Transcatheter vs Surgical Aortic Valve Replacement in Low Risk Patients:

3-Year Outcomes from the Evolut Low Risk Trial

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For the Evolut Low Risk Trial Investigators

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AMERICAN COLLEGE of CARDIOLOGY

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Evolut™
Low Risk
Trial

Disclosures

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below

Financial Relationship	**Company**
Research grants, consulting fees, honoraria, speakers bureau fees	Medtronic, Edwards Lifesciences

Evolut Low Risk Study Administration

Evolut™ Low Risk Trial

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Echo Core Laboratory: Jae Oh, Mayo Clinic

Statistical Analyses: Jian Huang, Medtronic

Sponsor: Medtronic

Background

Evolut™ Low Risk Trial

- Now approved for all patients with aortic stenosis regardless of surgical risk, TAVR has become the dominant form of AVR in the US.
- Current ACC/AHA guidelines recommend that heart teams utilize a shared decision-making process when discussing AVR with patients aged 65-80 years.[1]
- In younger lower-risk patients the faster recovery and short-term benefits after TAVR must be balanced with long-term durability, however limited intermediate and long-term data exist to guide such discussions in this patient population.

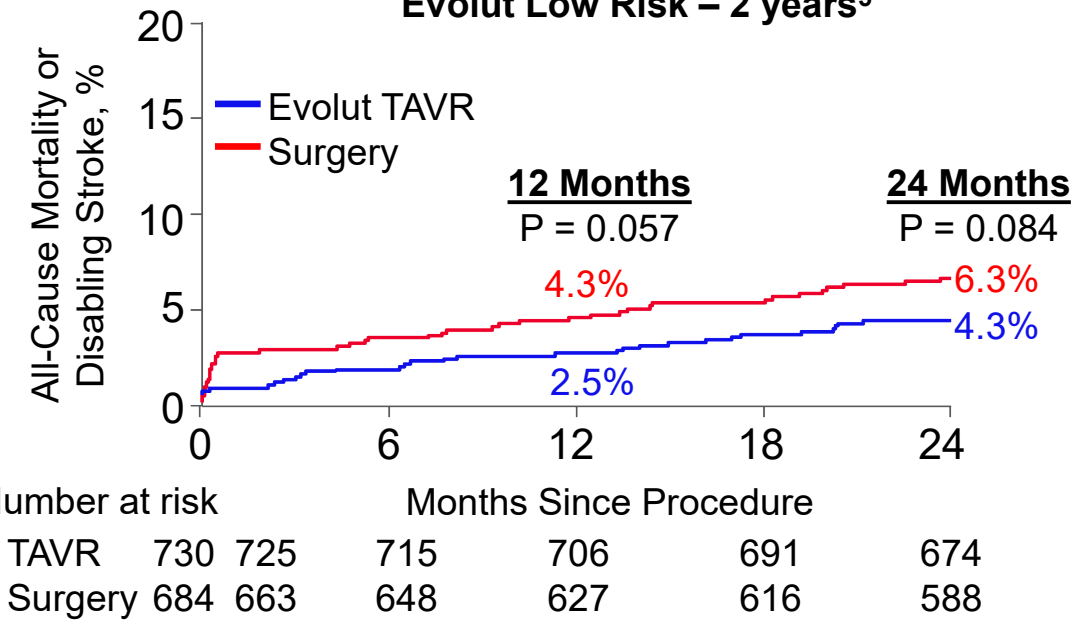
[1]Otto CM, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease. JACC 2021;77:e25-e197.

Background

Evolut™ Low Risk Trial

- Randomized data of TAVR vs surgery from high and intermediate risk patients demonstrate similar survival outcomes at 5 years.[1-4]
- Data in low-risk patients have shown promising short-term outcomes, but continued follow-up to guide shared decision is needed.

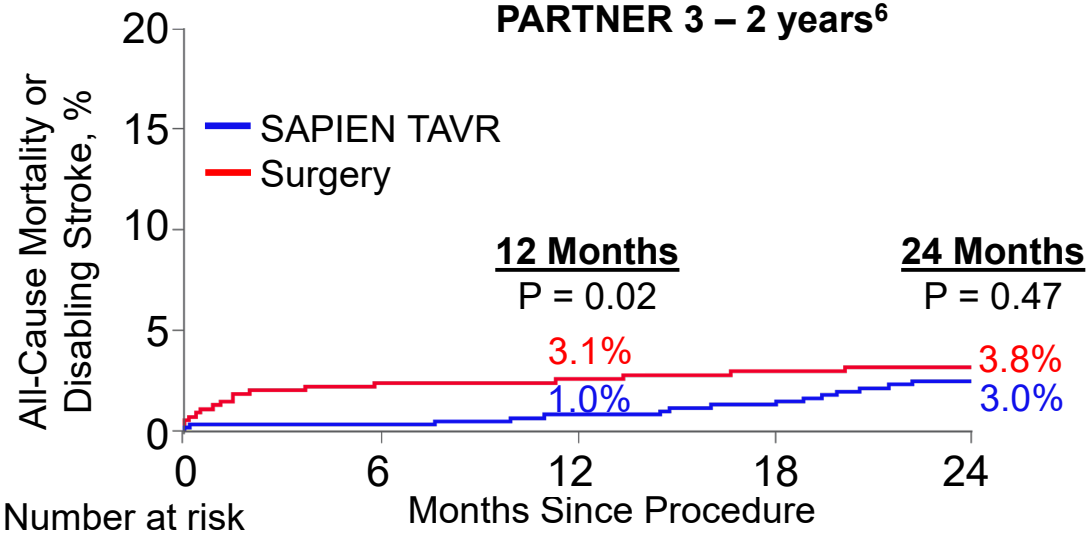
Evolut Low Risk – 2 years[5]



Number at risk

TAVR	730	725	715	706	691	674
Surgery	684	663	648	627	616	588

PARTNER 3 – 2 years[6]



Number at risk

TAVR	496	493	490	483	472	
Surgery	454	431	424	410	400	

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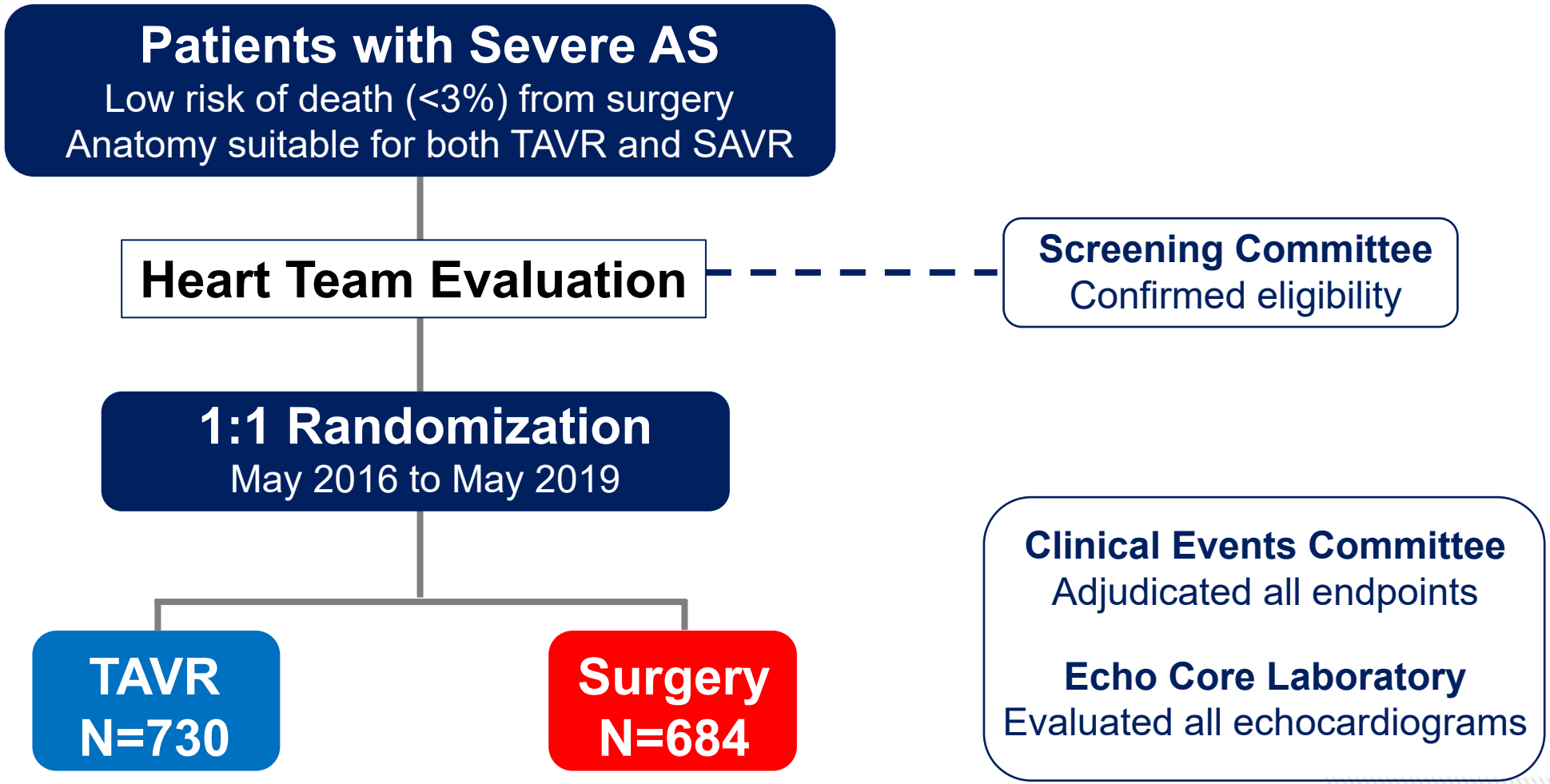
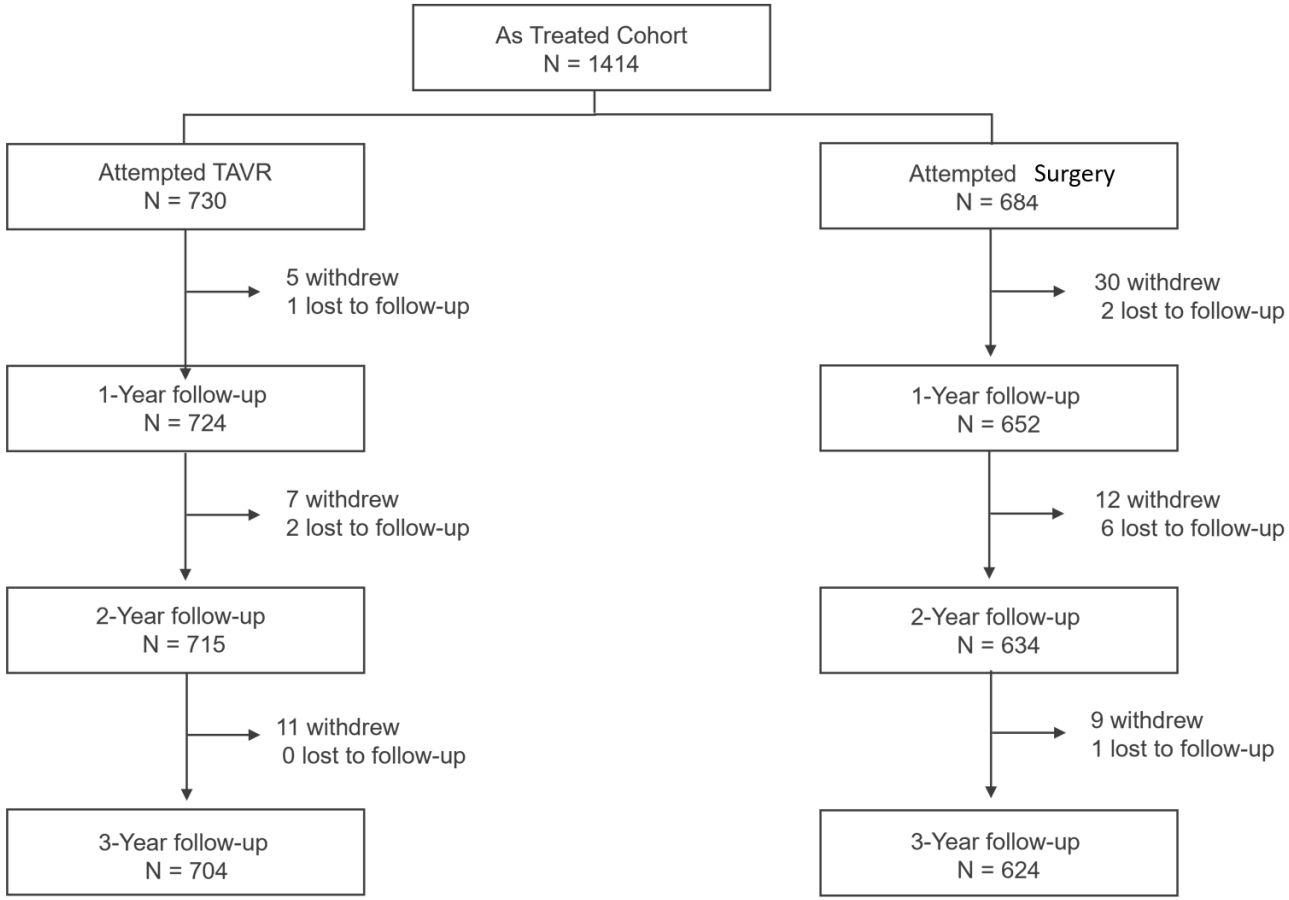
[1]Gleason TG, et al. JACC 2018;72:2687-2696. [2]Mack MJ, et al. Lancet 2015;385:2477-2484. [3]Van Mieghem NM, et al. JAMA Cardiol 2022;7:1000-1008. [4]Makkar RR, et al. NEJM 2020;382:799-809. [5]Forrest JK, et al. JACC 2022;79:882-896. [6]Leon MB, et al. JACC 2021;77:1149-1161.

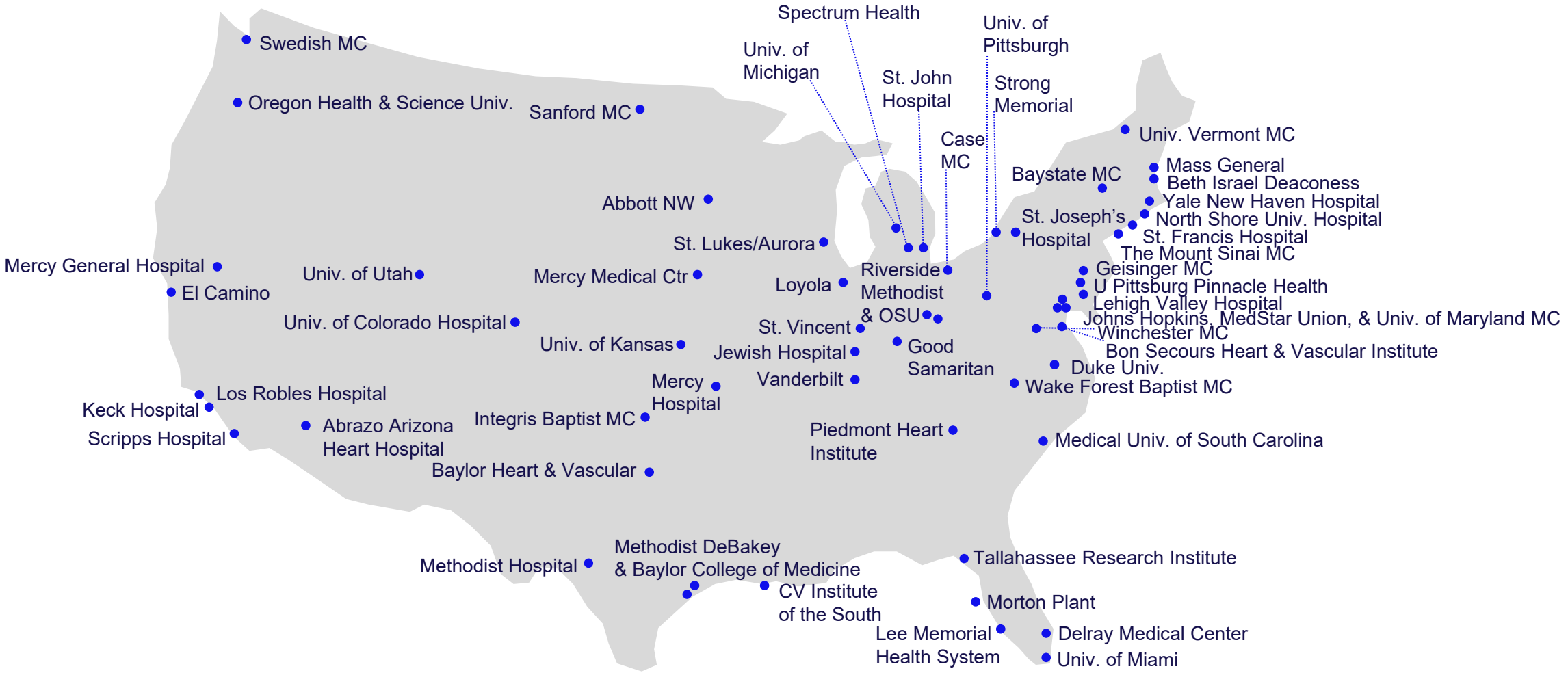
Evolut Low Risk Study Design

Evolut™ Low Risk Trial

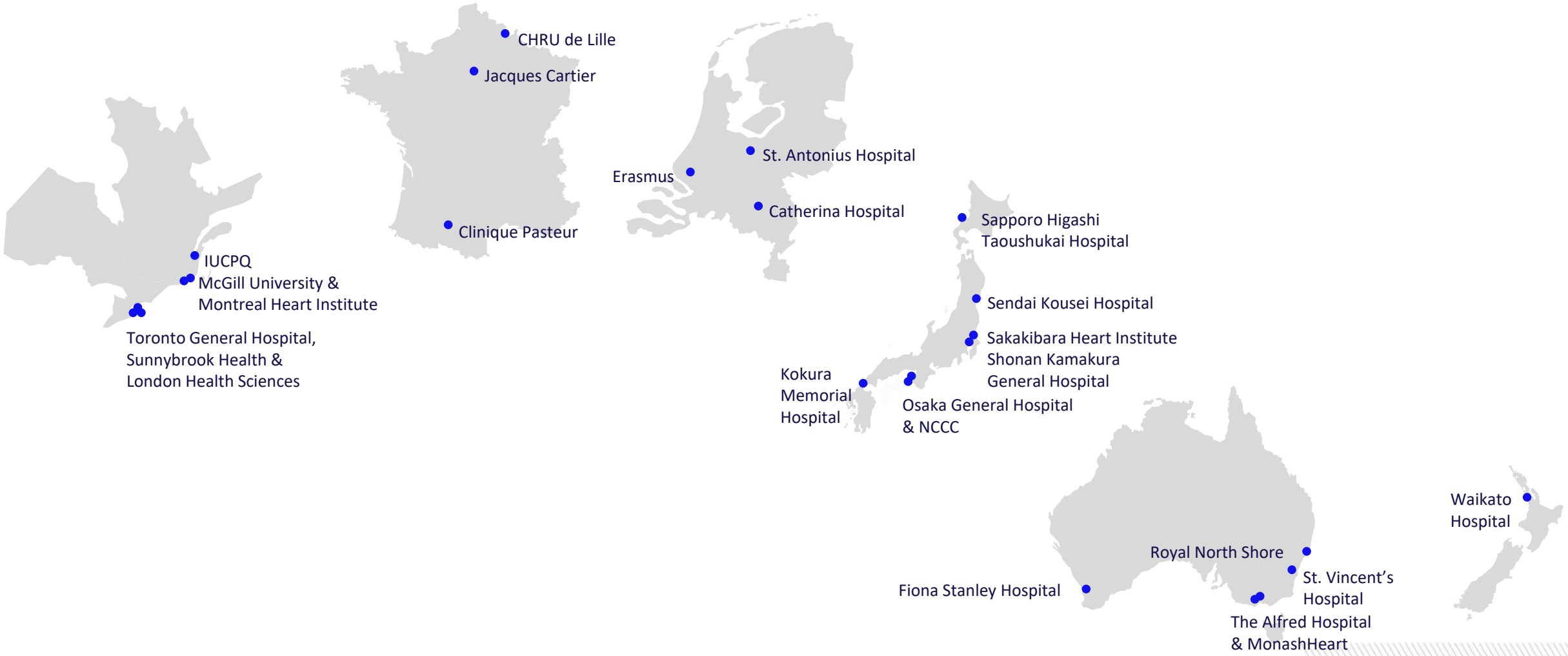



As Treated Cohort
N = 1414
Attempted TAVR
N = 730
5 withdrew
1 lost to follow-up
1-Year follow-up
N = 724
7 withdrew
2 lost to follow-up
2-Year follow-up
N = 715
11 withdrew
0 lost to follow-up
3-Year follow-up
N = 704
Attempted Surgery
N = 684
30 withdrew
2 lost to follow-up
1-Year follow-up
N = 652
12 withdrew
6 lost to follow-up
2-Year follow-up
N = 634
9 withdrew
1 lost to follow-up
3-Year follow-up
N = 624

Participating Sites in the United States



Australia, Canada, Europe, Japan, and New Zealand



Baseline Characteristics

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Mean ± SD or %	Evolut TAVR (N = 730)	Surgery (N = 684)
Age	74.1 ± 5.8	73.7 ± 5.9
Female	36.4	34.1
Left ventricular ejection fraction, %	61.7 ± 7.9	61.9 ± 7.7
STS-PROM score, %	2.0 ± 0.7	1.9 ± 0.7
NYHA class III/IV	24.9	28.2
Hypertension	84.8	82.6
Chronic lung disease, COPD	15.1	18.0
Previous CABG	2.5	2.0
Previous PCI	14.1	12.9
Atrial fibrillation/atrial flutter	15.4	14.4
Pre-existing permanent pacemaker or defibrillator	3.3	3.8

No significant differences between treatment groups

Primary Endpoint: All-Cause Mortality or Disabling Stroke

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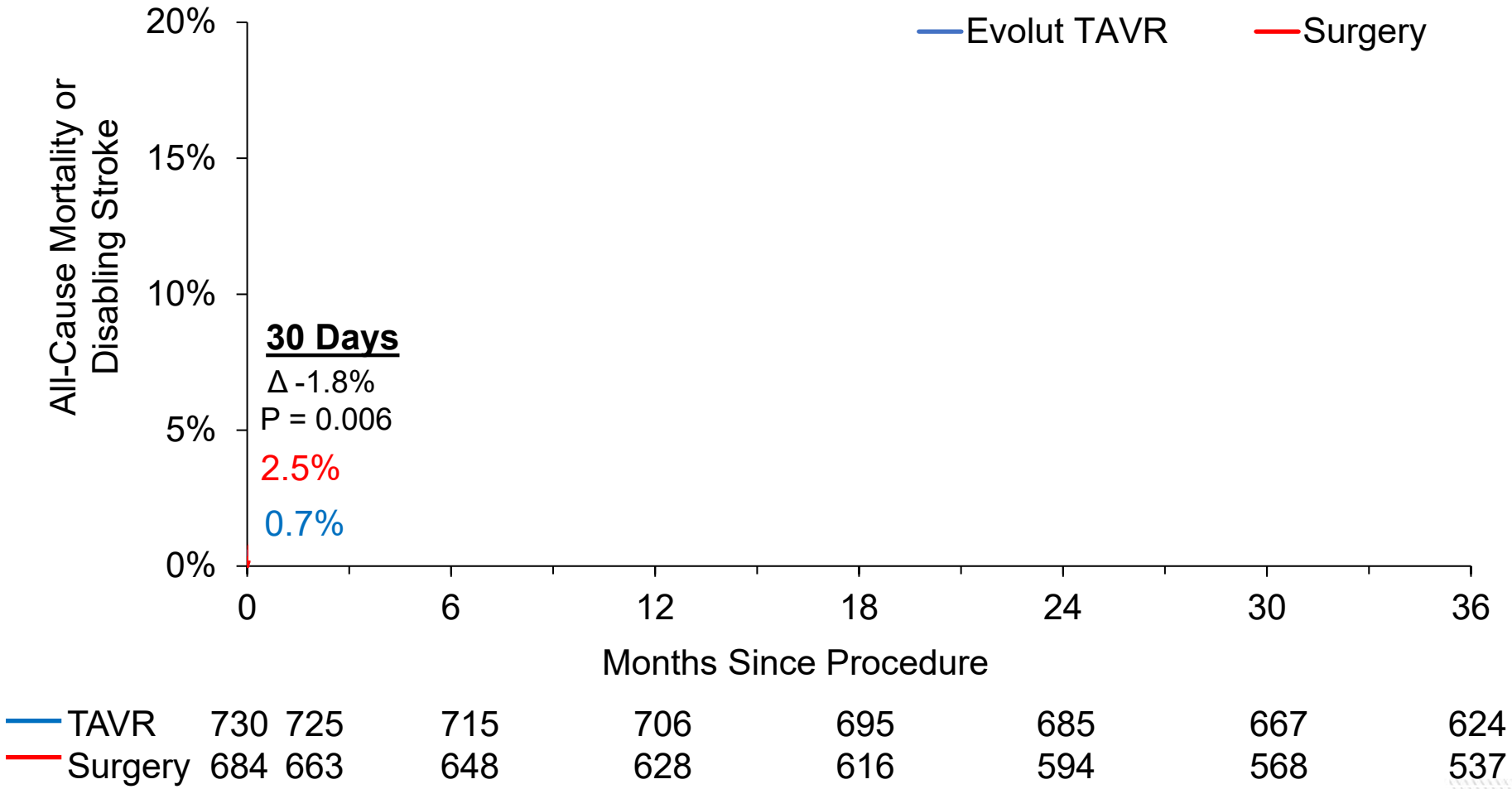

All-Cause Mortality and Disabling Stroke

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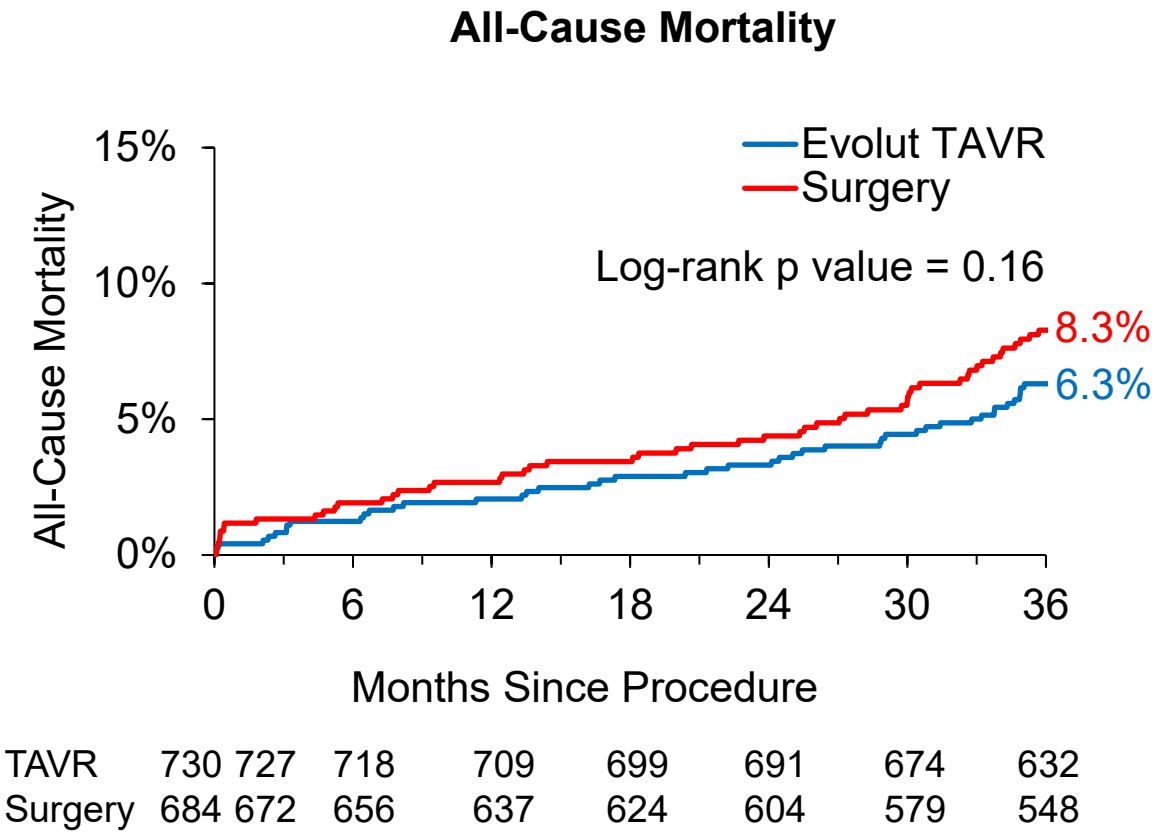

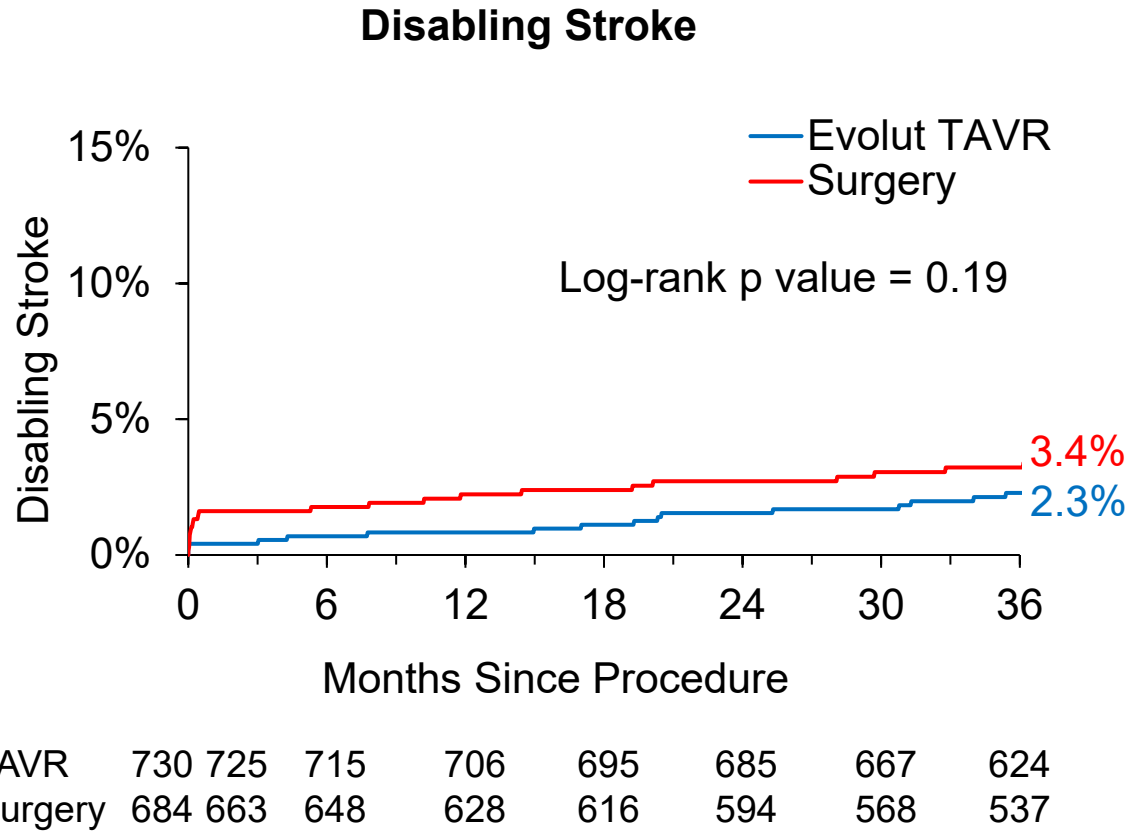

3-Year Death or Disabling Stroke by Baseline Variables

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Variable	KM rate at 3 years		HR (95% CI)	P value for Interaction
	Evolut TAVR	Surgery		
Age, years				0.95
< 75	5.7	8.0	0.71 (0.40-1.26)	
≥ 75	9.1	13.0	0.68 (0.43-1.07)	
Sex				0.41
Male	7.8	11.7	0.64 (0.41-0.98)	
Female	6.8	7.8	0.89 (0.46-1.73)	
BMI, kg/m^2				0.71
≤ 30	6.6	9.9	0.65 (0.39-1.10)	
> 30	8.2	10.8	0.75 (0.45-1.23)	
STS Score, %				0.55
< 2	5.8	9.0	0.62 (0.37-1.06)	
≥ 2	9.4	12.0	0.77 (0.47-1.26)	
NYHA				0.71
I/II	6.7	9.7	0.78 (0.41-1.47)	
III/IV	9.7	11.9	0.77 (0.47-1.26)	
Baseline KCCQ				0.43
≤ 72	8.1	12.7	0.62 (0.38-0.99)	
> 72	6.5	7.8	0.83 (0.47-1.45)	
COPD				0.63
No	7.8	10.9	0.89 (0.35-2.25)	
Yes	7.6	8.8	0.83 (0.47-1.45)	

Clinical Outcomes Through 3 Years

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Kaplan-Meier estimate, %	Evolut TAVR (N=730)	Surgery (N=684)	Log-rank P Value
All-cause mortality or disabling stroke	7.4	10.4	0.051
All-cause mortality	6.3	8.3	0.16
Cardiovascular death	4.1	5.6	0.18
All stroke	7.4	6.6	0.55
Disabling stroke	2.3	3.4	0.19
AV hospitalization[a]	7.4	9.2	0.20
All-cause mortality, disabling stroke, or AV hospitalization	13.2	16.8	0.050
Myocardial infarction	3.4	2.3	0.25
Permanent pacemaker implant[b]	23.2	9.1	<0.001
Atrial fibrillation	13.1	40.0	<0.001
Valve endocarditis	0.7	1.3	0.30

[a]Not adjudicated by the Clinical Events Committee (CEC). [b]Patients with pacemaker or ICD at baseline are not included. Not adjudicated by the CEC.

Valve Performance at 3 Years

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% (n)[a]	Evolut TAVR	Surgery	P Value
Paravalvular regurgitation	**N=541**	**N=447**	
None/trace	78.7 (426)	97.3 (435)	
≥ Mild	21.3 (115)	2.7 (12)	<0.001
≥ Moderate	0.9 (5)	0.2 (1)	0.16
Prosthesis-Patient Mismatch (VARC-3)	**N=489**	**N=394**	
None	89.4 (437)	74.9 (295)	
Moderate	9.2 (45)	20.3 (80)	
Severe	1.4 (7)	4.8 (19)	0.003
≥ Moderate	10.6 (52)	25.1 (99)	<0.001
Total valve thrombosis	0.7 (5)	0.6 (4)	0.84
Clinical valve thrombosis	0.3 (2)	0.2 (1)	0.61
Subclinical valve thrombosis	0.4 (3)	0.5 (3)	0.91
Reintervention	1.0 (7)	0.9 (6)	0.92

[a]PVR and PPM are reported as proportion % (n) and compared by chi-square test, with number of patients with echos at 3 years shown in the top row for each. Reintervention and valve thrombosis are reported as Kaplan-Meier estimate % (n) and compared by log-rank test.

Most TAVs in the study were Evolut R (73%) and did not have an external pericardial wrap.
PVR and PPM were based on Echo Core Laboratory assessment.

3-Year All-Cause Mortality or Disabling Stroke in the TAVR Cohort by PVR

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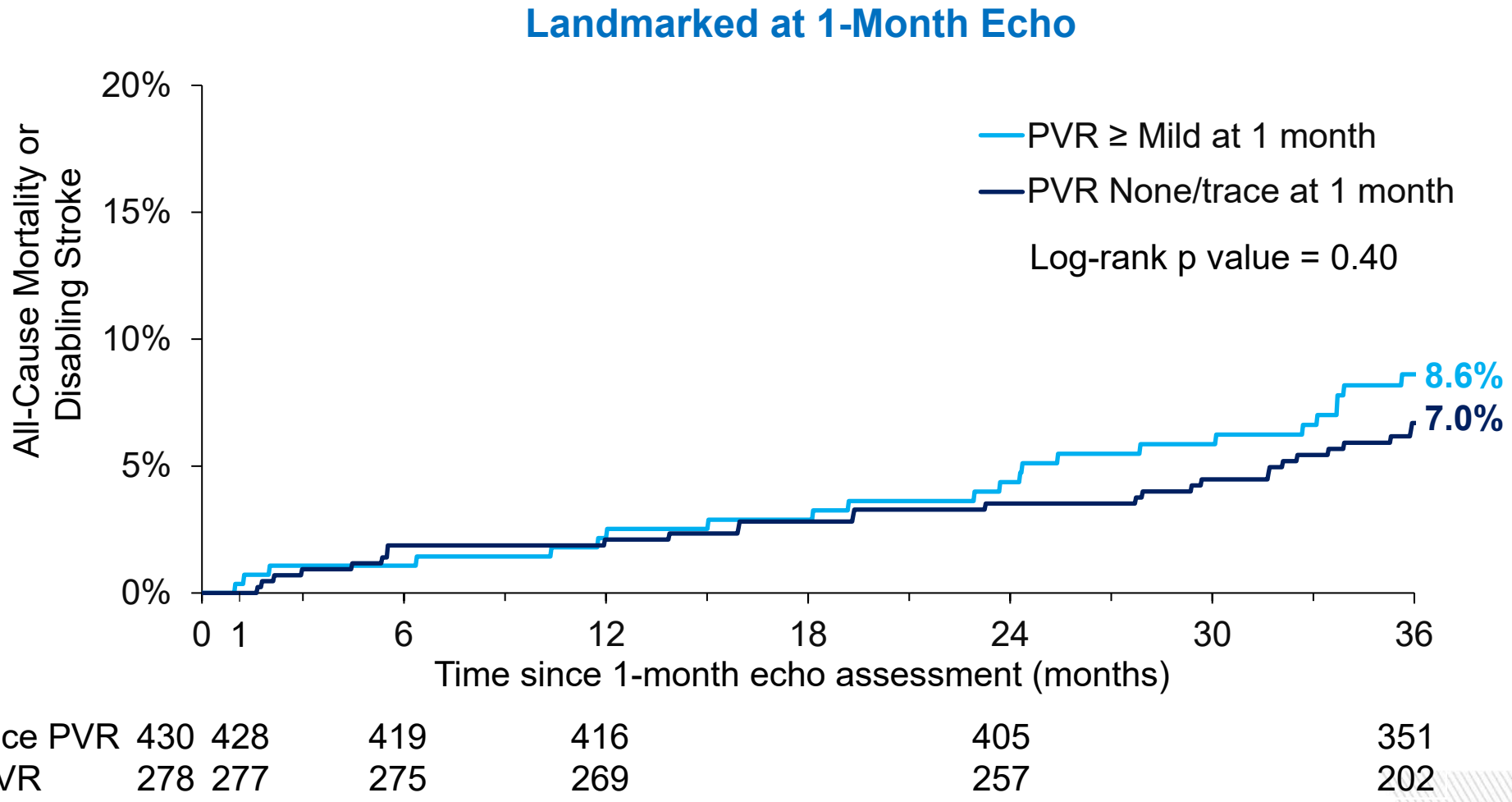
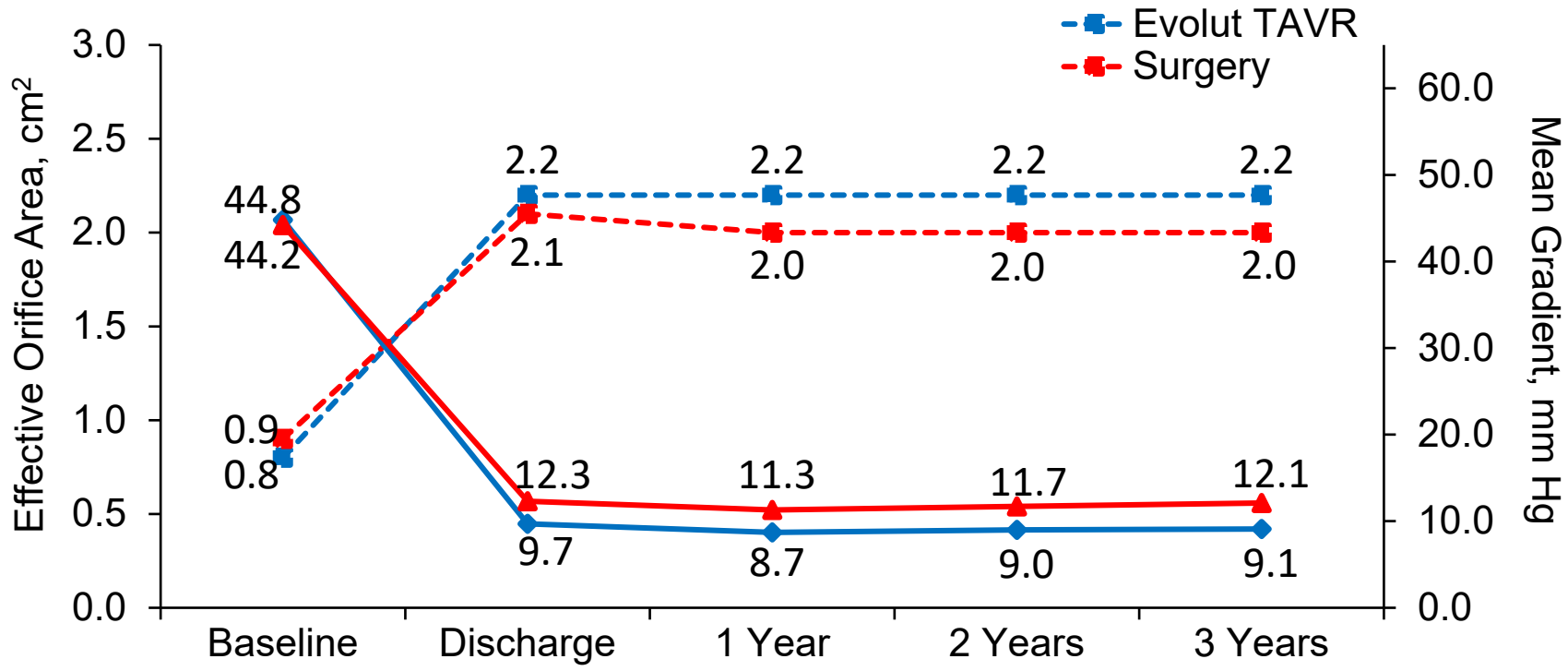


PVR = paravalvular regurgitation
PVR was based on Echo Core Laboratory assessment.

Valve Hemodynamics to 3 Years

Evolut™ Low Risk Trial

Significantly better MG and EOA with Evolut TAVR at all follow-up timepoints (p < 0.01)



No. of patients					
TAVR EOA	637	576	565	535	493
Surgery EOA	596	406	525	434	396
TAVR MG	717	703	662	607	547
Surgery MG	679	632	597	514	456

KCCQ Overall Summary Score

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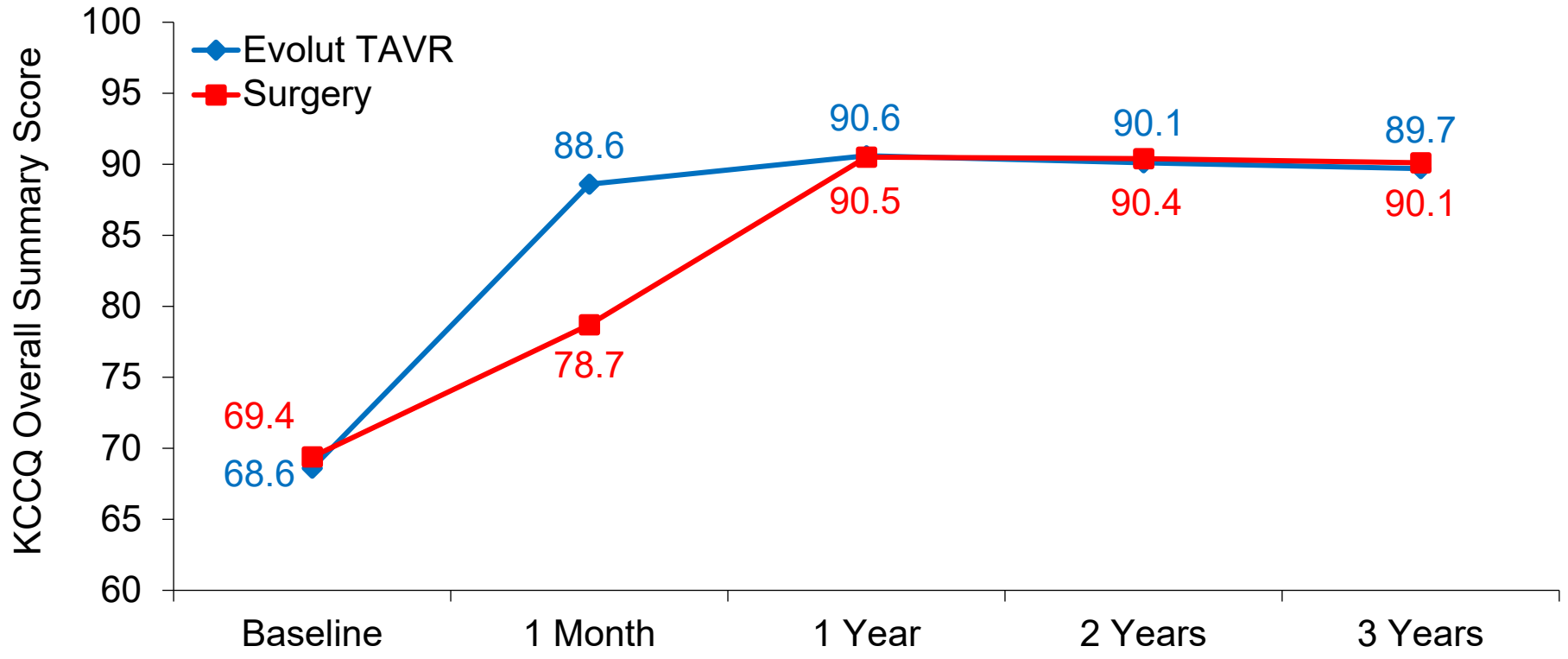

Change from Baseline				
TAVR	20.0 ± 21.1	21.6 ± 20.6	20.9 ± 20.8	20.1 ± 20.6
Surgery	9.2 ± 22.3	20.7 ± 20.3	20.0 ± 20.0	19.3 ± 21.1
P value	<0.001	0.42	0.44	0.53

Summary

Evolut™ Low Risk Trial

- At 3 years, the rate of all-cause mortality or disabling stroke was 7.4% with TAVR and 10.4% with surgery.
    - The absolute difference between treatment arms remained consistent over time, with a 30% relative reduction in hazard (p = 0.051) for death or disabling stroke.
- TAVR patients continued to have better valve hemodynamics at 3 years.
- Residual paravalvular regurgitation 3 years after TAVR was none/trace in nearly 80% of patients and there was no difference in >mild PVL.
- Rates of new pacemaker implantation were higher after TAVR and the frequency of new onset atrial fibrillation was more common after surgery.

Clinical Implications

Evolut™ Low Risk Trial

1. These results provide patients and heart teams important data to aid in the shared decision-making process.

2. The excellent valve performance and durable outcomes out to 3 years in low-risk patients affirms the role of TAVR in this population.

3. Longer-term data are needed and the potential impact that hemodynamics, valve design, new pacemakers, and other secondary endpoints have on long-term outcomes will be important to follow in this group of low-risk patients.

Manuscript published today in JACC

Evolut™ Low Risk Trial

Three-Year Outcomes After Transcatheter or Surgical Aortic Valve Replacement in Low-Risk Patients

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Thank you to the patients, physicians, and clinical study teams who made this work possible.