Faculty disclosure

Joelle Kefer

<u>*I disclose the following financial relationships:*</u>

Consultant for StJude Medical
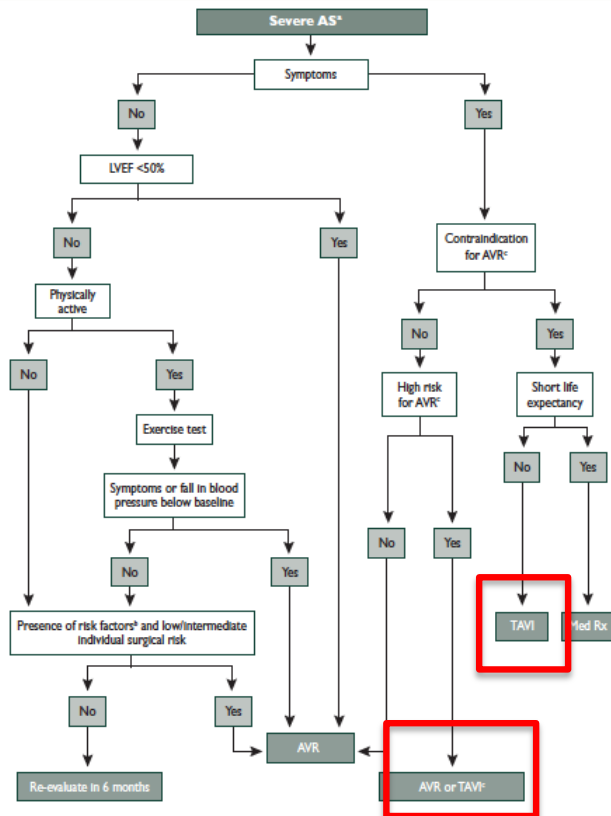**Receive grant/research support** from Abbott Vascular

AVR : risk of surgery

Table 7 Operative mortality after surgery for valvular heart disease

	EACTS (2010)	STS (2010)	UK (2004–2008)	Germany (2009)
Aortic valve replacement, no CABG (%)	2.9 (40 662)	3.7 (25 515)	2.8 (17 636)	2.9 (11 981)

A logistic EuroSCORE $\geq 20\%$ has been suggested as an indication for TAVI therapy but EuroSCORE is known to markedly overestimate operative mortality.[113] Use of the STS scoring system $>10\%$ may result in a more realistic assessment of operative risk.[40]

In the absence of a perfect quantitative score, the risk assessment should mostly rely on the clinical judgement of the 'heart team', in addition to the combination of scores.[113]

ESC/EACTS guidelines, Eur Heart J 2012

AVR : risk of surgery

Table 5. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

	Low Risk (Must Meet ALL Criteria in This Column)	Intermediate Risk (Any 1 Criterion in This Column)	High Risk (Any 1 Criterion in This Column)	Prohibitive Risk (Any 1 Criterion in This Column)
STS PROM*	<4% AND	4%–8% OR	>8% OR	Predicted risk with surgery of death or major morbidity (all-cause) >50% at 1 y OR
Frailty†	None AND	1 Index (mild) OR	≥2 Indices (moderate to severe) OR	
Major organ system compromise not to be improved postoperatively‡	None AND	1 Organ system OR	No more than 2 organ systems OR	≥3 Organ systems OR
Procedure-specific impediment§	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

*Use of the STS PROM to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 standard deviation of STS average observed/expected ratio for the procedure in question.

†Seven frailty indices: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, and urinary continence) and independence in ambulation (no walking aid or assist required or 5-meter walk in <6 s). Other scoring systems can be applied to calculate no, mild-, or moderate-to-severe frailty.

‡Examples of major organ system compromise: Cardiac—severe LV systolic or diastolic dysfunction or RV dysfunction, fixed pulmonary hypertension; CKD stage 3 or worse; pulmonary dysfunction with FEV1 <50% or $DLCO_2$ <50% of predicted; CNS dysfunction (dementia, Alzheimer's disease, Parkinson's disease, CVA with persistent physical limitation); GI dysfunction—Crohn's disease, ulcerative colitis, nutritional impairment, or serum albumin <3.0; cancer—active malignancy; and liver—any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy.

§Examples: tracheostomy present, heavily calcified ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, or radiation damage.

CKD indicates chronic kidney disease; CNS, central nervous system; CVA, stroke; $DLCO_2$, diffusion capacity for carbon dioxide; FEV1, forced expiratory volume in 1 s; GI, gastrointestinal; INR, international normalized ratio; LV, left ventricular; PROM, predicted risk of mortality; RV, right ventricular; STS, Society of Thoracic Surgeons; and VKA, vitamin K antagonist.

Initial concept of TAVI: clinical need
AS untreated in 32% cases @ high risk

Aortic stenosis

Transcatheter
aortic valve
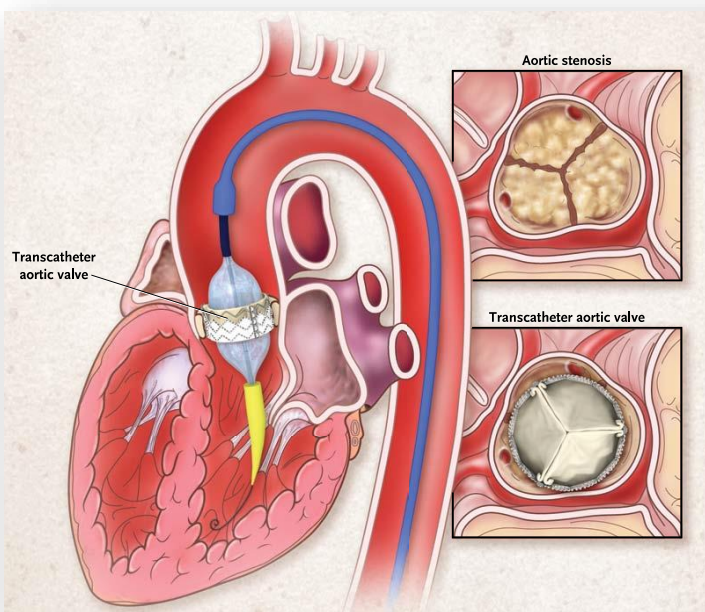
Transcatheter aortic valve
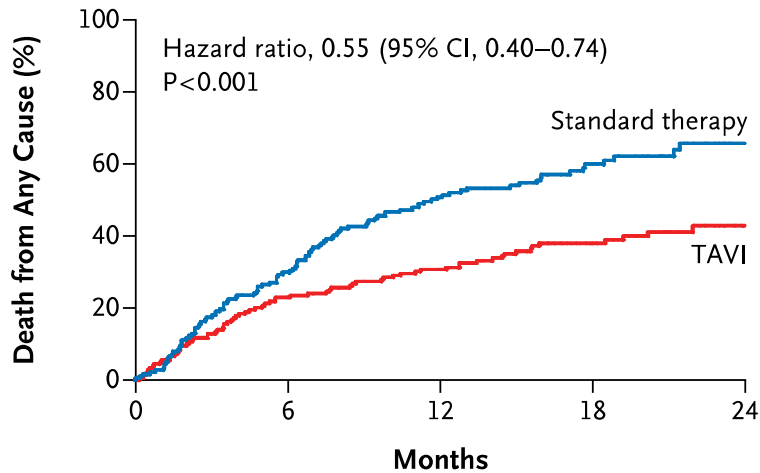
The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Implantation for Aortic Stenosis
in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D.,
Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D.,
Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D.,
Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D.,
John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D.,
and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Δ at 1 yr = 20.0%
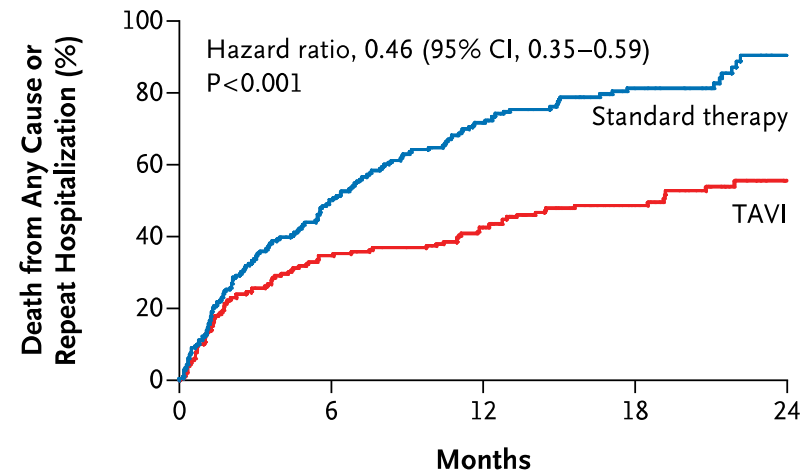NNT = 5.0 pts

Δ at 1 yr = 29.1%
NNT = 3.4 pts

A

Hazard ratio, 0.55 (95% CI, 0.40–0.74)
$P<0.001$

Standard therapy

TAVI

Death from Any Cause (%)

Months

No. at Risk

TAVI	179	138	122	67	26
Standard therapy	179	121	83	41	12

C

Hazard ratio, 0.46 (95% CI, 0.35–0.59)
$P<0.001$

Standard therapy

TAVI

Death from Any Cause or Repeat Hospitalization (%)

Months

No. at Risk

TAVI	179	117	102	56	22
Standard therapy	179	86	49	23	4

STS : 11.2 ± 5.8
Log Euroscore : 26.4 ± 17.2

Leon M et al, NEJM 2010

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D.,

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Intention-to-Treat Population		As-Treated Population	
	TAVR Group (N=394)	Surgical Group (N=401)	TAVR Group (N=390)	Surgical Group (N=357)
Age — yr	83.2±7.1	83.5±6.3	83.1±7.1	83.2±6.4
Female sex — no. (%)	183 (46.4)	189 (47.1)	183 (46.9)	170 (47.6)
NYHA class — no. (%)				
Class II	56 (14.2)	53 (13.2)	56 (14.4)	47 (13.2)
Class III	258 (65.5)	277 (69.1)	255 (65.4)	248 (69.5)
Class IV	80 (20.3)	71 (17.7)	79 (20.3)	62 (17.4)
STS PROM estimate†				
Mean estimate — %	7.3±3.0	7.5±3.2	7.3±3.0	7.5±3.4
<4% — no. (%)	33 (8.4)	42 (10.5)	33 (8.5)	40 (11.2)
4–10% — no. (%)	308 (78.2)	288 (71.8)	304 (77.9)	251 (70.3)
>10% — no. (%)	53 (13.5)	71 (17.7)	53 (13.6)	66 (18.5)
Logistic EuroSCORE — %‡	17.6±13.0	18.4±12.8	17.7±13.1	18.6±13.0
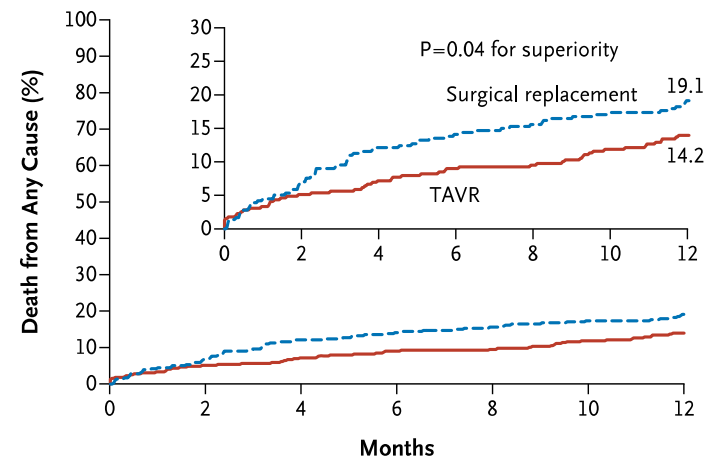
No. at Risk

TAVR	390	377	353	329
Surgical replacement	357	341	297	274

Figure 2. Kaplan–Meier Cumulative Frequency of Death from Any Cause.

The rate of death from any cause in the TAVR group was noninferior to that in the surgical group (P<0.001). A subsequent test for superiority at 1 year showed that TAVR was superior to surgical replacement (P=0.04). The inset shows the same data on an enlarged y axis.

TAVI devices developed over time

Second generation TAVI mitigate technical issues

30-day outcome in High risk patients

PARTNER II S3 High Risk ACC 2015

CE Mark Evolut R ACC 2015
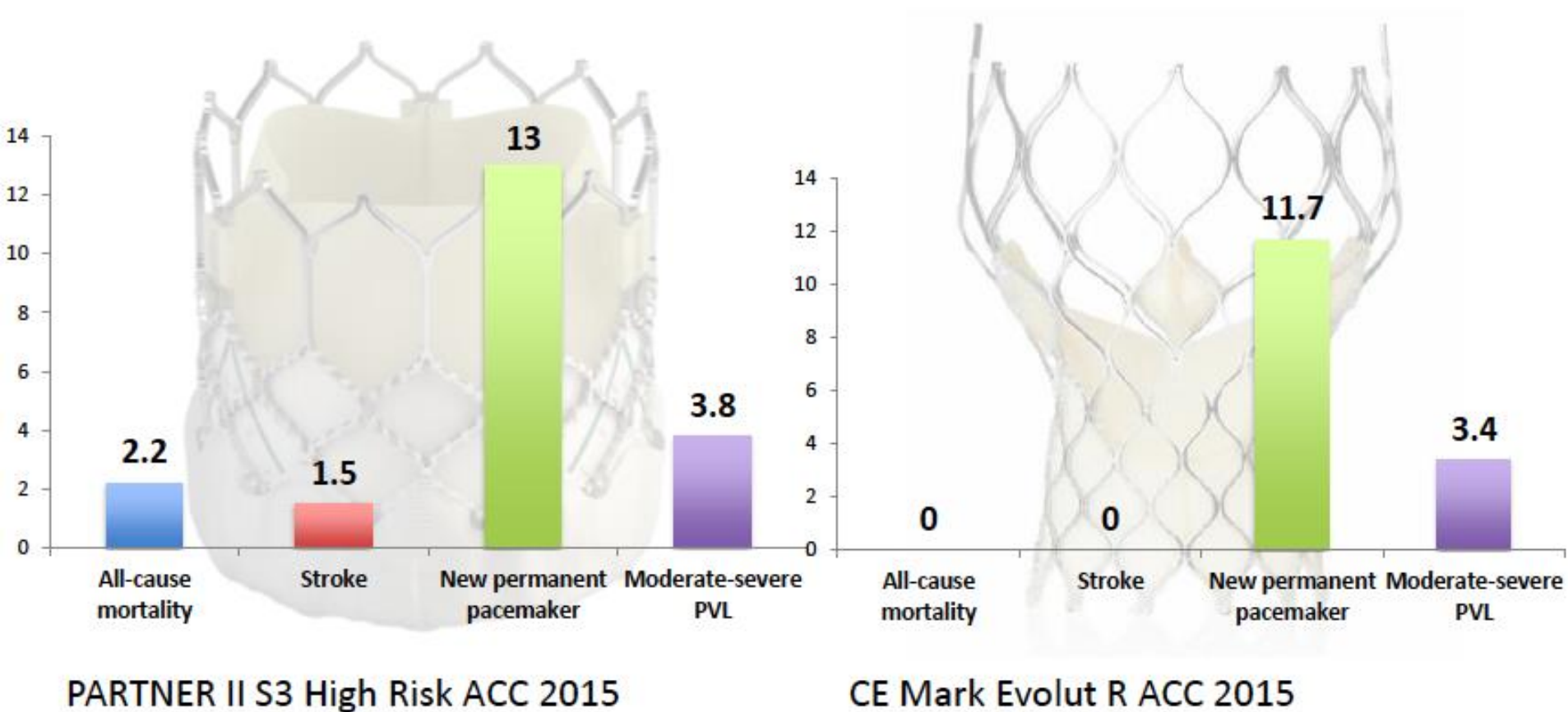
Paravalvular aortic regurgitation

■ Mild ■ Moderate / Severe

[1]Leon, et. al. presented at ACC 2013; [2]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [3]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [4]Manoharan, et al., et. al. presented at TCT 2014; [5]Kodali, et al., presented at ACC 2015; [6]Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; [7]Meredith, et al., presented at PCR London Valves 2014
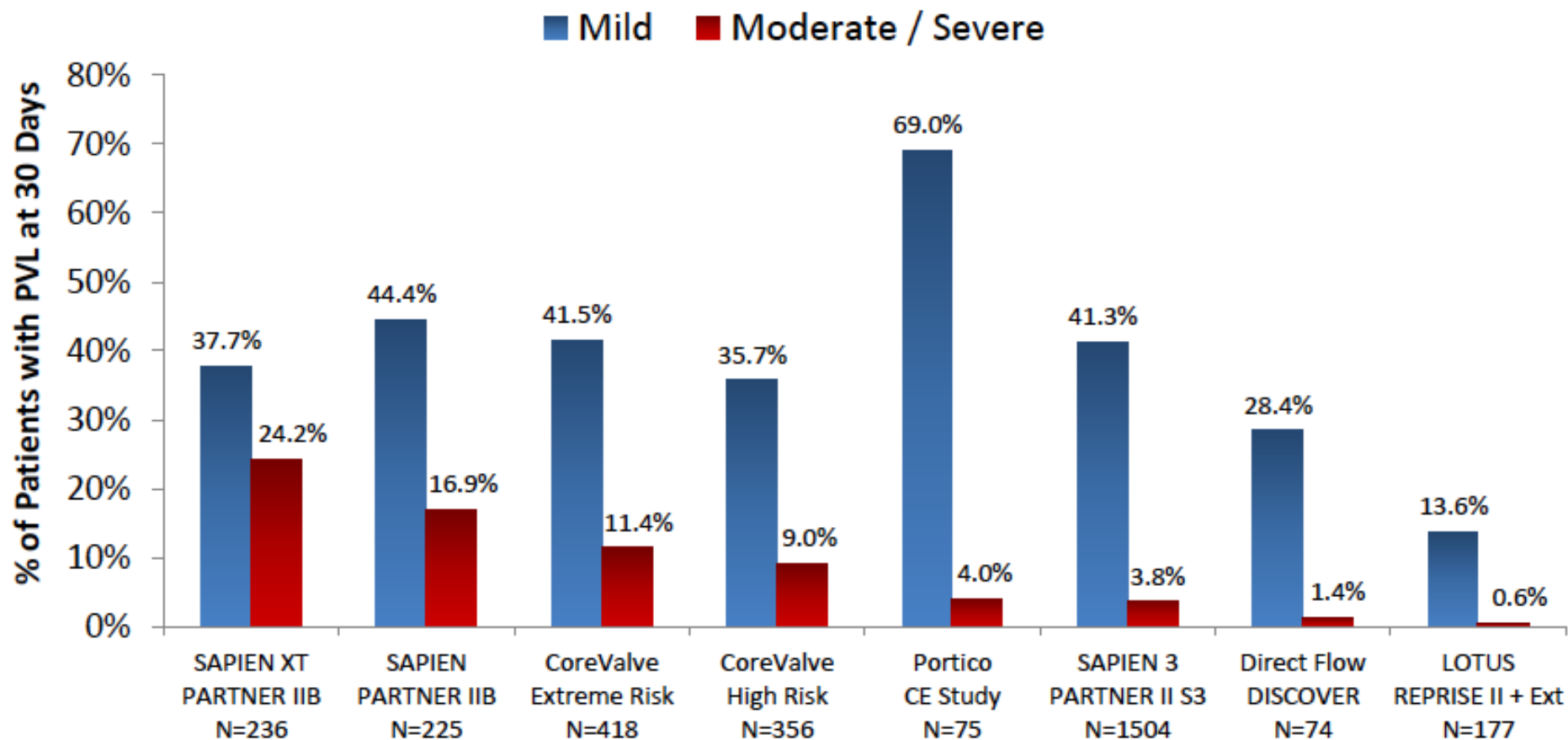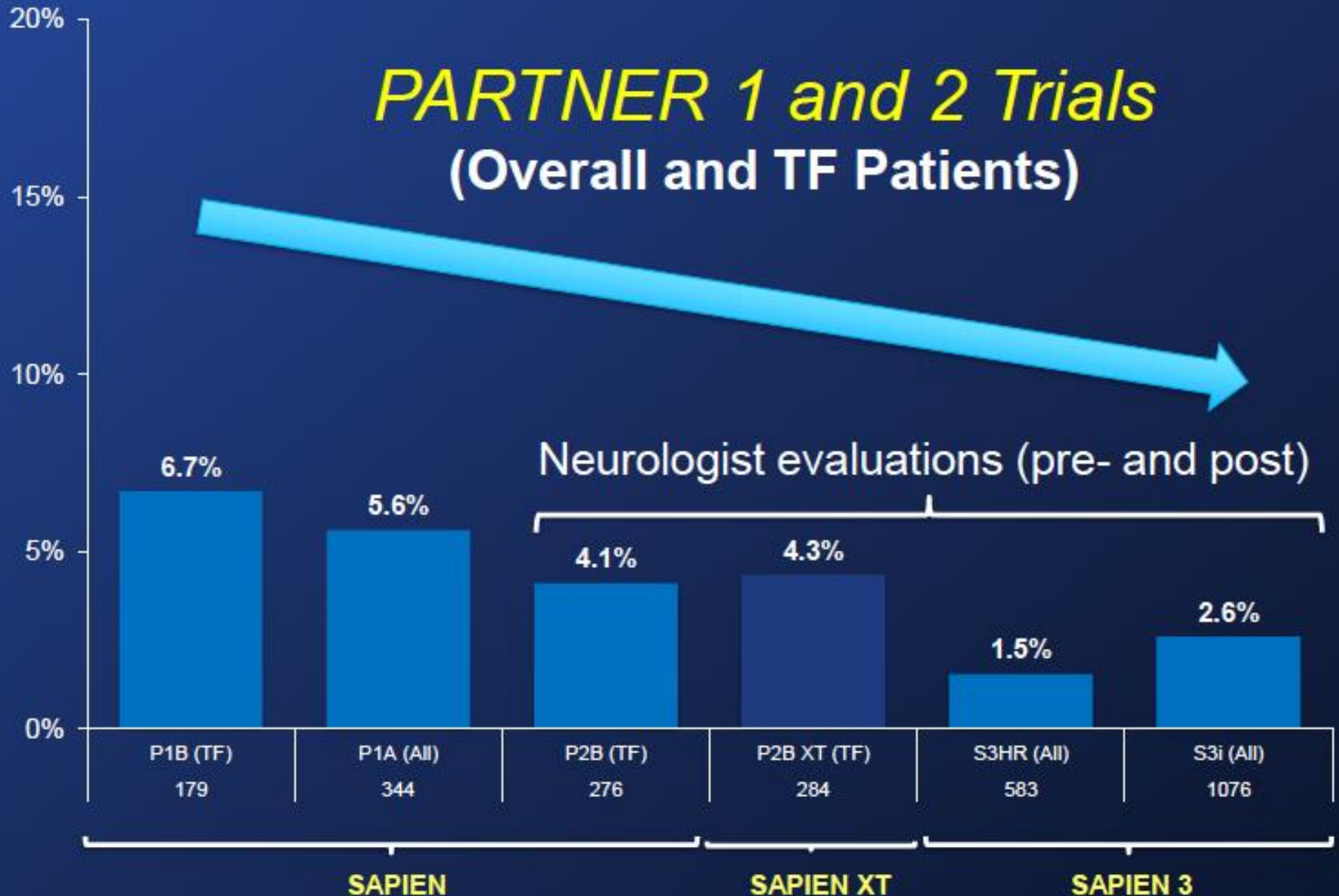
Strokes at 30 days

TAVI in intermediate risk patients

ADVANCE Registry : 1015 patients March'10 - July'11 implanted with Corevalve
Intermediate risk = Euroscore >10-20% : 30-d mortality 4.4% - Major stroke : 2%

Table 3 Outcomes at 30-day follow-up for all patients and by EuroSCORE[a]

	All Patients (n = 996)	EuroSCORE[b] ≤ 10% (n = 229)	EuroSCORE >10–20% (n = 406)	EuroSCORE (n = 360)
Primary endpoint				
MACCE (VARC)	8.0 (6.3, 9.7)	3.5	9.1	9.7
All-cause mortality	4.5 (3.2, 5.8)	2.6	4.4	5.8
Myocardial infarction (VARC)	0.2 (0.0, 0.5)	0.0	0.2	0.3
Emergent cardiac surgery or percutaneous reintervention	1.3 (0.6, 2.1)	0.4	1.3	2.0
Stroke (VARC)	3.0 (2.0, 4.1)	1.8	4.2	2.5
Additional VARC endpoints				
Cardiovascular mortality[f]	3.4 (2.3, 4.6)	1.7	3.5	4.5
Bleeding	29.0 (26.1, 31.9)	23.2	32.4	28.9
Life-threatening or disabling bleeding	4.0 (2.8, 5.3)	3.5	5.0	3.4
Major bleeding	9.7 (7.8, 11.6)	7.0	9.7	11.4
Minor bleeding	17.4 (15.0, 19.9)	15.8	20.1	15.6
Vascular complications[g]	20.7 (18.2, 23.3)	16.2	23.2	20.6
Major	10.9 (8.9, 12.8)	7.4	13.1	10.3
Minor	10.2 (8.2, 12.1)	9.2	10.1	10.9
Stroke or transient ischaemia attack	3.3 (2.2, 4.5)	1.8	5.0	2.5
Major stroke	1.2 (0.5, 1.9)	0.9	2.0	0.6
Minor stroke	1.8 (1.0, 2.7)	0.9	2.2	2.0
Transient ischaemia attack	0.4 (0.0, 0.8)	0.0	1.0	0.0
Acute kidney injury—stage III	0.4 (0.0, 0.8)	0.0	0.0	1.1
Additional endpoints				
New pacemaker implantation	26.3 (23.5, 29.1)	29.0	26.1	24.8
Death from any cause or major stroke	5.1 (3.8, 6.5)	2.6	5.7	6.1

B

Freedom from all-cause mortality (%)

Log-rank P-value <0.01

— All patients
— EuroSCORE (≤10%)
— EuroSCORE (>10-20%)
— EuroSCORE (>20%)

Months

No. at risk				
All	996	951	861	651
≤10%	229	223	212	163
>10%-20%	406	387	352	267
>20%	360	340	297	221

Linke et al, Eur H J 2014:35:2672-84
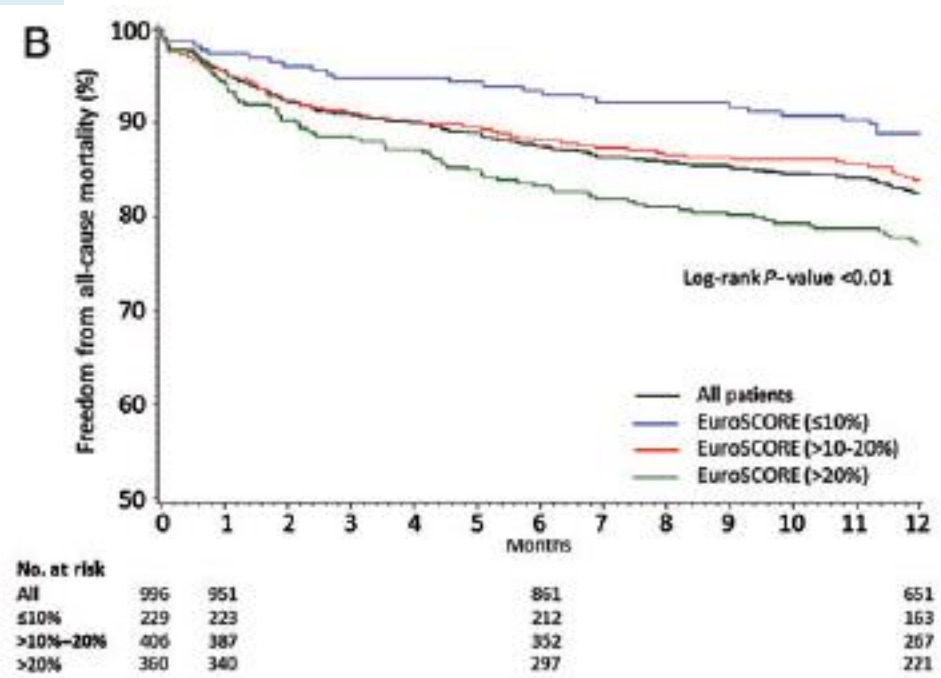
TAVI in intermediate risk patients

Matched TAVI (n=255) vs. SAVR (n=255)
STS 3-8%
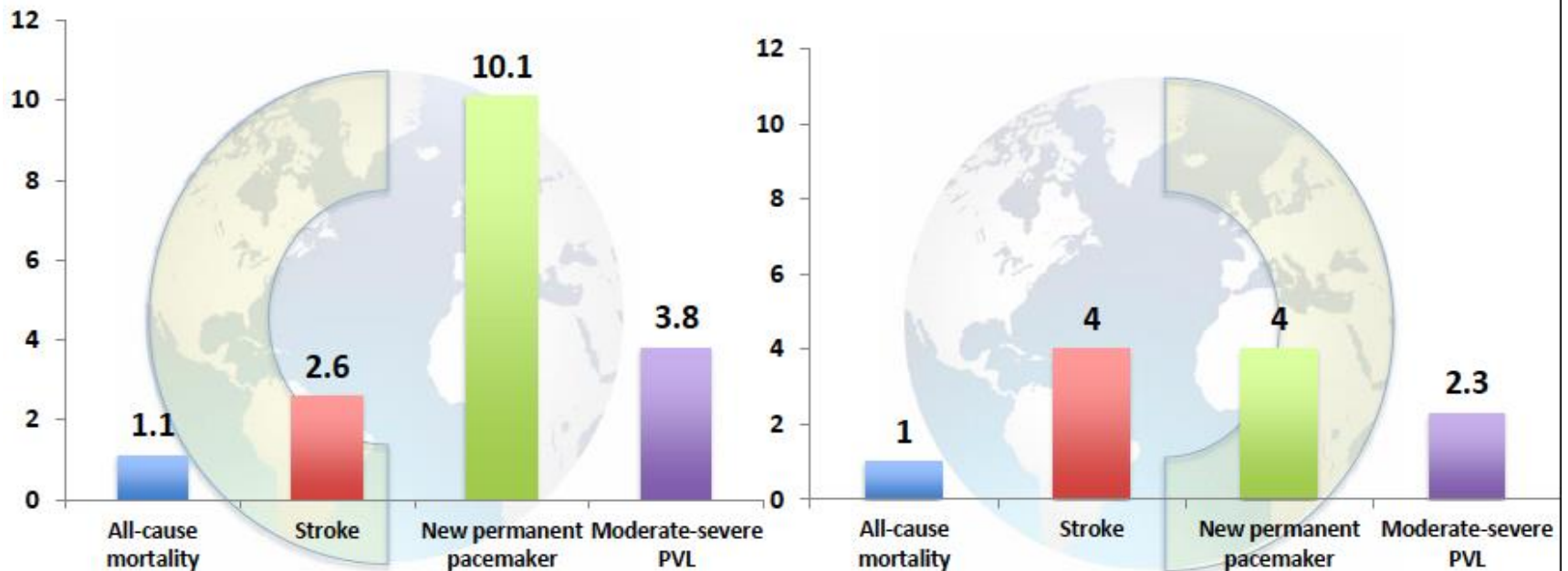
Piazza et al. J Am Coll Cardiol Interv 2013; 6:443-51
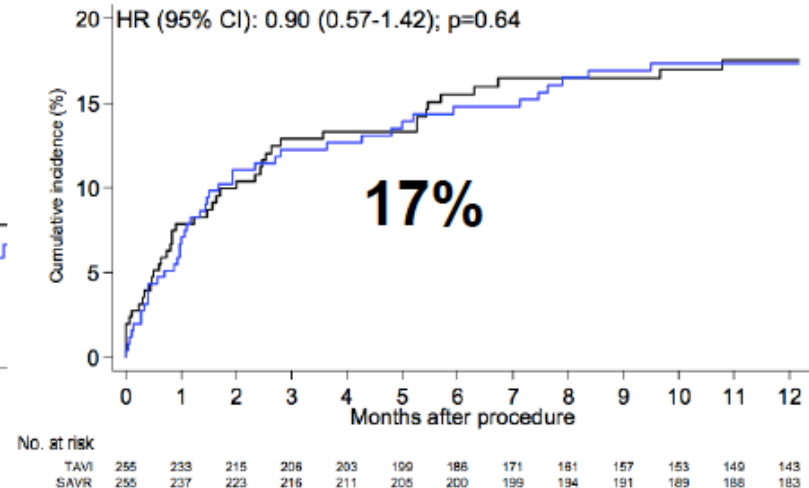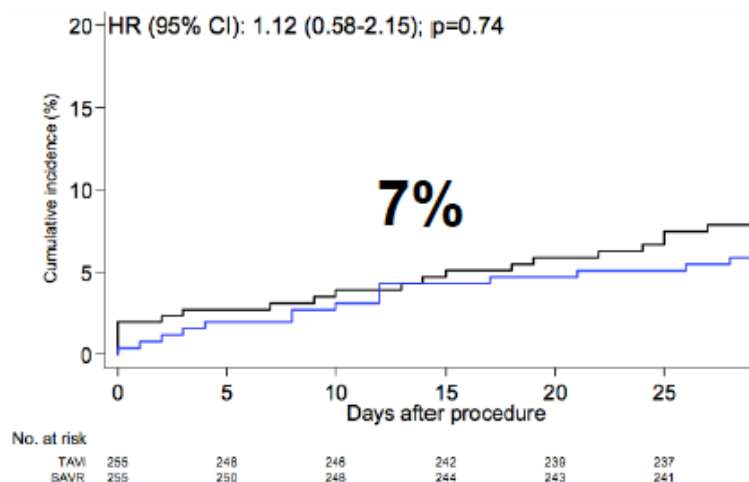
TAVI in intermediate risk patients

SAPIEN S3
Intermediate risk
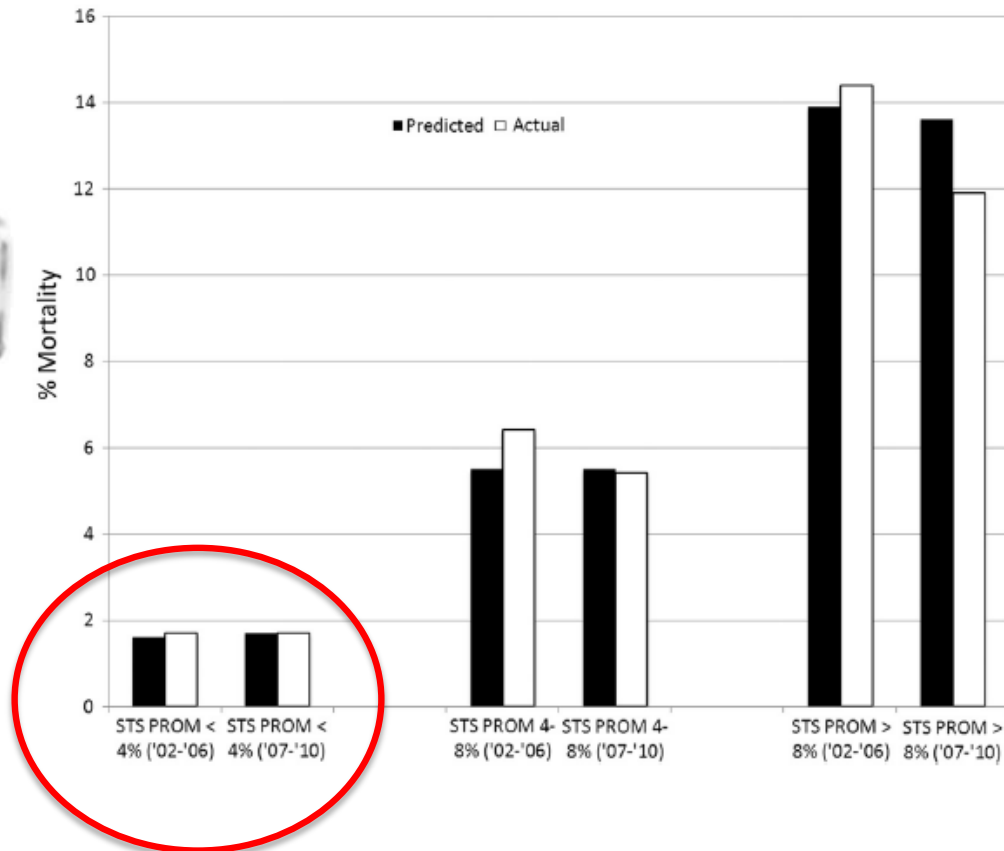
N = 1076; mean STS : 5.3%

N = 101; mean STS : 5.2%

US PARTNER 2 S3 - PRESENTED AT ACC 2015

SAPIEN 3 CE mark study - PRESENTED AT EUROPCR 2015

TAVI in low risk patients

STS database 2002-2010
n=141,905

6.2% — High risk (STS > 8%)

13.9% — Intermediate risk (STS 4-8%)

79.9% — Low risk (STS <4%)

Thourani et al; Ann Thorac Surg 2015;99:55

NOTION : RCT trial
TAVI vs SAVR in low risk patients

TABLE 1 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
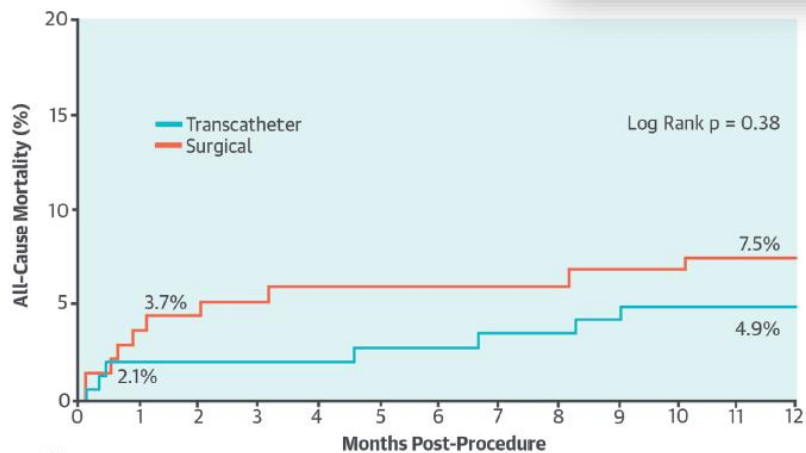
Thyregod et al, J Am Coll Cardiol 2015;65:2184-94
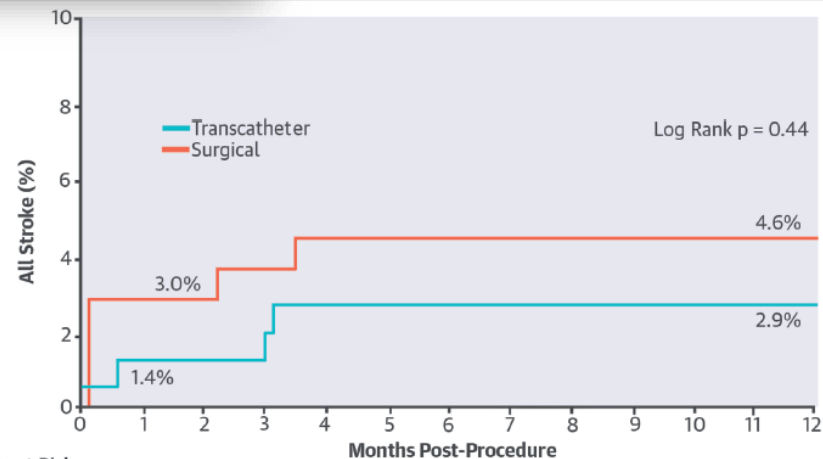
TAVI and SAVR : ≠ complications

TABLE 3 Clinical Outcomes in the As-Treated Population

	Index Hospitalization* or 30 Days†			1 Year		
	TAVR	**SAVR**	**p Value**	**TAVR**	**SAVR**	**p Value**
Major, life threatening, or disabling bleeding*	16 (11.3)	28 (20.9)	0.03			
Cardiogenic shock*	6 (4.2)	14 (10.4)	0.05			
Major vascular complications*	8 (5.6)	2 (1.5)	0.10			
Acute kidney injury stage II or III*	1 (0.7)	9 (6.7)	0.01			
All-cause death†	3 (2.1)	5 (3.7)	0.43	7 (4.9)	10 (7.5)	0.38
Cardiovascular death†	3 (2.1)	5 (3.7)	0.43	6 (4.3)	10 (7.5)	0.25
Neurological events†	4 (2.8)	4 (3.0)	0.94	7 (5.0)	8 (6.2)	0.68
Stroke†	2 (1.4)	4 (3.0)	0.37	4 (2.9)	6 (4.6)	0.44
Transient ischemic attack†	2 (1.4)	0 (0)	0.17	3 (2.1)	2 (1.6)	0.71
MI†	4 (2.8)	8 (6.0)	0.20	5 (3.5)	8 (6.0)	0.33
Valve endocarditis†	1 (0.7)	0 (0)	0.33	4 (2.9)	2 (1.6)	0.47
New-onset or worsening AF†	24 (16.9)	77 (57.8)	<0.001	30 (21.2)	79 (59.4)	<0.001
Permanent pacemaker implantation†	46 (34.1)	2 (1.6)	<0.001	51 (38.0)	3 (2.4)	<0.001

NOTION trial @ 2 yrs

Mortality, stroke or MI — P-Value (log-rank) = 0.43; SAVR 15.7% → 18.8%, TAVI 11.3% → 15.8%

All-cause mortality — P-value (log-rank) = 0.54; SAVR 7.5% → 9.8%, TAVI 4.9% → 8.0%

Presented by Lars Söndergaard
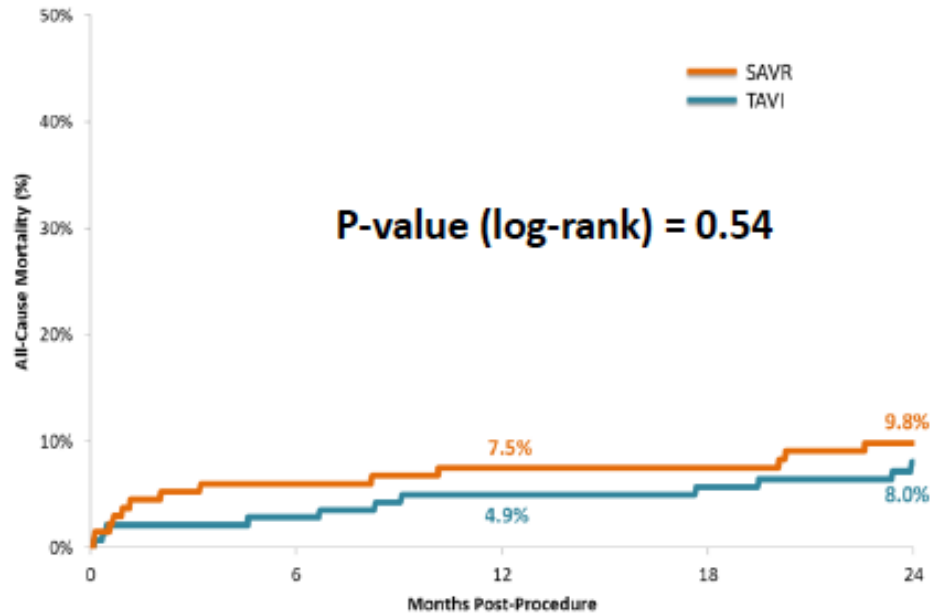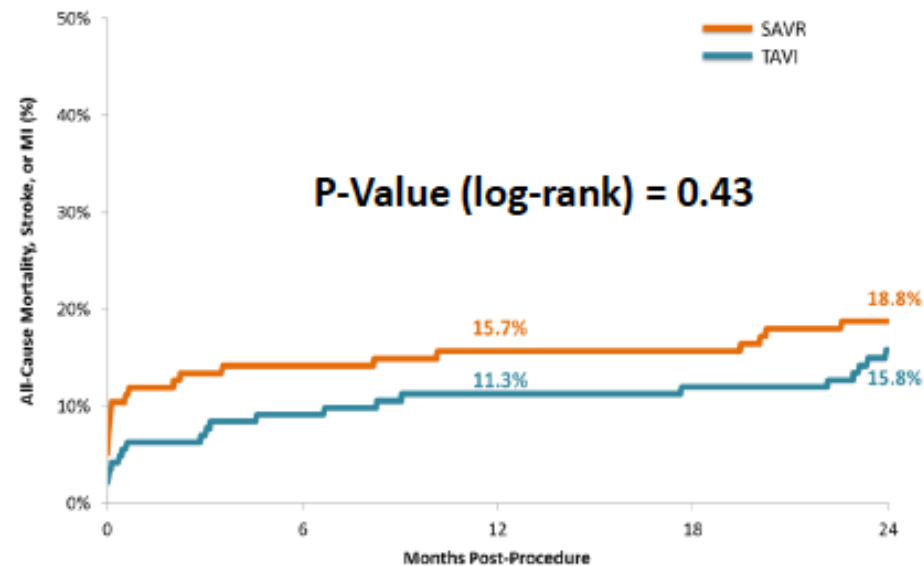
Advantages of TAVI
Mini invasive

Short recovery period and stay lenght,
no general anesthesia, no chest opening

DAY 1 after TF TAVI

15 min post-TAVI

Advantages of TAVI Haemodynamics

Larger aortic valve area and lower gradient after TAVI
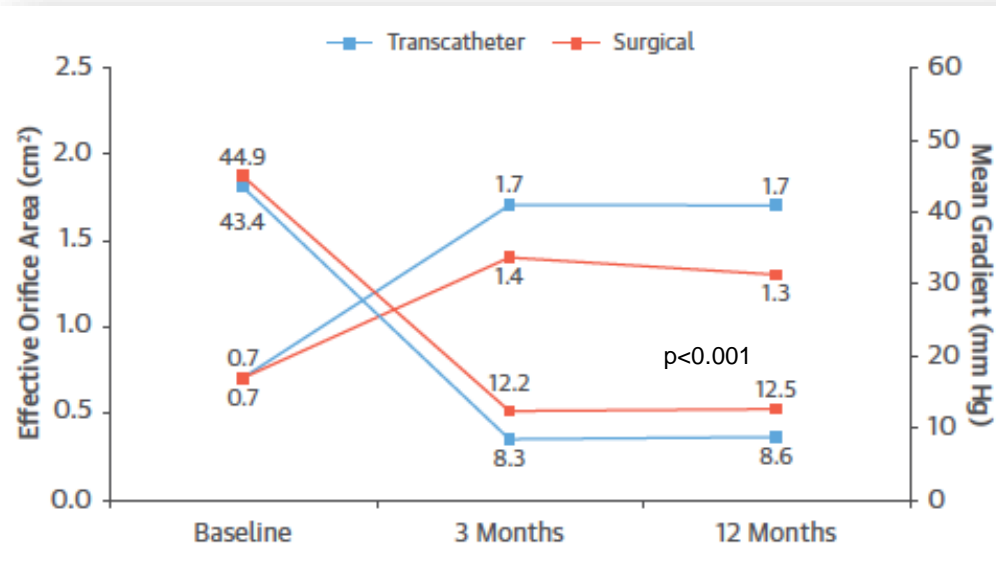
Table 2. Postprocedural Changes in AVA and Gradient

Variable	SAVR Group	TAVI Group	P, ANOVA	P, ANCOVA
AVA, cm²			<0.001	0.0009
Baseline	0.71±0.17	0.64±0.18*		
Discharge	1.47±0.42†	1.65±0.55*†		
1-y follow-up	1.39±0.40†	1.56±0.38*†		
Indexed AVA, cm²/m²			<0.001	0.0003
Baseline	0.38±0.09	0.36±0.10*		
Discharge	0.76±0.22†	0.92±0.32*†		
1-y follow-up	0.71±0.19†	0.87±0.20*†		
Mean gradient, mm Hg			0.005	0.04
Baseline	35±14	37±14		
Discharge	13±5†	10±5*†		
1-y follow-up	14±6†	9±4*†		

Thyregod et al, J Am Coll Cardiol 2015;65:2184-94

Clavel et al; Circ 2010:122:1928-1936

Advantages of TAVI

Bleeding/Atrial fibrillation/
Acute kidney injury
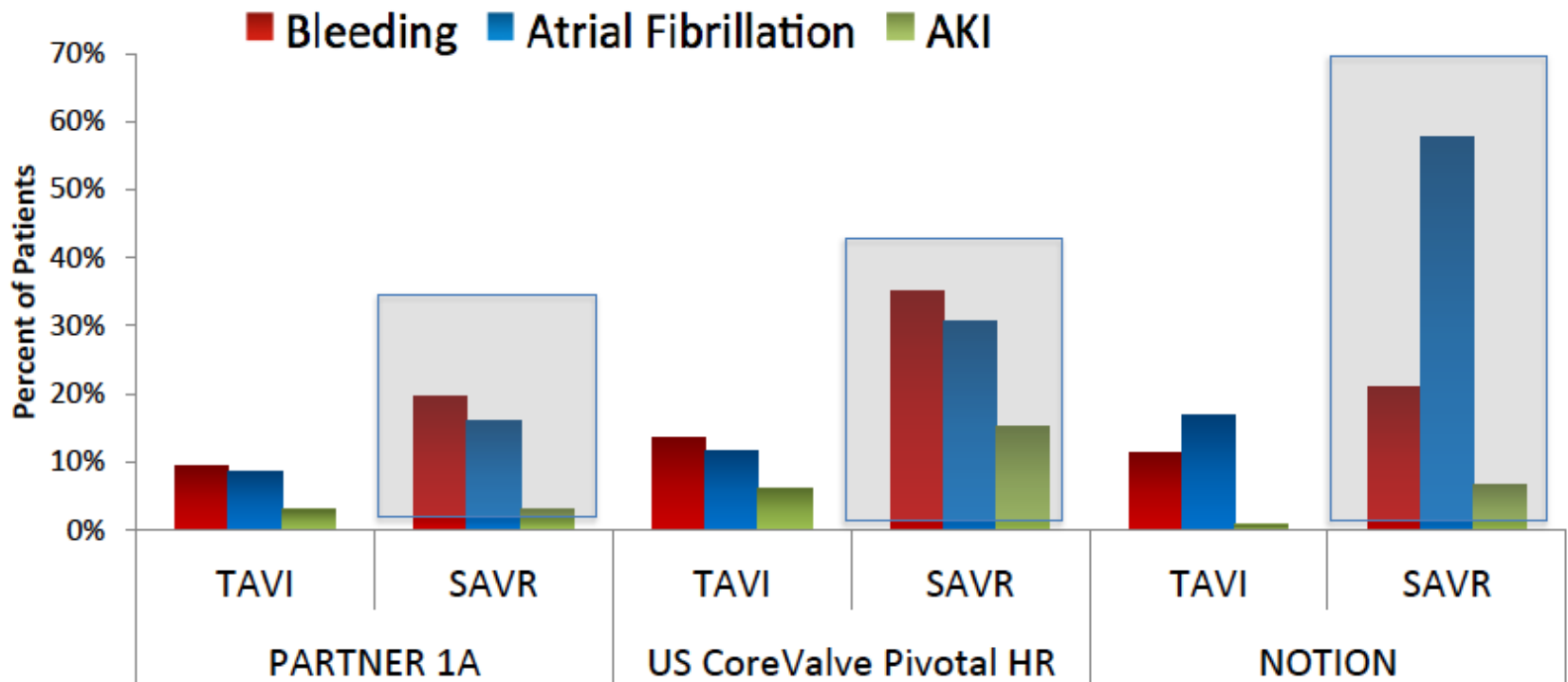
Disadvantages of TAVI : permanent pacemaker rate
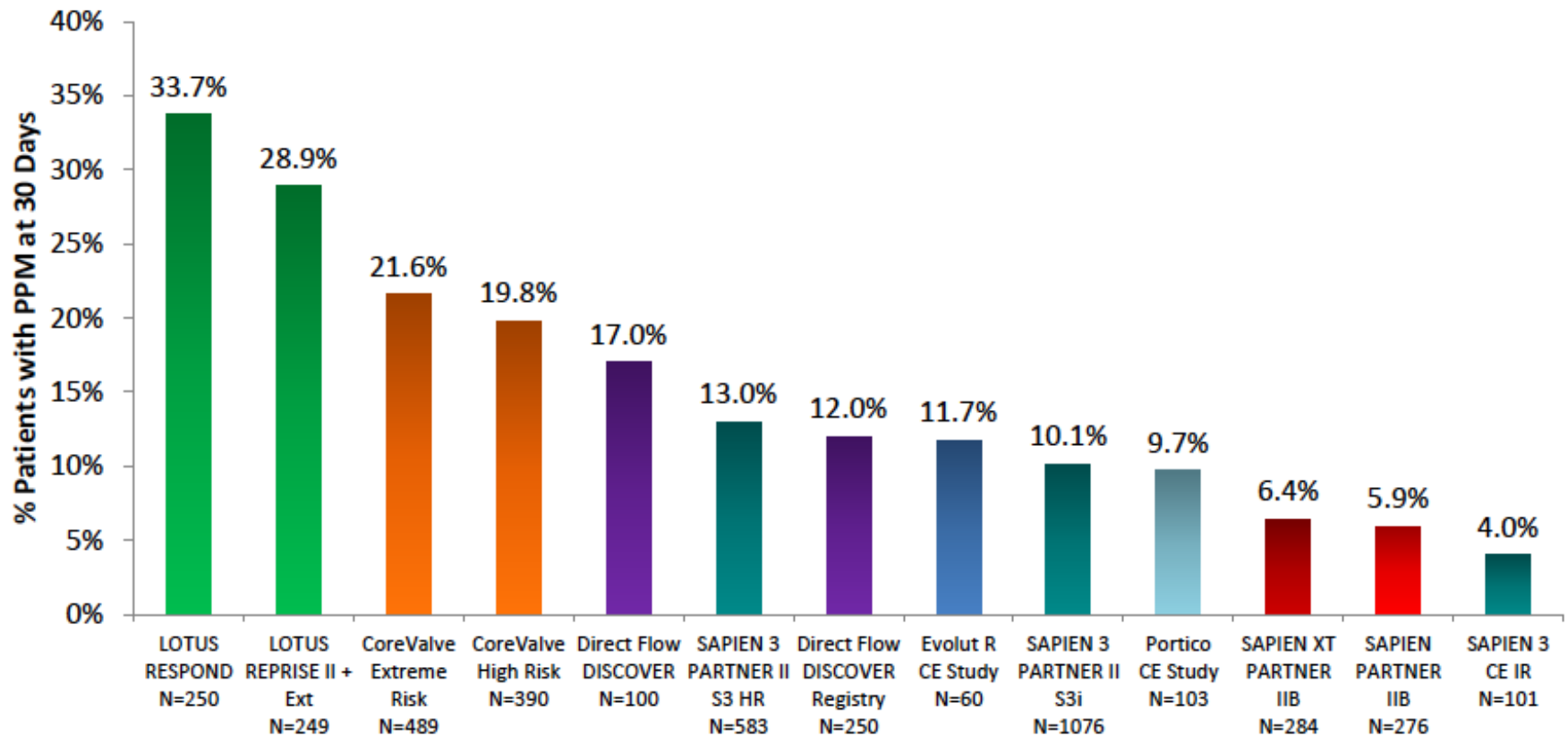
[1]Van Mieghem, et al., presented at EuroPCR 2015; [2]Meredith, et al., presented at PCR London Valves 2014; [3]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [4]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [5]Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; [6]Kodali, et al., presented at ACC 2015; [7]Naber, et al., presented at EuroPCR 2015; [8]Meredith, et al., presented at ACC 2015; [9]Kodali, et al., presented at ACC 2015; [10]Manoharan, et al., et. al. presented at TCT 2014; [11]Leon, et. al. presented at ACC 2013; [12]Vahanian, et al., presented at EuroPCR 2015

Disadvantages of TAVI

✓ New LBBB, new PCMK

✓ Major vascular complications

✓ PVL

Thyregod et al, J Am Coll Cardiol 2015;65:2184-94
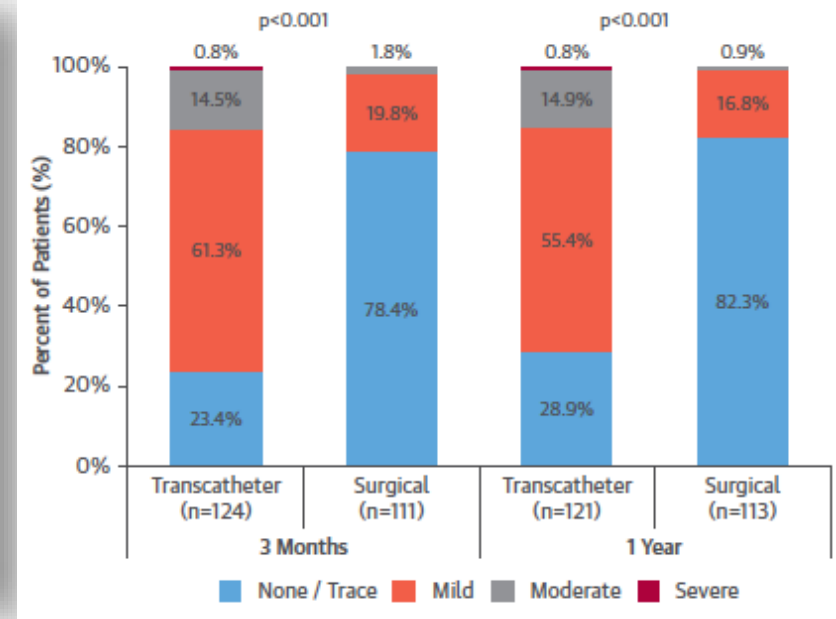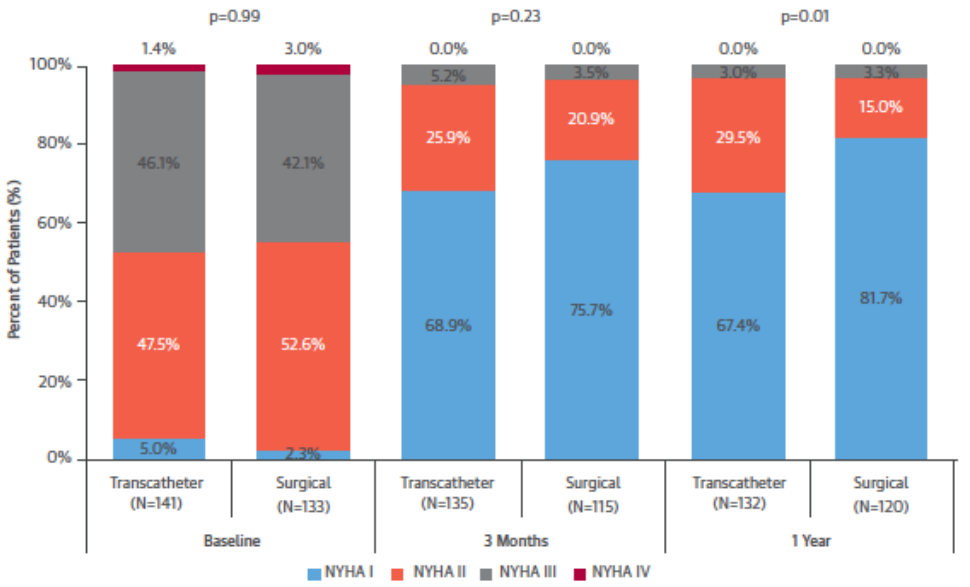
Remaining issues : durability

PARTNER 1A – 5 years
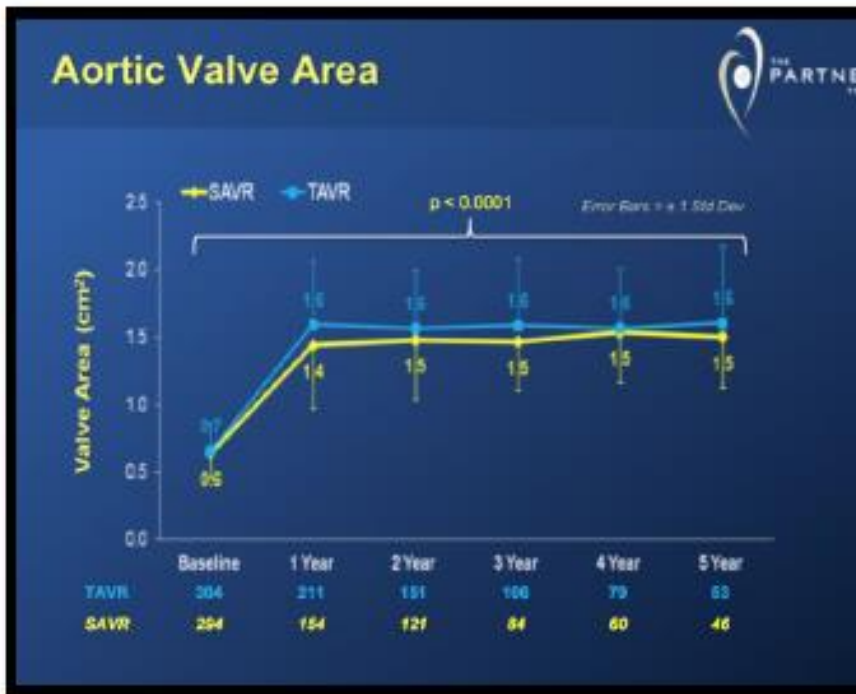
ADVANCE – 3 years
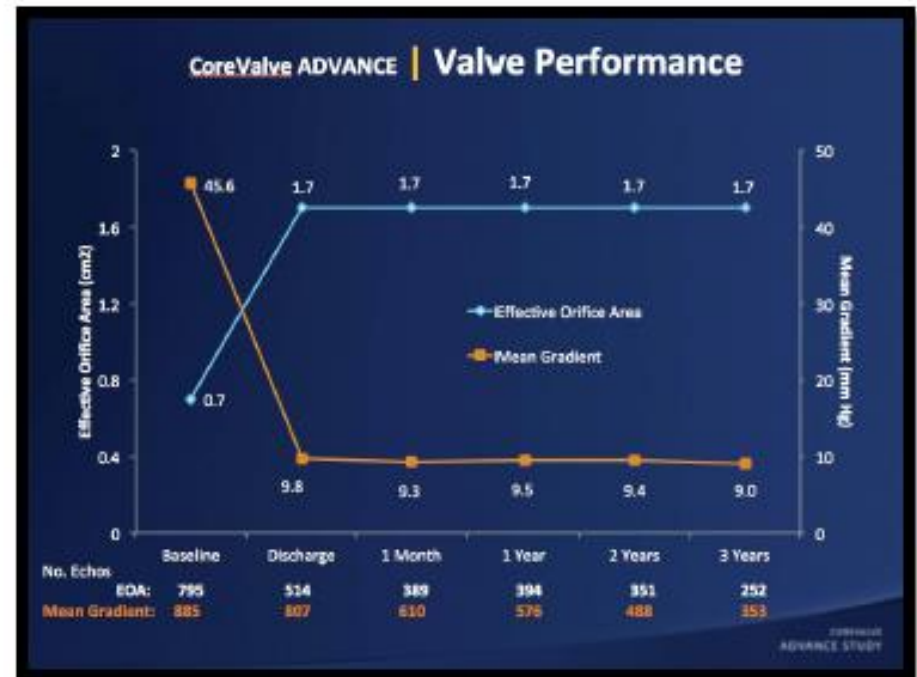
5-yr outcome

PARTNER 1A – 5 years

Mack et al, Lancet 2015;385:2475
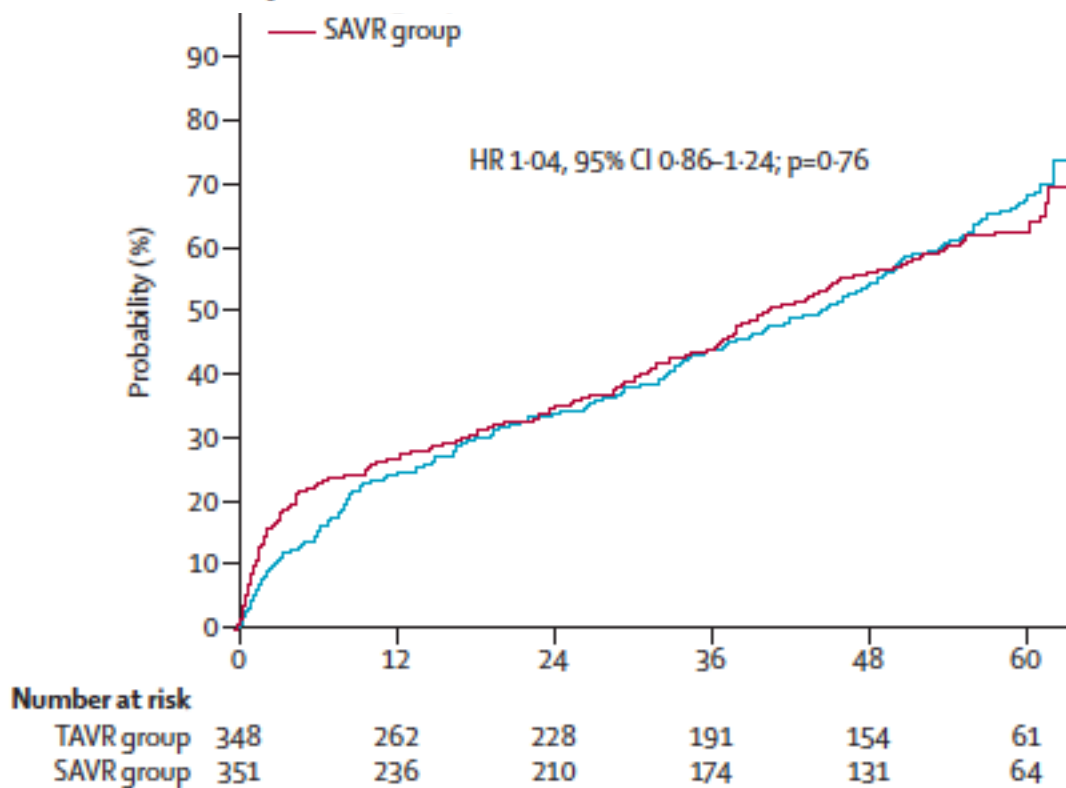
Remaining issues :
potential thrombus on the leaflets
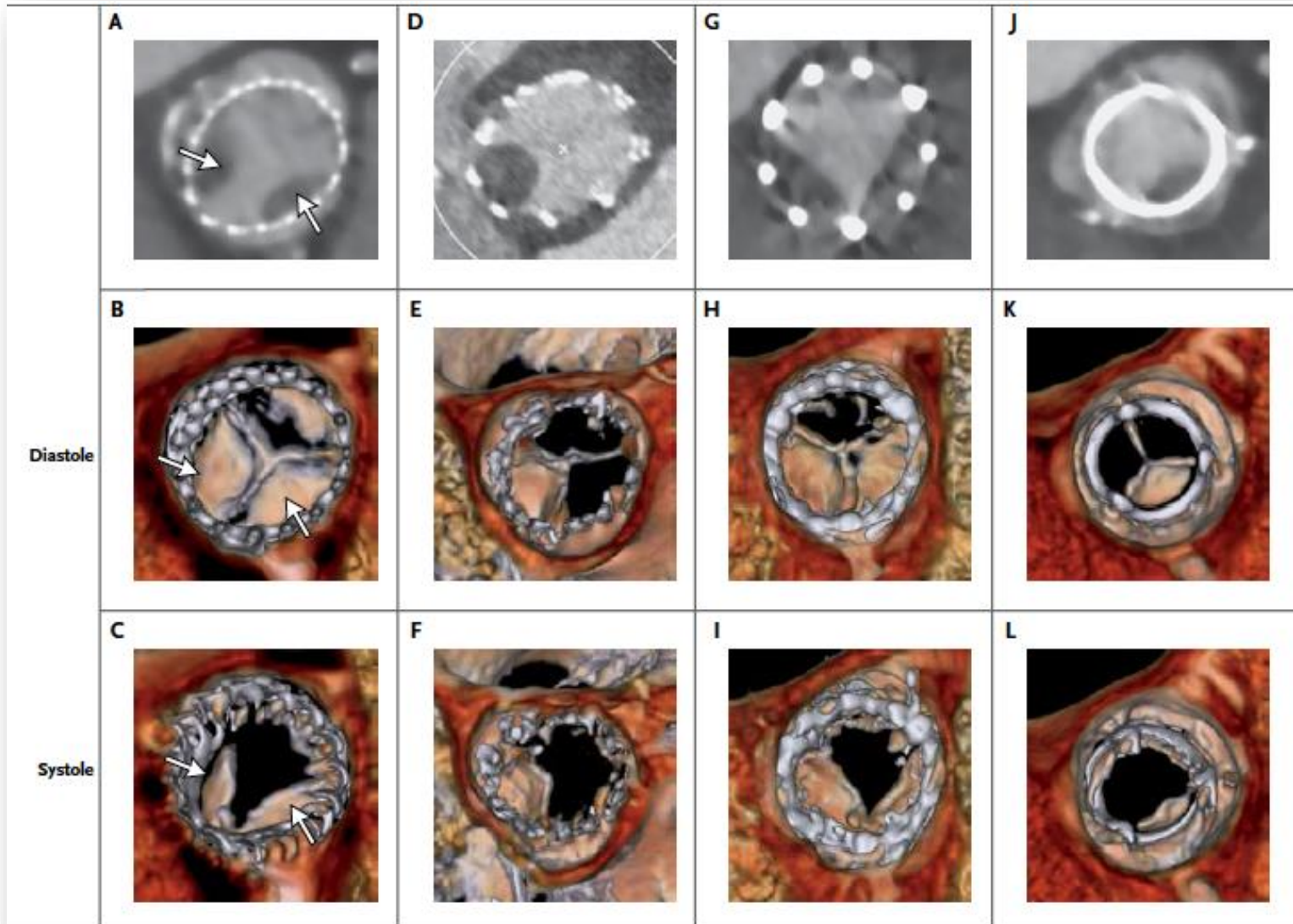
Remaining issues : antiplatelet/(N)OAC

BEFORE-	DURING	AFTER
Acetylsalicylic acid (ASA)	**UNFRACTIONATED HEPARIN**: target ACT ≥300"	ASA + CLOPIDOGREL
	Bivalirudin: **BRAVO** Bivalirudin and Aortic Valve intervention Outcomes	Acetylsalicylic acid (ASA) ARTE trial
	Low Molecular Weight Heparin	Non anti-VKA Oral Anticoagulant ± ASA: Atlantis Action GALILEO

TAVI in low risk patients : CONCLUSIONS

- Use of TAVI is exponential
- SAVR is a valuable therapy in low risk AS patients
- New generation TAVI mitigate technical issues
- Similar mortality in Notion RCT
- Different types of complications

- Ongoing trials : PARTNER II and SURTAVI