31 GIORNATE CARDIOLOGICHE TORINESI

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Don’t believe everything! Read carefully!

All that glitters is *not* gold!

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Disclosures

FB receives consulting fees from Abbott Medical

Background (1)

The indication for TAVI was expanded to intermediate risk patients on the basis of the major trials

B) Choice of intervention in symptomatic aortic stenosis		
Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on site and with structured collaboration between the two, including a Heart Team (heart valve centres).	I	C
The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in *Table 7*). In addition, the local expertise and outcomes data for the given intervention must be taken into account.	I	C
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
In patients who are at increased surgical risk (STS or EuroSCORE II ≥ 4% or logistic EuroSCORE I ≥ 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
Balloon aortic valvotomy may be considered as a bridge to SAVR or TAVI in haemodynamically unstable patients or in patients with symptomatic severe aortic stenosis who require urgent major non-cardiac surgery.	IIb	C
Balloon aortic valvotomy may be considered as a diagnostic means in patients with severe aortic stenosis or other potential causes for symptoms (i.e. lung disease) and in patients with severe myocardial dysfunction, pre-renal insufficiency or other organ dysfunction that may be reversible with balloon aortic valvotomy when performed in centres that can escalate to TAVI.	IIb	C

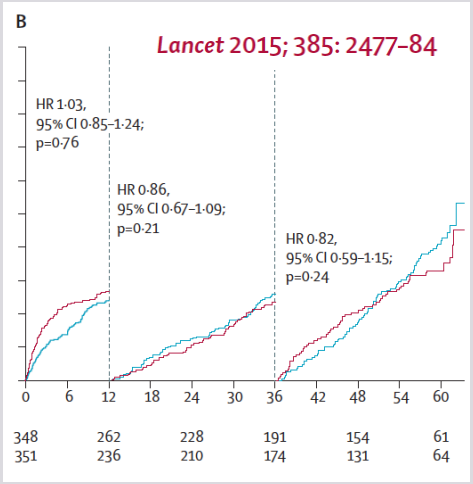
Available data from randomized controlled trials and large registries in elderly patients at increased surgical risk show that TAVI is superior in terms of mortality to medical therapy in extreme-risk patients,[91] non-inferior or superior to surgery in high-risk patients[94–97] and non-inferior to surgery and even superior when transfemoral access is possible in intermediate-risk patients.[98–102] In the two large studies on intermediate risk, the mean ages of patients were 82 and 80 years,[99,102] mean STS scores were 5.8% and 4.5%[99,102] and a high percentage were considered frail. Thus the results are valid only for comparable patient groups. Overall, rates of vascular complications, pacemaker

Background (1)

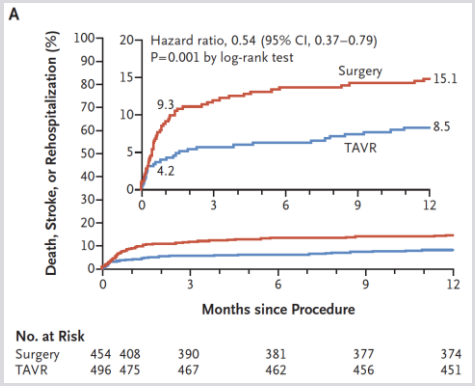
TAVI, what's happening at follow-up?

TRIALS SAY OK

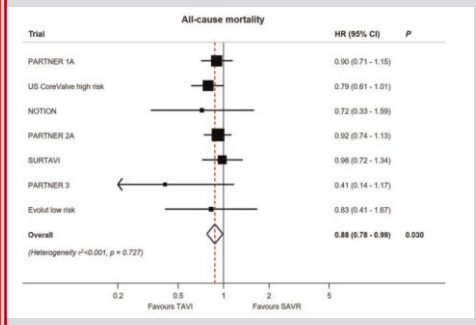
5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial



Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients



META SAY "WOW"



2.0% for high-, intermediate-, and low surgical risk trials, respectively. Transcatheter aortic valve implantation was associated with a significant reduction of all-cause mortality compared to SAVR (hazard ratio [HR] 0.88 [95% confidence interval (CI) 0.78–0.99], $P = 0.030$); an effect that was consistent across the entire spectrum of surgical risk

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis

European Heart Journal (2019) **0**, 1–11

TAVR Survival Surpasses SAVR in Low-Risk Patients: Meta-analysis

MEDSCAPE

Patrice Wendling
September 17, 2019

Read Comment

In a new study, use of transcatheter rather than surgical aortic valve replacement (TAVR/SAVR) reduced the risk of early death in low-risk patients with severe aortic stenosis, calling into question whether TAVR should be the preferred option.

In the pooled analysis of 4 randomized trials involving 2887 patients at low surgical risk, the 1-year risks with TAVR and SAVR for all-cause death were 2.1% vs 3.5% (relative risk [RR], 0.61; 95% CI, 0.39 - 0.96) and were 1.6% vs 2.9% for cardiovascular death (RR, 0.55; 95% CI, 0.33 - 0.90).

The magnitude of relative risk reduction was similar in the recently reported pivotal PARTNER 3 and Evolut Low Risk trials, which were included in this study along with the 2015 NOTION trial and a post-hoc SURTAVI analysis. The four trials have shown TAVR is noninferior or superior to SAVR on composite primary endpoints that included mortality; however, none were adequately powered to detect mortality differences in and of themselves, the authors reported in the September 24 issue of the *Journal of the American College of Cardiology*.

Top of the pyramid of evidence! But…

Background (1)

…there could be some limitations!

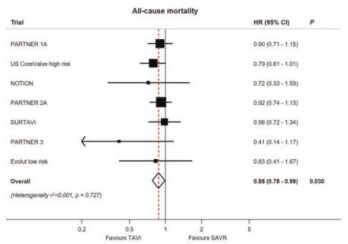
RC TRIALS

Composite outcomes: underpowered for singular outcomes

Not homogeneous definition of outcomes (neurologic event,…)

Sponsorship: could it be a bias?

META



European Heart Journal (2019) **0**, 1–11

Short follow-up

Effect size: HR? RR?

Background (2)

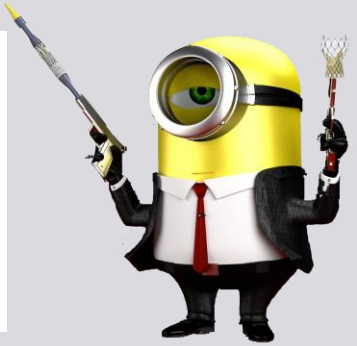
Prospective randomized studies are mainly made by companies

Surveys of randomized trials published between 1990 and 2000 raised awareness in the medical community that **trials funded by for-profit organizations were more likely to report positive findings than those funded by not-for-profit organizations**.

Contemporary data has confirmed that incentives surrounding for-profit organizations have the potential to influence clinical trial outcomes.

Table 2. Proportion of Trials Significantly Favoring Newer Treatments Over Standard of Care

Trials	No./Total % Not-for-Profit (n = 104)	Not-for-Profit and For-Profit (n = 62)	For-Profit (n = 137)	*P* for Trend
All	51/104 (49.0)	35/62 (56.5)	92/137 (67.2)	.005
Clinical end points	19/55 (34.6)	24/44 (54.6)	64/96 (66.7)	<.001
Drug	17/43 (39.5)	24/46 (54.4)	74/113 (65.5)	.002
Device	4/8 (50.0)	9/13 (69.2)	14/17 (82.4)	.07



Attempts to explain this phenomenon have focused largely on **design bias**, **interpretation bias**, **data suppression**, and **differential data quality**.

Reported Outcomes in Major Cardiovascular Clinical Trials Funded by For-Profit and Not-for-Profit Organizations: 2000-2005
JAMA. 2006;295:2270-2274

LET'S SEE

OUTCOMES

LANDMARK

INCLUSION CRITERIA

POTENTIAL BIAS FOR MISCLASSIFICATION

PROPENSITY SCORE

META-ANALYSIS OF HRs

OUTCOMES

PRIMARY OUTCOMES IN TAVI/SAVR RANDOMIZED STUDIES

What it is suggested by guidelines

Guidelines for reporting mortality and morbidity after cardiac valve interventions
J Thorac Cardiovasc Surg 2008;135:732-8

MORTALITY

Valve—related
Cardiac
All cause

MORBIDITY

Structural valve deterioration
Non-structural dysfunction
Thrombosis
Embolism
Bleeding
Endocarditis
Redo

COMPOSITE ENDPOINTS

LANDMARK AT 30-day

DURABILITY

Updated standardized endpoint definitions for transcatheter aortic valve implantation: The Valve Academic Research Consortium-2 consensus document* (J Thorac Cardiovasc Surg 2013;145:6-23)

TABLE 11. Composite endpoints

Device success
- Absence of procedural mortality AND
- Correct positioning of a single prosthetic heart valve into the proper anatomical location AND
- Intended performance of the prosthetic heart valve (no prosthesis–patient mismatch* and mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s, AND no moderate or severe prosthetic valve regurgitation*)

Early safety (at 30 days)
- All-cause mortality
- All stroke (disabling and nondisabling)
- Life-threatening bleeding
- Acute kidney injury—Stage 2 or 3 (including renal replacement therapy)
- Coronary artery obstruction requiring intervention
- Major vascular complication
- Valve-related dysfunction requiring repeat procedure (BAV, TAVI, or SAVR)

Clinical efficacy (after 30 days)
- All-cause mortality
- All stroke (disabling and nondisabling)
- Requiring hospitalizations for valve-related symptoms or worsening congestive heart failure†
- NYHA class III or IV
- Valve-related dysfunction (mean aortic valve gradient ≥20 mm Hg, EOA ≤0.9–1.1 cm^2‡ and/or DVI <0. 35 m/s, AND/OR moderate or severe prosthetic valve regurgitation*)

Time-related valve safety
- Structural valve deterioration
  - Valve-related dysfunction (mean aortic valve gradient ≥20 mm Hg, EOA ≤0.9-1.1 cm^2‡ and/or DVI <0.35 m/s, AND/OR moderate or severe prosthetic valve regurgitation*)
  - Requiring repeat procedure (TAVI or SAVR)
- Prosthetic valve endocarditis
- Prosthetic valve thrombosis
- Thrombo-embolic events (eg, stroke)
- VARC bleeding, unless clearly unrelated to valve therapy (eg, trauma)

Outcomes

PRIMARY OUTCOMES INTAVI/SAVR RANDOMIZED STUDIES

TABLE 1 | Results of major prospective randomized trials on TAVI vs. SAVR in high and intermediate to low risk patients.

	PARTNER 1A (6)	CoreValve HR (7)	PARTNER 2A (10)	NOTION (9)	SURTAVI (8)
Time of recruitment	May 2007–August 2009	February 2011–December 2012	December 2011 –November 2013	December 2009–April 2013	June 2012–June 2016
THV	SAPIEN	CoreValve	SAPIEN XT	CoreValve	CoreValve
Primary endpoint	All-cause death at 1 year	All-cause death at 1 year	All-cause death or diasbling stroke at 2 years	All-cause death, disabling stroke or myocardial infarction at 1 year	All-cause death or disabling stroke at 2 years

Front. Cardiovasc. Med. 5:92.
doi: 10.3389/fcvm.2018.00092

Composite endpoints different among studies and from guidelines

Durability at two years? What about valve-related death?

Landmark at 30-days? (Does the risk profile change over time?)

Outcomes

EX: SURTAVI COMPOSITE OUTCOMES

TRIAL END POINTS

The primary end point was a composite of death from any cause or disabling stroke at 24 months. (Trial end-point definitions are provided in Table S4 in the Supplementary Appendix.) Disabling stroke was defined according to the criteria of the Valve Academic Research Consortium-2 (VARC-2).[10]

N Engl J Med 2017;376:1321-31.

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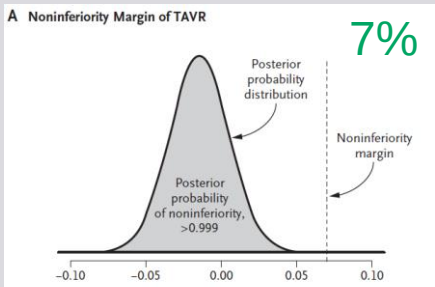
We determined that TAVR would be declared noninferior to surgery for the primary outcome if the posterior probability of noninferiority with a margin of 0.07 was more than 0.971,



TAVR Posterior Median	Surgery Posterior Median	Difference Posterior Median
	% (95% CI)	
12.6 (10.2 to 15.3)	14.0 (11.4 to 17.0)	−1.4 (−5.2 to 2.3)

Table 3. Clinical Outcomes at 30 Days, 12 Months, and 24 Months (Modified Intention-to-Treat Population).*

Outcome	30 Days			12 Months			24 Months		
	TAVR	Surgery	95% Credible Interval	TAVR	Surgery	95% Credible Interval	TAVR	Surgery	95% Credible Interval
					percent				
Death from any cause or disabling stroke	2.8	3.9	−2.8 to 0.7	8.1	8.8	−3.5 to 2.1	12.6	14.0	−5.2 to 2.3
Death from any cause	2.2	1.7	−0.9 to 1.8	6.7	6.8	−2.7 to 2.4	11.4	11.6	−3.8 to 3.3
Cardiovascular	2.0	1.7	−1.0 to 1.6	4.8	5.5	−2.9 to 1.5	7.7	8.0	−3.3 to 2.6
Valve-related	0.1	0.1	−0.3 to 0.3	0.1	0.3	−0.7 to 0.3	0.2	0.4	−0.9 to 0.5
Aortic-valve reintervention	0.9	0.2	−0.1 to 1.4	2.1	0.5	0.4 to 2.7	2.8	0.7	0.7 to 3.5
All stroke and TIA	4.5	6.5	−4.2 to 0.3	8.2	8.6	−3.1 to 2.4	10.0	11.0	−4.2 to 2.2
All stroke	3.4	5.6	−4.2 to −0.2	5.4	6.9	−3.9 to 0.9	6.2	8.4	−5.0 to 0.4
Disabling	1.2	2.5	−2.6 to 0.1	2.2	3.6	−3.1 to 0.4	2.6	4.5	−4.0 to 0.1
Nondisabling	2.2	3.1	−2.5 to 0.6	3.7	3.9	−2.2 to 1.7	4.4	4.7	−2.6 to 1.9
TIA	1.5	1.1	−0.7 to 1.5	3.2	2.0	−0.4 to 2.8	4.3	3.1	−0.9 to 3.2
Myocardial infarction	0.9	1.0	−1.0 to 0.9	2.0	1.6	−0.9 to 1.8	2.8	2.2	−1.1 to 2.4
Hospitalization for aortic-valve–related disease	2.9	4.2	−3.1 to 0.5	8.5	7.6	−1.8 to 3.6	13.2	9.7	0.1 to 7.0
MACCE	5.7	7.4	−4.0 to 0.7	13.2	12.8	−2.9 to 3.7	18.6	18.6	−4.2 to 4.2

Outcomes

EX: PARTNER 2A ENDPOINTS

END POINTS

The primary end point was a nonhierarchical composite of death from any cause or disabling stroke at 2 years in the intention-to-treat population; all the patients were followed for at least

?

Table 11 Composite endpoints

Clinical efficacy (after 30 days)

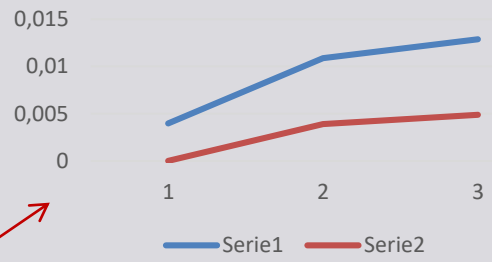
- All-cause mortality
- All stroke (disabling and non-disabling)
- Requiring hospitalizations for valve-related symptoms or worsening congestive heart failure[b]
- NYHA class III or IV
- Valve-related dysfunction (mean aortic valve gradient ≥20 mmHg, EOA ≤0.9–1.1 cm^{2c} and/or DVI <0. 35 m/s, AND/OR moderate or severe prosthetic valve regurgitation[a])

Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document[r]

Table 2. Clinical End Points at 30 Days, 1 Year, and 2 Years.*

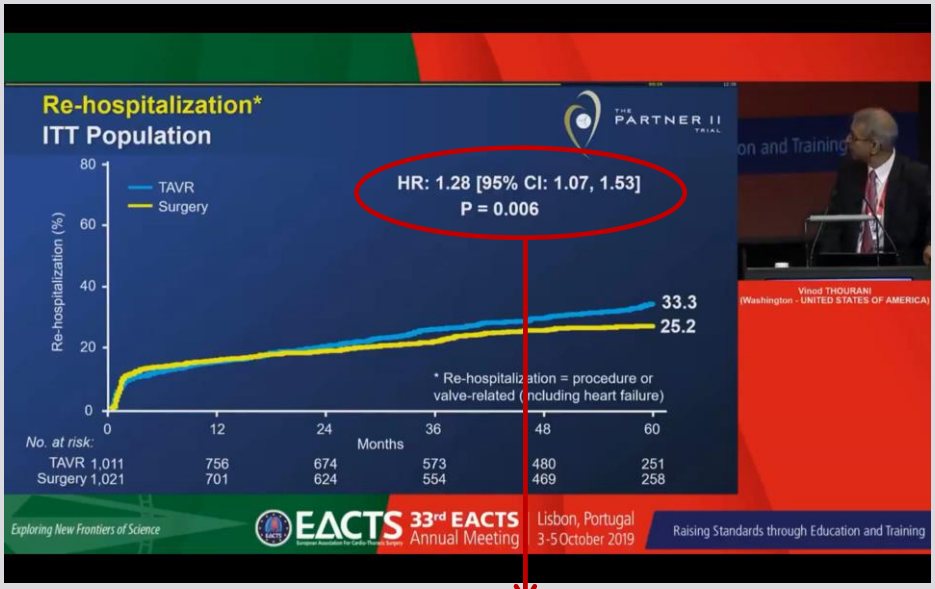
End Point	At 30 Days			At 1 Year			At 2 Years		
	TAVR (N=1011)	Surgery (N=1021)	P Value	TAVR (N=1011)	Surgery (N=1021)	P Value	TAVR (N=1011)	Surgery (N=1021)	P Value
	no. of patients (%)			*no. of patients (%)*			*no. of patients (%)*		
Death from any cause or disabling stroke	62 (6.1)	80 (8.0)	0.11	145 (14.5)	160 (16.4)	0.24	192 (19.3)	202 (21.1)	0.33
Death									
From any cause	39 (3.9)	41 (4.1)	0.78	123 (12.3)	124 (12.9)	0.69	166 (16.7)	170 (18.0)	0.45
From cardiac causes	33 (3.3)	32 (3.2)	0.92	70 (7.1)	77 (8.1)	0.40	97 (10.1)	104 (11.3)	0.38
Not from cardiac causes	6 (0.6)	9 (0.9)	0.41	53 (5.6)	47 (5.2)	0.71	69 (7.4)	65 (7.4)	0.98
Neurologic event									
Any event	64 (6.4)	65 (6.5)	0.94	99 (10.1)	93 (9.7)	0.76	121 (12.7)	103 (11.0)	0.25
Transient ischemic attack	9 (0.9)	4 (0.4)	0.17	23 (2.4)	16 (1.8)	0.38	34 (3.7)	20 (2.3)	0.09
Any stroke	55 (5.5)	61 (6.1)	0.57	78 (8.0)	79 (8.1)	0.88	91 (9.5)	85 (8.9)	0.67
Disabling stroke	32 (3.2)	43 (4.3)	0.20	49 (5.0)	56 (5.8)	0.46	59 (6.2)	61 (6.4)	0.83
Nondisabling stroke	23 (2.3)	18 (1.8)	0.43	30 (3.0)	24 (2.5)	0.44	33 (3.4)	27 (2.9)	0.51
Rehospitalization	64 (6.5)	62 (6.5)	0.99	142 (14.8)	135 (14.7)	0.92	183 (19.6)	156 (17.3)	0.22
Death from any cause or rehospitalization	99 (9.8)	101 (10.2)	0.78	234 (23.4)	225 (23.3)	0.97	303 (30.5)	281 (29.6)	0.67
Death from any cause, any stroke, or rehospitalization	140 (13.9)	153 (15.3)	0.37	274 (27.4)	276 (28.3)	0.64	344 (34.6)	326 (33.9)	0.75
Myocardial infarction	12 (1.2)	19 (1.9)	0.22	24 (2.5)	29 (3.0)	0.47	33 (3.6)	37 (4.1)	0.56
Major vascular complication	80 (7.9)	51 (5.0)	0.008	84 (8.4)	54 (5.3)	0.007	86 (8.6)	55 (5.5)	0.006
Life-threatening or disabling bleeding	105 (10.4)	442 (43.4)	<0.001	151 (15.2)	460 (45.5)	<0.001	169 (17.3)	471 (47.0)	<0.001
Acute kidney injury	13 (1.3)	31 (3.1)	0.006	32 (3.4)	48 (5.0)	0.07	36 (3.8)	57 (6.2)	0.02
New atrial fibrillation	91 (9.1)	265 (26.4)	<0.001	100 (10.1)	272 (27.2)	<0.001	110 (11.3)	273 (27.3)	<0.001
New permanent pacemaker	85 (8.5)	68 (6.9)	0.17	98 (9.9)	85 (8.9)	0.43	114 (11.8)	96 (10.3)	0.29
Endocarditis	0	0	—	7 (0.8)	6 (0.7)	0.84	11 (1.2)	6 (0.7)	0.22
Aortic-valve reintervention	4 (0.4)	0	0.05	11 (1.2)	4 (0.5)	0.10	13 (1.4)	5 (0.6)	0.09

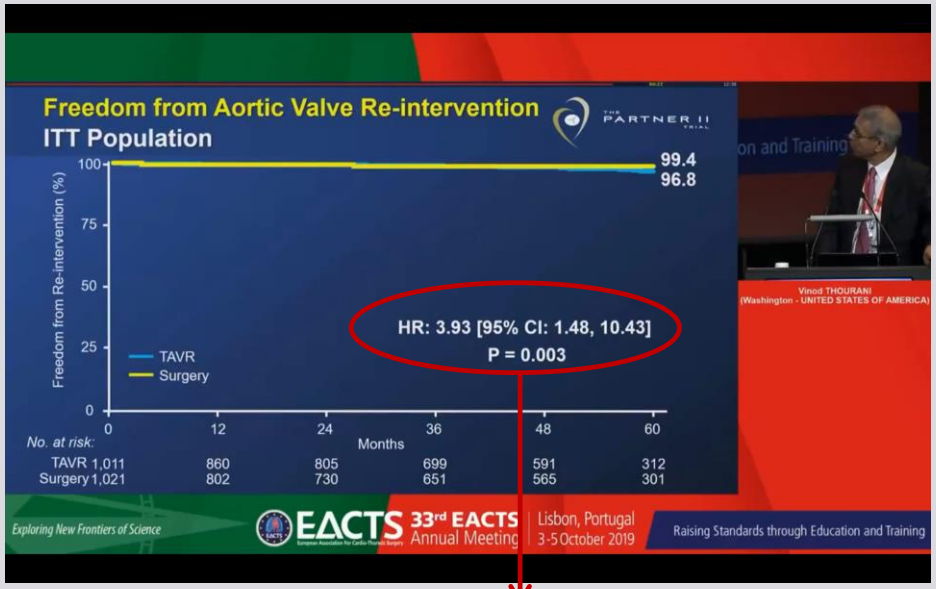
Crude reoperation rate



Outcomes

5 YEARS OUTCOMES FROM THE PARTNER 2A TRIAL





Hazard of Re-hospitalization at 5 years

28% higher in TAVI

Hazard of Re-Intervention at 5 years

4 times higher in TAVI

DURABILITY IS CRITICAL ISSUE …….

Outcomes

….BUT WE ARE FORGETTING IT!

TABLE 2 | Overview of currently active randomized trials on TAVI vs. SAVR in low to intermediate risk patients with severe aortic stenosis.

	DEDICATE	NOTION 2	PARTNER 3	CoreValve low risk
Reference/NCT number	Clinicaltrials.gov/NCT03112980	Clinicaltrials.gov/NCT02825134	Clinicaltrials.gov/NCT02675114	Clinicaltrials.gov/NCT02701283
Study start date	2017	2016	2016	2016
Study status	Recruiting	Recruiting	Recruiting	Recruiting
Estimated study completion date	2024	2024	2027	2026
Patients' risk profile	STS-PROM 2-6%	Patient age ≤75 years and STS-PROM <4%	STS-PROM <4%	Operative risk <3%
Study arms	TAVI* vs. SAVR* (1:1 randomization)	TAVI* vs. SAVR* (1:1 randomization)	TAVI (SAPIEN 3) vs. SAVR* (1:1 randomization)	TAVI (CoreValve Evolut R) vs. SAVR* (1:1 randomization)
Estimated enrollment	1,600	992	1,328	1,200
Primary Outcome	• Efficacy endpoint: Overall survival at 5 years • Safety endpoint: Overall survival at 1 year and 196 deaths (event-driven)	All-cause mortality, myocardial infarction or stroke at 1 year	All-cause mortality, stroke, or re-hospitalization at 1 year	All-cause mortality or disabling stroke at 2 years
Follow up time	5 years	1 year	10 years	10 years

Feasibility

Safety

Efficacy: Durability?

(22). Overall, the incidence of structural valve degeneration and aortic valve re-intervention were low but will naturally become an issue as follow-up length and patient numbers increase. Recently published definitions of prosthesis degeneration may aid comprehensive analysis of this important topic (23, 24). To eliminate durability concerns after TAVI, very solid durability data available for surgical bioprostheses over the course of more than a decade will need to be matched (25).

Front. Cardiovasc. Med. 5:92. doi: 10.3389/fcvm.2018.00092

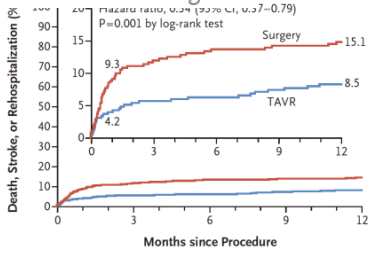
Outcomes

….and the choice is driven by the sample size need

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

PARTNER 3 Investigators



No. at Risk

Surgery	454	408	390	381	377	374
TAVR	496	475	467	462	456	451

END POINTS

The primary end point was a composite of death from any cause, stroke, or rehospitalization at 1 year after the procedure. All the patients un-

Why use composites? The main advantage of this approach is increased statistical efficiency. By measuring more than one result and combining the data in a single outcome, researchers have an easier time showing a statistically significant difference between the treatment group and controls. This allows for studies that require fewer patients, take less time, and ultimately are more cost-effective. However, this approach can also open the door to misdirection and statistical sleight of hand.

Problems with use of composite end points in cardiovascular trials: systematic review of randomised controlled trials

Conclusion The use of composite end points in cardiovascular trials is frequently complicated by large gradients in importance to patients and in magnitude of the effect of treatment across component end points. Higher event rates and larger treatment effects associated with less important components may result in misleading impressions of the impact of treatment.

BMJ

WHAT THIS STUDY ADDS

Almost half of a sample of recent prominently published cardiovascular trials used composite end points, which were often inadequately reported and showed large gradients in importance to patients

End points of least importance to patients typically contributed most events

Composite end points, as currently used in cardiovascular trials, may often be misleading

OUTCOMES & LANDMARK

WHY?

The assumption of hazard-proportionality in COX was violated

5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial

Lancet 2015; 385: 2477–84

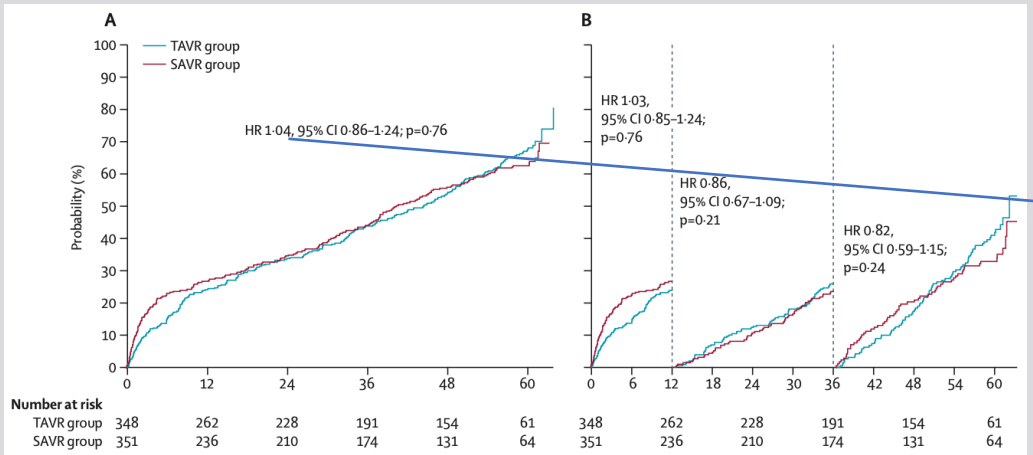
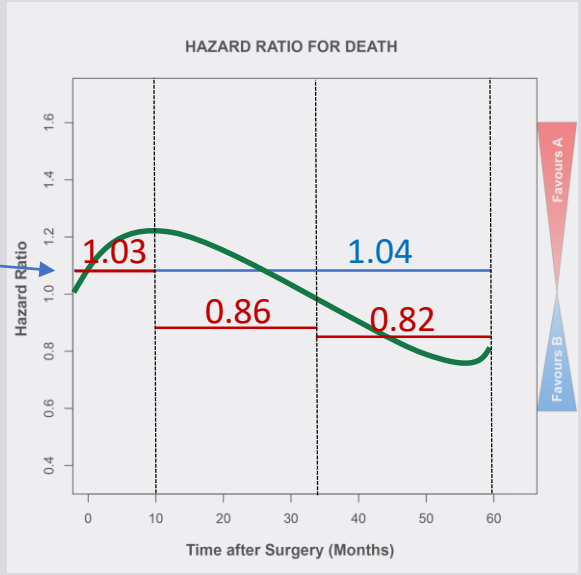
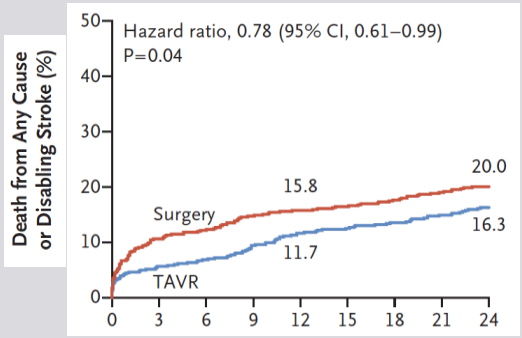


Figure 2: **Mortality and cardiovascular outcomes**
Kaplan-Meier analysis of all-cause death in the intention-to-treat population (A) and by landmark analysis (B);

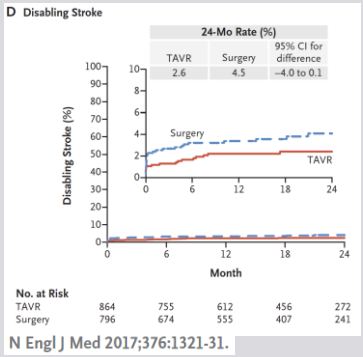


Outcomes: Landmark at 30 days

PARTNER 2A ENDPOINTS

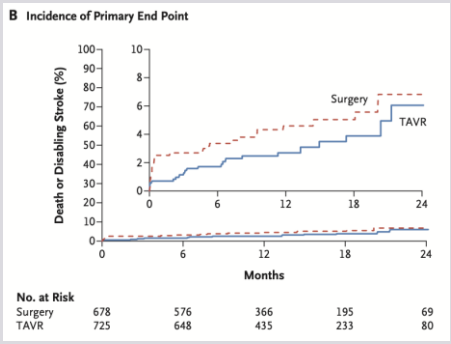


SURTAVI ENDPOINTS

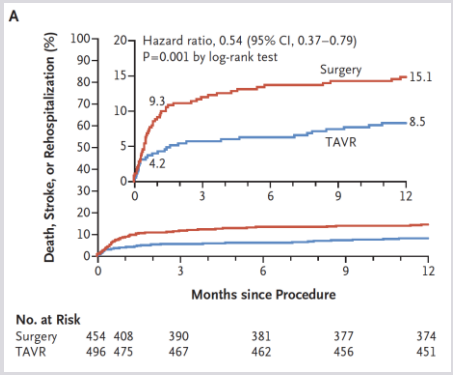


N Engl J Med 2017;376:1321-31.

EVOLUT R ENDPOINTS



PARTNER 3 ENDPOINTS



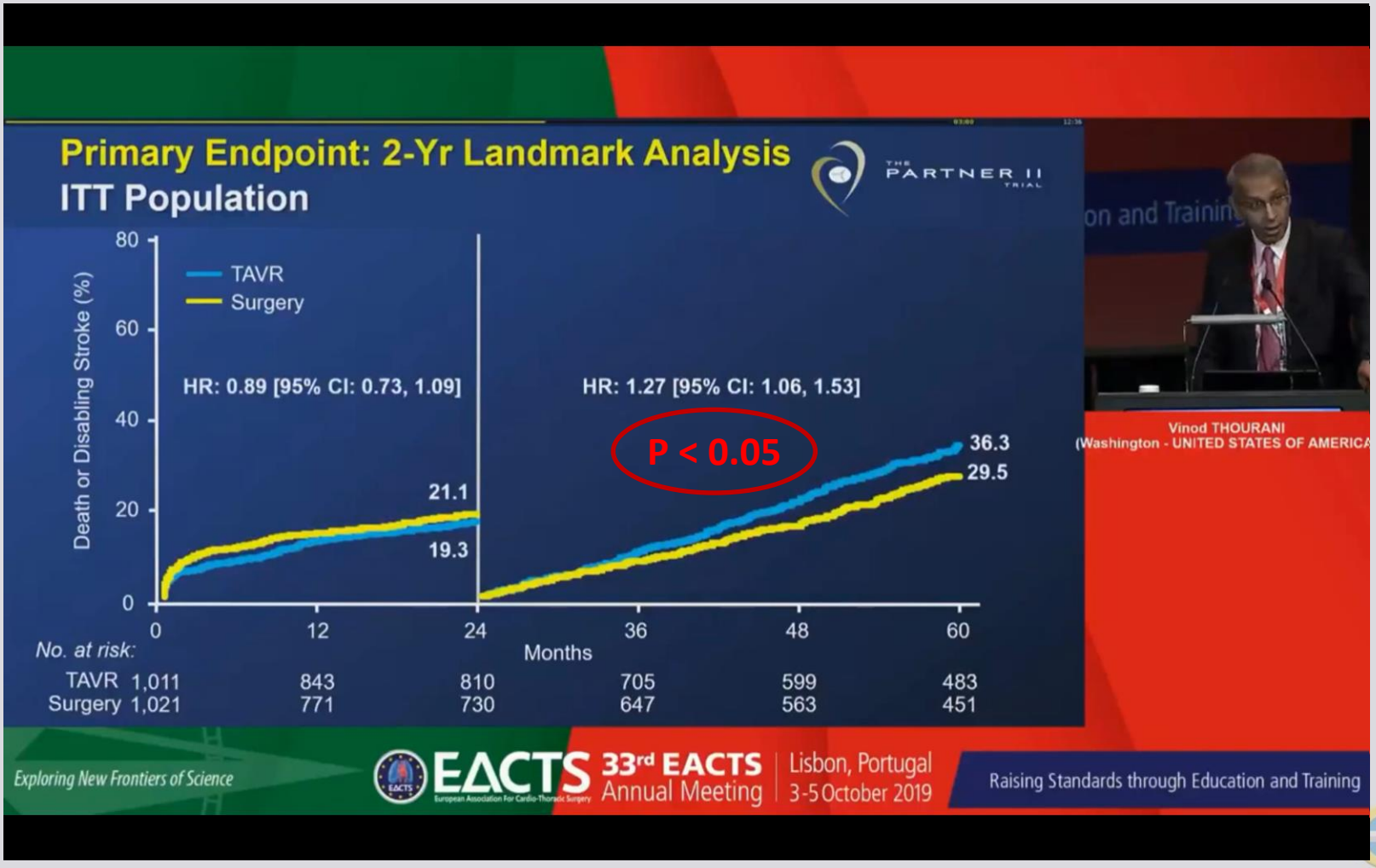
NO LANDMARKING HAS BEEN PERFORMED….

Differences are in the 30 day-2 months

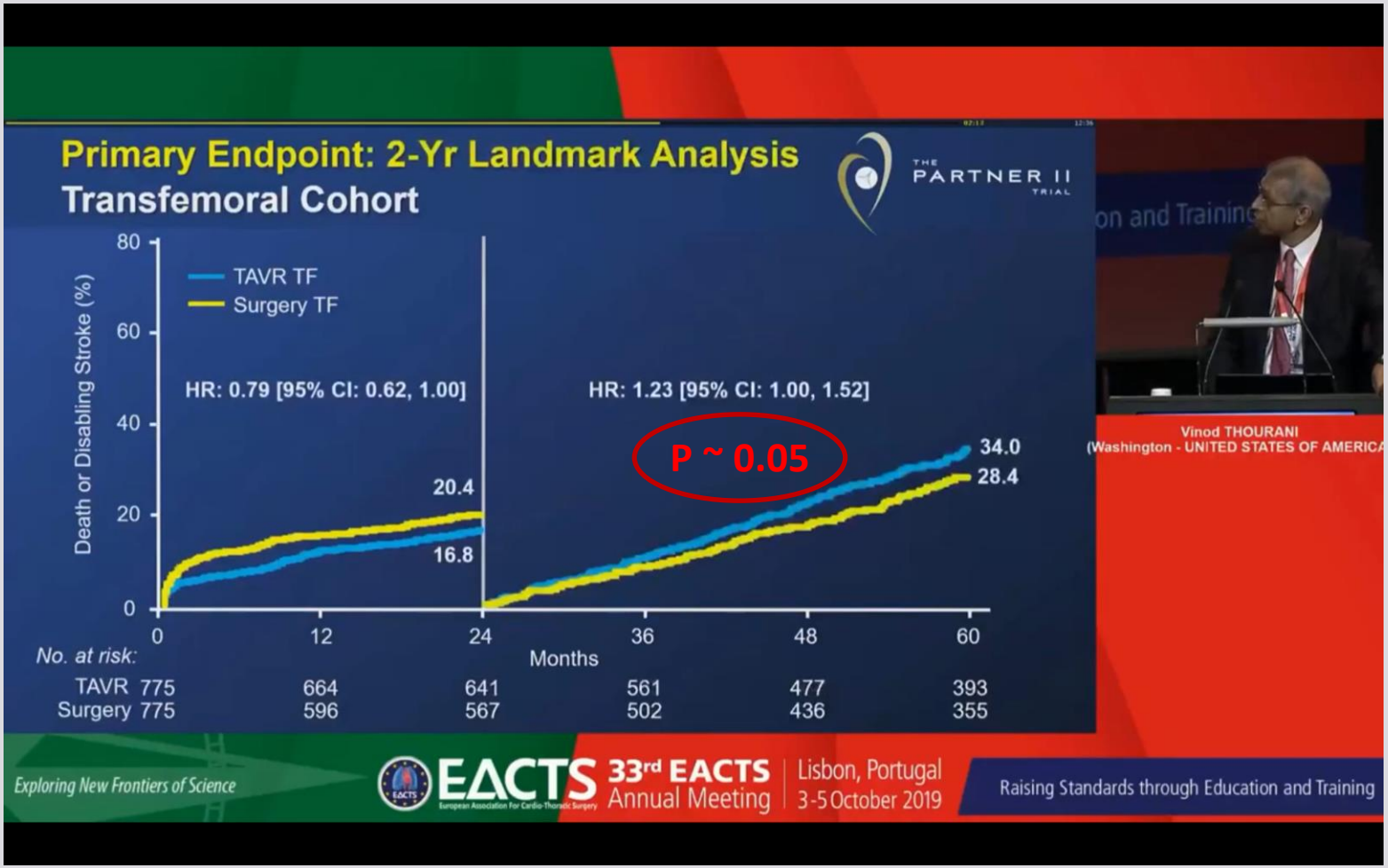
CURVES ARE PARALLEL AFTER A COUPLE OF MONTHS

PROPORTIONALITY OF HAZARDS COULD BE NOT RESPECTED

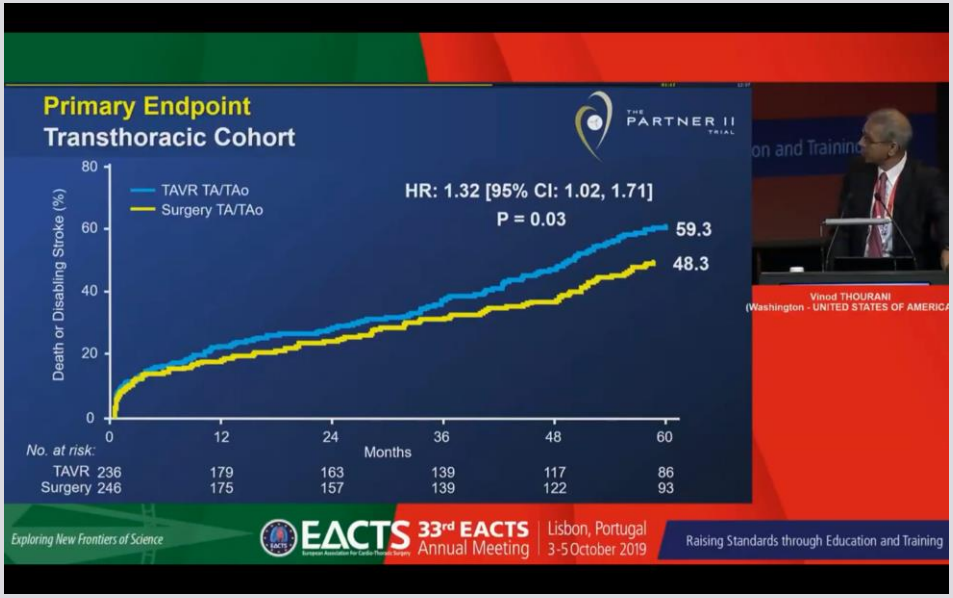
Outcomes: Landmark Analysis at follow-up

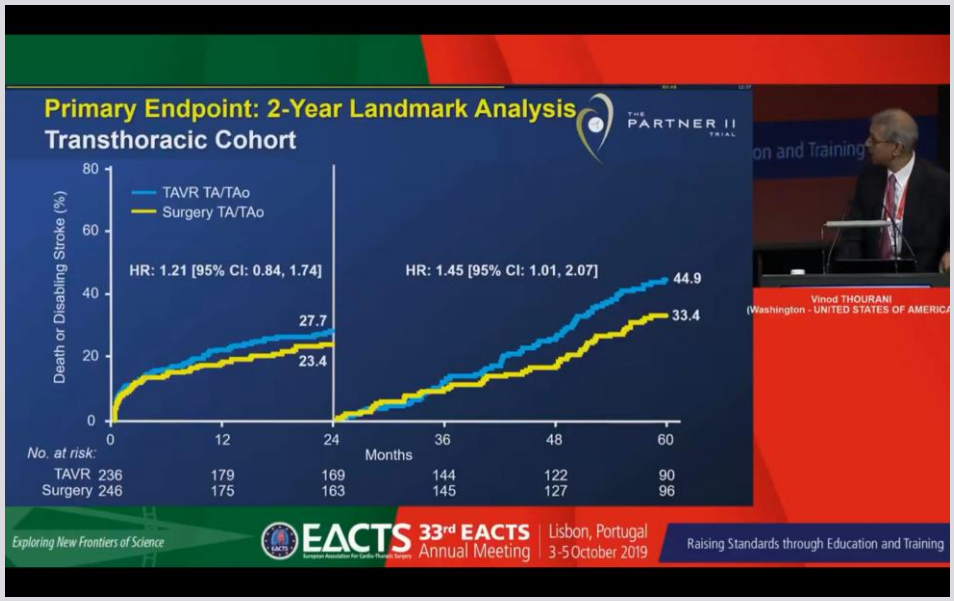


Outcomes: Landmark Analysis at follow-up



Outcomes: Landmark Analysis at follow-up





INCLUSION CRITERIA

Randomization, when properly conducted, avoids bias by distributing both known and unknown patient characteristics between the experimental conditions on the basis of the play of chance.

BMJ 2013;347:f6409 doi: 10.1136/bmj.f6409 (Published 11 November 2013)

ASSOCIATED PROCEDURES | TREATMENT GROUPS

PARTNER 2 Trial		SURTAVI Trial		EVOLUT R Trial		PARTNER 3 Trial	
Surgery	9.1% concomitant 14.5% CABG	Surgery	27.8%	Surgery	26.2%	Surgery	26.4%
TAVR	3.9% PCI	TAVR	14.5%	TAVR	6.9%	TAVR	7.9%
P-value < 0.0001		**P-value < 0.0001**		**P-value < 0.0001**		**P-value < 0.0001**	

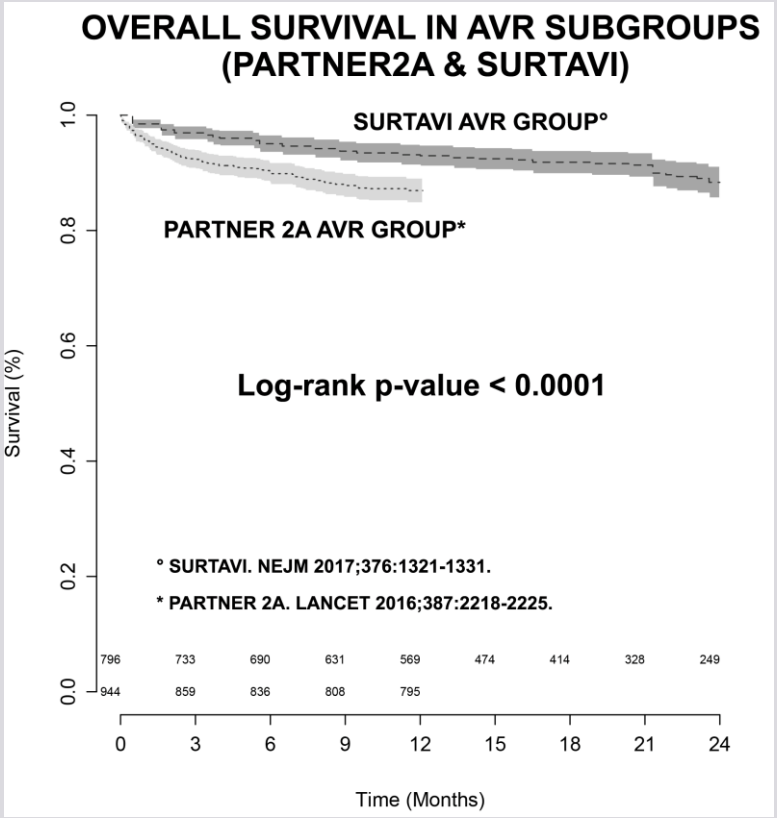
ASSOCIATED PCI/CABG | TREATMENT GROUPS

PARTNER 2 Trial		SURTAVI Trial		EVOLUT R Trial		PARTNER 3 Trial	
Surgery	14.5%	Surgery	22.1%	Surgery	13.6%	Surgery	12.8%
TAVR	3.9%	TAVR	14.5%	TAVR	6.9%	TAVR	6.5%
P-value < 0.0001		**P-value < 0.0001**		**P-value < 0.0001**		**P-value 0.0012**	

HOMOGENEOUS GROUPS?

Inclusion Criteria

Are the surgical arms homogeneous?



OTHER POTENTIAL BIASES? DATA MISCLASSIFICATION?

theheart.org Medscape Cardiology

News > Medscape Medical News

Deaths Linked to Transcatheter Valve Cases May Be 'Underreported'

Batya Swift Yasgur MA, LSW
October 15, 2019

2 Read Comments ADD TO EMAIL ALERTS

Deaths associated with some transcatheter valve-repair procedures may be underreported in a US Food and Drug Administration (FDA) adverse events database, leaving a misleading picture of the number of associated fatalities, a new report suggests.

It found that 17.5% of deaths associated with the *SAPIEN 3* (Edwards Lifesciences) transcatheter valve and 24.7% of those associated with *MitraClip* (Abbott Vascular) were misclassified as "injury" or "malfunction" events in the FDA's Manufacturer and User Facility Device Experience (MAUDE) database.

"We found that a significant number of deaths associated with these high-risk cardiac devices were not correctly classified," senior author Rita F. Redberg, MD, MSc, told *theheart.org | Medscape Cardiology.*

"Therefore, clinicians, patients, or anyone searching MAUDE — the primary source for adverse event data — to determine how many deaths were reported associated with these devices would get an erroneously low number for deaths reported to MAUDE, which is already only a small fraction of all adverse events, as most are not reported to MAUDE," said Redberg, from the University of California, San Francisco.

17.5% of DEATHS MISCLASSIFICATED

MAUDE:
ERRONEOUSLY LOW NUMBER OF REPORTED DEATHS

PS STUDY ON TAVI vs SAVR: A QUASI-RANDOMIZED STUDY?

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

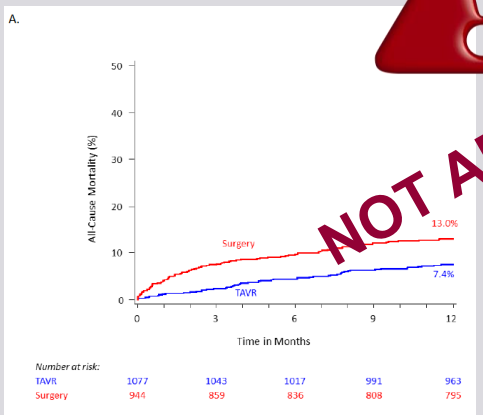
Lancet 2016; 387: 2218–25

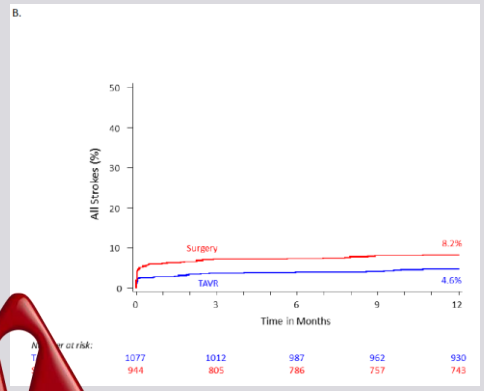
Propensity score methodology was used to reduce the confounding in the statistical comparison of outcomes of two treatment groups from the two different studies by accounting for differences in baseline patient characteristics.

Results

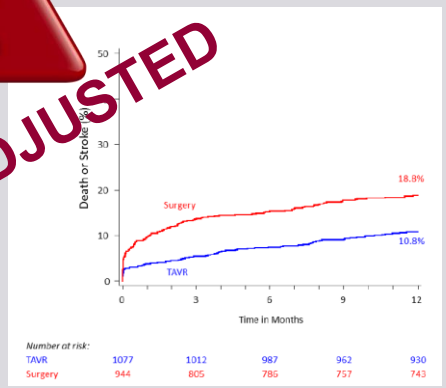
Time-to-event analyses for the SAPIEN 3 TAVR and PARTNER 2A surgery cohorts for all-cause death, all strokes, and the composite event of death and strokes are shown in the appendix, as are those for transfemoral-access TAVR only. Important differences between TAVR and surgery for each endpoint are observed in the first several months, with the curves then remaining parallel (appendix).

Lancet 2016; 387: 2218–25





NOT ADJUSTED

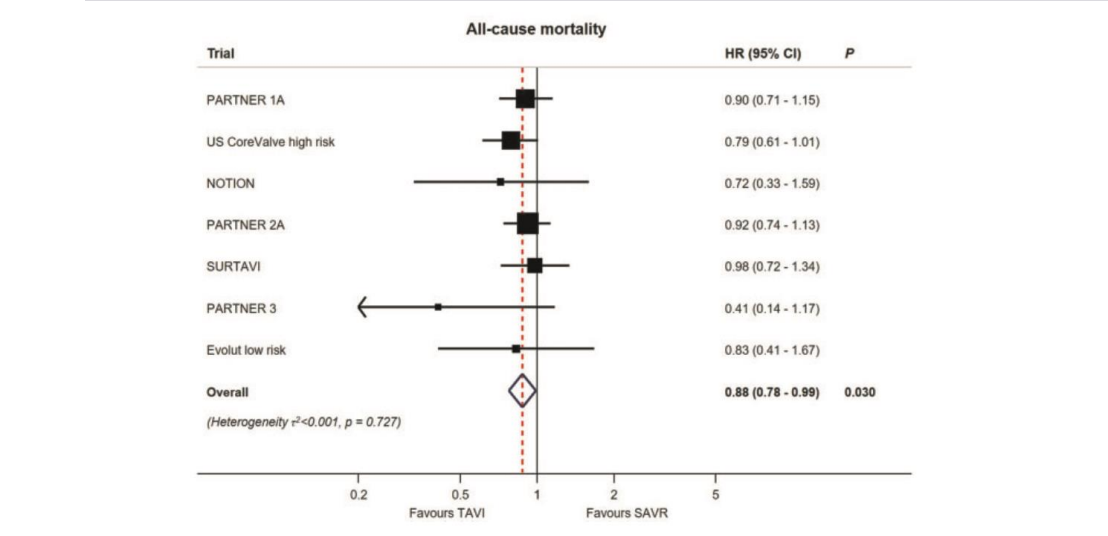


Appendix Figure 4. Time to Event Curves for A. All-Cause mortality, B. All Stroke, C. Composite of all-cause mortality and stroke

META-ANALYSIS. TOP OF PYRAMID OF EVIDENCE!

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis

European Heart Journal (2019) **0**, 1–11
doi:10.1093/eurheartj/ehz275



Conclusion Compared with SAVR, TAVI is associated with reduction in all-cause mortality and stroke up to 2 years irrespective of baseline surgical risk and type of THV system.

META-ANALYSIS. TOP OF PYRAMID OF EVIDENCE!

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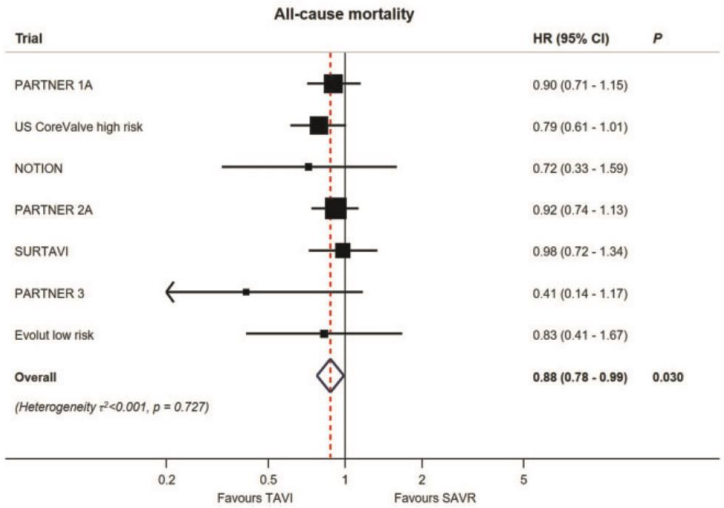
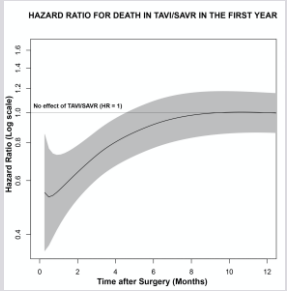


1) HRs and RR together?

ciple and utilized as-treated data, if ITT data were unavailable. Hazard ratios took precedence over risk ratios (RRs) to incorporate time-to-event data and allow for censoring. We derived RR using the number of events and participants in each treatment group when HR were unavailable. Disagreements between reviewers were resolved through consensus or third-party adjudication.

2) Proportionality of Hazards?



Not assessable by meta-analysis

META-ANALYSIS. TOP OF PYRAMID OF EVIDENCE!

Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis

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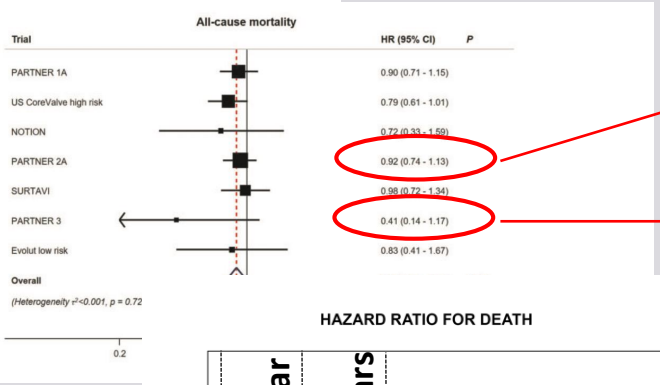
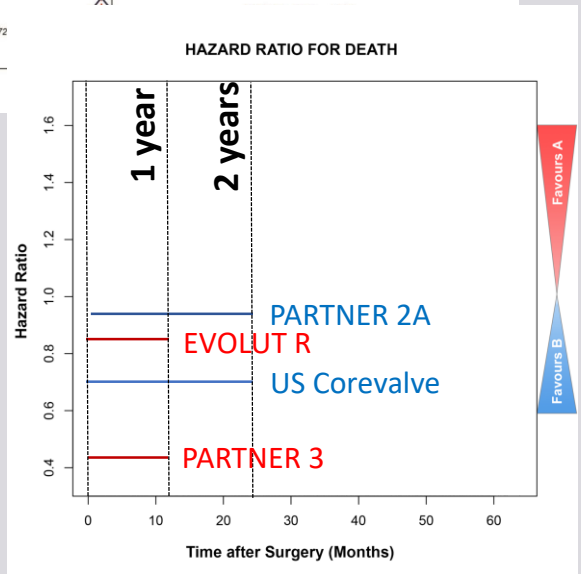
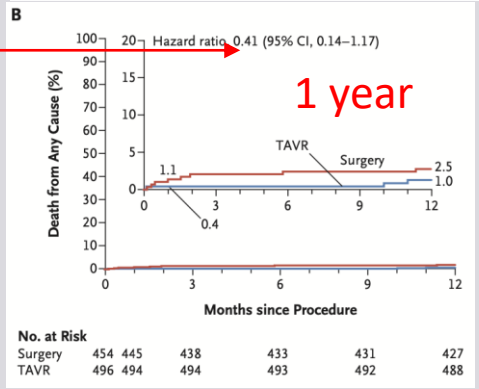






3) TOGETHER 1-2years ??

CONCLUSIONS

ARE YOU SURE THAT EVERYTHING THAT GLITTERS IS GOLD????

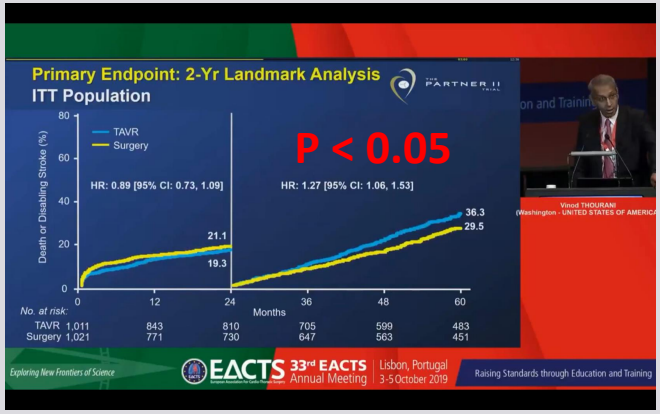
New perspectives: transcatheter aortic valve implantation in the year 2020

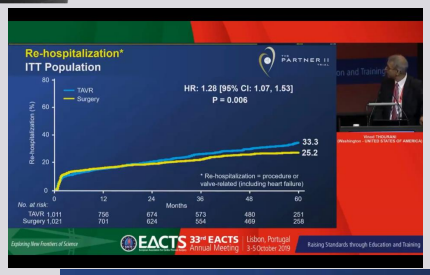
In 2020 transcatheter aortic valve implantation (TAVI) will be the default treatment in patients with aortic stenosis

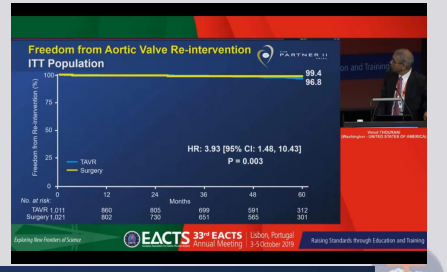
European Heart Journal (2015) **36**, 1200–1206

Why is this the case? Because more than half a million patients will have been treated by this technique worldwide, allowing its efficacy, safety, and durability to be assessed.

As a consequence of these good results of TAVI shown in randomized trials such as PARTNER 2 and SURTAVI and also in large dynamic registries, the technique will be performed in intermediate, and probably, low-risk patients'. Surgical valve replacement will be limited to patients with a contraindication to TAVI or those who need combined cardiac or aortic surgery.







- The current findings at 5 years mandate re-examination at later timepoints; follow-up has been extended in PARTNER 2A to 10 years