

Is TAVR with STS PROM < 3% better than SAVR?

Lessons learned from SURTAVI

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Disclosure Statement of Financial Interest

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Affiliation/Financial Relationship

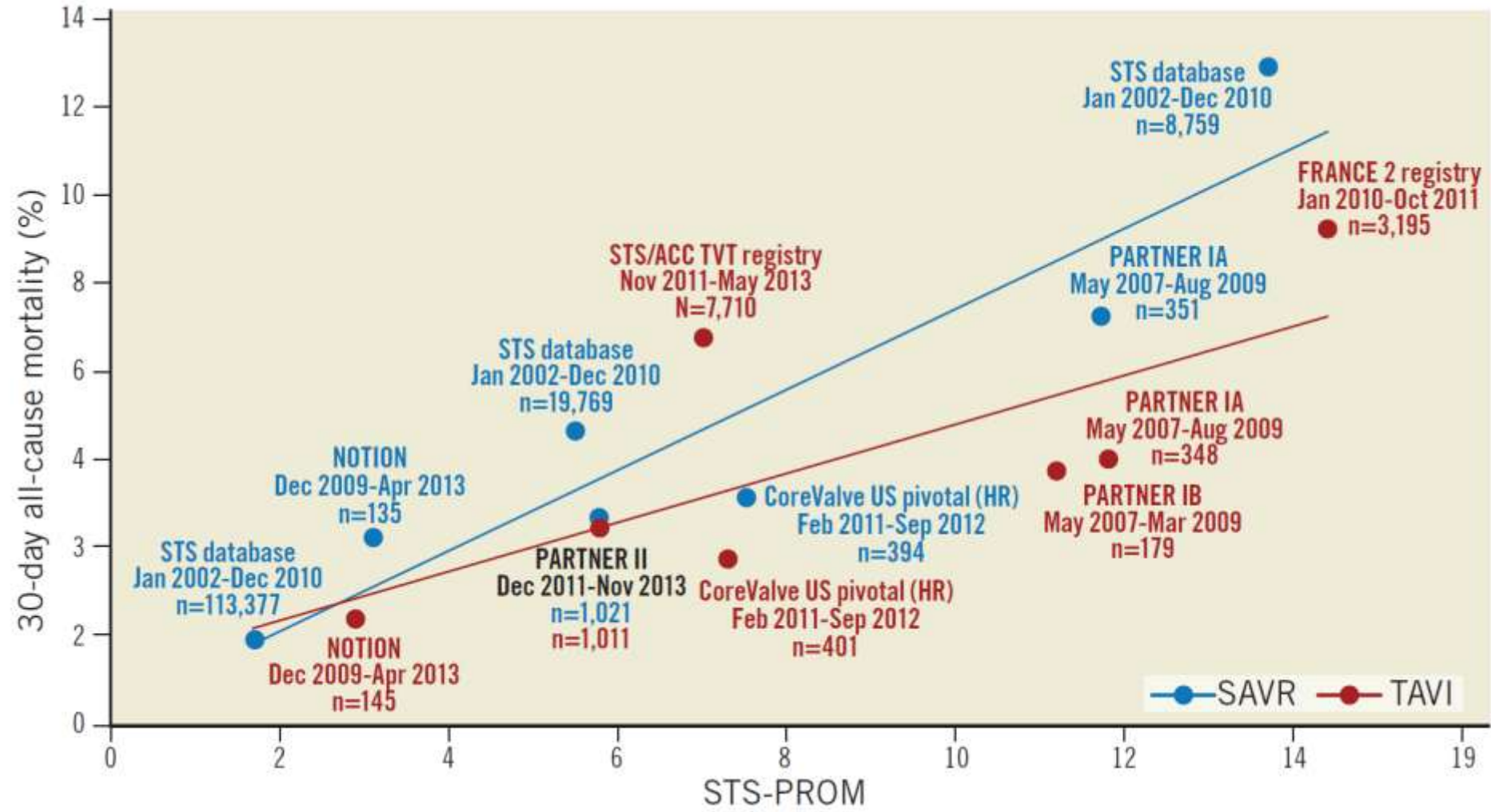
- Grant/Research Support
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Company

- Abbott
- Arterius
- Biosensors
- Medtronic
- Micell Technologies
- Philips/Volcano
- Sinomed
- Xeltis

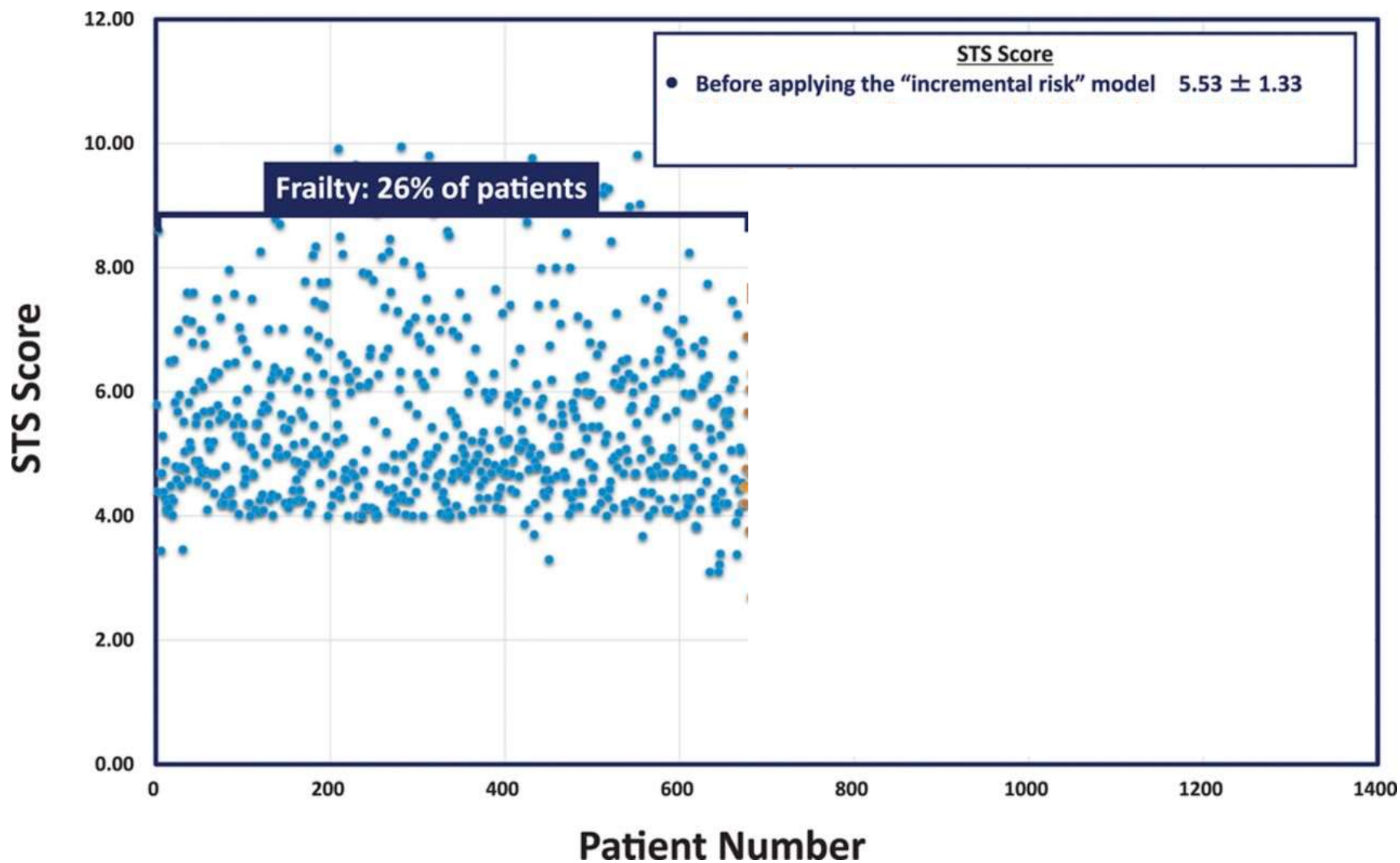
Is TAVR with STS PROM <3% better than SAVR?

30-day of observed all-cause mortality after TAVR and SAVR versus STS predicted rate of mortality



Is TAVR with STS PROM<3% better than SAVR?

The Society of Thoracic Surgeons (STS) score in SURTAVI trial.



Inclusion Criteria

Following agreement with the FDA (continued)

Version 6: (first patient was enrolled with version 3 on 19th Jun 2012)

- 1. Subject must have an STS mortality risk score $\geq 4\%$ and ≤ 10**

Medtronic SURTAVI Trial. Version 6.0

Version 8: (now applied in 75 centers; Nov 18th 2015)

- 1. Subject must have *co-morbidities such that Heart Team agrees predicted risk of operative mortality is $\geq 3\%$ at 30 days***

Medtronic SURTAVI Trial. Version 8.0

Heart Team Review and Decision (continued)

Version 8:

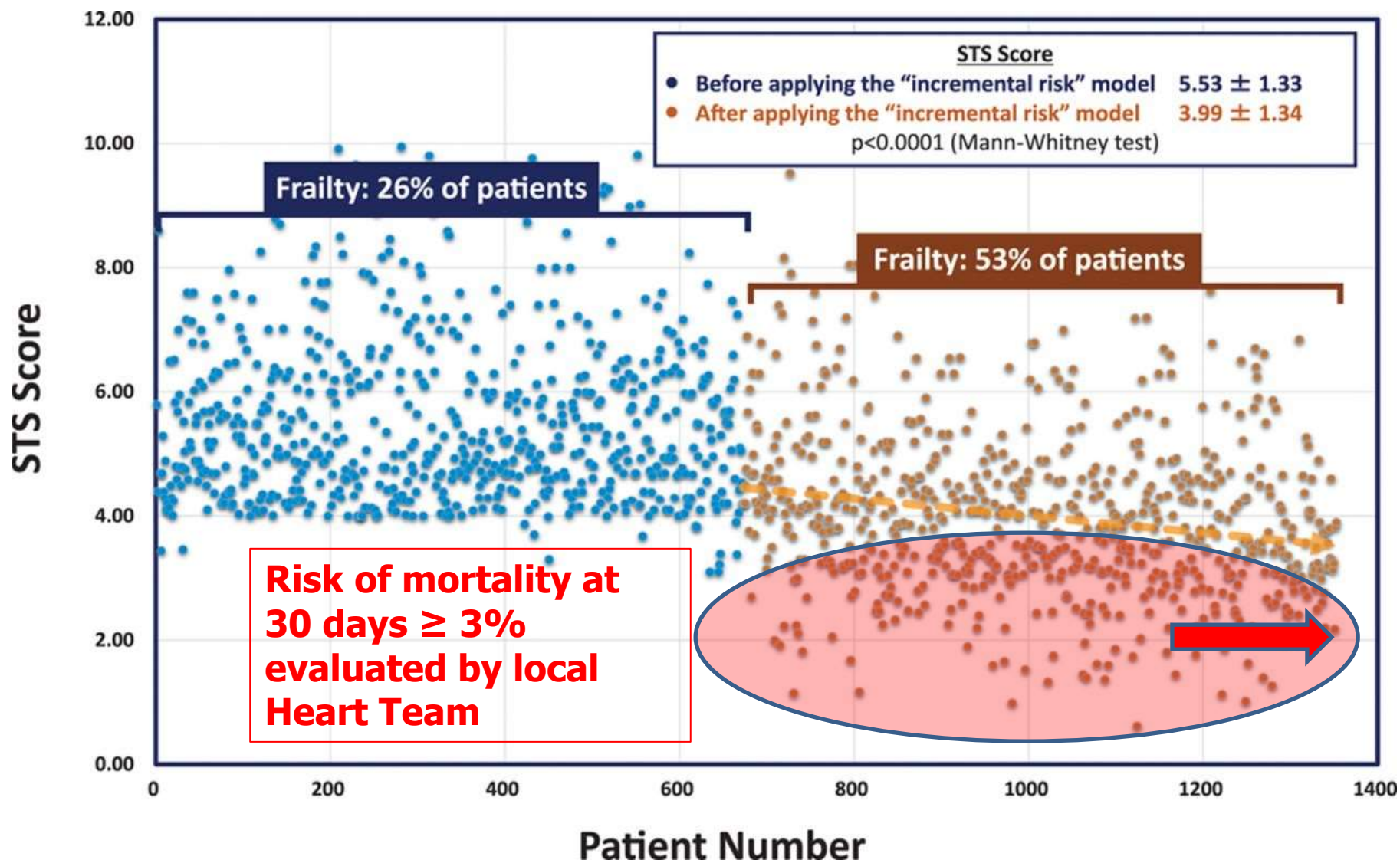
- Any additional risk factors not accounted for in the STS risk calculator that may increase the level of surgical risk:
 - Heart Team should consider the following potential incremental risks:
 - *Age ≥ 75*
 - BNP ≥ 550pg/mL or NT proBNP ≥ 3200pg/mL
 - *Prior Stroke/TIA*
 - FEV1 750-1000cc
 - Home / Supplemental oxygen
 - Nocturnal Bi-level Positive Airway Pressure
 - 5-Meter Gait Speed ≥ 6 seconds
 - Severe Diastolic Dysfunction (Grade III or IV)
 - Liver Disease (Child A or B)
 - Pulmonary Hypertension (systolic pressure 60-80mmHg)
 - *Frailty (e.g. BMI <21 kg/m², Albumin <3.3 g/dl, etc.)*
 - *Other risks, as deemed applicable*
 - Confirm the incremental risk, *as determined by the Heart Team, does not result in a risk definition higher than intermediate risk*

Medtronic SURTAVI Trial. Version 8.0

Yellow indicates it was already in STS

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The Society of Thoracic Surgeons (STS) score in SURTAVI trial.



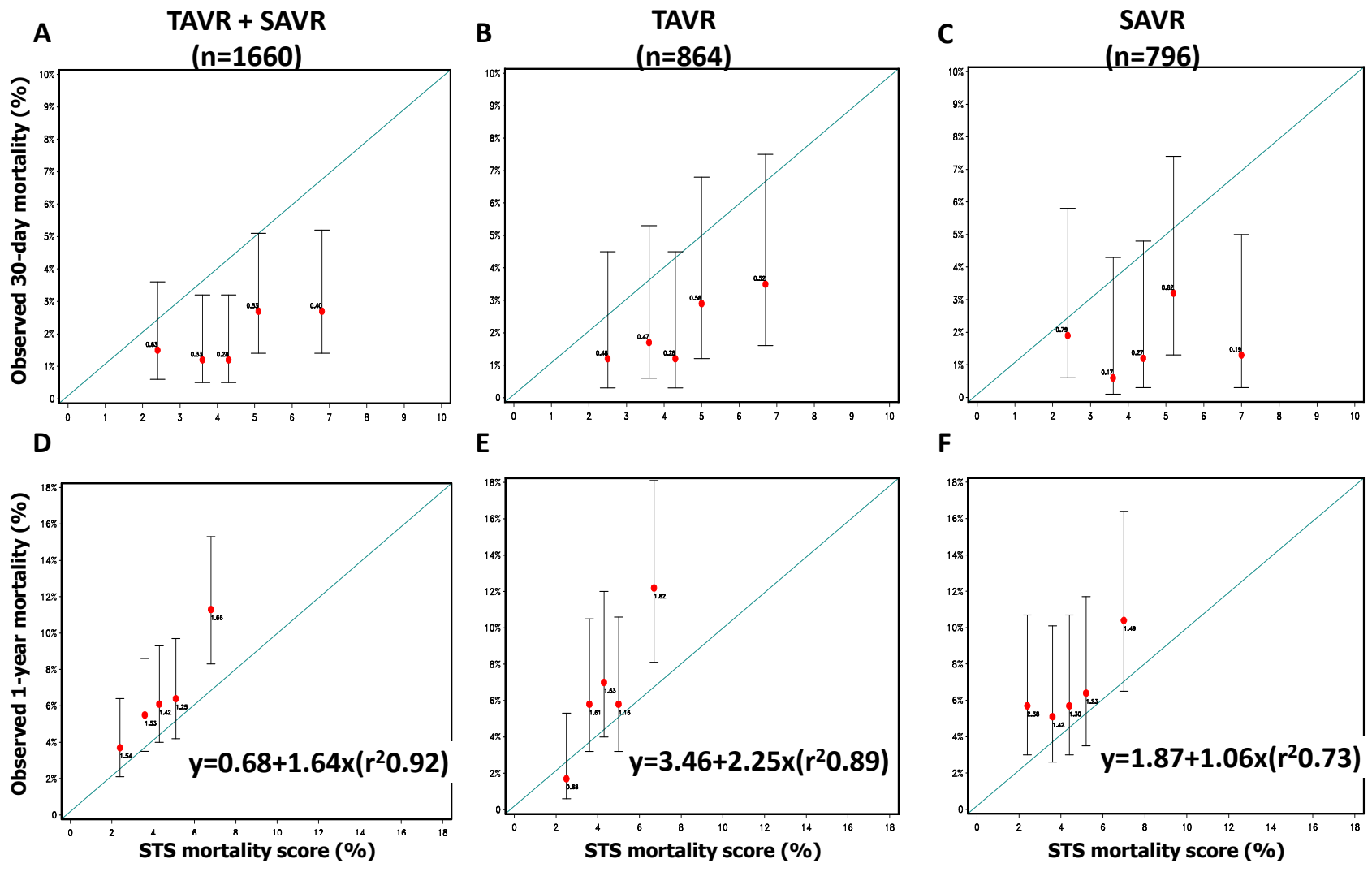
SURTAVI-Baseline characteristics

Potential incremental risks

Variable	Before version 8	After version 8
Age ≥ 75	86.0%	78.7% ↓
BNP>550 pg/ml	13.7%	14.6% ↗
NT proBNP ≥ 3200 pg/mL	13.7%	14.7% ↗
Severe diastolic dysfunction	1.6%	1.5% →
Pulmonary Hypertension (systolic pressure ≥ 60 mmHg)	3.0%	2.4% ↓
Prior Stroke/TIA	15.5%	11.2% ↓
Home/Supplemental oxygen	2.5%	2.2% ↘
Nocturnal Bi-PAP	4.5%	6.5% ↑
FEV1 750-1000 cc	2.4%	1.3% ↓
5-meter gait speed ≥ 6 seconds	25.9%	52.9% ↑
Liver disease (Child A, or B)	0.4%	0.4% →
Severe Aortic Calcification	8.0%	11.6% ↑

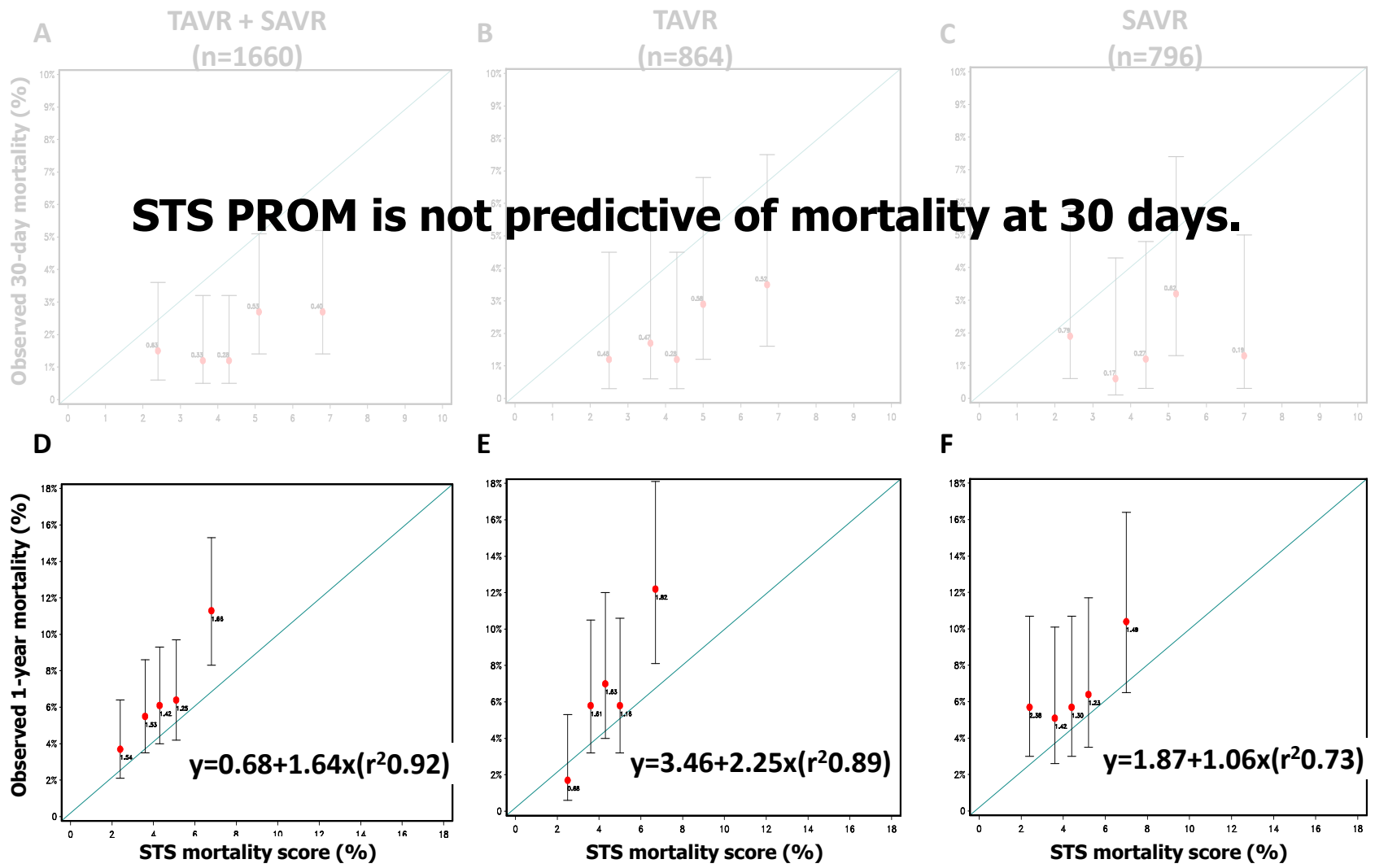
Is TAVR with STS PROM<3% better than SAVR?

Calibration - STS divided by quintiles 30-day and 1-year mortality (KM estimate)



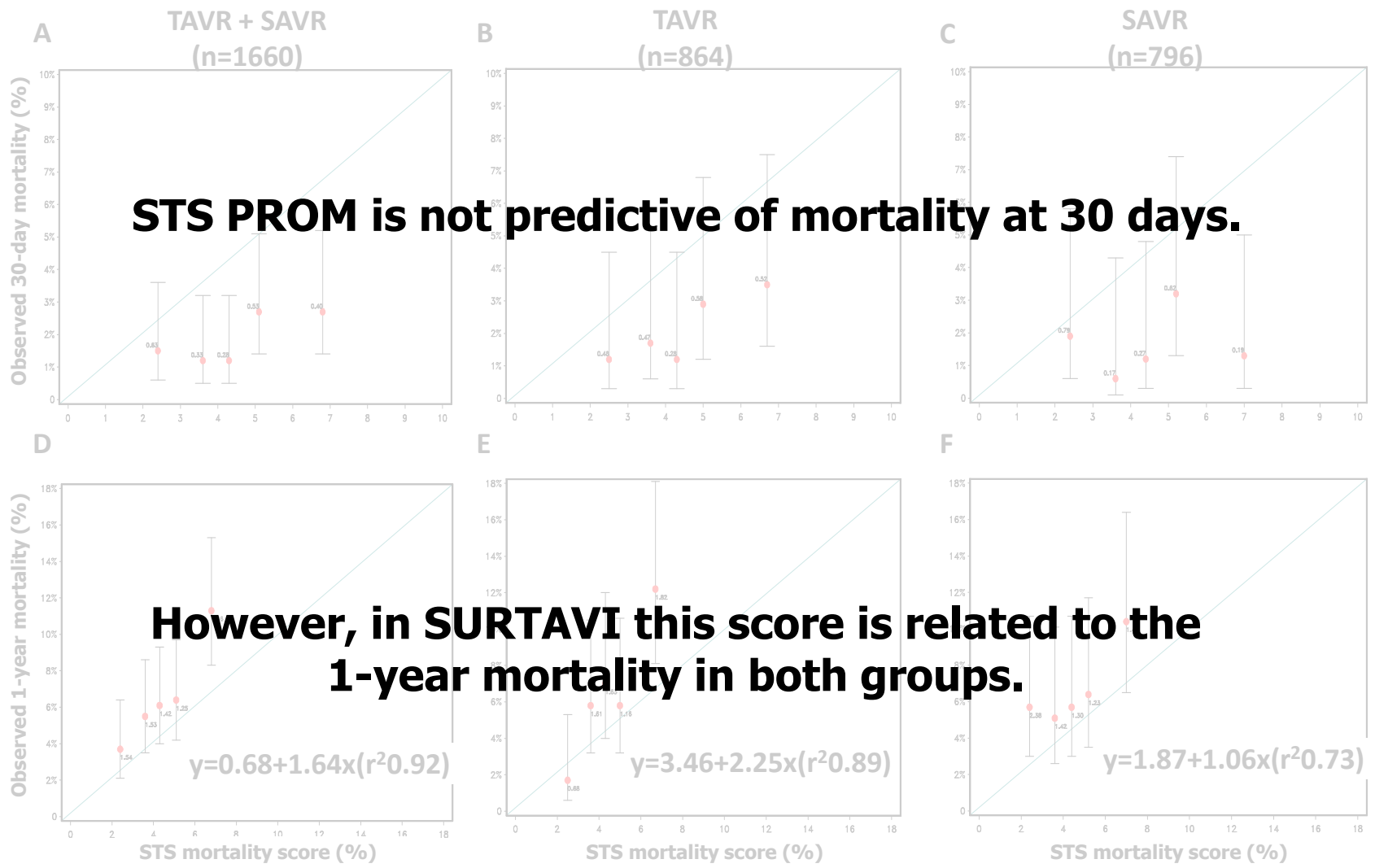
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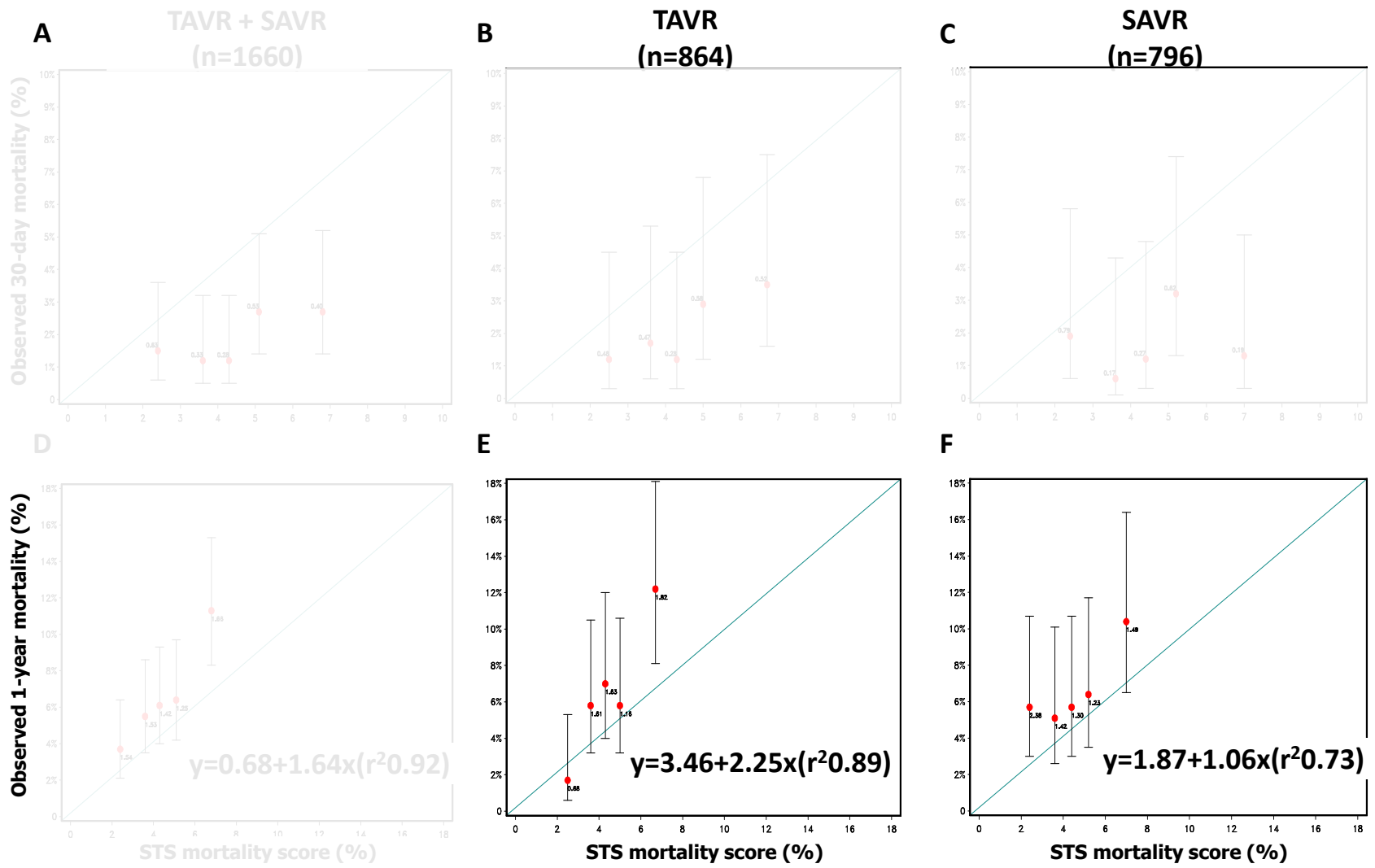
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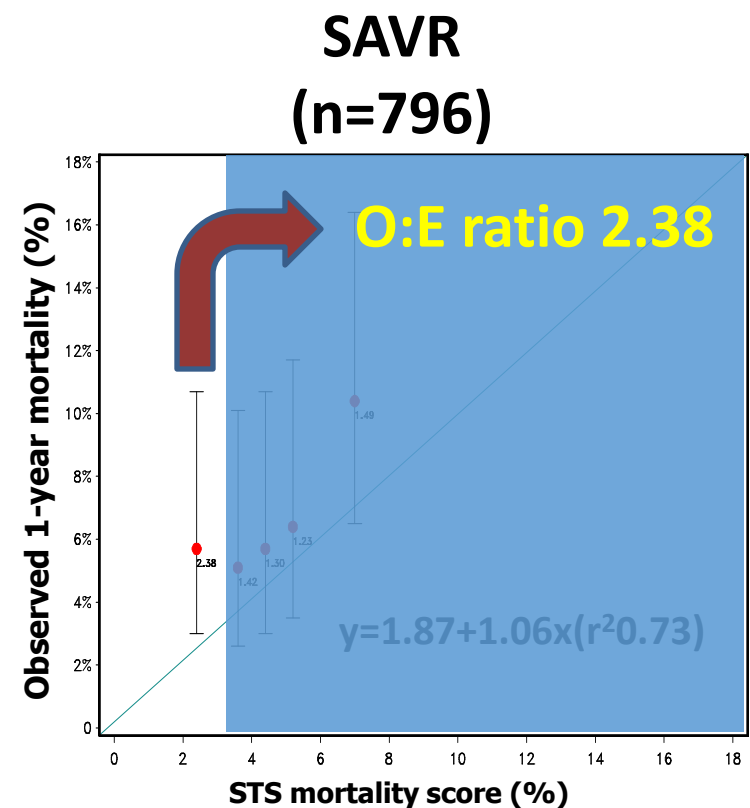
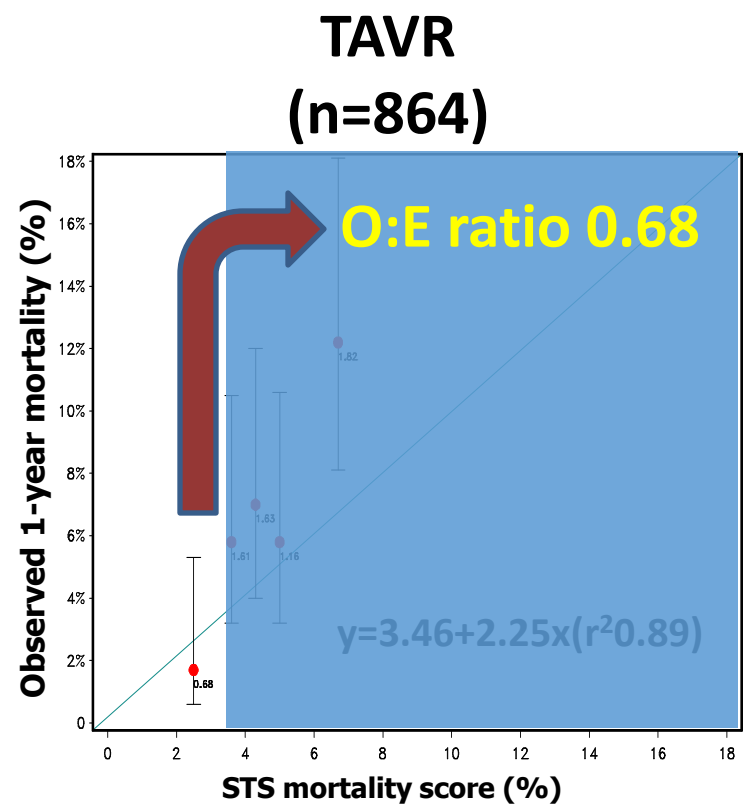
Is TAVR with STS PROM<3% better than SAVR?

Calibration - STS divided by quintiles 30-day and 1-year mortality (KM estimate)



Is TAVR with STS PROM<3% better than SAVR?

Calibration - STS divided by quintiles 1-year mortality TAVR vs. SAVR (KM estimate)



Observed over expected mortality, lower in TAVR than SAVR in the lower risk quintile

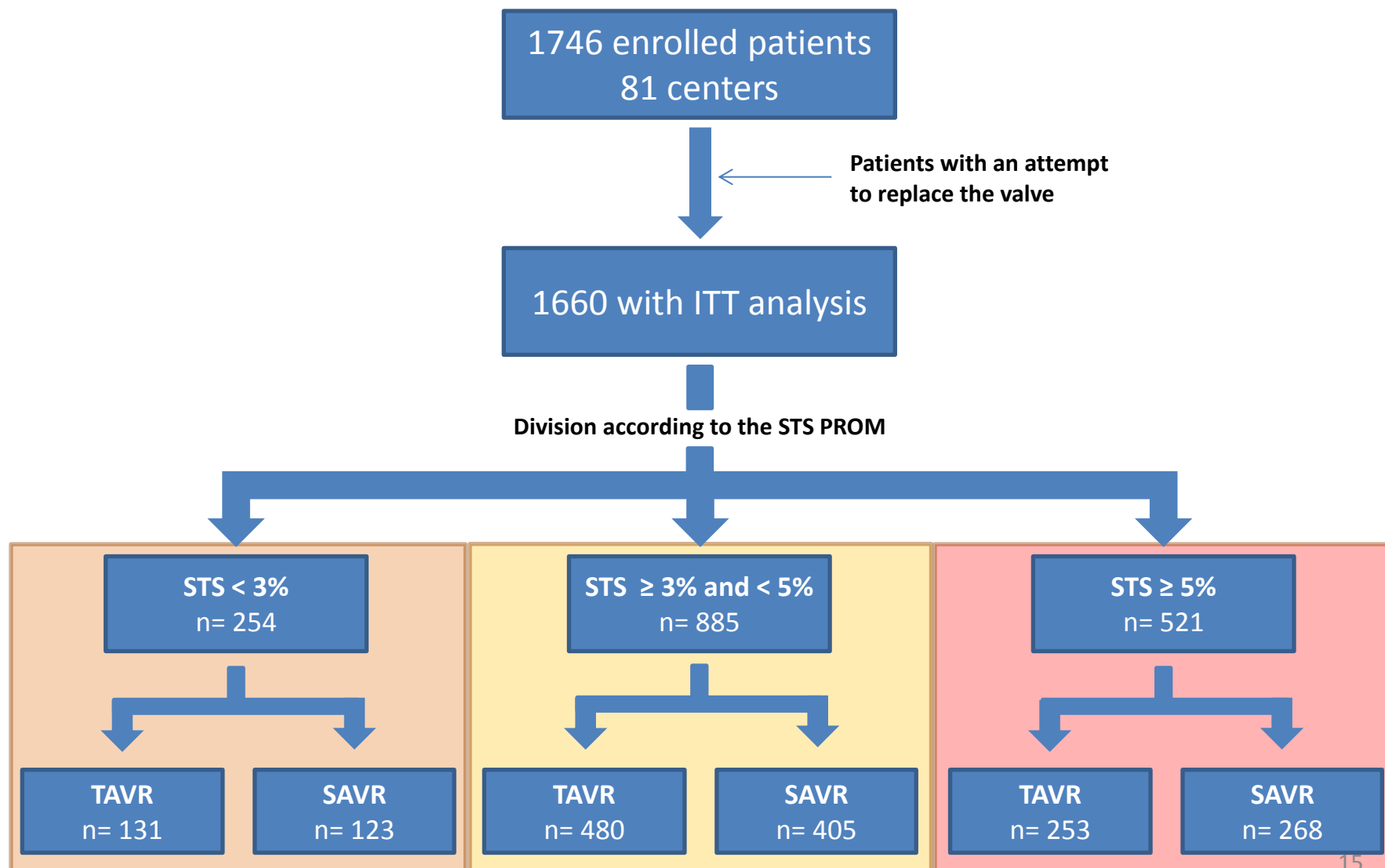
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There is a significant linear correlation between STS PROM and 1-year mortality.

STS Mortality Score (%)		STS Mortality Score (%)				
		1st quintile	2nd quintile	3rd quintile	4th quintile	5th quintile
SAVR + TAVR (n=1660)	n	331	332	333	332	332
	STS PROM (Mean ± SD)	2.4 ± 0.6	3.6 ± 0.3	4.3 ± 0.2	5.1 ± 0.3	6.8 ± 1.0
	1-Year Mortality - KM Estimate (n of subjects with events)	3.7% (12)	5.5% (18)	6.1% (20)	6.4% (21)	11.3% (37)
SAVR (n=796)	n	158	160	162	158	158
	STS PROM (Mean ± SD)	2.4 ± 0.6	3.6 ± 0.3	4.4 ± 0.2	5.2 ± 0.3	7.0 ± 1.0
	1-Year Mortality - KM Estimate (n of subjects with events)	5.7% (9)	5.1% (8)	5.7% (9)	6.4% (10)	10.4% (16)
TAVR (N=864)	n	173	172	173	173	173
	STS PROM (Mean ± SD)	2.5 ± 0.6	3.6 ± 0.2	4.3 ± 0.2	5.0 ± 0.3	6.7 ± 1.0
	1-Year Mortality - KM Estimate (n of subjects with events)	1.7% (3)	5.8% (10)	7.0% (12)	5.8% (10)	12.2% (21)

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Flowchart for the analysis of SURTAVI with STSPROM <3%.



Is TAVR with STS PROM<3% better than SAVR?

In each risk stratum (STS) there is no significant differences between SAVR and TAVR for 17 baseline demographic characteristic

	STS <3%			STS ≥3 to < 5%			STS ≥ 5%		
	TAVR	SAVR	p-value	TAVR	SAVR	p-value	TAVR	SAVR	p-value
Number of patients	131	123	-	480	405	-	253	268	-
Age, years	75.1 ± 6.5	75.4 ± 5.5	0.67	80.0 ± 5.7	79.9 ± 5.7	0.76	82.3 ± 5.6	81.4 ± 6.0	0.08
Male sex	89 (67.9)	84 (68.3)	0.95	284 (59.2)	227 (56.0)	0.35	125 (49.4)	127 (47.4)	0.64
Body surface area, m ²	2.0 ± 0.2	2.0 ± 0.2	0.84	1.9 ± 0.2	1.9 ± 0.2	0.82	1.9 ± 0.2	1.9 ± 0.2	0.23
STS PROM, %	2.3 ± 0.5	2.3 ± 0.5	0.99	4.0 ± 0.6	4.0 ± 0.6	0.56	6.2 ± 1.0	6.3 ± 1.1	0.17
Diabetes mellitus	30 (22.9)	21 (17.1)	0.25	163 (34.0)	144 (35.6)	0.62	102 (40.3)	112 (41.8)	0.73
Serum creatinine >2 mg/dl	0 (0.0)	1 (0.8)	0.48	6 (1.3)	5 (1.2)	0.98	8 (3.2)	11 (4.1)	0.57
Prior stroke	6 (4.6)	9 (7.3)	0.36	31 (6.5)	28 (6.9)	0.79	20 (7.9)	20 (7.5)	0.85
Peripheral vascular disease	25 (19.1)	18 (14.6)	0.34	140 (29.2)	112 (27.7)	0.62	101 (39.9)	108 (40.3)	0.93
Permanent pacemaker/ICD	9 (6.9)	6 (4.9)	0.50	47 (9.8)	35 (8.6)	0.56	31 (12.3)	38 (14.2%)	0.52
Coronary artery disease	63 (48.1)	63 (51.2)	0.62	306 (63.8)	251 (62.0)	0.59	172 (68.0)	197 (73.5)	0.17
Prior CABG	10 (7.6)	9 (7.3)	0.92	74 (15.4)	67 (16.5)	0.65	54 (21.3)	61 (22.8)	0.70
Prior PCI	28 (21.4)	18 (14.6)	0.16	96 (20.0)	85 (21.0)	0.72	60 (23.7)	66 (24.6)	0.81
Prior myocardial infarction	14 (10.7)	10 (8.1)	0.49	68 (14.2)	59 (14.6)	0.87	43 (17.0)	42 (15.7)	0.68
History of arrhythmia	36 (27.5)	34 (27.6)	0.98	150 (31.3)	120 (29.6)	0.60	89 (35.2)	96 (35.8)	0.88
Atrial fibrillation / flutter	33 (25.2)	28 (22.8)	0.65	129 (26.9)	93 (23.0)	0.18	81 (32.0)	90 (33.6)	0.70
NYHA Class III/IV	53 (40.5)	60 (48.8)	0.18	300 (62.5)	235 (58.0)	0.17	167 (66.0)	168 (62.7)	0.43
Body mass index <21 kg/m ²	2 (1.5)	6 (4.9)	0.16	11 (2.3)	10 (2.5)	0.86	7 (2.8)	5 (1.9)	0.49

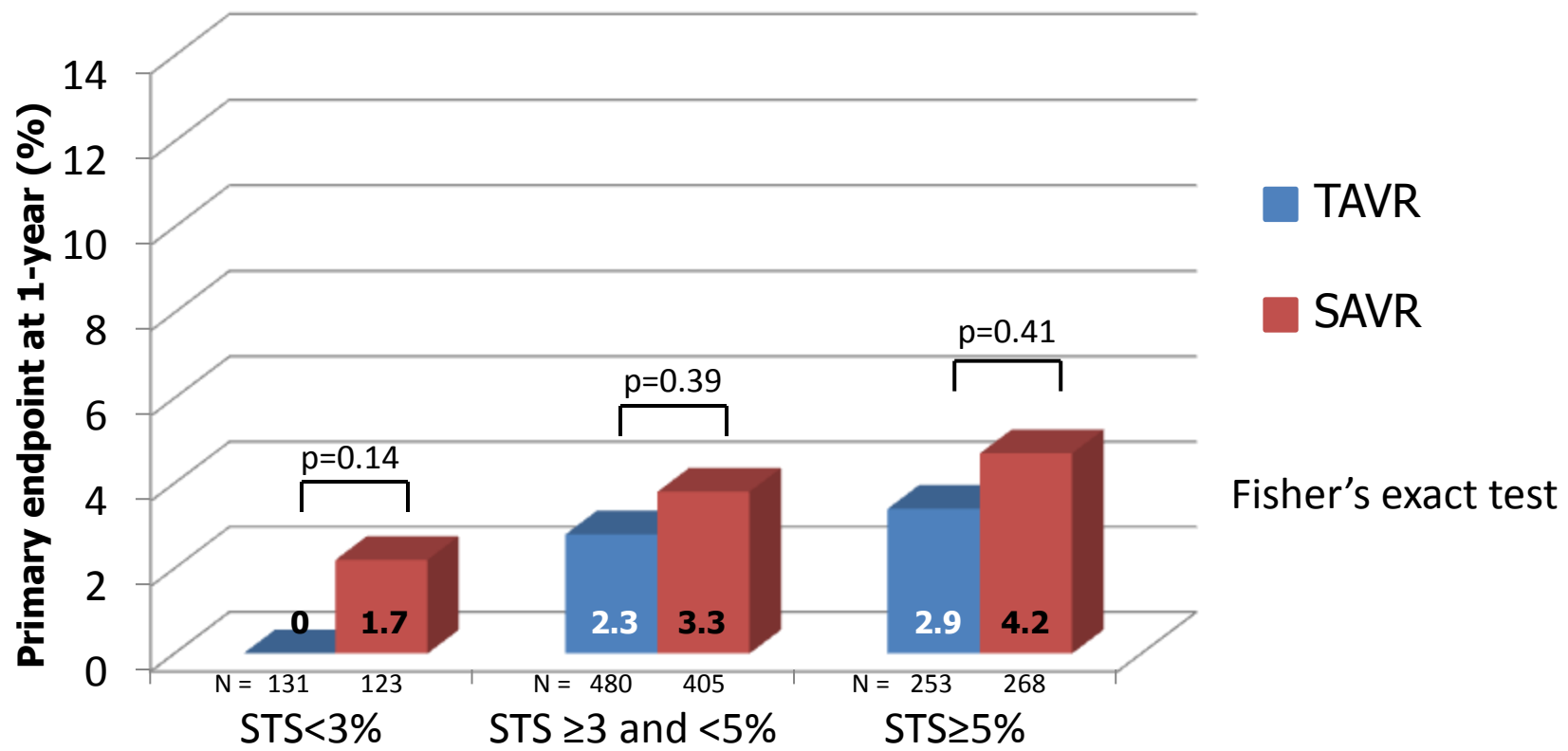
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There is a significant increase in age, risk factors and comorbidities following the risk stratum

	STS <3%	STS ≥ 3 to < 5%	STS $\geq 5\%$	p-value
	TAVR + SAVR	TAVR + SAVR	TAVR + SAVR	
Number of patients	254	885	521	
Age, years	75.2	80.0	81.8	< 0.0001
Male sex, %	68.1	57.7	48.4	< 0.0001
STS PROM, %	2.3	4.0	6.3	< 0.0001
Diabetes mellitus, %	20.1	34.7	41.1	< 0.0001
Serum <u>creatinine</u> >2 mg/dl, %	0.4	1.2	3.6	0.0016
Prior stroke, %	5.9	6.7	7.7	0.6195
Peripheral vascular disease, %	16.9	28.5	40.1	< 0.0001
Permanent pacemaker/ICD, %	5.9	9.3	13.2	0.0034
Coronary artery disease, %	49.6	62.9	70.8	< 0.0001
Prior CABG, %	7.5	15.9	22.1	< 0.0001
Prior PCI, %	18.1	20.5	24.2	0.1048
Prior myocardial infarction, %	9.4	14.4	16.3	0.0364
History of arrhythmia, %	27.6	30.5	35.5	0.0477
Atrial fibrillation / flutter, %	24.0	25.1	32.8	0.0031
NYHA Class III/IV, %	44.5	60.5	64.3	< 0.0001

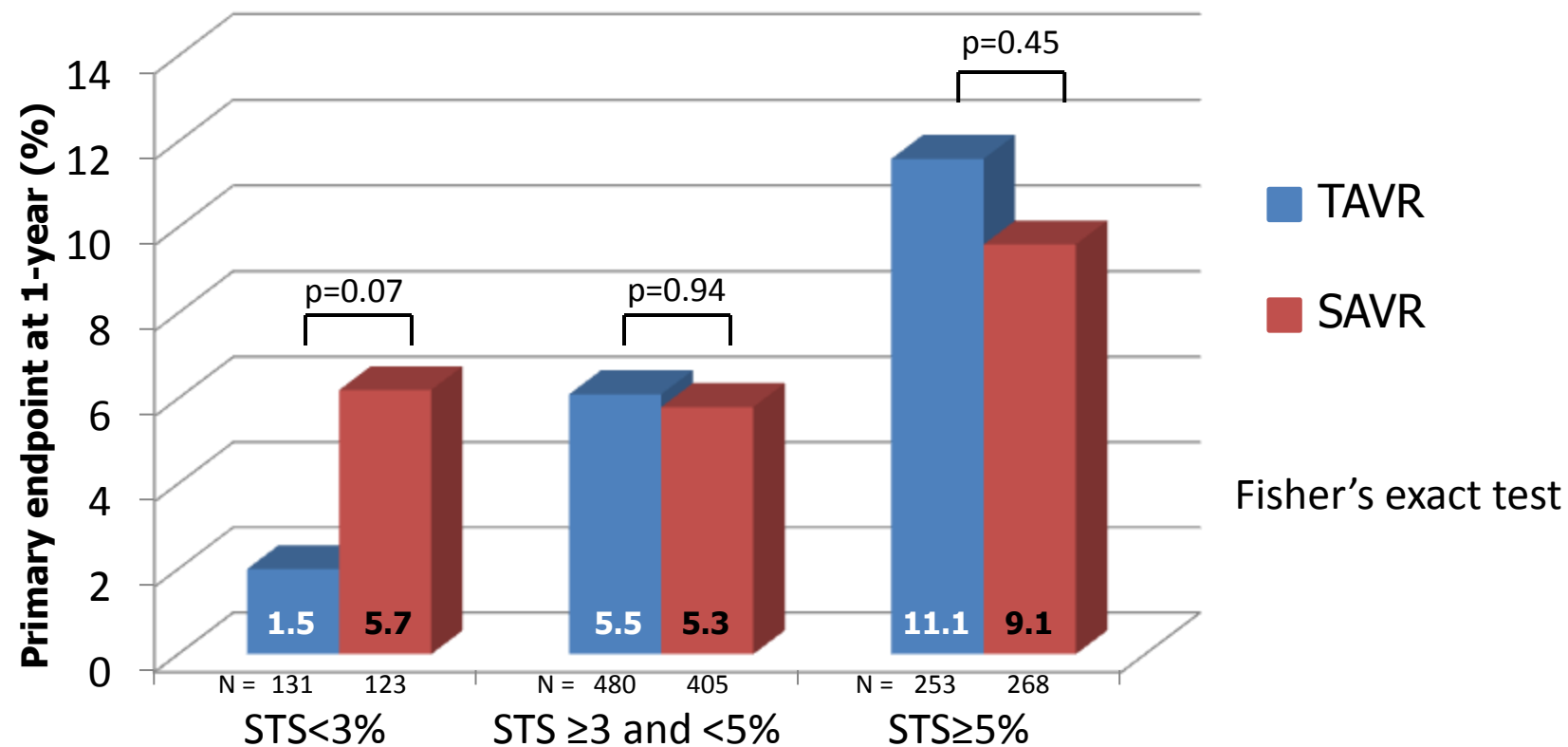
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Disabling stroke at 1-year (SURTAVI)



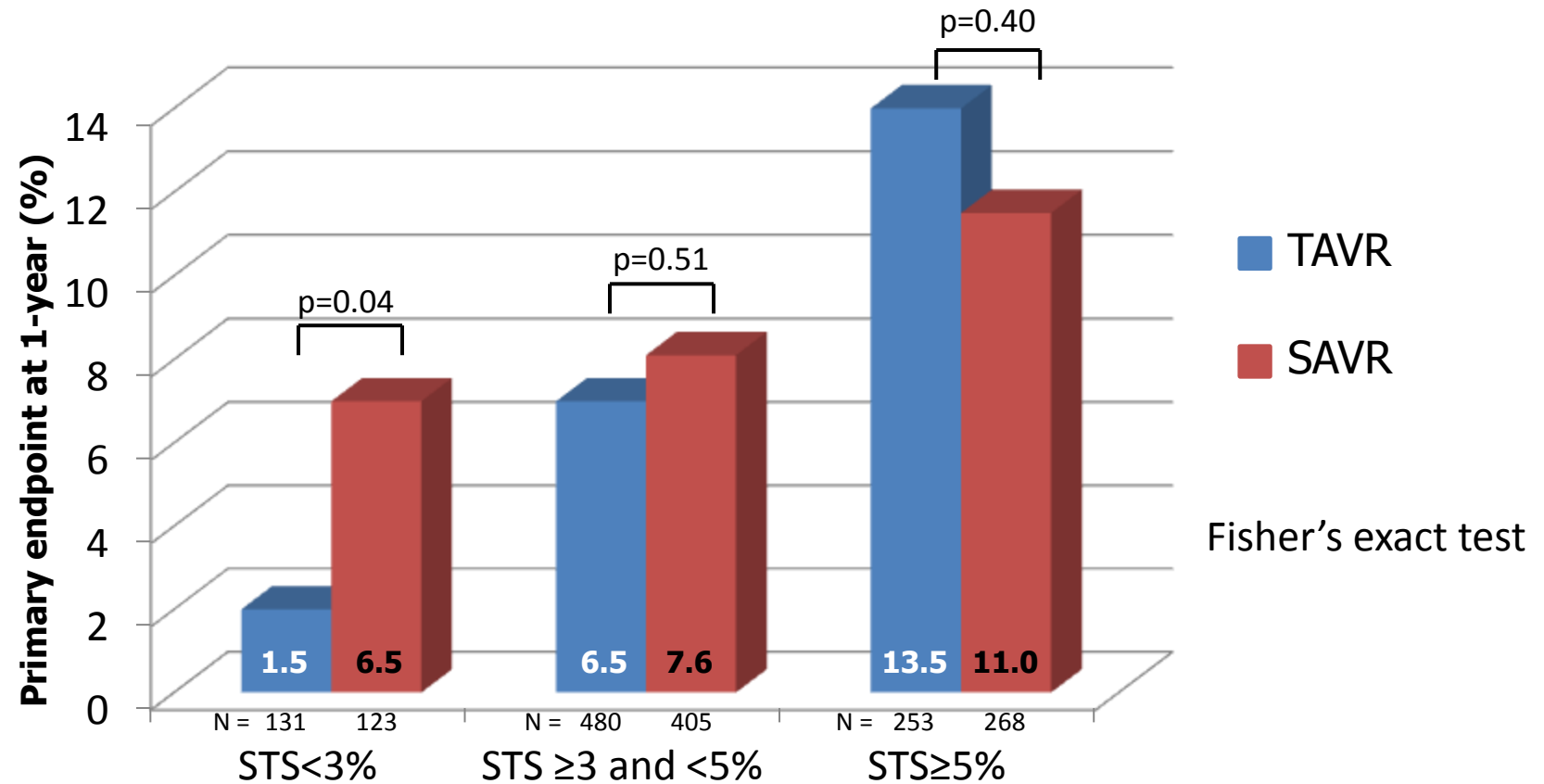
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All-cause death at 1-year (SURTAVI)



Is TAVR with STS PROM<3% better than SAVR?

All-cause death or disabling stroke at 1-year (SURTAVI)



Is TAVR with STS PROM<3% better than SAVR?

Conclusions

- When compared to SAVR with STS score of less than 3% in the context of a randomized trial :
 - ✓ TAVR could achieve a superior primary endpoint, traditionally based on all cause death or disabling stroke.
- However, this would request a prospective, adequately powered trial using specifically the inclusion criteria of STS-PROM of less than 3%.

Medtronic Transcatheter Aortic Valve Replacement in Low Risk Patients

ClinicalTrials.gov Identifier: NCT02701283

Study Design

Study Type	Interventional (Clinical Trial)
Estimated Enrollment	1200 participants
Allocation	Randomized
Intervention Model	Parallel Assignment
Masking	None (Open Label)
Primary Purpose	Treatment
Official Title	Transcatheter Aortic Valve Replacement With the Medtronic Transcatheter Aortic Valve Replacement System In Patients at Low Risk for Surgical Aortic Valve Replacement
Study Start Date	March 2016
Estimated Primary Completion Date	March 2018
Estimated Study Completion Date	March 2026

Recruitment Status : Recruiting
First Posted : March 8, 2016
Last Update Posted : November 17, 2017

The PARTNER 3 - Trial - The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients With Aortic Stenosis (P3)

ClinicalTrials.gov Identifier: NCT02675114

Study Design

Study Type	Interventional (Clinical Trial)
Estimated Enrollment	1328 participants
Allocation	Randomized
Intervention Model	Parallel Assignment
Masking	None (Open Label)
Primary Purpose	Treatment
Official Title	A Prospective, Randomized, Controlled, Multi-Center Study to Establish the Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low Risk Patients Who Have Severe, Calcific, Aortic Stenosis Requiring Aortic Valve Replacement
Actual Study Start Date	March 2016
Estimated Primary Completion Date	October 2018
Estimated Study Completion Date	March 2027

Recruitment Status : Recruiting
First Posted : February 5, 2016
Last Update Posted : November 22, 2017

Is TAVR with STS PROM<3% better than SAVR?

The Society of Thoracic Surgeons (STS) score overestimates the 30-day mortality after TAVR

- The STS score has been designed for risk stratification and prediction of 30-day mortality after cardiac surgery in general
- Since TAVR originated in patients who were inoperable or at high-risk for SAVR, the criteria for risk stratification were naturally borrowed from the surgical field.

