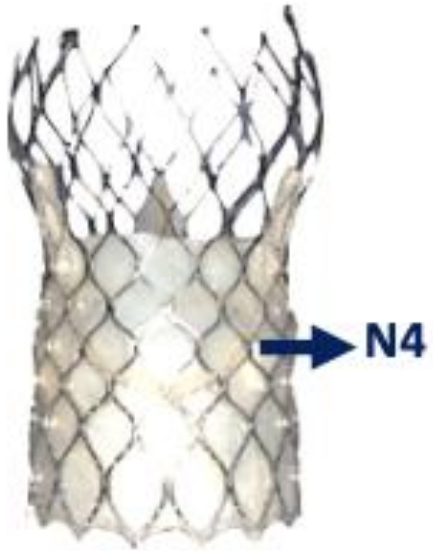
S3 Outflow at Node 5



59% leaflet overhang

INDEX THV EXPANSION

S3 Outflow at Node 5



+2.0 mm

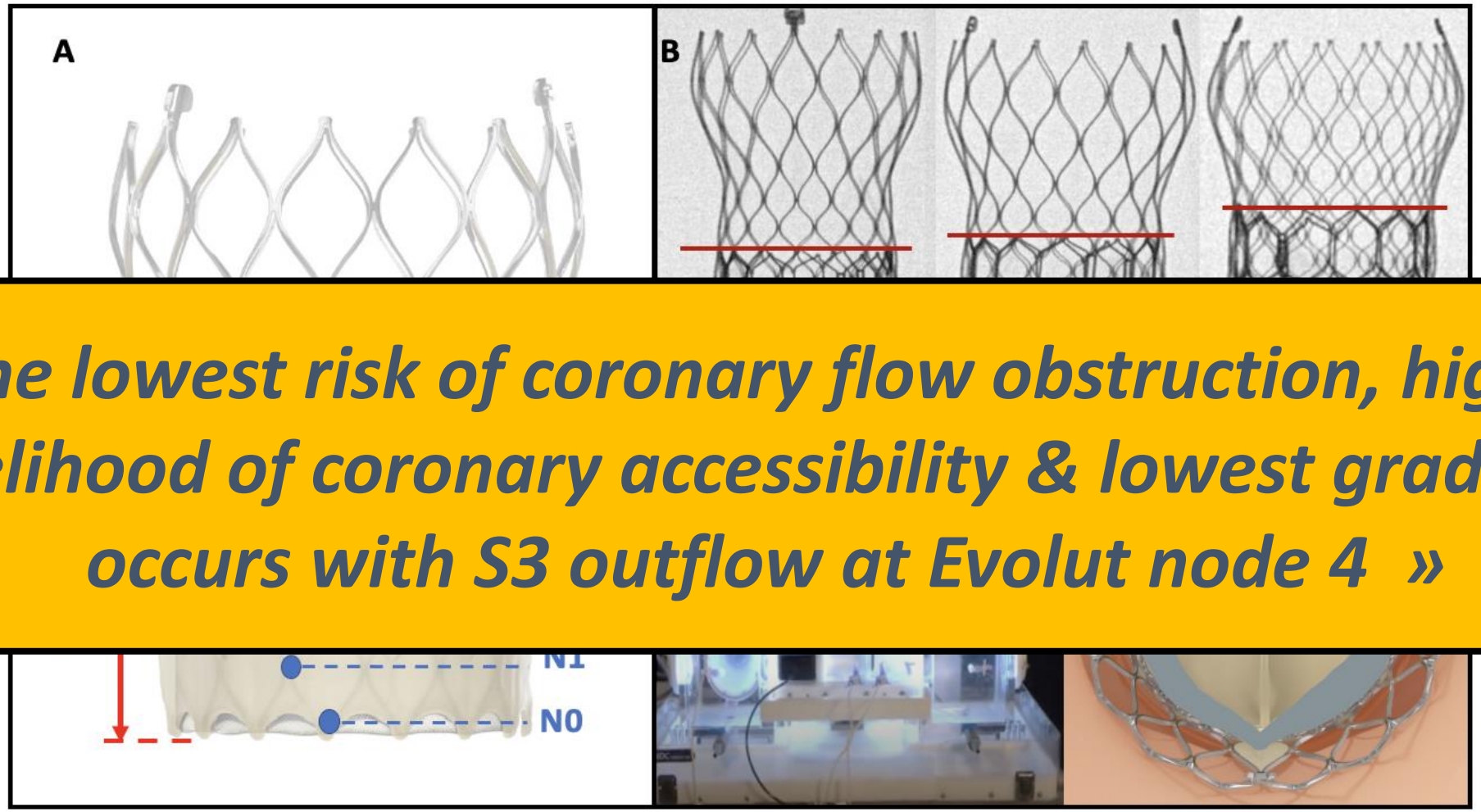
Tarantini G, et al. JACC Cardiol Intv 2022

Tarantini et al. Am J Cardiol 2023;192:228–244)

Redo TAVR
Implant methods & Leaflet Management.
Avoid high gradients and coronary obstruction.

SAPIEN 3 IN EVOLUT (AVOIDING HIGHER GRADIENTS)

CONCEPTUAL INTERACTION WITH SAPIEN 3 AND EVOLUT

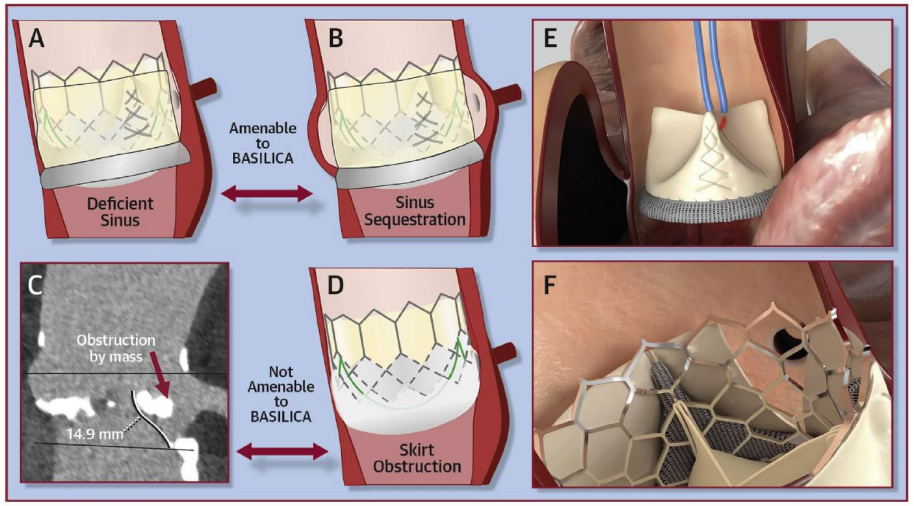


«The lowest risk of coronary flow obstruction, highest likelihood of coronary accessibility & lowest gradients occurs with S3 outflow at Evolut node 4 »

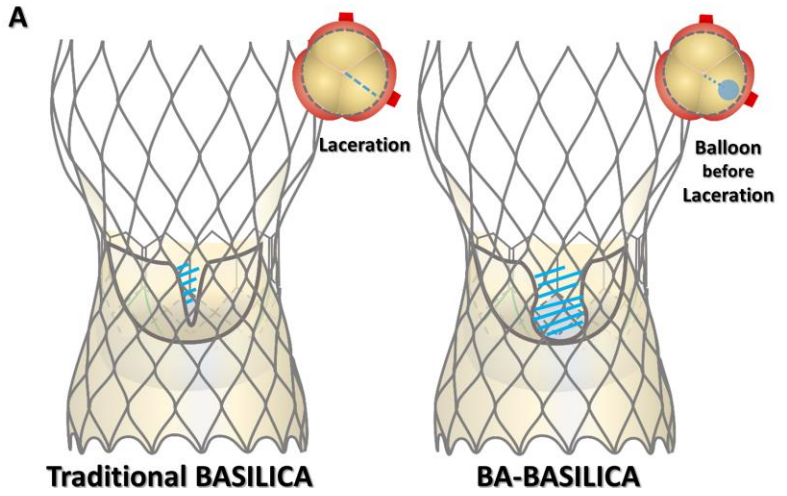
Akodad et al Submitted

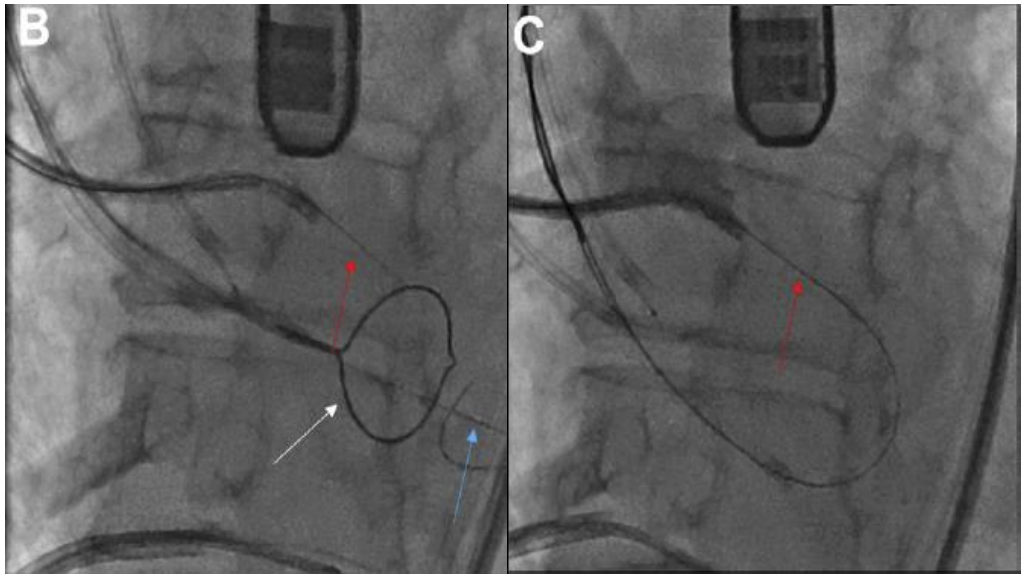
TAVR FOR SURGICAL VALVE FAILURE

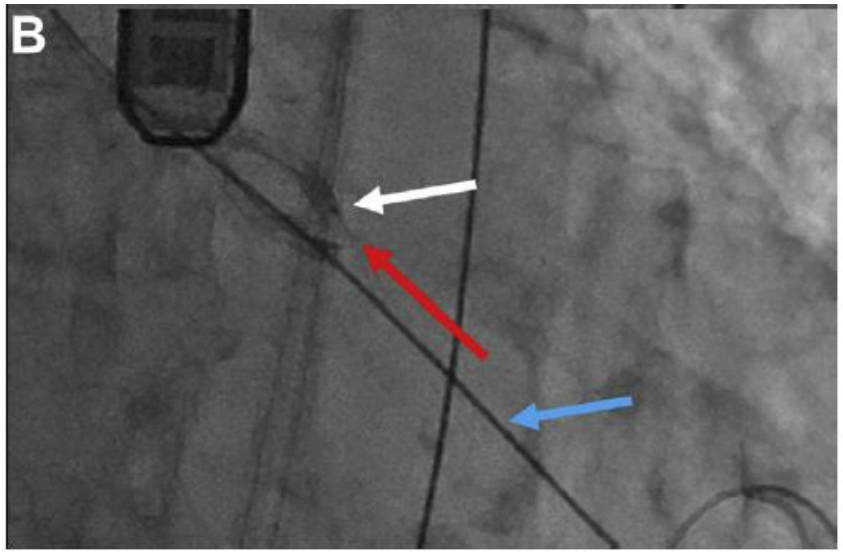
PREVENTING CORONARY OBSTRUCTION (BASILICA VS BA BASILICA?)



Lederman, R.J. et al. J Am Coll Cardiol Intv. 2019;12(13):1197-216.



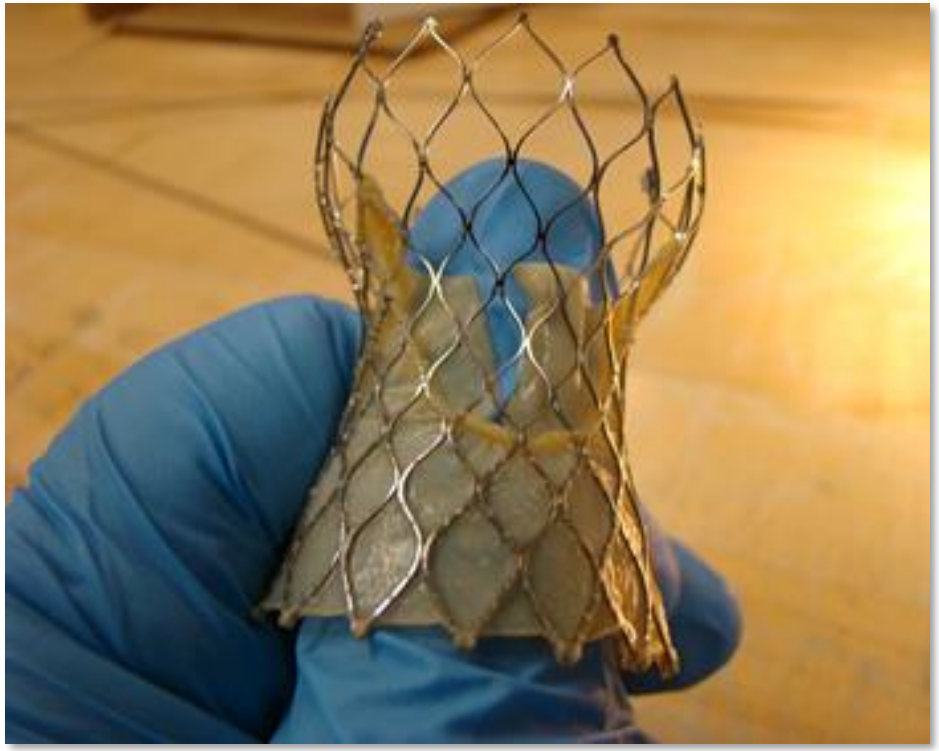




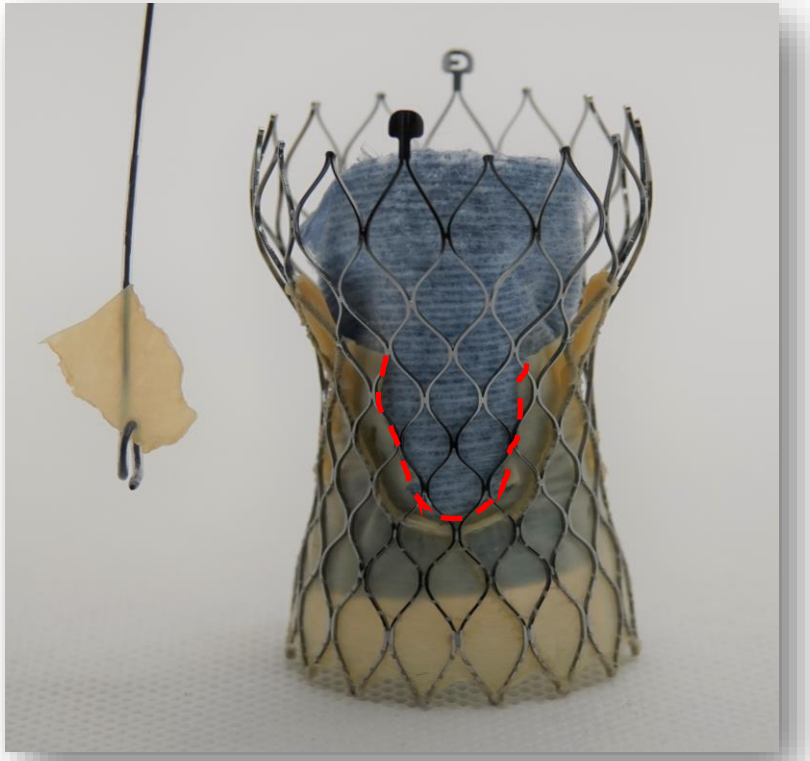
LEAFLET MODIFICATION FOR ACCESS AND FLOW

How Much Modification Is Needed? Risks? Benefits?

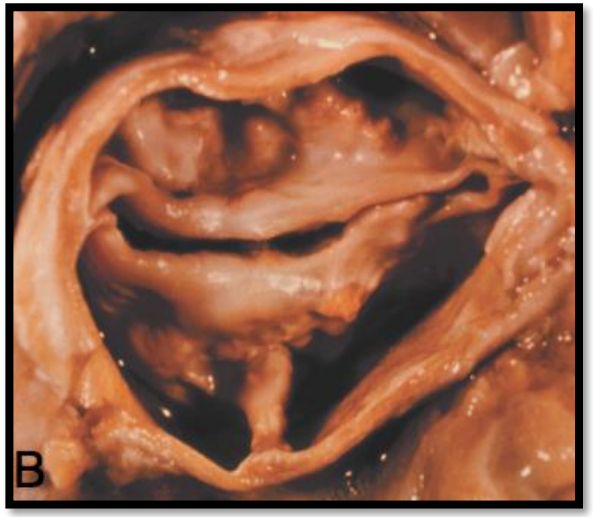
Leaflet Laceration



Leaflet Resection



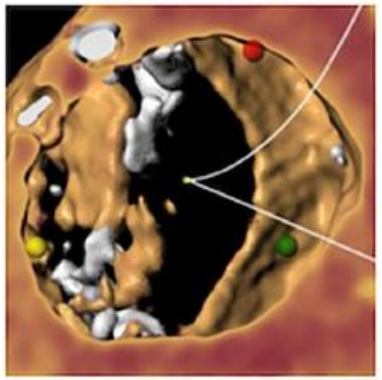
Bicuspid Aortic Valve Disease: Data Gaps?



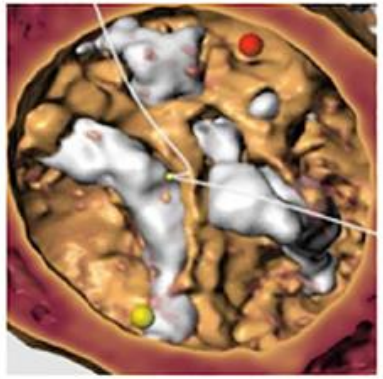
ANATOMICAL CONSIDERATIONS IN PATIENTS WITH BICUSPID VALVE

Suitable for TAVR → **NOT Suitable for SAVR**

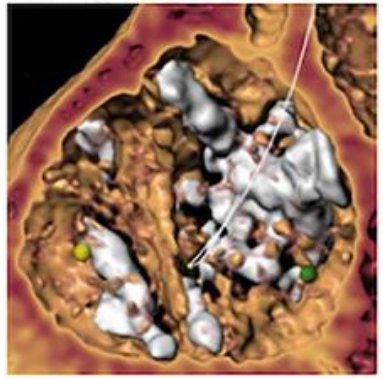
No Calcified Raphe or Excess Leaflet Calcificaton



Excess Leaflet Calcification



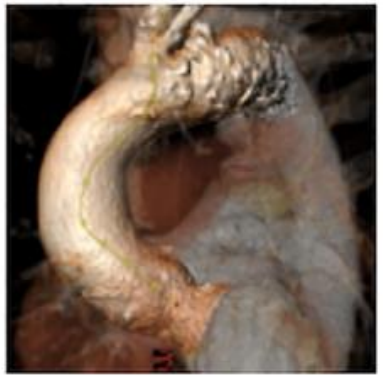
Calcified Raphe

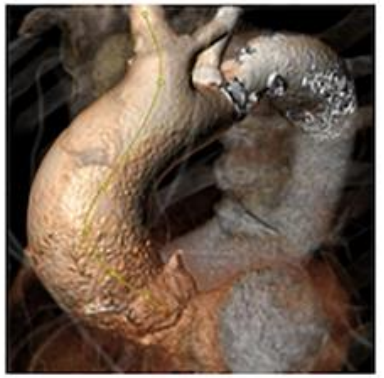


Calcified Raphe Plus Excess Leaflet Calcification & Calcified raphe

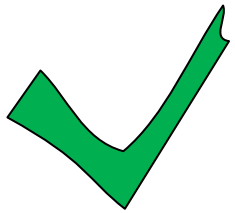
No dilation of ascending aorta

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





TAVR IN BICUSPID AORTIC VALVE DISEASE



What we know

- Feasible and safe
- One-year mortality similar to surgery and TAVI
- Better results with newest generation of THV
- A CT scan is mandatory for procedure planning
- Clacified raphe + highly calcified leaflets associated with poor outcomes

Warning

- Low but higher risk of stroke than TAV
- Higher risk of pacemaker implantation than SAVR
- Low but higher risk of annular rupture than TAV (BEV)
- Higher risk of ≥mild PVR than TAV or surgery

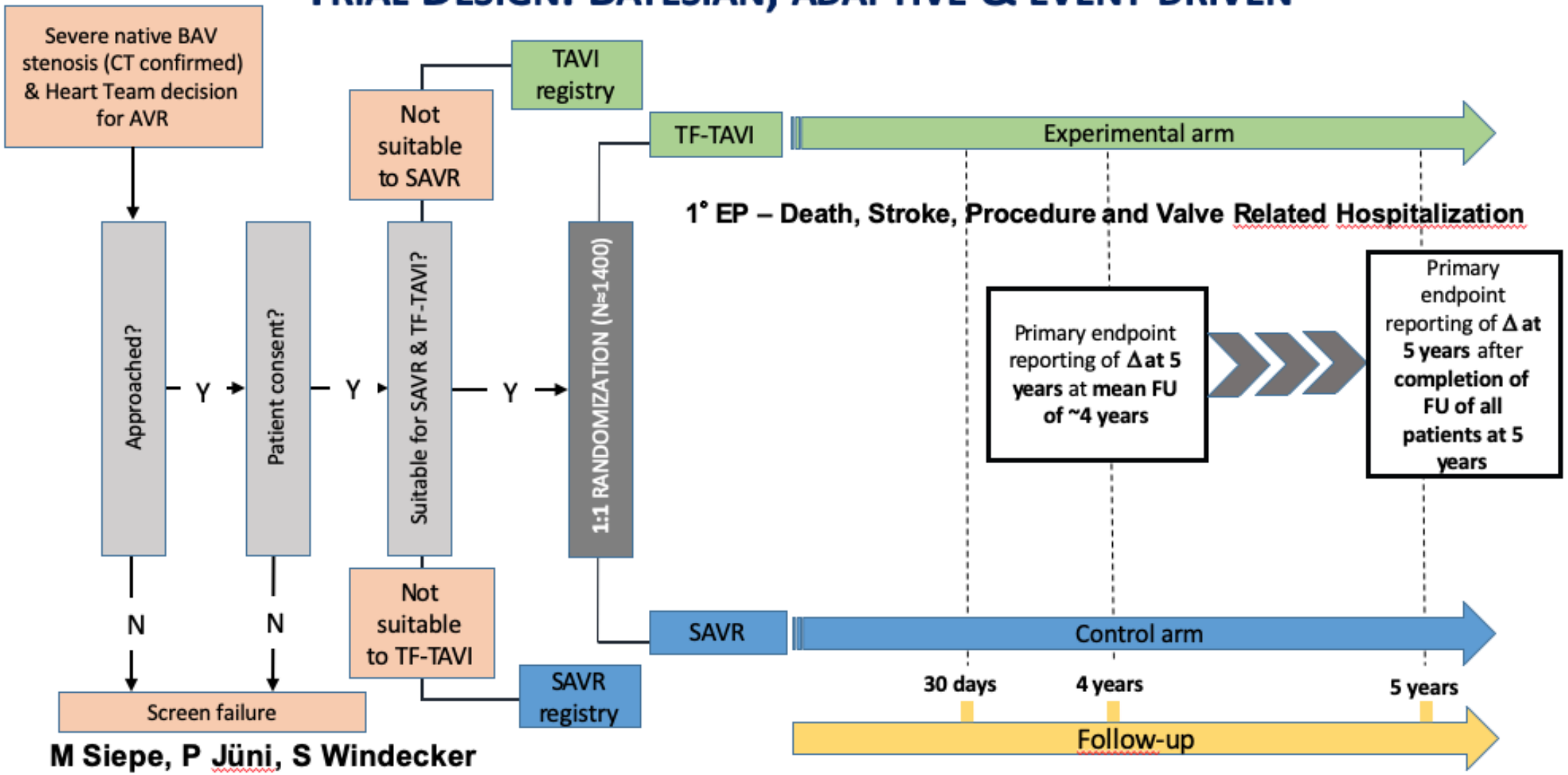
Remaining questions

- Anatomical features favorable/unfavorable for TAVI
- Optimal CT scan sizing 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

BELIEVERS Trial (PI: R.Makkar, V.Thourani)

Patients with severe *Bicuspid Aortic Valve* stenosis > 50 years old

TAVR and SAVR risk determined by committee

Permissibility of randomization will determined by the committee

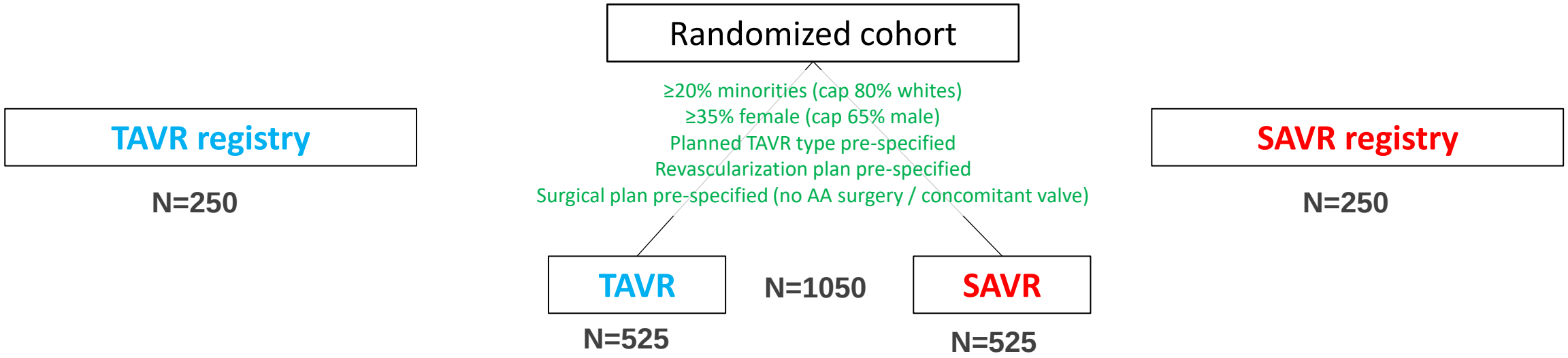
based on perceived equipoise, taking into account risk assessments

If risk assessment deemed too disparate, registry still permitted

Key exclusions for randomization:

Concomitant non coronary cardiovascular disease requiring cardiac surgery; SYNTAX≥32; AoMAX≥45mm*

(May still enter registries)



THERE IS A LOT MORE WE DONT KNOW!

- Patients with bicuspid AV are often young and may need one or more procedures during their lifetime
  - Choice of **SAVR vs TAVR as an index procedure**?
  - Plan for second and third procedures?

- Do patients who receive BAV TAVR have a higher rates of **subclinical thrombosis**?
  - Is **durability** of TAVR in bicuspid AS comparable?

- Do patients with BAV TAVR benefit from **cerebral protection**?

- How do **long term outcomes** of TAVR vs SAVR in bicuspid AS compare?

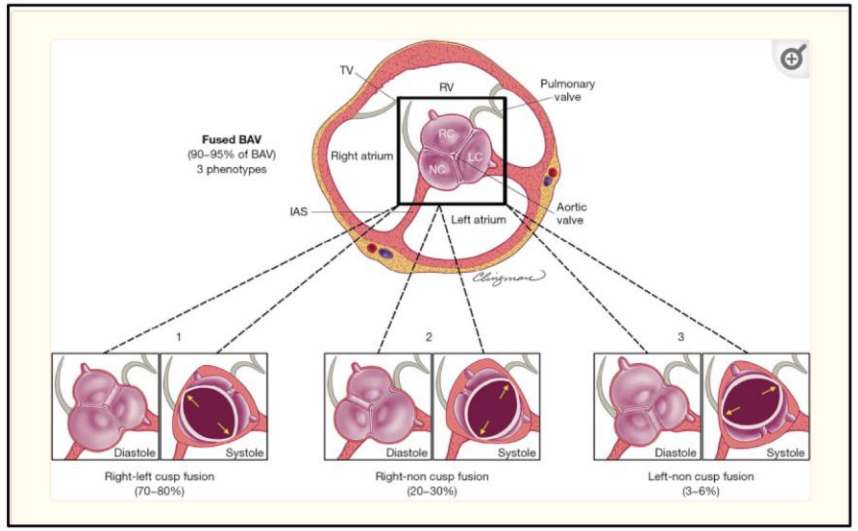
- Impact of **aortopathy** on outcomes after TAVR?

- Choice of **THV prothesis** in BAV TAVR?

- ***Optimal sizing methodology for BAV TAVR***

- ***Is Sievers classification still up to date***

ALTERNATIVE CLASSIFICATION OF BICUSPID VALVE DISEASE!



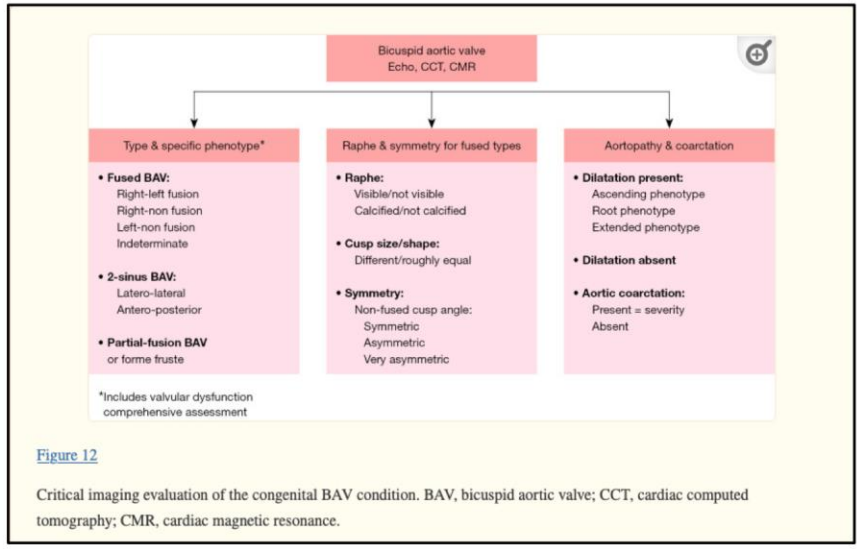
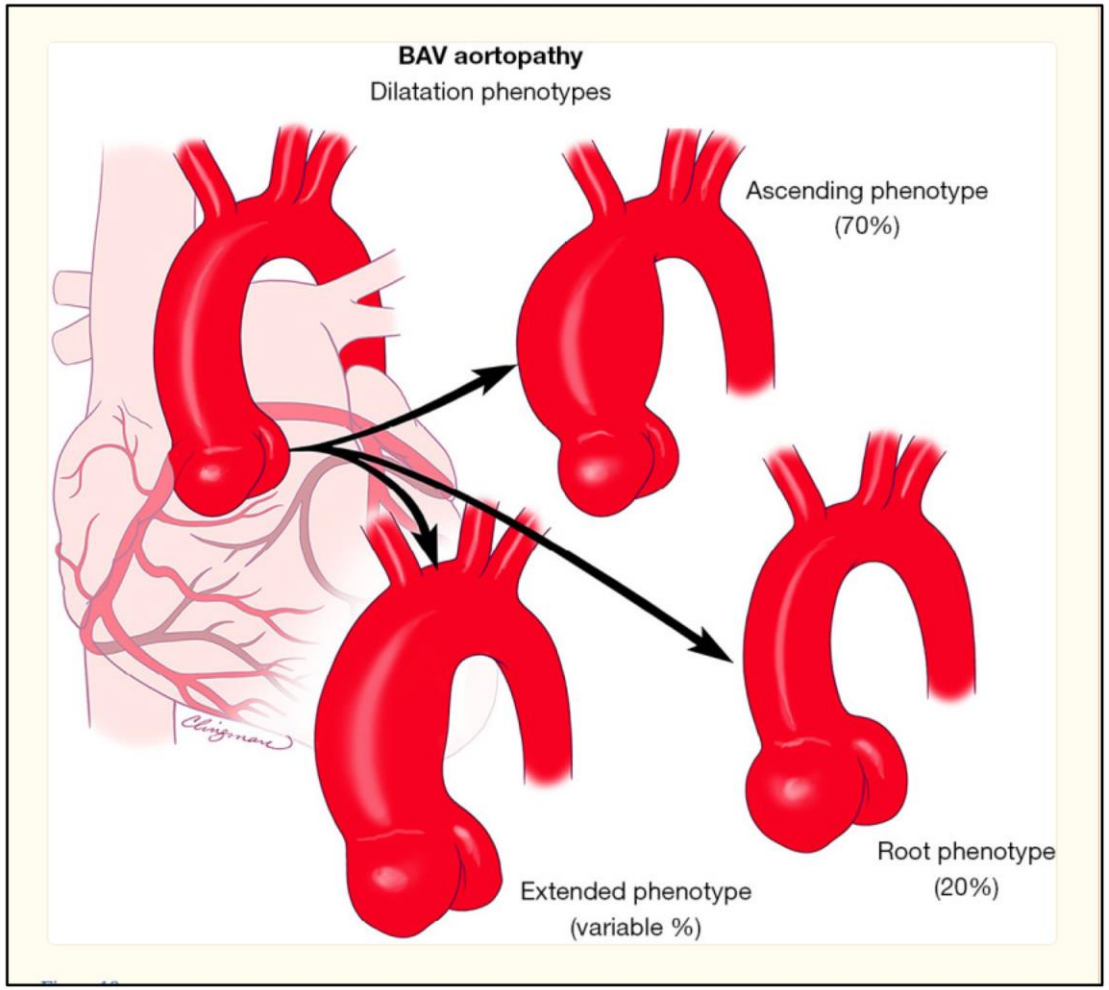


Figure 12

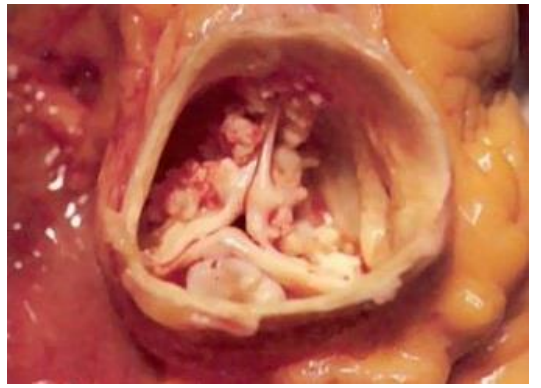
Critical imaging evaluation of the congenital BAV condition. BAV, bicuspid aortic valve; CCT, cardiac computed tomography; CMR, cardiac magnetic resonance.



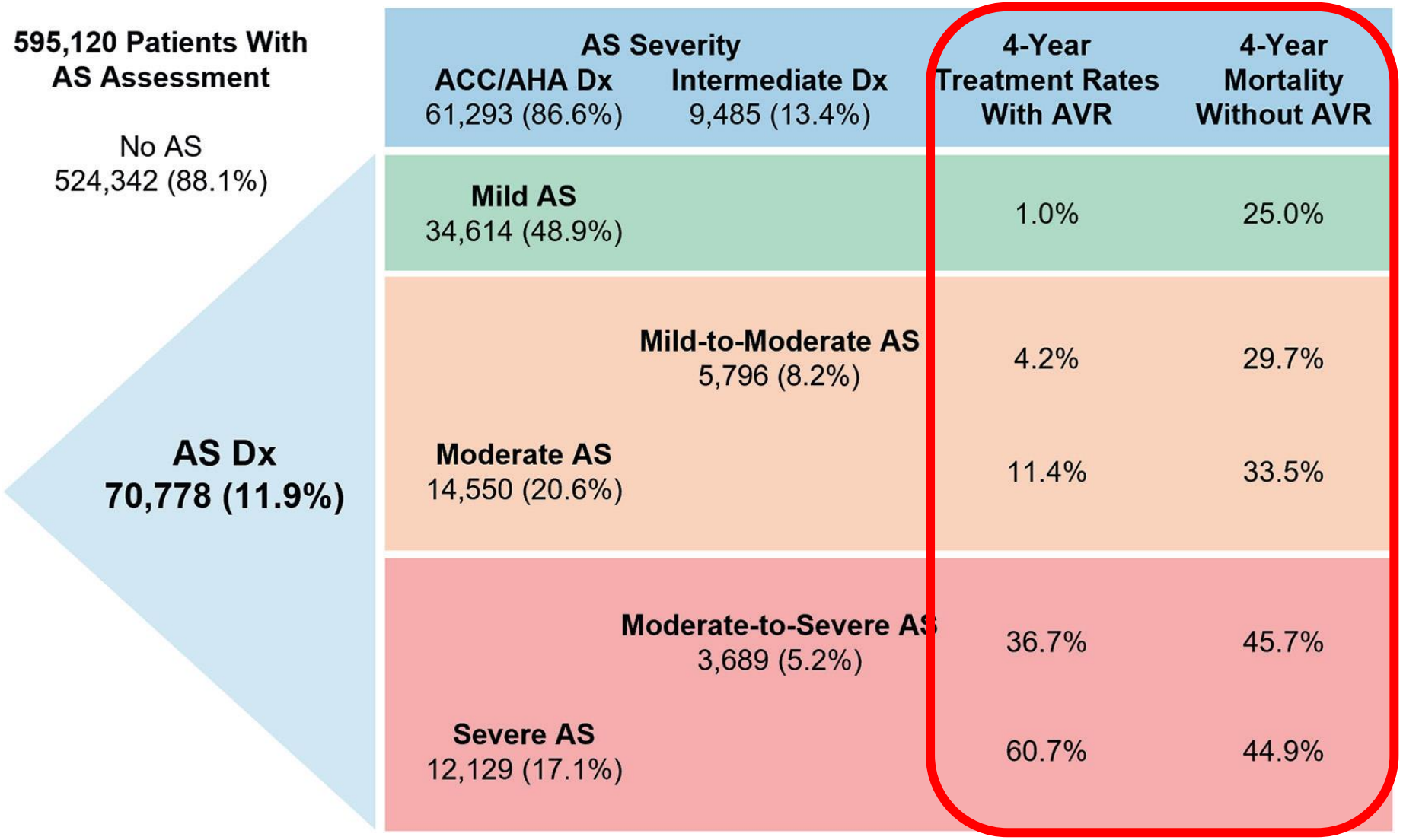
Michelena et al, J Thorac Cardiovasc Surh, 2021

The Conundrum of Asymptomatic and Moderate Aortic Stenosis,

And Why are we targeting them?



TAVR NEXT STEPS I MORTALITY IN UNTREATED AS



Généreux P, et al. J Am Coll Cardiol. 2023

CURRENT TREATMENT PARADIGM FOR MODERATE AORTIC STENOSIS

WATCHFUL WAITING IS INGRAINED IN CLINICAL PRACTICE

Current Guidelines

- Clinical and echo follow-up every 1-2 years for progression of AS, and medical therapy for hypertension and other cardiovascular conditions[1-3]
- AVR may be considered for patients undergoing cardiac surgery for another reason (IIb)

Issues with watchful waiting for moderate AS

- Rate of stenosis progression is highly variable[1,2]
- Moderate AS has been associated with significant cardiovascular events and mortality in observational studies.[4,5]
- Waiting for AS to progress to severe before intervening may result in irreversible cardiac damage and worse prognosis even with AVR[6]

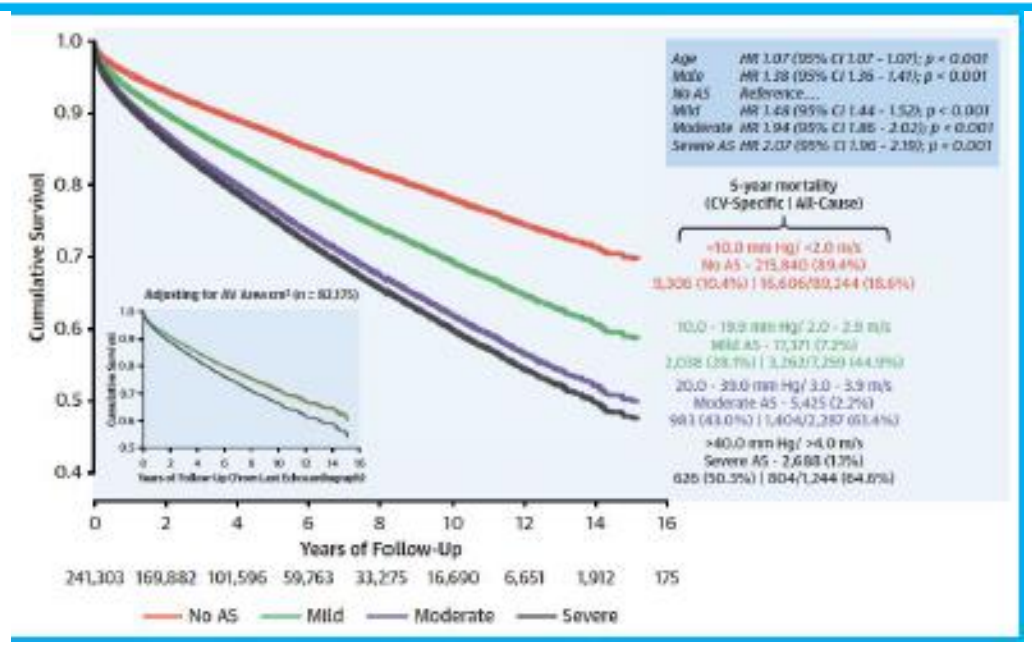
- [1] Nishimura RA, et al. J Am Coll Cardiol. 2017
- [2] Vahanian A, et al. Eur Heart J. 2022
- [3] Izumi C, et al. Circ J. 2020
- [4] Strange, G, et al. J Am Coll Cardiol. 2019
- [5] Coisne A et al. J Am Coll Cardiol 2022
- [6] Généreux P et al. J AM Cardiol. 2022

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,[a] Simon Stewart, PhD,[b] David Celermajer, MD, PhD,[c] David Prior, MBBS, PhD,[d] Gregory M. Scalia, MBBS (Hons), MMedSc,[e] Thomas Marwick, MBBS, PhD,[f] Marcus Ilton, MD,[g] Majo Joseph, MBBS,[h] Jim Codde, PhD,[i] David Playford, MBBS, PhD,[a] on behalf of the National Echocardiography Database of Australia contributing sites



Why?

-Misclassificatio

-Challen

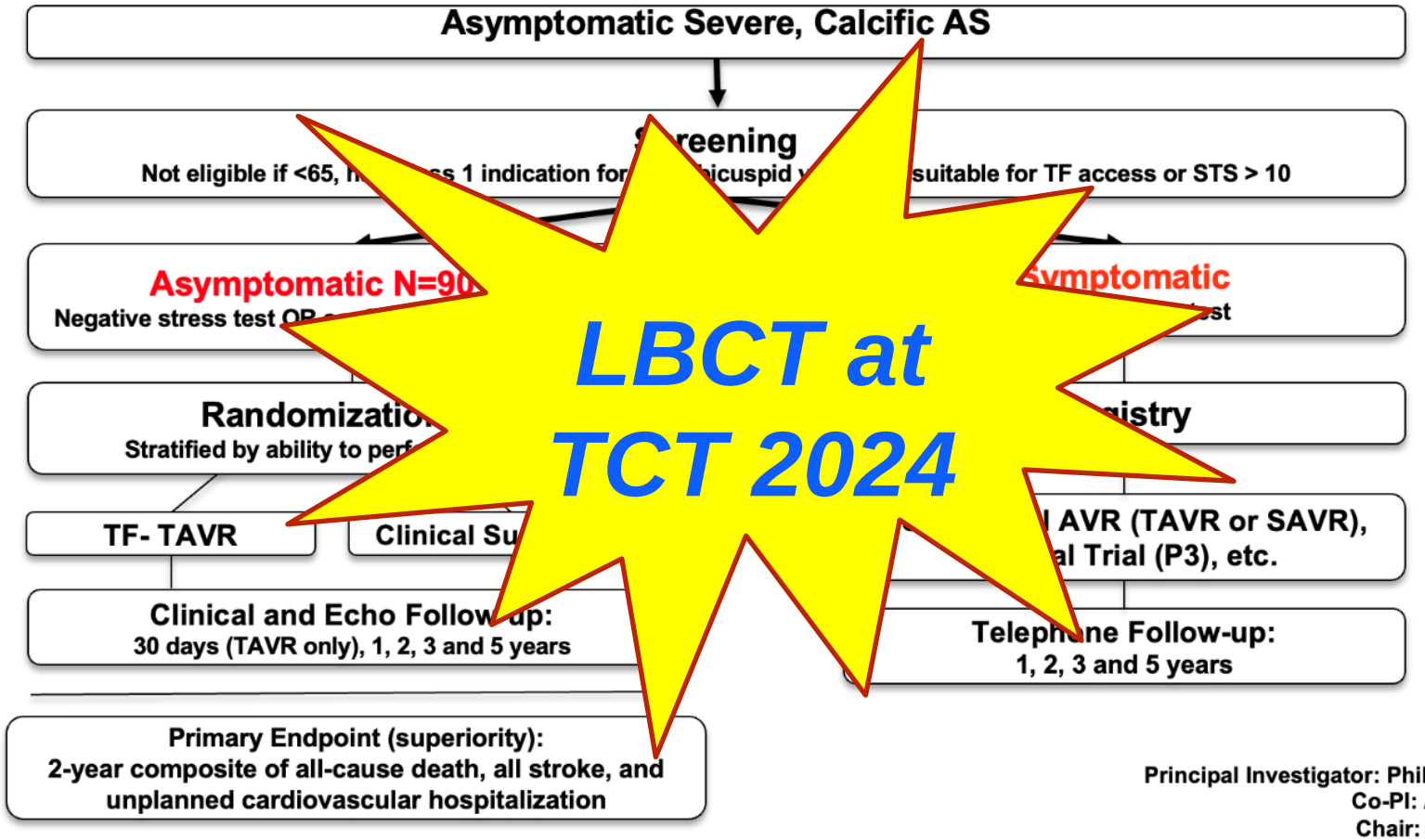
-Rapi

-To

Moderate AS is NOT a Benign Disease!

Upcoming trials for Asymptomatic and Moderate Aortic Stenosis

THE EARLY TAVR TRIAL



- ~90% Stress test
- TAVR only
- Biobank/Biomarkers
- TTE and CT Core Lab
- 10y FU

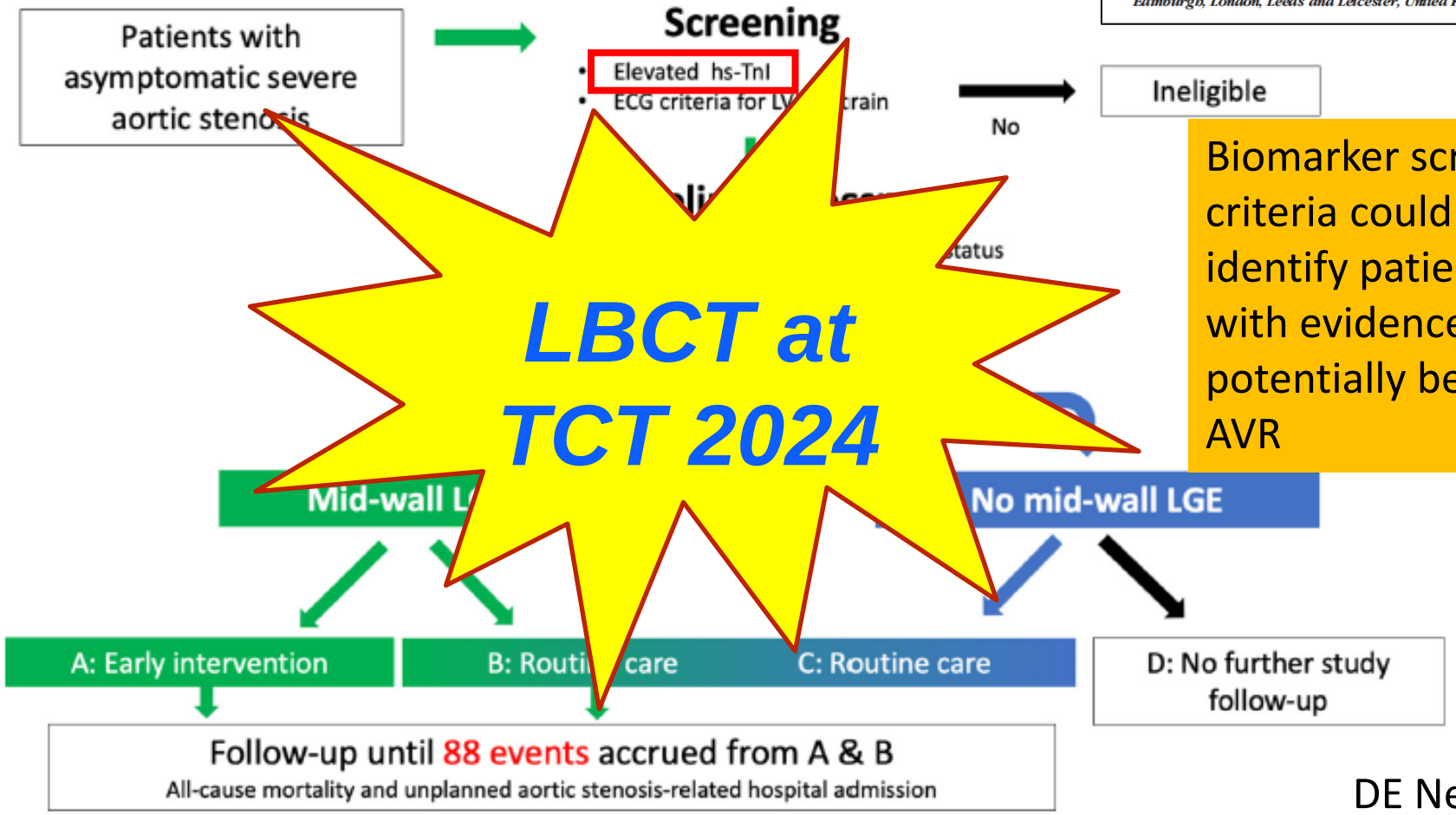
Principal Investigator: Philippe Généreux, MD
Co-PI: Allan Schwartz, MD
Chair: Martin B. Leon, MD

EVOLVED Trial (earlier AVR)

Biomarker screening

Rationale and design of the randomized, controlled Early Valve Replacement Guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe Aortic Stenosis (EVOLVED) trial

Rong Bing, [a,1] Russell J. Everett, [a,1] Christopher Tuck, [b] Scott Semple, [a] Steff Lewis, [b] Ronnie Harkess, [b] Nicholas L. Mills, [a] Thomas A. Treibel, [c] Sanjay Prasad, [d] John P. Greenwood, [e] Gerry P. McCann, [f] David E. Newby, [a] and Marc R. Dweck, [a]
Edinburgh, London, Leeds and Leicester, United Kingdom



LBCT at TCT 2024

Biomarker screening/inclusion criteria could be an important tool to identify patients with less severe AS with evidence of LV damage/injury potentially benefitting from earlier AVR

DE Newby and MR Dweck

Bing R et al. Am Heart J 2019

TRANSCATHETER AVR TRIALS IN MODERATE AORTIC STENOSIS

TAVR-UNLOAD (n=300)

Pri n

ar

PROGRESS (n=450-750)

FPI
Q4 ‘21

EXPAND II (n=650)

FPI
Q1 ‘22

TAVR vs. no TAVR

Mortality, adverse heart failure endpoints

Potential new treatment pathways

In TODAY'S FAST CHANGING TURBULENT WORLD, IT IS HARD TO PREDICT THE NEXT YEAR, NOT TO SPEAK ABOUT TEN YEARS…

However, The future of Medicine and specifically of Structural Heart is not something to predict, It is something to build..

This very year at the 22nd anniversary of TAVR, we can look back with pride and astonishment and implement the experience we built to the existing unmet needs, driving innovative therapeutic solutions forward