TAVI: Radical and Revolutionary:

Impact of TAVI in Low Risk Patients

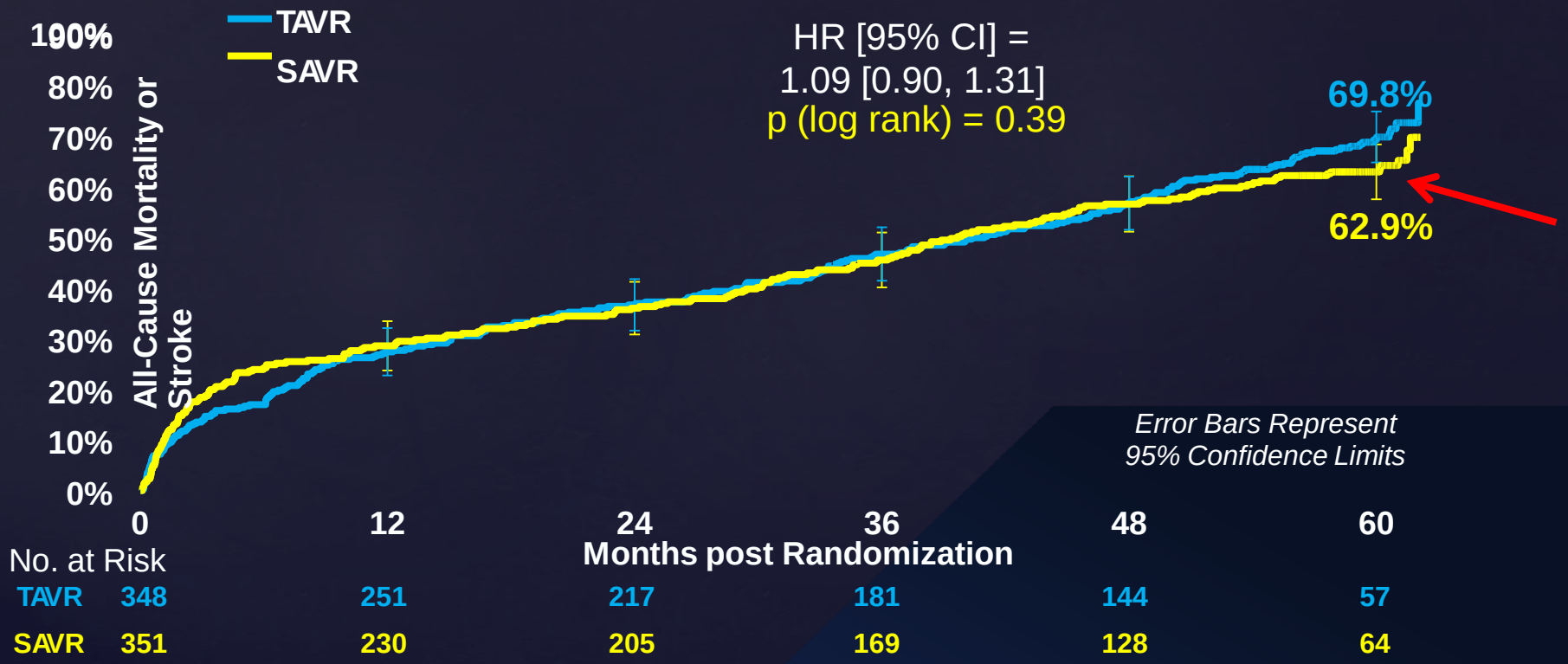
Joseph E. Bavaria, MD
Roberts-Measey Professor of Surgery
Vice Chair, Division of Cardiovascular Surgery
University of Pennsylvania Medical Center
Philadelphia, PA
President-Society of Thoracic Surgeons (STS)

NYC ACC December 2016

High Risk for Surgical AVR Patients
STS score > 8

All-Cause Mortality or Stroke (ITT)

All Patients 5-yr



No. at Risk

TAVR	348	251	217	181	144	57
SAVR	351	230	205	169	128	64

PARTNER Cohort A

1-Year outcomes published on-line June 5, 2011 @ NEJM.org and in print June 9, 2011

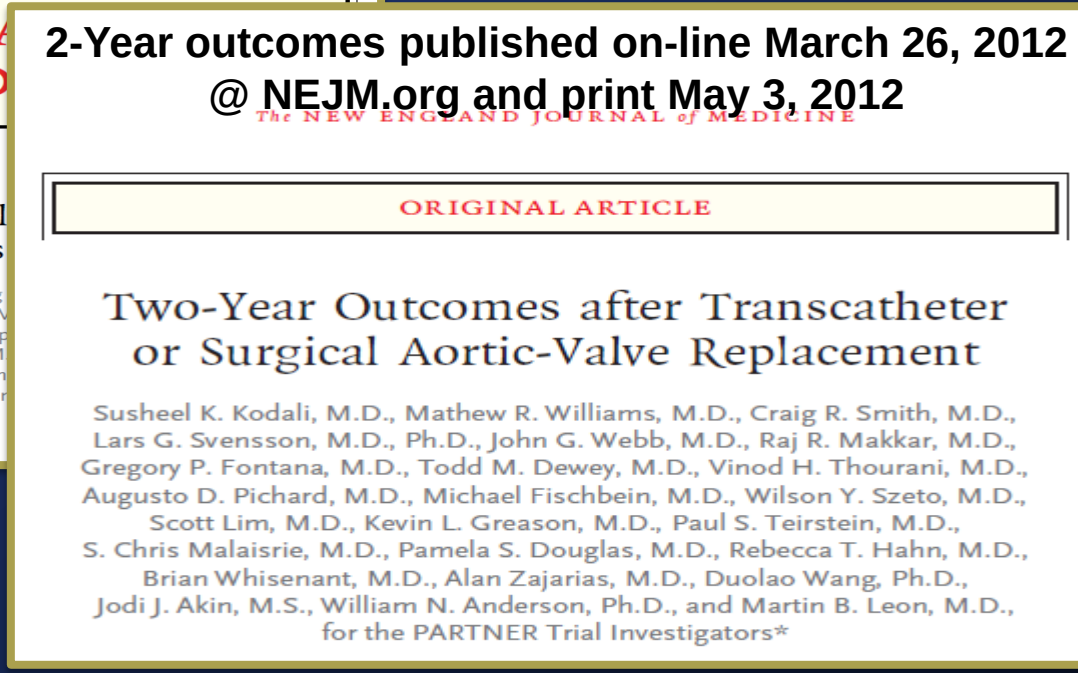
The NEW ENGLA
JOURNAL of MED

ESTABLISHED IN 1812 JUNE 9, 2011

Transcatheter and Surgical Aortic-Val
in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig
Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M
Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kap
Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M
Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson
and Stuart J. Pocock, Ph.D., for the PARTNER Trial In

2-Year outcomes published on-line March 26, 2012 @ NEJM.org and print May 3, 2012



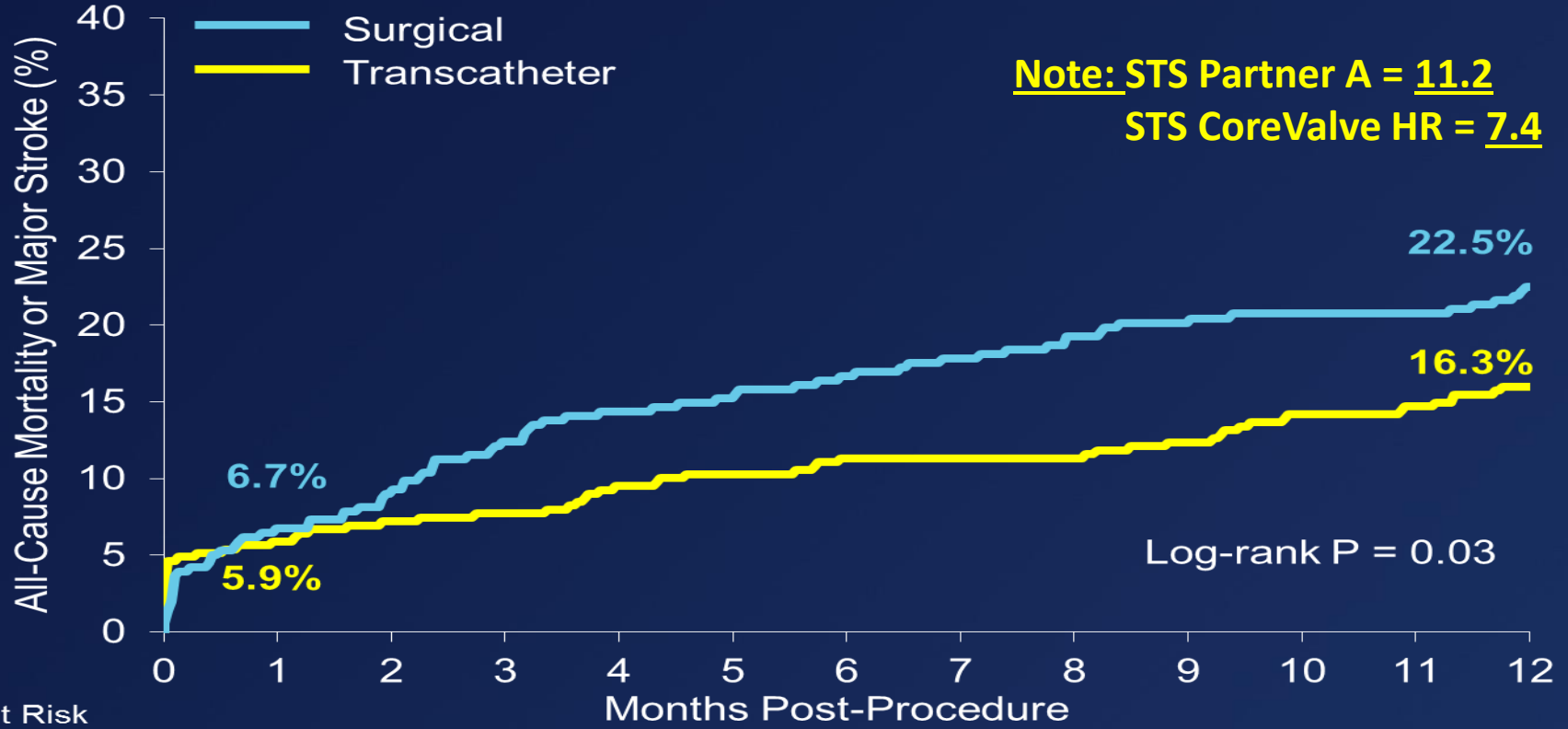
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

Susheel K. Kodali, M.D., Mathew R. Williams, M.D., Craig R. Smith, M.D., Lars G. Svensson, M.D., Ph.D., John G. Webb, M.D., Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Todd M. Dewey, M.D., Vinod H. Thourani, M.D., Augusto D. Pichard, M.D., Michael Fischbein, M.D., Wilson Y. Szeto, M.D., Scott Lim, M.D., Kevin L. Greason, M.D., Paul S. Teirstein, M.D., S. Chris Malaisrie, M.D., Pamela S. Douglas, M.D., Rebecca T. Hahn, M.D., Brian Whisenant, M.D., Alan Zajarias, M.D., Duolao Wang, Ph.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

All-Cause Mortality or Major Stroke



Note: STS Partner A = 11.2
STS CoreValve HR = 7.4

No. at Risk					
Surgical	357	333	289		263
Transcatheter	390	367	344		322

So …… Why a New TAVI trial into **INTERMEDIATE RISK** patients??

THE PARTNER TRIAL

THE PARTNER TRIAL

For all the Reasons explained …. The High Risk trials all showed equivalence to AVR. It is the next logical step

So the Real Question is ……. Why **NOT** a New TAVI trial into **INTERMEDIATE RISK** patients??

THE PARTNER TRIAL

- Surgical AVR vs TAVI

Results of Partner 2 Randomized Clinical Trial in Intermediate Risk patients (STS = 4-8)

No Difference!!

- Presented at ACC April 2016

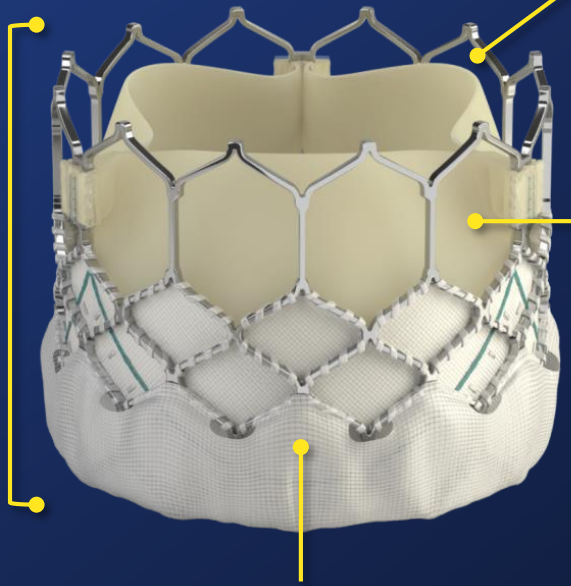
Intermediate Risk Patients
STS score > 3-4 to 8

Also, We have "New Stuff"

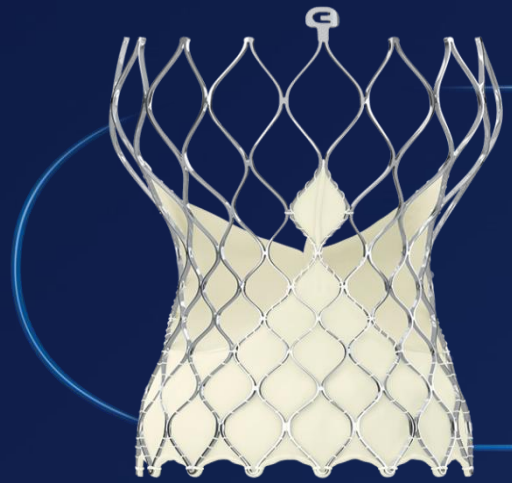
SAPIEN 3 Transcatheter Heart Valve

Distinguishing Features

THE PARTNER II TRIAL



CoreValve Evolut R System



Transcatheter Valve

Supra-annular design, optimized sealing

Catheter Delivery System

14Fr-equivalent profile

Loading System

Clinical and Echocardiographic Outcomes at 30 Days with the SAPIEN 3 TAVR System in Inoperable, High-Risk and Intermediate-Risk AS Patients

Susheel Kodali, MD
on behalf of The PARTNER Trial Investigators

ACC 2015 | San Diego | March 15, 2015

THE PARTNER II TRIAL

The PARTNER II S3 Trial: S3HR & S3i

Top 10 Enrollment Sites

THE PARTNER II TRIAL

S3HR

Cedars-Sinai Medical Ctr. Los Angeles, CA	73
Columbia University Medical Ctr. New York, NY	65
Emory University Atlanta, GA	63
University of Pennsylvania Philadelphia, PA	43
Heart Hospital Baylor Plano Plano, TX	30
Ochsner Hospital New Orleans, LA	26
University of Texas, Houston Houston, TX	25
Stanford University Medical Ctr.	24

S3i

Cedars-Sinai Medical Ctr. Los Angeles, CA	106
University of Pennsylvania Philadelphia, PA	66
Emory University Atlanta, GA	62
University of Texas, Houston Houston, TX	52
Columbia University Medical Ctr. New York, NY	48
Heart Hospital Baylor Plano Plano, TX	46
Cleveland Clinic Foundation Cleveland, OH	41
Newark Beth Israel Medical Ctr.	38

Baseline Patient Characteristics

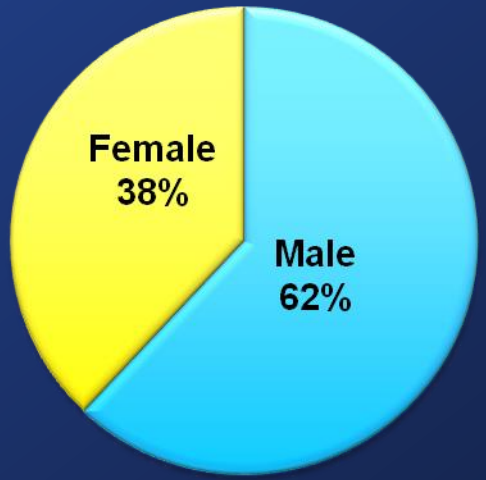
S3i Patients (Intermediate Risk STS 4-8)

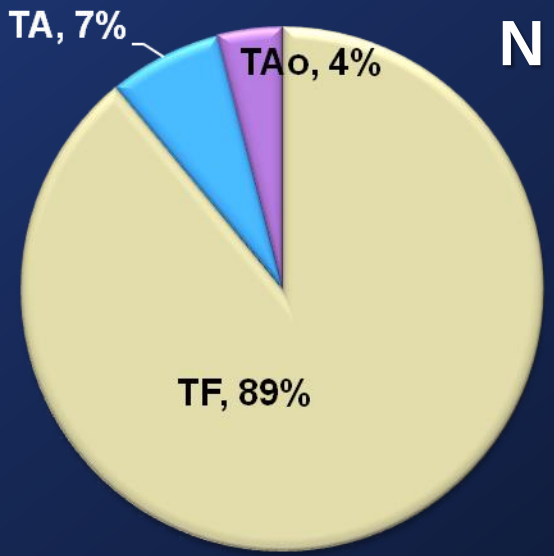
THE PARTNER II TRIAL

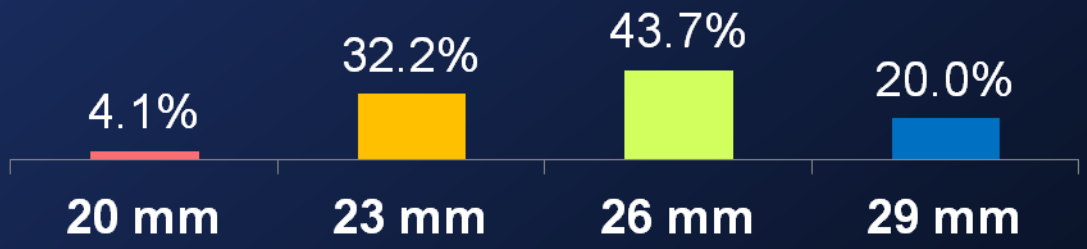
Average STS = **5.3%** (Median 5.2%)

Average Age = **81.9yrs**

N = 1076

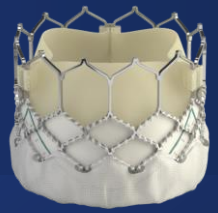






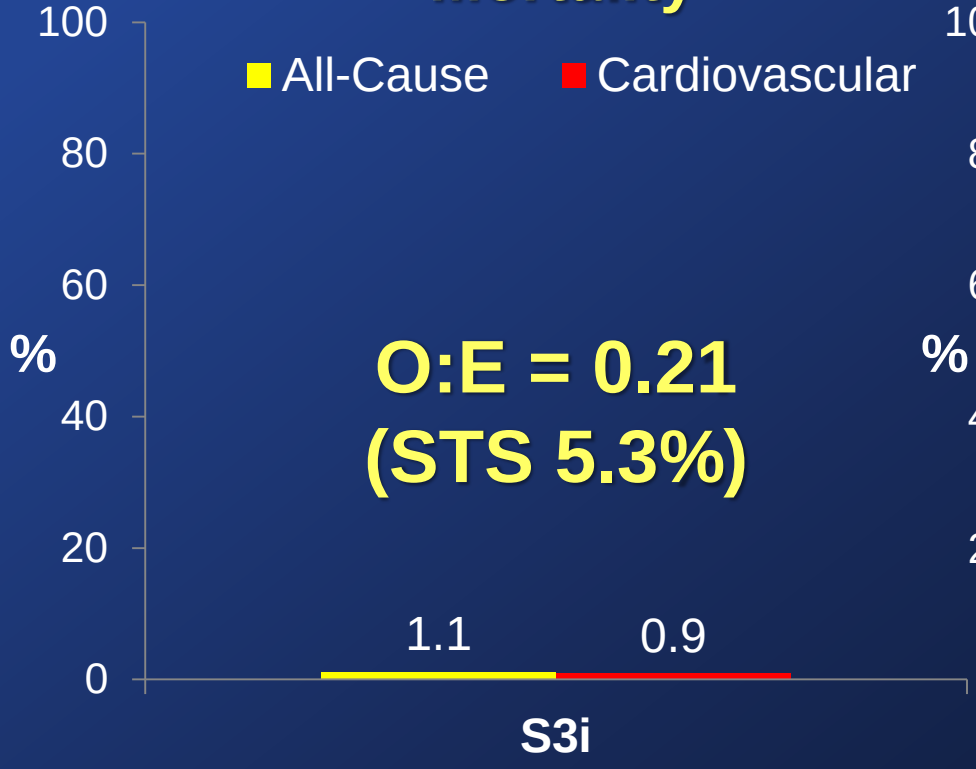
Mortality and Stroke: S3i

At 30 Days (As Treated Patients)

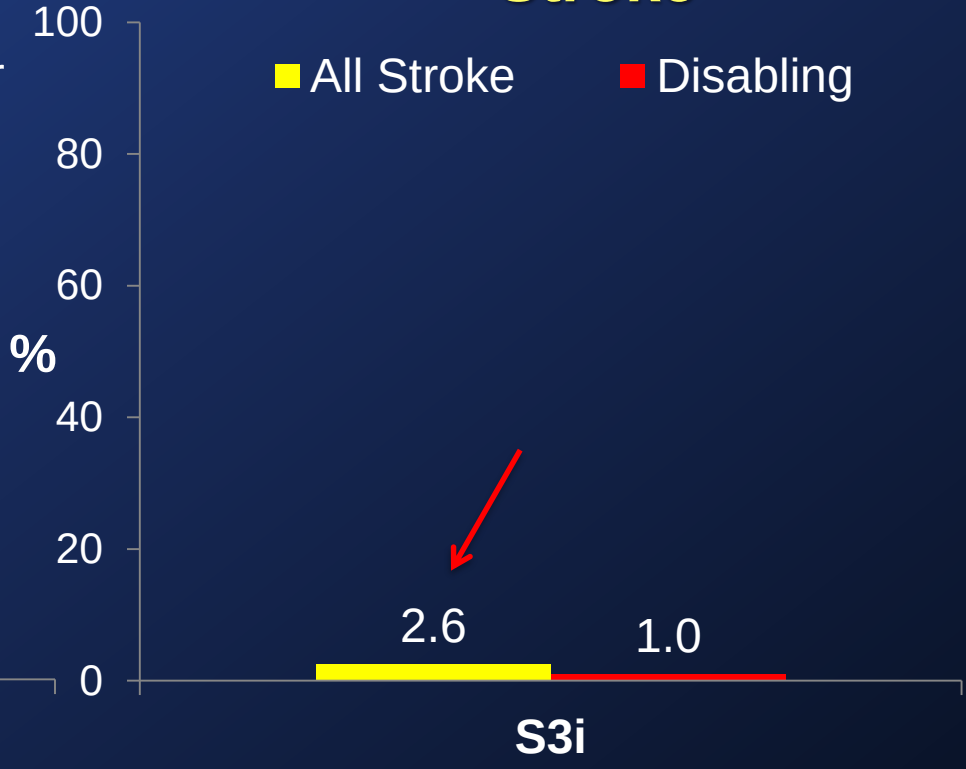


THE PARTNER II TRIAL

Mortality

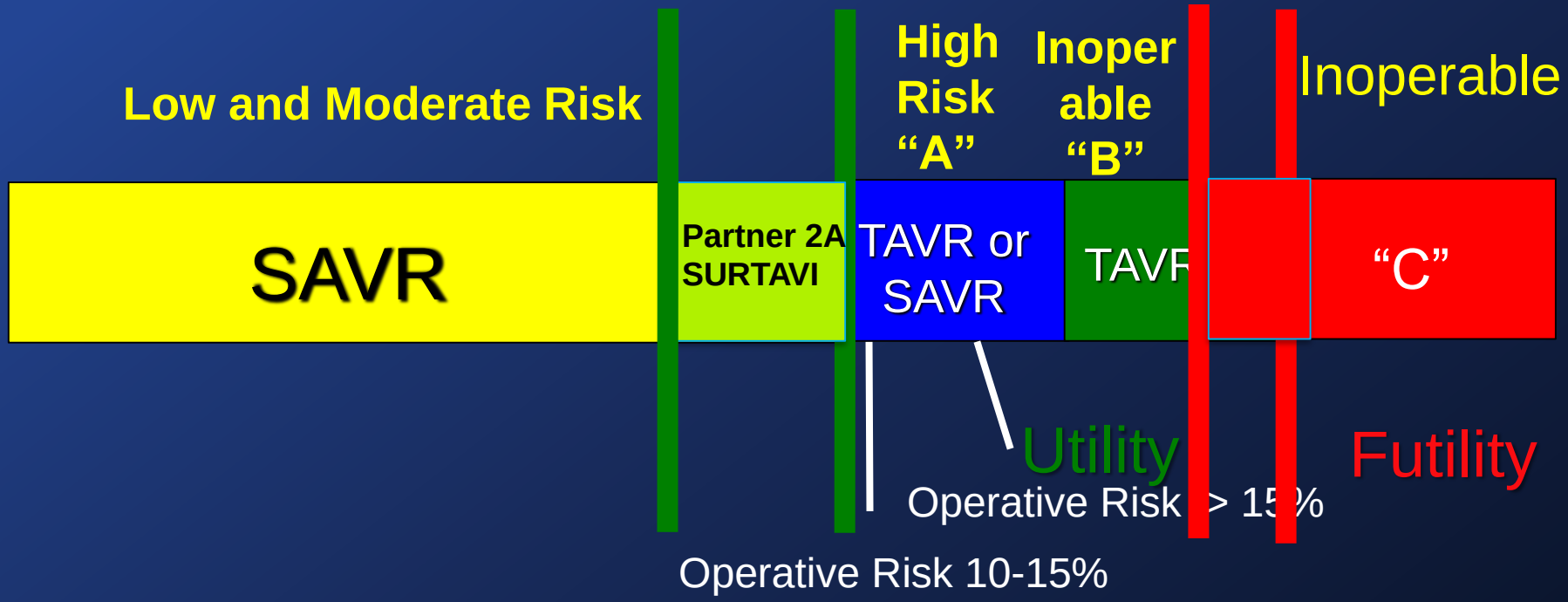


Stroke



Just Happened: Treatment of Aortic Stenosis

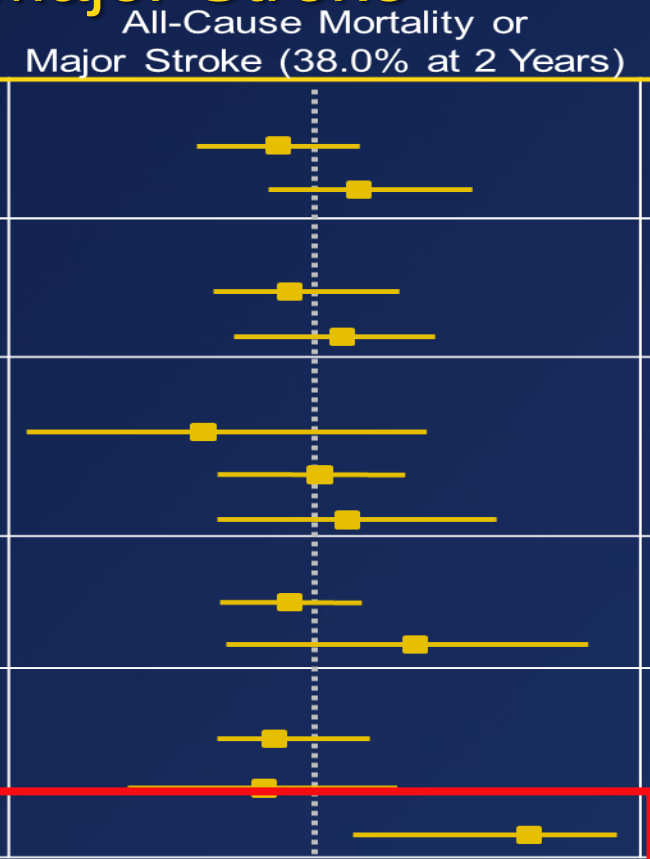
THE PARTNER II TRIAL



Adapted from S. Kodali and M. Leon

Subgroup Analysis
2-Year All-Cause Mortality or Major Stroke

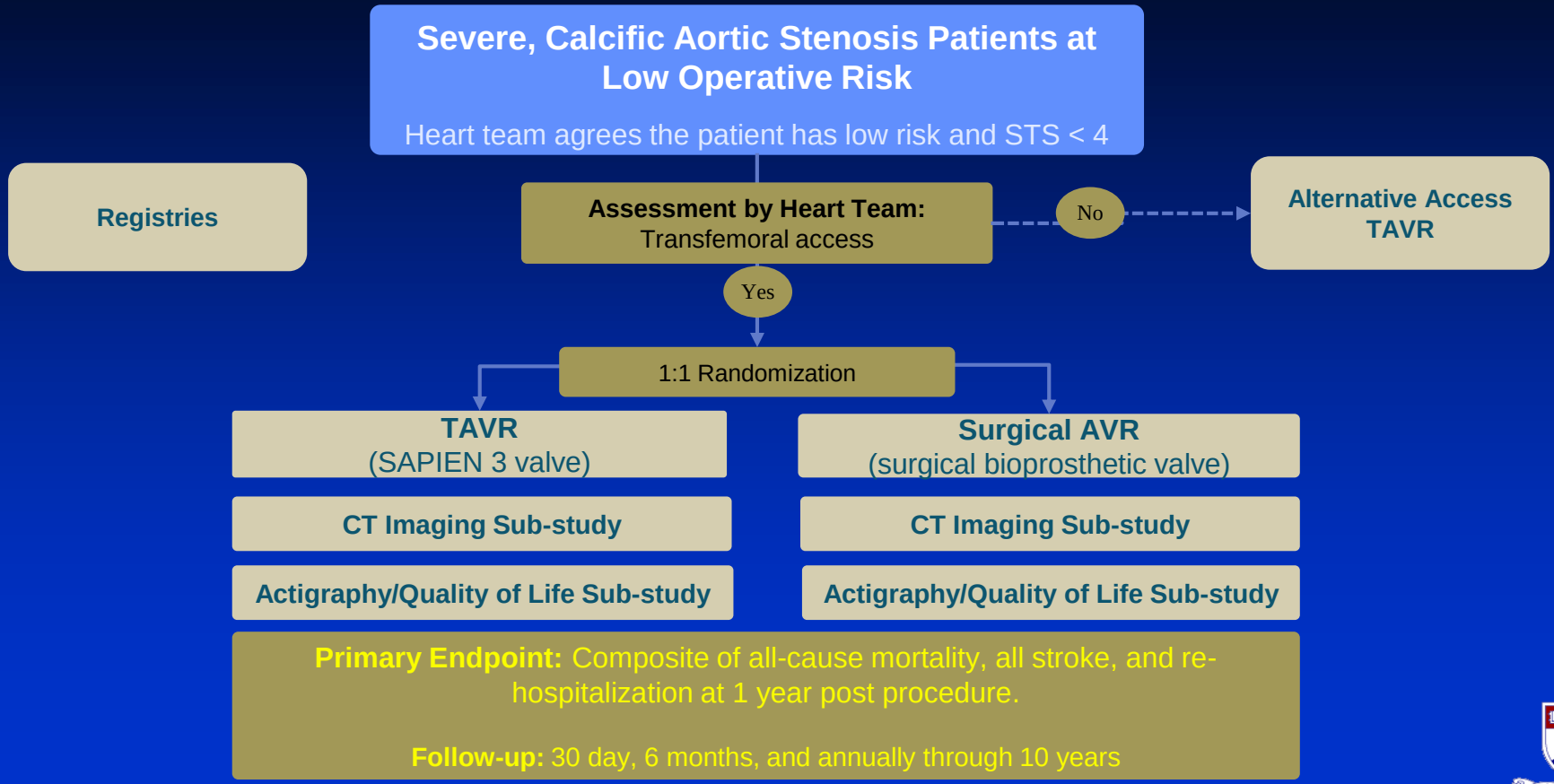
	Patients	KM (%) 2-Yr (95% CI)	P Value
Gender			0.1809
Female	255	35.1 (29.2, 41.0)	
Male	234	41.0 (34.7, 47.4)	
Age			0.4647
≤85	263	36.9 (31.0, 42.8)	
>85	226	39.2 (32.8, 45.7)	
NYHA			
II	40	30.3 (15.9, 44.6)	
III	313	38.1 (32.7, 43.6)	0.3805
IV	136	39.9 (31.7, 48.2)	0.3282
LVEF			0.1706
≥40%	404	36.8 (32.0, 41.5)	
<40%	83	43.6 (32.9, 54.3)	
STS Score			
<10%	272	35.8 (30.1, 41.6)	
10-15%	133	34.4 (26.2, 42.5)	0.8008
>15%	84	50.7 (39.9, 61.5)	0.0120



So NOW the Real Question is ……. Why **NOT** a New TAVI trial into **LOW RISK** patients??

THE PARTNER TRIAL

The PARTNER 3 Trial Study Design

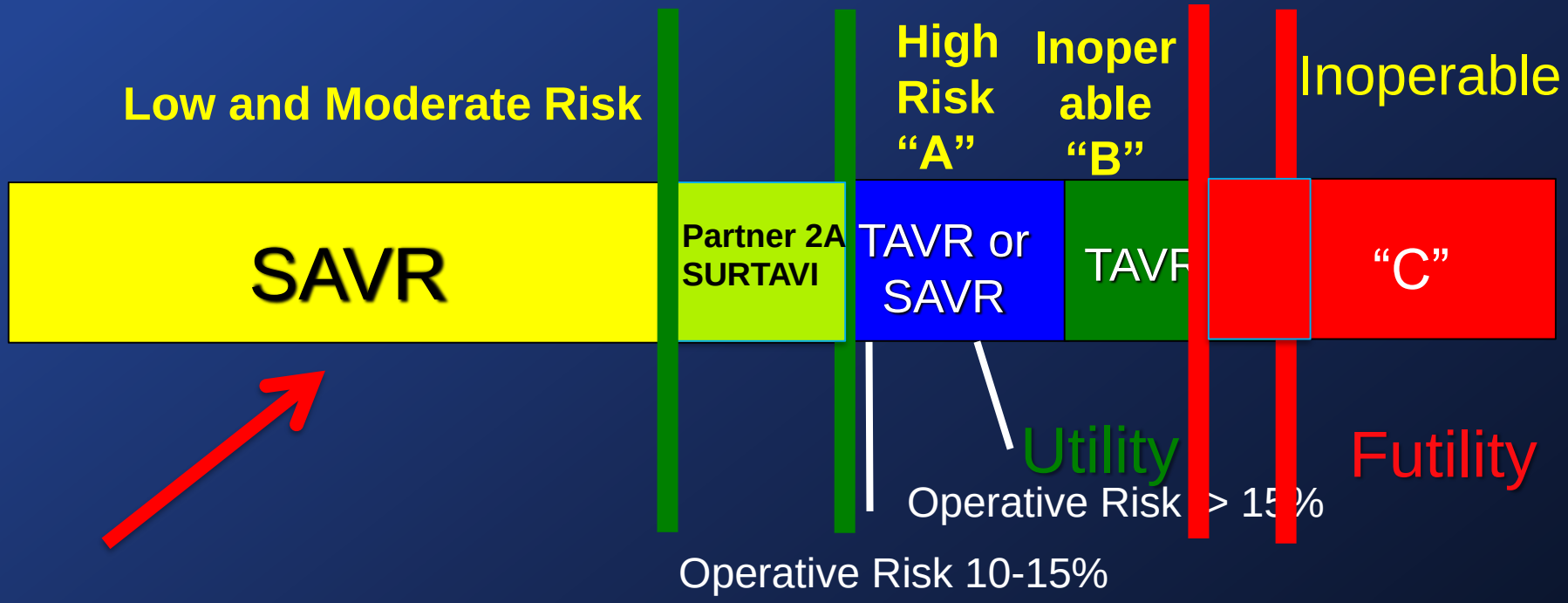


Some Key Exclusion Criteria in the FDA Trials

- Iliofemoral vessel characteristics that would preclude safe passage of the introducer sheath
- Evidence of an acute myocardial infarction ≤ 1 month (30 days) before randomization
- Aortic valve is unicuspid, bicuspid, or non-calcified
- Severe aortic regurgitation (>3+)
- Severe mitral regurgitation (>3+) or ≥ moderate stenosis
- Complex coronary artery disease:
  - Unprotected left main coronary artery
  - Syntax score > 32 (in the absence of prior revascularization)
  - Heart Team assessment that optimal revascularization cannot be performed
- Symptomatic carotid or vertebral artery disease or successful treatment of carotid stenosis within 30 days of randomization
- Leukopenia (WBC < 3000 cell/mL), anemia (Hgb < 9 g/dL), Thrombocytopenia (Plt < 50,000 cell/mL), history of bleeding diathesis or coagulopathy, or hypercoagulable states
- Hemodynamic or respiratory instability requiring inotropic support, mechanical ventilation or mechanical heart assistance within 30 days of randomization
- Hypertrophic cardiomyopathy with obstruction (HOCM)
- Ventricular dysfunction with LVEF < 30%

The Near Future: Treatment of Aortic Stenosis

THE PARTNER II TRIAL

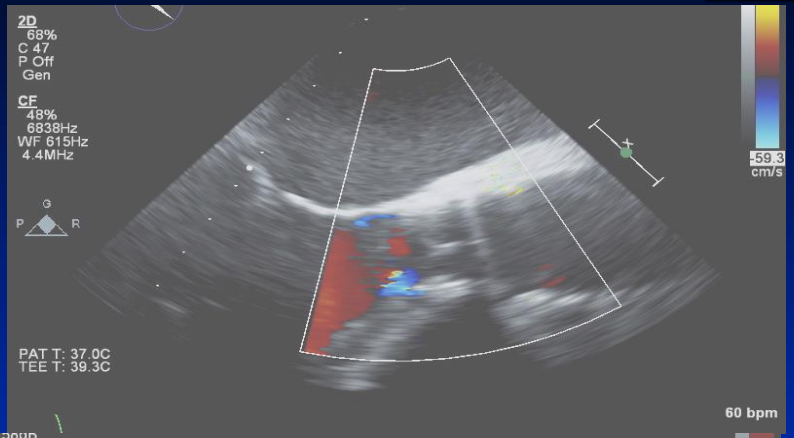


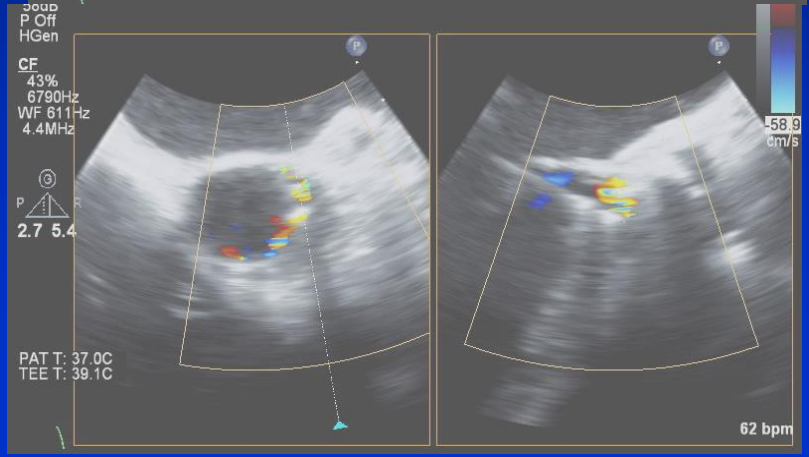
Adapted from S. Kodali and M. Leon

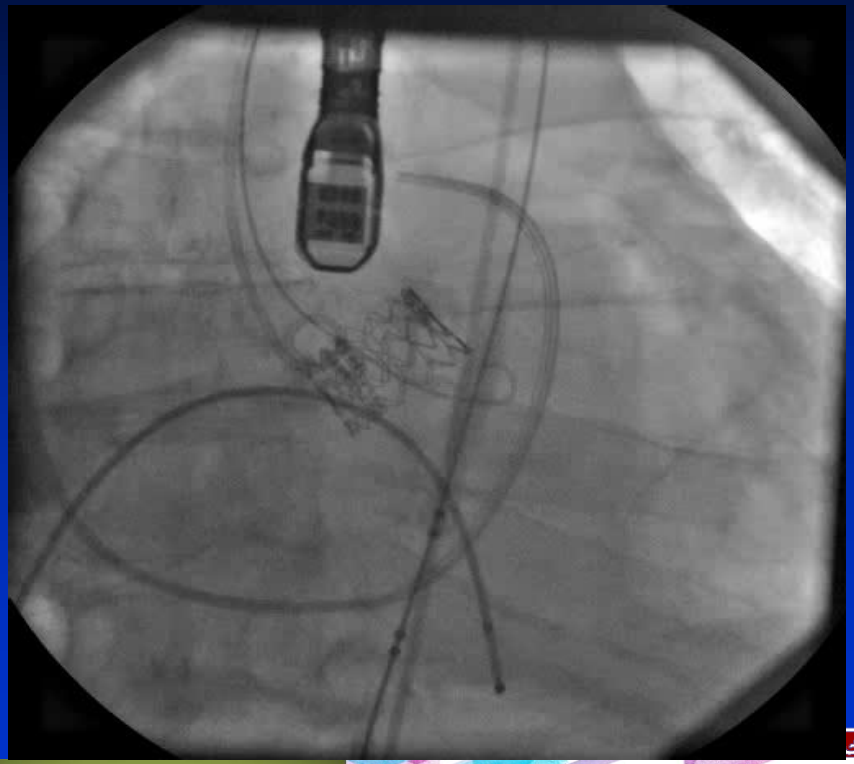
A few problems must be solved with TAVI, especially for application into LOW RISK Patients

But I think they will be solved!

What about TAVR Post Procedural AI: Will it be tolerated in LOW RISK patients??

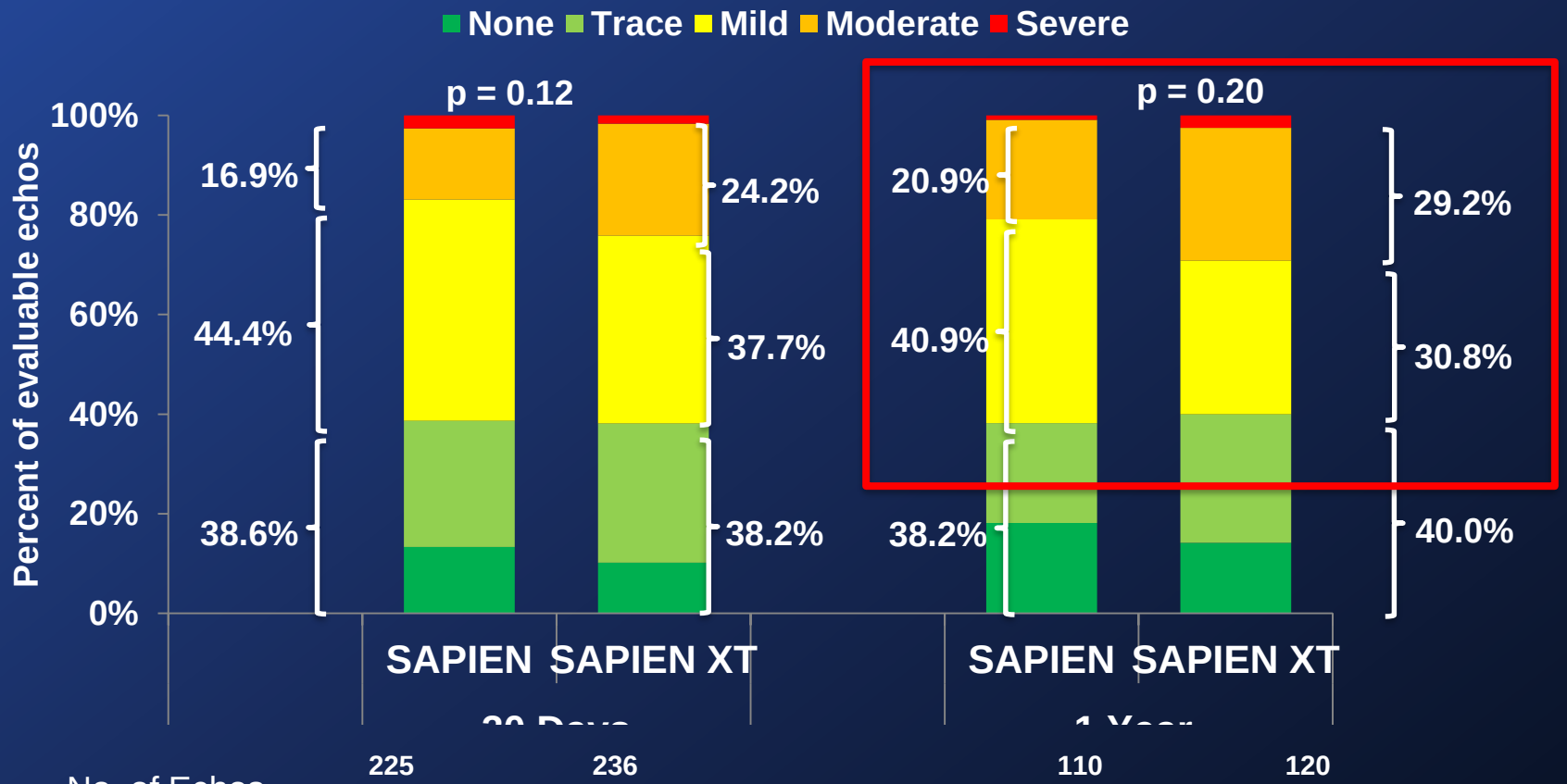




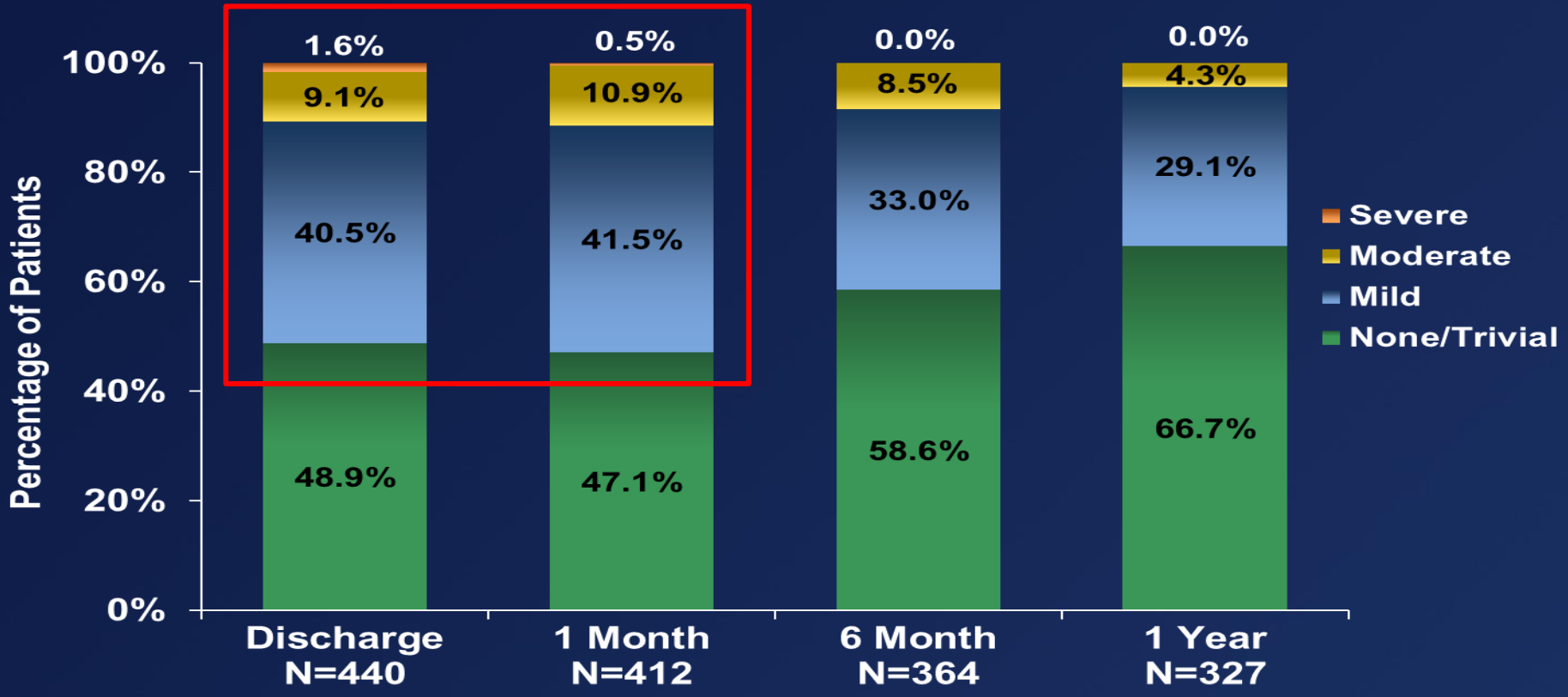


Paravalvular Aortic Regurgitation (AT, Valve Implant)

THE PARTNER II TRIAL

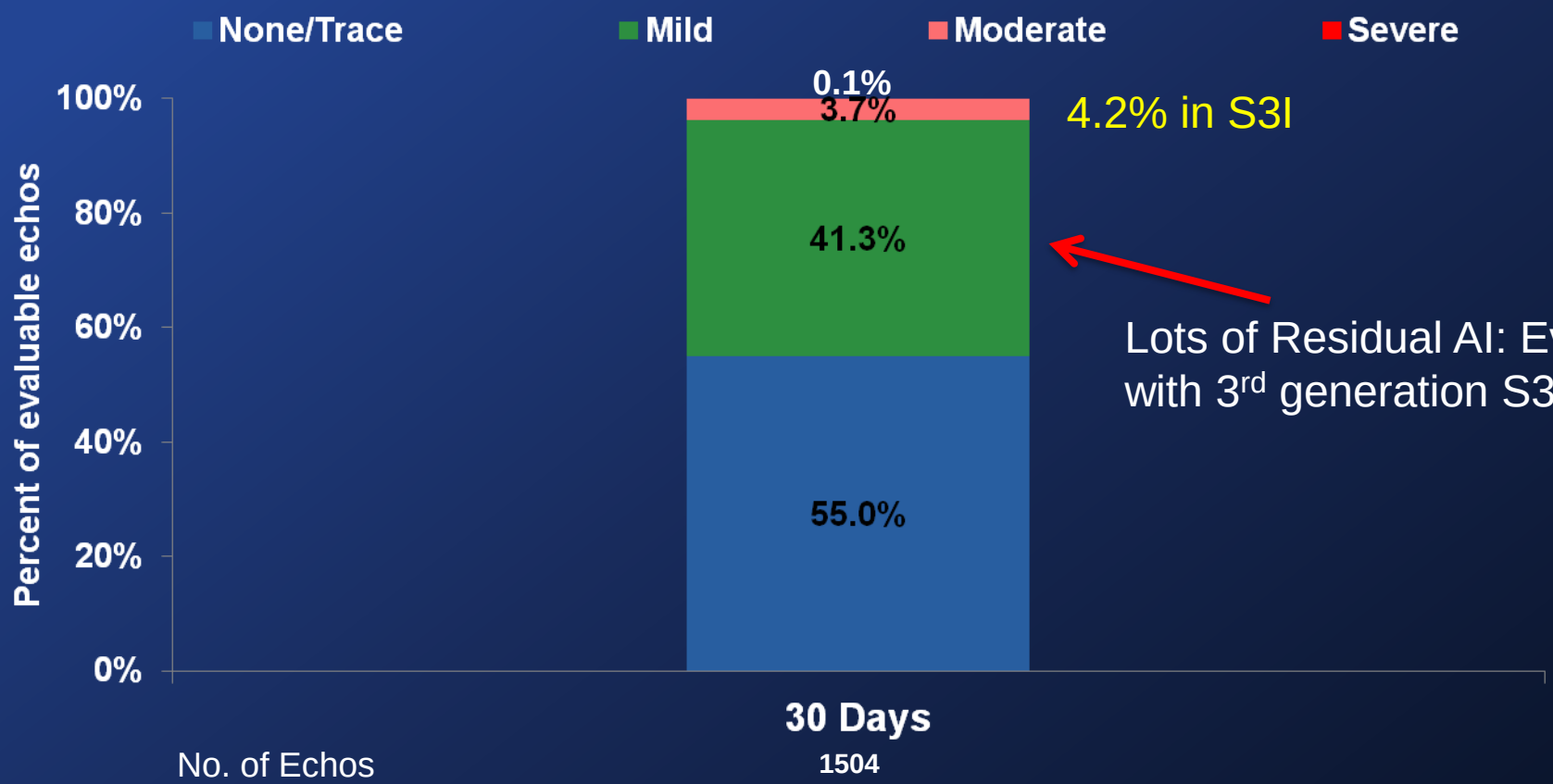


Paravalvular Regurgitation (For Corevalve)



Paravalvular Leak: S3HR & S3i
(Valve Implant Patients)

THE PARTNER II TRIAL



Clinical Performance Evolute CE Mark

Event, %	N=60
Absence of procedural mortality	100.0 (60/60)
Correct positioning of 1 valve in proper location	98.3 (59/60)
Mean gradient < 20 mm Hg or peak velocity < 3m/sec	98.3 (59/60)
Absence of moderate or severe regurgitation	93.3 (56/60)
Absence of patient prosthesis mismatch*	83.6 (46/55)
VARC-2 device success†	78.6 (44/56)

6.7%

*Effective orifice area could not be determined in 5 patients to calculate patient prosthesis mismatch.

†First time reporting of device success according to VARC-2 criteria

Source: Meredith IT, et al. Early Results from the CoreValve Evolut R CE Study [2101-295]. Presented at the Annual Meeting of the American College of Cardiology. March 14, 2015.

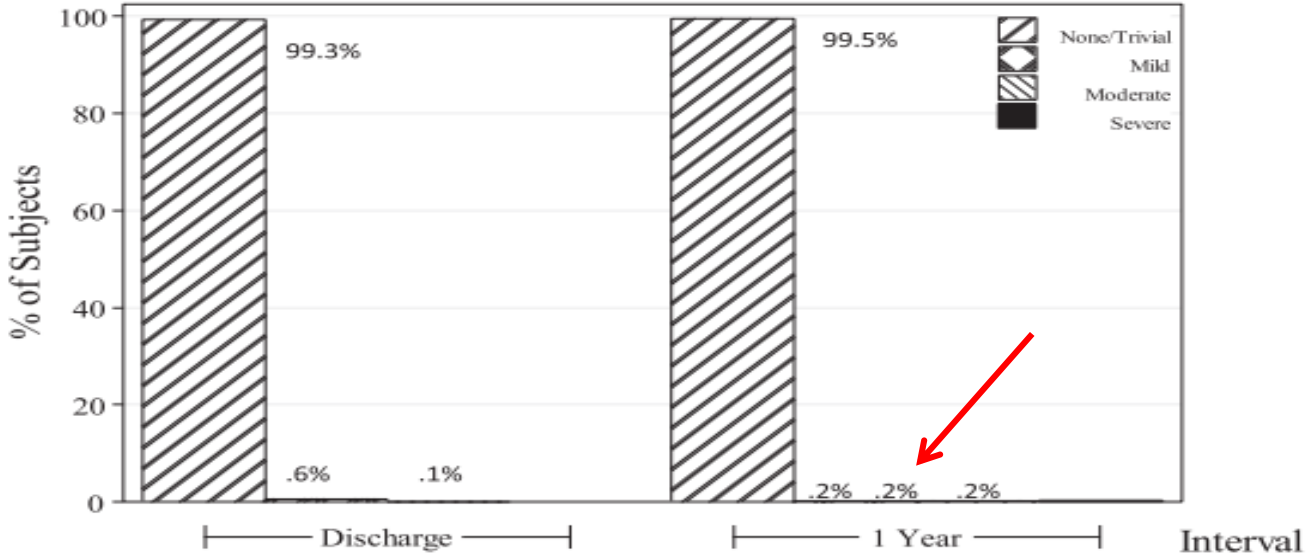
The St Jude Medical Trifecta aortic pericardial valve: Results from a global, multicenter, prospective clinical study

Joseph E. Bavaria, MD,[a] Nimesh D. Desai, MD, PhD,[a] Anson Cheung, MD,[b] Michael R. Petracek, MD,[c] Mark A. Groh, MD,[d] Michael A. Borger, MD,[e] and Hartzell V. Schaff, MD[f]

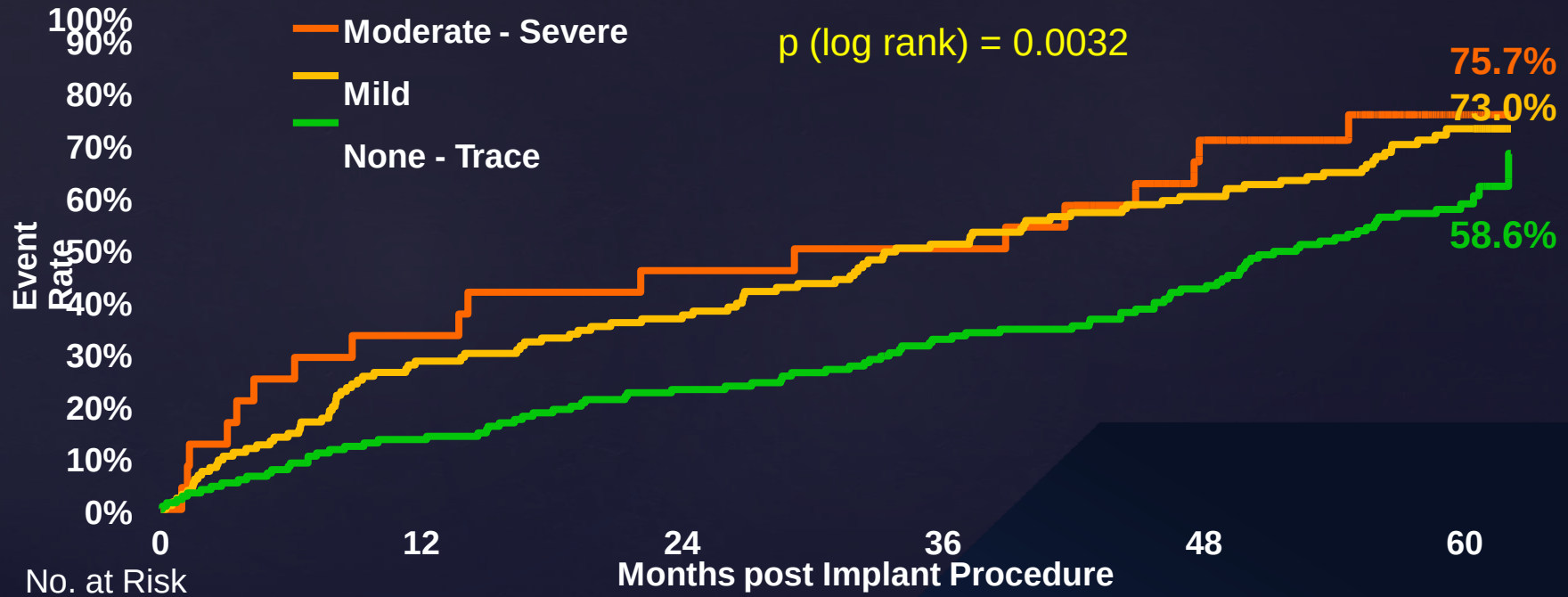
FIGURE 12. Paravalvular leak over time.

N=1,016 patients

STS = 4.02



Mortality and Post Procedural PVL
TAVR Patients



No. at Risk

M-S	24	16	13	12	7	2
Mild	137	98	84	65	52	11
N-T	158	135	120	105	88	34

TVT 2012

FRench **A**ortic **N**ational **C**orevalve and **E**dwards Registry

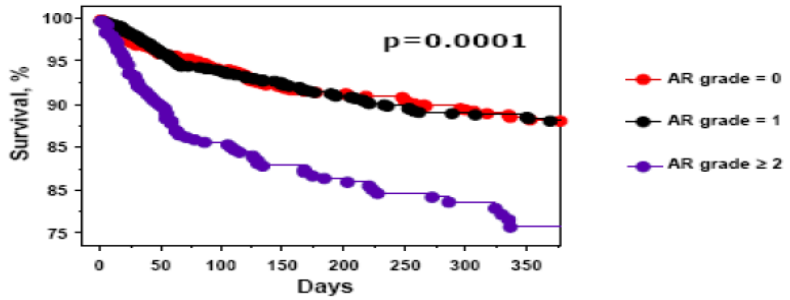
Predictor of 1-year Mortality

Multi-variate analysis

	Hazard ratio	95% CI
Logistic EuroScore (Increased 1%)	1.37	1.19- 1.58
NYHA (Class III or IV vs Class I or II)	1.49	1.09- 2.03
TA vs TF	1.45	1.09- 1.92
AR ≥ 2 vs ≤ 2/4	2.49	1.91- 3.25

>+1 AI is Bad!

euro PCR 1 year Actuarial mortality according to post-procedural aortic regurgitation



Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Corrado Tamburino, MD, PhD; Davide Capodanno, MD; Angelo Ramondo, MD; Anna Sonia Petronio, MD; Federica Ettori, MD; Gennaro Santoro, MD; Silvio Klugmann, MD; Francesco Bedogni, MD; Francesco Maisano, MD; Antonio Marzocchi, MD; Arnaldo Poli, MD; David Antoniucci, MD; Massimo Napodano, MD; Marco De Carlo, MD, PhD; Claudia Fiorina, MD; Gian Paolo Ussia, MD

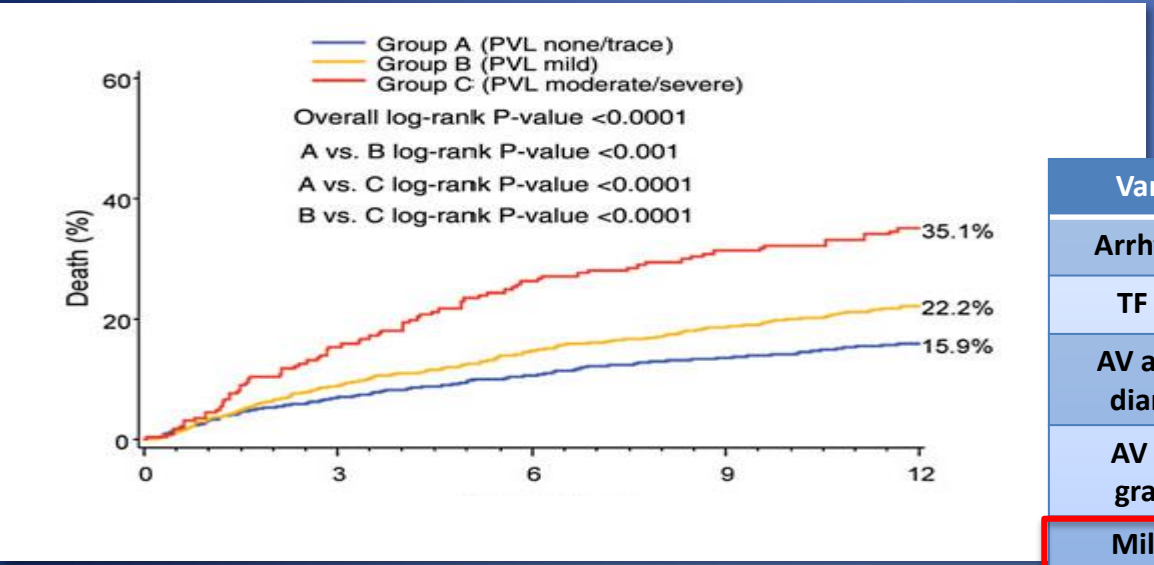
	Hazard Ratio	95% LCL	95% UCL	*P* Value
Late mortality				
Prior stroke	5.468	1.47	20.39	0.01
Post-procedural paravalvular leak ≥2+	3.785	1.57	9.10	0.003
Prior acute pulmonary edema	2.696	1.09	6.68	0.03
Chronic kidney disease	2.532	1.01	6.35	0.048

LCL indicates lower confidence limit; UCL indicates upper confidence limit.

>+1 AI is Bad!

Paravalvular Leak: Dilate, Plug or Watch?

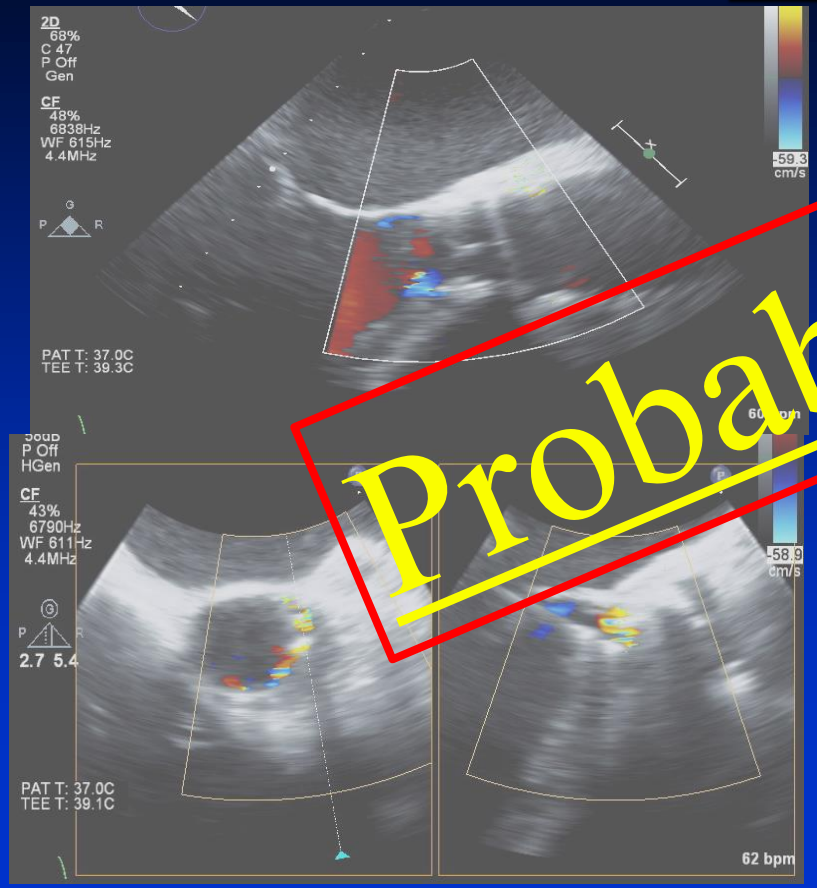
Mild or Moderate PVL: Should I be concerned?



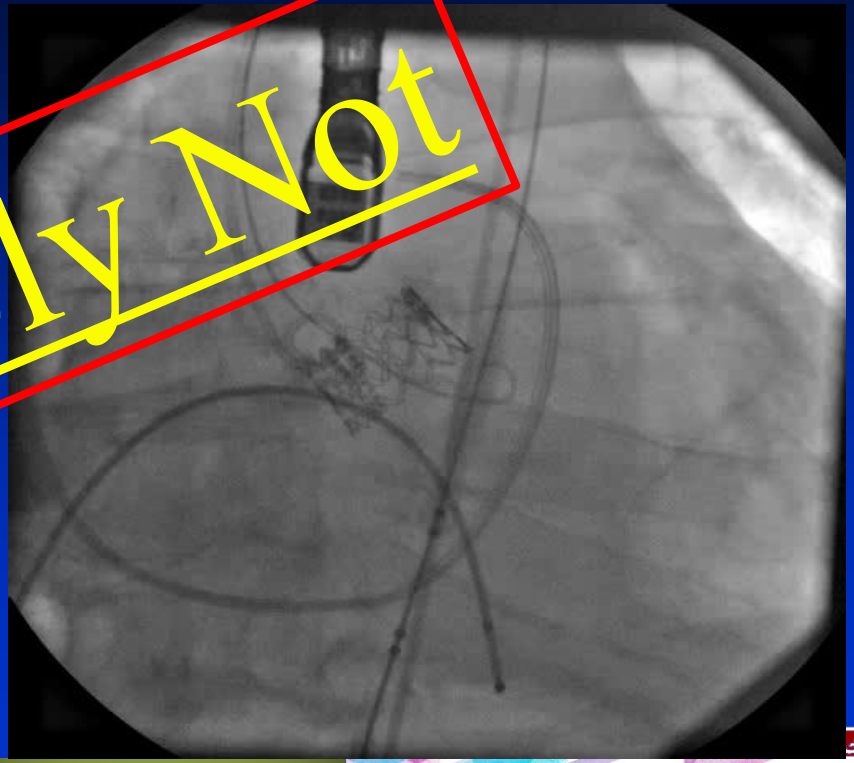
Variable	HR	95% CI	P-value
Arrhythmia	1.41	1.14-1.75	0.002
TF vs TA	0.73	0.59-0.91	0.005
AV annular diameter	1.07	1.03-1.11	0.001
AV mean gradient	0.98	0.97-0.99	<0.0001
Mild PVL	1.35	1.07-1.72	0.013
Mod/Sev PVL	2.20	1.6-3.03	<0.0001
Creat ≥ 2	1.35	1.04-1.74	0.023
BMI	0.95	0.93-0.97	<0.0001

Kodali S et al, Eur Heart J 2015

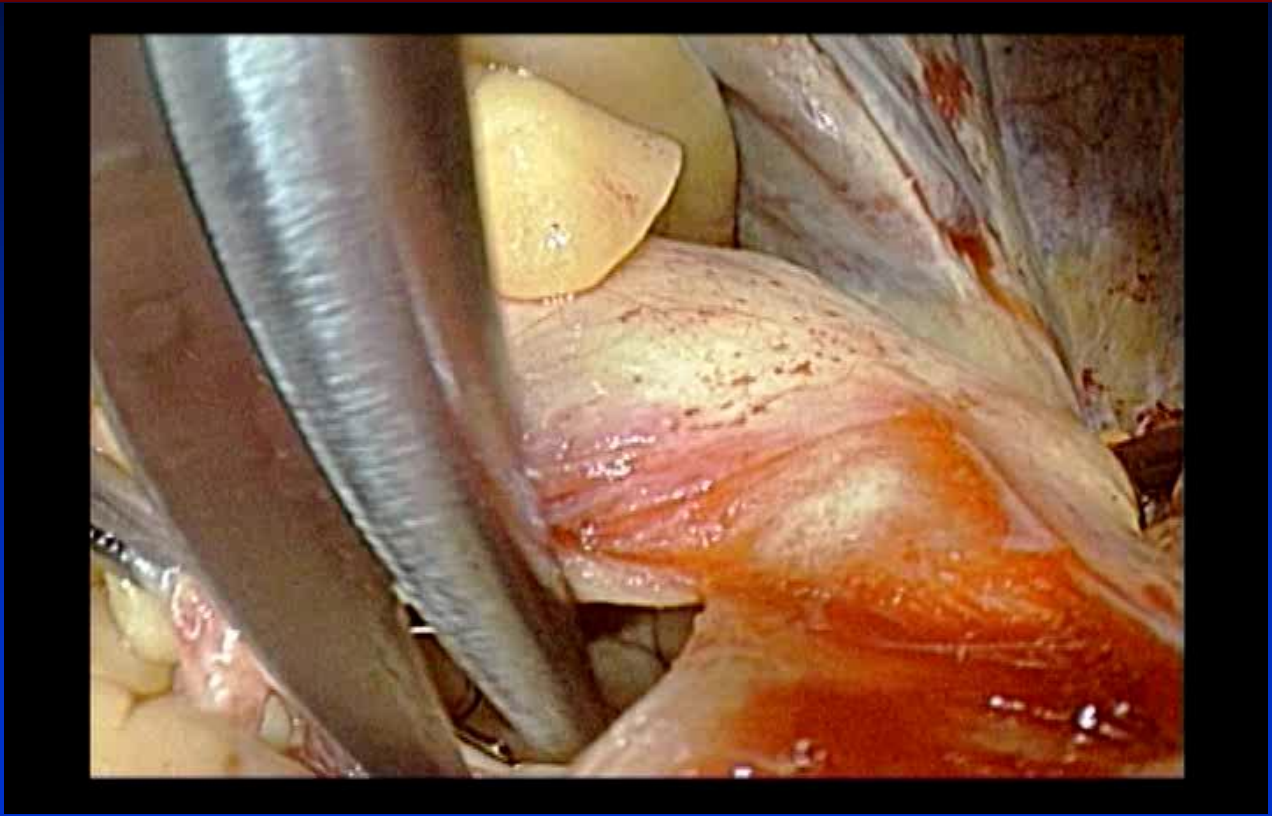
What about TAVR Post Procedural AI: Will it be tolerated in LOW RISK patients??



Probably Not



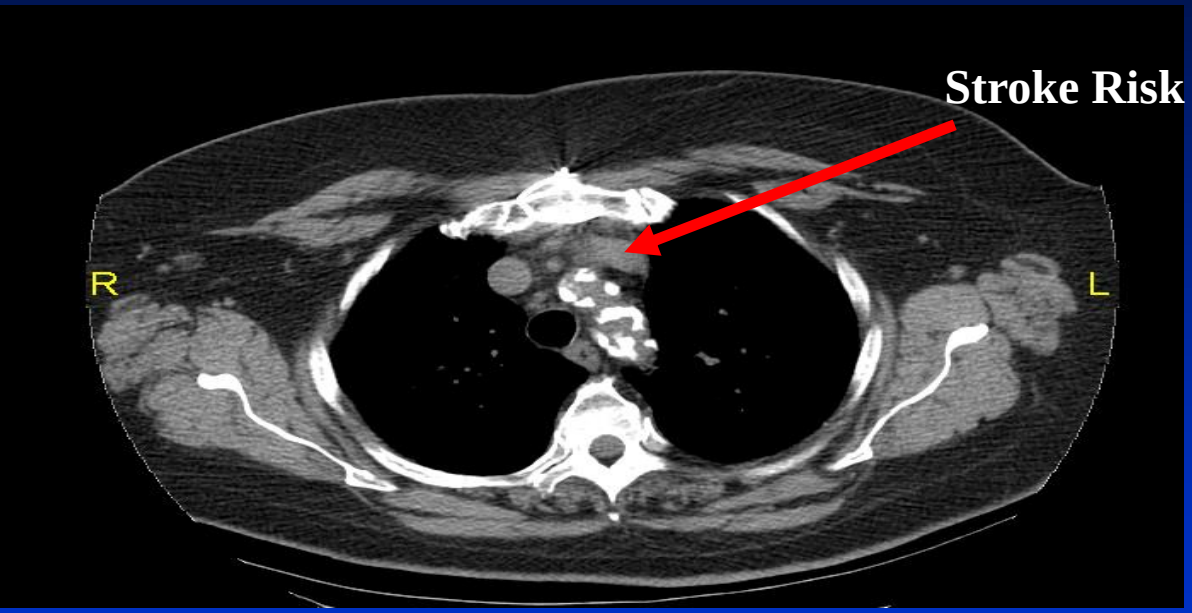
Conversion: Residual AR 2-3 + after TAVI
Valve explantation

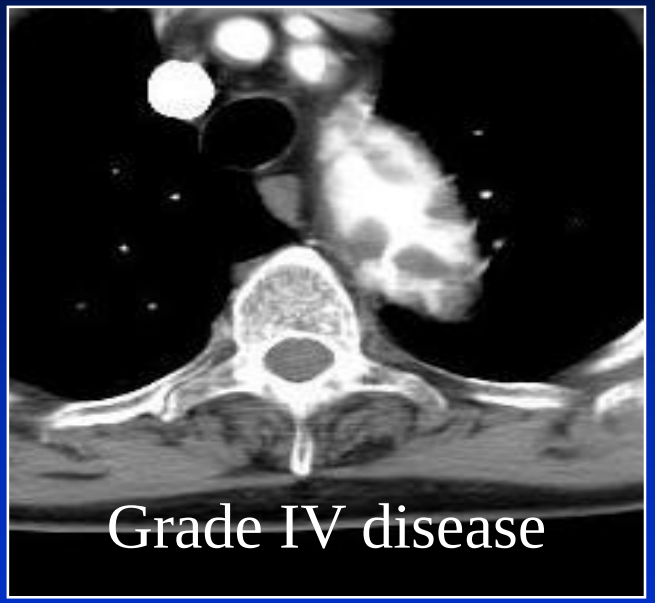


What about TAVR Post Procedural CVA: Will it be tolerated in LOW RISK patients???

Extensive Cerebral Vessel Calcium and Atheromatous disease off the Aortic Arch

A-P

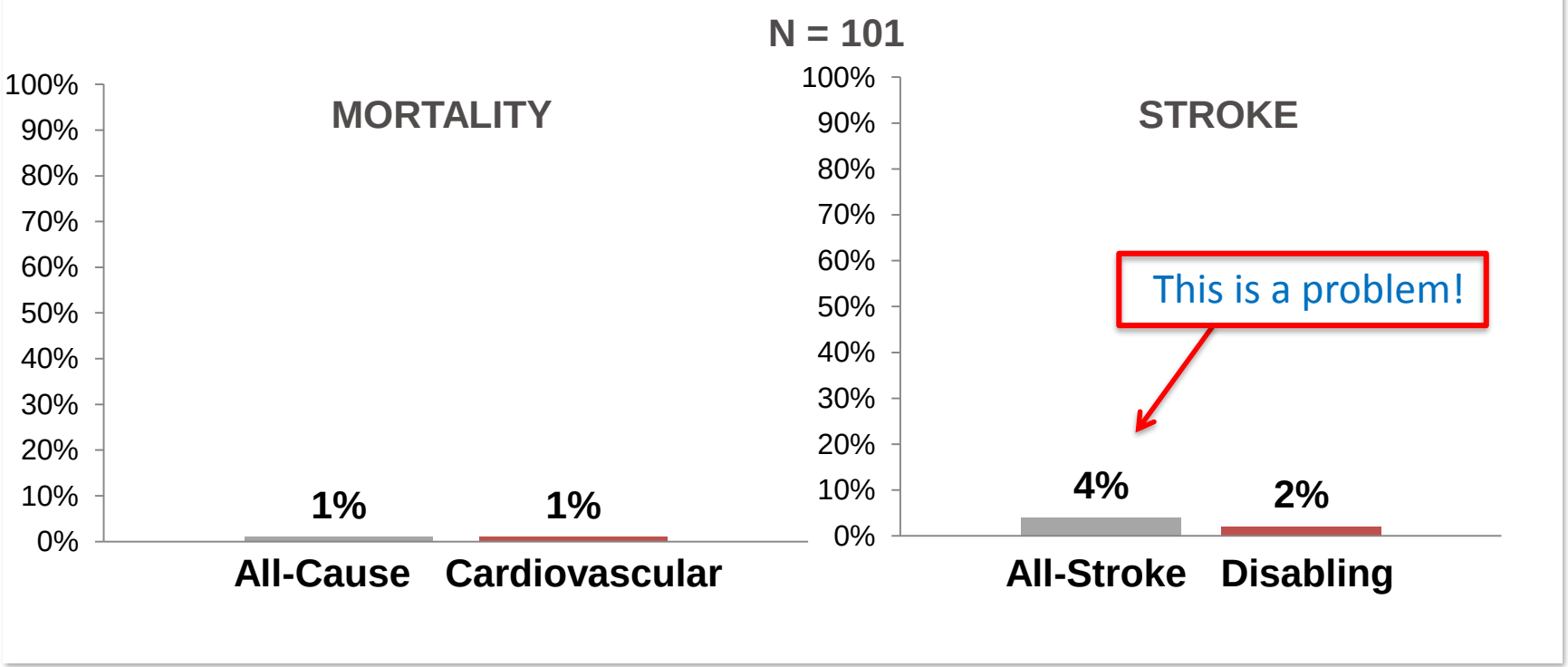




The High Initial TF stroke risk is coming down with both experience and improved devices

Open AVR

SAPIEN 3 CE IR
Clinical Outcomes at 30 Days



ALEC VAHANIAN, MD
HÔPITAL BICHAT
PARIS, FRANCE
ON BEHALF OF THE SAPIEN 3 INVESTIGATORS

What about Pacemakers??

Secondary Endpoints

Events*	1 Month	1 Year
Any Stroke, %	4.0	7.0
Major, %	2.3	4.3
Myocardial Infarction, %	1.2	2.0
Reintervention, %	1.1	1.8
VARC Bleeding, %	36.7	42.8
Life Threatening or Disabling, %	12.7	17.6
Major, %	24.9	28.5
Major Vascular Complications, %	8.2	8.4
Permanent Pacemaker Implant, %	21.6	26.2
Per ACC Guidelines, %	17.1	19.2

* Percentages obtained from Kaplan Meier estimates

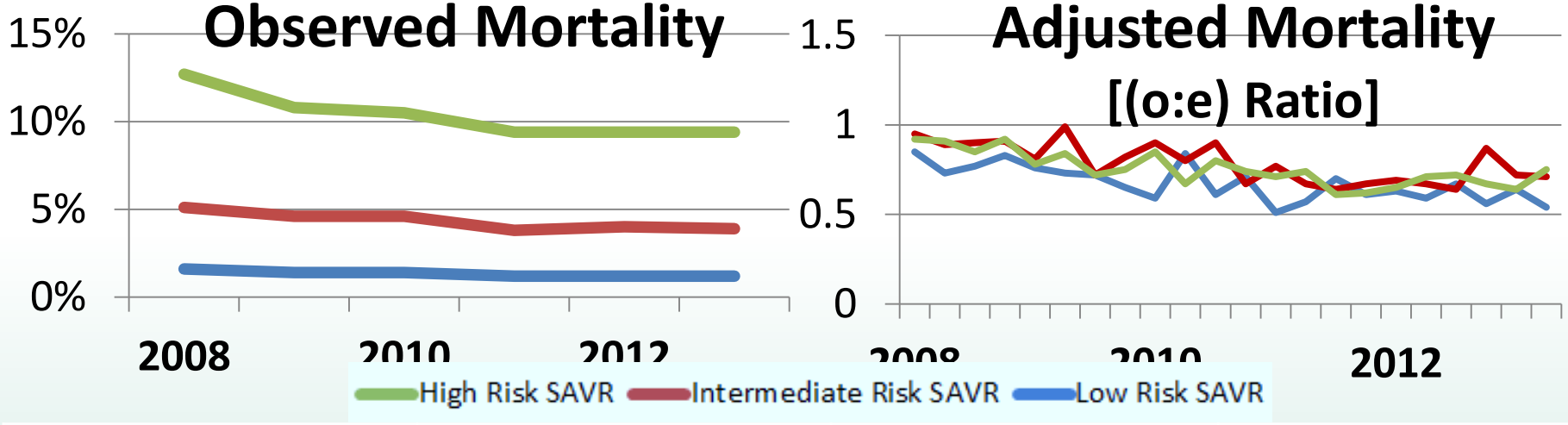
Other Clinical Events Intermediate Risk

At 30 Days (As Treated Patients)

THE PARTNER II TRIAL

Events (%)	S3HR Overall (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i Overall (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
Major Vascular Comps.	5.0	5.3	3.3	5.6	5.9	3.2
Bleeding - Life Threatening	6.3	5.5	10.9	5.4	4.4	12.9
Annular Rupture	0.3	0.2	1.1	0.2	0.2	0
Myocardial Infarctions	0.5	0.4	1.1	0.3	0.3	0
Coronary Obstruction	0.2	0	1.1	0.4	0.4	0
Acute Kidney Injury	1.0	0.8	2.2	0.5	0.3	1.6
New Permanent Pacemaker	13.0	13.2	12.0	10.1	10.4	7.2
Aortic Valve Re-intervention	1.0	0.8	2.2	0.7	0.8	0
Endocarditis	0.2	0.2	0	0.1	0.1	0

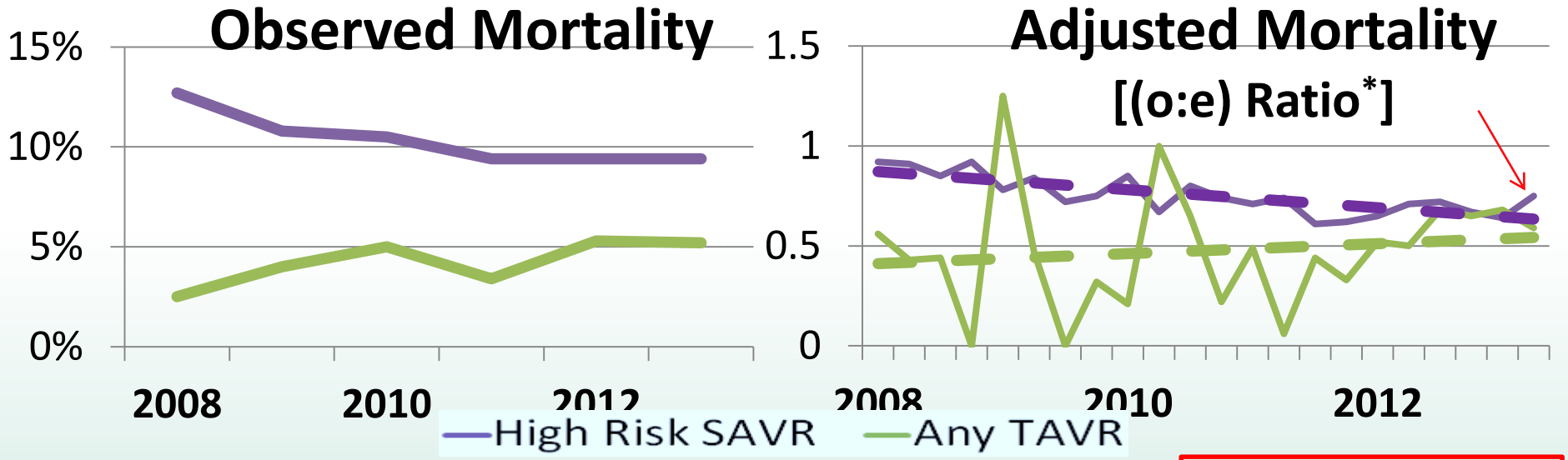
However, Therapy with Surgical AVR is also steadily improving especially recently



Surgical AVR Risk	2008 – 2009	2010 – 2011Q2	2011Q3 – 2013Q2
Low	0.60 (0.53, 0.68)	0.56 (0.49, 0.65)	0.50 (0.44, 0.57)
Intermediate	0.76 (0.68, 0.85)	0.66 (0.58, 0.76)	0.62 (0.55, 0.70)
High	0.86 (0.78, 0.94) →	0.74 (0.66, 0.82) →	0.62 (0.55, 0.69)

*o:e Ratio calculated using STS PROM calibrated for yr2007

*p<0.0001 across intervals



	2008 – 2009	2010 – 2011Q2	2011Q3 – 2013Q2
High Risk SAVR (o:e*)	0.86 (0.78, 0.94)	0.74 (0.66, 0.82)	0.62 (0.55, 0.69)
Any TAVR (o:e*)	**0.38 (0.18, 0.69)**	**0.36 (0.22, 0.54)**	**0.61 (0.55, 0.66)†**

*o:e Ratio calculated using STS PROM calibrated for yr2007

† p<0.0001

Transcatheter Aortic Valves: The Future …. Is Coming!

We will wait for the Low Risk Trials to Report … but ….

The TAVI Heart Team

Multi-Disciplinary TAVI TEAM Approach in Hybrid OR

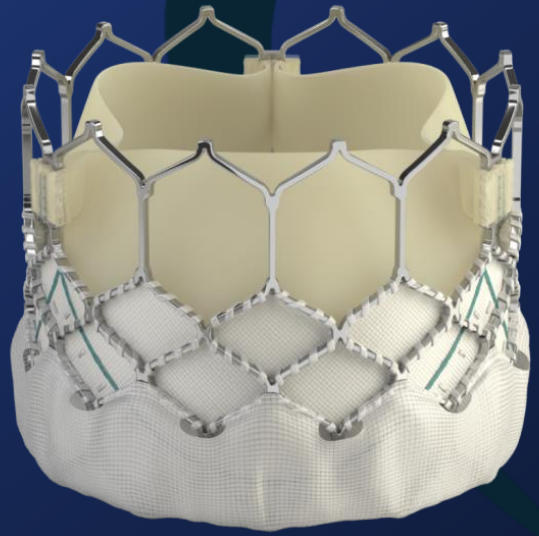
Interventional Cardiology assisting Cardiac Surgeon: TF case

Cardiac Surgeon assisting Interventional Cardiologist: TF Case

Now, More Junior Cardiac Surgeons and Interventional Cardiologists Doing Procedure

Weekly Penn Aortic Valve and TAVI Conference: Choosing the RIGHT and Proper Therapy for the Patient

Thank you!



THE PARTNER TRIAL