Five-Year Outcomes From the All-Comers Nordic Aortic Valve Intervention Randomized Clinical Trial in Patients with Severe Aortic Valve Stenosis

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On behalf of the NOTION Investigators

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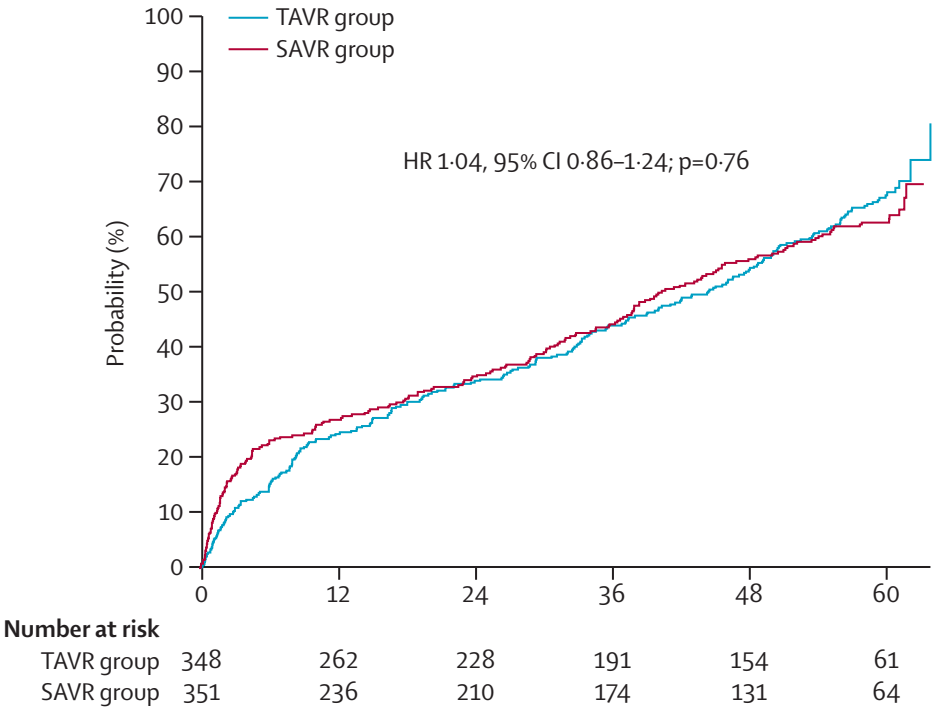
TAVR vs. SAVR in High-Risk Patients



All-cause death after 5 years

PARTNER 1

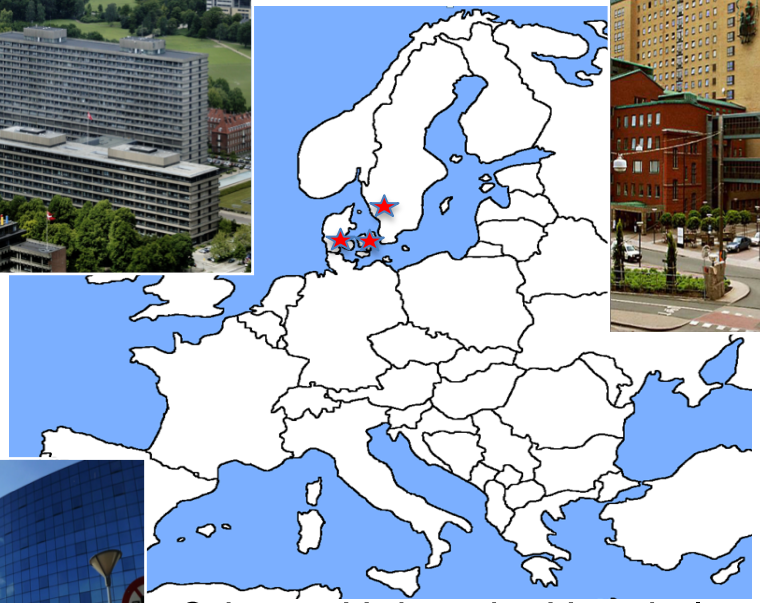
Mack MJ et al, Lancet 2015

Nordic Aortic Valve Intervention (NOTION) Trial

Objective:	To compare TAVR vs. SAVR in patients ≥ 70 years eligible for surgery (all-comers population/consecutive recruitment)
Primary outcome:	Composite rate of all-cause mortality, stroke or myocardial infarction at 1 year (VARC II-defined)
Secondary outcomes:	Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)
Design:	Prospective, multicenter, non-blinded, randomized trial
Enrollment period:	December 2009 - April 2013

Participating Centers

Rigshospitalet, Copenhagen University Hospital, Denmark



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Investigators and CEC

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- Peter Bo Hansen
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- Henrik Nissen
- Bo Juel Kjeldsen
- Petur Petursson

Enrollment Criteria

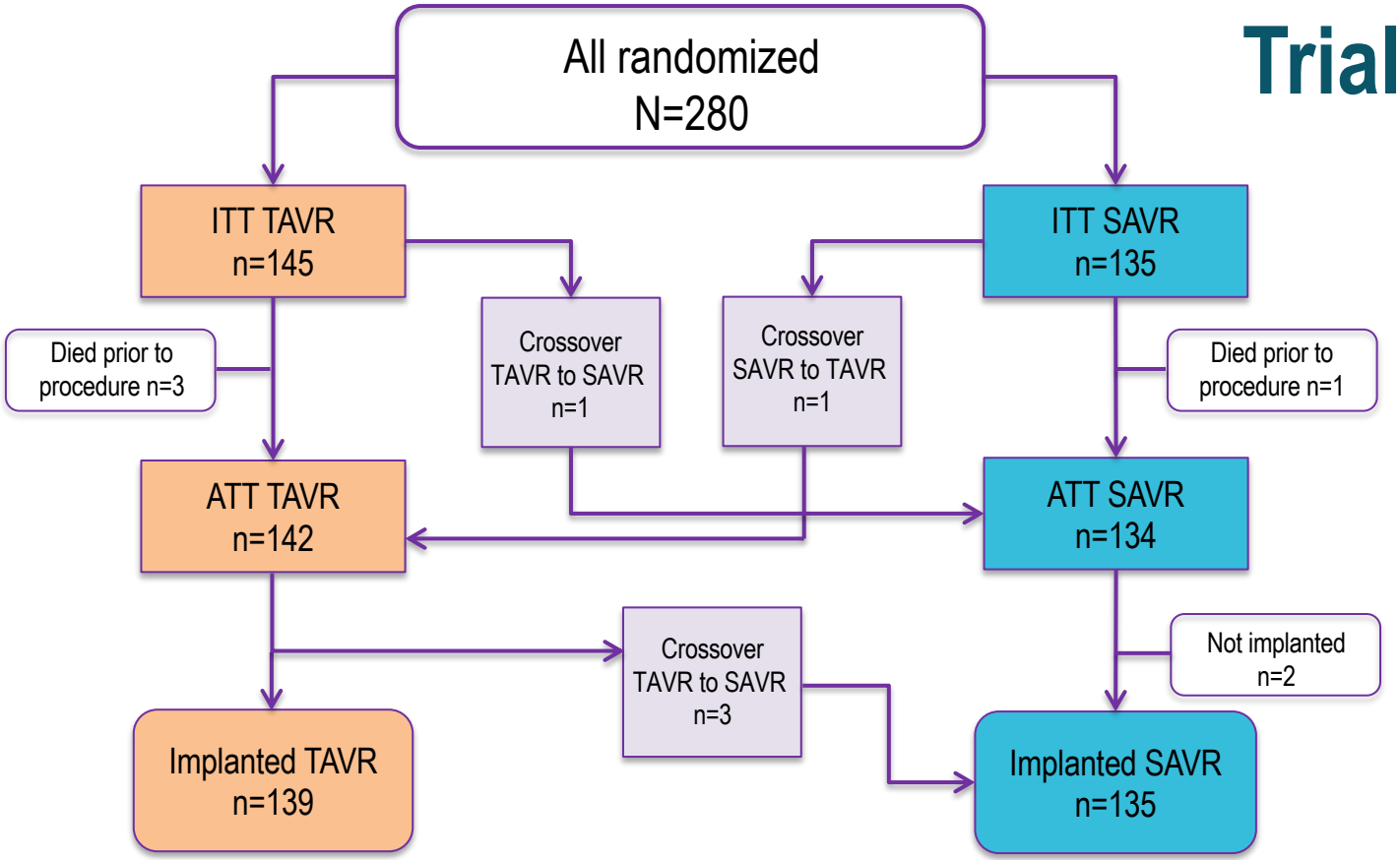
Main inclusion criteria

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

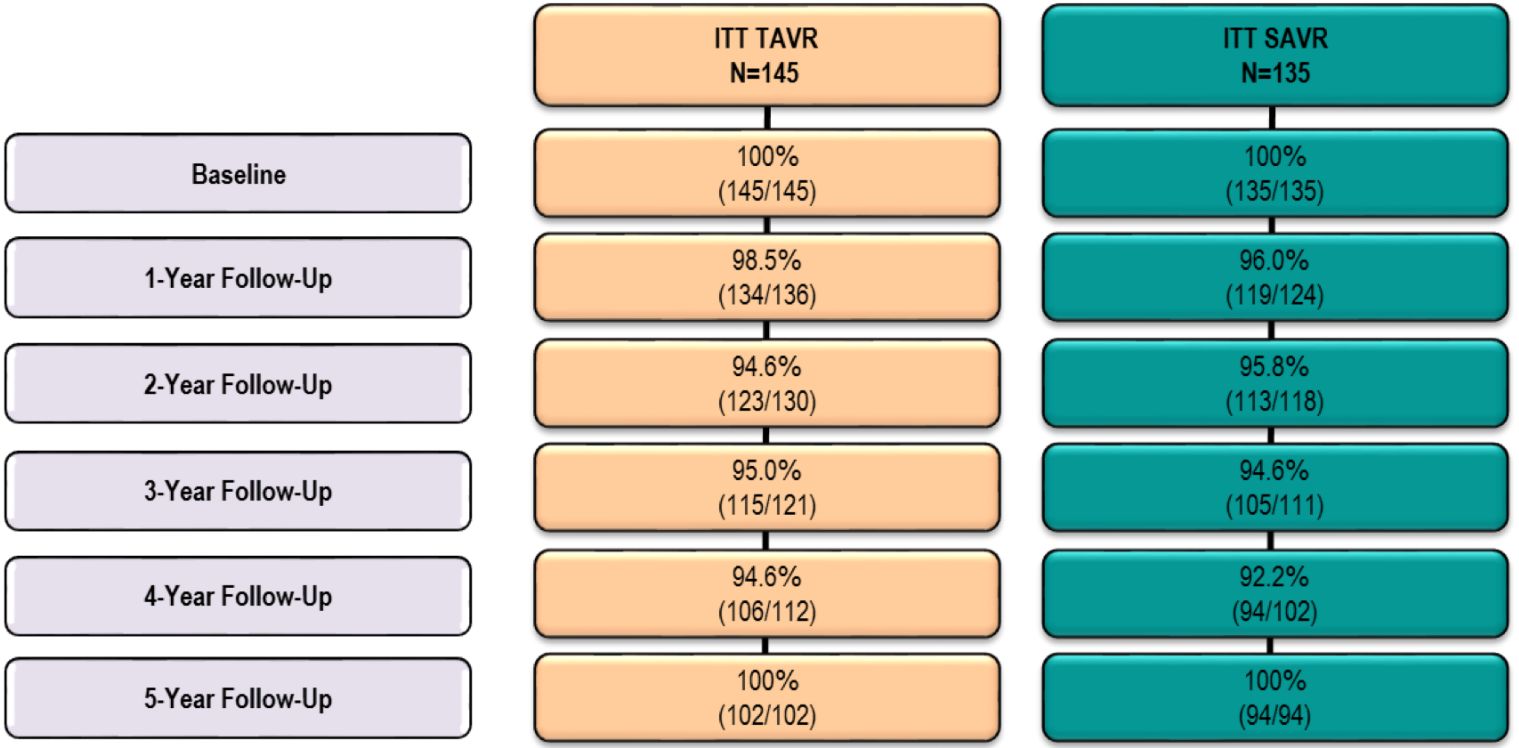
Main exclusion criteria

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

Trial Flow


All randomized
N=280
ITT TAVR
n=145
ITT SAVR
n=135
Died prior to procedure n=3
Crossover TAVR to SAVR n=1
Crossover SAVR to TAVR n=1
Died prior to procedure n=1
ATT TAVR
n=142
ATT SAVR
n=134
Crossover TAVR to SAVR n=3
Not implanted n=2
Implanted TAVR
n=139
Implanted SAVR
n=135

Compliance


ITT TAVR
N=145
ITT SAVR
N=135
Baseline
100%
(145/145)
100%
(135/135)
1-Year Follow-Up
98.5%
(134/136)
96.0%
(119/124)
2-Year Follow-Up
94.6%
(123/130)
95.8%
(113/118)
3-Year Follow-Up
95.0%
(115/121)
94.6%
(105/111)
4-Year Follow-Up
94.6%
(106/112)
92.2%
(94/102)
5-Year Follow-Up
100%
(102/102)
100%
(94/94)

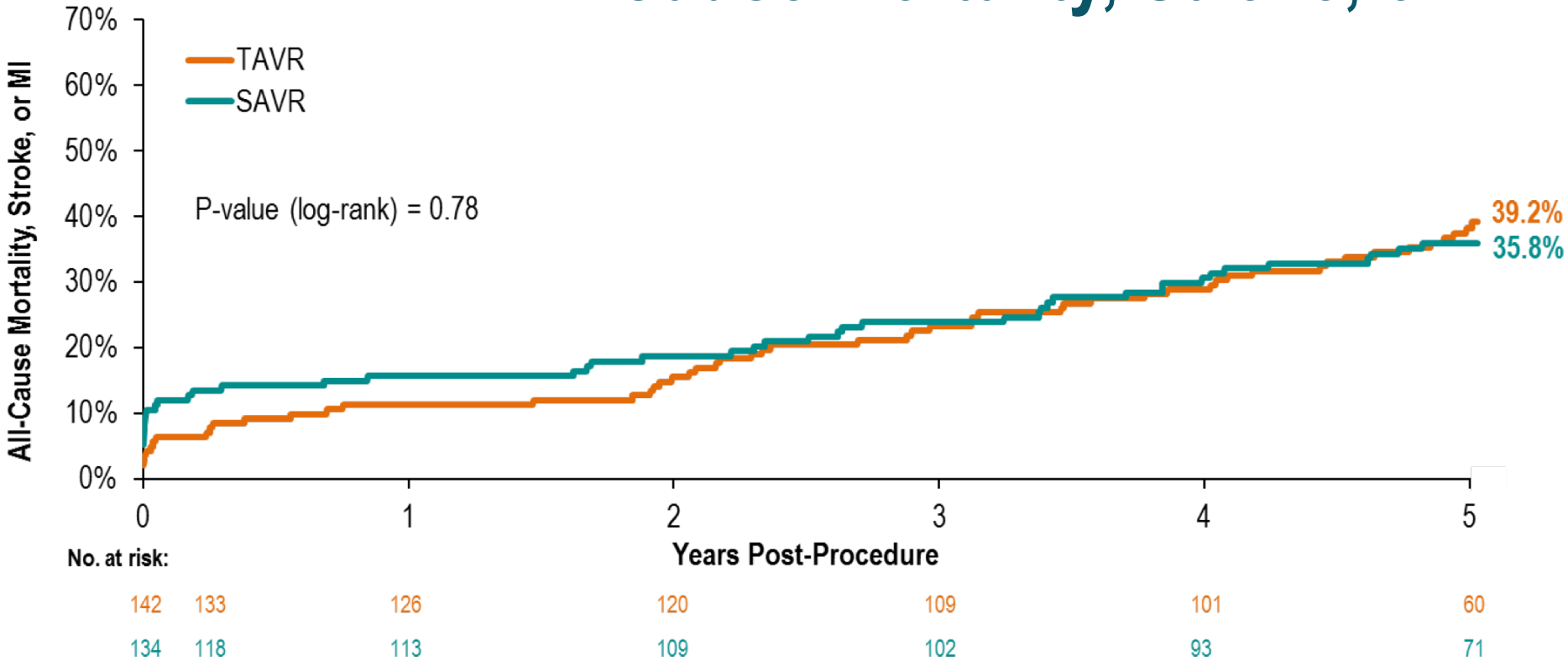
Baseline Characteristics

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

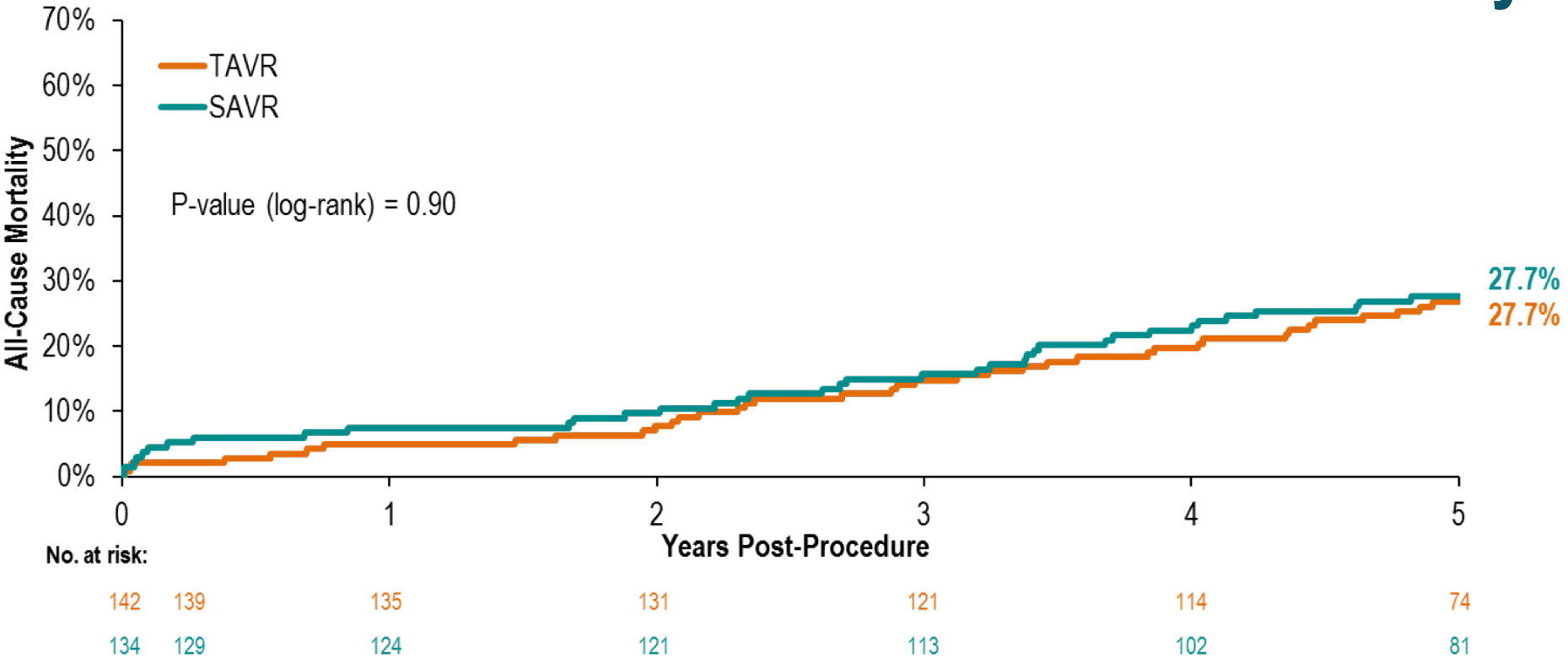
Baseline Characteristics

Characteristic, %	TAVR n=145	SAVR n=135	p-value
Diabetes	17.9	20.7	0.55
Peripheral vascular disease	4.1	6.7	0.35
Prior stroke	6.2	9.6	0.29
COPD	11.7	11.9	0.97
Creatinine > 2 mg/dl	1.4	0.7	>0.99
Prior myocardial infarction	5.5	4.4	0.68
Prior PCI	7.6	8.9	0.69

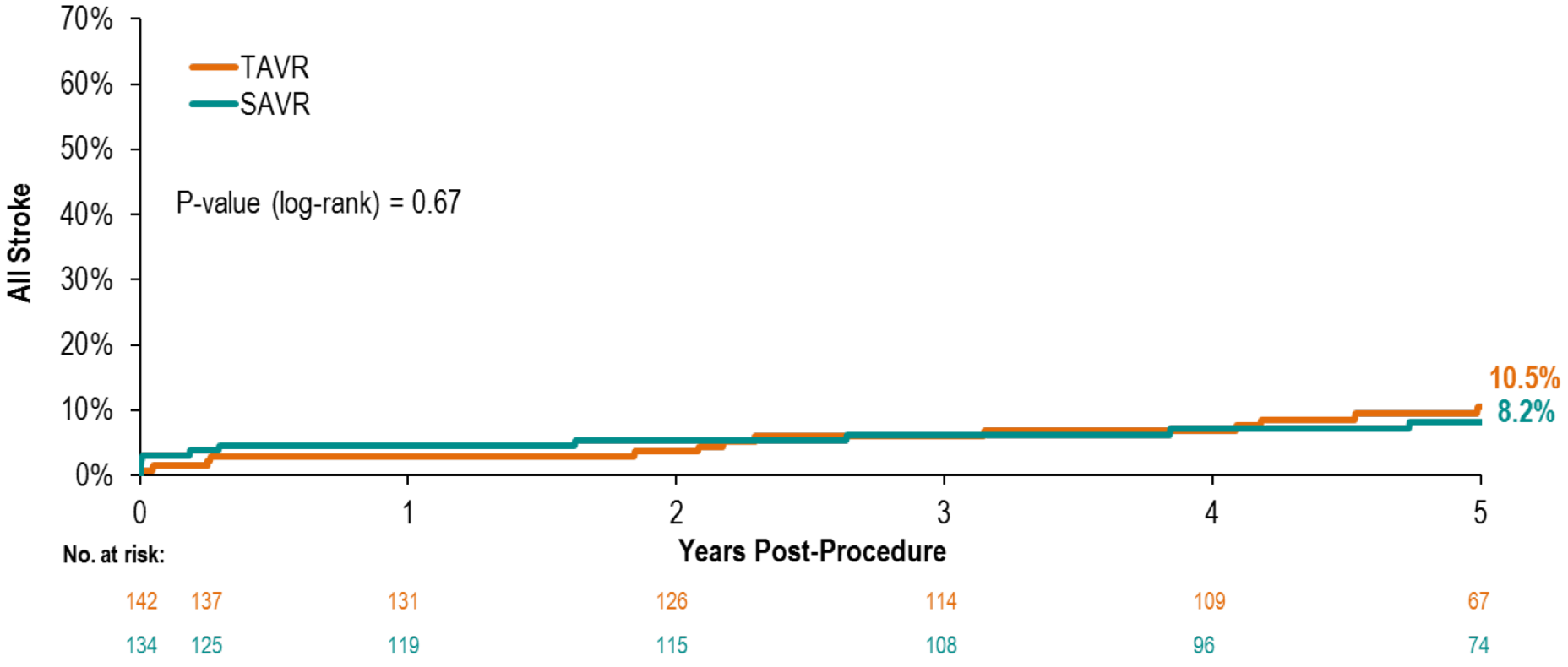
All-Cause Mortality, Stroke, or MI



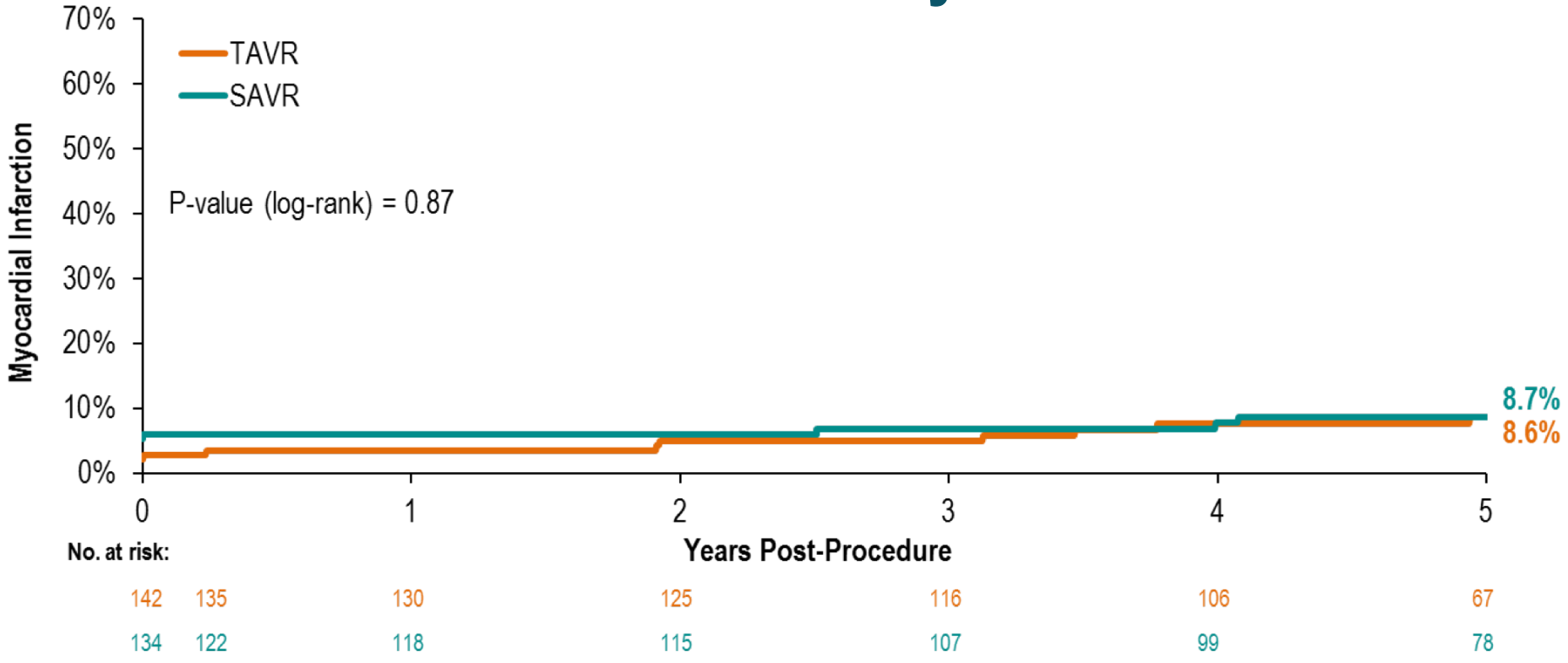
All-Cause Mortality



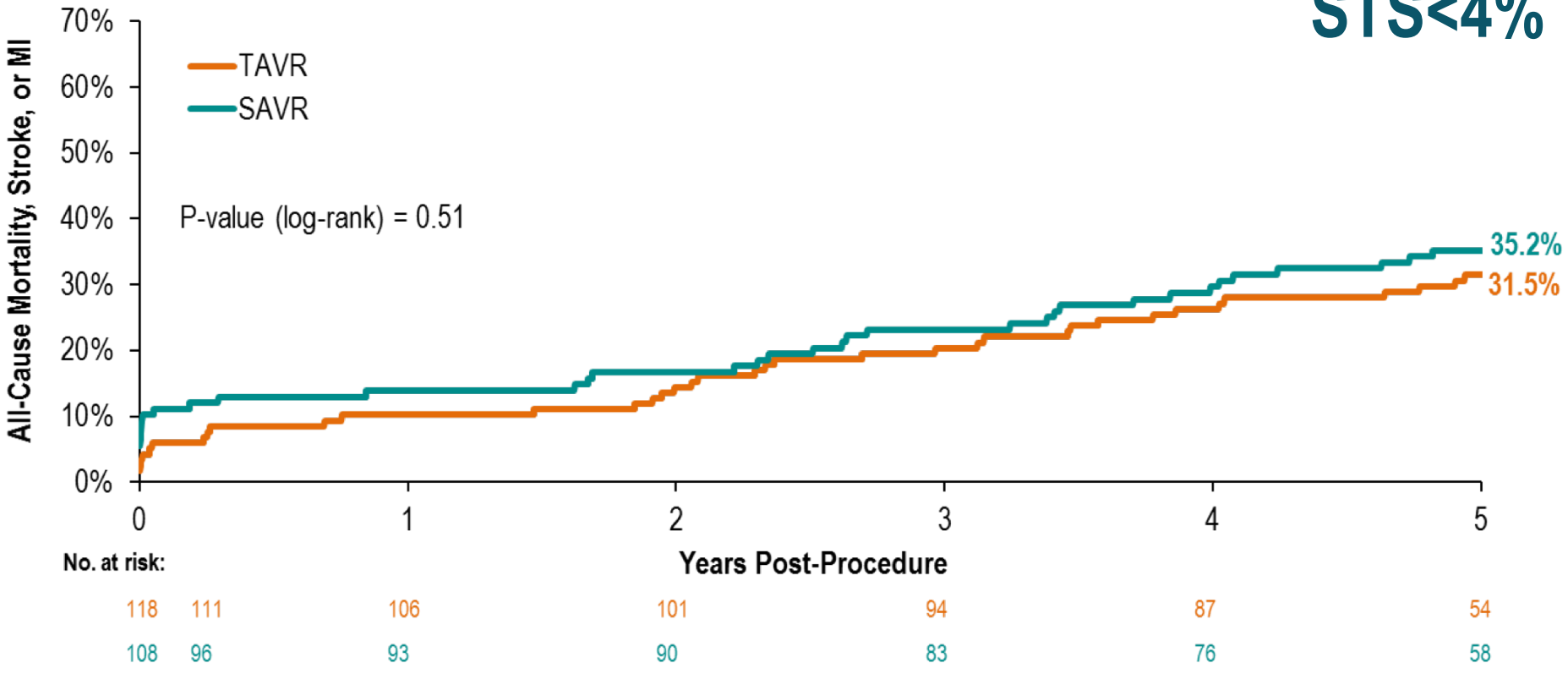
Stroke


70%
60%
50%
40%
30%
20%
10%
0%
All Stroke
TAVR
SAVR
P-value (log-rank) = 0.67
10.5%
8.2%
0
1
2
3
4
5
Years Post-Procedure
No. at risk:
142 137 131 126 114 109 67
134 125 119 115 108 96 74

Myocardial Infarction



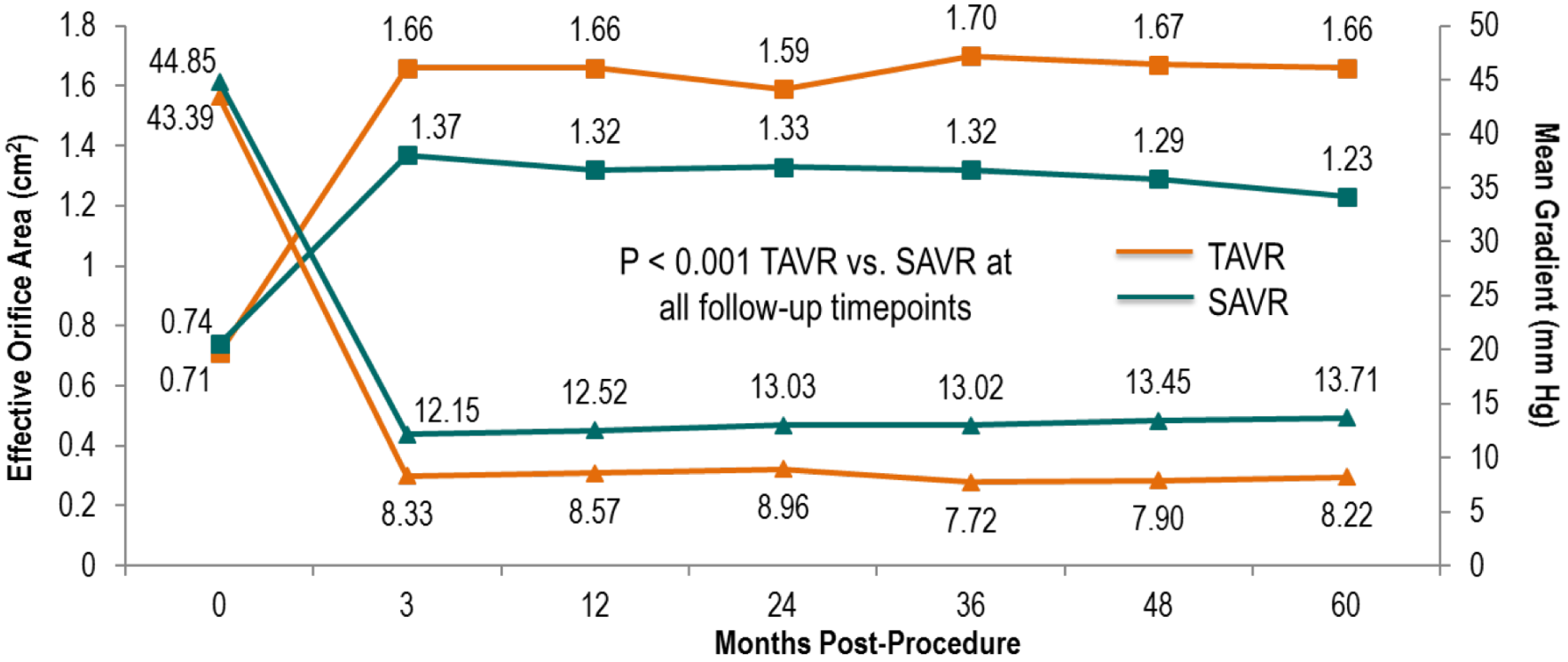
All-Cause Mortality, Stroke, or MI: STS<4%



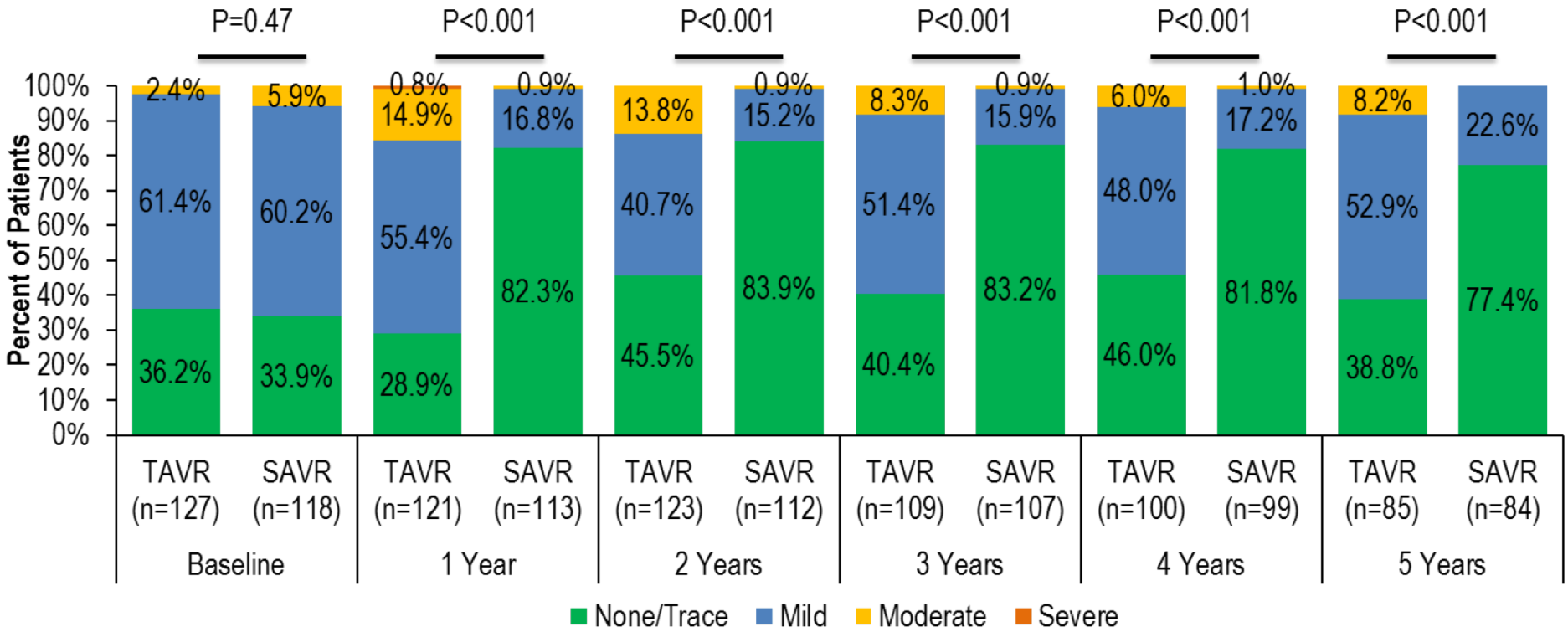
Secondary Outcomes

5-Year Outcome, Kaplan-Meier %	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	0.10

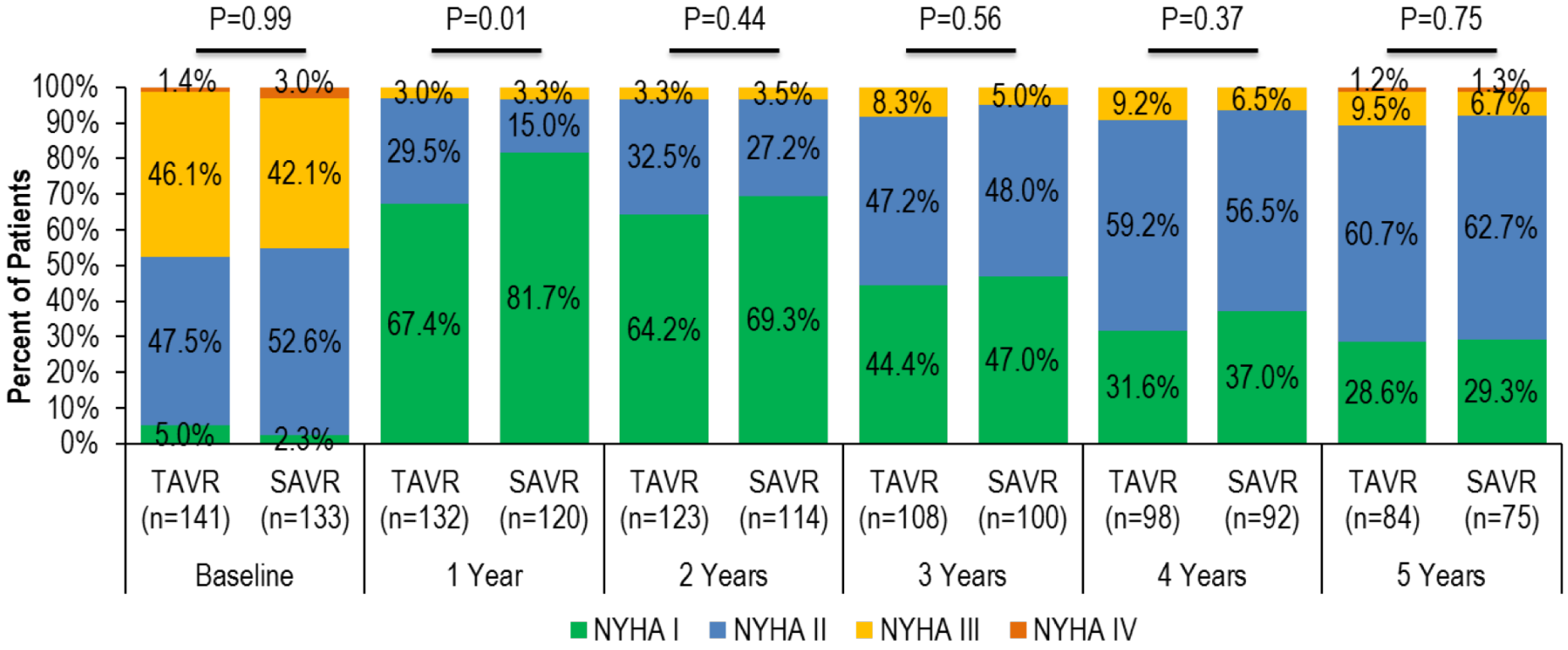
Aortic Valve Performance



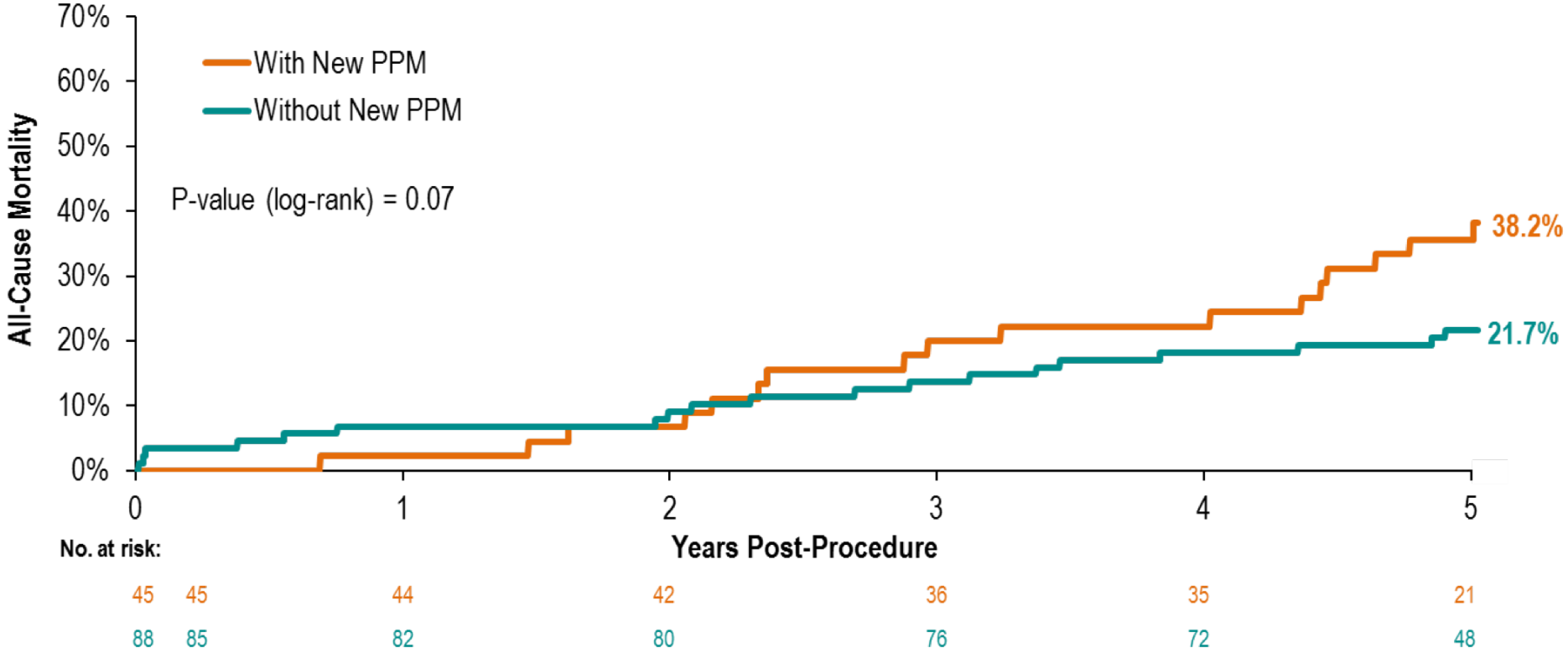
Aortic Valve Regurgitation



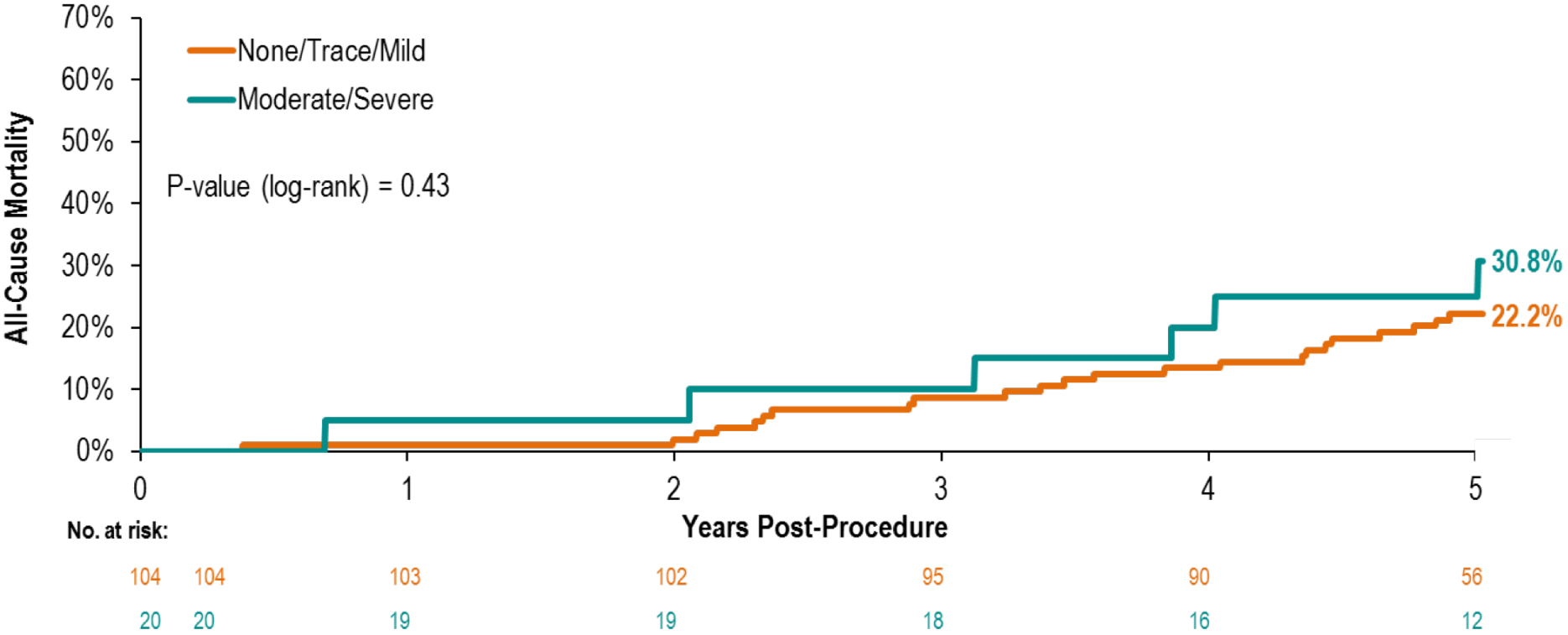
NYHA Class


P=0.99
P=0.01
P=0.44
P=0.56
P=0.37
P=0.75
Percent of Patients
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1.4%
46.1%
47.5%
5.0%
3.0%
42.1%
52.6%
2.3%
3.0%
29.5%
67.4%
3.3%
15.0%
81.7%
3.3%
32.5%
64.2%
3.5%
27.2%
69.3%
8.3%
47.2%
44.4%
5.0%
48.0%
47.0%
9.2%
59.2%
31.6%
6.5%
56.5%
37.0%
1.2%
9.5%
60.7%
28.6%
1.3%
6.7%
62.7%
29.3%
TAVR (n=141)
SAVR (n=133)
TAVR (n=132)
SAVR (n=120)
TAVR (n=123)
SAVR (n=114)
TAVR (n=108)
SAVR (n=100)
TAVR (n=98)
SAVR (n=92)
TAVR (n=84)
SAVR (n=75)
Baseline
1 Year
2 Years
3 Years
4 Years
5 Years
NYHA I
NYHA II
NYHA III
NYHA IV

Association of New Pacemaker with Mortality for TAVR

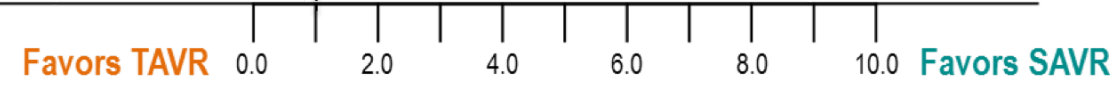


All-Cause Mortality by 3-Month AR Severity



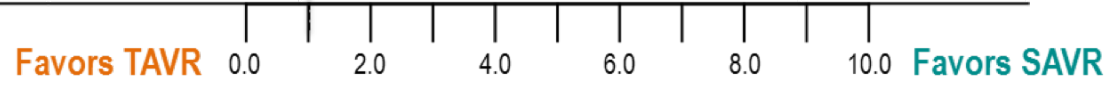
Subgroup Analysis for 5-Year Mortality

	All-Cause Mortality 5-Year KM Rates		Hazard Ratio (95% CI)	P
Variable	TAVR	SAVR		
Age (years)				0.19
<75y	6.9	18.5		
≥75y	33.0	30.0		
Gender				0.95
Male	31.7	31.5		
Female	23.0	23.4		
BMI (kg/m²)				0.77
≤30	29.3	28.3		
>30	20.0	23.5		
STS (%)				0.05
<4	21.2	26.9		
≥4	58.3	30.8		



Subgroup Analysis for 5-Year Mortality

	All-Cause Mortality 5-Year KM Rates		Hazard Ratio (95% CI)	P
Variable	TAVR	SAVR		
Hypertension				0.04
No	33.3	16.1		
Yes	25.5	31.1		
Peripheral Vascular Disease				0.88
No	28.2	28.1		
Yes	16.7	22.2		
Diabetes				0.99
No	27.3	27.4		
Yes	29.6	28.6		
LVEF (%)				0.42
≤40	22.2	40.0		
>40	21.6	19.2		



Conclusions

- NOTION is the first trial to report on 5-year outcomes after TAVR vs. SAVR in lower risk patients (82% with STS < 4%)
- After 5 years, there were no differences in all-cause mortality, stroke, myocardial infarction, or these combined
- There was no difference in prosthetic valve re-intervention
- Prosthetic opening area was larger and mean gradient lower for TAVR and remained unchanged over time
- TAVR continued to have more mild/moderate prosthetic regurgitation
- New pacemaker implantation after TAVR trended to be associated with increased mortality
- Determining the longevity of TAVR prostheses will require longer term follow-up