Is TAVR Ready for All Patients with Aortic Valve Disease?

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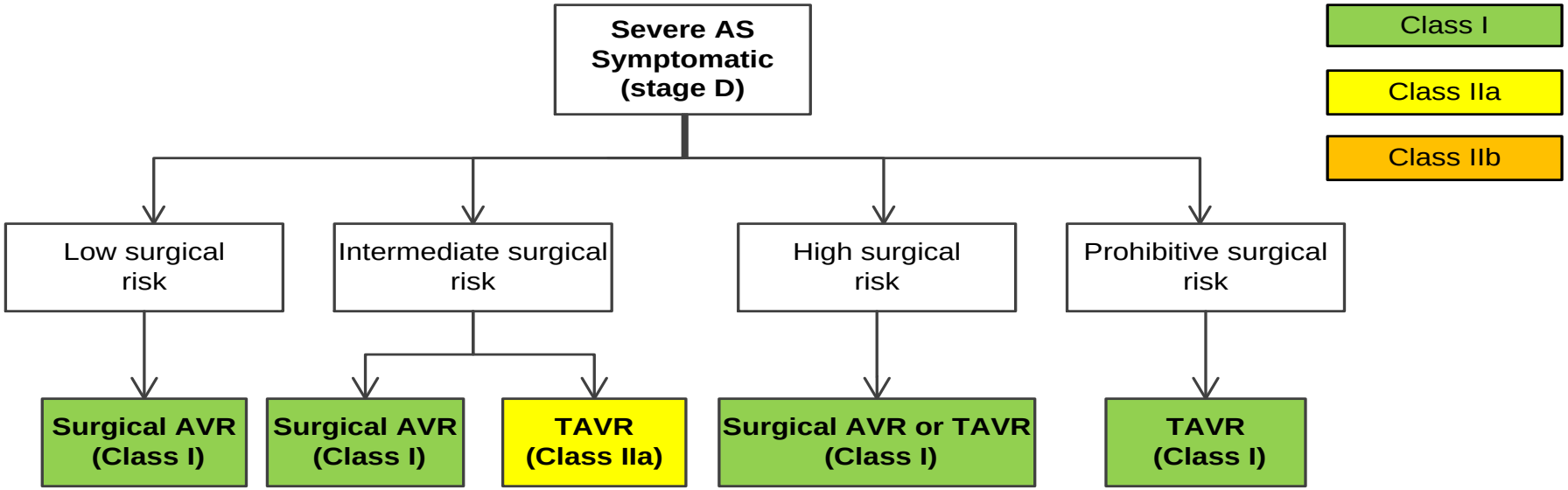
COI Disclosures

- **Modest Consulting fees: Janssen, Medtronic**

Objectives

- Discuss current indications for TAVR – Those with proven benefit
- Highlight New Randomized Trial Data
- Identify Future Studies/Indications + Next Frontiers

Choice of TAVR Versus Surgical AVR in the Patient With Severe Symptomatic AS (Modified)

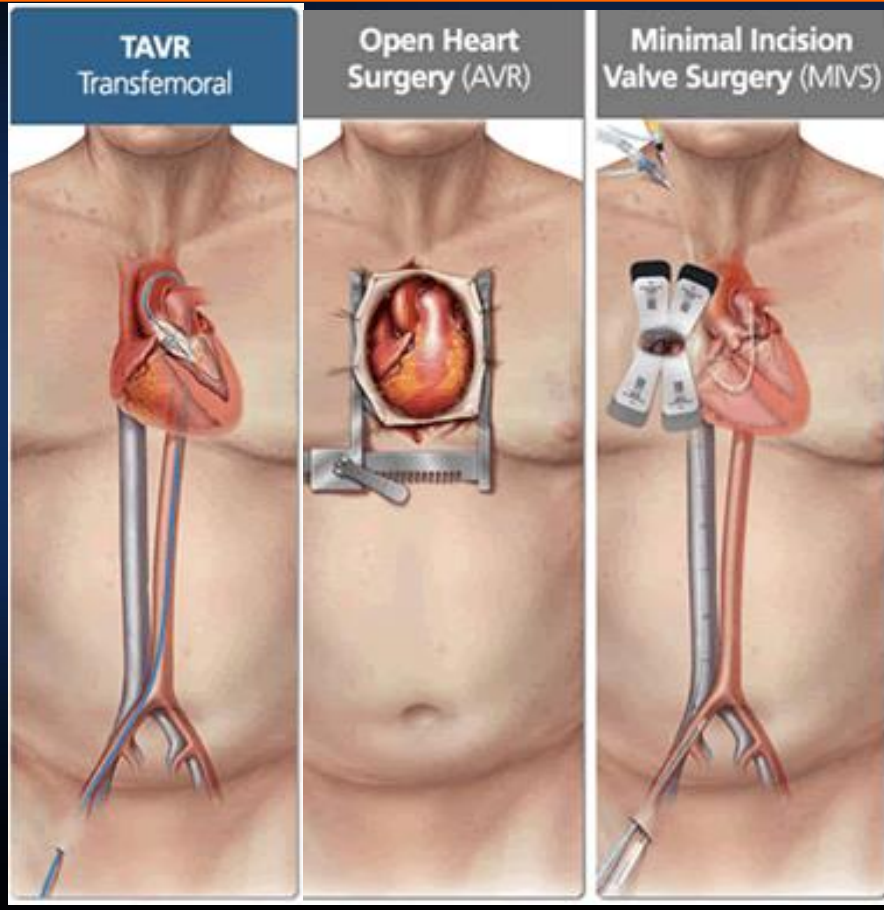


TAVR is Beneficial to Many Patients

- TAVR reduces mortality in patients at extreme risk or unable to have conventional surgery
- TAVR is noninferior to surgery in patients at high risk
- TAVR is noninferior and in some cases superior to surgery in intermediate risk patients

Potential Advantages of TAVR

- Less Invasive, lower risk of bleeding
- Shorter Length of Stay and Recovery
- Similar rates of mortality and stroke (based on High/Intermediate risk trials)



Concerns about TAVR in Low Risk Pts

- Paravalvular leak and pacemaker risk
- Valve Performance and Longevity
- Anatomic Considerations (i.e. Bicuspid AoV etc.)
- Young pts likely to need multiple AVRs

Device Evolution

- New generation devices are safer and more effective
- Less pacemaker and paravalvular leak
- Smaller profile and sheath size

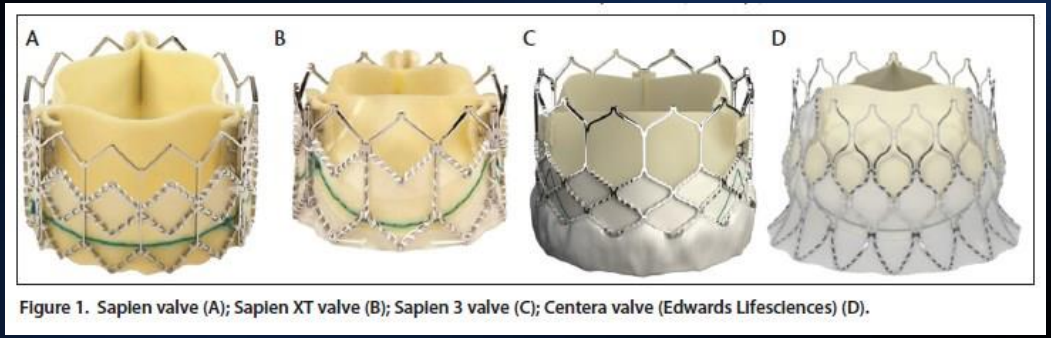
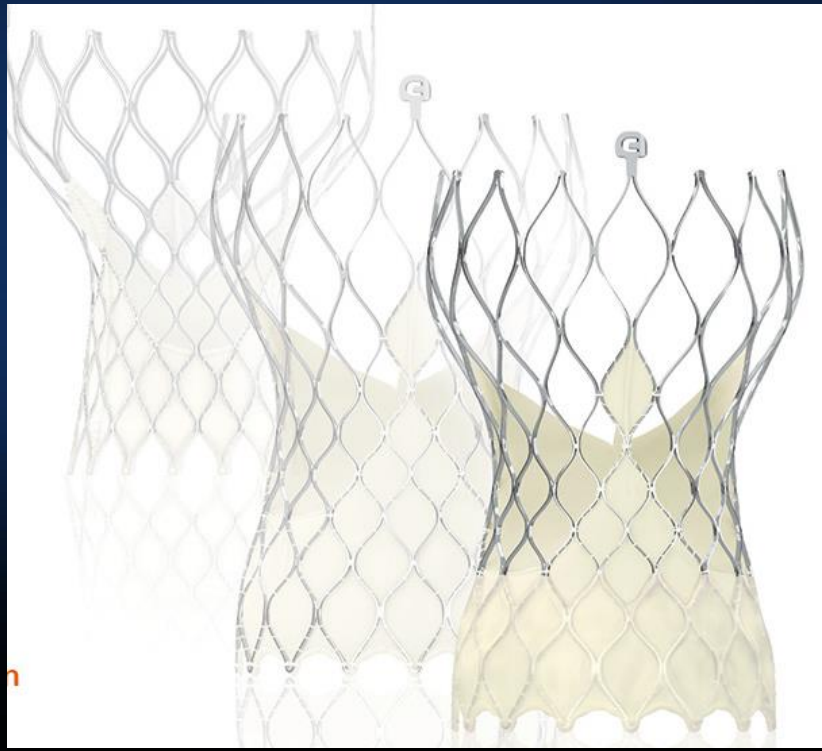
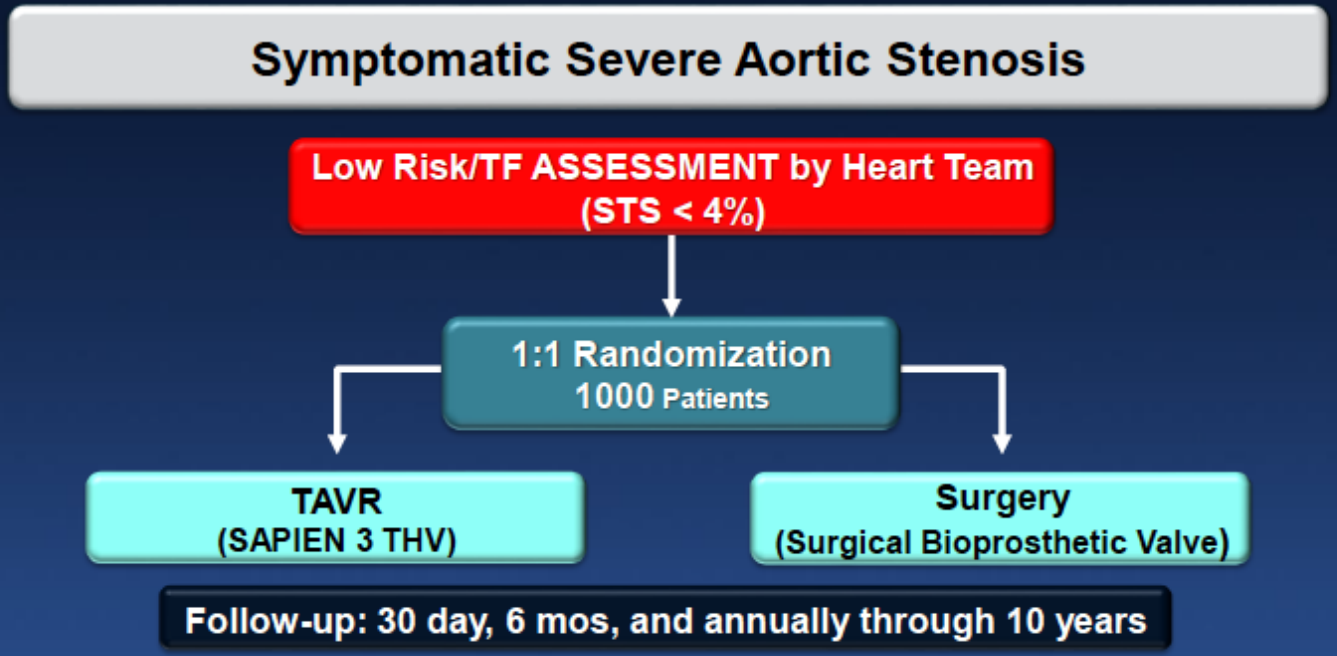


Figure 1. Sapien valve (A); Sapien XT valve (B); Sapien 3 valve (C); Centera valve (Edwards Lifesciences) (D).



THE PARTNER 3 TRIAL

PARTNER 3 Study Design



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

Baseline Patient Characteristics

% or mean ± SD

Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)	Other Co-Morbidities	TAVR (N=496)	Surgery (N=454)
Age (years)	73.3 ± 5.8	73.6 ± 6.1	Diabetes	31.3%	30.2%
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI – kg/m^2	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	1.9 ± 0.7	1.9 ± 0.6	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	27.7%	28.0%	Atrial Fibrillation (h/o)	15.7%	18.8%
Prior CABG	3.0%	1.8%	Permanent Pacemaker	2.4%	2.9%
Prior CVA	3.4%	5.1%	Left Bundle Branch Block	3.0%	3.3%
Peripheral Vascular Disease	6.9%	7.3%	Right Bundle Branch Block	10.3%	13.7%

*p = 0.01

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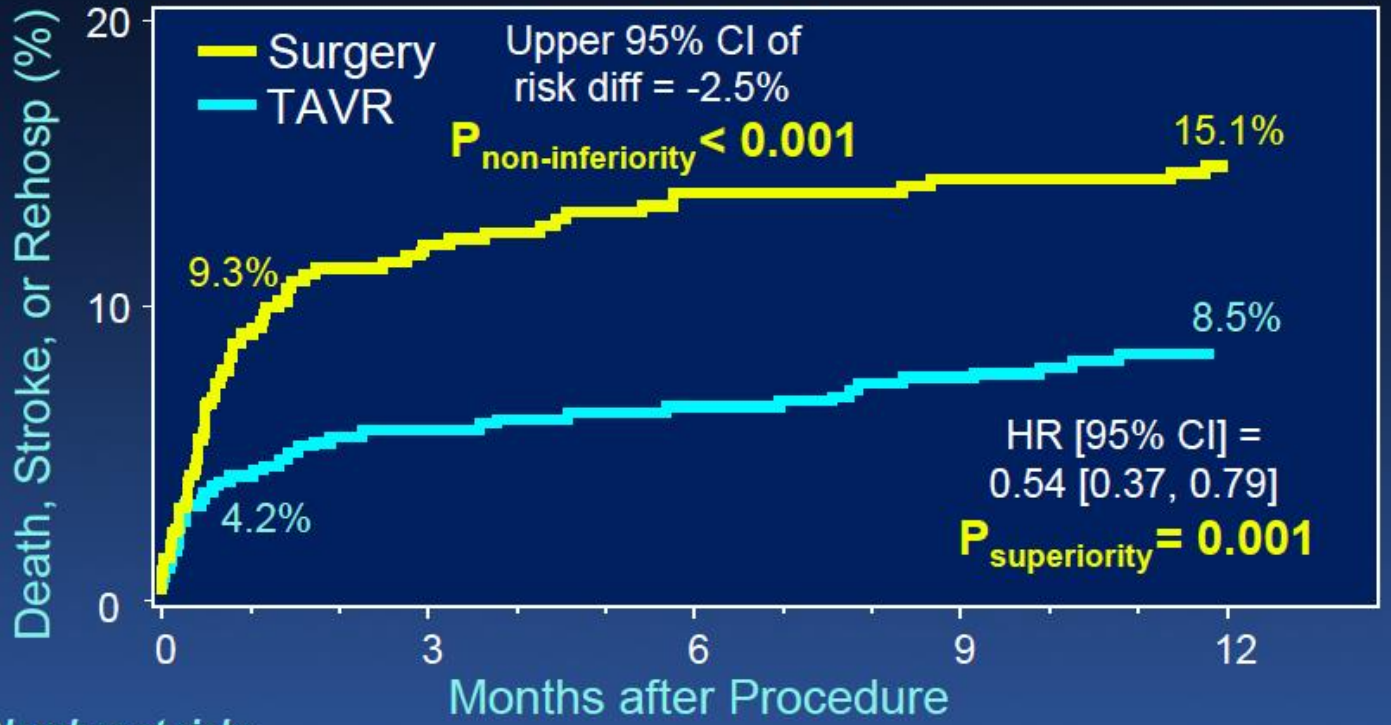
Primary Endpoint



Number at risk:

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

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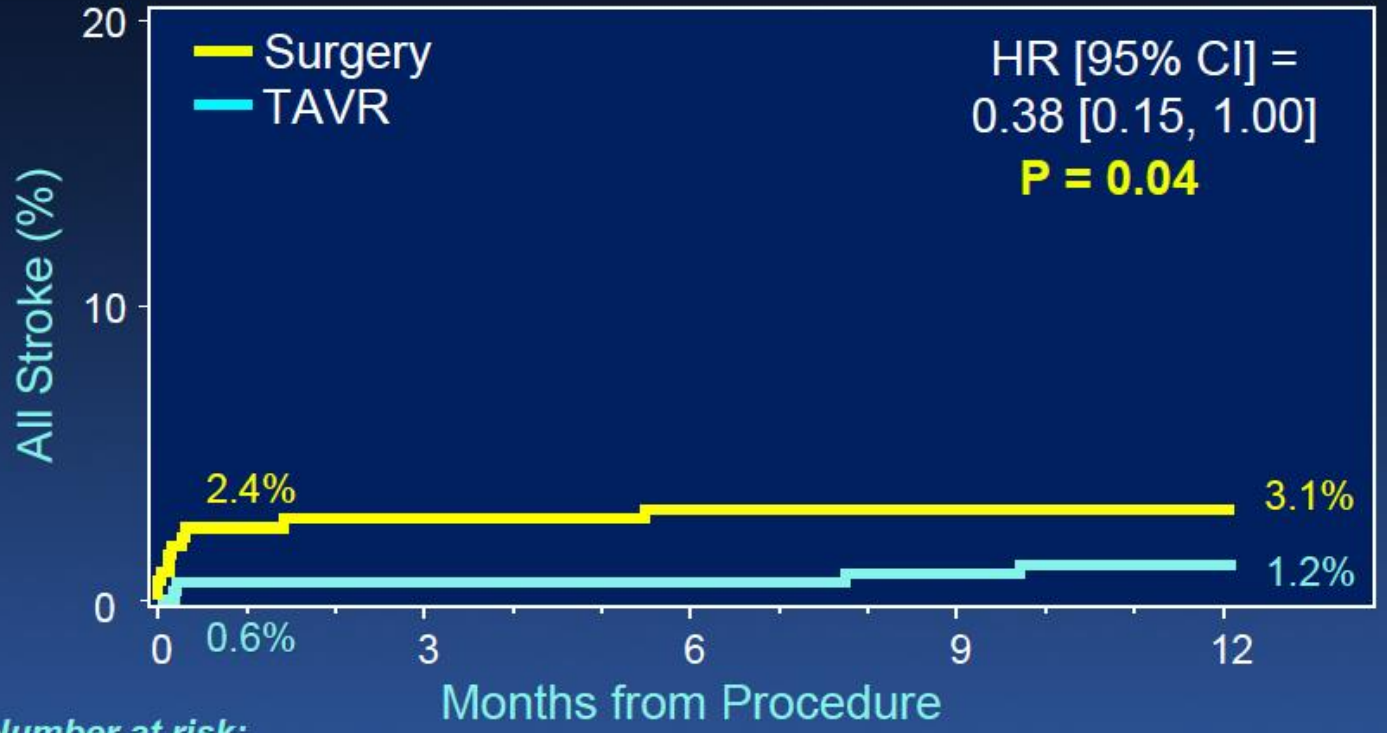
All Stroke



Number at risk:

Surgery	**454**	**435**	**427**	**423**	**421**	**417**
TAVR	**496**	**491**	**491**	**489**	**487**	**484**

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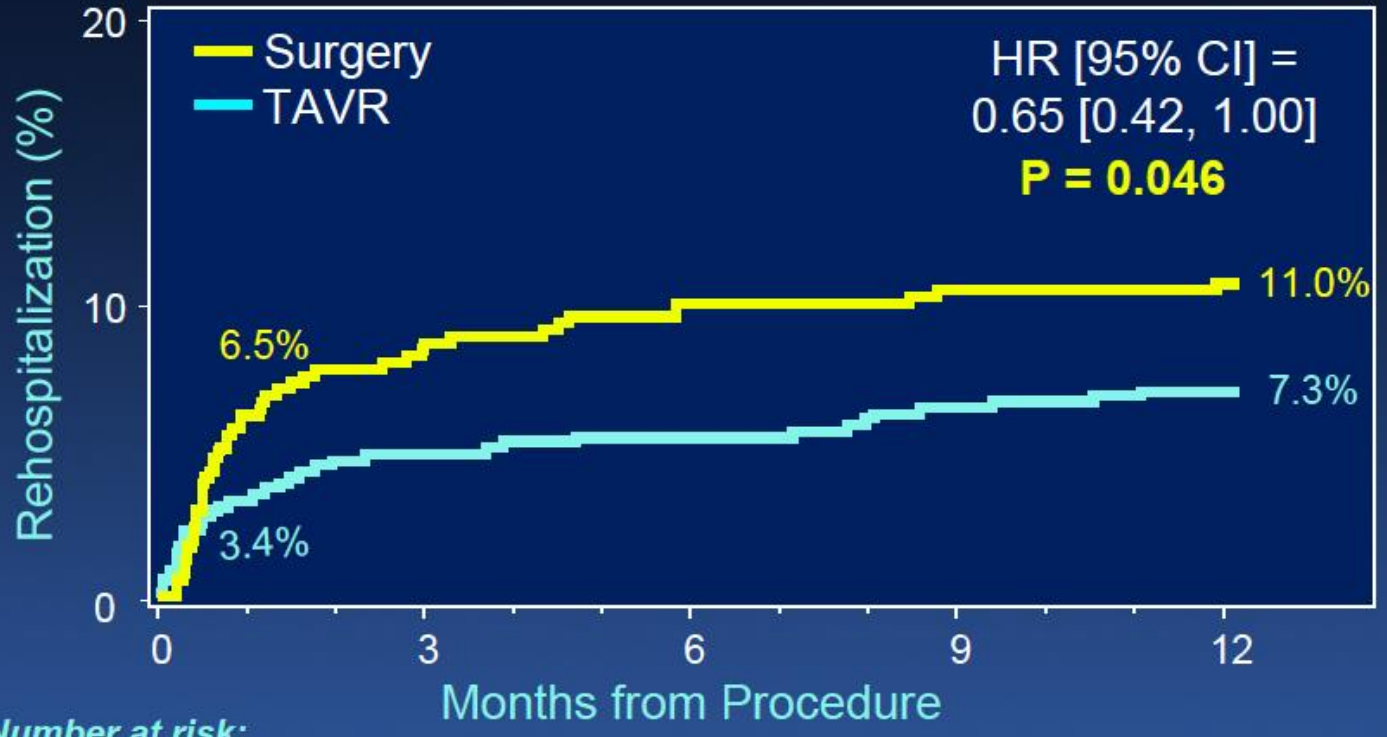
Rehospitalization



Number at risk:

Surgery	**454**	**416**	**399**	**389**	**385**	**382**
TAVR	**496**	**477**	**469**	**465**	**459**	**453**

THE PARTNER 3 TRIAL

Other Secondary Endpoints

Outcomes % (no. of pts)	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
Bleeding - Life-threat/Major	3.6% (18)	24.5% (111)	<0.001	7.7% (38)	25.9% (117)	<0.001
Major Vascular Complics	2.2% (11)	1.5% (7)	0.45	2.8% (14)	1.5% (7)	0.19
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21
New LBBB	22.0% (106)	8.0% (35)	<0.001	23.7% (114)	8.0% (35)	<0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0% (0)	0% (0)	NA	0.6% (3)	0.5% (2)	0.76
Endocarditis	0% (0)	0.2% (1)	0.29	0.2% (1)	0.5% (2)	0.49
Asymp Valve Thrombosis	0.2% (1)	0% (0)	0.34	1.0% (5)	0.2% (1)	0.13

Event rates are KM estimates (%) and p-values are based on Log-Rank test

* Event rates are incidence rates and p-value is Fisher's Exact test

THE PARTNER 3 TRIAL

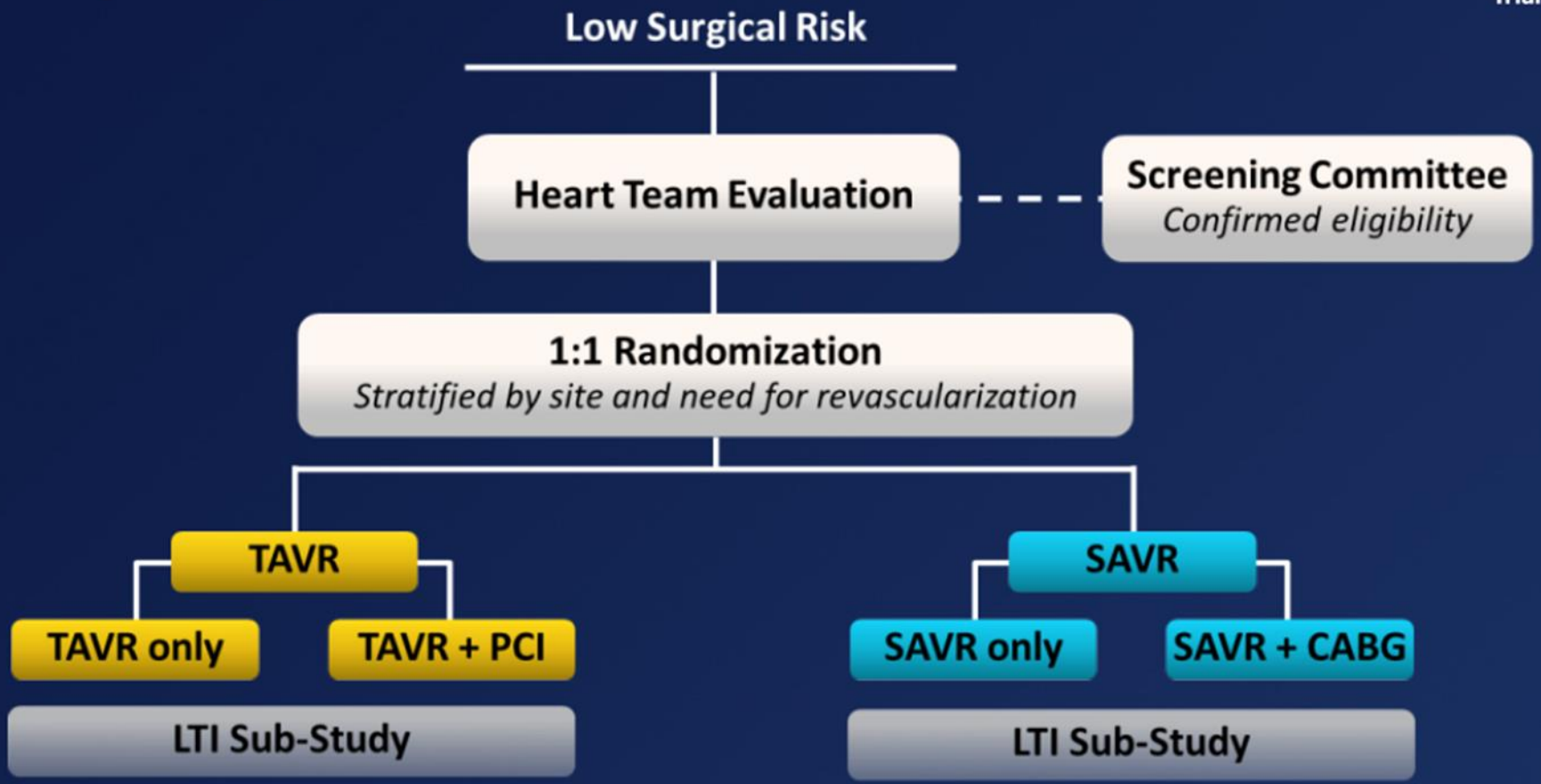
The PARTNER 3 Trial

Clinical Implications

- *Based upon these findings, TAVR, through 1-year, should be considered the preferred therapy in low surgical risk aortic stenosis patients!*
- *PARTNER randomized trials over the past 12 years, clearly indicate that the relative value of TAVR compared with surgery is independent of surgical risk profiles.*
- *The choice of TAVR vs. surgery in aortic stenosis patients should be a shared-decision making process, respecting patient preferences, understanding knowledge gaps (esp. in younger patients), and considering clinical and anatomic factors.*

Study Design

Evolut™ Low Risk Trial



Baseline Characteristics

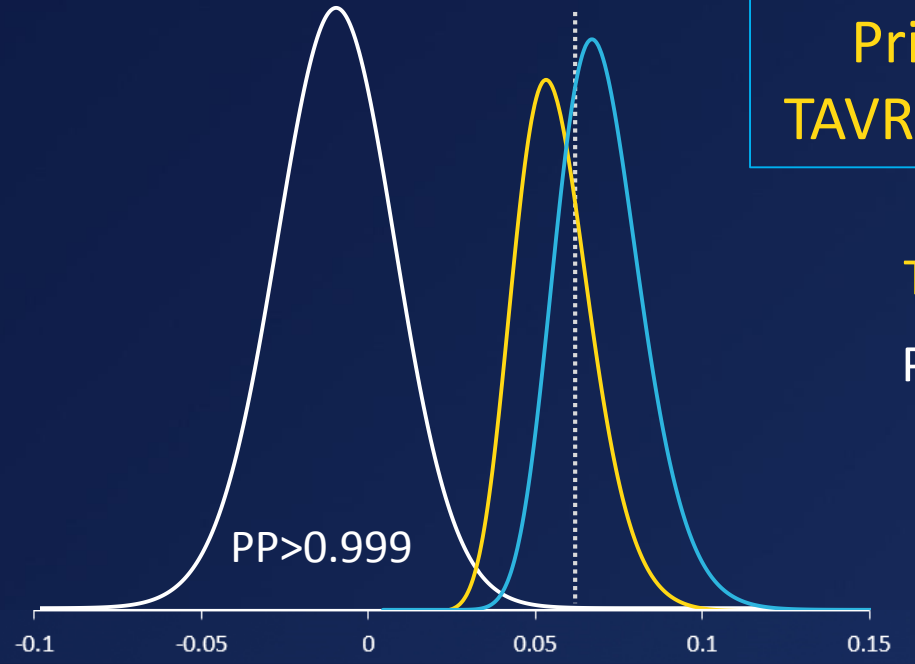
Evolut™ Low Risk Trial

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
Age, years	74.1 ± 5.8	73.6 ± 5.9
Female sex	36.0	33.8
Body surface area, m^2	2.0 ± 0.2	2.0 ± 0.2
STS PROM, %	1.9 ± 0.7	1.9 ± 0.7
NYHA Class III or IV	25.1	28.5
Hypertension	84.8	82.6
Chronic lung disease (COPD)	15.0	18.0
Cerebrovascular disease	10.2	11.8
Peripheral arterial disease	7.5	8.3

There are no significant differences between groups.

Primary Endpoint

All-Cause Mortality or Disabling Stroke at 2 Years



Primary Endpoint Met
TAVR is noninferior to SAVR

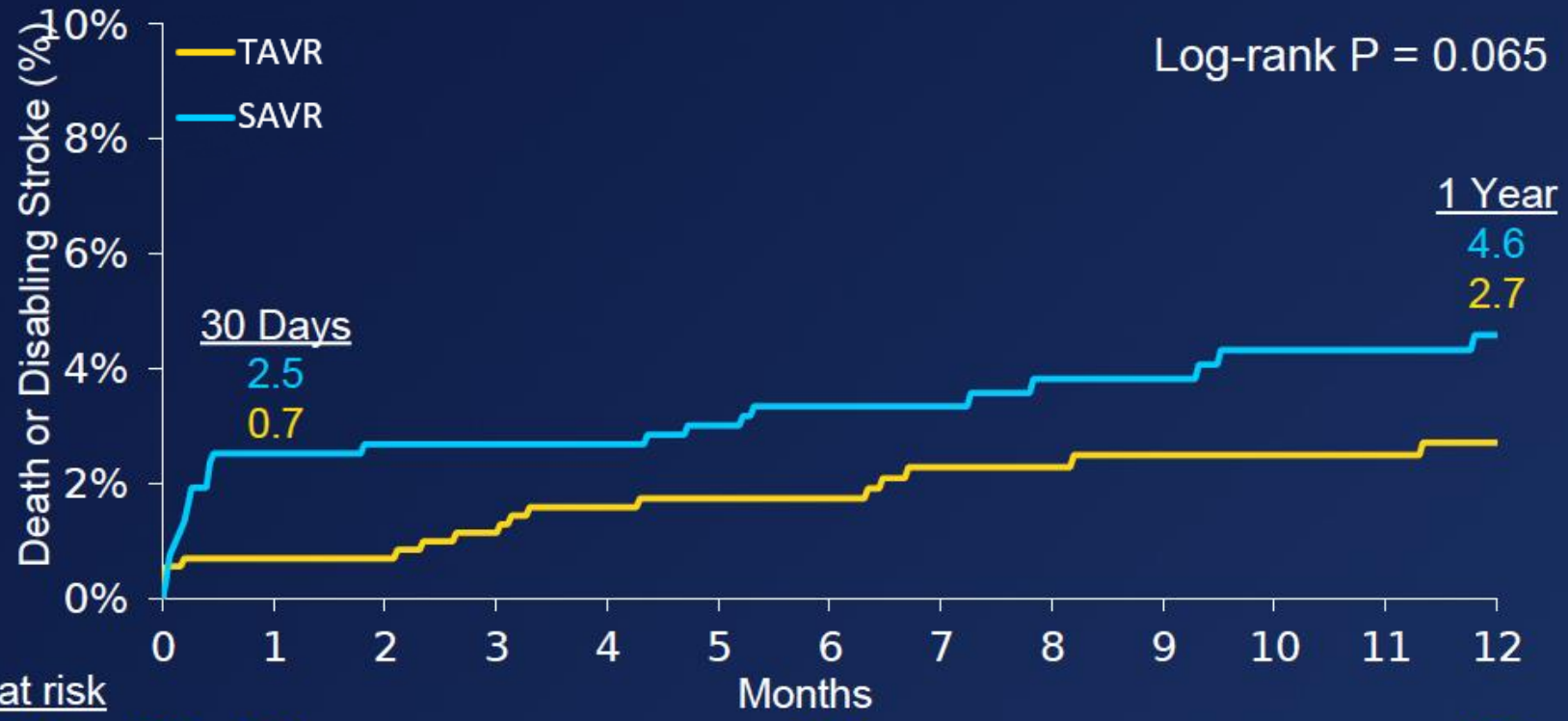
TAVR 5.3% SAVR 6.7%

Posterior probability of noninferiority > 0.999

TAVR –SAVR difference = -1.4% (95% BCI; -4.9, 2.1)

K-M All-Cause Mortality or Disabling Stroke at 1 Year

Evolut™ Low Risk Trial



K-M Disabling Stroke at 1 Year

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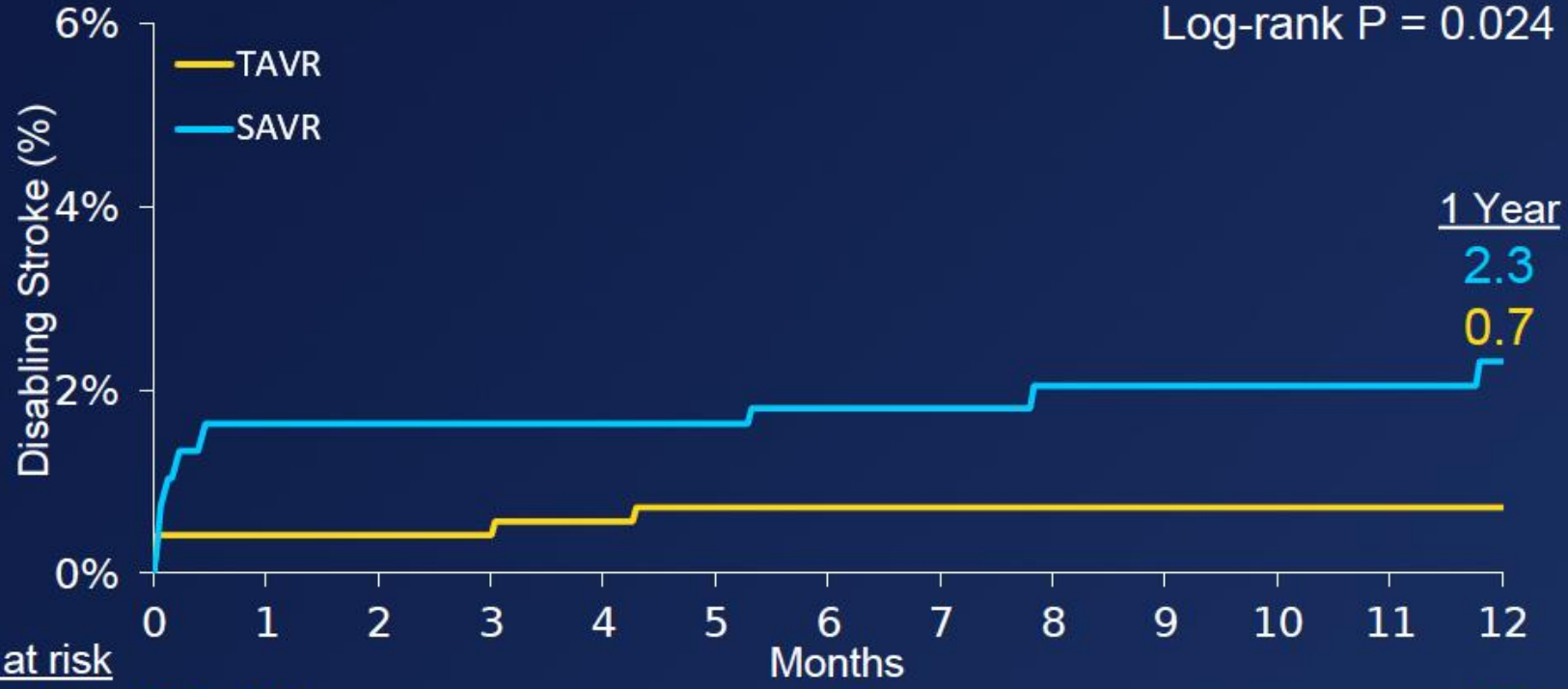
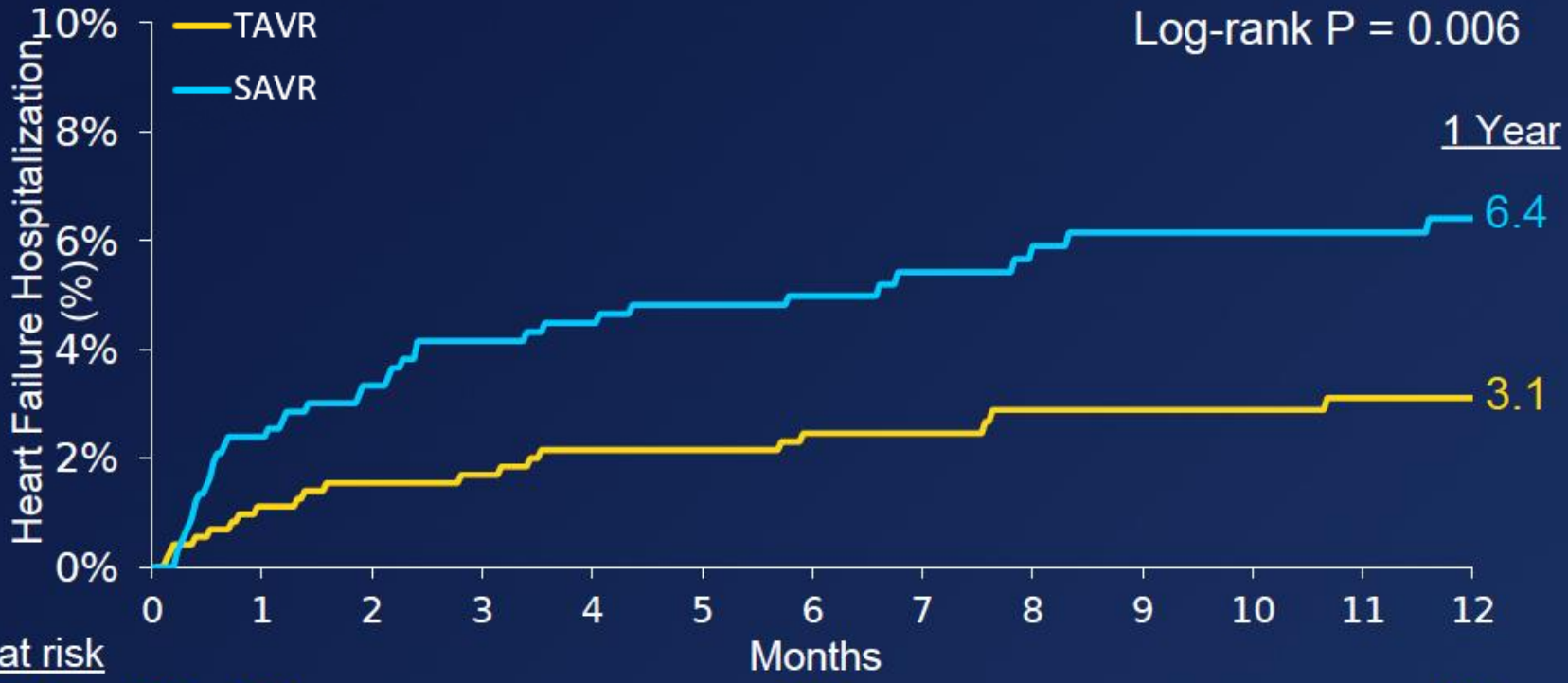


K-M Heart Failure Hospitalization at 1 Year

Evolut™ Low Risk Trial



Clinical Outcomes at 30 Days

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Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety endpoint*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)
Aortic valve reintervention	0.4	0.4	(-0.8, 0.7)

* Significantly favors TAVR; * Significantly favors SAVR

BCI = Bayesian credible interval

Valve Hemodynamics

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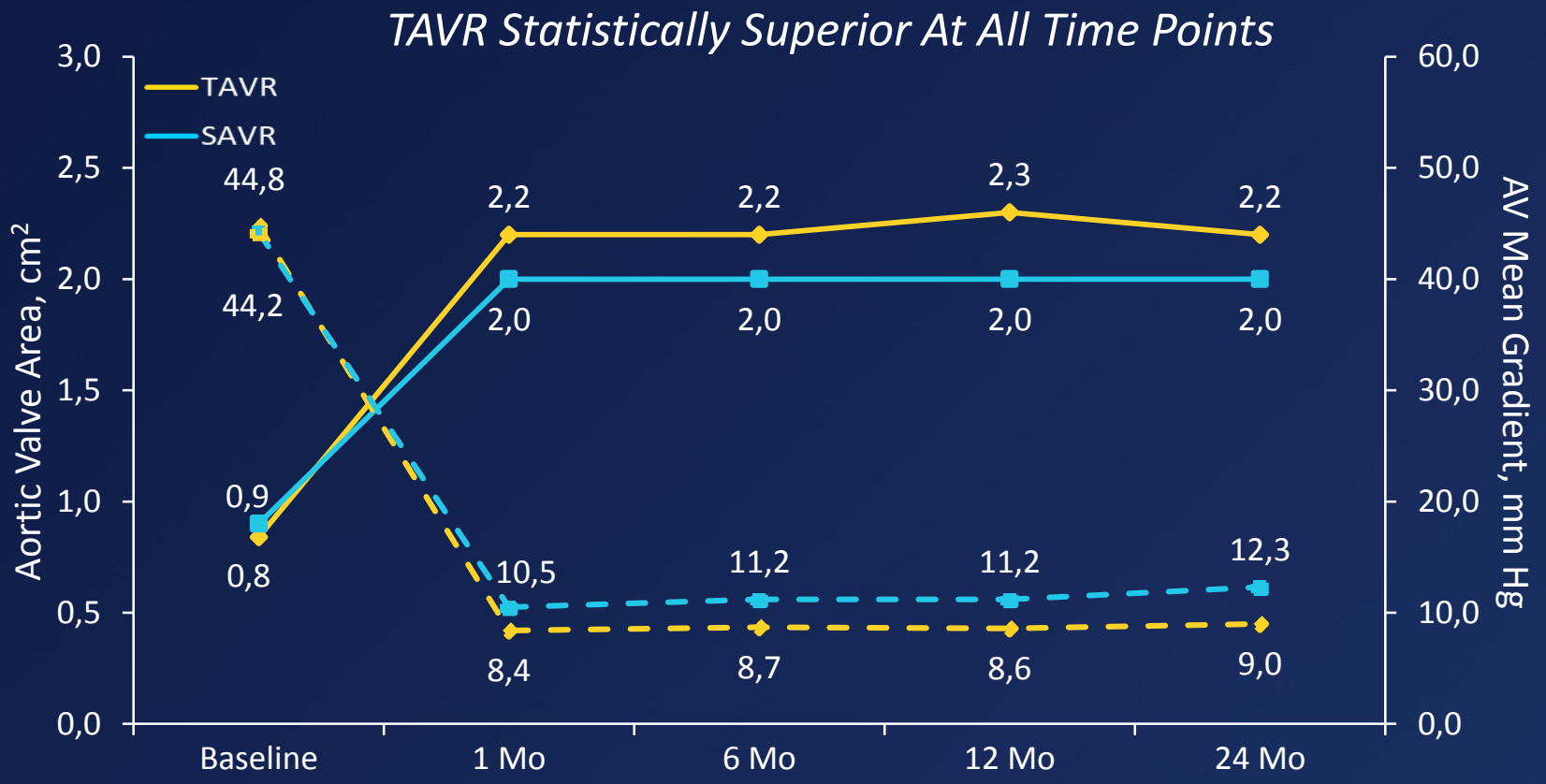


Implanted population. Core lab assessments.

Conclusion

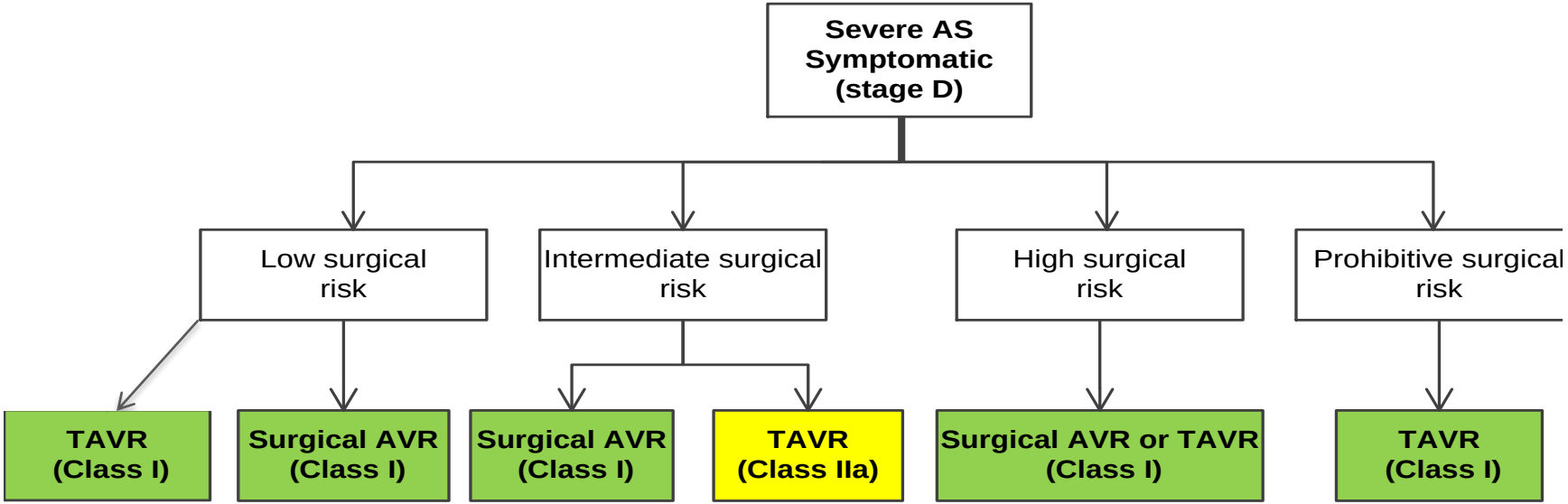
Evolut™ Low Risk Trial

TAVR may be a preferred strategy to surgery in patients with severe aortic stenosis at low risk of surgical mortality.

Remaining questions

- 10 yr follow up for durability of valves
- Medtronic CoreValve vs. Sapien S3
  - CoreValve showed better hemodynamics but higher pacemaker rates – will these differences be significant?
- NOTION 2 trial – Low risk pts <75 years of age

Choice of TAVR Versus Surgical AVR in the Patient With Severe Symptomatic AS (Modified)



The Next Frontiers for TAVR

- Asymptomatic patients – EARLY TAVR
- Bicuspid Valve patients – Several registries
- Pure Native Valve Aortic Regurgitation

Conclusions

- TAVR is beneficial in most patients at high, intermediate and low risk and has been aided by the evolution of TAVR technology

- More studies being performed on asymptomatic patients and bicuspid valve patients (need comparison with SAVR)