euroPCR @ SOLACI

Clinical evidence of TAVR in intermediate risk patients: Lessons from clinical trials

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Disclosures

- Speaker Fees: AZ, The Medicines Company, Abbott Vascular, KSH, Microport
- Advisory Boards: Abiomed, Abott Vascular, KSH, Microport, Medicines Company, Sinomed
- Institutional Research Support: Medtronic, Abbott Vascular

Trial Evidence

- Randomised controlled trials
  - TAVI in inoperable patients
  - TAVI in high risk patients
  - TAVI in intermediate risk patients
- Registry data
- Upcoming trials and next questions

WHAT IS INTERMEDIATE RISK ?

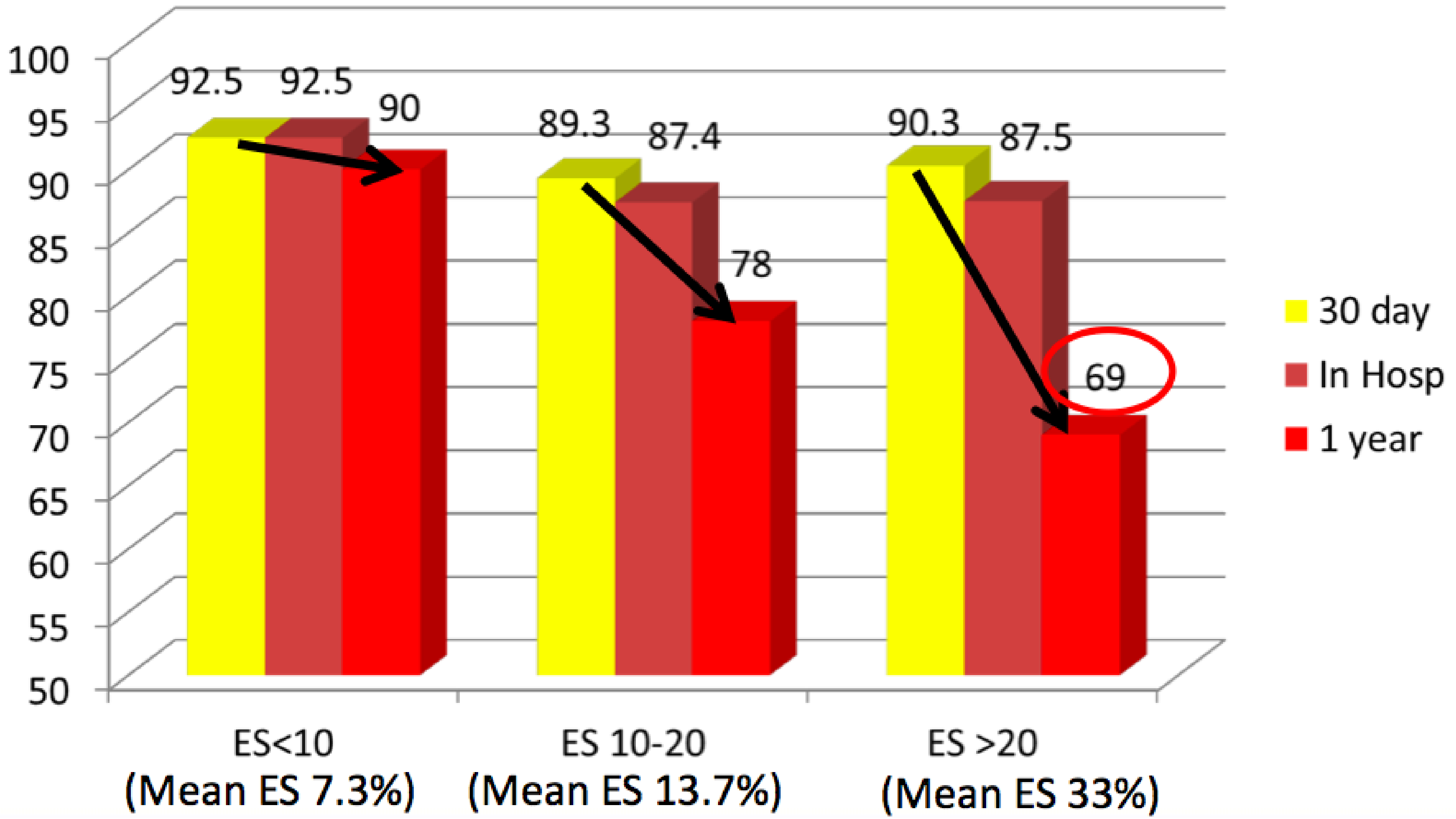
euro PCR 2013

Aortic Valve Replacement in Octogenarians: Utility of Risk Stratification With EuroSCORE

Sergey Leontyev, MD, Thomas Walther, MD, PhD, Michael A. Borger, MD, PhD, Sven Lehmann, MD, Anne K. Funkat, PhD, Ardawan Rastan, MD, PhD, Jörg Kempfert, MD, Volkmar Falk, MD, PhD, and Friedrich W. Mohr, MD, PhD

Department of Cardiac Surgery, Heart Center, University of Leipzig, Leipzi

(Ann Thorac Surg 2009;87:1440–5)



Co-morbidity ‘invisible’ to the Euroscore

- Frailty
- Poor mobility
- Depression/lack of motivation
- Cognitive impairment
- Porcelain aorta
- Liver disease
- Chest wall deformity

Risk Assessment before Valve Intervention

« 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 a combination of scores »

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 &
European Journal of Cardio-Thoracic Surgery 2012 -
doi:10.1093/ejcts/ezs455).

Intermediate risk

- **SURTAVI -** inclusion criteria STS ≥4 and ≤10%
- **PARTNER 2 -** Cohort A STS ≥4
- **UK TAVI -** STS ≥4 and ≤12%

but all specify decision to be made by Heart Team

Intermediate risk

- Patients who are operable
- Absence of severe comorbidities
- Risk score in the medium/low range

DATA

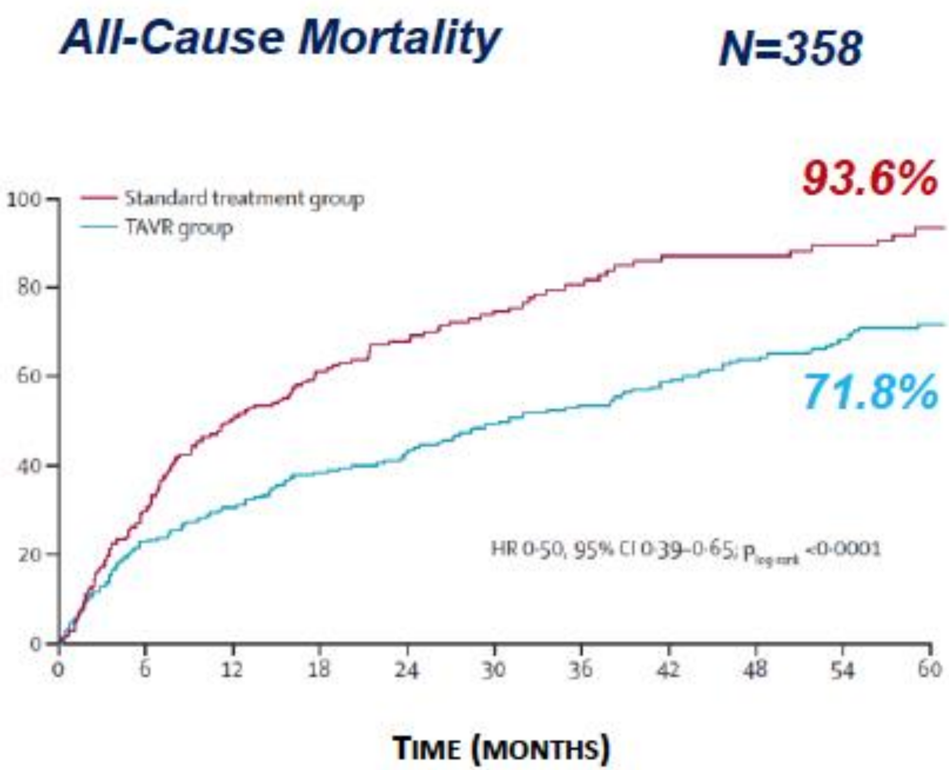
TAVI vs Medical Rx: Inoperable Patients

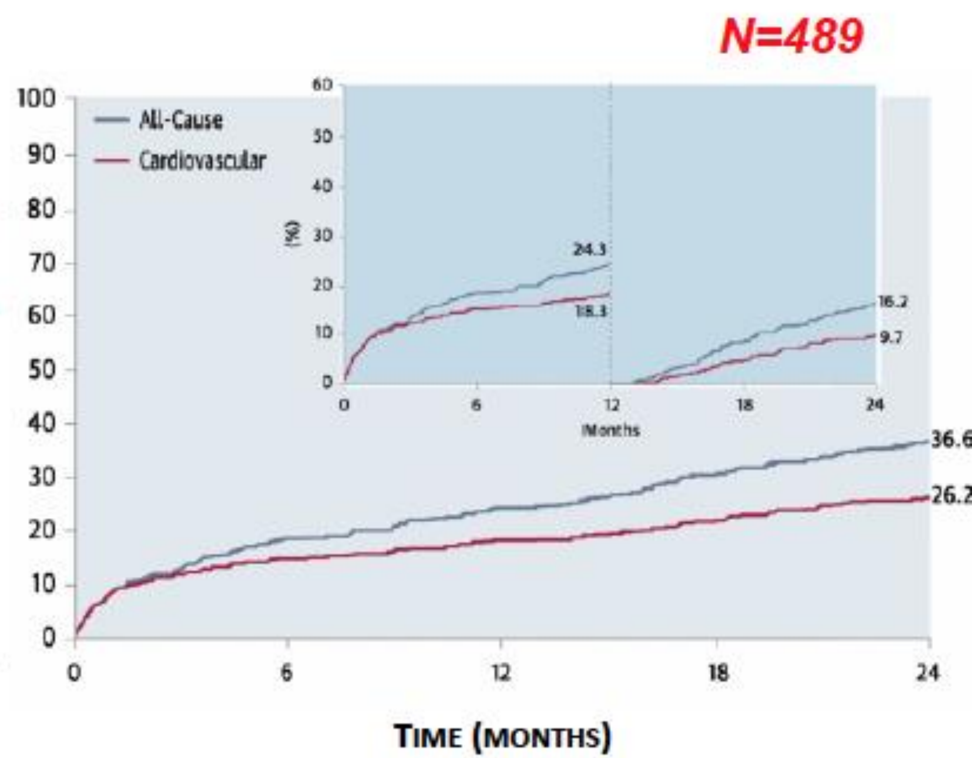
PARTNER 1B: 5-Year Follow-up

Kapadia SR et al. *Lancet* 2015

CoreValve Extreme-Risk: 2-Year Follow-up

Yakubov SJ et al. *J Am Coll Cardiol* 2015



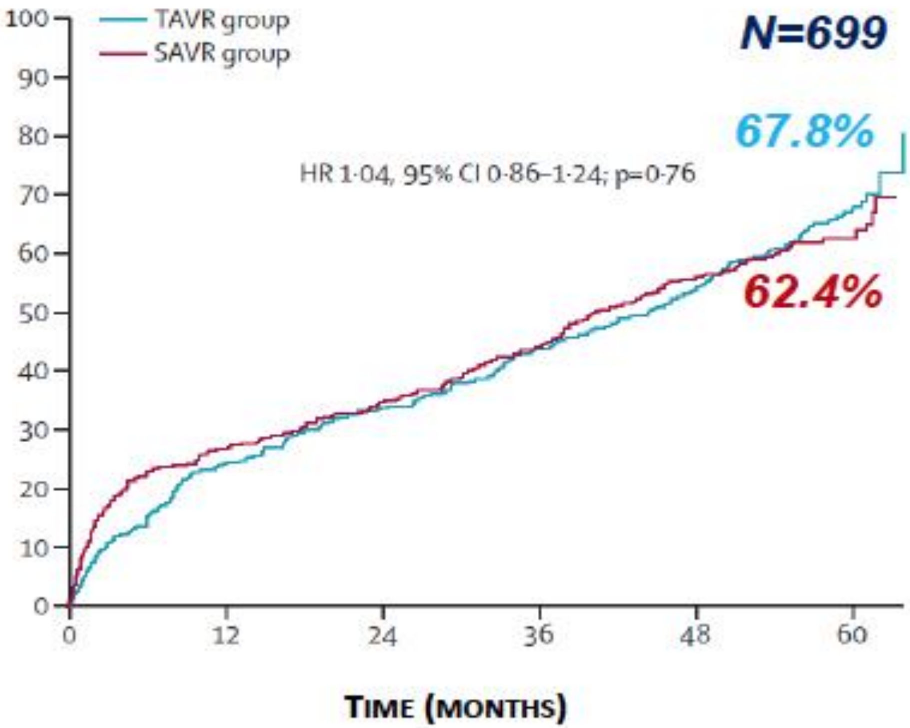


TAVI vs SAVR: High Risk Patients

PARTNER 1A: 5-Year Follow-up

Mack MJ et al. *Lancet* 2015

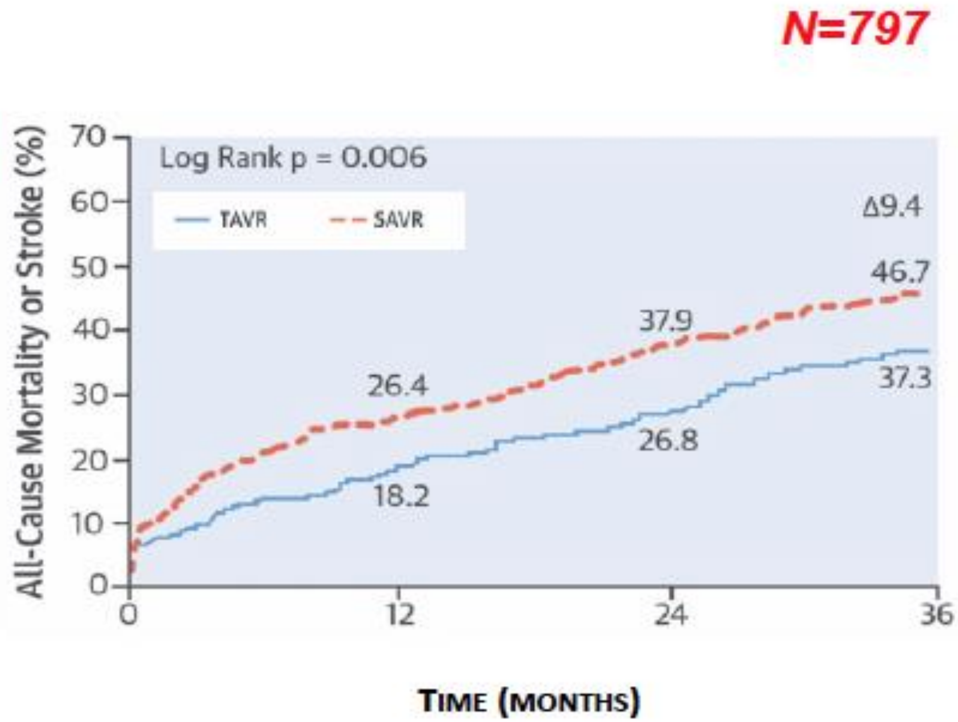
All-cause Mortality



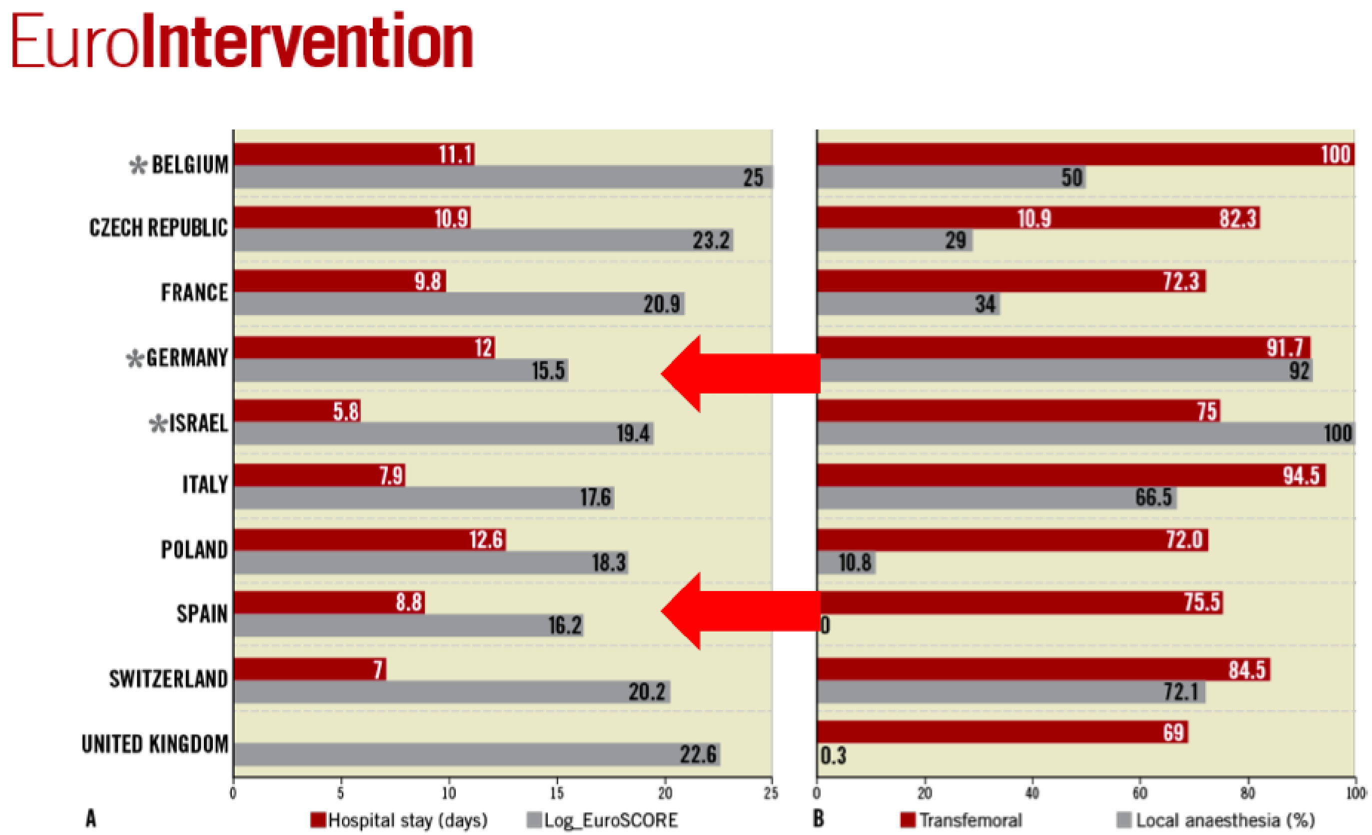
CoreValve High-Risk: 3-Year Follow-up

Deeb M et al. *J Am Coll Cardiol* 2016

All-cause Mortality or Stroke



European sentinel registry



EuroIntervention 2012; 8-online publish-ahead-of-print December 2012

The 2011-12 pilot European Sentinel Registry of Transcatheter Aortic Valve Implantation: in-hospital results in 4,571 patients

euro PCR 2013

Improvements in Transcatheter Aortic Valve Implantation Outcomes in Lower Surgical Risk Patients

A Glimpse Into the Future

Ruediger Lange, MD, PHD, Sabine Bleiziffer, MD, Domenico Mazzitelli, MD, Yacine Elhmidi, MD, Anke Opitz, MD, Marcus Krane, MD, Marcus-Andre Deutsch, MD, Hendrik Ruge, MD, Gernot Brockmann, MD, Bernhard Voss, MD, Christian Schreiber, MD, Peter Tassani, MD, PHD, Nicolo Piazza, MD, PHD

Munich, Germany

Objectives The purpose of this study was to investigate the evolution of patient selection criteria for transcatheter aortic valve implantation (TAVI) and its impact on clinical outcomes.

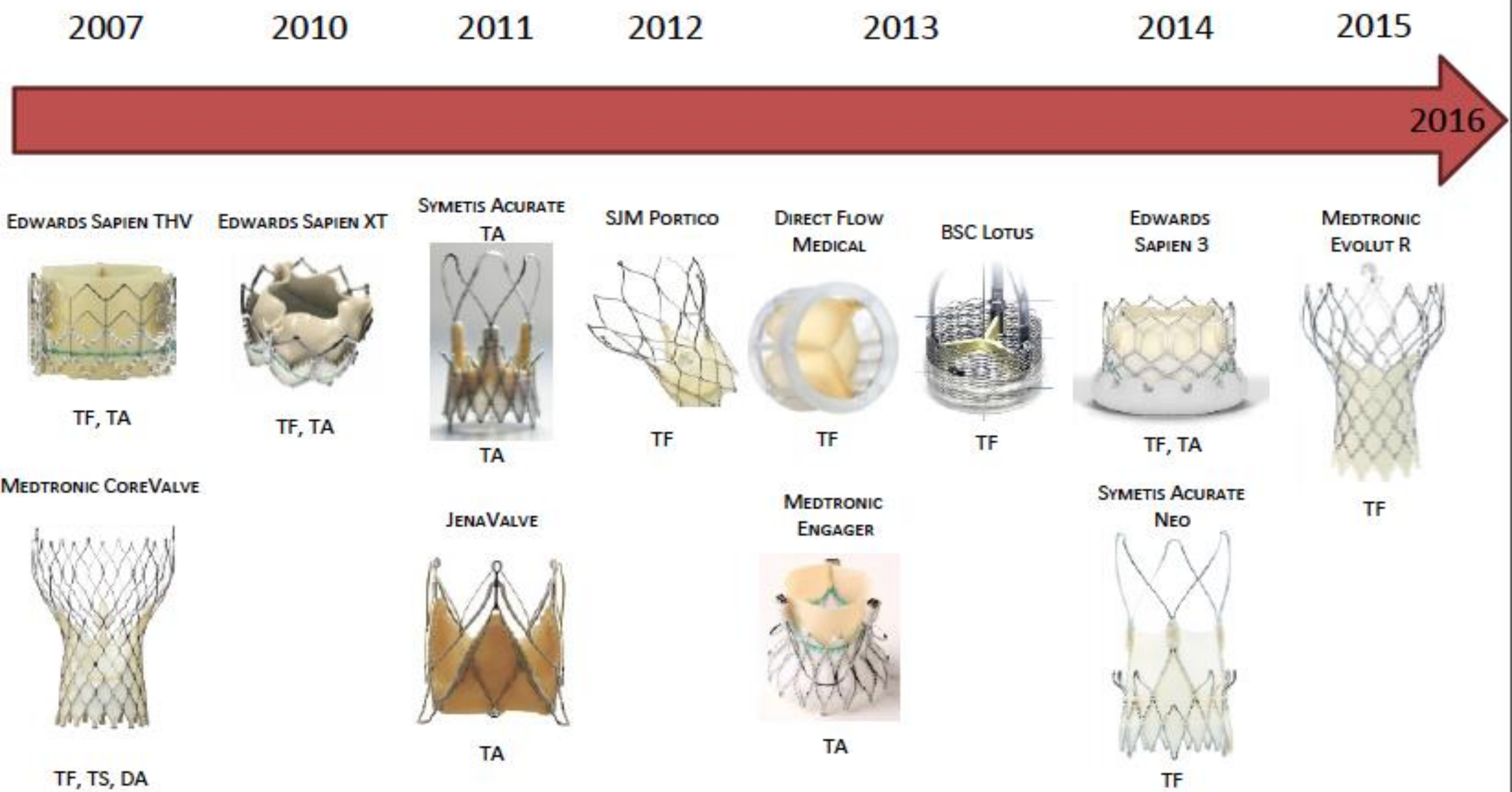
Background Anecdotal evidence suggests that patient selection for TAVI is shifting toward lower surgical risk patients. The extent of this shift and its impact on clinical outcomes, however, are currently unknown.

Methods We conducted a single-center study that subcategorized TAVI patients into quartiles (Q1 to Q4) defined by enrollment date. These subgroups were subsequently examined for differences in baseline characteristics and 30-day and 6-month mortality rate. The relationship between quartiles and mortality rate was examined using unadjusted and adjusted (for baseline characteristics) Cox proportional hazard models.

Results Each quartile included 105 patients (n = 420). Compared with Q4 patients, Q1 patients had higher logistic EuroSCORES (25.4 ± 16.1% vs. 17.8 ± 12.0%, p < 0.001), higher Society of Thoracic Surgeons scores (7.1 ± 5.5% vs. 4.8 ± 2.6%, p > 0.001), and higher median N-terminal pro–B-type natriuretic peptide levels (3,495 vs. 1,730 ng/dl, p = [illegible]). From Q1 to Q4, the crude 30-day and 6-month mortality rate decreased significantly from 11.4% to 3.8% (unadjusted hazard ratio [HR]: 0.33; 95% confidence interval [CI]: 0.11 to 1.01; p = 0.053) and from 23.5% to 12.4% (unadjusted HR: 0.49; 95 CI: 0.25 to 0.95; p = 0.07), respectively. After adjustment for baseline characteristics, there were no significant differences between Q1 and Q4 in 30-day mortality rate (adjusted HR ratio: 0.29; 95% CI: 0.08 to 1.08; p = 0.07) and 6-month mortality rate (HR: 0.67; 95% CI: 0.25 to 1.77; p = 0.42).

Conclusions The results of this study demonstrate an important paradigm shift toward the selection of lower surgical risk patients for TAVI. Significantly better clinical outcomes can be expected in lower than in higher surgical risk patients undergoing TAVI. (J Am Coll Cardiol 2012;59:280–7)

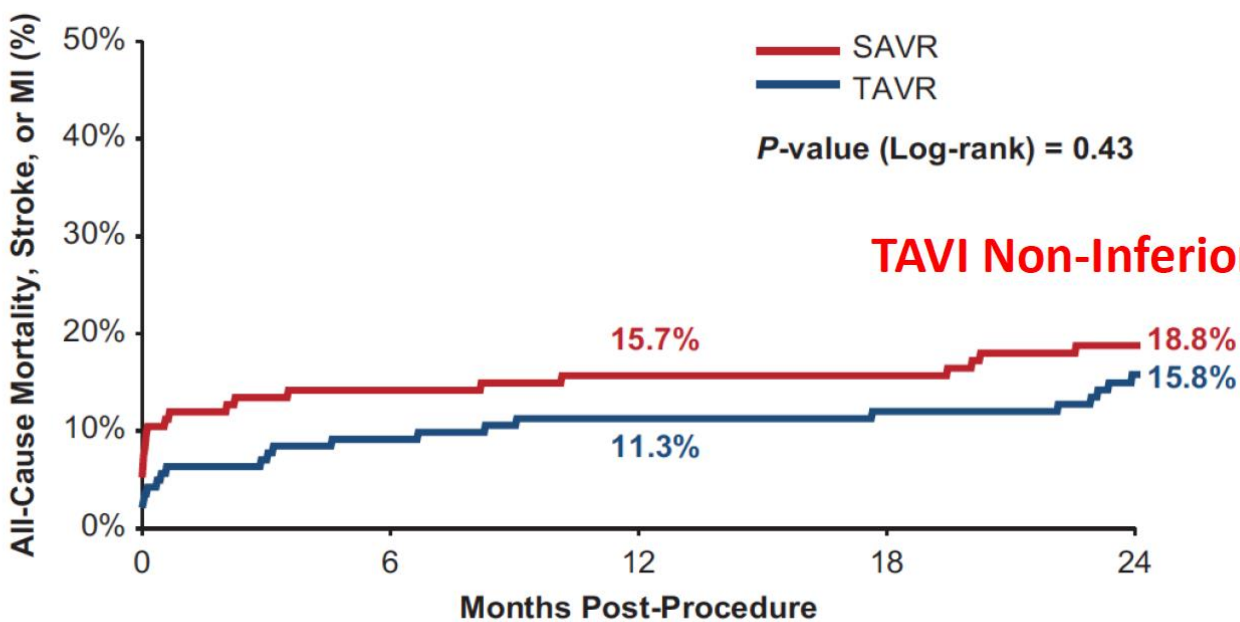
TAVI 2002-2016: Devices with CE Mark Approval



Notion

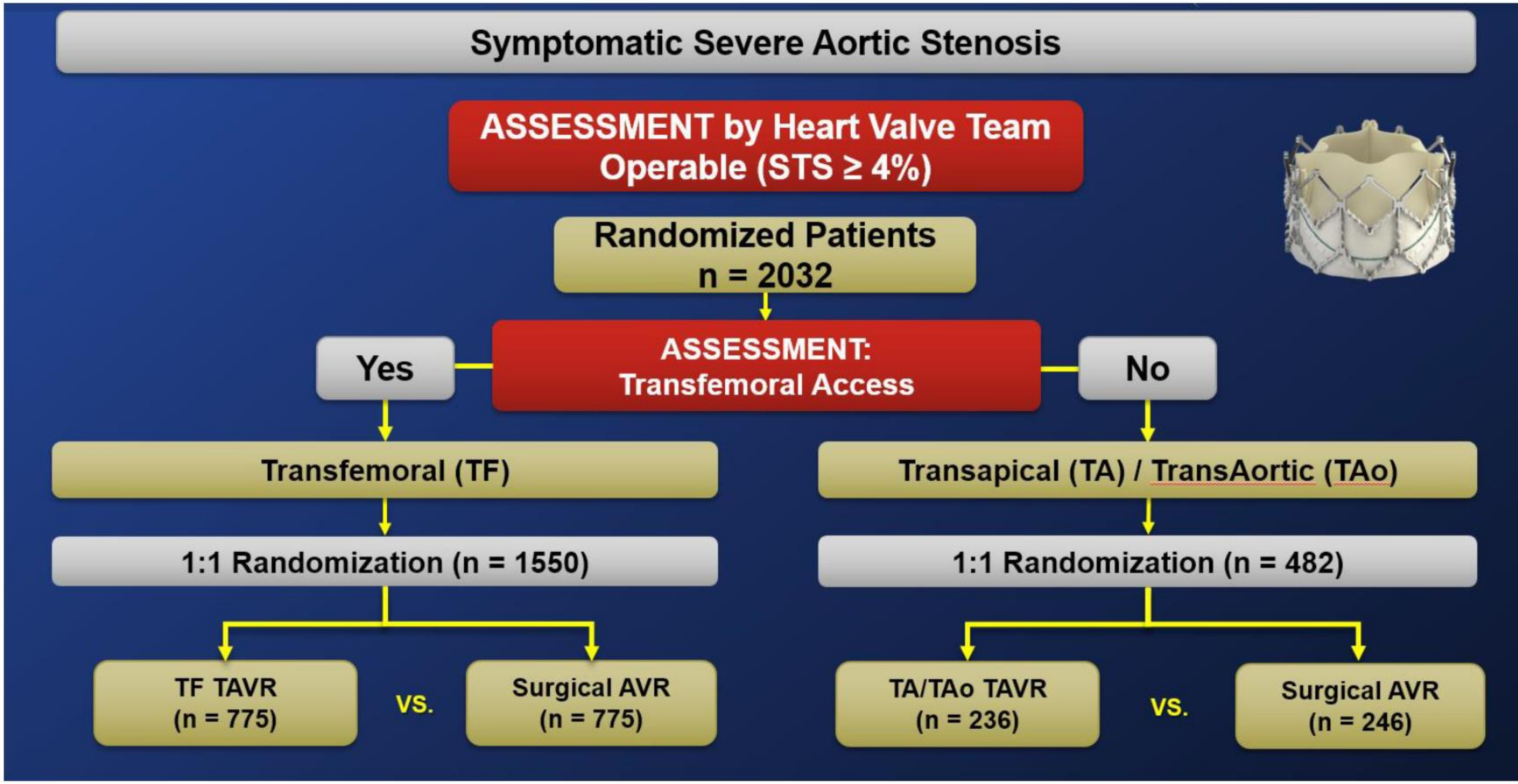
- TAVI with Corevalve vs SAVR
- Age > 70Y (mean 79Y)
- STS score: 3 (80% considered low risk)
- Logistic Euroscore: 9

All-cause mortality, stroke or MI



Sondergaard et al. Circ cardiovasc Interv 2016

Partner IIA



Primary Endpoint: All-Cause Mortality or Disabling Stroke at Two Years

Partner IIA

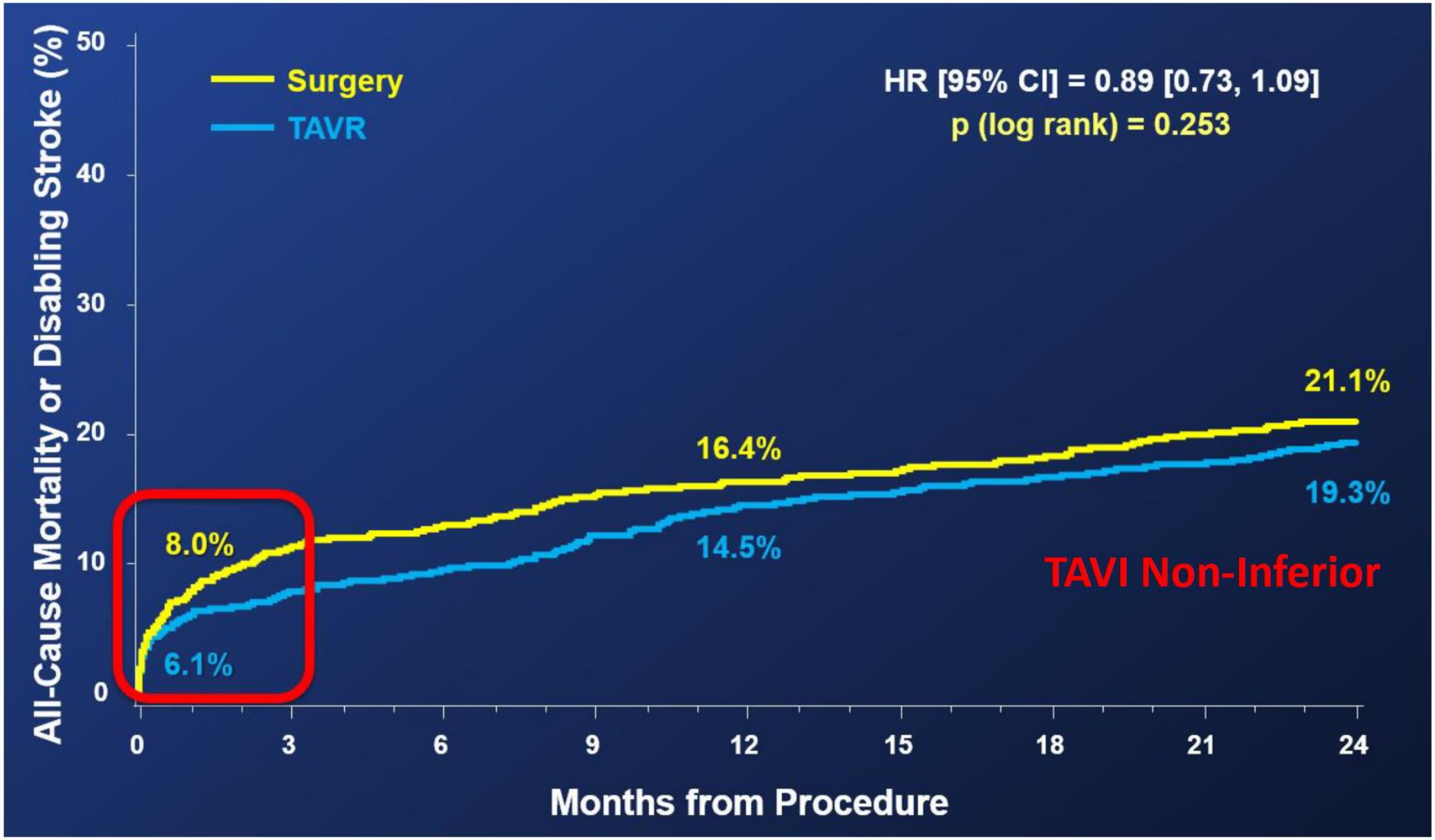
Some important baseline characteristics

Characteristic	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Age - yrs	81.5 ± 6.7	81.7 ± 6.7	0.63
STS Score - %	5.8 ± 2.1	5.8 ± 1.9	0.29

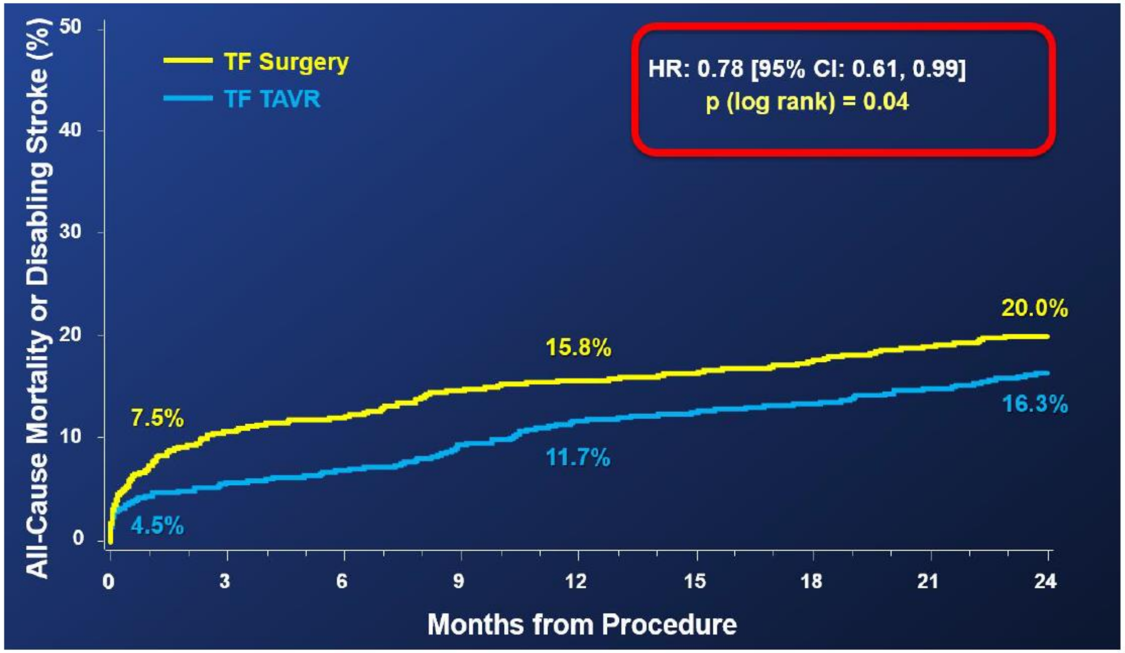
Some important outcomes

Events (%)	30 Days			2 Years		
	TAVR (n = 1011)	Surgery (n = 1021)	p-value*	TAVR (n = 1011)	Surgery (n = 1021)	p-value*
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	27.3	<0.001
New Permanent Pacemaker	8.5	6.9	0.17	11.8	10.3	0.29

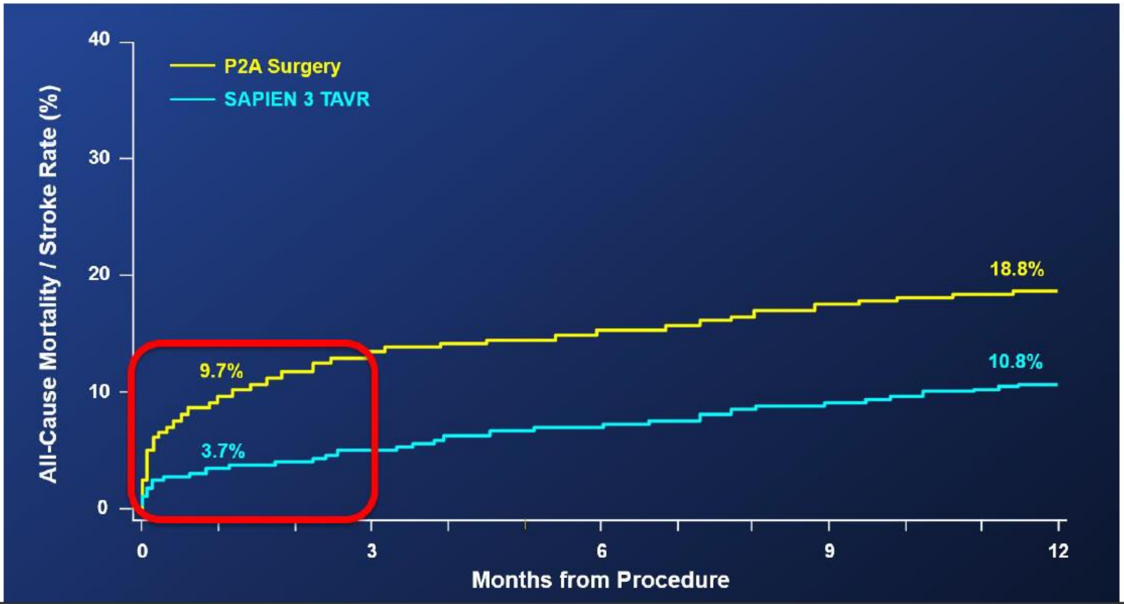
Partner IIA Primary Endpoint



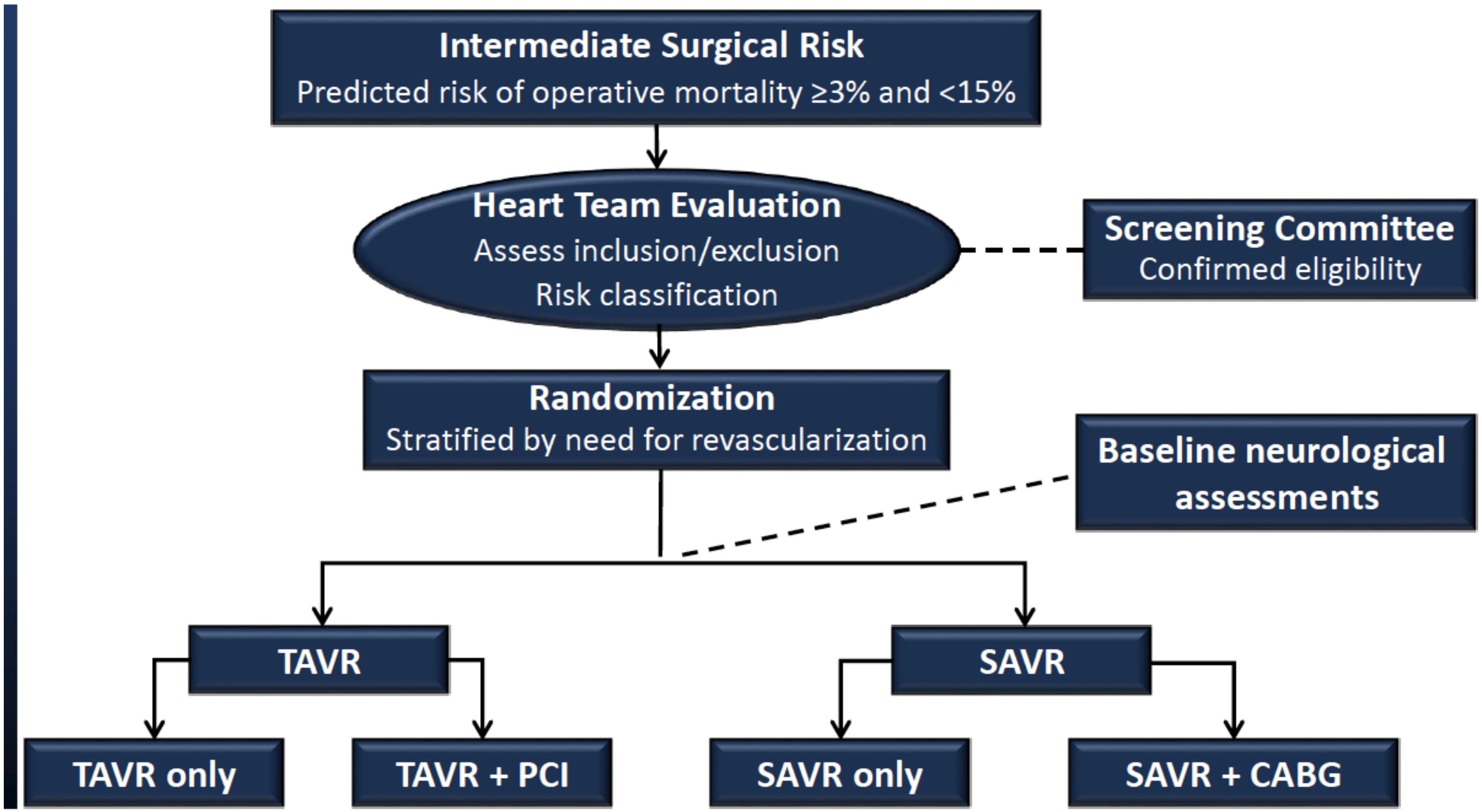
Partner IIA - TF



Partner II – S3i

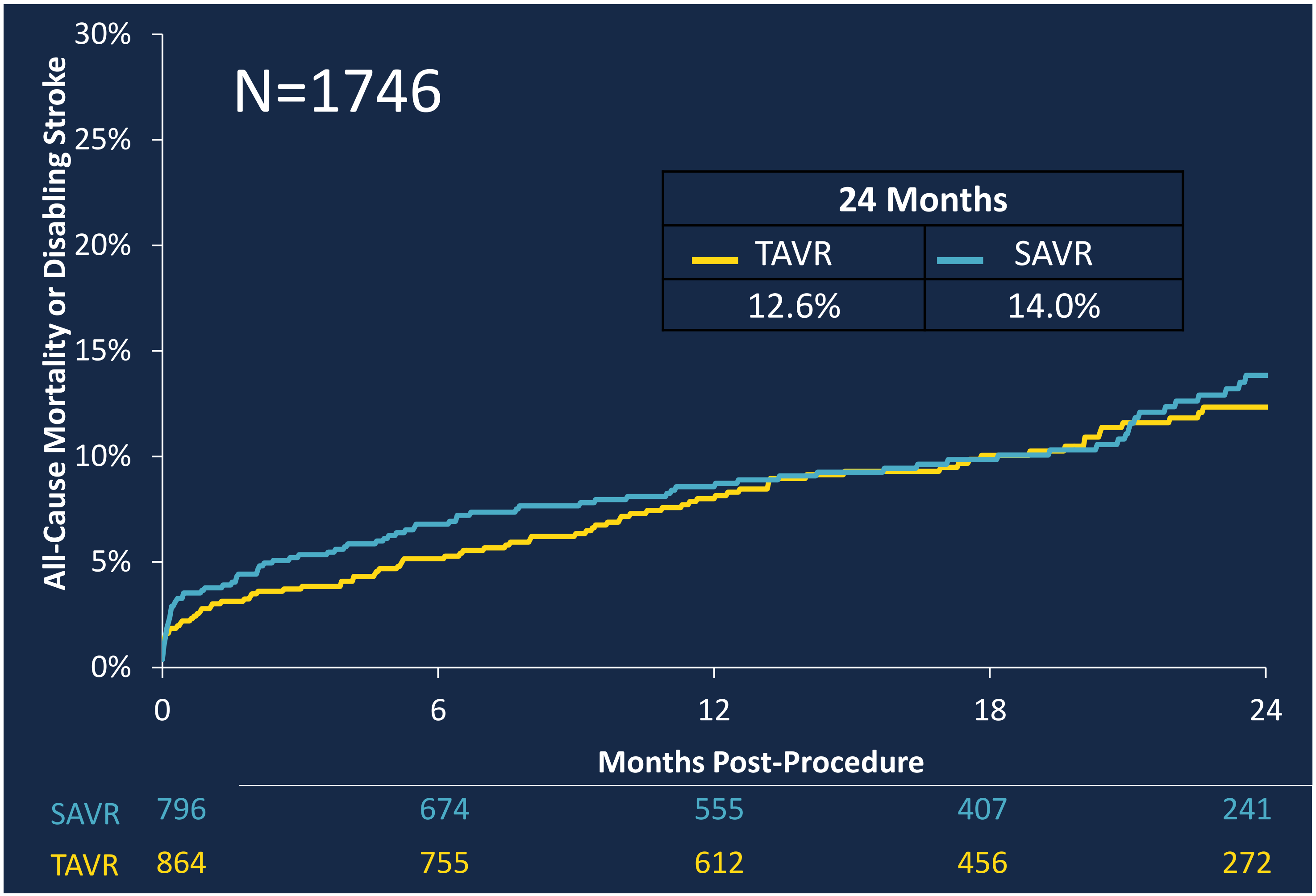


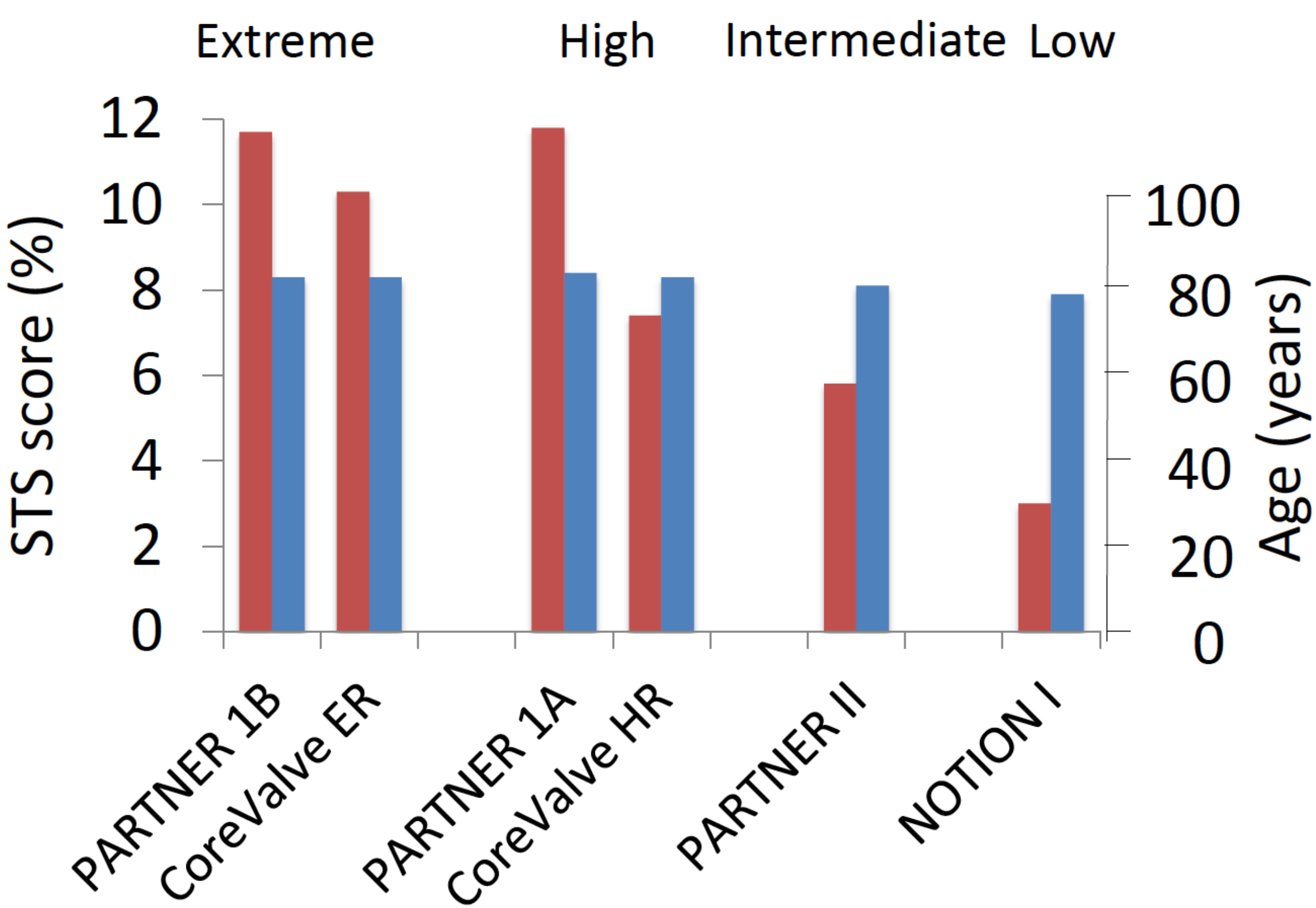
SURTAVI



Reardon M, et al. New Engl J Med 2017

SURTAVI Trial: All Death or Disabling Stroke





Extreme
High
Intermediate
Low
STS score (%)
Age (years)
12
10
8
6
4
2
0
100
80
60
40
20
0
PARTNER 1B
CoreValve ER
PARTNER 1A
CoreValve HR
PARTNER II
NOTION I

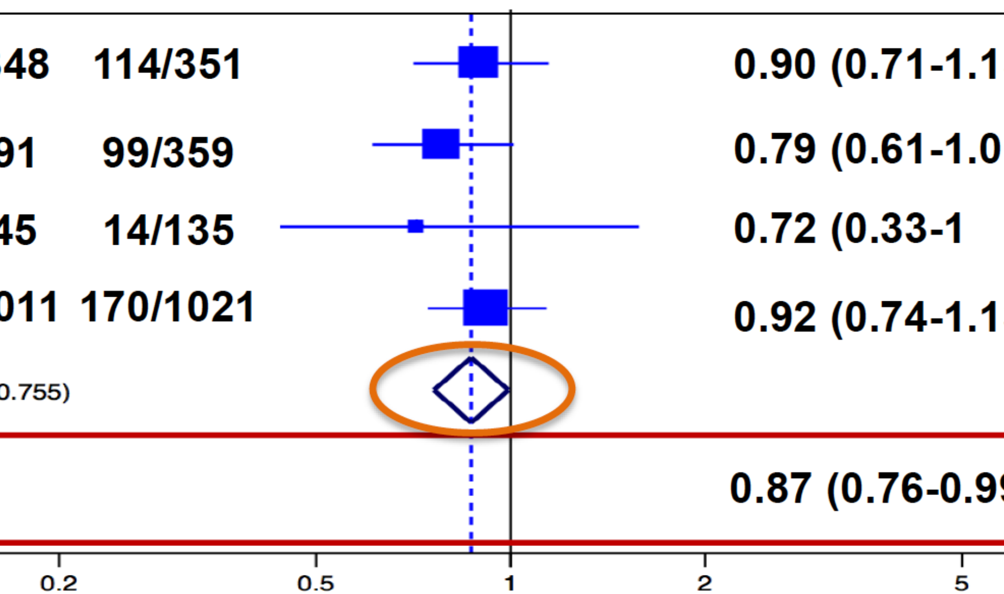
All-cause mortality benefits for TAVI

ALL-CAUSE MORTALITY AT 2 YEARS
4 RANDOMIZED TRIALS (N =3,806)

Trial	TAVR	SAVR	HR (95% CI)
PARTNER 1A	116/348	114/351	0.90 (0.71-1.15)
US CoreValve	85/391	99/359	0.79 (0.61-1.01)
NOTION	11/145	14/135	0.72 (0.33-1
PARTNER 2A	166/1011	170/1021	0.92 (0.74-1.13)

Overall (Heterogeneity $\tau^2 < 0.001$, $p = 0.755$)

Overall	**0.87 (0.76-0.99), P=0.038**



Favours TAVI   Favours SAVR

TAVI Superior

Siontis et al. *EHJ* 2016

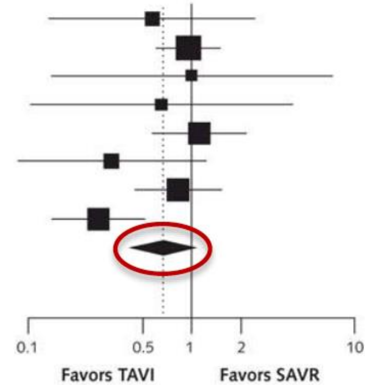
Outcome in low/intermediate risk patients

Early

Study (Reference)	TAVI Events, *n*	TAVI Total, *n*	SAVR Events, *n*	SAVR Total, *n*	OR (95% CI)	Weight (Random), %*
NOTION (9, 10)	3	139	5	135	0.57 (0.13–2.45)	6.8
PARTNER 2A (11)	39	1011	41	1021	0.96 (0.61–1.50)	22.5
Latib et al (12)	2	111	2	111	1.00 (0.14–7.23)	4.1
Osnabrugge et al (13)	2	42	3	42	0.65 (0.10–4.10)	4.6
Piazza et al (14)	20	255	18	255	1.12 (0.58–2.17)	17.5
Schymik et al (15)	3	216	9	216	0.32 (0.09–1.21)	7.9
Tamburino et al (16)	20	650	24	650	0.83 (0.45–1.51)	18.8
Thourani et al (17)	12	1077	38	944	0.27 (0.14–0.52)	17.7
Random-effects model	101	3501	140	3374	0.67 (0.42–1.07)	100

Heterogeneity: I^2 = 49.3%; tau-squared = 0.1642; P = 0.0545

Test for overall effect: P = 0.0836

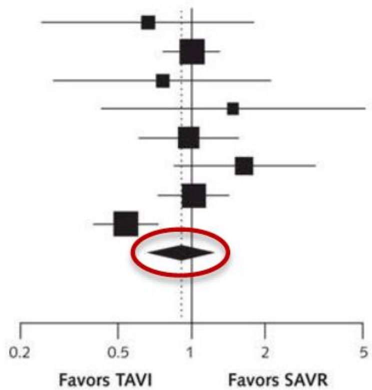


Mid-term

Study (Reference)	TAVI Events, *n*	TAVI Total, *n*	SAVR Events, *n*	SAVR Total, *n*	OR (95% CI)	Weight (Random), %*
NOTION (9, 10)	7	139	10	135	0.66 (0.24–1.80)	5.8
PARTNER 2A (11)	123	1011	124	1021	1.00 (0.77–1.31)	20.8
Latib et al (12)	7	111	9	111	0.76 (0.27–2.13)	5.5
Osnabrugge et al (13)	7	42	5	42	1.48 (0.43–5.10)	4.1
Piazza et al (14)	42	255	43	255	0.97 (0.61–1.55)	14.8
Schymik et al (15)	25	216	16	216	1.64 (0.85–3.16)	10.3
Tamburino et al (16)	83	601	82	603	1.02 (0.73–1.41)	18.9
Thourani et al (17)	79	1077	121	944	0.54 (0.40–0.73)	19.8
Random-effects model	373	3452	410	3327	0.91 (0.67–1.23)	100

Heterogeneity: I^2 = 58.2%; tau-squared = 0.0741; P = 0.0192

Test for overall effect: P = 0.4768

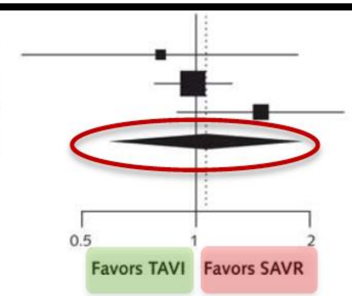


Late

Study (Reference)	TAVI Events, *n*	TAVI Total, *n*	SAVR Events, *n*	SAVR Total, *n*	OR (95% CI)	Weight (Random), %*
NOTION (9, 10)	11	139	13	135	0.81 (0.35–1.87)	9.5
PARTNER 2A (11)	166	1011	170	1021	0.98 (0.78–1.24)	67.1
Schymik et al (15)	43	216	31	216	1.48 (0.89–2.46)	23.4
Random-effects model	220	1366	214	1372	1.06 (0.59–1.91)	100

Heterogeneity: I^2 = 18.7%; tau-squared = 0.0138; P = 0.2921

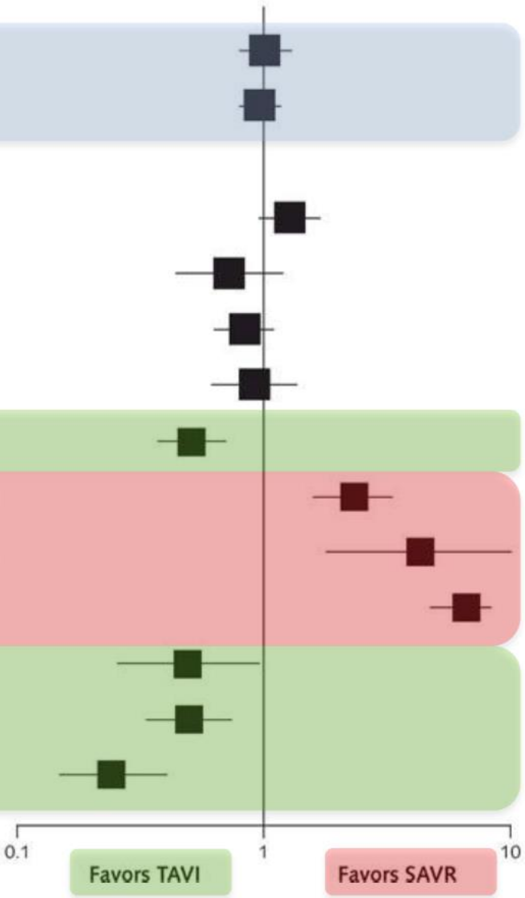
Test for overall effect: P = 0.7011



Ann Intern Med. 2016;165(5):334-344

TAVI vs SAVR

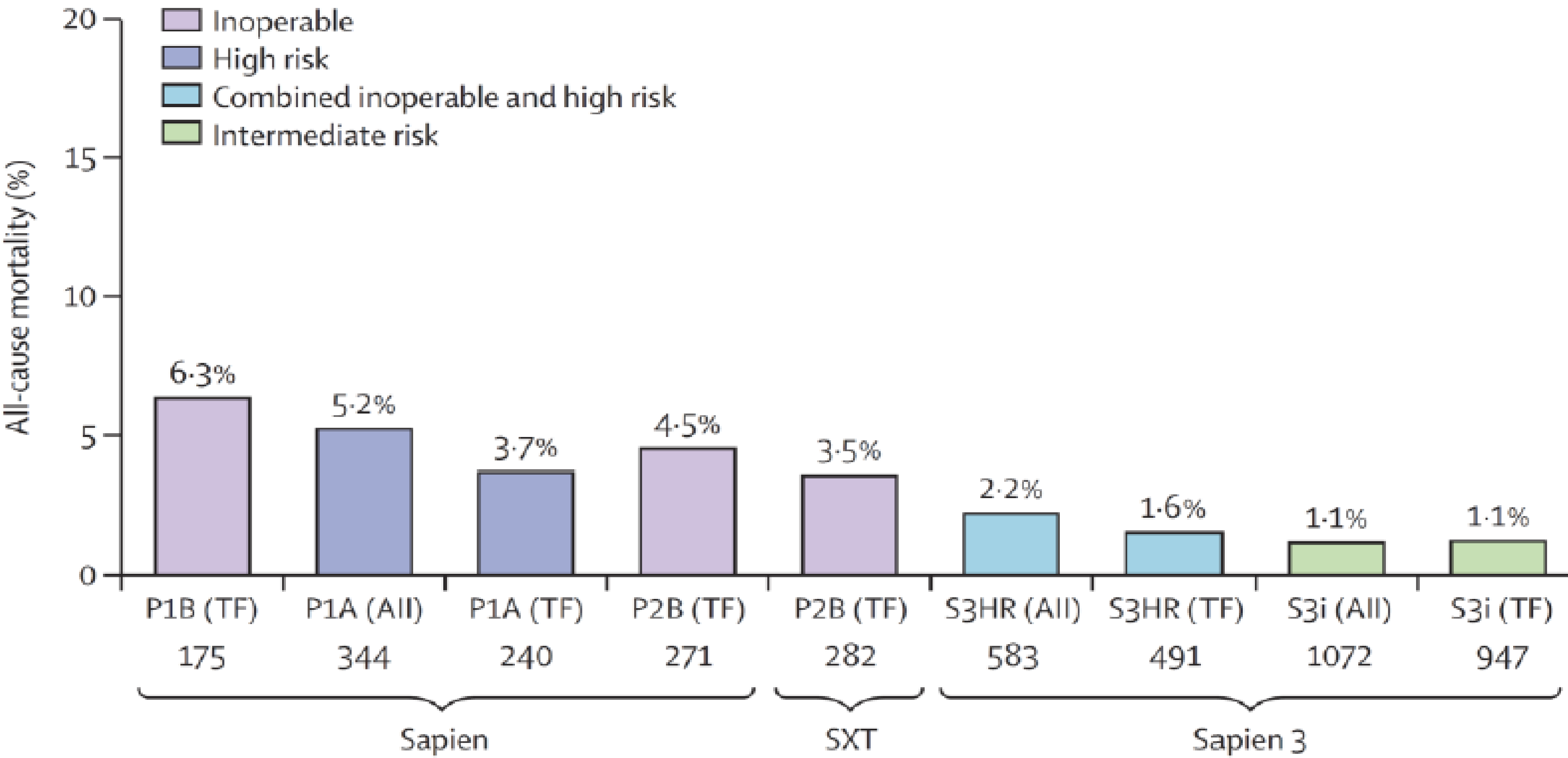
	Studies, *n*	Patients, *n*	OR (95% CI)	*P*	I^2, %	P_{int}
Primary outcomes						
Early all-cause mortality	35	16 386	1.01 (0.81–1.26)	0.90	37	0.14
Midterm all-cause mortality	23	11 222	0.96 (0.81–1.14)	0.64	40	0.48
Secondary outcomes						
Long-term all-cause mortality	10	5505	1.28 (0.97–1.69)	0.08	62	0.01
Early CV mortality	10	6656	0.73 (0.45–1.19)	0.18	33	0.41
Early stroke	30	14 236	0.84 (0.64–1.09)	0.17	18	0.24
Midterm stroke	9	7433	0.92 (0.62–1.35)	0.63	53	0.46
Early MI	19	11 835	0.51 (0.38–0.69)	0.001	0	0.33
Early PM implantation	25	13 086	2.32 (1.62–3.31)	0.001	67	0.76
Early vascular complication	15	11 167	4.32 (1.82–10.3)	0.001	81	0.12
Early paravalvular leak	15	7631	6.66 (5.26–8.45)	0.001	0	0.61
Early major bleeding	14	9808	0.49 (0.26–0.95)	0.04	96	0.45
Early AKI	15	9809	0.50 (0.34–0.73)	0.002	65	0.35
Early NOAF	9	6087	0.24 (0.15–0.40)	0.001	77	0.35



Ann Intern Med. 2016;165(5):334-344

Rationale for TAVI in Low Risk Patients

All-cause Mortality at 30 Days



Bonow et al. Lancet 2016

TAVI in Low Risk Patients: Ongoing Trials

PARTNER 3 *NCT02675114*	**CoreValve** *NCT02701283*	**NOTION-2** *NCT02825134*
Low surgical risk as assessed by Heart Team		
STS < 4%	*STS < 3%*	*STS < 4%*
Sample Size		
N=1,228	*N=1,200*	*N=992*
1:1 Randomization TAVI Vs. SAVR		
SAPIEN 3	*Evolut R*	*Any CE-approved device*
Primary Endpoint		
All-cause mortality, Any strokes, or re-hospitalization at 1 year	*All-cause mortality, any stroke, life-threatening bleeding, major vascular complications, or AKI at 30-day*	*All-cause mortality, myocardial infarction, or any stroke at 1-year*

To be continued