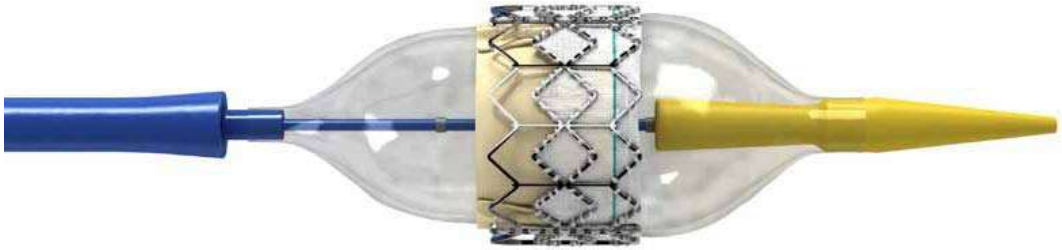
The Transcatheter Aortic Valve Replacement (TAVR)Program at Southcoast Health



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Cardiovascular Care Center

Southcoast Health

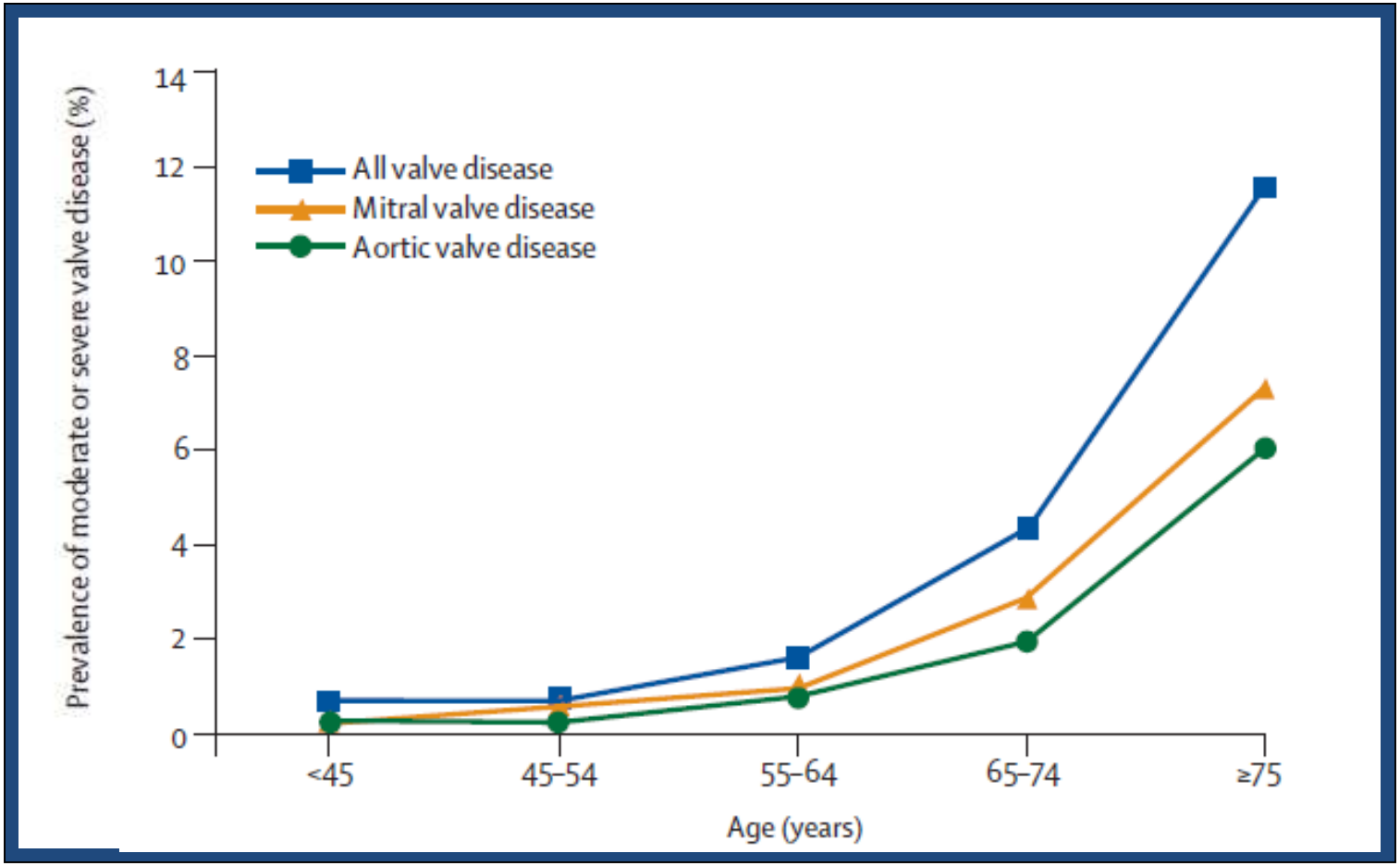
Disclosures

- Edwards Lifesciences: speaking honorarium

Outline

- Prevalence, Pathophysiology, and Prognosis for Severe Aortic Stenosis
- Transcatheter Aortic Valve Replacement (TAVR) and patient selection
- Recent Evidence and Future Direction for TAVR
- The Southcoast TAVR Program

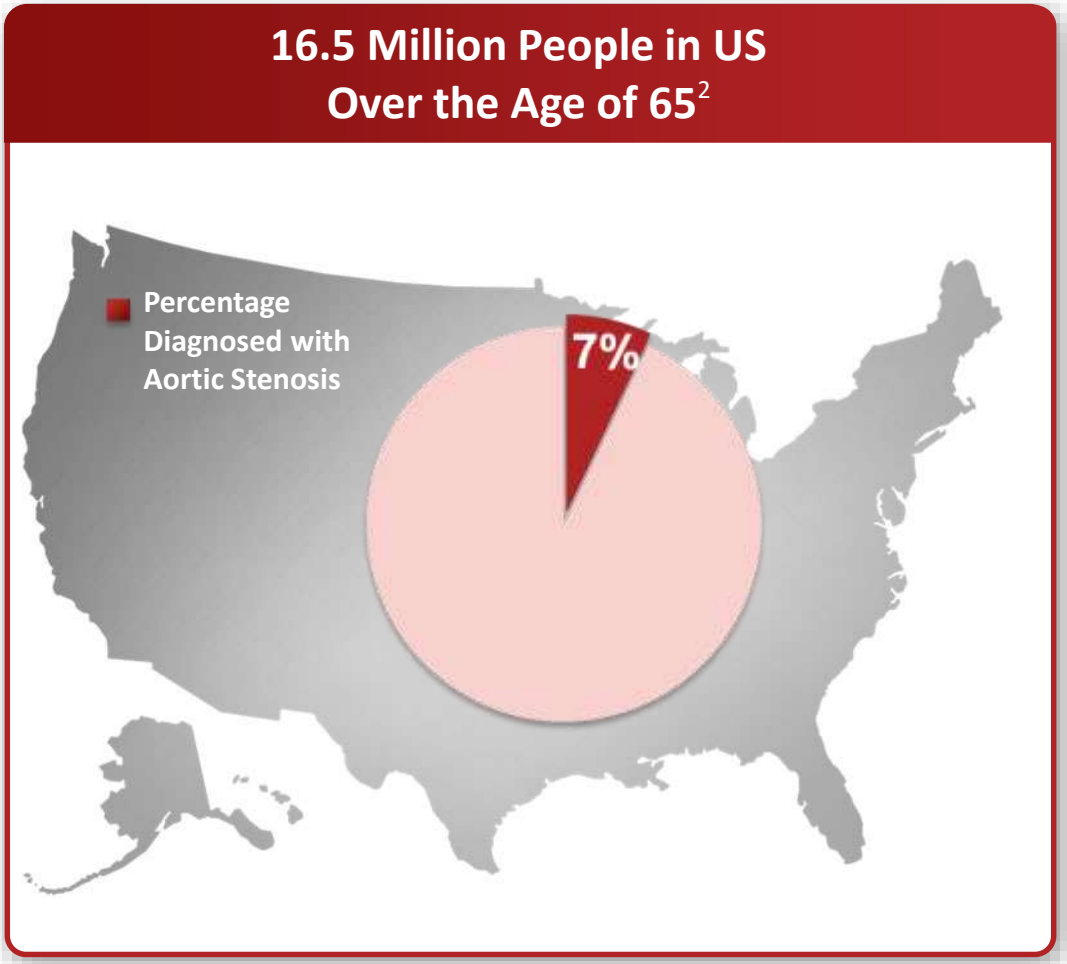
Prevalence of Valve Disease by Age



Nkomo et al. Lancet. 2006; 368: 1005-11.

Prevalence of Aortic Stenosis

- Aortic stenosis is estimated to be prevalent in up to 7% of the population over the age of 65.[1]
- This prevalence increases with each decade of life after 65.



1. Ramaraj R, Sorrell VL. Degenerative aortic stenosis. Br Med J 2008;336: 550–5.

Echocardiographic Guidelines are the Gold Standard in Assessing Severe Aortic Stenosis

Grading the Severity of Aortic Stenosis per the ACC/AHA Guidelines			
Indicator	Mild	Moderate	Severe
Jet velocity (m/s)	< 3.0	3.0 - 4.0	> 4.0
Mean gradient (mmHg)	< 25	25 - 40	> 40
Valve area (cm^2)	> 1.5	1.0 – 1.5	< 1.0
Valve area index (cm^2/m^2)	N/A	N/A	< 0.6

*Doppler-Echocardiographic measurements

- According to the 2008 ACC/AHA guidelines, severe aortic stenosis is defined as:
  - Aortic valve area (AVA) less than 1.0 cm^2
  - Mean gradient greater than 40 mmHg or jet velocity greater than 4.0 m/s

Calcific Aortic Stenosis: Mechanisms

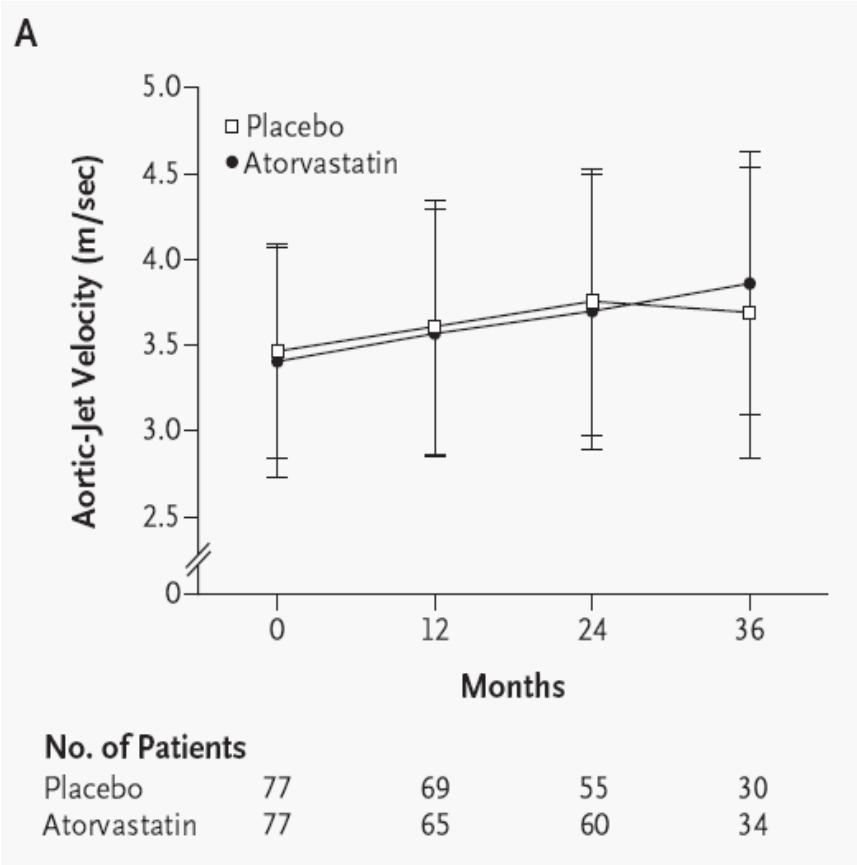
- Calcific aortic stenosis is a biologically active process
- Lipid accumulation
  - LDL accumulation and oxidation
- Inflammation
  - T-cells, monocytes, inflammatory mediators, cytokines
- Calcification
  - Osteoblast expression, bone formation

Do Statins Slow the Progression of Aortic Stenosis?

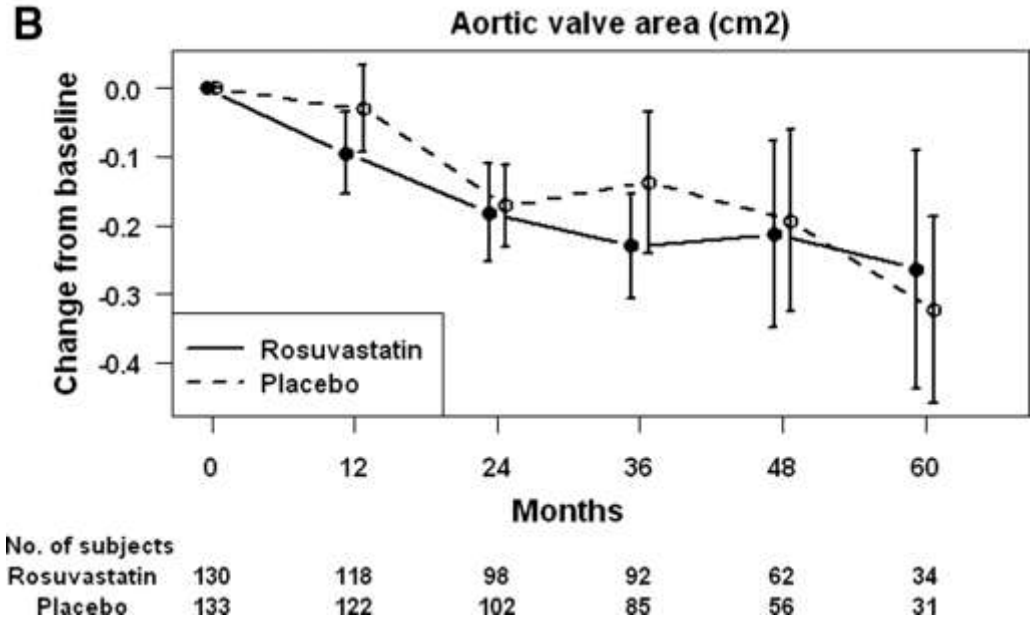
- Six retrospective studies had found statin therapy was associated with a reduced rate of AS progression
- However, three prospective randomized trials have failed to show a decrease in hemodynamic progression of AS or a delay in AVR…

Helske S, Otto CM. Circulation 2009;119:2653-2655

Randomized Trials of Statin Therapy and Progression of Aortic Stenosis

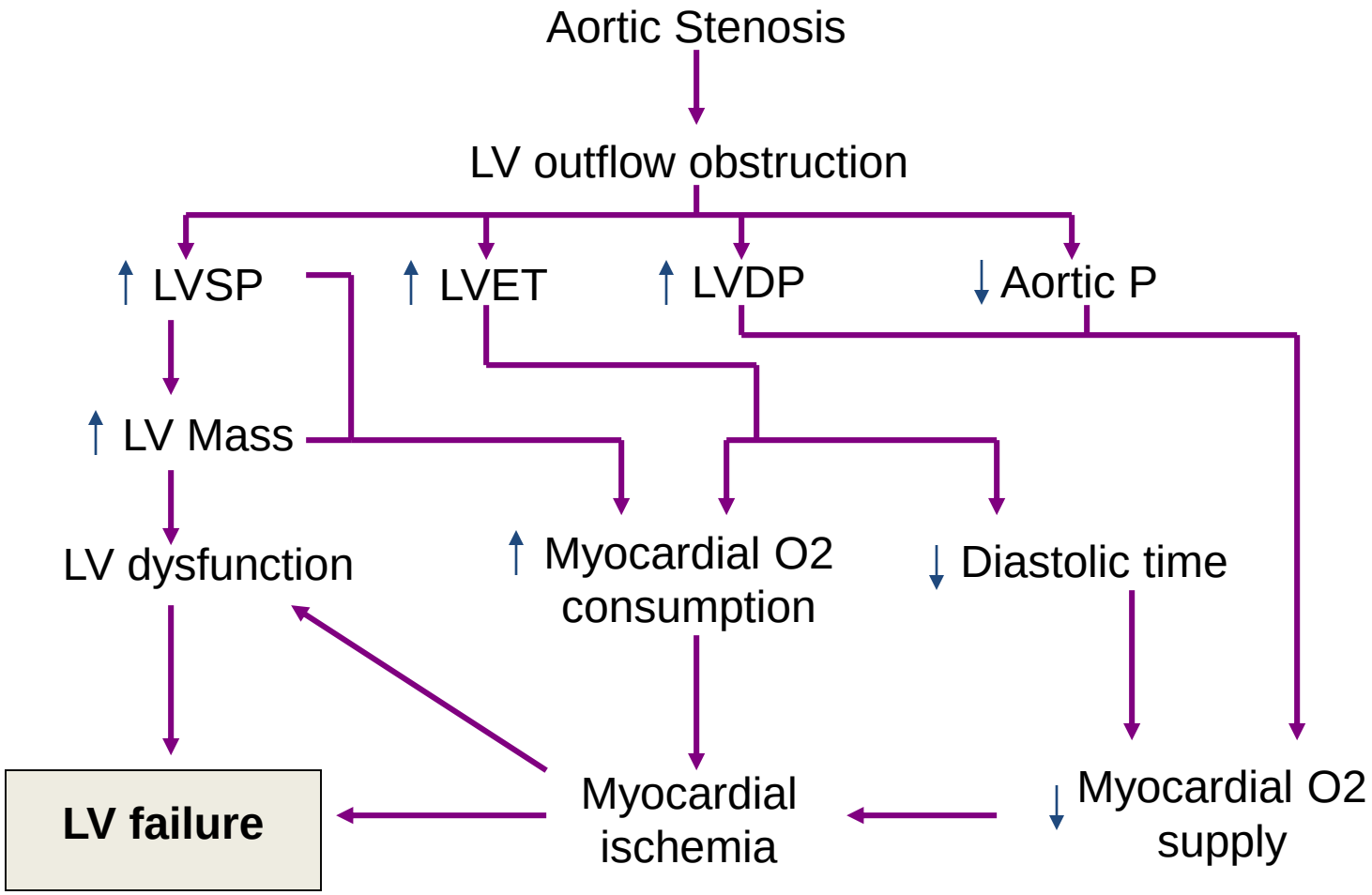


SALTIRE Trial: Cowell SJ, et al.
N Engl J Med 2005;352:2389-97

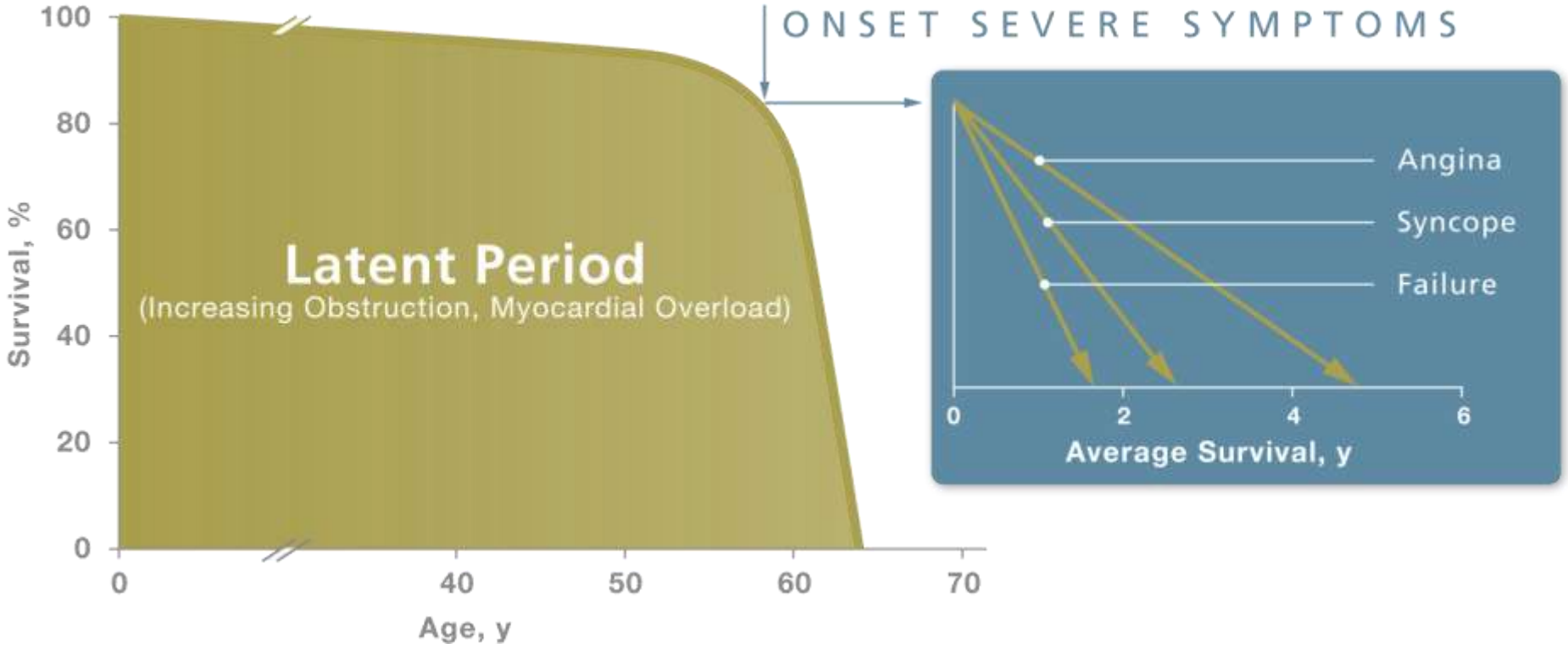


ASTRONOMER (AS Progression Observation, Measuring Effects of Rosuvastatin)
Chan K L et al. Circulation 2010;121:306-314

Pathophysiology Aortic Stenosis



Prognosis

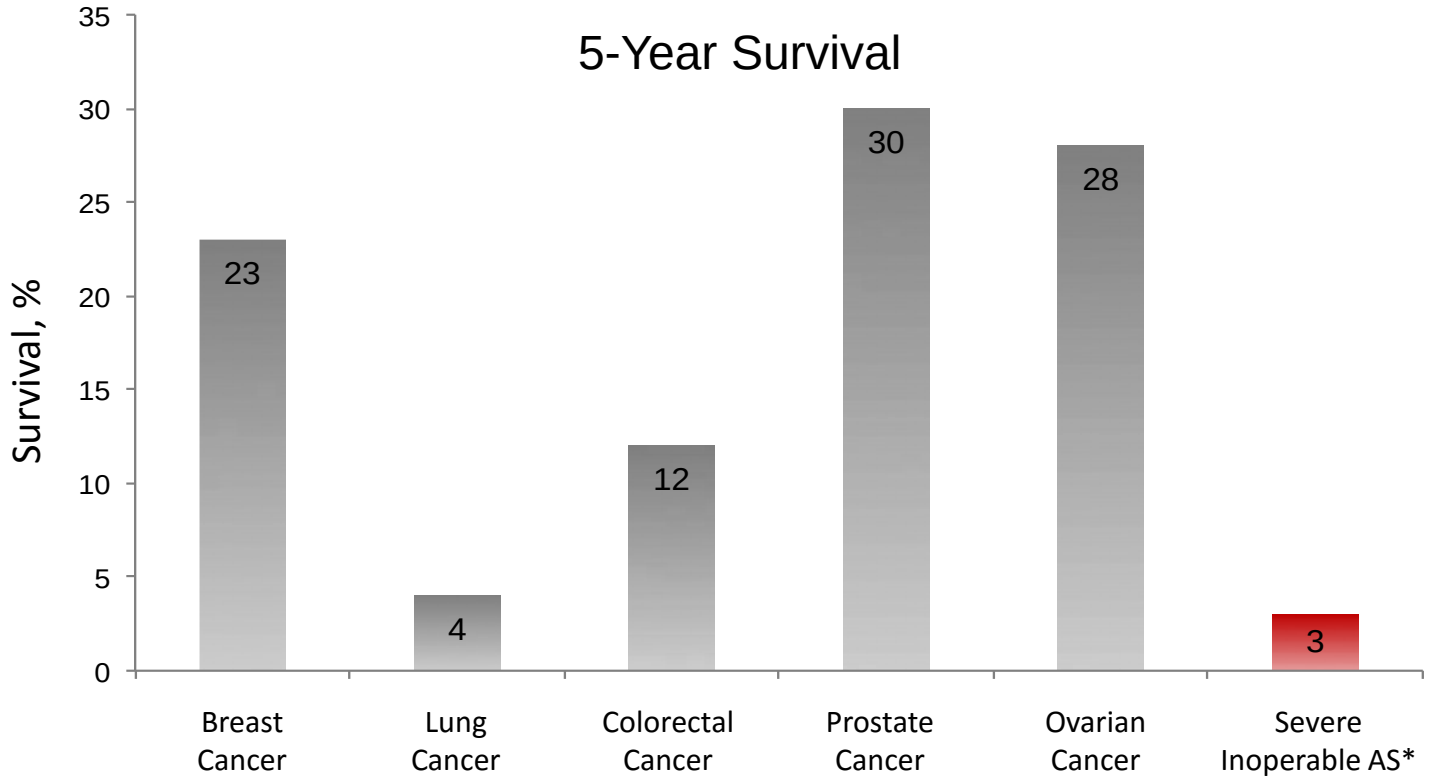


Survival after onset of symptoms
is 50% at 2 years and 20% at 5 years.

Rationale for Treadmill Testing in the "Asymptomatic" Patient with Severe Aortic Stenosis

- Quantitative evaluation of exercise capacity
- Assessment of blood pressure response with exertion
- Evaluate left ventricular function with exercise
- Assess RVSP with activity

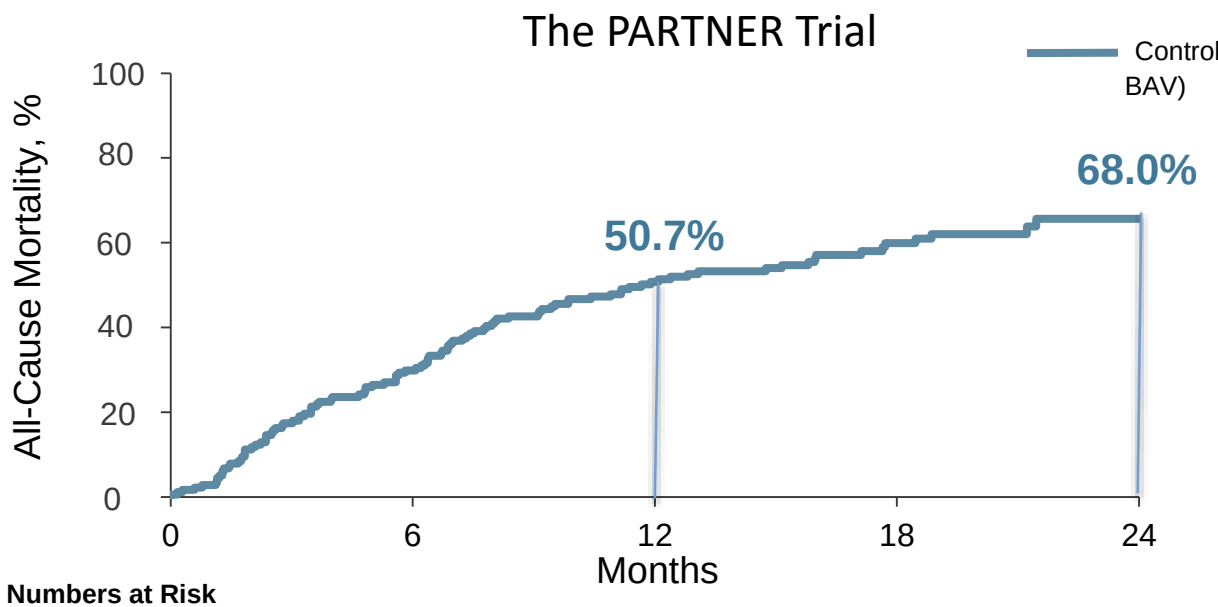
Sobering Perspective



*Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis

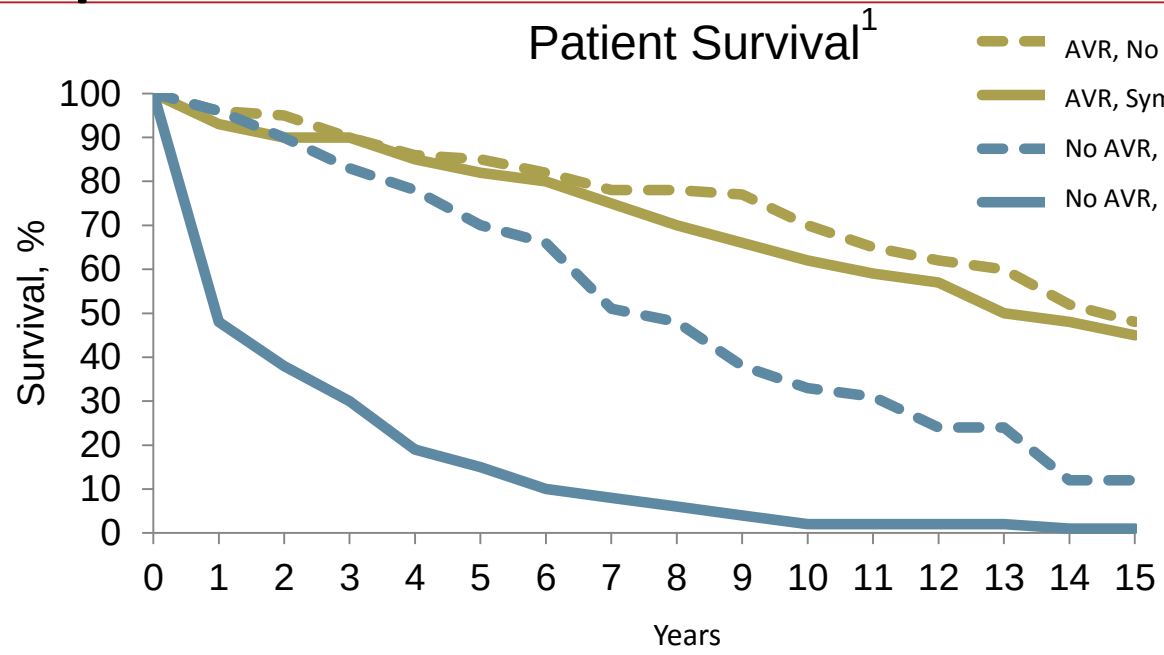
Inoperable PARTNER Cohort: All-Cause Mortality



- As seen previously, survival after onset of symptoms in patients with aortic stenosis is 50% at 2 years[1]
- The PARTNER Trial showed that in inoperable patients with severe aortic stenosis who did not receive a valve replacement, 50% died within *1 year*
- Despite the frequent utilization of BAV, standard therapy did not do much to alter the dismal course of disease for inoperable patients with severe aortic stenosis

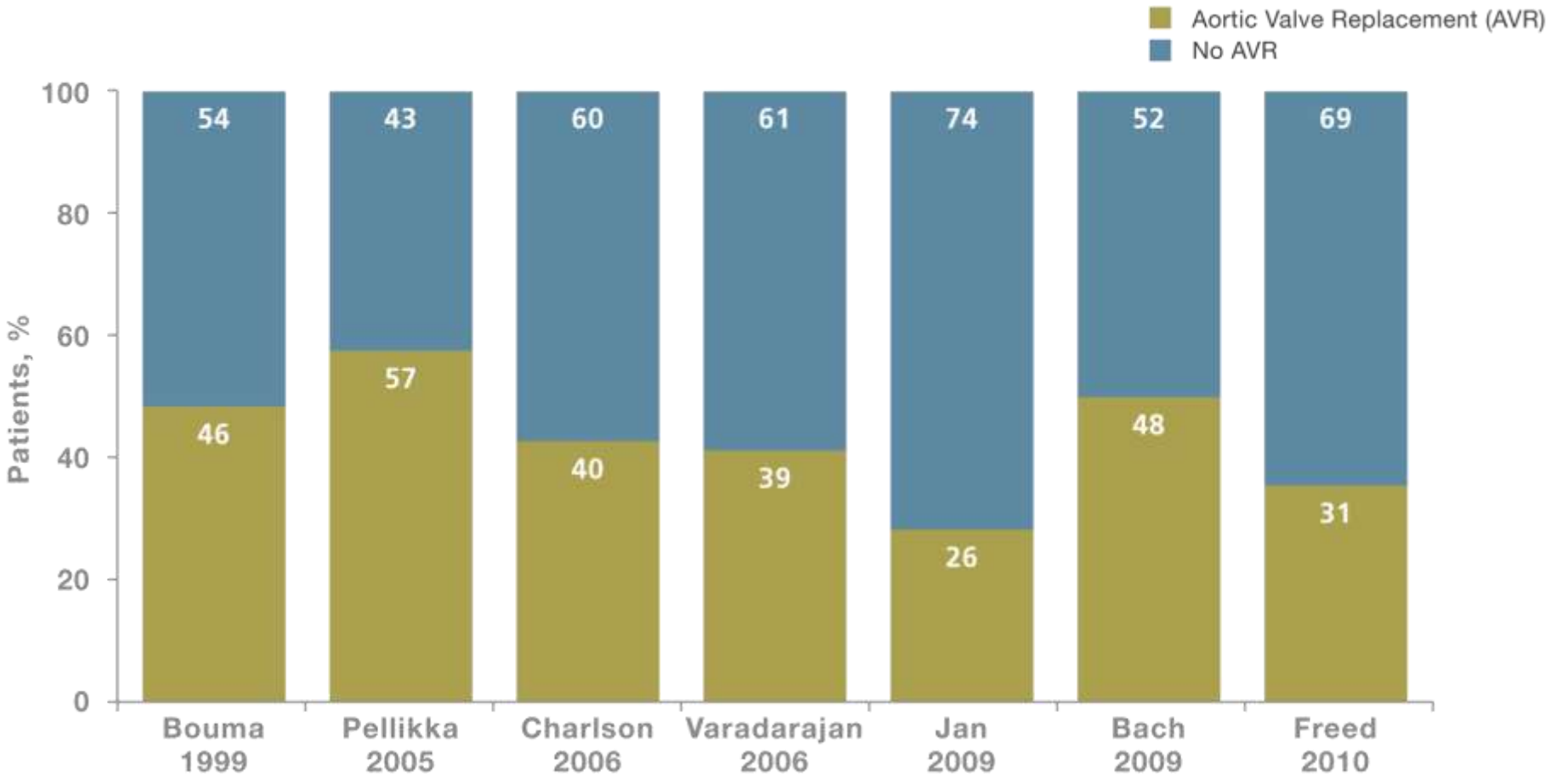
Leon et al, NEJM 2010; 363:1597-1607

Aortic Valve Replacement Greatly Improves Survival

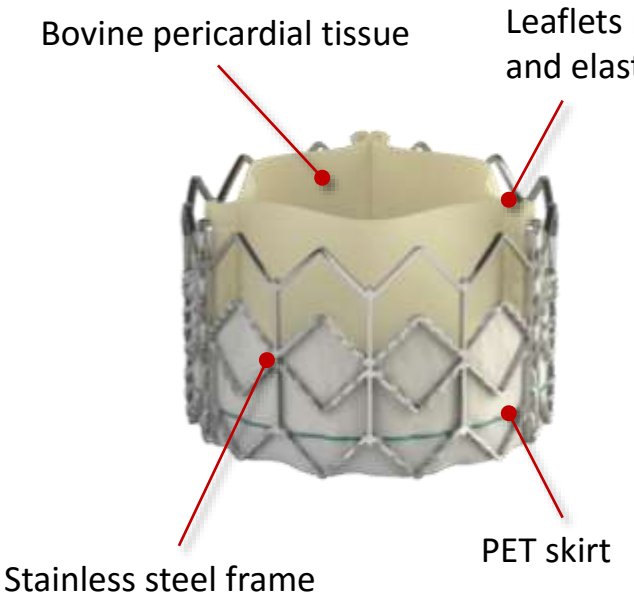


- Study data demonstrate that early and late outcomes were similarly good in both symptomatic and asymptomatic patients
- It is important to note that among asymptomatic patients with SAS, omission of surgical treatment was the most important risk factor for late mortality

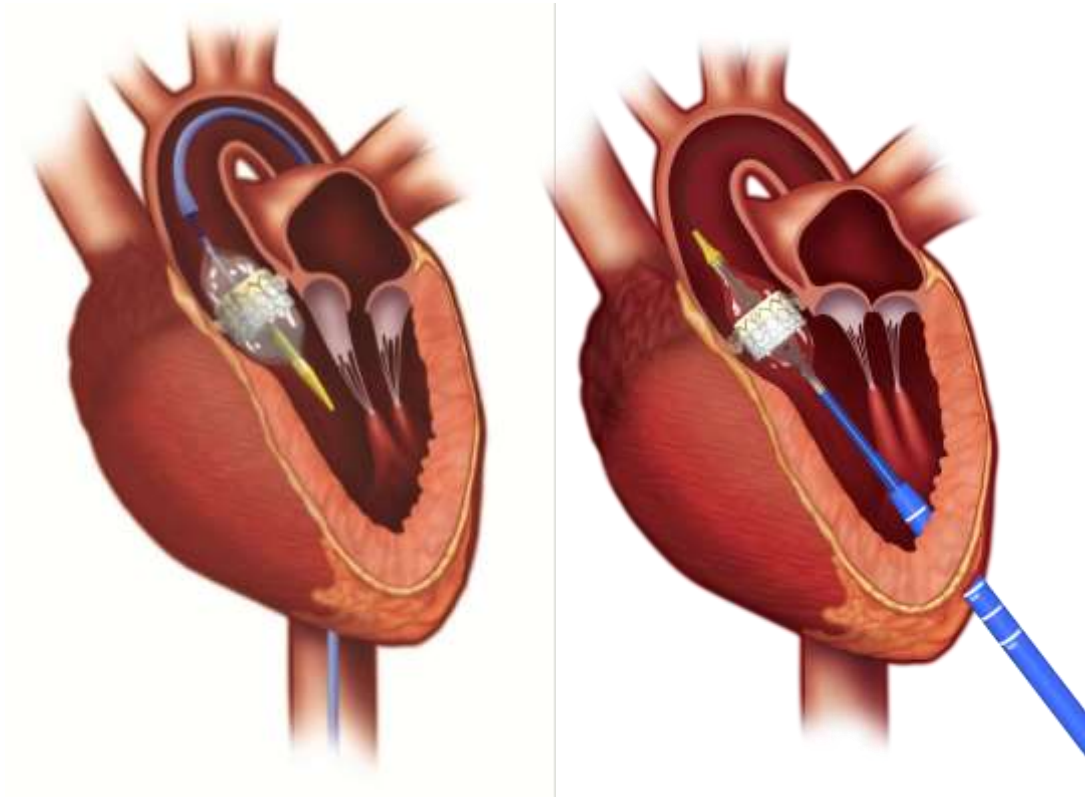
Frequently not treated



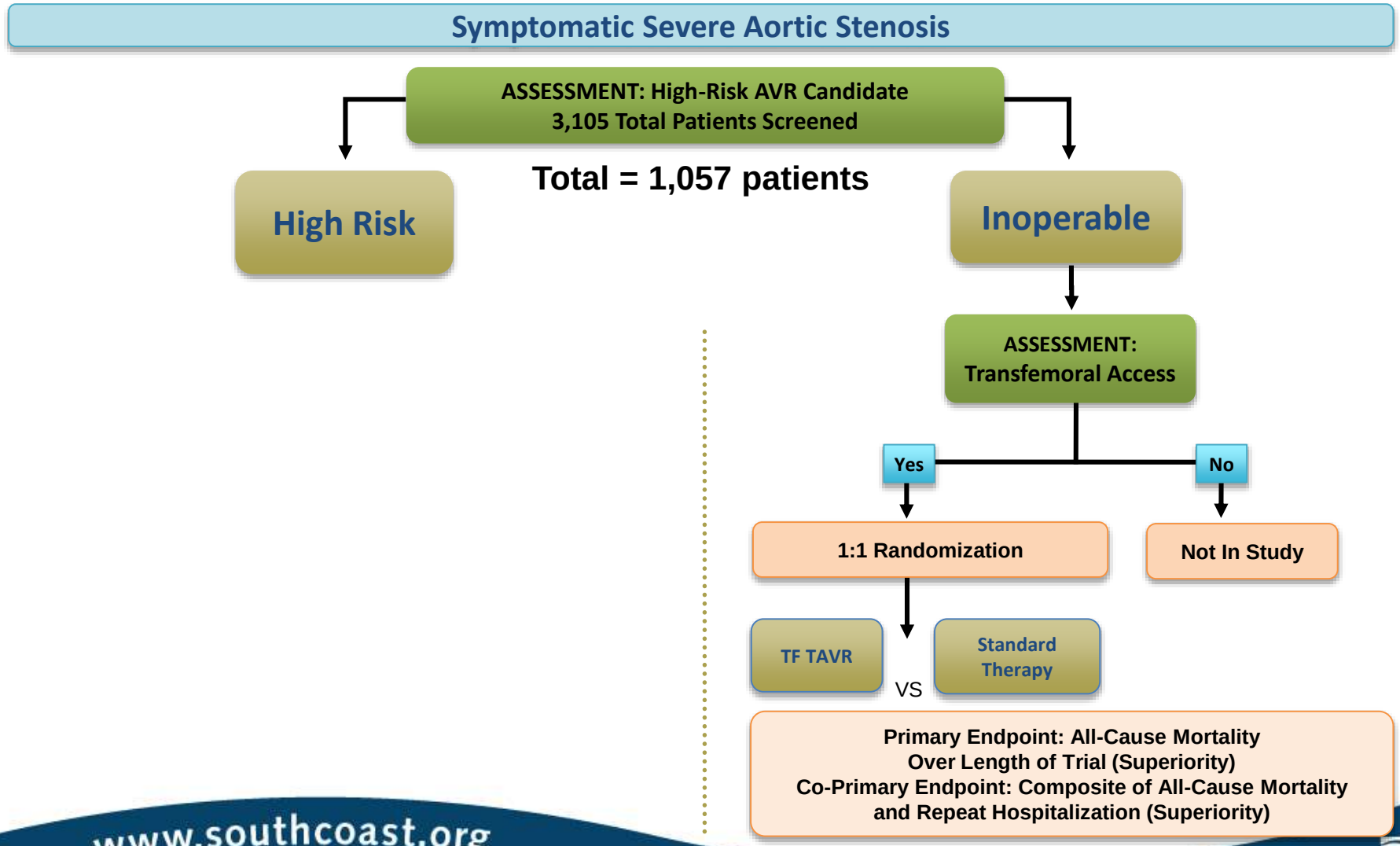
Transcatheter Aortic Valve Replacement (TAVR)



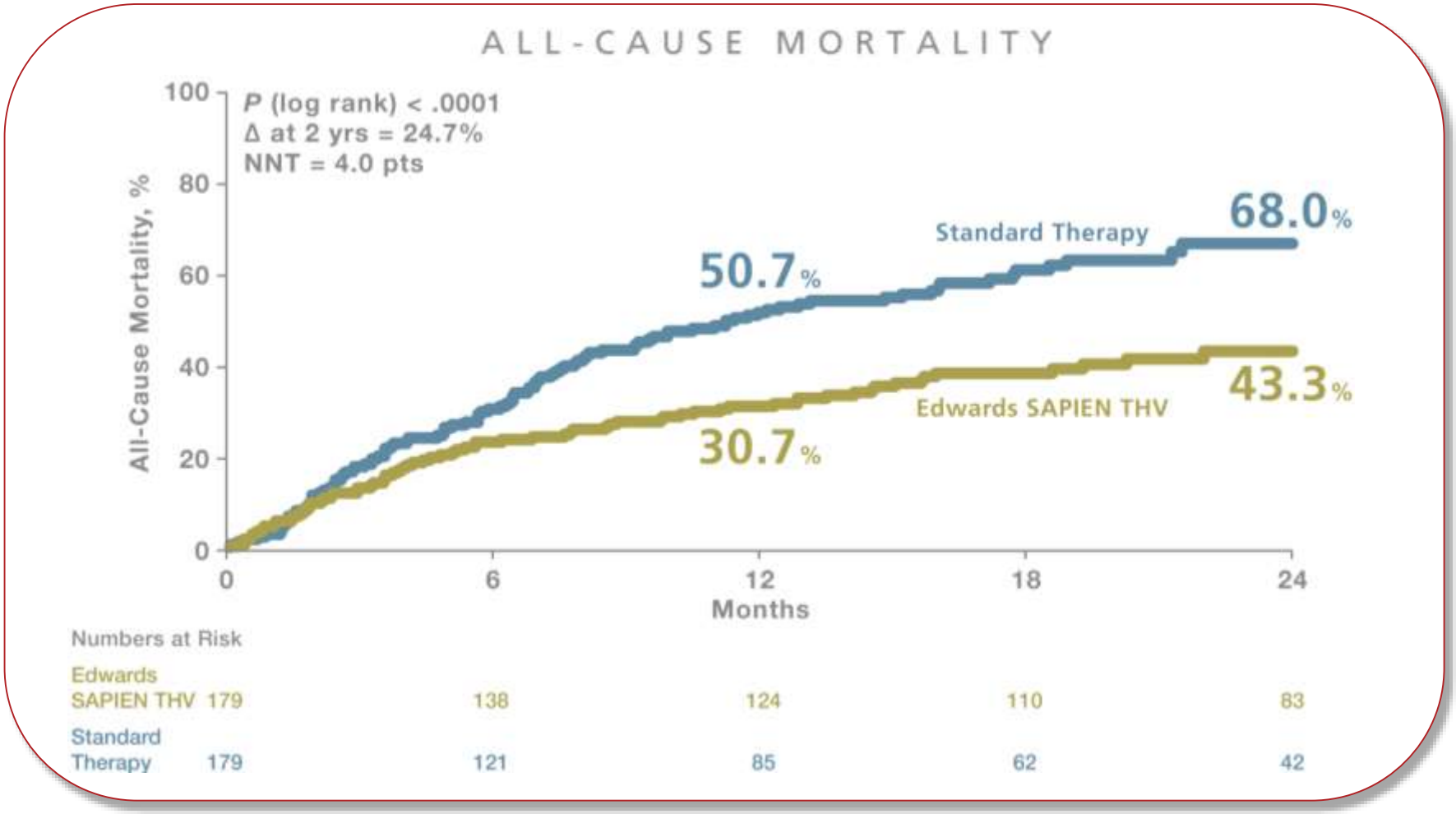
Approach



PARTNER Study Design



Edwards SAPIEN THV Improved Survival



THE PARTNER TRIAL COHORT B

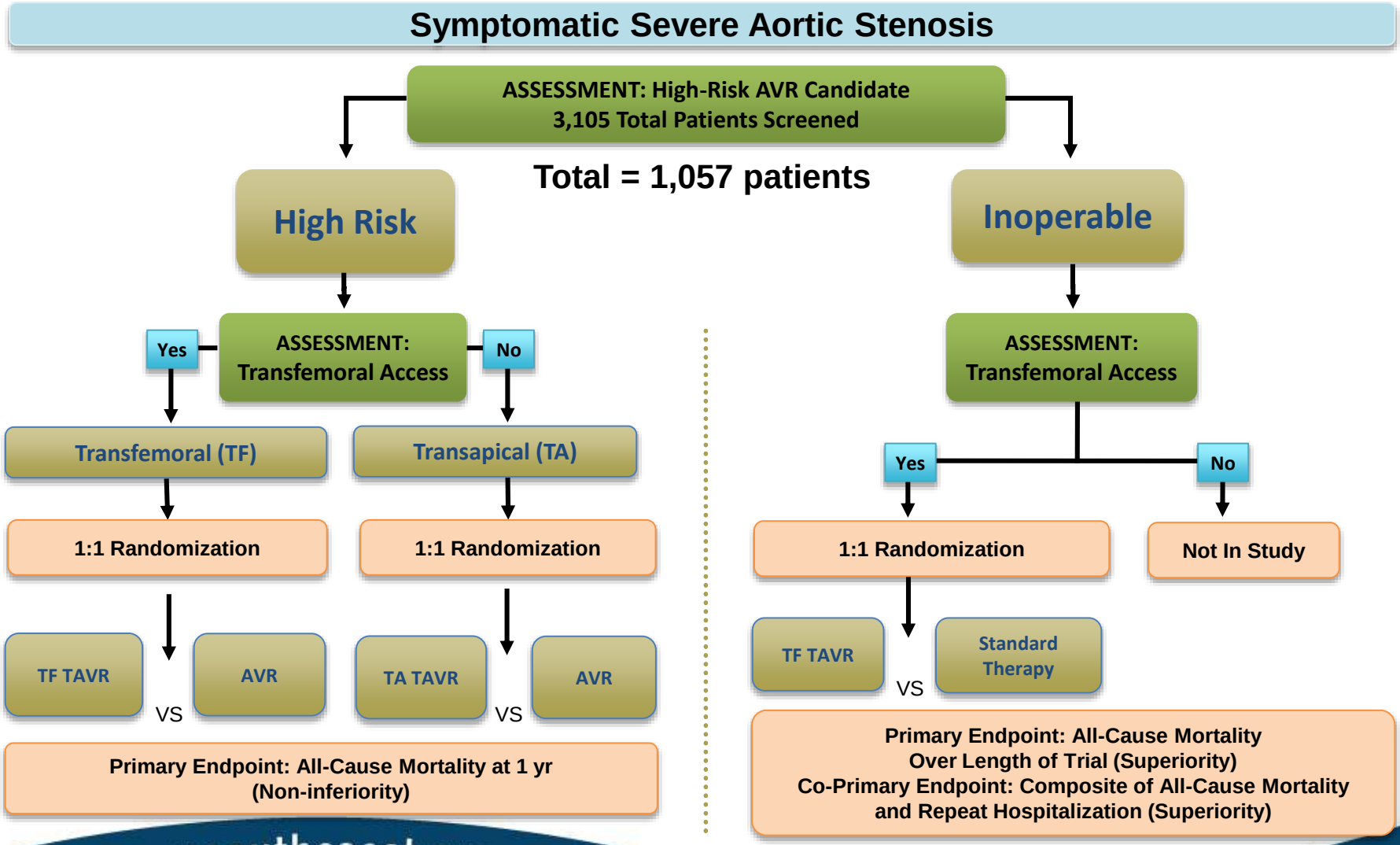
Treatment for Inoperable Aortic Stenosis

FDA Approves Transcatheter Valve for Patients with Inoperable AS

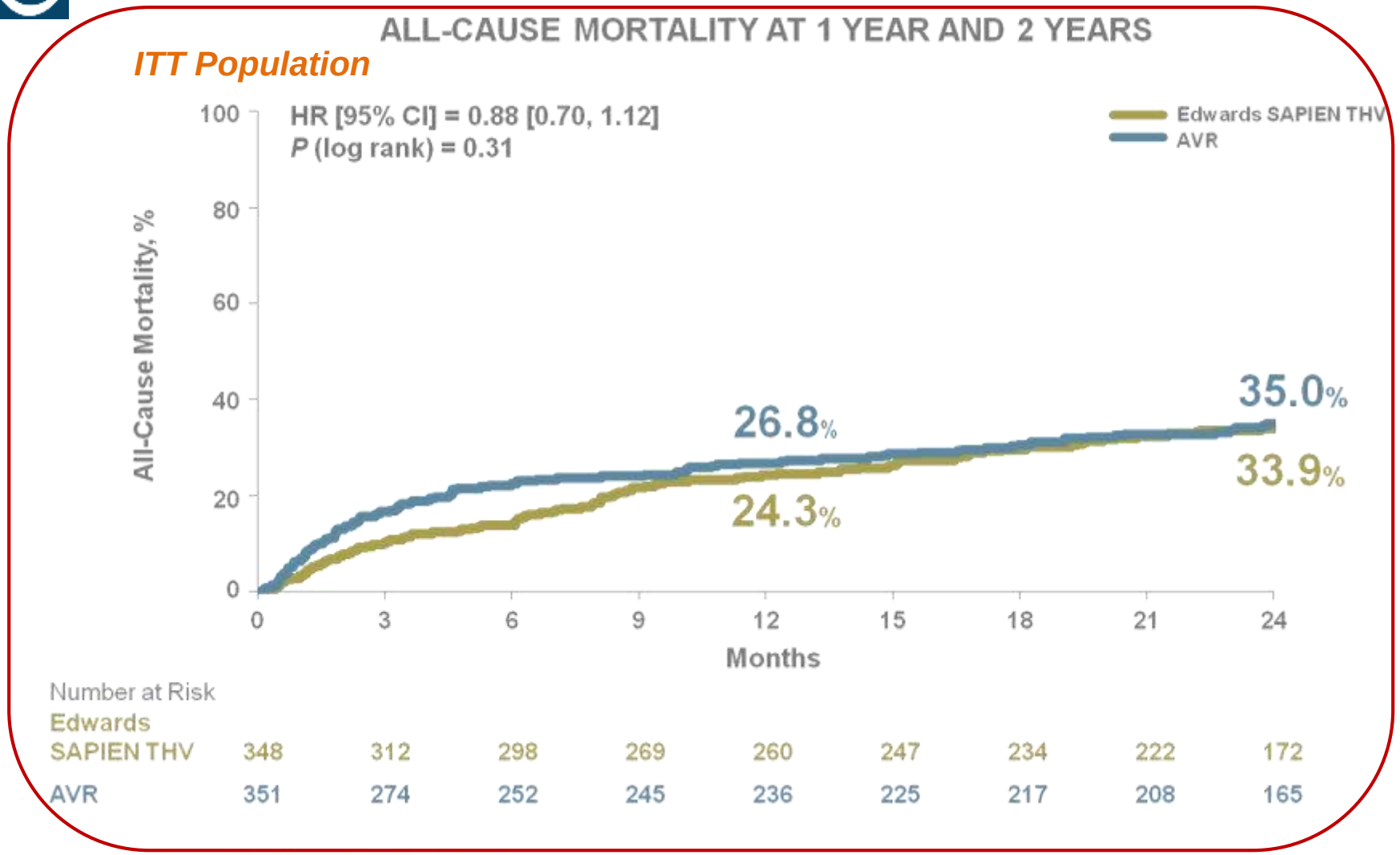
Cardiology Today Intervention, January/February 2012

The Sapien transcatheter heart valve has been approved by the FDA for the treatment of patients with severe aortic stenosis who are ineligible for surgery. The approval makes the device the first artificial heart valve available in the United States that can replace an aortic heart valve without surgery.

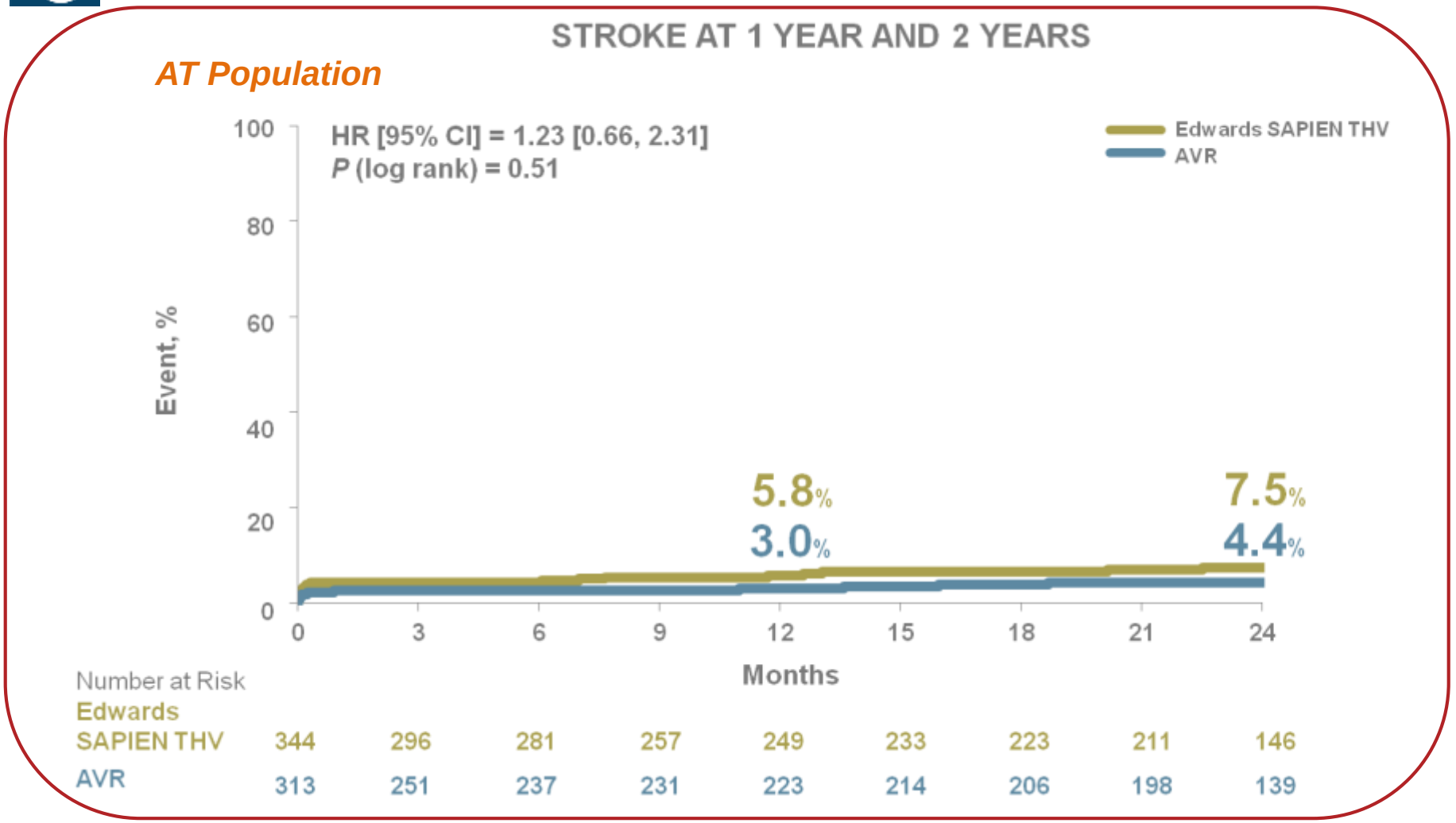
PARTNER Study Design



All-Cause Mortality



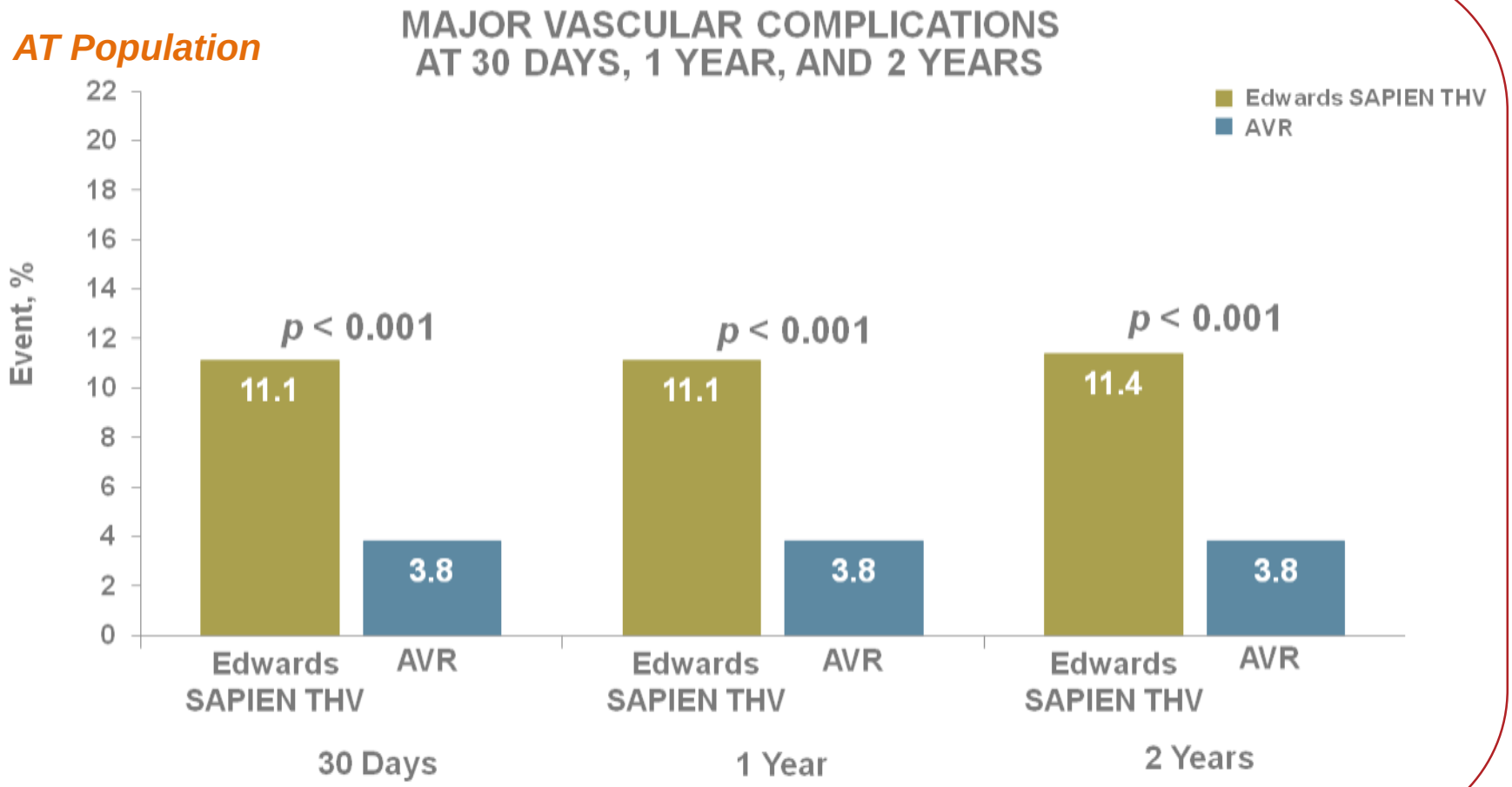
All Strokes



THE PARTNER TRIAL COHORT A

Major Vascular Complications

AT Population

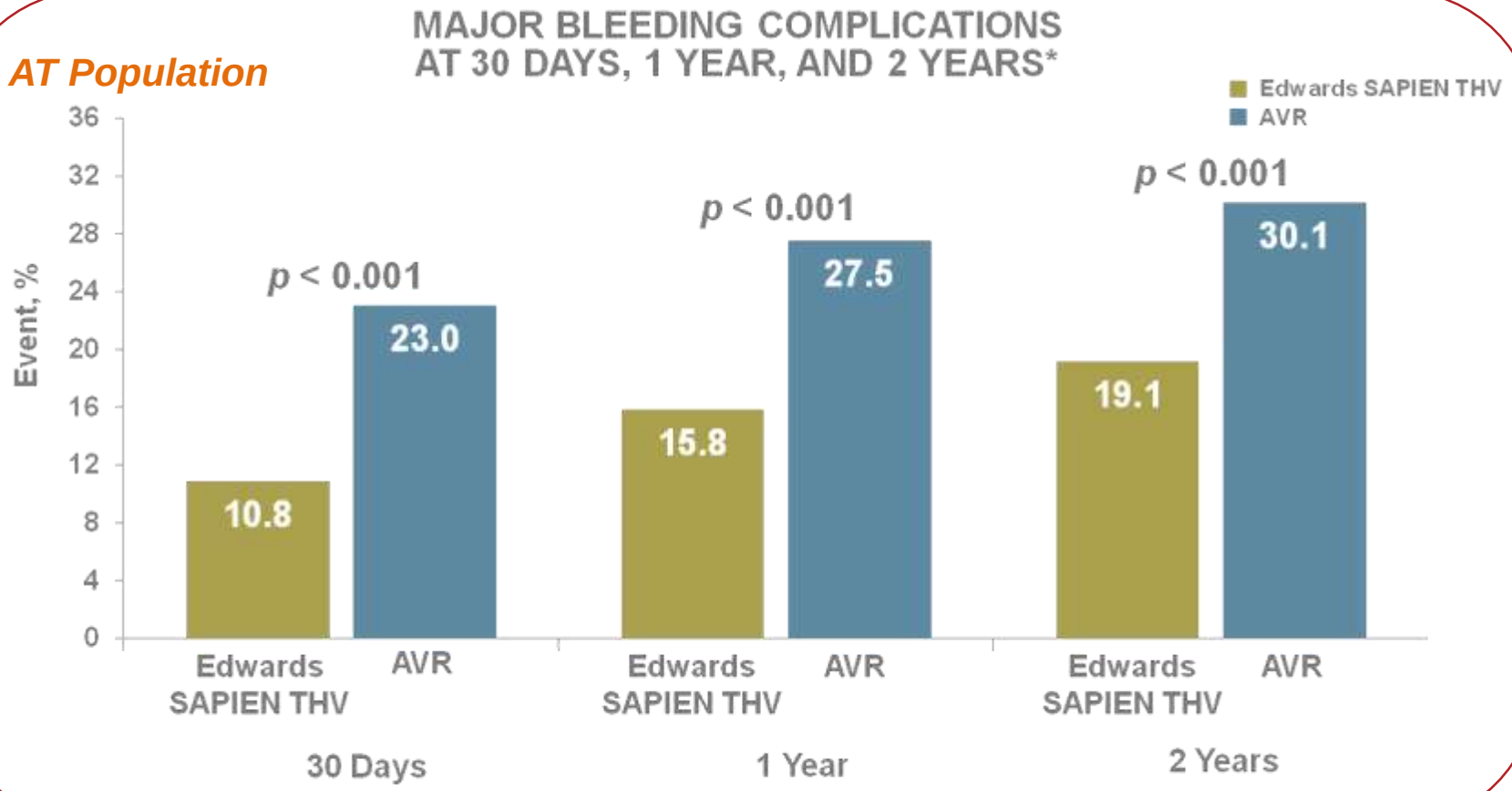


Kaplan-Meier estimates.

THE PARTNER TRIAL COHORT A

Major Bleeding

AT Population



Kaplan-Meier estimates. *Major bleeding is defined as any episode of major internal or external bleeding that caused death, hospitalization or permanent injury (e.g., vision loss) or necessitated transfusion of greater than 3 units PRBCs within a 24-hour period, pericardiocentesis, open and/or endovascular procedure for repair or hemostasis.

THE PARTNER TRIAL COHORT A

Treatment for High Risk Surgical Patients

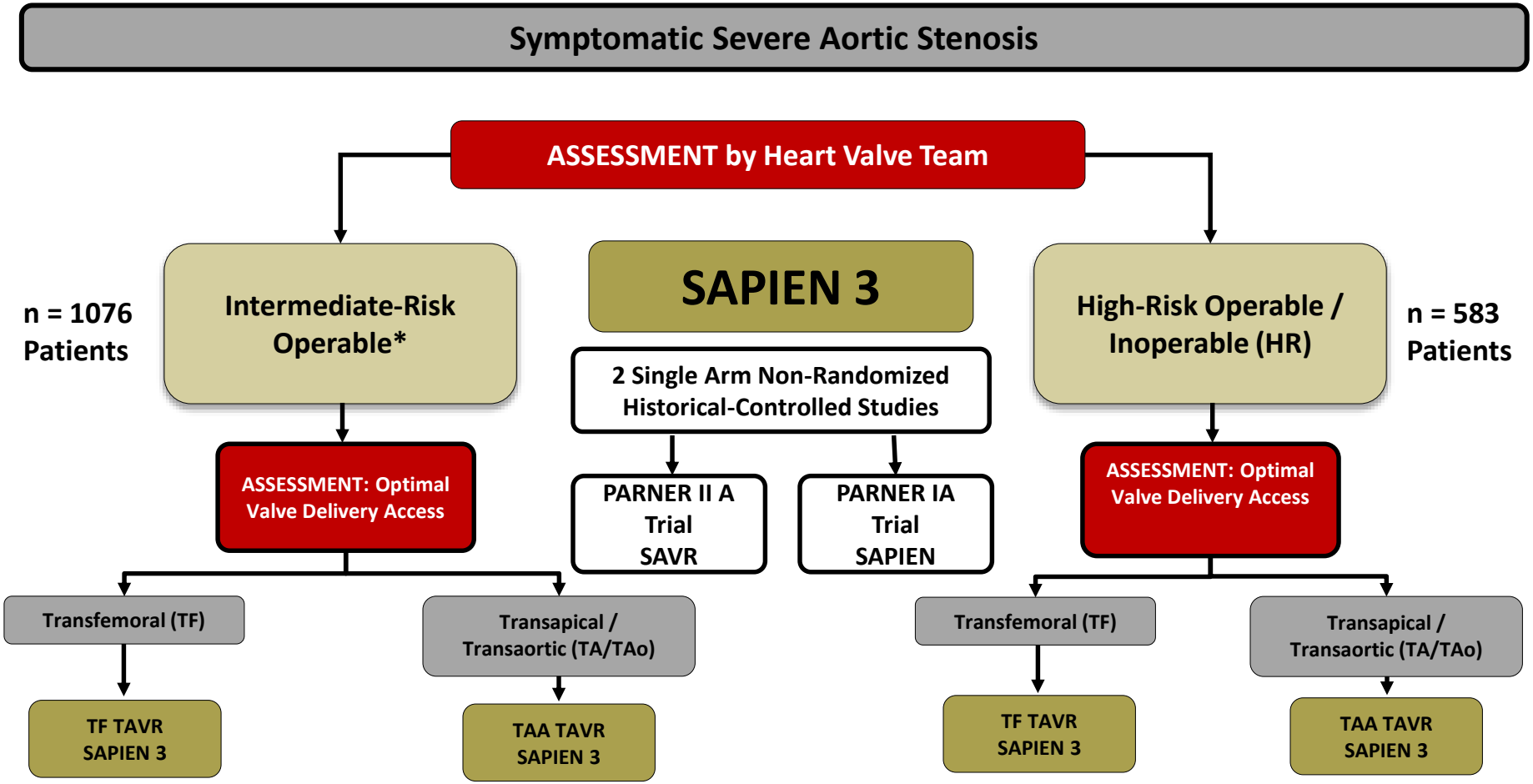
October 19, 2012

FDA Approves The Sapien Transcatheter Heart Valve For High Risk Patients [1]

by Larry Husten • Interventional Cardiology & Surgery • Tags: Sapien, TAVI, TAVR, transcatheter aortic valve replacement

The FDA today approved an expanded indication for Edwards Lifesciences' Sapien transcatheter heart valve (THV). The device can now be implanted in patients who are eligible for aortic valve replacement surgery but at high risk for serious surgical complications or death. Previously the Sapien valve was approved only for use in patients who were not eligible for surgery.

The PARTNER II Trial with the SAPIEN 3 Valve
Study Design



*The SAPIEN 3 valve is only indicated for patients at high or greater risk.

Clinical Outcomes Improve as Therapy Evolves

Low Mortality and Stroke Rates
Patient selection, procedural techniques, device evolution

RetroFlex 3
Delivery System

NovaFlex+
Delivery System

Edwards Commander
Delivery System

Improved Vascular Access
Lower profile devices expands treatment possibilities

RetroFlex 3
Introducer Sheath

Edwards eSheath
Introducer Set

Edwards eSheath
Introducer Set*

Increased Treatment Range
Larger and smaller valves

SAPIEN Valve
23 and 26 mm

SAPIEN XT Valve
23, 26, 29 mm

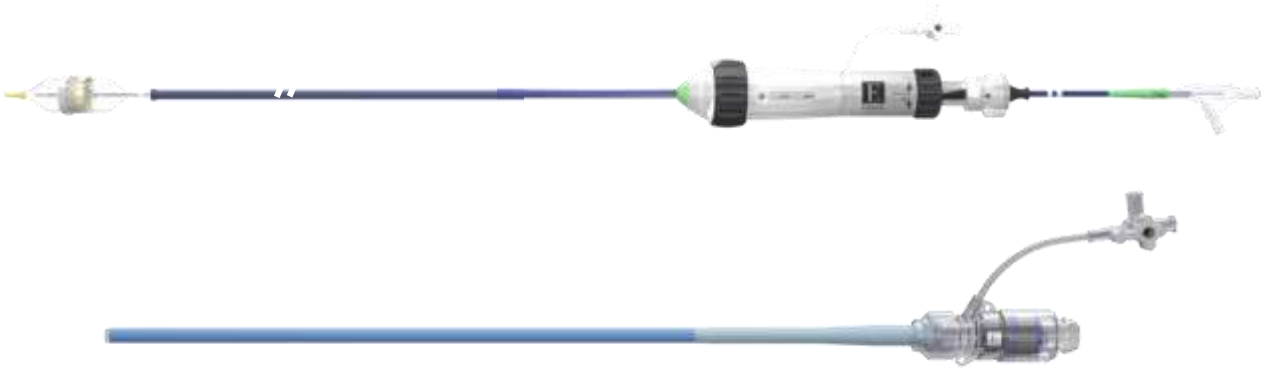
SAPIEN 3 Valve
20, 23, 26, 29 mm

*only used with 20,23,26 valve sizes

Low Profile Demonstrates > 50% Reduction in Major Vascular Complications*

Low Profile 14F / 16F eSheath Introducer Sheath Compatible

SAPIEN 3



SAPIEN 3 Valve Size	20 mm	23 mm	26 mm	29 mm
Edwards eSheath Introducer Set	14F	14F	14F	16F
Minimum Access Vessel Diameter	5.5 mm	5.5 mm	5.5 mm	6.0 mm

*PARTNER II Trial high-risk TF SAPIEN 3 valve cohort (VARC II) versus SAPIEN XT valve cohort (VARC I) 30-day results.

Baseline Patient Characteristics

SAPIEN 3 Valve HR Patients

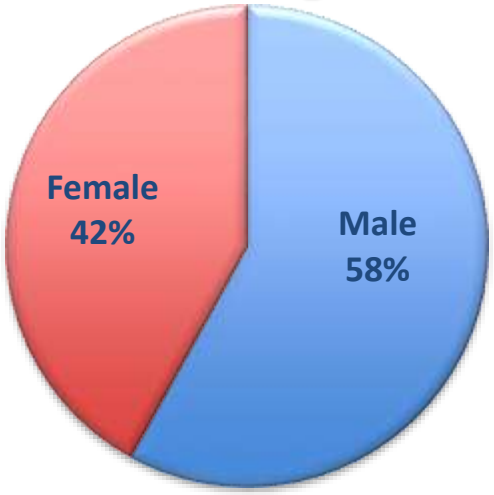
Average STS =

8.6%

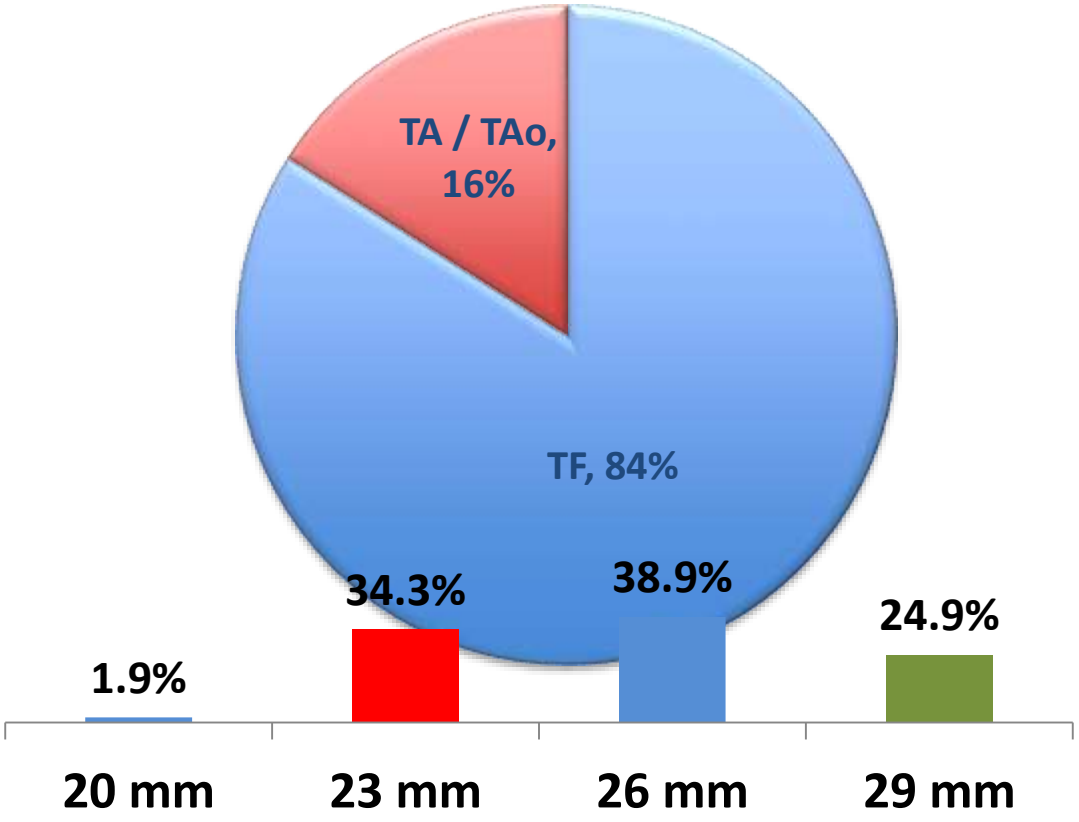
(Median 8.4%)

Average Age =

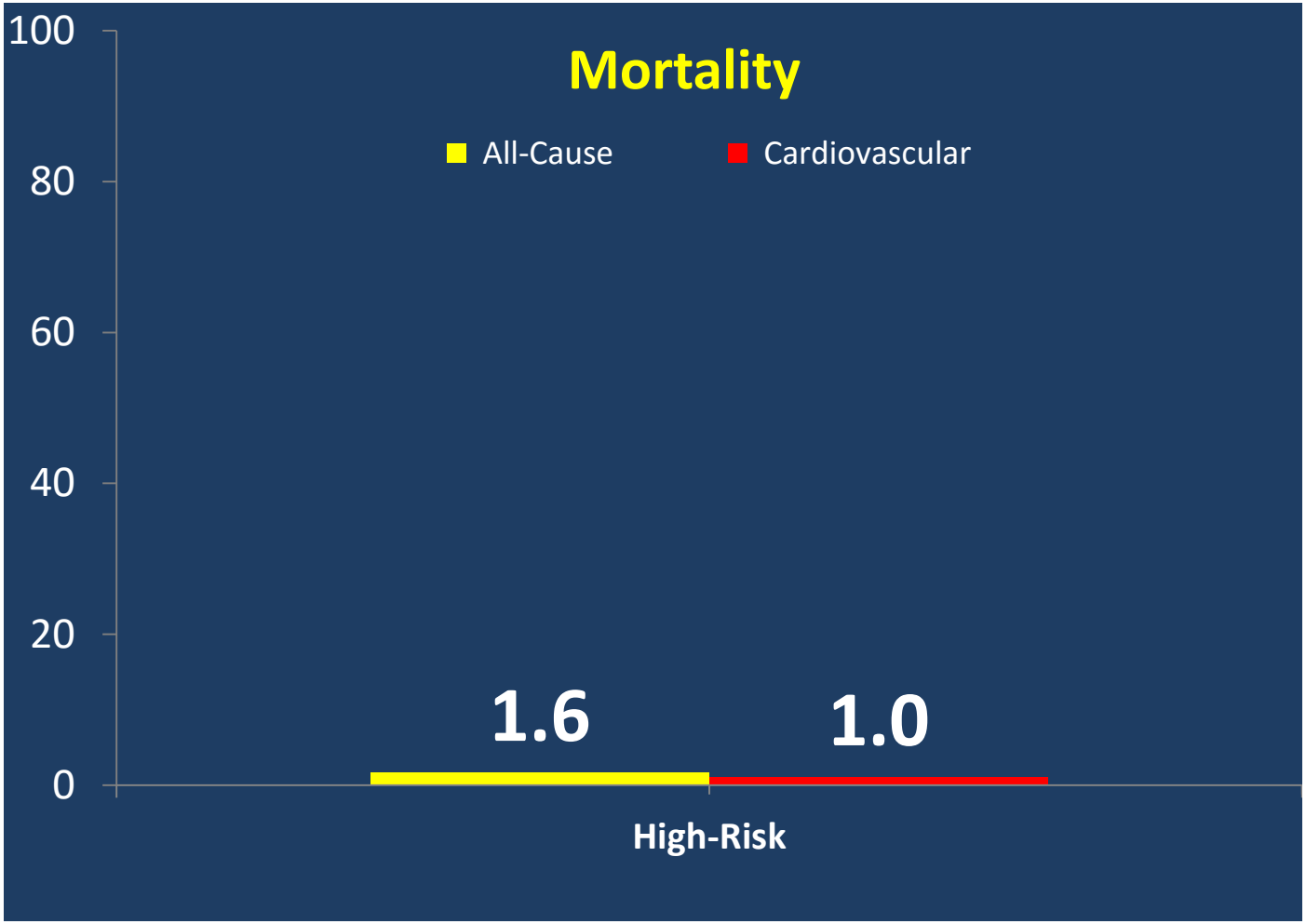
82.6yrs



N = 583

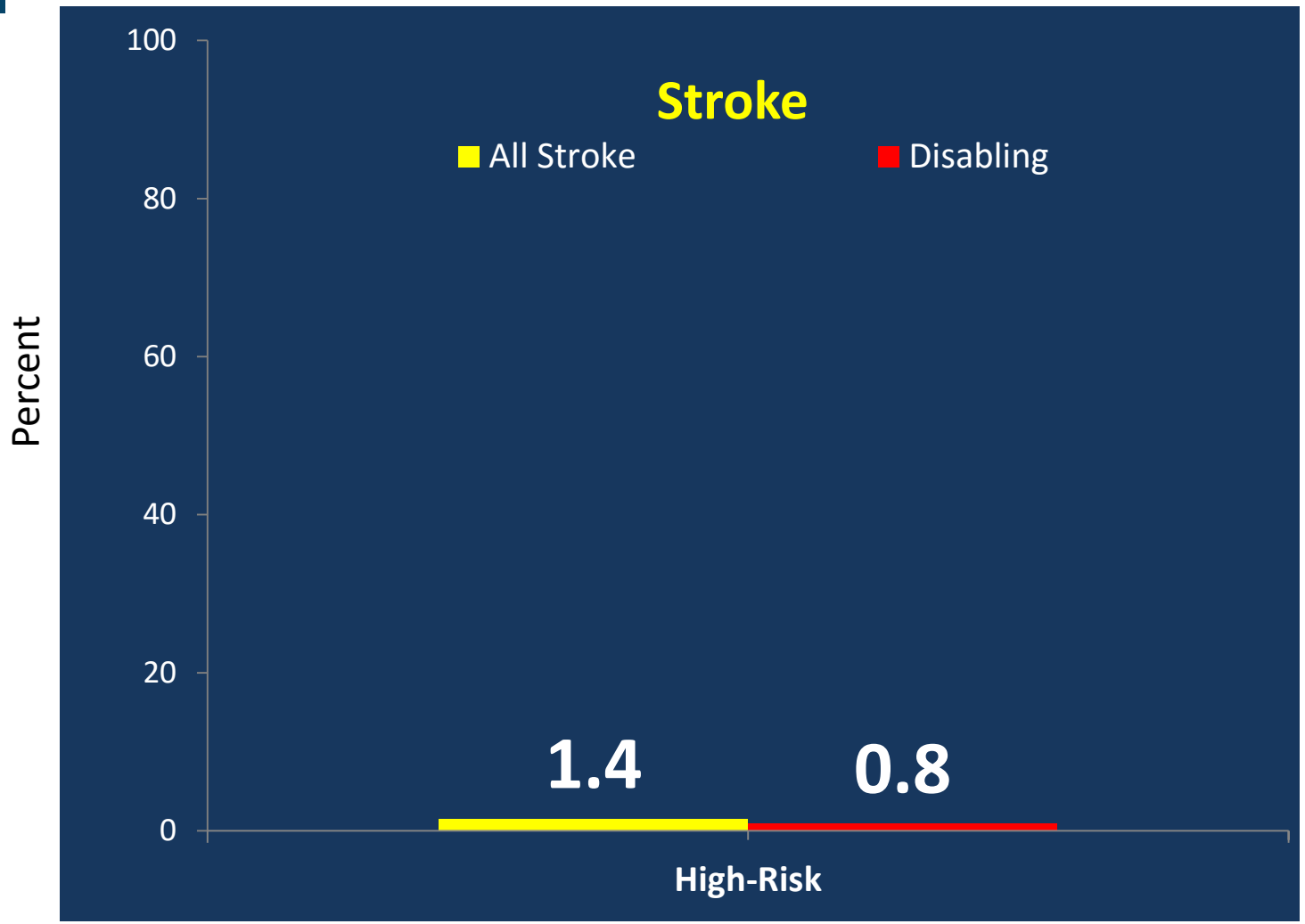


Mortality at 30 Days (As Treated Patients)



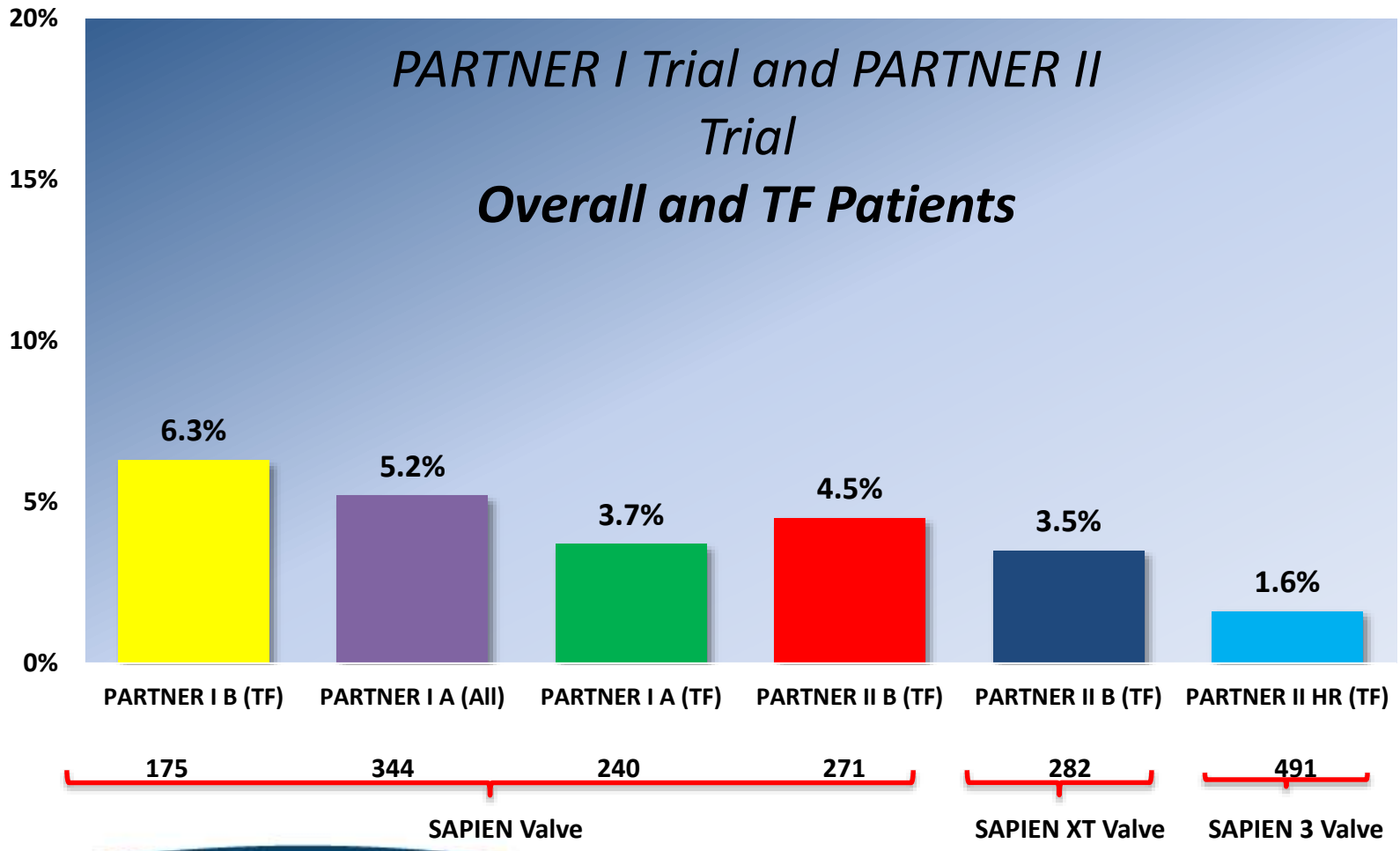
Transfemoral n=491

Stroke at 30 Days (As Treated Patients)

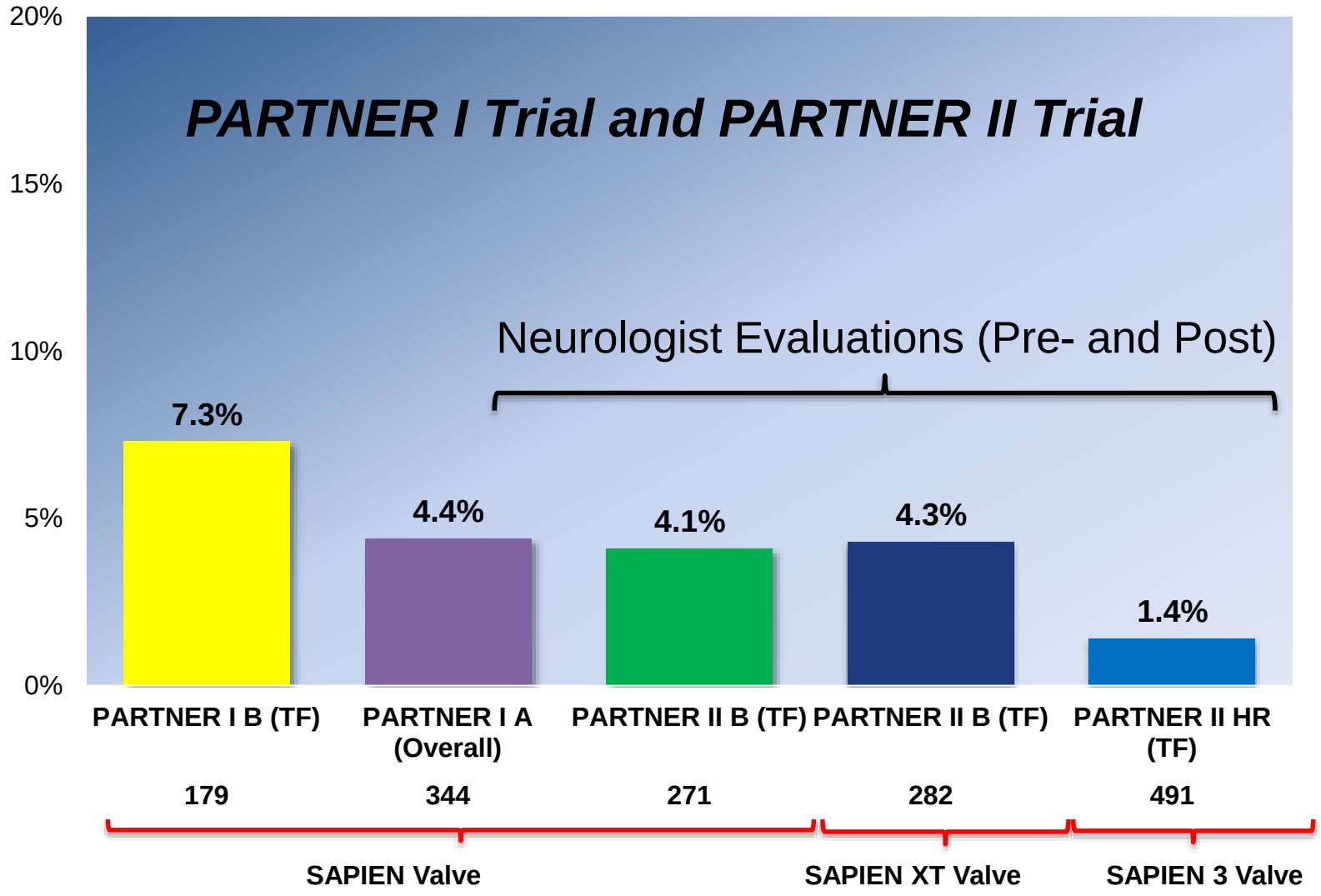


Transfemoral n=491

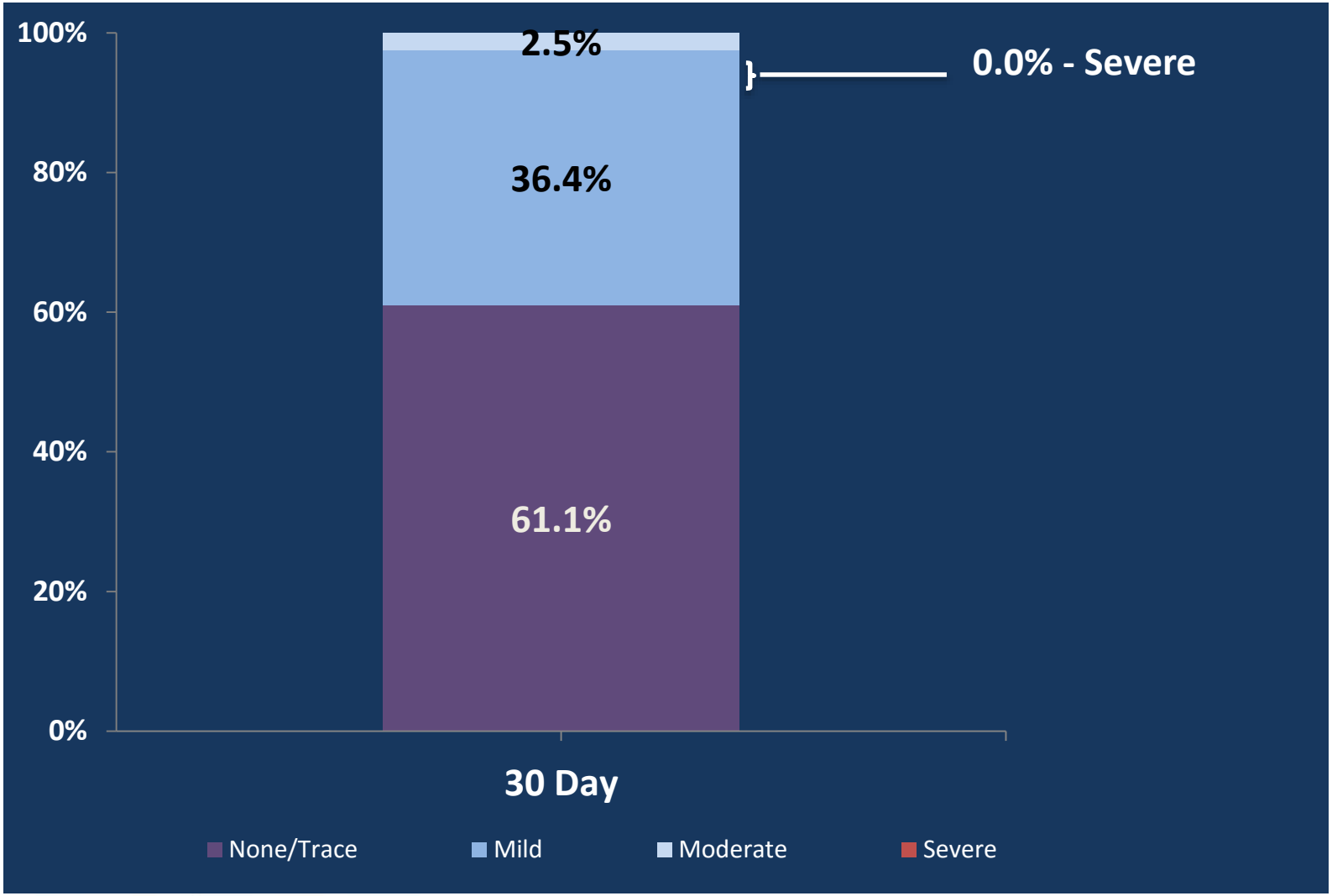
All-Cause Mortality at 30 Days
(As Treated Patients)



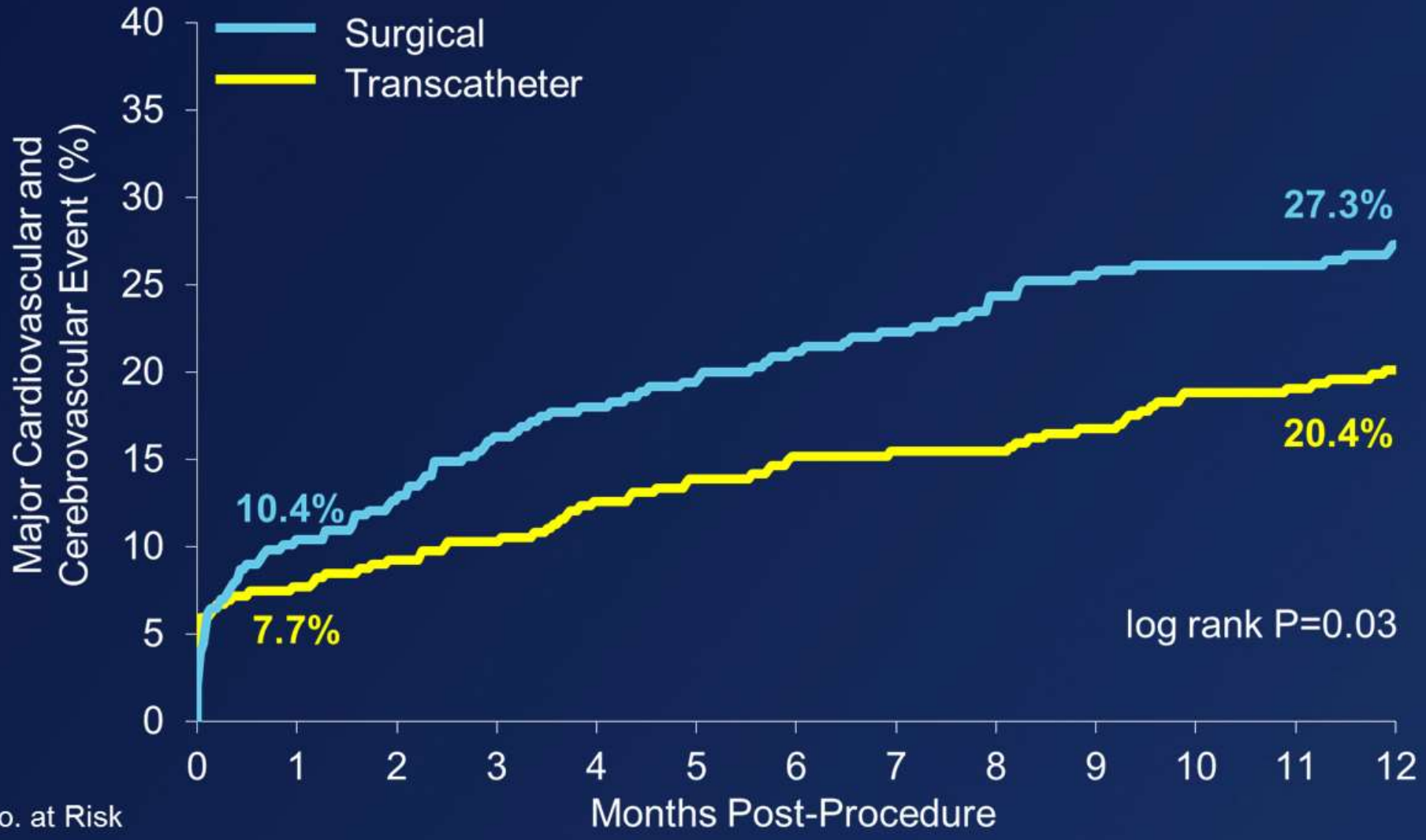
All Strokes at 30 Days



Paravalvular Leak
(At 30 Days - Transfemoral Cohort)



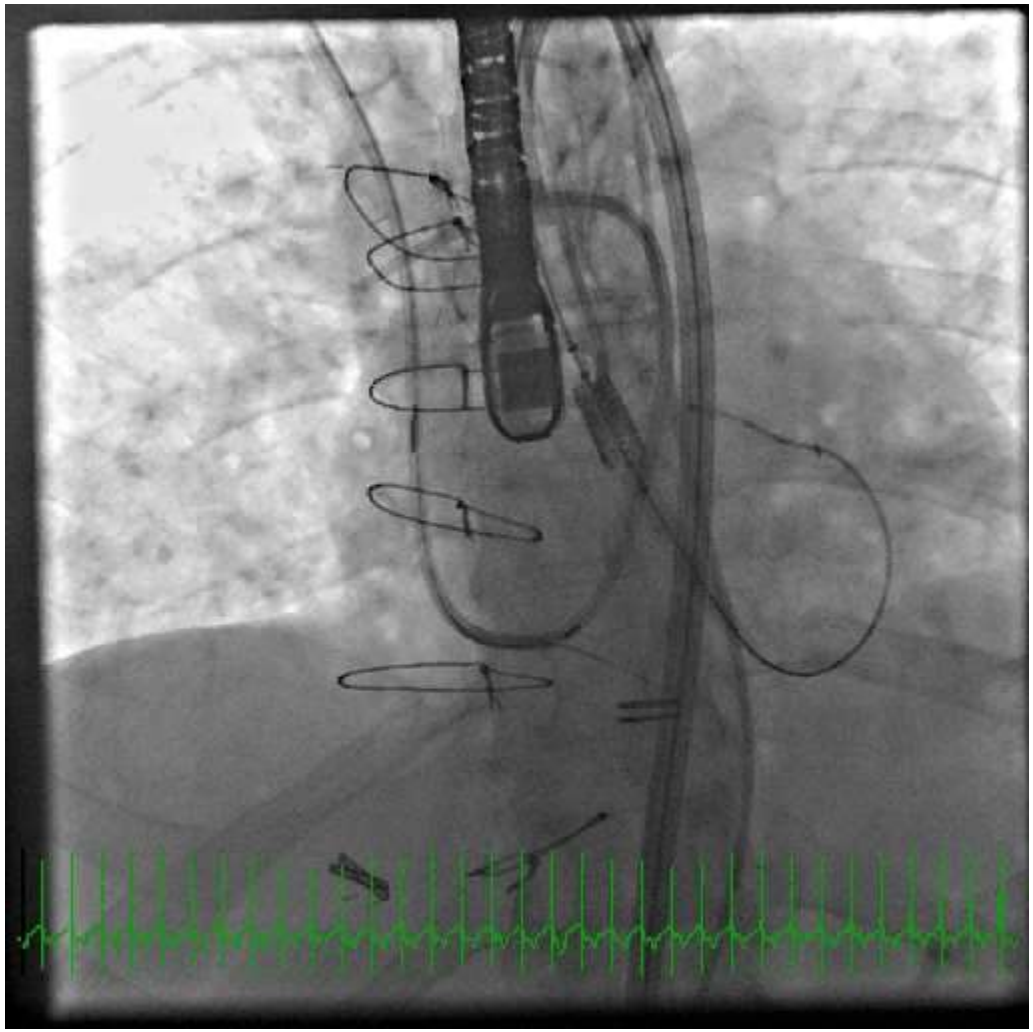
1 Year MACCE


Surgical
Transcatheter
Major Cardiovascular and Cerebrovascular Event (%)
40
35
30
25
20
15
10
5
0
27.3%
20.4%
10.4%
7.7%
log rank P=0.03
0
1
2
3
4
5
6
7
8
9
10
11
12
Months Post-Procedure
No. at Risk
Surgical 357 320 273 247
Transcatheter 390 360 329 306

CoreValve Evolut R

- 14F Delivery system
- Nitinol self expanding valve
- Full recapture is possible
- Ease of use
- Initial valve in valve indication
- Larger annular sizes

Transfemoral TAVR

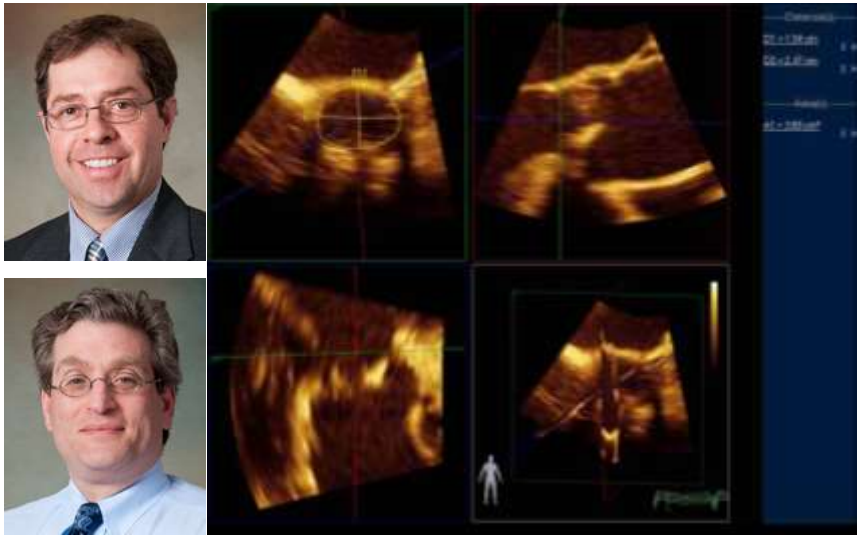


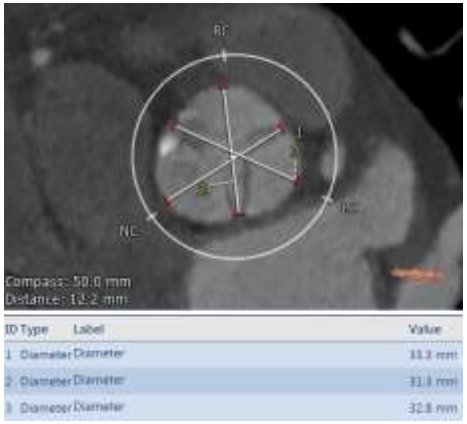
Development of the Transcatheter Aortic Valve Replacement Program at Southcoast Health

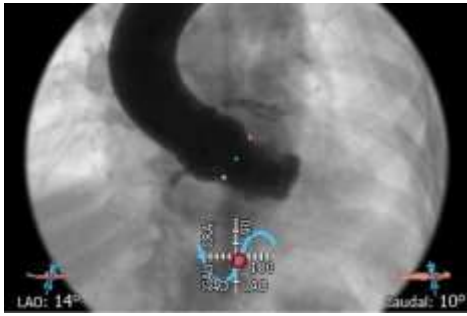
The Surgical Program at Southcoast

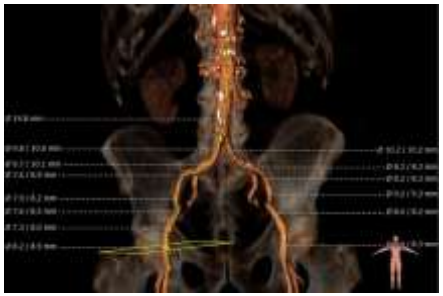
- Since joining Southcoast in 2012 Dr. James Fingleton has performed over 50 mitral valve repairs.
- Average 20/yr which is an important marker
- Dr. Iraklis Gerogiannis and Dr. Fingleton have performed several complex aorta surgeries (valve sparing root, Bentall, aneurysm, dissections)
- Over 60 minimally invasive aortic valve replacements

Valve Imaging Program









- Through the tremendous efforts of Dr. Abadi and Dr. Schneider we have a superb advanced valve imaging program- <u>invasive echocardiography</u>
- Dr. John Mungovan, chief of radiology and Liz Przeszlo we have excellent CT imaging

The Heart Valve Team at Southcoast

The Goal of the Southcoast Valve Clinic

- To provide a comprehensive evaluation by the cardiologists and cardiac surgeon.
- Provide an expeditious and coordinated evaluation (CT, echo, etc.).
- Offer the best path to a diverse range of therapies: traditional surgery, minimally invasive surgery, transcatheter valve therapy, or balloon valvuloplasty. . .decided upon by a multidisciplinary team
- Provide clear and accessible follow up communication with the referring physician.

Southcoast Future Direction

- A shift towards more trans-femoral access = quicker recovery
- Percutaneous access
- Conscious sedation
- Shorter Hospitalizations
- A “paired down” TAVR procedure and work up?
- Reduced costs of product
- Diversify Procedures

A NEW SPACE!!!!!

Conclusion

- Severe symptomatic aortic stenosis is common.
- Symptoms can be subtle, but when present and assoc with comorbities = poor prognosis.
- TAVR has emerged as a viable treatment approach in high risk surgical patients ?moderate.
- The TAVR program has had tremendous results here at Southcoast.

Thank You