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





20 mins



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

- Research Support
- Consulting Activities*
- Equity

Company

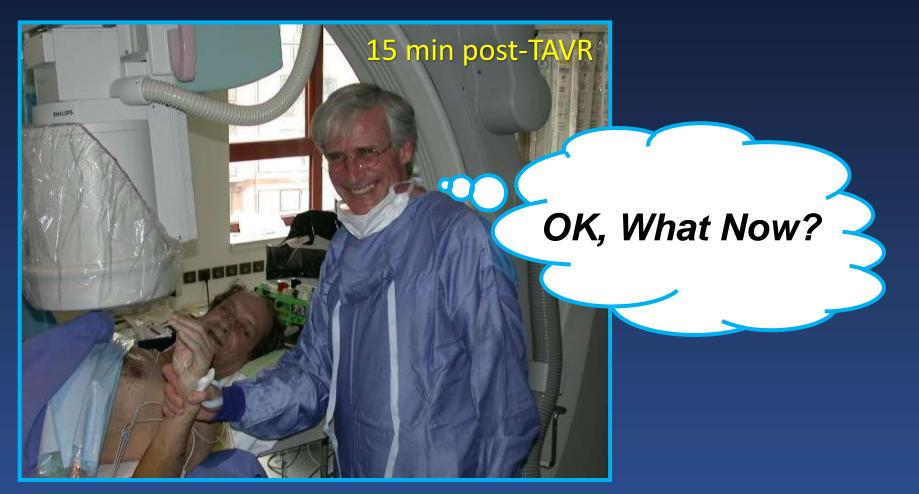
Abbott, Boston Scientific, Edwards Lifesciences, Medtronic Abbott, Boston Scientific, Edwards Lifesciences, Gore, Medtronic Ancora, Conveyor, East End Medical, K2, Medinol, Pi-Cardia, Triventures, Venus MedTech, Valve Medical, XenterMD

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





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









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

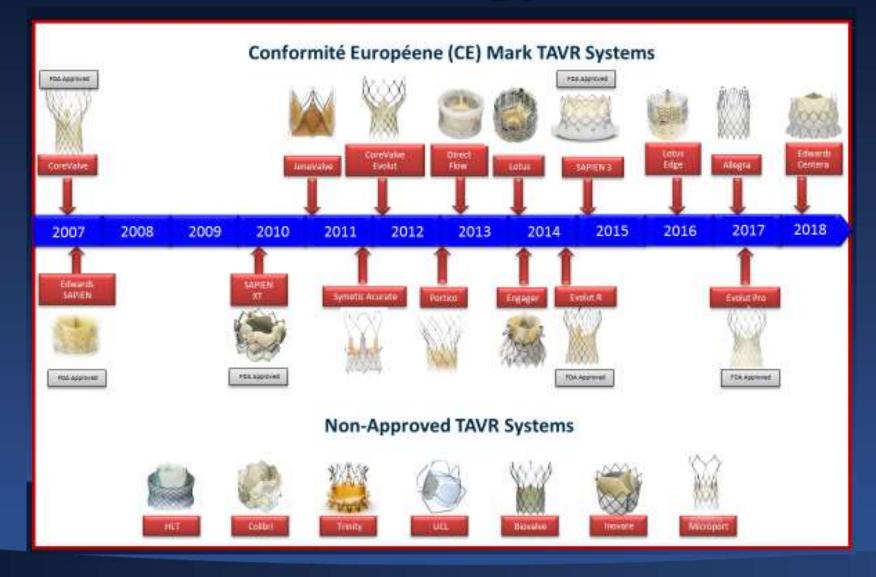
MDT Evolut R (PRO+) Edwards Sapien 3 (Ultra)



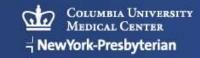




TAVR Technology Evolution







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





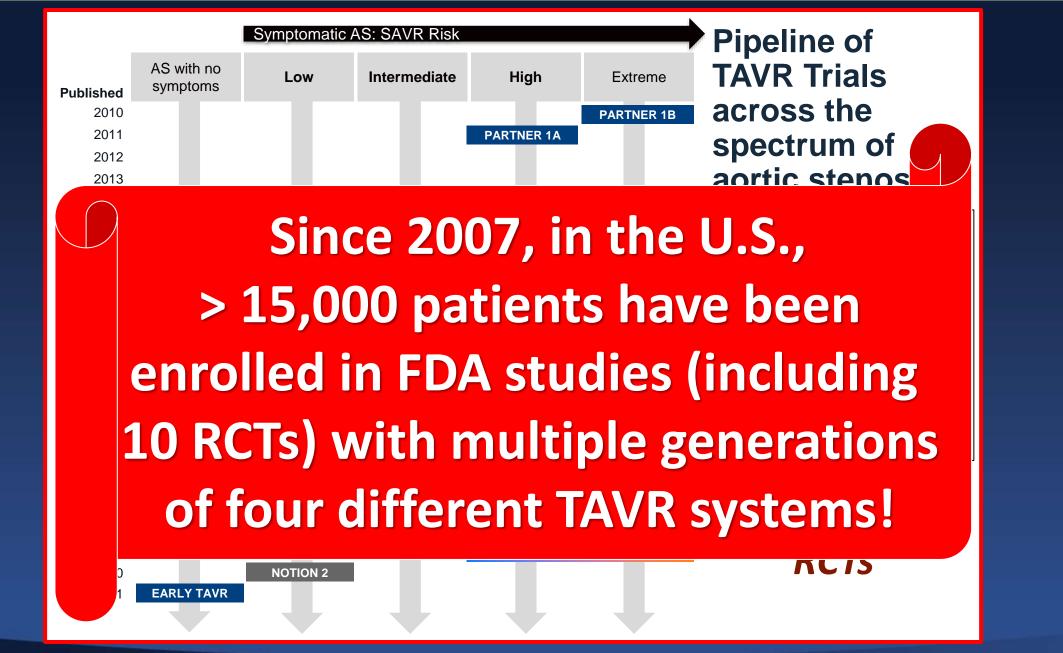
TAVR Procedural Refinements The minimalist strategy

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!*

id ambulation and early discharge plans (1-2 days)







Cardiovascular Research Foundation

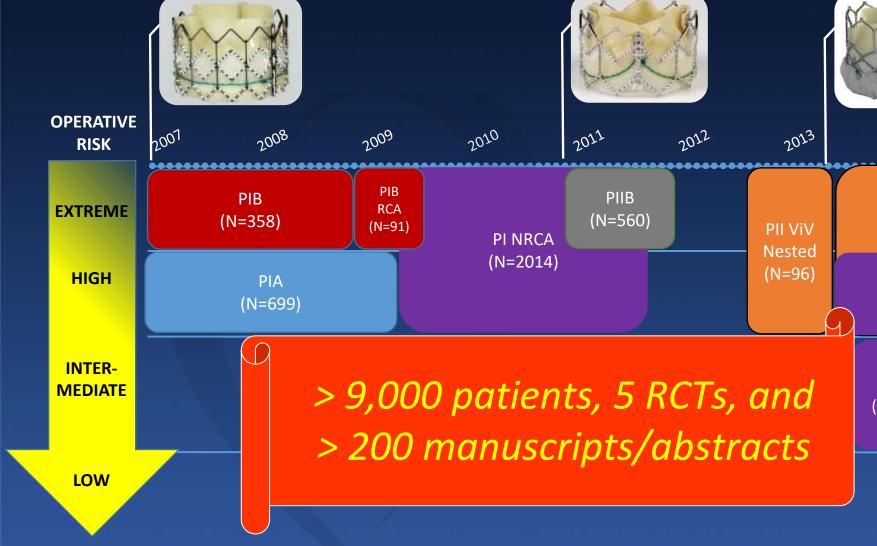
Capodanno D, Leon MB. EuroIntervention 2016



The PARTNER Trial Phenomenon

SAPIEN XT

SAPIEN 3



PARTNER 3

TRIAL

SAPIEN

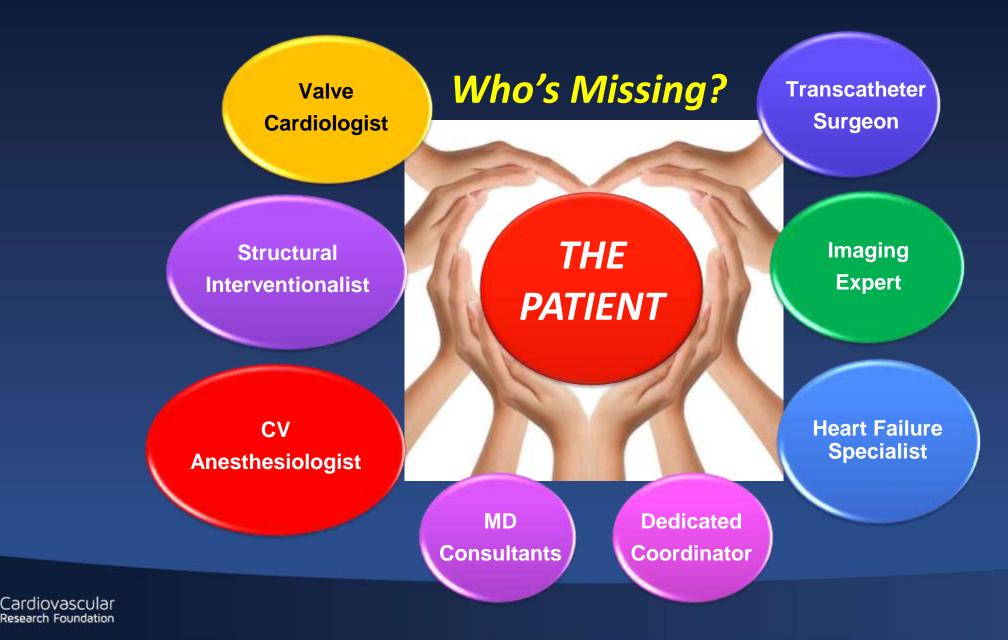
TAVR (XT) vs. TAVR (SAPIEN) TAVR-only Registry **TAVR Valve in Valve Registry** 2014 2015 2016 2017 PII ViV CA (N=269) PII S3HR (N=583) PII S3i PII S3i (N=1078) (N=1078) PIII

TAVR vs. Standard Therapy

(N=1000)

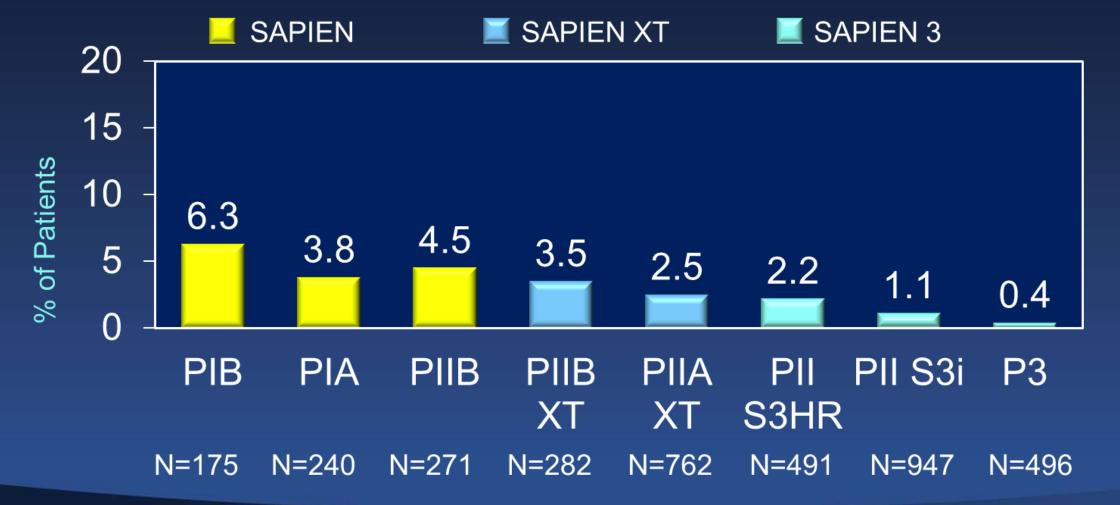
TAVR vs. SAVR

The HEART TEAM 3.0



Columbia University Medical Center

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



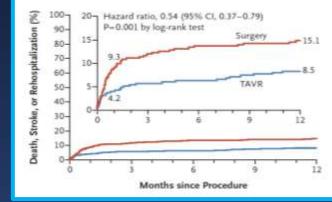
N Engl J Med 2019

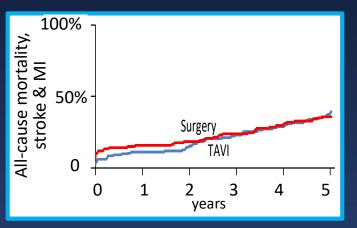




TAVR Low-Risk Trials (4 RCTs - 3,661 patients)

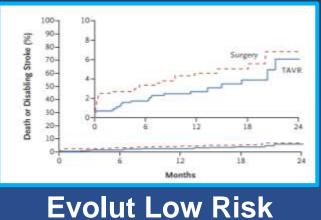




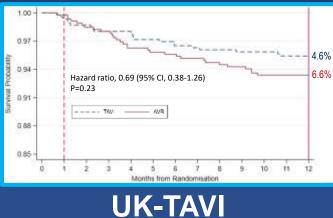


NOTION





PARTNER 3

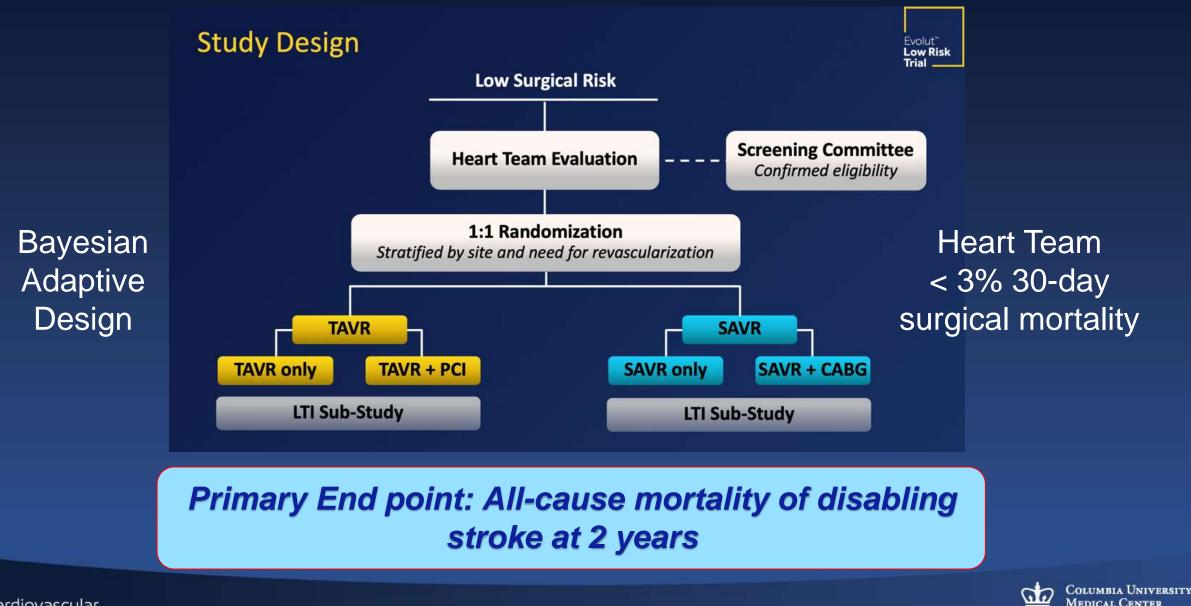




Columbia University Medical Center

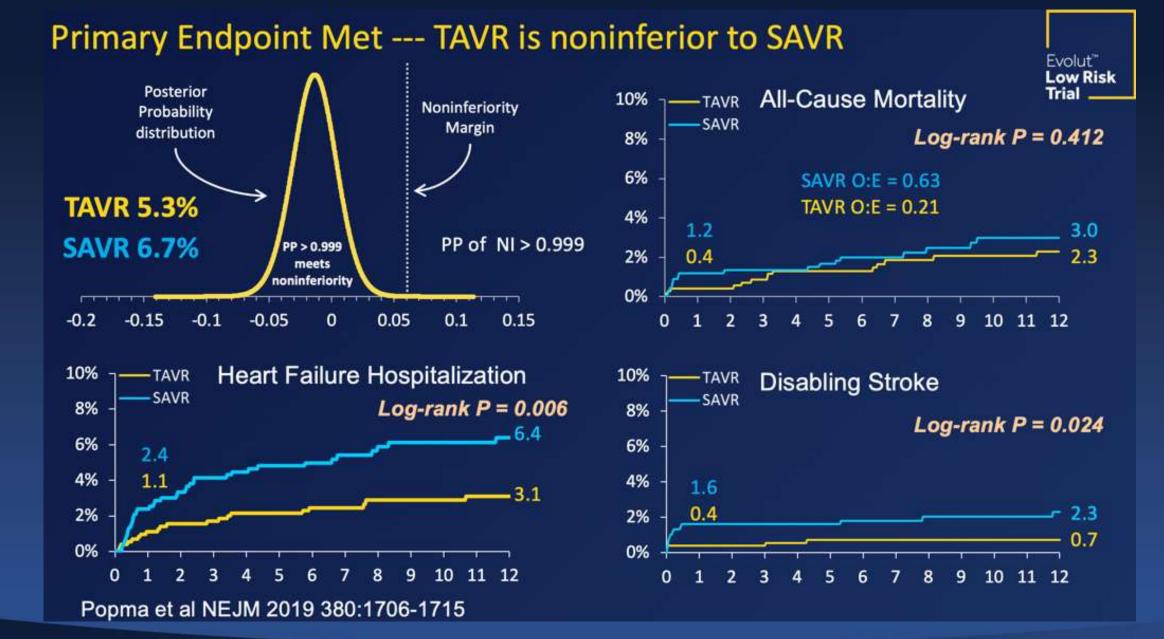


Evolut Low-Risk TAVR Trial



- NewYork-Presbyterian



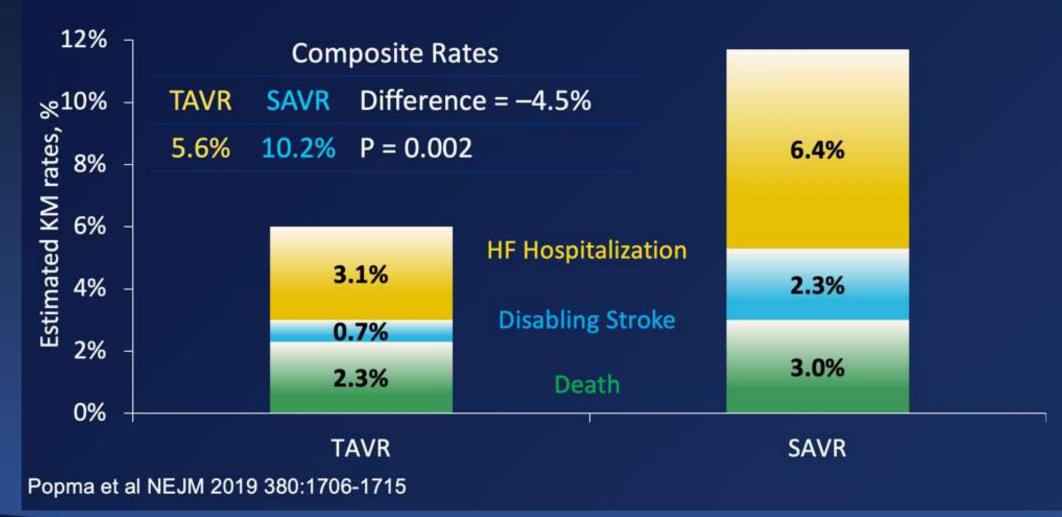






LR RCT: Death, Disabling Stroke, and Heart Failure Hospitalizations to 1 Year



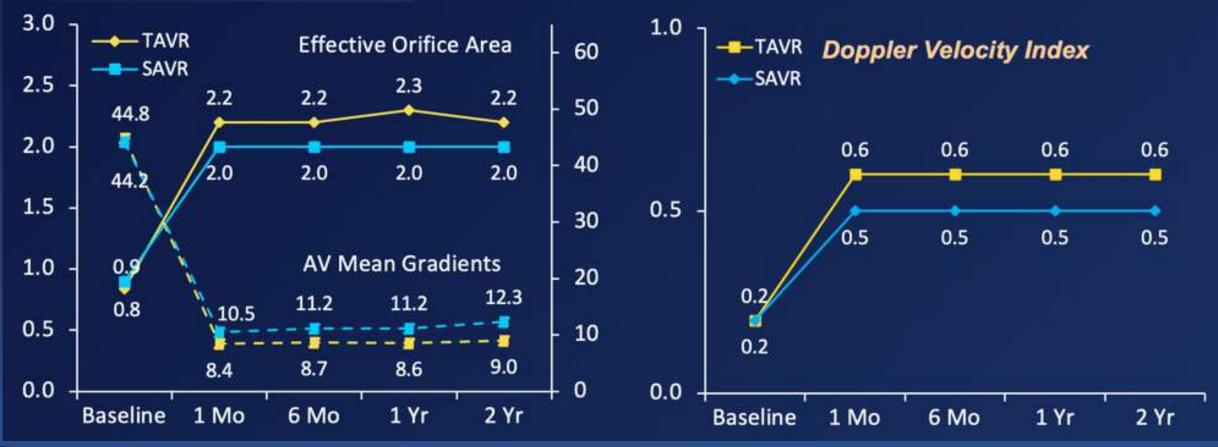








Evolut Low-Risk TAVR Trial: Serial Echo Findings thru 2 yrs



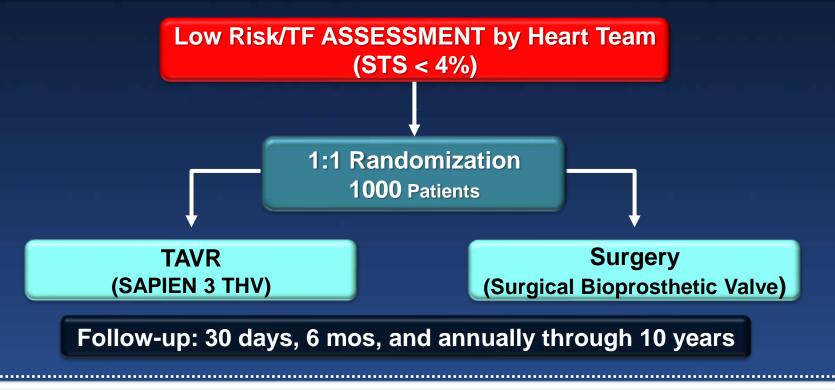






PARTNER 3 Study Design

Symptomatic Severe Aortic Stenosis

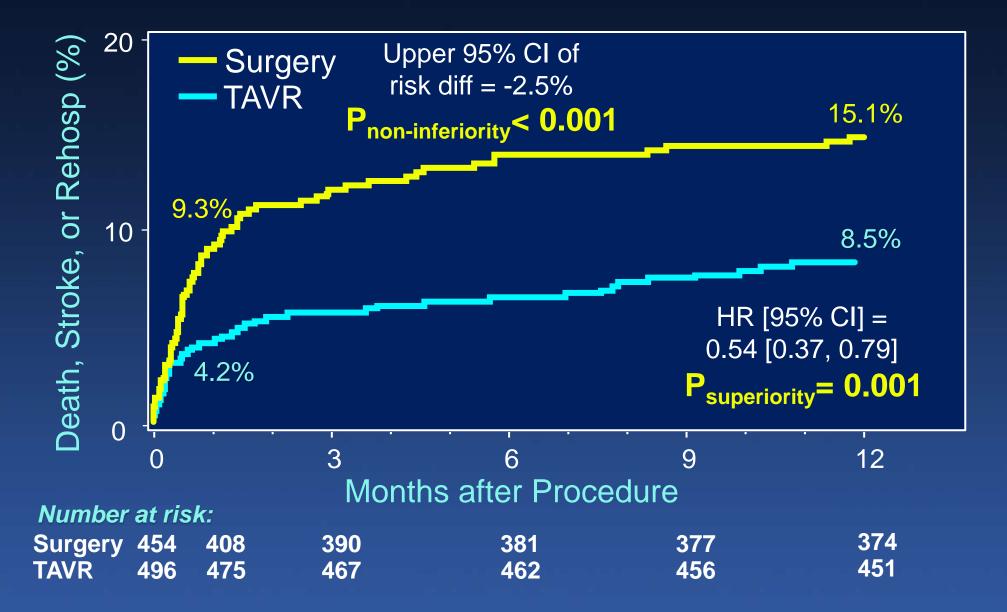


PRIMARY ENDPOINT: Composite of all-cause mortality, stroke, or CV re-hospitalization at 1 year post-procedure

Primary Endpoint

PARTNER 3

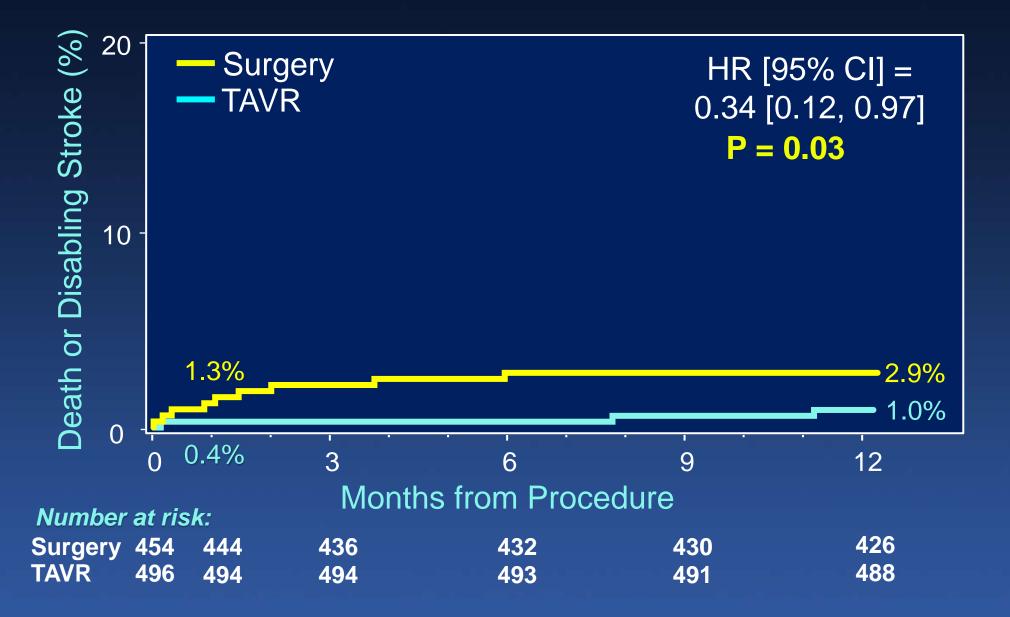
TRIAL



Death or Disabling Stroke

PARTNER 3

TRIAL



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</p>
- 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



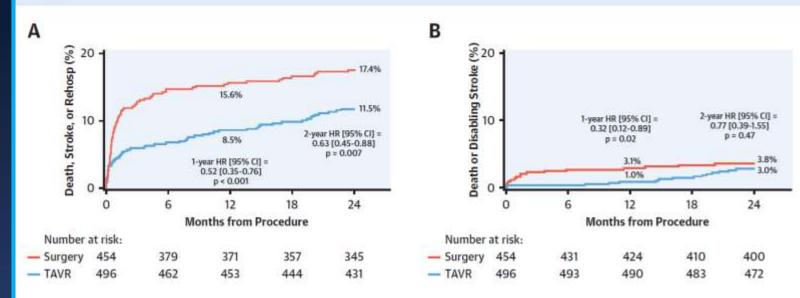
"This is an historic moment, and all of us here should remember it as such."

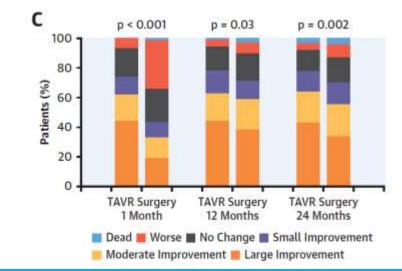
Eugene Braunwald, ACC 2019













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

Columbia University Medical Center

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



White the set of the s





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

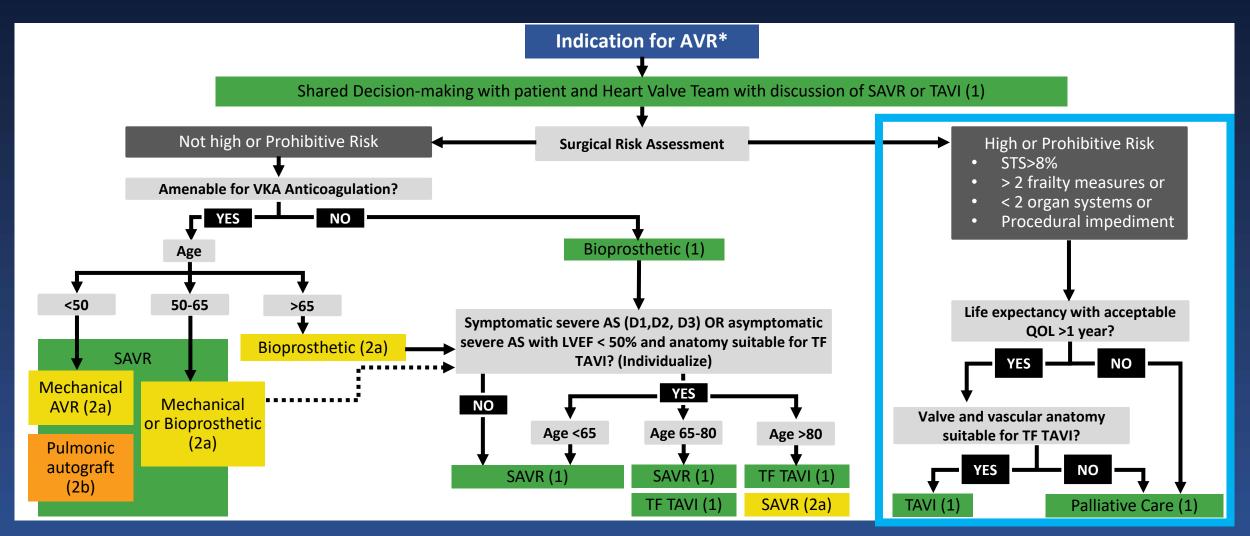
"Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information. †ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison.

> COLUMBIA UNIVERSITY MEDICAL CENTER



J Am Coll Cardiol 2020

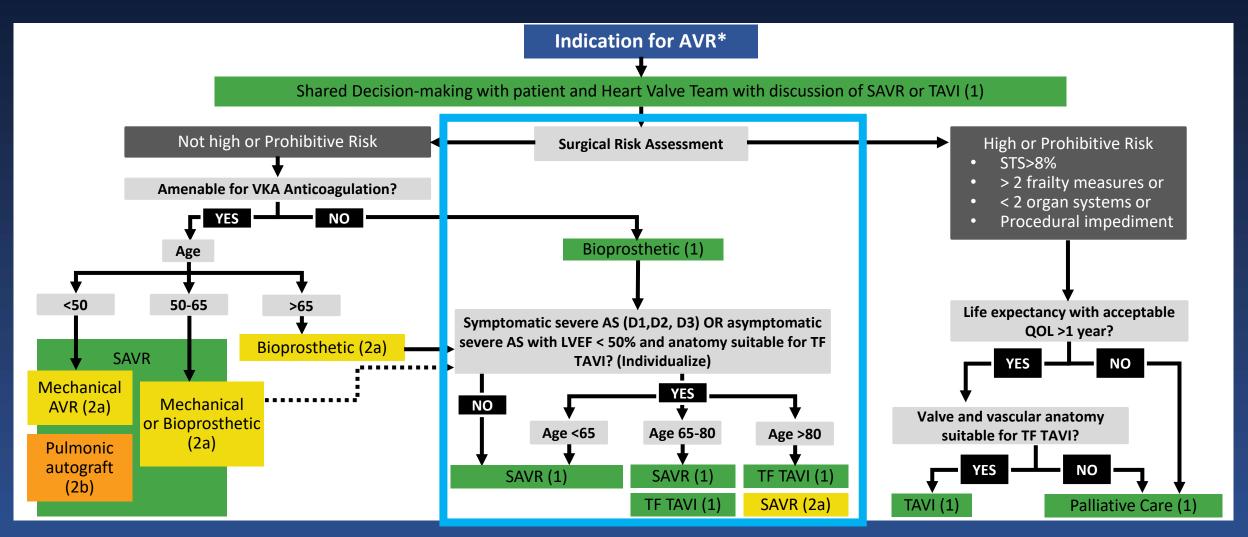
gendre i for dotalied information. one Connection on Clinical Frantise Guilddony Linnon.





J Am Coll Cardiol 2020







J Am Coll Cardiol 2020

Cardiovascular

Research Foundation

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 (Cl 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 (Cl 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 (Cl 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 (Cl 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...







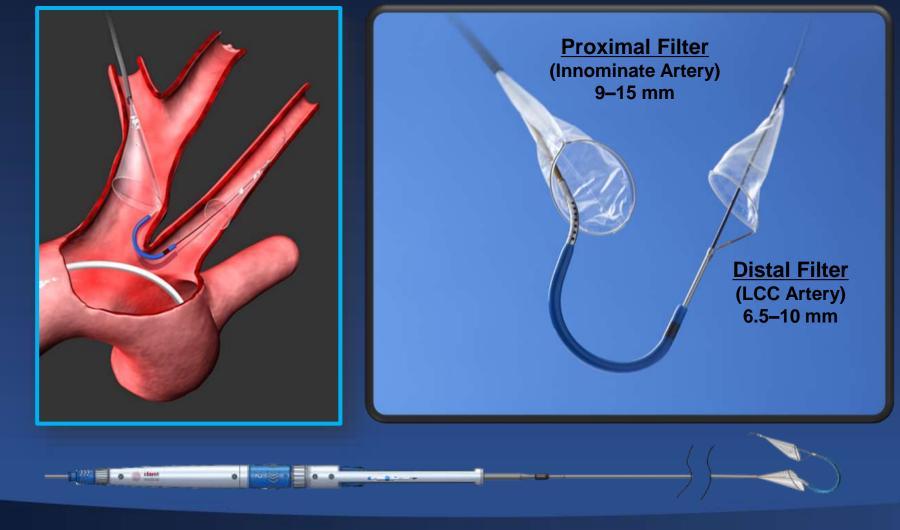
TAVR – Future Directions *Still <u>MANY</u> Knowledge Gaps*

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





TAVR Accessory Devices Cerebral Embolic Protection (CEP)

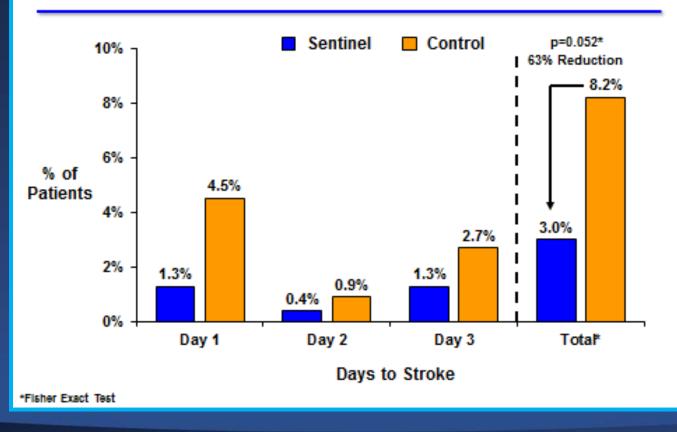






SENTINEL CEP Randomized Trial Clinical Outcomes

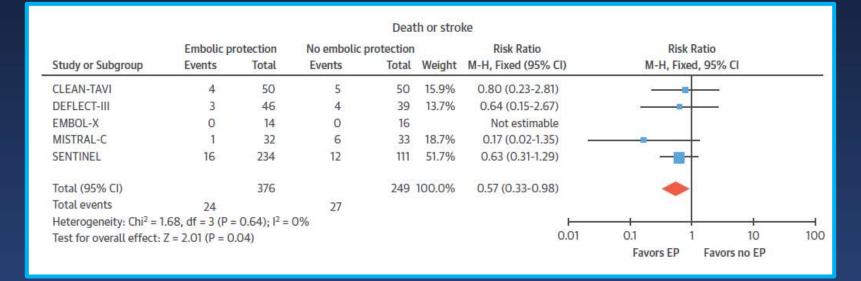
Stroke Diagnosis ≤72 hours (ITT)







CEP Meta-analysis *Five Studies (n = 625 patients)*



• 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; l² = 0%)
- NNT = 22 to reduce one stroke or death



Giustino G et al. JACC 2017



TAVR – Future DirectionsStill 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)





Background

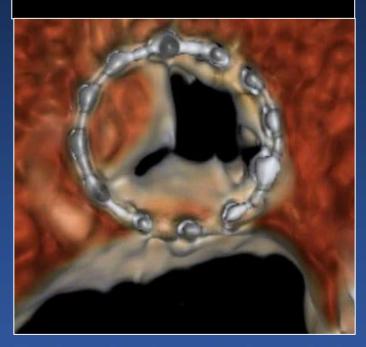
Subclinical Leaflet Thrombosis characterized by hypoattenuated leaflet thickening (HALT) and reduced leaflet motion has been frequently observed in transcatheter and surgical aortic bioprosthetic valves.

Hypoattenuating leaflet thickening (HALT)

Reduced leaflet motion



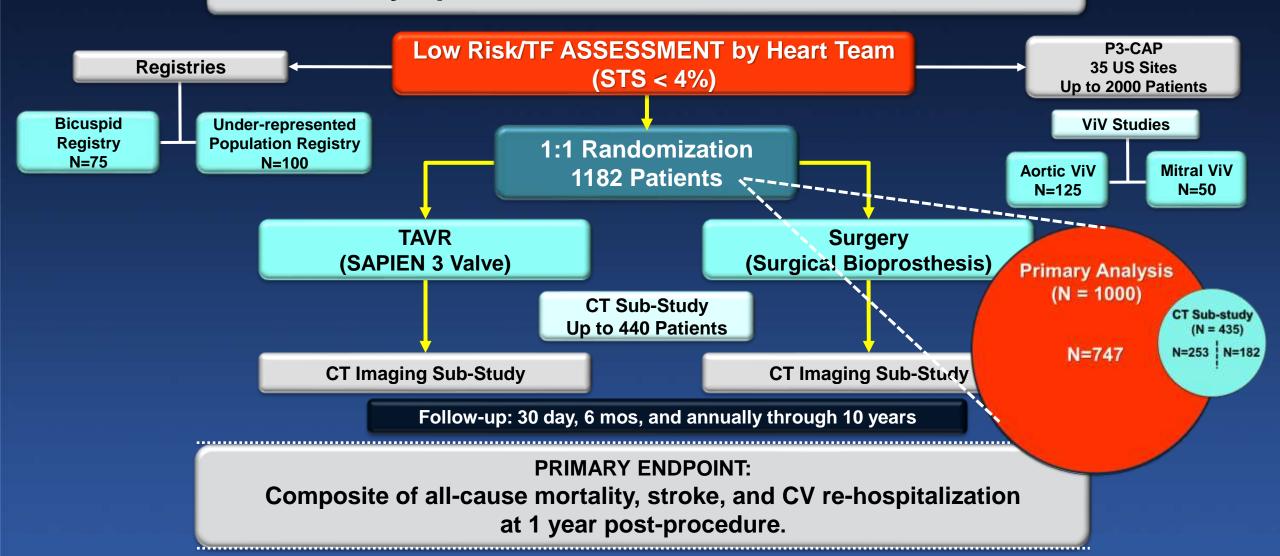
PARTNER 3



Makkar R. et al. NEJM 2015

PARTNER 3 PARTNER 3 Trial Study Design

Symptomatic Severe Aortic Stenosis



Incidence of HALT at 30 Days and 1 Year TAVR vs SAVR

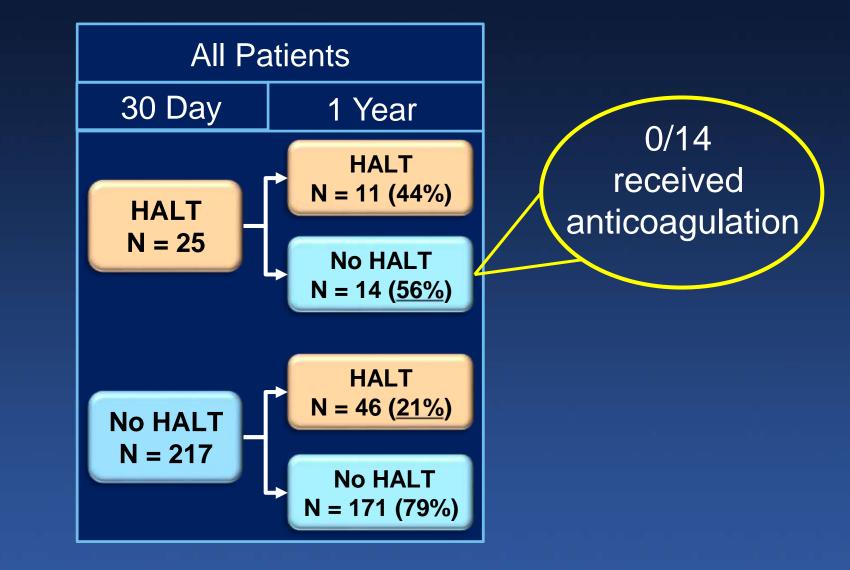
Per Protocol Population

		30 Days			1 Year			
Outcomes (%)	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

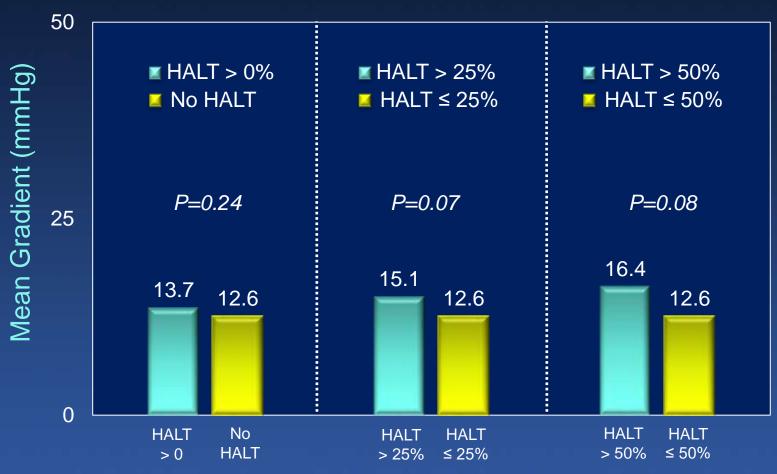


HALT from 30D to 1Y Per Protocol Population





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

BARTNER 3 30-day HALT and Clinical Events

All Patients with Evaluable CTs – TAVR & SAVR

	Ι	Day 7-30	Day :	Day 31-365		
Clinical Events (n)	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		
ΤΙΑ	0	1	1	2		
Retinal Artery Embolism	0	0	1	1		

*Defined according to VARC2 definition

TAVR – Future DirectionsStill MANY Knowledge Gaps

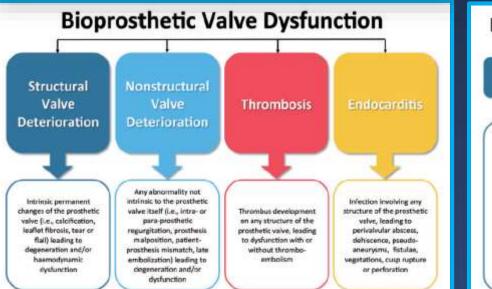
- Use of cerebral embolic protection to reduce strokes systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- Bioprosthetic valve durability (SVD and BVF) new definitions

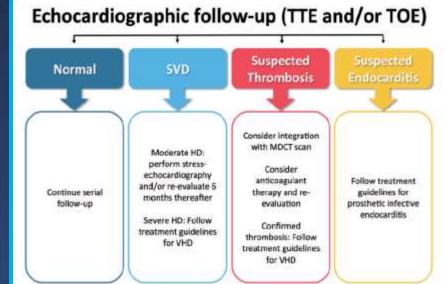




Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society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

Davide Capodanno¹*[†], Anna S. Petronio^{2†}, Bernard Prendergast³, Helene Eltchaninoff⁴, Alec Vahanian⁵, Thomas Modine⁶, Patrizio Lancellotti⁷, Lars Sondergaard⁸, Peter F. Ludman⁹, Corrado Tamburino¹, Nicolò Piazza¹⁰, Jane Hancock³, Julinda Mehilli¹¹, Robert A. Byrne¹², Andreas Baumbach¹³, Arie Pieter Kappetein¹⁴, Stephan Windecker¹⁵, Jeroen Bax¹⁶, and Michael Haude¹⁷ 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

Eltchaninoff, et al. EIJ 2018 0.6% 8 years 8 years Holy, et al. EIJ 2018 0.0% Eltchaninoff, et al. EIJ 2018 3.2% Barbanti, et al. JAHA 2018 2.4% Holy, et al. EIJ 2018 4.5% 3.6% Antonazzo Panico, et al. EIJ 2019 Blackman, et al. JACC 2019 0.4% Barbanti, et al. JAHA 2018 4.5% Sondergaard, et al. JACC 2019 0.7% 7 years Antonazzo Panico, et al. EIJ 2019 2.5% Abdel-Wahab, et al. EuroPCR 2019 0.5% 5 years 7 years Didier, et al. Circulation 2018 2.5% Duetsch, et al. EIJ 2018 3.7% Gleason, et al. JACC 2019 0.0% 6 years 7.5% Sondergaard, et al. JACC 2019 Vollenbroich, et al. IJC 2019 0.2% 3.7% 1.3% BVF at 6 to 8 years SVD at 5 to 8 years Weighted incidence Weighted incidence (95% CI 0.7-1.9) (95% CI 2.7-4.6)

Severe SVD



Capodanno D, et al. Eurointervention 2019

Bioprosthetic valve failure (BVF)

COLUMBIA UNIVERSITY

MEDICAL CENTER

- NewYork-Presbyterian

60

TAVR – Future DirectionsStill 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 DirectionsStill MANY Knowledge Gaps

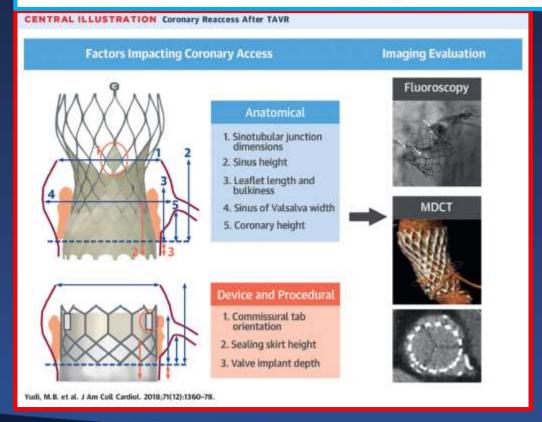
- Use of cerebral embolic protection to reduce strokes systematic or selective use
- Importance of valve leaflet thickening (CT studies) and valve thrombosis (clinical)
- Bioprosthetic valve durability (SVD and BVF) new definitions
- Safety and durability of TAV-in-TAV procedures and safety of failed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

TAVR – Future DirectionsStill 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 Kanlan-Meier e	otimotoo londmor	rad at 20 days				

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

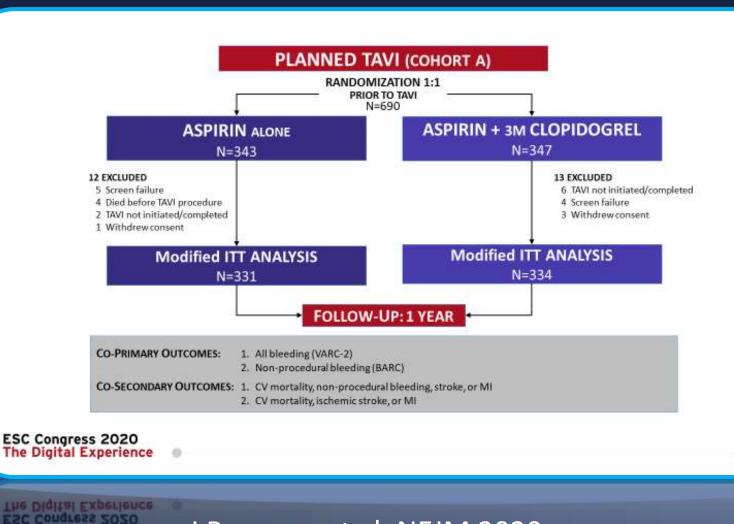
TAVR – Future Directions *Still <u>MANY</u> Knowledge Gaps*

• Optimal antithrombotic pharmacotherapy after TAVR (both antiplatelet and anti-thrombotic meds)





The POPULAR TAVI Trial SAPT vs. DAPT



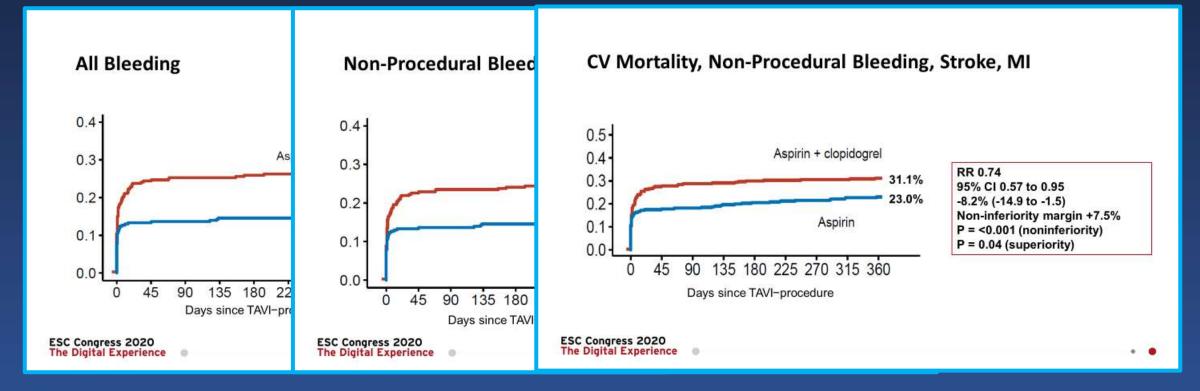
Cardiovascular Research Foundation

J Brouwer et al; NEJM 2020

Columbia University Medical Center

The POPULAR TAVI Trial SAPT vs. DAPT

KEY Endpoints





J Brouwer et al; NEJM 2020



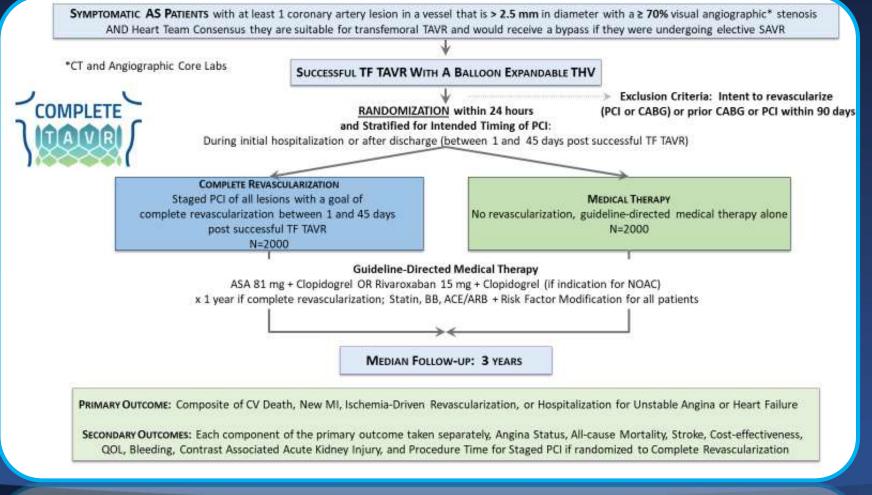
TAVR – Future DirectionsStill MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both antiplatelet 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

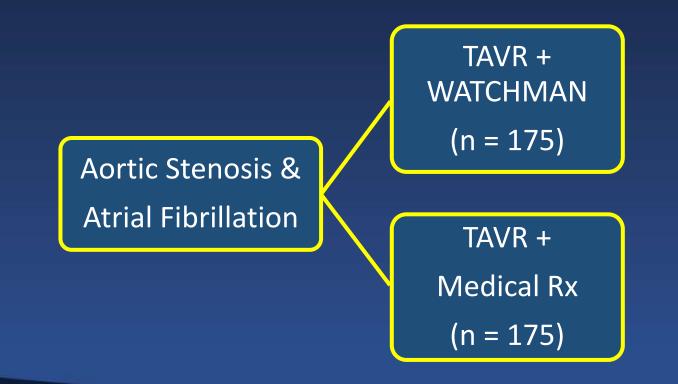




SECONDARY OUTCOMES: Each component of the primary outcome taken separately. Angina Status, All-cause Miortality, Stroke, Cost-effectiveness, QDL, Bleeding, Contrast Associated Acute Kidney Injury, and Procedure Time for Staged PCL & randomized to Complete Revascularization Columbia University Medical Center

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 DirectionsStill MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both antiplatelet 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)

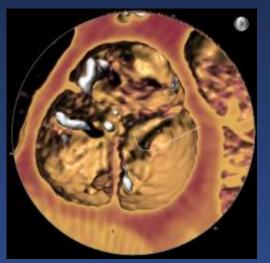




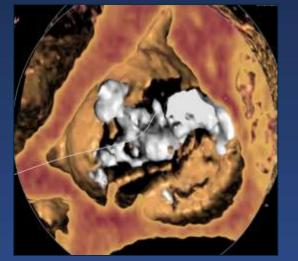
Bicuspid Aortic Valve Classification CTA System

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

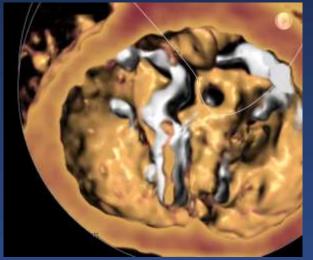
Tricommissural



3 commissures V-like orifice "functional or acquired" Bicommissural Raphe-type



2 commissures, 1 raphe Slit-like orifice Bicommissural Non Raphe-type



2 commissures, no raphe Slit-like orifice





Jilaihawi H. JACC Imaging 2016

Evolut LR BAV Registry

JAMA Cardiology | Original Investigation

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

John C. Farrer, MD, Hard Ranbar, MD G. Mollard Dink, ND Fran Zar, MD, Howerk L, Jong MD, HO, Need S. Oberran, MD, Markey J. Chestali, MD: Histoir M, Michaelsa, MD, Mark A, Marg, MD, Anthry A, Sales, MD, Jan Frang, MD, ME, John Y. Papers, MD, Michael J, Barchan, MD

Interactionance: The instruments of transcontenue and is value replacement (TAVII) in low-mat patients with becaused and by value denoisis have not been studied in a large scale, multicentered, prospective fashese.

OR LECTION To evaluate the procedural safety, efficacy, and 30-day subtaneous of their an patients with becaused antic clements at low surgest risk.

BEYER, SET Net, AND PARTICIPANTS The Low The Bicagol Study is a properties, single are bid intelly with industrive backases inter to developed from the total Low Takis Readwroad Data 7 Aldree ong participanting in the Lokat Like Mike Readwraid That Mark Developed States where and participanting in the Lokat Like Mike Readwraid That Mixer Developed 2016 to October 2016. Tigglie partners in the interest brought are to a state American Seart Association/Internation/Comparison of Cardinagy guideline industries for anticwide registerizers.

BITERVENTIONS Patients underwerst attarcepted implant of an Exclusion Exclusion transcatheter acritic velve, with valve size based on annular measurements.

NUME CONTENTES ADDI MERCATES. The properties of privacy and posts was the income and all cause montality or disabiling strate at 30 days. The prospective privacy efficacy end posts and device scattes defined as the damment of proceeding memory and posts and the bioproteints' heart value in the proper automatical occides, and the absence of neuro their and a antis: engineering and posts. The second post and an anti-

BIALTA A Littla of 500 patients underwent au ettempoint implicit. Buildie claust implication bioluber mans ang mit 2010.033 yans. 640 (66) Implicito 12:23, 2017. Maid Sawen Tpati Administration Sergence score of 14.810.093. Mole patients (1058: 5027.01 And Sawen Tpati Administration ampholitagy. The matchinoches of all clauses multiply or Subdet/matchines us 379, 600% CL 0.396, 537.01 at 32.05 apr. The altware success rate warrs (5).3% (10% CL 0.9556; 460%). All CL displates the mans static parameter parameter was implicated in 22 patients (05.9%). Separatem band guarter than statigaramabanda linki.

CONCLUSIONS AND RELEVANCE Transcatheter active valve replacement in low surgical risk patients with builepid active valve staroosts activered beneaties to day results, with low rotes of doots and strates and/high device success rate.

A PARTY OF A PARTY OF

TIMA, NEWSTRATION Clevelatisals.gov.tdeet/fair: 14/103035-04

www.emm.20047

Male Conduct des Els COLLiness III. Registration Decision 2, 2020 article: Generationing failber, MICE, factorit, VIII: Disponsion of Internet Modation (Confirming Face) for Despire Cachine Graphic, State Face States (Confirming Face), States Dates (Confirming Face), States Harm, CT (MCS), States, Survey upplicability States

COLUMN TWO IS NOT

a 2000 American Medical Association, All rights sweeted. SSOC 8 ULTERT Sep 1 St. L 2007 PLACE Split 1

Outcomes at 30 Days

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.



Forrest, J et al; JAMA Cardiology 2020



Low Risk Bicuspid Study

18

Evolut LR BAV Registry

JAMA Cardiology | Original Investigation

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

John C. Farrer, MD. Hard Randson, MD. G. Millard Derli, MD. Fran Zier, MD. Howert, L. Img, MD. HO, Neud, S. Oberran, MD. Markey J. Chemical, MD: Herman M. Millarden, MD. Molek, Mang, MD. Julie, A Sada, MD. Jan Floren, MD. MT, John J. Papers, MD. McLands, J. Barchan, MD

INFORTANCE. The outcomes of transcriberer aerts, value replacement (14/40) in low risk partnersts with becaused acritic valve stancesis have not been studied in a large scale. multicentered, prospective fashion

OBJECTIVE To evaluate the procedural safety, efficacy, and 30 day instrument of Horizon patients with becaused as to stenous at low surgeul risk.

DESIGN, SETTING, AND PARTICIPANTS The Low Risk discussed bauty is a properties, single are this study with inclusion/exclusion interto developed from the Exclusion and Risk Randoment Total. Follow-up is planned for 10 years, Patients underwest UVW at 25 carties in the Dated States who were also participating in the Excite Lose finit Randomized hist hom December 2018 to October 2019. Eligible patients had severe bicoupit actic solve starsion and met American Heart Associat Arrenican College of Cardiology gladeline industrions for aortic valve replacement.

INTERVENENCES Patients under went attempted implant of an Evolution Evolutions transcatteter acros valve, with valve use based on annular measurements.

MUR DOTTOMES AND MEASURES. The proper thad primary and point was the reall-cause mortality or shadding stroke at 30 days. The prespectful primary efficacy endpoint was device success defined as the absence of procedural mortality. He carrier position of 1 bioprosthetic heart value in the proper anatomical location, and the absence of more than mild acris: mgurgitation postprocedure.

series 75 A total of 150 patients underwant as attempt include mean age of 70.3 (5.5) years, 48.0% female (n = 72), and a mean facinity of Theracic Surgeons score of 1.4 (0.0%). Most patients (106: 50.7%) had Savers type I salve morphology. The incidence of all cause mortality or disabling stroke was 1.7% (95% C). 0.3% 5.3% at 30 days. The device success rate was 05.3% (\$5% 0.96.5% 0.0%). At 30 days, the mean (50) Air gradient was 76 (3.7) owning and effective orthon area was 2.3 (0.7) cm² A new permanent pacentalier was implanted in 22 patients (253%), to patients had granter than mild personnal a losi.

CONCLUSIONS AND RELEVANCE Transcatheter auftit, salve replacement in low surgical risk patients with the uspid acris; waive statoosis achieved favorable 30-day results, with low rates of death and stroke and high device success rate.

8 2000 American Medical Association. All rights reserved

LATE OF L AND THE

DETTFUT: Sep 3 95.1 2020

TIMA, INTUSTIGATION Cleacedinals gov/destifier: 14/1000/15-04

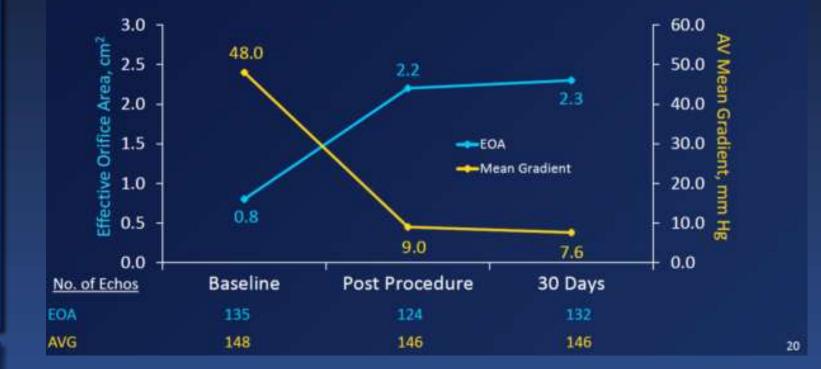
- and 1990

and Condition day The ad unline Debater (19920)

1000 at 100 UT 2020 has

Valve Hemodynamics







Forrest, J et al; JAMA Cardiology 2020



Evolut LR BAV Registry

JAMA Cardiology | Original Investigation

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

John C. Farrer, MD. Hard Randson, MD. G. Milliard Derli, MD. Fran Ziek, MD. Howert, E. Imry, MD. Hou, New S. Oberran, MD. Hardy J. Chemical, MD: Herman J. McDelena, MD: Abuel A. Marg, MD. Jeffley A. Sados, MD. Jan Filang, MD. MT, John Y. Frynes, MD. McDelei, J. Barchan, MD

INFORVANCE: The outcomes of transcathems anetic value explanament (1AM) in low-end patients with becaused and to value structure have not been studied in a large scale, multicentered, prospective fashion.

OR LECTION To evaluate the procedural valvey, efficacy, and 30-day solutiones of their erpatients with becaused and to demonstration wages a risk.

BEYNER, SETTING, AND PARTICIPANTS, The Low The Bicaupit Study is a properties, single are that fundy with inclusive/inclusion intervie developed from the Coalet in the Risk Background Back Fallow equipation of the Types, whitein audientes Study 2014 22 southers in the Linked States when were also participating in the Coalet Line Risk Radionaux Table To be come of the OccUPM 2015 Tables Parenter in the Next Advanced Tables To be and American States And Coalet Line States and met American States when the anatowhen registrement.

INTERVENTIONS Patients underwent attempted implant of an Exist or Exist motranscatheter aertic value, with value size based on annular muzauments.

NAME OVERCOME ADDRESS THE properties of privacy and post was the incidence of all cases envirolity or disabling strate at 30 days. The properties primary efficacy endpaces and device social defined as the durament of proceeding anothing the cases (problem) of bioproducts: heart value in the proper automical location, and the absence of neurother millial and the angularians programmation.

Black TA, Aulika El Sci-patiento sudewant au interruption traplace, Baulika el Discutantecco Selucióne mana que 1702-0133 yans e Al Colo Baulicio 172, 2014 a di anume tocingi el Monace Sengenos scotte el Vel BLORN. More patiento 1016: 502-0134 had taivens tipes I año morpholitagy. The subscotte of al Canama mutitaly or sUbdingtamine and 378, 10795 CJ. 0.376-5, 378 ki al 30-days. The elivine success rates ward 53. 56 (1976 CJ. 0.956; 46.0164). (Al Canama el Canama de La Canama el Canama el

COMPLICIONS AND HELPANCE Transactions acrity salve replacement in low surgest this patients with humped and to valve standout actioned because 30 day results, with low rates of douth and strains and high device success rate.

6 2000 American Medical Association, All rights reserved v8/20/20/20/20/07 30/20/06/09/09/ Paul // 10/20/06/09/09/

COLORIDAD DATE OF THE OWNER OWN

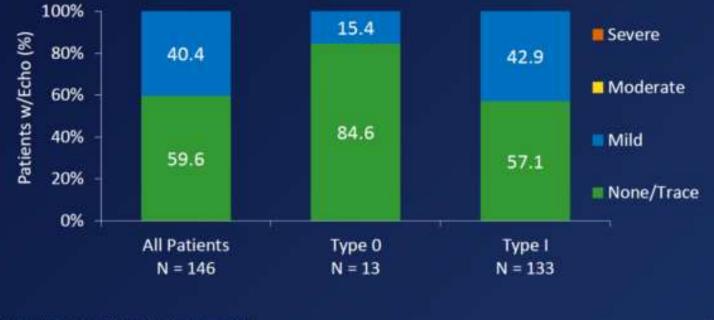
DOTFUT Sep 3 36.4 2020

THEM, MULTINATION Clinicalitials goo identifier, NCT03015-04

and in 1970.4

state Conduct data 12,000 January 2,0020

Total Aortic Valve Regurgitation



Implant population. Core lab assessments.



Forrest, J et al; JAMA Cardiology 2020



22

volut

Low Risk

Bicuspid Study



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



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



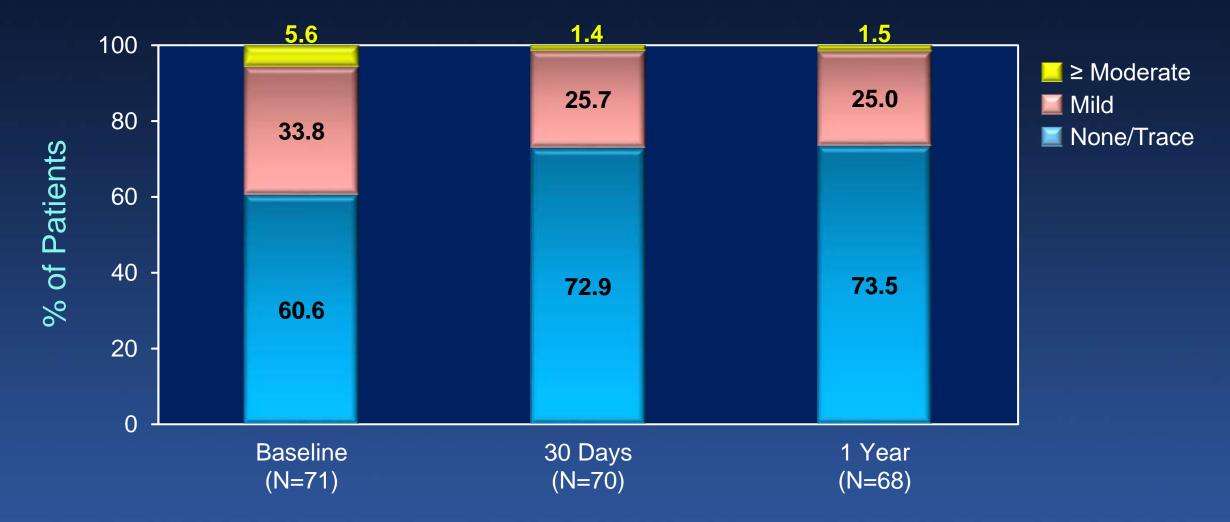
Primary Endpoint

	30 D	ays	1 Year
Outcomes	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)



Aortic Regurgitation Bicuspid Registry



TAVR – Future DirectionsStill MANY Knowledge Gaps

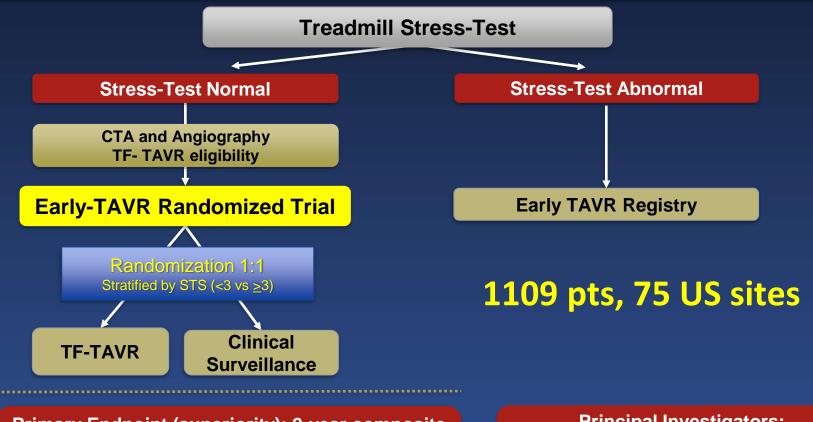
- Optimal antithrombotic pharmacotherapy after TAVR (both antiplatelet and anti-thrombotic meds)
- Management of severe AS in the setting of concomitant diseases (e.g. severe CAD, CKD, multi-valve disease, and AF)
- Management of bicuspid aortic valve disease (TAVR vs. SAVR)
- Management of asymptomatic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



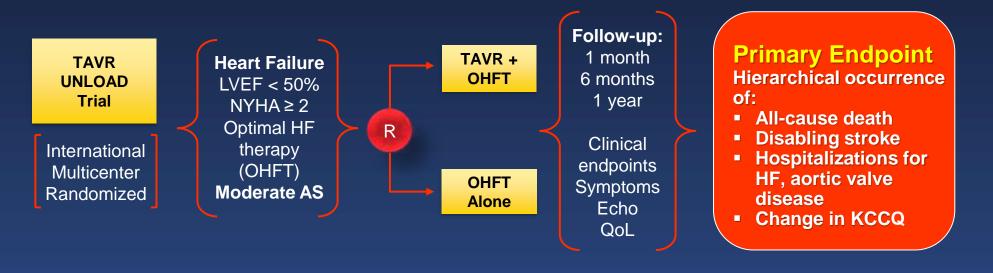
Primary Endpoint (superiority): 2-year composite of all-cause mortality, all strokes, and repeat hospitalizations (CV) Principal Investigators: Philippe Généreux, Allan Schwartz Chair: Martin B. Leon





TAVR UNLOAD Trial - Moderate AS + HF (300 patients, 1:1 Randomized)

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



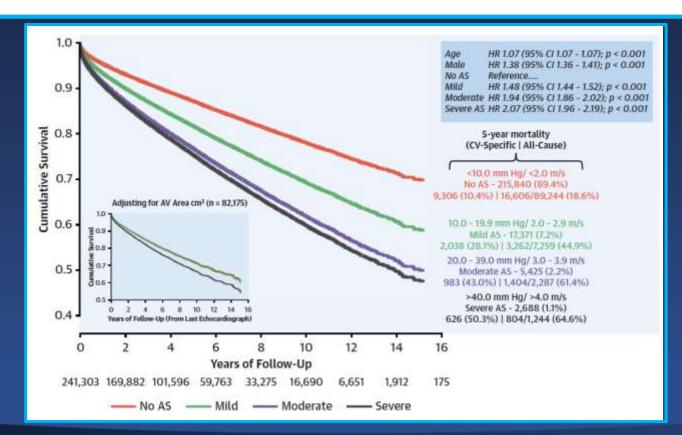






Poor Long-Term Survival in Patients With Moderate Aortic Stenosis

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



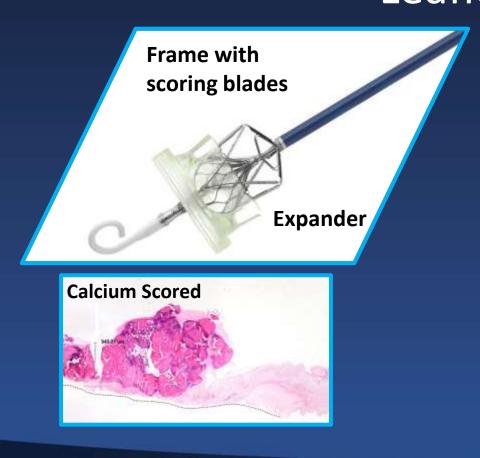
TAVR – Future DirectionsStill MANY Knowledge Gaps

- Optimal antithrombotic pharmacotherapy after TAVR (both antiplatelet 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 <u>Lifelong</u> Therapy Choices Age matters (symptomatic severe AS)

< 50 yo	50-65 yo	65-75yo	> 75 yo
<section-header></section-header>	<section-header><section-header></section-header></section-header>	 SAVR or DAVR TAVR ideal or SAVR adverse SDM= shared decisions 	<section-header></section-header>



Think SEQUENCING...



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

Featured Case Reports

Genereux

CCI 2016

Palisaitis

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.

Demers

Key words: TAVR; TAVI; discharge





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

It's is All About the Patients!



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





