Aortic Valvular Stenosis, Asymptomatic, Severe, Age 60 Years

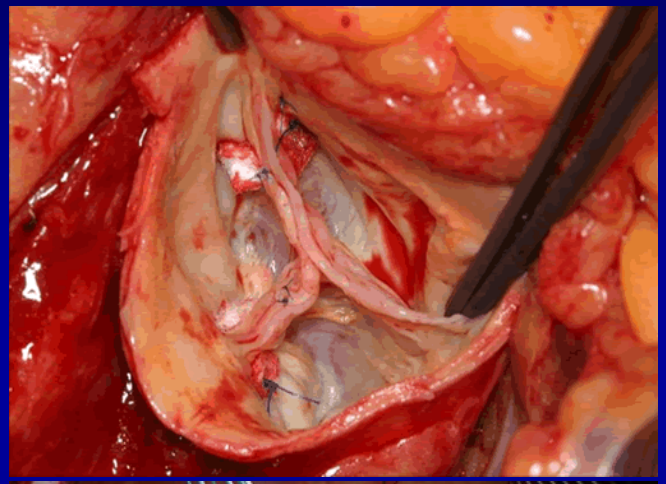
From Medical Therapy, to Surgical AVR, To Transcatheter AVR/Valvuloplasty

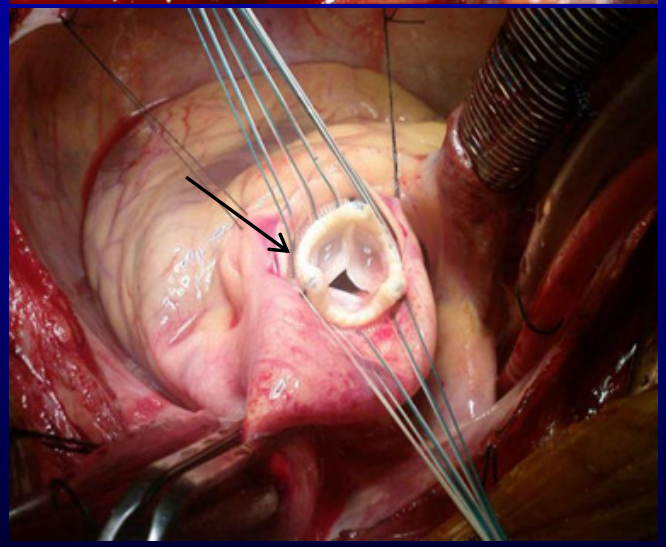
The Interventionalist's View

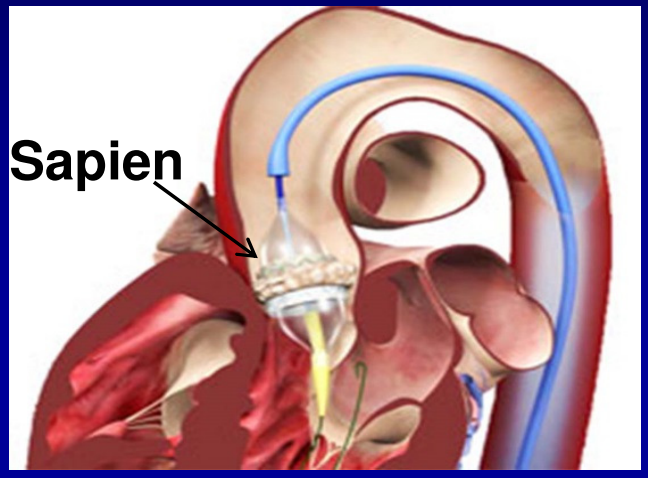
Samin K Sharma, MD, FACC, FSCAI
Director Clinical & Interventional Cardiology
Zena and Michael a Weiner Professor of Medicine
President Mount Sinai Heart Network
Mount Sinai Hospital, NY

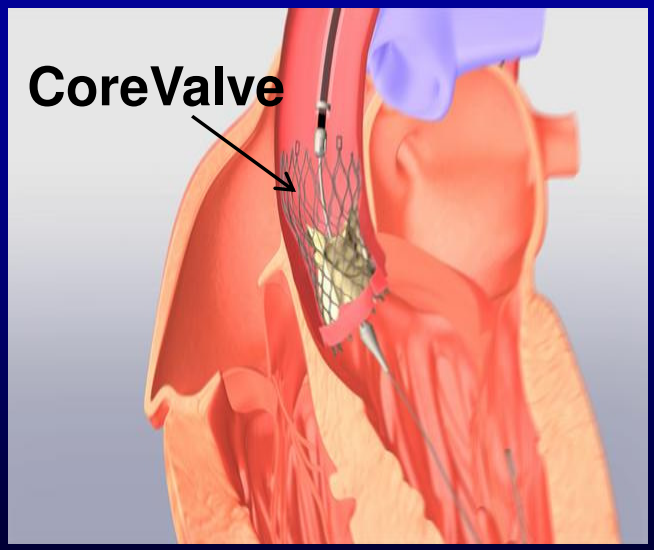
Interventional Choices for AS:

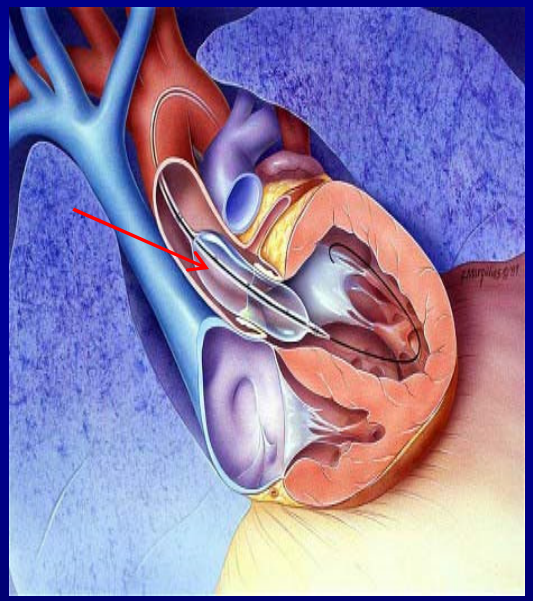
SAVR	TAVR	BAV



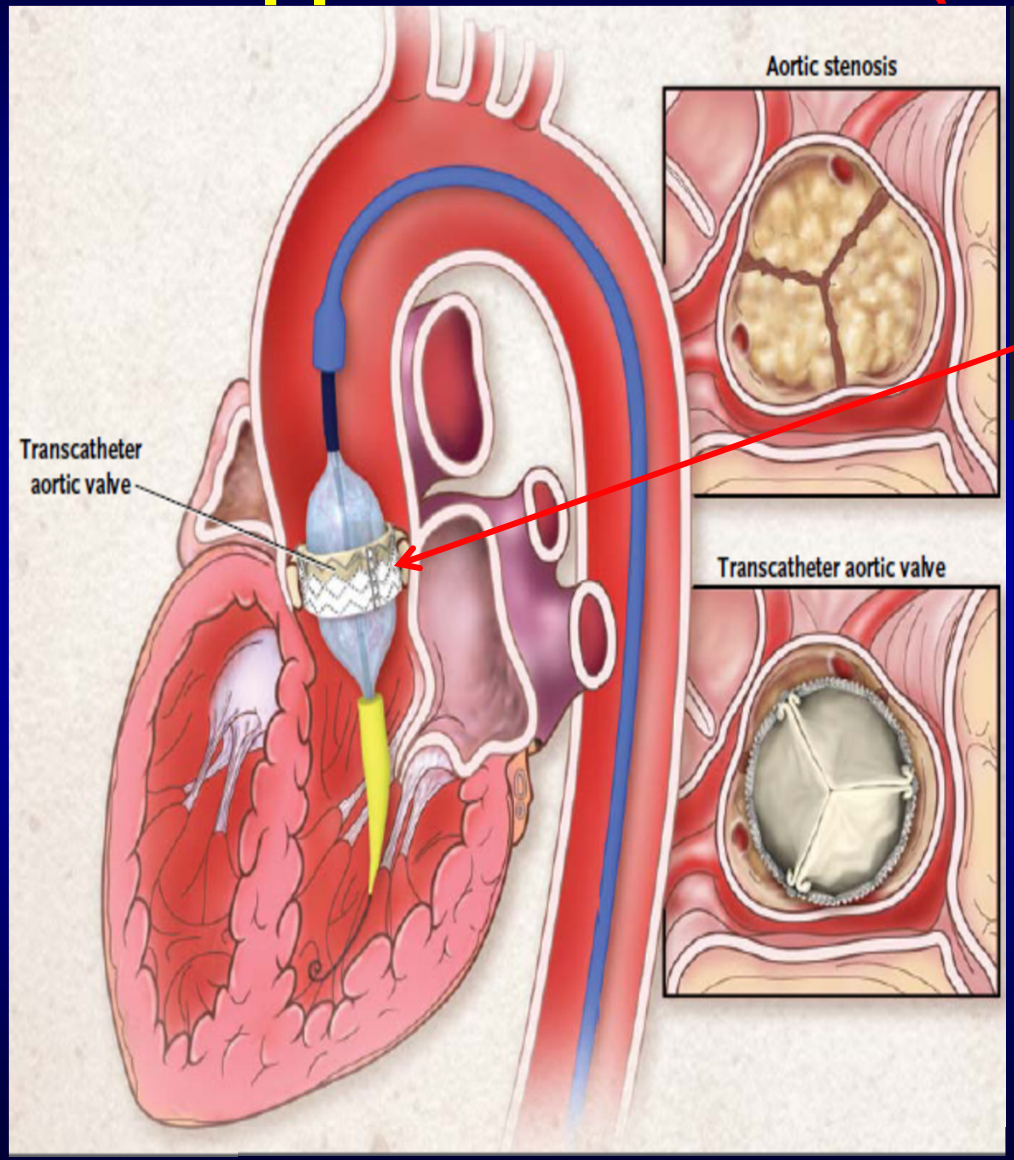


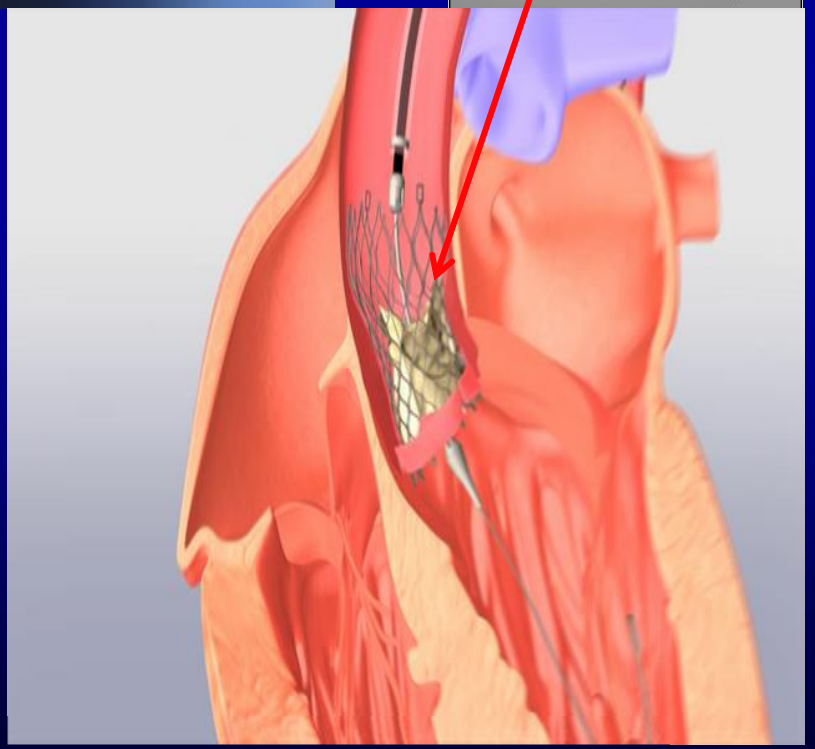






Transcatheter Aortic Valves:
FDA Approved Devices (All for Symptomatic AS)

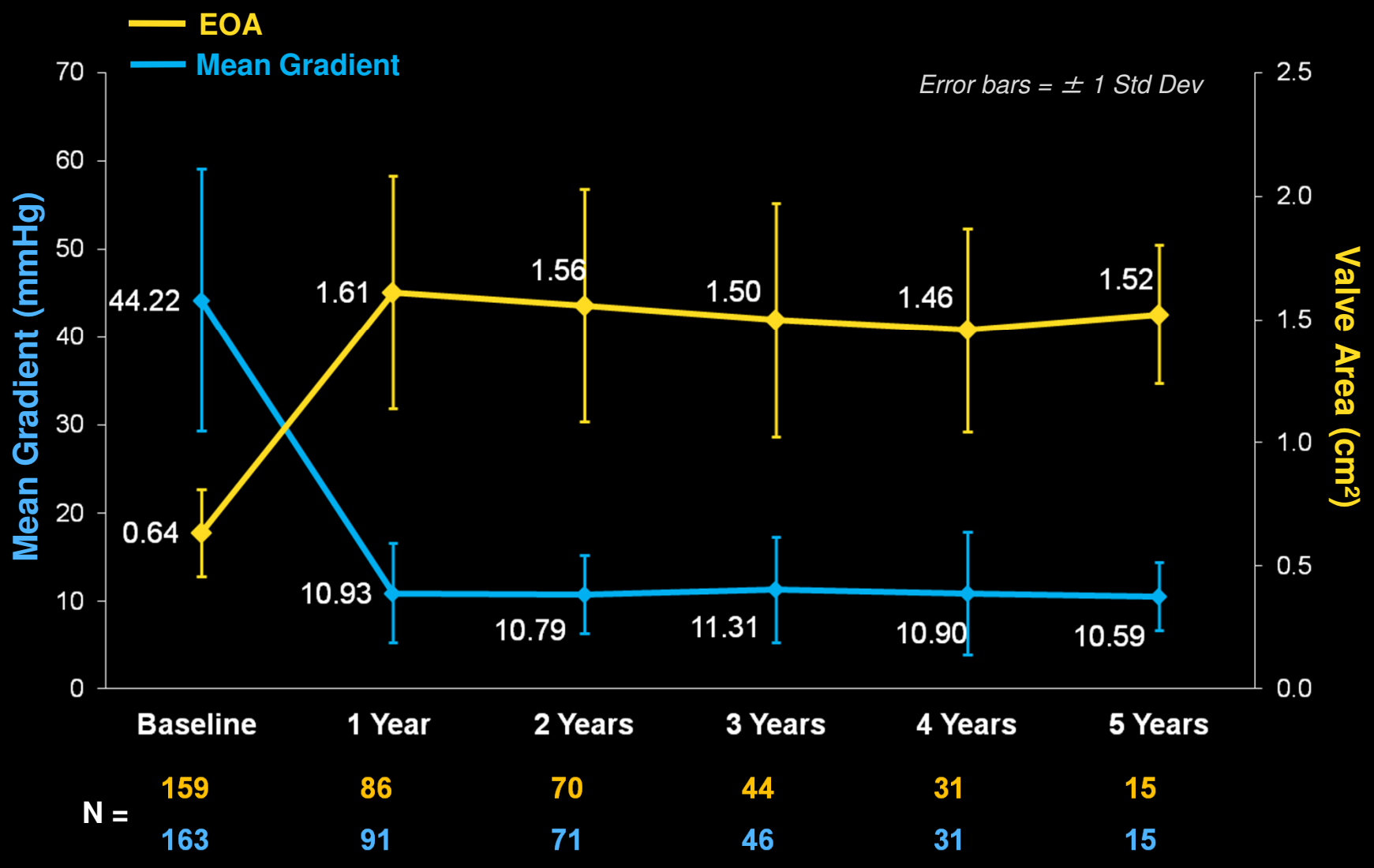




Edwards-Sapien

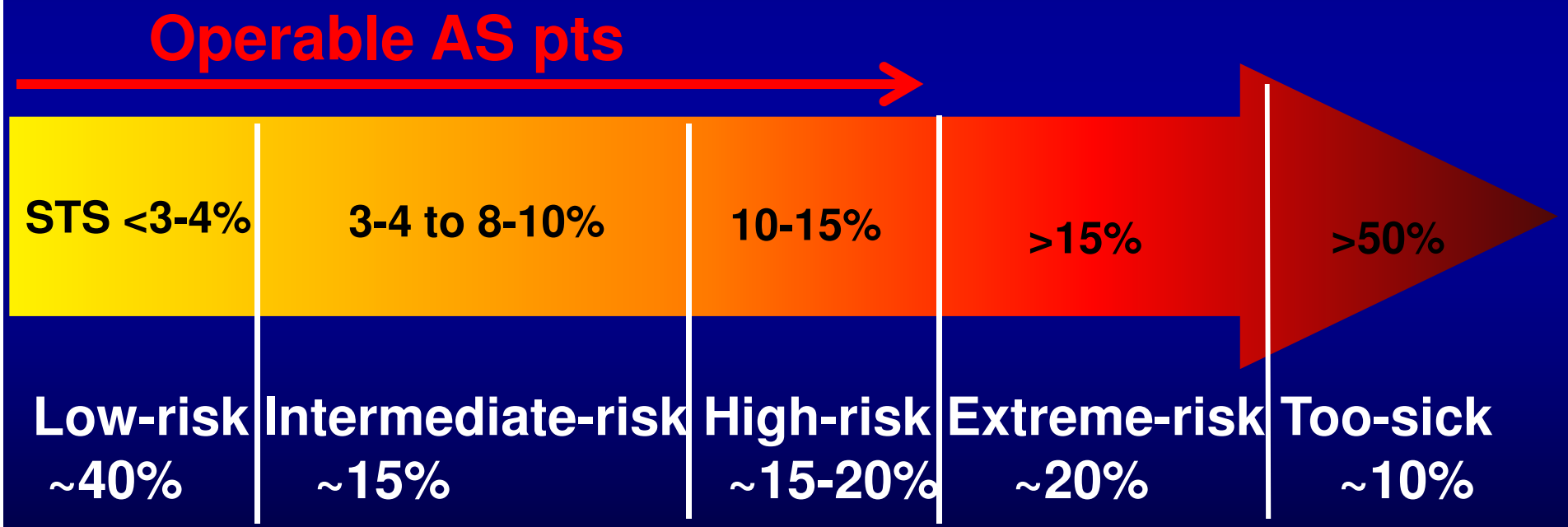
CoreValve

PARTNER Trial: Aortic Mean Gradient & Valve Area



Transcatheter Aortic Valves Replacement (TAVR)

Surgical risk is a continuum (STS risk score)



TAVR for Extreme Risk AS Cases
Or In-operable AS Cases

STS Morbidity/Mortality risk of >15-50%

Two Trials: PARTNER IB (Completed): ES Valve
CoreValve Trial (Completed)

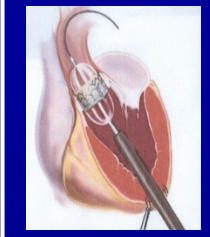
PARTNER US Trial: Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High Risk AVR Candidate
3105 Total Patients Screened

In-operable Gp Cohort B — **n=358**

ASSESSMENT: Transfemoral Access



Yes / No

1:1 Randomization

Not In Study

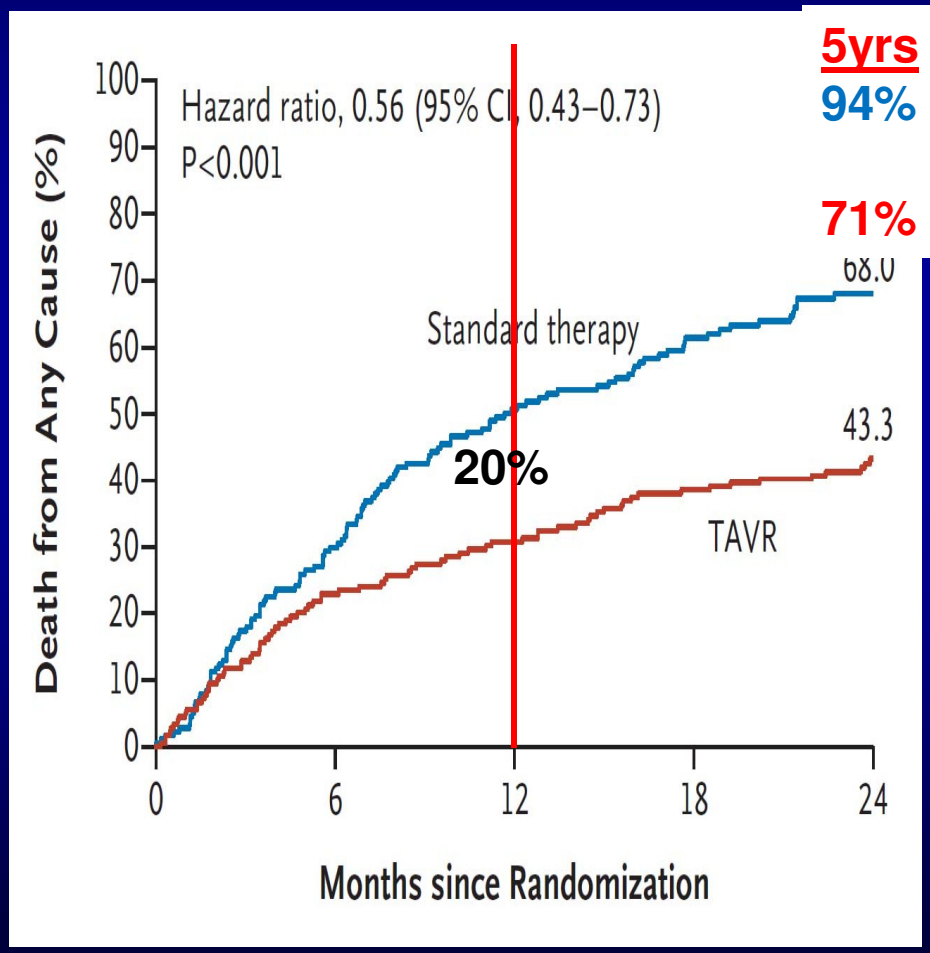
TAVR Trans Femoral vs **Standard Therapy (usually BAV)**

Primary Endpoint: All Cause Mortality over length of trial (Superiority)

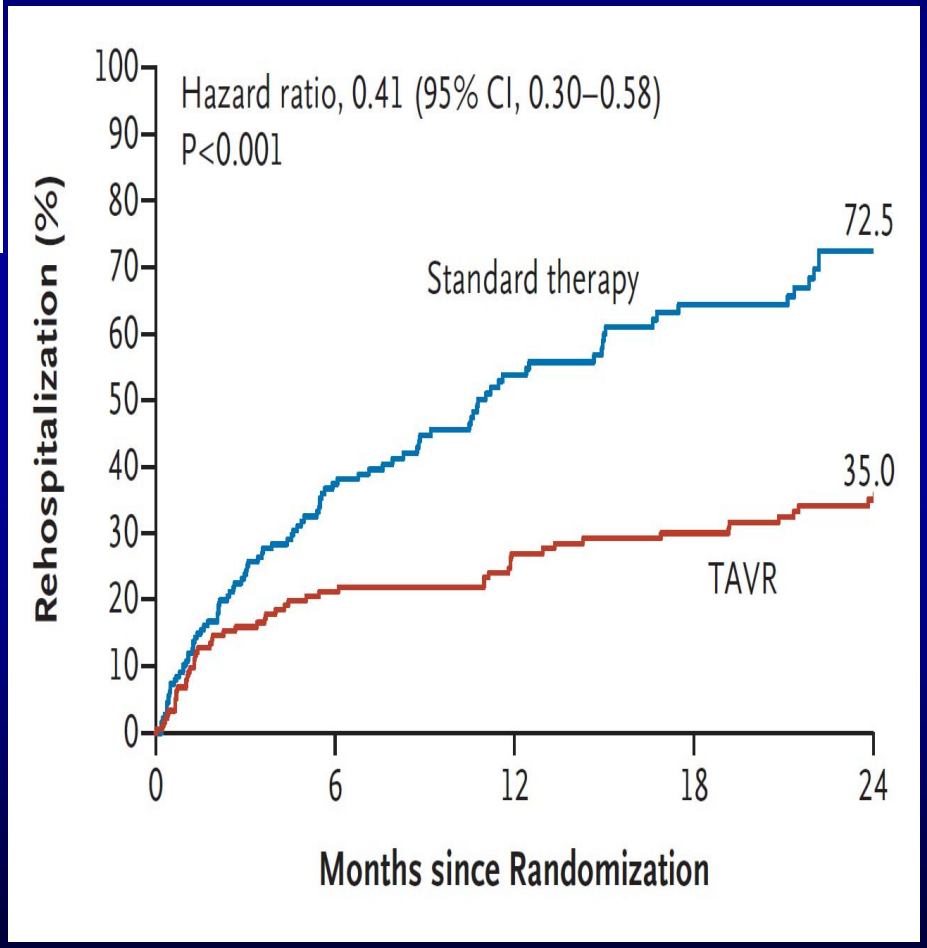
Leon et al, NEJM 2010;363:1597

PARTNER Trial Cohort B: Time-to-Event Analysis of Key Endpoints During 2 Years Follow-up

Rate of Death From Any Cause



Rate of Re-hospitalization



Makkar et al., NEJM 2012;366:1696

CoreValve Pivotal Trials Study Design

CoreValve US Pivotal Trials

Extreme Risk
(Inoperable; STS mortality/morbidity >50%)

Iliofemoral Access
for 18 Fr Sheath

Presented in TCT 2013

Yes

No

CoreValve Iliofemoral

N=487

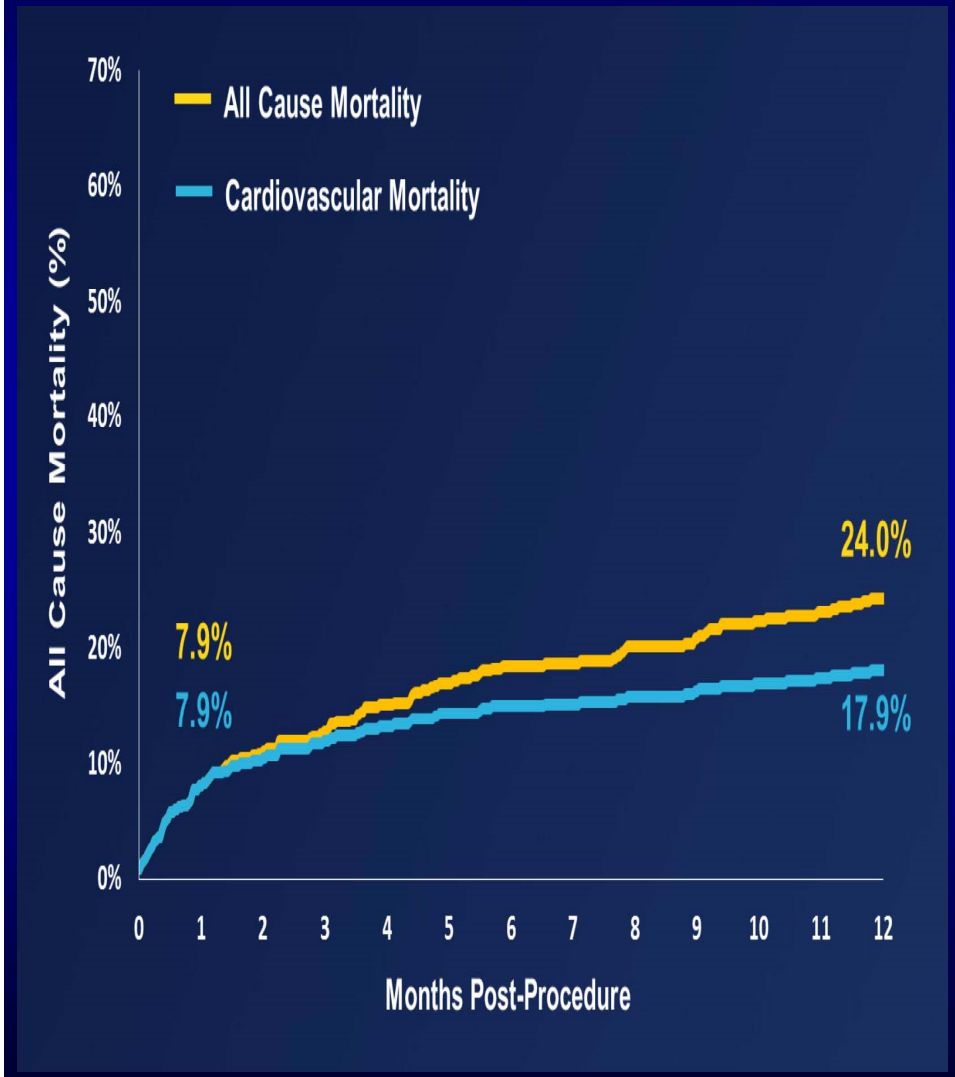
CoreValve Non-Iliofemoral

N=147

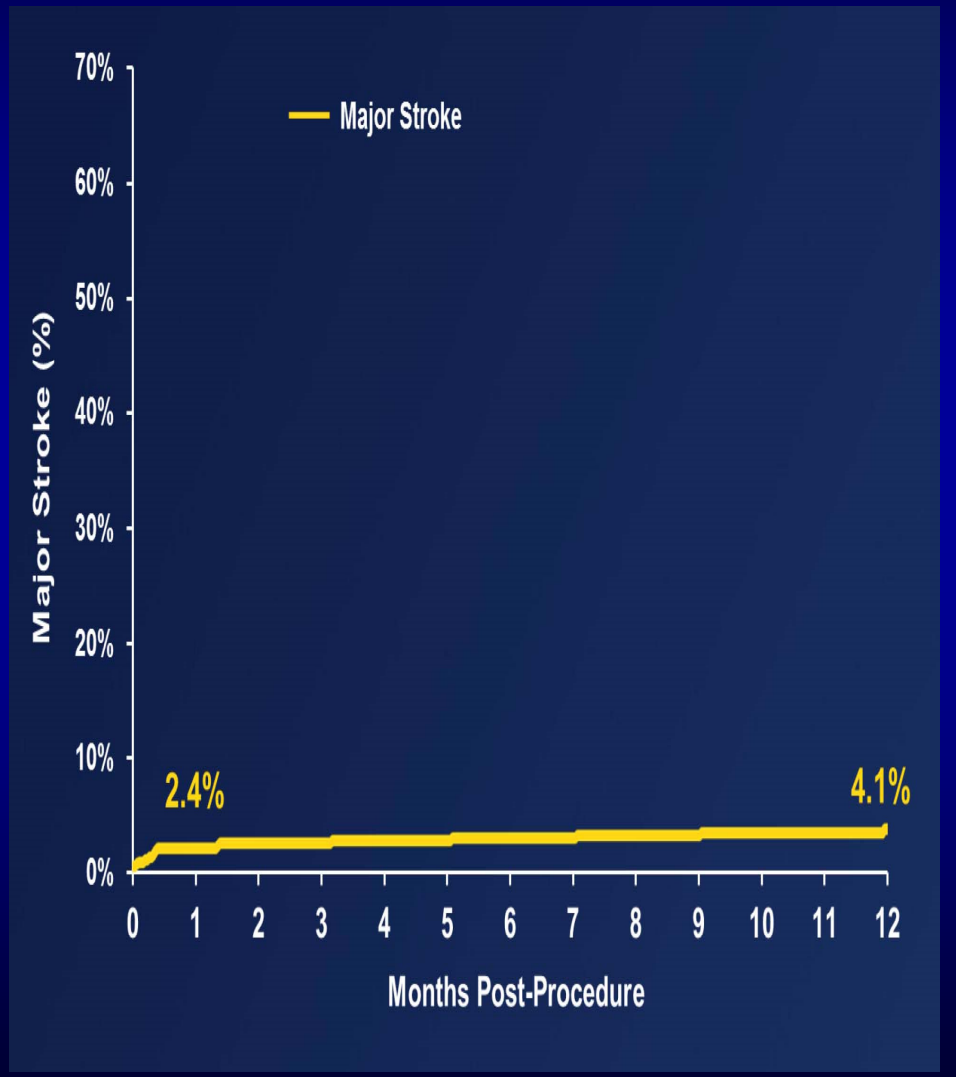
CoreValve Extreme Risk Study: Primary Endpoints

N= 487

1 Year Mortality



Major Stroke



Popma et al, TCT 2013; JACC May 2014

TAVR for High Risk AS Cases

STS Mortality risk of 10-15%

Two Trials: PARTNER IA (Completed): ES Valve
Pivotal CoreValve Trial (Completed)

PARTNER US Trial: Study Design

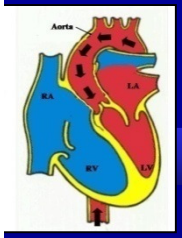
Symptomatic Severe Aortic Stenosis

ASSESSMENT: High Risk AVR Candidate
3105 Total Patients Screened

n= 700

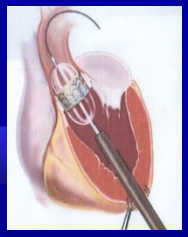
High-surgical risk Gp
STS >10% Cohort A

ASSESSMENT: Transfemoral Access



High Risk TF

High Risk TA



1:1 Randomization

1:1 Randomization

TAVR Trans Femoral vs **Surgical AVR**

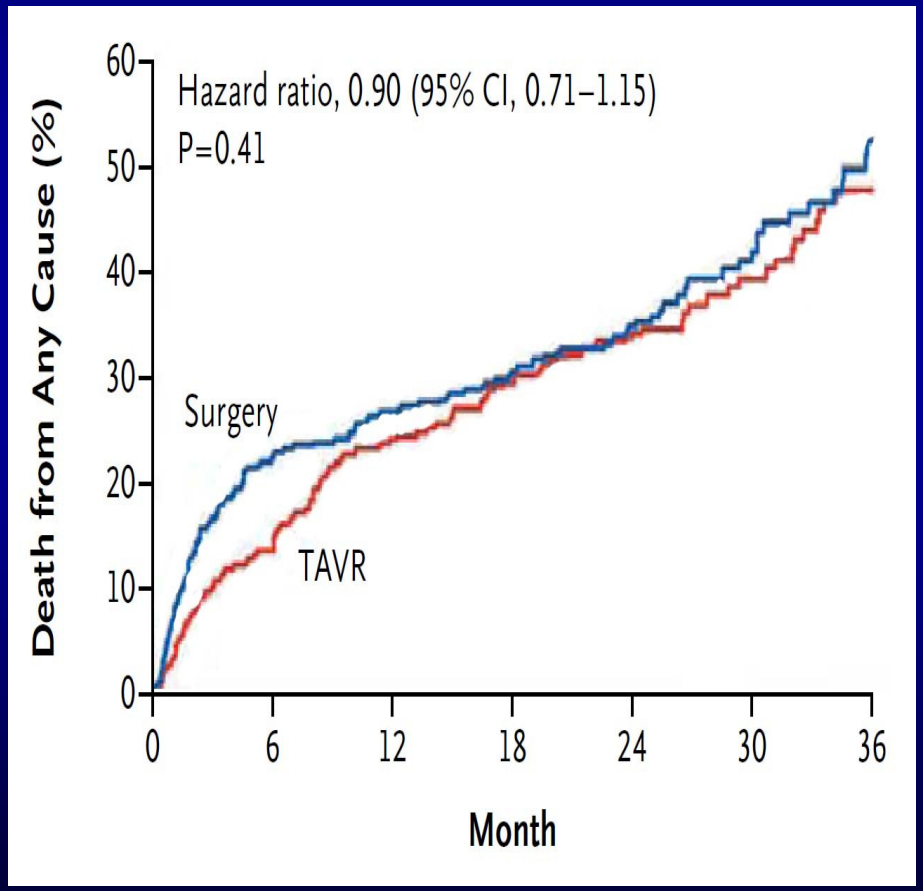
TAVI Trans Apical vs **Surgical AVR**

Primary Endpoint: All Cause Mortality (1 yr)
(Non-inferiority)

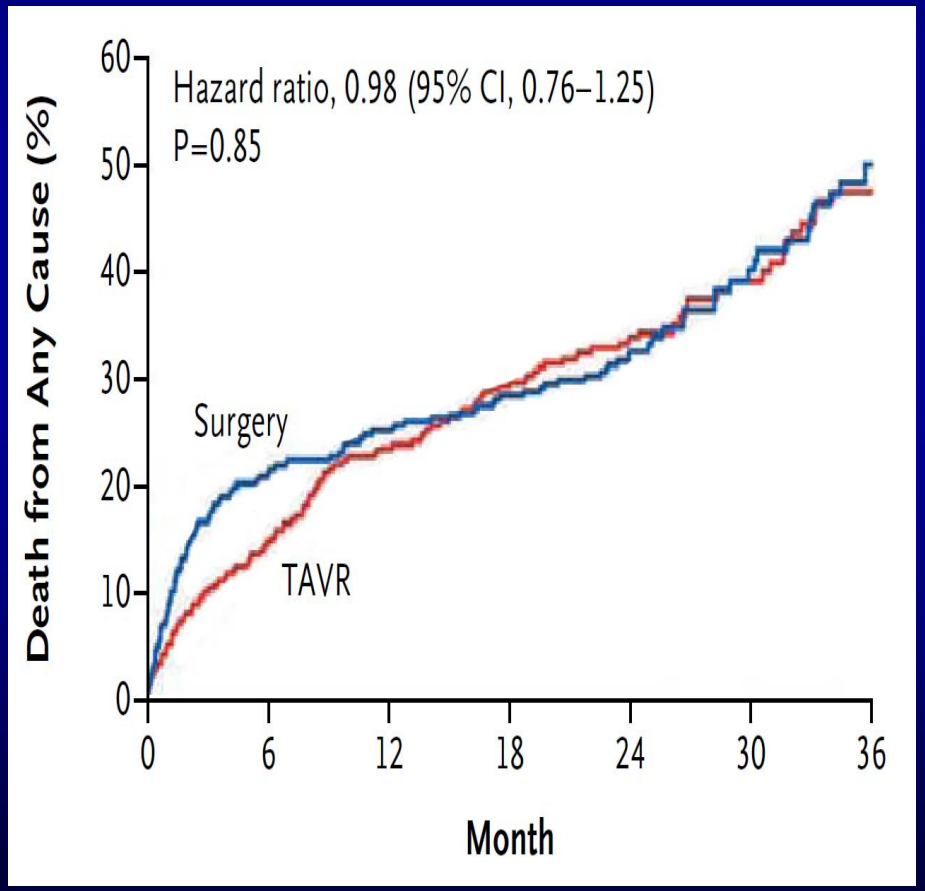
Leon et al, NEJM 2010;363:1597

PARTNER Trial Cohort A: Time-to-Event Curves for Primary Endpoints at 3-Yrs

Death from Any Cause, Intention-to-Treat Population

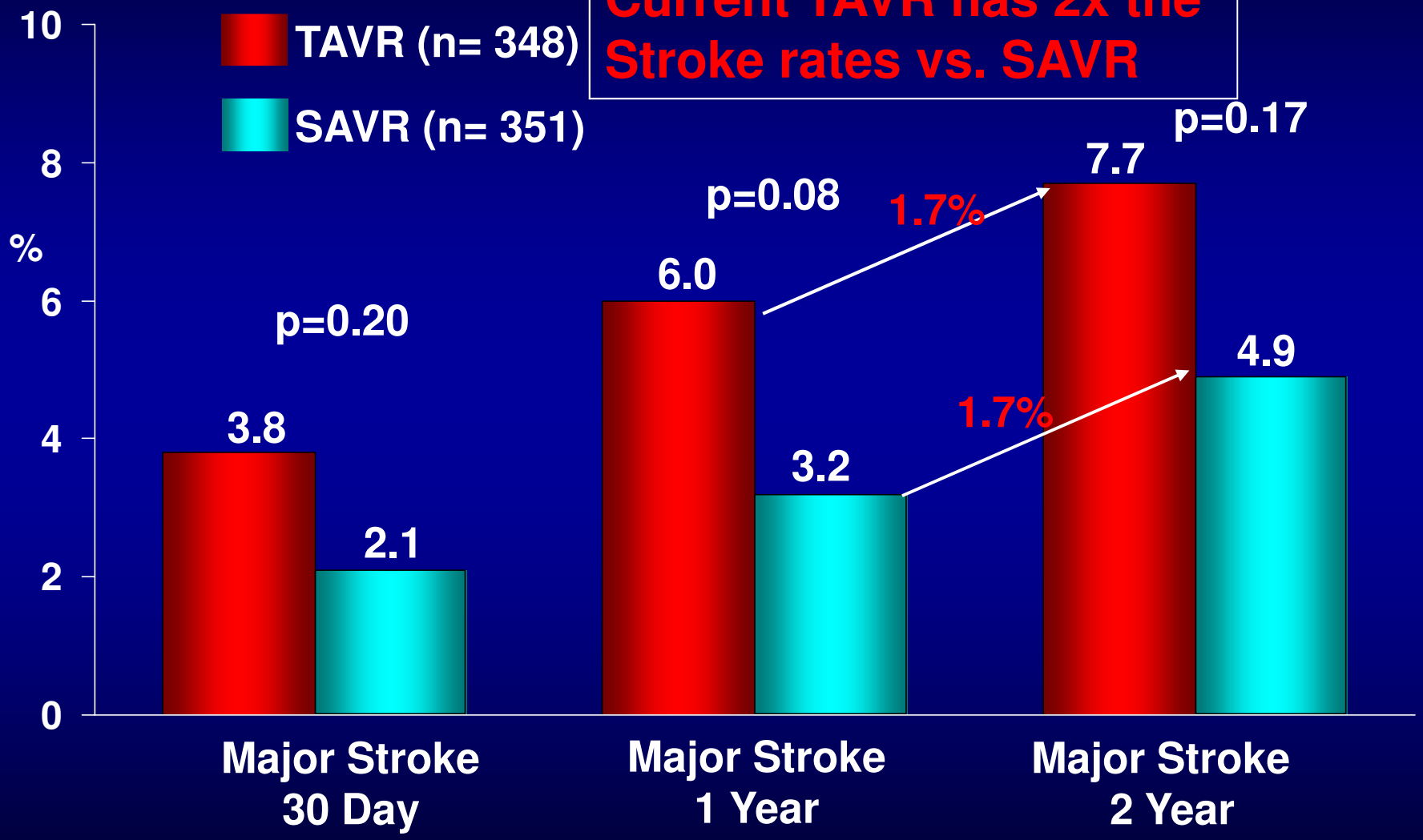


Death from Any Cause, As-Treated Population



Kodali et al., NEJM 2012;366:1686

Partner Trial Cohort A: Stroke at 2 Year



Smith C et al. NEJM 2011;364:2187.
Kodali S et al. NEJM 2012;366:1686.

CoreValve Pivotal Trials Study Design

CoreValve US Pivotal Trials

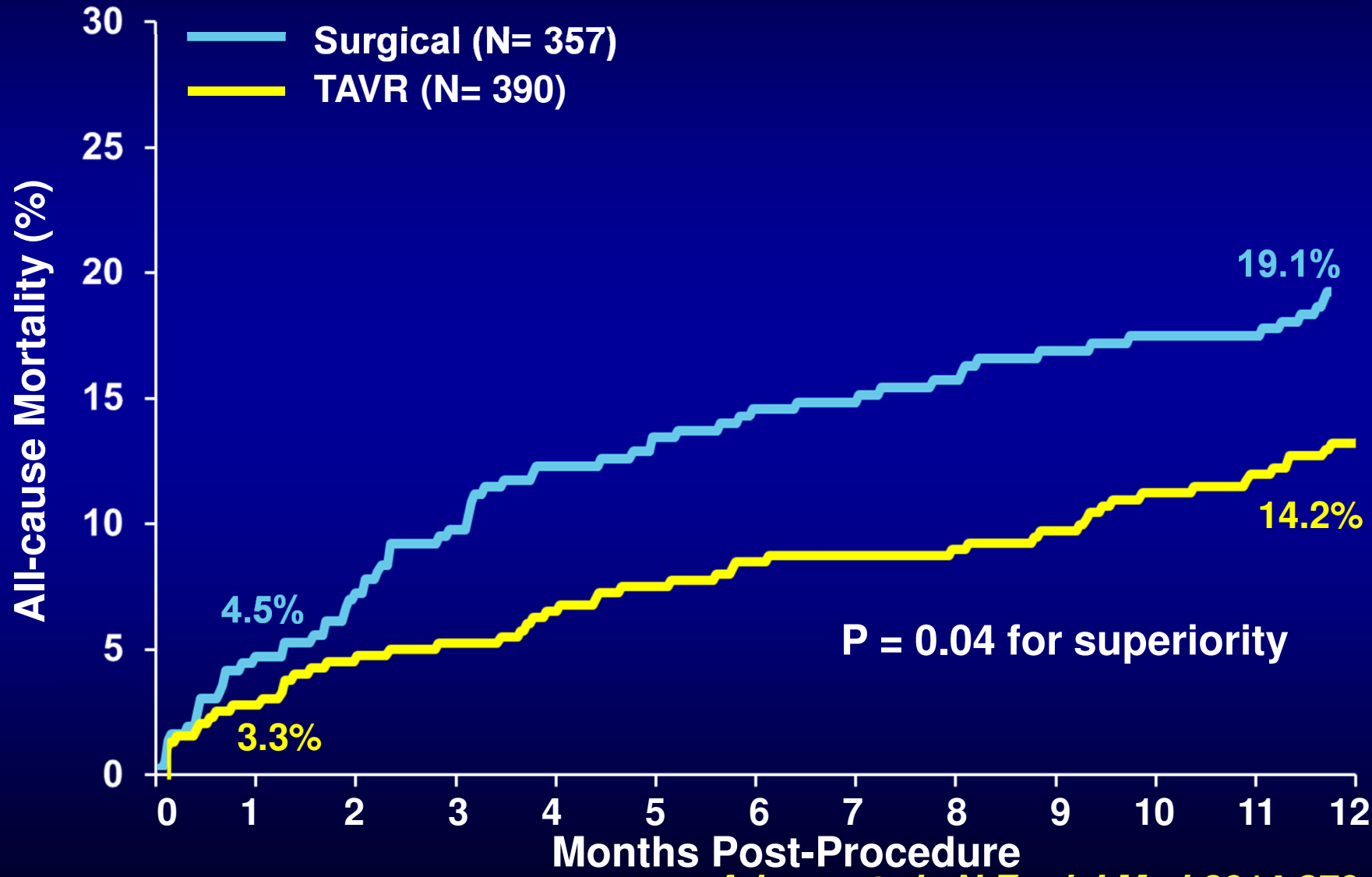
High Risk
Incremental STS mortality >15%

Randomization 1:1
N=790
Presented in ACC 2014

Versus

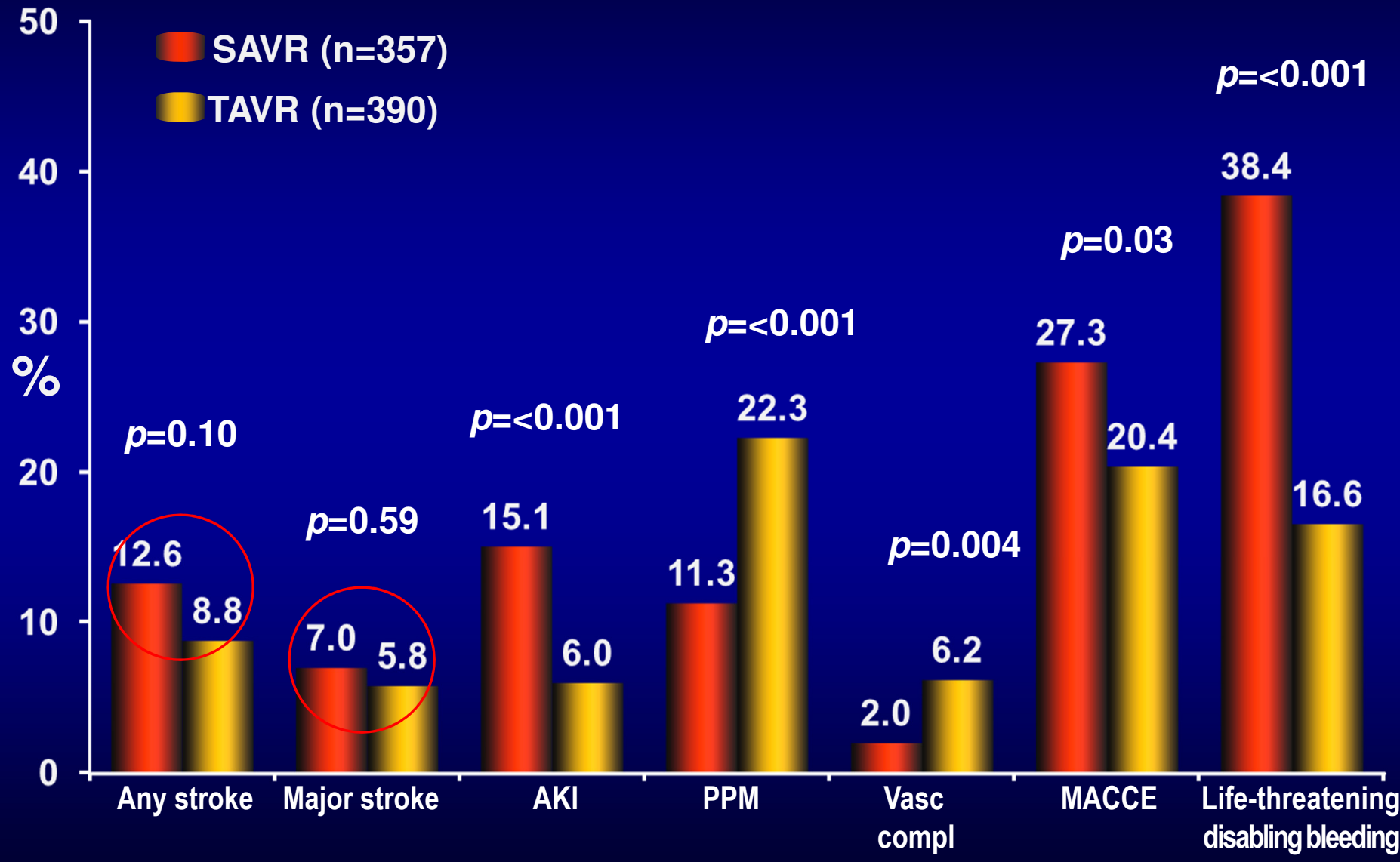
CoreValve	SAVR
N=392	N=388

CoreValve High Risk Pivotal trial: Primary Endpoint-- 1 Year All-cause Mortality



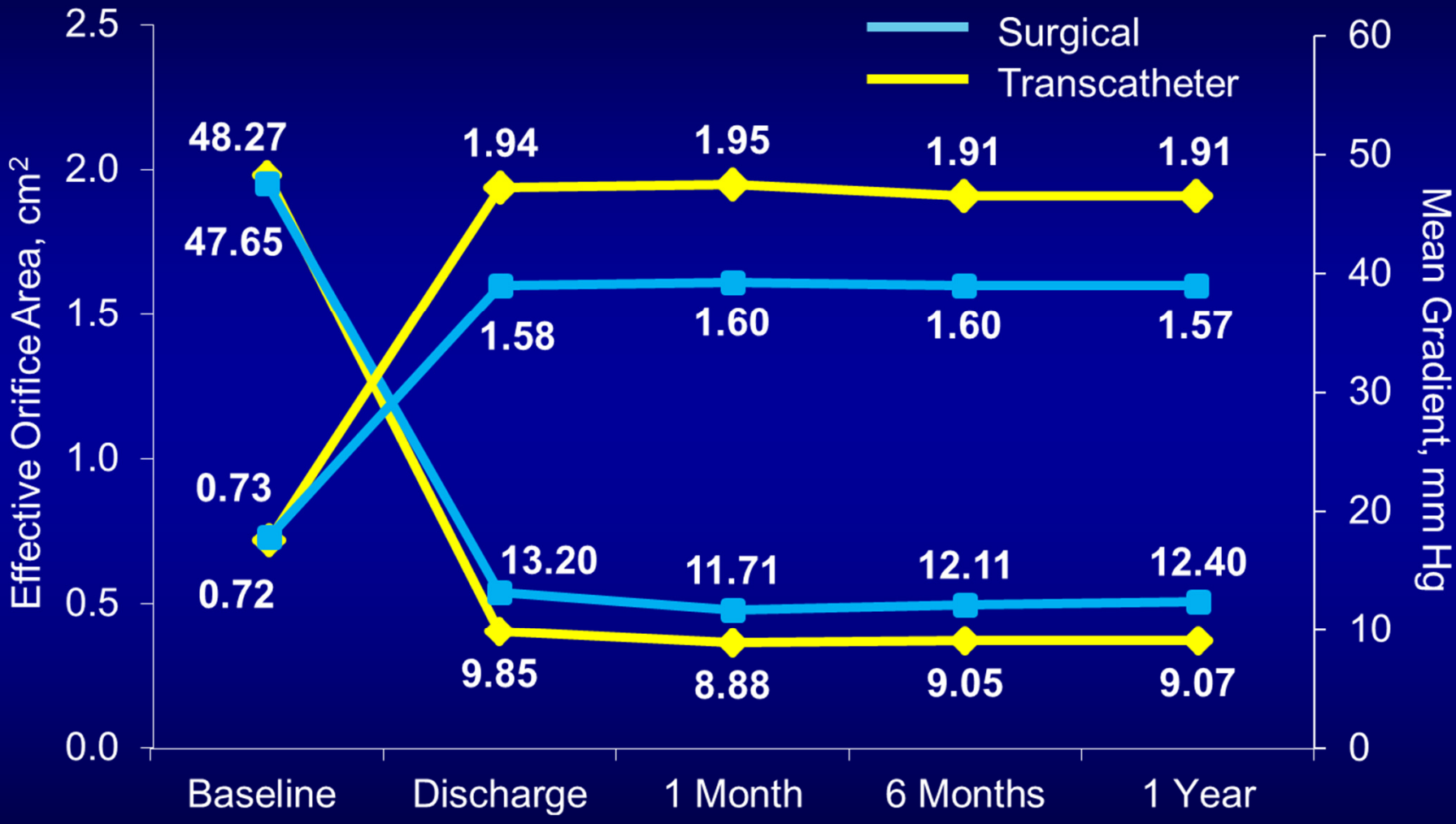
Adams et al., N Engl J Med 2014;370:1790

CoreValve High-risk Pivotal Trial: 1-Year Results



Adams et al., N Engl J Med 2014;370:1790

CoreValve: Echocardiographic Findings



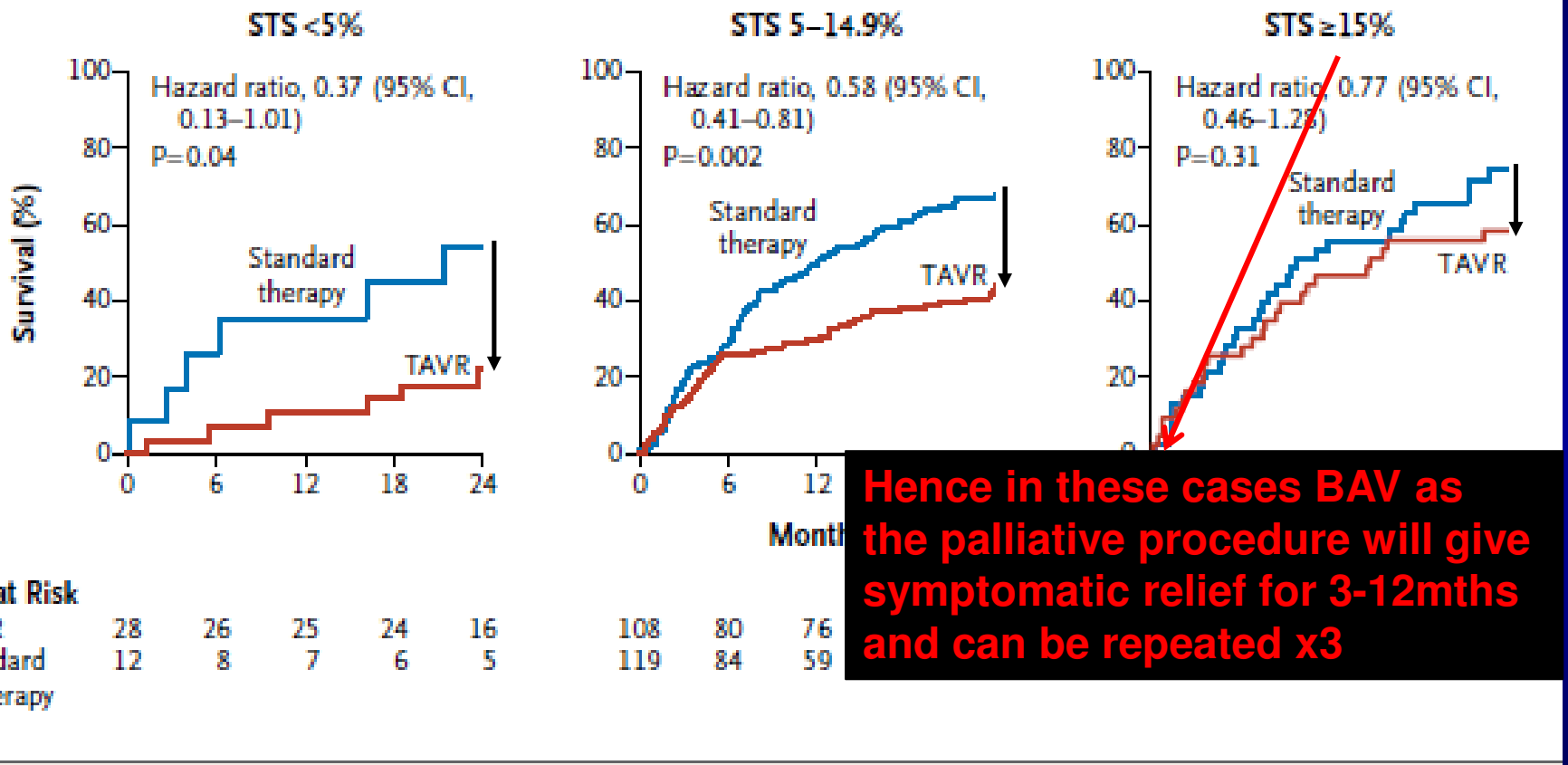
Post implant, there were significant differences ($P < 0.001$) between TAVR and SAVR at each time point for both EOA and mean gradient.

TAVR for Futile AS Cases

STS Morbidity/Mortality risk of >50%

Data from PARTNER IB Trial ES Valve

Partner Trial Cohort B: TAVR for Inoperable Severe Aortic Stenosis; Impact of Co-morbidities



Hence in these cases BAV as the palliative procedure will give symptomatic relief for 3-12mths and can be repeated x3

Figure 2. Two-Year Mortality, Stratified According to the Society of Thoracic Surgeons (STS) Risk Score.

Stratification according to STS categories (<5%, 5 to 14.9%, and ≥15%, on a scale of 0% to 100%, with higher scores indicating greater surgical risk) revealed a significant association with 2-year mortality.

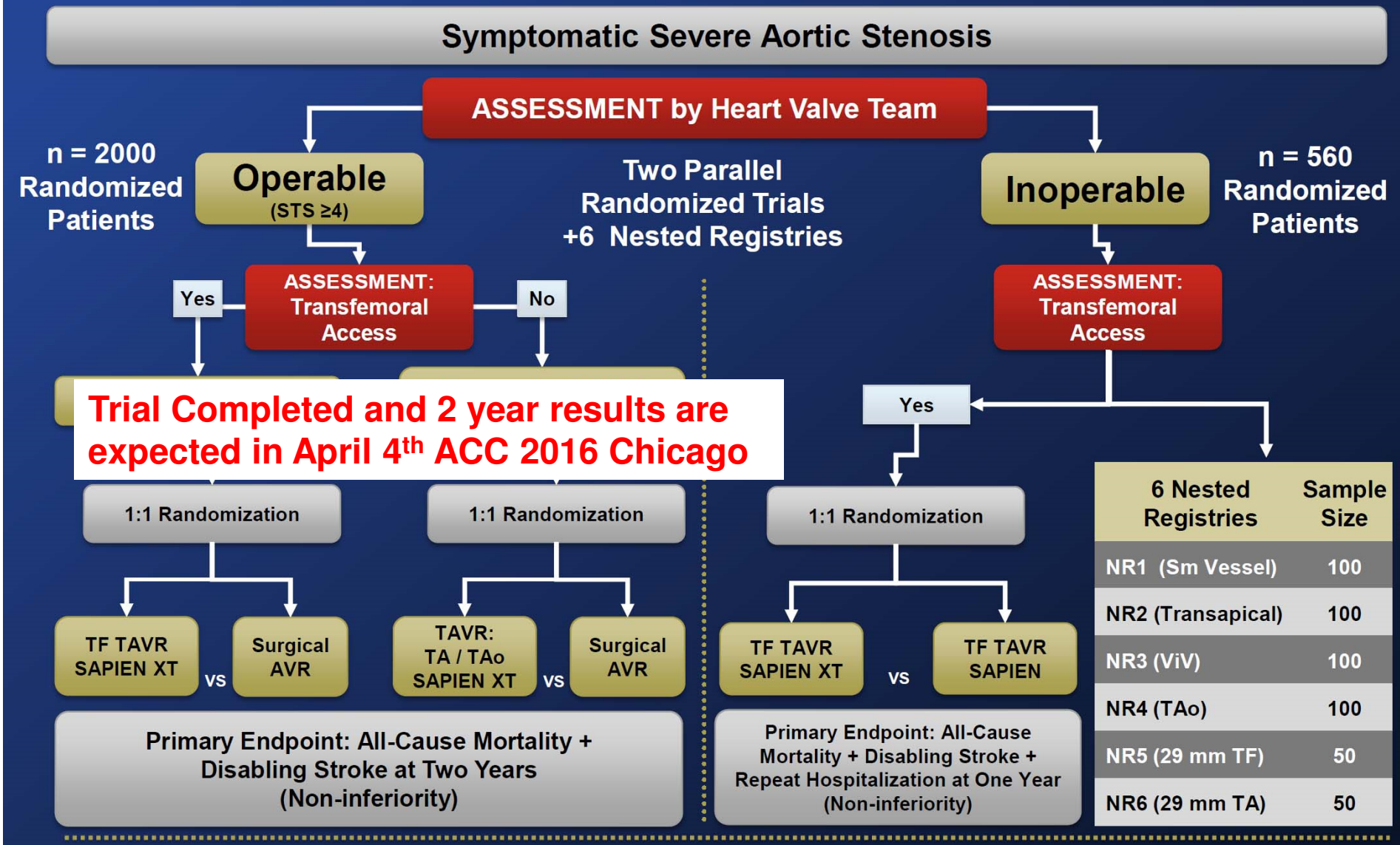
Makkar et al., NEJM 2012;366:1696

TAVR for Intermediate Risk AS patients

STS mortality risk of 3-4 to 8-10%

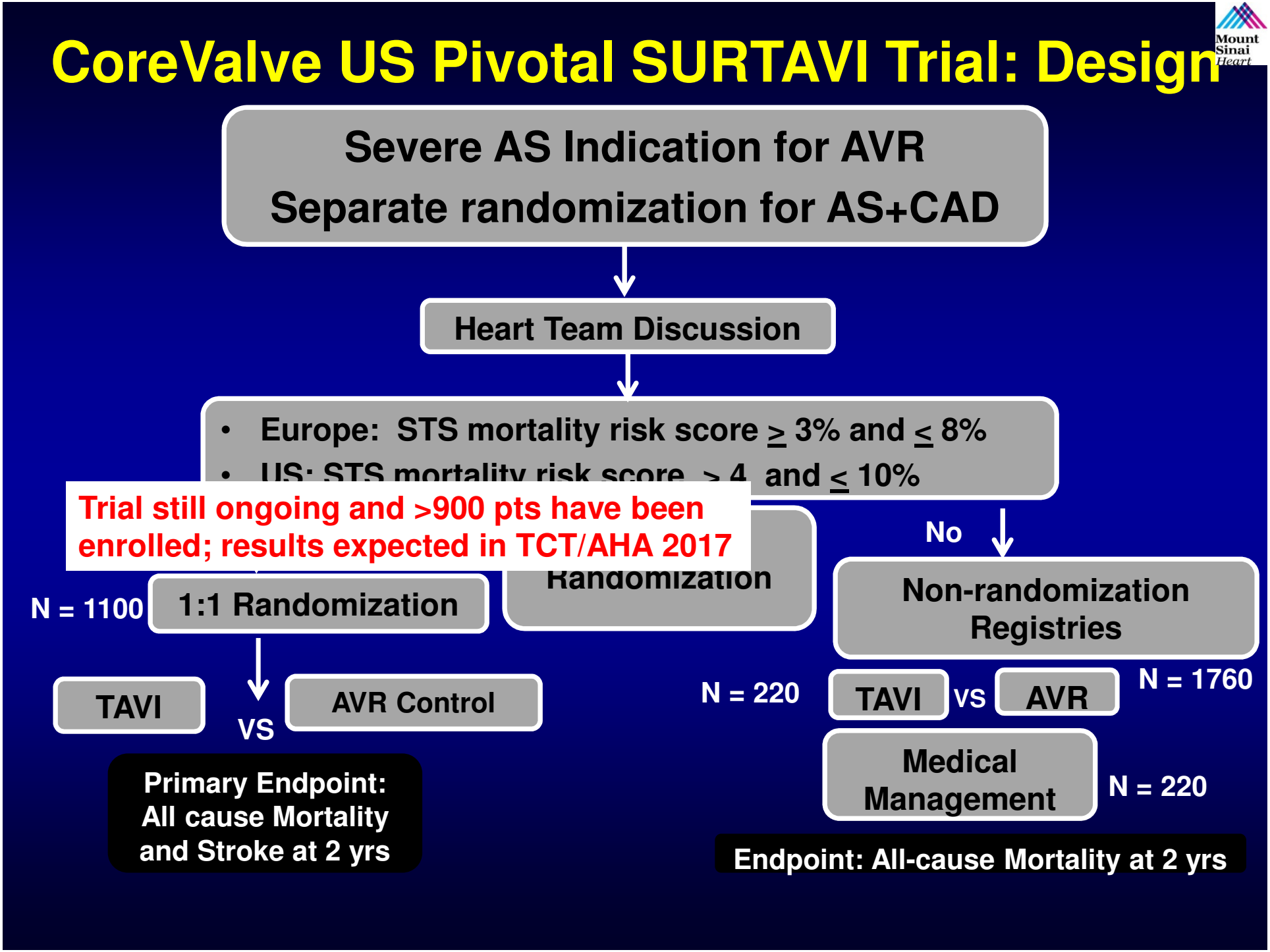
Two Trials: PARTNER IIA (completed)
SURTAVI Trial (ongoing)

The PARTNER II Trial Study Design



6 Nested Registries	Sample Size
NR1 (Sm Vessel)	100
NR2 (Transapical)	100
NR3 (ViV)	100
NR4 (TAo)	100
NR5 (29 mm TF)	50
NR6 (29 mm TA)	50

CoreValve US Pivotal SURTAVI Trial: Design



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MINI-FOCUS ON TAVI

CLINICAL RESEARCH

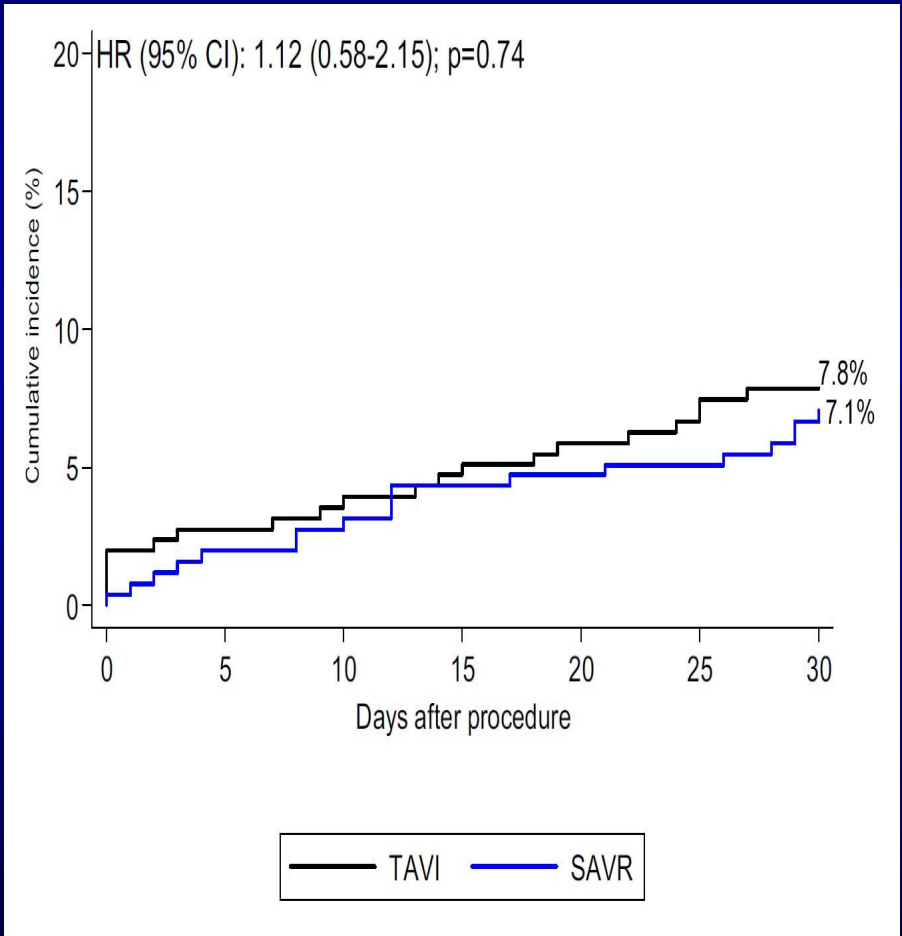
A 3-Center Comparison of 1-Year Mortality Outcomes Between Transcatheter Aortic Valve Implantation and Surgical Aortic Valve Replacement on the Basis of Propensity Score Matching Among Intermediate-Risk Surgical Patients

Nicolo Piazza, MD, PHD,*† Bindu Kalesan, PHD,‡ Nicolas van Mieghem, MD,§
Stuart Head, MSC,‖ Peter Wenaweser, MD,¶ Thierry P. Carrel, MD,# Sabine Bleiziffer, MD,*†
Peter P. de Jaegere, MD, PHD,§ Brigitta Gahl,# Robert H. Anderson, MD, PHD,**
Arie-Pieter Kappetein, MD, PHD,‖ Ruediger Lange, MD, PHD,*†
Patrick W. Serruys, MD, PHD,§ Stephan Windecker, MD,¶ Peter Jüni, MD‡

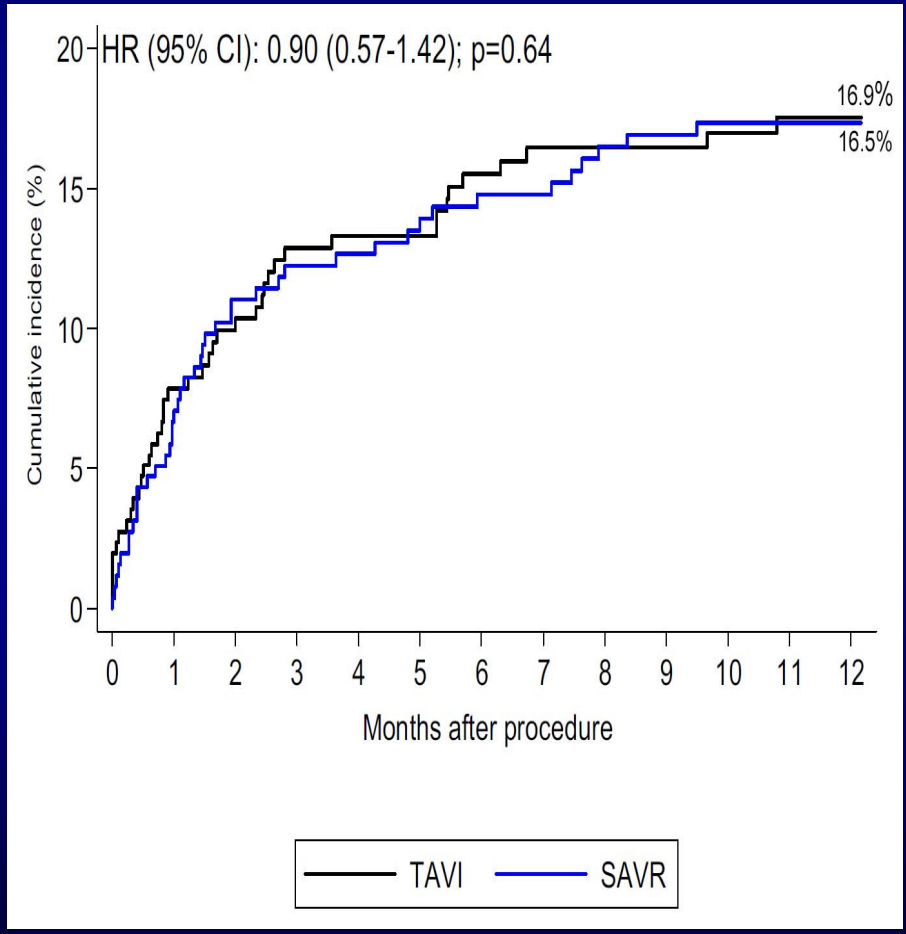
Munich, Germany; Bern, Switzerland; Rotterdam, the Netherlands; Montreal, Canada; and Newcastle-Upon-Tyne, United Kingdom

TAVR vs. SAVR in Intermediate Surgical Risk
Cumulative Incidence of All-Cause Mortality

All-Cause Mortality at 30 Days



All-Cause Mortality at 1 Year



Piazza et al., JACC Cardiovasc Interv 2013;6:443

TAVR for Low Risk AS patients

STS mortality risk of <3-4%

One Trials: Notion Trial (Completed)- CoreValve

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Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

1-Year Results From the All-Comers NOTION Randomized Clinical Trial

Hans Gustav Hørsted Thyregod, MD,* Daniel Andreas Steinbrüchel, MD, DMSc,* Nikolaj Ihlemann, MD, PhD,† Henrik Nissen, MD, PhD,‡ Bo Juel Kjeldsen, MD, PhD,§ Petur Petursson, MD,‖ Yanping Chang, MS,¶ Olaf Walter Franzen, MD,† Thomas Engstrøm, MD, DMSc,† Peter Clemmensen, MD, DMSc,† Peter Bo Hansen, MD,# Lars Willy Andersen, MD, DMSc,# Peter Skov Olsen, MD, DMSc,* Lars Søndergaard, MD, DMSc†

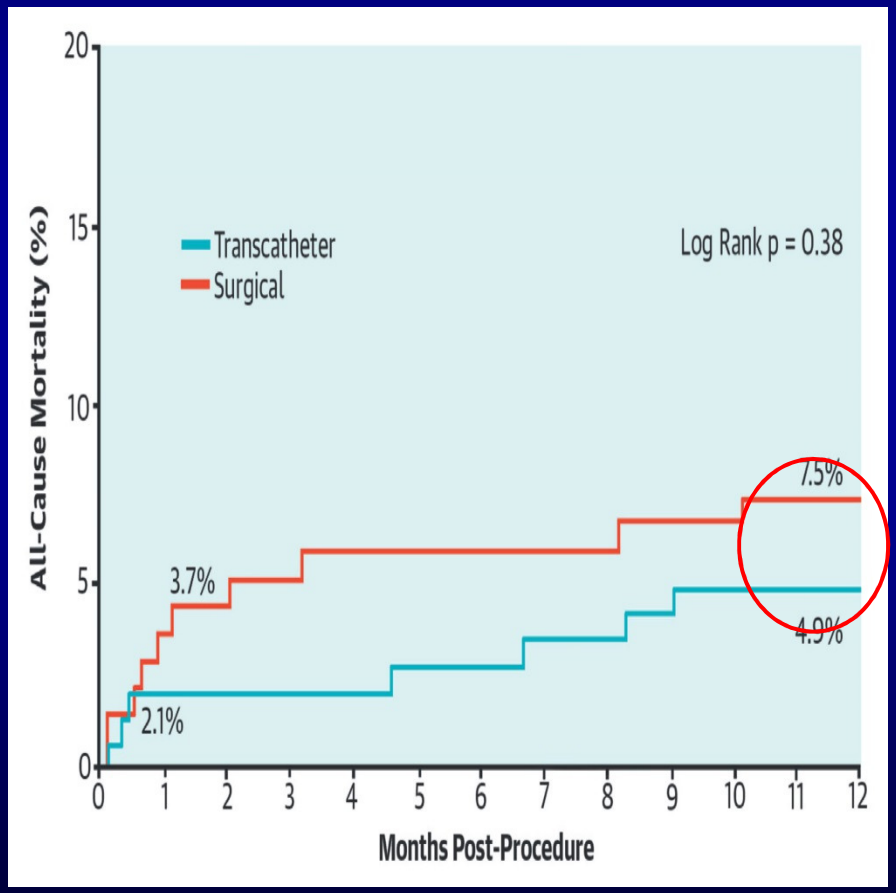
NOTION Trial: Baseline Characteristics

	TAVR* (n = 145)	SAVR* (n = 135)
Age, yrs	79.2 ± 4.9	79.0 ± 4.7
Male	78/145 (53.8)	71/135 (52.6)
NYHA functional classification		
I	7/144 (4.9)	3/134 (2.2)
II	67/144 (46.5)	70/134 (52.2)
III	67/144 (46.5)	57/134 (42.5)
IV	3/144 (2.1)	4/134 (3.0)
STS-PROM score, %	2.9 ± 1.6	3.1 ± 1.7
Logistic EuroSCORE, %	8.4 ± 4.0	8.9 ± 5.5
Logistic EuroSCORE II, %	1.9 ± 1.2	2.0 ± 1.3
Additive EuroSCORE, %	7.4 ± 1.4	7.5 ± 1.4
Diabetes mellitus	26/145 (17.9)	28/135 (20.7)
Creatinine level >2 mg/dl	2/145 (1.4)	1/135 (0.7)
History of hypertension	103/145 (71.0)	103/135 (76.3)
Peripheral vascular disease	6/145 (4.1)	9/135(6.7)
Prior cerebrovascular accident	24/145 (16.6)	22/135 (16.3)
Chronic lung disease	17/145 (11.7)	16/135 (11.9)
Cardiac risk factors		
Prior PCI	11/145 (7.6)	12/135 (8.9)
Pre-existing pacemaker	5/145 (3.4)	6/135 (4.4)
Prior MI	8/145 (5.5)	6/135 (4.4)
Prior AF/atrial flutter	40/144 (27.8)	34/133 (25.6)

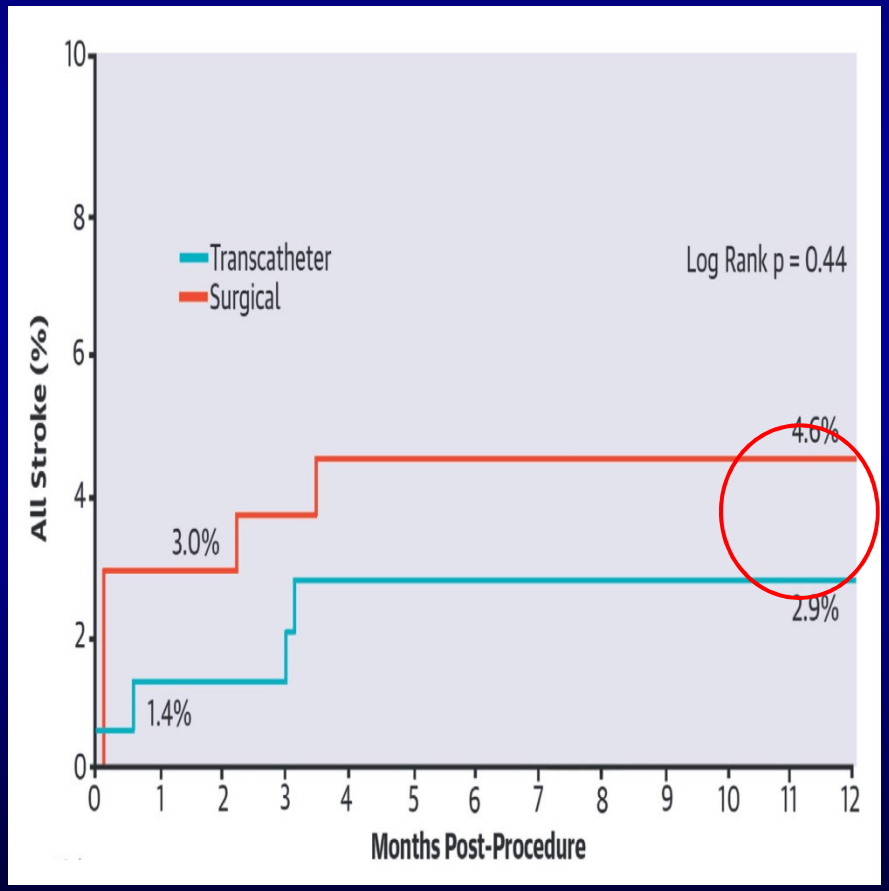
Thyregod et al., J Am Coll Cardiol 2015;65:2184

NOTION Trial: TAVR vs SAVR in Severe Aortic Valve Stenosis

All-Cause Morality at 1 Year

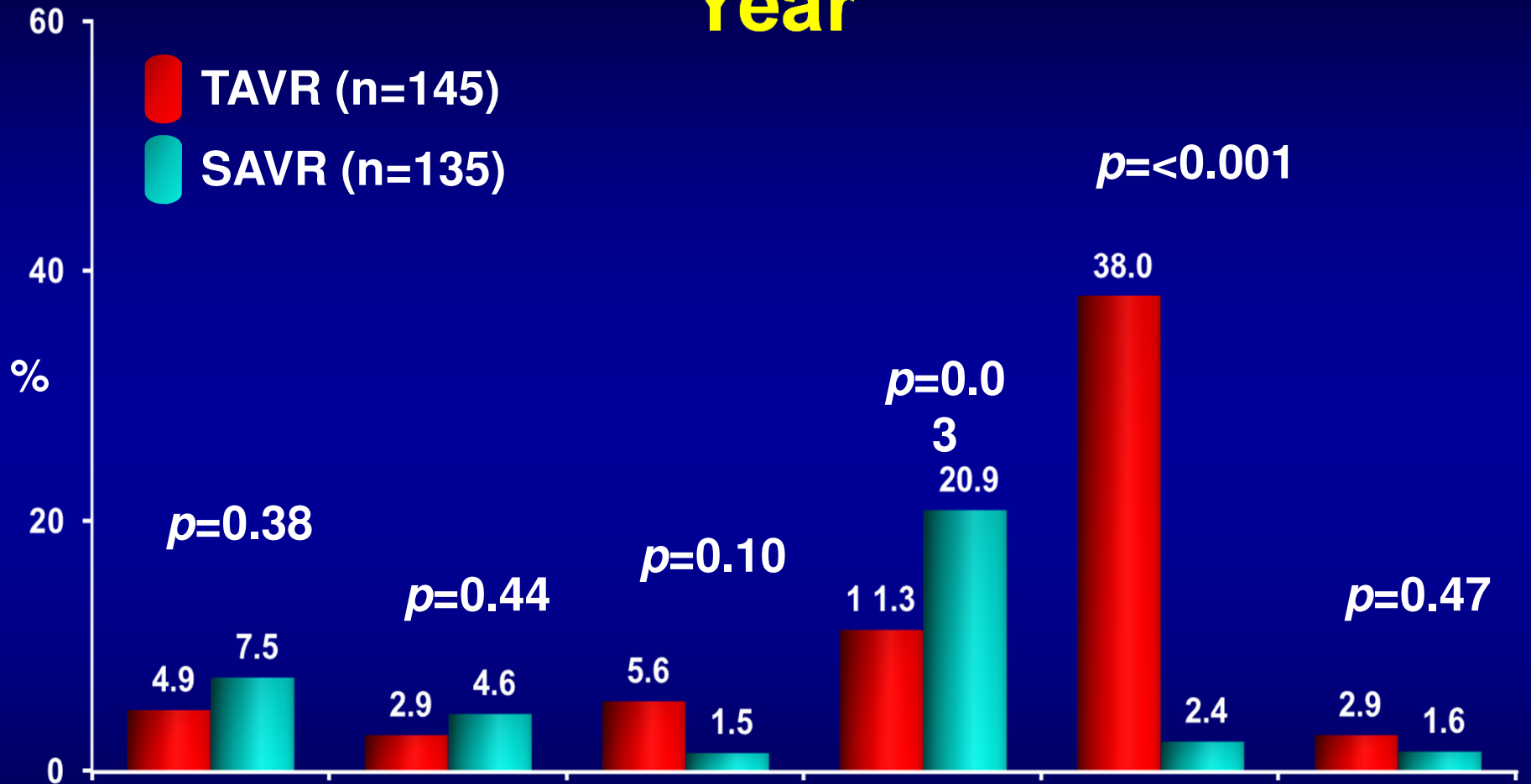


All-Strokes at 1 Year



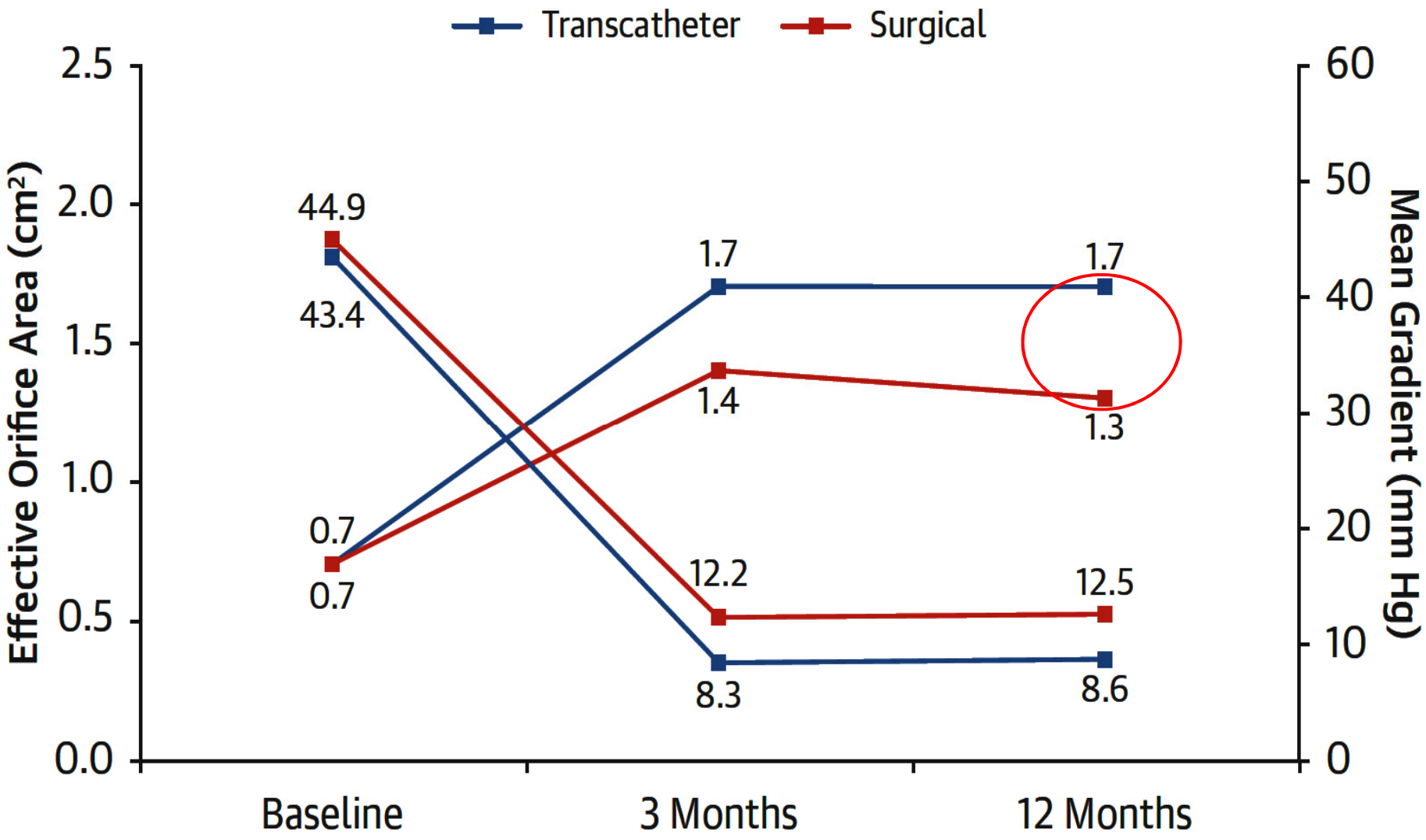
Thyregod et al., J Am Coll Cardiol 2015;65:2184

NOTION Trial: Clinical Outcomes at 1 Year



Thyregod et al., J Am Coll Cardiol 2015;65:2184

NOTION Trial: Aortic Valve



Thyregod et al., J Am Coll Cardiol

Randomized TAVR Trials by Risk Group

	Trial	STS Score (%)		Mortality (%)		Stroke (%)		>Mild AR (%)		Pacemaker (%)	
Extreme Risk		TAVR	ST	TAVR	ST	TAVR	ST	TAVR	ST	TAVR	ST
	PARTNER 1B	11.2	12.1	30.7	50.7	10.0	4.5	10.5	4.2	4.5	7.8
	CoreValve ER	10.3	-	24.3	-	7.0	-	13.8	-	21.6	-
	Groups	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
High Risk	PARTNER 1A	11.8	11.7	24.2	26.8	6.0	3.1	6.8	1.9	5.7	5.0
	CoreValve	7.3	7.5	14.2	19.1	8.8	12.6	7.1	1.4	22.3	11.3
Intermediate Risk	PARTNER 2A SURTAVI			Results Awaited ACC 2016 Ongoing Enrollment							
Lower Risk	Notion	2.9	3.1	4.9	7.5	2.9	4.6	15.7	0.9	38.0	2.4

Transcatheter Aortic Valves Replacement (TAVR)

Surgical risk is a continuum: *Symptomatic AS*

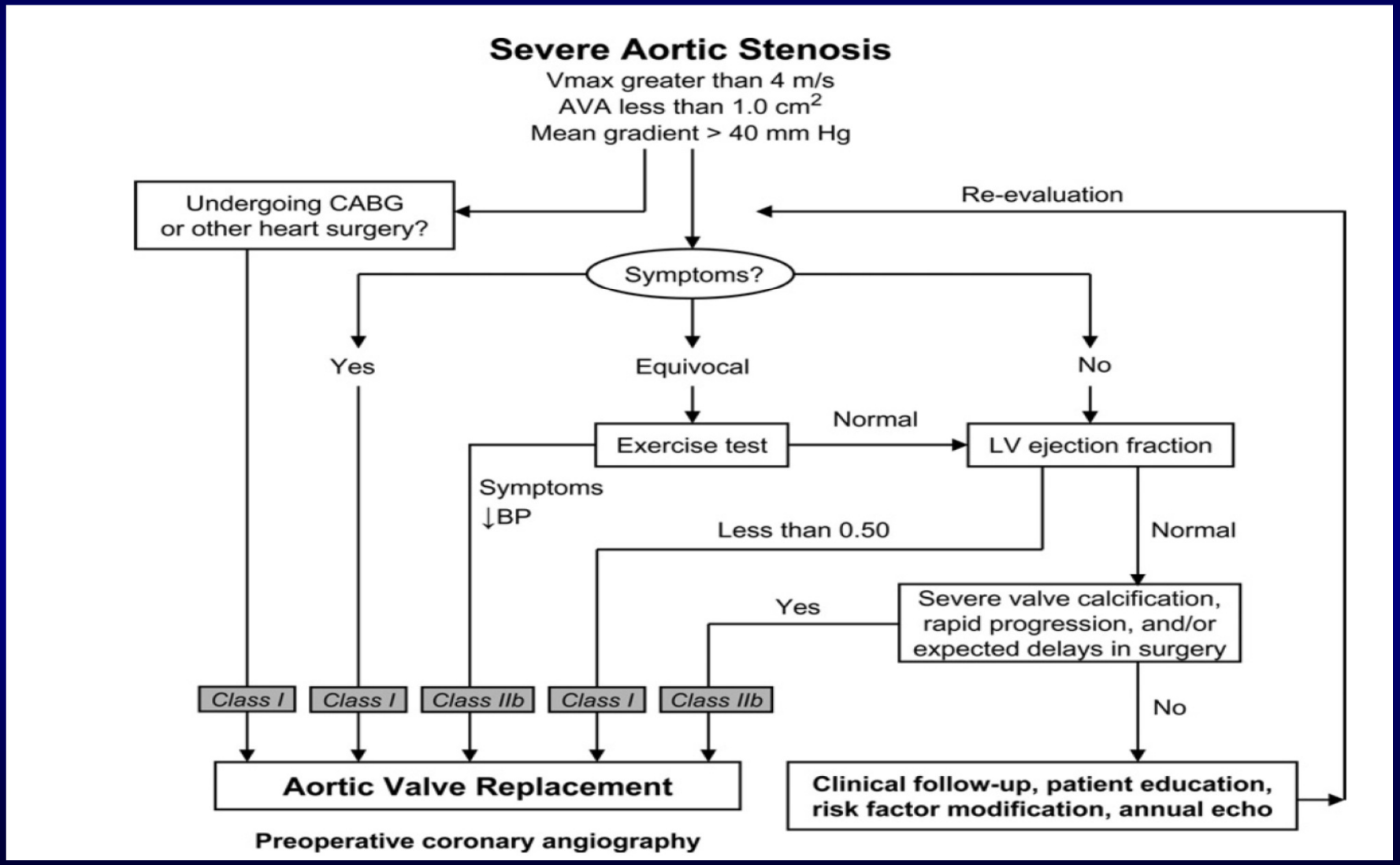
Pt with prohibitive surgical risk are appropriate for TAVR even with low STS risk: hostile mediastinum, egg-shell aorta, RT prior CABG with IM stuck to mediastinum severe COPD, extreme frailty

Operable AS pts

STS: <3%	3-4 to 8-10%	10-15%	15-50%	>50%
Low-risk	Intermediate-risk	High-risk	Extreme-risk	Too-sick
~40%	~15%	~15-20%	~20%	~10%

Aortic Stenosis and SAVR

ACC/AHA Guidelines Flowchart



Bonow R, Carabello BA, et al. Circulation 2006; 114: e84-231.

Summary of Recommendations for AS: Choice of Surgical or Transcatheter Intervention

Recommendations	COR	LOE
Surgical AVR is recommended in patie… low or intermediate surgical risk		
For patients in whom TAVR or high-ris… Valve Team should collaborate to provide optimal patient care		
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

Hence 60year old asymptomatic pt with severe AS
If qualifies for SAVR, could be appropriate for TAVR
In the appropriate STS risk group

BAV may provide palliative symptomatic benefit in these pts

Nishimura et al., J Thorac Cardiovasc Surg 2014;148:e1

Structural Heart Webcast Series

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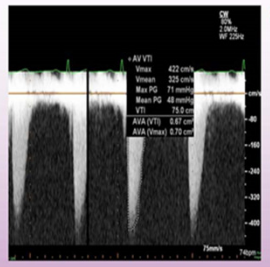
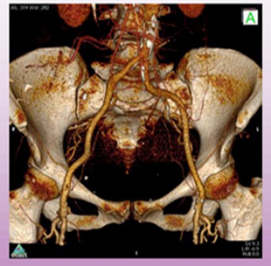
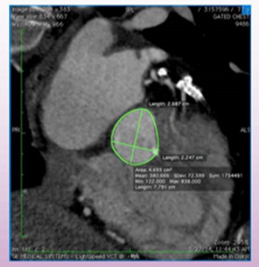
9:00 – 10:00 am







Live From The Mount Sinai Hospital

www.structuralheartlivecases.org

Mount Sinai Heart

2nd Tuesday of the Month

9-10am:

Next webcast February 9th 2016

This is a great addition to our monthly;

- CCClivecases.org for 5+ yrs.

- Peripheralinterventions.org for 3+ yrs.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

R.R. Makkar, G. Fontana, H. Jilaihawi, T. Chakravarty, K.F. Kofoed, O. de Backer, F.M. Asch, C.E. Ruiz, N.T. Olsen, A. Trento, J. Friedman, D. Berman, W. Cheng, M. Kashif, V. Jelnin, C.A. Kliger, H. Guo, A.D. Pichard, N.J. Weissman, S. Kapadia, E. Manasse, D.L. Bhatt, M.B. Leon, and L. Søndergaard

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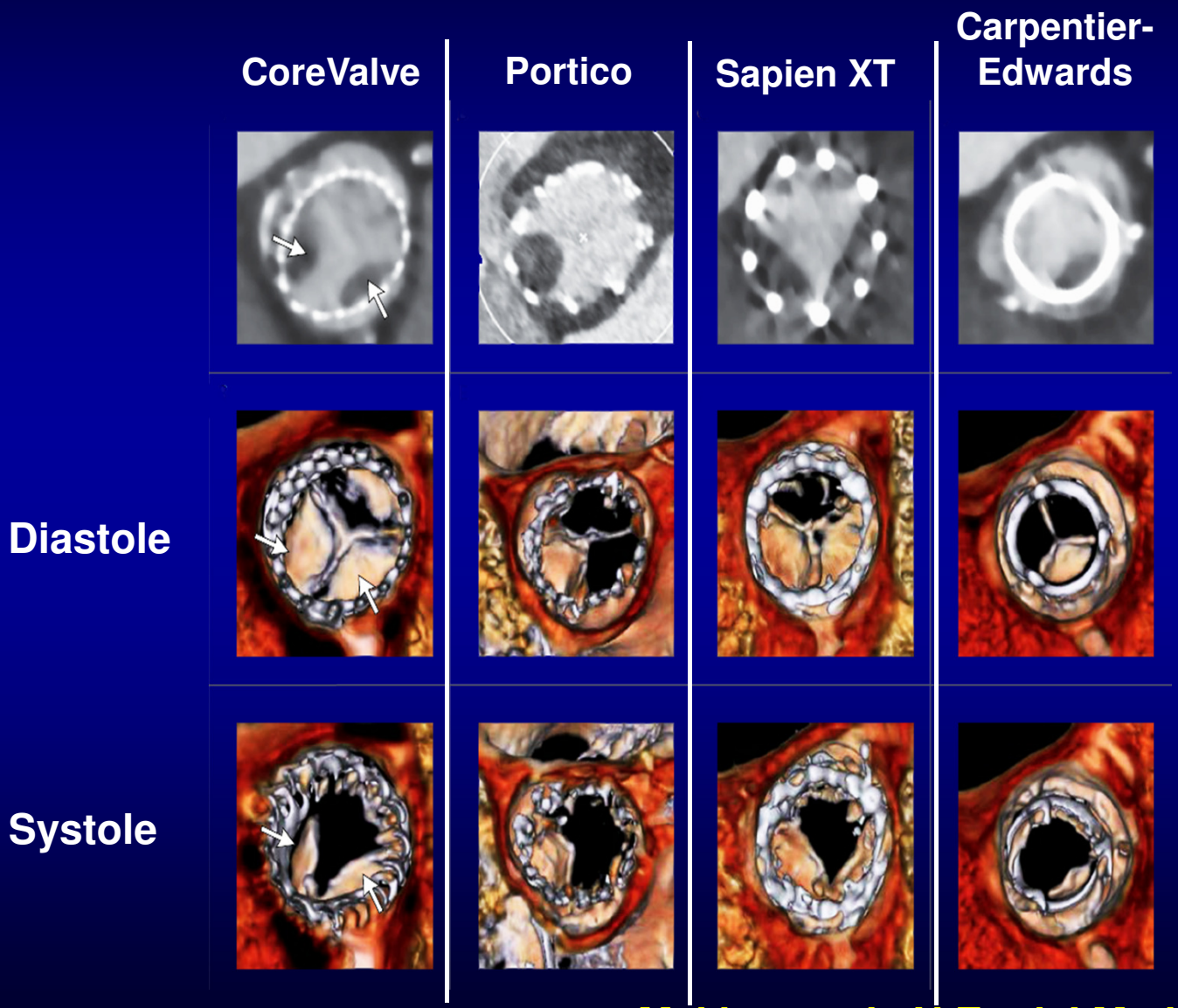
ORIGINAL ARTICLE

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

CONCLUSIONS

Reduced aortic-valve leaflet motion was shown in patients with bioprosthetic aortic valves. The condition resolved with therapeutic anticoagulation. The effect of this finding on clinical outcomes including stroke needs further investigation. (Funded by St. Jude Medical and Cedars–Sinai Heart Institute; Portico-IDE ClinicalTrials.gov number, NCT02000115; SAVORY registry, NCT02426307; and RESOLVE registry, NCT02318342.)

Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types



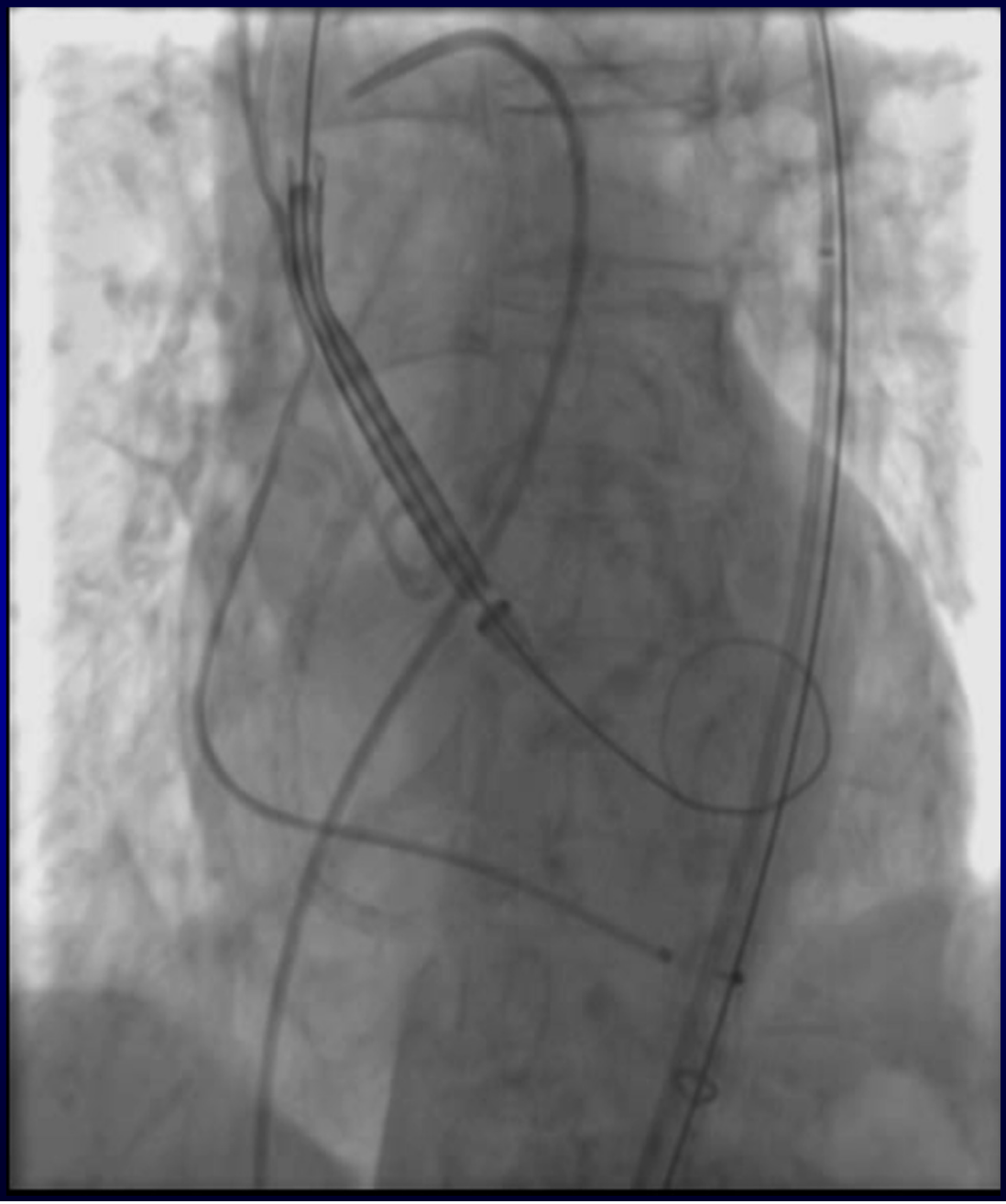
Makkar et al., N Engl J Med 2015;373:2015

Clinical Outcomes

Outcome	Normal Leaflet Motion	Reduced Leaflet Motion	P Value
	number of patients		
PORTICO IDE study			
Patients in study	33	22	
Death	1	2	0.56
Myocardial infarction	1	1	>0.99
Stroke or transient ischemic attack	0	2	0.16
Stroke	0	2	0.16
Transient ischemic attack	0	0	>0.99
Pooled registries (RESOLVE and SAVORY cohorts)			
Patients in group	115	17	
Death	0	0	>0.99
Myocardial infarction	0	0	>0.99
Stroke or transient ischemic attack	1	3	0.007
Stroke	1	0	>0.99
Transient ischemic attack	0	3	0.002

Makkar et al., N Engl J Med 2015;373:2015

SET 3 – RM R7



SET 3 – RM R10

SET 3 – RM R12

SET 3 – RM R13

SET 3 – RM R15

SET 3 – RM R18