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CARDIOVASCULAR RESEARCH TECHNOLOGIES

TAVI with ACURATE neo2 vs. Sapien/Evolut: A SWEDEHEART Target Trial Emulation Study

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Conflicts of interest

Boston Scientific: Institutional research support, Consulting

Edwards Lifesciences: Consulting

Anteris: Consulting

One-year clinical outcomes of TAVI with Acurate neo2 vs. Sapien/Evolut: A SWEDEHEART target trial emulation study

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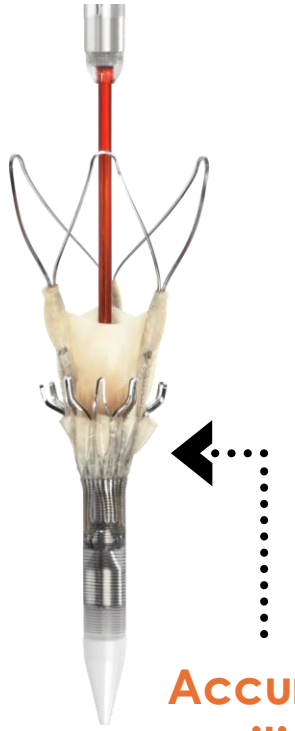
ACURATE neo2: Nitinol Self-expanding TAVI

Open upper frame

Supra-annular leaflets

ACTIVE PVseal™





Accurate positioning

Top-down deployment with upper- and lower- crown anchoring provides first-time precise procedures[2]

- Boston Scientific
- Investigational in US
- Next gen ACURATE Prime now in Europe

Annulus treatment range

Treats 20 mm to 27 mm annulus diameters

One-year Outcomes of ACURATE *neo2* vs Approved TAVR Devices in All-risk Patients with Severe AS: **the ACURATE IDE Trial**

Michael Reardon, MD

Houston Methodist DeBakey Heart & Vascular Center

Houston, TX

On behalf of the ACURATE IDE Investigators

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ACURATE IDE Trial Design

Prospective, multicenter, randomized study
N=1500 patients with symptomatic severe native aortic stenosis indicated for TAVR

Operators pre-specify valve type to be used if randomized to Control

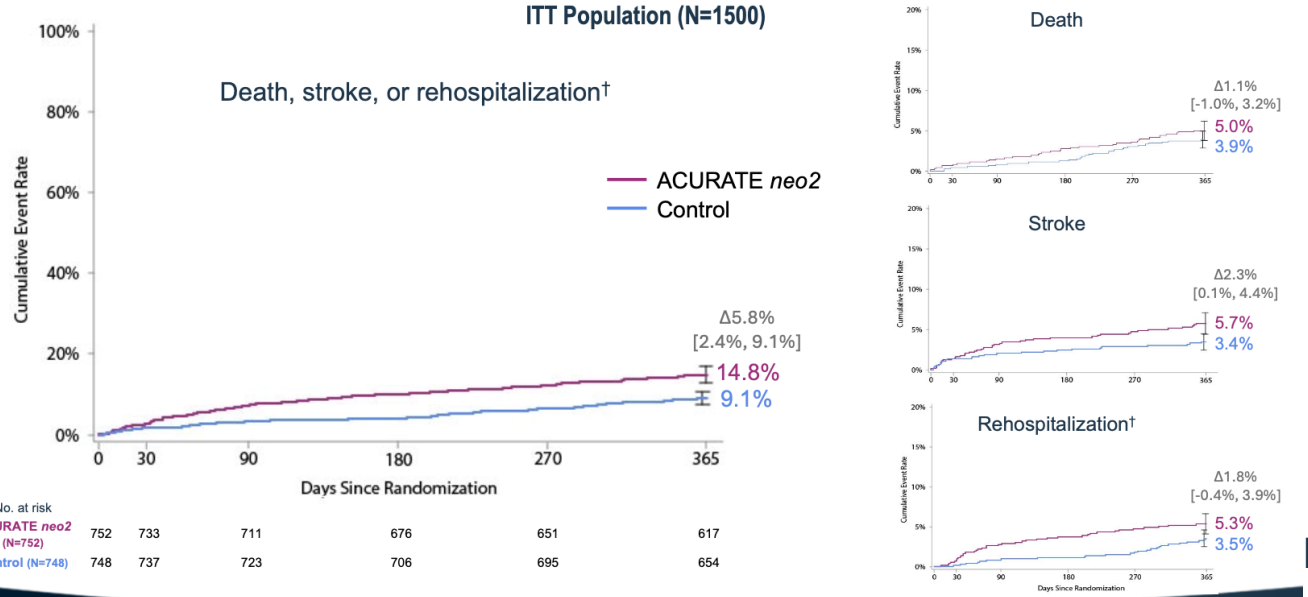
1:1 Randomization

- ACURATE *neo2* N=752
- Mixed Control N=748
  - Evolut N=244: CoreValve Evolut R, Evolut PRO, Evolut PRO+, Evolut FX
  - SAPIEN N=504: SAPIEN 3, SAPIEN 3 Ultra

- **Primary Endpoint: Composite of all-cause mortality, stroke or rehospitalization† at 1 year**
- Follow-Up: Discharge/7d post-procedure, 30d, 6mo, 1-10y post-procedure

† Hospitalization for valve-related symptoms or worsening congestive heart failure (NYHA class III or IV); per VARC-2 definition

Kaplan-Meier Analysis through 1 Year

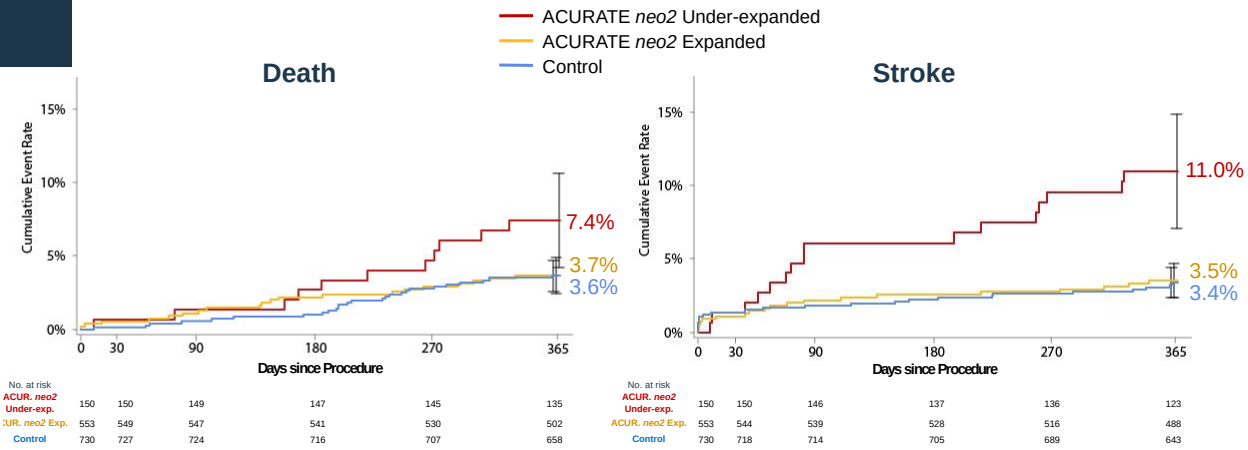


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Note: Control devices include CoreValve Evolut R, Evolut PRO, Evolut PRO+, and Evolut FX and SAPIEN 3, SAPIEN 3 Ultra
† Hospitalization for valve-related symptoms or worsening congestive heart failure (NYHA class III or IV); per VARC-2 definition

- 21% of ACURATE underexpanded by fluoroscopy

Post-Hoc Clinical Analysis: Valve Frame Expansion



Death and stroke at 1 year are comparable for ACURATE *neo2* Expanded and Control

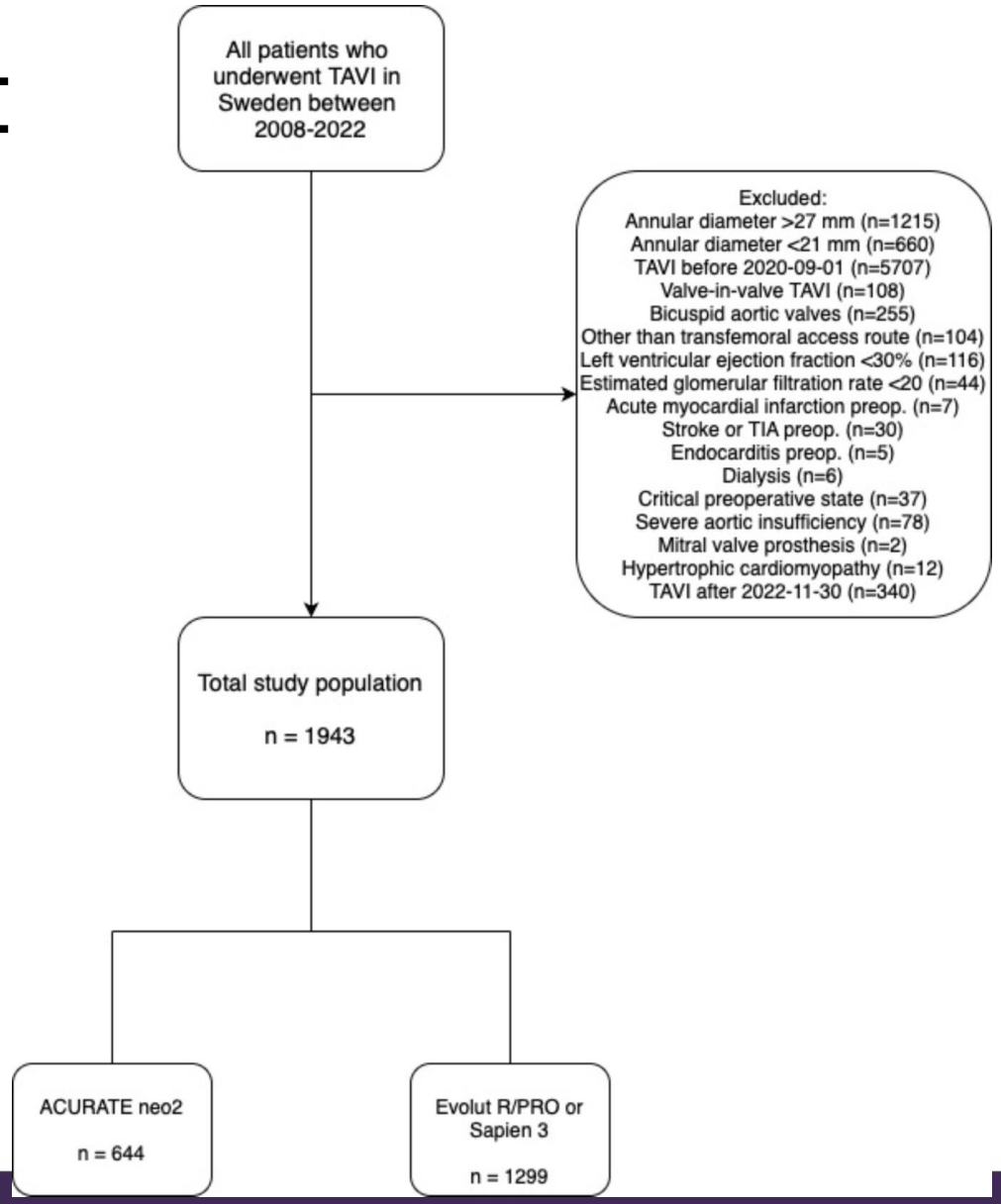
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Table S1. Target trial protocol.

Protocol components	Target trial specification	Target trial emulation	Data sources for emulation
Aim	To study differences in clinical outcomes after TAVI with an Acurate neo2 valve vs Evolut R, Evolut PRO or Sapien 3 valves.	Same as target trial	
Eligibility criteria	Age >18 TAVI after September 1, 2020 TAVI before November 30, 2022 Annular diameter <27 mm and >21 mm Primary TAVI Tricuspid aortic valve Transfemoral access route Left ventricular ejection fraction >30% Estimated glomerular filtration rate >20 Exclusion criteria: Acute myocardial infarction within 1 month Stroke or TIA within 6 months Endocarditis within 6 months Dialysis Critical preoperative state Severe aortic insufficiency Mitral valve prosthesis Hypertrophic cardiomyopathy	Same as target trial	SWEDEHEART (subregister SWENTRY) The Swedish National Patient Register
Treatment strategies	TAVI with the ACURATE neo2 vs TAVI with Evolut R, Evolut PRO or Sapien 3	Same as target trial	SWEDEHEART (subregister SWENTRY)
Treatment assignment	Randomized nonblinded	Nonblinded and nonrandomized	
Follow-up start	At treatment assignment	Same as target trial	
Follow-up end	First occurrence of death, heart failure hospitalization, stroke, at one year after TAVI, or 31 December 2022	Same as target trial	
Outcome	Primary: composite outcome of all-cause mortality, heart failure hospitalization, and stroke Secondary: individual components of the primary outcome, acute myocardial infarction, percutaneous coronary intervention, major bleeding, myocardial infarction, cardiovascular mortality	Same as target trial	The Swedish National Patient Register
Causal contrast	Intention-to-treat effect	Observational analogue of intention-to-treat effect	
Statistical methods	Bayesian non-inferiority. Kaplan-Meier, Cox regression	Balancing weighting, Kaplan-Meier, Aalen-Johansen, flexible parametric survival modelling, restricted mean survival time	

Target trial emulation

Study flowchart



Total 1943 TAVI

644 ACURATE neo2

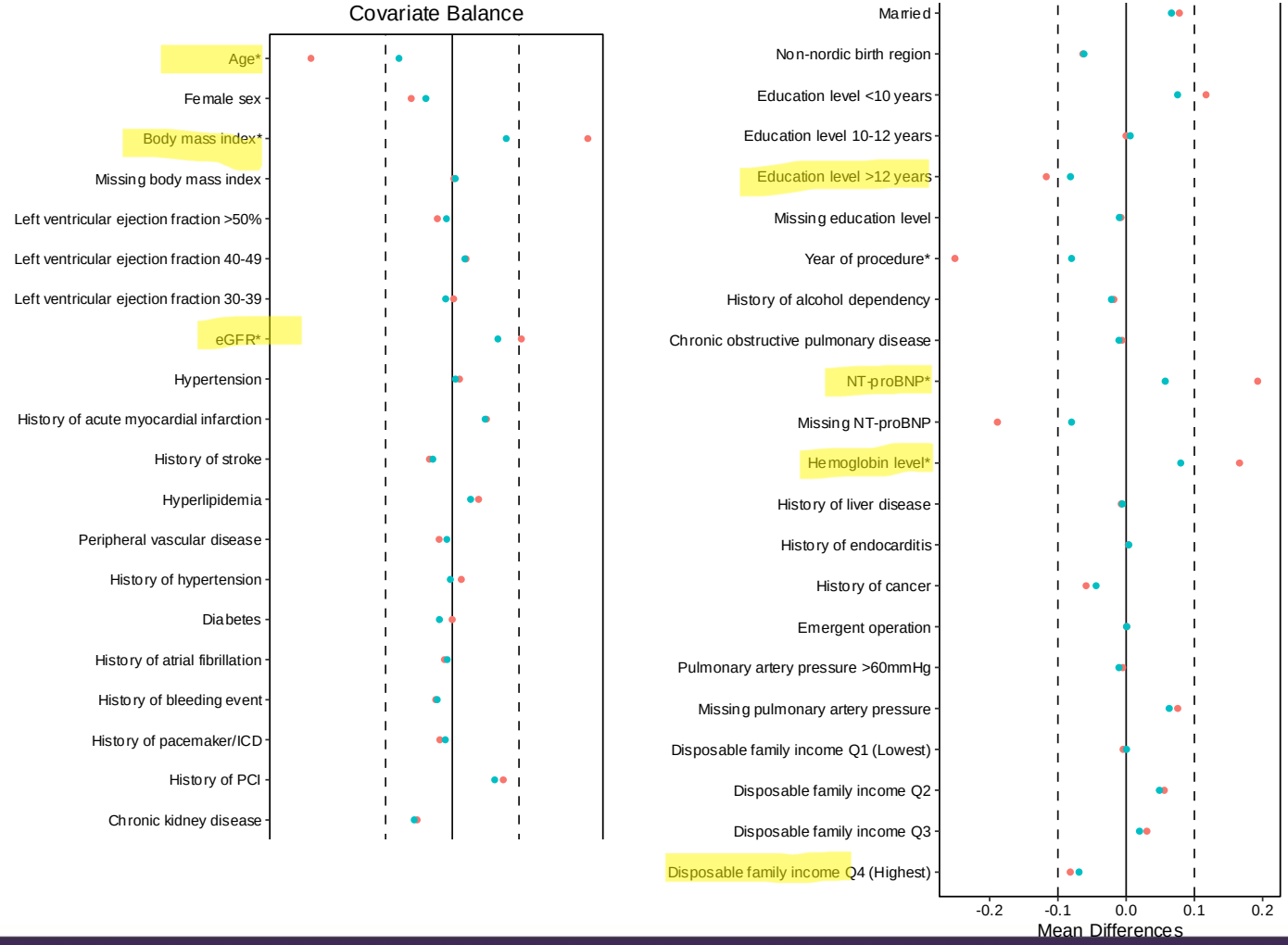
826 Edwards Sapien3
473 Medtronic Evolut

Baseline data (crude)

Variable	Overall	ACURATE neo2	Control	p
No.	1943	644	1299	
Age, years, median [IQR]	81.2 (6.1)	82.1 (5.8)	80.8 (6.2)	<0.001
Female sex	49.8 %	53.9 %	47.7 %	0.012
LVEF				0.409
>50%	81.9 %	83.4 %	81.1 %	
40-49%	12.2 %	10.9 %	12.9 %	
30-39%	5.9 %	5.7 %	5.9 %	
Aortic mean pressure gradient, mmHg, mean (SD)	47.7 (13.0)	47.9 (12.1)	47.6 (13.4)	0.644
NT-proBNP, ng/L, mean (SD)	2323.2 (4072.2)	1811.2 (2586.1)	2518.7 (4498.0)	0.003
eGFR, mL/min/1.73 m^2				0.404
15-29	3.1 %	3.6 %	2.9 %	
30-44	14.3 %	14.9 %	13.9 %	
45-59	26.7 %	28.3 %	25.9 %	
>60	55.9 %	53.3 %	57.2 %	
Hypertension	91.7 %	91.0 %	92.1 %	0.470
COPD	17.1 %	17.5 %	16.9 %	0.785
Previous myocardial infarction	17.2 %	13.8 %	18.9 %	0.006
Previous stroke	20.8 %	23.1 %	19.7 %	0.091
Diabetes	29.8 %	29.8 %	29.8 %	1.000
Previous atrial fibrillation	38.7 %	39.4 %	38.3 %	0.650
Previous pacemaker/ICD	10.2 %	11.5 %	9.6 %	0.231
Previous PCI	30.1 %	25.0 %	32.6 %	0.001

Adjusted by balancing weighting (Love plot)

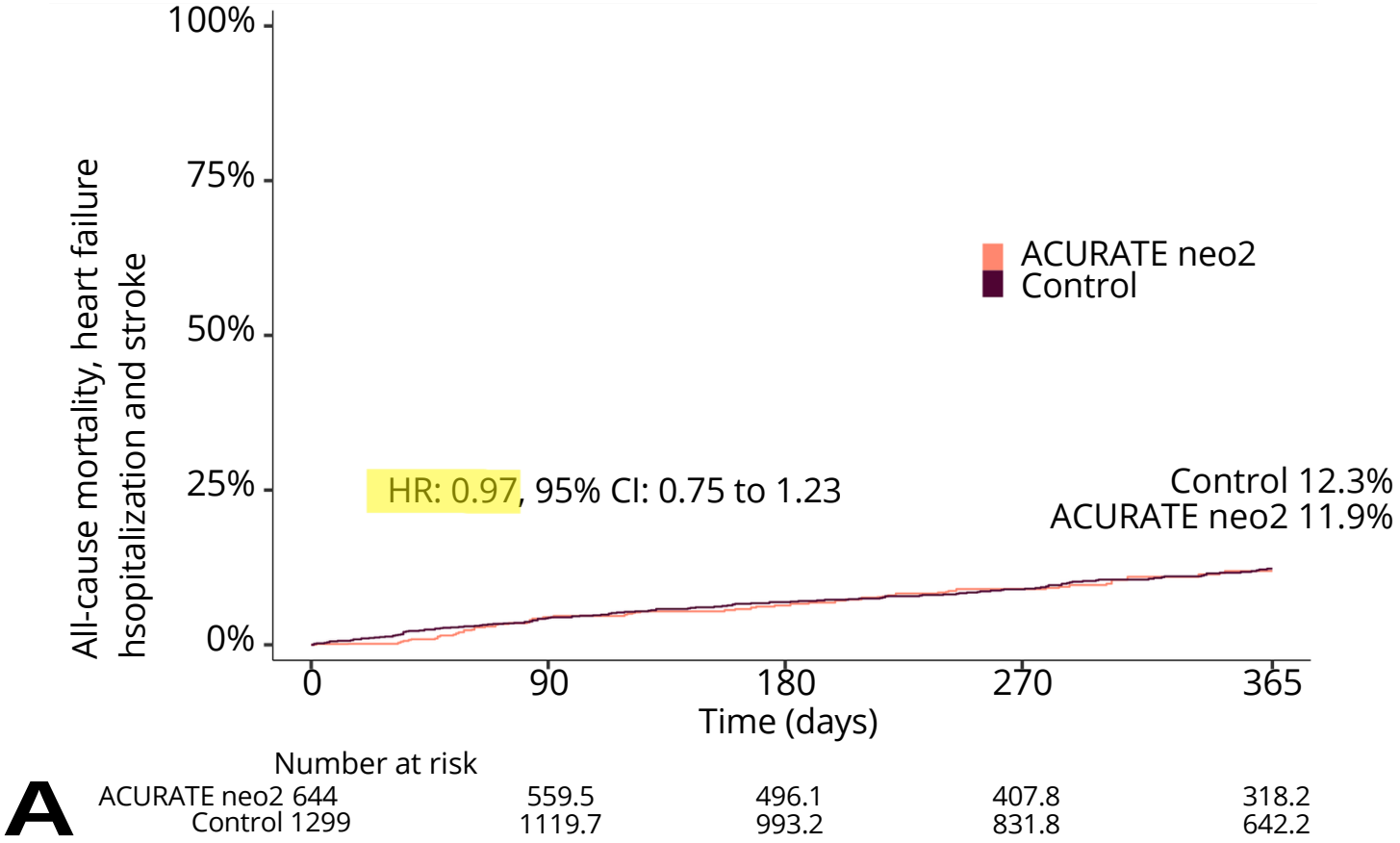
* = standardized mean difference



Procedural data

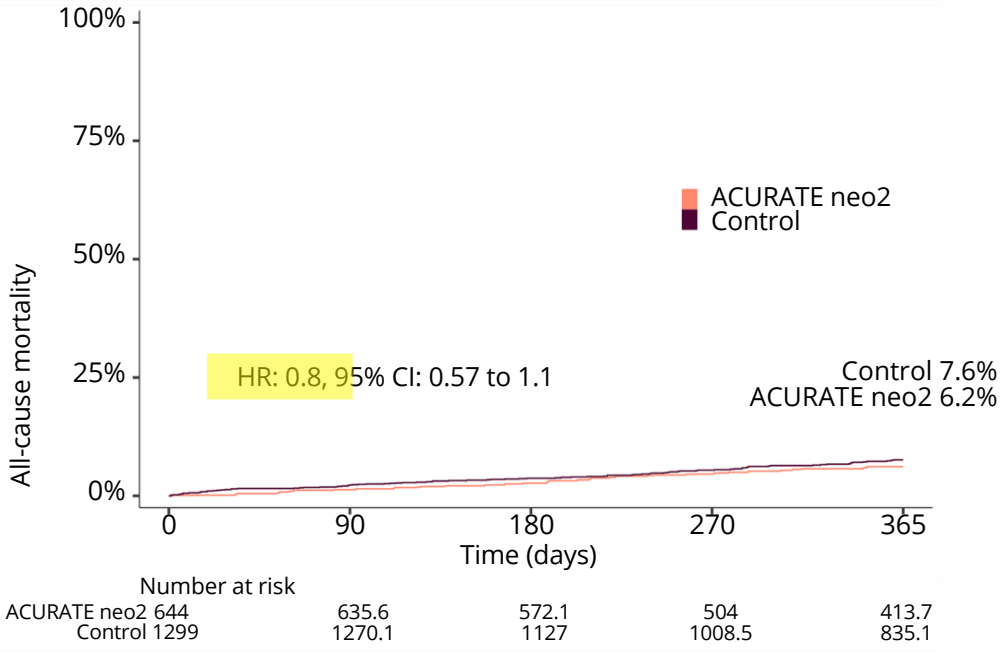
Variable	Overall	ACURATE neo2	Control	p
Prosthesis size, mm				<0.001
≤23	21.9 %	18.3 %	23.6 %	
24-26	39.7 %	37.4 %	40.9 %	
≥27	38.4 %	44.3 %	35.5 %	
Annulus diameter, mm, mean (SD)	24.1 (1.7)	24.0 (1.5)	24.1 (1.8)	0.059
Pre-dilatation	60.9 %	99.8 %	41.6 %	<0.001
Pre-dilatation balloon undersizing, mm, mean (SD)	2.3 (1.6)	1.2 (0.8)	3.6 (1.4)	<0.001
Annulus diameter and pre-dilatation balloon size difference				<0.001
≤1mm	27.4 %	47.3 %	3.7 %	
1-2mm	30.4 %	45.6 %	12.4 %	
>2mm	42.2 %	7.2 %	83.9 %	
Post-dilatation	22.7 %	44.7 %	11.8 %	<0.001
Post-dilatation balloon undersizing, mm, mean (SD)	0.8 (1.0)	0.8 (0.7)	0.8 (1.3)	0.911
Annulus diameter and post-dilatation balloon size difference				0.001
≤1mm	71.2 %	74.3 %	65.4 %	
1-2mm	23.1 %	22.9 %	23.5 %	
>2mm	5.7 %	2.8 %	11.1 %	

Primary Endpoint

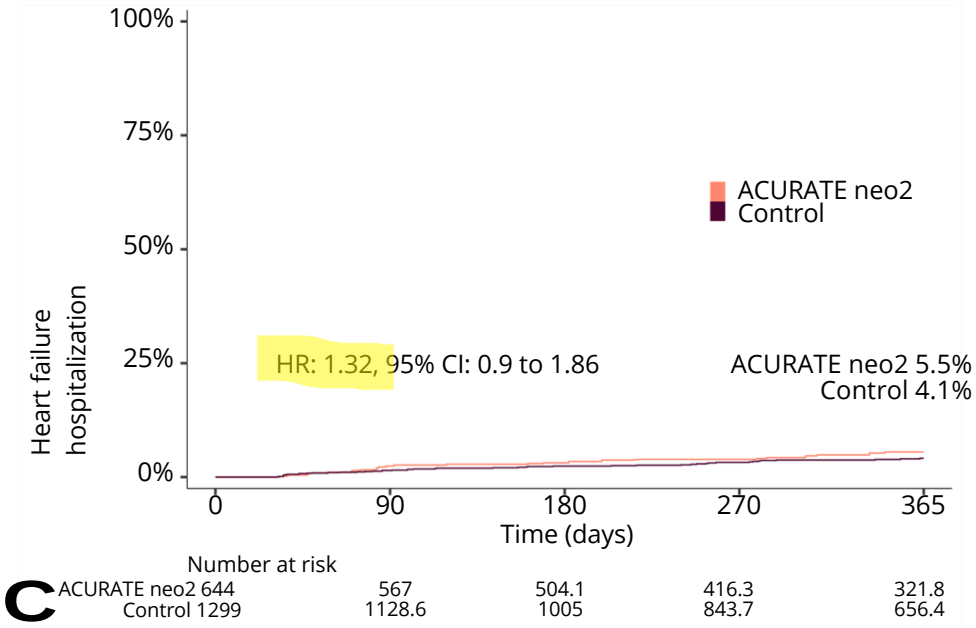


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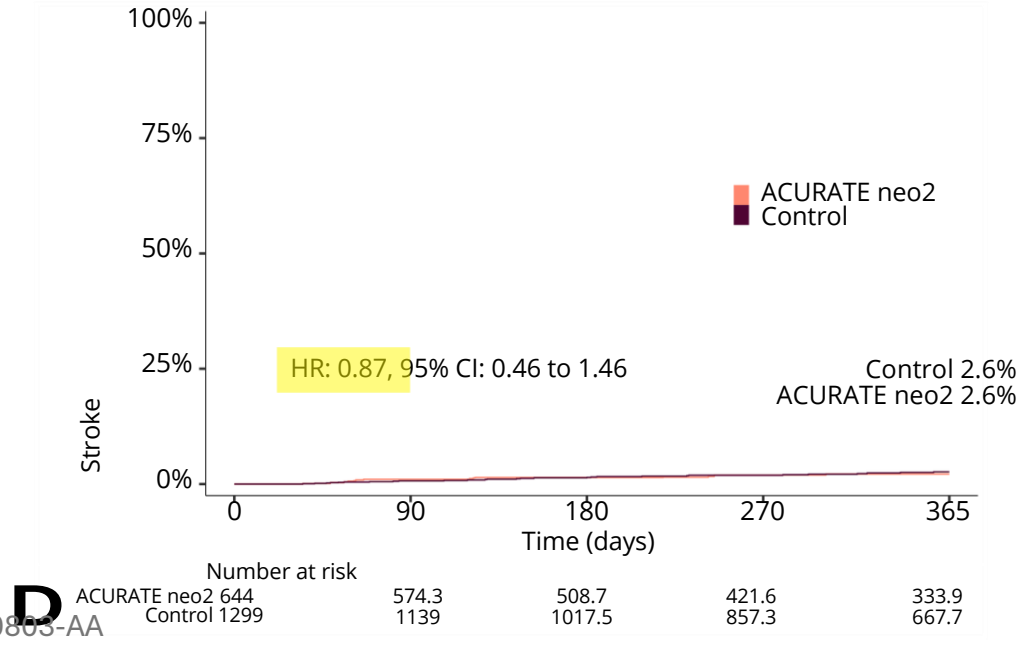
Components



B



C



D

Additional endpoints

Weighted cumulative incidence of acute myocardial infarction, percutaneous coronary intervention and major bleeding event at 3 and 12 months.				
	Events / PY	HR (95% CI)	3 months	12 months
Acute myocardial infarction				
ACURATE neo2	3 / 481	0.66 (0.20-1.55)	0.3 (0.0-2.4)	0.6 (0.2-2.2)
Control	17 / 1005	NA	0.4 (0.2-0.9)	1.5 (1.0-2.5)
Percutaneous coronary intervention				
ACURATE neo2	4 / 481	0.85 (0.25-2.02)	0.1 (0.0-0.8)	0.7 (0.3-2.0)
Control	9 / 1009	NA	0.3 (0.1-0.8)	0.9 (0.4-1.7)
Major bleeding event				
ACURATE neo2	27 / 468	1.03 (0.67-1.49)	2.4 (1.4-3.9)	4.2 (2.8-6.3)
Control	47 / 989	NA	2.1 (1.4-3.0)	4.2 (3.1-5.5)
Cardiovascular death				
ACURATE neo2	23 / 642	0.54 (0.30-0.88)	0.5 (0.2-1.6)	2.6 (1.5-4.4)
Control	57 / 1477	NA	1.6 (1.1-2.5)	4.3 (3.5-6.0)

Acute myocardial infarction, percutaneous coronary intervention major bleeding event and cardiovascular death outcomes estimated using Aalen-Johansen to account for the competing risk of death.
PY = person-years

Postdilatation - not dangerous

Variable	Overall	No post-dilatation	Postdilatation	p
No	644	356	288	
Peri-procedural tamponade %	0.2	0.3	0.0	1.000
Peri-procedural valve embolization %	0.5	0.8	0.0	0.327
Major vascular complication %	1.2	0.8	1.7	0.509
VARC2 major bleeding %	2.5	2.0	3.1	0.489
Aortic mean pressure gradient, mmHg, mean (SD)	9.1 (3.9)	9.5 (4.2)	8.6 (3.5)	0.019
Paravalvular leakage				0.012
Moderate %	2.8	2.3	3.5	
Acute kidney injury %	2.8	2.2	3.5	0.486
In-hospital stroke %	0.6	1.1	0.0	0.195
In-hospital TIA %	0.2	0.3	0.0	1.000
In-hospital myocardial infarction %	0.2	0.3	0.0	1.000
Pacemaker implantation within 30 days %	5.6	7.0	3.8	0.113
30-day mortality %	0.5	0.6	0.3	1.000

Analysis of ACURATE group
Crude data

Comparison IDE vs SWEDEHEART (ACURATE group)

	IDE trial	SWEDEHEART
Age, years	78.0	82.1
Preop AS mean gradient, mmHg	44.7	47.9
Predile done (%)	99.6%	99.8%
Predil balloon within 1mm of anular size (%)	19%	47%
Postdil done (%)	26.1%	44.7%
Postdil balloon within 1mm of anular size (%)	49%	74%
Postop mean gradient, mmHg	9.0	9.1
New pacemaker 30d (%)	11.2%	5.6%

Emulated trial, observational data, outcomes from official complete databases
Same inclusion/exclusion criteria, same primary outcome definitions as ACURATE IDE trial
Adjusted analysis by balancing weighting



ACURATE neo2
n=644

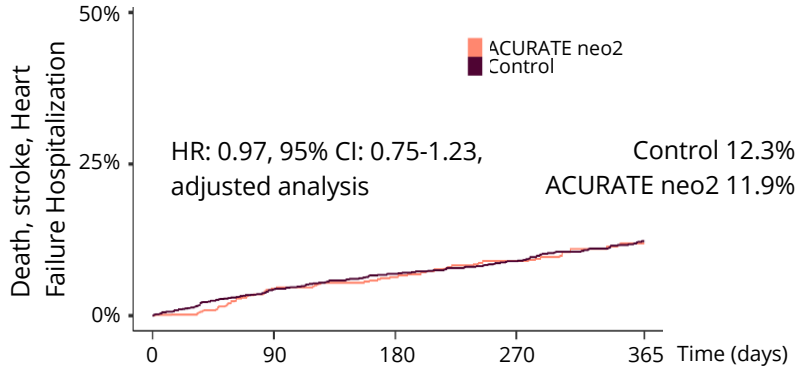
Evolut/Sapien3
n=1299



Primary endpoint at 12 months

Combination of

- Death
- Stroke
- Heart Failure Hospitalization



Secondary endpoints at 12 months, adjusted analysis

		Hazard ratio	95% Confidence Interval	ACURATE neo2	Evolut/Sapien3
	Death	0.80	0.57-1.10	6.2%	7.6%
	Stroke	0.87	0.46-1.46	2.2%	2.6%
	Heart Failure Hospitalization	1.32	0.90-1.86	5.5%	4.1%

Limitations

- Observational data
- No imaging (frame underexpansion could not be estimated)

Conclusions

- Mortality, heart failure hospitalization and stroke was not different between ACURATE and Sapien/Evolut TAVI in Swedish observational data
- Rigorous pre- and postdilatation was used
- Not difficult – most often same balloon for pre/postdilatation
- Post-dilatation was not associated with adverse events
- SE EU Europe US USA – can learn from each other