TAVR Shifting to lower risk: Ready or too fast?

Corrado Tamburino, MD, PhD

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TAVI in low-risk patients

Why not?

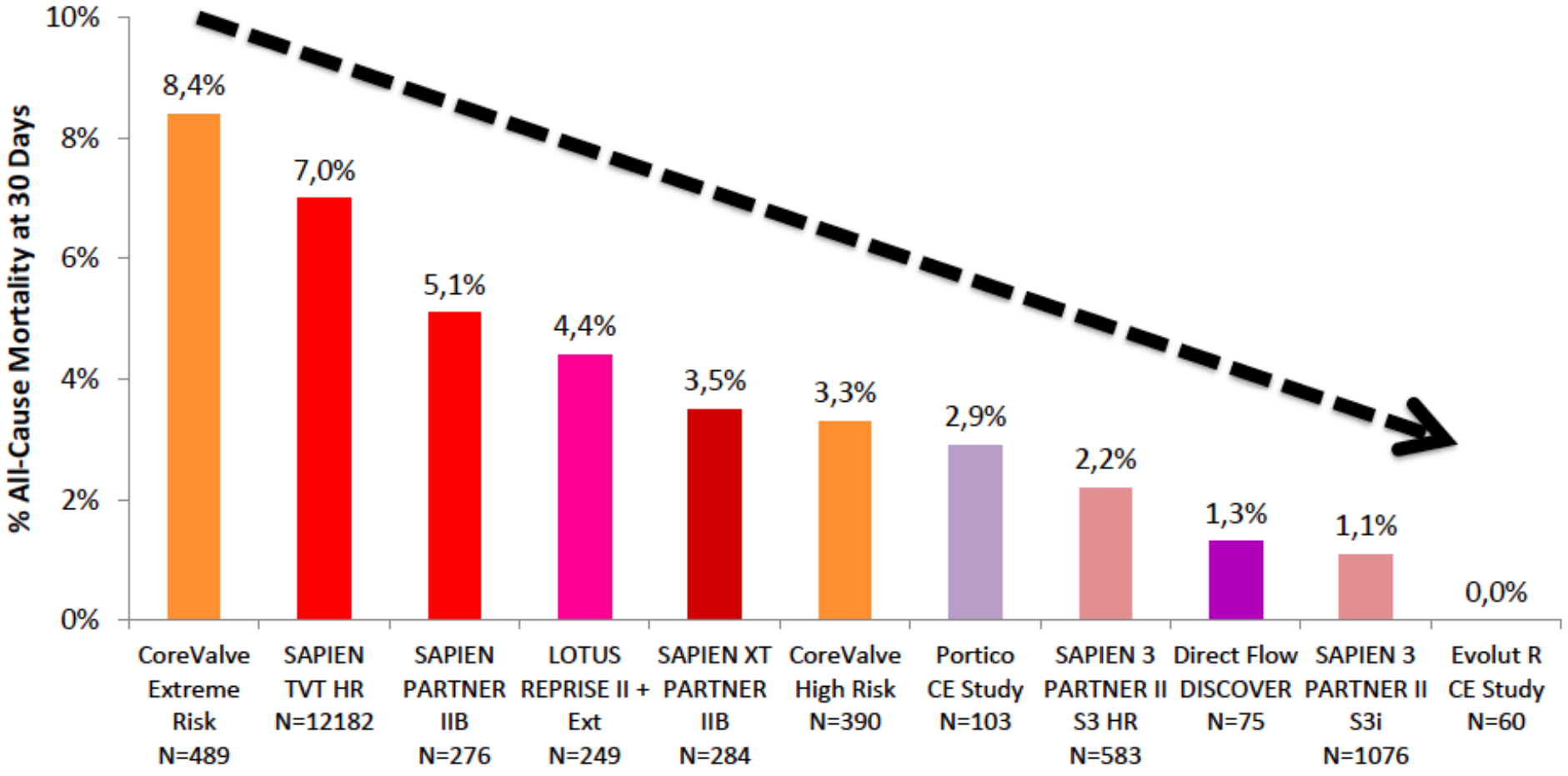
Complications

Evidence

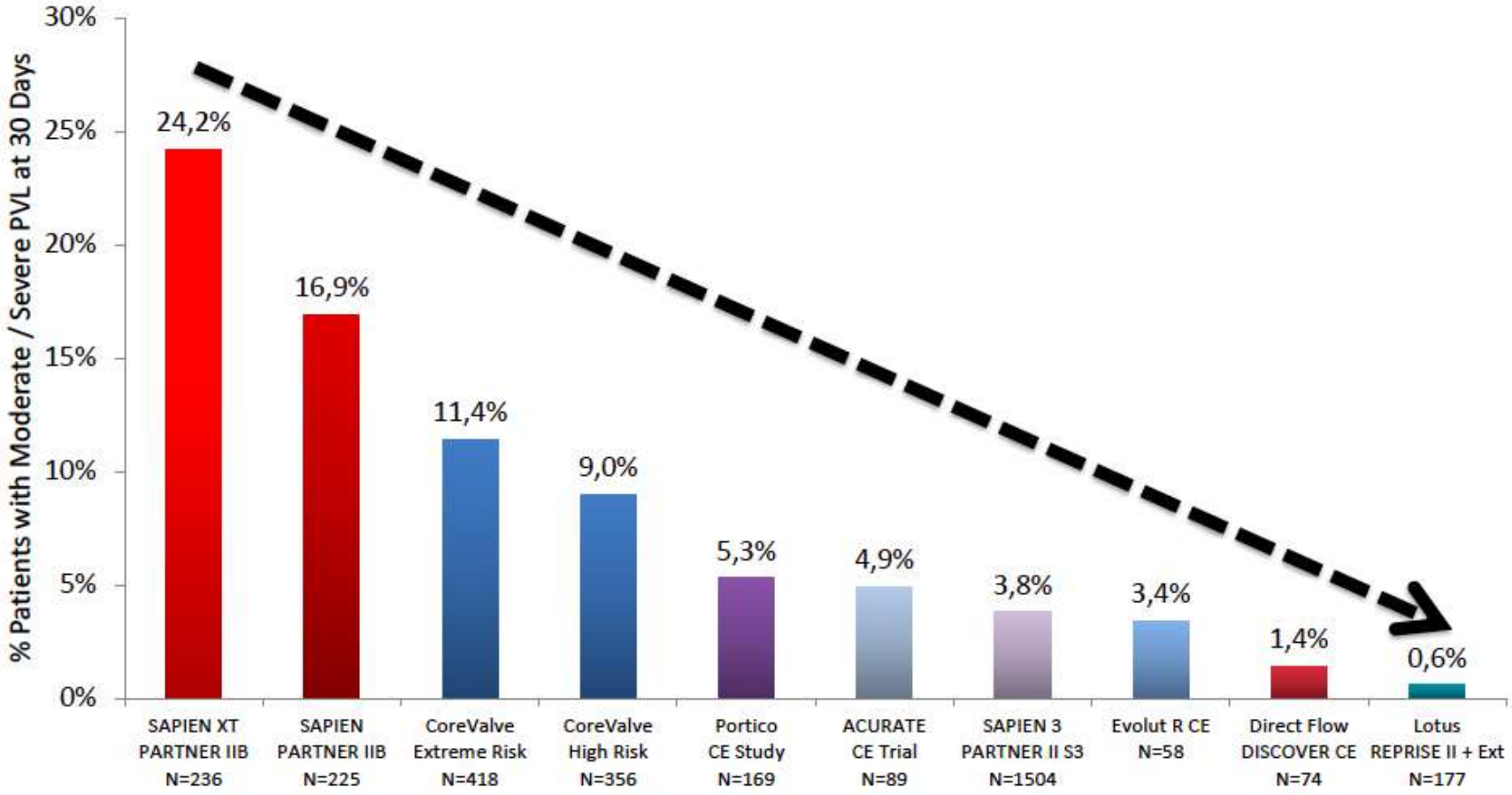
Durability

Costs

TAVI: 30-day All-cause Mortality

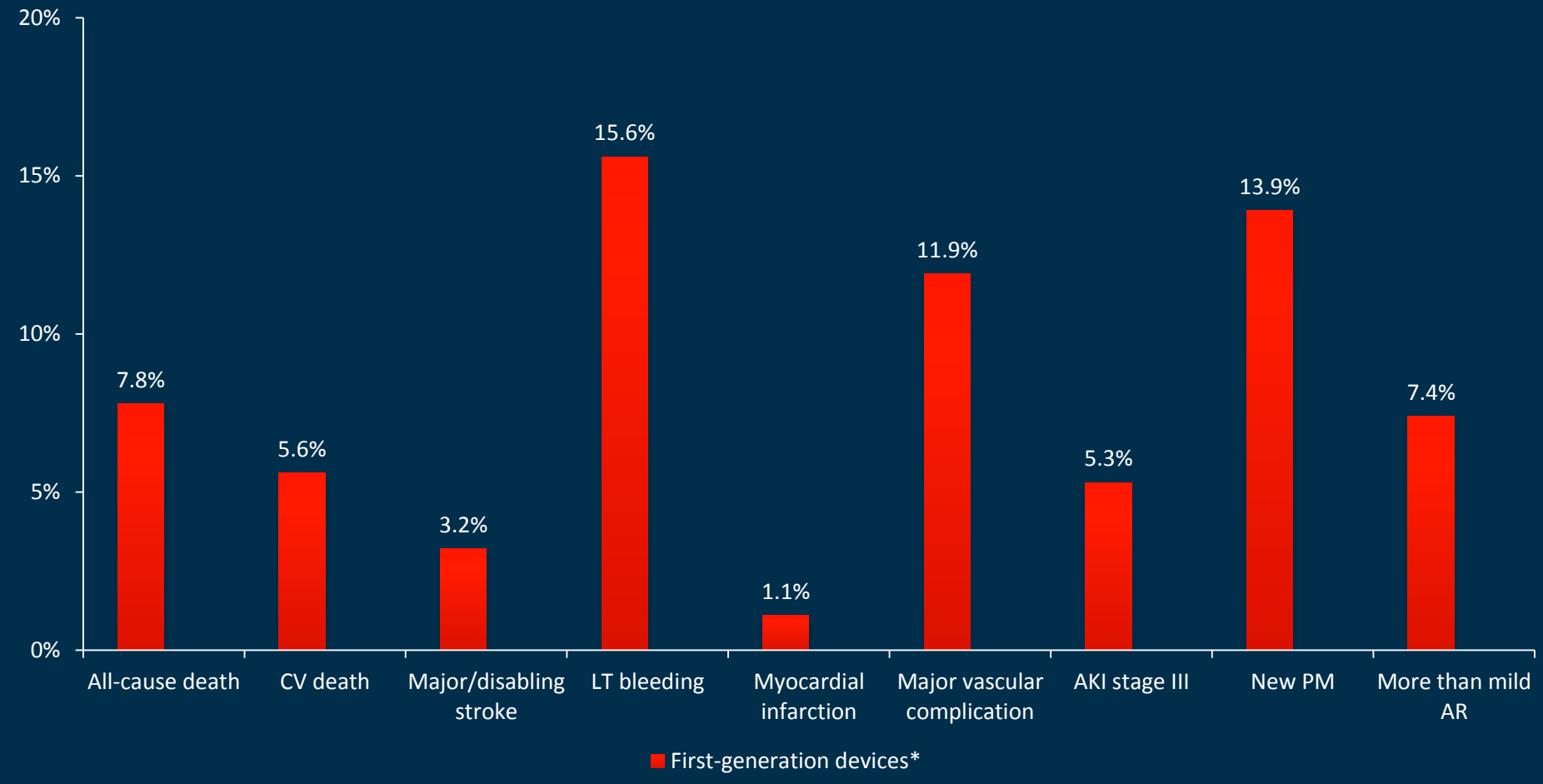


Paravalvular Leak



Transcatheter Aortic Valve Implantation

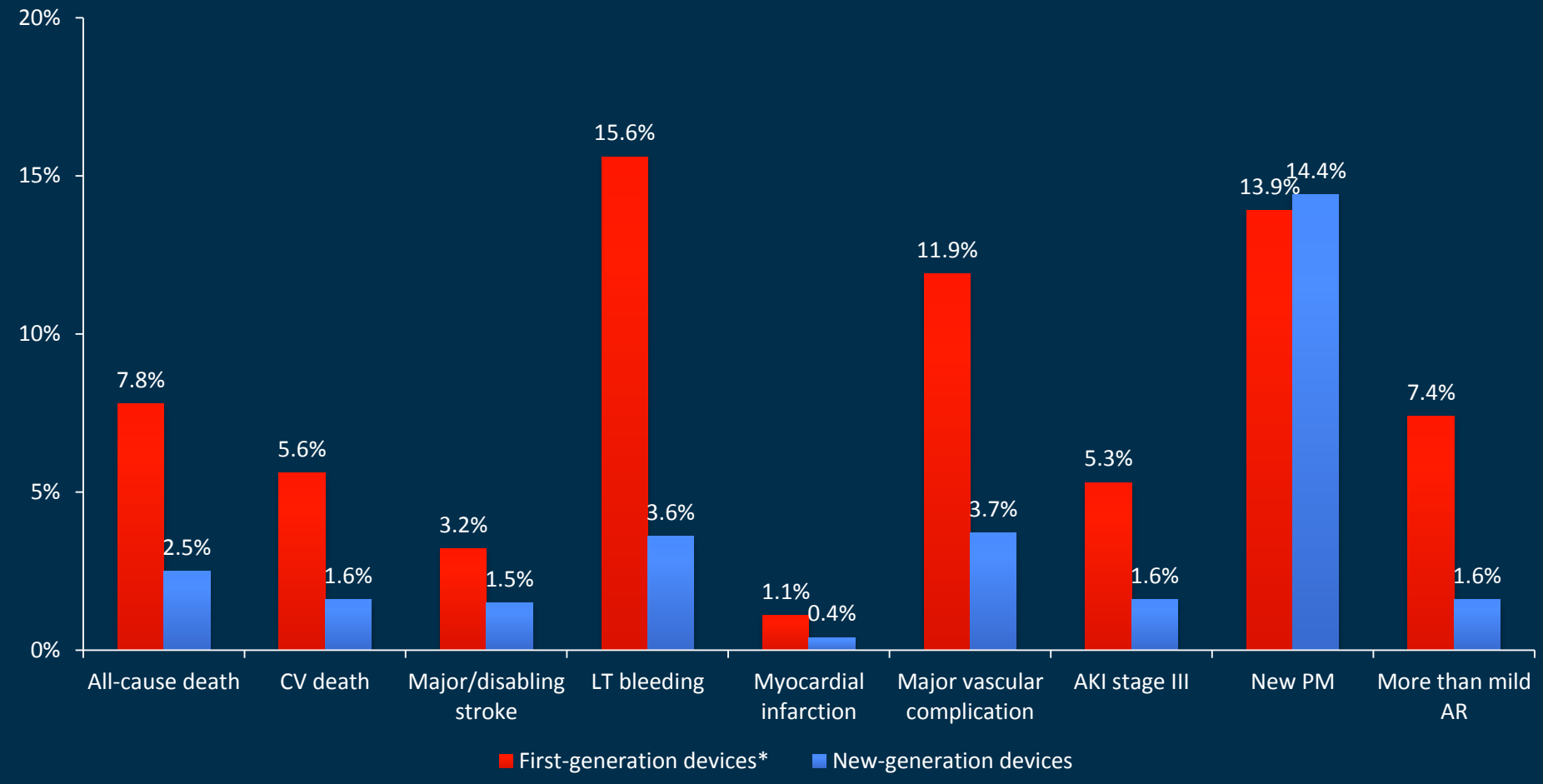
First- vs. Second-generation devices



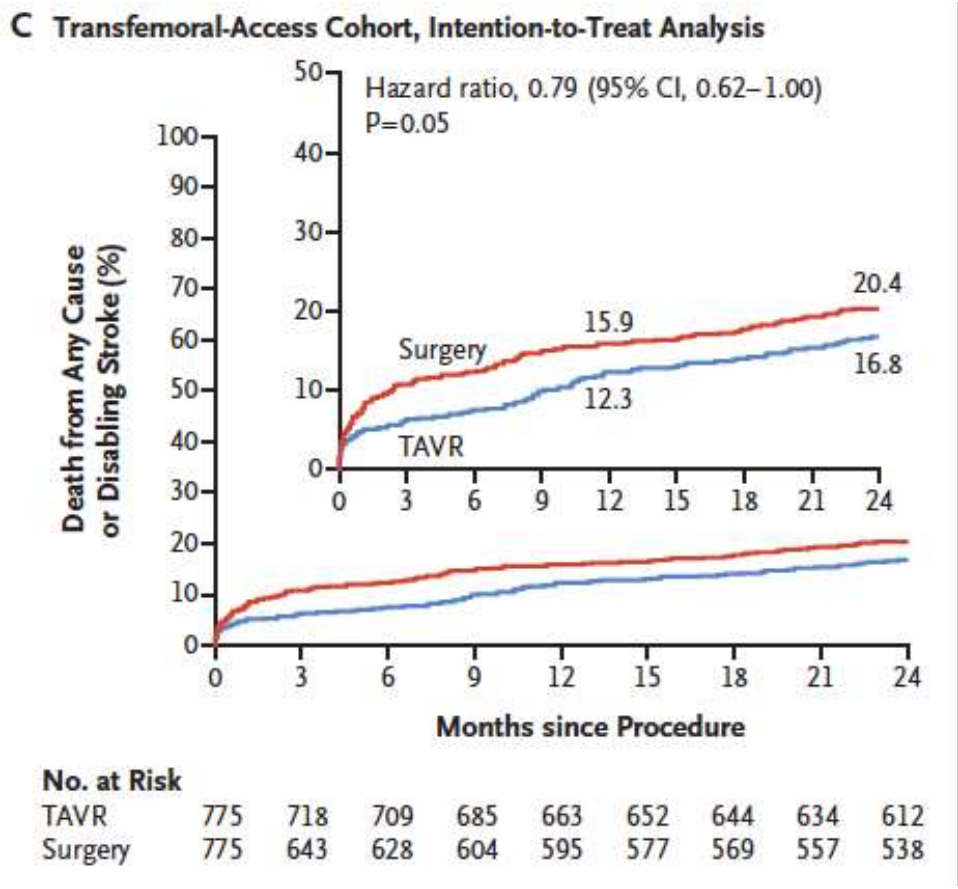
*Genereux et al. JACC 2013

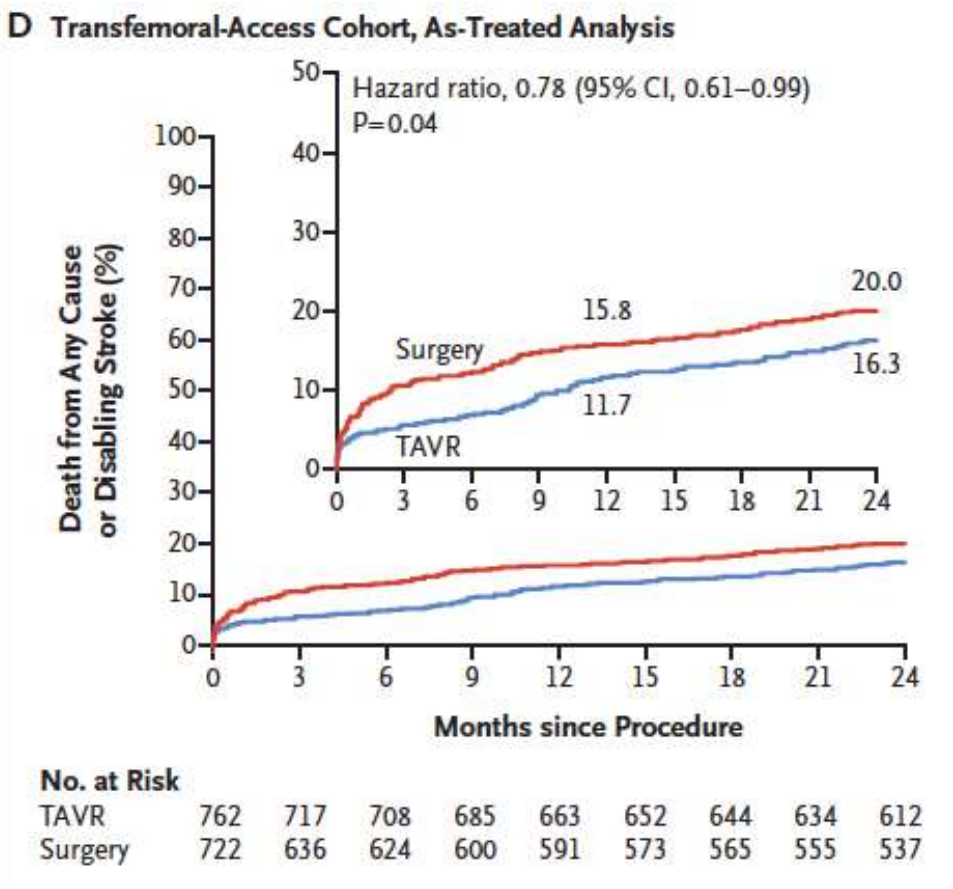
Transcatheter Aortic Valve Implantation

First- vs. Second-generation devices



PARTNER II Trial
Transfemoral procedures – Primary Outcome

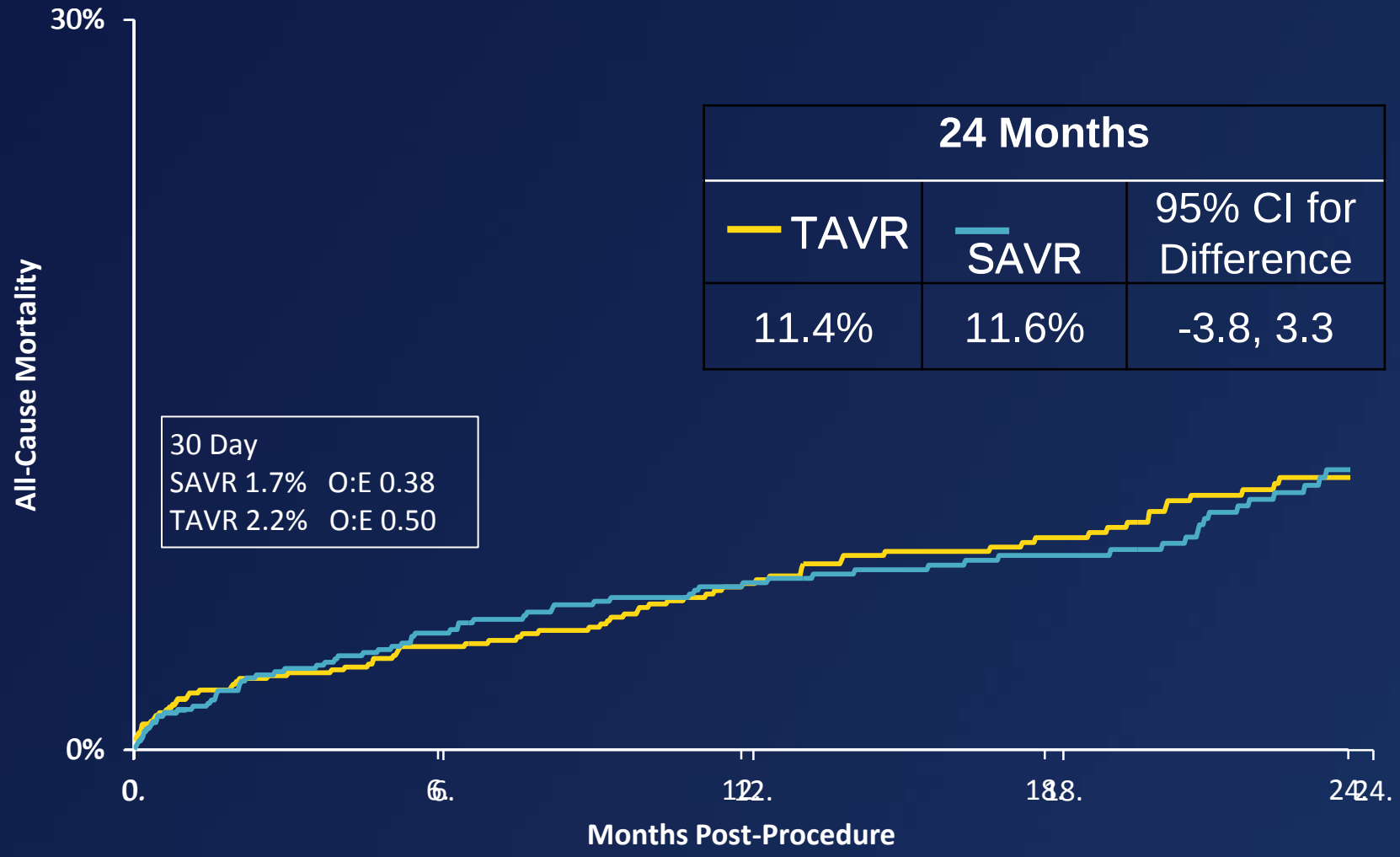




Leon MB et al, NEJM 2016

End Point	At 30 Days			At 2 Years		
	TAVR (N=1011)	Surgery (N=1021)	P Value	TAVR (N=1011)	Surgery (N=1021)	P Value
	no. of patients (%)			*no. of patients (%)*		
Death from any cause or disabling stroke	62 (6.1)	80 (8.0)	0.11	192 (19.3)	202 (21.1)	0.33
Death						
From any cause	39 (3.9)	41 (4.1)	0.78	166 (16.7)	170 (18.0)	0.45
From cardiac causes	33 (3.3)	32 (3.2)	0.92	97 (10.1)	104 (11.3)	0.38
Not from cardiac causes	6 (0.6)	9 (0.9)	0.41	69 (7.4)	65 (7.4)	0.98
Neurologic event						
Any event	64 (6.4)	65 (6.5)	0.94	121 (12.7)	103 (11.0)	0.25
Transient ischemic attack	9 (0.9)	4 (0.4)	0.17	34 (3.7)	20 (2.3)	0.09
Any stroke	55 (5.5)	61 (6.1)	0.57	91 (9.5)	85 (8.9)	0.67
Disabling stroke	32 (3.2)	43 (4.3)	0.20	59 (6.2)	61 (6.4)	0.83
Nondisabling stroke	23 (2.3)	18 (1.8)	0.43	33 (3.4)	27 (2.9)	0.51
Rehospitalization	64 (6.5)	62 (6.5)	0.99	183 (19.6)	156 (17.3)	0.22
Death from any cause or rehospitalization	99 (9.8)	101 (10.2)	0.78	303 (30.5)	281 (29.6)	0.67
Death from any cause, any stroke, or rehospitalization	140 (13.9)	153 (15.3)	0.37	344 (34.6)	326 (33.9)	0.75
Myocardial infarction	12 (1.2)	19 (1.9)	0.22	33 (3.6)	37 (4.1)	0.56
Major vascular complication	80 (7.9)	51 (5.0)	0.008	86 (8.6)	55 (5.5)	0.006
Life-threatening or disabling bleeding	105 (10.4)	442 (43.4)	<0.001	169 (17.3)	471 (47.0)	<0.001
Acute kidney injury	13 (1.3)	31 (3.1)	0.006	36 (3.8)	57 (6.2)	0.02
New atrial fibrillation	91 (9.1)	265 (26.4)	<0.001	110 (11.3)	273 (27.3)	<0.001
New permanent pacemaker	85 (8.5)	68 (6.9)	0.17	114 (11.8)	96 (10.3)	0.29
Endocarditis	0	0	—	11 (1.2)	6 (0.7)	0.22
Aortic-valve reintervention	4 (0.4)	0	0.05	13 (1.4)	5 (0.6)	0.09
Coronary obstruction	4 (0.4)	6 (0.6)	0.53	4 (0.4)	6 (0.6)	0.53

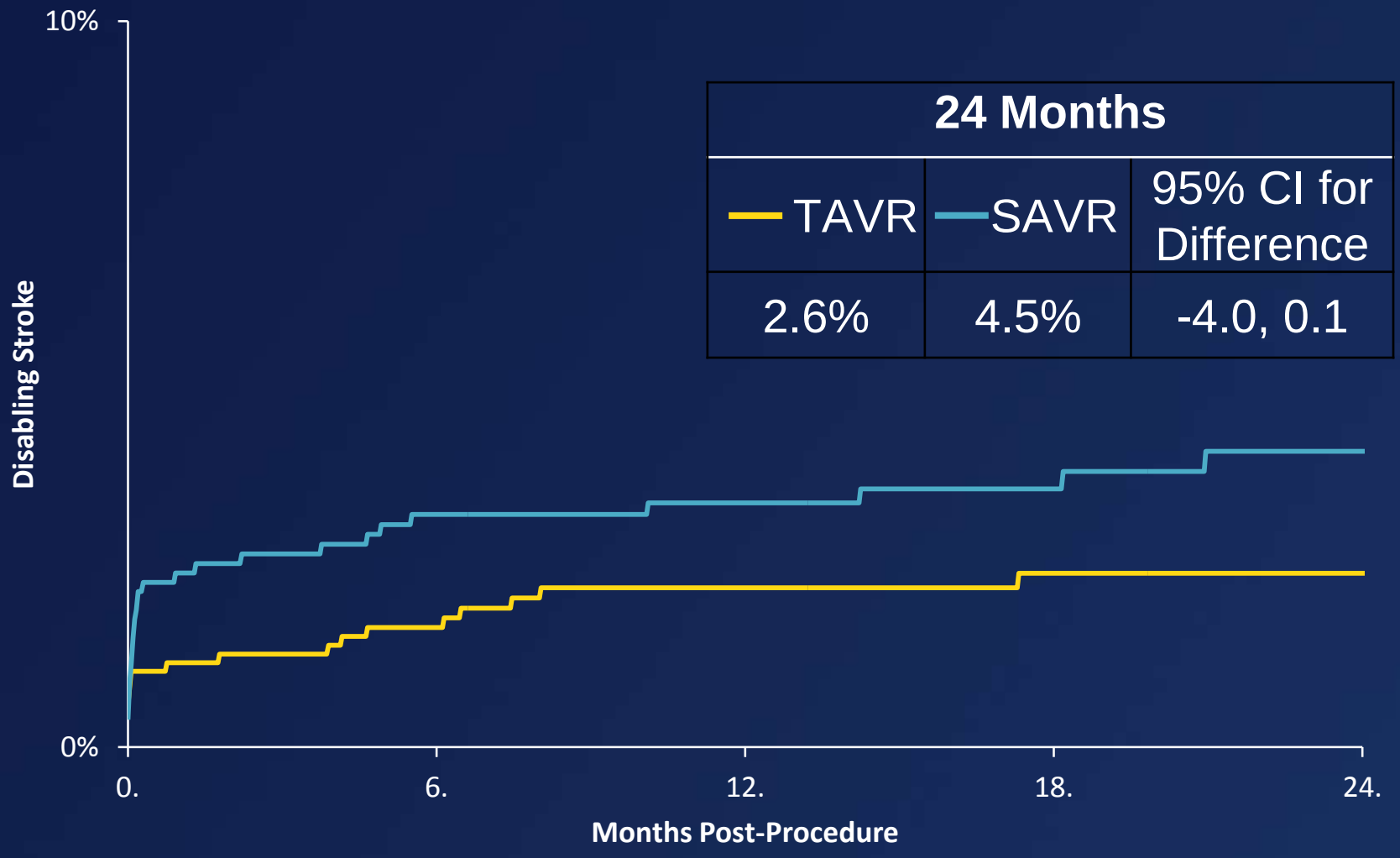
All-Cause Mortality



24 Months		
TAVR	SAVR	95% CI for Difference
11.4%	11.6%	-3.8, 3.3

No. at Risk					
SAVR	796	690	569	414	249
TAVR	864	762	621	465	280

Disabling Stroke



24 Months		
TAVR	SAVR	95% CI for Difference
2.6%	4.5%	-4.0, 0.1

No. at Risk

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

SURTAVI Trial
All procedures – Primary Outcome 30 days

Table 2. Procedure-Related Complications at 30 Days (Modified Intention-to-Treat Population).*

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

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

Vinod H Thourani, 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

	30 days						1 year					
	SAPIEN 3 TAVR			Surgical valve replacement			SAPIEN 3 TAVR			Surgical valve replacement		
	Events (n)	Cumulative KM estimates	Numbers at risk	Events (n)	Cumulative KM estimates	Numbers at risk	Events (n)	Cumulative KM estimates	Numbers at risk	Events (n)	Cumulative KM estimates	Numbers at risk
Death												
From any cause	12	1·1%	1063	38	4·0%	902	79	7·4%	963	121	13·0%	795
Cardiac death	10	0·9%	1063	29	3·1%	902	47	4·5%	963	74	8·1%	795
Non-cardiac death	2	0·2%	1063	9	1·0%	902	32	3·1%	963	47	5·3%	795
Neurological events												
Transient ischaemic attack	4	0·4%	1059	4	0·4%	898	18	1·8%	945	15	1·7%	782
Any stroke	29	2·7%	1035	57	6·1%	852	49	4·6%	930	75	8·2%	743
Disabling stroke	11	1·0%	1053	41	4·4%	868	24	2·3%	953	54	5·9%	764
Non-disabling stroke	18	1·7%	1045	16	1·7%	886	25	2·4%	940	22	2·4%	773
Death from any cause or disabling stroke	22	2·0%	1053	75	8·0%	868	90	8·4%	953	155	16·6%	764
Rehospitalisation	49	4·6%	1017	62	6·8%	845	119	11·4%	865	135	15·1%	697
Myocardial infarction	3	0·3%	1060	18	1·9%	889	3	0·3%	961	28	3·1%	780
Life-threatening or disabling bleeding	50	4·6%	1018	440	46·7%	493	..	..	..	..	..	..
Major vascular complication	66	6·1%	1000	51	5·4%	860	..	..	..	..	..	..
Acute kidney injury (stage 3)	5	0·5%	1058	31	3·3%	879	..	..	..	..	..	..
New atrial fibrillation	54	5·0%	1012	265	28·3%	649	63	5·9%*	912	272	29·2%	564
New permanent pacemaker	109	10·2%	955	68	7·3%	836	132	12·4%*	842	85	9·4%	721

p value<0.01

Thourani et al, Lancet 2016

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1-Year Outcomes After Transfemoral Transcatheter or Surgical Aortic Valve Replacement

Results From the Italian OBSERVANT Study

Corrado Tamburino, MD,*† Marco Barbanti, MD,*† Paola D'Errigo, RS,‡ Marco Ranucci, MD,§ Francesco Onorati, MD,‖ Remo Daniel Covello, MD,¶ Francesco Santini, MD,# Stefano Rosato, RS,§ Gennaro Santoro, MD,** Danilo Fusco, RS,†† Claudio Grossi, MD,‡‡ Fulvia Seccareccia, RS,‡ for the OBSERVANT Research Group

Ferrarotto Hospital
University of Catania

OBSERVANT

In-hospital Outcomes & 30-day mortality

	SAVR N=650 *LES II 5.1±6.2*	TAVI N=650 *LES II 4.9±5.1*	P value
Renal failure, n (%)	64 (10.9)	36 (6.1)	0.004
New PPM, n (%)	23 (3.6)	98 (15.5)	<0.001
AMI, n (%)	5 (0.8)	3 (0.5)	0.479
Stroke, n (%)	14 (2.2)	8 (1.3)	0.180
Infection			
Wound, n (%)	10 (1.6)		
Lung or other organs, n (%)	24 (3.9)	29 (4.7)	0.191
Sepsis, n (%)	11 (1.8)	4 (0.6)	
RBC Transfusions: number of units	3.6±3.6	2.3±2.2	0.002
ICU stay (days)	3.8±7.7	3.2±4.7	0.077
Total hospital stay (days)	12.6±1.34	8.8±8.5	<0.001
Death (30 days), n (%)	24 (3.8)	20 (3.2)	0.546

TAVI and Low-risk

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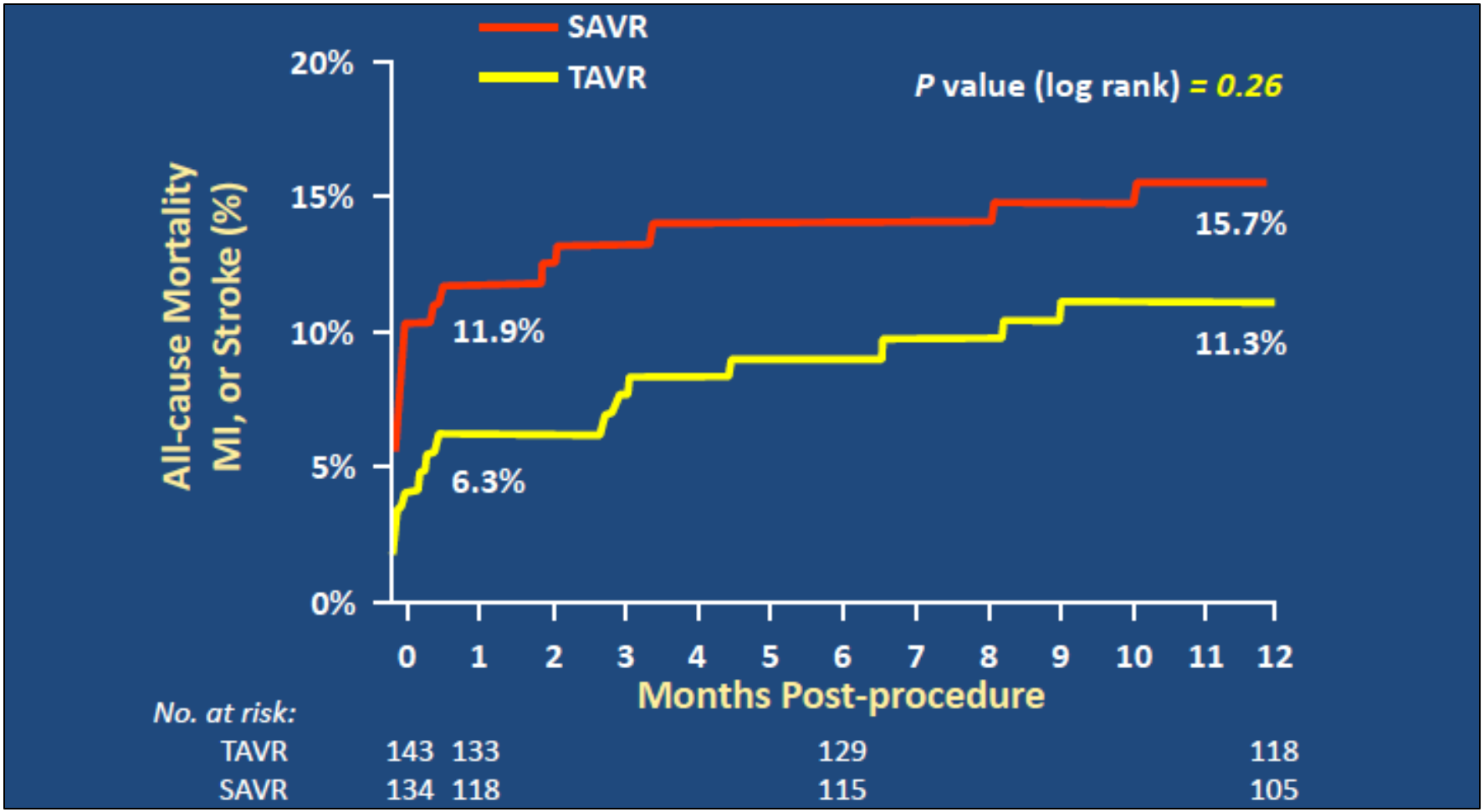
Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

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

TAVI and Low-risk



NOTION 2y

	Surgery (n = 135)	TAVR (n = 145)	*P* Value
All-Cause Mortality	9.8%	8.0%	.54
CV Mortality	9.1%	6.5%	.40
Stroke	5.4%	3.6%	.46
MI	6.0%	5.1%	.69
A-fib	60.2%	22.7%	< .001
Pacemaker	4.2%	41.3%	< .001

Valve performance was better after TAVR, with a higher effective orifice area and lower mean gradient at 2 years compared with surgery (*P* < .001 for both). Mild/severe aortic regurgitation was more common in the TAVR arm through 2 years (54.4% vs 16.1%; *P* < .001). Also, at 1 year, more surgery than TAVR patients were in NYHA class I, but this difference disappeared at 2 years (*P* = .44).

TAVI and Low-risk

Annals of Internal Medicine

REVIEW

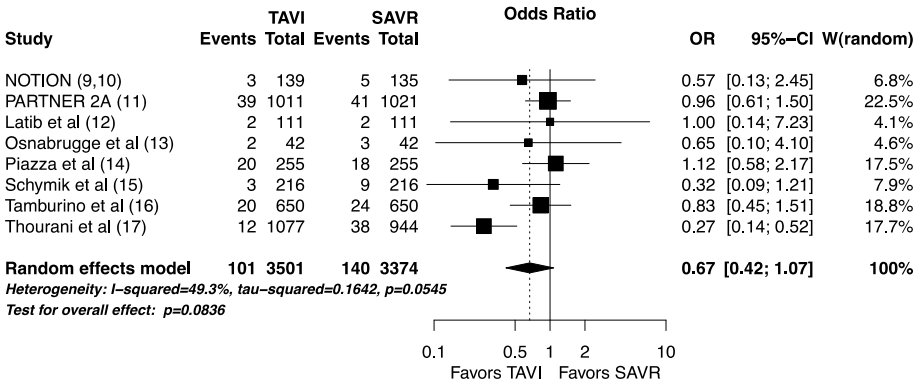
Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement

A Systematic Review and Meta-analysis

Giuseppe Gargiulo, MD; Anna Sannino, MD; Davide Capodanno, MD, PhD; Marco Barbanti, MD; Sergio Buccheri, MD; Cinzia Perrino, MD, PhD; Piera Capranzano, MD; Ciro Indolfi, MD, PhD; Bruno Trimarco, MD; Corrado Tamburino, MD, PhD; and Giovanni Esposito, MD, PhD

ALL-CAUSE MORTALITY IN LOW-TO-INTERMEDIATE RISK PATIENTS

Early all-cause mortality

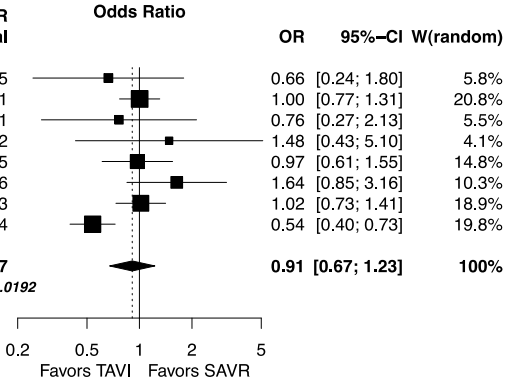


Study	TAVI Events	TAVI Total	SAVR Events	SAVR Total	OR	95%–CI	W(random)
NOTION (9,10)	3	139	5	135	0.57	[0.13; 2.45]	6.8%
PARTNER 2A (11)	39	1011	41	1021	0.96	[0.61; 1.50]	22.5%
Latib et al (12)	2	111	2	111	1.00	[0.14; 7.23]	4.1%
Osnabrugge et al (13)	2	42	3	42	0.65	[0.10; 4.10]	4.6%
Piazza et al (14)	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–squared=49.3%, tau–squared=0.1642, p=0.0545

Test for overall effect: p=0.0836

Mid-term all-cause mortality

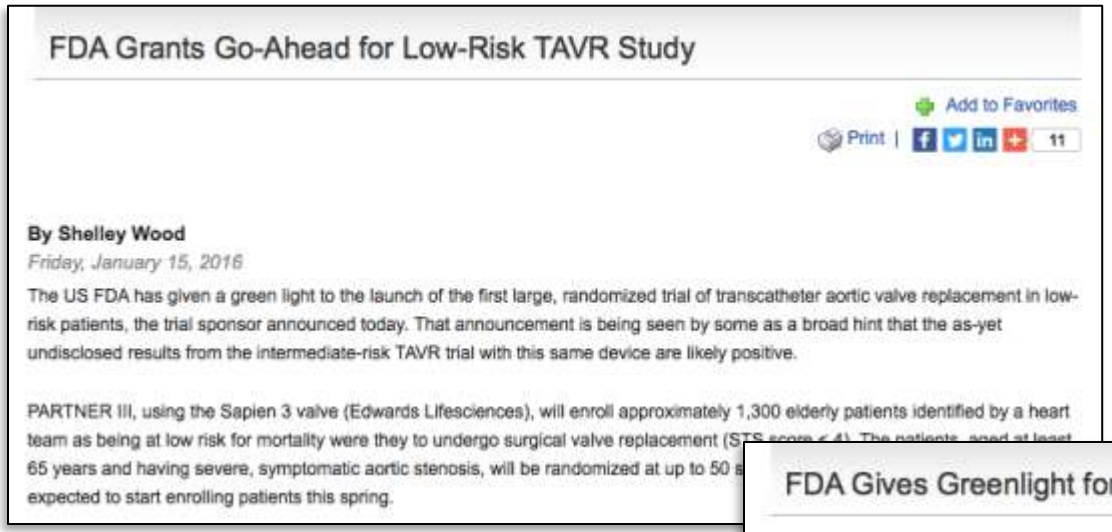


Study	TAVI Events	TAVI Total	SAVR Events	SAVR Total	OR	95%–CI	W(random)
NOTION (9,10)	7	139	10	135	0.66	[0.24; 1.80]	5.8%
PARTNER 2A (11)	123	1011	124	1021	1.00	[0.77; 1.31]	20.8%
Latib et al (12)	7	111	9	111	0.76	[0.27; 2.13]	5.5%
Osnabrugge et al (13)	7	42	5	42	1.48	[0.43; 5.10]	4.1%
Piazza et al (14)	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–squared=58.2%, tau–squared=0.0741, p=0.0192

Test for overall effect: p=0.4768

No strong evidences of TAVI in low risk patients are available!



FDA Grants Go-Ahead for Low-Risk TAVR Study

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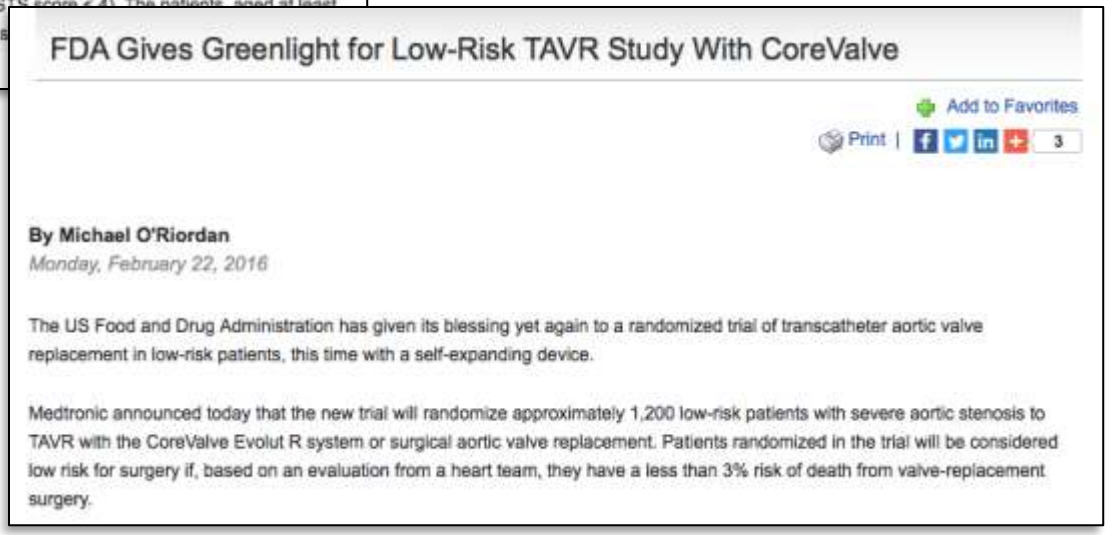
By Shelley Wood

Friday, January 15, 2016

The US FDA has given a green light to the launch of the first large, randomized trial of transcatheter aortic valve replacement in low-risk patients, the trial sponsor announced today. That announcement is being seen by some as a broad hint that the as-yet undisclosed results from the intermediate-risk TAVR trial with this same device are likely positive.

PARTNER III, using the Sapien 3 valve (Edwards Lifesciences), will enroll approximately 1,300 elderly patients identified by a heart team as being at low risk for mortality were they to undergo surgical valve replacement (STS score < 4). The patients, aged at least 65 years and having severe, symptomatic aortic stenosis, will be randomized at up to 50 s
expected to start enrolling patients this spring.



FDA Gives Greenlight for Low-Risk TAVR Study With CoreValve

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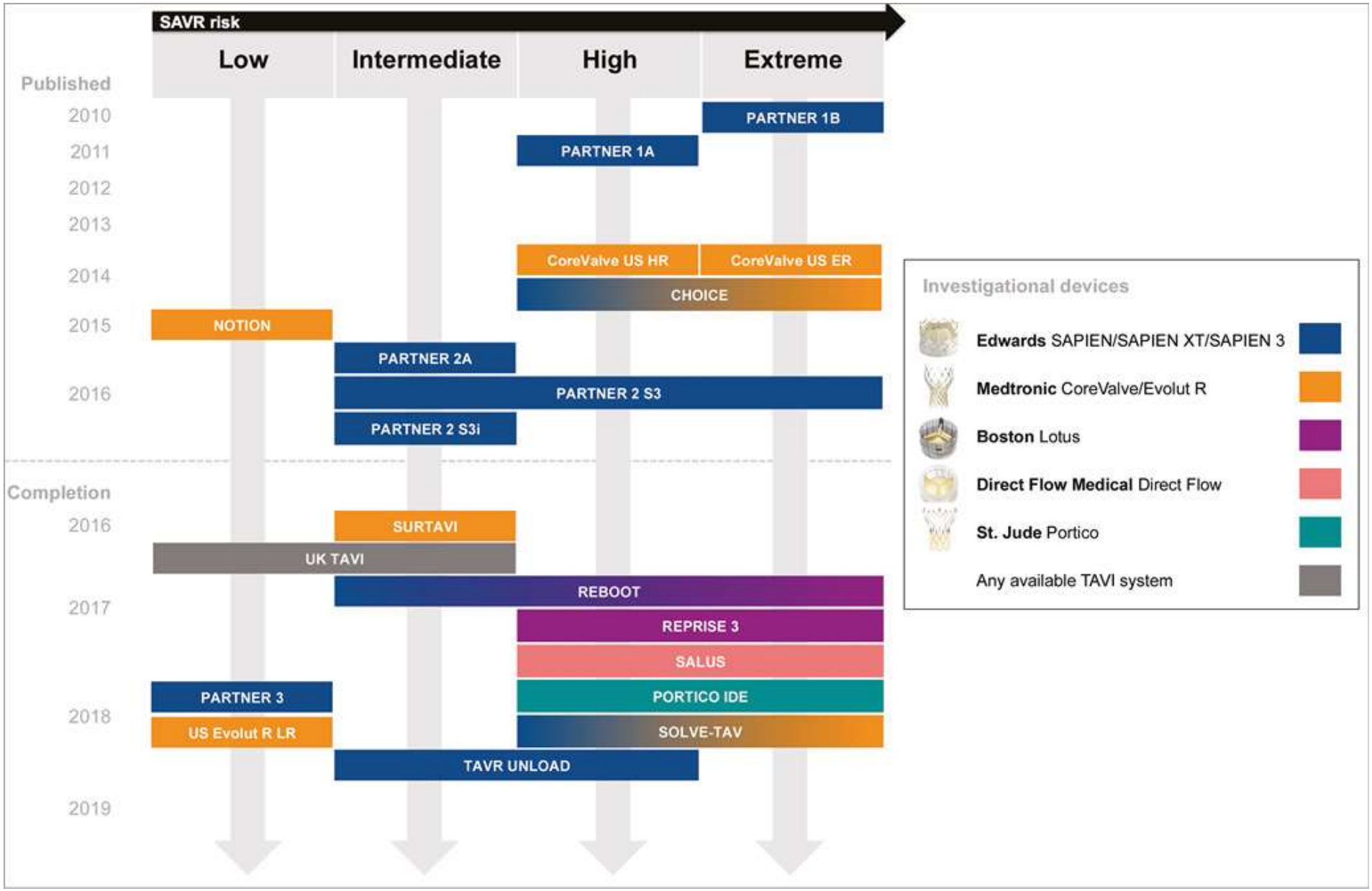
By Michael O'Riordan

Monday, February 22, 2016

The US Food and Drug Administration has given its blessing yet again to a randomized trial of transcatheter aortic valve replacement in low-risk patients, this time with a self-expanding device.

Medtronic announced today that the new trial will randomize approximately 1,200 low-risk patients with severe aortic stenosis to TAVR with the CoreValve Evolut R system or surgical aortic valve replacement. Patients randomized in the trial will be considered low risk for surgery if, based on an evaluation from a heart team, they have a less than 3% risk of death from valve-replacement surgery.

SOURCE: tctmd.com

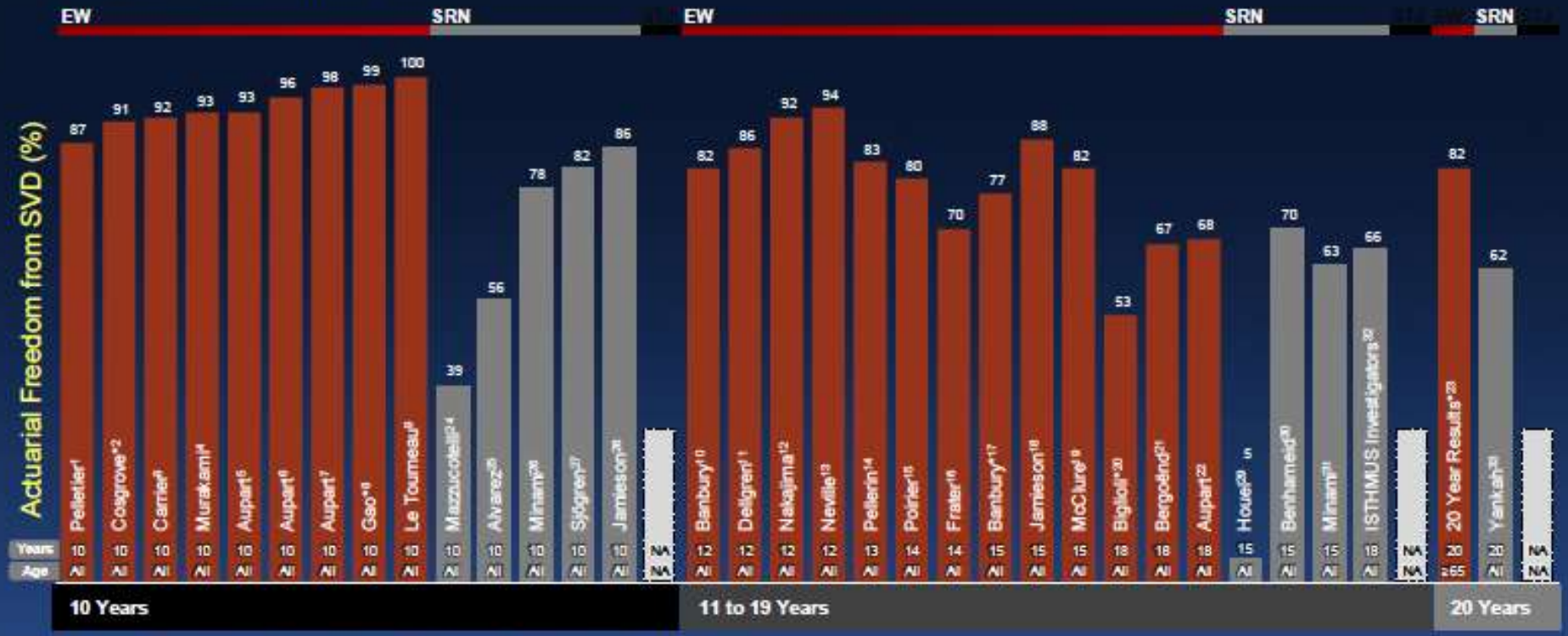


Capodanno D, Eurointervention 2016

Freedom from Structural Valve Deterioration of Pericardial Aortic Bioprostheses

Actuarial Freedom from Structural Valve Deterioration

Pericardial Aortic Bioprostheses



* Freedom from explant / prosthesis replacement / reoperation due to SVD

Methodology: Comprehensive literature searches were conducted utilizing a combination of key words. See references section for key words, filters, and a search results summary.
Note: Patients and results are a subset of each study. See references section for total cohort size, patient mean age, and at risk population size.

Original Investigation

Trends in Aortic Valve Replacement for Elderly Patients in the United States, 1999-2011

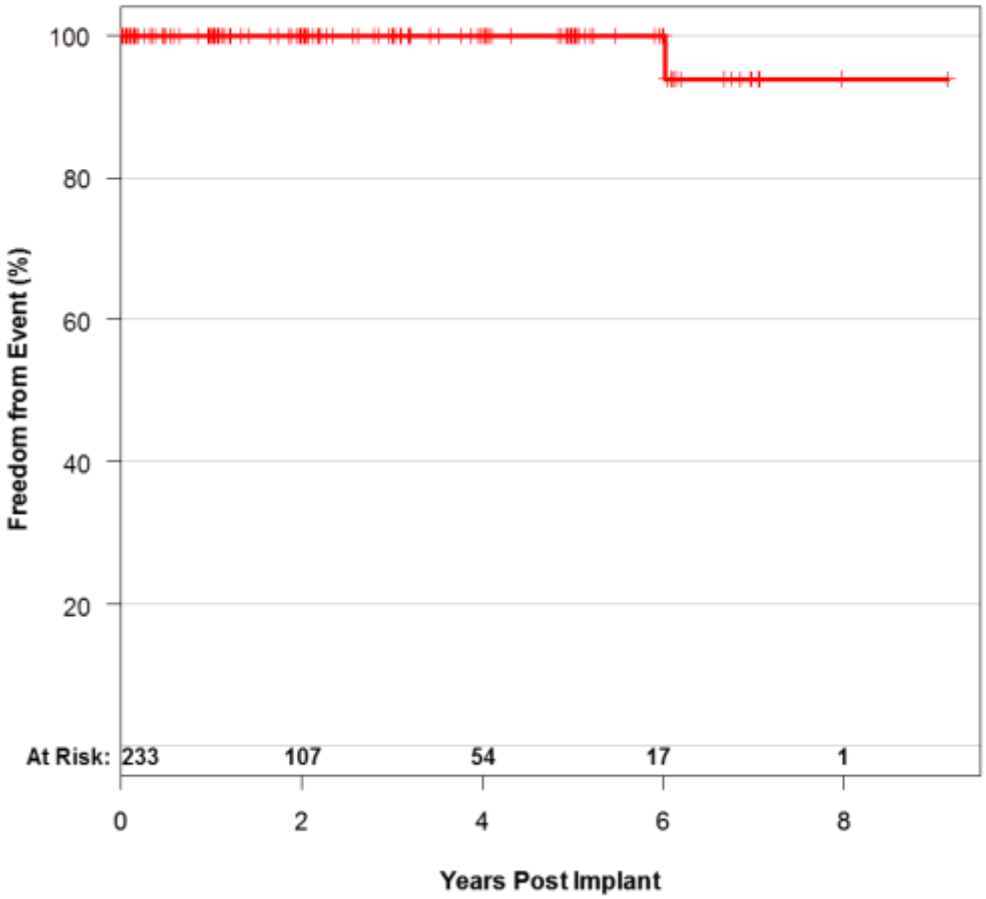
José Augusto Barreto-Filho, MD, PhD; Yun Wang, PhD; John A. Dodson, MD; Mayur M. Desai, PhD, MPH; Lissa Sugeng, MD, MPH; Arnar Geirsson, MD; Harlan M. Krumholz, MD, SM

Table 3. Outcomes of Aortic Valve Replacement Surgery, 1999-2011

	% (95% CI)						
	1999	2001	2003	2005	2007	2009	2011
Overall							
No. of patients	24 568	26 598	28 186	28 687	28 039	30 418	31 380
In-hospital mortality rates, %	7.1 (6.81-7.46)	6.7 (6.42-7.03)	6.5 (6.24-6.82)	5.5 (5.26-5.79)	5.1 (4.82-5.34)	4.9 (4.62-5.10)	3.8 (3.56-3.99)
30-d Mortality rates							
Overall	7.6 (7.27-7.93)	7.3 (6.97-7.60)	7.1 (6.85-7.45)	6.0 (5.69-6.24)	5.5 (5.25-5.79)	5.5 (5.21-5.72)	4.2 (3.95-4.39)
Age, y							
65-74	5.9 (5.43-6.35)	5.7 (5.29-6.19)	5.6 (5.15-6.02)	4.6 (4.17-4.96)	4.5 (4.16-4.97)	4.2 (3.86-4.61)	3.3 (2.94-3.59)
75-84	8.2 (7.72-8.70)	7.8 (7.37-8.28)	7.6 (7.15-8.02)	6.3 (5.96-6.75)	5.6 (5.26-6.02)	5.7 (5.34-6.10)	4.4 (4.07-4.73)
≥85	12.3 (11.0-13.8)	10.8 (9.60-12.1)	11.1 (9.99-12.4)	9.3 (8.27-10.4)	8.1 (7.18-9.10)	8.1 (7.23-8.94)	5.8 (5.12-6.49)

THV Durability
CHU Rouen

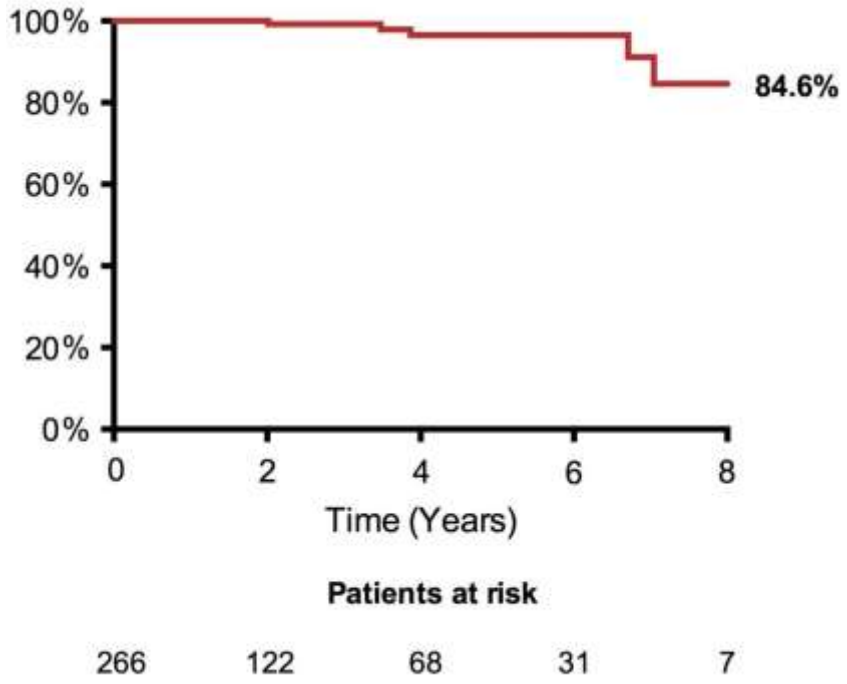
- 239 pts from 2002-2011 (> 5 years FU)
- Freedom from either reoperation, or if asymptomatic, echo mean valve gradient >40 mmHg or severe AR (effective ROA > 0.3cm2)
- *Among survivors, none with MG >40 and only 1 pt with severe AR resulting in ViV procedure*



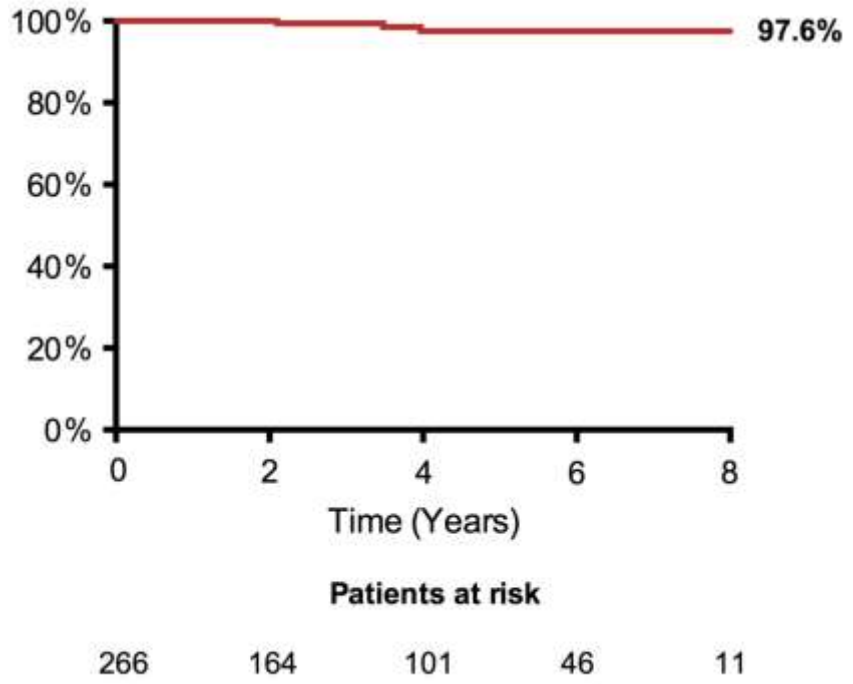
THV Durability
Vancouver

- 266 pts from before 2011 (> 5 years FU)

Freedom from severe failure

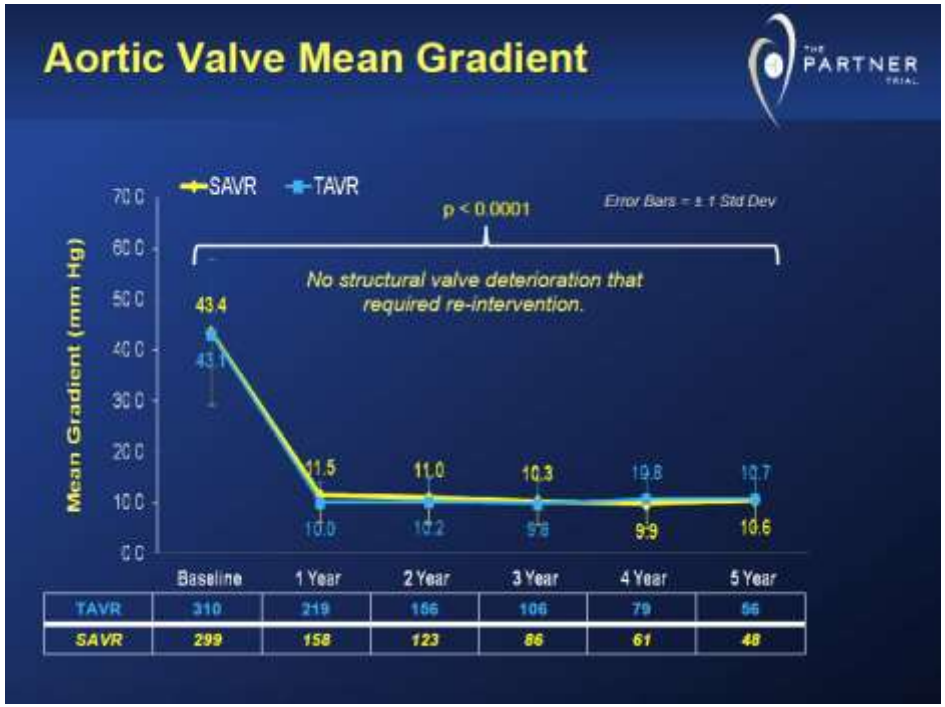


Freedom from reintervention



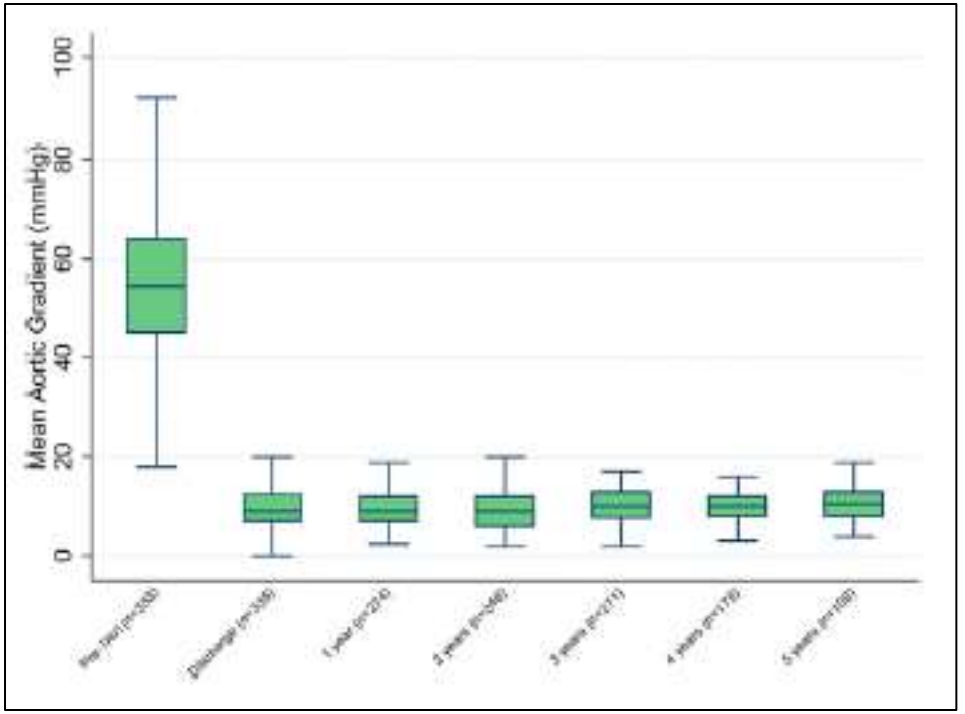
Transcatheter Aortic Valve Implantation
THV durability

PARTNER I



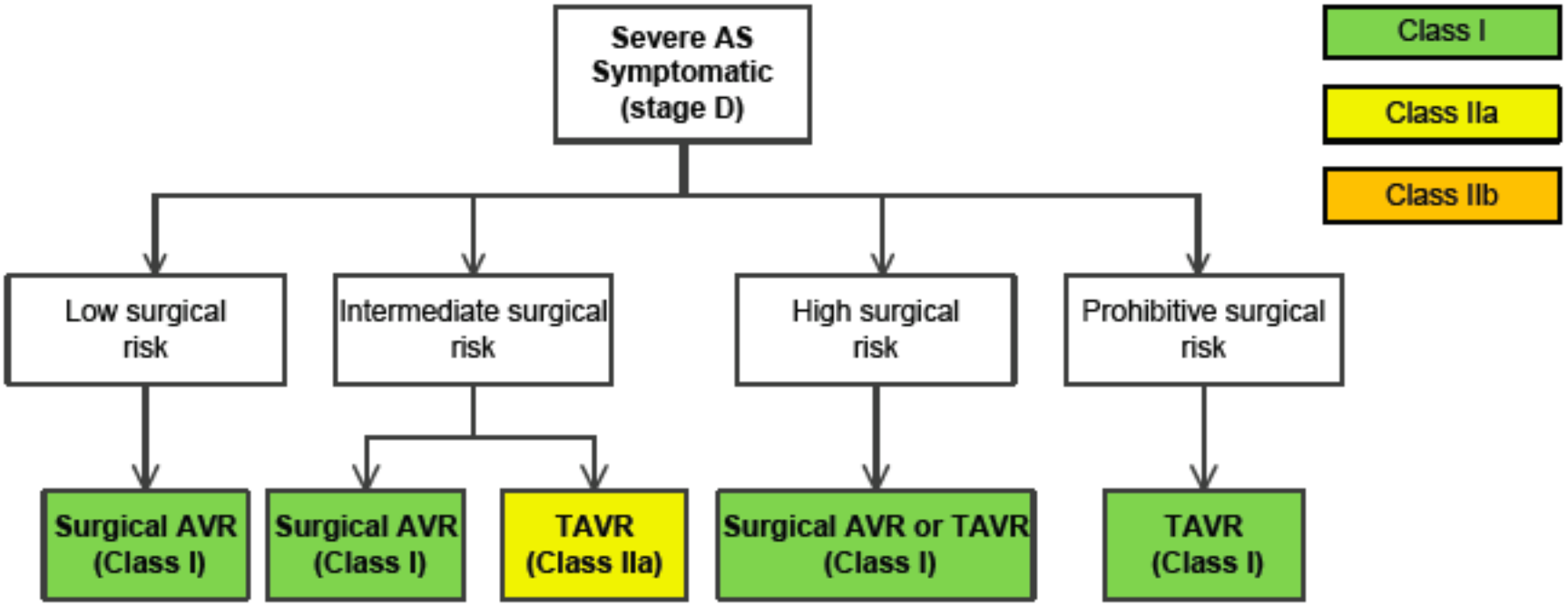
Mack et al. Lancet 2015

Italian CV Registry

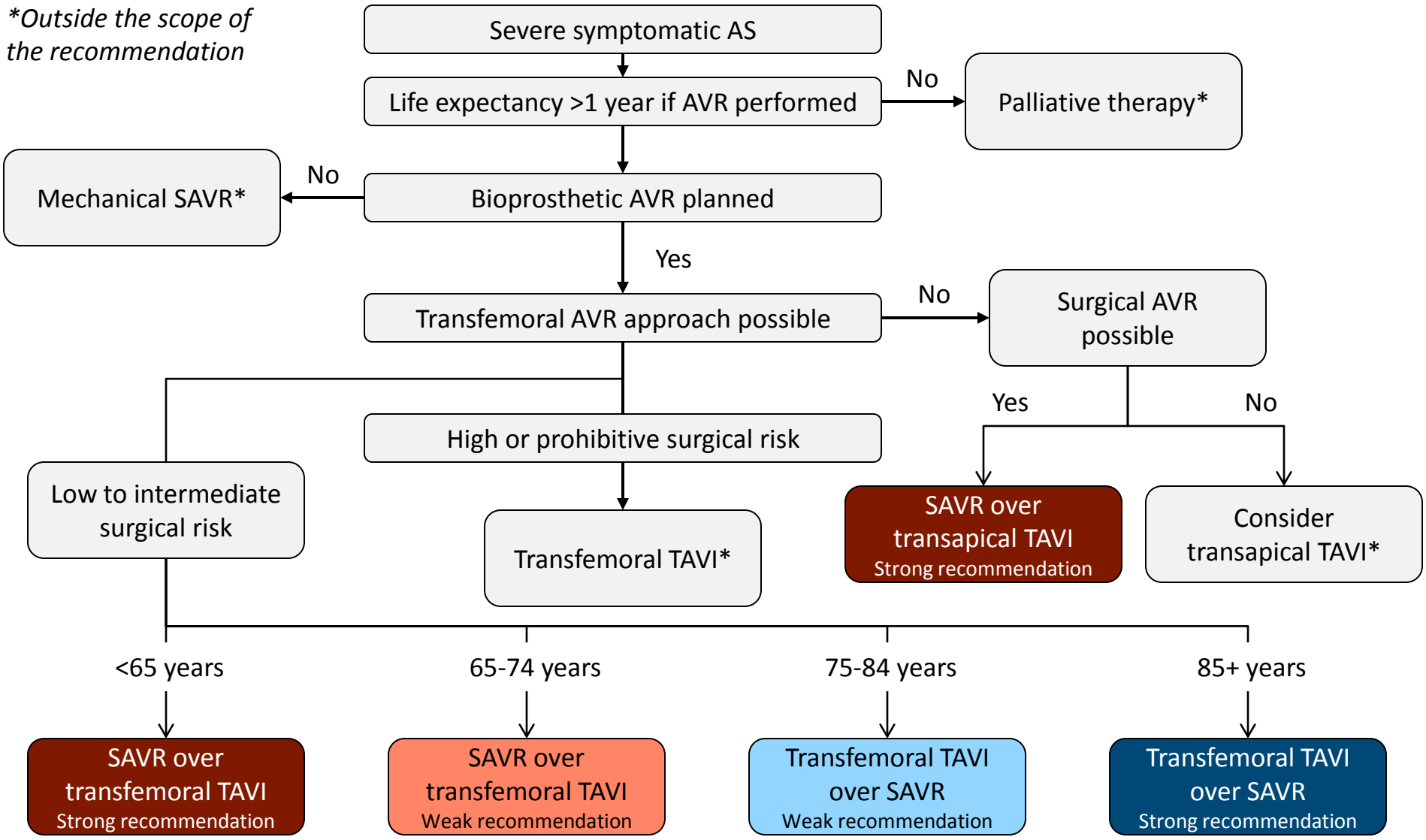


Barbanti et al. JACC Intv 2015

Transcatheter Aortic Valve Implantation
New Guidelines **AHA/ACC 2017**



Management of severe AS - *A Clinical Practice Guideline*



Per O Vandvik et al. BMJ 2016;354:i5085

Closing Remarks

- Over the next decade a remarkable growth in TAVI procedures is predicted
- The growing adoption of TAVI in lower-risk population has been driven by:
  - the multi-disciplinary heart team
  - rapid technology enhancement
  - simplification of the procedure
  - striking reduction in complications
  - global trends and accepted clinical practices
- The current TAVI guidelines (AHA/ACC), are more close to the clinical practice
- The ultimate role of TAVI is yet to be determined. But we can anticipate a future time when the choice of a procedure over the other one (TAVI or surgery) will be a risk-benefit assessment based on clinical and anatomic factors, and not an imprecise risk stratification model