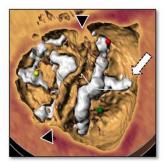


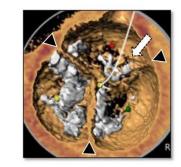
Update in TAVR for Bicuspid Aortic Valve Stenosis



Interventional Cardiology/ Structural Heart Disease Jackson Memorial Health System University of Miami Miller School of Medicine

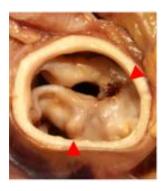


















DISCLOSURE

Camilo Gomez, MD

No relevant financial relationship reported





TAVR for Bicuspid Aortic Valve Stenosis Objectives

- Review Bicuspid Aortic Valve (BAV) anatomy and challenges for TAVR
- Discuss latest clinical evidence and outcomes
- Explore future directions and ongoing trials



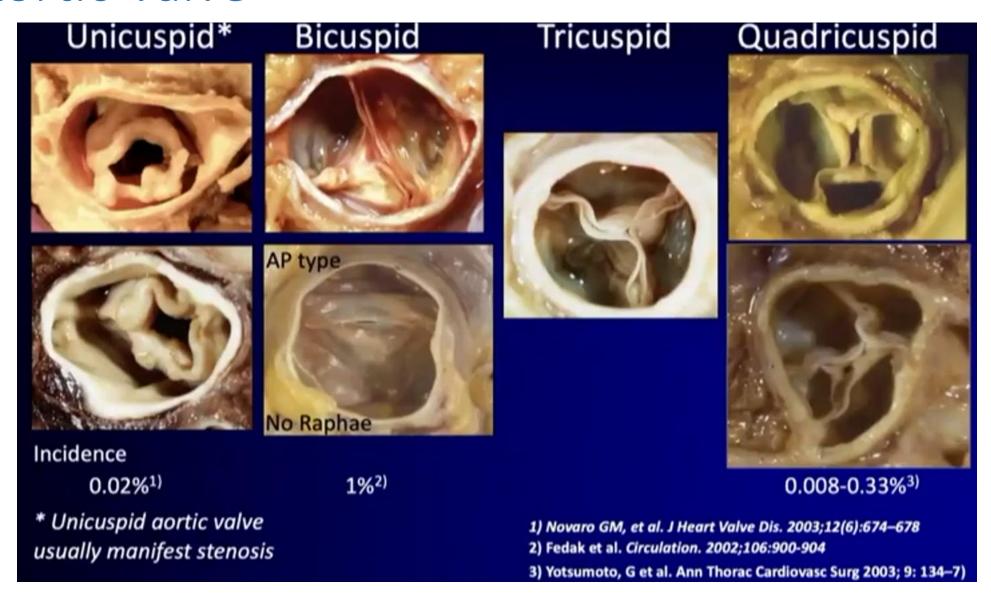


Bicuspid Aortic Valve (BAV) Stenosis- What we know





Aortic Valve



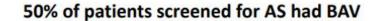
Surgically Removed Aortic Valves and their Etiology

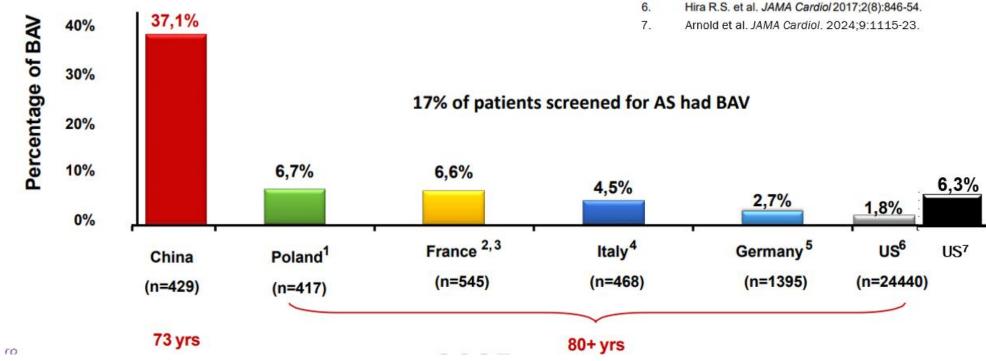
| Etiology | Mayo Clinic (1965) | University of Minnesota (1979-1983) | London (1976-1979) | Mayo Clinic (1990) | AFIP (1990-1997) | Toronto (2008) |
|---------------------------|-----------------------|---|-----------------------|-----------------------|---------------------|-------------------|
| Bicuspid | 49% | 49% | 56% | 36% | 30% | 32% |
| Post-rheumatic | 33% | 23% | 24% | 9% | 13% | 11% |
| Tricuspid degenerative | 0% | 28% | 12% | 51% | 49% | 64% |
| Unicuspid | 10% | 1% | 0% | 0% | 6% | 3% |
| Other | 7% | 0% | 8% | 2% | 2% | 1% |





Prevalence of BAV in the TAVR Population







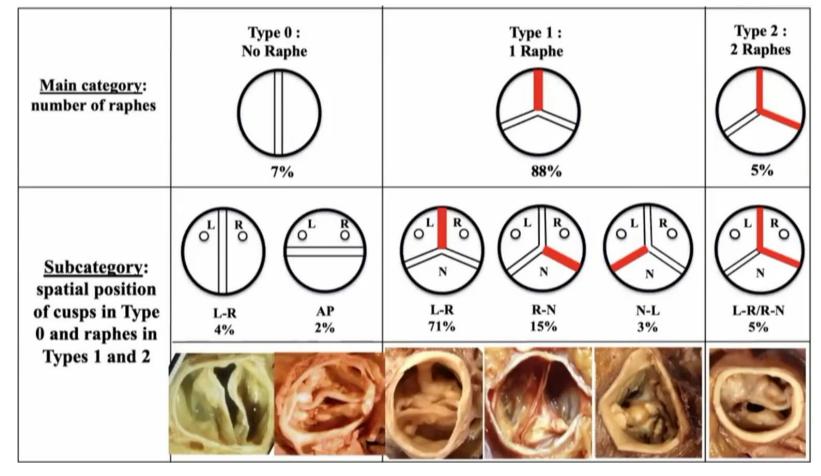
Mao Chen. PCR. 2022 Modified June 2025 Kleiman N NY Valves 2025

Kochman J. et al. *Am J Cardiol* 2014;114(5):757-62. Himbert D. et al. *Am J Cardiol* 2012;110(6):877-83. Hayashida K. et al. *Circ CV Interv* 2013;6(3):284-91.

Costopoulos C. et al. Am J Cardiol 2014;113(8):1390-3. Bauer T.et al. Am J Cardiol 2014;113(3):518-21.



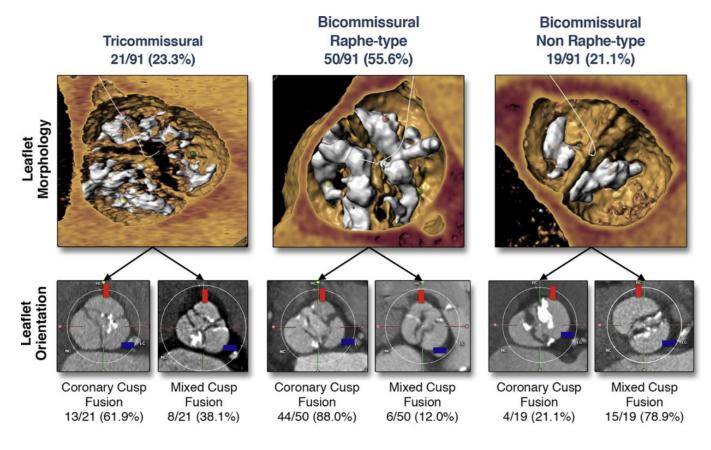
Bicuspid Aortic Valve (BAV) Anatomy - Sievers



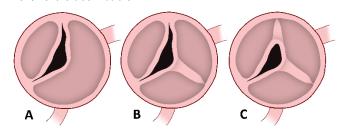




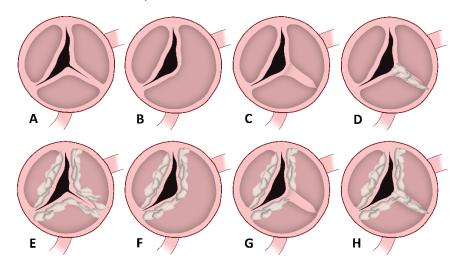
CT Derived Classification



I. Sievers classification



II. TAVR-directed bicuspid aortic valve CT classification



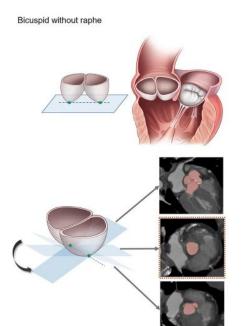
Jilaihawi et al (computed tomography [CT]-derived) classification

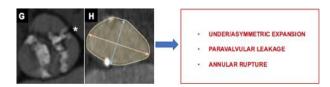


N Van Mieghem. Mastering Structural Heart Disease 2023

TAVR Challenges in BAV Anatomy

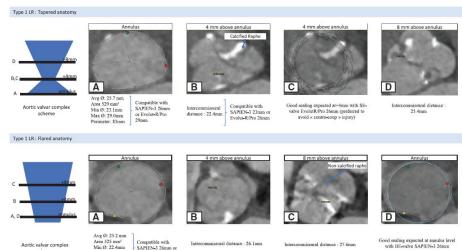
- 1. Dimensions of the AV complex (Larger)
 - Annulus Area 521±21 mm² vs 463±20 mm²
 - Ascending Aorta 36.7±5.4 mm² vs 30.4±3.4 mm²

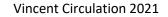




2. Geometry

- In general circular at the annulus
- Supra-annular = Elliptical
- AV complex shape (annulus to leaflets) = Nontubular (flared or tapered) in 2/3 of patients





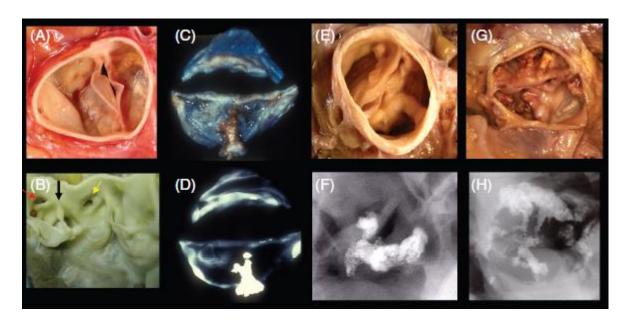
- SAPIEN-3 26mm or Evolut-R/Pro 29mm





TAVR Challenges in BAV Anatomy

• 3. Heavily Calcification

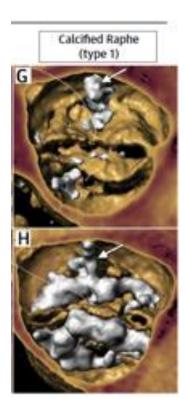


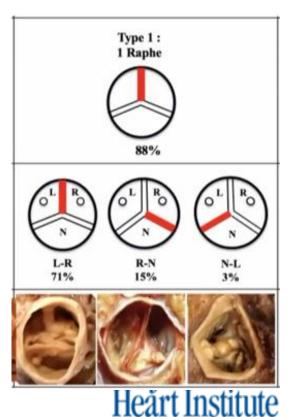
Y Sato, R Virmani CV Path Institute Mastering Structural Heart Disease 2023



• 4. Calcified raphe

- Plus Asymmetrical morphology AV complex
- May prevent optimal expansion of THV
- <u>L-R Cusp</u> → Conduction disturbances (Compression force contralateral stent frame towards NC)

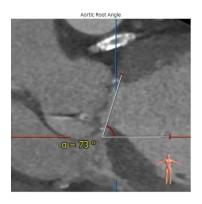


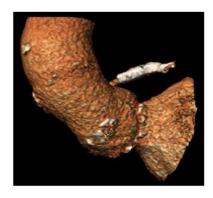


TAVR Challenges in BAV Anatomy

5. Horizontal Aorta

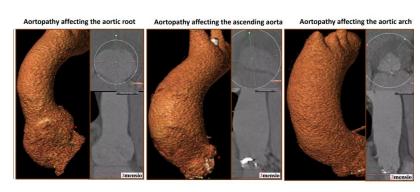
 Difficulties crossing and positioning of the THV within a vertical annulus.







- Shorter membranous septum length => Conduction disorders
- 6. Coronaries
 - Coronary anomalies (L dominance, separate ostia)
 - Coronary ostia close proximity to the commissure (But coronary high is similar or higher than TAV)
- 7. Concomitant Aortopathy
 - Cannot be addressed by TAVR



Makkar Euro PCR 2024



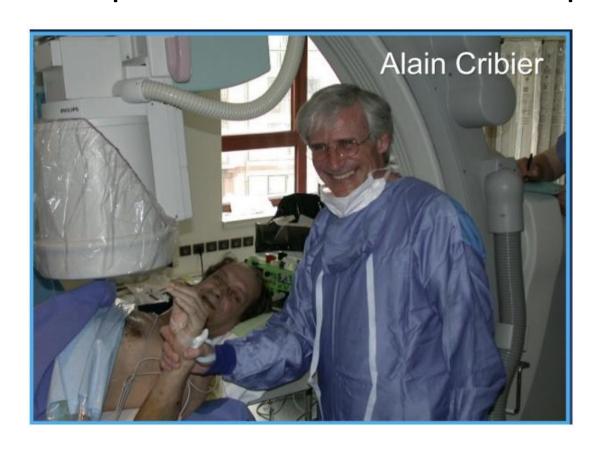


Clinical Evidence and Outcomes





First-in-man TAVR was performed in a Bicuspid Aortic Valve – April 16, 2002



57 yo man in cardiogenic shock, AVA 0.6, EF 15%

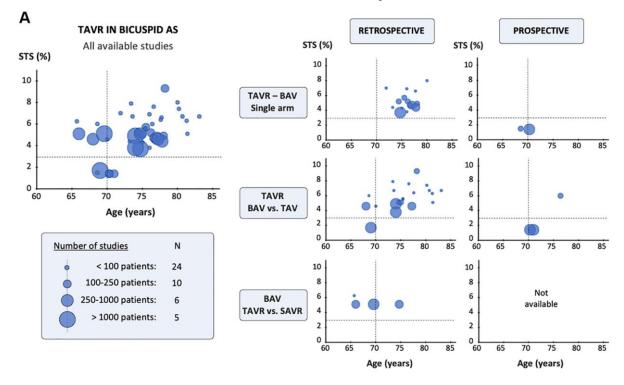


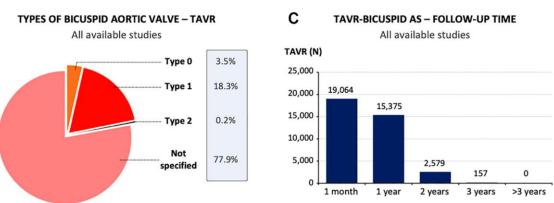


Current Evidence on TAVR on Bicuspid AS

В

- No large prospective studies
- No RCTs BAV excluded from all pivotal RCTs
- No long term follow up
- Bicuspid morphology type rarely examined









TAVR in Bicuspid Aortic Valve – *Recent Data*

| Study / Registry | N | Population | Key Findings | Implications | |
|---------------------------------------|---------------|-----------------------------|---|---|--|
| Evolut Low-Risk BAV Substudy | 150 | Low-risk BAV | 30d mortality 0.7%, stroke 1.4%, PVL 0%, pacemaker 14% | Excellent short-term safety in selected BAV | |
| LRT Bicuspid Trial | 61 | Low-risk BAV | 30d mortality 1.6%, stroke 0%, PVL 3.3%, pacemaker 11.5% | Safe and feasible in selected BAV with favorable anatomy | |
| STS/ACC TVT Registry (2023) | >20,000 | All-risk BAV | Comparable mortality to tricuspid; \downarrow PVL with newer valves, \uparrow PPI | Outcomes improving with experience and newer devices | |
| TriNetX Registry (2024) | ~12,000 | Matched TAVR vs SAVR in BAV | TAVR associated with 2x ↑ mortality and ↑ HF over ~2 years | Suggests SAVR superiority in BAV for long-term outcomes | |
| NOTION-2 (2024) RCT | ~90 (26% BAV) | Low-risk ≤75 yrs | Higher event rate 14.3% events with TAVR vs 3.9% SAVR (HR ~3.8, p=0.07) | Trend toward worse outcomes with TAVR in BAV; not statistically significant | |
| Meta-analysis – Yu et al. (2023) | 14,000+ | BAV vs tricuspid TAVR | No mortality/stroke difference; 个 PPI , 个 AKI in BAV | Acceptable short-term safety, but procedural risks slightly higher | |
| Meta-analysis – Zhou et al. (2023) | >200,000 | Pooled BAV data | ↑ 30d mortality (OR 1.23), ↑ stroke (OR 1.39), ↓ mortality with new-gen valves | New-generation devices improve outcomes, but risk persists | |
| Medicare Data (2018–2022) | 11,289 | BAV patients | Lower in-hospital mortality with TAVR; but worse long-term mortality/stroke | Early advantage, but long-term caution in younger BAV patients | |
| Low-risk cohort study (2024) | N/A | Matched BAV vs SAVR | No difference in composite (death/stroke/readmission); better hemodynamics with TAVR | Suggest TAVR is viable in carefully selected low-risk BAV | |
| Durability Study (2023) | ~5-year FU | BAV vs tricuspid TAVR | No significant difference in structural valve deterioration or valve failure | TAVR in BAV may have acceptable mid-term durability | |



ily

Comparative data on TAVR vs SAVR in BAV: A tale of two (STS and TVT) registries

RICHARD E. CLARK MEMORIAL PAPER FOR ADULT CARDIAC SURGERY

Benchmarking Outcomes of Surgical Aortic Valve Replacement in Patients With Bicuspid Aortic Valves



Sameer A. Hirji, MD, MPH, ¹ Zachary Wegermann, MD, ² Sreekanth Vemulapalli, MD, ² Paige Newell, MD, ¹ Maria Grau-Sepulveda, MD, ² Sean O'Brien, PhD, ² Vinod H. Thourani, MD, ³ Vinay Badhwar, MD, ⁴ and Tsuyoshi Kaneko, MD⁵

| Age (mean) | 70 years |
|---------------------|----------|
| STS Score (mean) | 1.28 % |
| NYHA Class III/IV | 18.8 % |
| 30-day Mortality | 1.3 % |
| 30-day Stroke | 1.2 % |
| 1-year Mortality | 3.2 % |
| Permanent pacemaker | 5.8% |

| Permanent pacemaker | 5.8% | | |
|--|--------|--|--|
| New-onset atrial fibrillation | 36.6 % | | |
| Acute Renal Failure | 1.1 % | | |
| Reoperation for bleeding or redo valve | 3.4% | | |

JAMA | Original Investigation

Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke Among Patients at Low Surgical Risk

Raj R. Makkar, MD; Sung-Han Yoon, MD; Tarun Chakravarty, MD; Samir R. Kapadia, MD; Amar Krishnaswamy, MD; Pinak B. Shah, MD; Tsuyoshi Kaneko, MD; Eric R. Skipper, MD; Michael Rinaldi, MD; Vasilis Babaliaros, MD; Sreekanth Vemulapalli, MD; Alfredo Trento, MD; Wen Cheng, MD; Susheel Kodali, MD; Michael J. Mack, MD; Martin B. Leon, MD; Vinod H. Thourani, MD

| Age (mean) | 69 | | | |
|-------------------------------|--------|--|--|--|
| STS Score (mean) | 1.7 | | | |
| NYHA Class III/IV | 55.1 % | | | |
| 30-day Mortality | 0.9 % | | | |
| 30-day Stroke | 1.4 % | | | |
| 1-year Mortality | 4.6 % | | | |
| Permanent pacemaker | 6.2% | | | |
| New-onset atrial fibrillation | 1.0% | | | |
| New Dialysis Requirement | 0.1 % | | | |
| | | | | |

0.1%

Need for second valve



Evolut Low Risk Bicuspid Study- 5 Year Results

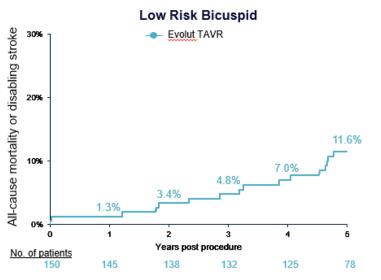
222 Patients screened Bicuspid valve and AVA < 1.0 cm² or gradient > 40 mm STS PROM < 3.0 Potentially suitable for TAVR

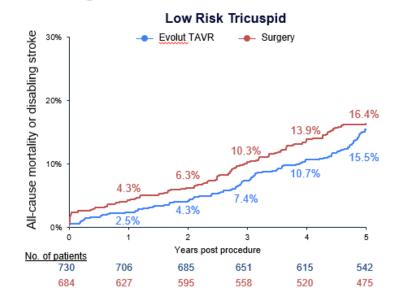
150 Enrolled

60 Excluded

- 17 Had tricuspid valve
- 15 Annular dimension
- 5 STS risk > Low
- 5 Ascending aorta > 45 mm
- 4 SOV diameter
- 2 LVOT calcification
- 5 Other non-anatomic

All-cause mortality or disabling stroke



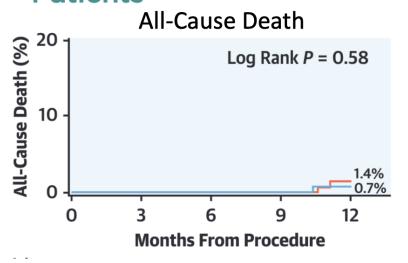


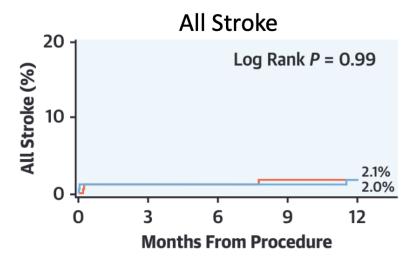


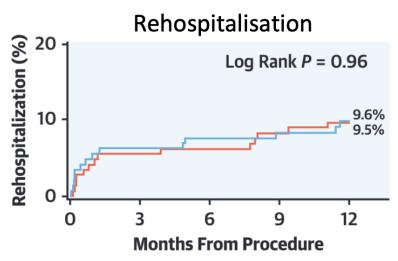


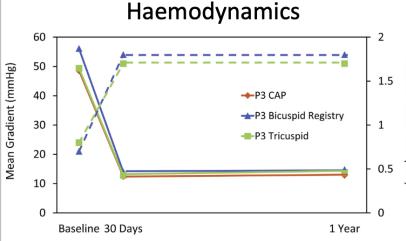
The PARTNER 3 Bicuspid Registry for Transcatheter Aortic Valve Replacement in Low-Surgical-Risk Patients

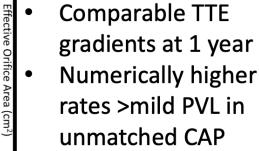
Tricuspid vs. Bicuspid TAVR comparison in 148 PM pairs from PARTNER 3 trial and PARTNER 3 BAV Registry

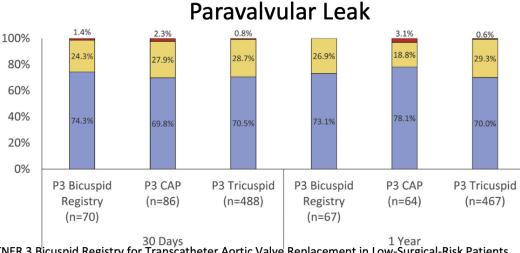










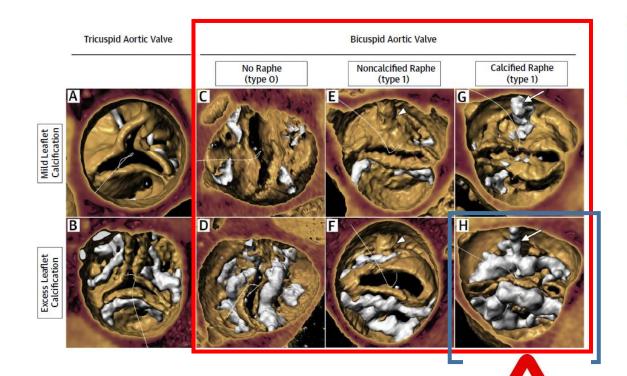


Mathew R. Williams, et al The PARTNER 3 Bicuspid Registry for Transcatheter Aortic Valve Replacement in Low-Surgical-Risk Patients

JACC: Cardiovascular Interventions, Volume 15, Issue 5, 14 March 2022, Pages 523-532

Impact of Bicuspid Phenotype







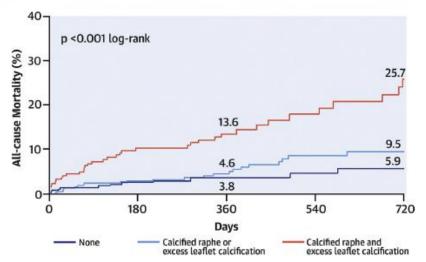
No Calcified Raphe or Excess Leaflet Calcification (31.3%)





Calcified Raphe Plus Excess Leaflet Calcification (26.0 %)



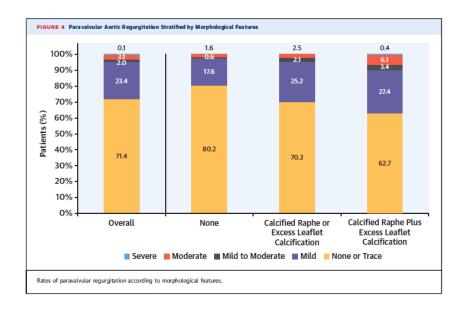






Impact of Bicuspid Phenotype

PVL



| | | mor priorogreat reatures | | | | | |
|---|-----------------------------------|--------------------------|--|--|---------|--|--|
| | Overall (N = 1,034) | None (n = 324) | Calcified Raphe or Excess Leaflet Calc (n = 441) | Calcified Raphe Plus Excess Leaflet Calc (n = 269) | p Value | | |
| Procedural outcomes | | | | | | | |
| Conversion to surgery | 9 (0.9) | 1 (0.3) | 2 (0.5) | 6 (2.2) | 0.028 | | |
| Coronary obstruction | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | _ | | |
| Aortic root injury | 18 (1.7) | 3 (0.9) | 3 (0.7) | 12 (4.5) | < 0.001 | | |
| Implantation of second valve | 14 (1.4) | 4 (1.2) | 3 (0.7) | 7 (2.6) | 0.10 | | |
| Echocardiographic findings | | | | | | | |
| Aortic valve gradient, mm Hg | 10.6 ± 5.0 | 10.8 ± 5.4 | 10.4 ± 4.3 | 10.9 ± 5.6 | 0.37 | | |
| Effective orifice area, cm ² | 1.7 ± 0.5 | 1.7 ± 0.4 | 1.7 ± 0.5 | 1.8 ± 0.5 | 0.053 | | |
| LVEF, % | $\textbf{56.3} \pm \textbf{14.0}$ | 59.0 ± 13.3 | 55.3 ± 14.1 | 54.5 ± 14.4 | < 0.00 | | |
| Paravalvular regurgitation ≥mild* | 291 (28.6) | 63 (19.8) | 130 (29.7) | 98 (37.3) | < 0.00 | | |
| Paravalvular regurgitation ≥moderate* | 33 (3.2) | 5 (1.6) | 11 (2.5) | 17 (6.5) | 0.002 | | |
| Clinical outcomes | | | | | _ | | |
| Death at 30 days | | | | | | | |
| From any cause | 21 (2.0) | 5 (1.5) | 5 (1.1) | 11 (4.1) | 0.016 | | |
| From cardiac cause | 17 (1.6) | 4 (1.2) | 3 (0.7) | 10 (3.7) | 0.009 | | |
| Death at 1 yr | | | | | | | |
| From any cause | 55 (6.7) | 10 (3.8) | 16 (4.6) | 29 (13.6) | < 0.00 | | |
| From cardiac cause | 33 (3.9) | 6 (2.2) | 6 (2.7) | 21 (9.6) | < 0.00 | | |
| Death at 2 yrs | | | | | | | |
| From any cause | 74 (12.5) | 12 (5.9) | 24 (9.5) | 38 (25.7) | < 0.00 | | |
| From cardiac cause | 40 (5.9) | 6 (2.2) | 9 (3.6) | 25 (14.4) | < 0.001 | | |
| Stroke | 28 (2.7) | 9 (2.8) | 12 (2.7) | 7 (2.6) | >0.99 | | |
| Major vascular complication | 34 (3.3) | 8 (2.5) | 12 (2.7) | 14 (5.2) | 0.12 | | |
| Bleeding (life-threatening or major) | 37 (3.6) | 10 (3.1) | 14 (3.2) | 13 (4.9) | 0.46 | | |
| Acute kidney injury (stage 2 or 3) | 20 (1.9) | 7 (2.2) | 6 (1.4) | 7 (2.6) | 0.43 | | |
| Composite endpoint | 86 (8.3) | 20 (6.2) | 28 (6.3) | 38 (14.1) | < 0.00 | | |
| Aortic valve reintervention | 5 (0.7) | 2 (0.9) | 2 (0.6) | 1 (0.4) | 0.91 | | |
| New permanent pacemaker† | 118 (12.2) | 31 (10.3) | 50 (11.9) | 37 (15.1) | 0.23 | | |

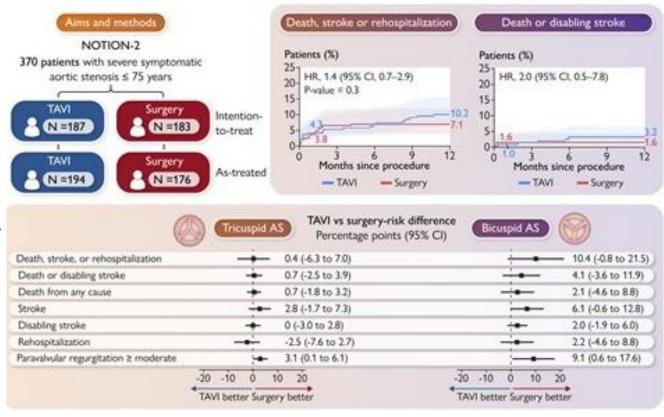
Morphological Features





Notion 2 Trial

- Low –risk pts randomized TAVR vs SAVR. ≤75 years of age with tricuspid or bicuspid AS
- N = 370 patients, median STS 1.1%
- Overall primary endpoint (death, stroke, HFH) @ 1 year: TAVI 10.2% vs. SAVR 7.1%, p = 0.3
- TAVR I risk of major bleeding & new-onset atrial fibrillation and I risk of non-disabling stroke, PPI& > mild PVL







Notion 2 Trial- Bicuspid Cohort

| Characteristic | TAVI (N = 49) | Surgery (N = 51) |
|--|------------------|---------------------|
| Age – years | 69.7±3.6 | 70.0±3.4 |
| Male sex – no. (%) | 27 (55.1) | 29 (56.9) |
| STS-PROM score – % [†] | 1.0 (0.8–1.3) | 1.1 (0.8–1.5) |
| Coronary artery disease – no. (%)^ | 6 (6.1) | 1 (2.0) |
| Previous myocardial infarction – no. (%) | 1 (2.0) | 1 (2.0) |

| Characteristic | TAVI (N = 49) |
|--|------------------|
| Implanted transcatheter aortic bioprosthesis – no. (%) | |
| Evolut R/Pro(+) | 27 (55.1) |
| SAPIEN 3 (Ultra) | 13 (26.5) |
| Portico/Navitor | 3 (6.1) |
| ACURATE neo(2) | 3 (6.1) |
| Lotus | 2 (4.1) |
| Myval | 1 (2.0) |

> Tricuspid Cohort

- →

 ↓ Systolic annular area < 500 mm2
 </p>





Notion 2 Trial- Valve Performance

1.9

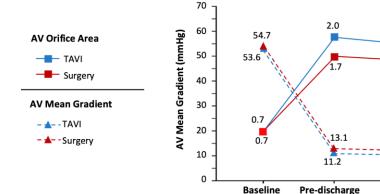
1.6

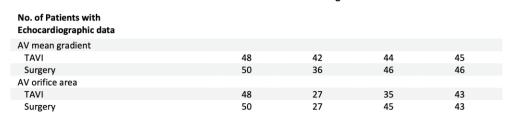
11.2

10.5

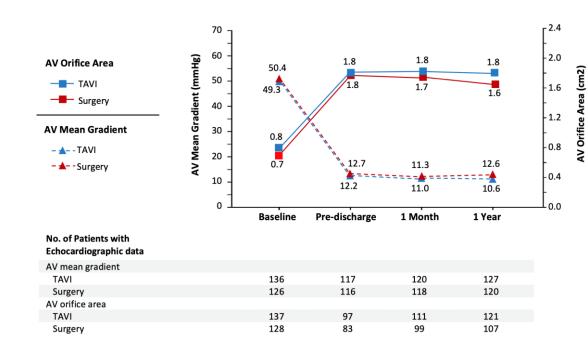
1 Month

Bicuspid Cohort





Tricuspid Cohort







- 2.0

1.6

1.2

- 0.8

- 0.4

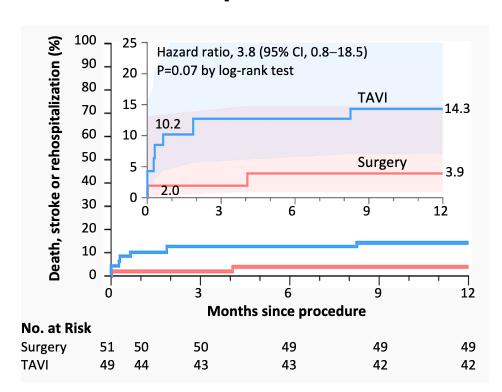
12.4

10.5

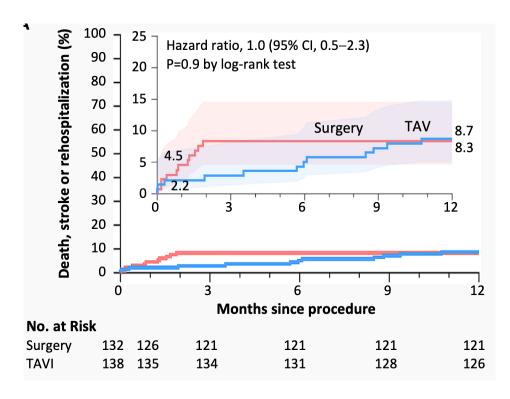
1 Year

Notion 2 Trial- Primary Endpoint

Bicuspid Cohort



Tricuspid Cohort

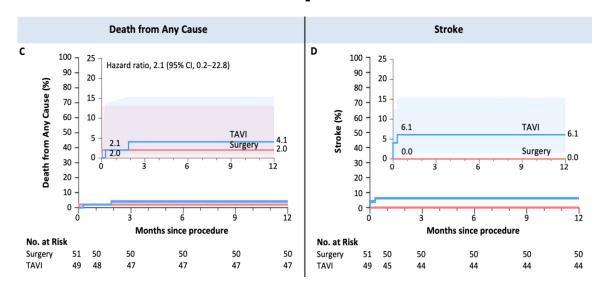




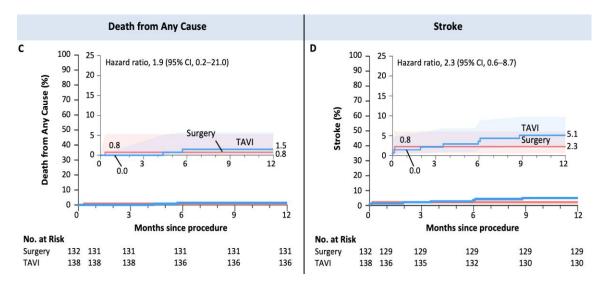
Event rate highest in bicuspid TAVR cohort & lowest in bicuspid SAVR cohort

Notion 2 Trial- Death and Stroke

Bicuspid Cohort



Tricuspid Cohort

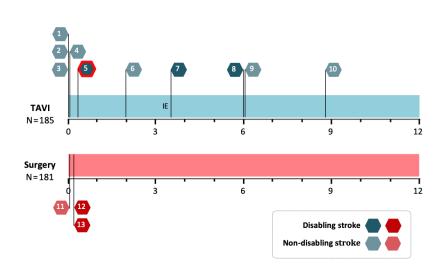


More strokes with TAVR





Notion 2 Trial- Stroke Events in Perspective



| Case | Native AV | AFib | Bio- prosthesis | CEP used | Stroke type & disability | Stroke timing | Imaging verified | Symptom resolution | Anti- thrombotics |
|---------|-------------------------|----------|--------------------|-------------|-----------------------------|------------------|---------------------|--------------------|----------------------|
| TAVI | | | | | | | | | |
| 1 | Tricuspid | Baseline | Portico | No | Ischemic, Non-disabling | Day 0 | Retino+ | Yes | DOAC |
| 2 | Bicuspid, type 1 R-L | Baseline | Evolut | No | Ischemic, Non-disabling | Day 0 | MR+ | Partial | DOAC |
| 3 (| Bicuspid, type 1 R-L | No | Evolut | No | Ischemic, Non-disabling | Day 0 | MR+ | No | SAPT |
| 4 | Tricuspid | No | Sapien | No | Ischemic, Non-disabling | Day 1 | CT+ | Yes | SAPT |
| 5 | Bicuspid, type 1 R-L | No | Sapien | No | Haemorrhagic Disabling | Day 9 | CT+ | Partial | DAPT |
| 6 | Tricuspid | No | Acurate | Yes | Ischemic, Non-disabling | Day 59 | MR+ | Yes | SAPT |
| 7 | Tricuspid | No | Acurate | No | Ischemic (IE), Disabling | Day 107 | MR+ | Died | DOAC SAPT |
| 8 | Tricuspid | No | Sapien | No | Ischemic, Disabling | Day 181 | MR+ | Partial | SAPT |
| 9 | Tricuspid | No | Acurate | Yes | Ischemic, Non-disabling | Day 185 | CT+ | Yes | DAPT |
| 10 | Tricuspid | Baseline | Portico | No | Ischemic, Non-disabling | Day 268 | MR+ | Yes | DOAC SAPT |
| Surgery | | | | | | | | | |
| 11 | Tricuspid | No | Inspiris | - | Ischemic, Non-disabling | Day 1 | CT+ | Yes | SAPT |
| 12 | Tricuspid | Baseline | Trifecta | - | Ischemic, Disabling | Day 5 | MR+ | Partial | DOAC SAPT |
| 13 | Tricuspid | No | Magna Ease | - | Ischemic, Disabling | Day 5 | CT+ | Died | SAPT |





Procedural Considerations for TAVR in BAV



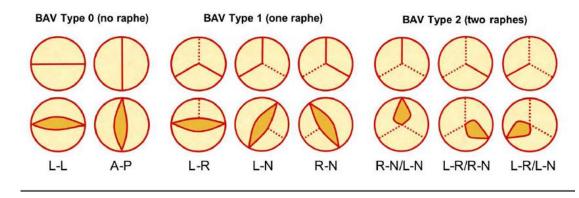


Patient selection and procedural planning are critical!

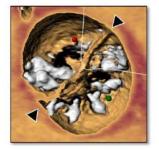




BAV Morphology Evaluation – *Identification of High Risk Anatomical Features*



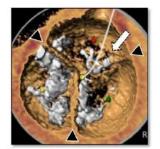
Bicommissural NON raphe-type



Bicommissural raphe-type



Tricommissural with calcific fusion



Anatomical challenges Procedural pitfalls AORTIC INJURY **AORTIC DILATATION PROGRESSION** DEVICE MALPOSITIONING CORONARY OBSTRUCTION UNDER/ASYMMETRIC EXPANSION PARAVALVULAR LEAKAGE STROKE UNDER/ASYMMETRIC EXPANSION PARAVALVULAR LEAKAGE ANNULAR RUPTURE

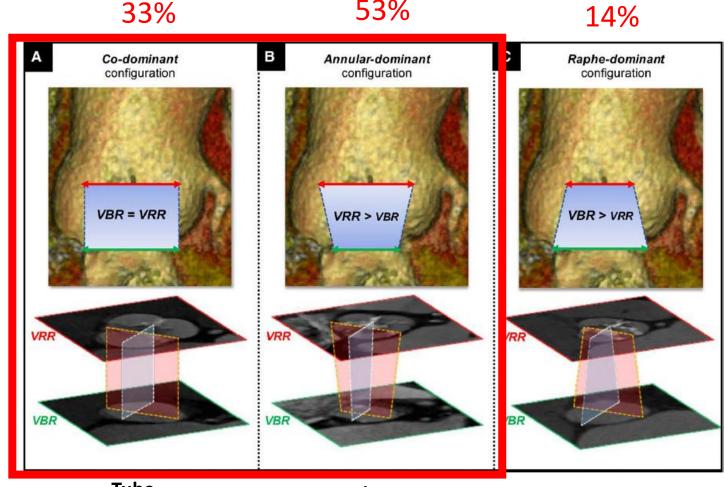






Prosthesis Size Selection

- Question 1: Is the intercommisural area the most constraining region?
- Question 2: Do we need to adjust sizing algorithms in this setting?



53%



Tube Sizing base on the annulus

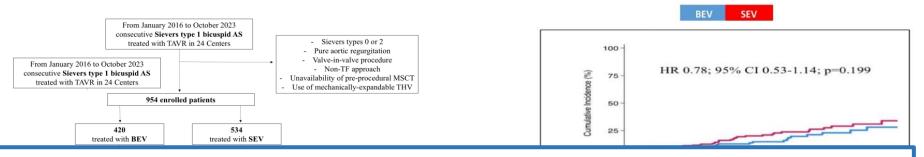
Flare Sizing base on the annulus

Taper Sizing base on the ICD



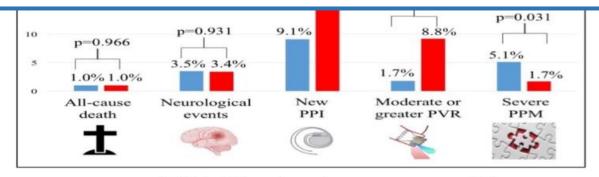


Composite of death, stroke or HF hospitalization

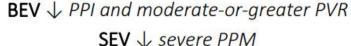


Median FU: 1.3 year BEV vs. SEV 15.7% vs 20.3%

A definitive recommendation of THF cannot be formulated!

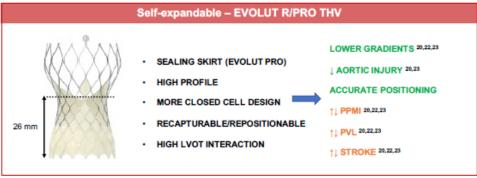


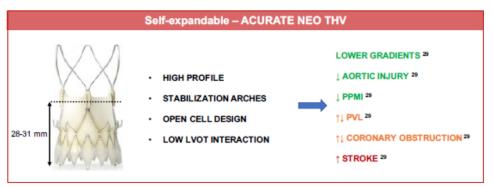


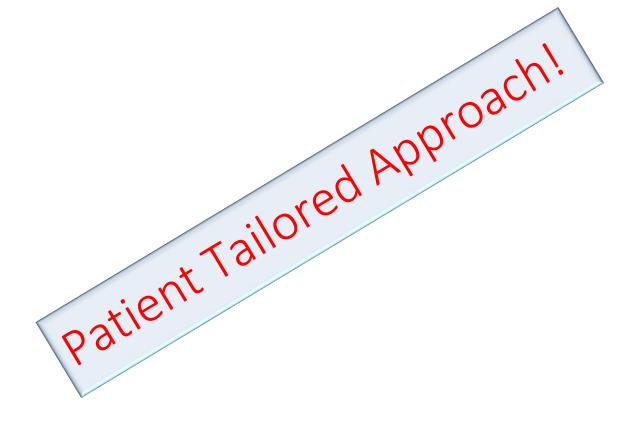


Jackson Heart Institute











DASI Simulations



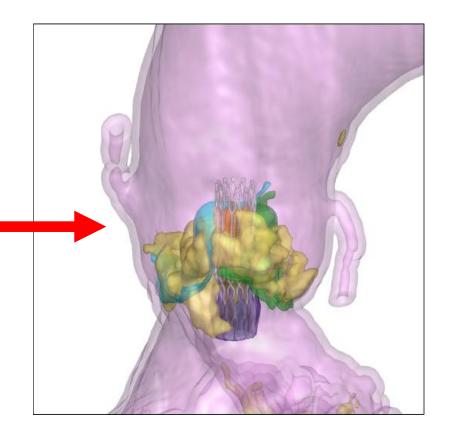
Simulations and Al-Driven Prediction Based Algorithms

Reduced Order Model (ROM)

Predicts:

1. Frame expansion

Displacement of surrounding tissues



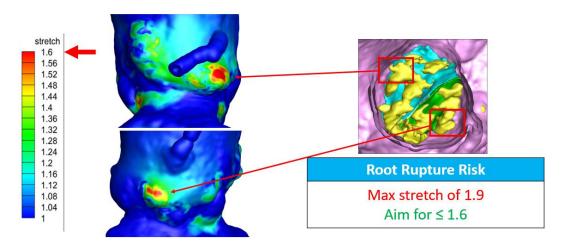








Root Rupture Risk



Coronary Obstruction Risk

| Left Coronary Ostium Diameter | | | | | |
|---|-----|--|--|--|--|
| Diameter (d) = 3.3 mm | | | | | |
| Distance from leaflet to coronary | | | | | |
| DLC = 10.2 mm | | | | | |
| Coronary Obstruction Risk Index* | | | | | |
| DLC/d = | 3.1 | | | | |
| Coronary Obstruction Risk Index Cut-off* • DLC/d < 0.7, high likelihood for Coronary Obstruction • DLC/d>0.7, low likelihood for Coronary Obstruction | | | | | |

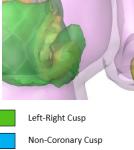
*Heitkemper M, Hatoum H, AzimianA et

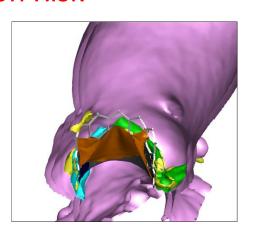
al. Modeling Risk of Coronary Obstruction During Transcatheter Aortic Valve Replacement.

J Thorac Cardiovasc Surg2020;159:829-838 e3.

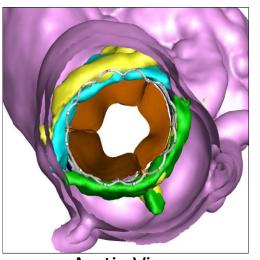
Jilaihawi NY Valves 2025

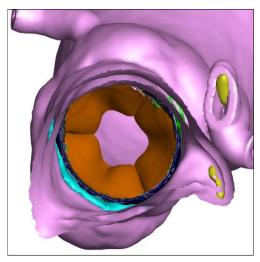






PVL Risk





Aortic View

Ventricular View

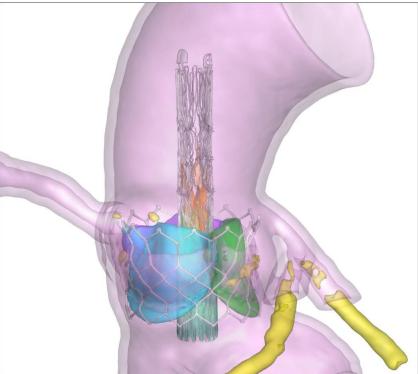
Paravalvular Leak Risk*

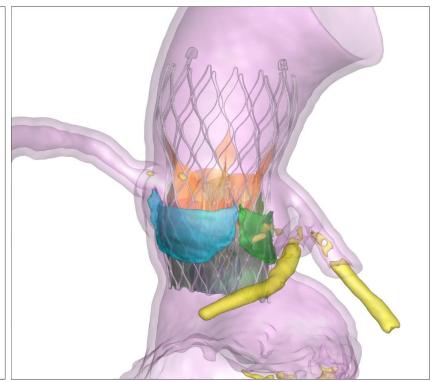
No Gap



Lifetime Management











What comes next?

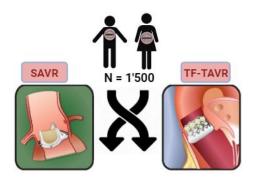




NAVIGATE BICUSPID - INVESTIGATOR INITIATED TRIAL



International, multi-center trial to evaluate the effectiveness and safety of transcatheter aortic valve intervention (TAVI) compared with surgical aortic valve replacement (SAVR) in patients with severe bicuspid aortic valve stenosis

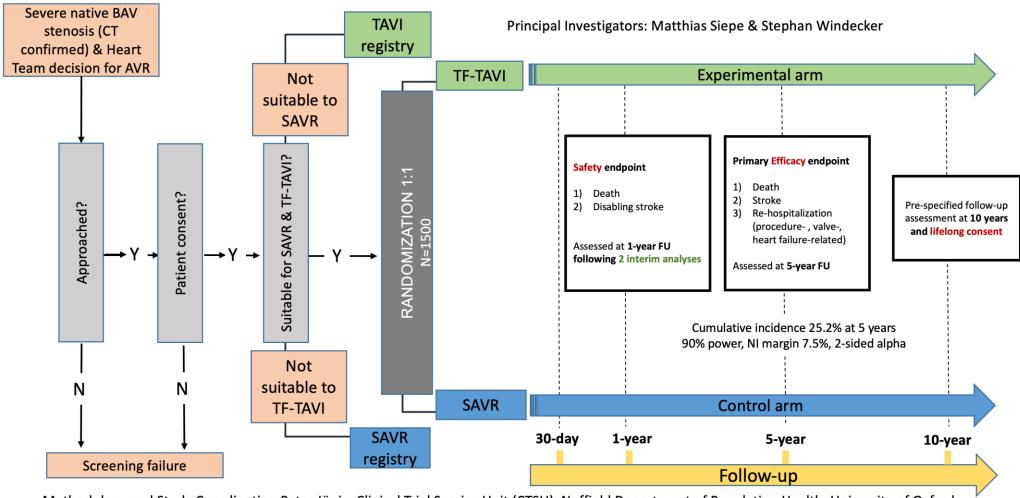






NAVIGATE BICUSPID - INVESTIGATOR INITIATED TRIAL





Methodology and Study Coordination Peter Jüni - Clinical Trial Service Unit (CTSU), Nuffield Department of Population Health, University of Oxford





BELIEVERS trial



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)

Randomized cohort

≥20% minorities (cap 80% whites) ≥35% female (cap 65% male) Planned TAVR type pre-specified Revascularization plan pre-specified

Surgical plan pre-specified (no AA surgery / concomitant valve)

TAVR

N = 525

N = 1050

SAVR

N = 525

SAVR registry

N = 250



TAVR registry

N = 250

Confidential



Conclusions

- BAV stenosis represent a complex anatomic scenario
- Unique challenges for TAVR
- Patient selection and preprocedural imaging are critical
- Advances in preprocedural imaging, AI simulations and devices will continue to improve outcomes.
- Lifetime management
- Need of RCT on
 - BAV vs TAV
 - BEV vs SEV
 - TAVR vs SAVR









Gracias!

