

XXIX Giornate Cardiologiche Torinesi

“ADVANCES IN CARDIAC ARRHYTHMIAS
AND GREAT INNOVATIONS IN CARDIOLOGY”

Turin, October 27-28, 2017
Centro Congressi Unione Industriale

TAVI long-term results: are they good
enough to
shift to intermediate risk patients?

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Città della Salute e della Scienza di Torino



2017 ESC/EACTS Guidelines for the management of valvular heart disease

SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10%^d and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation).⁹³

I

B

TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team.^{91,94}

I

B

3-Year Outcomes in High-Risk Patients Who Underwent Surgical or Transcatheter Aortic Valve Replacement



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 Thomas G. Gleason, MD,^e Joon Sup Lee, MD,^e James B. Hermiller, Jr, MD,^f John Heiser, MD,^g William Merhi, MD,^g
 George L. Zorn III, MD,^h Peter Tadros, MD,^h Newell Robinson, MD,ⁱ George Petrossian, MD,^j G. Chad Hughes, MD,^j
 J. Kevin Harrison, MD,^j Brijeshwar Maini, MD,^k Mubashir Mumtaz, MD,^k John Conte, MD,^l Jon Resar, MD,^l
 Vicken Aharonian, MD,^m Thomas Pfeffer, MD,^m Jae K. Oh, MD,ⁿ Hongyan Qiao, PhD,^o David H. Adams, MD,^p
 Jeffrey J. Popma, MD,^q for the CoreValve US Clinical Investigators

CoreValve US

Self-expanding TAVR was associated with a **sustained 3-year clinical benefit** over SAVR in patients with aortic stenosis at **HIGH risk for surgery**.



	TAVR Group (n = 391)	SAVR Group (n = 359)
Age, yrs	83.2 ± 7.1	83.3 ± 6.4
Male	207/391 (52.9)	188/359 (52.4)
STS Score, %	7.3 ± 3.0	7.5 ± 3.3
Logistic EuroSCORE, %	17.7 ± 13.0	18.8 ± 13.2

2017 ESC/EACTS Guidelines for the management of valvular heart disease

In patients who are at increased surgical risk (STS or EuroSCORE II \geq 4% or logistic EuroSCORE I \geq 10%^d or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics (see *Table 7*), with TAVI being favoured in elderly patients suitable for transfemoral access.^{91,94–102}

I

B

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

SURTAVI

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis



THE LANCET

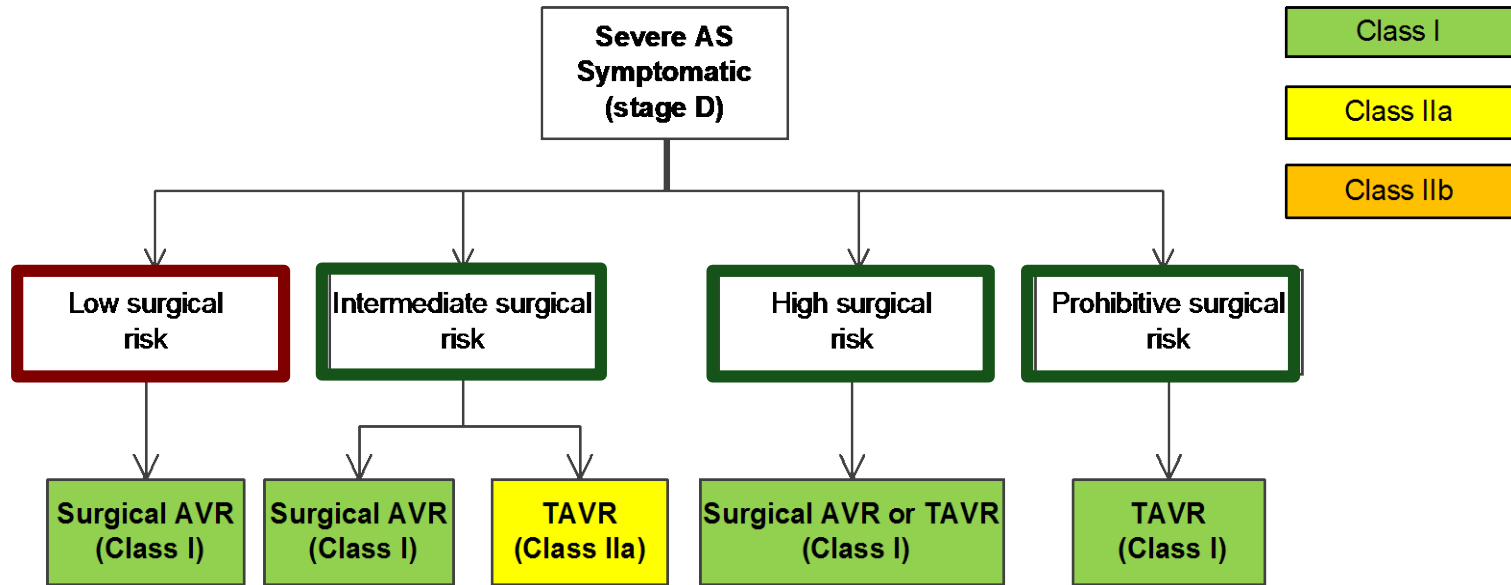
P2 S3i

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials 

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

IIa	B-R	<p>TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences (62-65).</p>	<p>NEW: New RCT showed noninferiority of TAVR to surgical AVR in symptomatic patients with severe AS at intermediate surgical risk.</p>
	<p>See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)</p>		

Figure 1. Choice of TAVR Versus Surgical AVR in the Patient With Severe Symptomatic AS

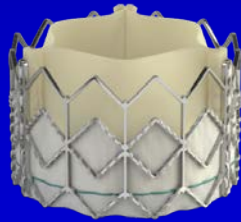




THE
PARTNER II
TRIAL

SAPIEN

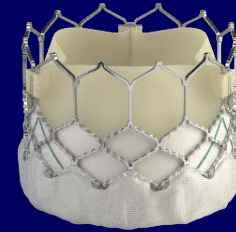
Valve
Technology



SAPIEN XT



SAPIEN 3



Sheath
Compatibility



22-24F

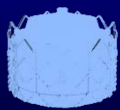


16-20F

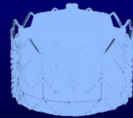


14-16F

Available
Valve Sizes



23 mm



26 mm



23 mm



26 mm



29 mm



20 mm



23 mm



26 mm



29 mm

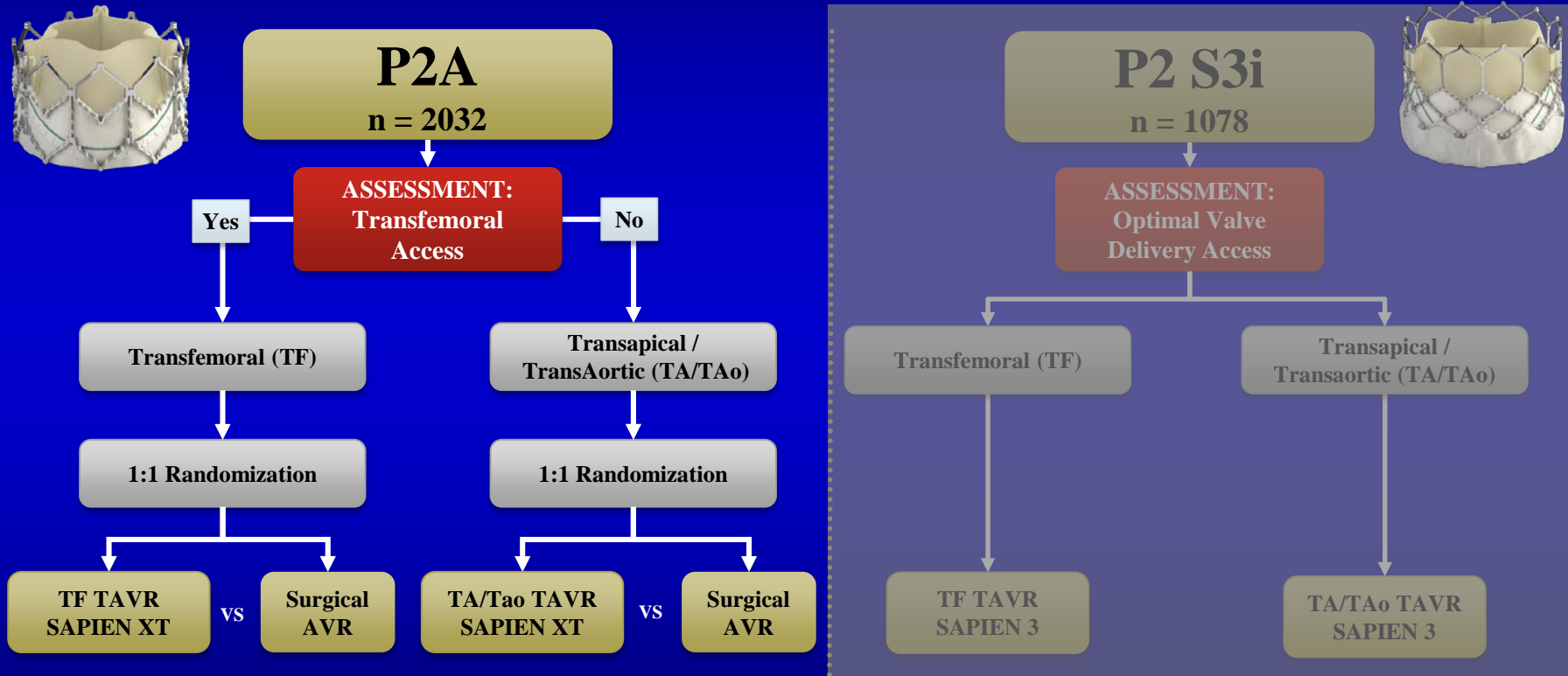
Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team

Intermediate Risk:

1. Determined by a multi-disciplinary Heart Team
2. Using a guideline **STS between 4-8%**, and
3. Adjudicated by case review committee

Intermediate Risk ASSESSMENT by Heart Valve Team



Primary Endpoint: All-Cause Mortality or Disabling Stroke at 24 months



Transcatheter or Surgical Aortic-Valve
Replacement in Intermediate-Risk Patients



2032 pts, 57 centers
2 years FU

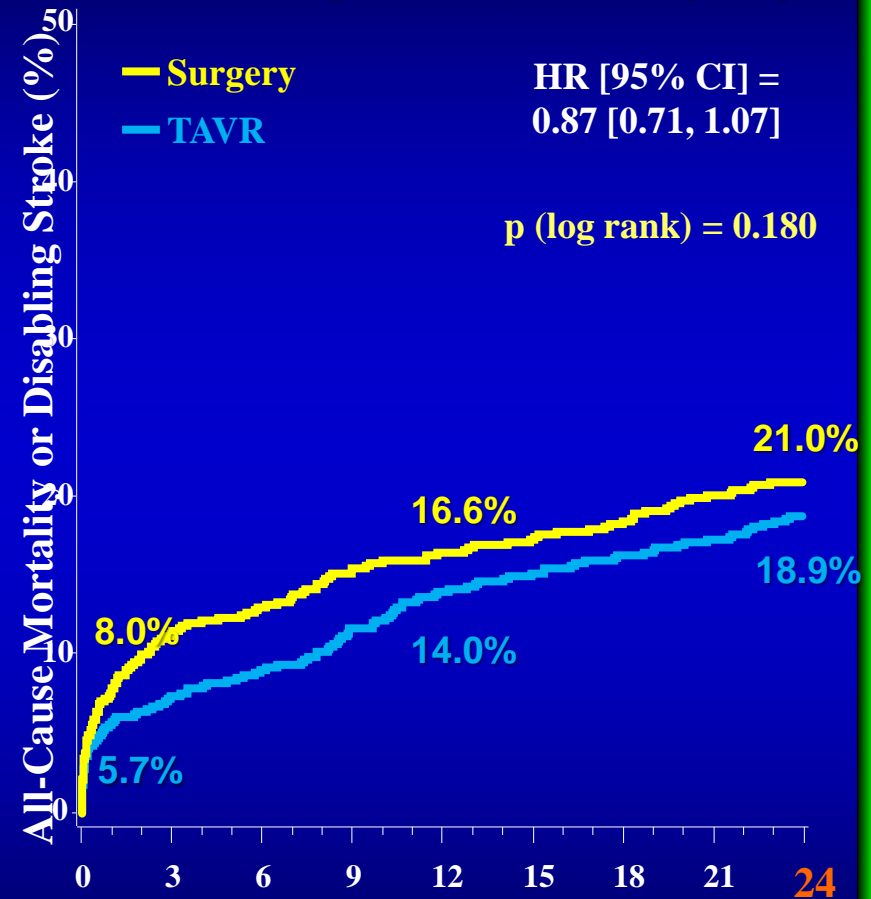
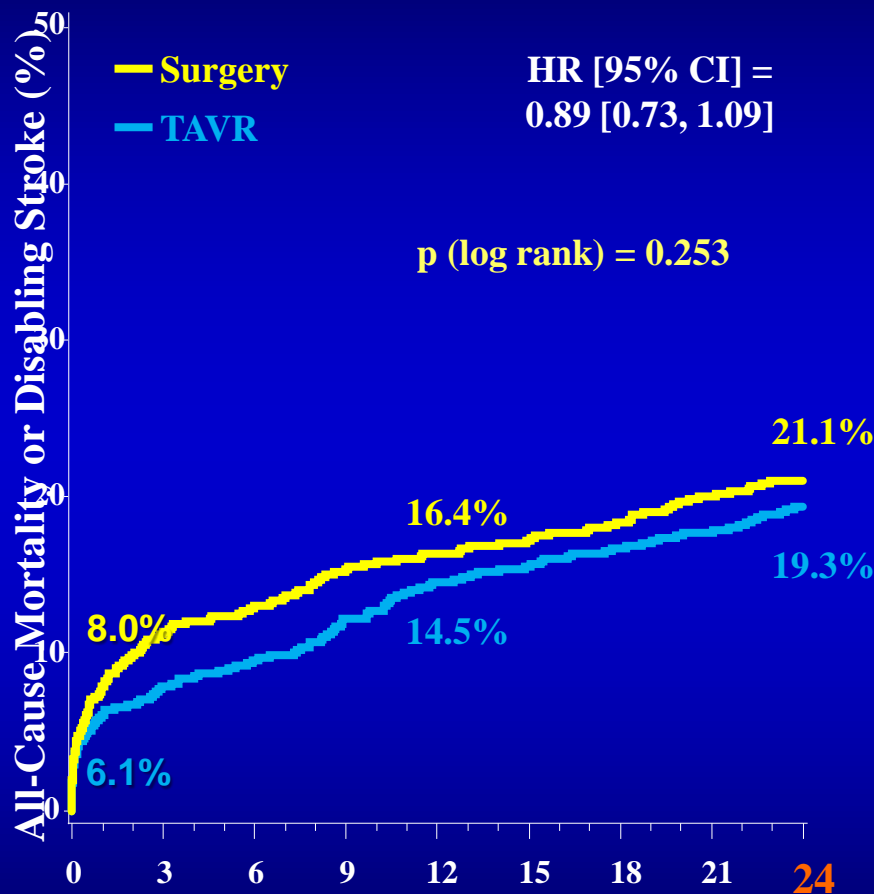
Characteristic	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Age - yrs	81.5 ± 6.7	81.7 ± 6.7	0.63
Male - %	54.2	54.8	0.79
STS Score - %	5.8 ± 2.1	5.8 ± 1.9	0.29
NYHA Class III or IV - %	77.3	76.1	0.53
CAD - %	69.2	66.5	0.20
Prior CABG - %	23.6	25.6	0.33
Cerebrovascular Disease - %	32.1	31.0	0.60
PVD - %	27.9	32.9	0.02

All-Cause Mortality or Disabling Stroke



Primary Endpoint (ITT)

Primary Endpoint (AT)



Number at risk:

	0	3	6	9	12	15	18	21	24
AVR	1021	838	812	783	770	747	735	717	695
TAVR	1011	918	901	870	842	825	811	801	774

Number at risk:

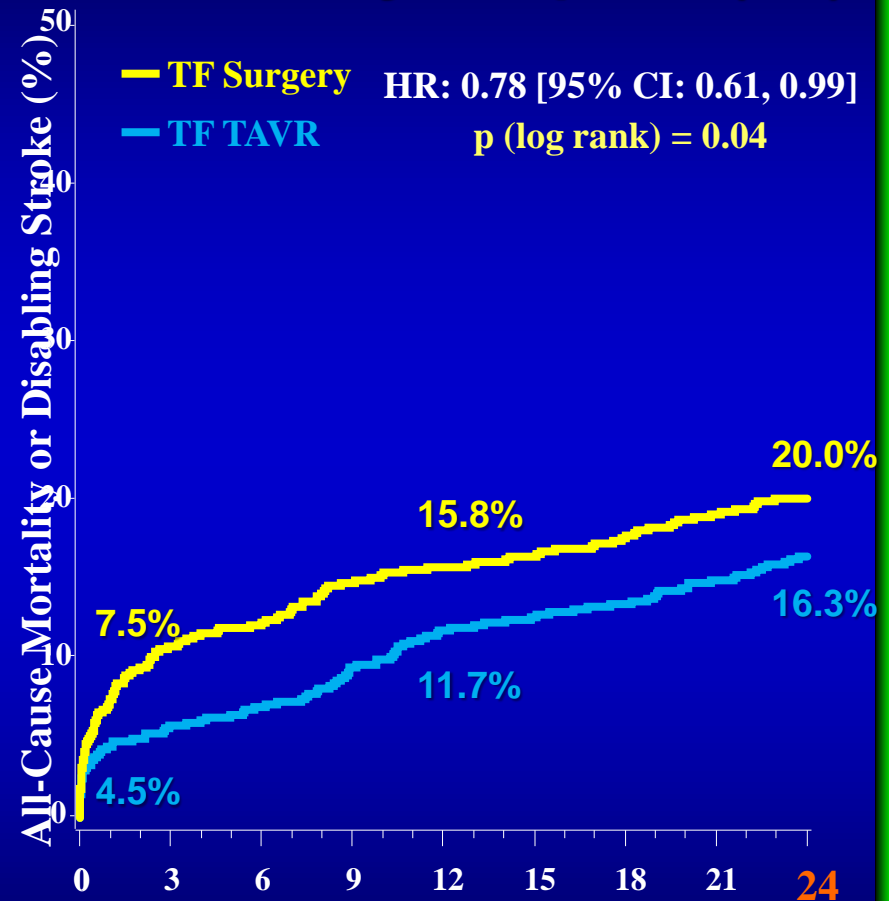
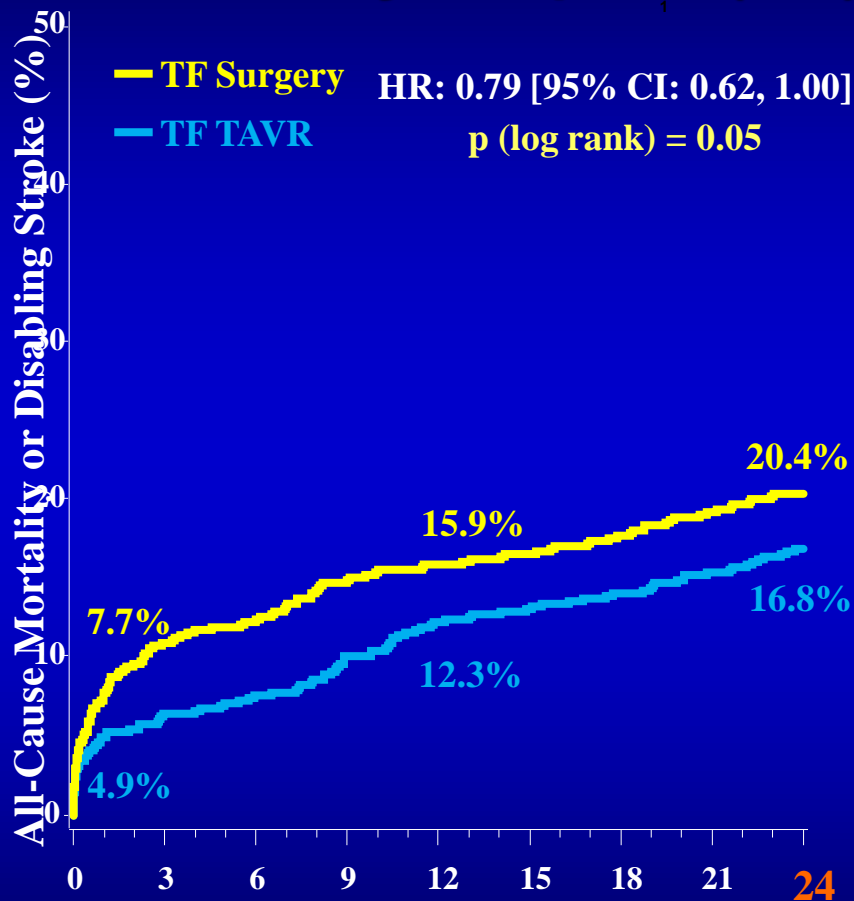
	0	3	6	9	12	15	18	21	24
AVR	944	826	807	779	766	743	731	715	694
TAVR	994	917	900	870	842	825	811	801	774

All-Cause Mortality or Disabling Stroke – TF



TF Primary Endpoint (ITT)

TF Primary Endpoint (AT)



	Months from Procedure								
Number at risk:	0	3	6	9	12	15	18	21	24
TF AVR	775	643	628	604	595	577	569	557	538
TF TAVR	775	718	709	685	663	652	644	634	612

	Months from Procedure								
Number at risk:	0	3	6	9	12	15	18	21	24
TF AVR	722	636	624	600	591	573	565	555	537
TF TAVR	762	717	708	685	663	652	644	634	612

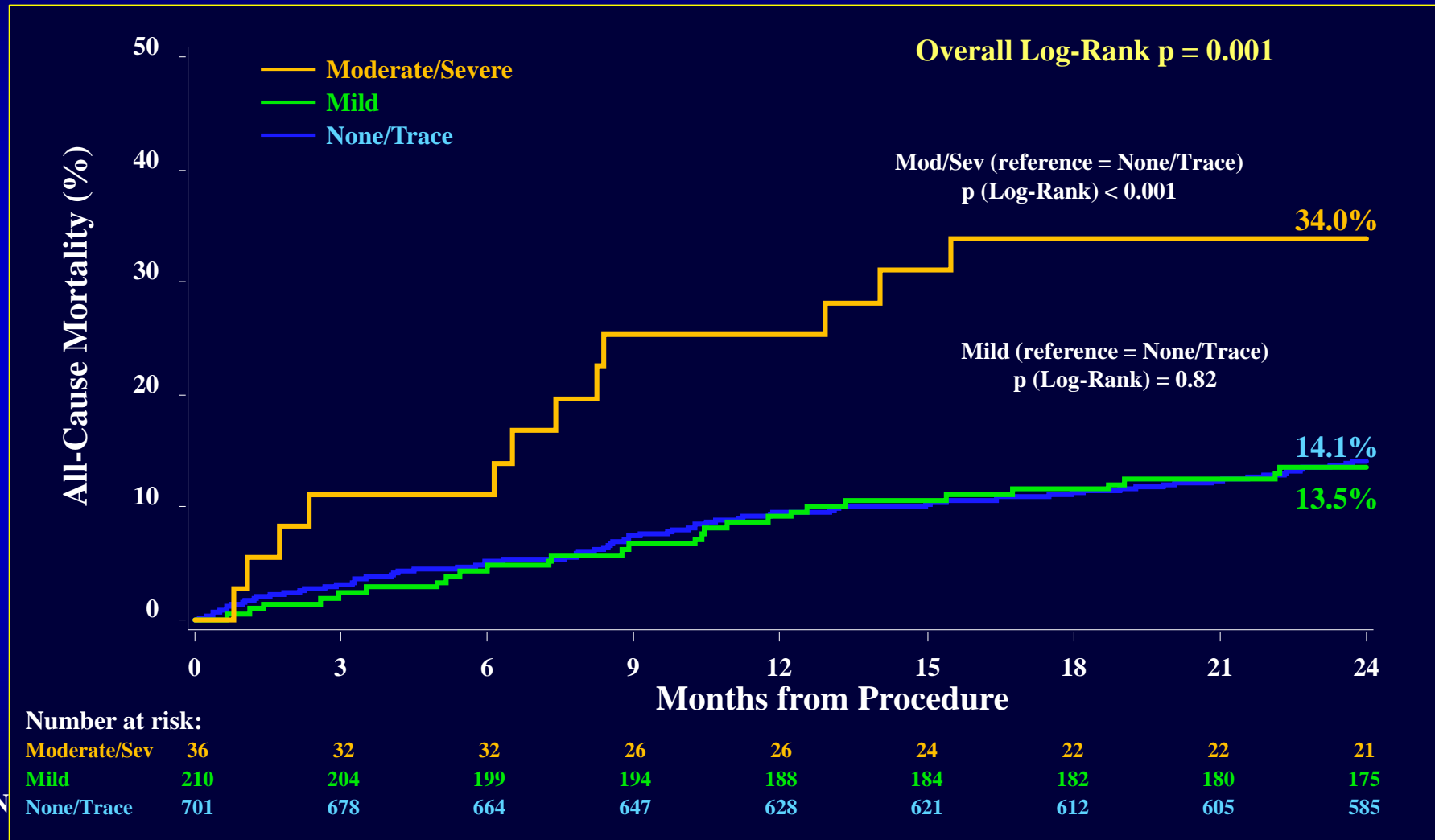
Other Clinical Endpoints (ITT)

At 30 Days and 2 Years



Events (%)	30 Days			2 Years		
	TAVR (n = 1011)	Surgery (n = 1021)	p-value*	TAVR (n = 1011)	Surgery (n = 1021)	p-value*
Rehospitalization	6.5	6.5	0.99	19.6	17.3	0.22
MI	1.2	1.9	0.22	3.6	4.1	0.56
Major Vascular Complications	7.9	5.0	0.008	8.6	5.5	0.006
Life-Threatening / Disabling Bleeding	10.4	43.4	<0.001	17.3	47.0	<0.001
AKI (Stage III)	1.3	3.1	0.006	3.8	6.2	0.02
New Atrial Fibrillation	9.1	26.4	<0.001	11.3	29.3	<0.001
New Permanent Pacemaker	8.5	6.9	0.17	11.8	10.3	0.29
Re-intervention	0.4	0.0	0.05	1.4	0.6	0.09
Endocarditis	0.0	0.0	NA	1.2	0.7	0.22

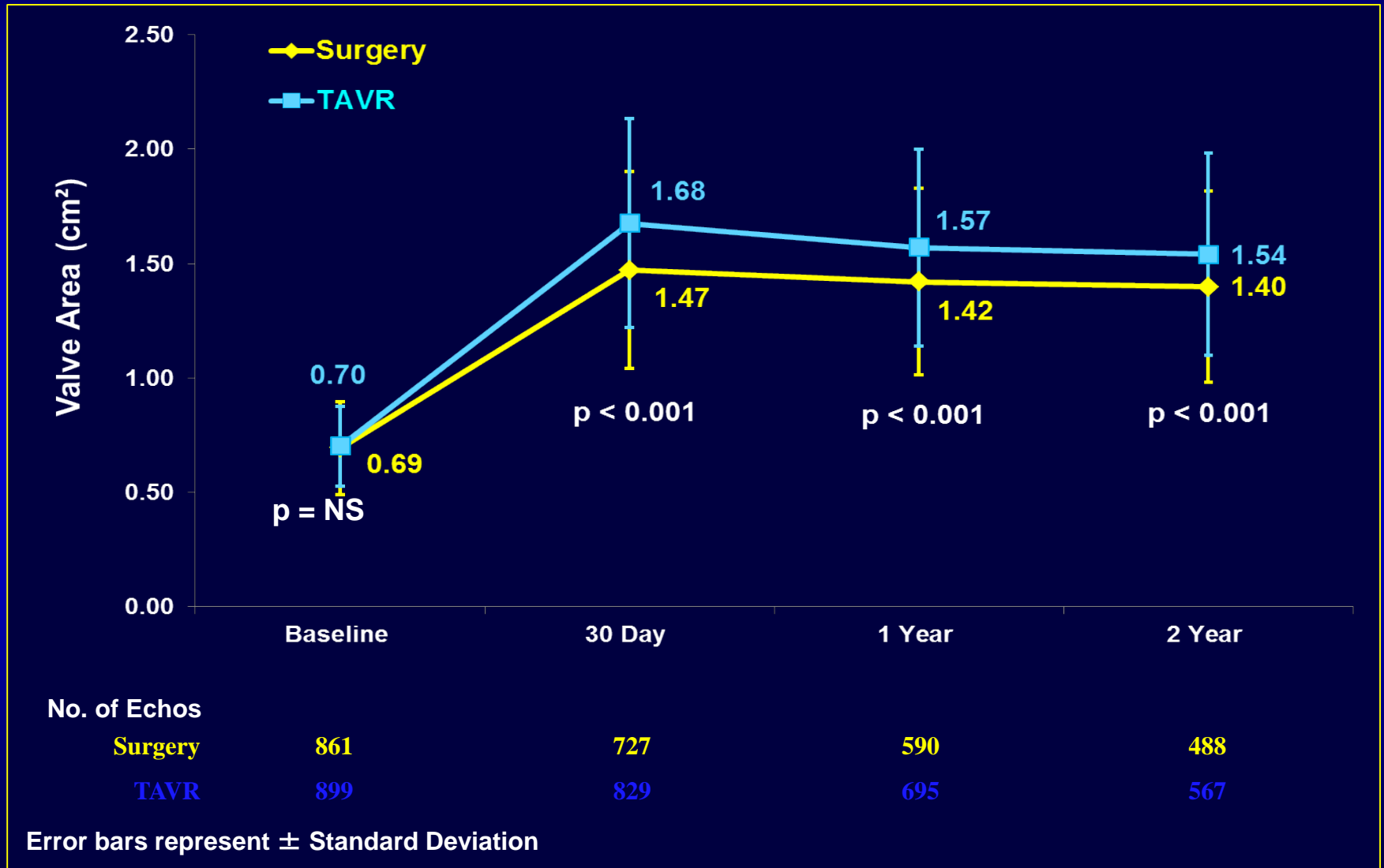
Paravalvular Regurgitation (VI)



TAVR 872 600

Surgery 757 514

Aortic Valve Area



- TAVR using SAPIEN XT and SVR were **similar (non-inferior) for the primary endpoint** (all-cause mortality or disabling stroke) at 2 years.

- In the **TF** subgroup (76% of patients), TAVR using SAPIEN XT significantly **reduced all-cause mortality or disabling stroke** vs. SVR (ITT: $p = 0.05$, AT: $p = 0.04$).

- TAVR **reduced AKI, severe bleeding, new AF, and LOS**
SVR reduced vascular complications and PVR

- In the SAPIEN XT TAVR cohort, moderate or severe PVR, but not mild PVR, was associated with increased mortality at 2 years.

Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis



Vinod H Hourani, Susheel Kodali, Raj R Makkar, Howard C Herrmann, Mathew Williams, Vasilis Babaliaros, Richard Smalling, Scott Lim, S Chris Malaisrie, Samir Kapadia, Wilson Y Szeto, Kevin L Greason, Dean Kereiakes, Gorav Ailawadi, Brian K Whisenant, Chandan Devireddy, Jonathon Leipsic, Rebecca T Hahn, Philippe Pibarot, Neil J Weissman, Wael A Jaber, David J Cohen, Rakesh Suri, E Murat Tuzcu, Lars G Svensson, John G Webb, Jeffrey W Moses, Michael J Mack, D Craig Miller, Craig R Smith, Maria C Alu, Rupa Parvataneni, Ralph B D'Agostino Jr, Martin B Leon

P2 S3i

- 1-year outcome of intermediate-risk pts from Sapien 3 observational study (**Kodali et al. EHJ 2016**) compared with intermediate-risk pts treated with **SVR** in the **PARTNER 2A** trial.
- Propensity score analysis (22 pre-specified baseline characteristics):
 - **963** pts treated with SAPIEN 3 TAVR
 - **747** with SVR.

Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year (Non-inferiority Propensity Score Analysis)

Characteristic	TAVR (n = 1077)	Surgery (n = 944)	p-value
Age - yrs	81.9 ± 6.6	81.6 ± 6.8	0.23
Male - %	61.7	55.0	0.002
BMI - kg/m ²	28.7 ± 6.1	28.4 ± 6.2	0.32
Median STS Score - %	5.2 [4.3, 6.3]	5.4 [4.4, 6.7]	0.0002
NYHA Class III or IV - %	72.5	76.1	0.07

Primary Endpoint - Non-inferiority

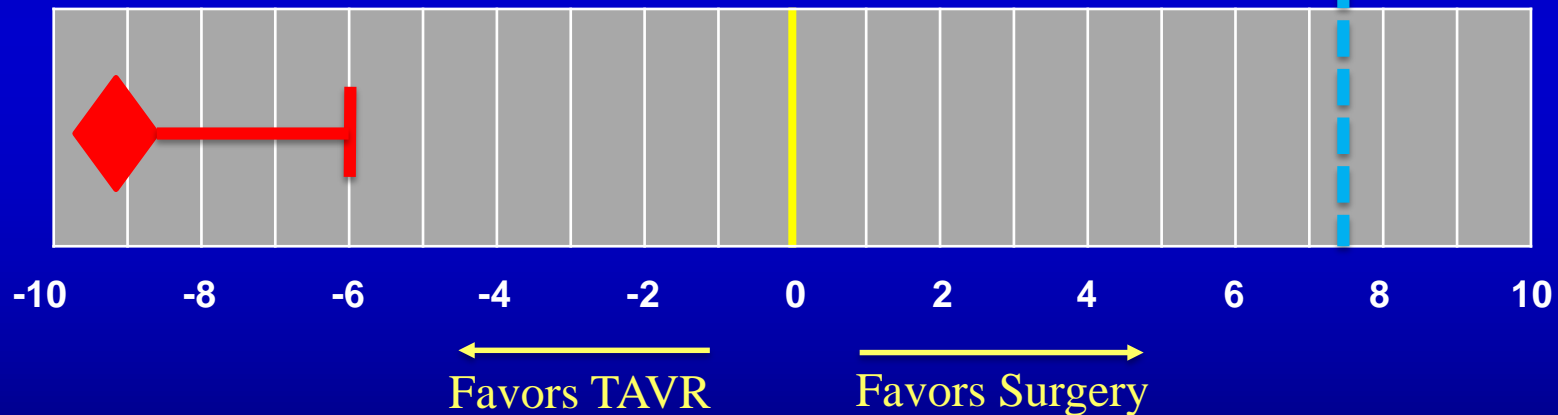
Death, Stroke, or AR \geq Mod at 1 Year (VI)



Weighted Difference **-9.2%**
Upper 1-sided 95% CI **-6.0%**

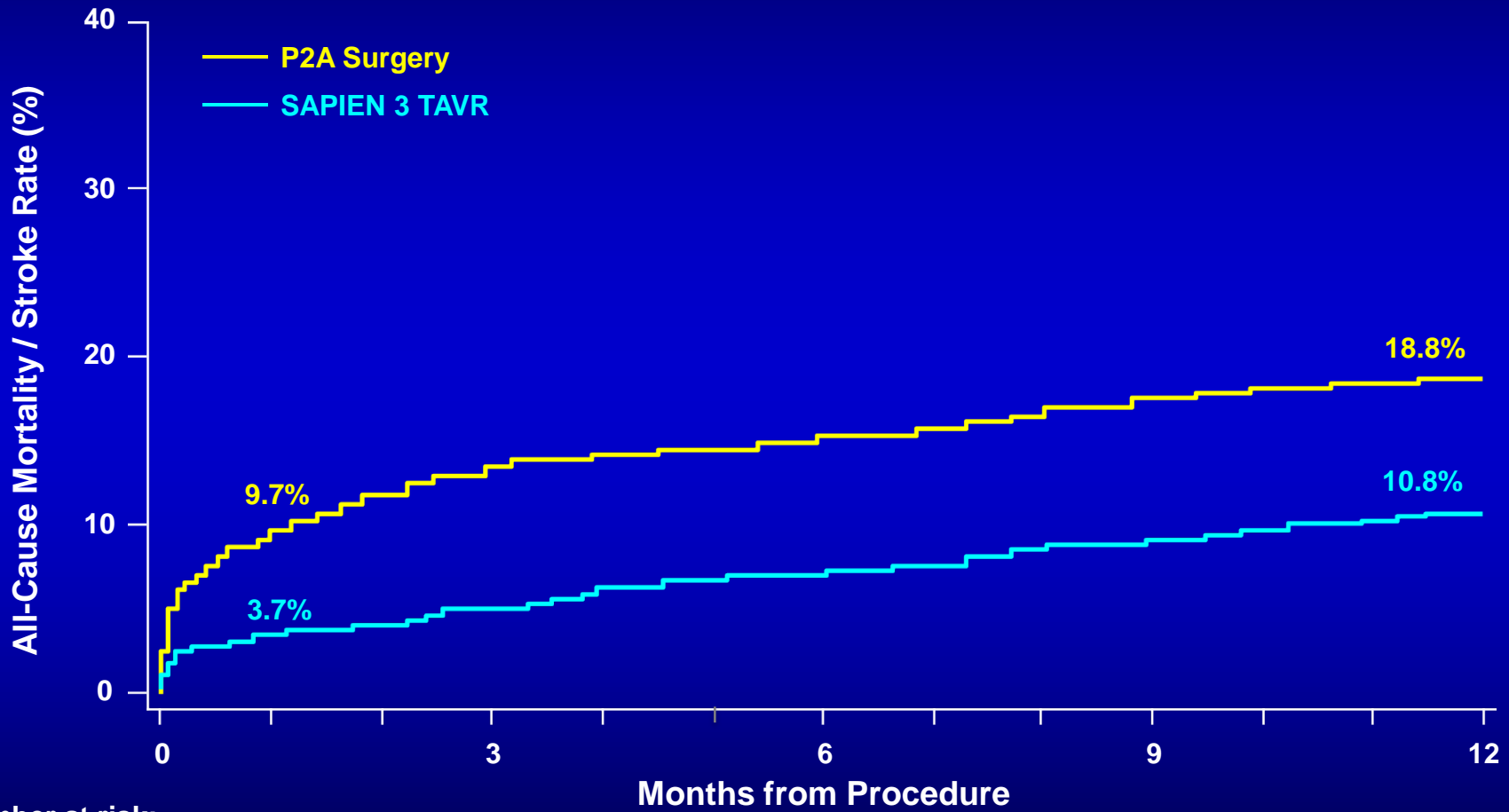
Non-Inferiority p-value **< 0.001**

Pre-specified non-inferiority margin = 7.5%



Primary Non-Inferiority Endpoint Met

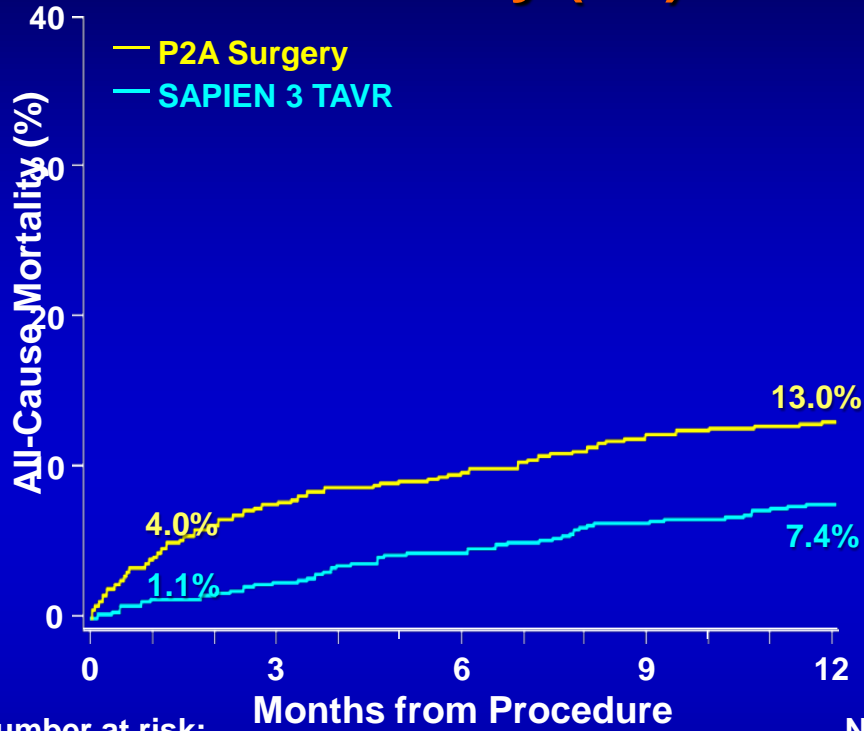
All-Cause Mortality and All Stroke (AT)



Number at risk:

	0	3	6	9	12
P2A Surgery	944	805	786	757	743
S3 TAVR	1077	1012	987	962	930

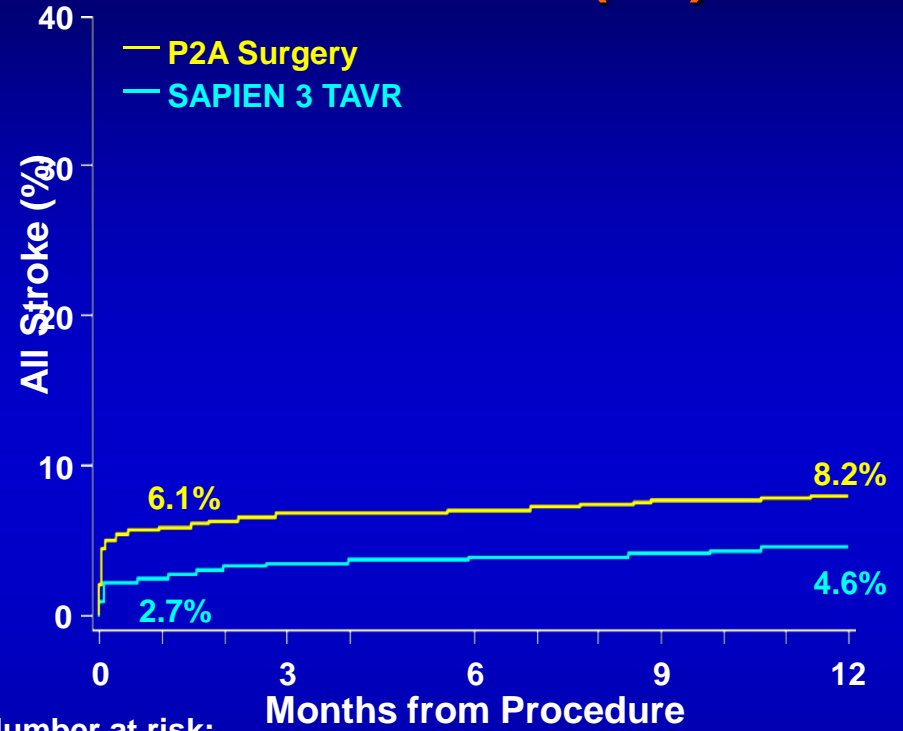
Mortality (AT)



Number at risk:

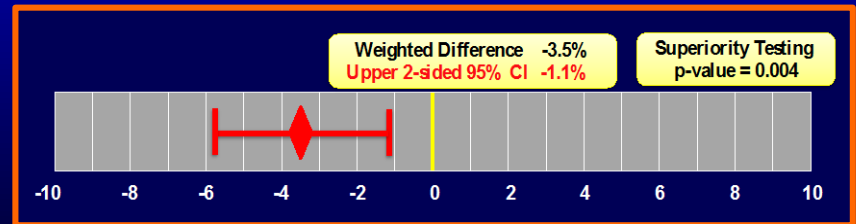
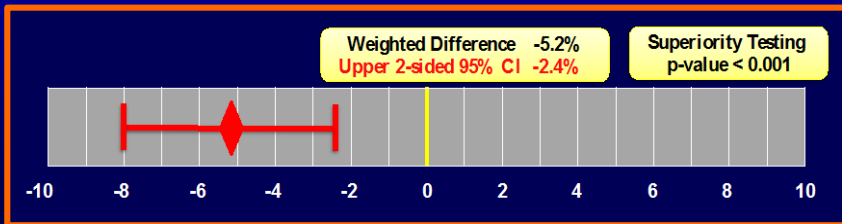
Months from Procedure	0	3	6	9	12
P2A Surgery	1077	859	836	808	795
S3 TAVR	1077	1043	1017	991	963

All stroke (AT)

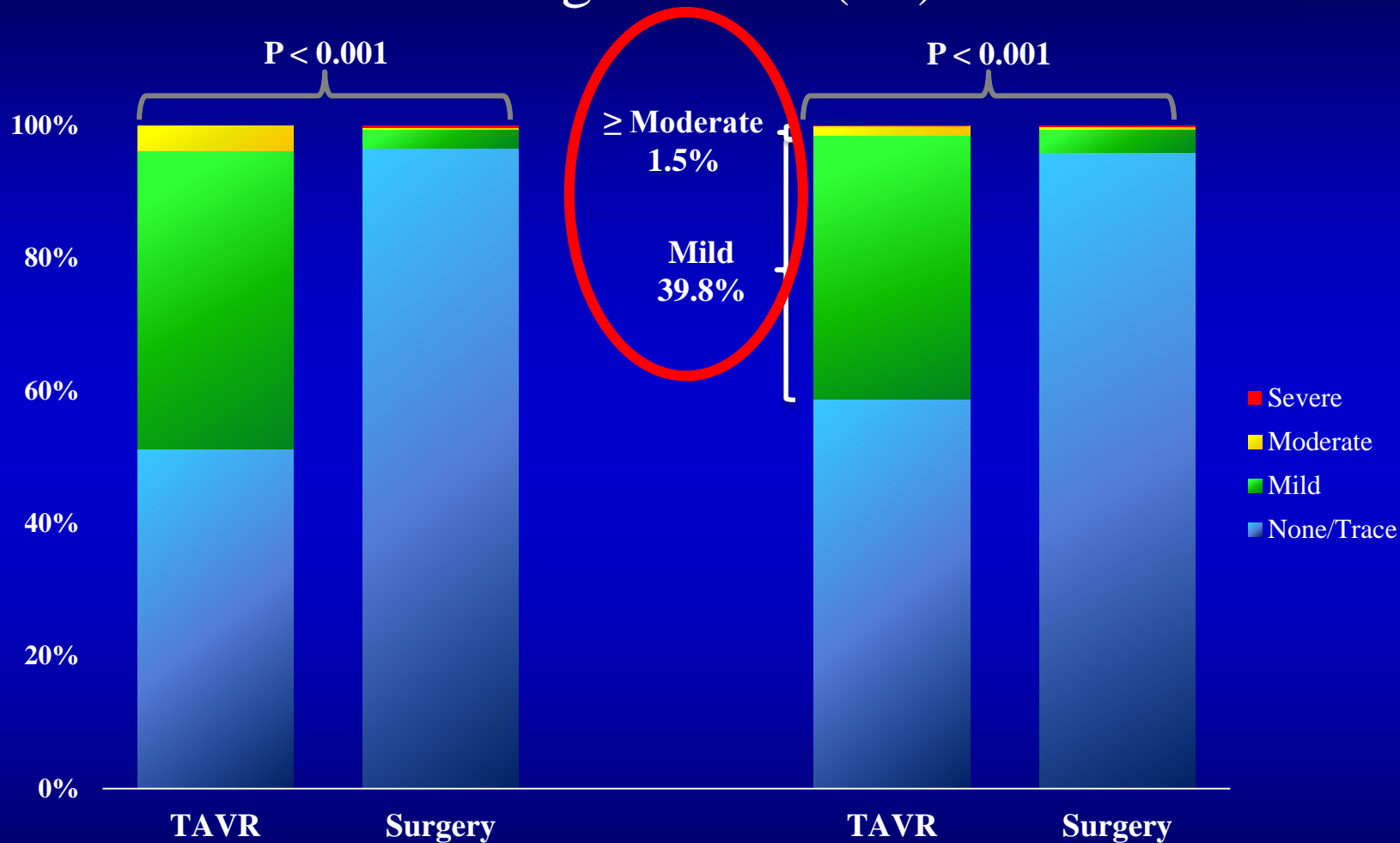


Number at risk:

Months from Procedure	0	3	6	9	12
P2A Surgery	1077	805	786	757	743
S3 TAVR	1077	1012	987	962	930



Paravalvular Regurgitation 3-Class Grading Scheme (VI)



No. of echos

30 Days

1 Year

P2A Surgery

755

610

S3i TAVR

992

875

In intermediate-risk patients, SAPIEN 3 TAVR resulted in **low 1-year rates** of **all-cause mortality** (7.4%), **all stroke** (4.6%), and **moderate or severe aortic regurgitation** (1.5%)

A **propensity score analysis** comparing SAPIEN 3 TAVR with surgery from PARTNER 2A in intermediate-risk patients at 1 year demonstrated:

- **Non-inferiority for the primary endpoint** (composite of all-cause mortality, all stroke, or AR \geq moderate)
- **Superiority of SAPIEN 3 TAVR for the primary endpoint, all-cause mortality, and all stroke**
- **Superiority of surgery for AR \geq moderate**

ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

M.J. Reardon, N.M. Van Mieghem, J.J. Popma, N.S. Kleiman, L. Søndergaard, M. Mumtaz, D.H. Adams, G.M. Deeb, B. Maini, H. Gada, S. Chetcuti, T. Gleason, J. Heiser, R. Lange, W. Merhi, J.K. Oh, P.S. Olsen, N. Piazza, M. Williams, S. Windecker, S.J. Yakubov, E. Grube, R. Makkar, J.S. Lee, J. Conte, E. Vang, H. Nguyen, Y. Chang, A.S. Mugglin, P.W.J.C. Serruys, and A.P. Kappetein, for the SURTAVI Investigators*

Intermediated surgical risk: an estimated risk of 30-day surgical death of 3 to 15%, according to the criteria of STS-PROM, as well as such nontraditional factors as coexisting *illnesses, frailty, and disability*.

Primary end point → a composite of death from any cause or disabling stroke at 24 months.

	TAVR (N=864)	Surgery (N=796)
Age — yr	79.7±6.1	79.7±6.1
Male sex — no. (%)	498 (57.6)	438 (55.0)
STS Mean—%	4.4±1.5	4.5±1.6
Logistic EuroSCORE	11.9±7.6	11.6±8.0
Previous stroke	57 (6.6)	57 (7.2)
Previous TIA	58 (6.7)	46 (4.8)
CAD	541 (62.6)	511 (64.2)
AF	243 (28.1)	211 (26.5)

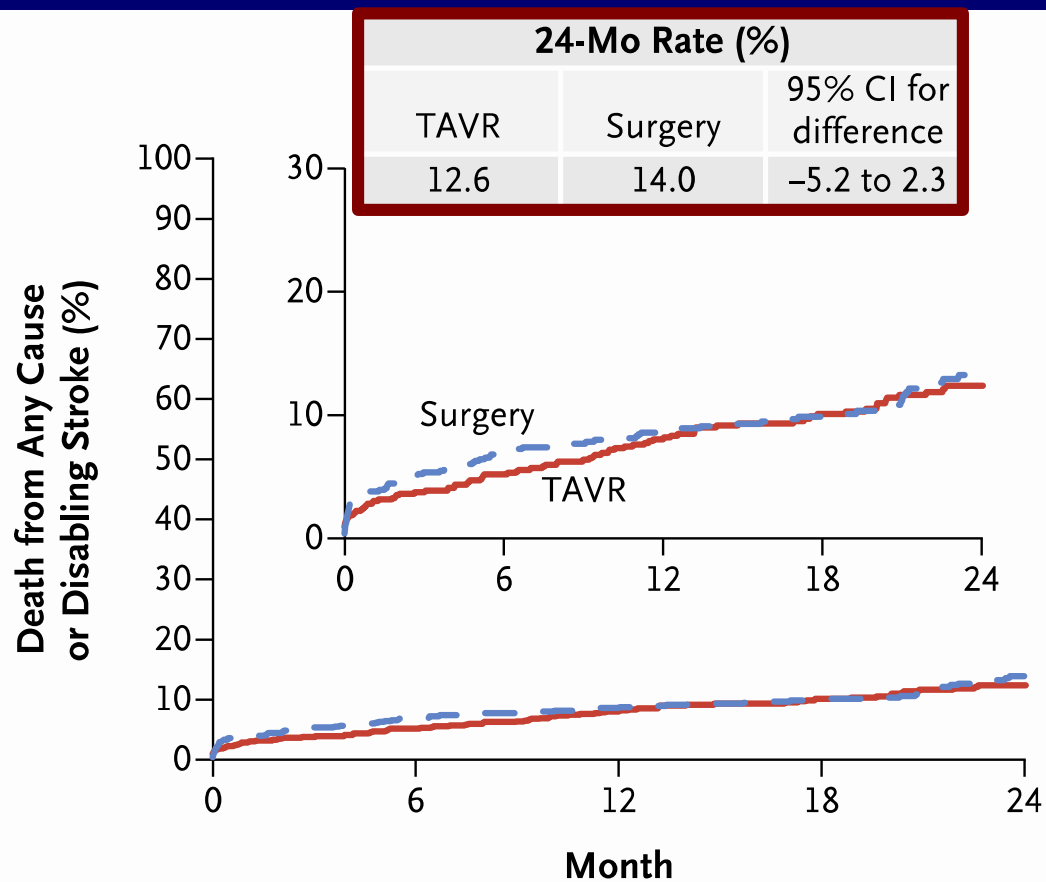


84%



16%

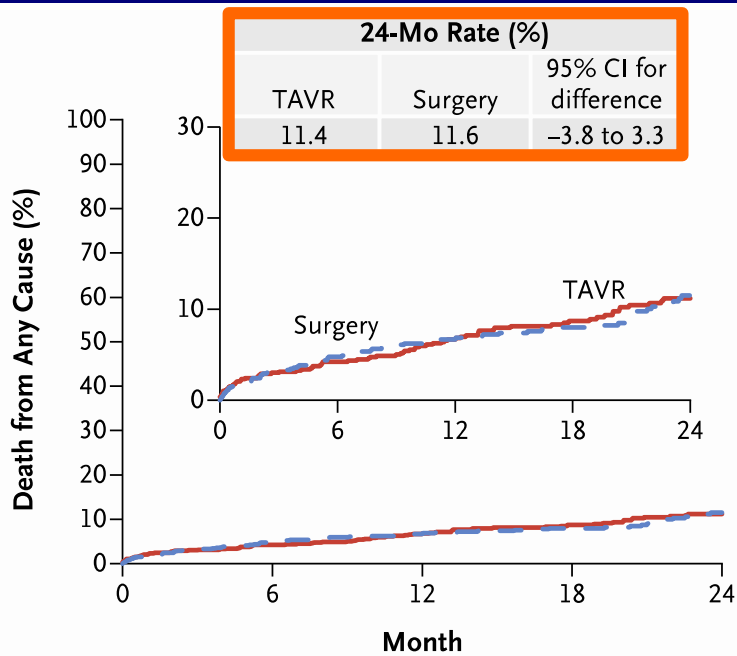
Death from Any Cause or Disabling Stroke



No. at Risk

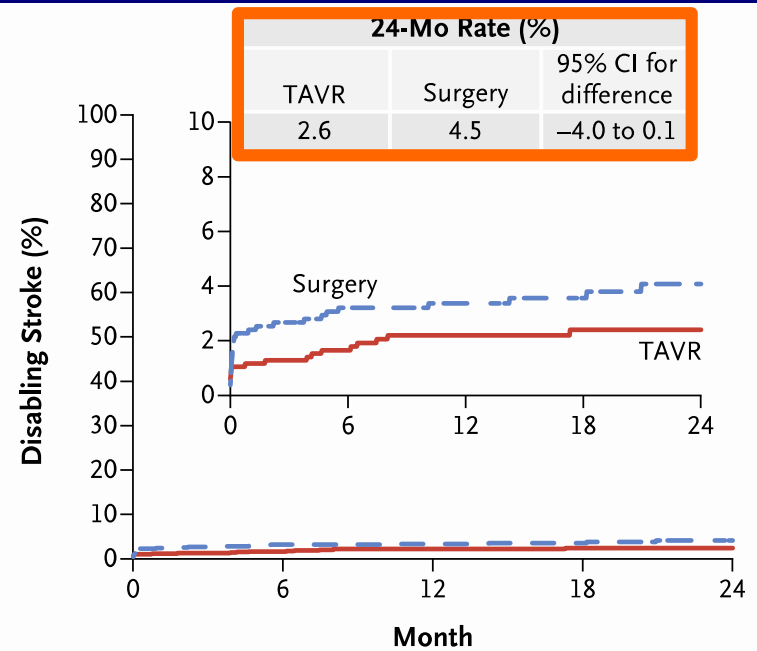
TAVR	864	755	612	456	272
Surgery	796	674	555	407	241

Death from Any Cause



No. at Risk	0	6	12	18	24
TAVR	864	762	621	465	280
Surgery	796	690	569	414	249

Disabling Stroke



No. at Risk	0	6	12	18	24
TAVR	864	755	612	456	272
Surgery	796	674	555	407	241

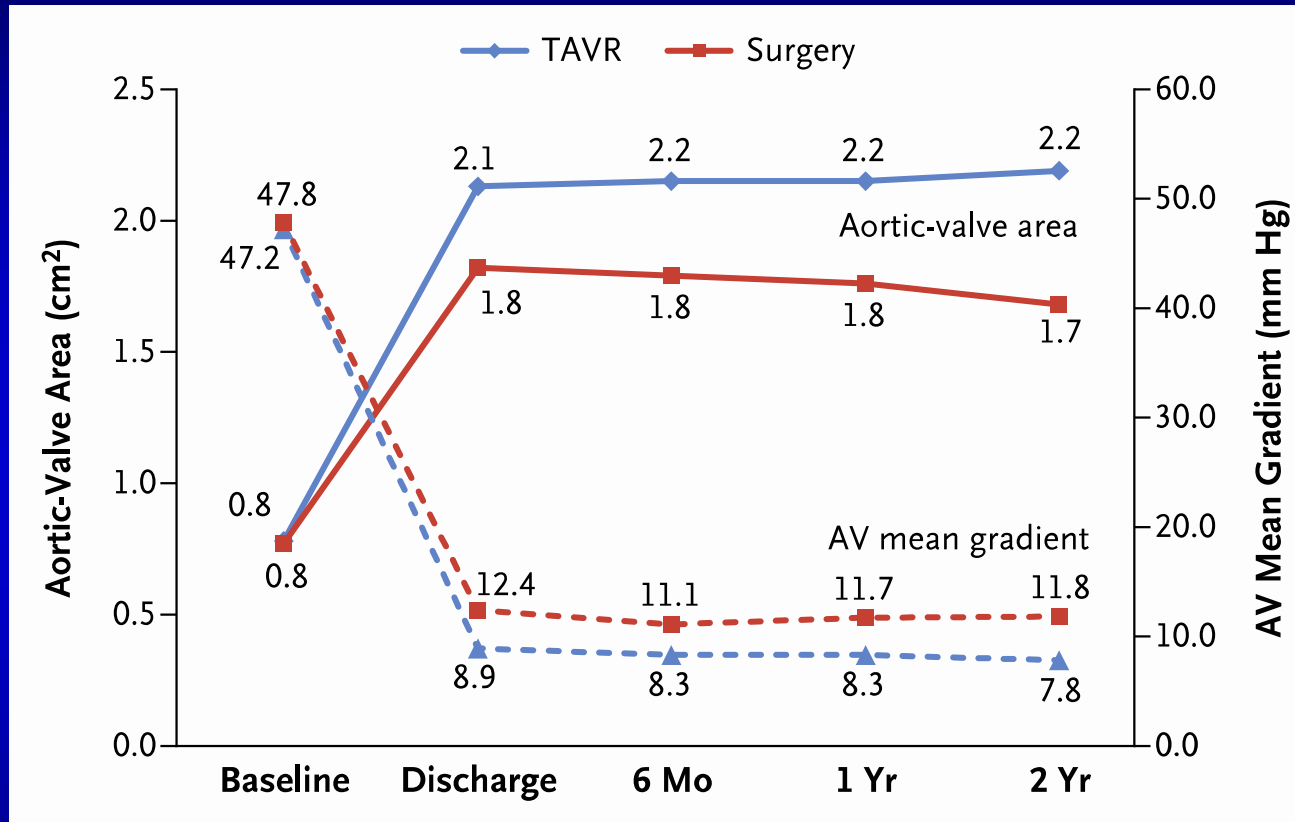
TAVR was a statistically non-inferior alternative to surgery with respect to death from any cause or disabling stroke at 24 months.

Procedure-Related Complications at 30 Days (Modified ITT)

Complication	TAVR (N=864)	Surgery (N=796)	95% Credible Interval for Difference
Life-threatening or major bleeding — %	12.2	9.3	-0.1 to 5.9
Transfusion of red cells — no. (%)			
0 units	756 (87.5)	469 (58.9)	24.4 to 32.5
1 unit	29 (3.4)	90 (11.3)	-10.5 to -5.5
2 to 4 units	48 (5.6)	136 (17.1)	-14.5 to -8.5
>4 units	31 (3.6)	101 (12.7)	-11.7 to -6.5
Acute kidney injury stage 2 or 3 — %	1.7	4.4	-4.4 to -1.0
Coronary-artery obstruction — %	0.2	0.0	-0.2 to 0.8
Major vascular complication — %	6.0	1.1	3.2 to 6.7
Cardiac perforation — %	1.7	0.9	-0.2 to 2.0
Cardiogenic shock — %	1.1	3.8	-4.2 to -1.1
Permanent pacemaker implantation — %	25.9	6.6	15.9 to 22.7
Atrial fibrillation — %	12.9	43.4	-34.7 to -26.4

Surgery was associated with higher rates of **AKI**, **AF**, and **transfusion requirements**, whereas TAVR had higher rates of **residual aortic regurgitation** and need for **pacemaker implantation**.

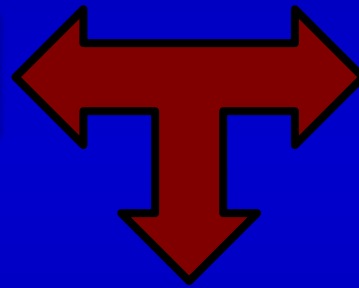
Echocardiographic findings



The mean AV gradient was significantly lower (dashed lines) and the effective AV orifice area was significantly larger (solid lines) in the TAVR group than in the surgery group at all time points after the procedure.

... and the low risk?

NOTION



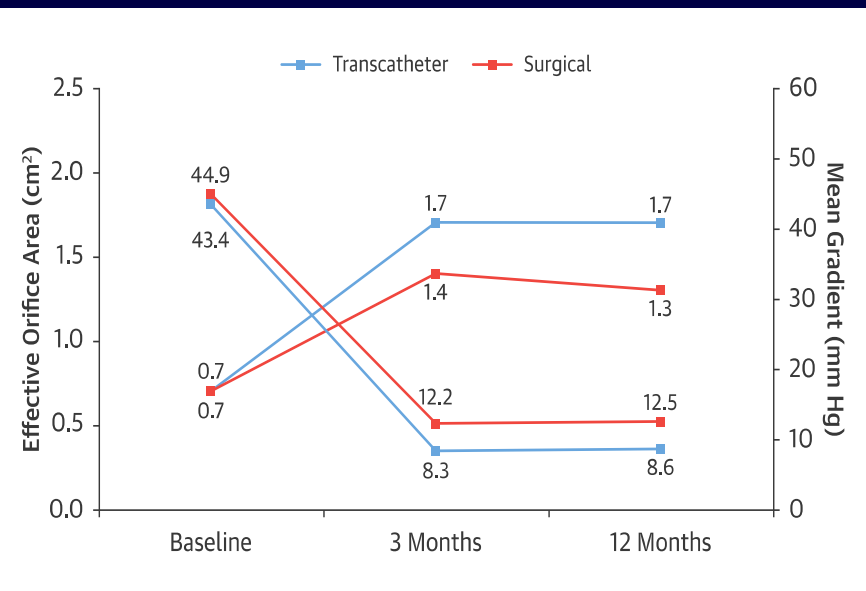
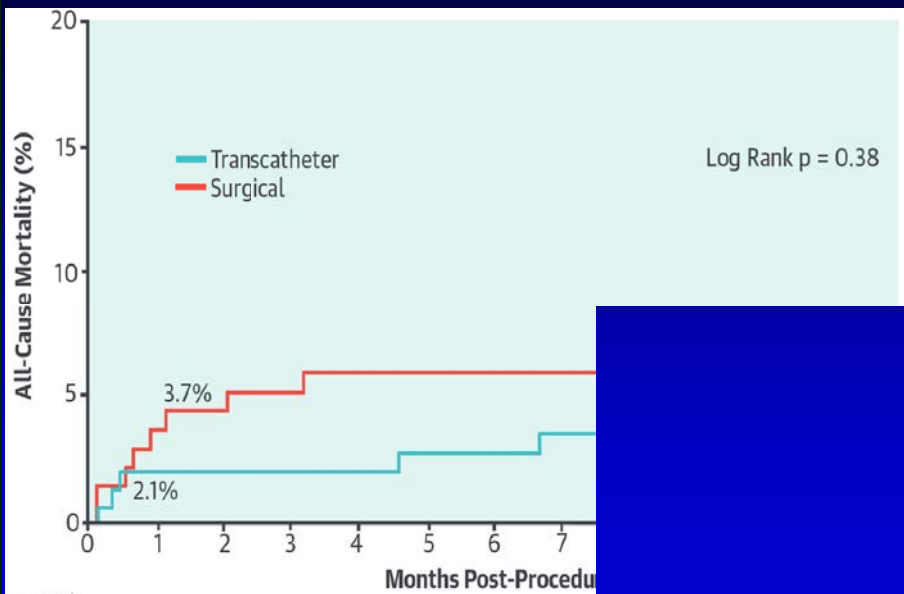
SURTAVI
STS PROM < 4%

STACCATO

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

Patients **>70 years old** with severe
AoV stenosis and no CAD were
randomized 1:1 to TAVR using a SE
bioprosthesis versus SAVR

	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)
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)



	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

ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

Intermediated surgical risk: an estimated risk of 30-day **surgical death of 3 to 15%**, according to the criteria of STS-PROM, as well as such nontraditional factors as coexisting *illnesses, frailty, and disability*.

STS <4%

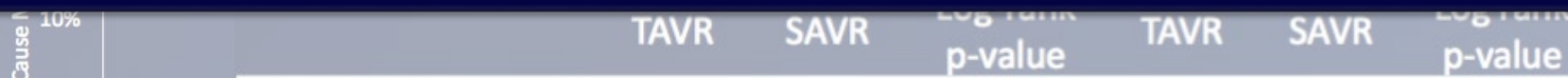
STS ≥4%

Variable	STS <4% N=644	STS ≥4% N=1016	P Value
Age, years	77.7 ± 6.0	81.1 ± 5.9	< 0.0001
Male sex	62.1%	52.8%	0.0002
STS PROM, %	3.0 ± 0.7	5.4 ± 1.2	< 0.0001
Diabetes mellitus	29.3%	37.7%	0.0005
Creatinine >2 mg/dl	0.6%	2.7%	0.0024
Permanent pacemaker	7.3%	10.7%	0.0196
Coronary artery disease	54.7%	68.9%	< 0.0001
Prior CABG	9.8%	20.9%	< 0.0001
Prior PCI	19.3%	22.5%	0.1110
Prior myocardial infarction	12.7%	15.2%	0.1681
Congestive heart failure	92.4%	98.2%	< 0.0001
History of arrhythmia	26.6%	34.8%	0.0004
Atrial fibrillation	21.6%	31.0%	< 0.0001
NYHA Class III/IV	51.9%	63.9%	< 0.0001

Death from Any Cause or Disabling Stroke



Self-expandable TAVR had **favorable outcomes** compared with surgery



Similar 12 month all cause mortality and stroke rates

	TAVR	SAVR	Log-rank p-value	TAVR	SAVR	Log-rank p-value
All-cause mortality	1.4%	1.3%	0.9045	3.8%	6.0%	0.2278

No. at Risk

Less frequent AF and AKI with TAVR, but more frequent use of PPM and AR

New Pacemaker	27.0%	6.7%	< 0.0001	30.7%	8.0%	< 0.0001
Acute Kidney Injury	3.8%	17.4%	< 0.0001	3.8%	17.4%	< 0.0001
Aortic valve hospitalization	3.2%	2.4%	0.5076	8.3%	3.5%	0.0249

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials

FREE



extremely high-risk

PARTNER 1A

US Corevalve

extremely high-risk

intermediate-risk

PARTNER 2A

NOTION

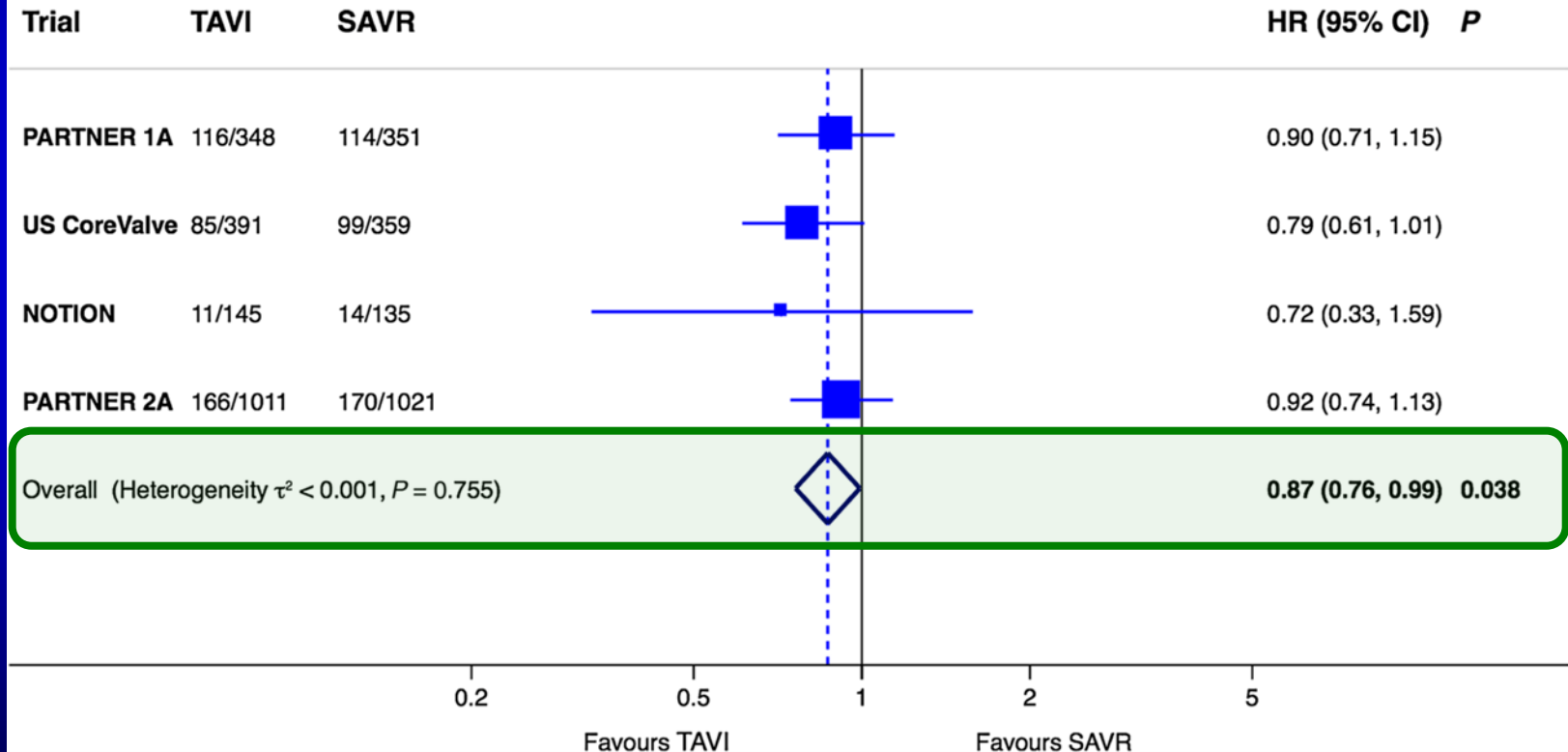
low-risk

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials

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Death from any cause

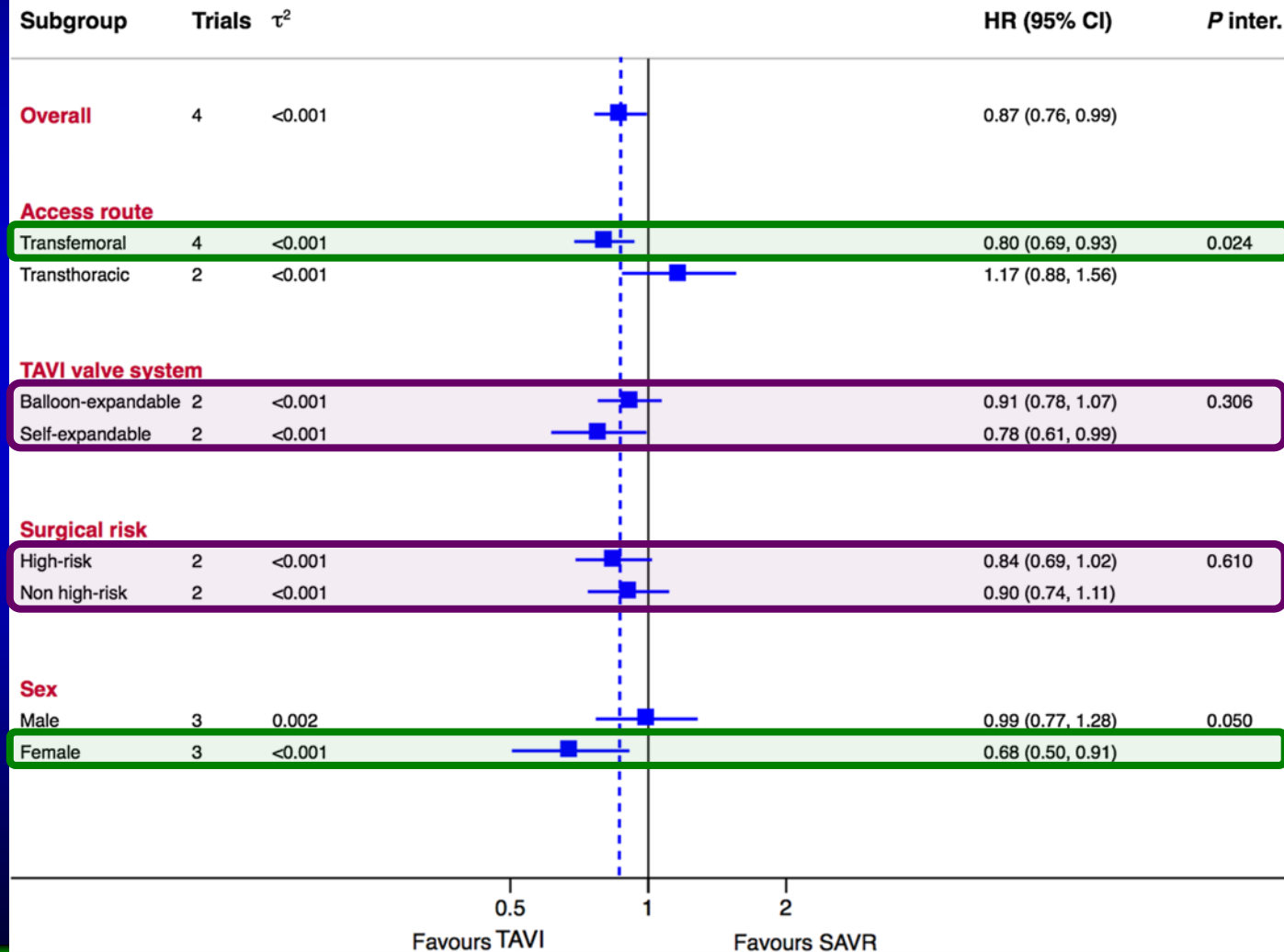


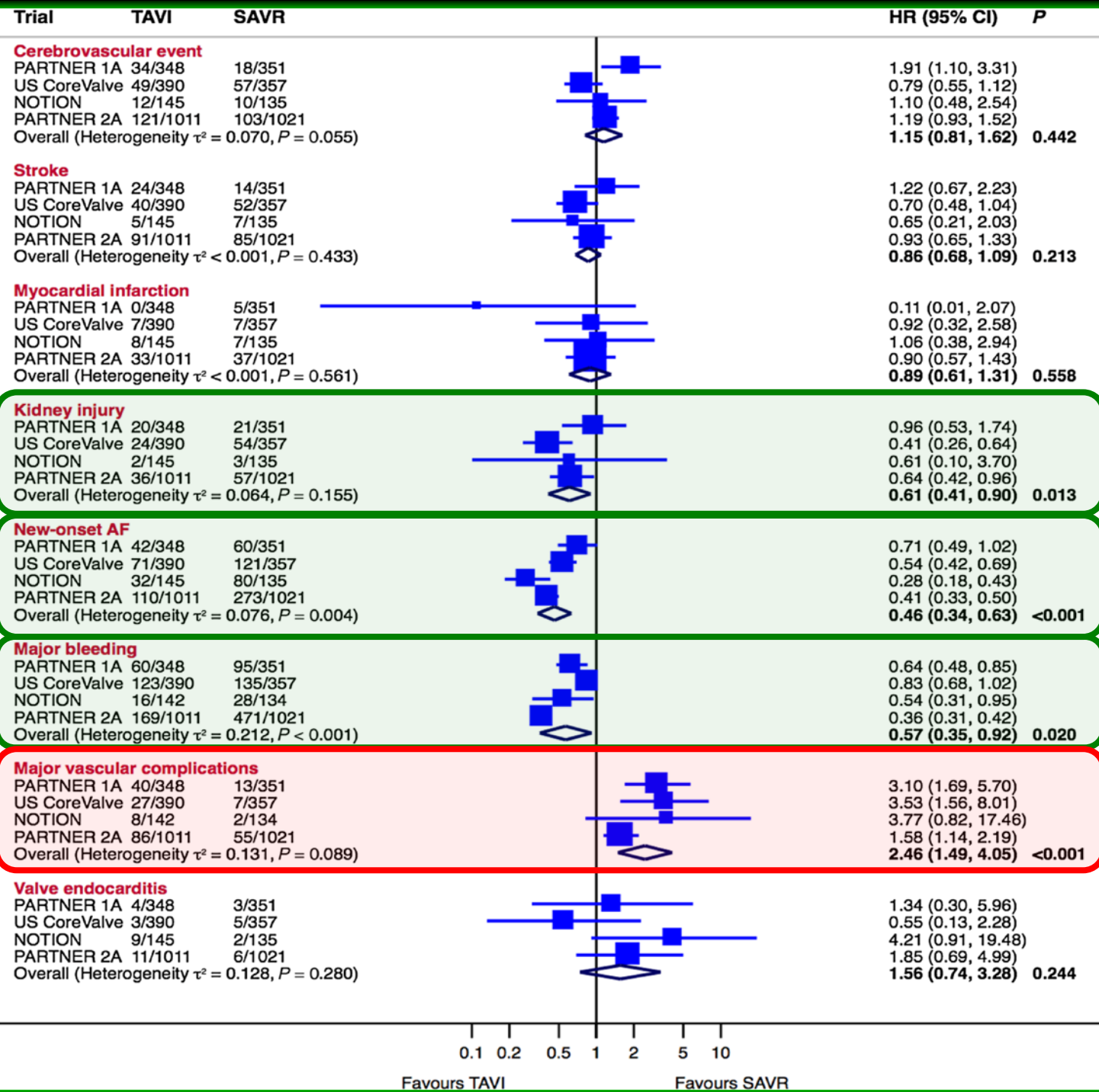
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Death from any cause



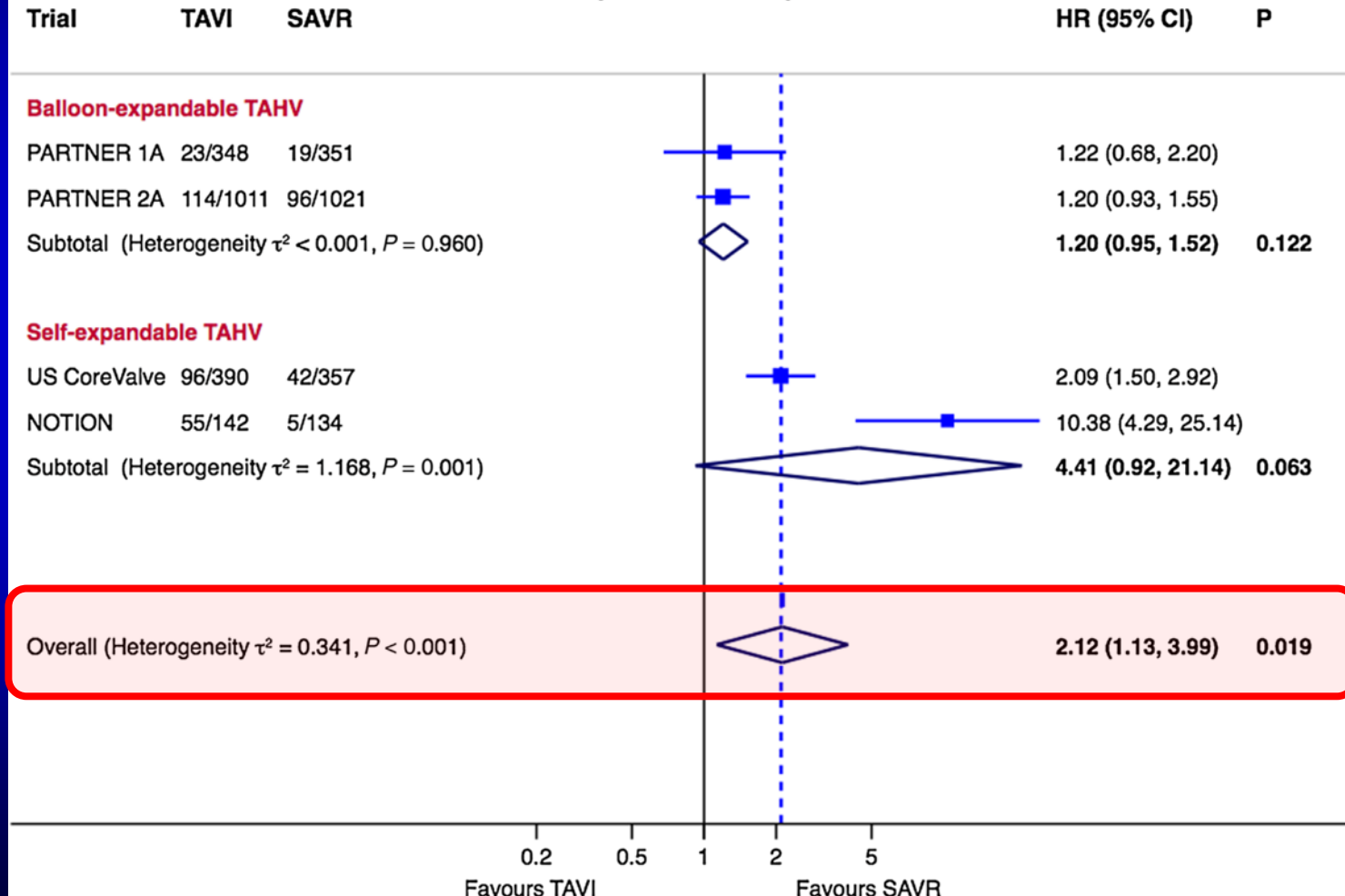


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Permanent pacemaker implantation

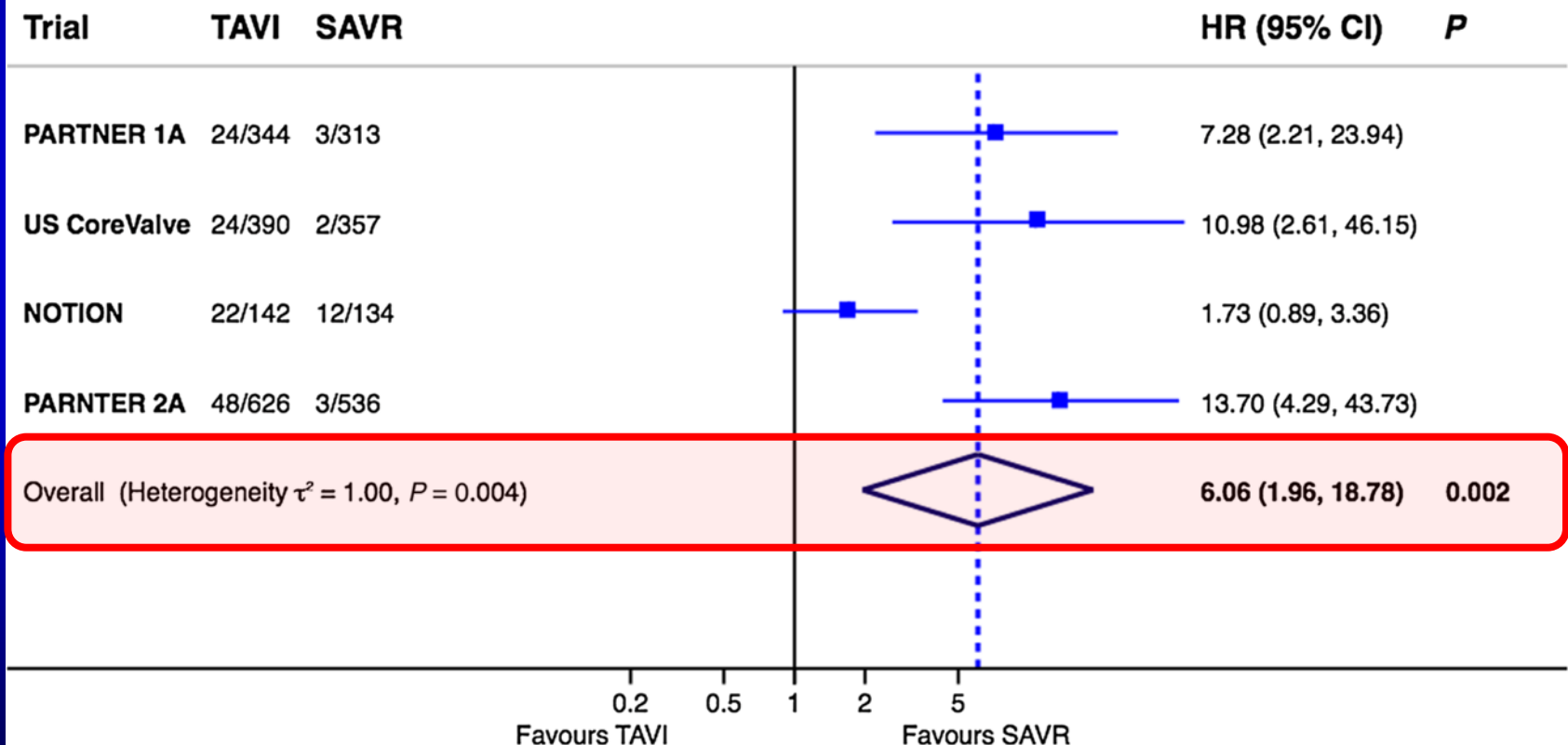


Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of severe aortic stenosis: a meta-analysis of randomized trials

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Paravalvular regurgitation



Conclusions

- 2017 European and American guideline for valvular heart disease introduced the role of **TAVR for intermediate-risk patients** with severe Ao stenosis
- Despite the calculated risk score was “lower”, the patients’ **age remains high** (80 y.o.)
- There are **few data about younger patients**
- When feasible, **trans-femoral** approach is associated with better results

Conclusions

- As for higher-risk patients, TAVR has **potential advantages** (lower incidence of AKI, death from any cause, major bleeding, new onset of AF) and **pitfalls** (major vascular complication, PPM, paravalvular regurgitation).

- In **lower-risk patients, low-risk procedure** and **optimal procedural results** are mandatory.



Post-procedural paravalvular regurgitation < moderate/severe
Preserved easy coronary access in younger patients
Low PPM rate



**Thank
you**