EARLY TAVR Trial

Confirmed Data and Data to be Reviewed

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
• Institutional Research Grant Support.	• Edwards Lifesciences

Learning Objectives

- To review clinical outcomes of EARLY TAVR vs clinical surveillance.
- To analyze conversion rates to AVR in clinical surveillance group.
- To compare outcomes of EARLY TAVR vs Delayed TAVR.

EARLY TAVR

901 patients (TAVR=455, Clinical surveillance=446), mean age 75.8 years, STS 1.8%.
Primary Endpoint: Death, stroke or CV hospitalization at 2 years

Prospective, multicenter RCT evaluating patients with asymptomatic, severe AS aged ≥ 65 years w/ an STS score ≤ 10% and LVEF ≥ 50%

Asymptomatic Assessment
Confirmed by negative treadmill stress test*

Randomization 1:1

Transfemoral-TAVR
(SAPIEN 3 or SAPIEN 3 Ultra THV)

Clinical Surveillance

PRIMARY ENDPOINT (Superiority)
Non-hierarchical composite of all-cause death, any stroke, or unplanned CV hospitalization at a minimum follow-up of 2 years

Genereux et al, TCT 2024.
Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

EARLY TAVR

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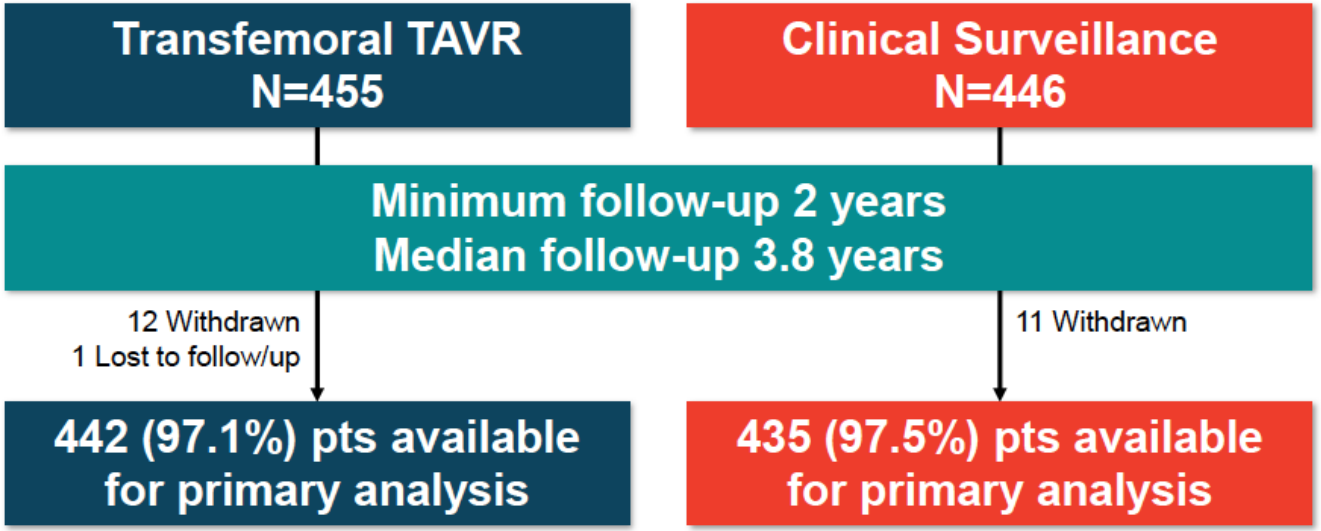
THE EARLY TAVR TRIAL

Patient Follow-up



Primary analysis evaluated in the ITT population

MAYO CLINIC Genereux et al, TCT 2024.
Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

EARLY TAVR

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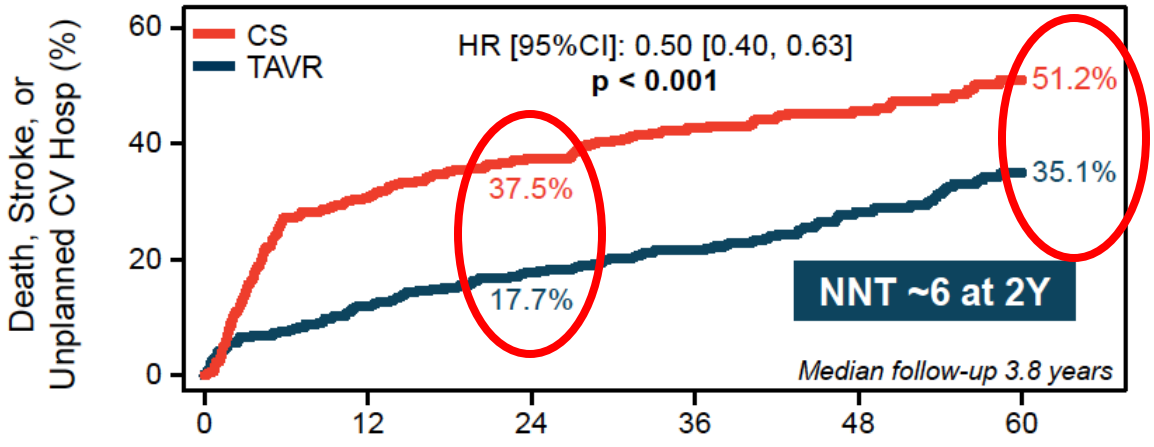
THE EARLY TAVR TRIAL

Primary Endpoint



No. at risk:

TAVR	455	390	363	285	142	103
CS	446	305	266	187	117	46

Genereux et al, TCT 2024.
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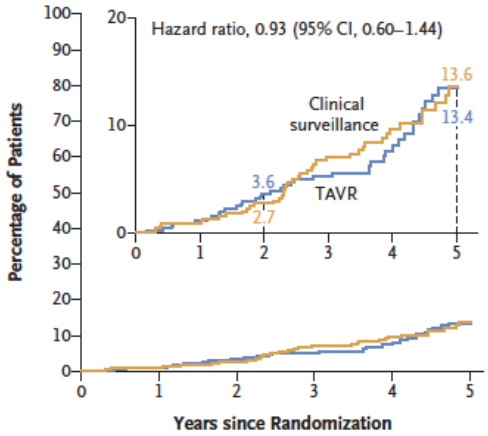
EARLY TAVR

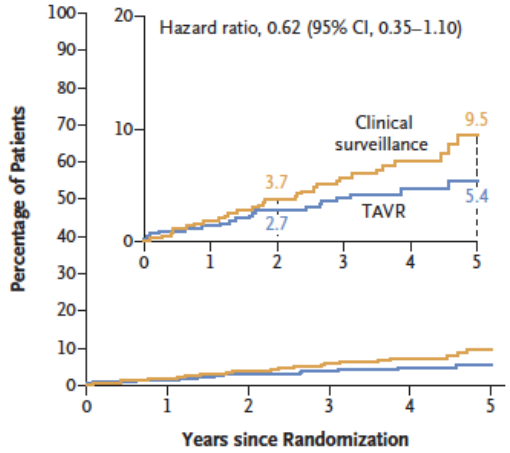
901 patients (TAVR=455, Clinical surveillance=446), mean age 75.8 years, STS 1.8%.
Primary Endpoint: Death, stroke or CV hospitalization at 2 years

B Death from Any Cause



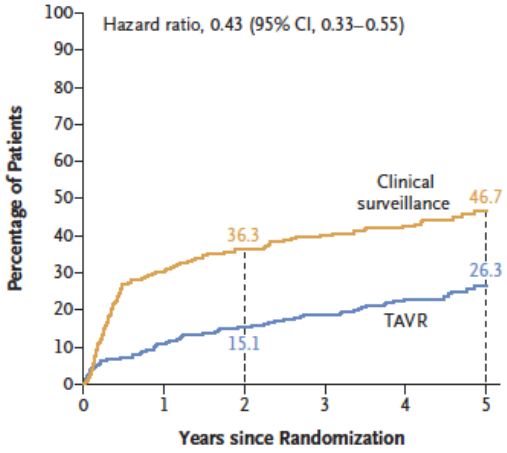
No. at Risk						
TAVR	455	439	425	346	187	136
Clinical surveillance	446	436	418	310	199	95

C Stroke



No. at Risk						
TAVR	455	433	415	335	180	130
Clinical surveillance	446	429	406	295	185	87

D Unplanned Hospitalization for Cardiovascular Causes



No. at Risk						
TAVR	455	392	365	287	142	103
Clinical surveillance	446	306	267	189	118	46

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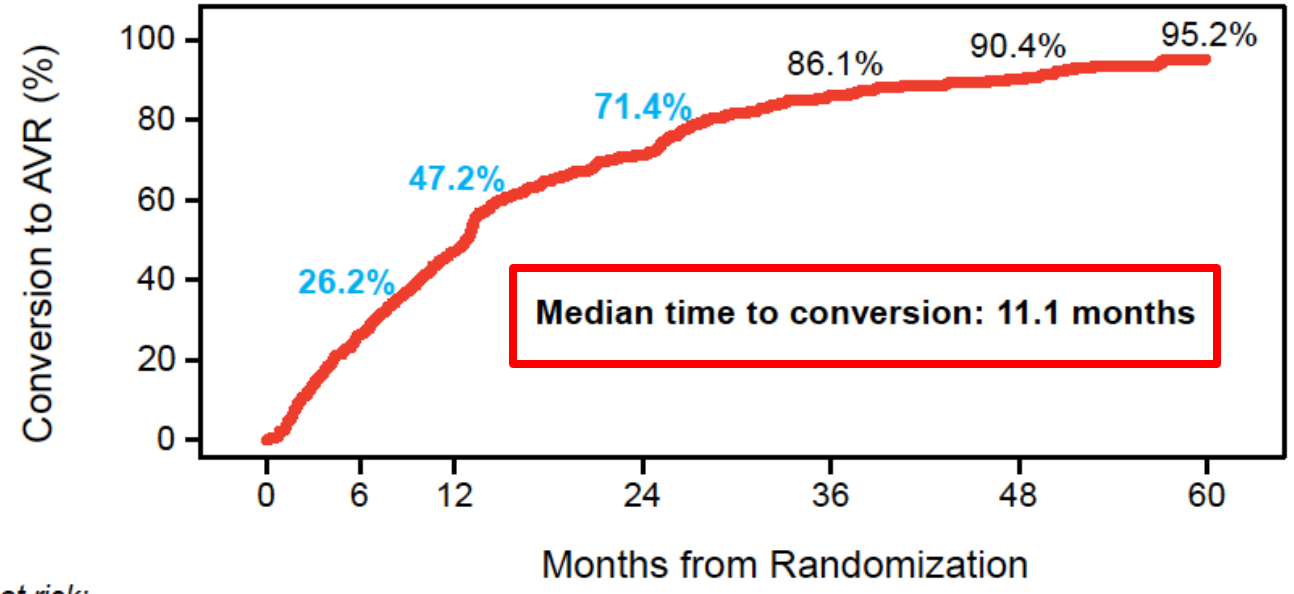
EARLY TAVR

901 patients (TAVR=455, Clinical surveillance=446), mean age 75.8 years, STS 1.8%.

THE EARLY TAVR TRIAL

Conversion to AVR in CS



No. at risk:

Clinical Surveillance	446	326	231	119	45	22	9

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Genereux et al, TCT 2024.

Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

EARLY TAVR

THE EARLY TAVR TRIAL Symptoms at Time of Conversion to AVR

CS Patients who Converted to AVR with Symptoms	Total (N=377)
Most Common Symptoms*	
Dyspnea	83.0%
Angina	24.9%
Dizziness	24.7%
Fatigue	22.0%
Syncope	7.2%
Multiple Symptoms	
Experienced 2 symptoms	34.5%
Experienced ≥ 3 symptoms	13.3%
Symptom/HF Severity	
NYHA II	70.0%
NYHA III/IV	30.0%
Accompanying Signs of Worsening AS*	
Peak velocity > 5 m/s	22.3%
LVEF drops to < 50%	4.8%
≥ 3-fold increase in NT-proBNP	6.7%

*Categories are not mutually exclusive

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EARLY TAVR

Clinical Presentation at Time of AVR Conversion

Patients classified based on acuity and severity of signs/symptoms

Asymptomatic
Includes pts who may have converted to AVR b/c they required additional medical procedures

Progressive Signs or Symptoms
NYHA II
Dyspnea
Angina
Fatigue
Dizziness
Increase in HF rx from baseline
≥ 1.5- to < 3-fold increase in NT-proBNP from baseline and age-specific threshold*

Advanced Signs or Symptoms / Acute Decompensation
NYHA III/IV
Dyspnea
Angina
Fatigue
Dizziness
Syncope
Atrial fibrillation
Ventricular arrhythmia
Resuscitated sudden death/cardiac arrest
Hospitalization for HF and/or pulmonary edema
LVEF drops to < 50%
≥ 3-fold increase in NT-proBNP from baseline and age-specific threshold*

*125 pg/mL for patients ≤ 75 years and 450 pg/mL for > 75 years

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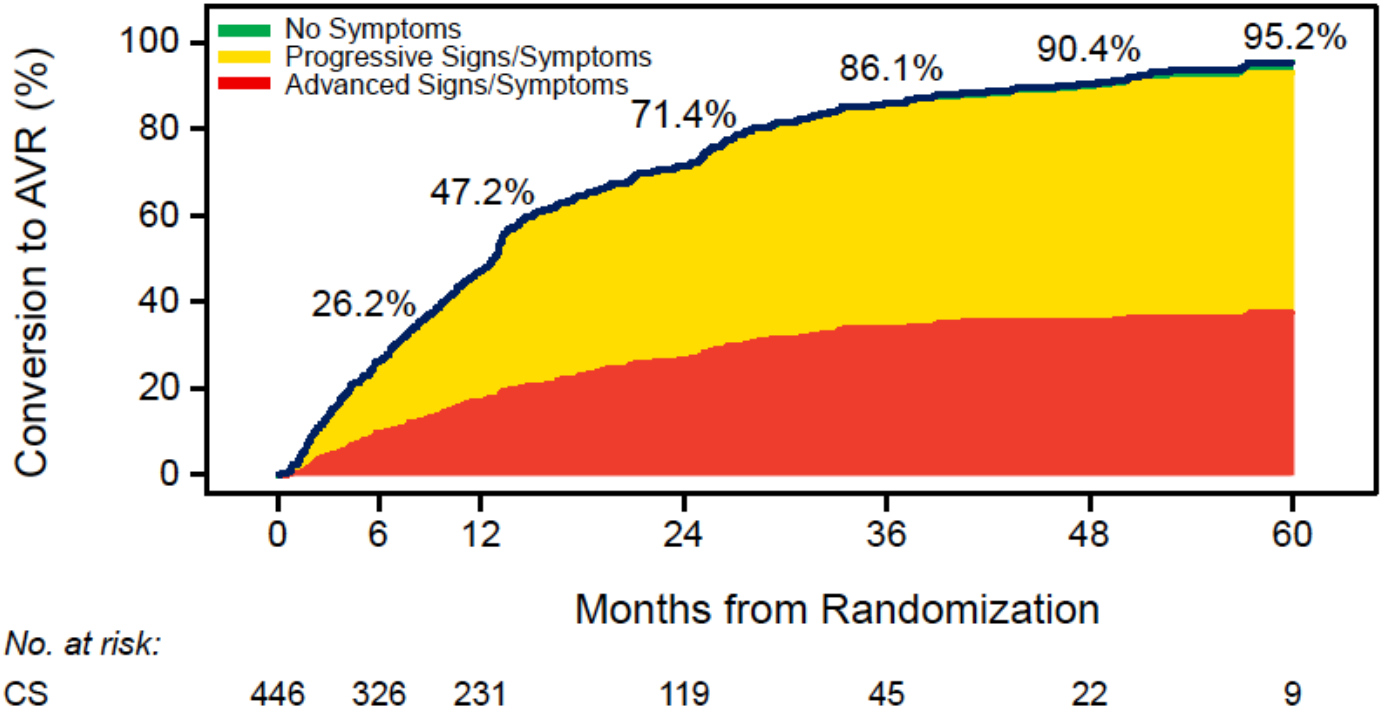
EARLY TAVR

Signs & Symptoms at Time of Conversion to AVR



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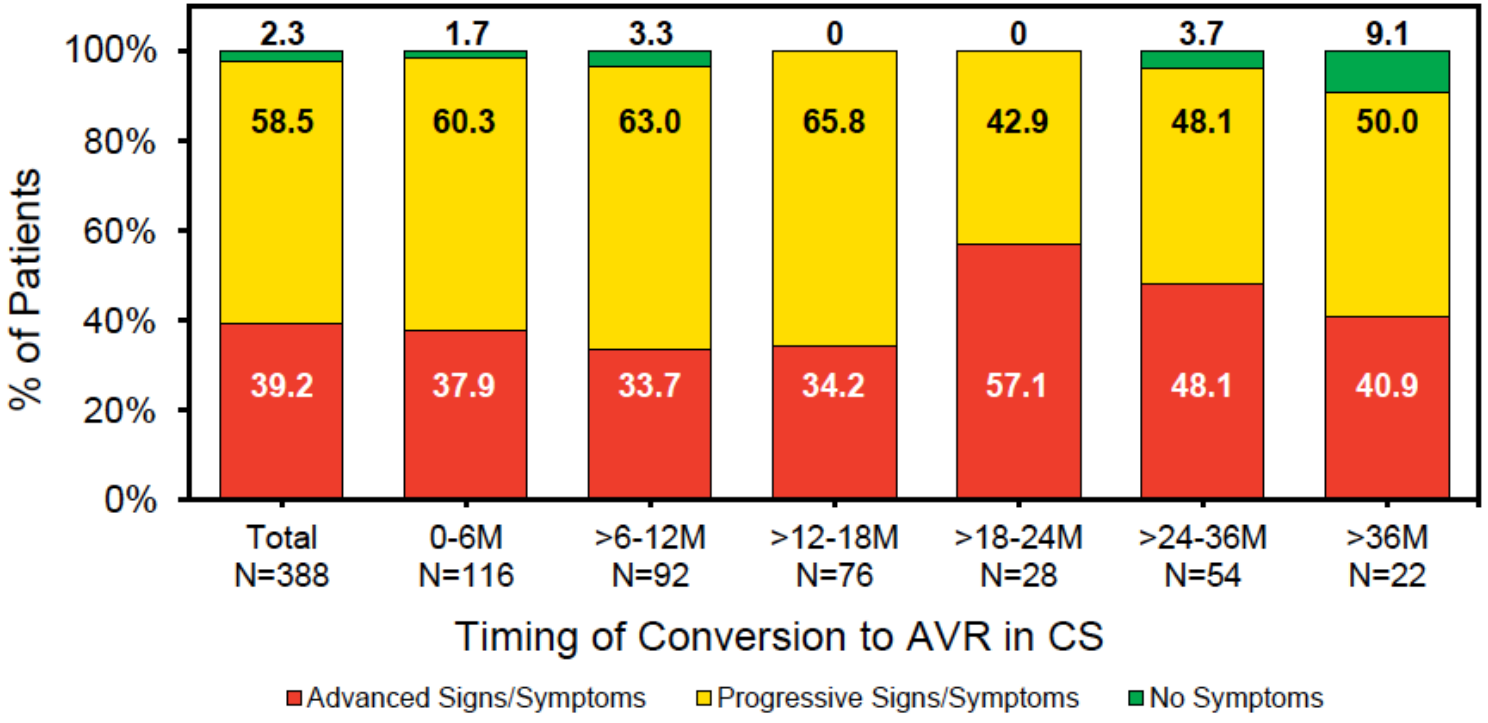
EARLY TAVR

Proportion of Patients Presenting with Advanced Signs/Symptoms was Consistent Through Time



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EARLY TAVR

THE EARLY TAVR TRIAL

Promptness of Treatment

Median (IQR) timing from:	Early TAVR (N=444)	CS with AVR (N=388)
Randomization to early TAVR	14 (9, 24) days	-
AVR indication to conversion*	-	32 (18, 58) days

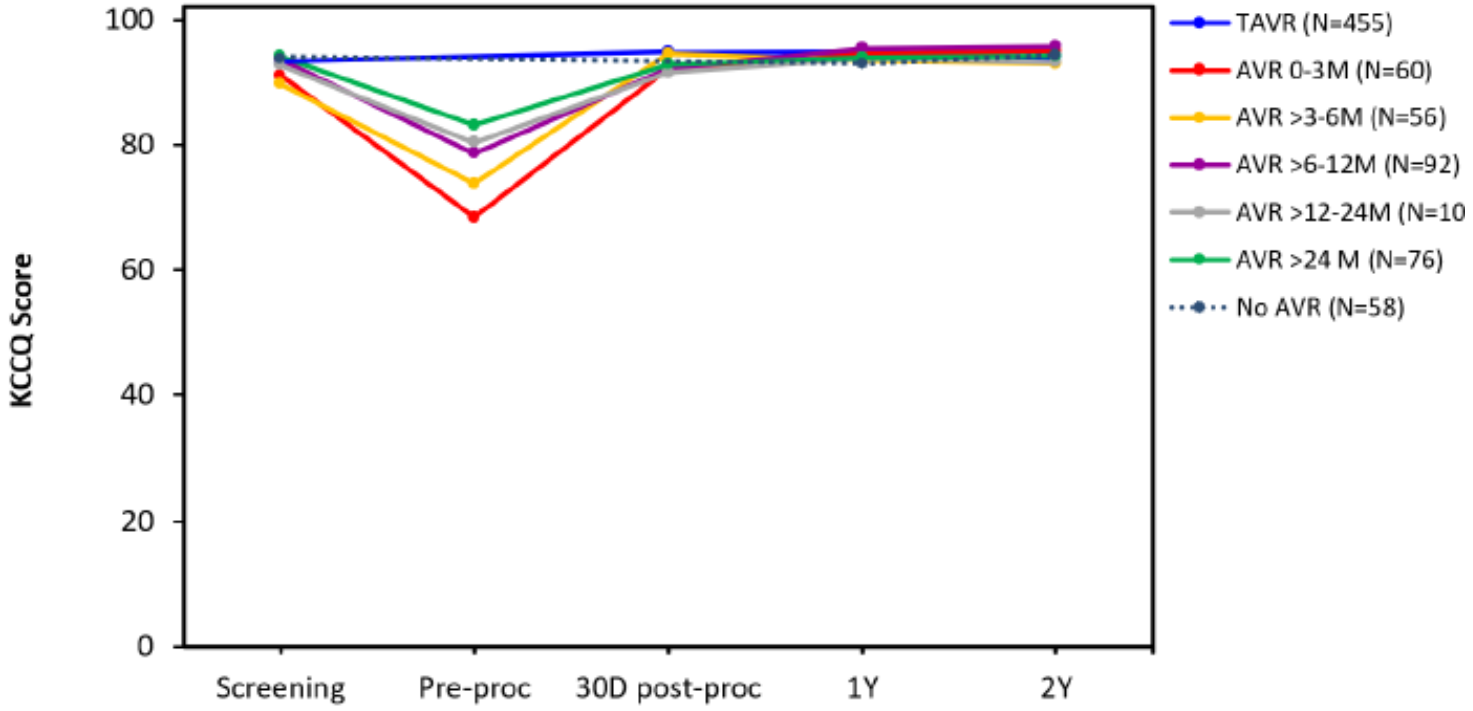
*N=381 (98.2%) underwent TAVR; N=7 (1.8%) underwent SAVR

87.9% of clinical surveillance patients who converted to AVR were treated within 3 months of indication for AVR

MAYO CLINIC Genereux et al, TCT 2024.
Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

EARLY TAVR

Figure S6. KCCQ Scores by Treatment and Timing of Conversion to AVR



Genereux et al, TCT 2024.

Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

EARLY TAVR

THE EARLY TAVR TRIAL — Periprocedural* Outcomes

Outcome – Kaplan-Meier Estimates	TAVR (N=444)	CS with AVR (N=388)
All-cause death	0.2%	0%
CV death	0%	0%
Non-CV death	0.2%	0%
Stroke	0.9%	1.8%
Disabling stroke	0%	1.0%
Non-disabling stroke	0.9%	0.8%
New onset atrial fibrillation	4.5%	3.1%
New permanent pacemaker	5.7%	8.4%
Life-threatening/disabling or major bleeding	2.5%	3.6%
Acute kidney injury (site-reported)	2.5%	3.4%
Major vascular complications	1.4%	1.0%
Myocardial infarction	0.5%	0.5%
Coronary obstruction requiring intervention	0%	0%

*Periprocedural defined as ≤ 30 days from index procedure in the TAVR arm or date of conversion to AVR in the CS arm

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Genereux et al, *NEJM 2025* Jan 16;392(3):217-227.

Outcomes of EARLY TAVR vs Delayed TAVR

901 patients (TAVR=455, Clinical surveillance=446), mean age 75.8 years, STS 1.8%.
Primary Endpoint: Death, stroke or CV hospitalization at 2 years

THE EARLY TAVR TRIAL

Purpose

- To compare outcomes between patients undergoing early TAVR and those randomized to clinical surveillance who underwent delayed AVR
- Assess the impact of clinical presentation at the time of conversion to AVR

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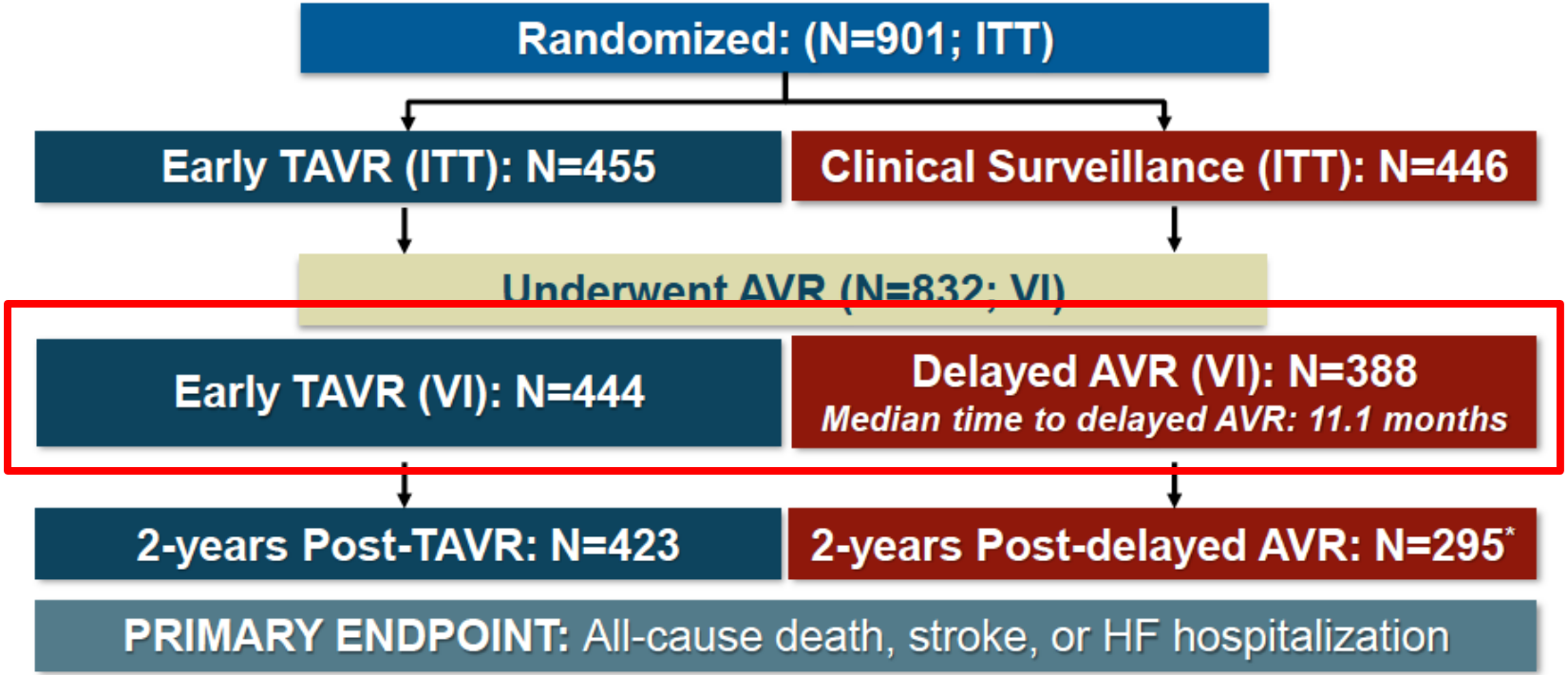
Genereux et al, ACC 2025.

Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL

Patient Flow: Valve Implanted Population



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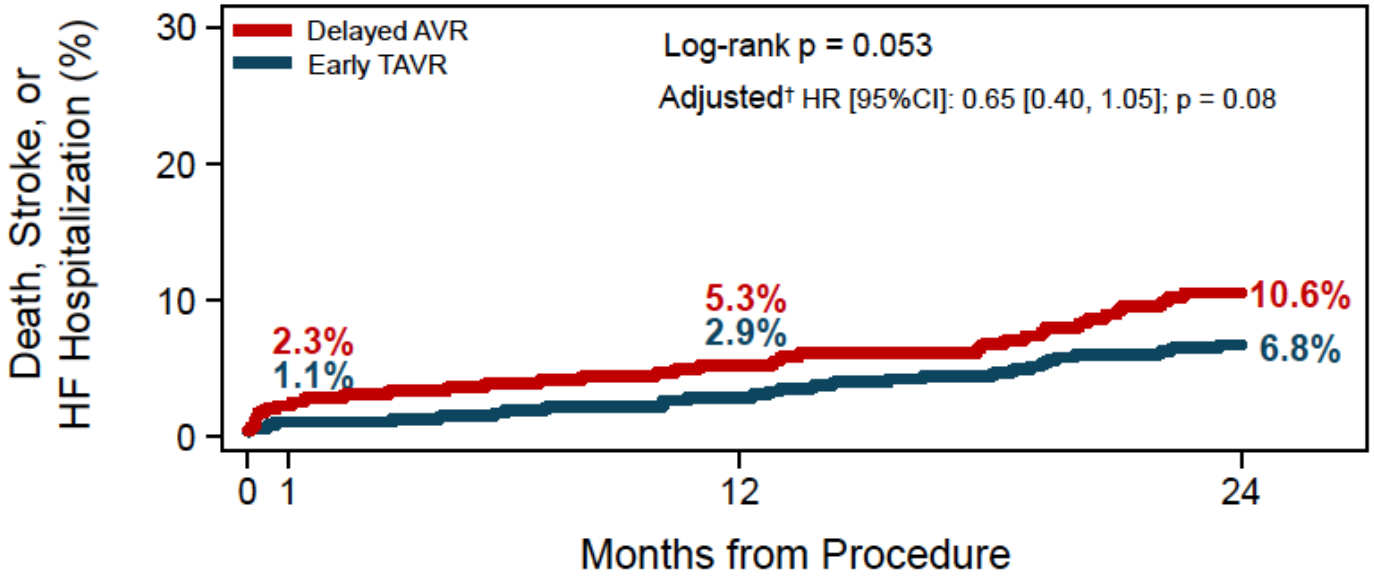
Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL — Death, Stroke, or HF Hospitalization*



No. at risk:

Early TAVR	444	439	430	409
Delayed AVR	388	375	340	277

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Genereux et al, ACC 2025.

EARLY TAVR

Clinical Presentation at Time of AVR Conversion

Patients classified based on acuity and severity of signs/symptoms

Asymptomatic
Includes pts who may have converted to AVR b/c they required additional medical procedures

Progressive Signs or Symptoms
NYHA II
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LVEF drops to < 50%
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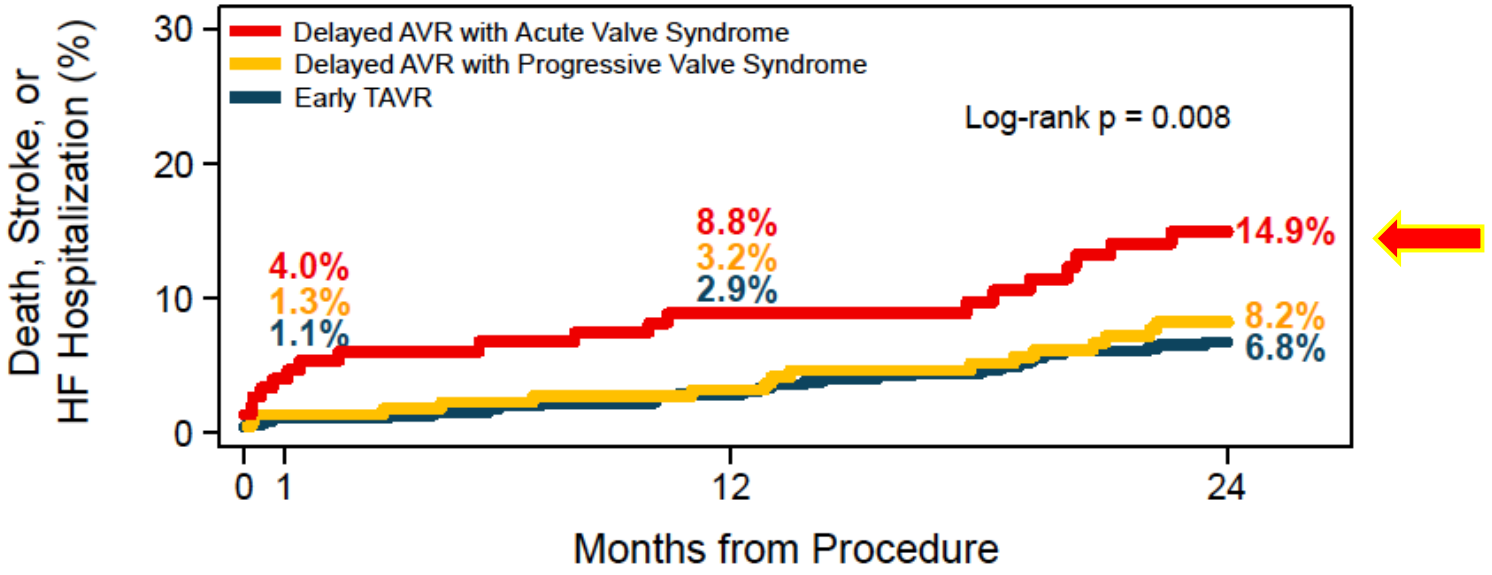
Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL — Death, Stroke, or HF Hospitalization*



No. at risk:

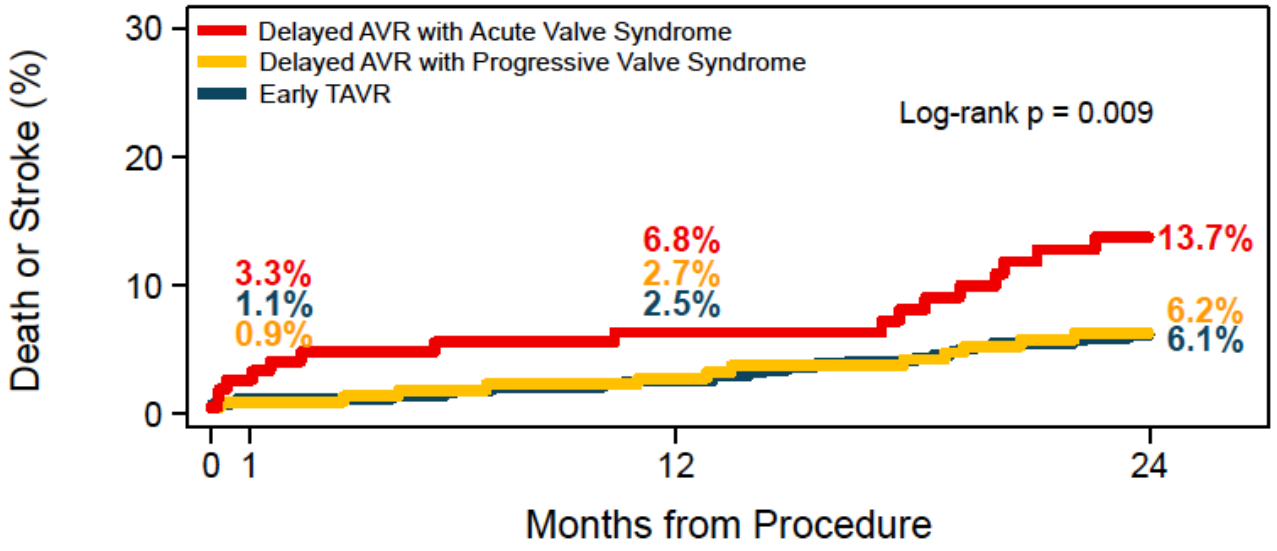
Early TAVR	444	439	430	409
Delayed AVR + PVS	227	222	207	175
Delayed AVR + AVS	152	144	125	96

Genereux et al, ACC 2025.

Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL

Death or Stroke



No. at risk:

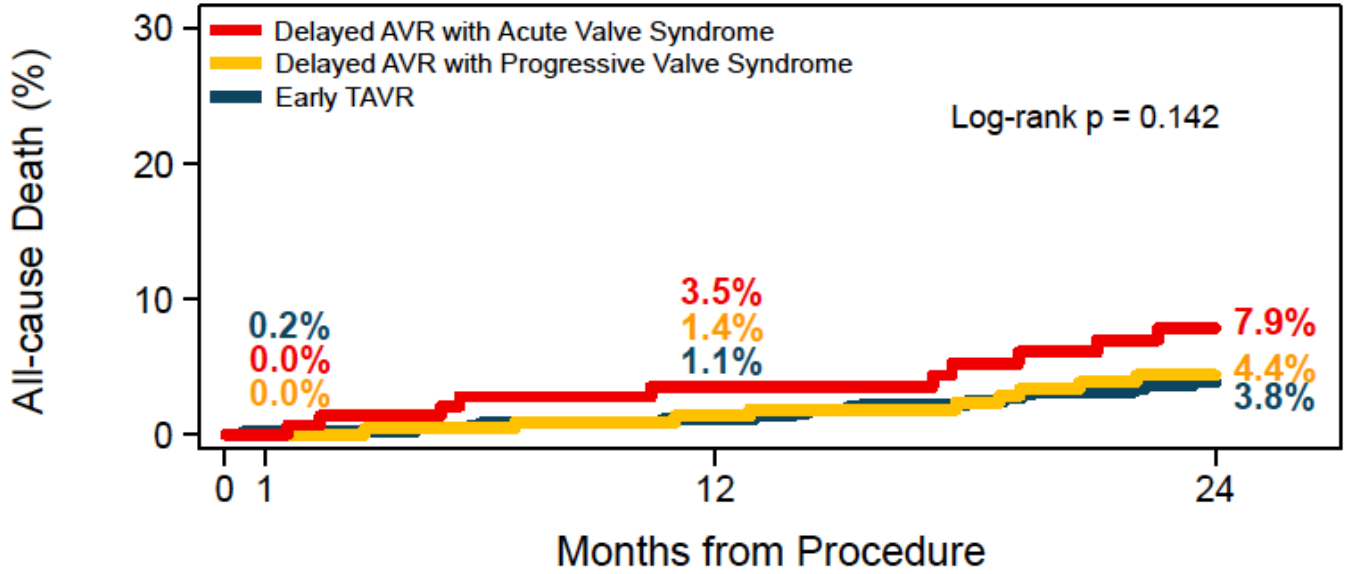
Early TAVR	444	439	432	412
Delayed AVR + PVS	227	223	208	179
Delayed AVR + AVS	152	145	128	98

Genereux et al, ACC 2025.

Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL

All-cause Death



No. at risk:

Early TAVR	444	443	438	422
Delayed AVR + PVS	227	225	211	183
Delayed AVR + AVS	152	149	131	104

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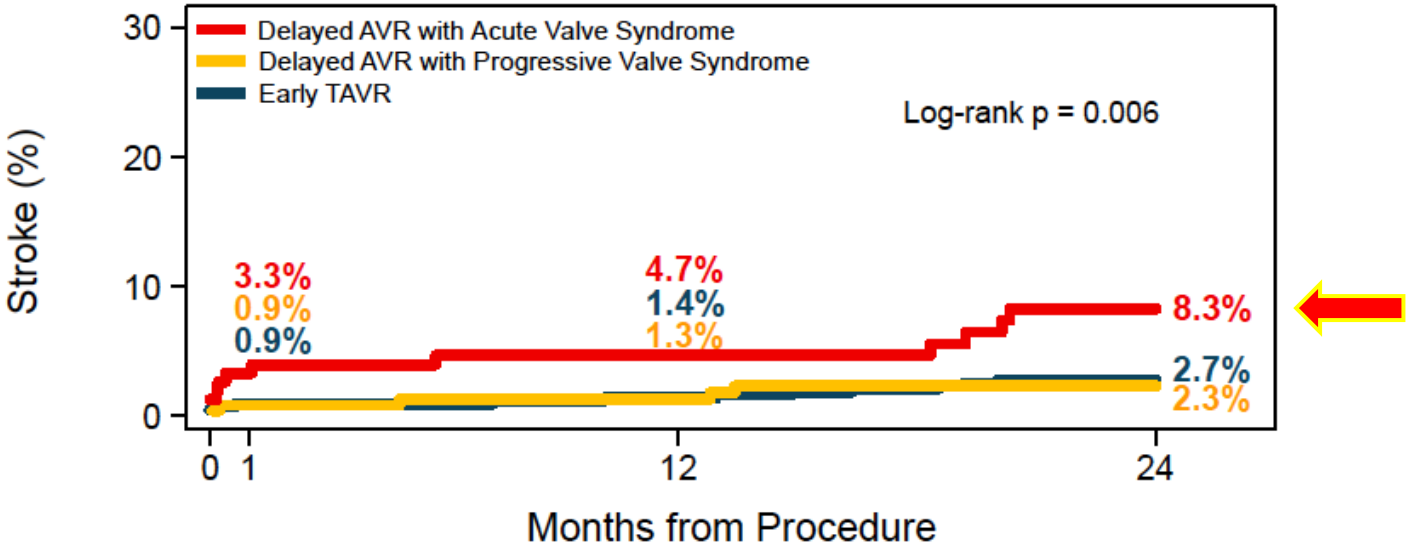
Genereux et al, ACC 2025.

Outcomes of EARLY TAVR vs Delayed TAVR

THE EARLY TAVR TRIAL

All Stroke



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Summary

- Early TAVR in asymptomatic is associated with lower composite rate of Death, Stroke or CV Hospitalization at 2 years than clinical surveillance.
- Median time to conversion was 11.1 months (95.2% converted within 5 years).
- 39.5% of crossovers presented with Acute Valve Syndrome (AVS).
- Delayed TAVR was associated with higher composite rate of Death, Stroke & HFH, primarily driven by higher stroke rates in patients presenting with AVS.
- Prompt TAVR in severe AS maybe be the preferred strategy to prevent progressions to Acute Valve Syndrome and associated poor outcomes.

On 5-1-25, the FDA approved Sapien 3 for asymptomatic severe AS

Thank You

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