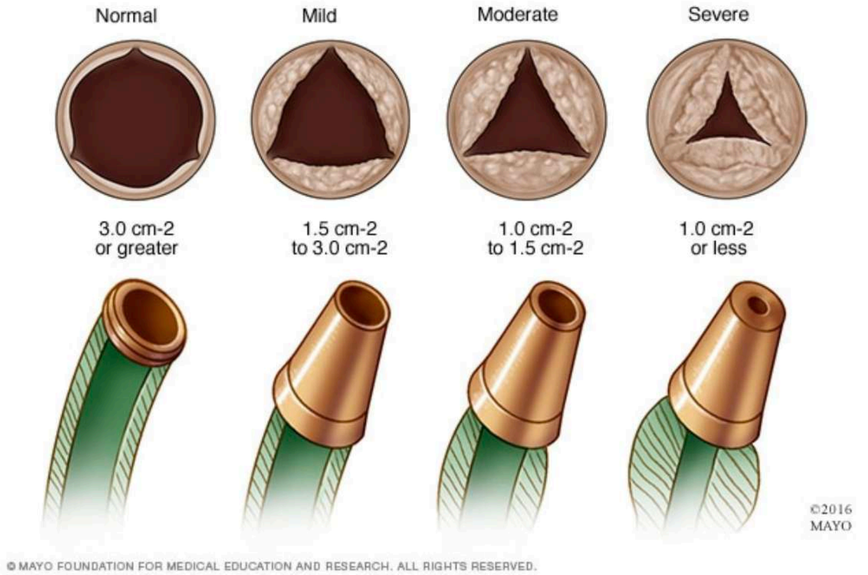
Developing Interventional Strategies for Management of Valvular Heart Disease

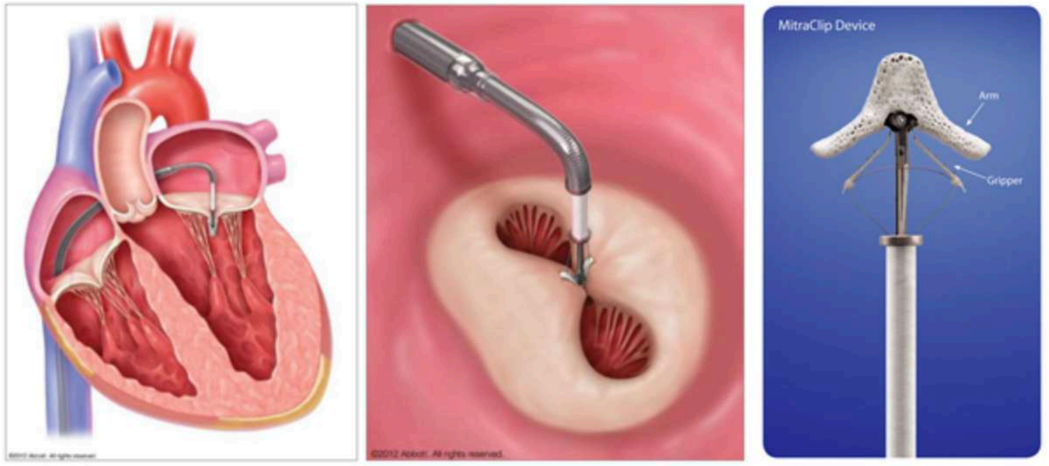
TAVR and MitraClip: Expanding Success and Indications

Paul Zellers, DO FACC

Objectives

- **Aortic Stenosis (AS)**
  - Aortic Valve Replacement (AVR): when to refer, when to fix
  - Evolution of Transcatheter Aortic Valve Replacement (TAVR)
  - TAVR Landmark Trials: outcomes, adverse events
  - TAVR vs SAVR: current guidelines
- **Mitral Regurgitation (MR)**
  - MitraClip technology
  - Primary vs Secondary MR
  - MitraClip landmark trials
  - Indications for MitraClip





Images contributed by Abbott Vascular

Aortic Stenosis

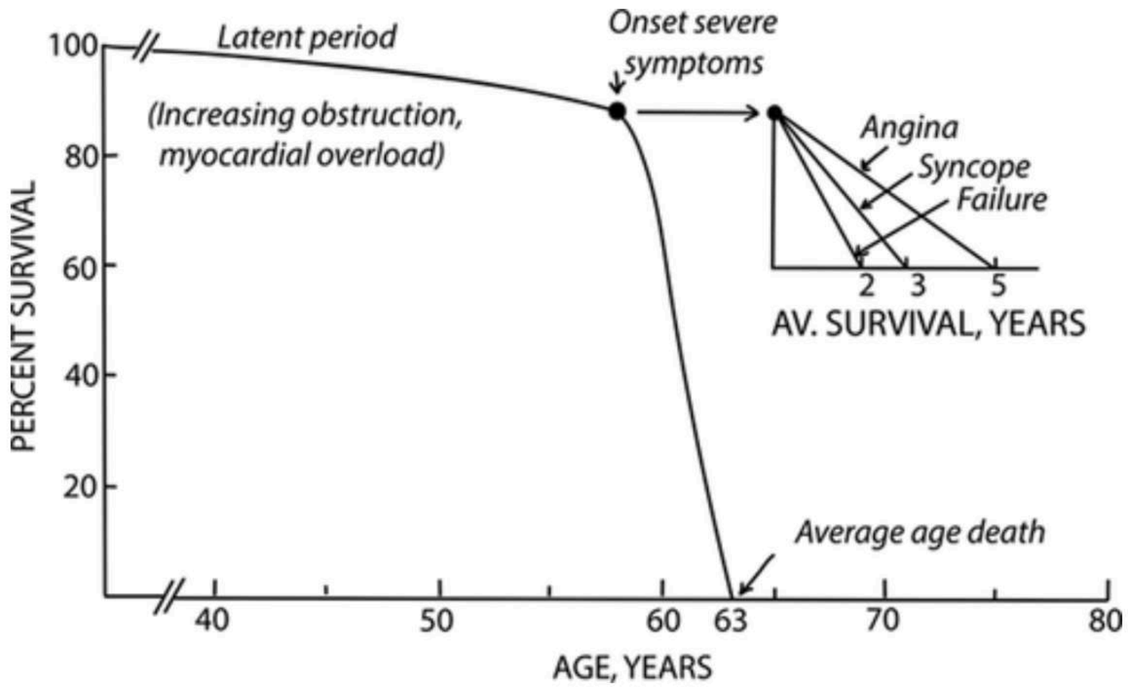
Pathology/Epidemiology

- Aortic stenosis causes progressive obstruction of the left ventricular outflow tract resulting in pressure hypertrophy of the left ventricle and ultimately heart failure.
- Valvular AS has several causes:
  - **Age related calcification/degeneration** - “wear and tear” manifesting usually in the 6th and 7th decades
  - Rheumatic
  - Congenital (bicuspid) - clinical manifestation earlier, 5th or 6th decade

Aortic Stenosis

Clinical Course

- Symptoms:
  - Chest pain - *myocardial ischemia, supply/demand mismatch*
  - Dyspnea - *Heart Failure*
  - Syncope - *multifactorial*



Aortic Stenosis

Surveillance

JACC Vol. 63, No. 22, 2014
June 10, 2014:e57–185

Table 4. Frequency of Echocardiograms in Asymptomatic Patients With VHD and Normal Left Ventricular Function

Stage	Valve Lesion			
Stage	**Aortic Stenosis***	**Aortic Regurgitation**	**Mitral Stenosis**	**Mitral Regurgitation**
Progressive (stage B)	Every 3–5 y (mild severity V_{max} 2.0–2.9 m/s) Every 1–2 y (moderate severity V_{max} 3.0–3.9 m/s)	Every 3–5 y (mild severity) Every 1–2 y (moderate severity)	Every 3–5 y (MVA >1.5 cm^2)	Every 3–5 y (mild severity) Every 1–2 y (moderate severity)
Severe (stage C)	Every 6–12 mo (V_{max} ≥ 4 m/s)	Every 6–12 mo Dilating LV: more frequently	Every 1–2 y (MVA 1.0–1.5 cm^2) Once every year (MVA <1.0 cm^2)	Every 6–12 mo Dilating LV: more frequently

Patients with mixed valve disease may require serial evaluations at intervals earlier than recommended for single valve lesions.

*With normal stroke volume.

LV indicates left ventricle; MVA, mitral valve area; VHD, valvular heart disease; and V_{max}, maximum velocity.

Aortic Stenosis

Surveillance

- Premature AVR carries risk of cardiac surgery
- Delayed AVR due to unrecognized symptoms can lead to poor outcomes
- Observational Study, 3 tertiary centers, 369 patients.

Evaluation of Patients With Severe Symptomatic Aortic Stenosis Who Do Not Undergo Aortic Valve Replacement

The Potential Role of Subjectively Overestimated Operative Risk

David S. Bach, MD; Derrick Siao, MD; Steven E. Girard, MD, PhD; Claire Duvernoy, MD; Benjamin D. McCallister, Jr, MD; Sarah K. Gualano, MD

Conclusions—One third of patients with severe AS are symptomatic but do not undergo AVR,

Circ Cardiovasc Qual Outcomes. 2009

Severe Aortic Stenosis

Outcomes

Evaluation of Patients With Severe Symptomatic Aortic Stenosis Who Do Not Undergo Aortic Valve Replacement

The Potential Role of Subjectively Overestimated Operative Risk

David S. Bach, Derrick Siao, Steven E. Girard, Claire Duvernoy, Benjamin D. McCallisterJr, and Sarah K. Gualano

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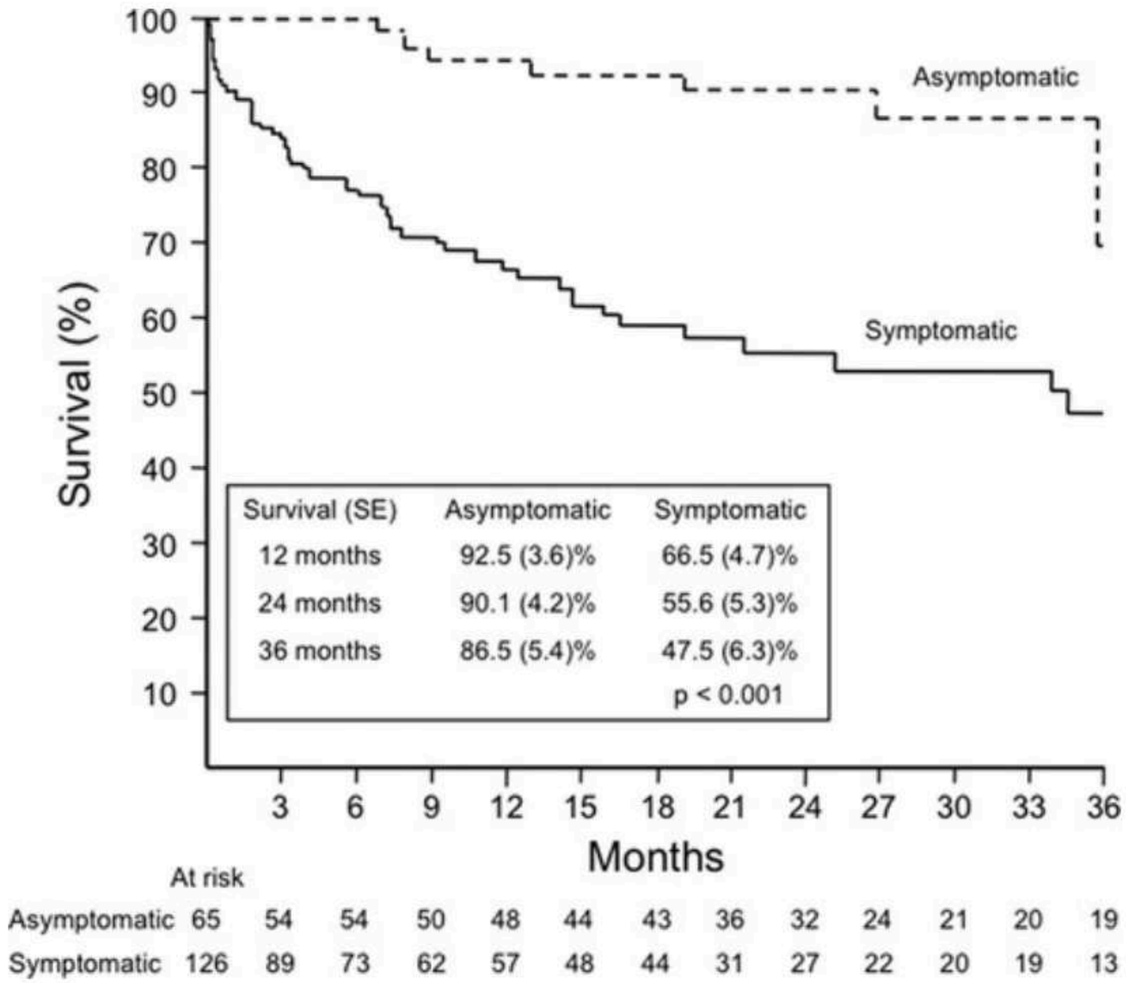
https://doi.org/10.1161/CIRCOUTCOMES.109.848259 |
Circulation: Cardiovascular Quality and Outcomes. 2009;2:533–539

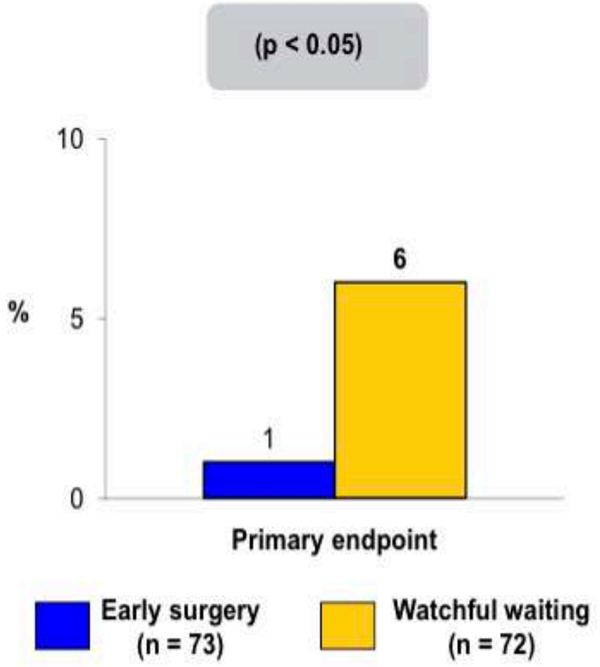


RECOVERY

#AHA19

AMERICAN COLLEGE of CARDIOLOGY

Trial Description: Patients with asymptomatic very severe aortic stenosis (peak velocity ≥4.5 m/sec) were randomized in a 1:1 fashion to either early surgery or watchful waiting. Patients were followed for 6.2 years.



RESULTS

- Primary endpoint, operative mortality or CV mortality at 4 years, for early surgery vs. watchful waiting: 1% vs. 6% ($p < 0.05$)
- CV mortality at 4 years: 1% vs. 15% ($p < 0.05$)
- All-cause mortality at 8 years: 10% vs. 32% ($p < 0.05$)
- Heart failure hospitalization: 0% vs. 11% ($p < 0.05$)

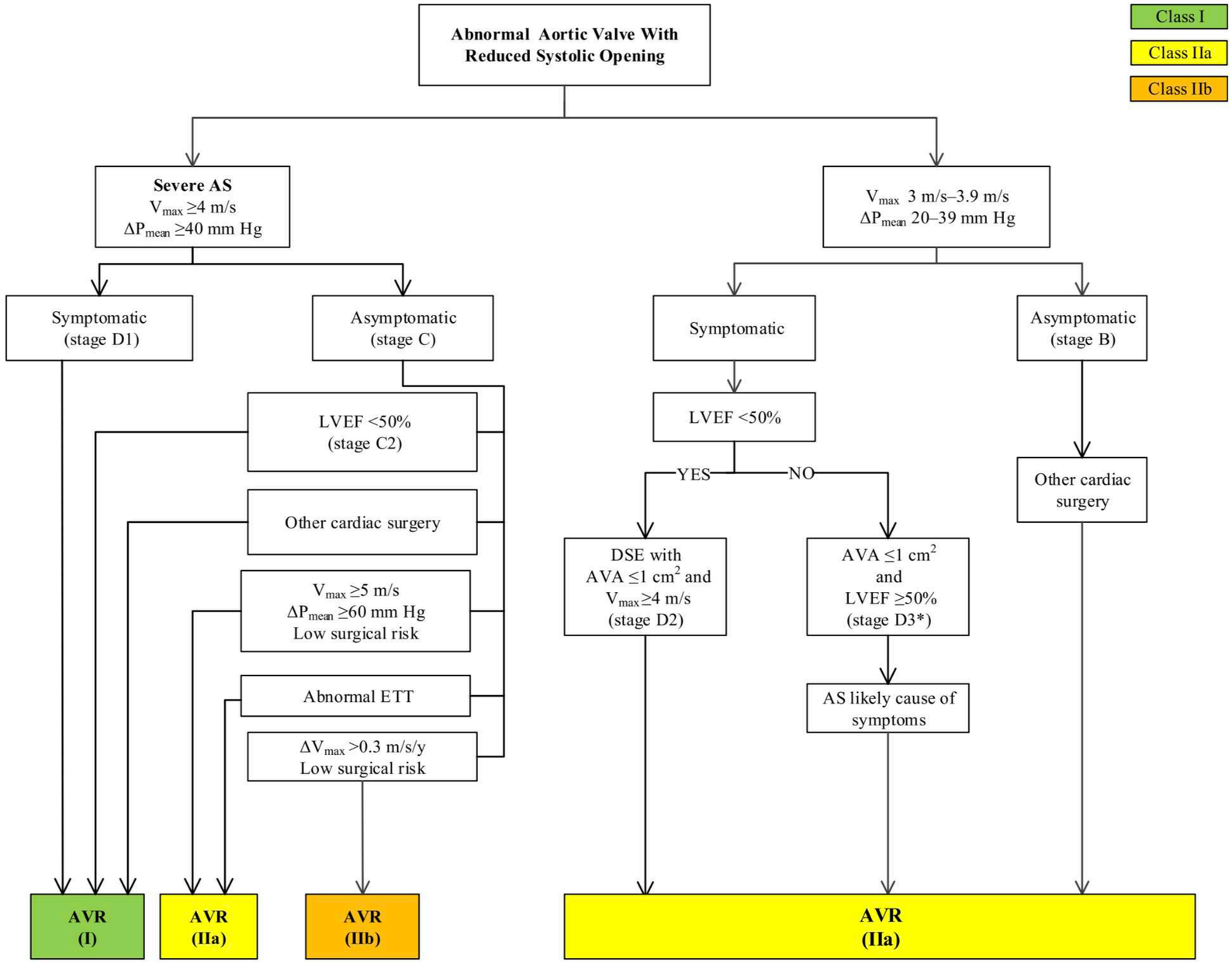
CONCLUSIONS

- Early surgery among patients with asymptomatic but very severe AS (AVA 0.75 cm^2, mean gradient ≥50 mm Hg, peak velocity ≥4.5 m/sec) results in improved survival out to 8 years compared with watchful waiting
- These are important findings, and will likely change guidelines on this topic

Kang DH, et al. N Engl J Med 2019;Nov 16:[Epub]

Aortic Stenosis

When to fix



PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With 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

Transcatheter Aortic Valve Replacement (TAVR)

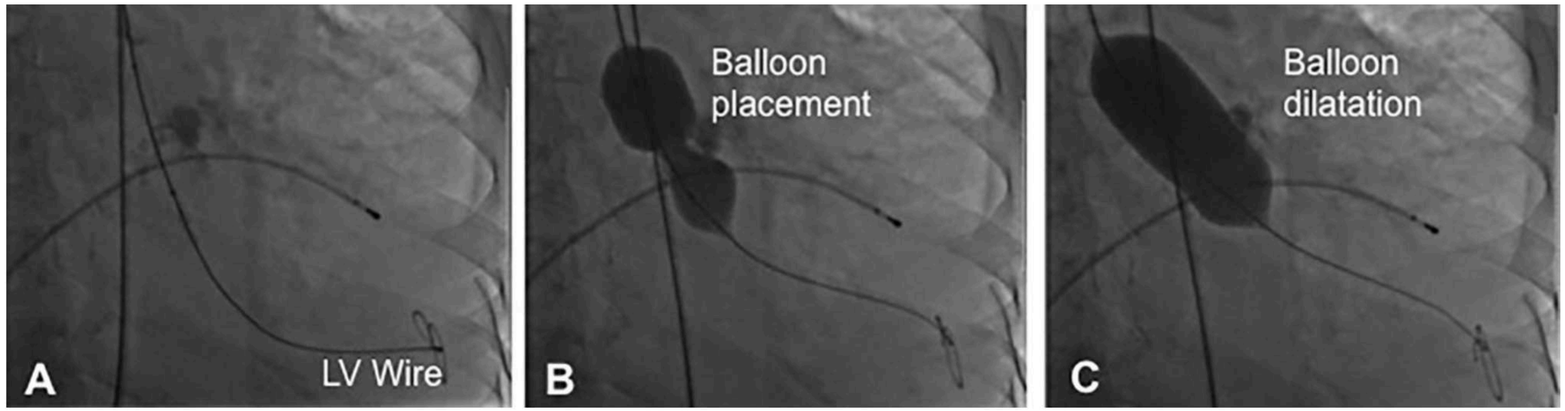
Concepts

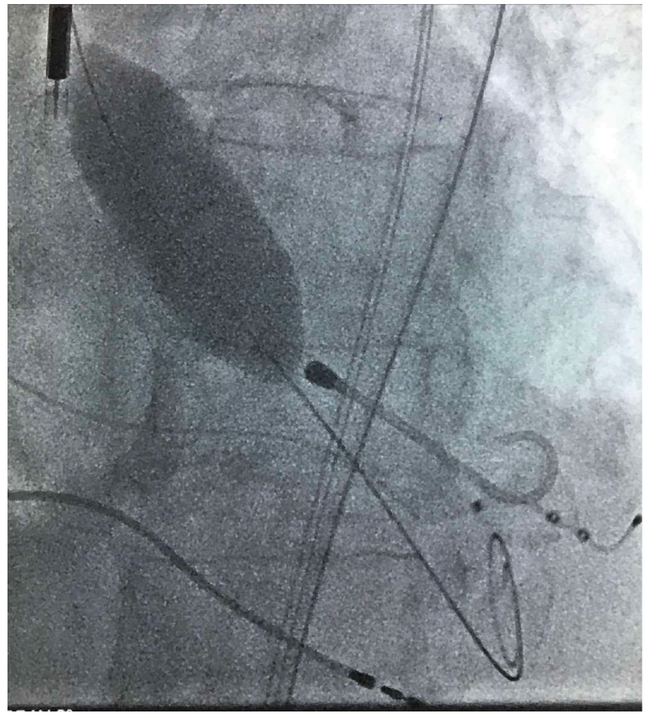
- For the past 50 years Aortic stenosis standard of care has been surgical aortic valve replacement (SAVR)
- 30-40% of patients with severe aortic stenosis are unsuitable for open heart surgery
    - Porcelain Aorta
    - Prior sternotomy, LIMA-LAD

Percutaneous Aortic Valve Intervention

History

- 1980’s - initial optimism for balloon valvuloplasty (BAV)
  - Procedural complications
  - No mortality benefit
  - Early restenosis
  - Palliative bridge

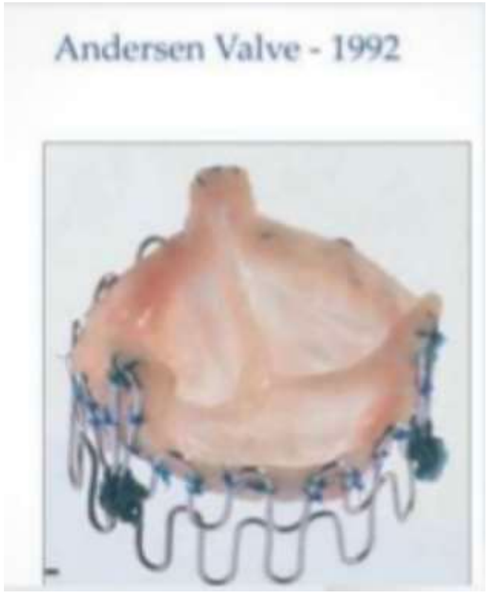


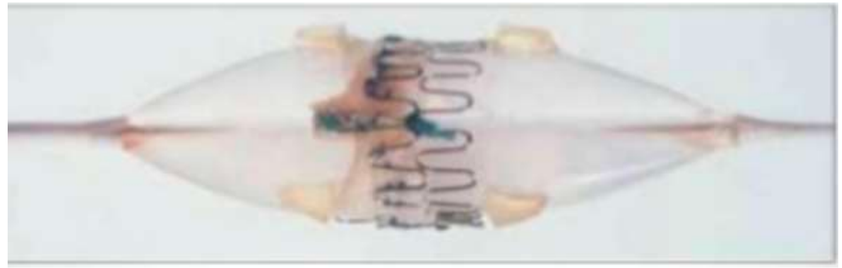


Percutaneous Aortic Valve Intervention

History

- 1992 Anderson et al - first report of porcine percutaneous AV fixed to steel frame via 50 prolene sutures mounted on a balloon. 41F catheter
    - 9 pig models (2 with significant PVL, 3 with coronary flow obstruction)
    - Too large for human use
- 2000 Bonhoeffer et al - bovine jugular vein valve on platinum stent, 12 yo boy in pulmonic position
- 2000 Cribier et al - balloon expandable bovine pericardial valve, 24F catheter (Sheep)
- 4/6/02 Cribier - 57 yo male with severe AS, h/o Aortobifem bypass. Antegrade. Valve on 30mm balloon, 24F
    - Normalization of AV gradients
    - Clinical Improvement in 2 days
    - Expired 3m later
- 2005 Paniagua - first retrograde TAVR
- 2006 Webb - 15/18 patients with successful implants. Rapid ventricular pacing





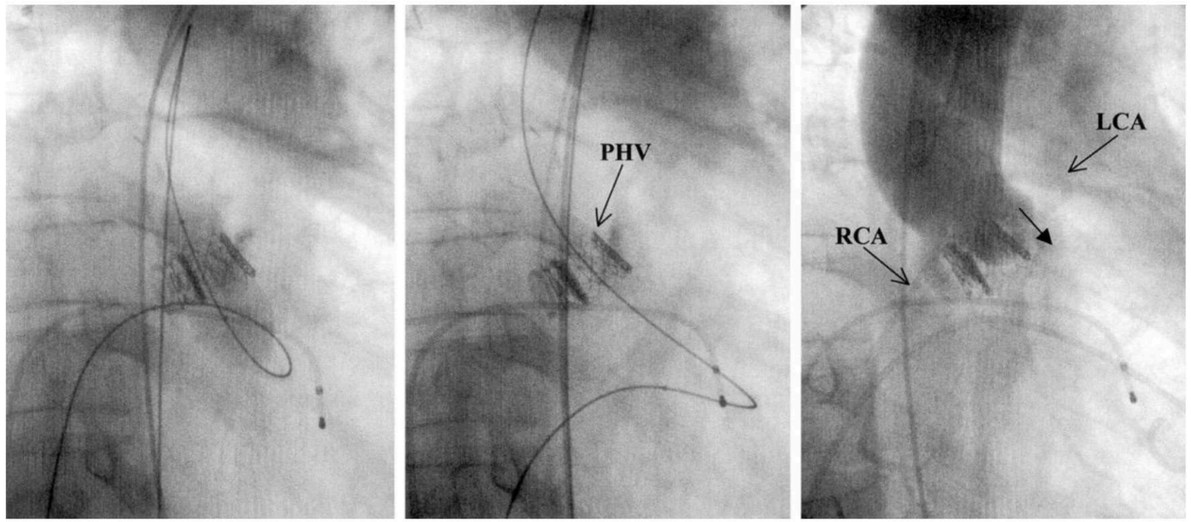
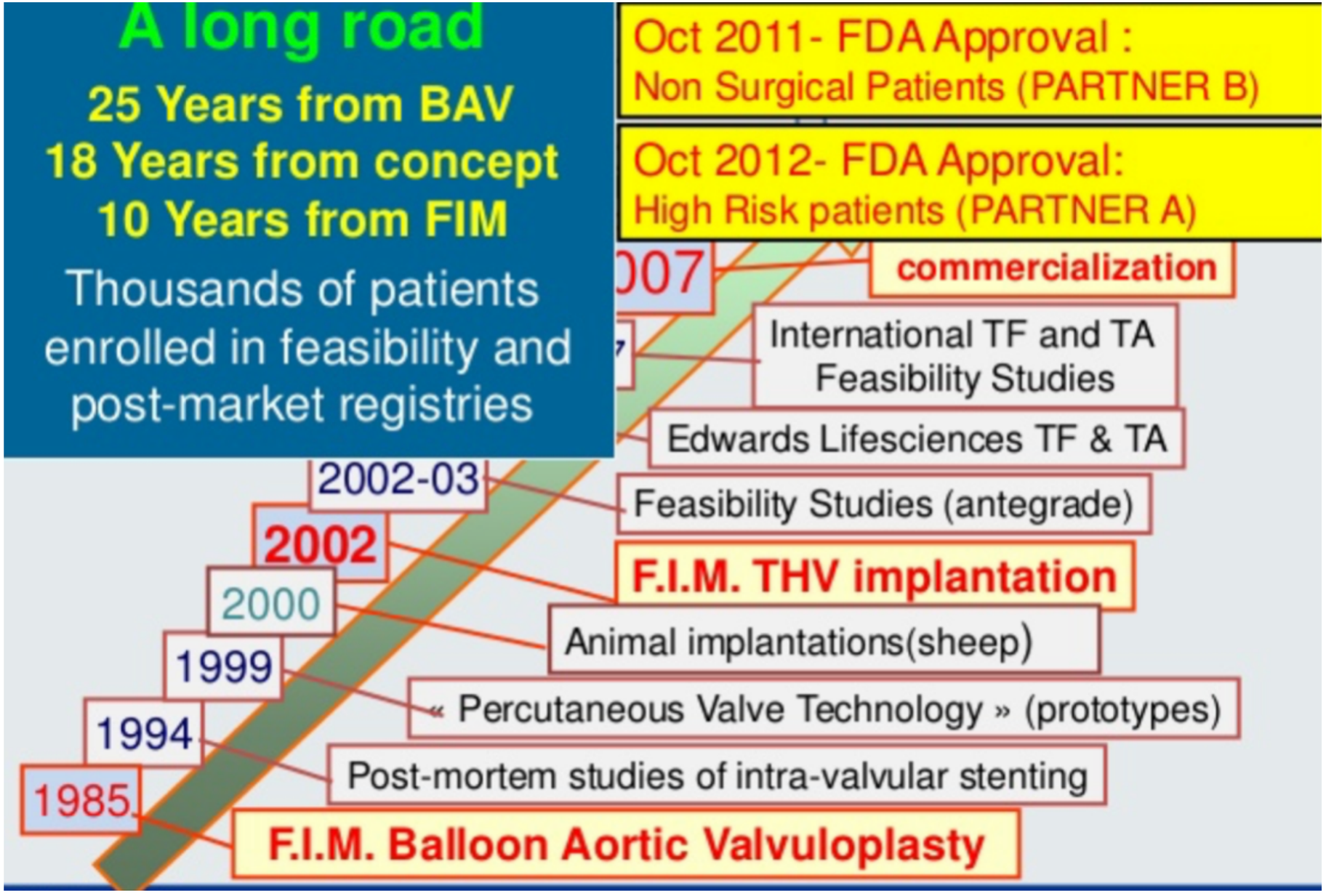
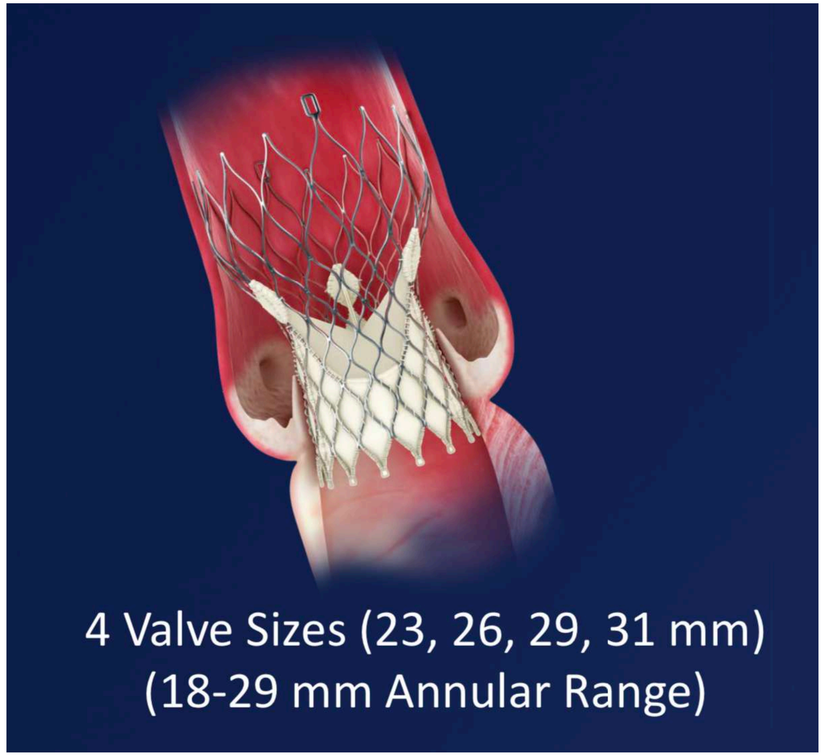


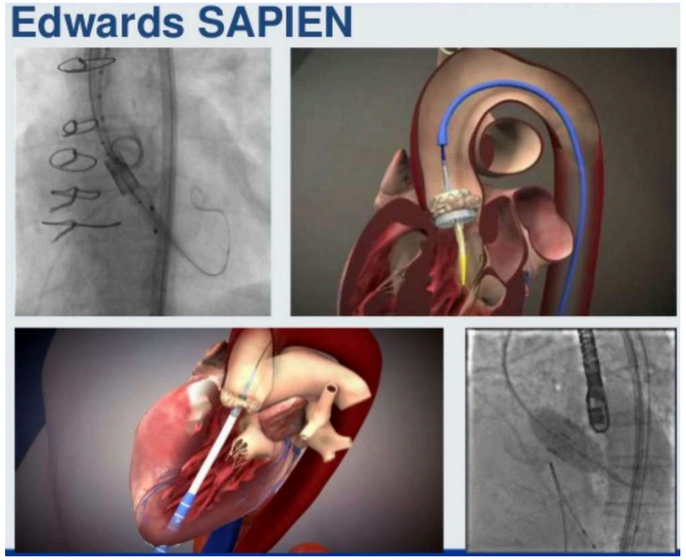
Figure 2. PHV delivery within the native calcific valve via antegrade approach. Left, Maximal balloon inflation (23 mm) for valve delivery. Middle, The PHV in position at mid part of the native aortic valve, pushing aside the calcific leaflets. Right, Supraaortic angiogram after PHV implantation showing no aortic regurgitation across the PHV and a mild paravalvular regurgitation (arrow). Both coronary ostia are patent and removed from the valve prosthesis [17]

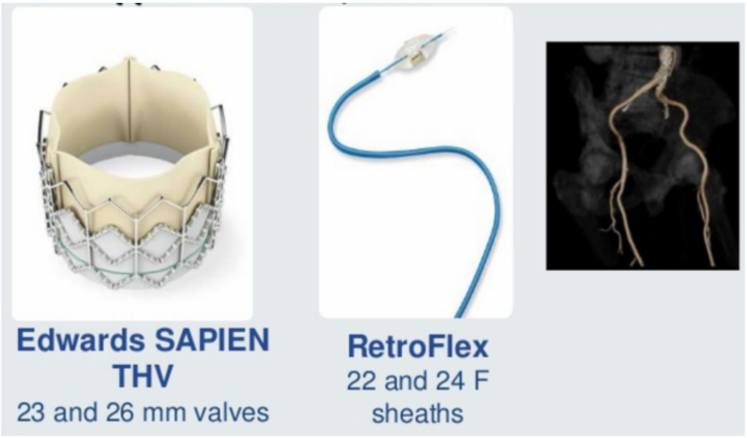

A long road
25 Years from BAV
18 Years from concept
10 Years from FIM
Thousands of patients enrolled in feasibility and post-market registries
Oct 2011- FDA Approval :
Non Surgical Patients (PARTNER B)
Oct 2012- FDA Approval:
High Risk patients (PARTNER A)
007
commercialization
International TF and TA Feasibility Studies
Edwards Lifesciences TF & TA
2002-03
Feasibility Studies (antegrade)
2002
F.I.M. THV implantation
2000
Animal implantations(sheep)
1999
« Percutaneous Valve Technology » (prototypes)
1994
Post-mortem studies of intra-valvular stenting
1985
F.I.M. Balloon Aortic Valvuloplasty

TAVR

A Tale of 2 Valves: Medtronic Corevalve, Edwards Sapien Valve

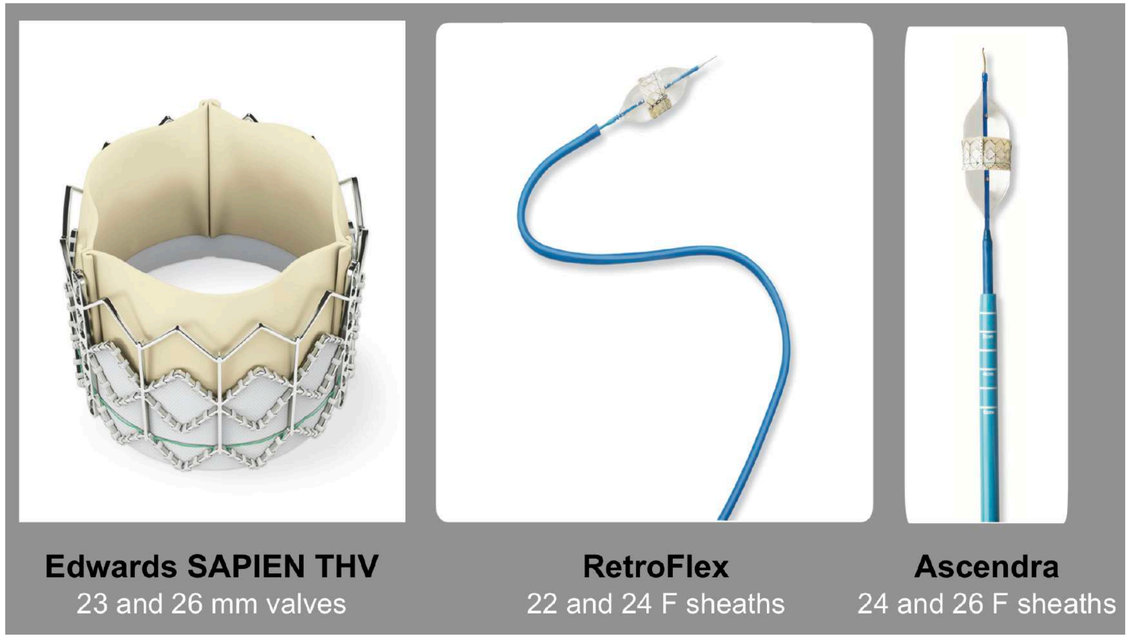






PARTNER A/B (NEJM 2010)

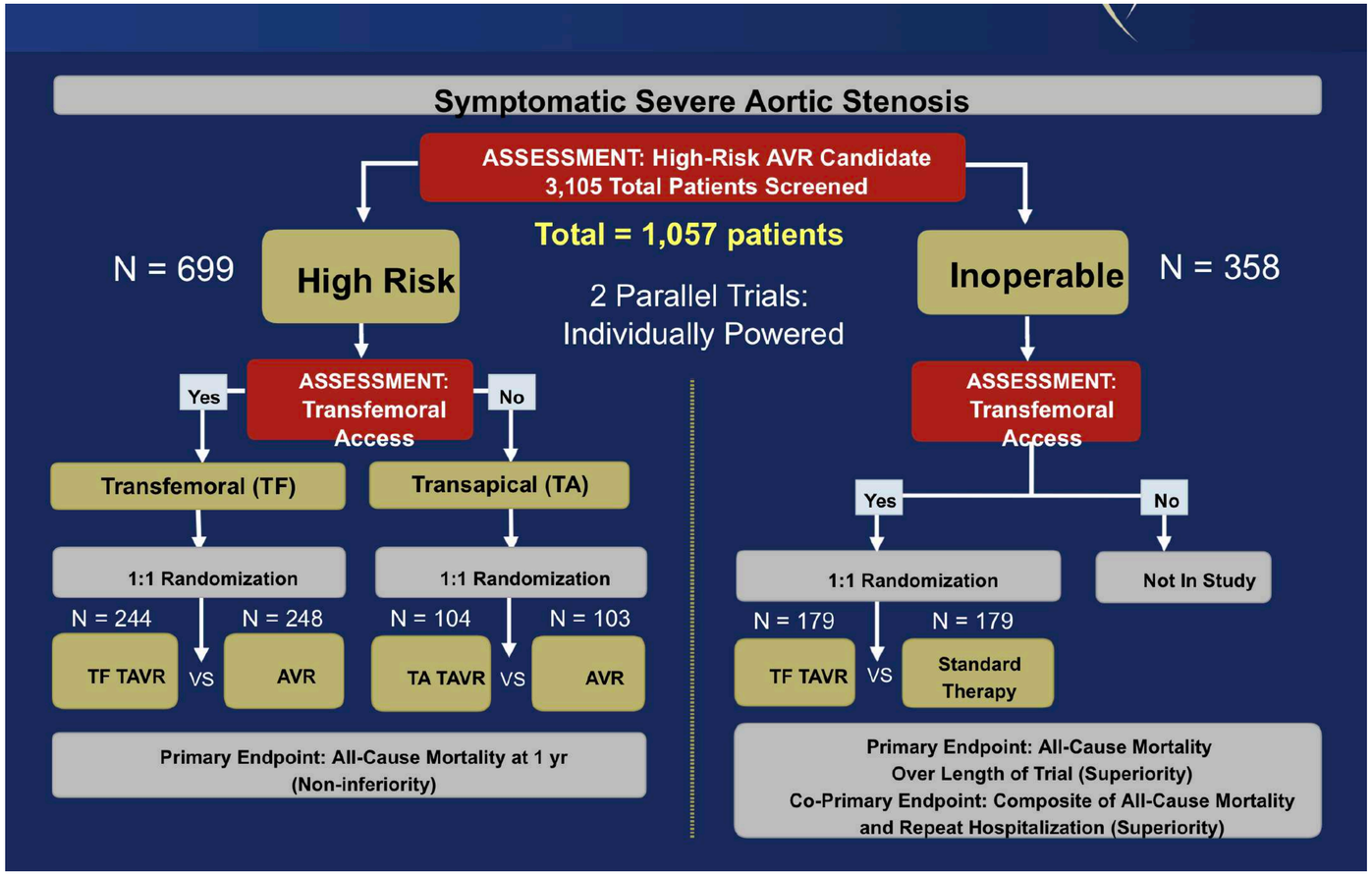
- TAVR vs SAVR in patients with severe aortic stenosis at high surgical risk, STS >10 (A)
- TAVR vs Medical therapy in patients with severe aortic stenosis whom are inoperable (B)



Edwards SAPIEN THV
23 and 26 mm valves

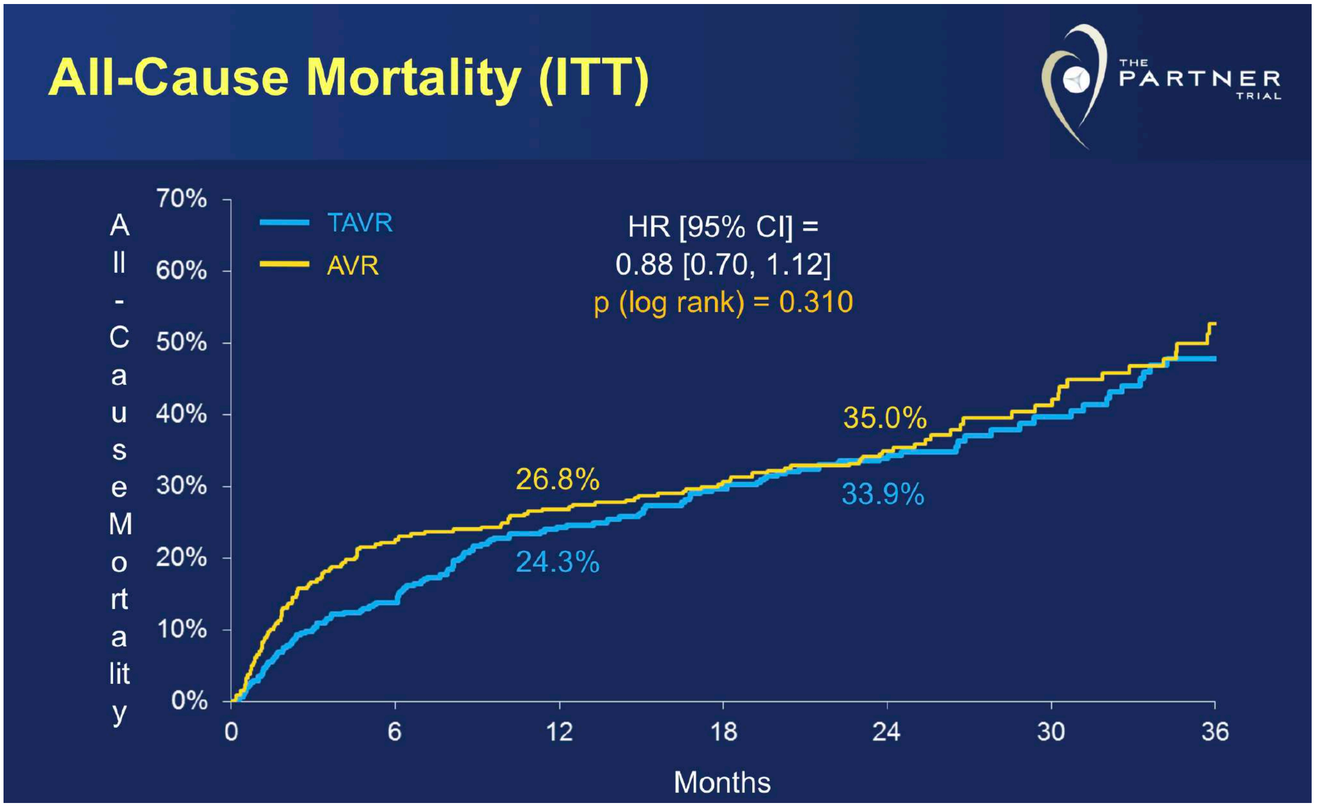
RetroFlex
22 and 24 F sheaths

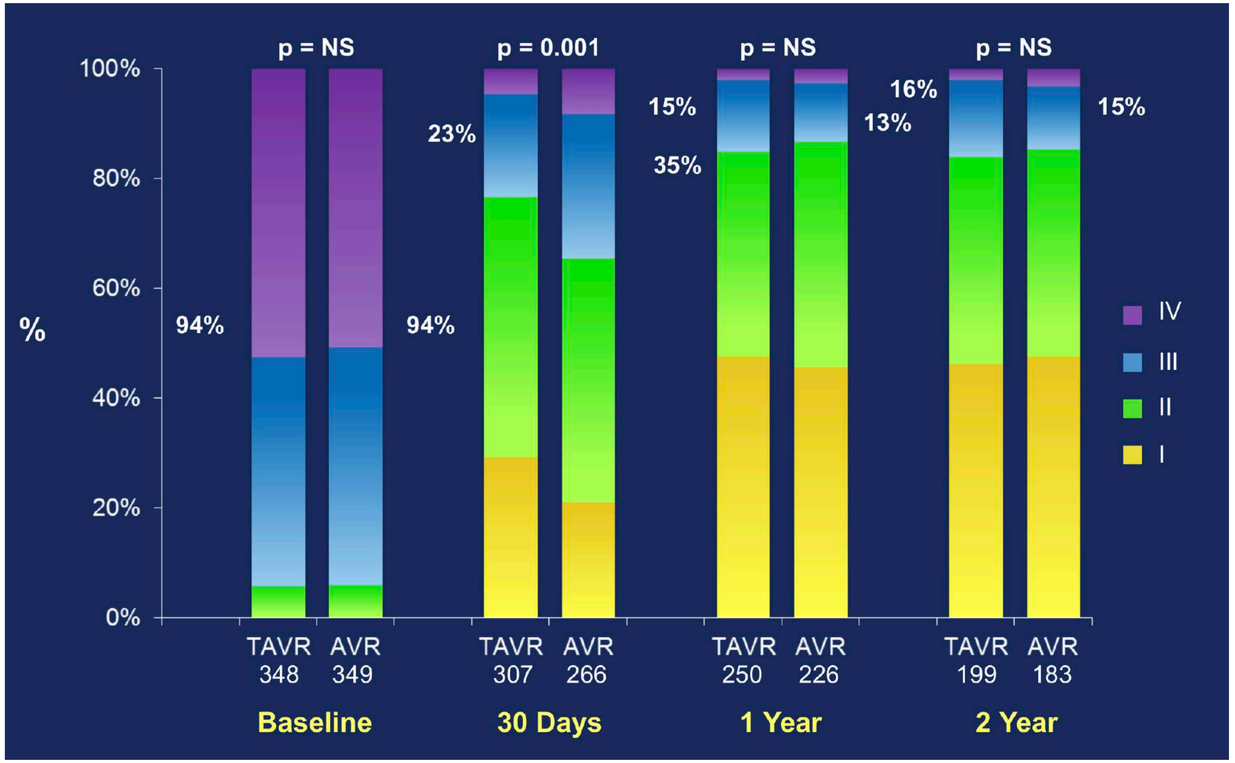
Ascendra
24 and 26 F sheaths



PARTNER A

Outcomes

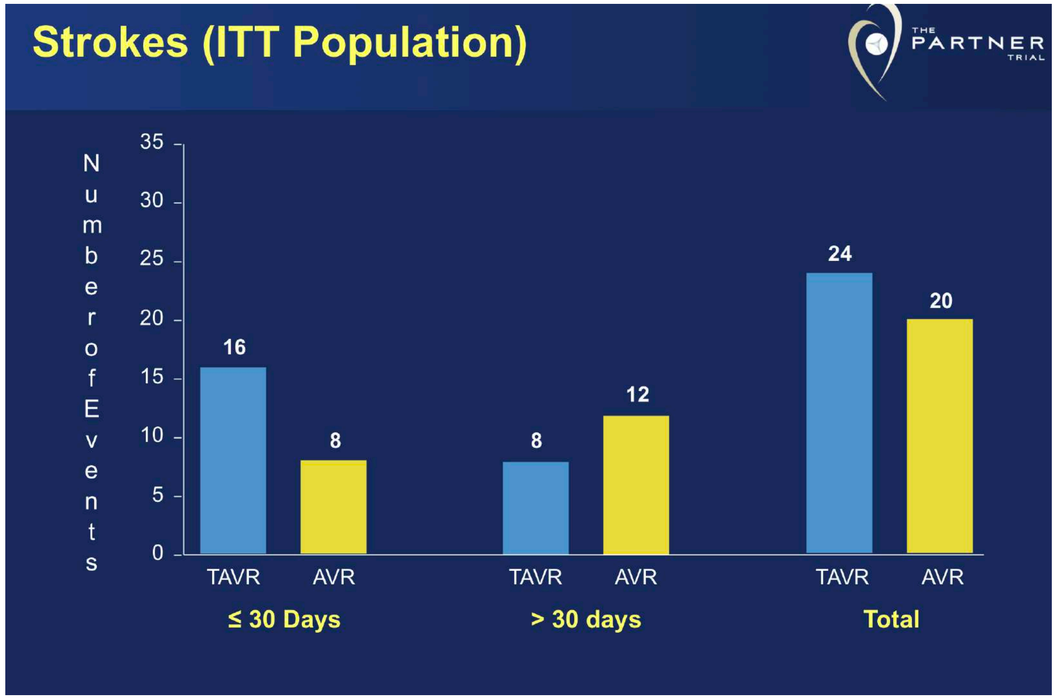




TCT 2014

Partner A

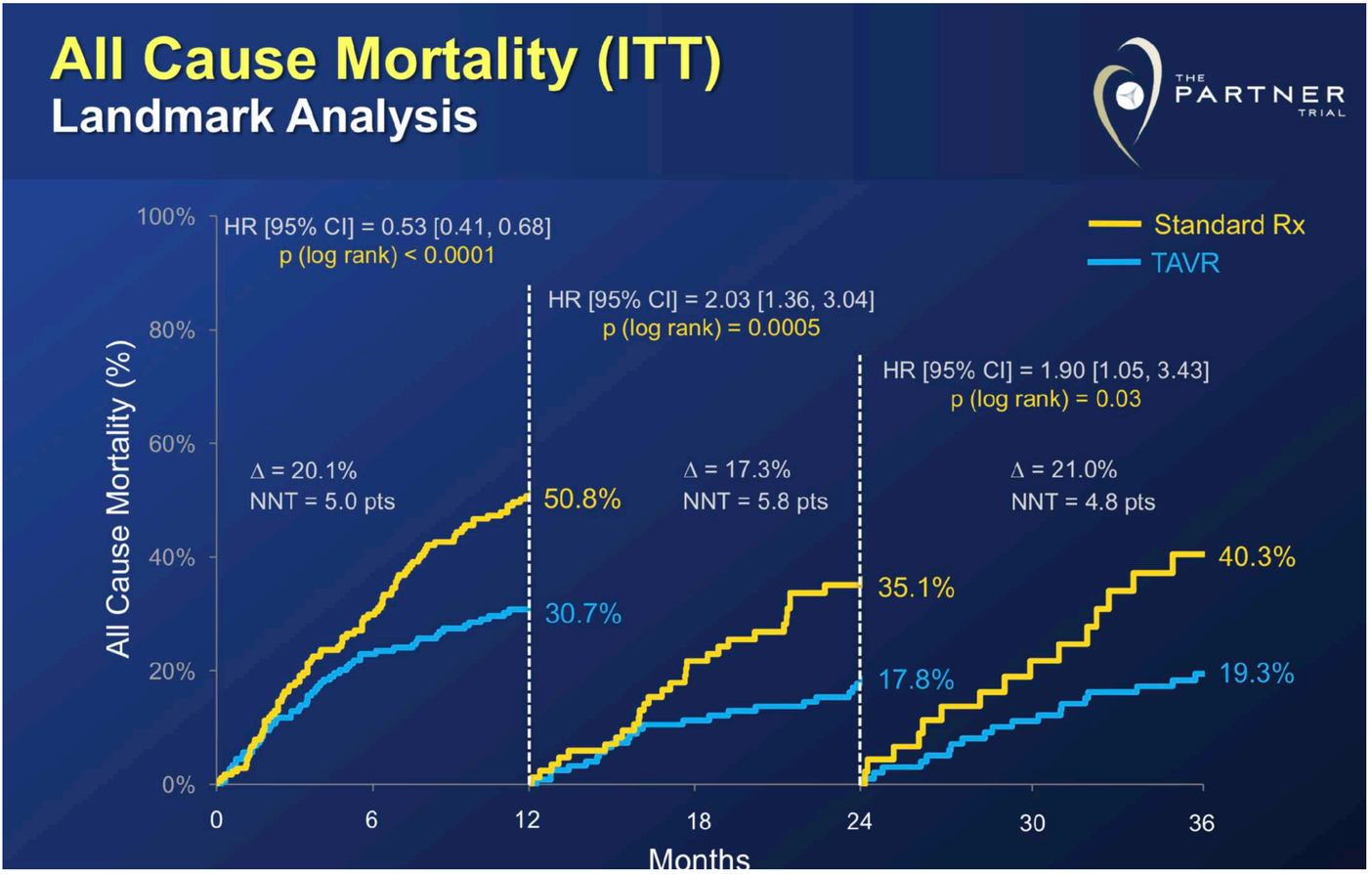
Adverse Events

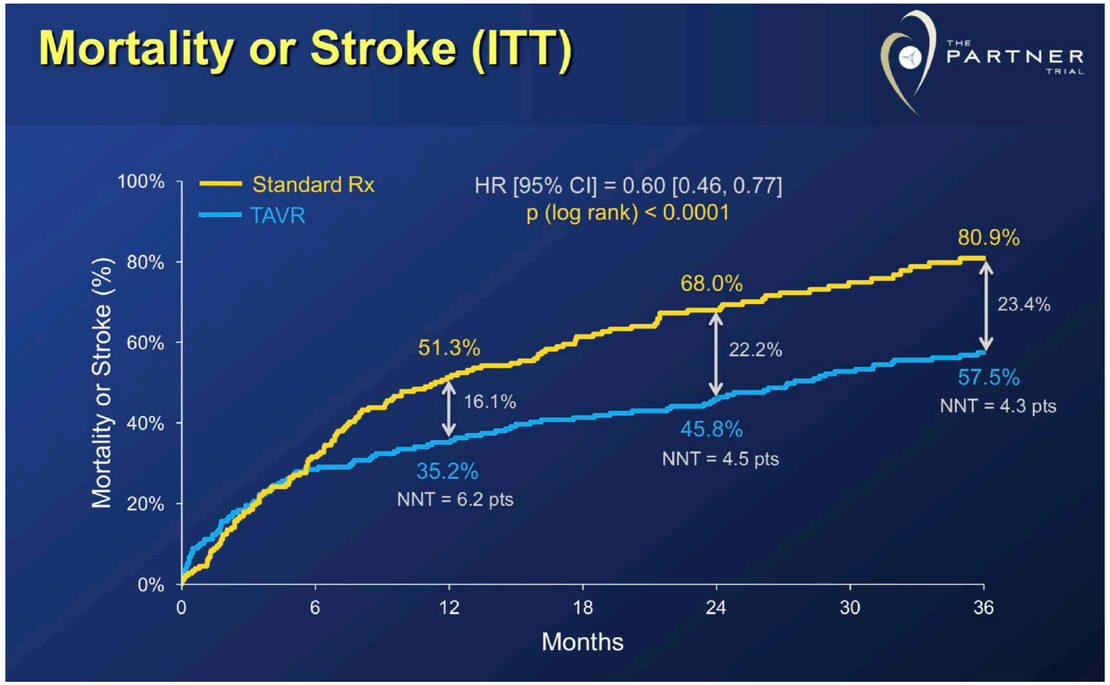


Outcome	1 Year			2 Years		
	AVR (N = 351)	*TAVR (N = 348)*	*p-value*	*AVR (N = 351)*	*TAVR (N = 348)*	*p-value*
Major Vascular complications	13 (3.8)	39 (11.3)	<0.001	13 (3.8)	40 (11.6)	<0.001
Major bleeding – no. (%)	88 (26.7)	52 (15.7)	<0.001	95 (29.5)	60 (19.0)	0.002
New PM – no. (%)	16 (5.0)	21 (6.4)	0.44	19 (6.4)	23 (7.2)	0.69
Endocarditis – no. (%)	3 (1.0)	2 (0.6)	0.63	3 (1.0)	4 (1.5)	0.61
SVD§ requiring AVR	0	0		0	0	
MI – no. (%)	2 (0.6)	0	0.16	4 (1.5)	0	0.05
Acute kidney inj* – no. (%)	20 (6.5)	18 (5.4)	0.57	21 (6.9)	20 (6.2)	0.75

PARTNER B

Outcomes



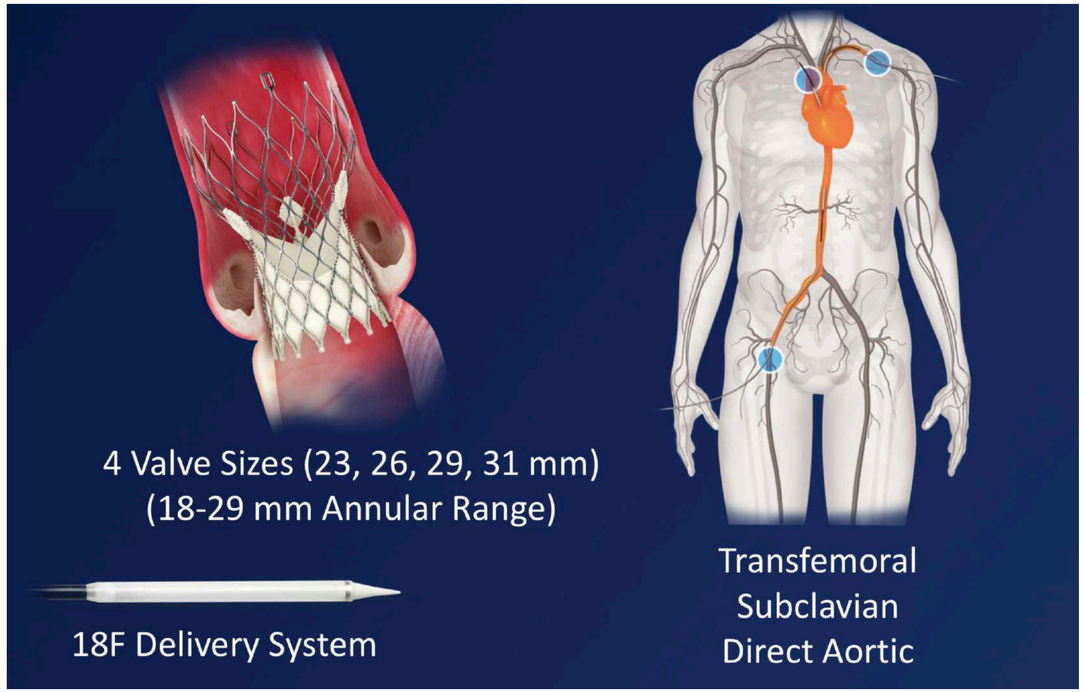


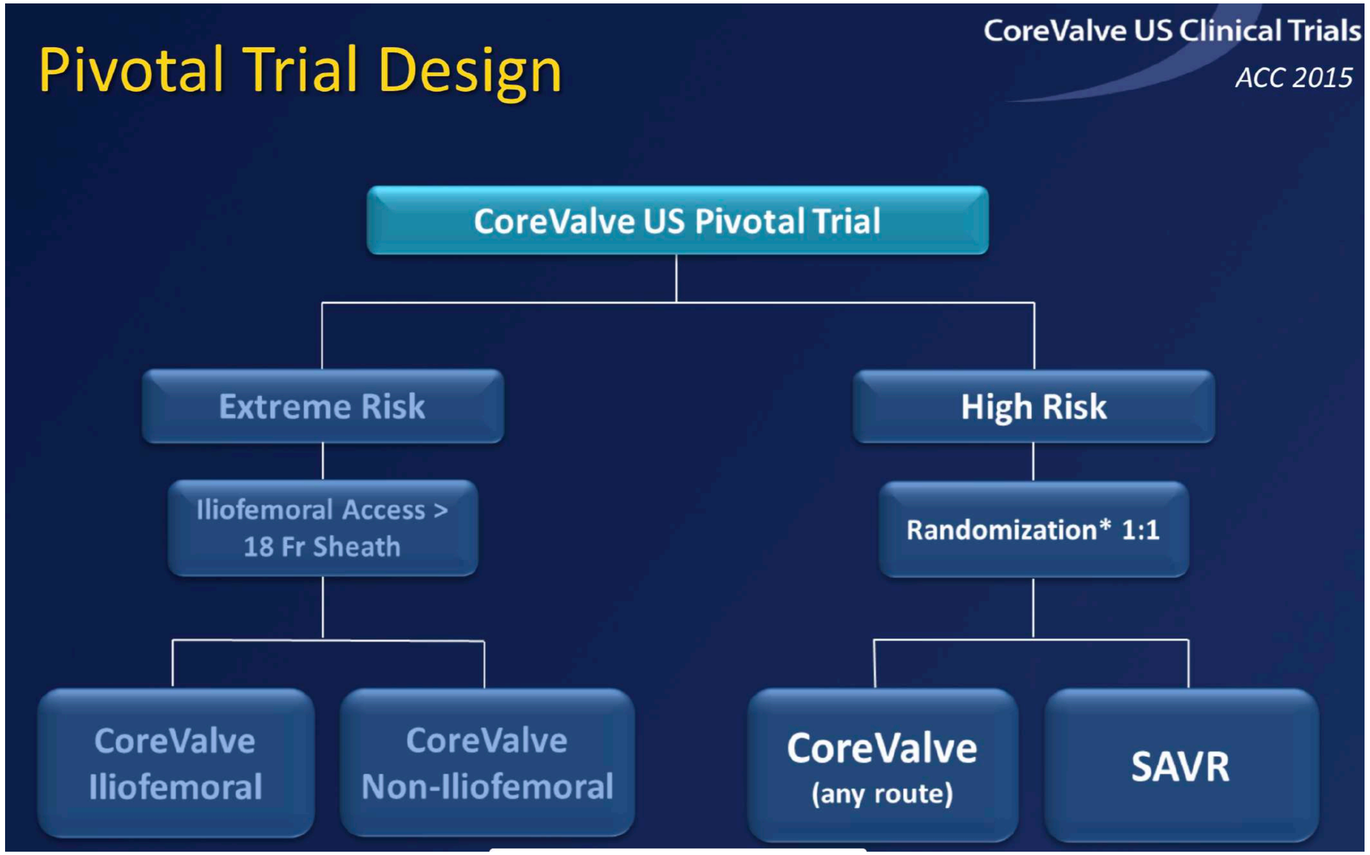
TCT 2014

US Corevalve

High/Extreme Risk

- A randomized comparison of self-expanding Transcatheter versus surgical aortic valve replacement in patients with severe AS deemed high risk for surgery





US Corevalve

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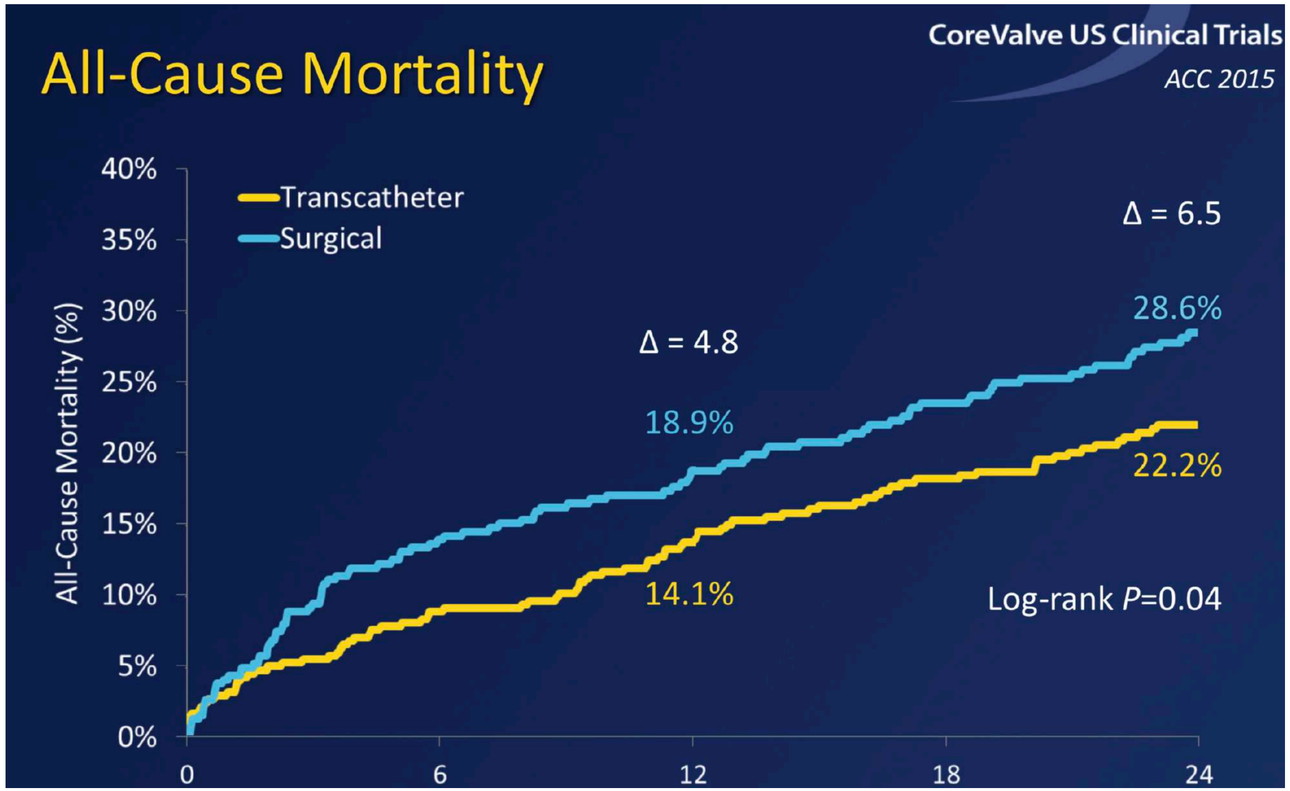
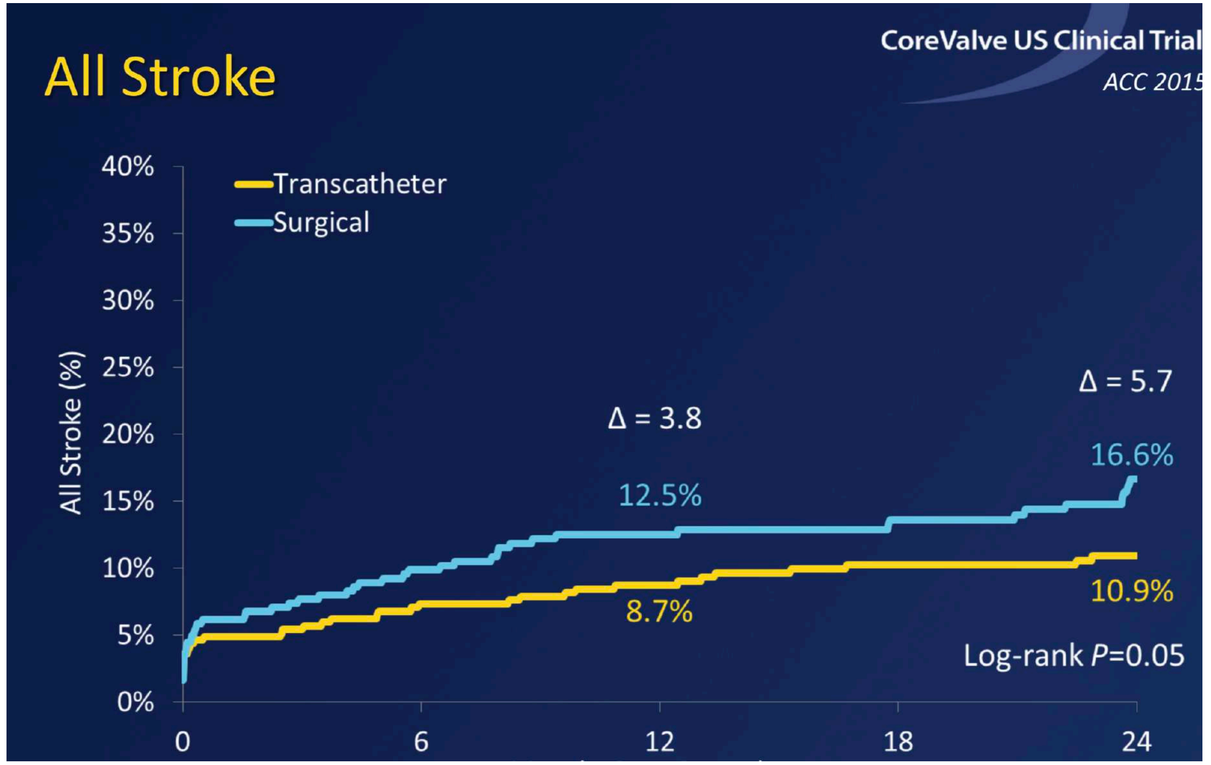




US CoreValve

Adverse Events

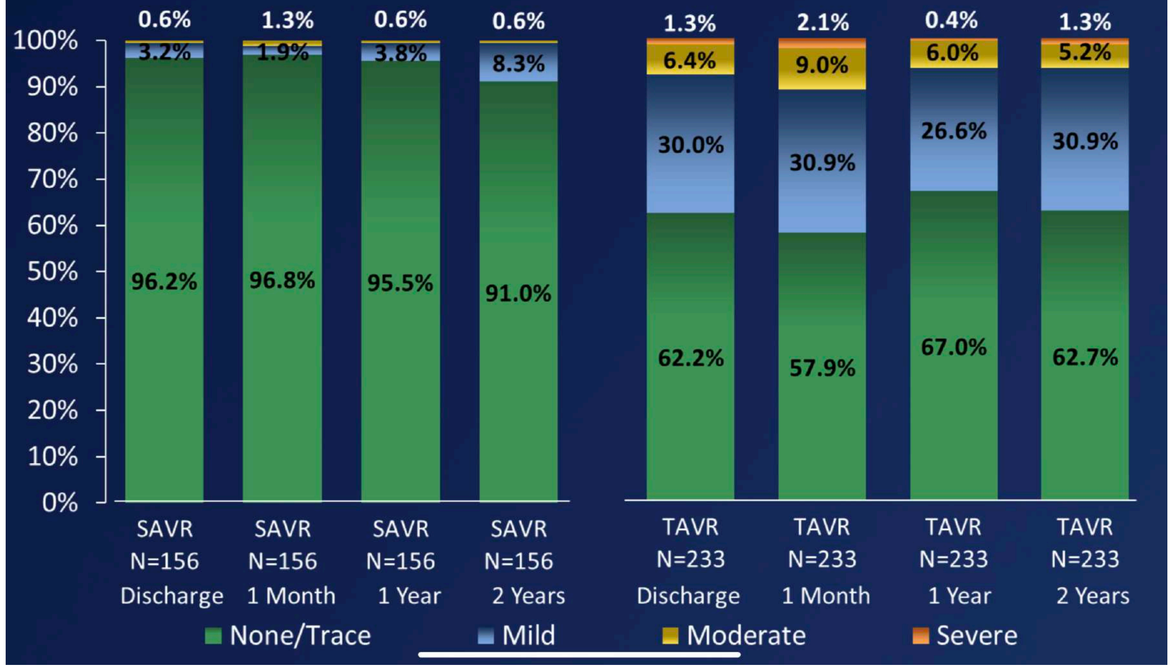
Other Clinical Endpoints

CoreValve US Clinical Trials
ACC 2015

Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	*P*	TAVR	SAVR	*P*	TAVR	SAVR	*P*
Vascular complications (major)	6.2	1.7	0.002	6.4	2.0	0.003	7.1	2.0	0.001
Pacemaker implant	20.0	7.1	<0.001	22.5	11.6	<0.001	25.8	12.8	<0.001
Bleeding (life threatening or disabling)	13.6	35.1	<0.001	16.5	38.4	<0.001	18.1	39.6	<0.001
New onset or worsening atrial fibrillation	11.7	31.0	<0.001	16.4	33.2	<0.001	19.5	34.9	<0.001
Acute kidney injury	6.2	15.1	<0.001	6.2	15.1	<0.001	6.2	15.1	<0.001

Paravalvular Regurgitation (Paired)

ACC 2015



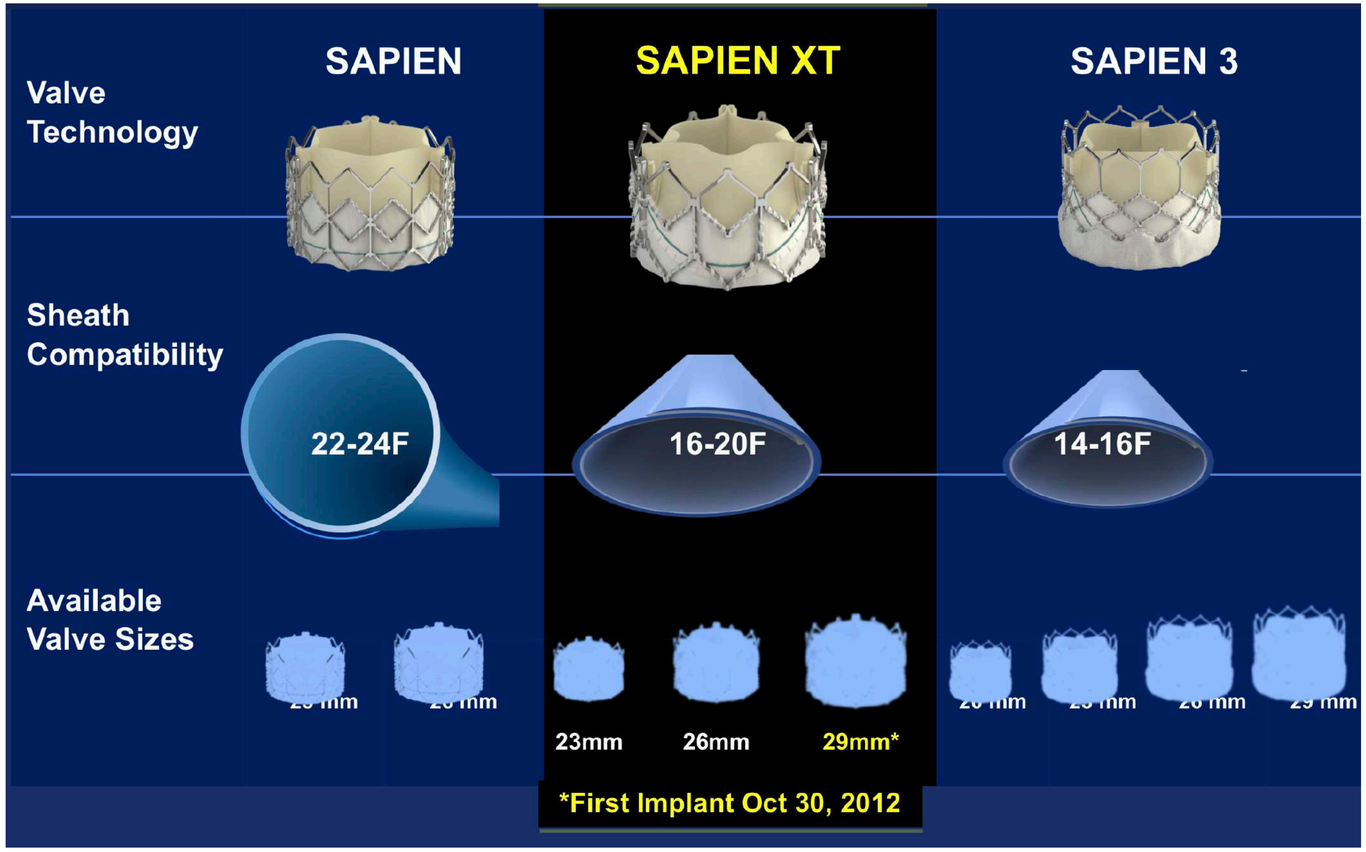
ACC AHA Guidelines 2014

AVR for Aortic Stenosis

Recommendations	COR	LOE
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk	I	A
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)	IIa	B
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B

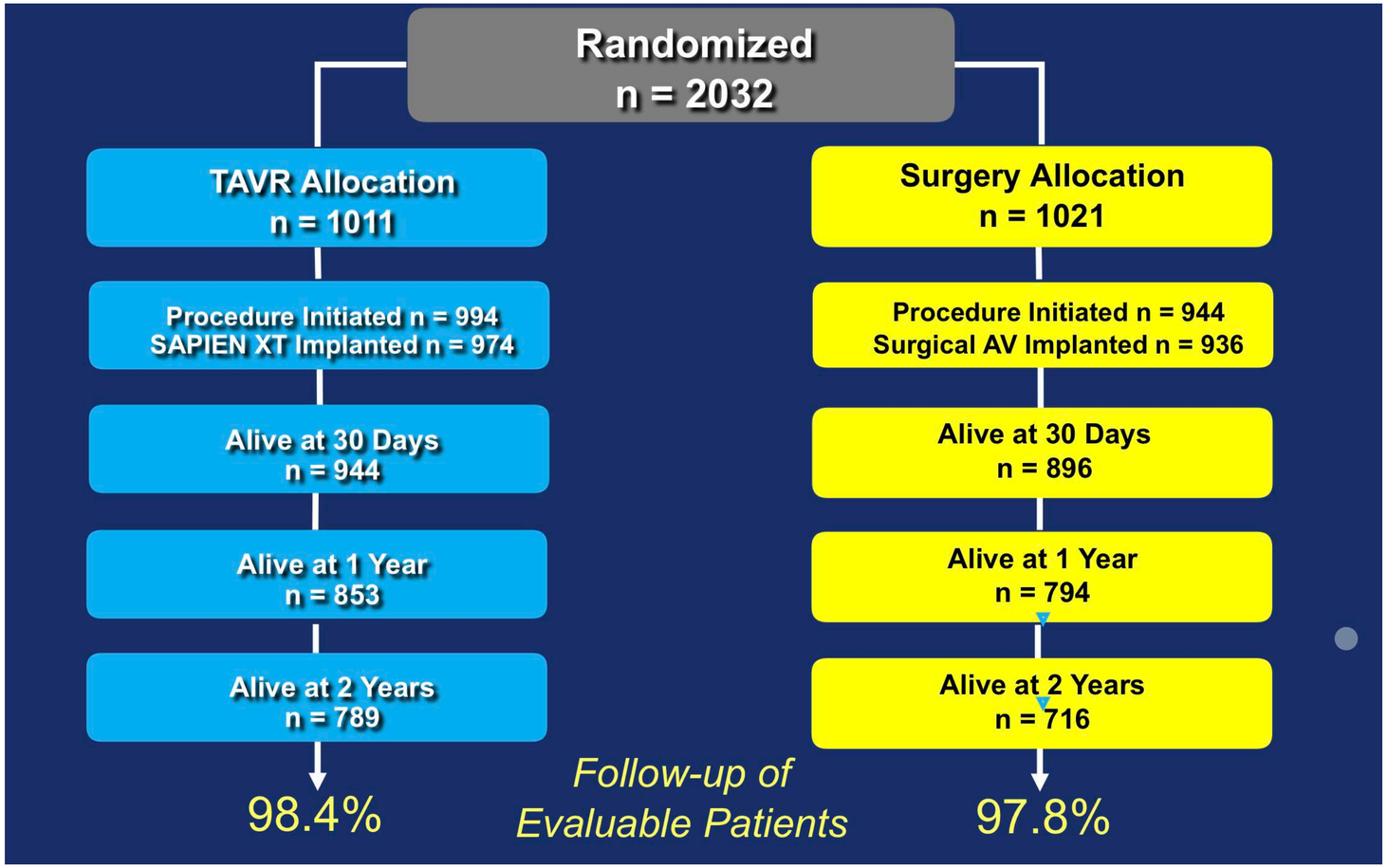
Severe Aortic Stenosis

Intermediate Risk: STS>4



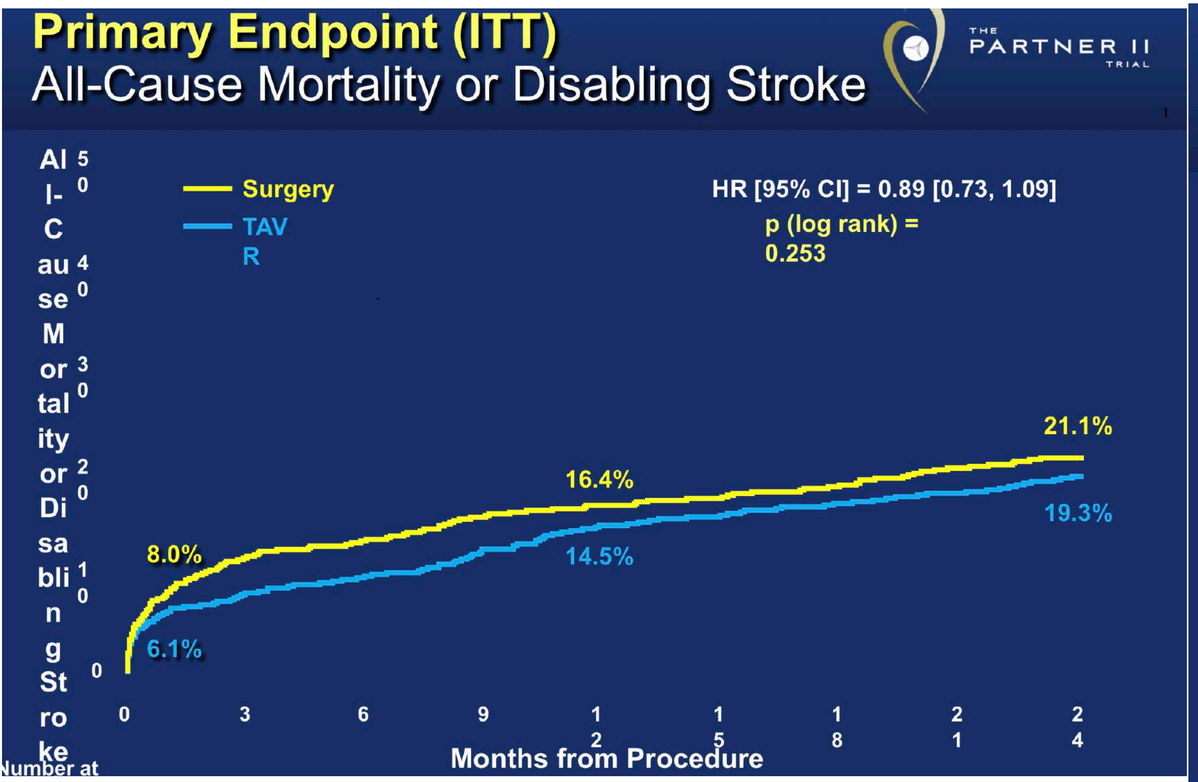
PARTNER 2

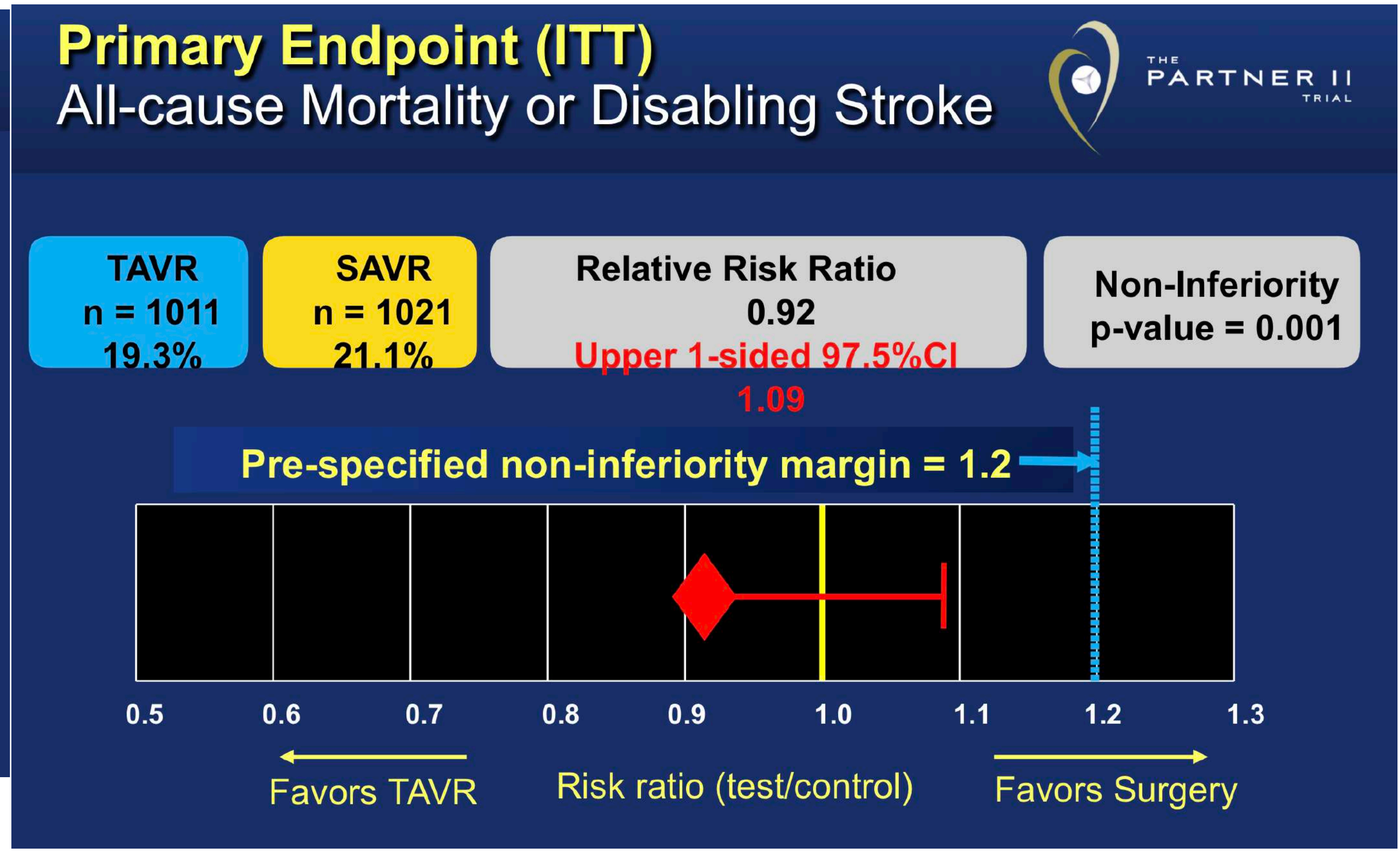
- To compare safety and effectiveness of TAVR with second generation Sapien XT versus SAVR in intermediate risk patients.



Partner 2

Outcomes





Partner 2

Adverse Events

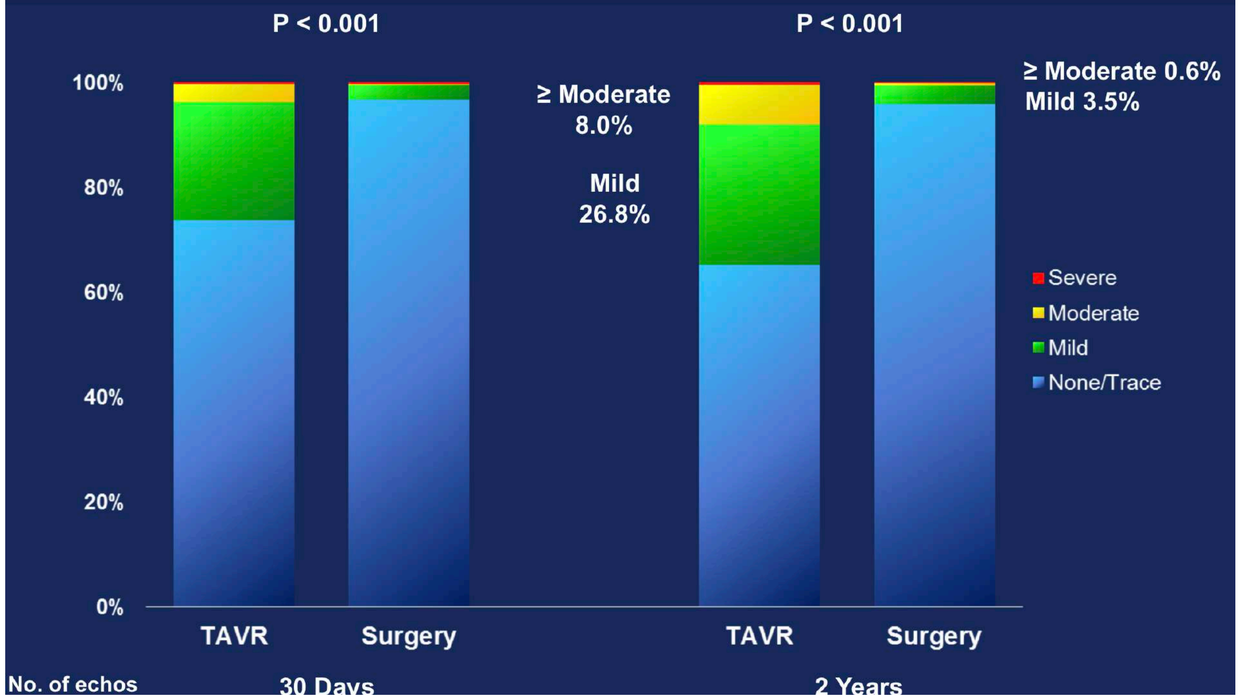
Other Clinical Endpoints (ITT)
At 30 Days and 2 Years

THE PARTNER II TRIAL

Events (%)	30 Days			2 Years		
	TAVR (n = 1011)	Surgery (n = 1021)	p-value*	TAVR (n = 1011)	Surgery (n = 1021)	p-value*
Rehospitalization	6.5	6.5	0.99	19.6	17.3	0.22
MI	1.2	1.9	0.22	3.6	4.1	0.56
Major Vascular Complications	7.9	5.0	0.008	8.6	5.5	0.006
Life-Threatening / Disabling Bleeding	10.4	43.4	<0.001	17.3	47.0	<0.001
AKI (Stage III)	1.3	3.1	0.006	3.8	6.2	0.02
New Atrial Fibrillation	9.1	26.4	<0.001	11.3	29.3	<0.001
New Permanent Pacemaker	8.5	6.9	0.17	11.8	10.3	0.29
Re-intervention	0.4	0.0	0.05	1.4	0.6	0.09
Endocarditis	0.0	0.0	NA	1.2	0.7	0.22

Paravalvular Regurgitation (VI)
3-Class Grading Scheme

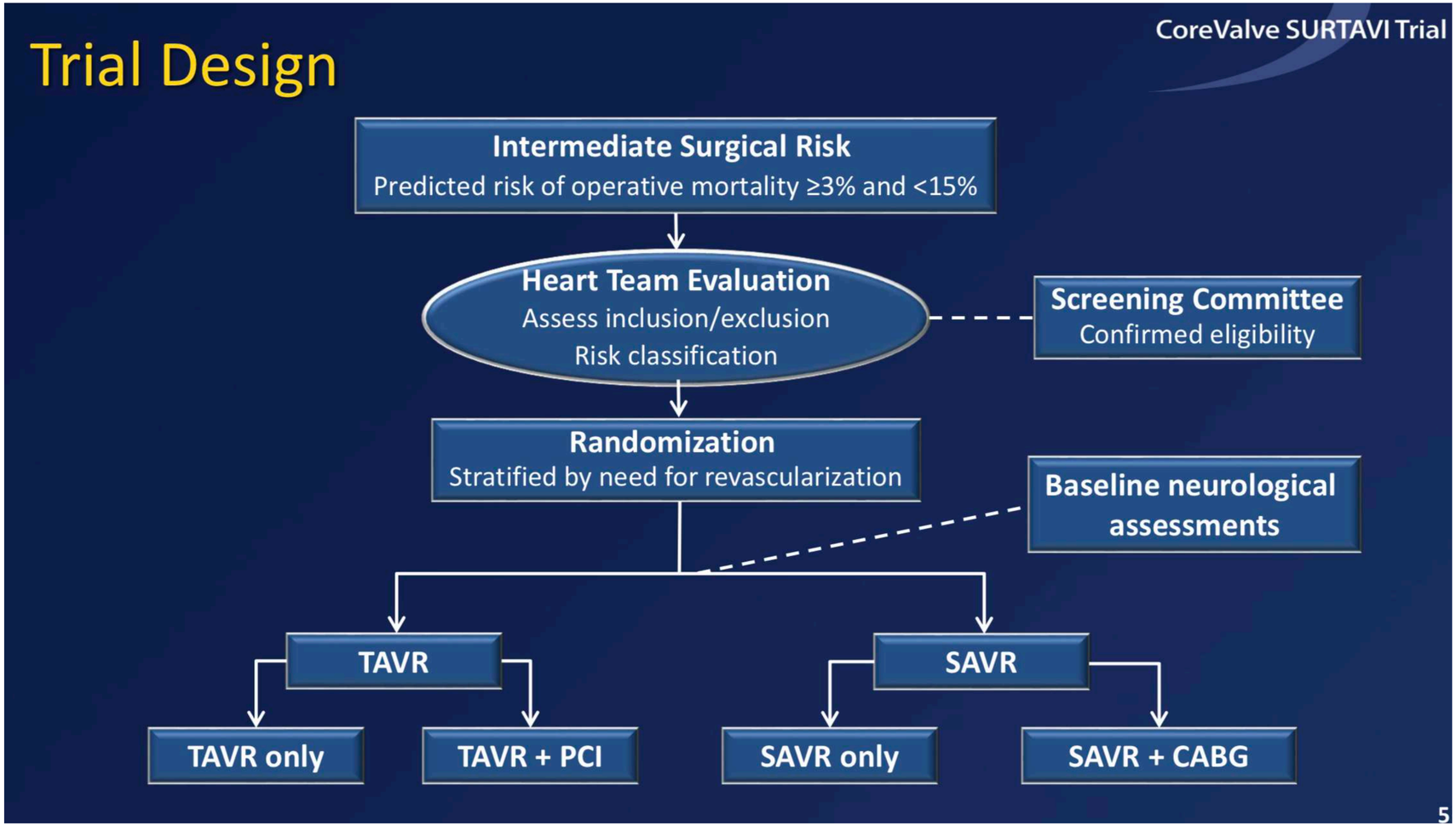
THE PARTNER II TRIAL



ACC 2016

SURTAVI

- Safety and efficacy of TAVR with self expanding prosthesis versus SAVR in intermediate risk patients with severe AS



Study Timeline

2012 2013 2014 2015 *April* 2016

First patient enrolled
June 19, 2012

Enrollment completed
June 30, 2016

CoreValve: 23, 26 and 29 mm (US)

Evolut R (US)

CoreValve: 23, 26 and 29 mm (CAN, EU)

Primary endpoint assessment
Dec 2016

CoreValve: 31 mm (US, CAN, EU)

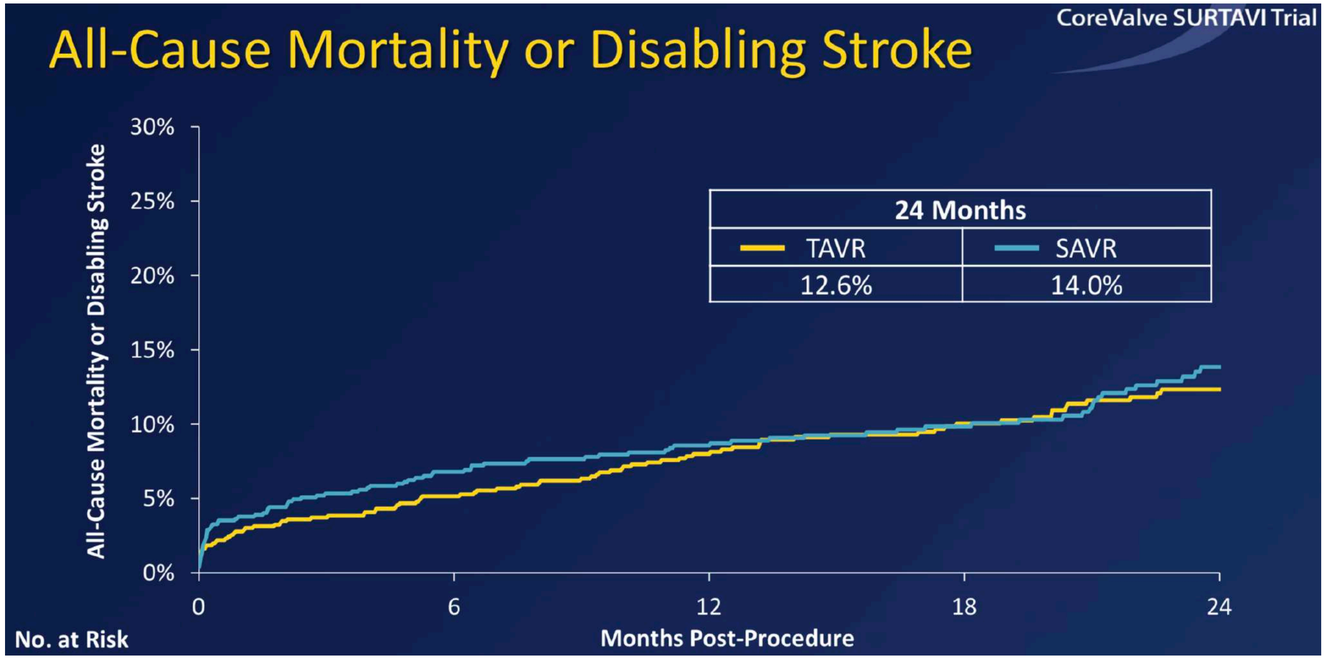
CoreValve (n=724)

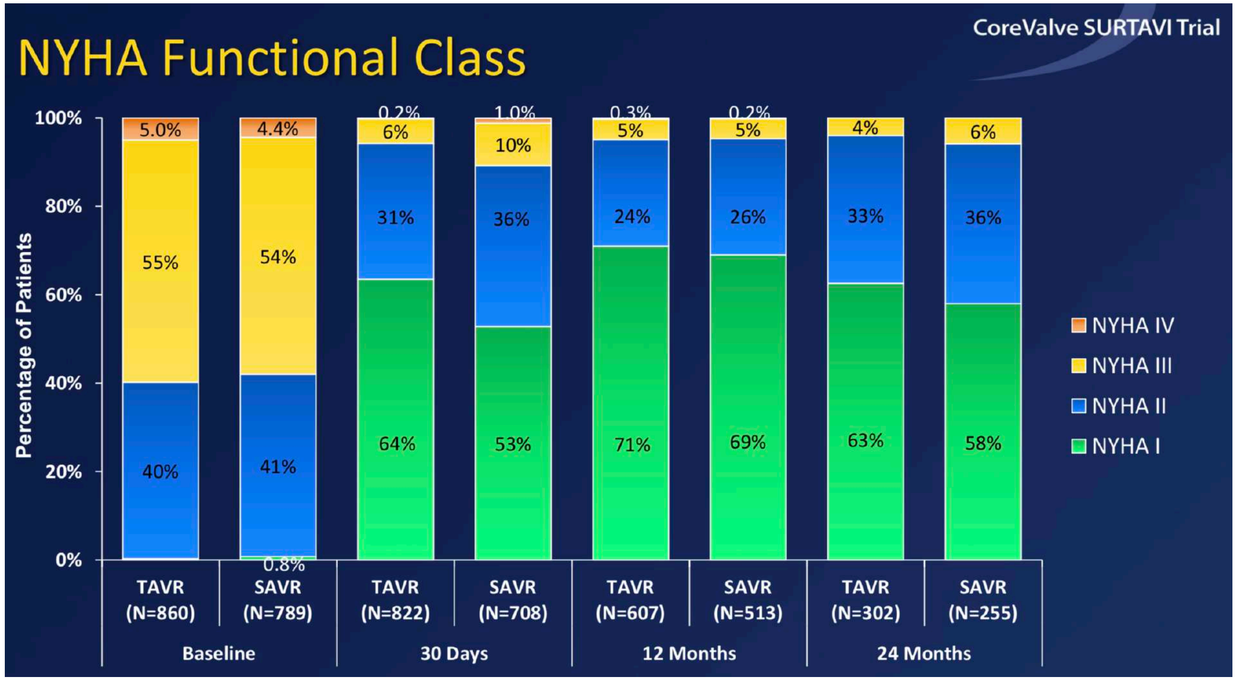
94% TF
4% DA
2% SCA

Evolut R (n=139)

SURTAVI

Outcomes





ACC 2017

SURTAVI

Adverse Events

30-Day Safety and Procedure-related Complications

CoreValve SURTAVI Tria

	TAVR (N=864)	SAVR (N=796)	95% CI for Difference
All-cause mortality or disabling stroke	2.8	3.9	-2.8, 0.7
All-cause mortality	2.2	1.7	-0.9, 1.8
Disabling stroke	1.2	2.5	-2.6, 0.1
All stroke	3.4	5.6	-4.2, -0.2
Overt life-threatening or major bleeding	12.2	9.3	-0.1, 5.9
Transfusion of PRBCs* - n (%)			
0 units	756 (87.5)	469 (58.9)	24.4, 32.5
2 – 4 units	48 (5.6)	136 (17.1)	-14.5, -8.5
≥ 4 units	31 (3.6)	101 (12.7)	-11.7, -6.5
Acute kidney injury, stage 2-3	1.7	4.4	-4.4, -1.0
Major vascular complication	6.0	1.1	3.2, 6.7
Cardiac perforation	1.7	0.9	-0.2, 2.0
Cardiogenic shock	1.1	3.8	-4.2, -1.1
Permanent pacemaker implant	25.9	6.6	15.9, 22.7
Atrial fibrillation	12.9	43.4	-34.7, -26.4

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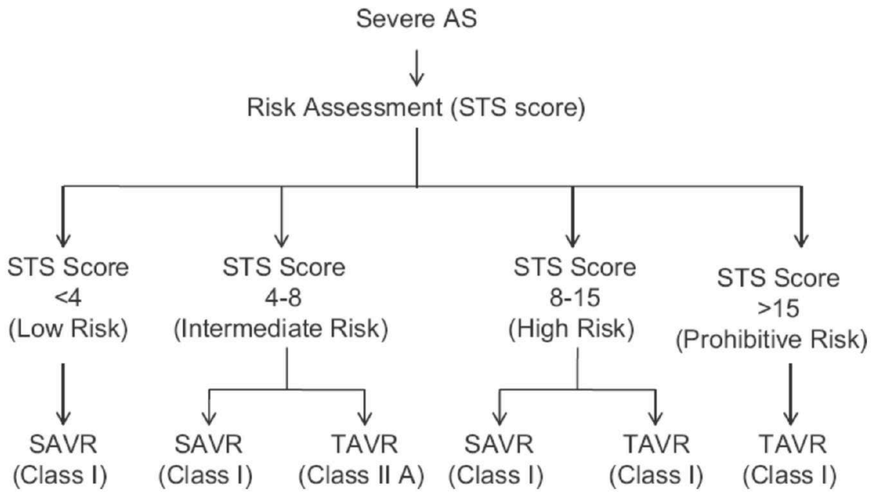
CLINICAL PRACTICE GUIDELINE: FOCUSED UPDATE

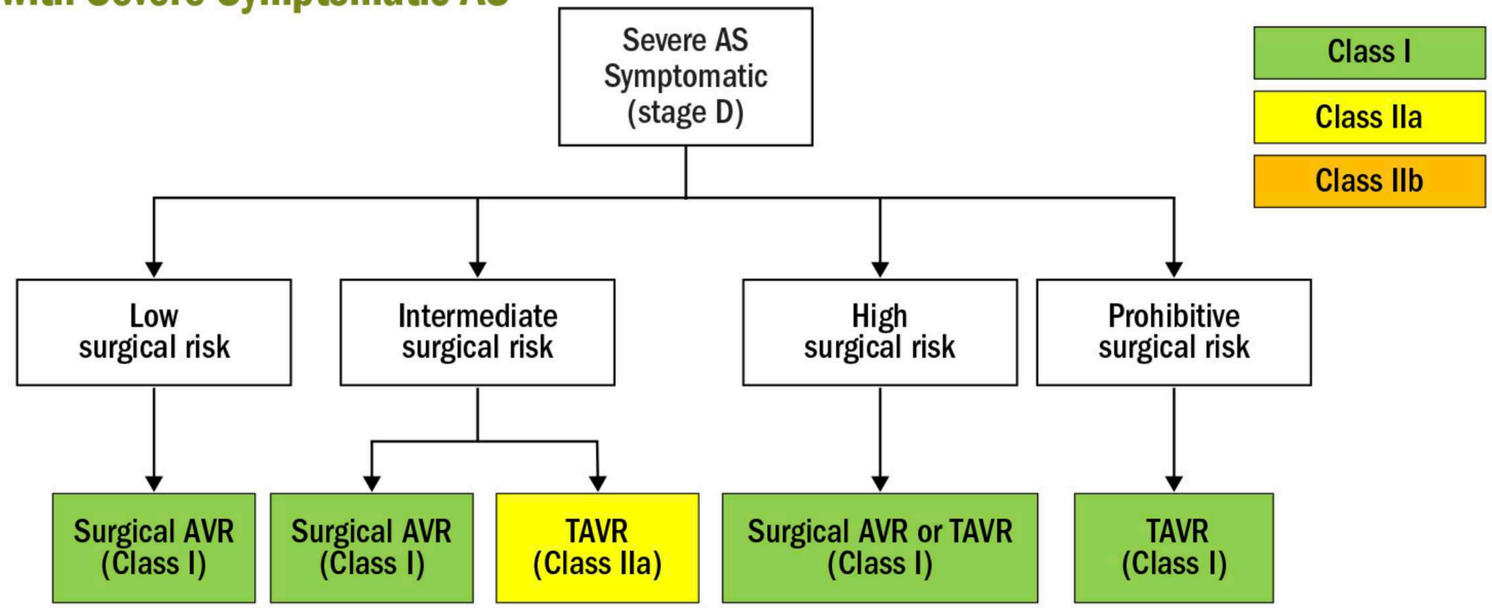
2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Developed in Collaboration With 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



Choice of TAVR Versus Surgical AVR in the Patient with Severe Symptomatic AS



AS = Aortic stenosis; AVR = Aortic Valve Replacement; TAVR = Transcatheter Aortic Valve Replacement

Severe Aortic Stenosis

Low Risk Patients: STS <4

ORIGINAL ARTICLE

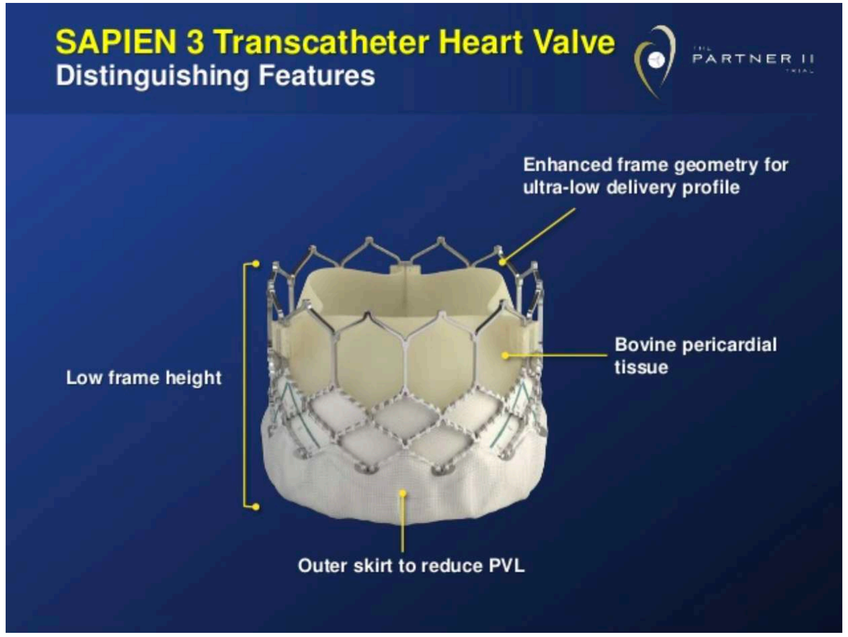
Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

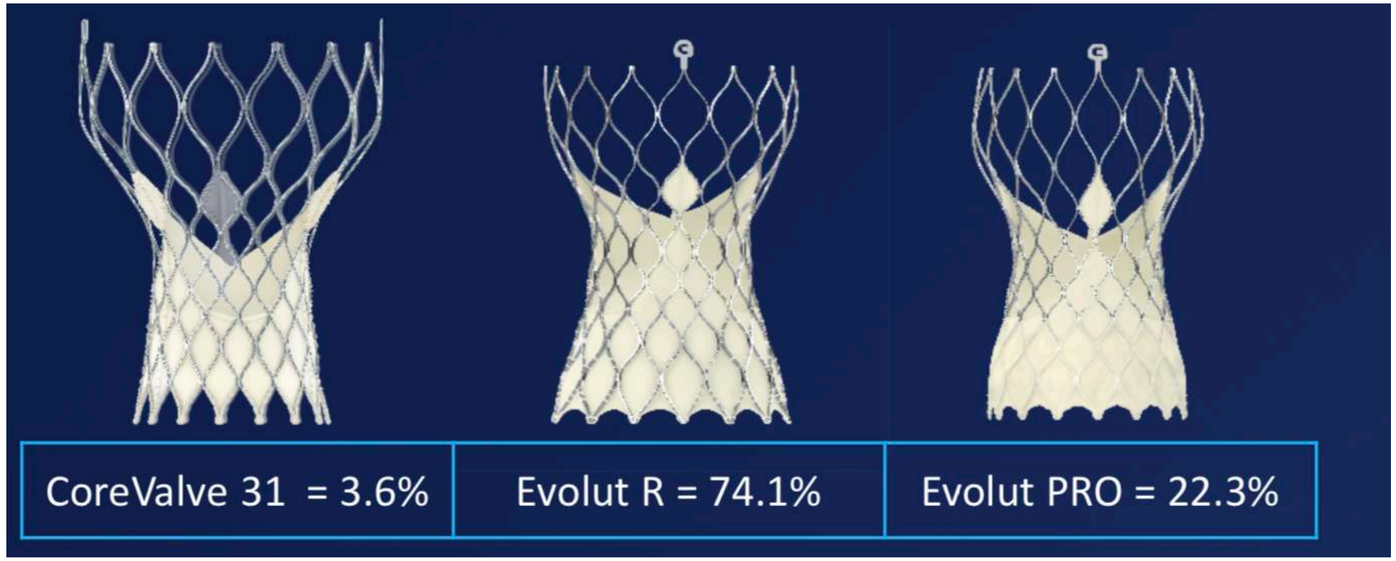
Michael J. Mack, M.D., Martin B. Leon, M.D., Vinod H. Thourani, M.D., Raj Makkar, M.D., Susheel K. Kodali, M.D., Mark Russo, M.D., Samir R. Kapadia, M.D., S. Chris Malaisrie, M.D., David J. Cohen, M.D., Philippe Pibarot, D.V.M., Ph.D., Jonathon Leipsic, M.D., Rebecca T. Hahn, M.D., et al., for the PARTNER 3 Investigators*

ORIGINAL ARTICLE

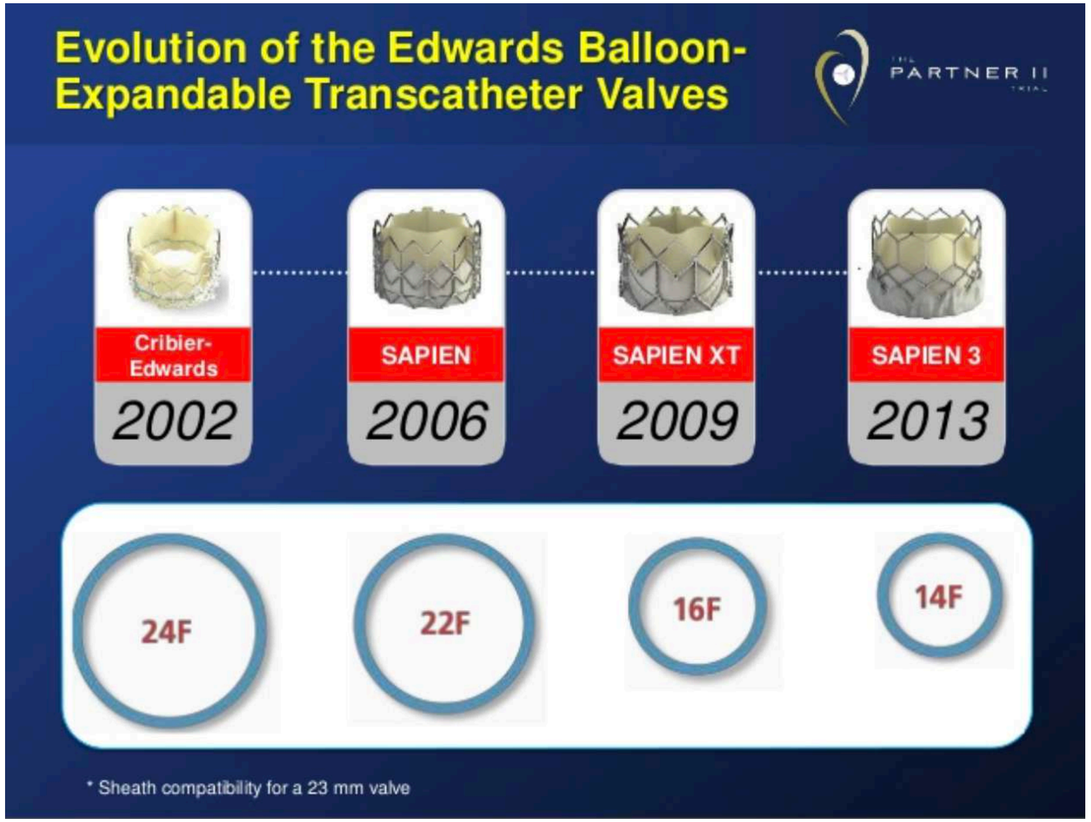
Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

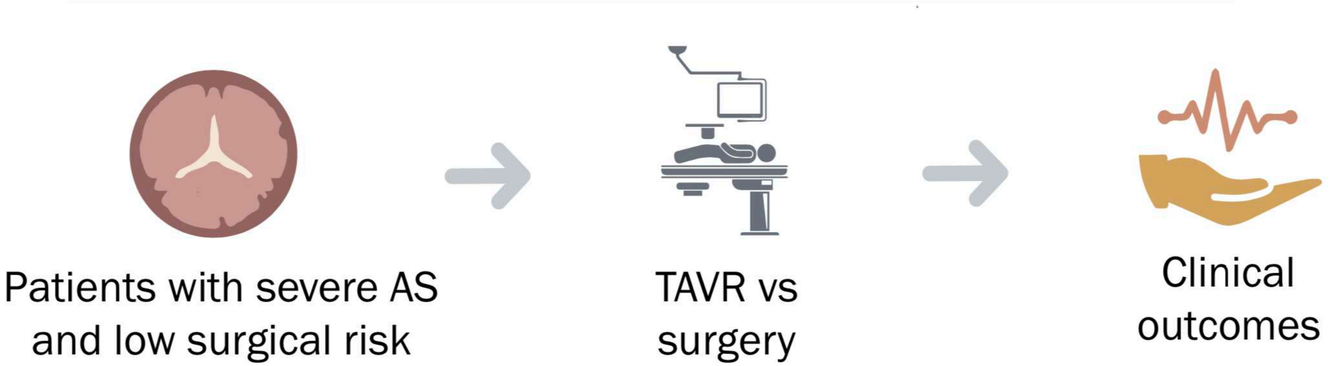
Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., et al., for the Evolut Low Risk Trial Investigators*



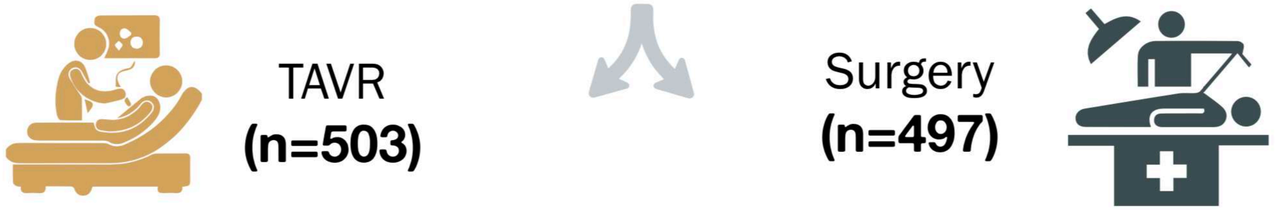


PARTNER 3

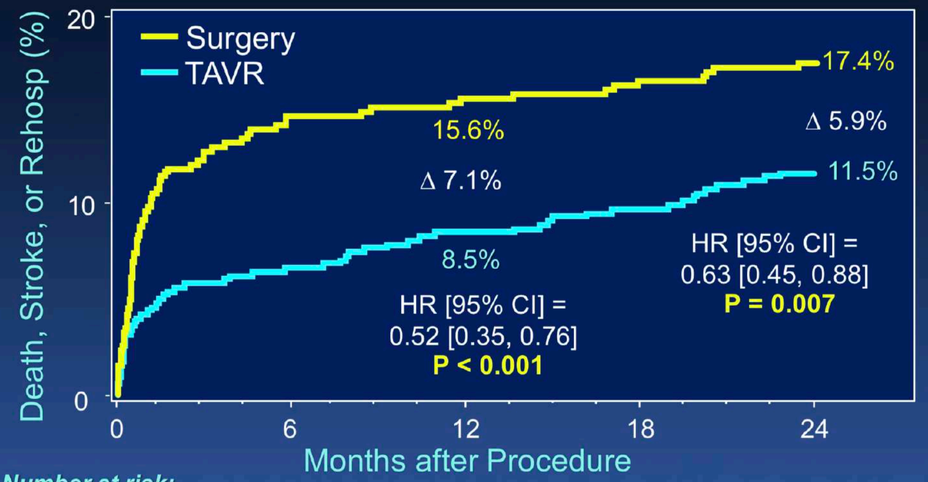




1000 patients (mean age, 73 years), male population (69.3%), with lower STS-PROM scores (mean 1.9%) and fewer comorbidities (low-risk surgical candidates)



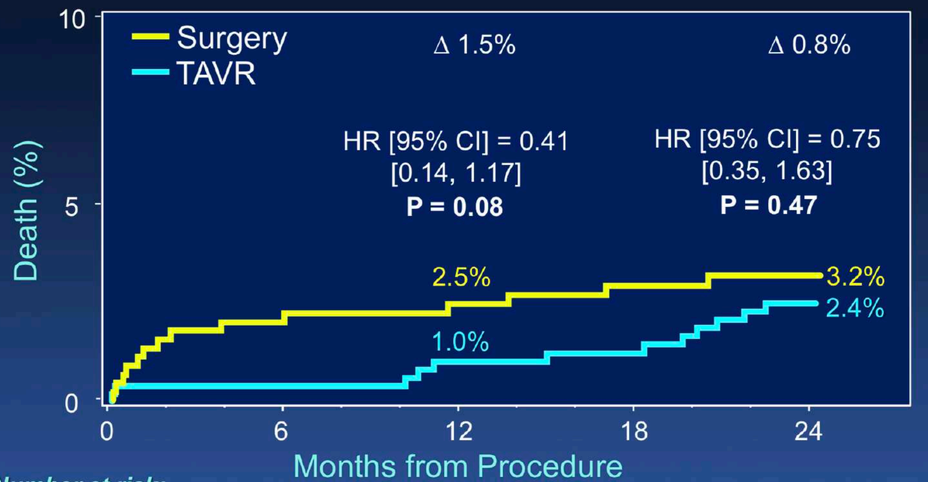
Primary Endpoint



Number at risk:

Surgery	454	378	370	352	339
TAVR	496	462	452	436	422

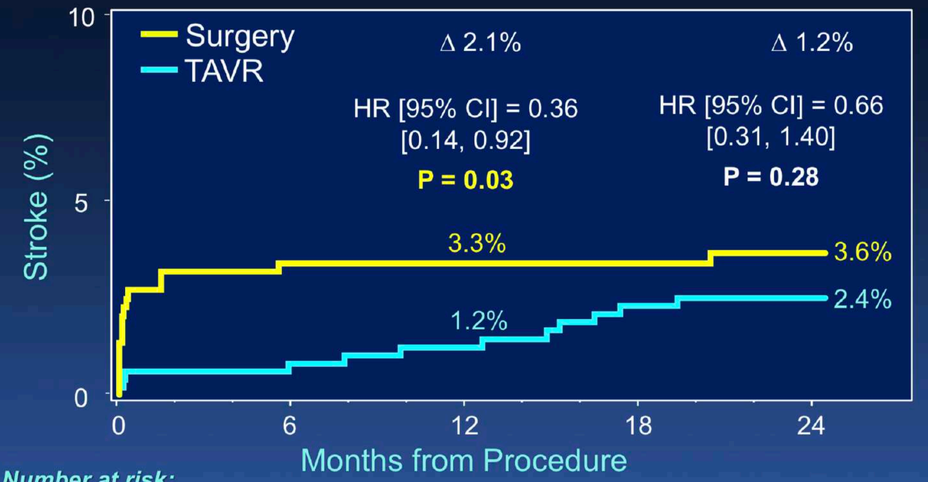
Death



Number at risk:

Surgery	454	432	425	408	397
TAVR	496	493	489	477	466

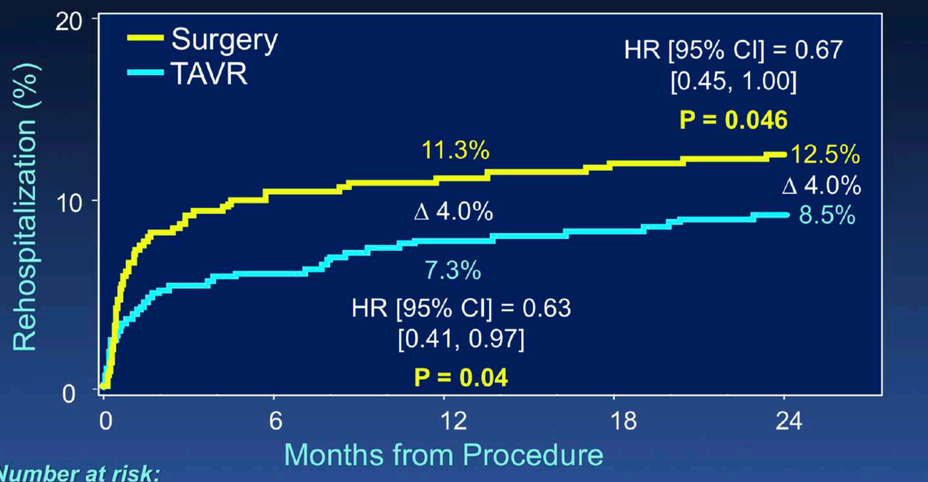
Stroke



Number at risk:

Surgery	454	421	414	398	386
TAVR	496	489	485	468	456

Rehospitalization

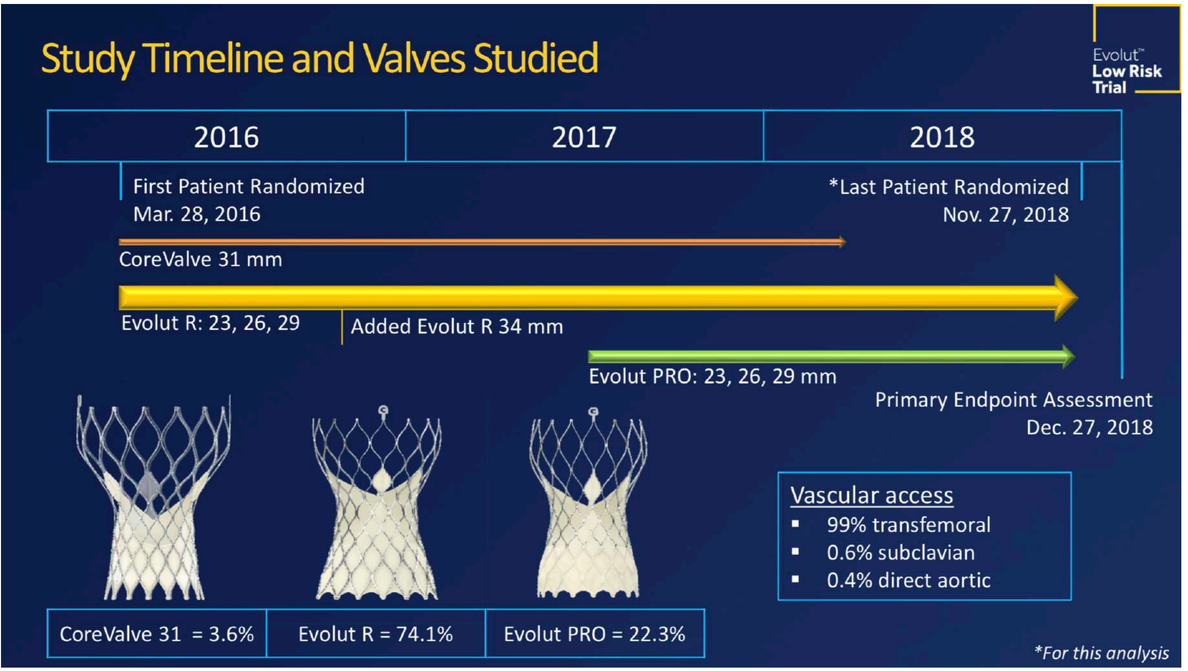


Number at risk:

Surgery	454	387	379	360	348
TAVR	496	465	454	441	427

TCT 2019

Evolut LR



Patients with severe AS and low surgical risk → TAVR with self-expanding valve vs. surgery → Clinical outcomes

1,468 patients with severe aortic stenosis with suitable anatomy for TAVR or surgery and no more than 3% risk of death by 30 days with surgery were randomized to:

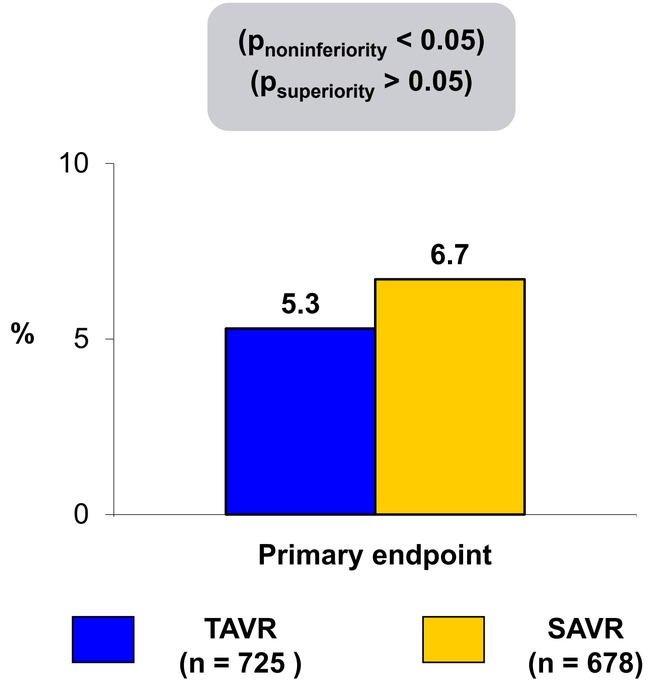
TAVR with self-expanding valve **(n=734)**

Surgery **(n=734)**

Evolut Low Risk

#ACC19

Trial Description: Patients with severe aortic stenosis with low STS PROM score (<3%) were randomized in a 1:1 fashion to either TAVR with CoreValve Evolut or SAVR. They were followed for 24 months.



RESULTS

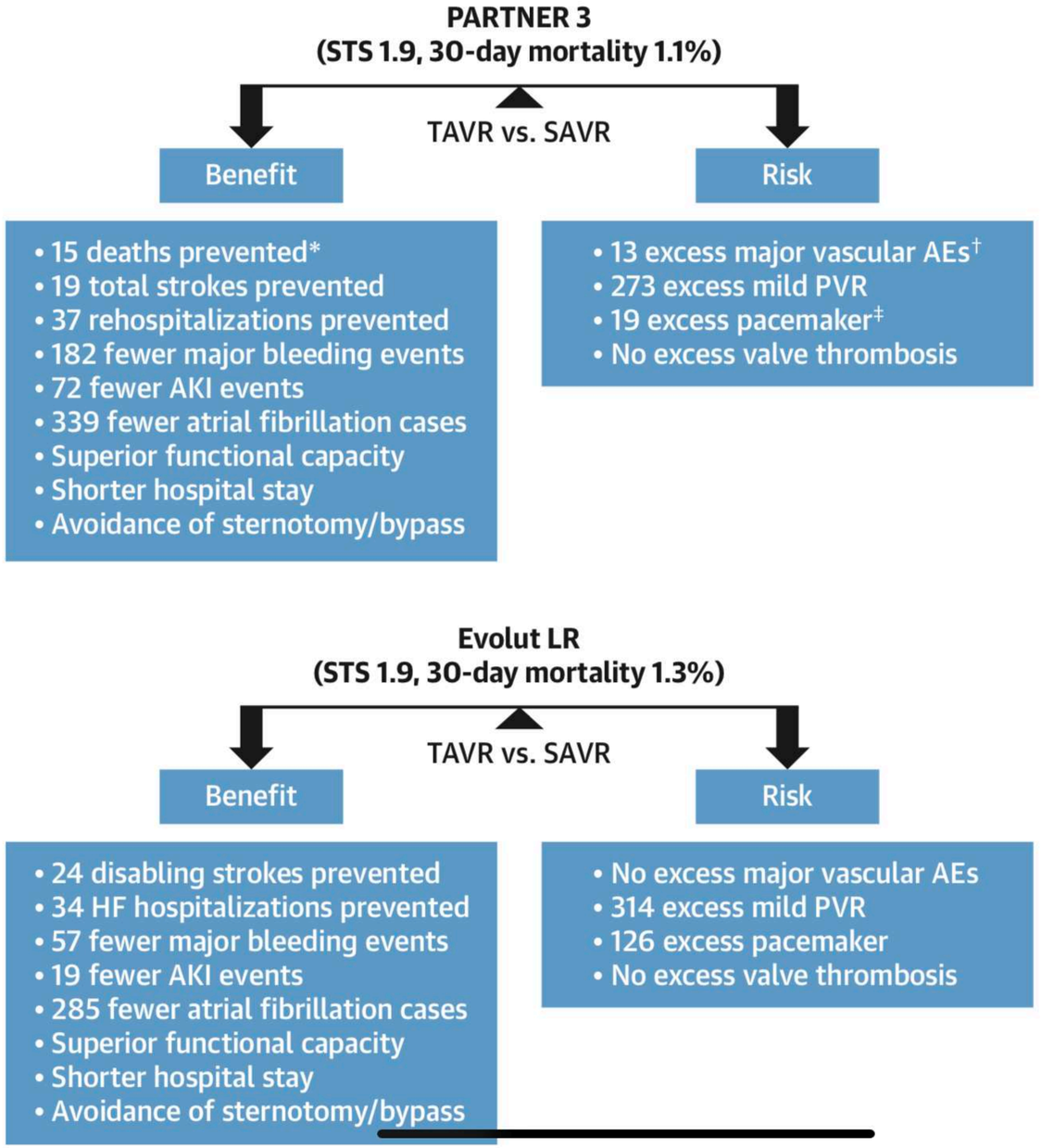
- Primary endpoint: All-cause mortality/disabling stroke for TAVR vs. SAVR at 24 months: 5.3% vs. 6.7%, $p < 0.05$ for noninferiority, $p > 0.05$ for superiority
- Disabling stroke at 2 years: 1.1% vs. 3.5%, $p < 0.05$; mortality: both 4.5%, $p > 0.05$
- New permanent pacemaker at 30 days: 17.4% vs. 6.1%, $p < 0.05$; moderate-severe paravalvular leak (PVL): 3.5% vs. 0.5%, $p < 0.05$; mean aortic gradient at 1 year: 8.6 vs. 11.2 mm Hg, $p < 0.05$, mean EOA at 1 year: 2.3 vs. 2.0, $p < 0.05$

CONCLUSIONS

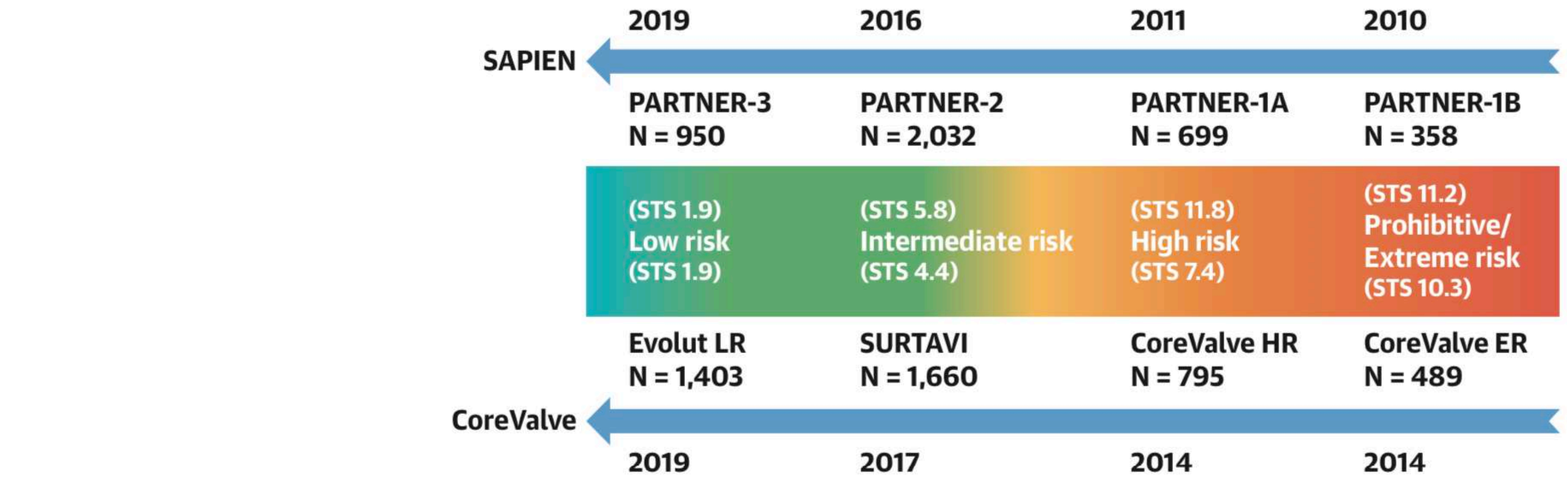
- TAVR with the self-expanding CoreValve Evolut valve was noninferior to SAVR for treatment of severe symptomatic aortic stenosis in low-risk patients
- Strokes, atrial fibrillation, and severe bleeding were higher with SAVR; need for permanent pacemaker and moderate-severe PVL was higher with TAVR
- Landmark trial; longer-term results are awaited

Popma JJ, et al. N Engl J Med 2019;Mar 17:[Epub]

FIGURE 1 Benefit/Risk Balance in the Pivotal Trials for Low-Risk Patients With Severe Symptomatic Aortic Stenosis, PARTNER 3 and Evolut LR



CENTRAL ILLUSTRATION Evolution of TAVR Over the Last Decade



U.S. Food and Drug Administration approval				
- *SAPIEN*	8/2019	8/2016	10/2012	11/2011
- *CoreValve*	8/2019	7/2017	6/2014	1/2014
Center for Medicare and Medicaid Services National Coverage Determination (Coverage with Evidence Development)	6/2019	5/2012	5/2012	5/2012
2017 ACC/AHA guideline recommendations	No	Class IIa, Level of Evidence: B	Class I, Level of Evidence: A	Class I, Level of Evidence: A

Kaul, S. J Am Coll Cardiol. 2020;76(8):985-91.

The pivotal trial for each risk category is shown for the balloon-expandable SAPIEN and self-expanding CoreValve and Evolut bioprostheses along with the current status of FDA approval (including date of approval), CMS National Coverage Determination through CED (including the date of approval), and the latest ACC/AHA guideline recommendations issued in 2017 that preceded the publication of the pivotal trials in low-risk patients with severe aortic stenosis. Notably, the CMS National Coverage Determination does not specify which surgical risks are to be covered but refers to "the treatment of symptomatic aortic valve stenosis when furnished according to the United States FDA approved indication" (24), allowing for immediate coverage of low-risk patients following FDA approval in August 2019. Not shown is Boston Scientific LOTUS Edge Valve System that was approved by the FDA for high-risk patients and above in April 2018. A total of 8,386 patients have been evaluated in 8 pivotal trials. CMS = Center for Medicare and Medicaid Services; FDA = U.S. Food and Drug Administration.

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ACC CLINICAL DOCUMENT

2017 ACC Expert Consensus Decision Pathway for Transcatheter Aortic Valve Replacement in the Management of Adults With Aortic Stenosis

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents

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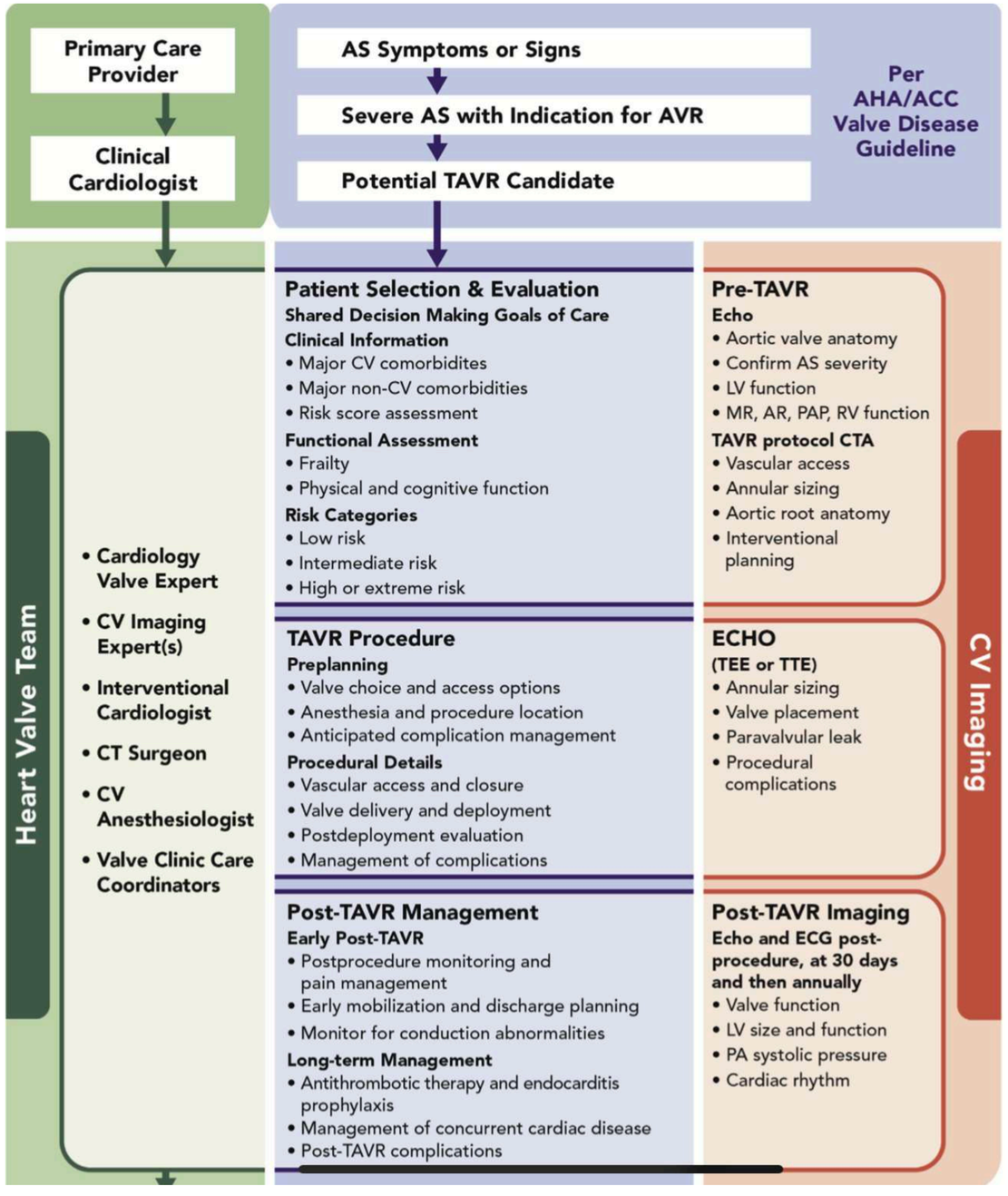
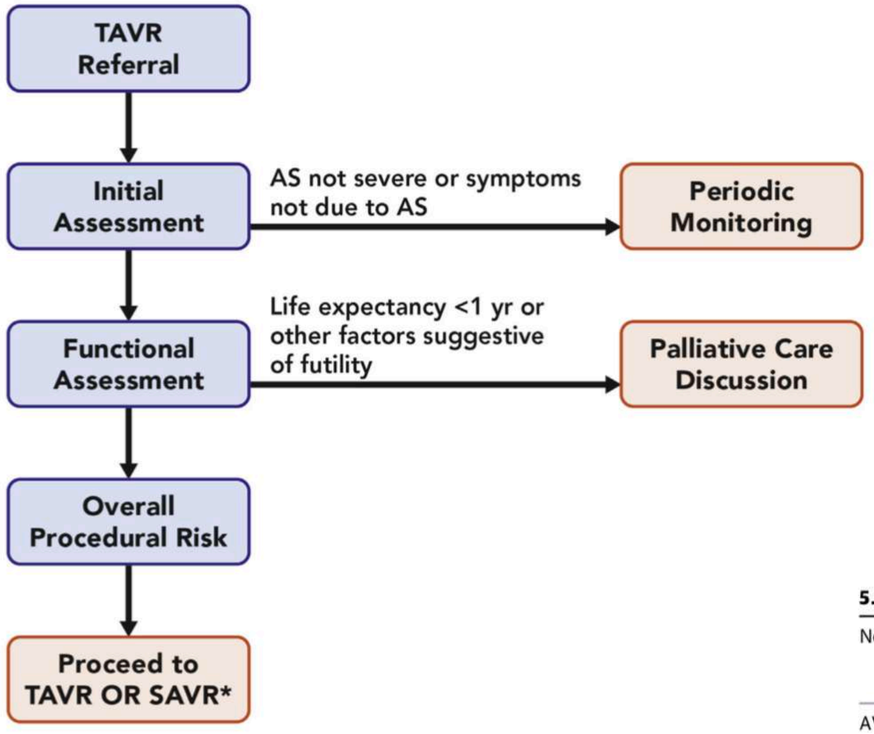


Severe Aortic Stenosis

The valve, the patient, the procedure

FIGURE 2 Pre-TAVR Considerations by the Heart Valve Team



Abbreviations:
AS = aortic stenosis, AVR = aortic valve replacement, TAVR = transcatheter aortic valve replacement

*per current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease

5.1.4 Overall Procedural Risk

Risk categories	☐ Low risk	☐ STS-PROM <4% and ☐ No frailty and ☐ No comorbidity and ☐ No procedure specific impediments
	☐ Intermediate risk	☐ STS-PROM 4%-8% or ☐ Mild frailty or ☐ 1 major organ system compromise not to be improved postoperatively or ☐ A possible procedure-specific impediment
	☐ High risk	☐ STS-PROM >8% or ☐ Moderate-severe frailty or ☐ >2 major organ system compromises not to be improved postoperatively or ☐ A possible procedure-specific impediment
	☐ Prohibitive risk	☐ PROMM >50% at 1 year or ☐ ≥3 major organ system compromises not to be improved postoperatively or ☐ Severe frailty ☐ Severe procedure-specific impediments

5.1.5 Integrated Benefit-Risk of TAVR and Shared Decision-Making

No current indication for AVR	☐ AS not severe or ☐ No AS symptoms or other indication for AVR	☐ Periodic monitoring of AS severity and symptoms ☐ Re-evaluate when AS severe or symptoms occur
AVR indicated but SAVR preferred over TAVR	☐ Lower risk for surgical AVR ☐ Mechanical valve preferred ☐ Other surgical considerations	☐ SAVR recommended in lower-risk patients ☐ Valve durability considerations in younger patients ☐ Concurrent surgical procedure needed (e.g., aortic root replacement)
TAVR candidate with expected benefit > risk	☐ Symptom relief or improved survival ☐ Possible complications and expected recovery ☐ Review of goals and expectations	☐ Discussion with patient and family ☐ Proceed with TAVR imaging evaluation and procedure
Severe symptomatic AS but benefit < risk (futility)	☐ Life expectancy <1 year ☐ Chance of survival with benefit at 2 years <25%	☐ Discussion with patient and family ☐ Palliative care inputs ☐ Palliative balloon aortic valvuloplasty in selected patients

TAVR Outcome Trends

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 21, 2020

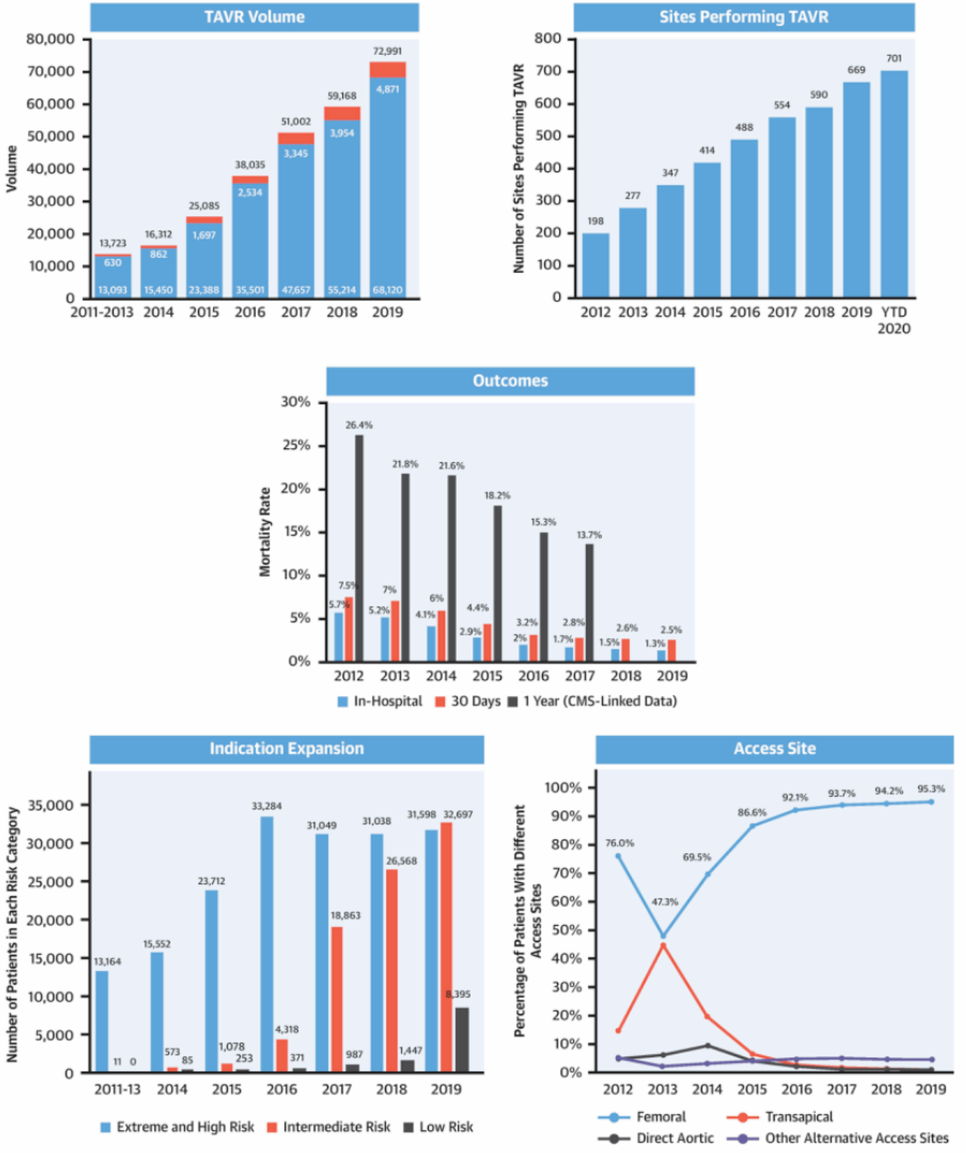
THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

STS-ACC TVT Registry of Transcatheter Aortic Valve Replacement

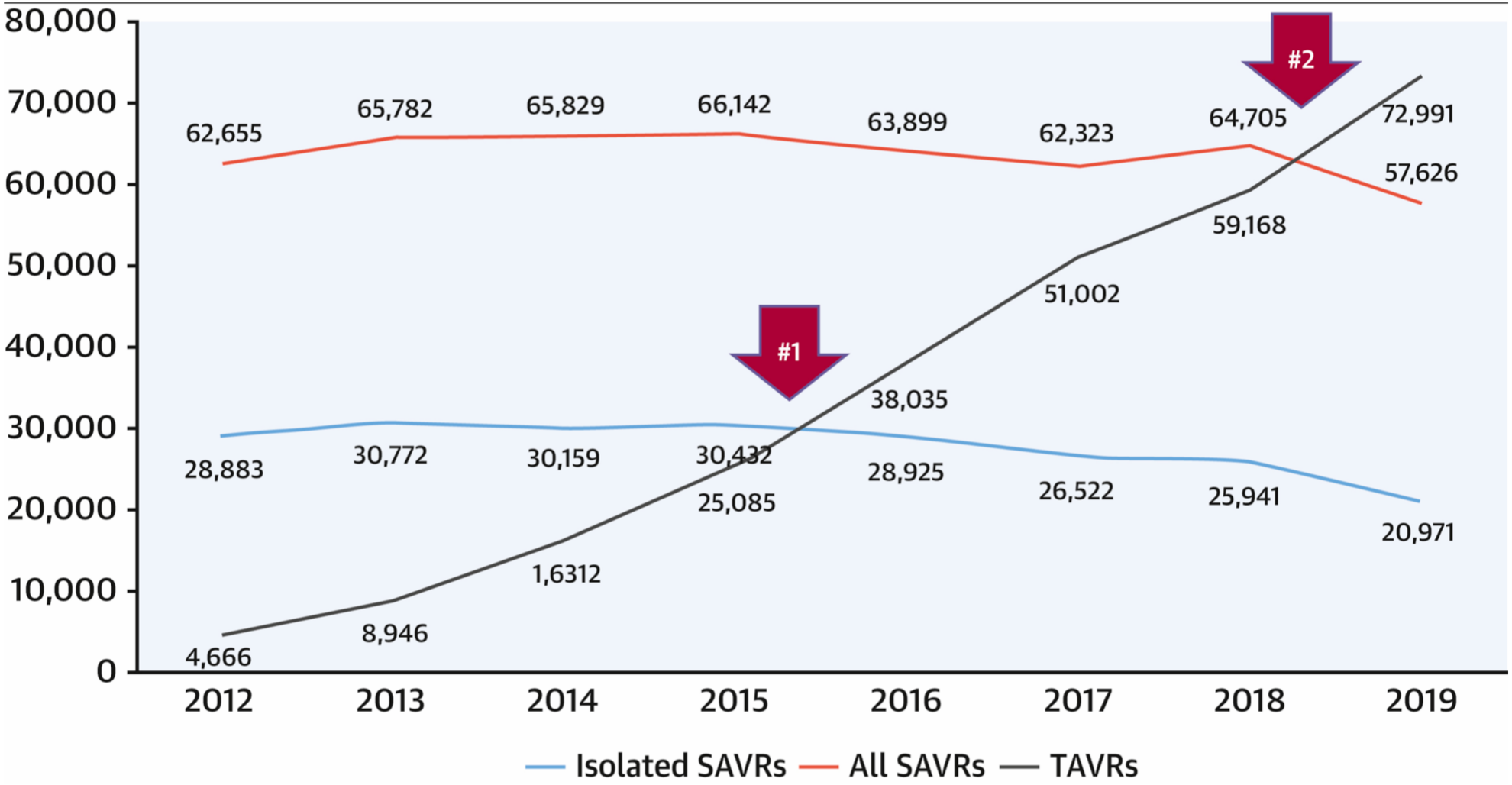
John D. Carroll, MD,[a] Michael J. Mack, MD,[b] Sreekanth Vemulapalli, MD,[c] Howard C. Herrmann, MD,[d] Thomas G. Gleason, MD,[e] George Hanzel, MD,[f] G. Michael Deeb, MD,[g] Vinod H. Thourani, MD,[h] David J. Cohen, MD, MSc,[i] Nimesh Desai, MD, PhD,[j] Ajay J. Kirtane, MD, SM,[k] Susan Fitzgerald, MSN, RN,[l] Joan Michaels, MSN, RN,[l] Carole Krohn, BSN, RN,[m] Frederick A. Masoudi, MD, MSPH,[a] Ralph G. Brindis, MD, MPH,[n] Joseph E. Bavaria, MD[j]

CENTRAL ILLUSTRATION: The State of Transcatheter Aortic Valve Replacement: Trends in the United States From 2011 to 2019



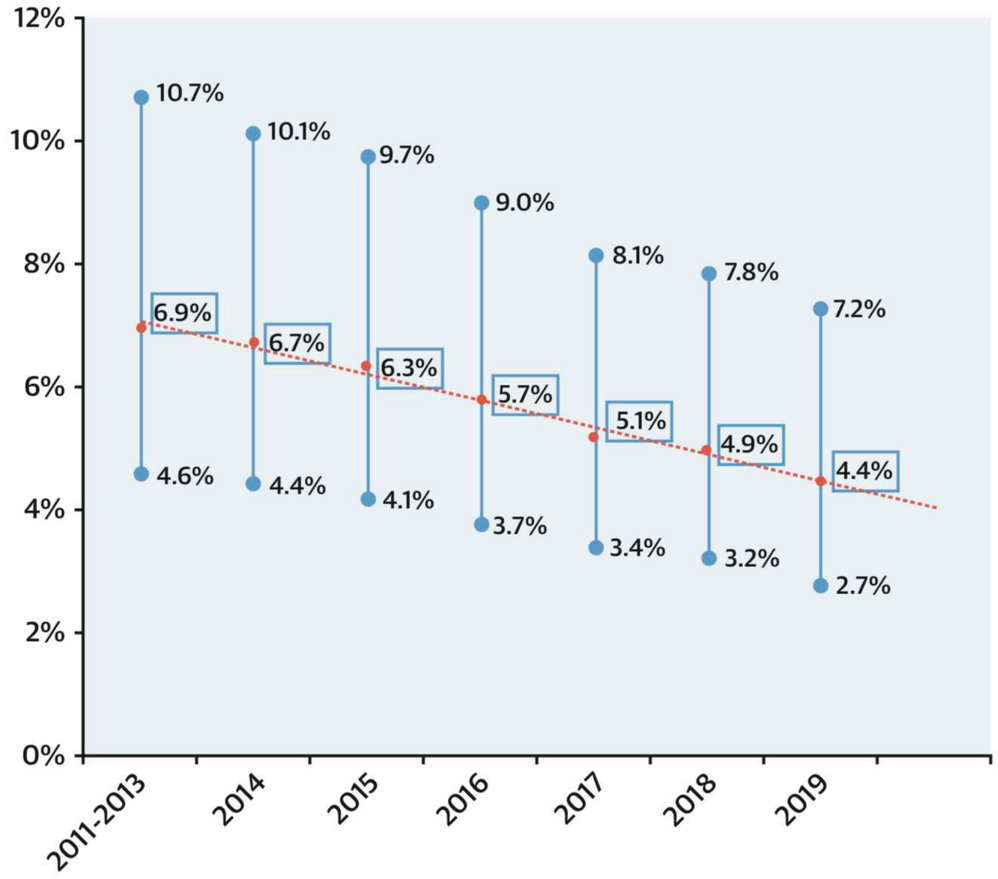
Carroll, J.D. et al. J Am Coll Cardiol. 2020;76(21):2492-516.

AVR Volume


80,000
70,000
60,000
50,000
40,000
30,000
20,000
10,000
0
2012
2013
2014
2015
2016
2017
2018
2019
#1
#2
62,655
65,782
65,829
66,142
63,899
62,323
64,705
57,626
28,883
30,772
30,159
30,432
28,925
26,522
25,941
20,971
4,666
8,946
1,6312
25,085
38,035
51,002
59,168
72,991
Isolated SAVRs
All SAVRs
TAVRs

Patient Risk

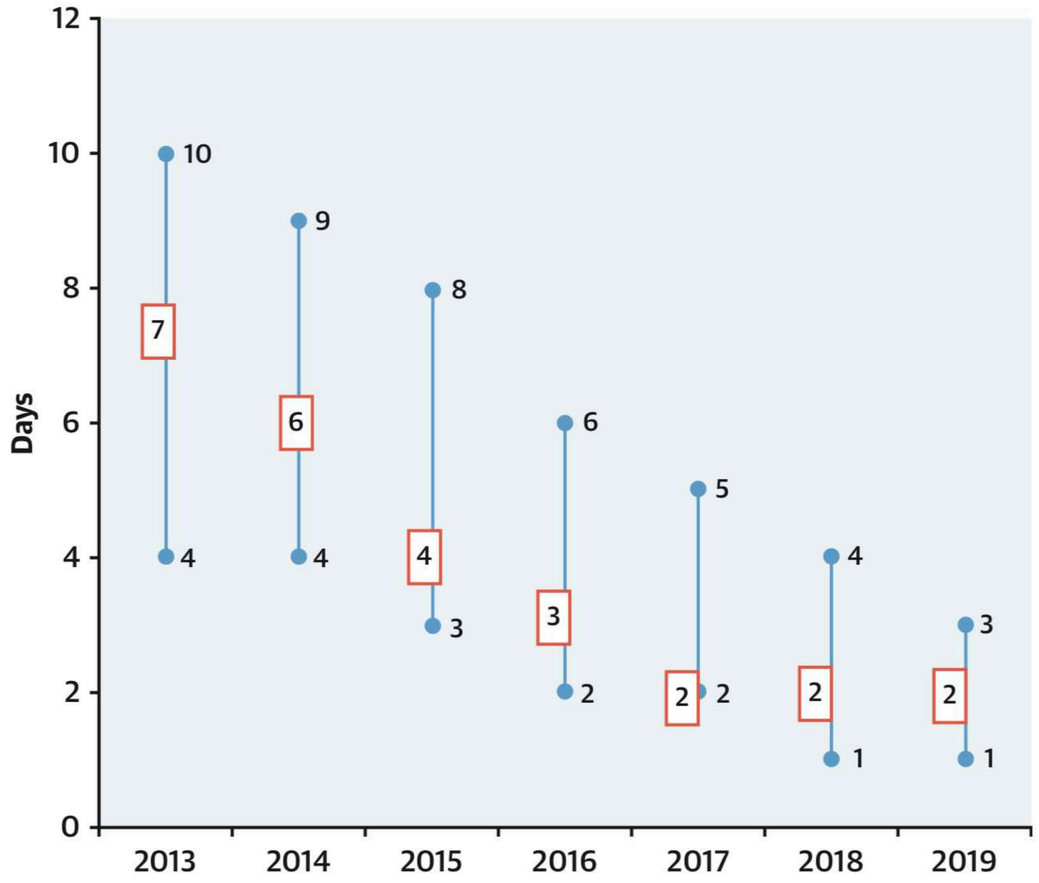
FIGURE 4 Risk Profile of Patients



The median (value in **blue box**), 25th, and 75th quartile values of the Society of Thoracic Surgeons (STS) 30-day predicted risk of mortality (PROM) score for isolated surgical aortic valve replacement for patients undergoing transcatheter aortic valve replacement through 2019. The decline in STS PROM values coincides with expansion of TAVR indication to intermediate- and low-risk patients.

Hospital Stay

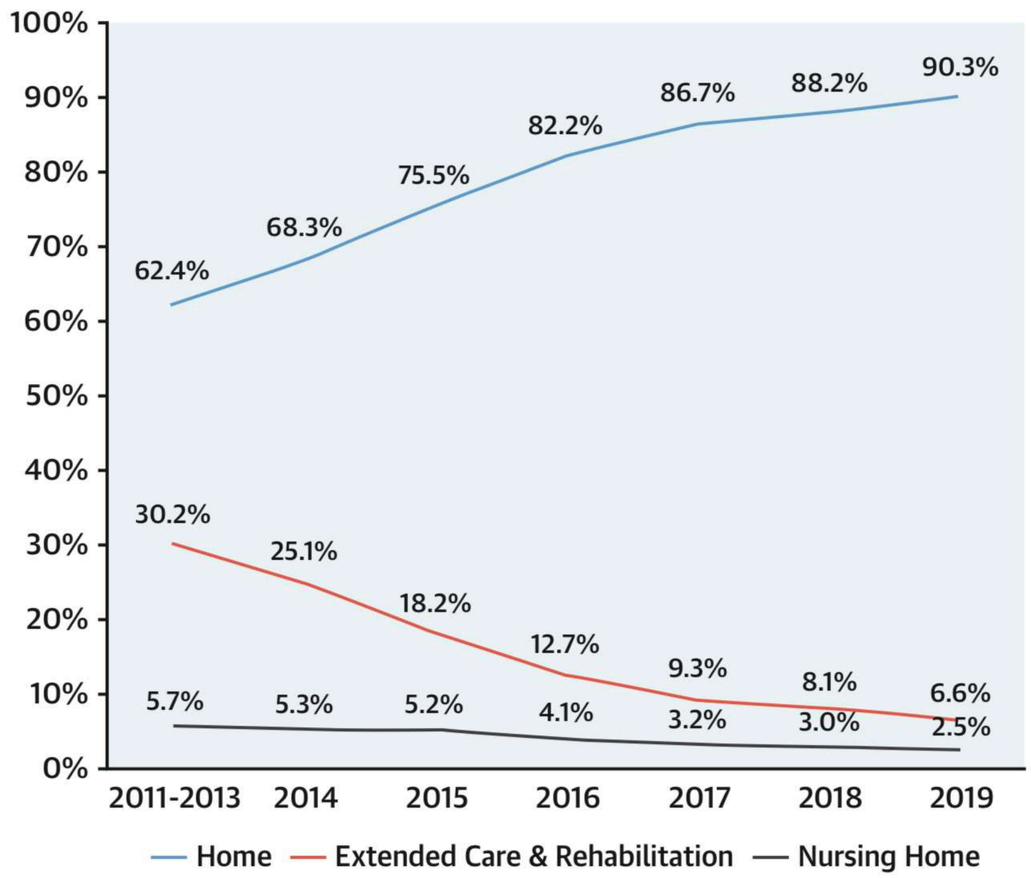
FIGURE 6 Length of Hospital Stay



Median length of stay values in **red boxes** between 2013 and 2019. The **bars** represent the 25th and 75th percentiles.

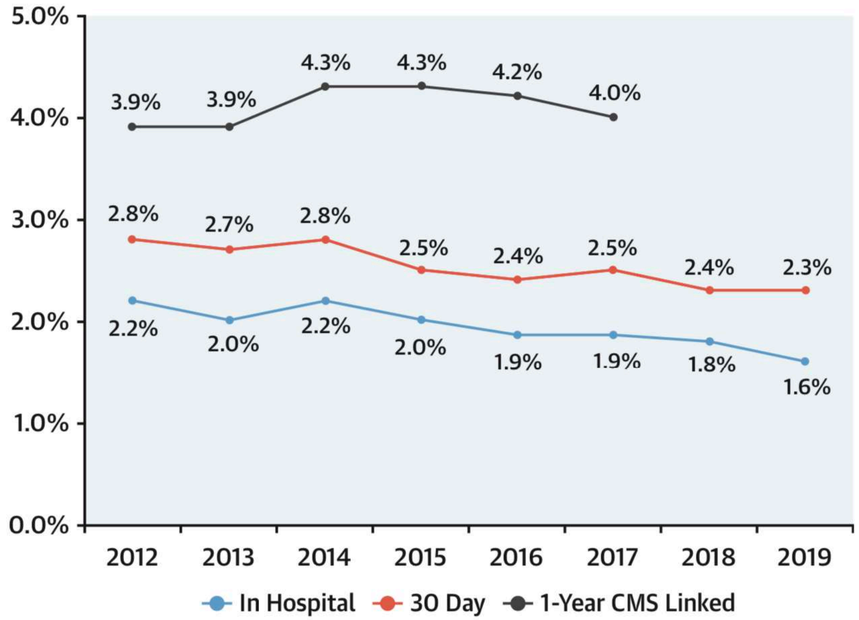
Disposition

FIGURE 7 Discharge Disposition



Proportions of patients discharged directly to home **(blue)**, to a rehabilitation facility **(red)**, and to a nursing home **(gray)** between 2011 and 2019.

FIGURE 8 Stroke Rates After TAVR



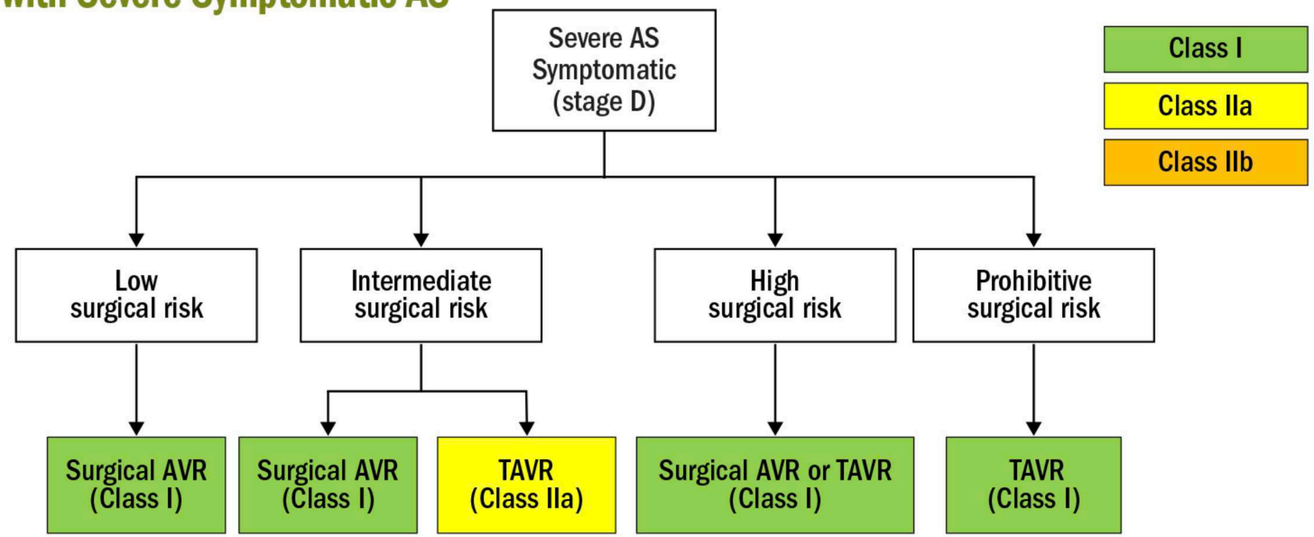
Yearly average rate of stroke after TAVR from 2012 through 2019. In-hospital rates are in **blue**, 30-day in **red**, and 1-year in **gray** (1-year values are from CMS-linked data, unavailable after 2017). There has been a small, slow, downward trend in stroke rates. CMS = Centers for Medicare & Medicaid; TAVR = transcatheter aortic valve replacement.

TAVR for AS

Summary

- Severe aortic stenosis is a condition that carries significant morbidity and mortality, especially if symptomatic
- AS typically affects the elderly population, surgical risk can be high/prohibitive
- TAVR a proven safe alternative to surgery in these patients
- Advances in technology and procedure itself has significantly reduced complications
- TAVR now an alternative to surgery in many patients of all risk categories

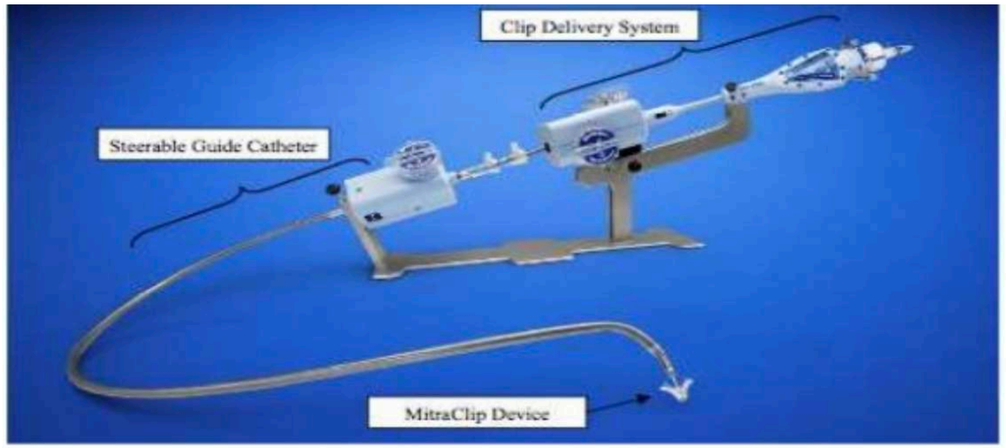
Choice of TAVR Versus Surgical AVR in the Patient with Severe Symptomatic AS



AS = Aortic stenosis; AVR = Aortic Valve Replacement; TAVR = Transcatheter Aortic Valve Replacement

Percutaneous Interventions- Mitral Valve

MitraClip



redit: Abbott

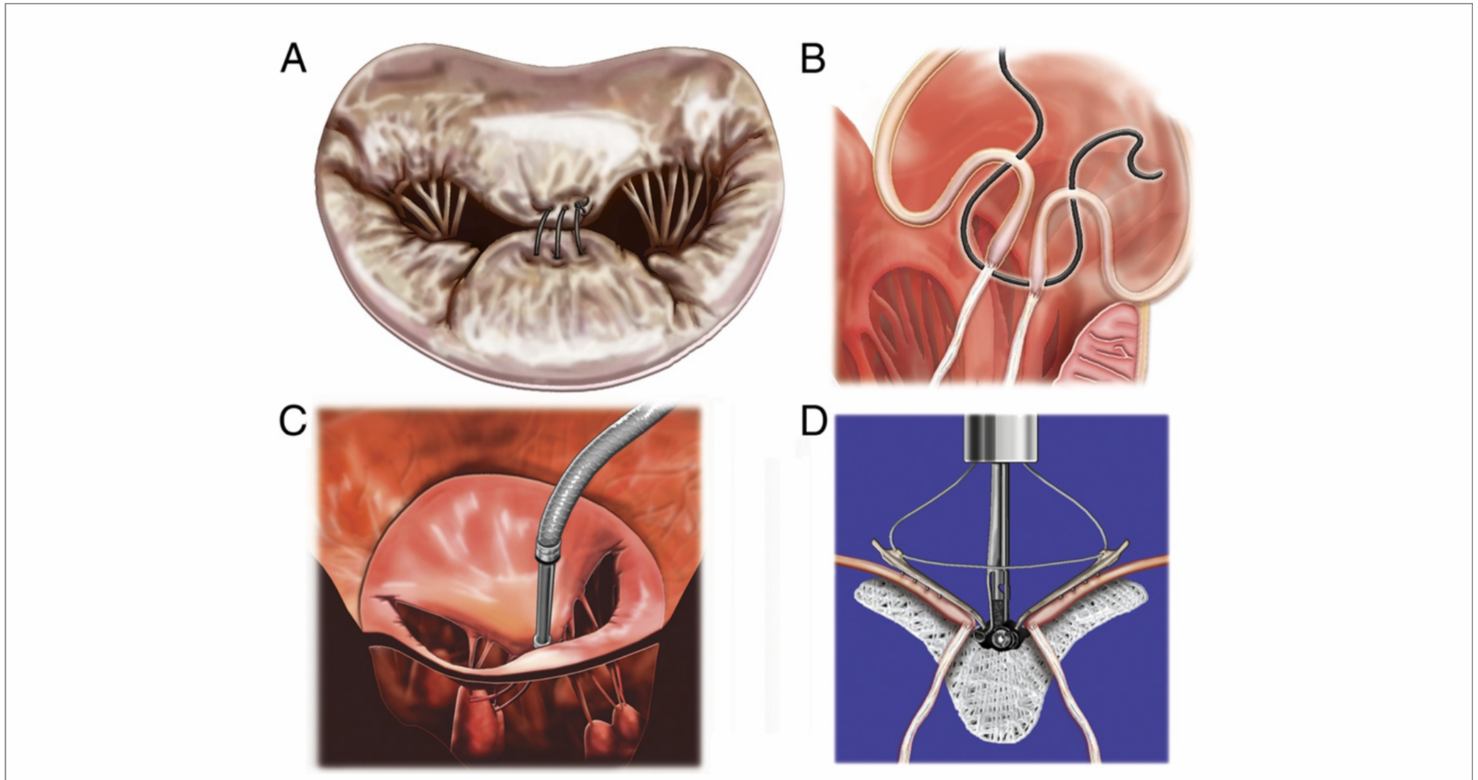


Figure 1 **Surgical Edge-to-Edge Technique Versus MitraClip**

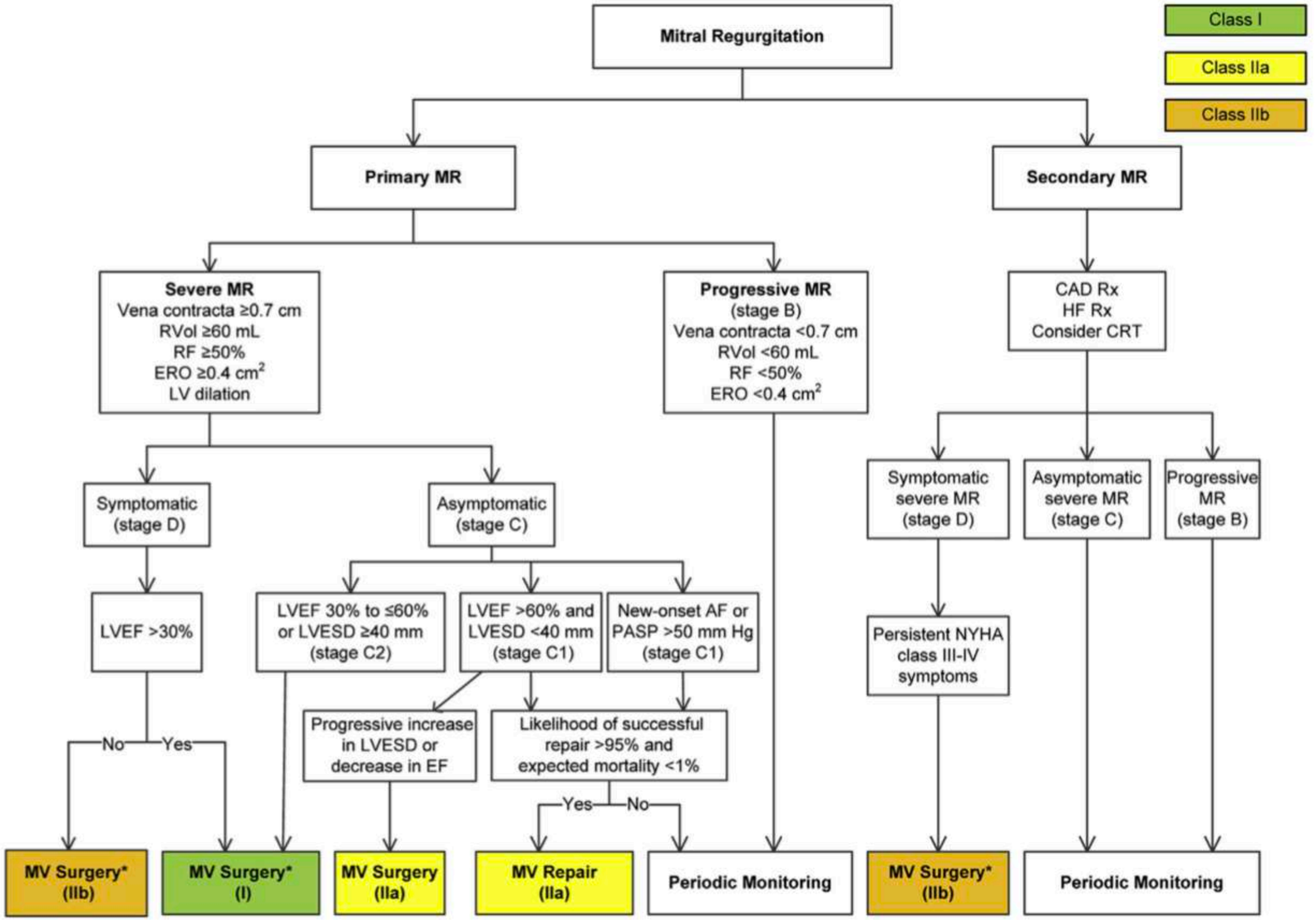
(A) The surgical technique involves a continuous suture of the free edge of the leaflets at the site of the regurgitation. In case the lesion is in the A2-P2 area, a double orifice valve is created. **(B)** The sutures engage the free edge of the facing leaflets, suture bite depth depends on the amount of redundant tissue (larger in case of degenerative disease, and minimal in case of functional mitral regurgitation). **(C)** The MitraClip (Abbott Vascular, Menlo Park, California) is implanted in the A2-P2 region, similarly to the surgical technique. The drawing illustrates the clip partially open, to demonstrate tissue penetration into the clip. Once proper leaflet grasping is confirmed, the clip is closed to enhance coaptation. **(D)** The free edges of the leaflets are engaged between the clip arms and the grippers. The clip is closed with leaflet facing. Compared with surgery where tissue is imbricated into the suture with no evidence of planar surface of coaptation, the MitraClip is designed to induce a linear apposition of leaflets to enhance coaptation. Figure illustration by Craig Skaggs.

Mitral Regurgitation (Chronic)

- Primary (degenerative) Mitral Regurgitation: disease of the mitral valve
  - Myxomatous
  - Rheumatic
- Secondary (functional) Mitral Regurgitation:
  - Ischemic
  - dilated cardiomyopathy
- Symptoms:
  - Dyspnea on exertion
  - Orthopnea/PND
  - Fatigue
  - palpitations (atrial fibrillation)

Mitral Regurgitation

Guidelines



EVEREST II (2011)

Randomized Comparison of Percutaneous Mitral Valve Repair and Surgery for Mitral Regurgitation

Key Inclusion/Exclusion Criteria
EVEREST II RCT

Inclusion

- Candidate for MV Surgery
- Moderate to severe (3+) or severe (4+) MR
  - Symptomatic
    - >25% EF & LVESD ≤55mm
  - Asymptomatic with one or more of the following
    - LVEF 25-60%
    - LVESD ≥40mm
    - Pulmonary hypertension
    - Atrial fibrillation

ACC/AHA Guidelines
JACC 52:e1-e142, 2008

Exclusion

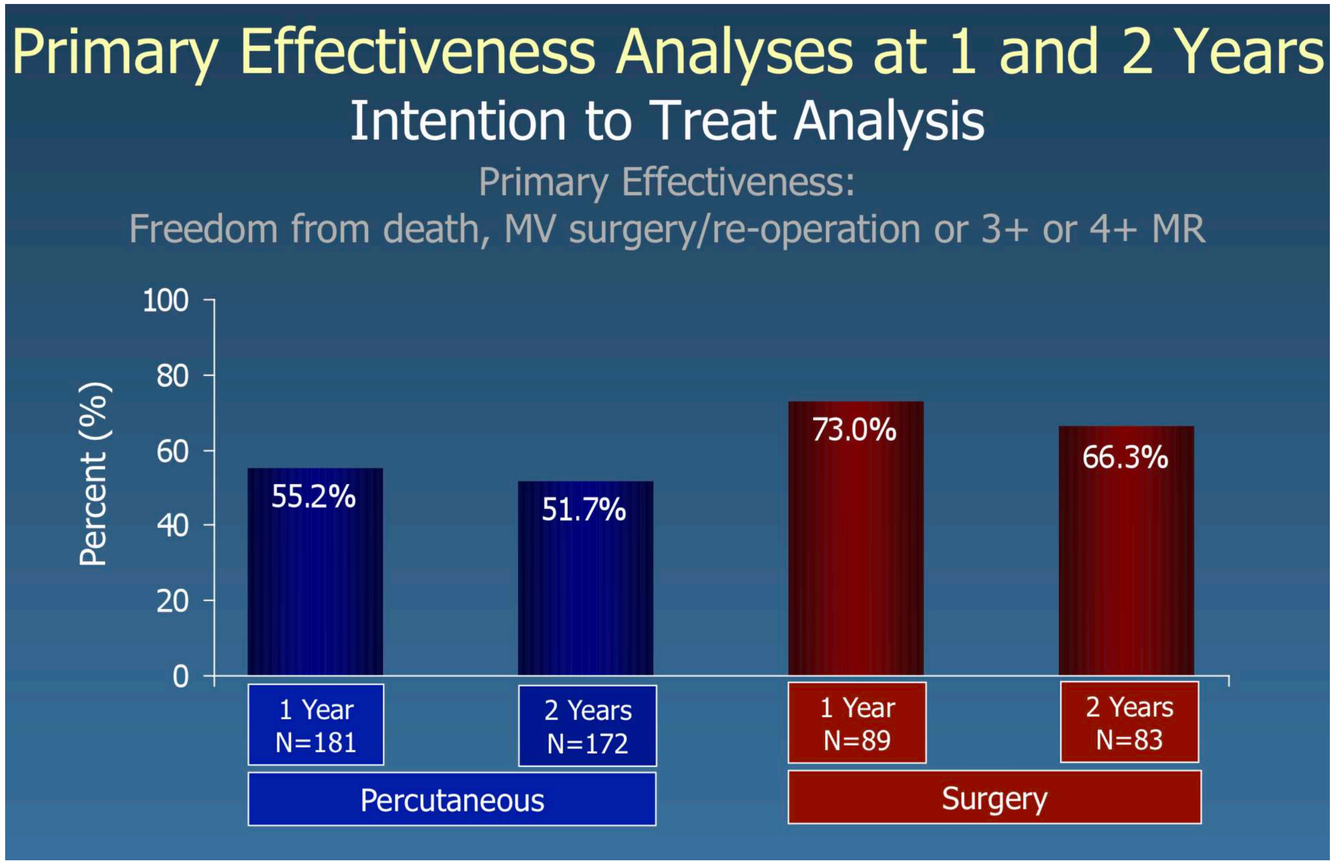
- AMI within 12 weeks
- Need for other cardiac surgery
- Renal insufficiency
  - Creatinine >2.5mg/dl
- Endocarditis
- Rheumatic heart disease
- MV anatomical exclusions
  - Mitral valve area <4.0cm^2
  - Leaflet flail width (≥15mm) and gap (≥10mm)
  - Leaflet tethering/coaptation depth (>11mm) and length (<2mm)

Baseline Demographics & Co-morbidities
Intention to Treat

Patient Demographics	Percutaneous % N=184	Surgery % N=95	P-value
Age (mean)	67 years	66 years	0.32
Male	63	66	0.60
History of CHF	91	78	0.005
Coronary artery disease	47	46	>0.99
Prior myocardial infarction	22	21	>0.99
Previous cardiovascular surgery	22	19	0.54
Atrial fibrillation	34	39	0.42
COPD (with or without home O_2)	15	15	>0.99
Moderate to Severe Renal Failure	3	2	0.72
Diabetes	8	11	0.50

EVEREST II

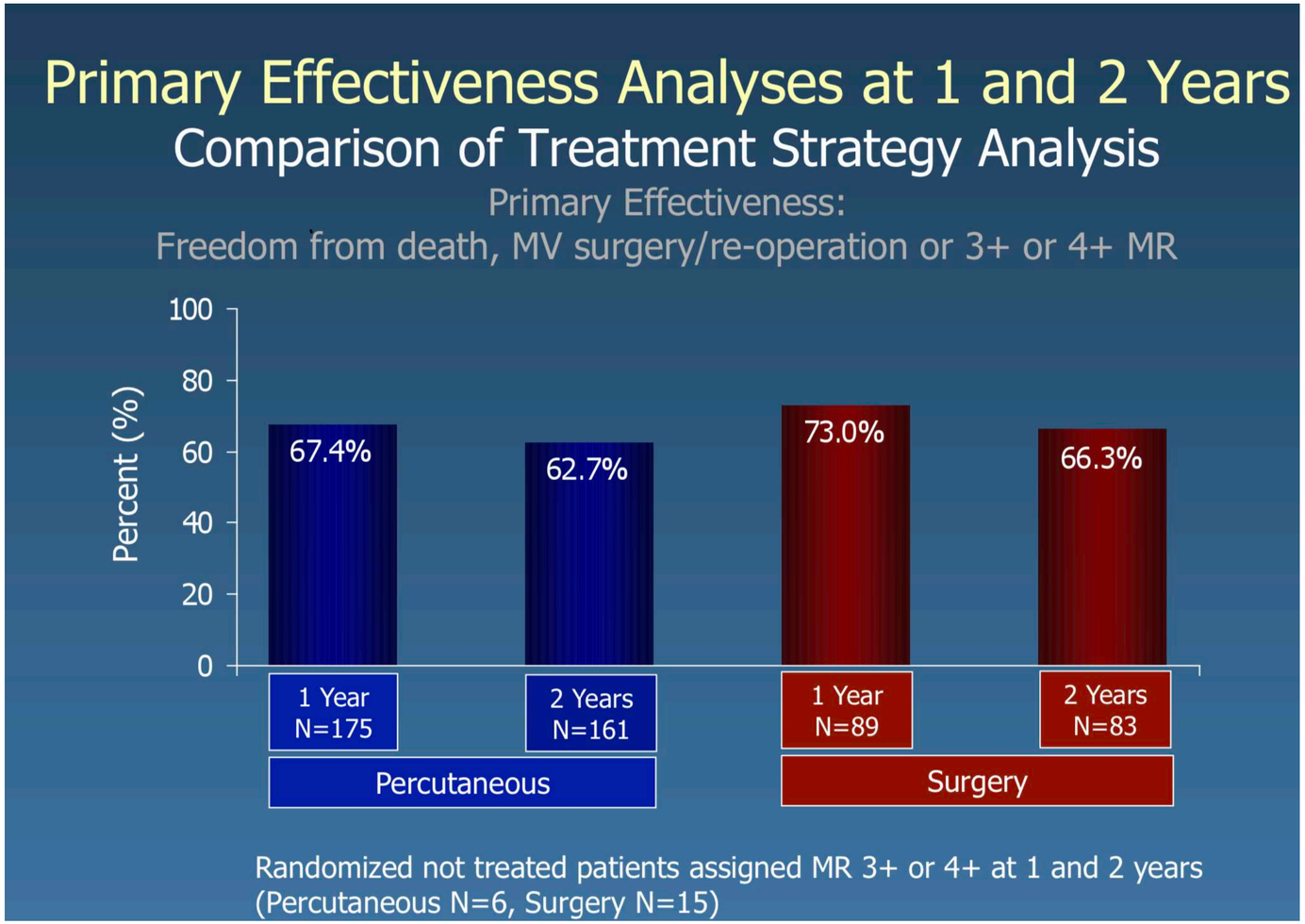
Outcomes (ITT)



Components of Failure	Percutaneous		Surgery		P-value Percutaneous vs Surgery at 2 years
	1 Year N=181	2 Years N=172	1 Year N=89	2 Years N=83	
Death	11 (6.1%)	19 (11.0%)	5 (5.6%)	9 (10.8%)	>0.999
MV Surgery / Re-operation	37 (20.4%)	38 (22.1%)	2 (2.2%)	3 (3.6%)	<0.001
3+ or 4+ MR *	38 (21.0%)	34 (19.8%)	18 (20.2%)	18 (21.7%)	0.84
Freedom from death, MV surgery / re-operation or 3+ or 4+ MR †	100 (55.2%)	89 (51.7%)	65 (73.0%)	55 (66.3%)	<0.001

EVEREST II

Outcomes (Comparison of Treatment)



2. Comparison of Treatment Strategies
   - Mitral valve surgery following unsuccessful in-hospital percutaneous repair not considered an "endpoint" event

MitraClip

Degenerative Mitral Regurgitation

- FDA approval October 2013: *“The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant **symptomatic** mitral regurgitation (MR ≥3+) due to **primary abnormality** of the mitral apparatus **[degenerative MR]** in patients who have been determined to be at **prohibitive risk** for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.*"

MitraClip

Data

- EVEREST II
  - Not as effective as surgery in reducing MR
  - Safer than surgery
  - Despite residual MR, reductions in LV chamber volumes and clinical outcomes assessed by QOL questionnaires similar. Similar findings in 4-5 yr f/u.
- Until 2019, registry data for MitraClip therapy for functional/secondary MR in high surgical risk patients (STS 13.2).

COAPT TRIAL

The COAPT Trial

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in 614 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT

Follow-up at 30d, 6mo, 1y, 18mo, 2y, 3y, 4y, 5y

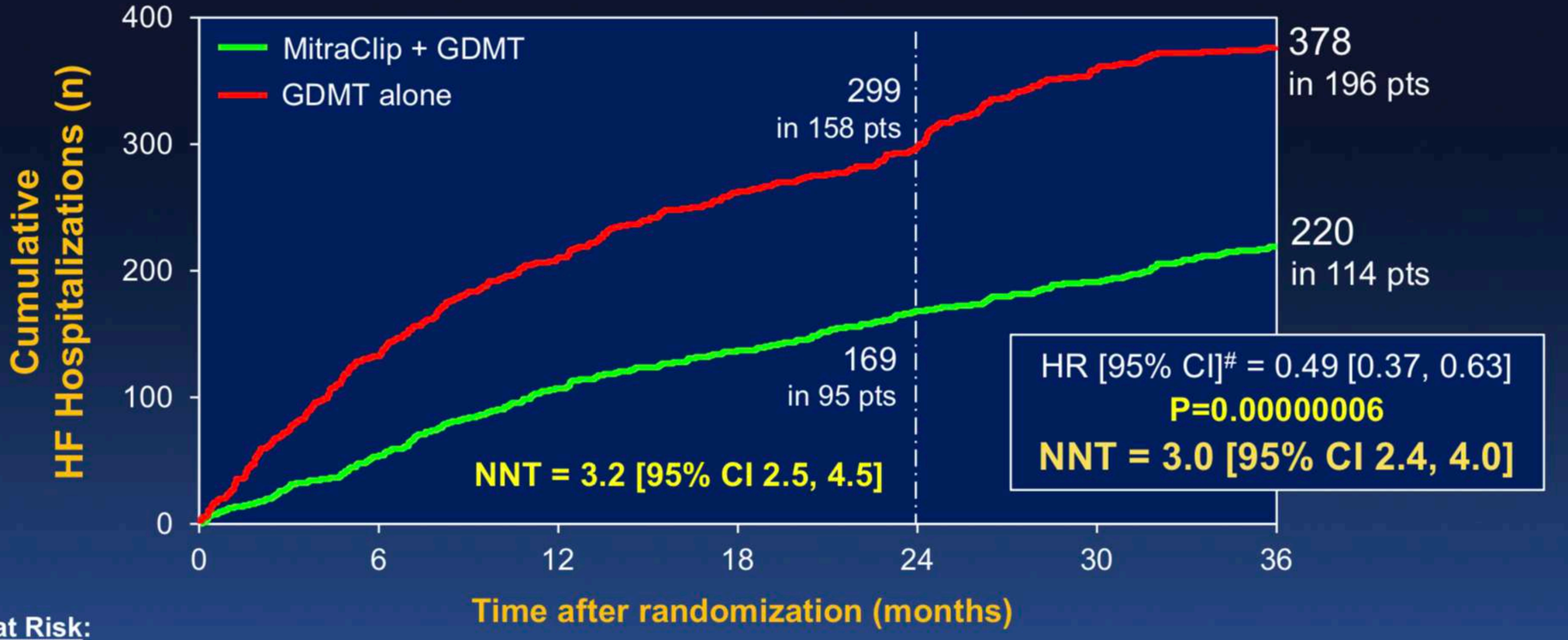
*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

COAPT TRIAL

Primary Effectiveness Endpoint

All Hospitalizations for HF within 36 months

All patients, ITT, including crossovers



# at Risk:							
MitraClip + GDMT	302	269	238	219	189	128	93
GDMT alone	312	272	223	185	144	89	68

tct2019

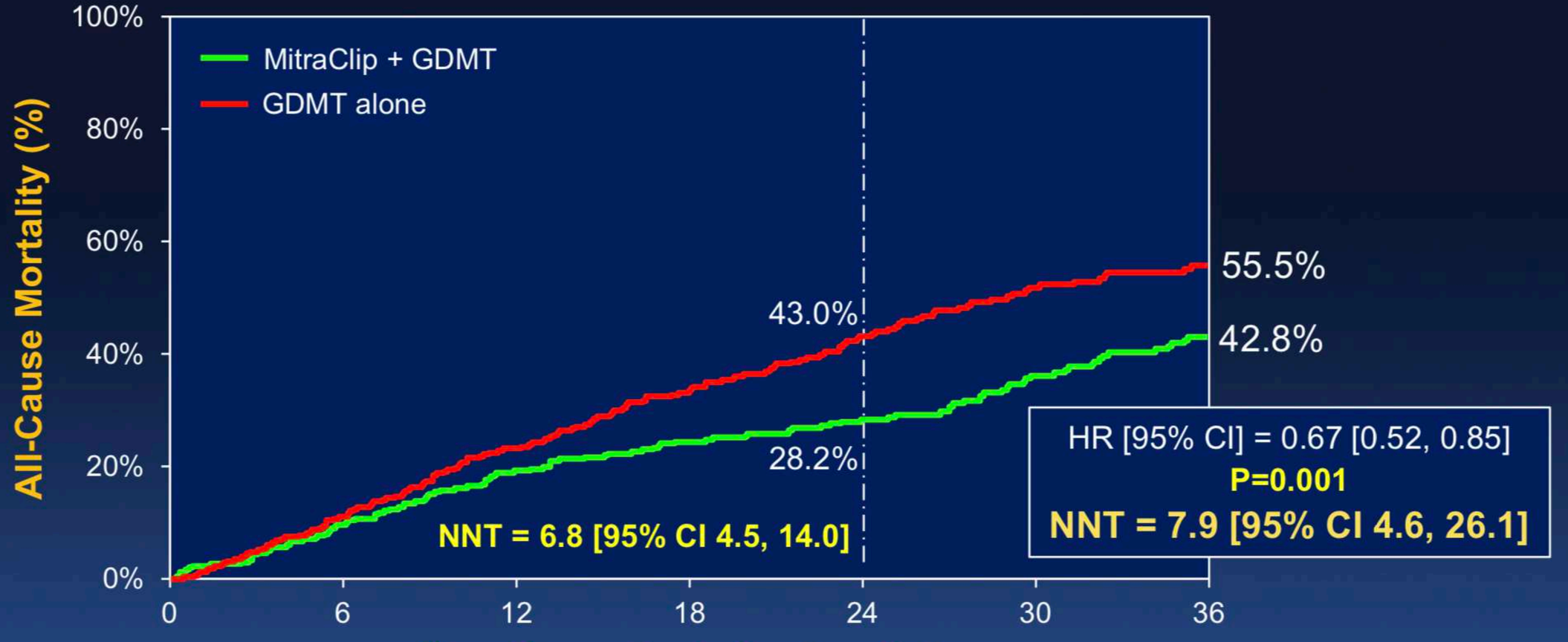
#Joint frailty model

Cardiovascular® Research Foundation

COAPT TRIAL

All-Cause Mortality

All patients, ITT, including crossovers



# at Risk:							
MitraClip + GDMT	302	269	238	219	189	128	93
GDMT alone	312	272	223	186	145	91	70

tct2019

Event rates are Kaplan-Meier time-to-first event estimates

Cardiovascular® Research Foundation

COAPT TRIAL

Primary Safety Endpoint (MitraClip arm)

Freedom from Device-related Complications

n=293 pts with MitraClip procedure attempted

	0-30 Days	0-12 Months	0-24 Months	0-36 Months
All	**1.4% (4)**	**3.3% (9)**	**5.2% (13)**	**8.7% (18)**
- Device-related complications	**1.4% (4)**	**1.4% (4)**	**1.4% (4)**	**1.4% (4)**
• Single leaflet device attachment	0.7% (2)	0.7% (2)	0.7% (2)	0.7% (2)
• Device embolization	0.3% (1)	0.3% (1)	0.3% (1)	0.3% (1)
• Endocarditis requiring surgery	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
• Mitral stenosis requiring surgery	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
• Any device-related complication requiring non-elective CV surgery	0.3% (1)	0.3% (1)	0.3% (1)	0.3% (1)
- Progressive heart failure	**0.0% (0)**	**2.0% (5)**	**3.8% (9)**	**7.4% (14)**
• Left ventricular assist device implant	0.0% (0)	1.2% (3)	2.6% (6)	5.4% (10)
• Heart transplant	0.0% (0)	0.8% (2)	1.3% (3)	2.6% (5)

Event rates are Kaplan-Meier time-to-first event estimates;
Includes only first occurrence of each event

MitraClip

HF and Secondary MR

- FDA March 14, 2019: *Expanded approval for treatment of patients with* ***structurally normal mitral valves*** *who develop* ***heart failure*** *and* ***moderate to severe MR*** *despite receiving optimal treatment including HF medications or, for certain patients, cardiac resynchronization therapy.*

MitraClip

Summary

- A percutaneous therapy not strongly reflected in our Valve Guidelines as of yet
- As of 2013 FDA approved, and a reasonable option for patients with symptomatic severe (3+/4+) MR in high surgical risk patients versus surgery with comparable outcomes (**death, freedom from re-operation, freedom from 3-4 MR**, HF/QOL scores, LV volume improvement)
- Must be anatomically feasible: central MR preferred, flail gap <15mm, little calcium
- As of 2019 FDA approved for patients with Heart Failure and moderate to severe MR who are still symptomatic on GDMT with **reduced mortality** and **HF hospitalizations**

Thank You!