The Long TAVR Journey: A Chain of RCTs, Guideline Changes, and Future Directions

Martin B. Leon, MD

Columbia University/NY Presbyterian Hospital

Cardiovascular Research Foundation

New York City

26th TCTAP VIRTUAL 2021

20 mins

Cardiovascular Research Foundation

Columbia University Medical Center

NewYork-Presbyterian

Disclosures - Martin B. Leon, MD

TCTAP 2021; Seoul, South Korea; April 21-24, 2021

Within the past 12 months, I or my spouse/partner have had a financial interest, arrangement or affiliation with the organization(s) listed below.

Financial Relationship	Company
• Research Support	Abbott, Boston Scientific, Edwards Lifesciences, Medtronic
• Consulting Activities*	Abbott, Boston Scientific, Edwards Lifesciences, Gore, Medtronic
• Equity	Ancora, Conveyor, East End Medical, K2, Medinol, Pi-Cardia, Triventures, Venus MedTech, Valve Medical, XenterMD

*Medical or scientific advisory boards (no direct physician payments)

Dr. Alain Cribier - *First-in-Man PIONEER*

April 16, 2002

TAVR - 2021

The "TAVR revolution" was not a random event!
It was the inevitable result of decades of bold progressive iteration in surgery, cardiac imaging and transcatheter therapies.

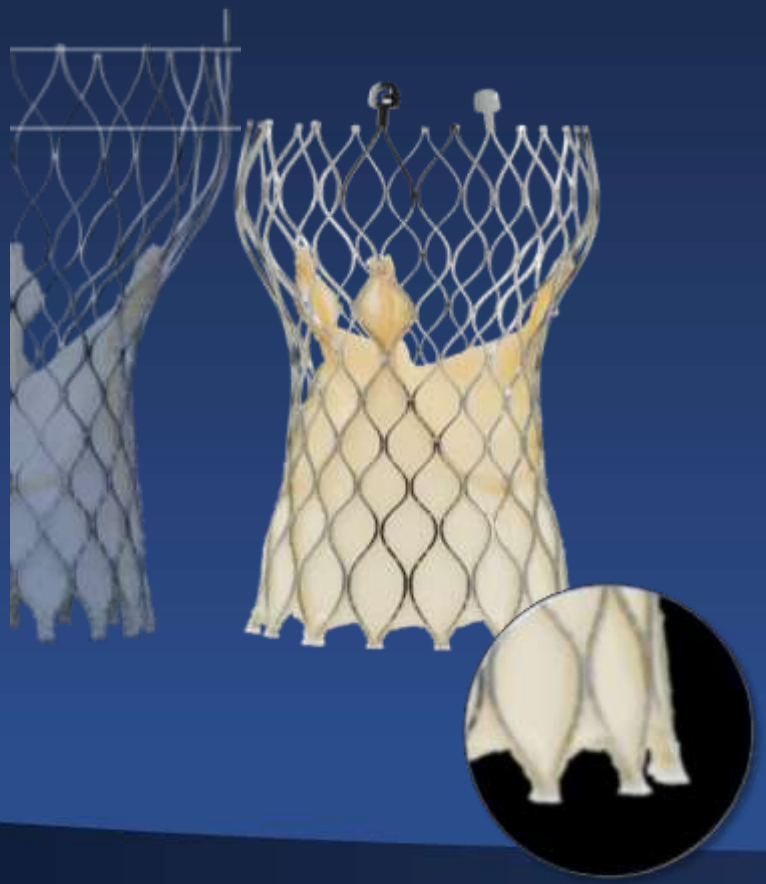
TAVR - 2021

No one could have predicted…

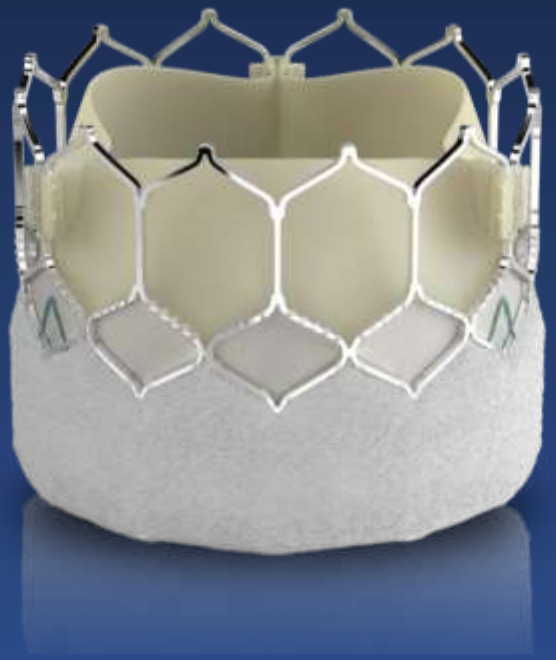
1. Rapid TAVR technology evolution
2. TAVR procedural refinements and simplification
3. Avalanche of TAVR clinical evidence
4. Heart valve team acceptance
5. Dramatic reduction in complications and improved outcomes

Current "Standards" for TAVR

MDT Evolut R (PRO+)



Edwards Sapien 3 (Ultra)



TAVR Technology Evolution

TAVR - 2021

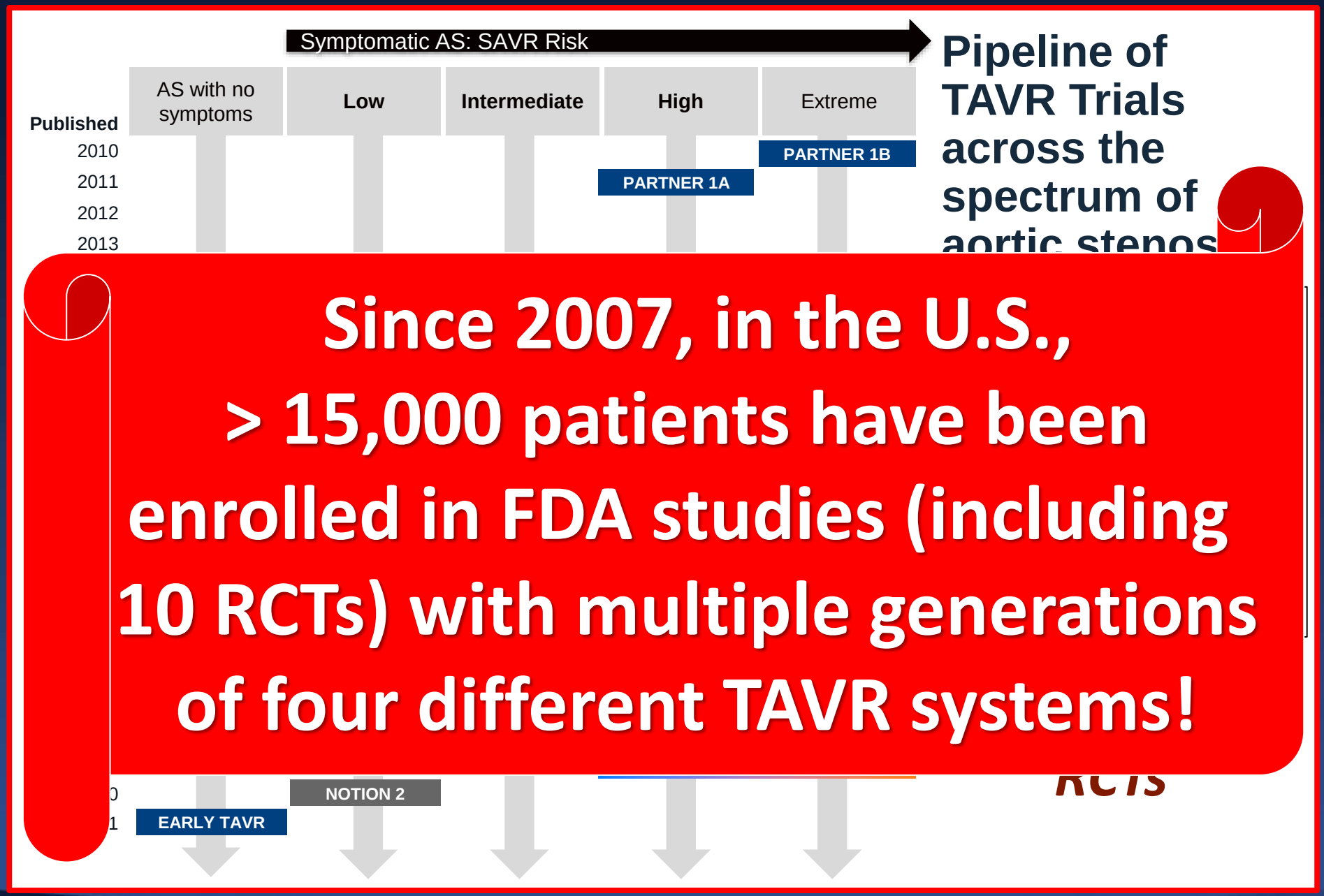
Accessory Technologies

- Cerebral embolic protection devices
- Dedicated pre-shaped guidewires
- Expandable and in-line sheaths
- Large hole closure devices
- Dedicated pacemaker catheters (and wires)
- Specialized balloons
- Aortic valve remodeling technologies
- Advanced imaging systems

TAVR Procedural Refinements

The minimalist strategy

- M th
- **Almost all TAVR cases worldwide are now candidates for some version of "minimalist" procedural strategy!**
- ***Median LOS after TAVR is 1-2 days at Columbia-NYP Hospital!***
- d
- id ambulation and early discharge plans (1-2 days)


Symptomatic AS: SAVR Risk
AS with no symptoms
Low
Intermediate
High
Extreme
Published
2010
2011
2012
2013
PARTNER 1B
PARTNER 1A
NOTION 2
EARLY TAVR
Pipeline of TAVR Trials across the spectrum of aortic stenos
RCTs
Since 2007, in the U.S., > 15,000 patients have been enrolled in FDA studies (including 10 RCTs) with multiple generations of four different TAVR systems!

The PARTNER Trial Phenomenon

THE PARTNER 3 TRIAL

SAPIEN

SAPIEN XT

SAPIEN 3

- TAVR vs. Standard Therapy
- TAVR vs. SAVR
- TAVR (XT) vs. TAVR (SAPIEN)
- TAVR-only Registry
- TAVR Valve in Valve Registry

OPERATIVE RISK

EXTREME

HIGH

INTER-MEDIATE

LOW

2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017

PIB (N=358)

PIB RCA (N=91)

PIA (N=699)

PI NRCA (N=2014)

PIIB (N=560)

PII ViV Nested (N=96)

PII ViV CA (N=269)

PII S3HR (N=583)

PII S3i (N=1078)

PII S3i (N=1078)

PIII (N=1000)

> 9,000 patients, 5 RCTs, and
> 200 manuscripts/abstracts

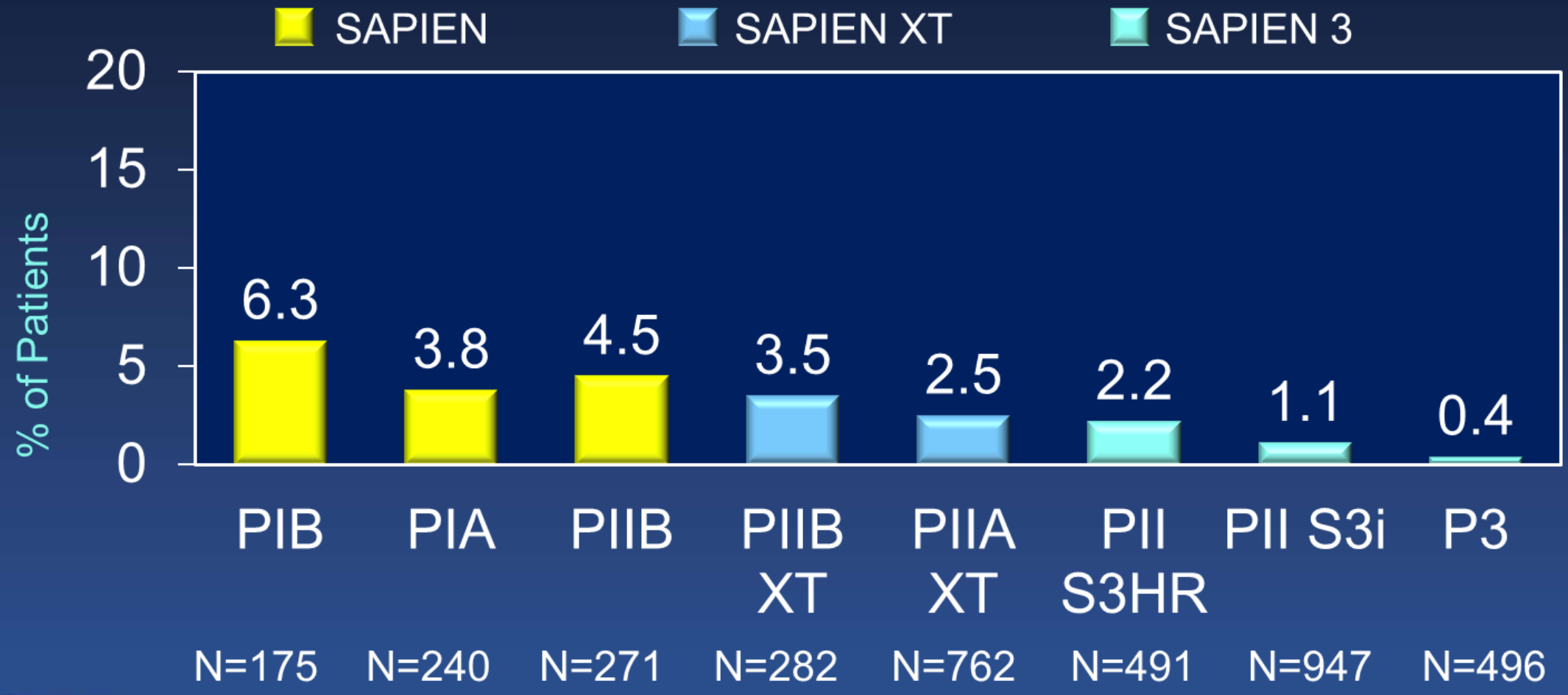
The HEART TEAM 3.0

Who's Missing?

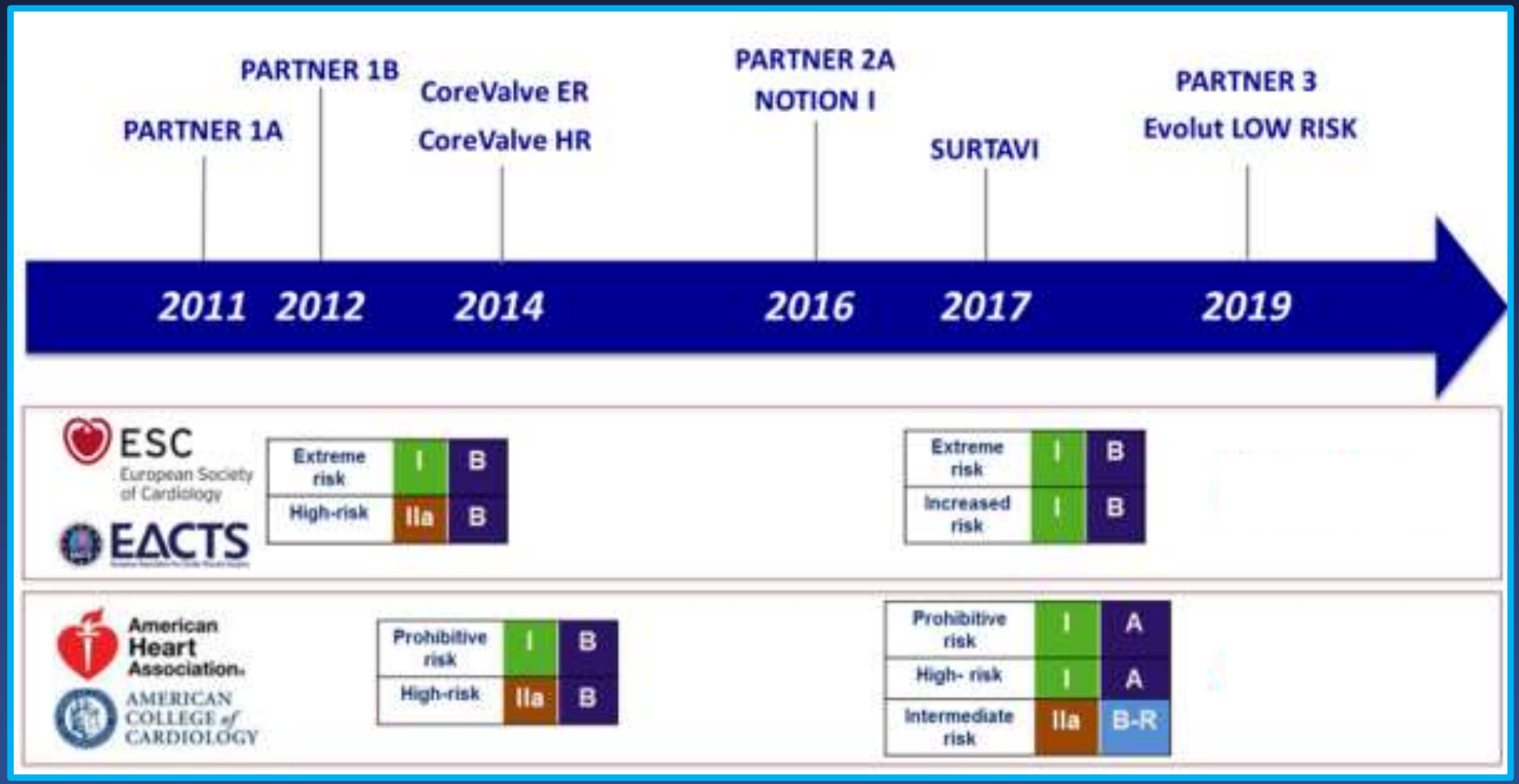
- Valve Cardiologist
- Transcatheter Surgeon
- Structural Interventionalist
- Imaging Expert
- CV Anesthesiologist
- Heart Failure Specialist
- MD Consultants
- Dedicated Coordinator

Improved TAVR Clinical Outcomes

TAVR 30-day Mortality (PARTNER trials)



TAVR Evidence and Guidelines



The Importance of Low-Risk Patients

STS Database (141,905 pts)

Contemporary Real-World Outcomes of Surgical Aortic Valve Replacement in 141,905 Low-Risk, Intermediate-Risk, and High-Risk Patients

Vinod H. Thourani, MD, Rakesh M. Suri, MD, DPhil, Rebecca L. Gunter, MD, Shubin Sheng, PhD, Sean M. O'Brien, PhD, Gorav Ailawadi, MD, Wilson Y. Szeto, MD, Todd M. Dewey, MD, Robert A. Guyton, MD, Joseph E. Bavaria, MD, Vasilis Babaliaros, MD, James S. Gammie, MD, Lars Svensson, MD, PhD, Mathew Williams, MD, Vinay Badhwar, MD, and Michael J. Mack, MD

Ann Thorac Surg 2015;99:55-61

The 'holy grail' is the 80% of aortic stenosis patients receiving surgery who are in the low-risk category!

TAVR Low-Risk RCTs

PARTNER 3 Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

EVOLUT Low Risk Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

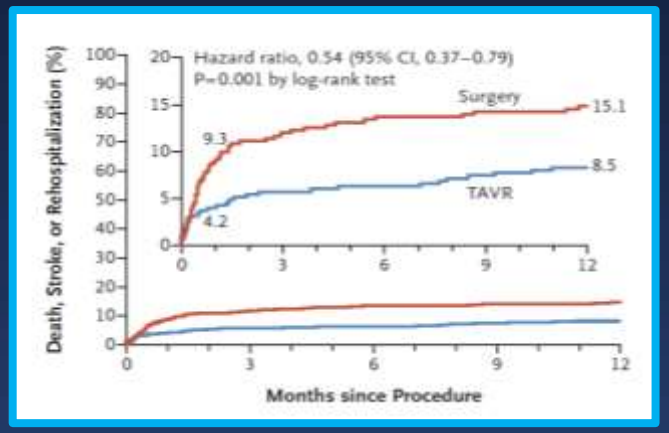
Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mum
John C. Heiser,
Paul S.
David H. F
John K. Forrest
Nicole Piaz
George F
Michael J. Bi
and Micha
, Tanvir Bajwa, M.D.,
Judah Askew, M.D.,
cuti, M.D.,
Zorn III, M.D.,
tony Walton, M.D.,
obinson, M.D.,
K. Oh, M.D.,
. Mugglin, Ph.D.,
l Investigators*

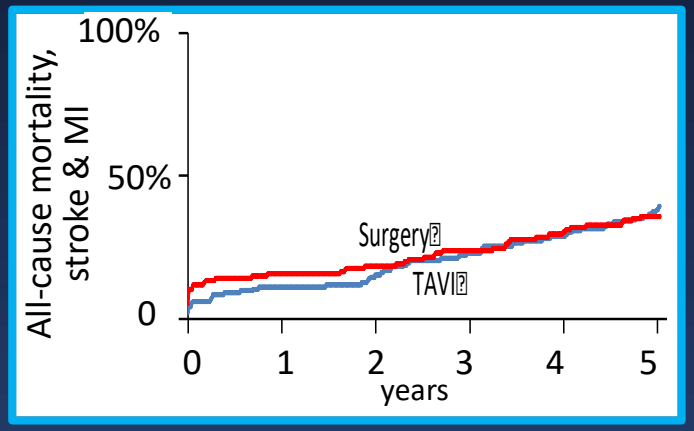
N Engl J Med 2019

TAVR Low-Risk Trials

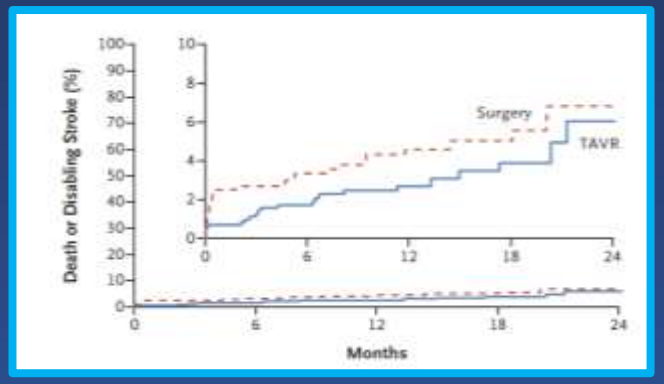
(4 RCTs - 3,661 patients)



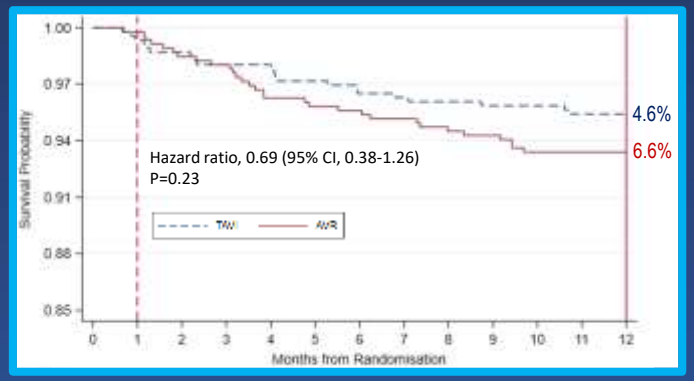
PARTNER 3



NOTION



Evolut Low Risk



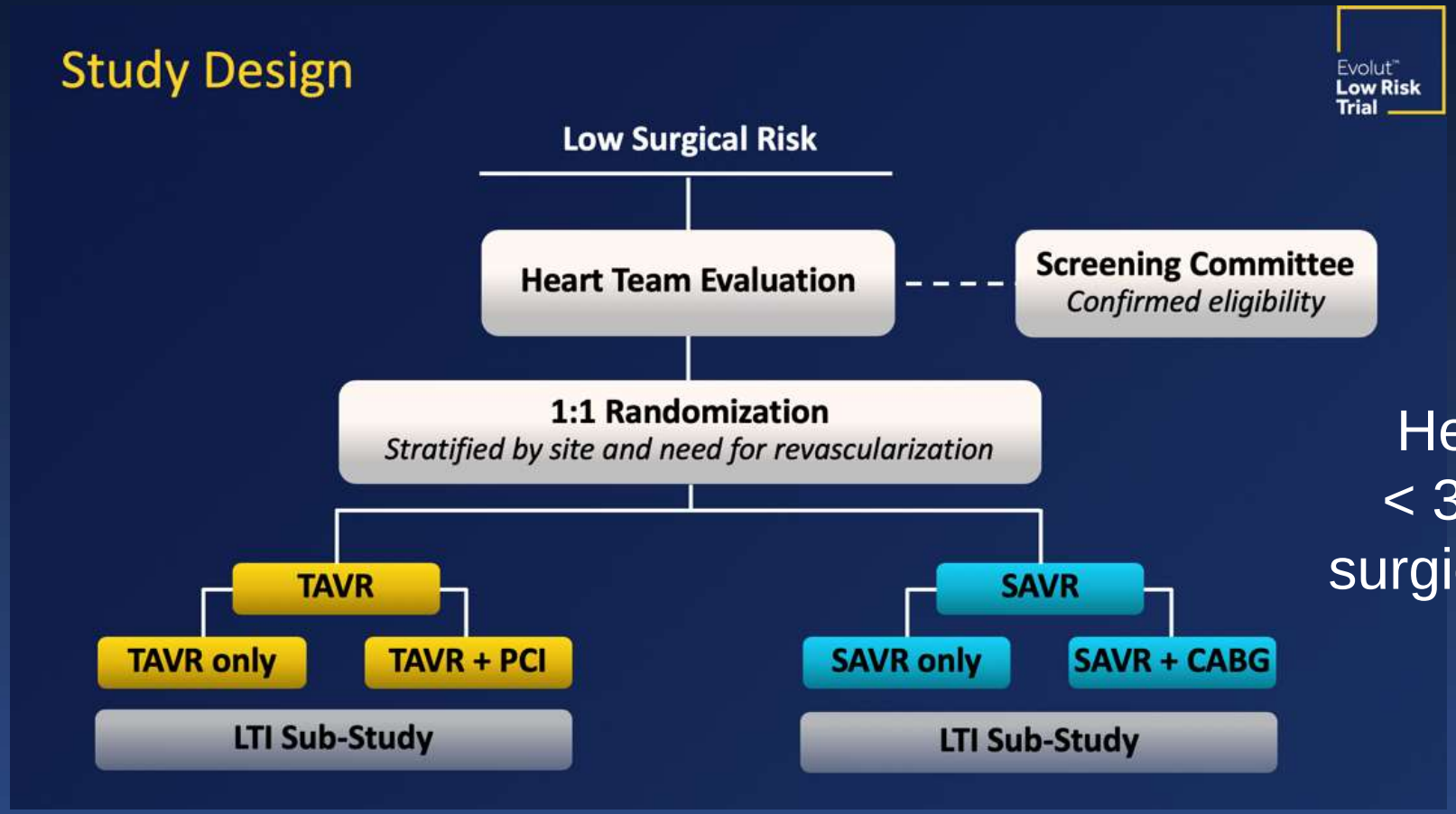
UK-TAVI

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

Evolut Low-Risk TAVR Trial

Bayesian Adaptive Design

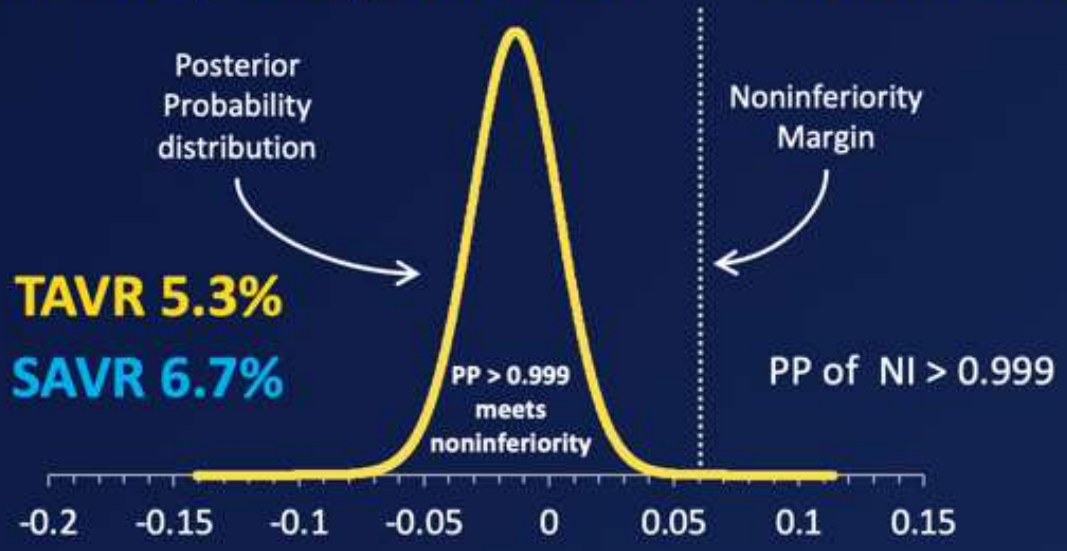


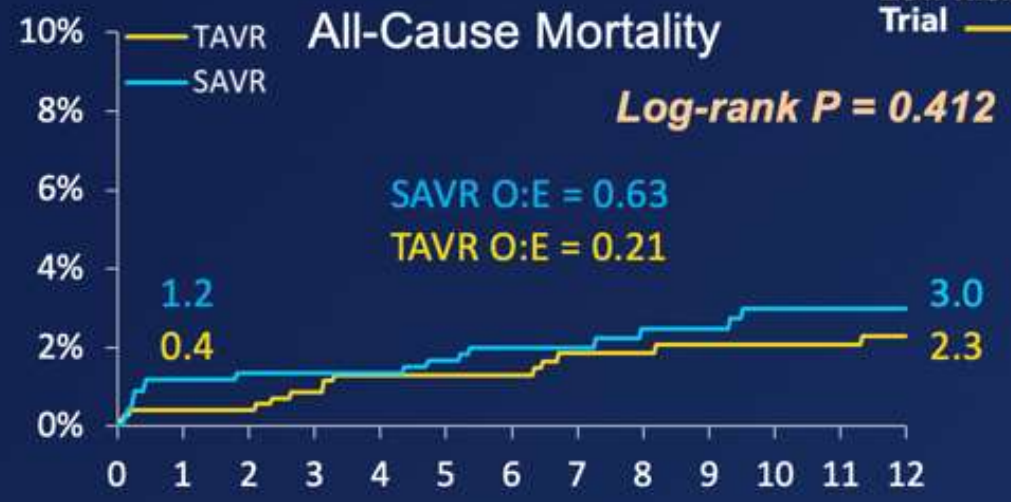
Heart Team
< 3% 30-day surgical mortality

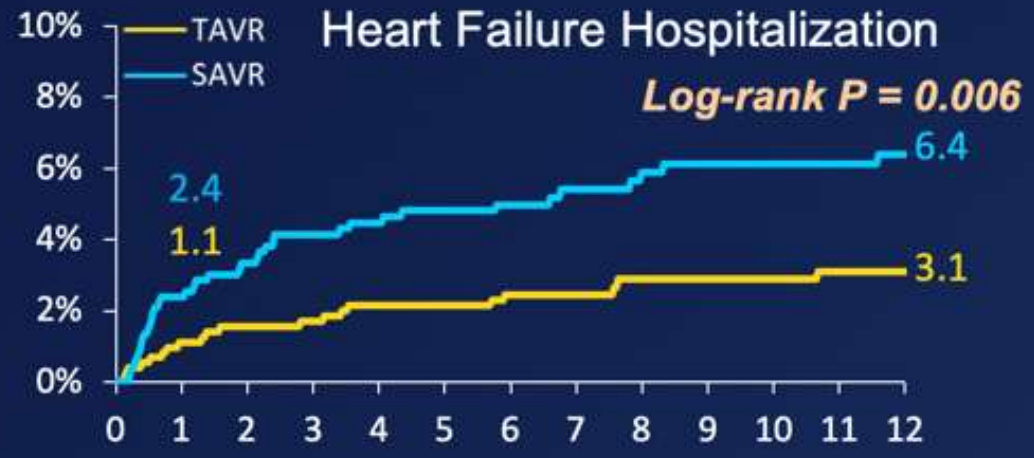
Primary End point: All-cause mortality of disabling stroke at 2 years

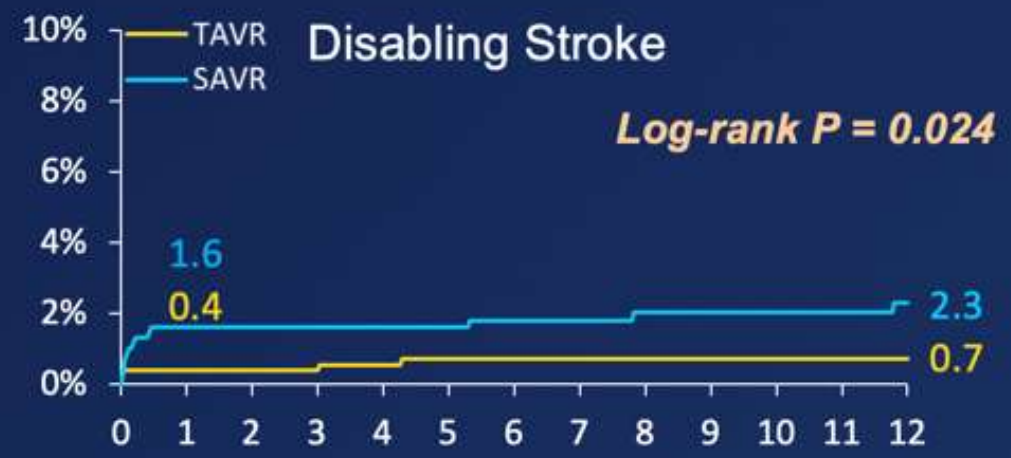
Primary Endpoint Met --- TAVR is noninferior to SAVR

Evolut™ Low Risk Trial









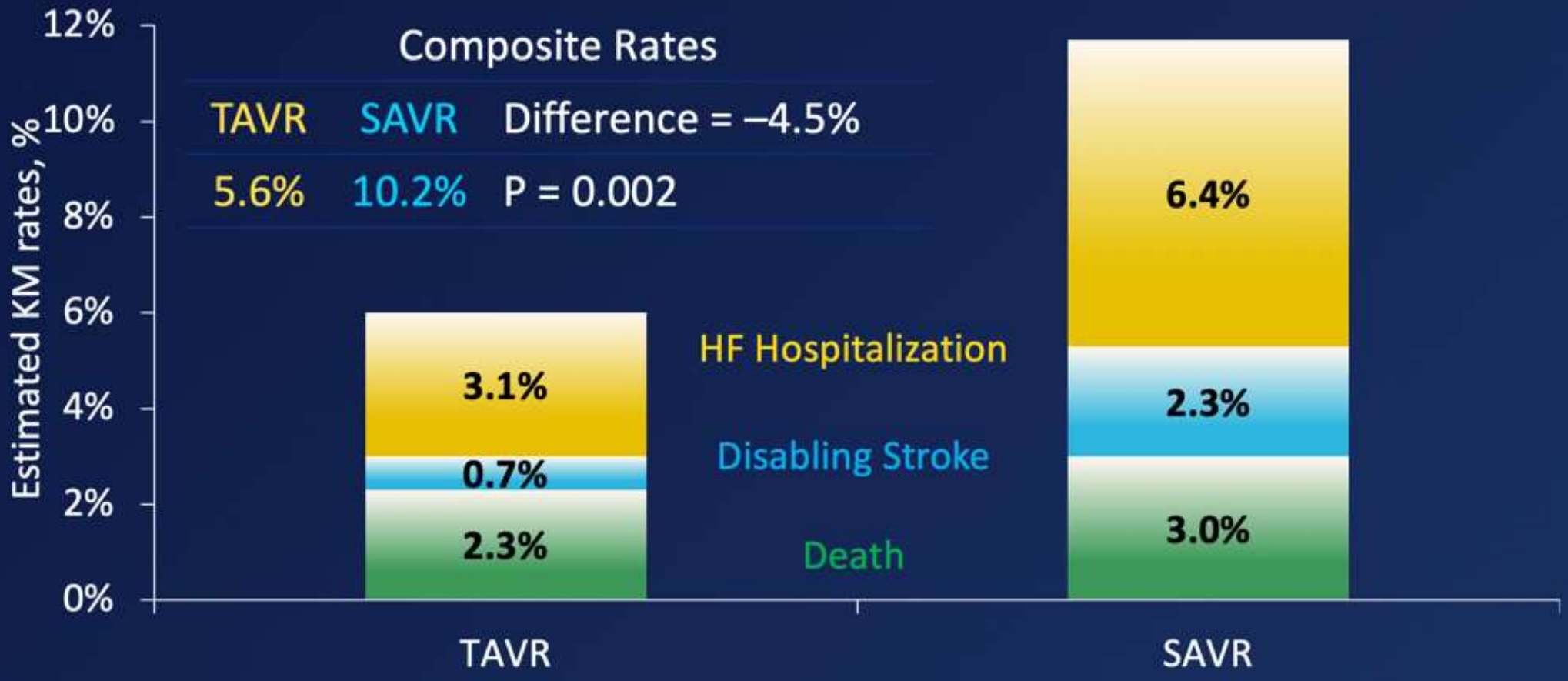
Popma et al NEJM 2019 380:1706-1715

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

LR RCT: Death, Disabling Stroke, and Heart Failure Hospitalizations to 1 Year

Evolut™ Low Risk Trial

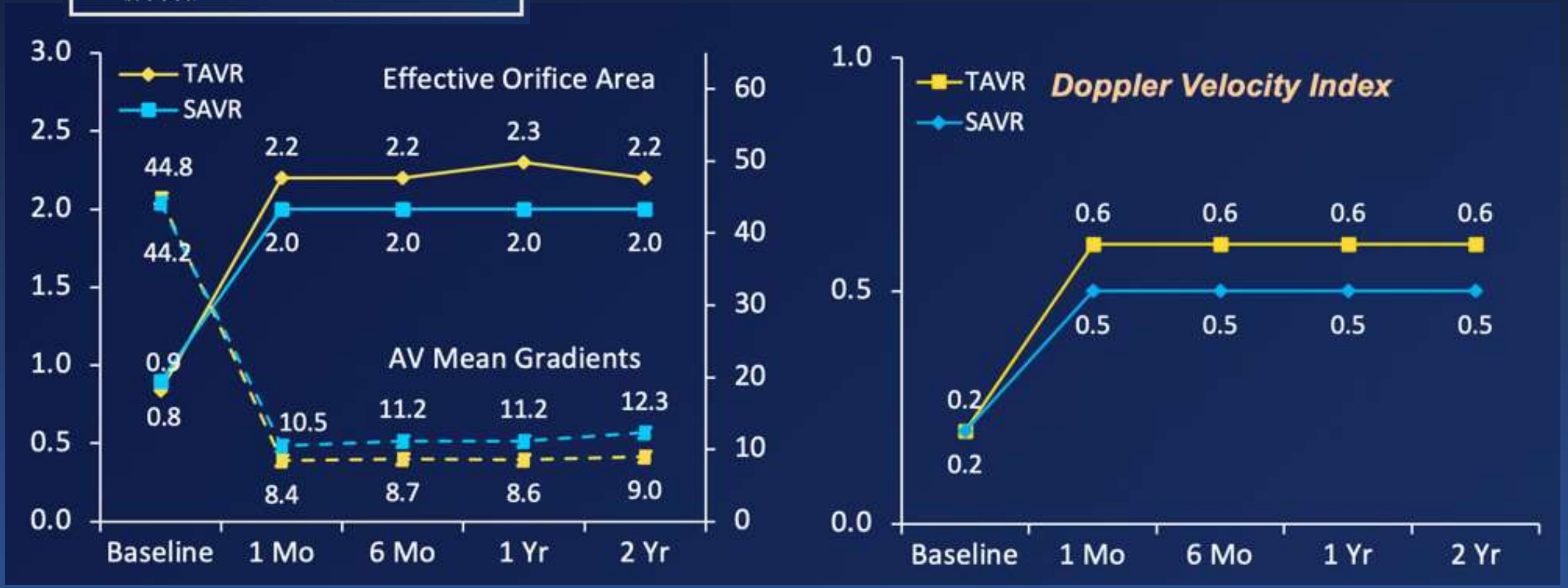


Popma et al NEJM 2019 380:1706-1715

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

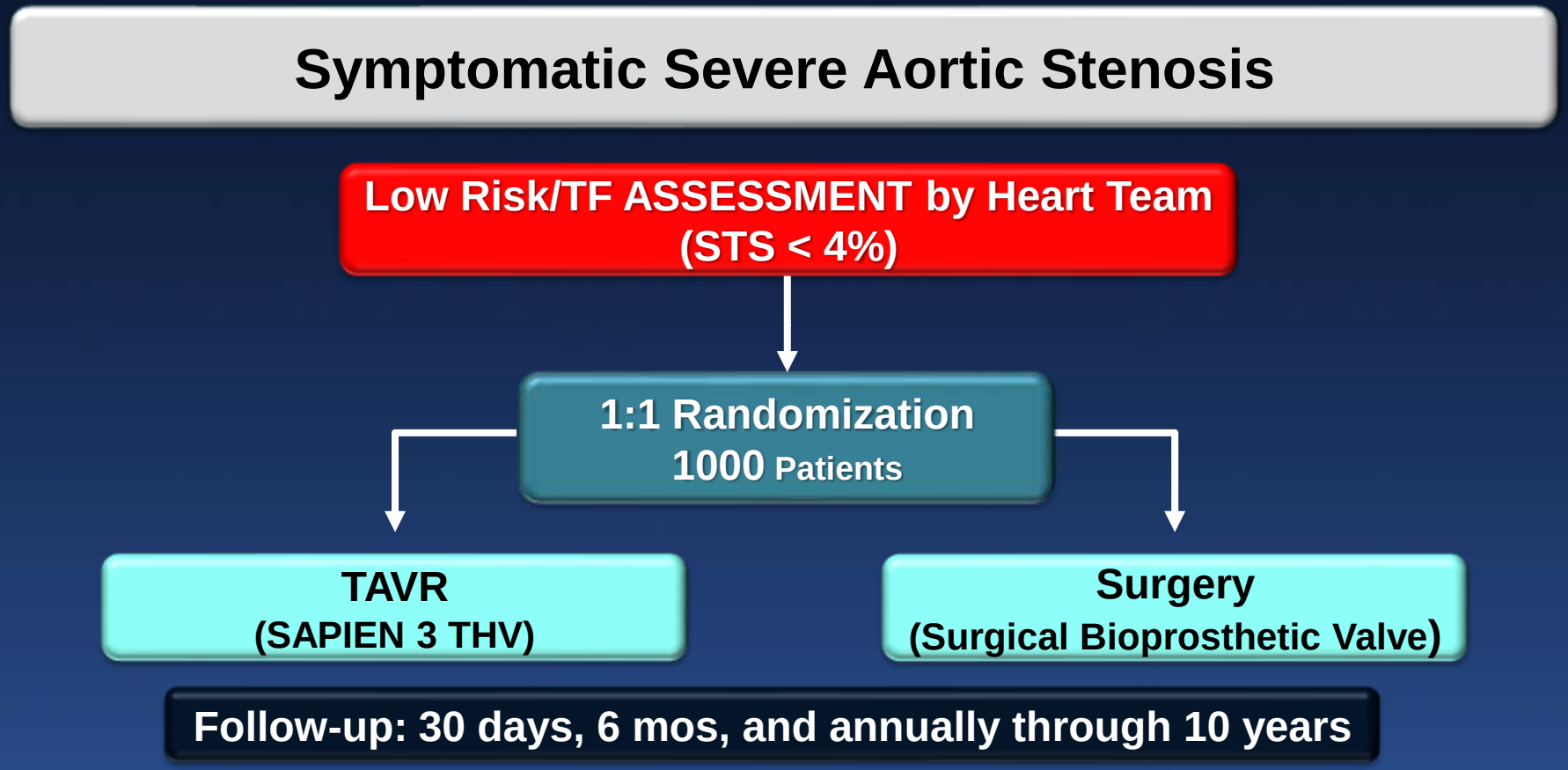
Evolut Low-Risk TAVR Trial: Serial Echo Findings thru 2 yrs



Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

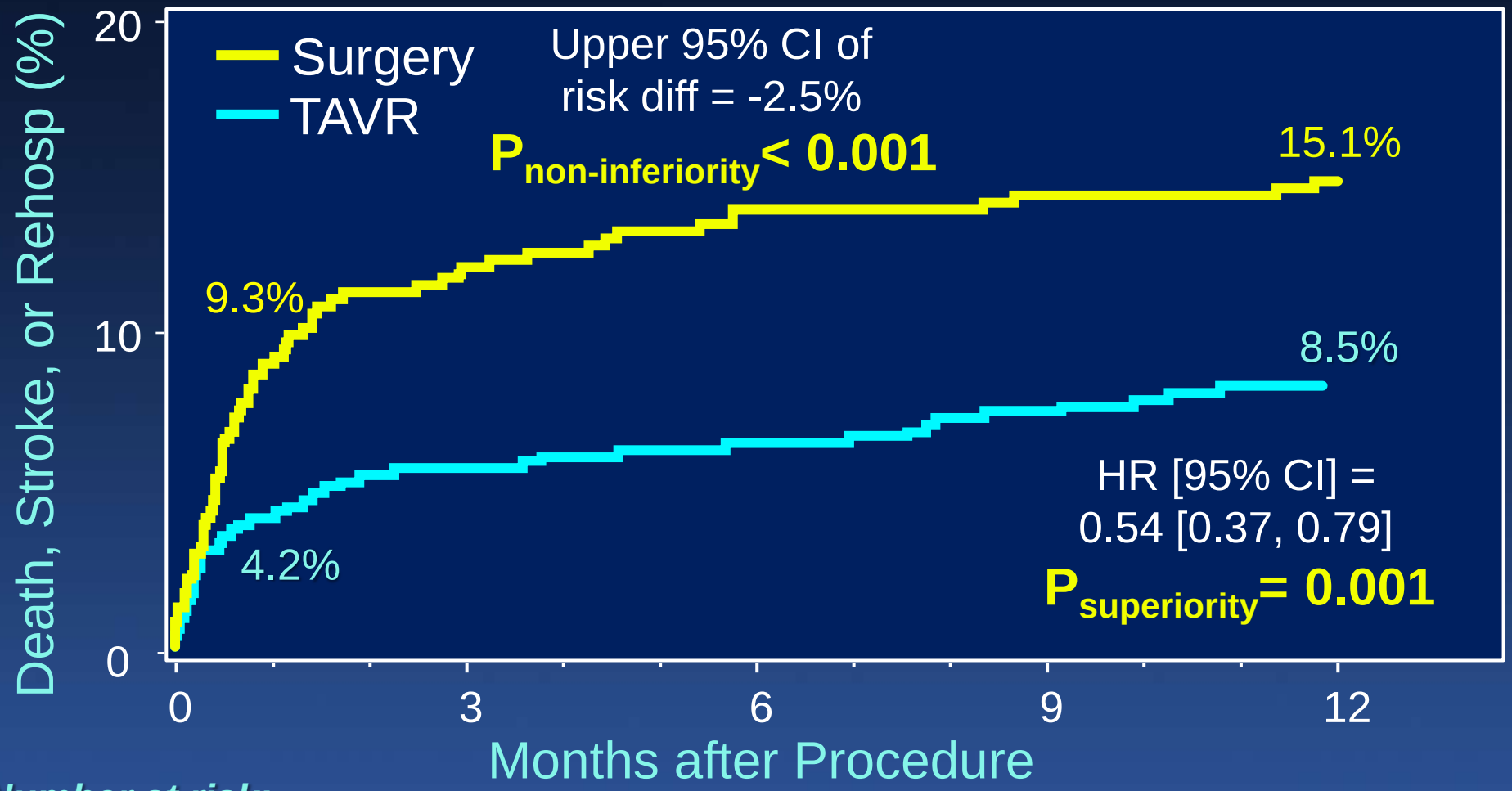
PARTNER 3 Study Design



PRIMARY ENDPOINT:
Composite of all-cause mortality, stroke, or CV re-hospitalization at 1 year post-procedure

THE PARTNER 3 TRIAL

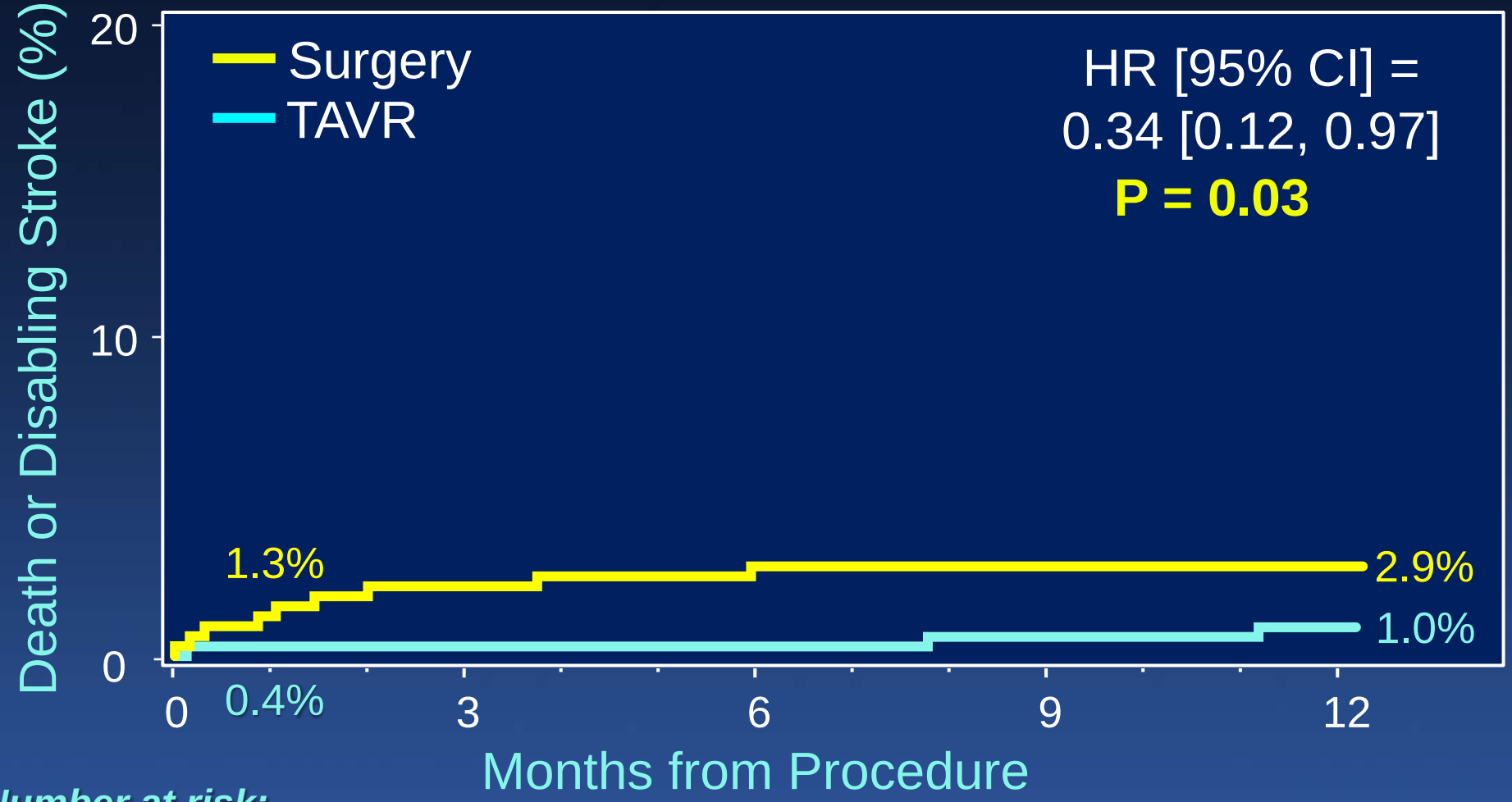
Primary Endpoint



Number at risk:

Surgery	**454**	**408**	**390**	**381**	**377**	**374**
TAVR	**496**	**475**	**467**	**462**	**456**	**451**

Death or Disabling Stroke



Number at risk:

Surgery	**454**	**444**	**436**	**432**	**430**	**426**
TAVR	**496**	**494**	**494**	**493**	**491**	**488**

The Low-Risk Patient TAVR Journey

Clinical Care Pathway

- Same-day admission
- 3/4 pts no general anesthesia (sedated, awake)
- Femoral artery puncture, no chest wall incision or CPB
- < 1 hour procedure
- 3/4 pts no ICU – Tx to floor
- Discharge in 1-2 days; 96% pts to home or self-care

Clinical Outcomes

- Rare procedural complications
- @ 30 days: mortality 0.4% and zero serious strokes!
- Less pain, bleeding, AKI and post-procedure arrhythmias
- Improved early recovery – QoL and increased activities
- @ 1 year: mortality 1% and serious strokes 0.2%

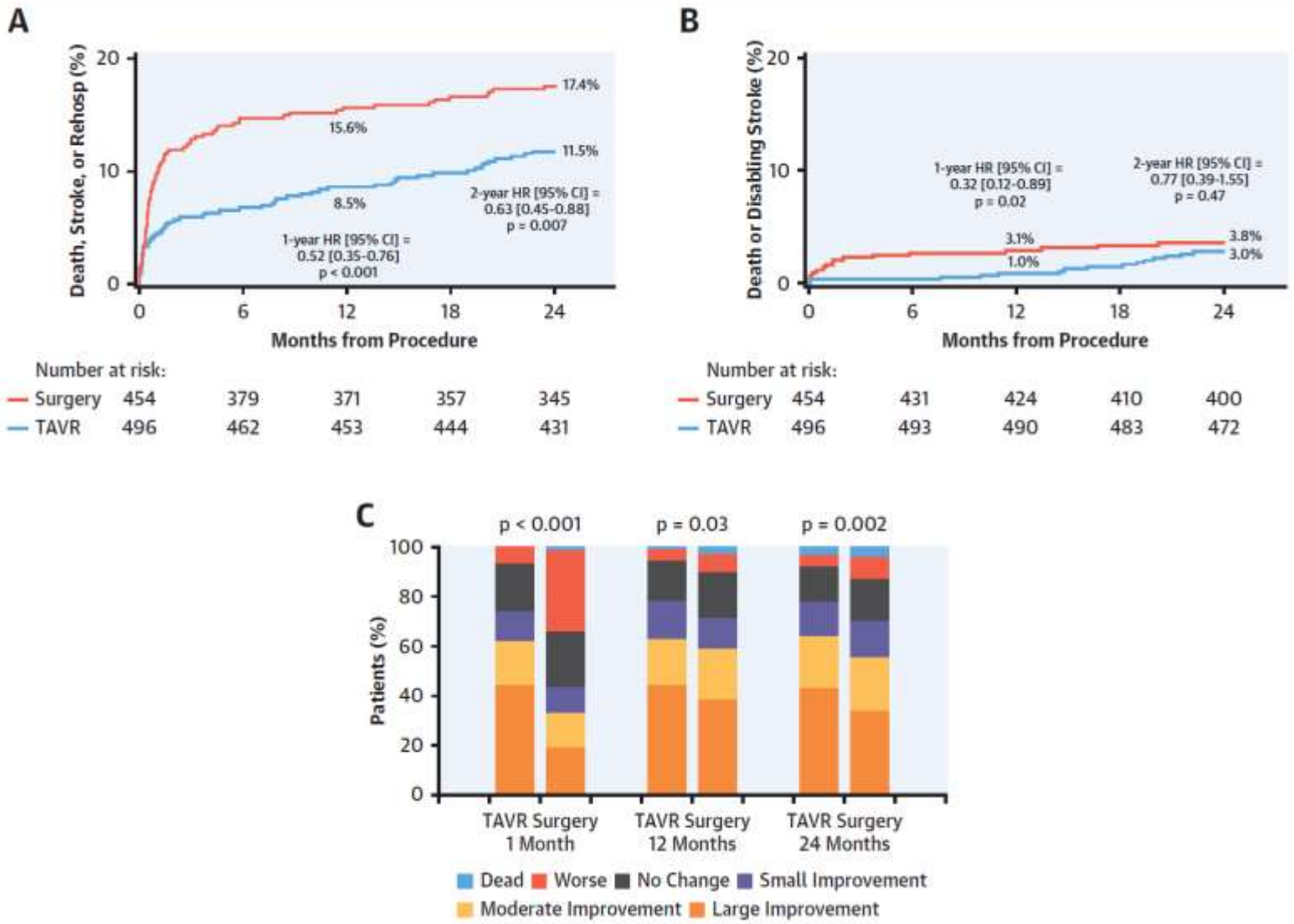
The Low-Risk TAVR Trials

An AS Treatment Paradigm Shift

"This is an historic moment, and all of us here should remember it as such."

Eugene Braunwald, ACC 2019

CENTRAL ILLUSTRATION Time-to-Event Curves and Disease-Specific Health Status in TAVR Versus Surgery Through 2 Years



Cardiovascular Research Foundation

Leon MB et al. J Am Coll Cardiol 2021;77: 1149-61

Columbia University Medical Center
NewYork-Presbyterian

After the Low-Risk Trials

An AS Treatment Paradigm Shift

- *The favorable outcomes of TAVR are consistent across the entire surgical risk spectrum suggesting that surgical risk estimation should no longer be the primary basis to guide the choice between TAVR and SAVR.*

After the Low-Risk Trials

An AS Treatment Paradigm Shift

- The favorable outcomes of TAVR are consistent across the entire surgical risk spectrum suggesting that surgical risk estimation should no longer be the primary basis to guide the choice between TAVR and SAVR.
- *CAVEAT: many patients (~30%) were excluded from the low-risk RCTs*

TAVR Low-Risk Trials

(4 RCTs - 3,661 patients)

Who's in?

- High-flow severe AS
- Low-risk patients (av STS ≈ 2)
- Transfemoral only
- Mean age 74 years
  - <25% aged <70 years
- Predominantly male

Who's out?

- Low-flow severe AS
- Bicuspid morphology
- Some small/large annulus patients
- Multivalve disease
- Severe CAD, CKD and low EF
- "High-risk" TAVR anatomy

After the Low-Risk Trials

An AS Treatment Paradigm Shift

- The favorable outcomes of TAVR are consistent across the entire surgical risk spectrum suggesting that surgical risk estimation should no longer be the primary basis to guide the choice between TAVR and SAVR.
- CAVEAT: many patients (~30%) were excluded from the low-risk RCTs
- *There will be a shift from a surgery-first to a TAVR-first strategy for most AS patients. The Heart Team will weigh clinical and anatomic characteristics to identify the best treatment option for individual patients with transfemoral TAVR replacing surgery as the default therapy in most cases!*

After the Low-Risk Trials

An AS Treatment Paradigm Shift

Who do we offer TAVR?

Who do we offer surgery?

2020 ACC/AHA Guidelines for VHD

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Developed in collaboration with and endorsed by the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

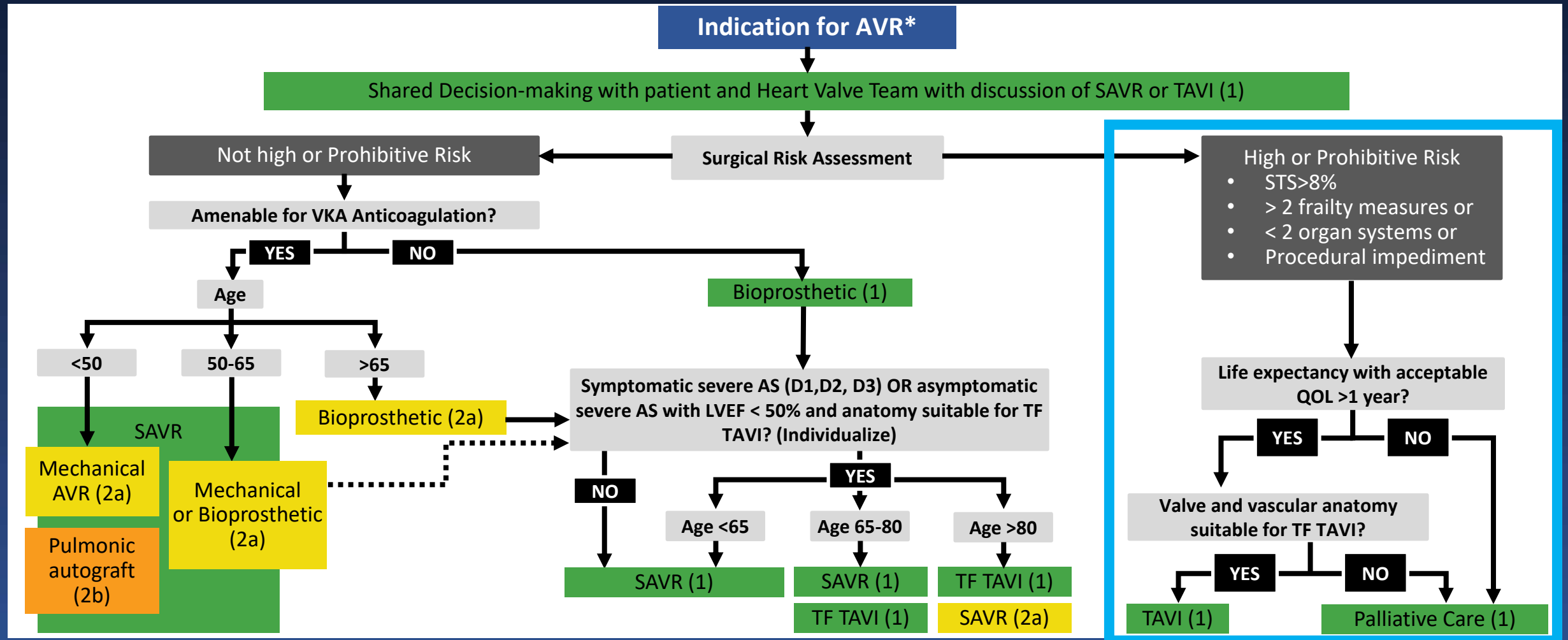
Writing Committee Members*

Catherine M. Otto, MD, FACC, FAHA, *Co-Chair*
Rick A. Nishimura, MD, MACC, FAHA, *Co-Chair*
Robert O. Bonow, MD, MS, MACC, FAHA
Blase A. Carabello, MD, FACC, FAHA
John P. Erwin III, MD, FACC, FAHA
Federico Gentile, MD, FACC
Hani Jneid, MD, FACC, FAHA
Eric V. Krieger, MD, FACC
Michael Mack, MD, MACC
Christopher McLeod, MBCHB, PhD, FAHA
Patrick T. O'Gara, MD, MACC, FAHA†
Vera H. Rigolin, MD, FACC, FAHA
Thoralf M. Sundt III, MD, FACC, FAHA
Annemarie Thompson, MD
Christopher Toly

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information.
†ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison.

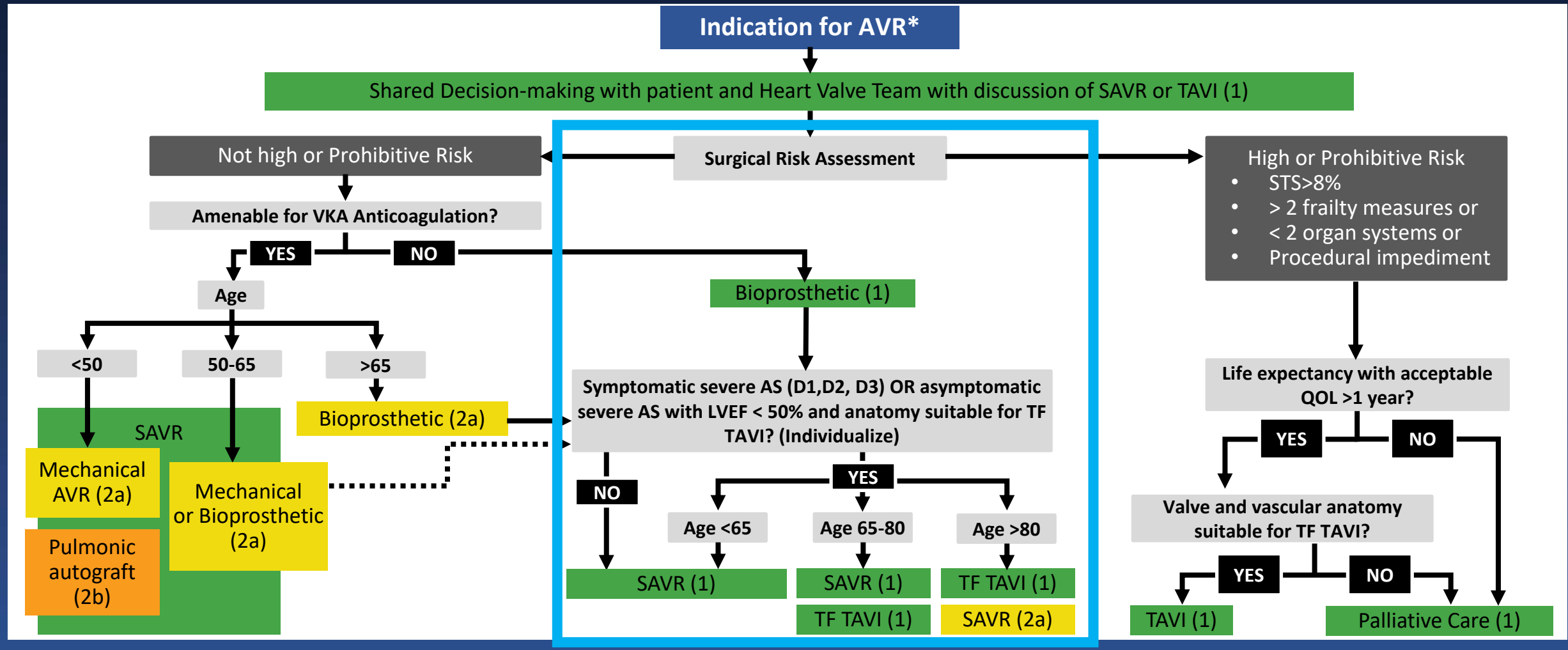
J Am Coll Cardiol 2020

2020 ACC/AHA Guidelines for VHD



J Am Coll Cardiol 2020

2020 ACC/AHA Guidelines for VHD



J Am Coll Cardiol 2020

2020 ACC/AHA Guidelines for VHD

Absolute Effect Estimates per 1000 Patients for Outcomes Comparing TF-TAVI to SAVR

Age Group	> 85 yrs		75-85 yrs		65-75 yrs		< 65 yrs	
Outcomes (RR < 1 favors TAVI)	SAVR	TAVI	SAVR	TAVI	SAVR	TAVI	SAVR	TAVI
Mortality (2 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	242	197	152	122	92	73	72	57
Stroke RR 0.80 (CI 95& CI 0.63-1.01)	99	79	99	79	70	56	50	40
Aortic valve reintervention (2 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	3	10	3	10	3	10	3	10
Aortic valve reintervention (10 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	61	198	61	198	61	198	61	198
Permanent pacer RR 2.46 (CI 95% 1.17 - 5.15)	92	226	92	226	92	226	92	226
Life threatening bleeding 0.39 (CI 95% 0.29 - 0.54)	413	161	413	166	413	161	413	161
Atrial fibrillation RR 0.43 (CI 95% 0.35 - 0.52)	312	134	312	134	312	134	100	43
Moderate-severe heart failure RR 1.29 (CI 95% 1.08 - 1.55)	69	87	69	87	69	87	69	87
Myocardial infarction RR 0.87 (CI 95% 0.59 - 1.29)	36	31	36	31	36	31	36	31
Acute kidney injury RR 0.38 (CI 95% 0.27 - 0.54)	85	32	85	32	85	32	85	32

J Am Coll Cardiol 2020 (data supplement #12)

2020 ACC/AHA Guidelines for VHD

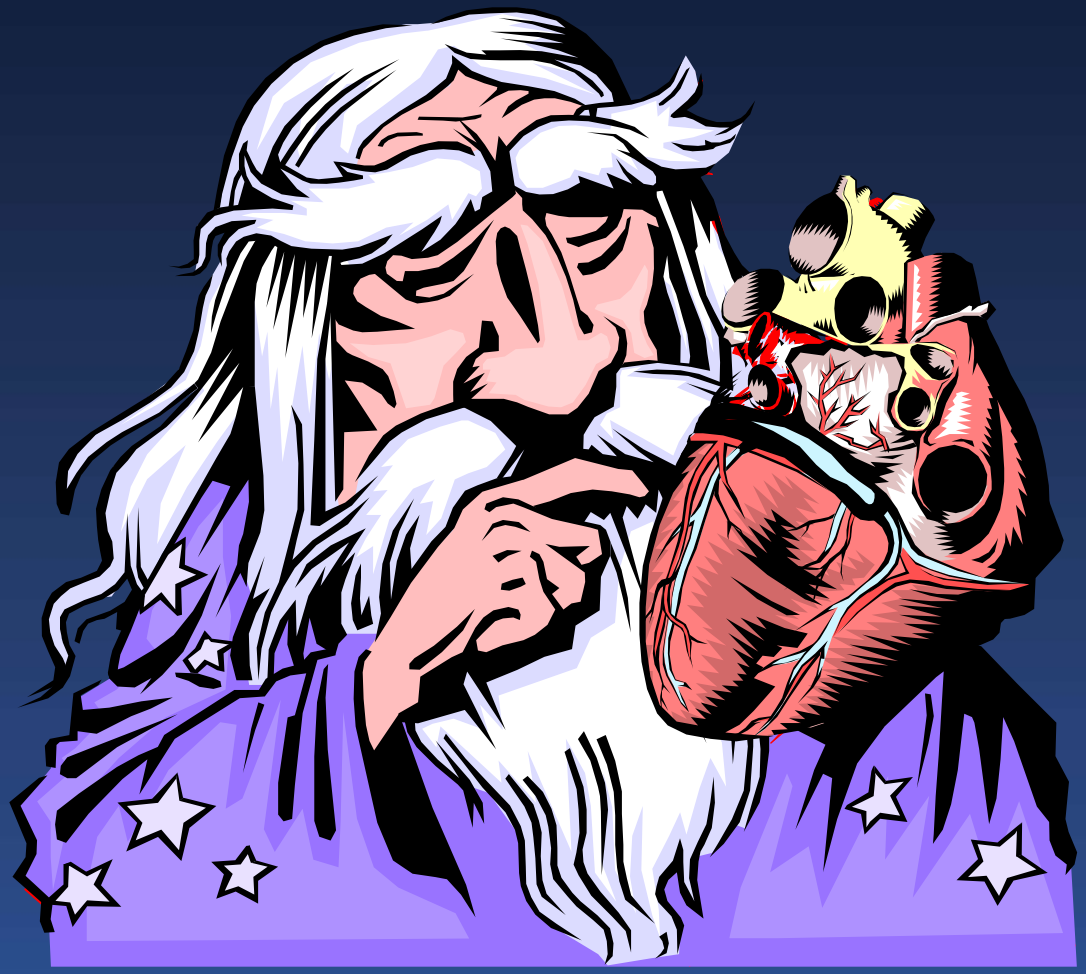
Absolute Effect Estimates per 1000 Patients for Outcomes Comparing TF-TAVI to SAVR

Age Group	> 85 yrs		75-85 yrs		65-75 yrs		< 65 yrs	
Outcomes (RR < 1 favors TAVI)	SAVR	TAVI	SAVR	TAVI	SAVR	TAVI	SAVR	TAVI
Mortality (2 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	242	197	152	122	92	73	72	57
Stroke RR 0.80 (CI 95& CI 0.63-1.01)	99	79	99	79	70	56	50	40
Aortic valve reintervention (2 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	3	10	3	10	3	10	3	10
Aortic valve reintervention (10 yrs) RR 3.25 (CI 95% 1.29 - 8.14)	61	198	61	198	61	198	61	198
Permanent pacer RR 2.46 (CI 95% 1.17 - 5.15)	92	226	92	226	92	226	92	226
Life threatening bleeding 0.39 (CI 95% 0.29 - 0.54)	413	161	413	166	413	161	413	161
Atrial fibrillation RR 0.43 (CI 95% 0.35 - 0.52)	312	134	312	134	312	134	100	43
Moderate-severe heart failure RR 1.29 (CI 95% 1.08 - 1.55)	69	87	69	87	69	87	69	87
Myocardial infarction RR 0.87 (CI 95% 0.59 - 1.29)	36	31	36	31	36	31	36	31
Acute kidney injury RR 0.38 (CI 95% 0.27 - 0.54)	85	32	85	32	85	32	85	32

J Am Coll Cardiol 2020 (data supplement #12)

TAVR – Future Directions

What the future will bring…



TAVR – Future Directions

Still MANY Knowledge Gaps

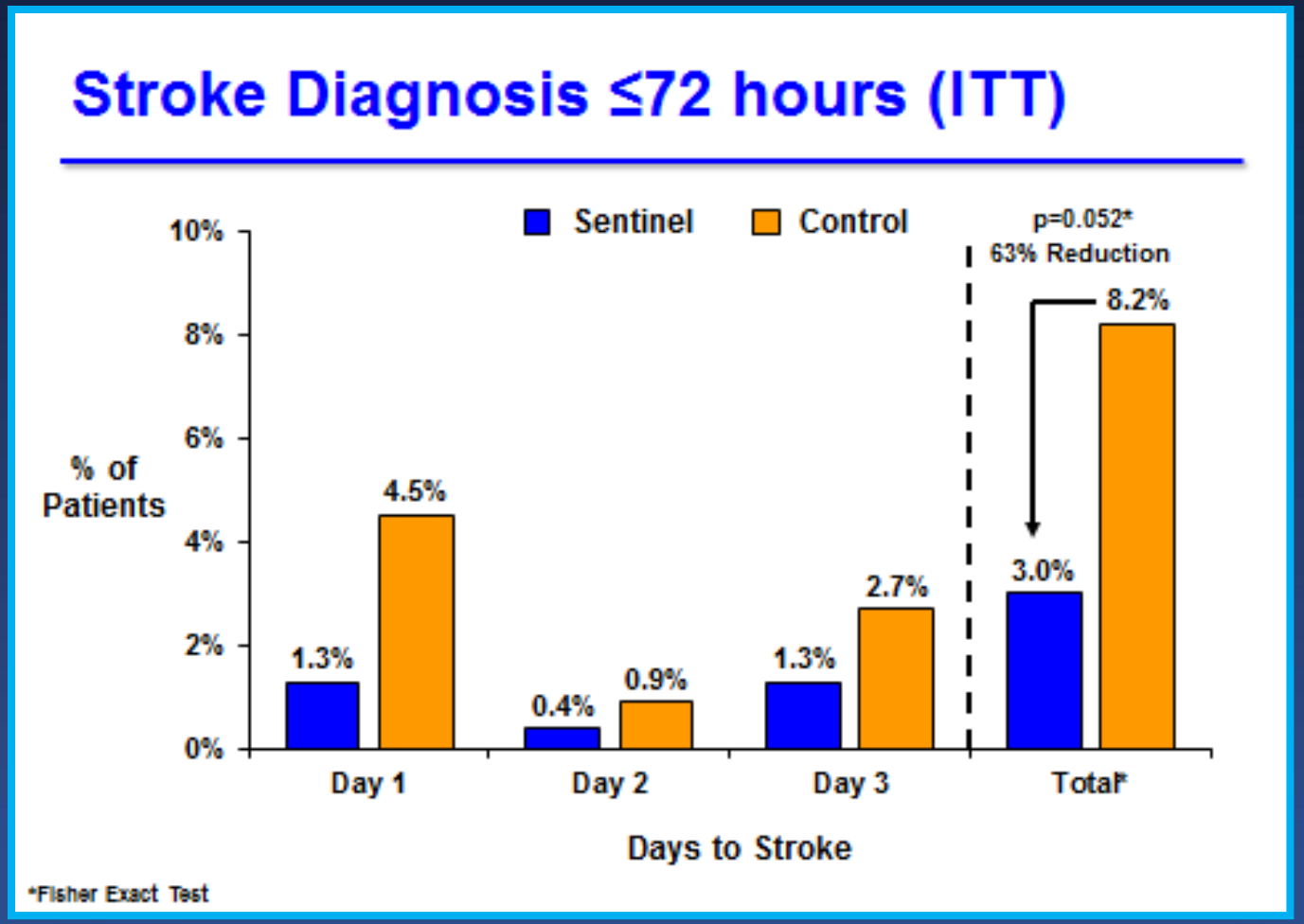
- ***Use of cerebral embolic protection to reduce strokes – systematic or selective use***

TAVR Accessory Devices

Cerebral Embolic Protection (CEP)

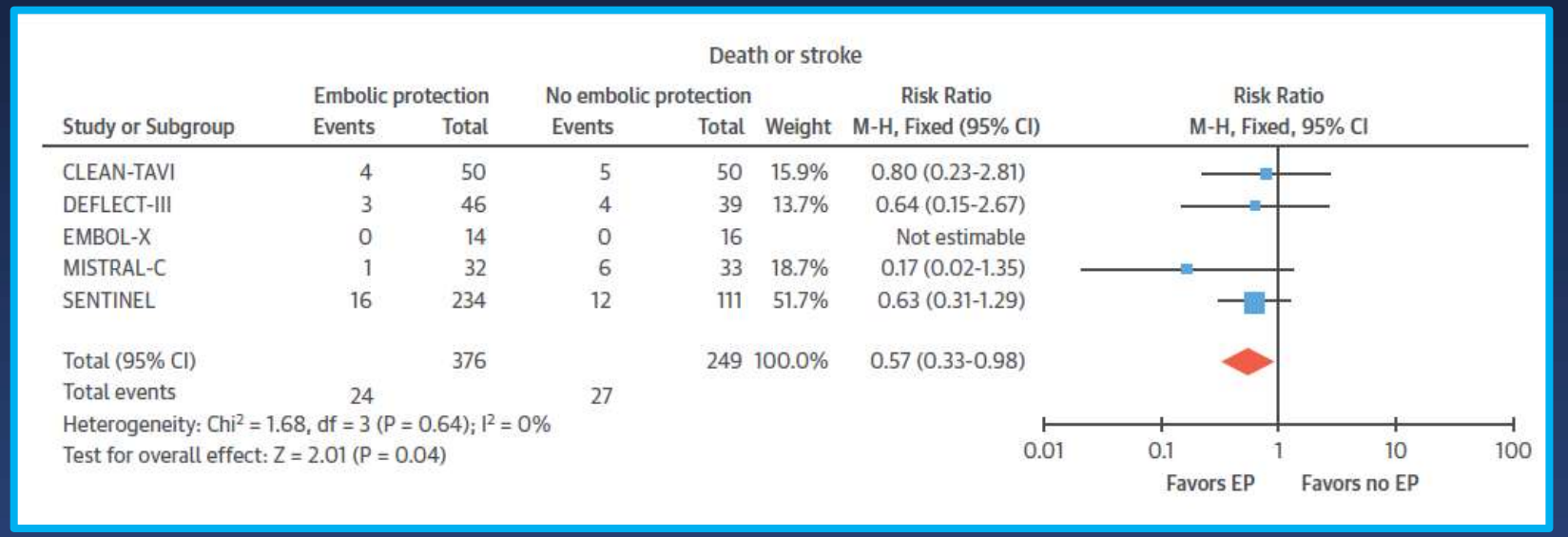
SENTINEL CEP Randomized Trial

Clinical Outcomes



CEP Meta-analysis

Five Studies (n = 625 patients)



Death or stroke

Study or Subgroup	Embolic protection Events	Total	No embolic protection Events	Total	Weight	Risk Ratio M-H, Fixed (95% CI)
CLEAN-TAVI	4	50	5	50	15.9%	0.80 (0.23-2.81)
DEFLECT-III	3	46	4	39	13.7%	0.64 (0.15-2.67)
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	6	33	18.7%	0.17 (0.02-1.35)
SENTINEL	16	234	12	111	51.7%	0.63 (0.31-1.29)
Total (95% CI)		376		249	100.0%	0.57 (0.33-0.98)
Total events	24		27			

Heterogeneity: $Chi^2 = 1.68$, df = 3 (P = 0.64); $I^2 = 0\%$

Test for overall effect: Z = 2.01 (P = 0.04)

Risk Ratio M-H, Fixed, 95% CI

0.01 0.1 1 10 100

Favors EP Favors no EP

- Meta-analysis of 5 RCTS of CEP in TAVR (625 pts; 376 with CEP and 249 without CEP)
- > 40% reduction in risk of stroke or death (6.4% vs 10.8%; RR: 0.57; 95% CI: 0.33-0.98; p=0.04; $I^2 = 0\%$)
- ***NNT = 22 to reduce one stroke or death***

Cardiovascular Research Foundation

Giustino G et al. JACC 2017

Columbia University Medical Center
NewYork-Presbyterian

TAVR – Future Directions

Still MANY Knowledge Gaps

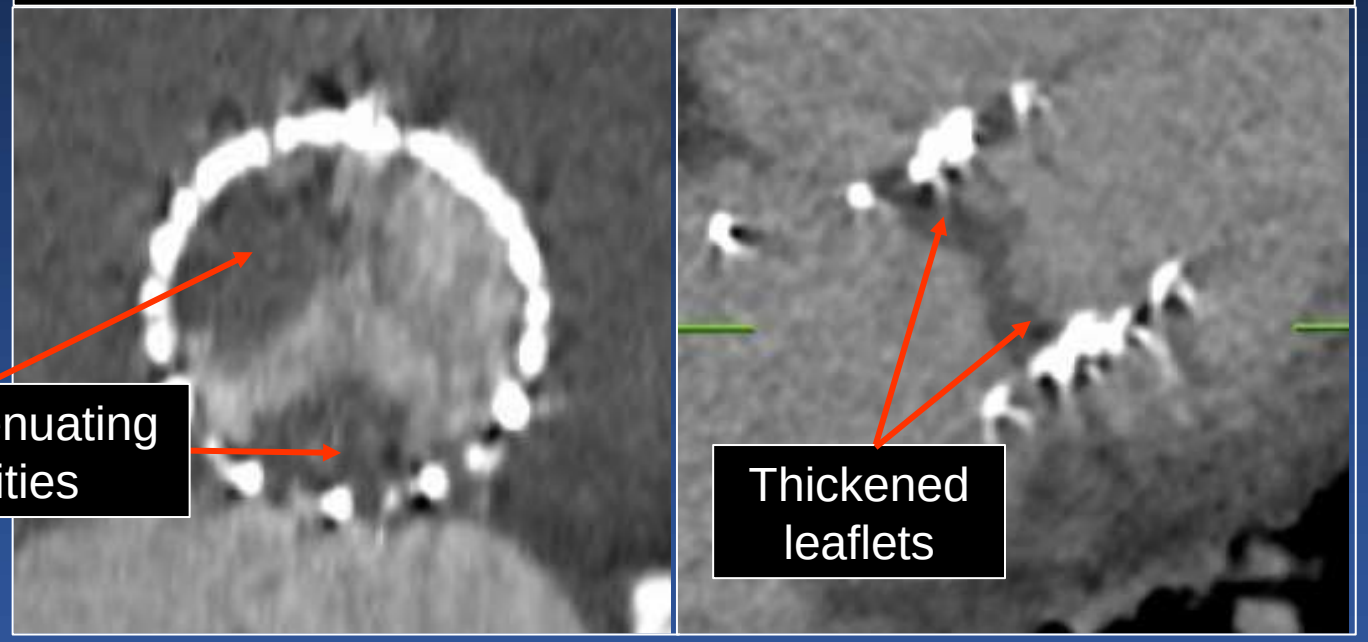
- Use of cerebral embolic protection to reduce strokes – systematic or selective use
- ***Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)***

THE PARTNER 3 TRIAL

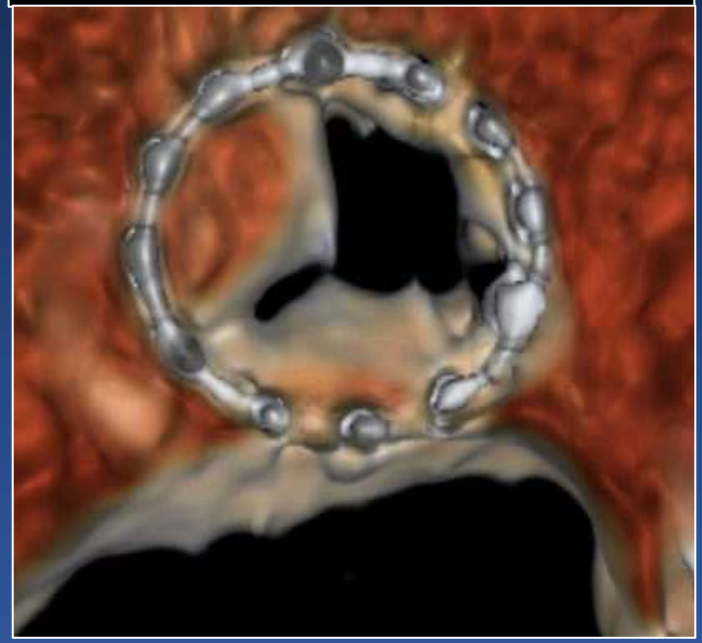
Background

Subclinical Leaflet Thrombosis characterized by hypo-attenuated leaflet thickening (HALT) and reduced leaflet motion has been frequently observed in transcatheter and surgical aortic bioprosthetic valves.

Hypoattenuating leaflet thickening (HALT)

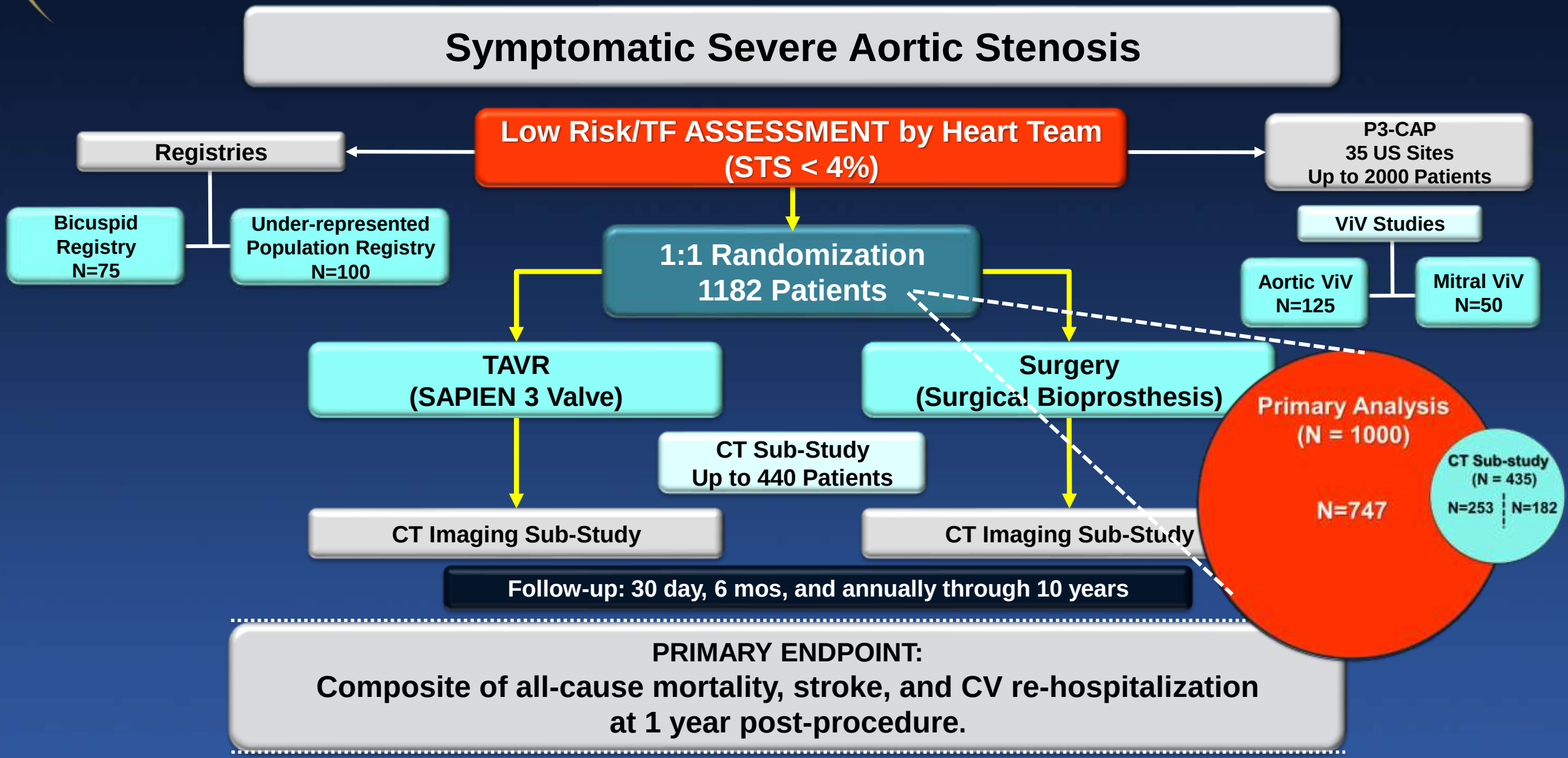


Reduced leaflet motion



Makkar R. et al. NEJM 2015

PARTNER 3 Trial Study Design



Incidence of HALT at 30 Days and 1 Year

TAVR vs SAVR

Per Protocol Population

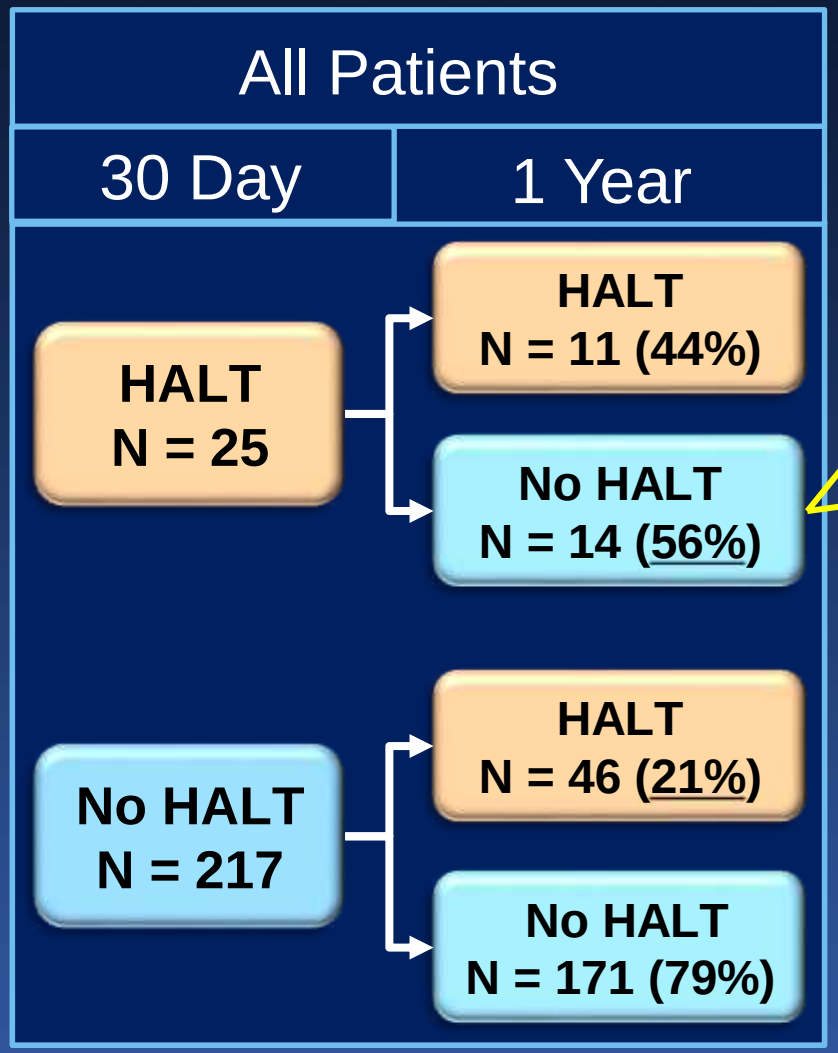
Outcomes (%)	30 Days			1 Year		
	TAVR (N=165)	Surgery (N=119)	P-value	TAVR (N=153)	Surgery (N=109)	P-value
HALT	13.3	5.0	0.03	27.5	20.2	0.19
1 Leaflet	81.8	66.7		64.3	68.2	
2 Leaflets	9.1	33.3		23.8	31.8	
3 Leaflets	9.1	0		11.9	0	

Event rates are binary and p-value is based on Fisher's Exact test

THE PARTNER 3 TRIAL

HALT from 30D to 1Y

Per Protocol Population

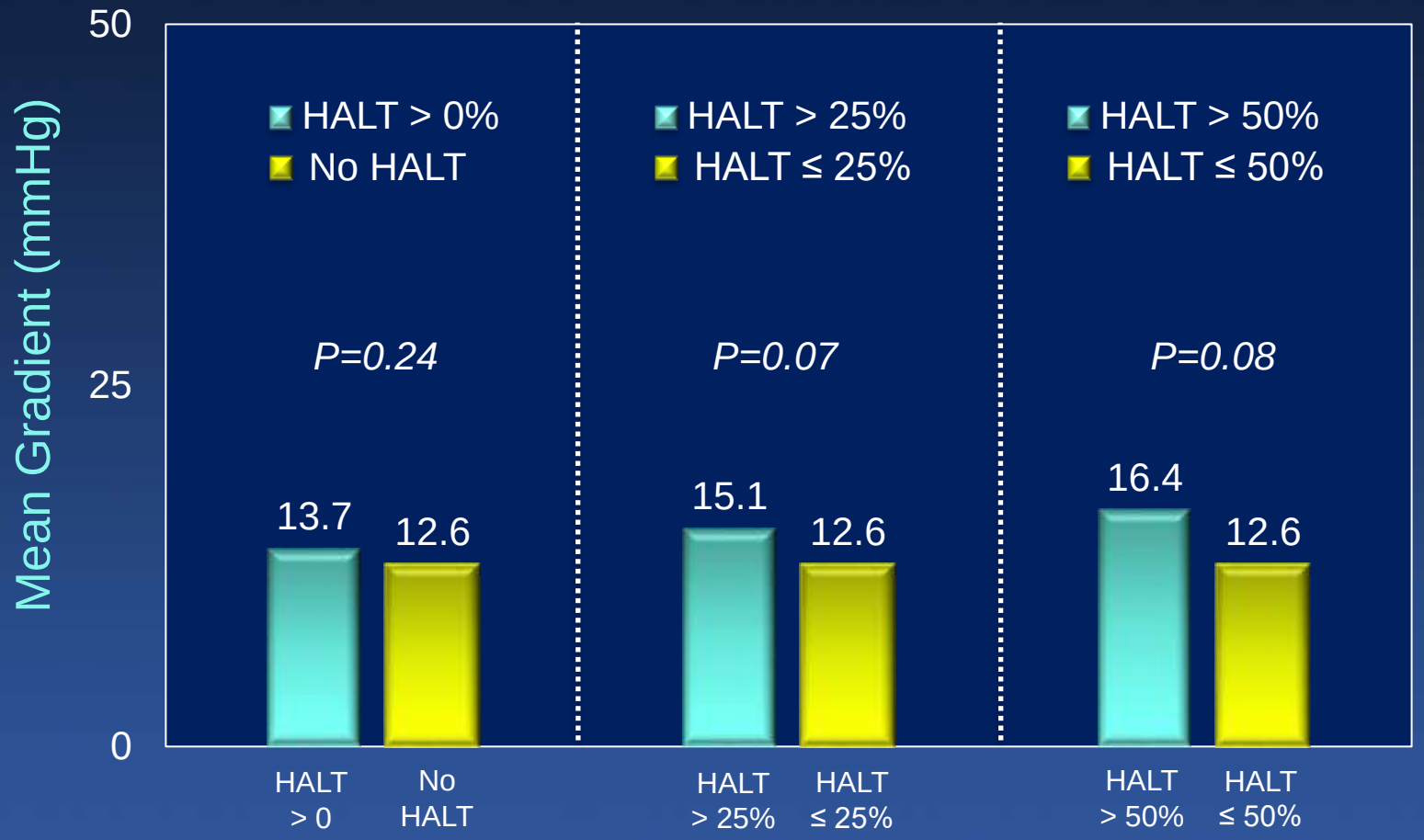


0/14 received anticoagulation

THE PARTNER 3 TRIAL

Mean Aortic Valve Gradient and Severity of HALT at 1 year

All Patients with Evaluable CTs – TAVR & SAVR



P-values are based on t-test

30-day HALT and Clinical Events

All Patients with Evaluable CTs – TAVR & SAVR

Clinical Events (n)	Day 7-30		Day 31-365	
	HALT at 30 Days (N=35)	No HALT at 30 Days (N=311)	HALT at 30 Days (N=35)	No HALT at 30 Days (N=311)
Death	0	0	0	4
Heart Failure	0	1	1	6
Angina	0	0	0	9
Myocardial Infarction	0	0	0	3
Clinical Valve Thrombosis*	0	0	3	1
Stroke	1	0	0	1
TIA	0	1	1	2
Retinal Artery Embolism	0	0	1	1

*Defined according to VARC2 definition

TAVR – Future Directions

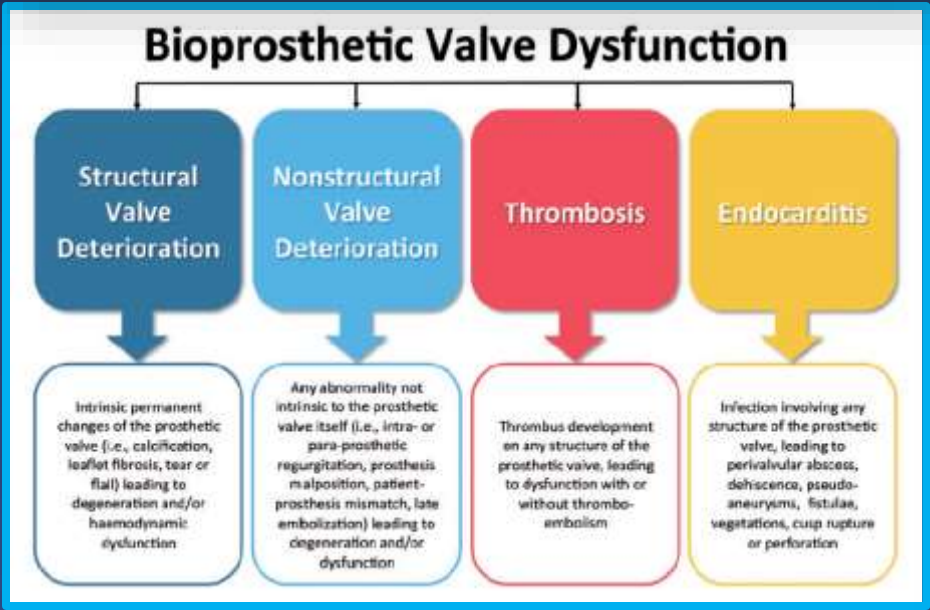
Still MANY Knowledge Gaps

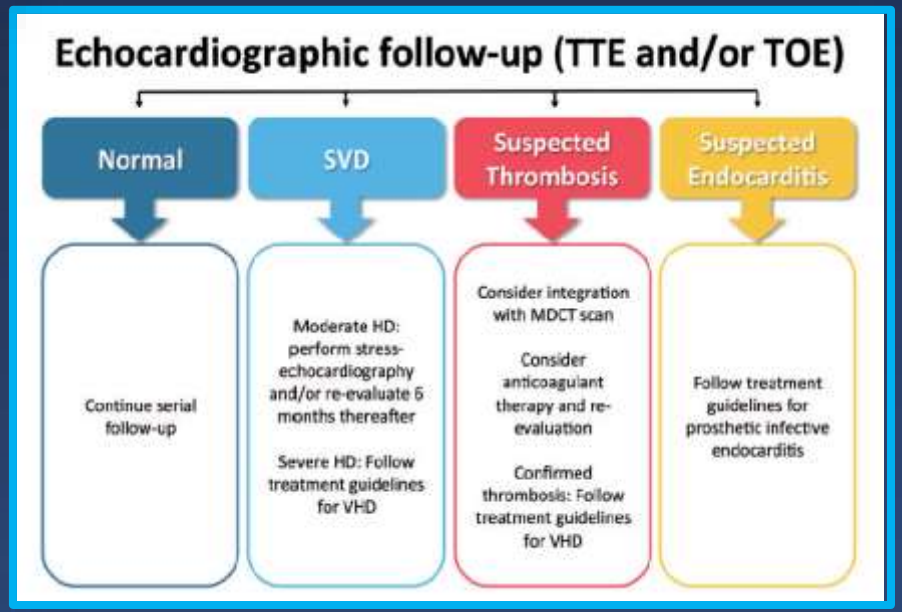
- Use of cerebral embolic protection to reduce strokes – systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- ***Bioprosthetic valve durability (SVD and BVF) – new definitions***

Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Davide Capodanno[1*†], Anna S. Petronio[2†], Bernard Prendergast[3], Helene Eltchaninoff[4], Alec Vahanian[5], Thomas Modine[6], Patrizio Lancellotti[7], Lars Sondergaard[8], Peter F. Ludman[9], Corrado Tamburino[1], Nicolò Piazza[10], Jane Hancock[3], Julinda Mehilli[11], Robert A. Byrne[12], Andreas Baumbach[13], Arie Pieter Kappetein[14], Stephan Windecker[15], Jeroen Bax[16], and Michael Haude[17]

New EU guidance with standardized definitions and endpoints to assess bioprosthetic aortic valve deterioration and failure



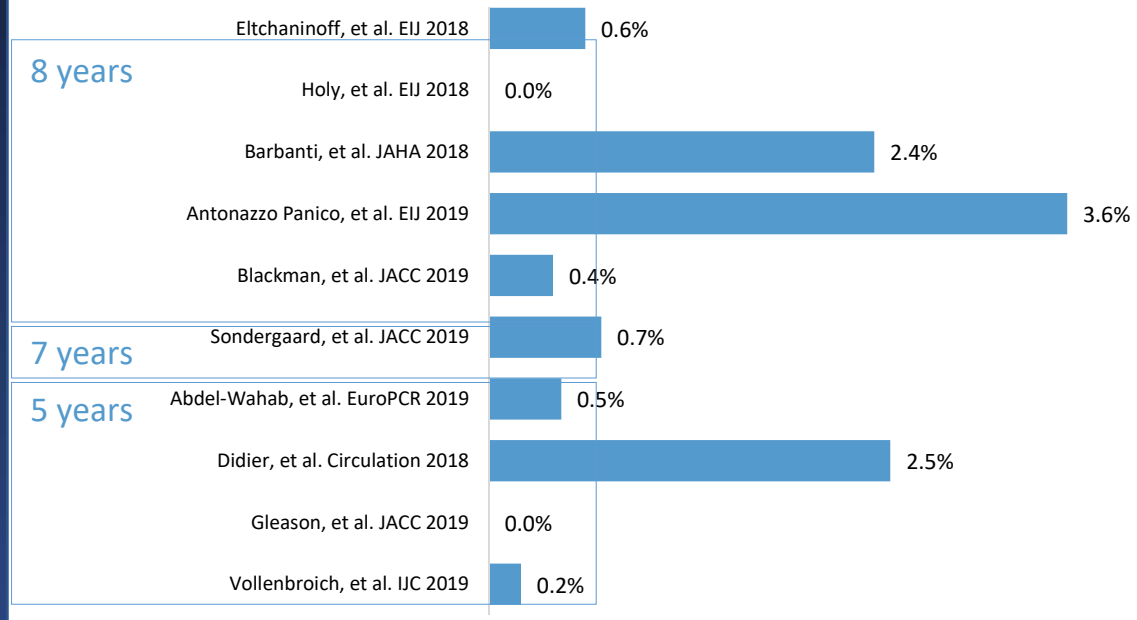


Capodanno D et al. Europ Heart J 2017

Long-term Durability of TAVR

ESC/EACTS definitions

Severe SVD

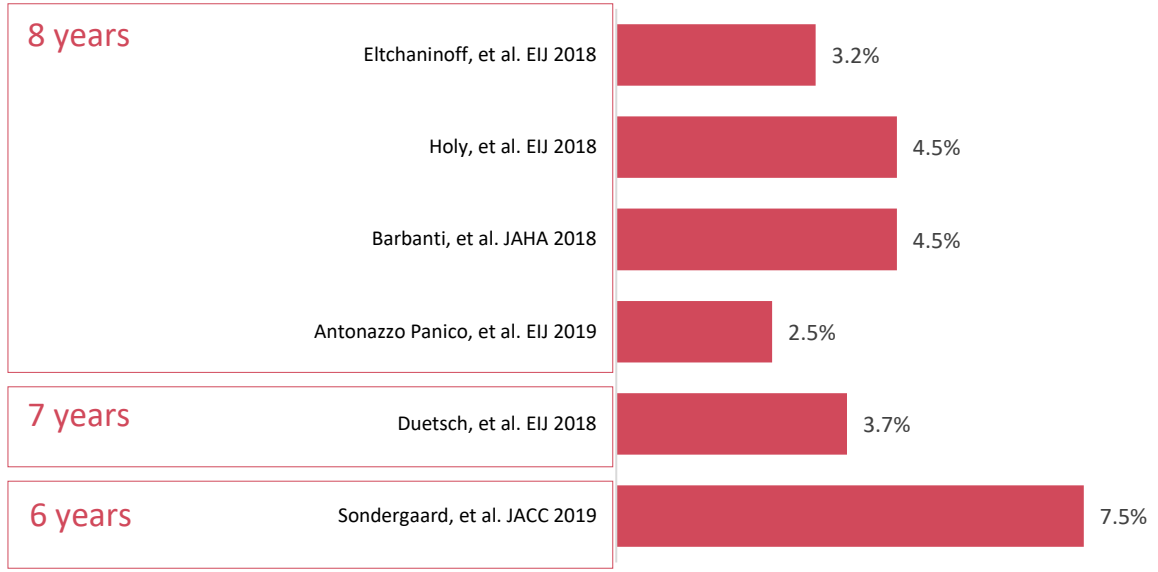


SVD at 5 to 8 years
Weighted incidence

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)

Capodanno D, et al. Eurointervention 2019

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

TAVR – Future Directions

Still MANY Knowledge Gaps

- Use of cerebral embolic protection to reduce strokes – systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- Bioprosthetic valve durability (SVD and BVF) – new definitions
- ***Safety and durability of TAV-in-TAV procedures and safety of failed TAVR surgical explantation***

All TAVR systems will certainly demonstrate evidence of valve degeneration during long-term (> 5 years) assessments. Is TAV-in-TAV a viable option?

Surgically explanted Sapien and CorveValve THVs

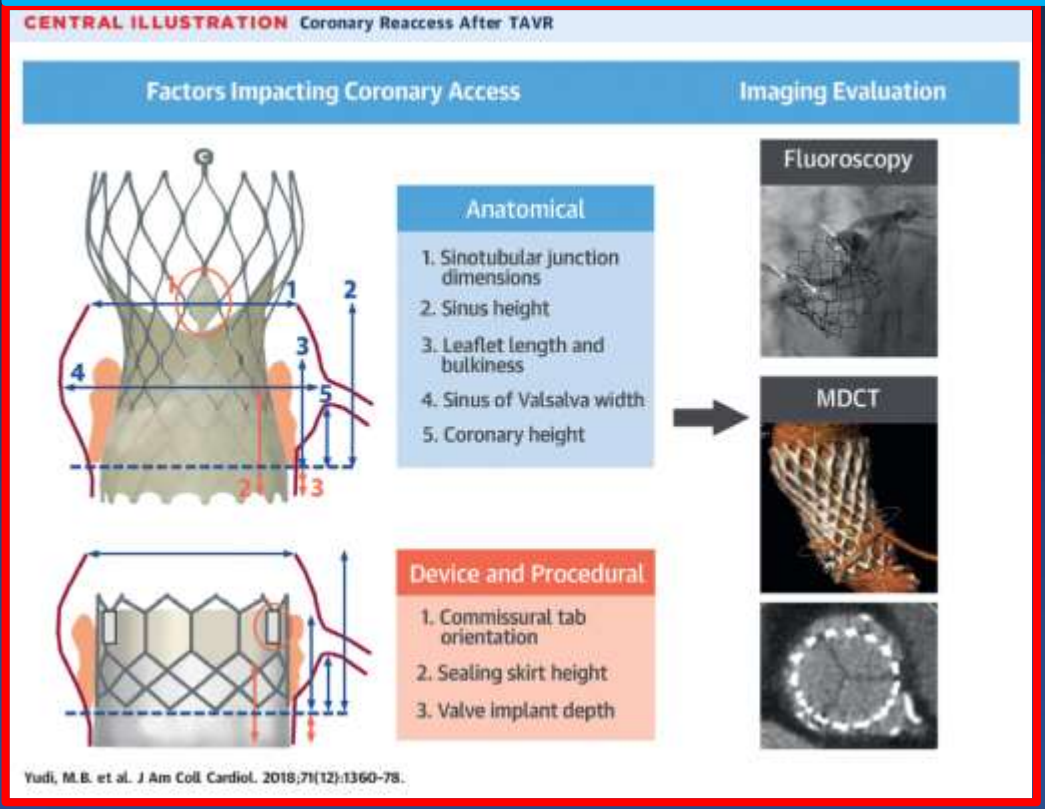
TAVR – Future Directions

Still MANY Knowledge Gaps

- Use of cerebral embolic protection to reduce strokes – systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- Bioprosthetic valve durability (SVD and BVF) – new definitions
- Safety and durability of TAV-in-TAV procedures and safety of failed TAVR surgical explantation
- ***Issues relating to coronary 'access' (esp. w CAD and younger pts)***

Coronary Angiography and Percutaneous Coronary Intervention After Transcatheter Aortic Valve Replacement

Matias B. Yudi, MBBS,[a] Samin K. Sharma, MD,[a] Gilbert H.L. Tang, MD, MSc, MBA,[b] Annapoorna Kini, MD[a]



Esp. relevant in patients with known CAD, in young low-risk patients with probable future 'valve-in' procedures, and during ACS events

Yudi et al. JACC 2018; 71:1360-78

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

TAVR – Future Directions

Still MANY Knowledge Gaps

- Use of cerebral embolic protection to reduce strokes – systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- Bioprosthetic valve durability (SVD and BVF) – new definitions
- Safety and durability of TAV-in-TAV procedures and safety of failed TAVR surgical explantation
- Issues relating to coronary 'access' (esp. w CAD and younger pts)
- ***Management of post-TAVR conduction disturbances (new pacemakers and especially new LBBB)***

Results (PARTNER 1 and 2)
30 Day to Two-Year Clinical Outcomes

Endpoint	LBBB (n = 215)	PPM (n = 315)	No PPM or LBBB (n = 2460)	P-value LBBB vs. None	P-value PPM vs. None	P-value PPM vs. LBBB
Death (all-cause)	24.0	18.0	16.0	0.003	0.32	0.12
CV Death	16.9	11.8	9.0	0.003	0.08	0.29
Rehospitalization	19.5	13.6	12.3	0.006	0.38	0.17
Death/Rehospitalization	34.4	28.6	24.9	0.003	0.08	0.16
LVEF	51.7	54.8	58.5	<0.0001	<0.0001	0.003

Event rates are Kaplan-Meier estimates landmarked at 30 days.
LVEF values reported are least-squares means from a linear mixed effects model

Tamim M. Nazif, MD and Jose M. Dizon, MD on behalf of The PARTNER Trial Investigators

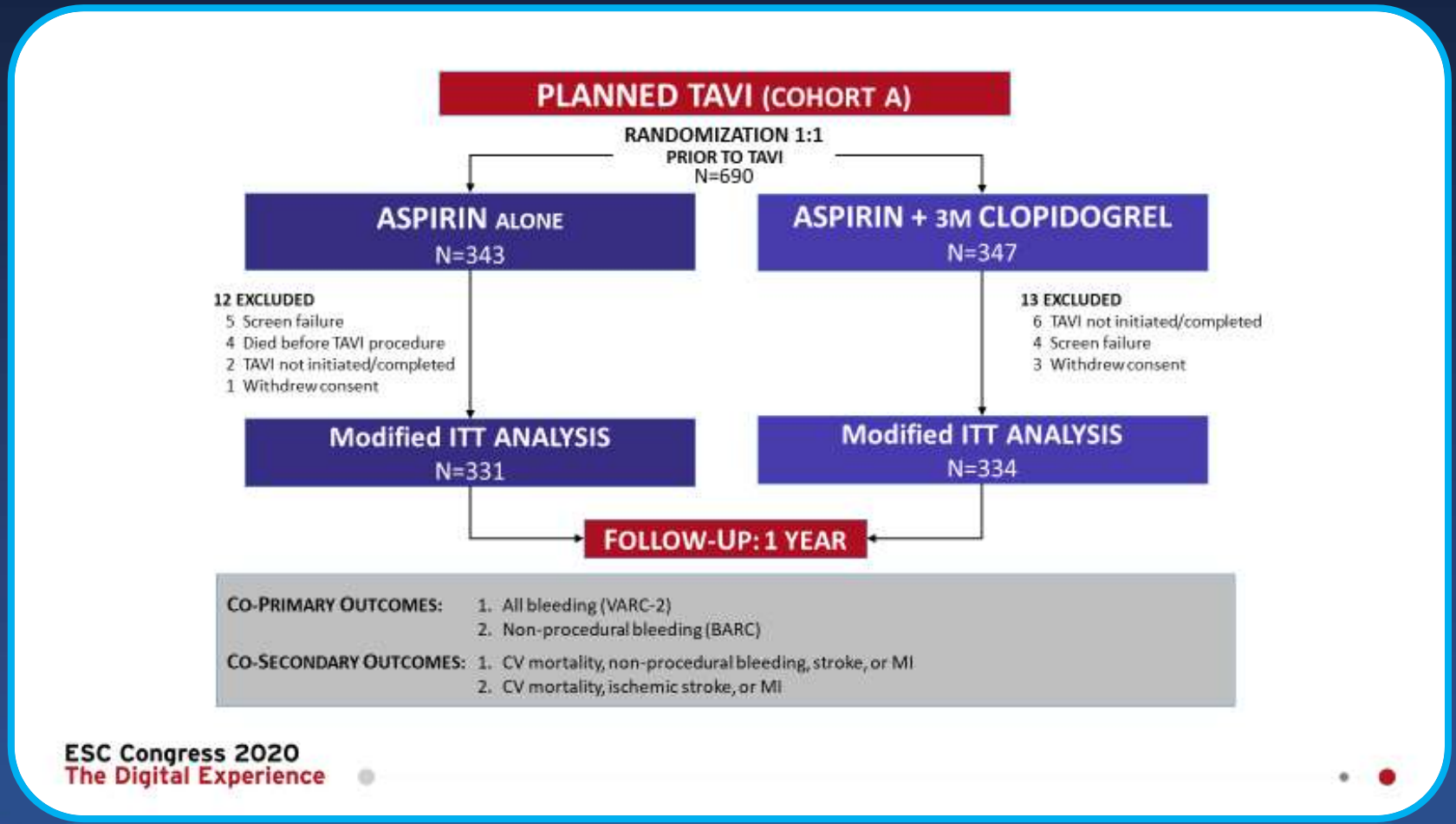
TAVR – Future Directions

Still MANY Knowledge Gaps

- ***Optimal antithrombotic pharmacotherapy after TAVR (both anti-platelet and anti-thrombotic meds)***

The POPULAR TAVI Trial

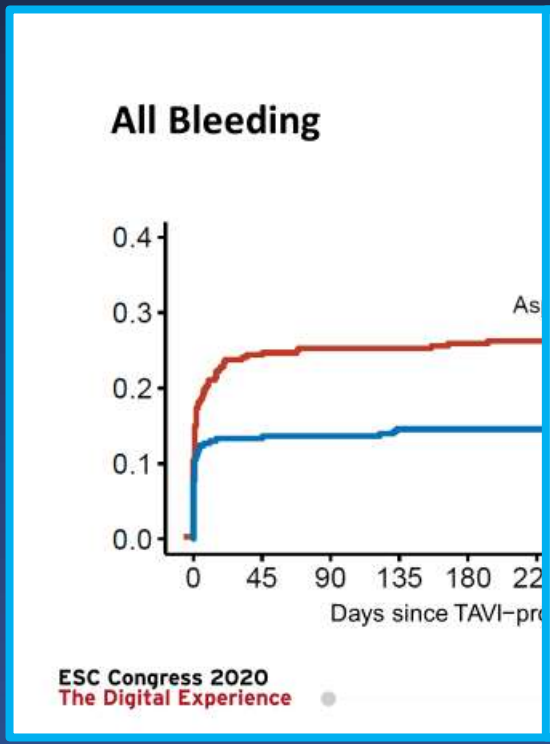
SAPT vs. DAPT

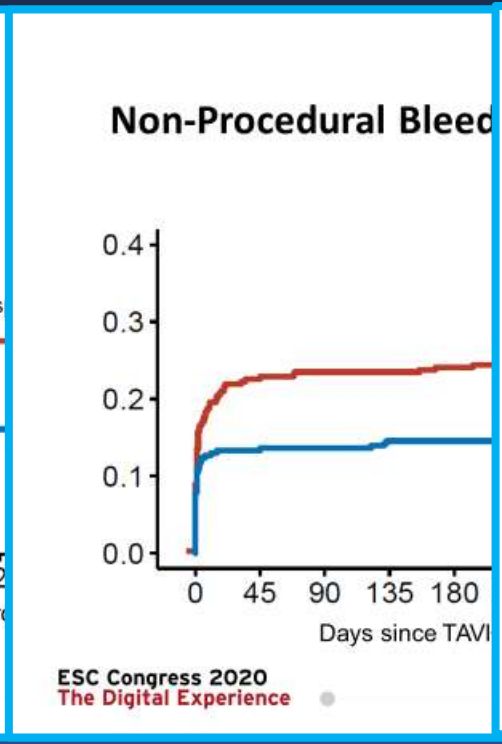


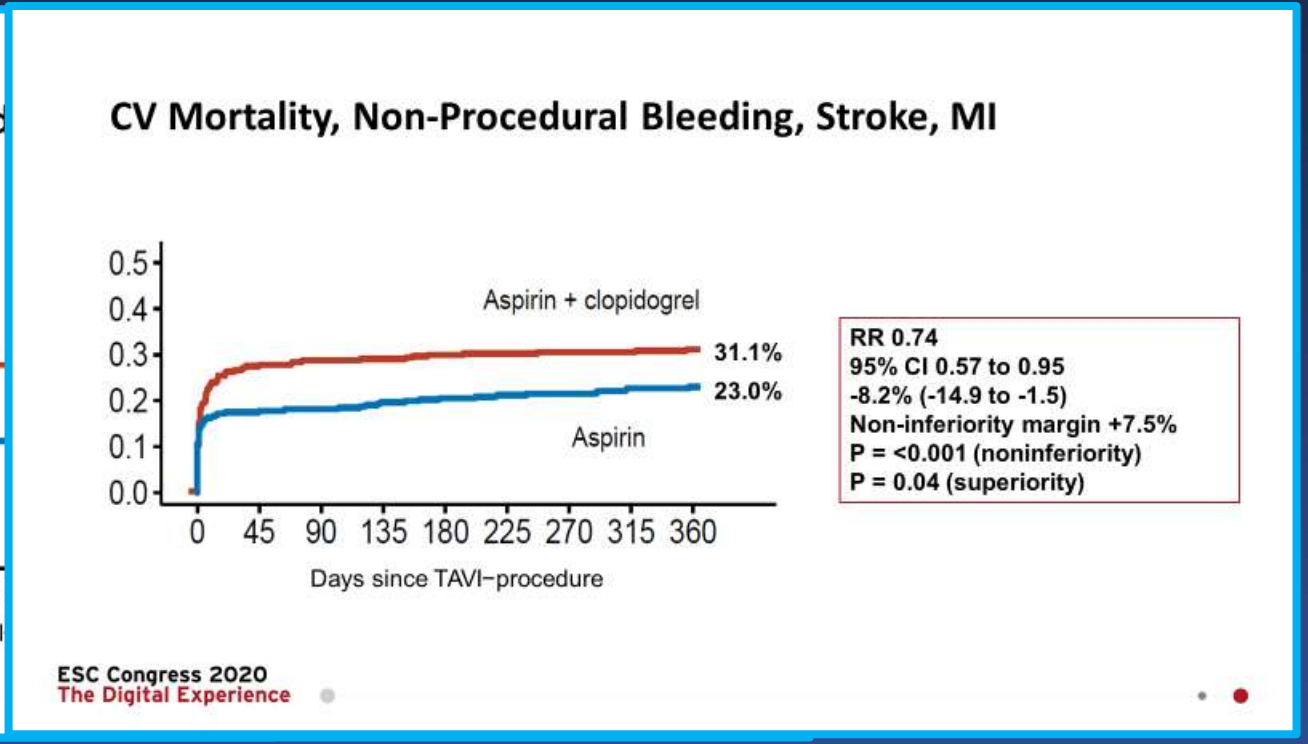
J Brouwer et al; NEJM 2020

The POPULAR TAVI Trial
SAPT vs. DAPT

KEY Endpoints







J Brouwer et al; NEJM 2020

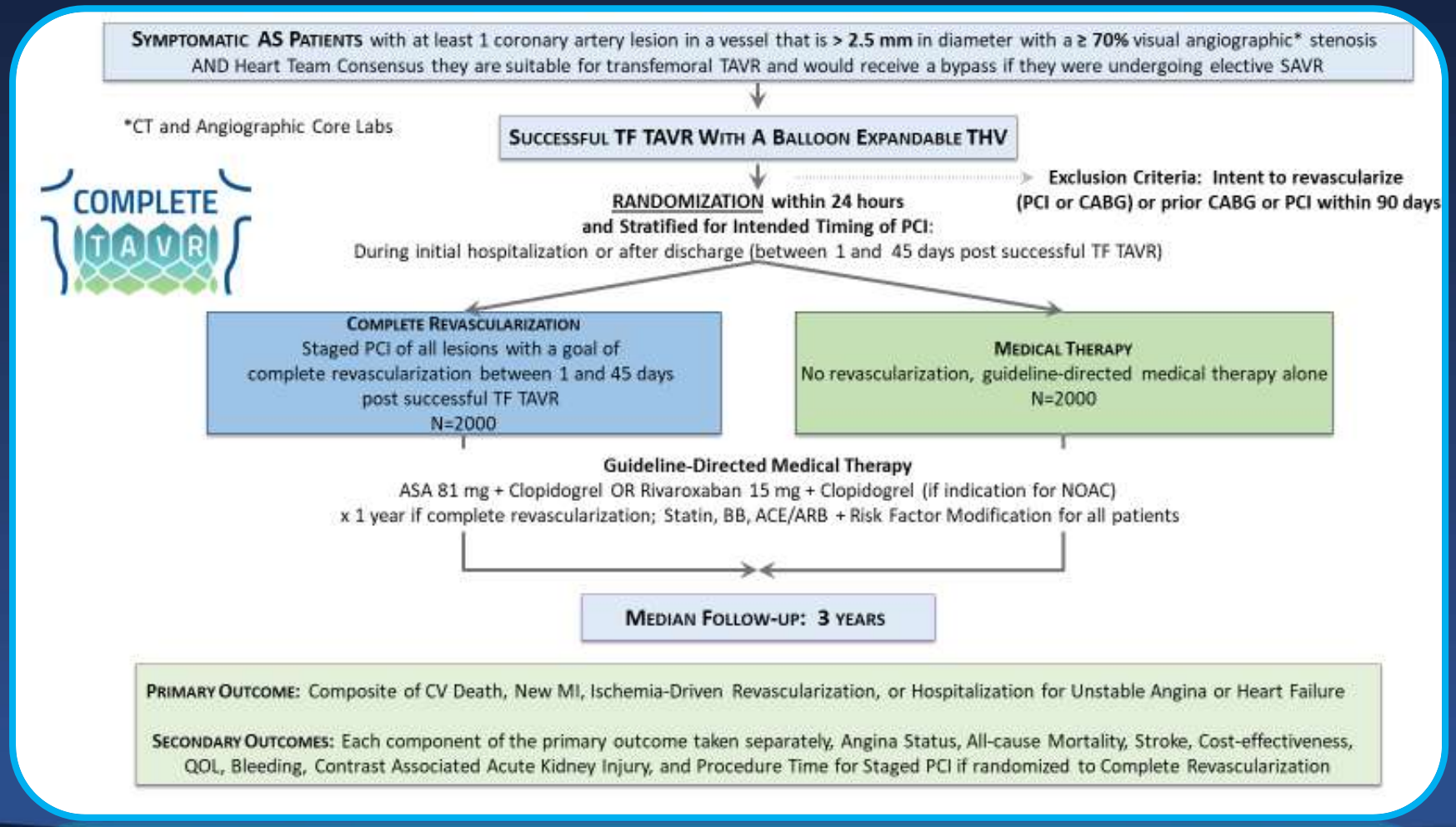
TAVR – Future Directions

Still MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both anti-platelet and anti-thrombotic meds)
- ***Management of severe AS in the setting of concomitant diseases (e.g. severe CAD, CKD, multi-valve disease, and AF)***

AS and CAD

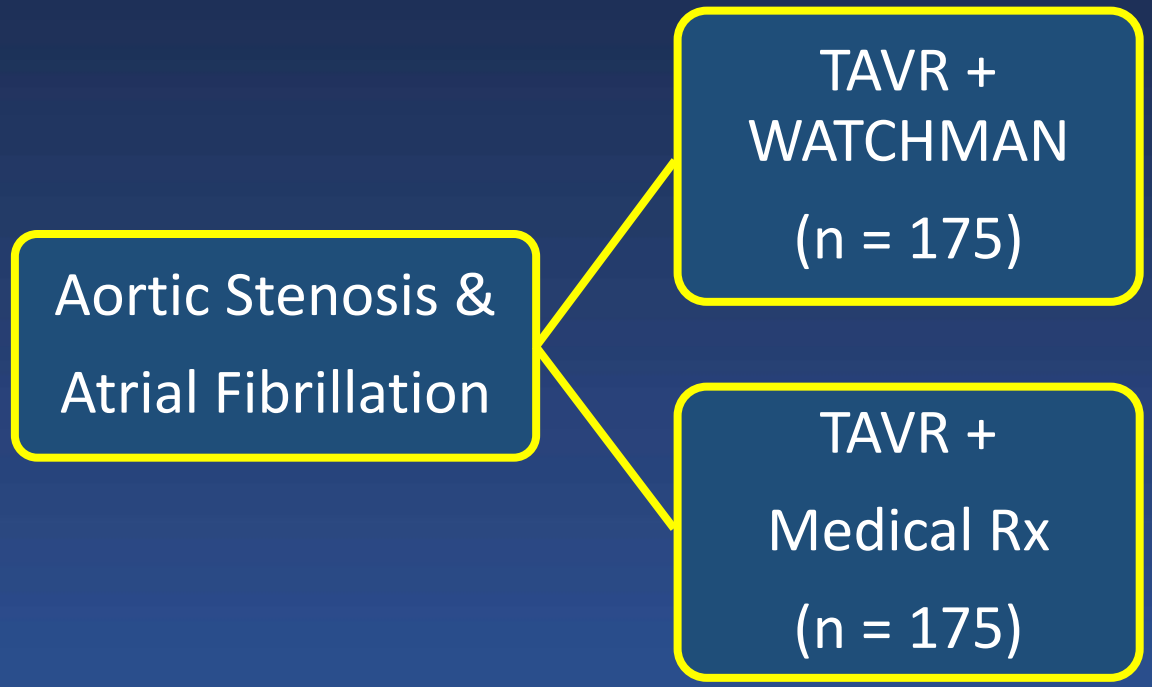
COMPLETE-TAVR



AS and Atrial Fibrillation

Watch-TAVR

National PIs: Samir Kapadia & Martin Leon
Grant support: Boston Scientific



1º Outcome:
- Death, stroke, bleeding @ 1 year

2º Outcome:
- Components of primary
- Any thromboembolism
- Cardiovascular death
- Re-hospitalization
- QoL (KCCQ-12)
- Procedural costs

TAVR – Future Directions

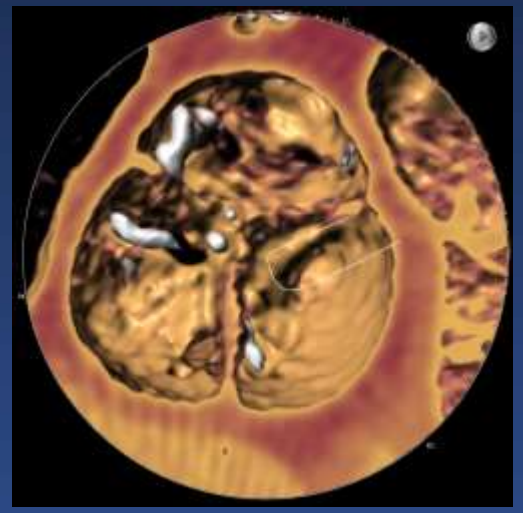
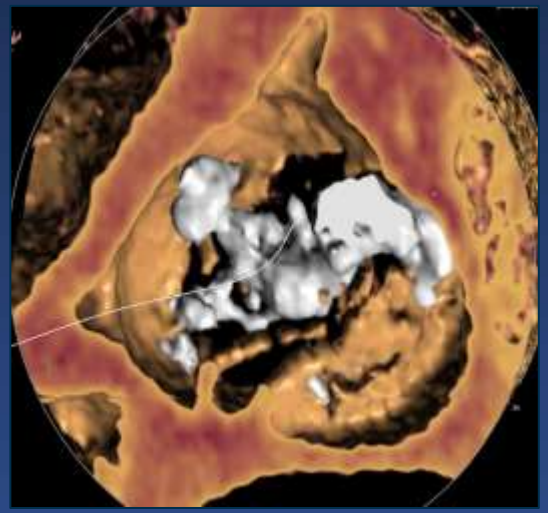
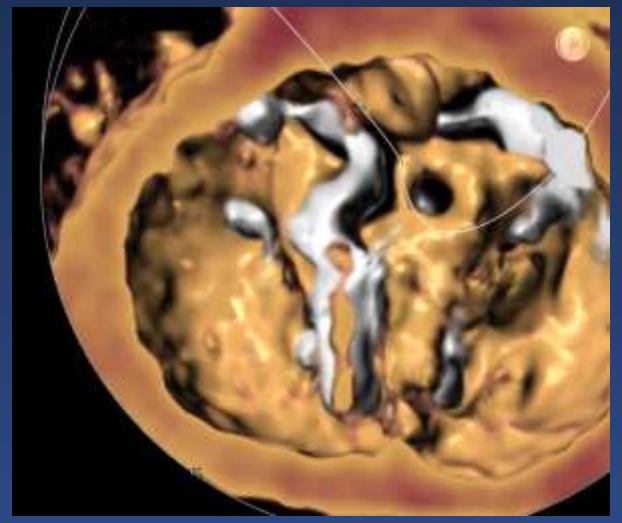
Still MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both anti-platelet and anti-thrombotic meds)
- Management of severe AS in the setting of concomitant diseases (e.g. severe CAD, CKD, multi-valve disease, and AF)
- ***Management of bicuspid aortic valve disease (TAVR vs. SAVR)***

Bicuspid Aortic Valve Classification

CTA System

(from 14 centers in North America, Europe and Asia)

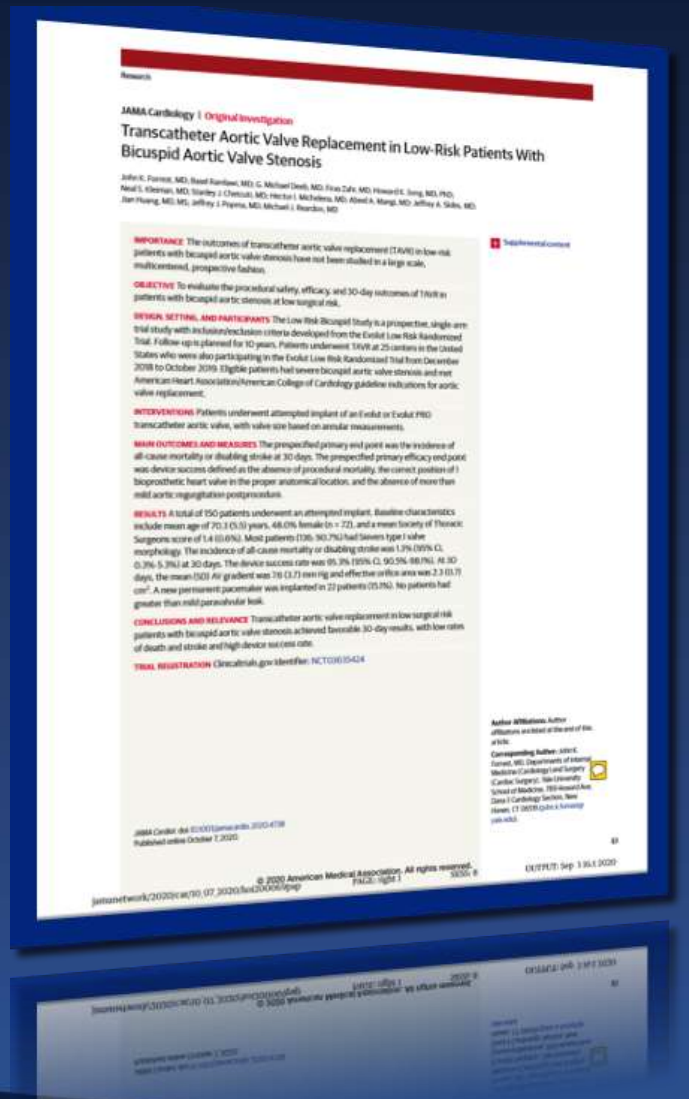
Tricommissural	*Bicommissural Raphe-type*	*Bicommissural Non Raphe-type*
		
3 commissures V-like orifice "functional or acquired"	2 commissures, 1 raphe Slit-like orifice	2 commissures, no raphe Slit-like orifice

Cardiovascular Research Foundation

Jilaihawi H. JACC Imaging 2016

Columbia University Medical Center
NewYork-Presbyterian

Evolut LR BAV Registry


JAMA Cardiology | Original Investigation

Transcatheter Aortic Valve Replacement in Low-Risk Patients With Bicuspid Aortic Valve Stenosis

Outcomes at 30 Days

Evolut™ Low Risk Bicuspid Study

No. of patients (KM estimates as %)	N = 150
All-cause mortality or disabling stroke	2 (1.3)
All-cause mortality	1 (0.7)
Disabling stroke	1 (0.7)
Non-disabling stroke	5 (3.3)
Major vascular complication	2 (1.3)
Aortic dissection	0 (0.0)
Annular rupture	0 (0.0)
Permanent pacemaker*	22 (14.7)
Permanent pacemaker†	22 (15.1)
Coronary artery obstruction	1 (0.7)

*Includes patients with baseline permanent pacemaker. †Excludes patients with baseline permanent pacemaker.

18

Cardiovascular Research Foundation

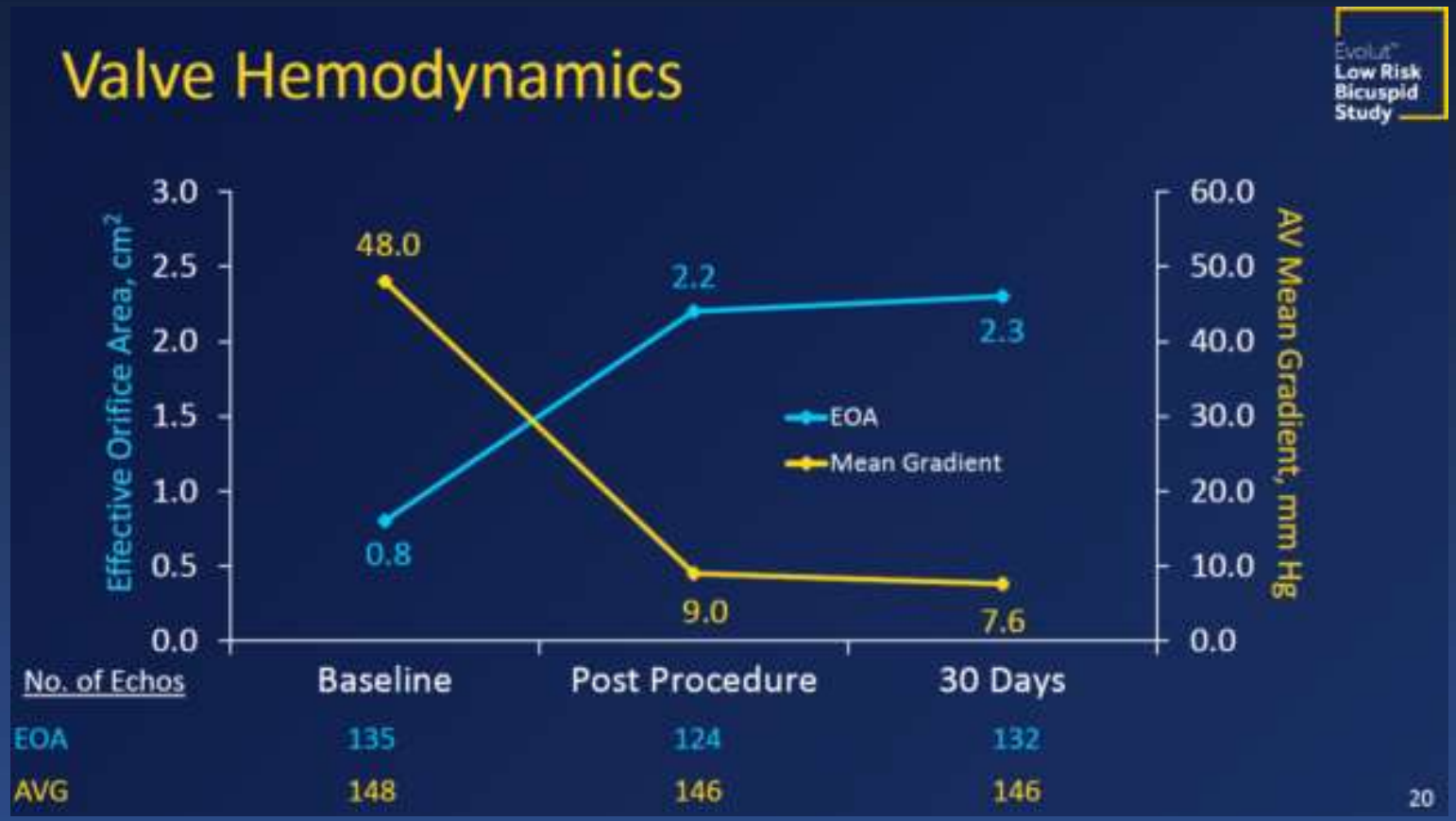
Forrest, J et al; JAMA Cardiology 2020

Columbia University Medical Center
NewYork-Presbyterian

Evolut LR BAV Registry

JAMA Cardiology | Original Investigation

Transcatheter Aortic Valve Replacement in Low-Risk Patients With Bicuspid Aortic Valve Stenosis



Forrest, J et al; JAMA Cardiology 2020

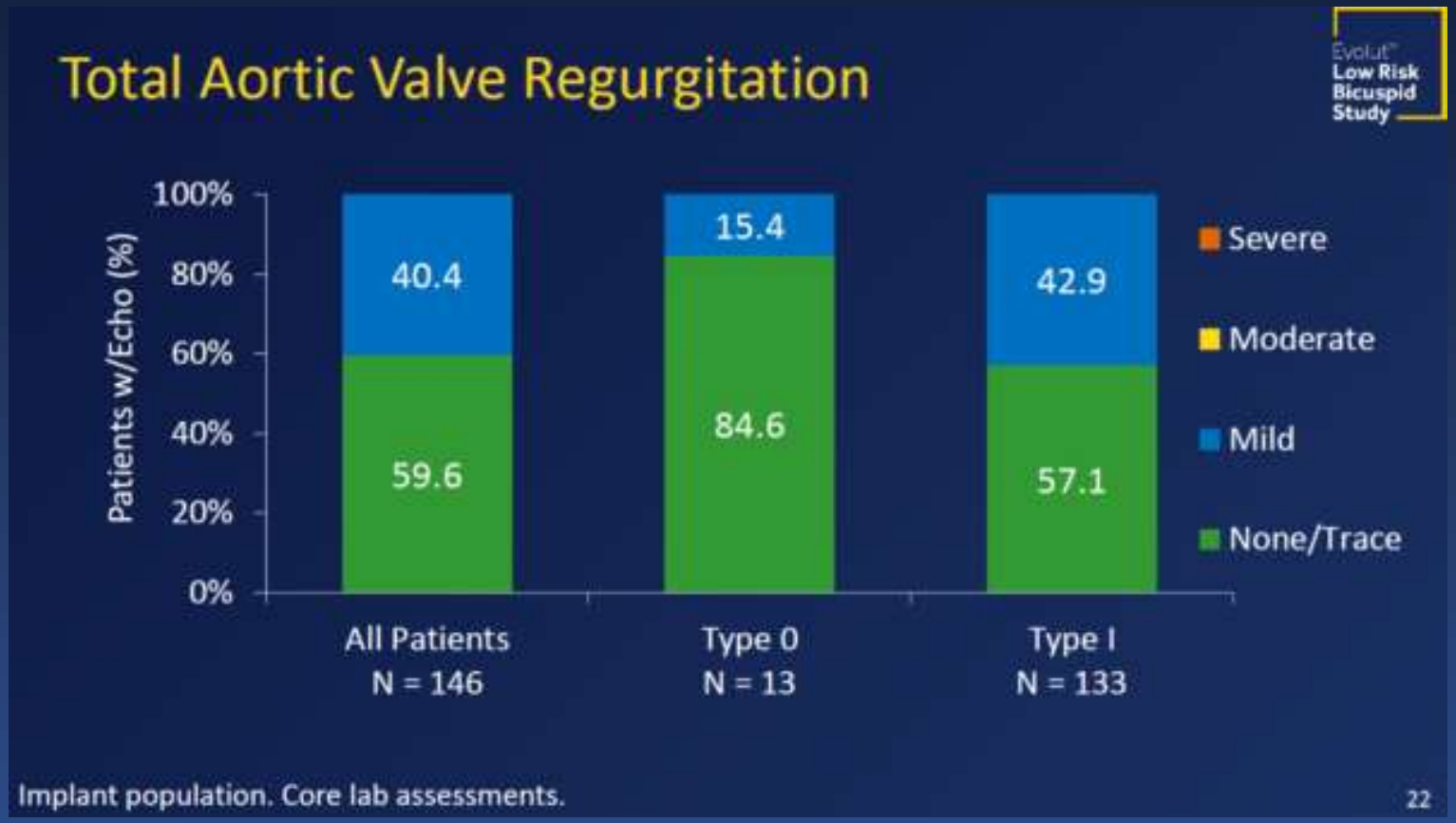
Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

Evolut LR BAV Registry

JAMA Cardiology | Original Investigation

Transcatheter Aortic Valve Replacement in Low-Risk Patients With Bicuspid Aortic Valve Stenosis



Forrest, J et al; JAMA Cardiology 2020

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

THE PARTNER 3 TRIAL

The PARTNER 3 Bicuspid Registry for SAPIEN 3 TAVR in Low-risk Patients

CRF TCT CONNECT

Mathew R. Williams, MD &
John G. Webb, MD
on behalf of the PARTNER 3 Trial Investigators

THE PARTNER 3 TRIAL

Primary Endpoint

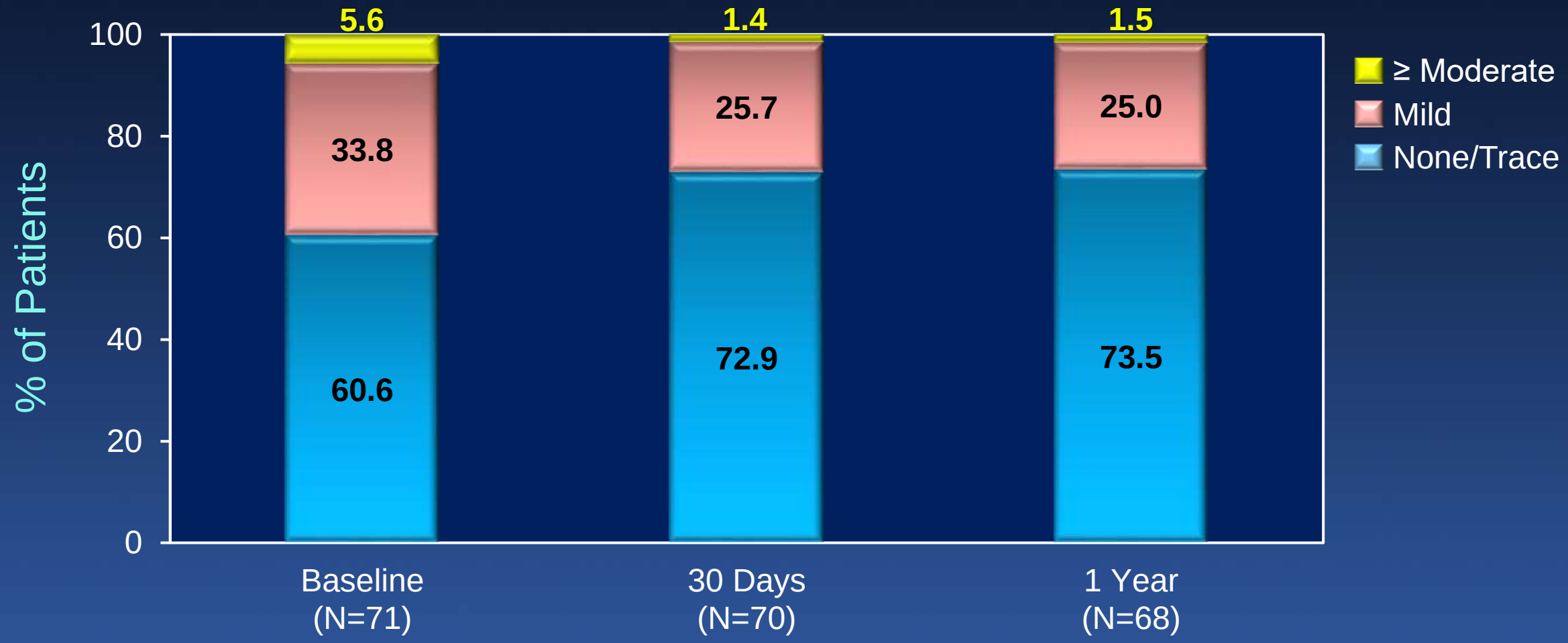
Outcomes	30 Days		1 Year
	Registry (N=71)	CAP (N=98)	Registry (N=71)
Composite	7.0% (5)	6.0% (6)	8.5% (6)
All-cause death	0%	0%	1.4% (1)
All Stroke	2.8% (2)	0%	2.8% (2)
Disabling	0%	0%	0%
CV Rehospitalization	4.2% (3)	6.0% (6)	5.6% (4)

Event rates are KM estimates % (no. of patients)

THE PARTNER 3 TRIAL

Aortic Regurgitation

Bicuspid Registry



TAVR – Future Directions

Still MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both anti-platelet and anti-thrombotic meds)
- Management of severe AS in the setting of concomitant diseases (e.g. severe CAD, CKD, multi-valve disease, and AF)
- Management of bicuspid aortic valve disease (TAVR vs. SAVR)
- ***Management of asymptomatic severe AS and symptomatic moderate AS (subgroups)***

The EARLY TAVR Trial

Asymptomatic Severe AS and 2D-TTE (PV ≥4m/s or AVA ≤1 cm²)
Exclusion if patient is symptomatic, age <65 yo, EF<50%, concomitant surgical indications, or STS >8

Treadmill Stress-Test

Stress-Test Normal

CTA and Angiography
TF- TAVR eligibility

Early-TAVR Randomized Trial

Randomization 1:1
Stratified by STS (<3 vs ≥3)

TF-TAVR

Clinical Surveillance

Stress-Test Abnormal

Early TAVR Registry

1109 pts, 75 US sites

Primary Endpoint (superiority): 2-year composite of all-cause mortality, all strokes, and repeat hospitalizations (CV)

Principal Investigators:
Philippe Généreux, Allan Schwartz
Chair: Martin B. Leon

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

TAVR UNLOAD Trial - Moderate AS + HF

(300 patients, 1:1 Randomized)

PIs: Nicolas M. Van Mieghem and Martin B. Leon

TAVR UNLOAD Trial

International Multicenter Randomized

Heart Failure
LVEF < 50%
NYHA ≥ 2
Optimal HF therapy (OHFT)
Moderate AS

R

TAVR + OHFT

OHFT Alone

Follow-up:
1 month
6 months
1 year

Clinical endpoints
Symptoms
Echo
QoL

Primary Endpoint
Hierarchical occurrence of:
- **All-cause death**
- **Disabling stroke**
- **Hospitalizations for HF, aortic valve disease**
- **Change in KCCQ**

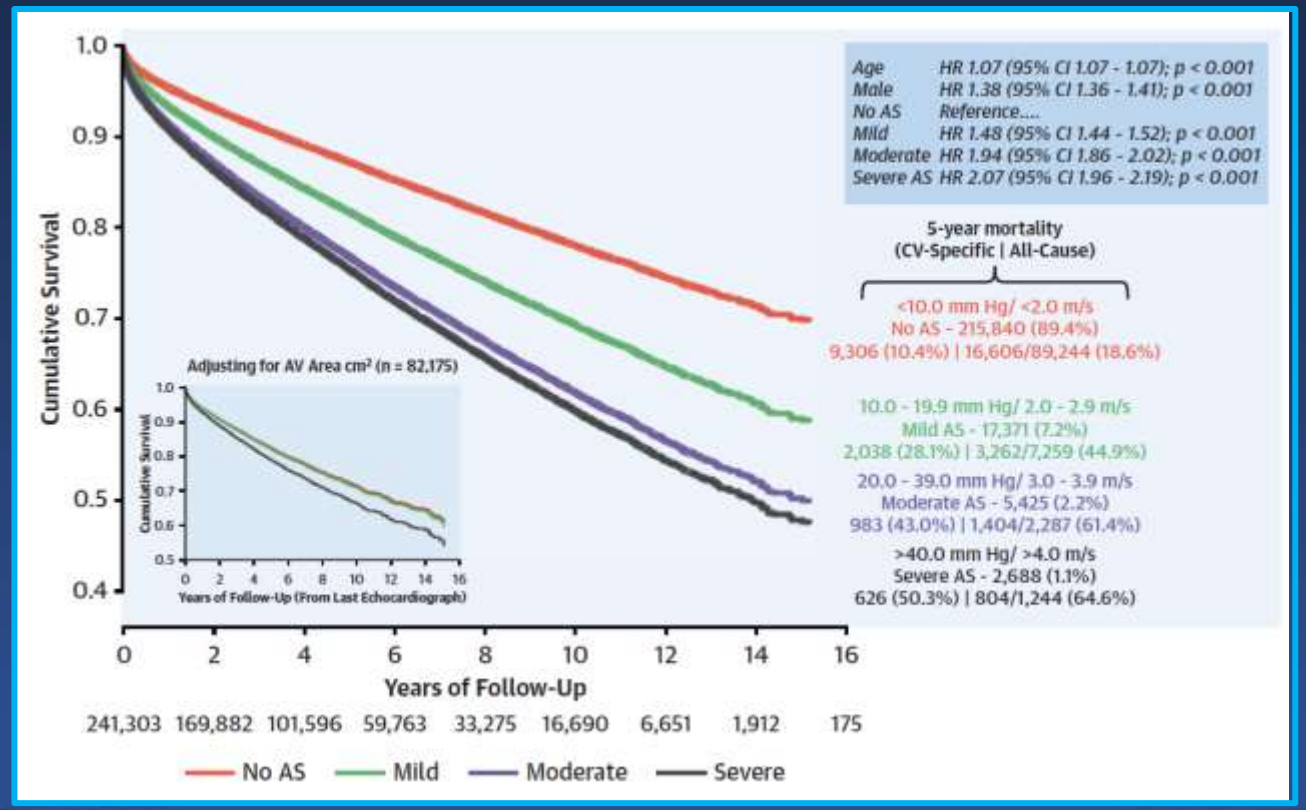
Reduced AFTERLOAD
Improved LV systolic and diastolic function

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

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



Strange G et al; J Am Coll Cardiol 2019

TAVR – Future Directions

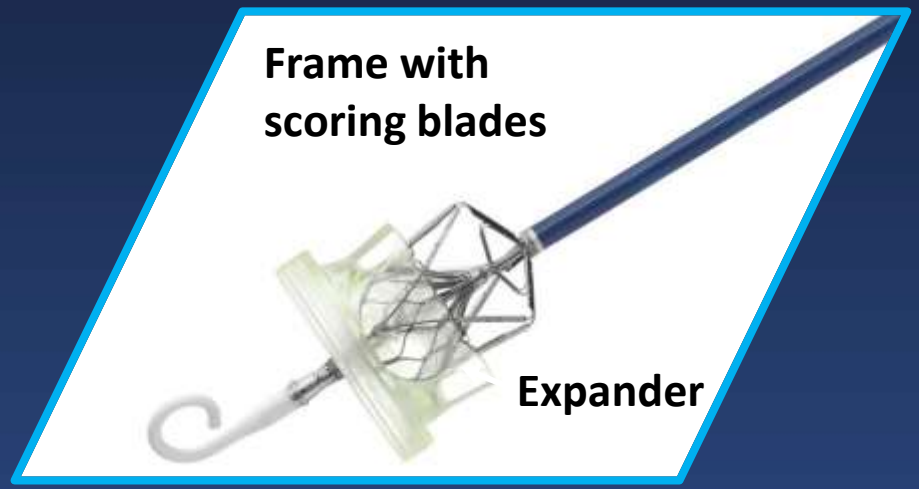
Still MANY Knowledge Gaps

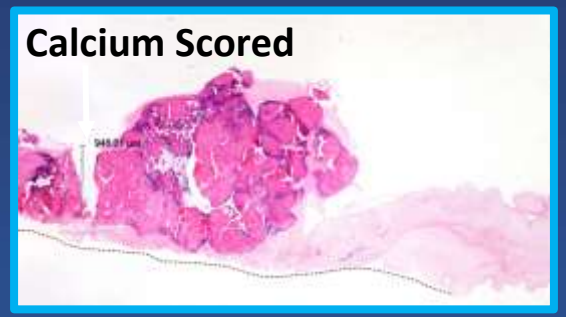
- Optimal antithrombotic pharmacotherapy after TAVR (both anti-platelet and anti-thrombotic meds)
- Management of severe AS in the setting of concomitant diseases (e.g. severe CAD, CKD, multi-valve disease, and AF)
- Management of bicuspid aortic valve disease (TAVR vs. SAVR)
- Management of asymptomatic severe AS and symptomatic moderate AS (subgroups)
- ***Life journey w AS in younger patients (aortic valve remodeling, multiple procedures, which comes first = sequencing?)***

TAVR – Future Directions

Aortic Valve Remodeling

Leaflex AVRT





- Mechanical scoring blades fracture leaflet calcium and improve leaflet mobility
- 13 Fr catheter
- Non-occlusive (no PM)
- Can be used as (1) stand-alone, (2) bridge to TAVR/SAVR or (3) preparation for TAVR (heavily calcified valves)

Aortic Stenosis *Lifelong* Therapy Choices

Age matters (symptomatic severe AS)

< 50 yo	50-65 yo	65-75yo	> 75 yo
• SAVR • MV>BV	• SAVR • MV or BV • TAVR only if SAVR adverse	• SAVR or TAVR • TAVR ideal or SAVR adverse • SDM	• TAVR • SAVR only if TAVR adverse
MV= mechanical valve BV= bioprosthetic valve	Adverse= clinical or anatomic factors	SDM= shared decisions	

Think SEQUENCING…

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

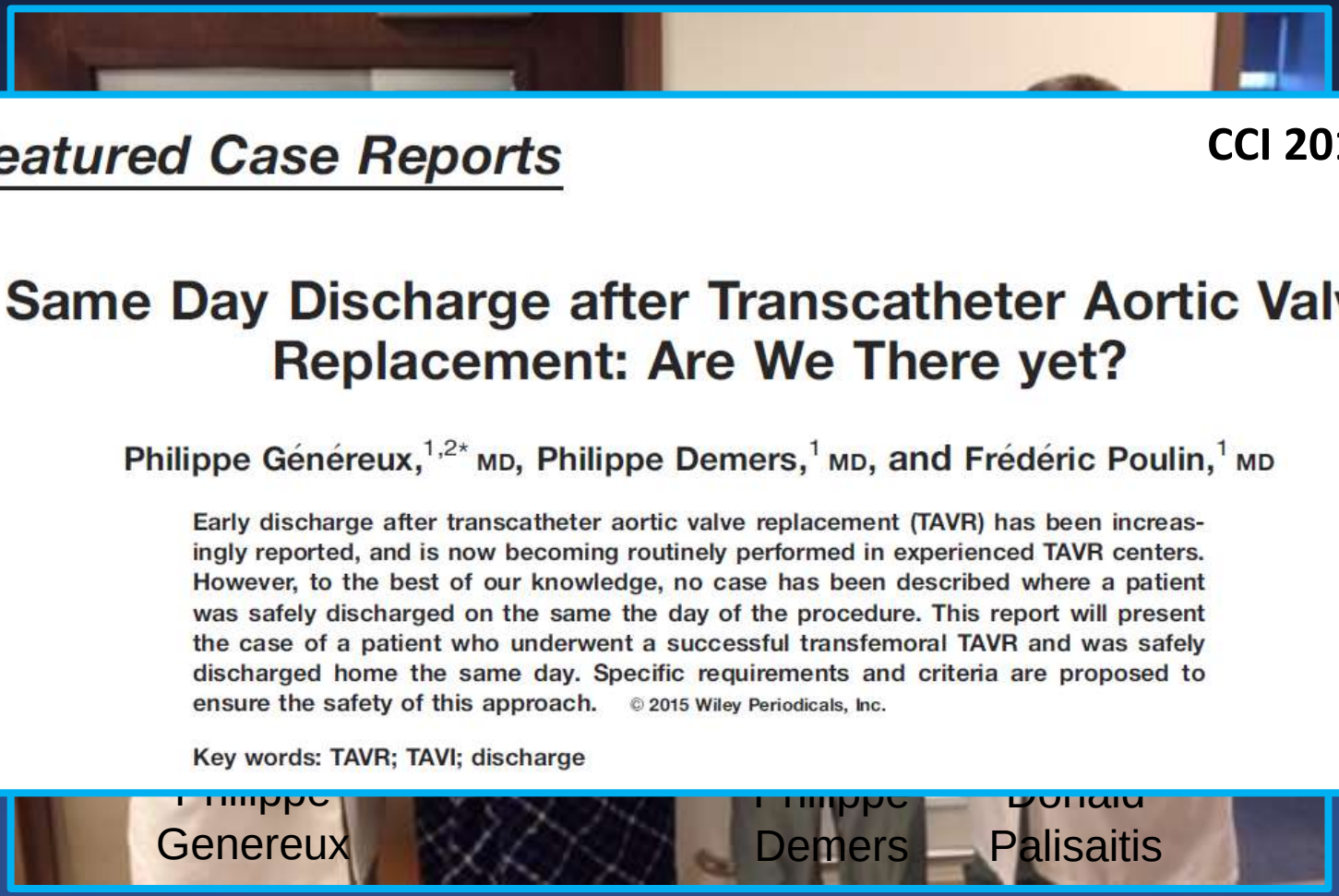
The Patients are Simply AMAZING!

Patient #1

92 yo man with critical AS… TAVR at CUMC on 2/8/06… Playing golf in Palm Springs on 3/8/06!!!

“Outpatient” Same-Day TAVR

Sacre-Coeur Hospital; Montreal, CN



CCI 2016

Featured Case Reports

Same Day Discharge after Transcatheter Aortic Valve Replacement: Are We There yet?

Philippe Généreux,[1,2*] MD, Philippe Demers,[1] MD, and Frédéric Poulin,[1] MD

Early discharge after transcatheter aortic valve replacement (TAVR) has been increasingly reported, and is now becoming routinely performed in experienced TAVR centers. However, to the best of our knowledge, no case has been described where a patient was safely discharged on the same the day of the procedure. This report will present the case of a patient who underwent a successful transfemoral TAVR and was safely discharged home the same day. Specific requirements and criteria are proposed to ensure the safety of this approach. © 2015 Wiley Periodicals, Inc.

Key words: TAVR; TAVI; discharge

Genereux P et al. Catheter Cardiovasc Interv 2016;87:980-2

Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

It's is All About the Patients!

Remember,
your patients are
the point-of-care!!!