



IX Congresso
Novas Fronteiras
em Medicina
Cardiovascular

22 a 24 de Fevereiro 2019

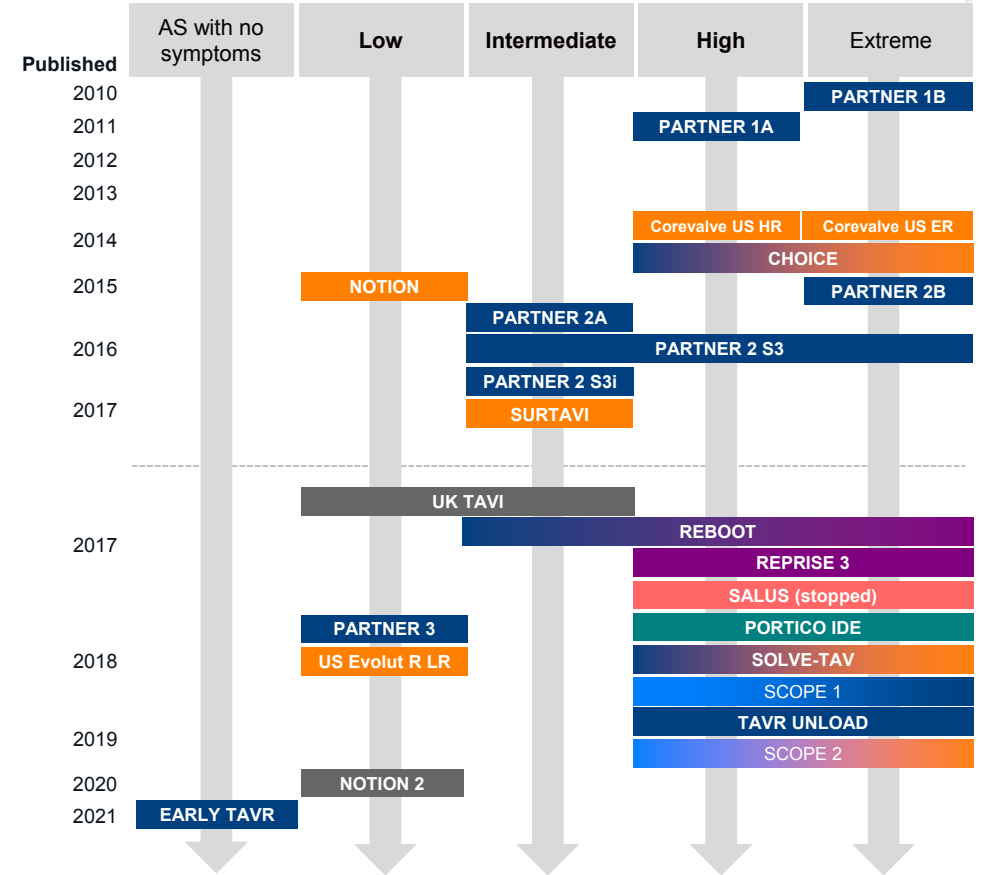
The Village Praia
D'El Rey - Óbidos

THE EXTENSION OF TAVR TO LOW RISK PATIENTS: ARE WE THERE?

E. Infante de Oliveira

Symptomatic AS: SAVR Risk 

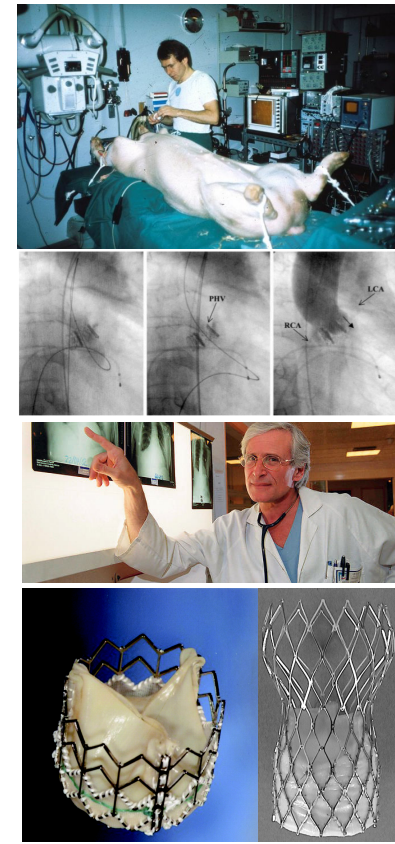
Pipeline of TAVR Trials across the spectrum of aortic stenosis



Investigational devices

-  Edwards Sapien/Sapien XT/S3
-  Medtronic CoreValve/Evolut R
-  Boston Lotus
-  Direct Flow Medical Direct Flow
-  Abbott Vascular Portico
-  Symetis Acurate Neo
-  Any available TAVR system

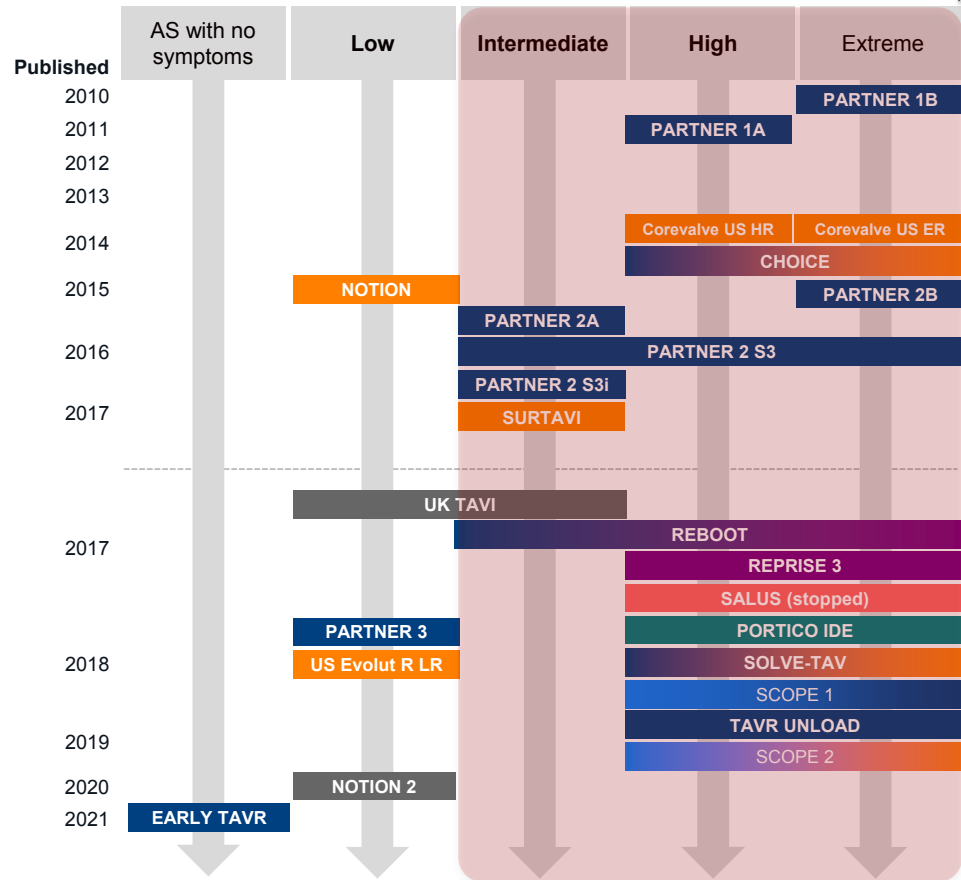
24 TAVR RCTs



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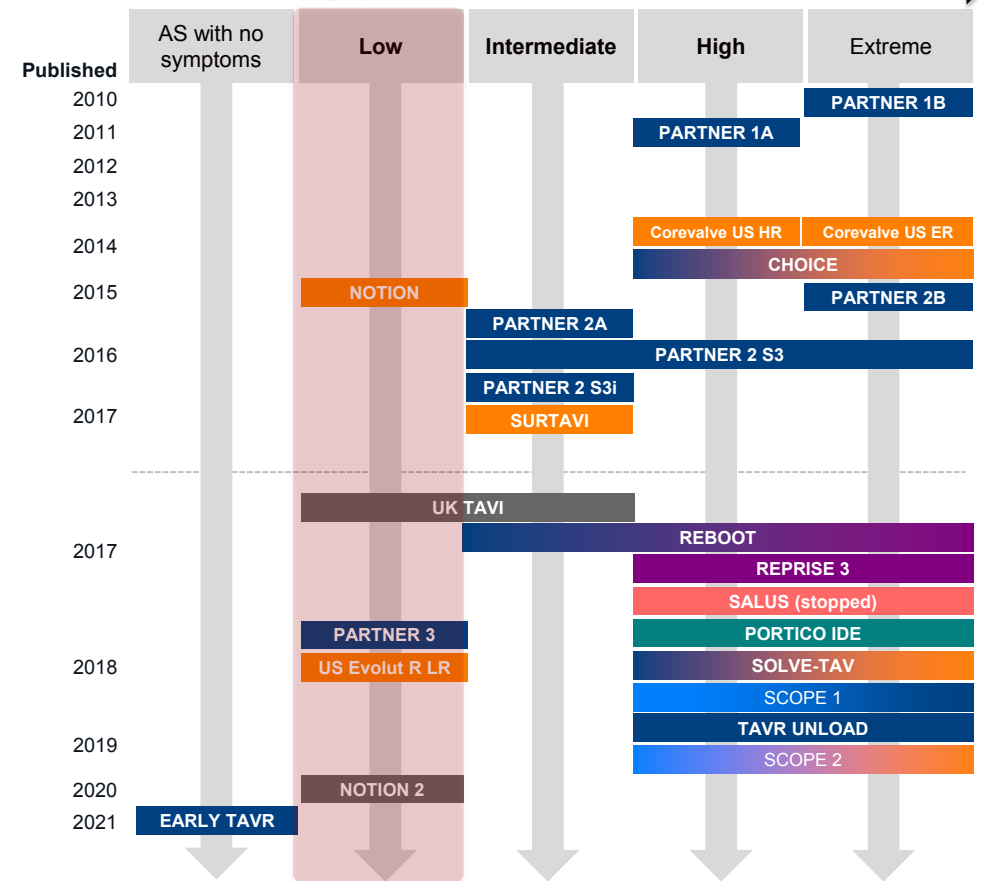
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**24 TAVR
RCTs**



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24 TAVR RCTs



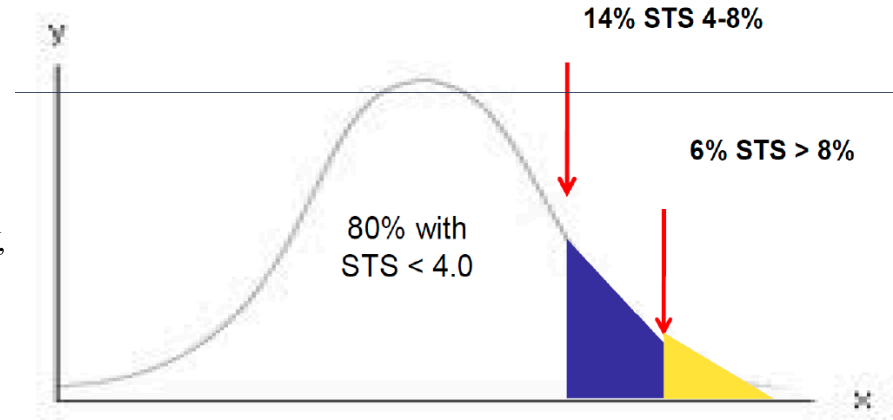
THE EXTENSION OF TAVR TO LOW RISK PATIENTS: ARE WE THERE?



Contemporary Real World Outcomes of Surgical Aortic Valve replacement in 141,905 low-risk, intermediate-risk and high risk patients.

Thourani VH, Suri RM, Gunter RL, Sheng S, O'Brien SM, Ailawai G, Szeto, WY, Dewey TM, Guyton RA, Bavaria JE, Babaliaros V, Gammie JS, Svensson L, Williams M, Badwar V, Mack MJ

Annals of Thoracic Surgery 2015; 99 (1) 55-61



Patient Population

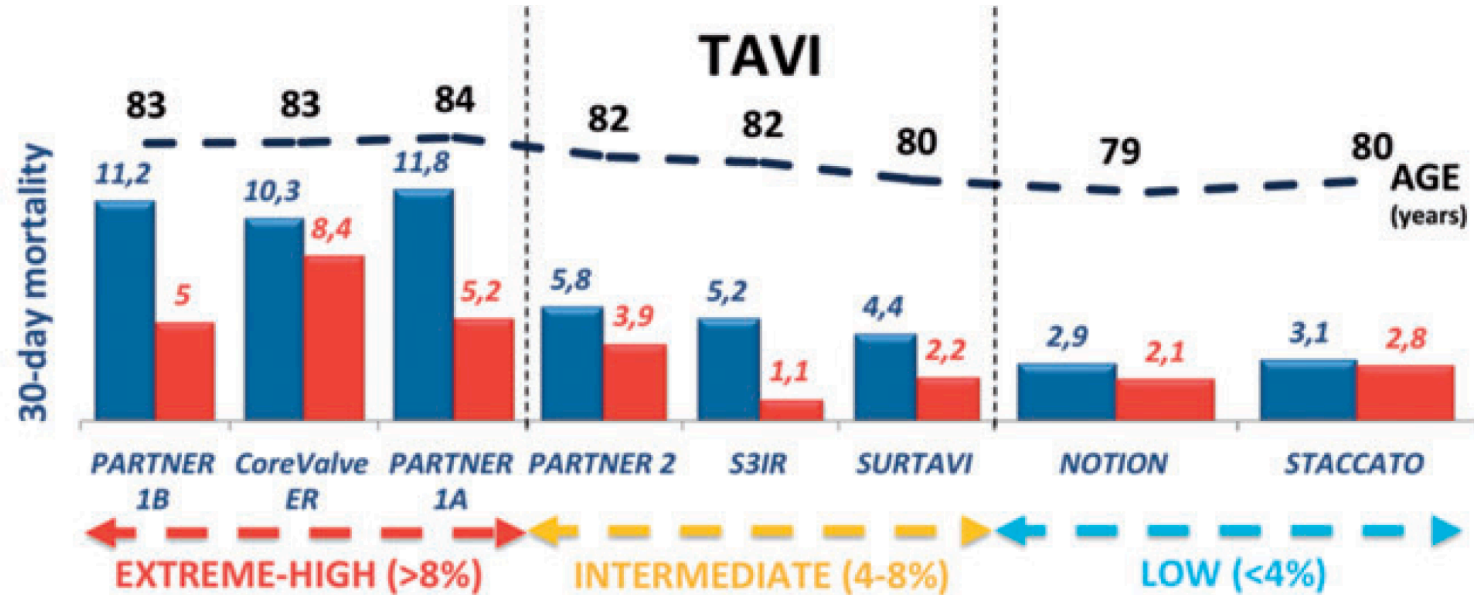
- 80% of “Low Risk” pts based on an STS < 4%
- Does not account for non traditional risk factors of co-morbidity, frailty, disability





TAVT trials – all same age!

European Heart Journal (2019) 40, 414–421



TAVR for low risk pts

- Short term outcomes
- Long term durability
- Economical impact (cost-effectiveness)



NOTION trial

Enrollment Criteria

Main inclusion criteria

- Severe aortic valve stenosis
- Age ≥ 70 years
- Life expectancy ≥ 1 year
- Suitable for self-expanding TAVR and SAVR

Main exclusion criteria

- Severe CAD
- Severe other valve disease
- Prior heart surgery
- Need for acute treatment
- Recent stroke or myocardial infarction
- Severe lung disease
- Severe renal disease



NOTION trial

Baseline Characteristics

Characteristic, % or mean $\pm$ SD	TAVR n=145	SAVR n=135	p-value
Age (yrs)	79.2 $\pm$ 4.9	79.0 $\pm$ 4.7	0.71
Male	53.8	52.6	0.84
STS score	2.9 $\pm$ 1.6	3.1 $\pm$ 1.7	0.30
STS score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 $\pm$ 4.0	8.9 $\pm$ 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

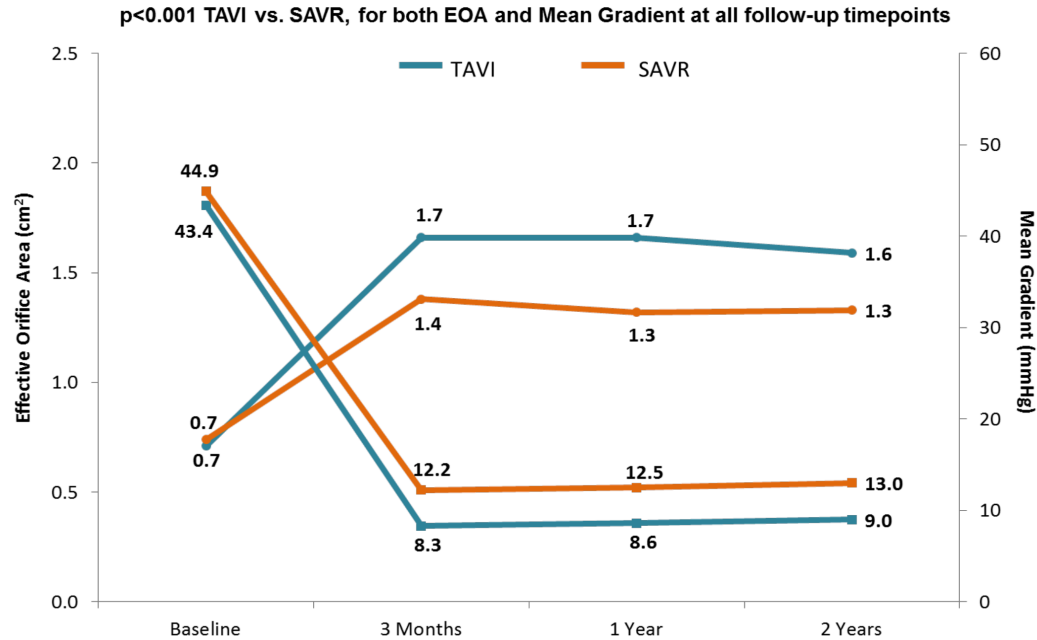


NOTION trial

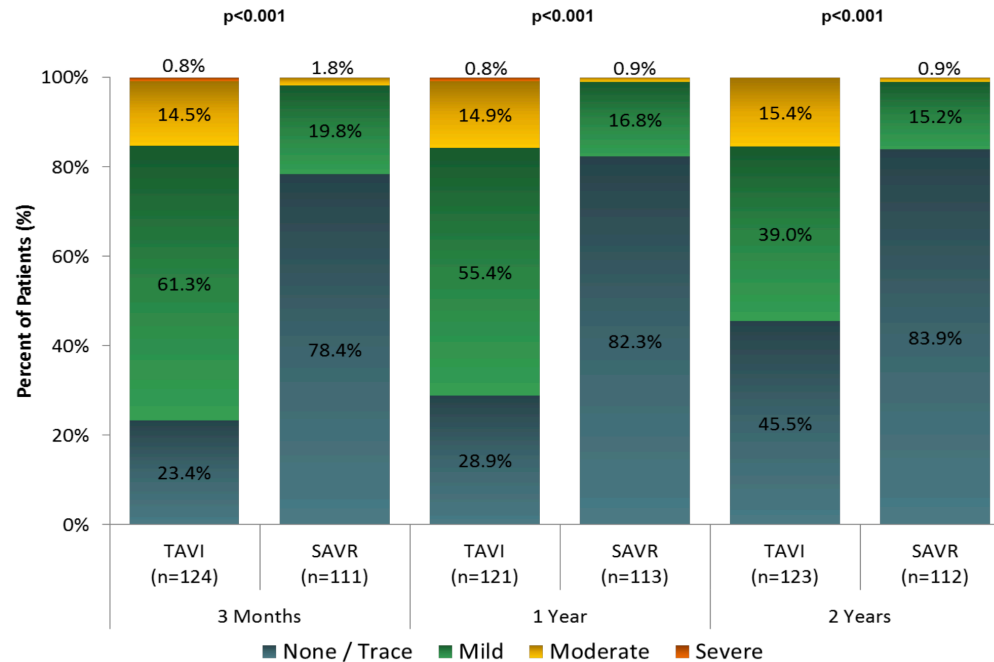
Outcome, %	1 Year			2 Years		
	TAVI	SAVR	p-value	TAVI	SAVR	p-value
Death, any cause	4.9	7.5	0.38	8.0	9.8	0.54
Death, cardiovascular	4.3	7.5	0.25	6.5	9.1	0.40
Stroke	2.9	4.6	0.44	3.6	5.4	0.46
TIA	2.1	1.6	0.71	6.0	3.3	0.30
Myocardial infarction	3.5	6.0	0.33	5.1	6.0	0.69
Atrial fibrillation	21.2	59.4	<0.001	22.7	60.2	<0.001
Pacemaker	38.0	2.4	<0.001	41.3	4.2	<0.001
Aortic valve re-intervention	0.0	0.0	na	0.0	0.0	na



NOTION trial – valve performance

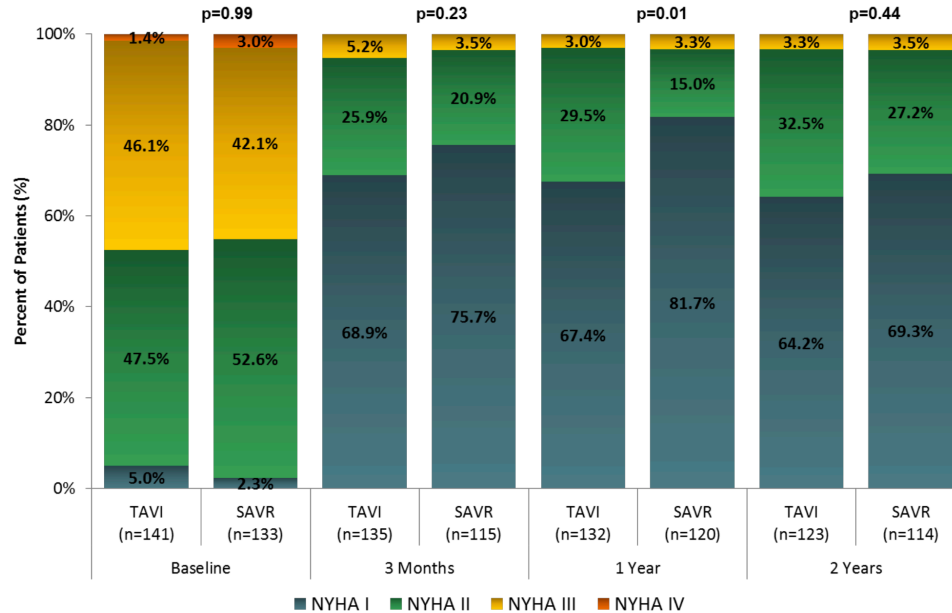


NOTION trial – Valve regurgitation / PVL





NOTION trial – NYHA class



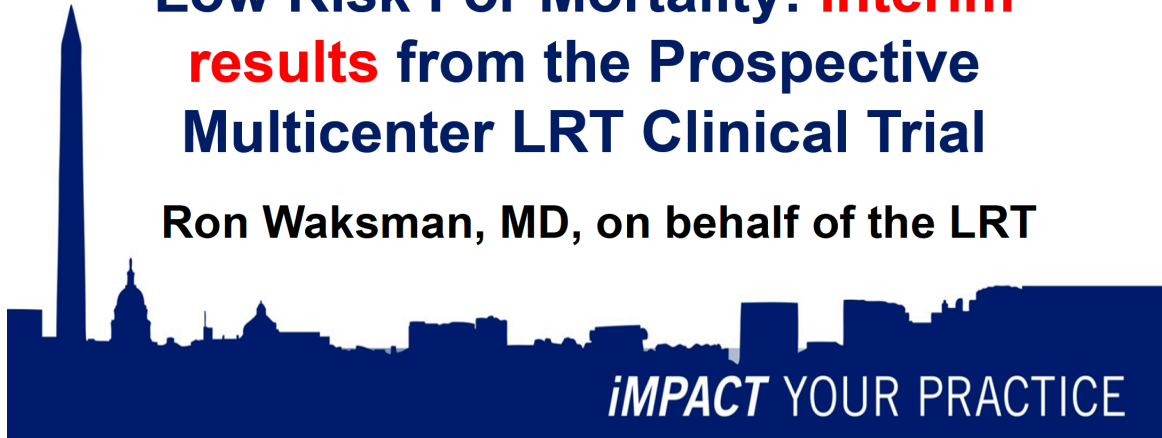
Can we improve short term outcomes?





Transcatheter Aortic Valve Replacement for Patients with Severe Aortic Stenosis who are at Low Risk For Mortality: **Interim results** from the Prospective Multicenter LRT Clinical Trial

Ron Waksman, MD, on behalf of the LRT



Medstar LR: 30-Day Adverse Events

	LRT	NOTION	SAPIEN 3 IR
Type of transcatheter valve	Edwards Sapien 3, Medtronic Evolut R or Evolut PRO	Medtronic CoreValve	Edwards Sapien 3
	N=125	N=145	N=1077
Age (years)	74.6 ± 5.7	79.2 ± 4.9	81.9 ± 6.6
STS score (%)	1.9 ± 0.5	2.9 ± 1.6	5.2 (4.3–6.3)
All-cause mortality	0.0%	2.1%	1.1%
Disabling stroke	0.0%	1.4%	1.0%
Paravalvular leak (≥ moderate)	0.0%	15.3% [†]	3.8%
Major vascular complications	4.0%	5.6%	6.1%
Major and life-threatening bleeding	4.0%	11.3%	4.6%
New PPM implantation	4.8%	34.1%	10.2%





PARTNER 3 – Low Risk Trial

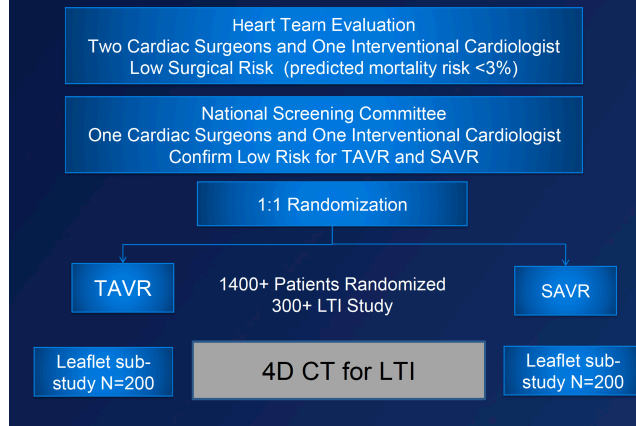
Primary Outcome:

- All cause mortality, all stroke, and rehospitalization one year after the procedure

Inclusion Criteria:

- 65 years of age or older with STS < 4 (MDT < 2%)
- Symptomatic, severe, calcific aortic stenosis with the following TTE criteria: Jet velocity ≥ 4.0 m/s or mean gradient ≥ 40 mmHg AND AVA ≤ 1.0 cm² or AVA index ≤ 0.6 cm²/m²
- Aortic valve annulus 273 mm² 683 mm²
- Adequate iliofemoral access with minimum average vessel diameter of 5.5mm (20, 23, 26mm) and 6.0mm (29mm)

Evolut R Low Risk Patient Selection



The NOTION-2 Trial

Inclusion criteria

- Severe symptomatic aortic stenosis, STS score $\leq 4\%$ & age ≤ 75 years
- Anticipated usage of bioprosthetic aortic valve
- Bicuspid aortic valves and coronary artery disease allowed

Primary end-point

- Composite rate of all-cause mortality, stroke & MI at 1 year

Design

- RCT, 1:1 between TF-TAVR vs. SAVR, non-inferior design, N=992
- Any bioprosthetic aortic valve allowed



TAVR for low risk pts

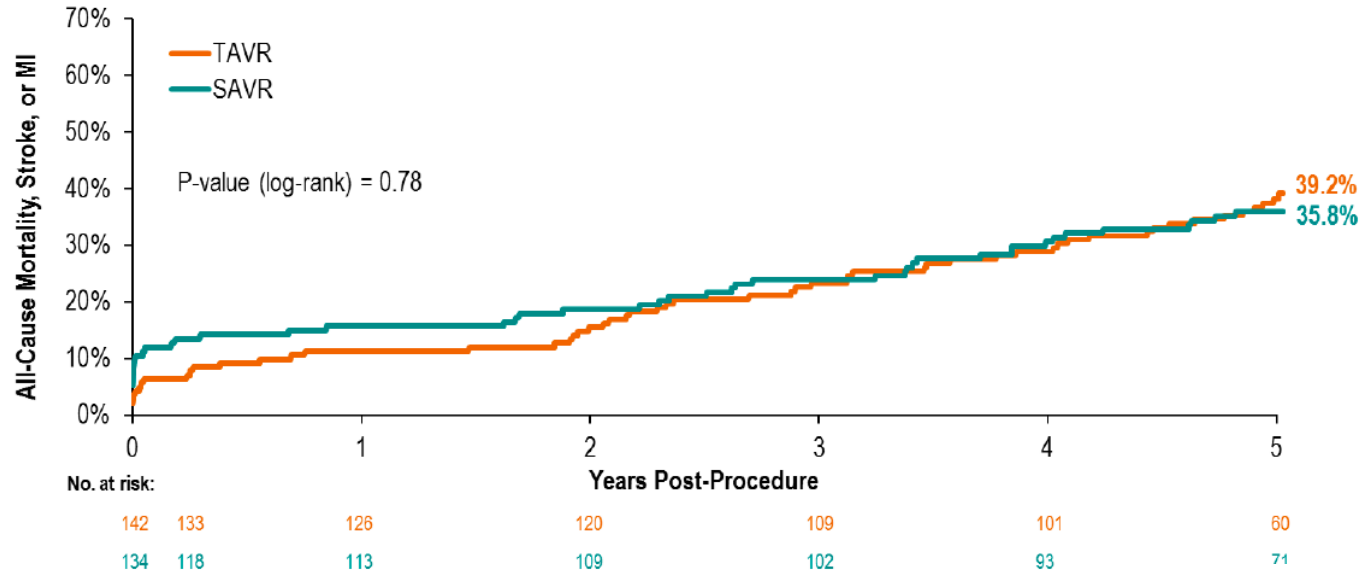
- Short term outcomes
- Long term durability
- Economical impact (cost-effectiveness)



NOTION trial

J Am Coll Cardiol 2019;73:546-53

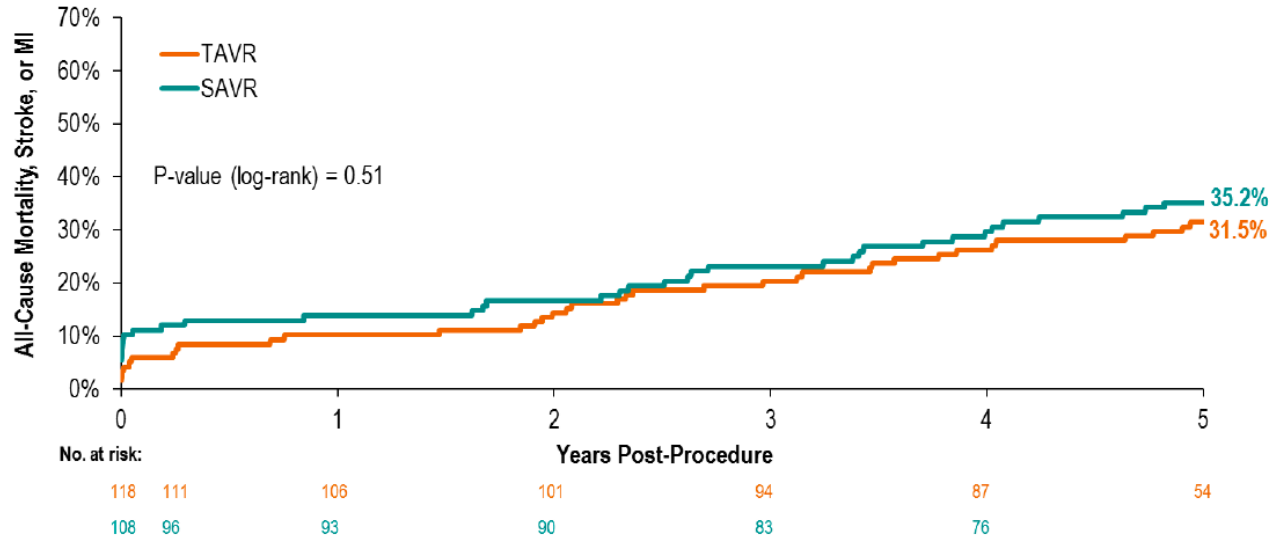
All-Cause Mortality, Stroke, or MI



NOTION trial

J Am Coll Cardiol 2019;73:546-53

All-Cause Mortality, Stroke, or MI: STS<4%



NOTION trial

J Am Coll Cardiol 2019;73:546–53

Secondary Outcomes

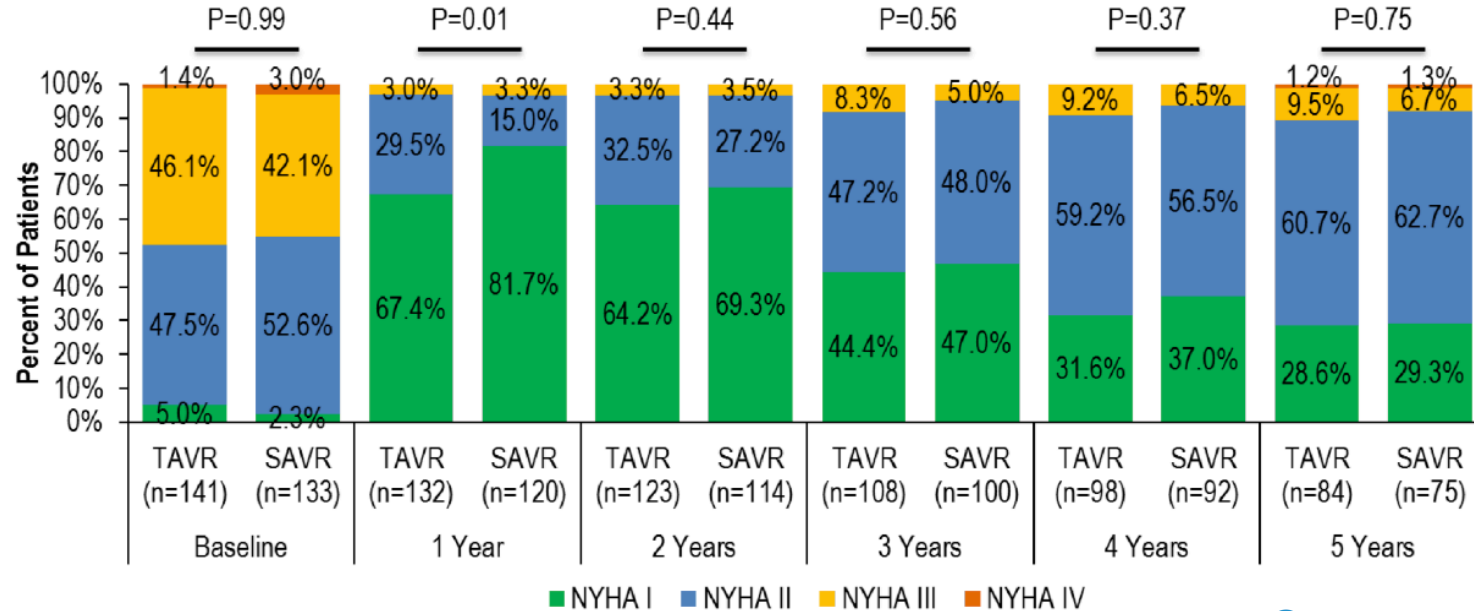
5-Year Outcome, %	TAVR	SAVR	p-value
Death, any cause	27.7	27.7	0.90
Death, cardiovascular	21.0	22.5	0.75
Stroke	10.5	8.2	0.67
TIA	6.8	4.1	0.35
Myocardial infarction	8.6	8.7	0.87
Atrial fibrillation	25.2	62.2	<0.001
Pacemaker	41.8	8.4	<0.001
Aortic valve re-intervention	2.5	0.0	0.09
Valve endocarditis	11.3	5.8	



NOTION trial

J Am Coll Cardiol 2019;73:546-53

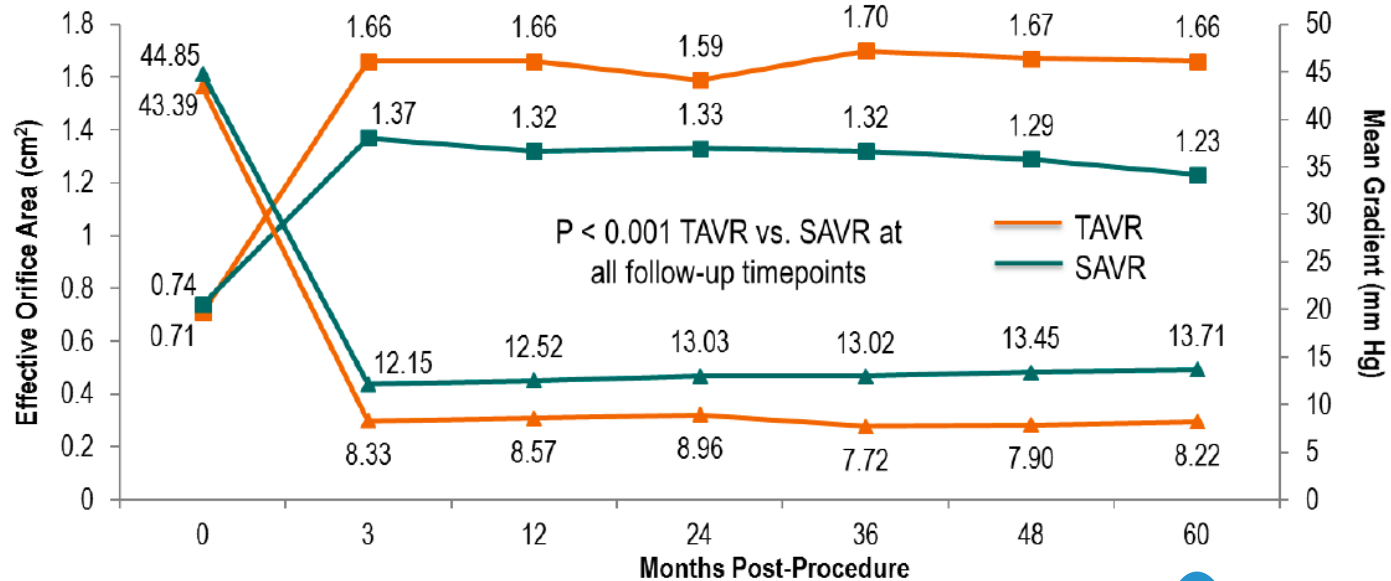
NYHA Class



NOTION trial

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Aortic Valve Performance



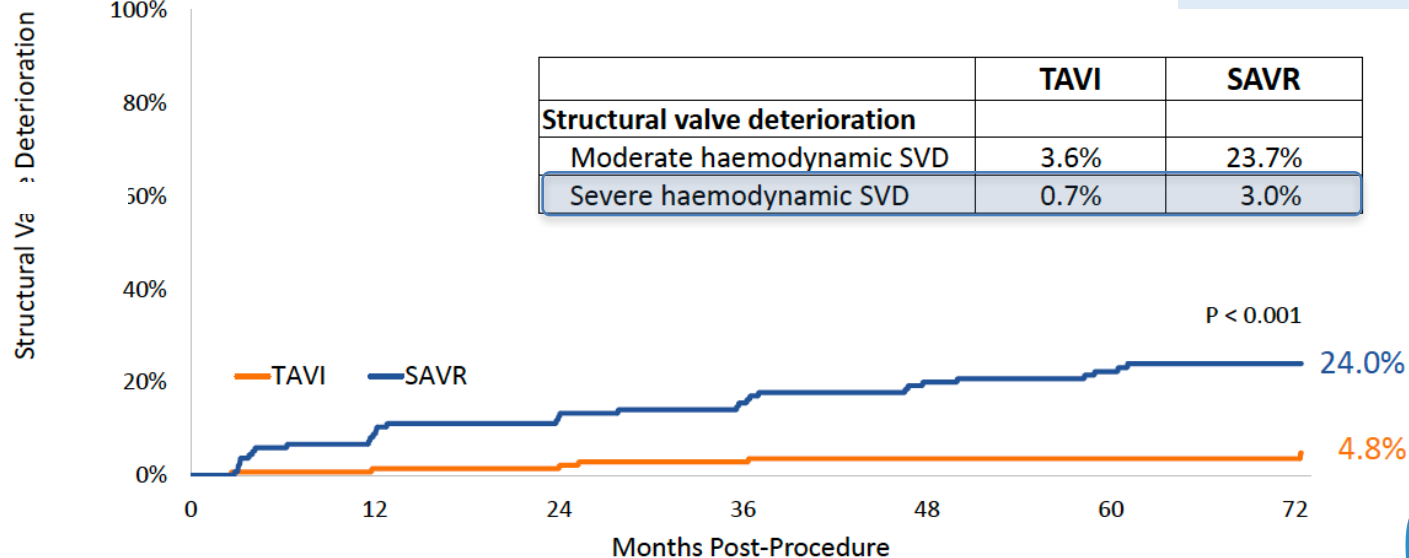


NOTION trial

J Am Coll Cardiol 2019;73:546–53

Structural Valve Deterioration

	TAVR (n = 139)	SAVR (n = 135)	p Value
Bioprosthetic valve dysfunction	56.1	66.7	0.073
Components			
Structural valve deterioration	4.8	24.0	<0.0001
Nonstructural valve deterioration	54.0	57.8	0.52
Thrombosis	0.0	0.0	NA
Endocarditis	5.8	5.9	0.95



5x higher!



NOTION trial

J Am Coll Cardiol 2019;73:546–53

TABLE 2 Transcatheter and Surgical Valve Sizes

Surgical Valve Types	19 mm	21 mm	23 mm	25 mm	27 mm	All
Mosaic	18.2 (2/11)	28.6 (12/42)	17.4 (8/46)	42.4 (14/33)	33.3 (1/3)	27.4 (37/135)
Epic	27.3 (3/11)	26.2 (11/42)	37.0 (17/46)	21.2 (7/33)	33.3 (1/3)	28.9 (39/135)
Trifecta	54.5 (6/11)	26.2 (11/42)	23.9 (11/46)	9.1 (3/33)	33.3 (1/3)	23.7 (32/135)
Perimount	0.0 (0/11)	14.3 (6/42)	13.0 (6/46)	6.1 (2/33)	0.0 (0/3)	10.4 (14/135)
Sorin Mitroflow	0.0 (0/11)	4.8 (2/42)	8.7 (4/46)	21.2 (7/33)	0.0 (0/3)	9.6 (13/135)
All	11	42	46	33	3	135
CoreValve Sizes	23 mm	26 mm	29 mm	31 mm		
	1.4 (2/139)	38.1 (53/139)	42.4 (59/139)	7.9 (11/139)		

Values are % (n/N) or n.



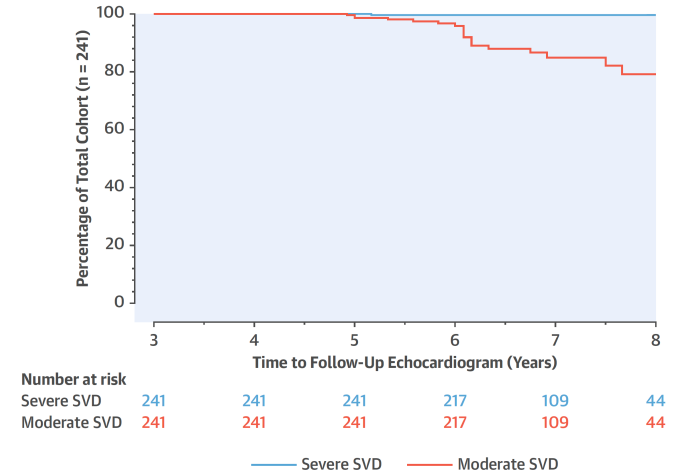


Long-Term Durability – UK-TAVI

J Am Coll Cardiol 2019;73:537–45

- 91% remained free of degeneration between 5-10y.
- incidence of severe degeneration was <1%
- moderate degeneration occurred in 1 in 12 patients

CENTRAL ILLUSTRATION Freedom From Structural Valve Deterioration Over Time: Kaplan-Meier Curve



Blackman, D.J. et al. J Am Coll Cardiol. 2019;73(5):537–45.



Future trials

European Heart Journal (2019) 40, 422–440

Table 2 Ongoing randomized clinical trials of TAVI in lower risk patients⁷

Trial ID	PARTNER 3 NCT02675114	Evolut R low risk NCT02701283	NOTION 2 NCT02825134	EARLY TAVR NCT03042104
Number of patients	1328	1200	992	1109
Comparator	SAVR	SAVR	SAVR	Clinical surveillance (no intervention)
Design	Randomized, non-inferiority	Randomized, non-inferiority	Randomized, non-inferiority	Randomized
Definition of low risk	Heart Team predicted peri-operative mortality <2% (STS <4%)	Heart Team predicted 30-day SAVR mortality <3% (STS <3%)	STS <4%, age ≤75 years	Asymptomatic patient
Transcatheter heart valve in TAVI arm	SAPIEN 3 only, transfemoral approach	Evolut R or CoreValve	Any CE approved transcatheter heart valve, only transfemoral approach	SAPIEN 3
Follow-up	Up to 10 years	Up to 5 years	Up to 5 years	2 years
Primary endpoint	All-cause mortality, all stroke, and rehospitalization at 1 year	All-cause mortality or disabling stroke at 2 years	All-cause mortality, MI, and stroke at 1 year	Non-hierarchical composite of all-cause mortality, all stroke, and unplanned CV hospitalization

Adapted from Tarantini et al.⁷

CV, cardiovascular; MI, myocardial infarction; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons.



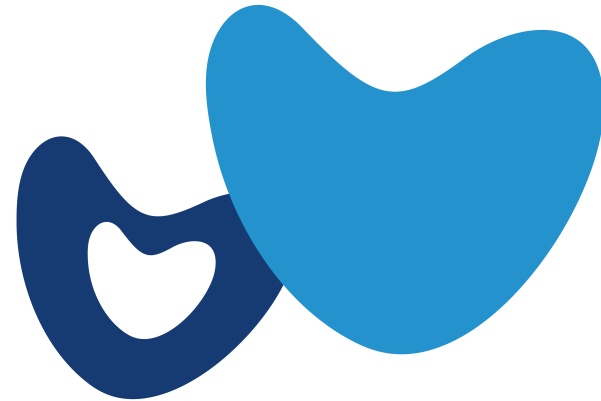
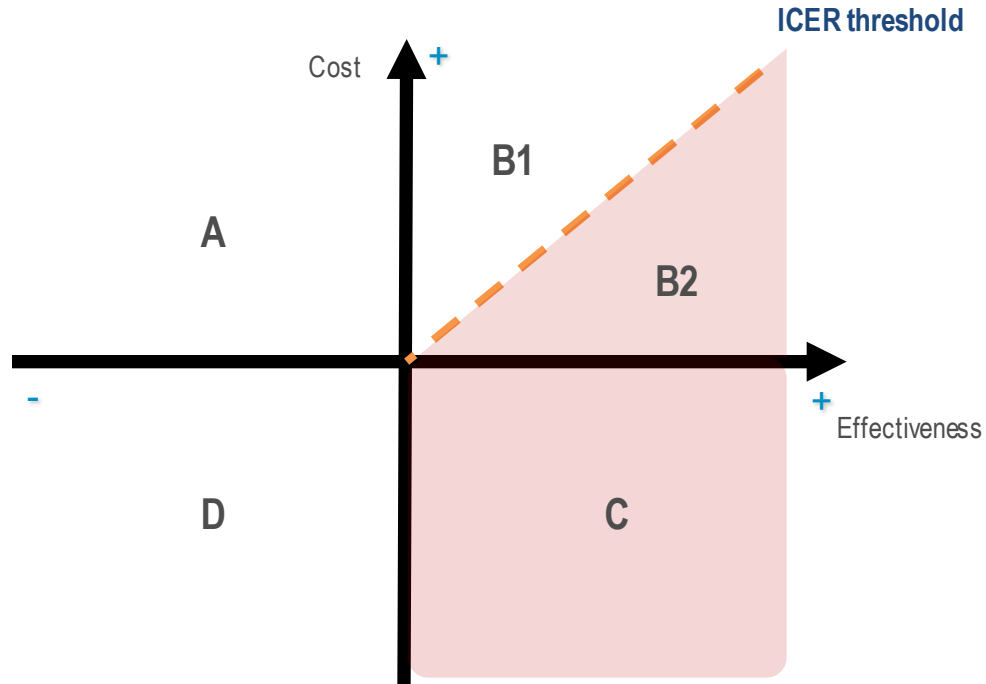
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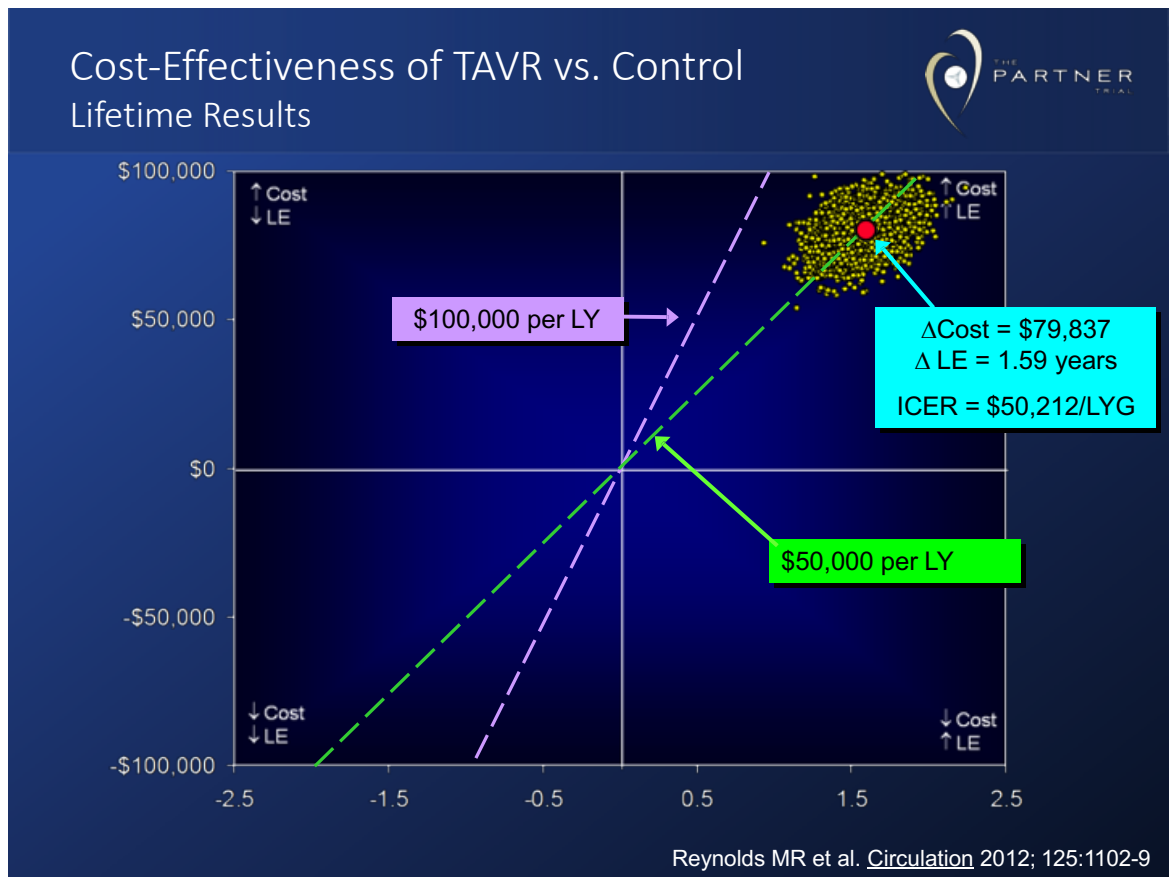
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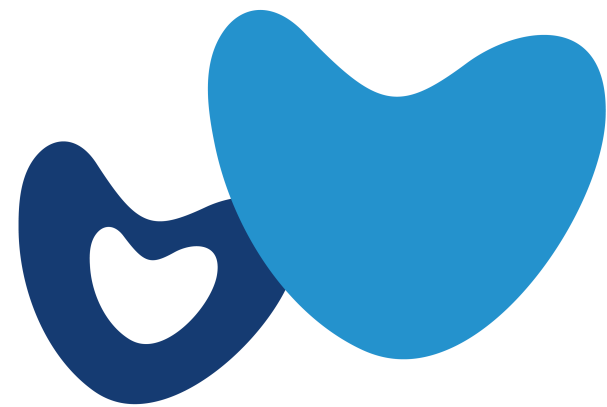


Cost-effectiveness 101



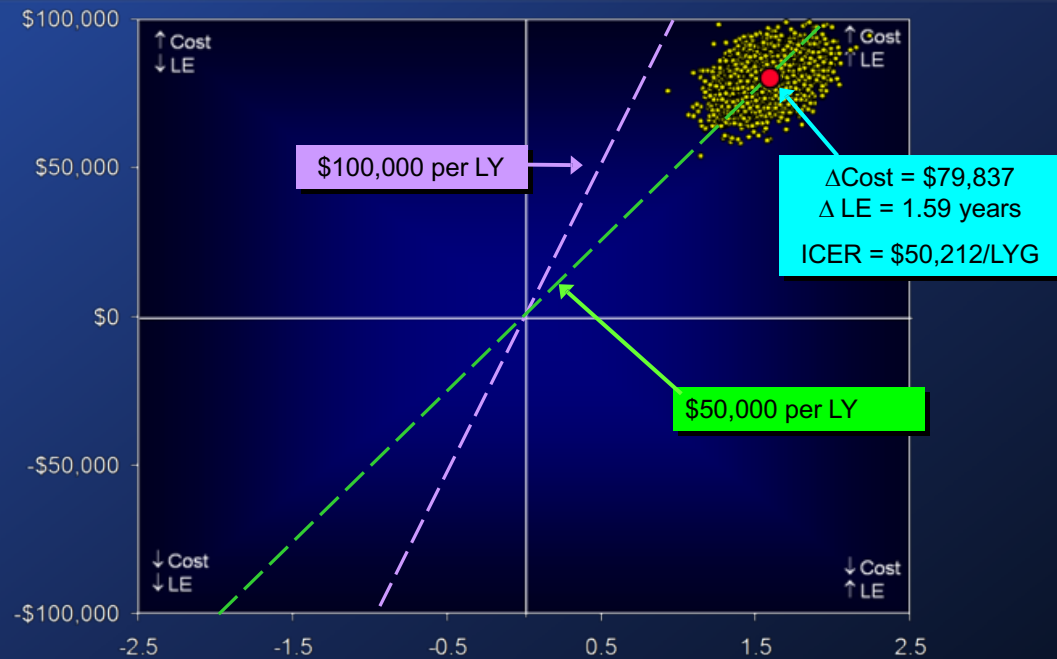


Extreme & high risk





Cost-Effectiveness of TAVR vs. Control Lifetime Results

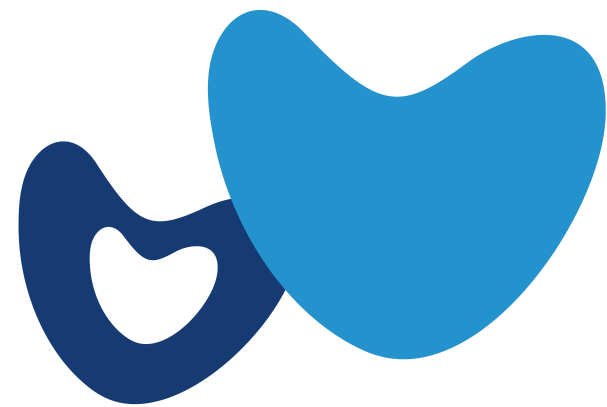


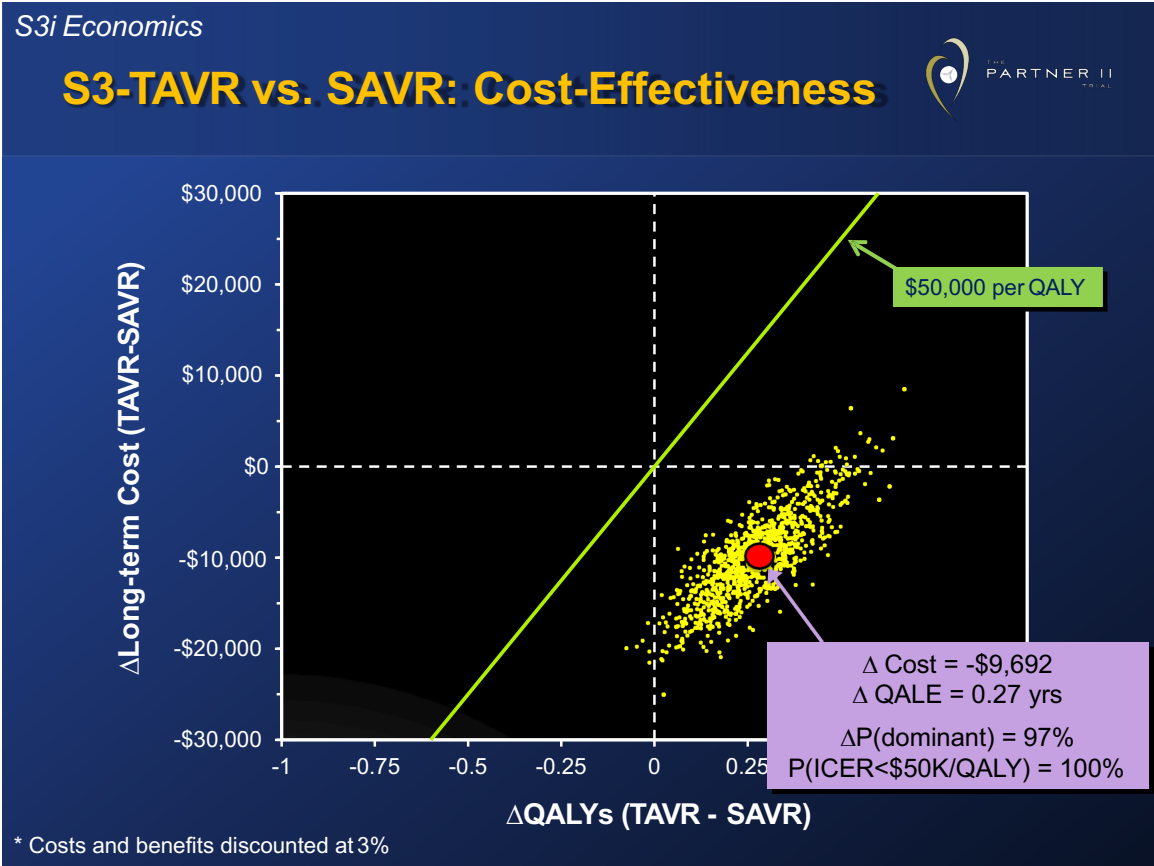
Reynolds MR et al. Circulation 2012; 125:1102-9

Extreme & high risk

Why doesn't TAVR save money?

- Control patients die too quickly
- TAVR patients expensive to keep alive





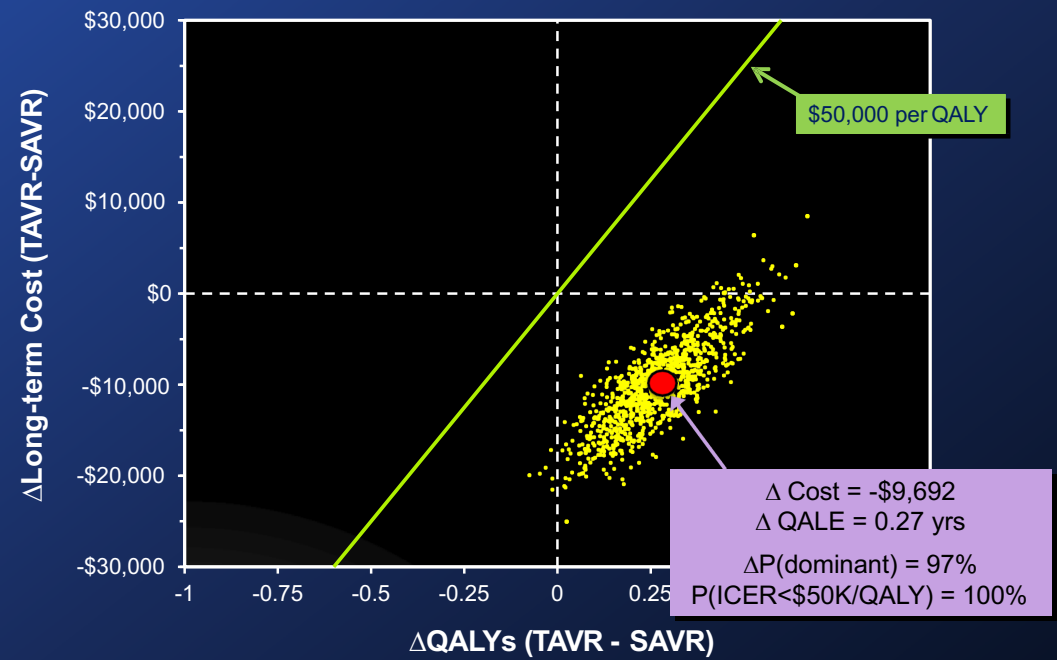
Intermediate risk





S3i Economics

S3-TAVR vs. SAVR: Cost-Effectiveness



* Costs and benefits discounted at 3%

Intermediate risk

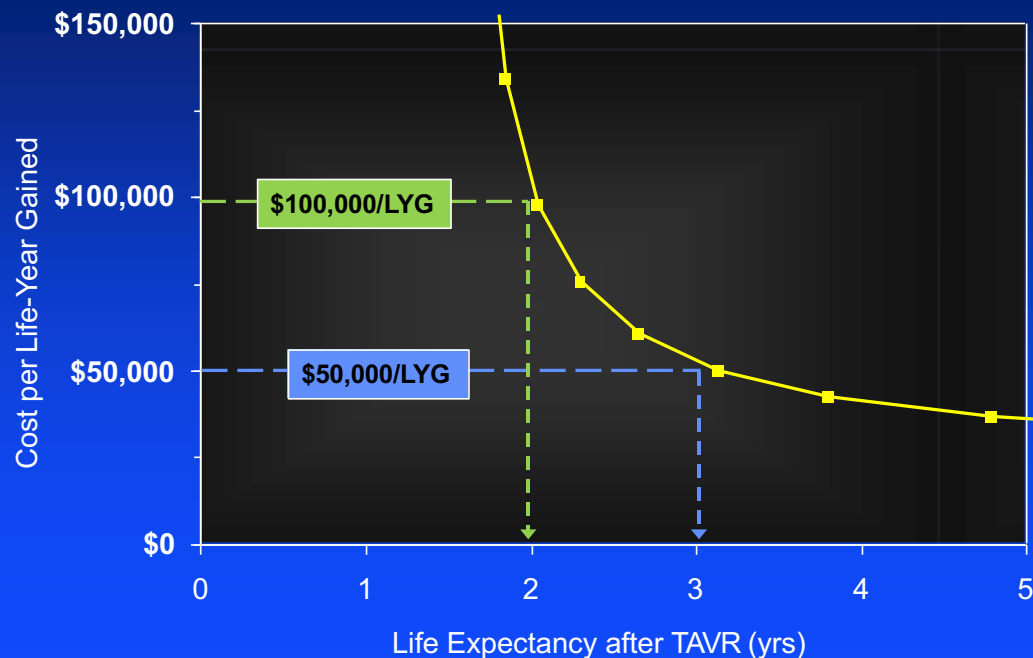
Why are the S3 results more favorable?

- Even shorter LOS (median 3 vs. 5 days)
- Greater f/u cost savings due to reduced rehospitalization as well as rehab
- Patient preference & faster recovery
- Improved QoL

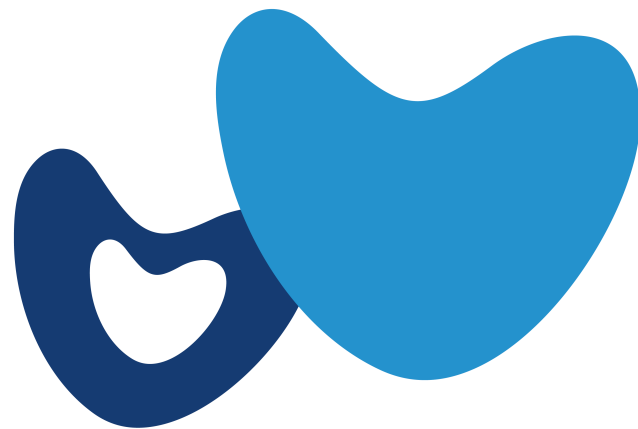




Relationship between Cost-Effectiveness and Post-TAVR Life Expectancy

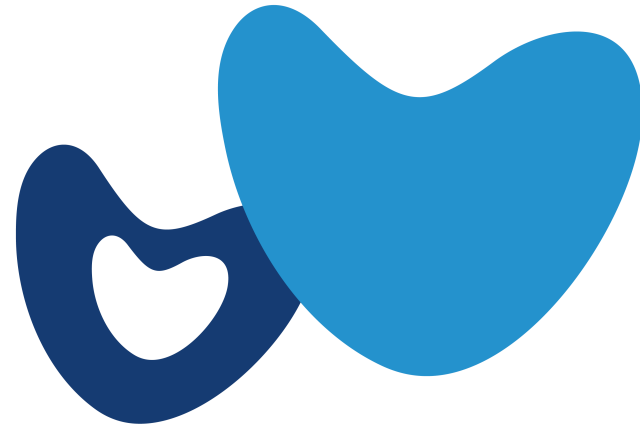
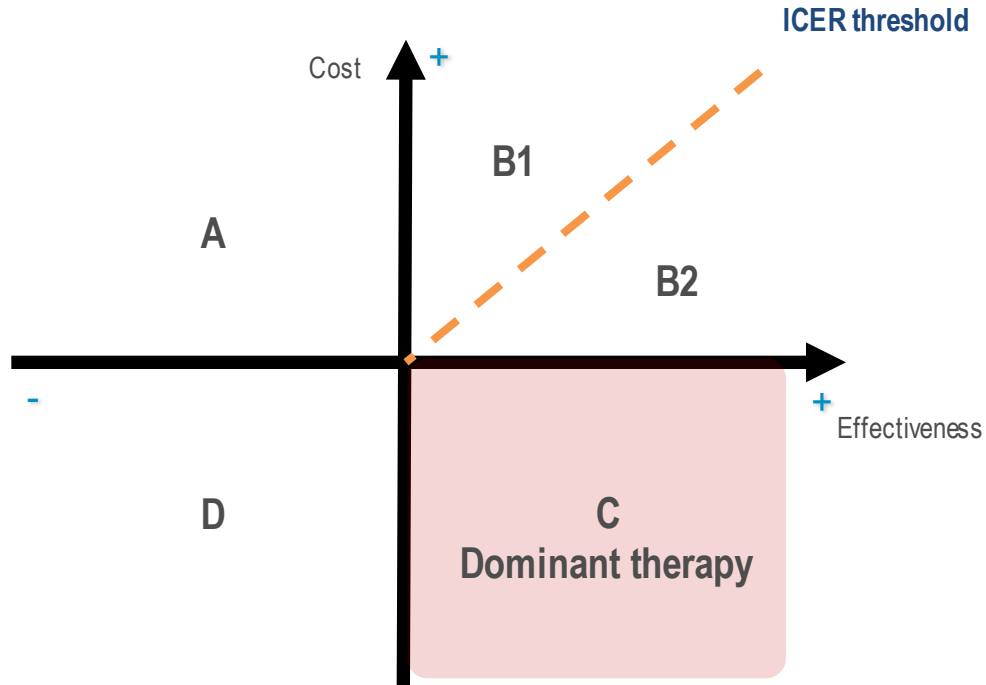


Lower risk equals to greater life expectancy and greater cost effectiveness



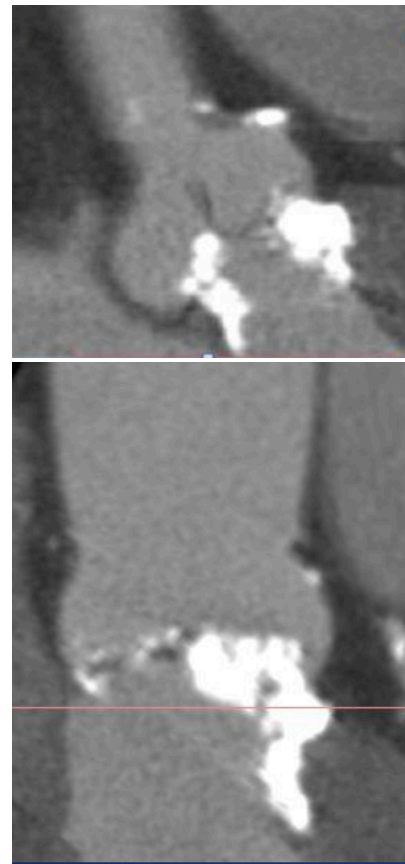


Cost-effectiveness 101



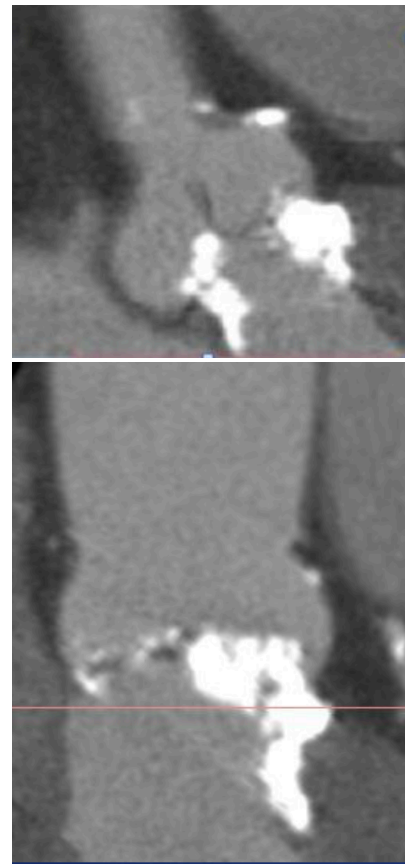
Adverse frontiers

- bicuspid disease in younger patients
- LVOT calcification
- long term coronary access



In conclusion

- So far looks promising
 - More data is on the way
 - I bet TAVR is going to win!
-
- Despite STS score, consider TAVR if the patient is a candidate to a biological prosthesis





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