Seven-year Outcomes of the PARTNER 3 Low-risk Trial

Michael J. Mack, MD &
Martin B. Leon, MD
on behalf of the PARTNER 3 Trial Investigators

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Disclosures: Michael J. Mack, MD

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Within the past 36 months, I or my spouse/partner has had a financial interest/arrangement or affiliation with the organization(s) listed below.

Financial Relationship	Company
• Institutional Research Support	NA
• Consulting Fees	NA
• Trial Co-PI	Abbott, Edwards Lifesciences
• Trial Study Chair	Medtronic

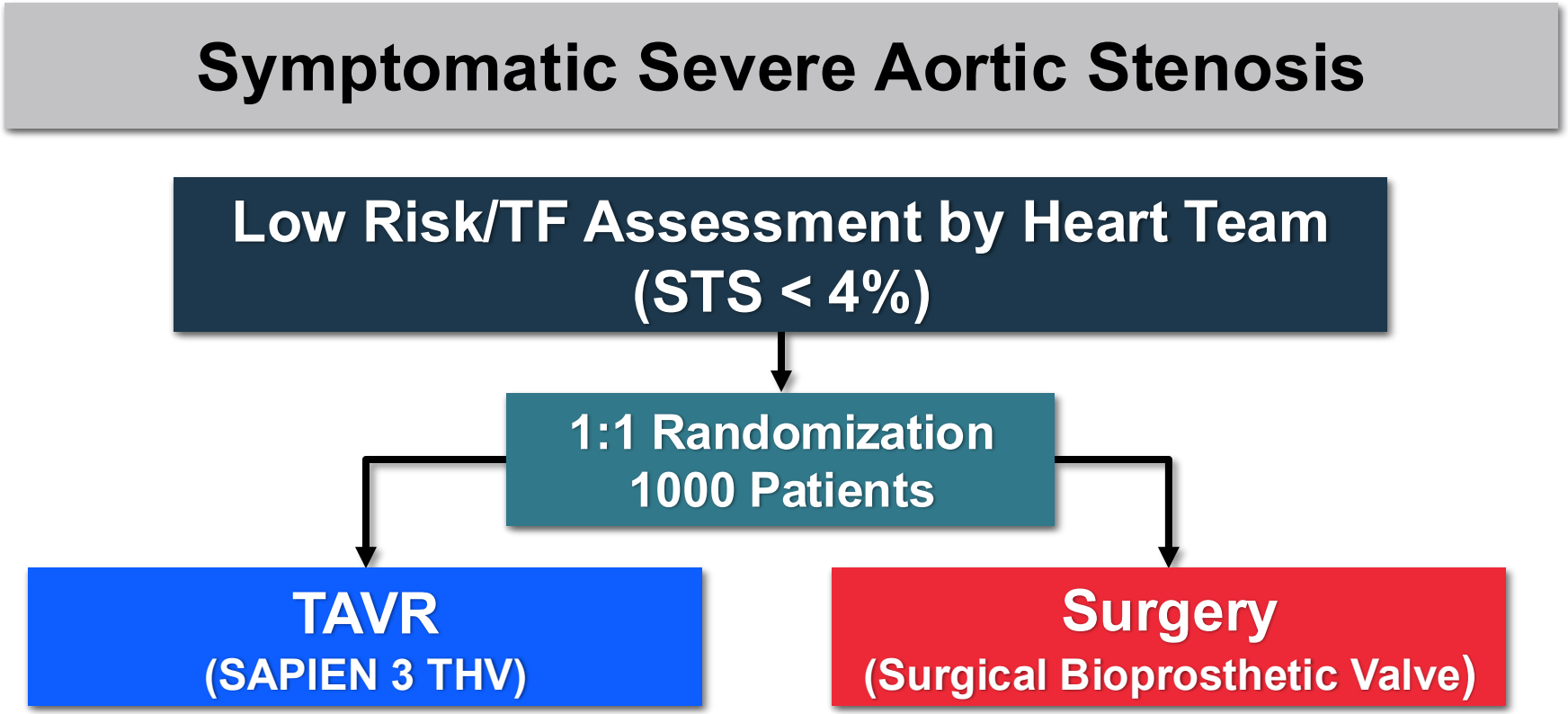
Background

- The PARTNER 3 low-risk randomized trial showed superior outcomes for TAVR vs Surgery at 1 year, but between-group differences attenuated through 5-year follow-up.
- Favorable surgical bioprosthetic valve durability has been reported for 10 or more years, but early valve failure can occur as soon as 5 to 7 years.
- As TAVR is increasingly performed in younger patients with longer life expectancy, understanding long-term transcatheter and surgical valve durability is essential to inform patient-centered decision making.

Purpose

To report the clinical, echocardiographic, and valve durability outcomes of the PARTNER 3 Trial at ***7 years*** for low-risk patients with symptomatic severe AS treated with balloon-expandable, SAPIEN 3 TAVR vs. Surgery

PARTNER 3 Study Design



Clinical follow-up: 30 days, 6 mos, & 1 – 10 yrs annually;
Echo follow-up: 30 days, 6 mos, 1 – 5 yrs annually, 7, & 10 yrs

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Methodology Considerations
For Long-term Follow-up

- One-year endpoints and definitions were supplemented with outcomes more relevant to long-term follow-up, especially valve durability and late clinical events.
- Challenges of long-term follow-up include data missingness, withdrawal/lost to follow-up, and the competing risk of death as patients age.
- To improve completeness of follow-up, FDA-mandated annual **vital status sweeps (VSS)** were performed by sites using patient/family phone calls, medical records, and/or publicly-available data.

Primary Endpoints

Primary Endpoint 1

- **Non-hierarchical composite** of all-cause death, all stroke, or rehospitalization* (time to first event)
- Assessed as the KM rate difference at 7 years
- Also depicted as a hazard ratio (HR)

Primary Endpoint 2

- **Hierarchical composite** of all-cause death, disabling stroke, non-disabling stroke, and rehospitalization* days
- Assessed using the ***win ratio*** method

*Rehosp related to the valve, procedure, or heart failure

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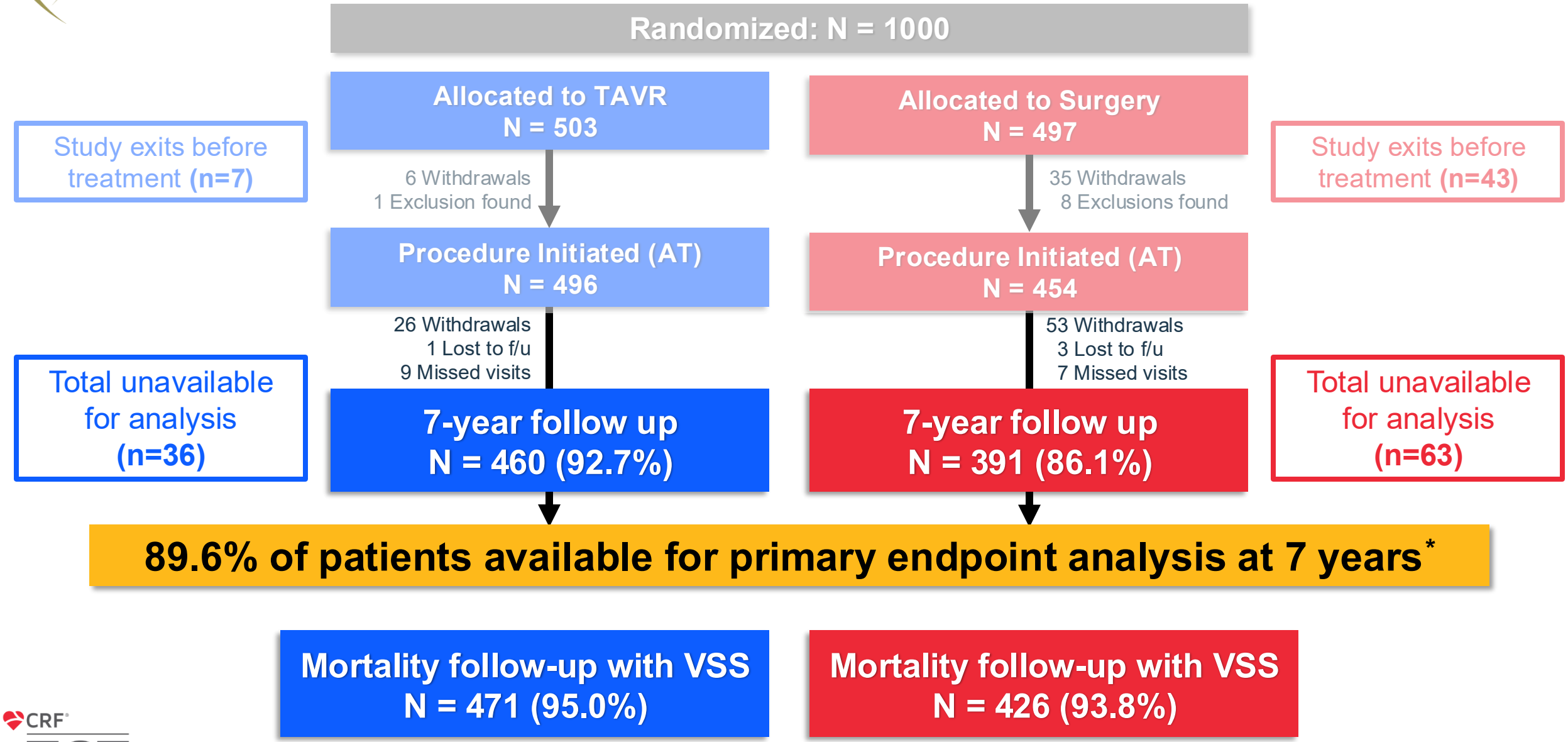
Patient Disposition



*Includes patients evaluable for the primary composite endpoint; does not include VSS data

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Baseline Characteristics

% or mean ± SD

Demographics & Vascular Disease	TAVR (N=496)	Surgery (N=454)	Other Comorbidities	TAVR (N=496)	Surgery (N=454)
Age (years)	**73.3 ± 5.8**	**73.6 ± 6.1**	Diabetes	31.3%	30.2%
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI (kg/m^2)	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	**1.9 ± 0.7**	**1.9 ± 0.6**	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	**27.7%**	**28.0%**	**Atrial Fibrillation (h/o)**	**15.7%**	**18.8%**
Prior CVA	3.4%	5.1%	**Permanent Pacemaker**	**2.4%**	**2.9%**
Peripheral Vascular Disease	6.9%	7.3%	Left Bundle Branch Block	3.0%	3.3%

*$P = 0.01$

Abbreviations: BMI: Body Mass Index; CVA: CerebroVascular Accident; COPD: Chronic Obstructive Pulmonary Disease

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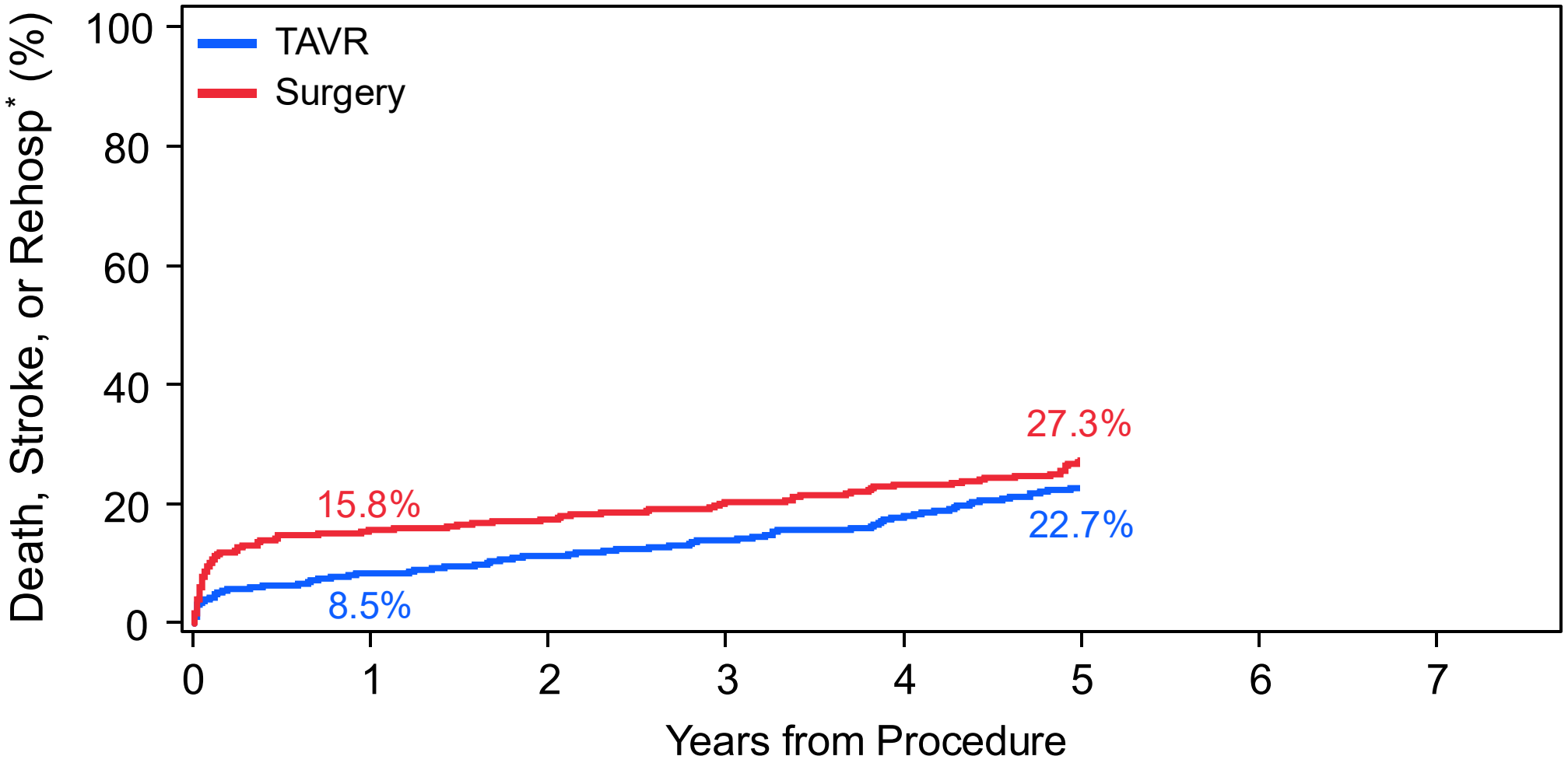
Primary Endpoint 1



Number at risk:

TAVR	496	453	435	418	394	366	333	288
Surgery	454	371	349	328	310	288	265	229

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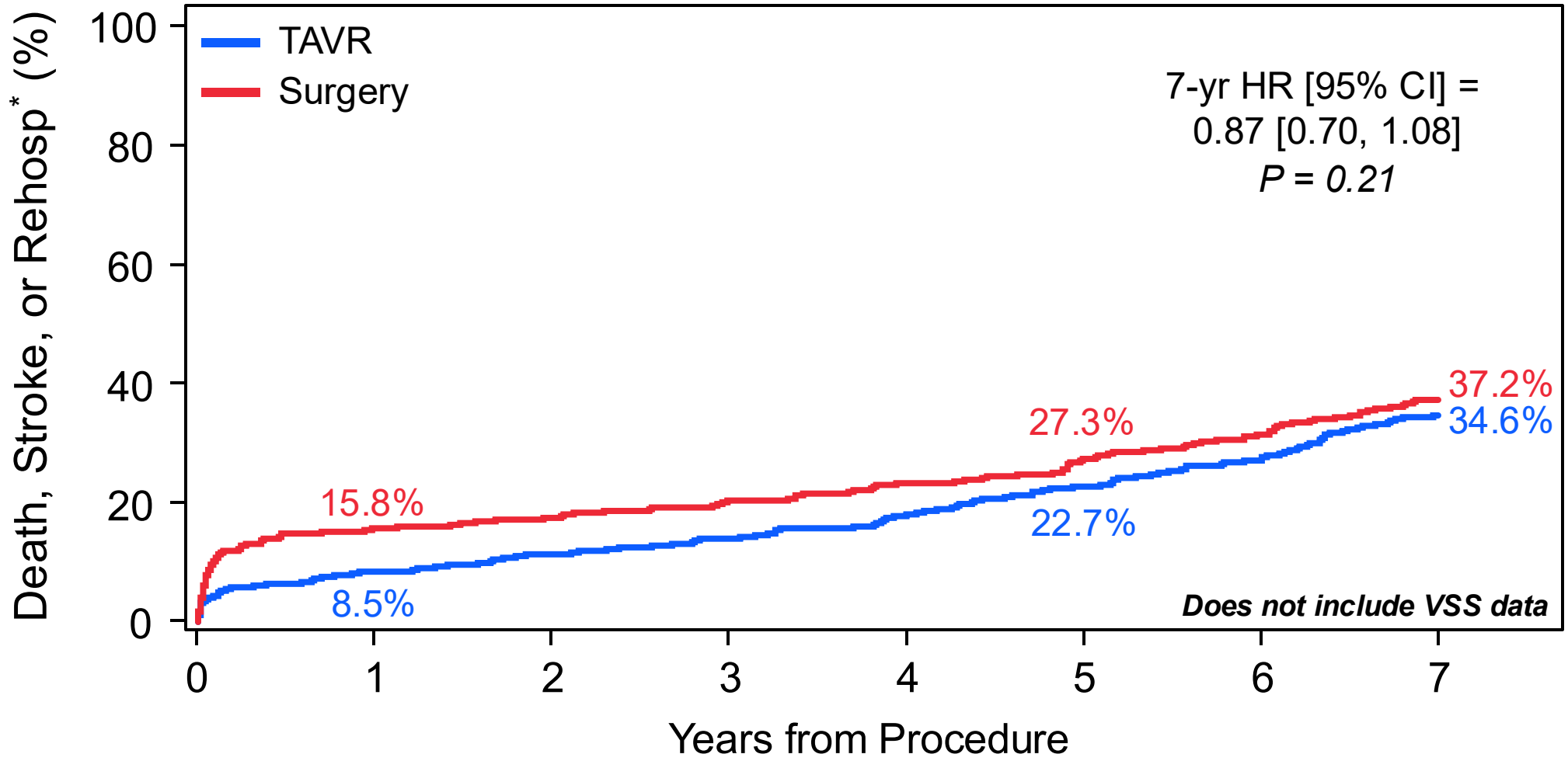

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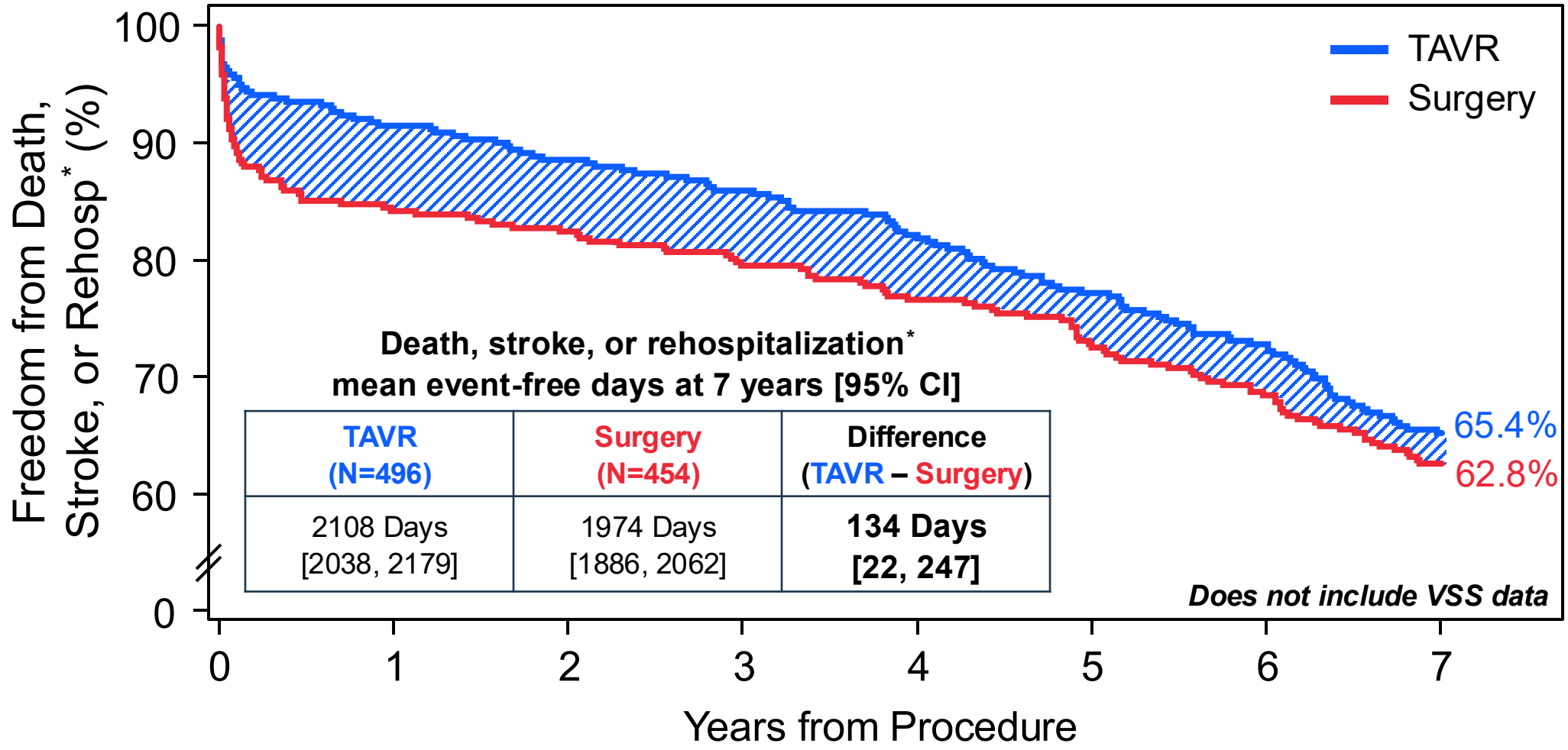
Restricted Mean Event-free Time



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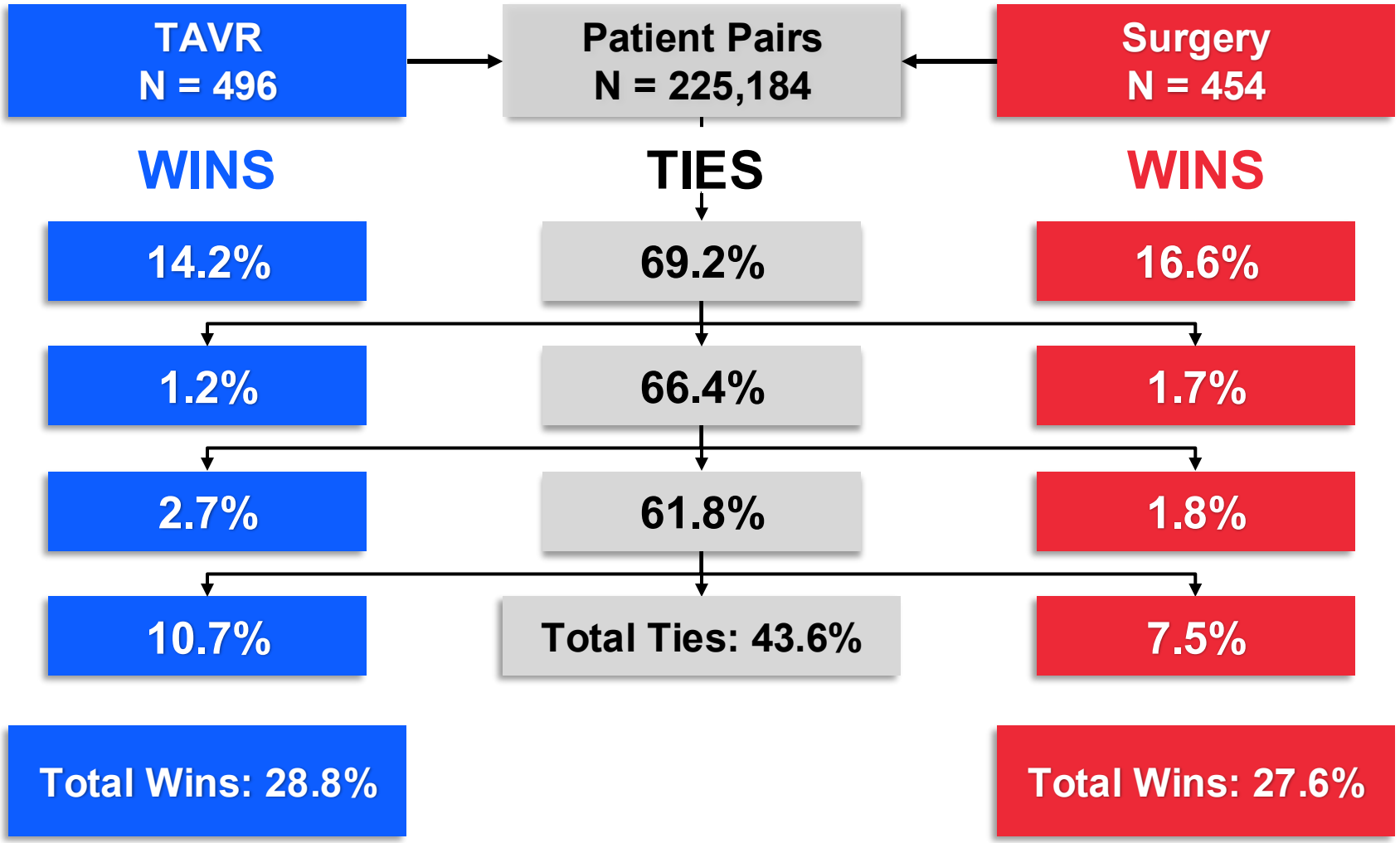
Primary Endpoint 2



Hierarchical Components:

1. All-cause Death (with VSS)
2. Disabling Stroke
3. Non-disabling Stroke
4. Rehospitalization Days
   (valve-, procedure-, or HF-related)

Win Ratio [95%CI] = $\frac{28.8}{27.6}$ = 1.04 [0.84, 1.30]; P = 0.70

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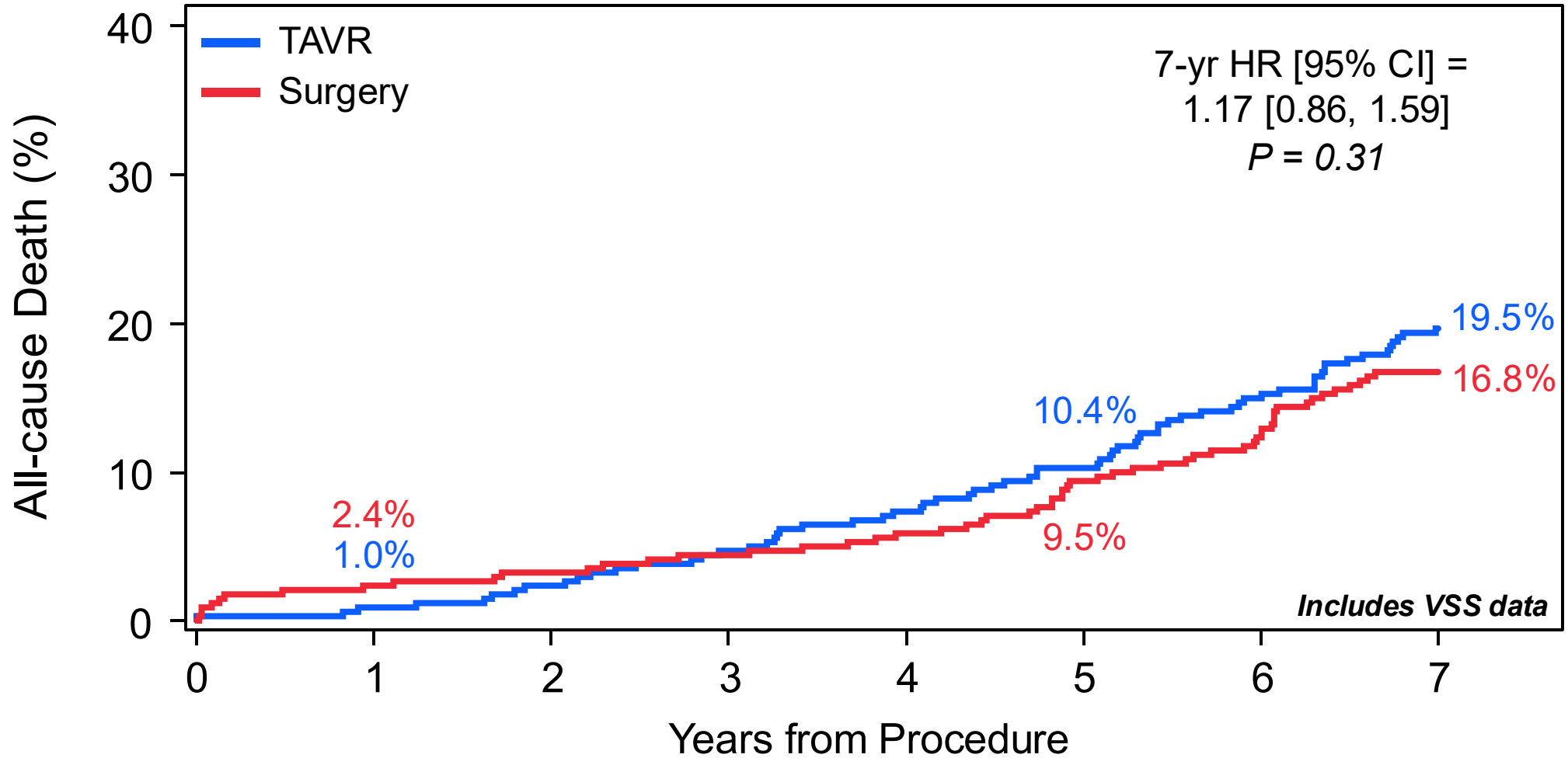
All-cause Death



Number at risk:

TAVR	496	490	481	468	449	433	405	377
Surgery	454	441	430	418	407	390	375	353

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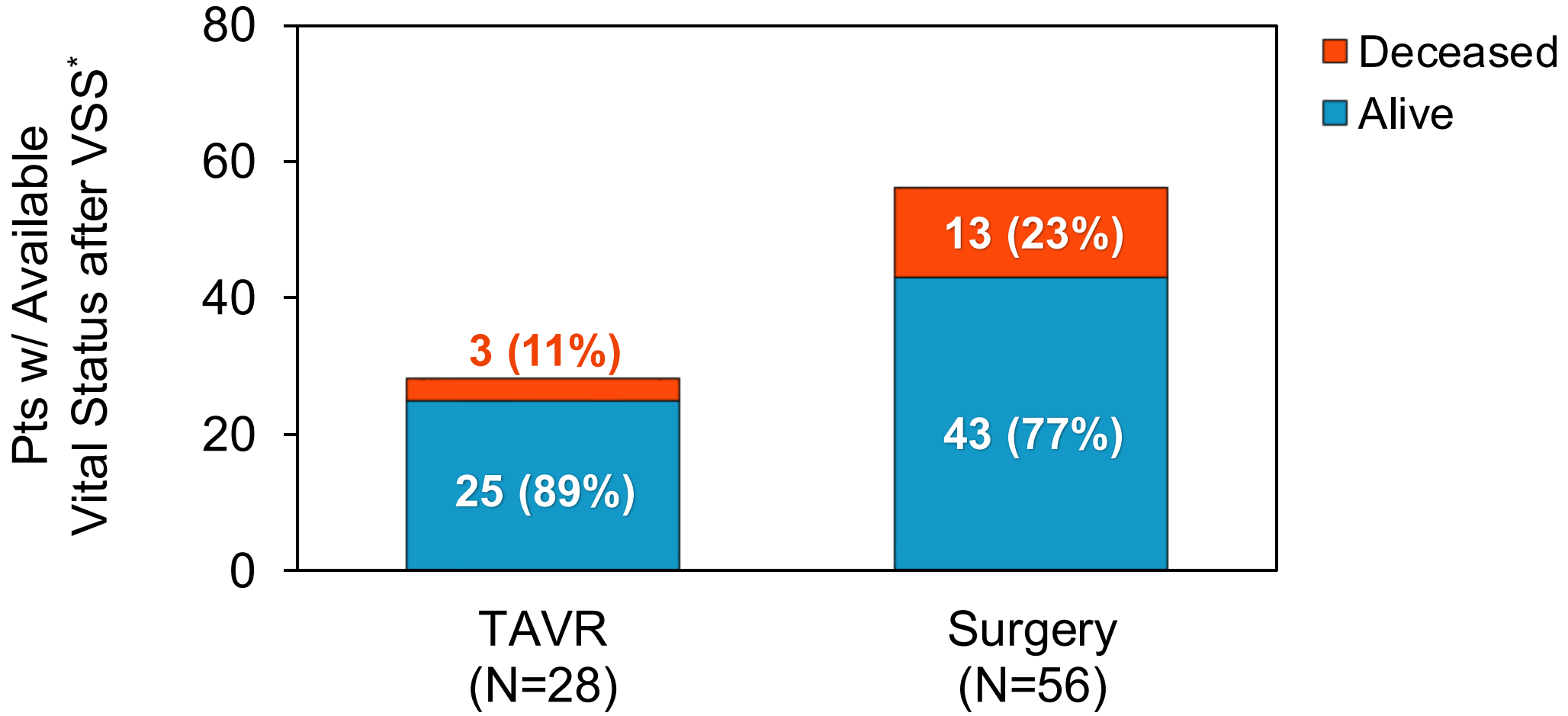
Vital Status Sweep (VSS)



VSS showed higher mortality in the Surgery arm among study exits

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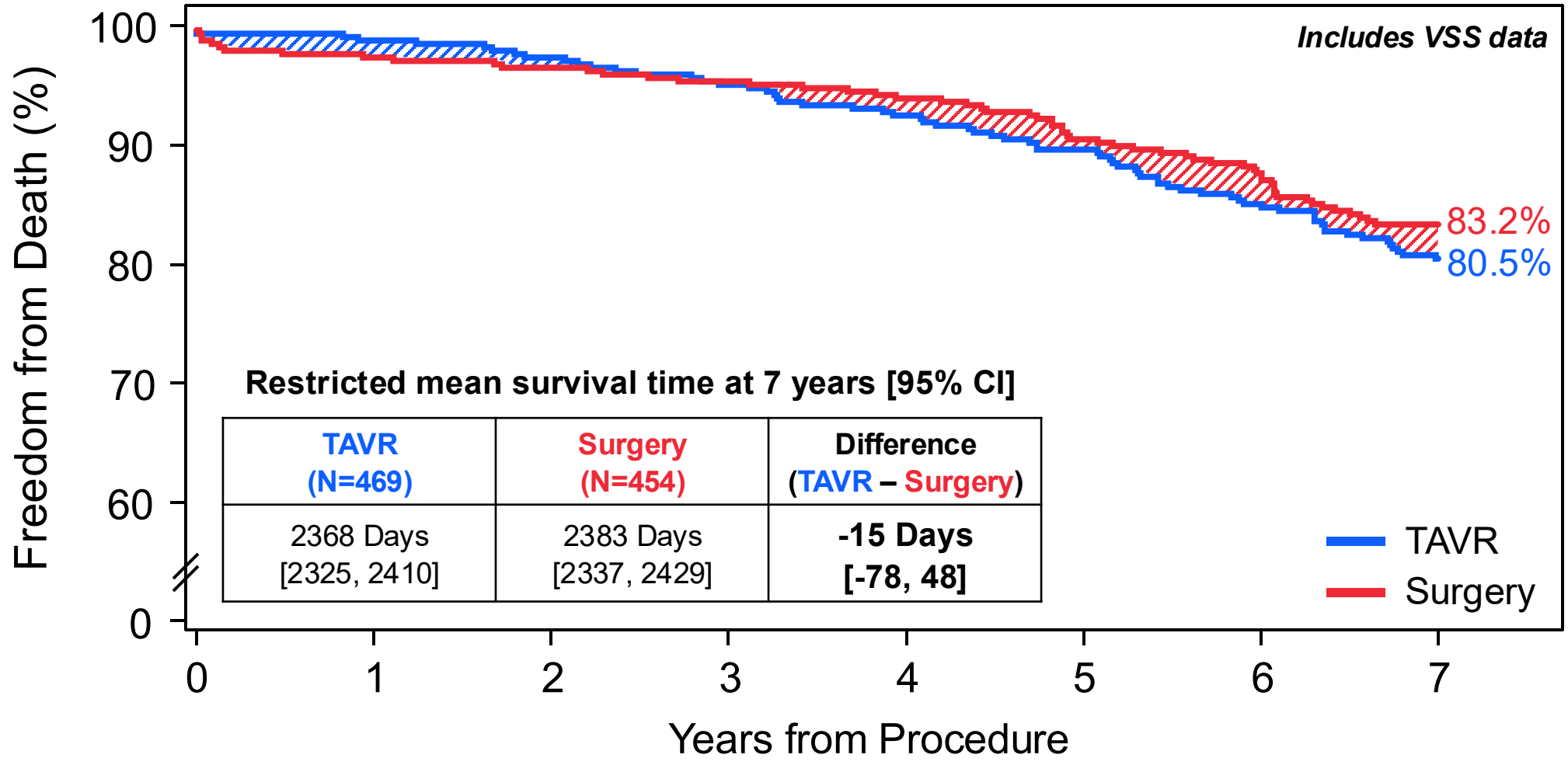
*VSS was performed by sites on patients who withdrew, were lost to follow-up, or missed a visit

Restricted Mean Survival Time



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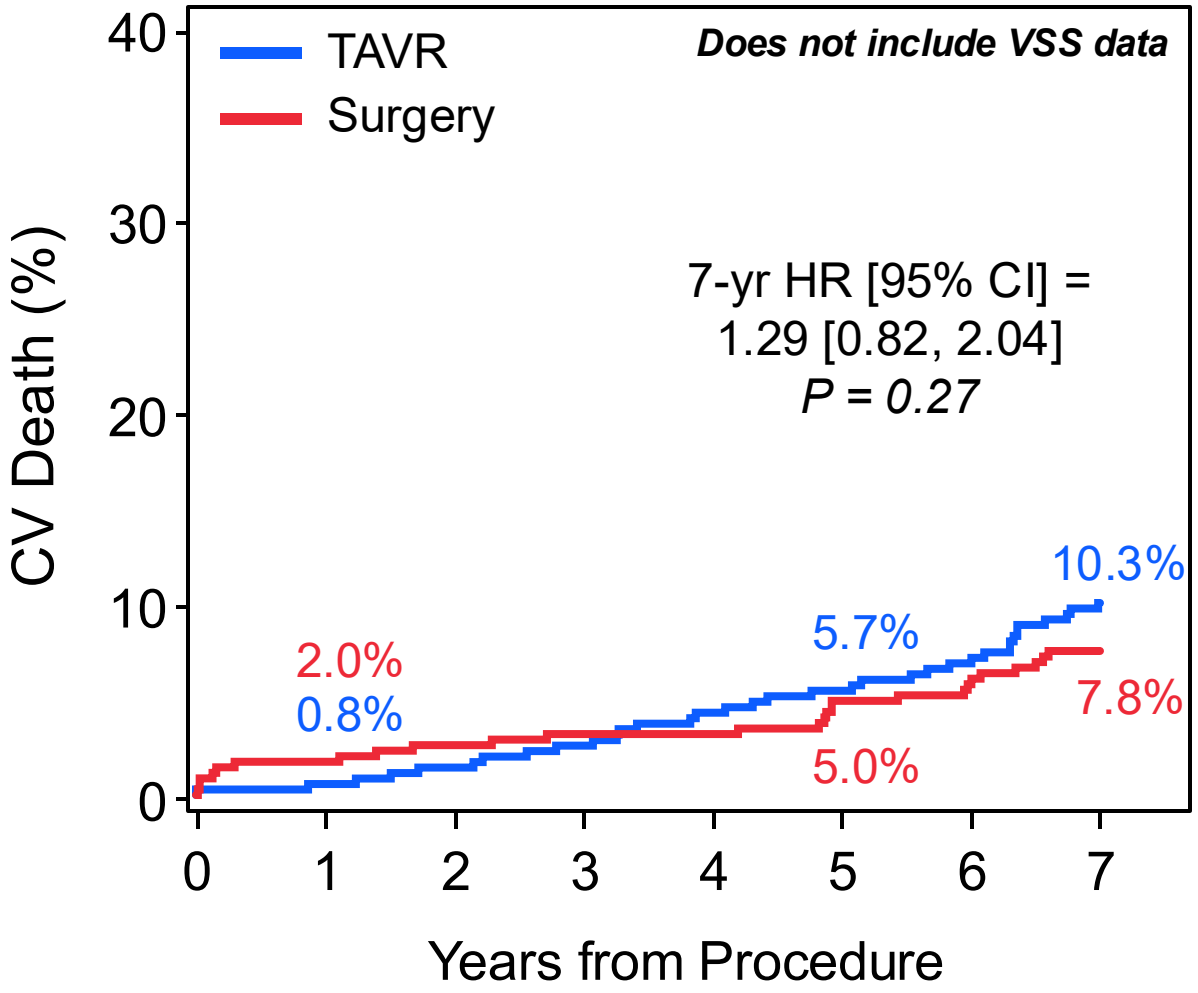
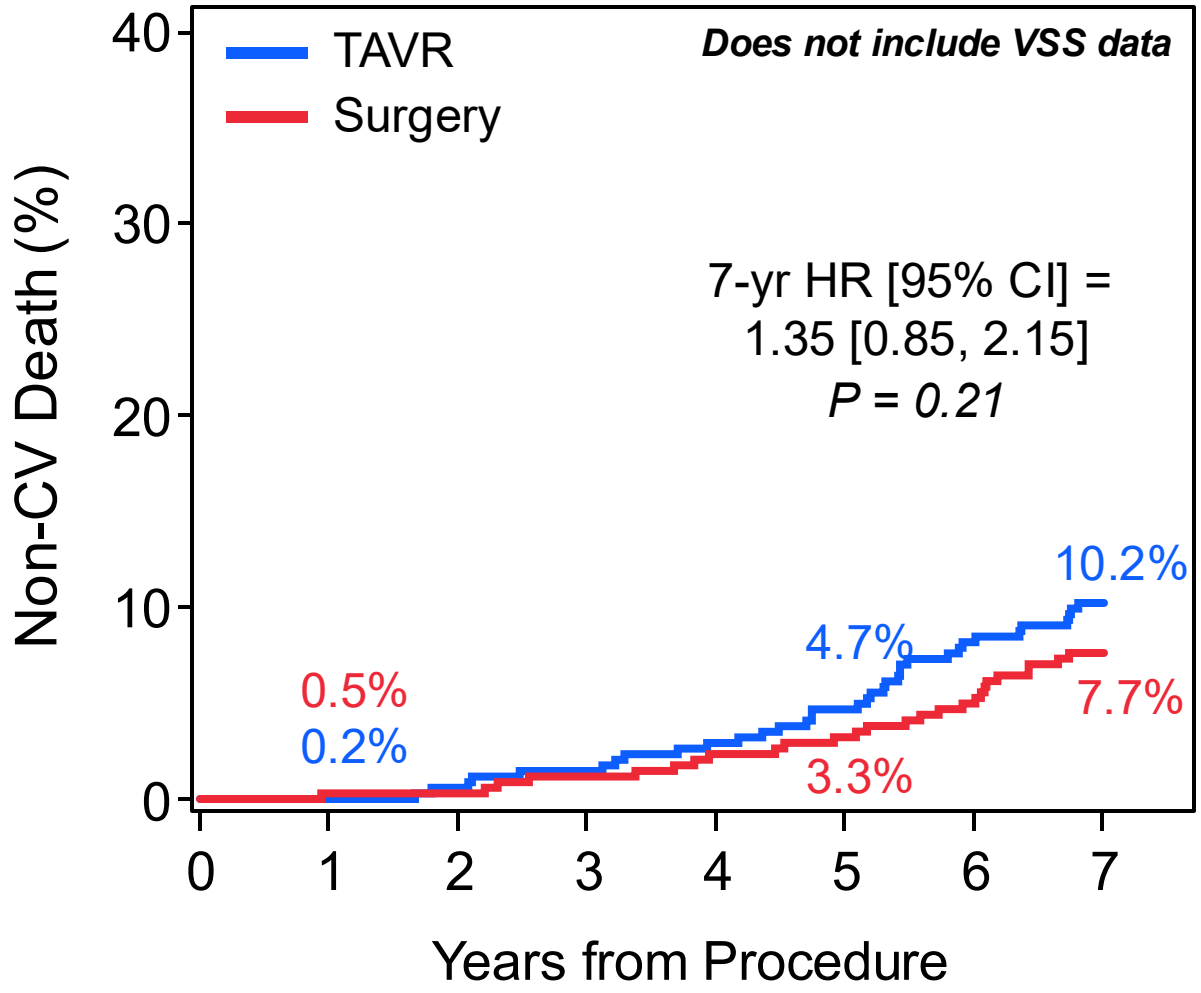
CV and Non-CV Death



No. at risk:

TAVR	496	490	480	465	443	422	388	352
Surgery	454	427	410	395	381	361	343	310



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Causes of Death 0 – 7 Years

CV Causes

Cause, No. of pts	TAVR	Surgery
Totals	**N=46**	**N=31**
Cardiac Cause	**18 (39.1%)**	**12 (38.7%)**
Acute MI	0	2
Cardiac Arrest	3	1
Cardiogenic Shock	1	1
CHF	7	6
Endocarditis	3	1
Sudden Cardiac Death	4	1
Non-coronary Vascular Conditions	**14 (30.4%)**	**6 (19.4%)**
Procedure-related	2	2
Stroke	6	4
Traumatic Head Injury from Fall	6	0
Unknown	**14 (30.4%)**	**13 (41.9%)**

Non-CV Causes

Cause, No. of pts	TAVR	Surgery
Totals	**N=45**	**N=29**
Cancer	18	11
Respiratory Failure*	12	10
Sepsis	8	3
Neurodegenerative Disease	1	2
Cirrhosis	1	1
MVA	1	1
GI Bleed	0	1
Homicide	1	0
Acute Renal Failure	1	0
Suicide	1	0
Toxic Metabolic Encephalopathy	1	0

*Due to COVID-19, chronic respiratory disease, or pneumonia

Vital-status Sweep

No. of VSS deaths	TAVR	Surgery
VSS (cause not determinable)	**3**	**13**

Abbreviations: MI: Myocardial Infarction; CHF: Congestive Heart Failure; MVA: Motor Vehicle Accident; GI: GastroIntestinal; VSS: Vital-Satus Sweep

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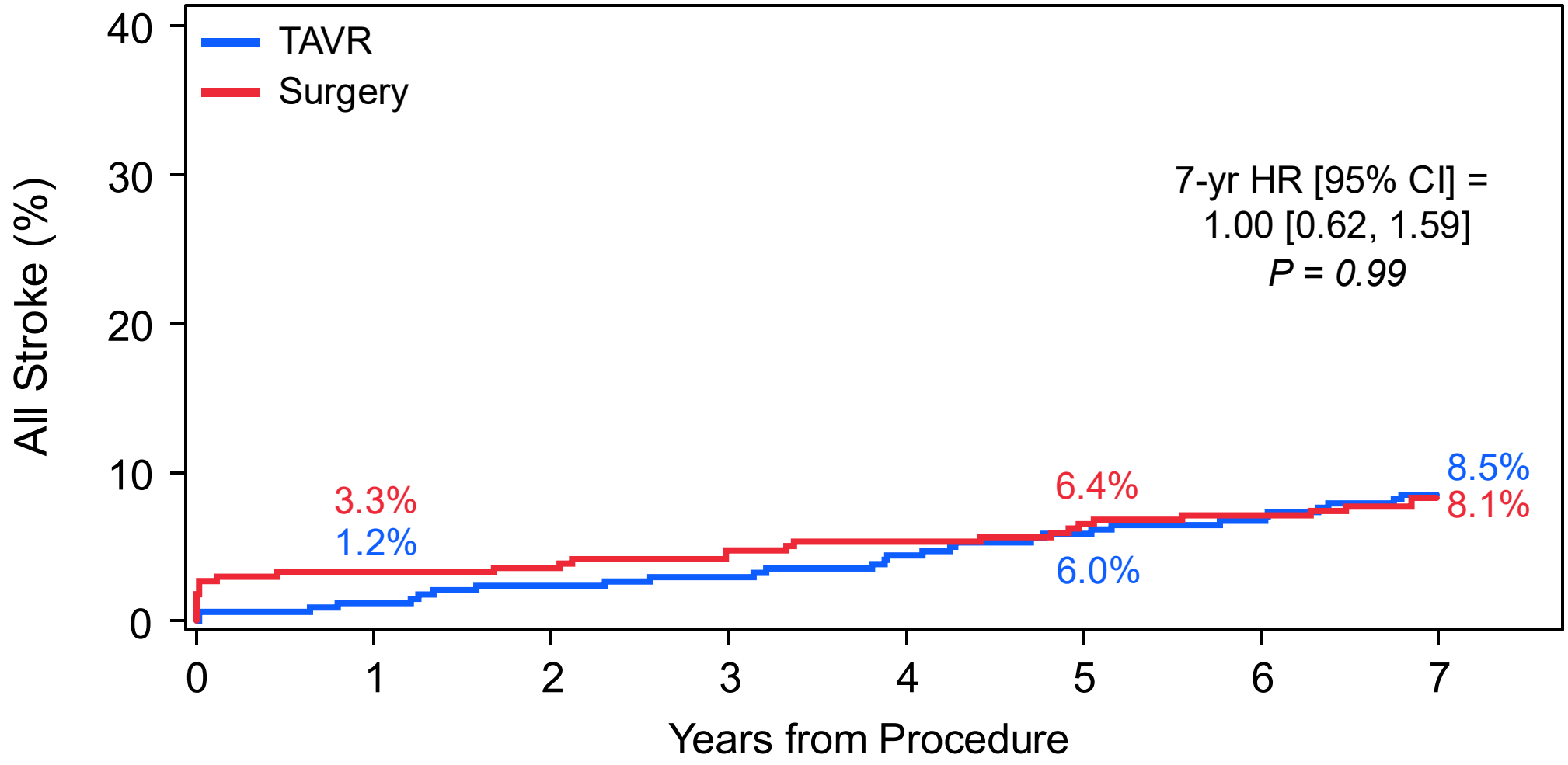
All Stroke



Number at risk:

TAVR	496	486	470	454	432	407	372	333
Surgery	454	416	398	379	363	344	326	291

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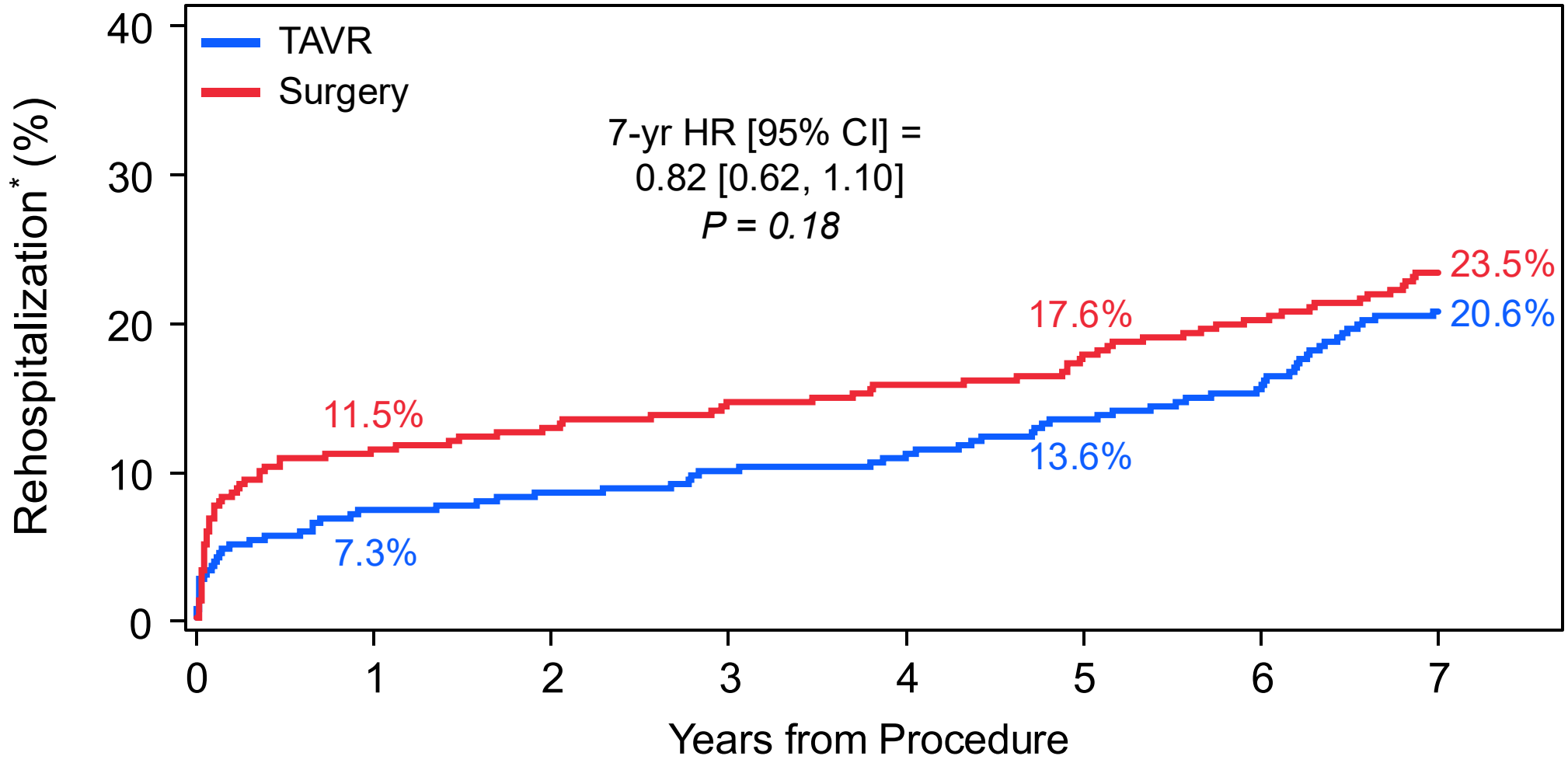
Rehospitalization



Number at risk:

TAVR	496	455	440	422	399	375	342	298
Surgery	454	380	359	339	322	301	277	240

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*Related to the valve, procedure, or heart failure

Additional Clinical Endpoints

KM% (No. of patients)

Endpoints	0 – 7 Years			
	TAVR (N=496)	Surgery (N=454)	HR [95% CI]	*P-value*
Death or disabling stroke*	21.7% (102)	16.8% (68)	1.31 [0.96, 1.78]	0.08
Aortic valve reintervention	6.7% (28)	6.0% (22)	1.11 [0.63, 1.94]	0.72
Endocarditis	2.9% (12)	2.8% (11)	0.94 [0.42, 2.14]	0.89
Clinical valve thrombosis†	**2.8% (13)**	**0.5% (2)**	**5.70 [1.29, 25.25]**	**< 0.01**
New-onset atrial fibrillation	**17.7% (69)**	**43.5% (158)**	**0.30 [0.23, 0.41]**	**< 0.0001**
New pacemaker	17.3% (78)	12.8% (51)	1.38 [0.97, 1.97]	0.07
Serious bleeding	15.6% (71)	18.5% (77)	0.79 [0.57, 1.09]	0.14
MI	6.0% (25)	5.6% (22)	0.99 [0.56, 1.75]	0.96
Revascularization	7.3% (31)	7.7% (31)	0.86 [0.53, 1.42]	0.57
PCI	6.6% (28)	6.6% (26)	0.94 [0.55, 1.60]	0.81
CABG	1.0% (4)	1.4% (6)	0.59 [0.17, 2.10]	0.41

*Does not include VSS data

†Per VARC-3; there was 1 new event in each arm from 5-7 years

Abbreviations: MI: Myocardial Infarction

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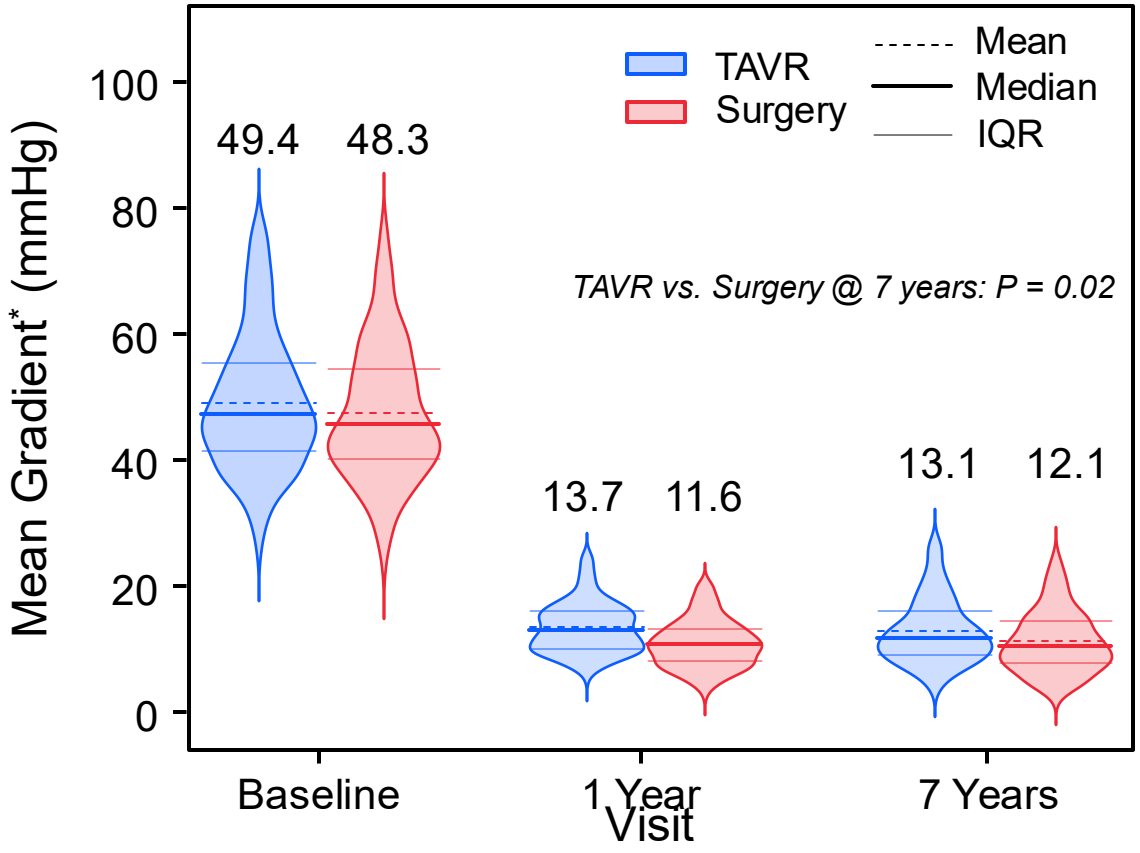
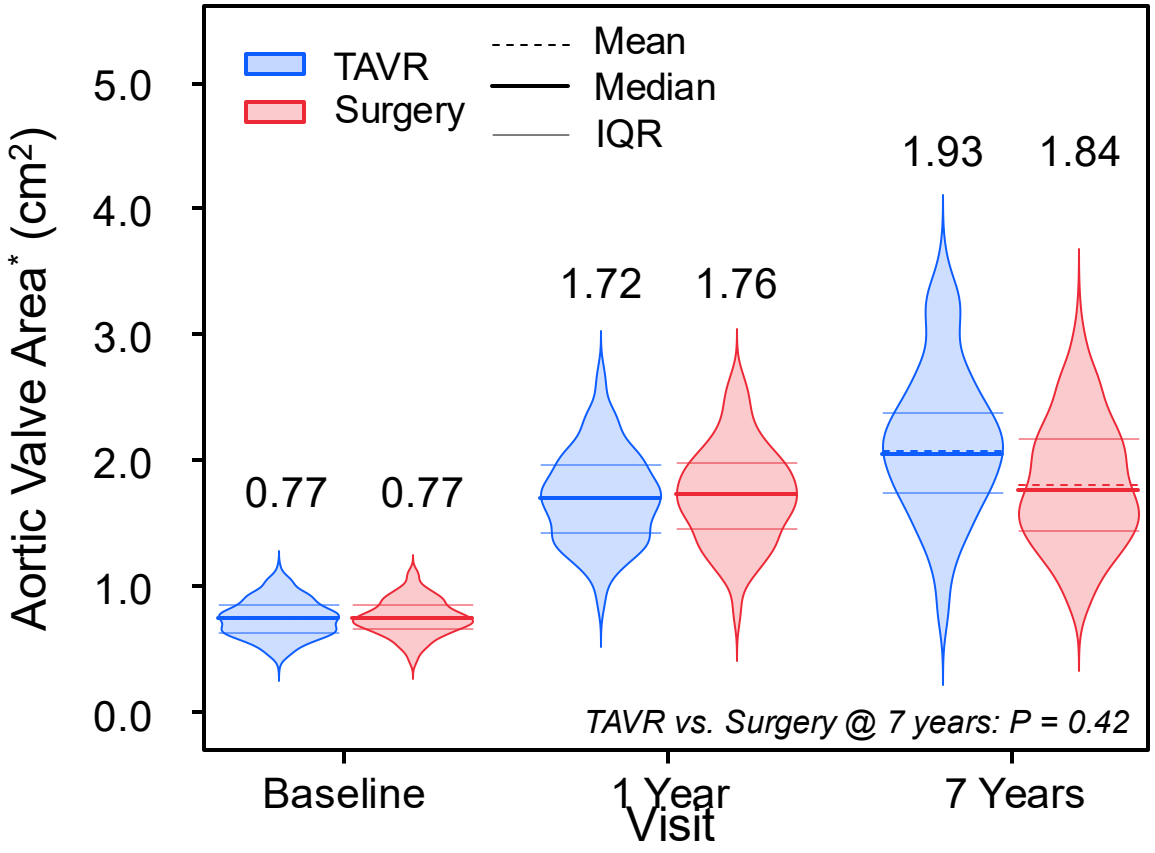
Valve Hemodynamics

Mean Gradient



No. of Echos			
TAVR	483	473	287
Surgery	442	391	246

Aortic Valve Area



No. of Echos			
TAVR	458	449	283
Surgery	424	371	241

**Mean values are shown; Pts w/ explants/ViVs were censored post-reintervention*

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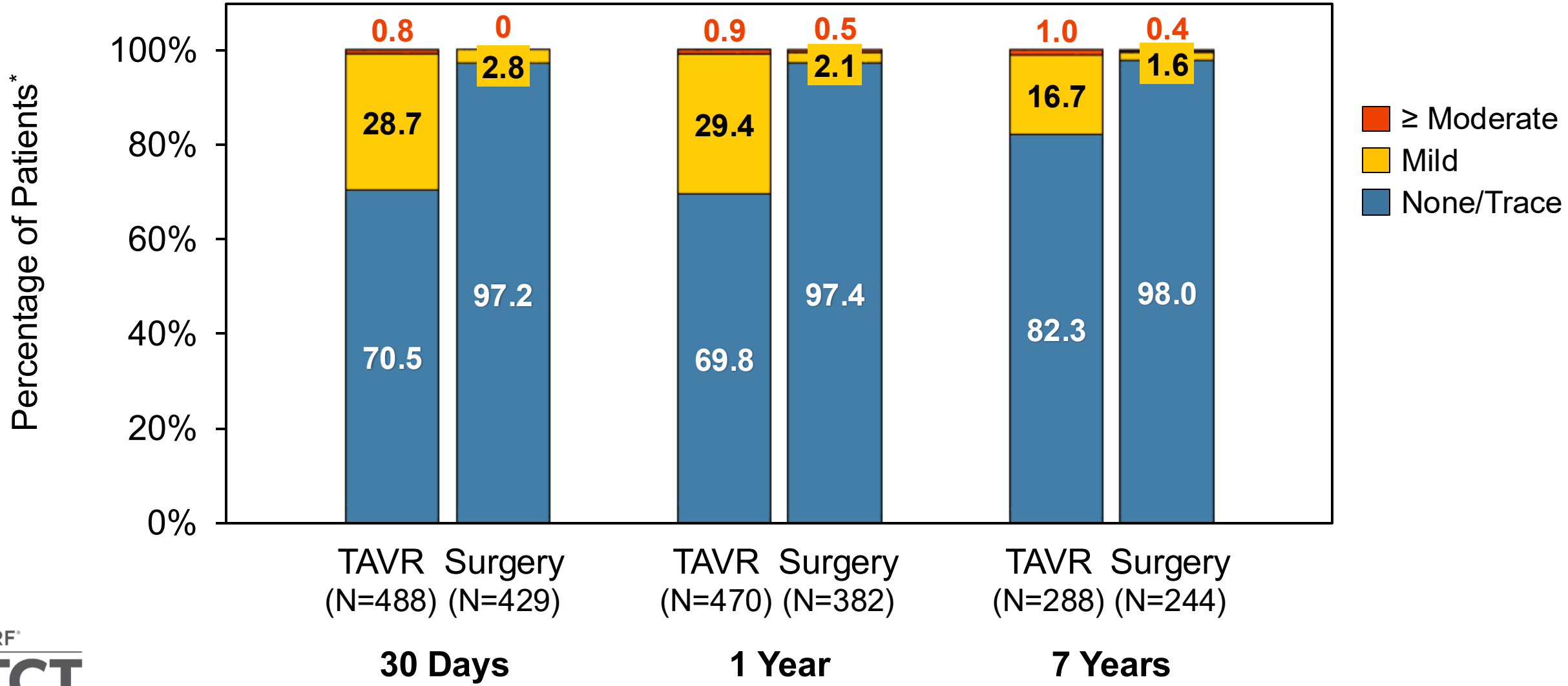
Paravalvular Regurgitation

≥ mild P < 0.0001 at all time points



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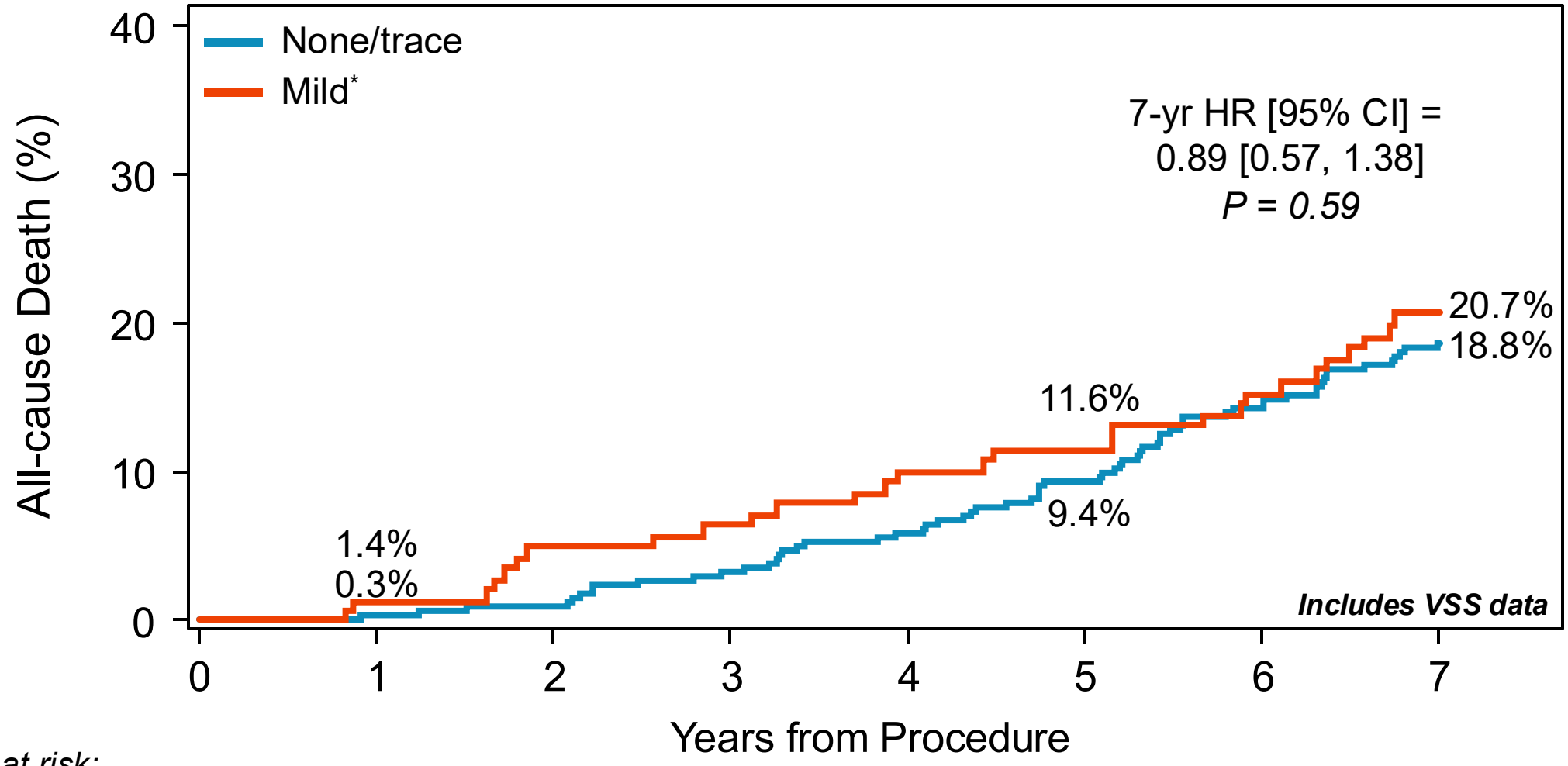
All-cause Death

By 30-day PVR – TAVR Only



Number at risk:

None/trace	344	342	339	330	317	304	284	266
Mild*	140	138	132	129	123	120	112	102

**Only 4 patients had moderate PVR at 30 days and none of them died*

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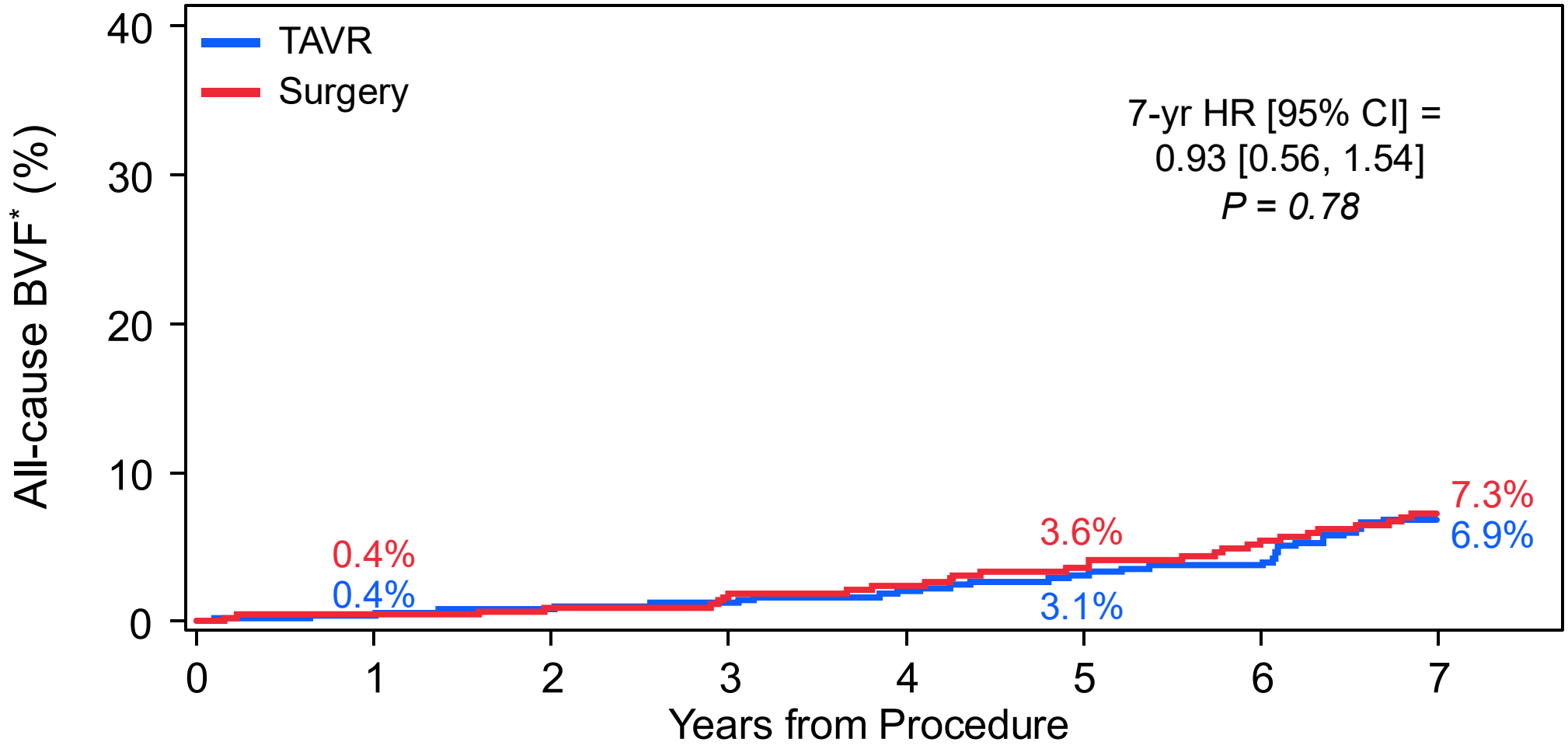
All-cause BVF (VARC-3)



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Surgery	454	426	407	390	372	348	327	288

**Cumulative incidence with death as a competing risk; HR estimated using the Fine and Gray method*

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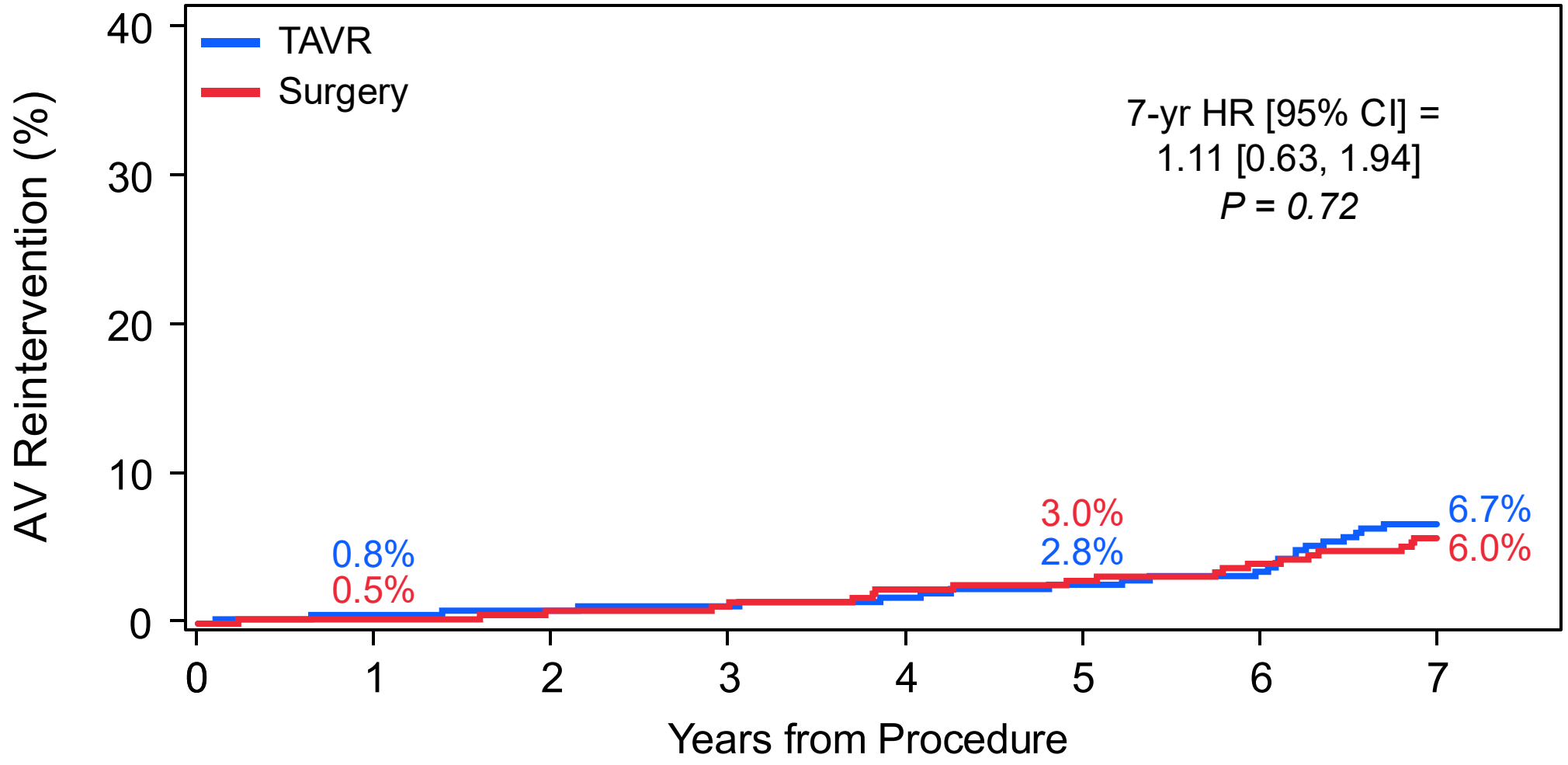
Aortic Valve Reintervention



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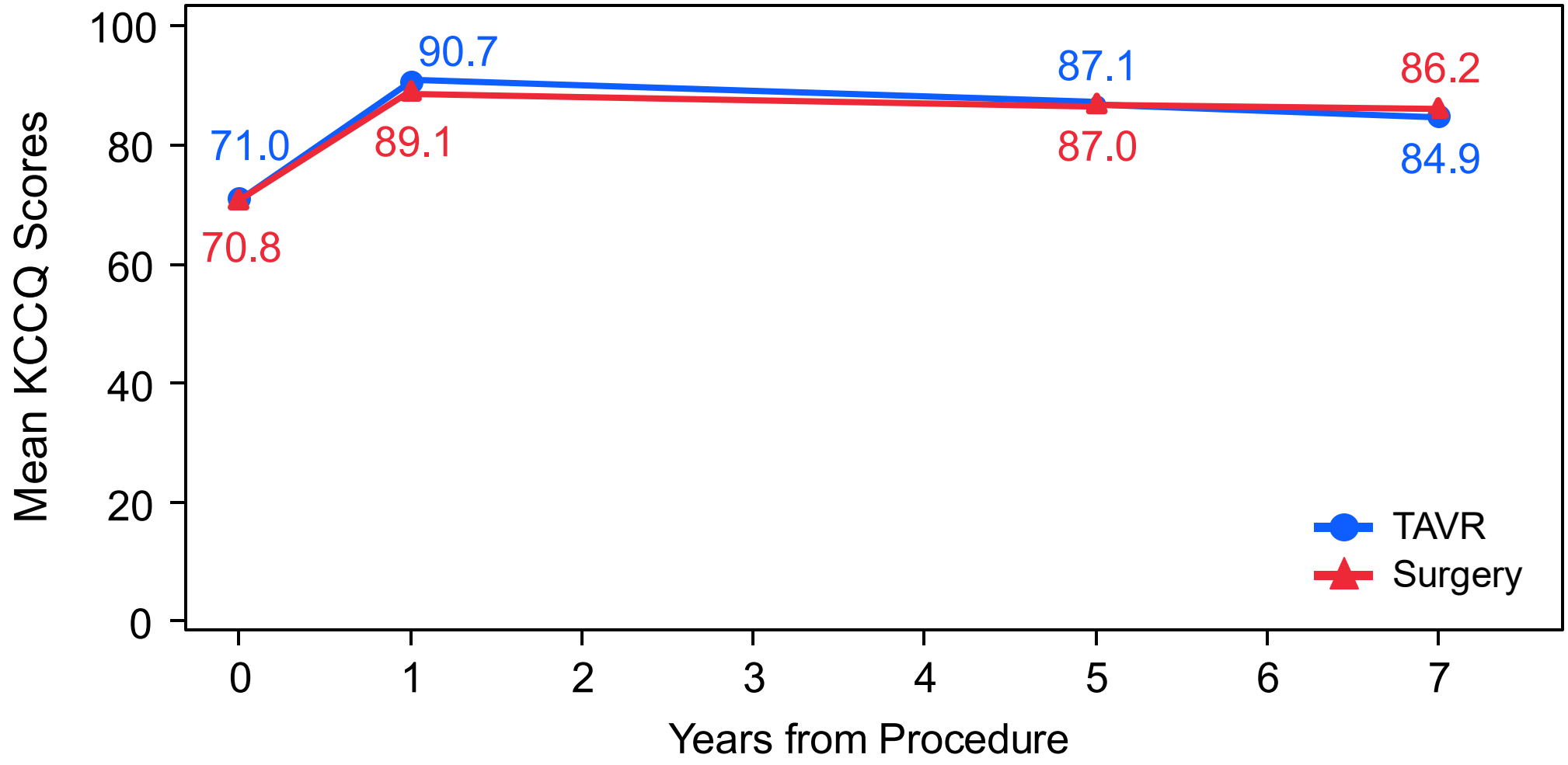
Mean KCCQ Overall Summary Scores



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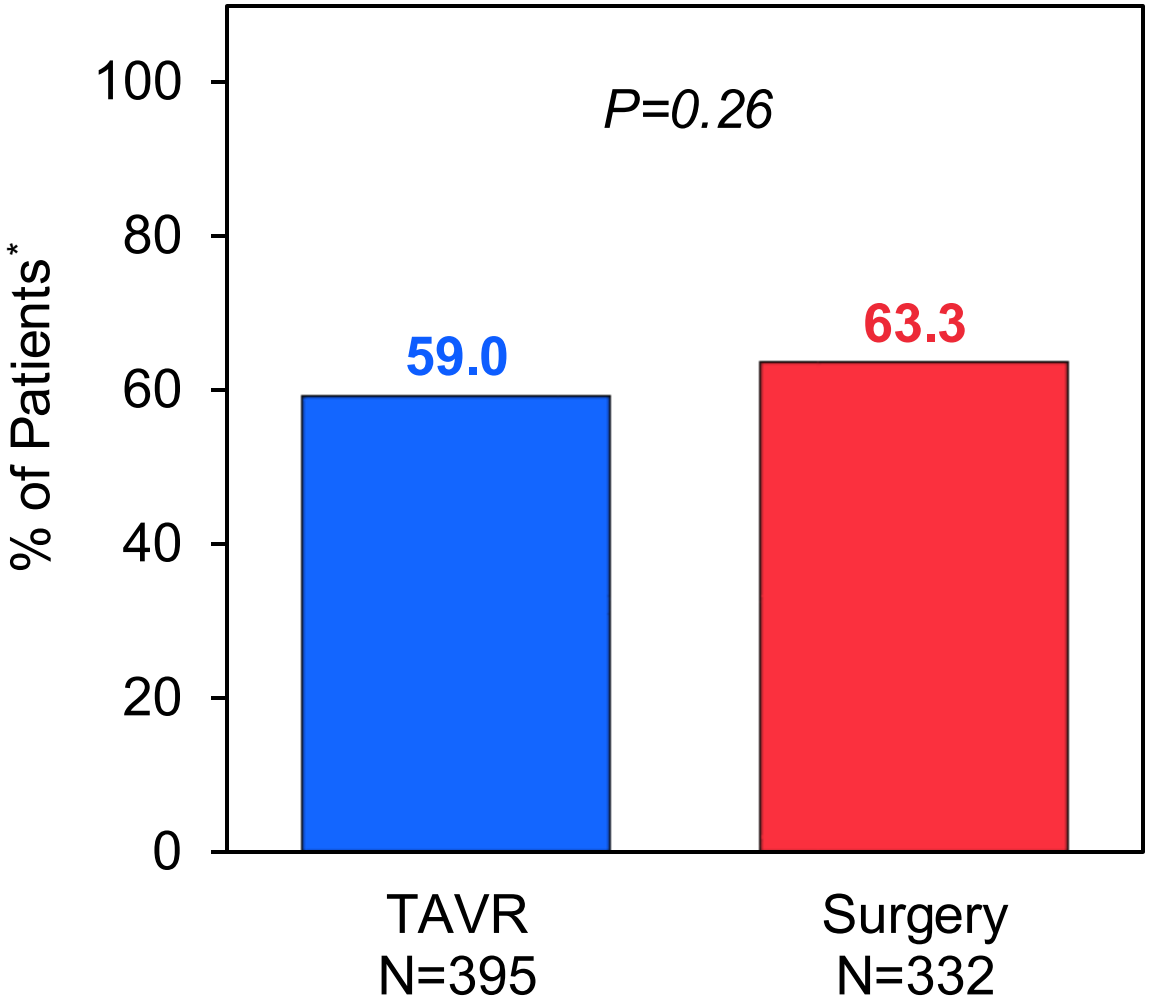
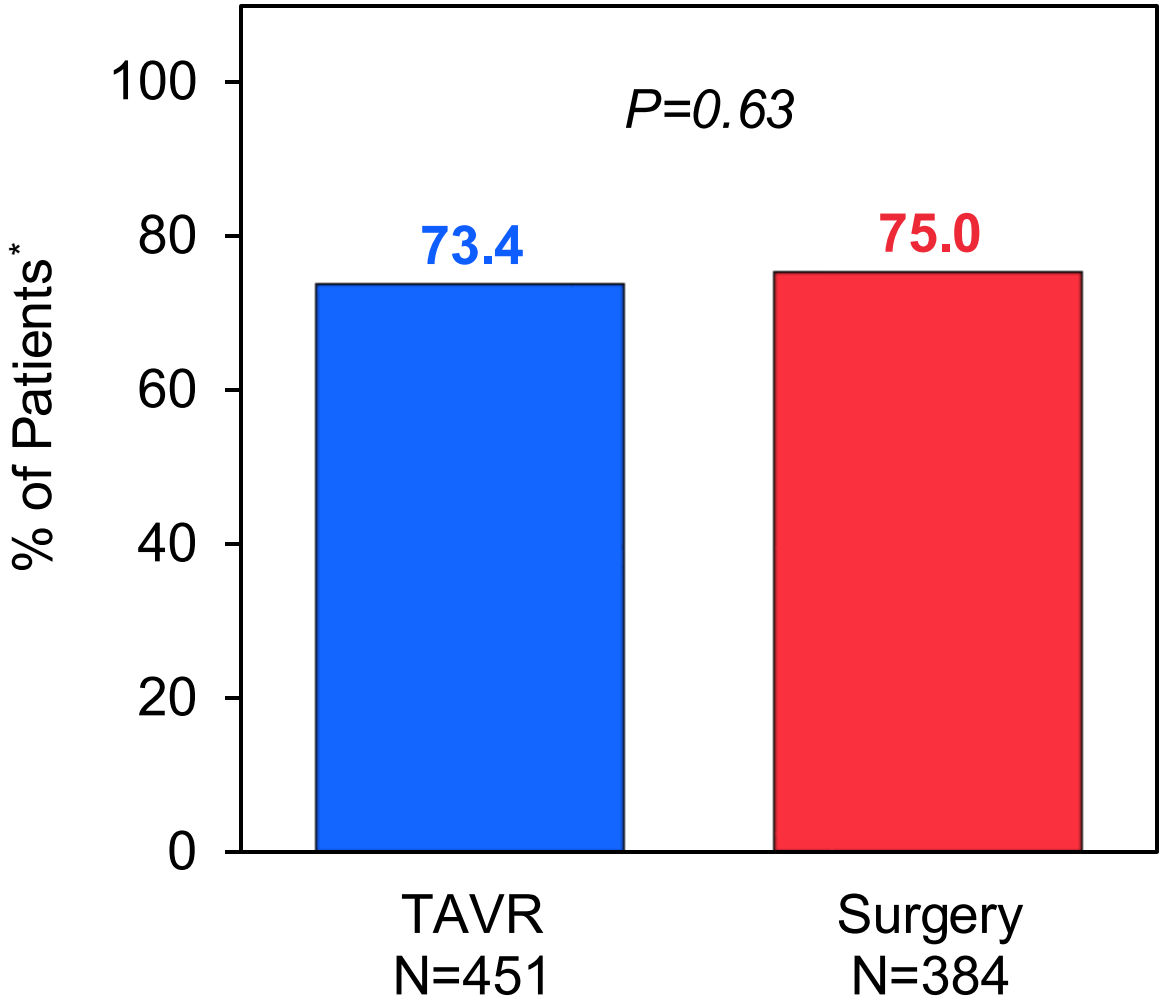
QOL and Valve Durability at 7 Years



Alive with a KCCQ Score > 75



Alive with a Durable Valve (no BVF)

**Pts known to be deceased per VSS were included in the denominator*

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Limitations and Context

- Results only apply to the enrolled population (bicuspid aortic valves, unsuitable TF access, and complex CAD excluded).
- Disproportionate withdrawal in the surgical arm could bias findings.
- Vital status sweeps, while essential for capturing complete mortality data, cannot be incorporated into composite outcomes or correct for possible biases in under-reporting of important nonfatal events.
- Long-term follow-up assessments in older patients can be confounded by competing non-valve-related events.
- Results are reported through 7 years; 10-year follow-up is planned.

Conclusions

Among patients with symptomatic severe AS at low surgical risk treated with SAPIEN 3 TAVR or Surgery, over 7 years of follow-up:

- **BOTH** TAVR and Surgery were associated with similar clinical event rates, with no significant differences in the 2 primary endpoints.
- The attenuation in primary endpoint differences observed at 5 years continued through 7 years.
- Marked 1-year improvements in hemodynamics and patient-reported outcomes were maintained and similar for both therapies.
- Valve function and durability were excellent and similar in both groups.

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