**UC DAVIS HEALTH**

**Heart & Vascular Center**

# 2024 Northern California Structural Heart Summit

## TAVR in Moderate or Asymptomatic Aortic Stenosis: How early is too early?

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# Conflicts of Interest

- I have performed consulting/proctoring for Medtronic Structural Heart for Evolut FX+ in the previous 24 months.

- UC Davis was a participant in a trial discussed here today.

# TAVR in Moderate or Asymptomatic AS

- Objectives
  - Very brief review of current guidelines for TAVR/SAVR

  - Look at recent surgical evidence for earlier surgery

  - Assess very recent trial data for TAVR in asymptomatic severe AS

  - Look at trials still in progress for moderate AS and TAVR

# The Paradigm, Since 1968



VALVULAR AORTIC STENOSIS IN ADULTS
AVERAGE COURSE
(Post Mortem Data)
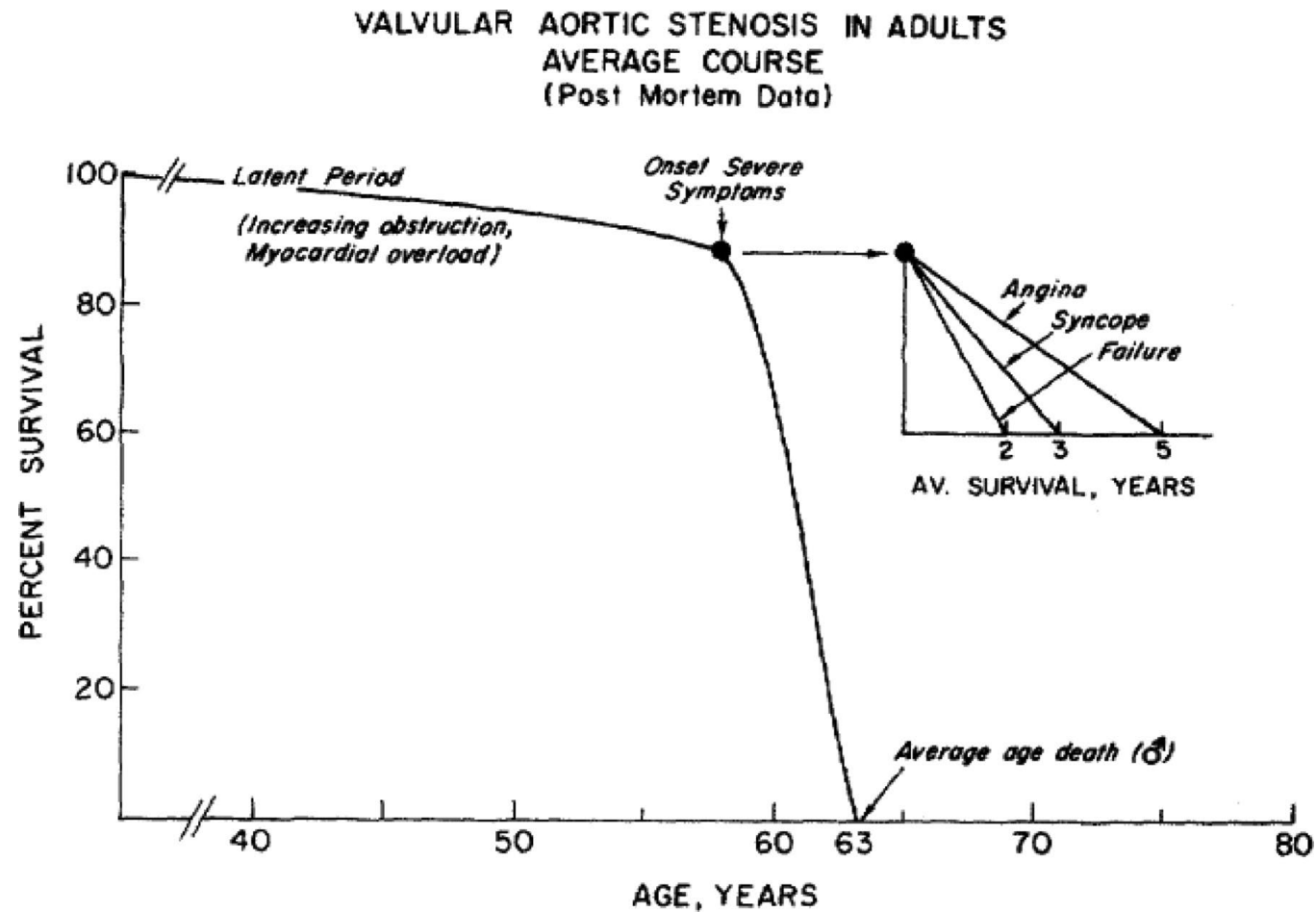
From Ross and Brauwald, Circulation. 1968 Jul;38(1 Suppl):61-7.

**B) Asymptomatic patients with severe aortic stenosis**

| Recommendation | Class | Level |
|---|---|---|
| Intervention is recommended in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <50%) without another cause.[9,238,239] | I | B |
| Intervention is recommended in asymptomatic patients with severe aortic stenosis and demonstrable symptoms on exercise testing. | I | C |
| Intervention should be considered in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <55%) without another cause.[9,240,241] | IIa | B |
| Intervention should be considered in asymptomatic patients with severe aortic stenosis and a sustained fall in BP (>20 mmHg) during exercise testing. | IIa | C |
| Intervention should be considered in asymptomatic patients with LVEF >55% and a normal exercise test if the procedural risk is low and one of the following parameters is present:<br>• Very severe aortic stenosis (mean gradient ≥60 mmHg or $V_{max}$ >5 m/s).[9,242]<br>• Severe valve calcification (ideally assessed by CCT) and $V_{max}$ progression ≥0.3 m/s/year.[164,189,243]<br>• Markedly elevated BNP levels (>3× age- and sex-corrected normal range) confirmed by repeated measurements and without other explanation.[163,171] | IIa | B |
| SAVR should be considered in patients with moderate aortic stenosis[h] undergoing CABG or surgical intervention on the ascending aorta or another valve after Heart Team discussion. | IIa | C |

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*European Heart Journal*, Volume 43, Issue 7, 14 February 2022, Pages 561–632

| Stage | Definition |
|---|---|
| A | At risk of AS |
| B | Progressive AS |
| **C: Asymptomatic severe AS** | |
| C1 | Asymptomatic severe AS |
| C2 | Asymptomatic severe AS with LV systolic dysfunction |
| **D: Symptomatic severe AS** | |
| D1 | Symptomatic severe high-gradient AS |
| D2 | Symptomatic severe low-flow, low-gradient AS with reduced LVEF |
| D3 | Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS |

*Circulation*. 2021;143:e72-e227

**Recommendations for Timing of Intervention of AS**
Referenced studies that support the recommendations are summarized in Online Data Supplements 8 and 9 to 16.

| COR | LOE | Recommendations |
|---|---|---|
| 1 | A | 1. In adults with severe high-gradient AS (Stage D1) and symptoms of exertional dyspnea, HF, angina, syncope, or presyncope by history or on exercise testing, AVR is indicated.[1–7] |
| 1 | B-NR | 2. In asymptomatic patients with severe AS and an LVEF <50% (Stage C2), AVR is indicated.[8–11] |
| 1 | B-NR | 3. In asymptomatic patients with severe AS (Stage C1) who are undergoing cardiac surgery for other indications, AVR is indicated.[12–16] |
| 1 | B-NR | 4. In symptomatic patients with low-flow, low-gradient severe AS with reduced LVEF (Stage D2), AVR is recommended.[17–24] |
| 1 | B-NR | 5. In symptomatic patients with low-flow, low-gradient severe AS with normal LVEF (Stage D3), AVR is recommended if AS is the most likely cause of symptoms.[25–27] |
| 2a | B-NR | 6. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when an exercise test demonstrates decreased exercise tolerance (normalized for age and sex) or a fall in systolic blood pressure of ≥10 mmHg from baseline to peak exercise.[13,28–30] |
| 2a | B-R | 7. In asymptomatic patients with very severe AS (defined as an aortic velocity of ≥5 m/s) and low surgical risk, AVR is reasonable.[15,31–35] |
| 2a | B-NR | 8. In apparently asymptomatic patients with severe AS (Stage C1) and low surgical risk, AVR is reasonable when the serum B-type natriuretic peptide (BNP) level is >3 times normal.[32,36–38] |
| 2a | B-NR | 9. In asymptomatic patients with high-gradient severe AS (Stage C1) and low surgical risk, AVR is reasonable when serial testing shows an increase in aortic velocity ≥0.3 m/s per year.[39,40] |
| 2b | B-NR | 10. In asymptomatic patients with severe high-gradient AS (Stage C1) and a progressive decrease in LVEF on at least 3 serial imaging studies to <60%, AVR may be considered.[8–11,33] |
| 2b | C-EO | 11. In patients with moderate AS (Stage B) who are undergoing cardiac surgery for other indications, AVR may be considered. |
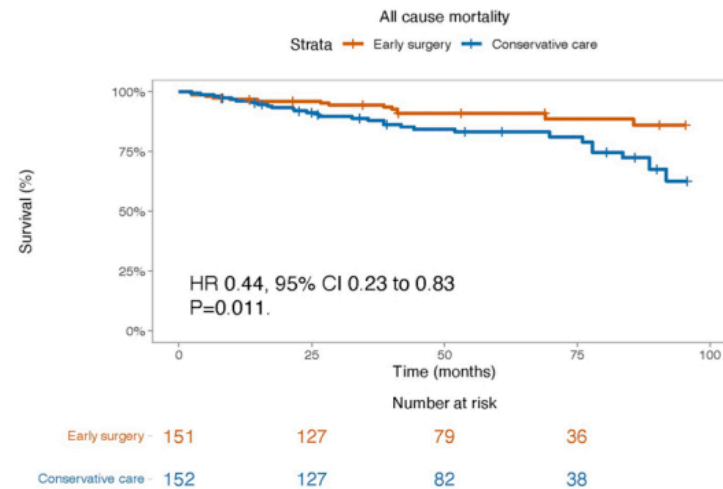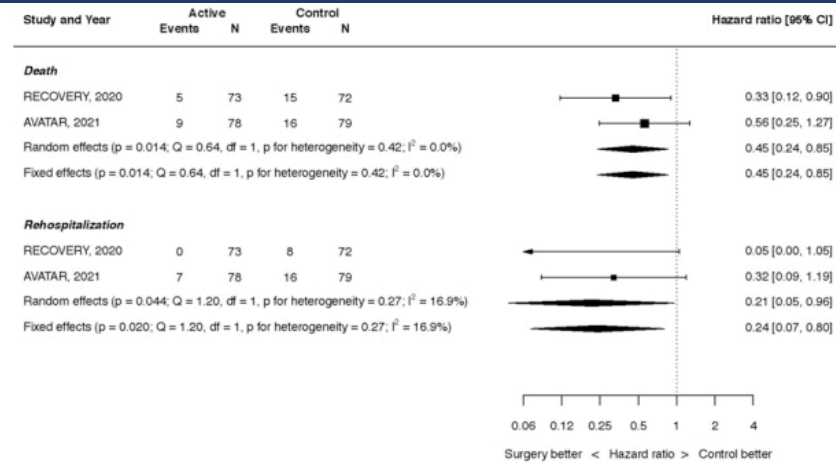
J Soc Cardiovasc Angiogr Interv. 2022 May 25;1(4):100383

# EARLY TAVR

- Truly asymptomatic

- Had to be free of symptoms on age adjusted treadmill protocol

- True C1 aortic stenosis only (EF ≥ 50%, AVA ≤ 1 cm$^2$ or AVAi ≤ 0.6cm$^2$/m$^2$ and mean gradient ≥ 40 mmHg or peak velocity ≥ 4 m/s)

- STS score ≤ 10 and age ≥ 65 years

- 677 patients screened and excluded
  - 146 had a positive stress test
  - 131 were deemed symptomatic or other exclusion per the PI indicating class I need for AVR
  - 213 were excluded due to anatomical considerations (TF-TAVR only, no altenative access)

- Minimum follow up 2 years post-randomization, median follow up 3.8 years

Transcatheter Aortic-Valve Replacement for Asymptomatic Severe Aortic Stenosis. N Engl J Med. 2024 Oct 28.
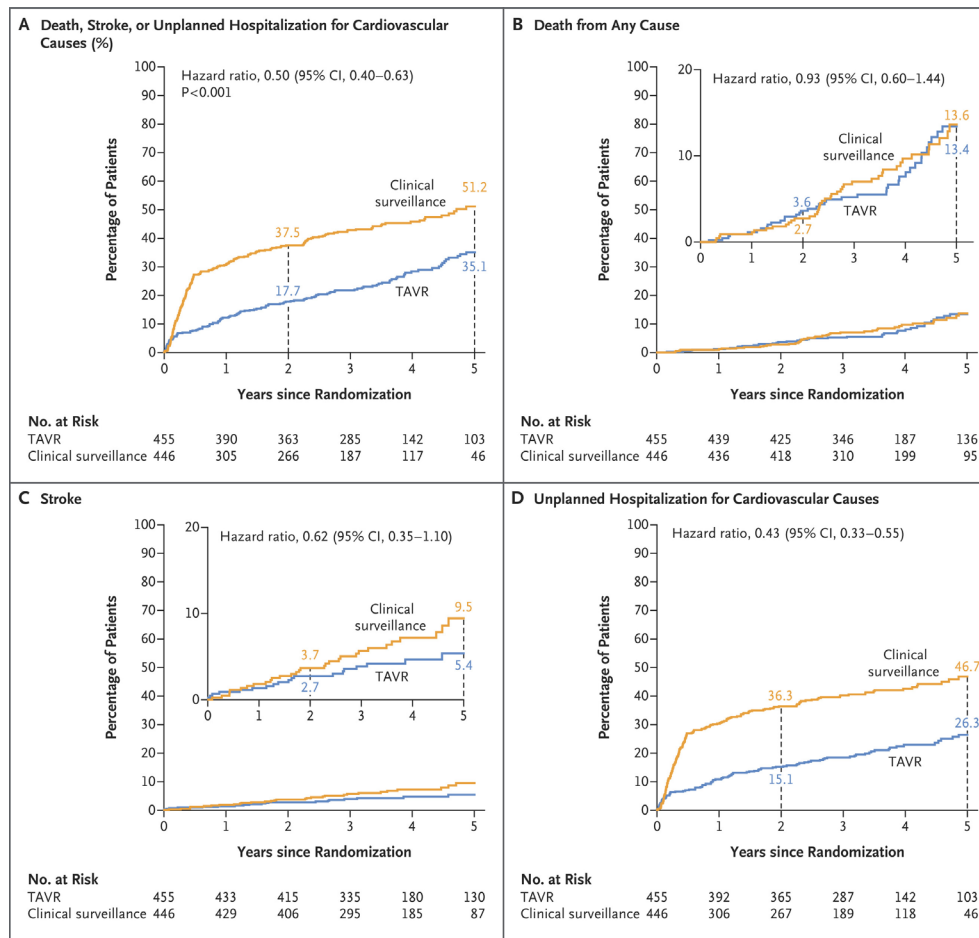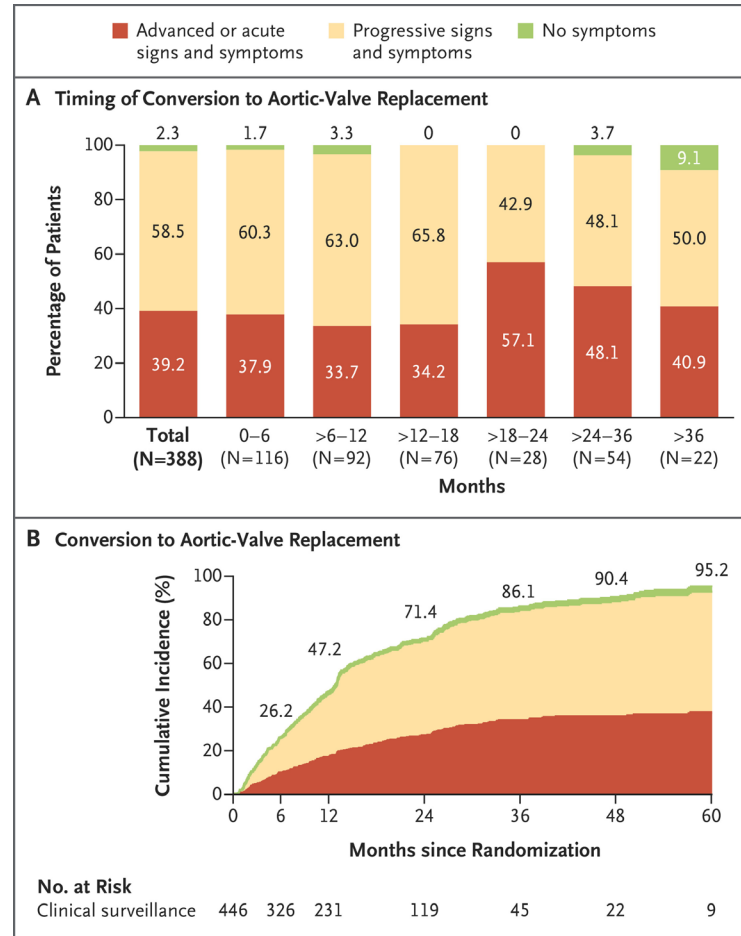
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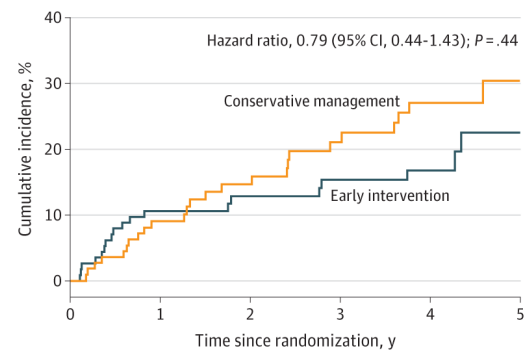
# EVOLVED

- Severe AS with peak velocity ≥ 4 m/s or ≥ 3.5 m/s and AVAi ≤ 0.6cm$^2$/m$^2$

- Asymptomatic but no treadmill requirement

- No concomitant severe aortic insufficiency or mitral insufficiency

- EF ≥ 50%

- Reduced GFR or other contraindication to MRI was exclusionary

- Screened for LV damage with hypertrophy on EKG or Troponin I ≥ 6 ng/L

- These patients then underwent cardiac MR

- Patients with midwall myocardial fibrosis were randomized to early AVR (SAVR or TAVR) vs guideline directed management

- Could be co-enrolled in the EASY-AS trial (another asymptomatic trial)
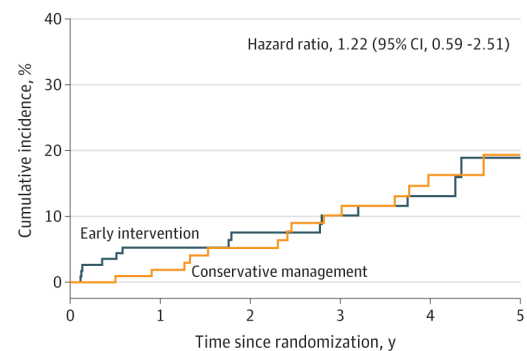
- SAV vs TAV chosen by the local heart team

A. All-cause death or unplanned aortic stenosis–related hospitalization

B. All-cause death

C. Unplanned aortic stenosis–related hospitalization

JAMA. Published online October 28, 2024

# EVOLVED
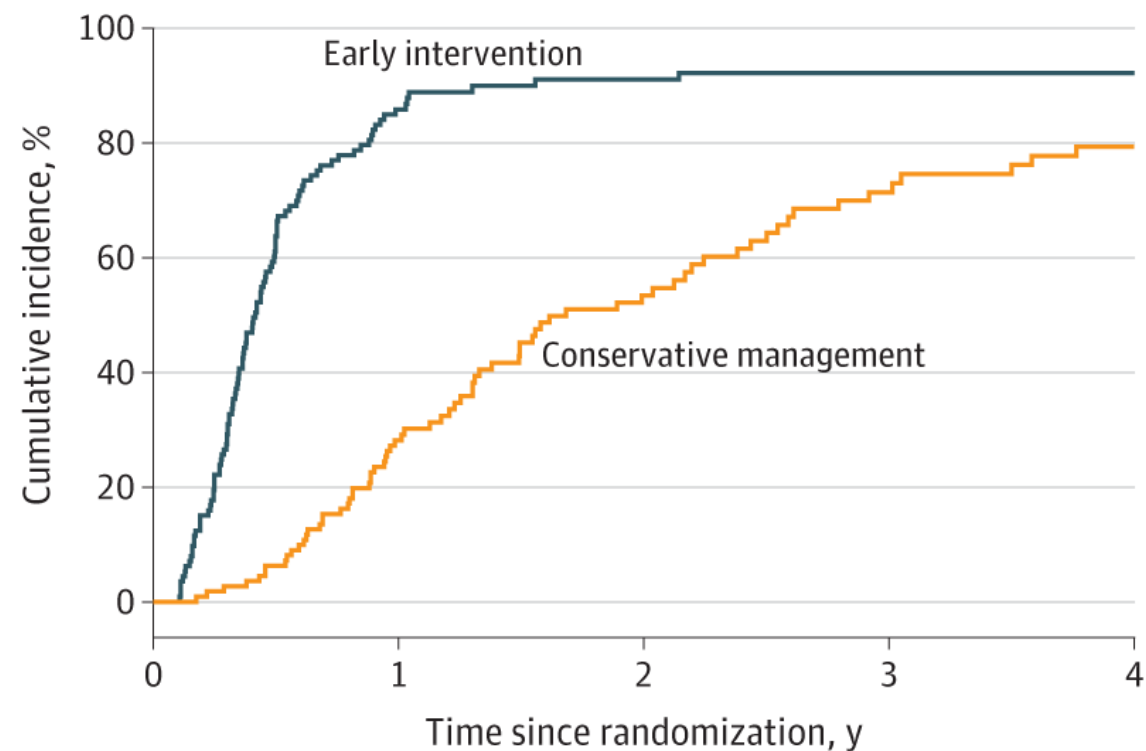
| | Early Intervention (n=113) | Conservative Management (n=111) |
|---|---|---|
| Did not receive intervention during follow-up, No. (%) | 7 (6) | 26 (23) |
| Type of surgery, No. (%) | | |
| - Elective surgery | 103 (97) | 72 (85) |
| - Urgent inpatient surgery | 3 (3) | 13 (15) |
| Surgical Aortic Valve Replacement, No. (%) | 80 (75) | 47 (55) |
| - Biological prosthesis | 73 (91) | 44 (94) |
| - Mechanical prosthesis | 7 (9) | 3 (6) |
| Transcatheter aortic valve intervention, No. (%) | 26 (25) | 38 (45) |
| - Transfemoral | 25 (96) | 37 (97) |
| - Other | 1 (4) | 1 (3) |
| Concomitant Procedure, No. (%) | | |
| - Coronary artery bypass grafting | 20 (19) | 13 (15) |
| - Aortic root repair or replacement | 6 (6) | 4 (5) |
| Primary indication for aortic valve intervention, No. (%) | | |
| - Symptom development | N/A | 61 (72) |
| - Reduction in ejection fraction | N/A | 1 (1) |
| - Abnormal exercise test | N/A | 1 (1) |
| - Rapid progression of aortic stenosis | N/A | 22 (26) |

JAMA. Published online October 28, 2024

# TAVR UNLOAD

- Randomized transfemoral TAVR vs. clinical aortic stenosis surveillance (CASS) for symptomatic patients with moderate AS and HFrEF

- TAVR for those who progressed to severe in the CASS group

- NYHA II-IV patients with LVEF 20-50%

- Moderate AS definition
  - AVA between 1 and 1.5 cm2 on resting echocardiogram
  - If AVA ≤ 1 cm2 but suspect low flow, dobutamine echo is performed
  - AVA <1 cm2 but indexed AVA >0.6 cm2/m2 on either rest or dobutamine
  - AVA >1.5 cm2 but indexed AVA <0.9cm2/m2 on either rest or dobutamine

- Randomized 1:1 to TAVR vs CASS

- Hierarchical primary endpoint of all-cause death, disabling stroke, disease related hospitalizations and HF hospitalization equivalents, and change in KCCQ-OSS

# TAVR UNLOAD



**FIGURE 2** Primary Endpoint at Longest and 1-Year Follow-Up
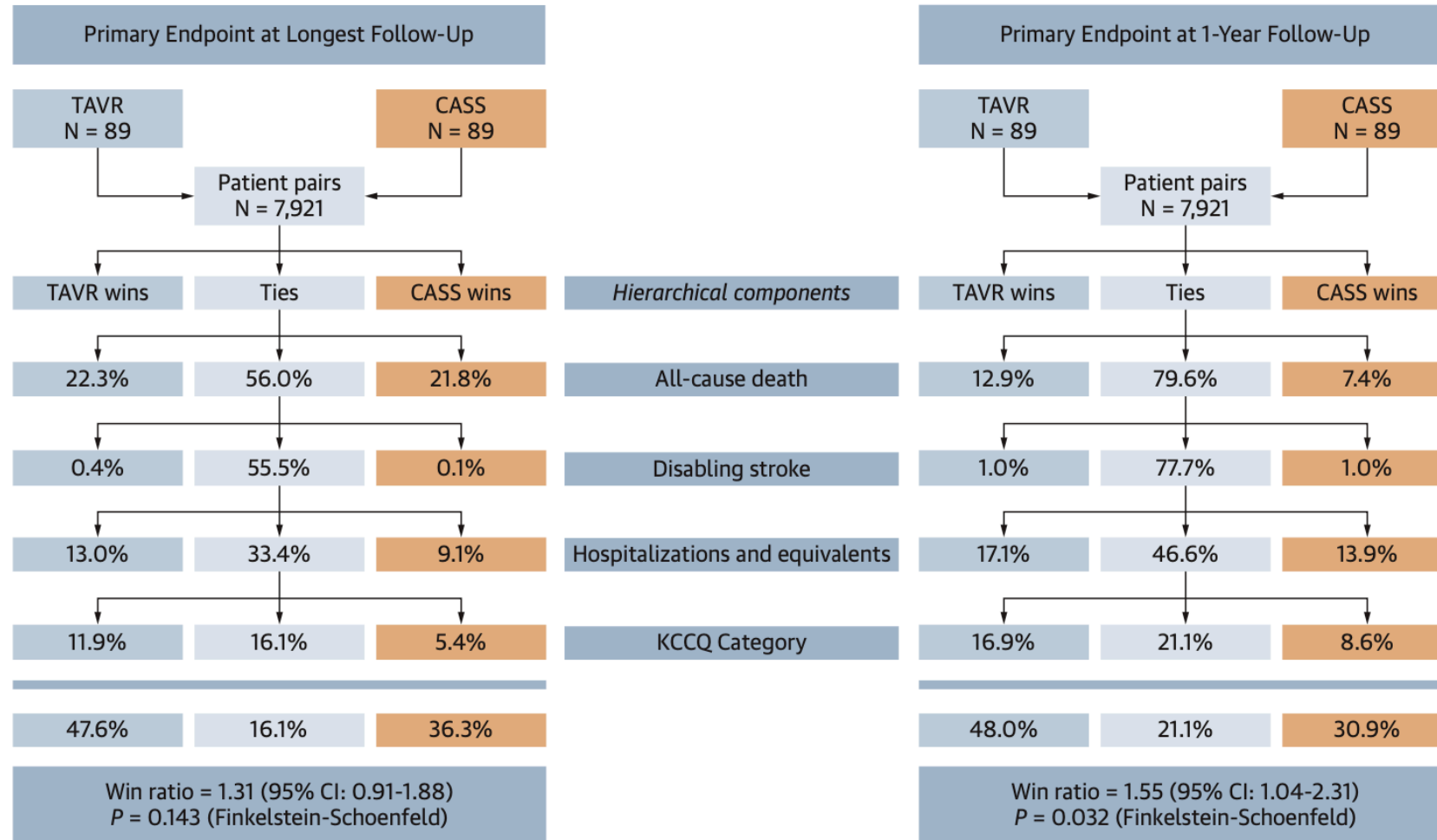
TAVR UNLOAD. JACC. 2024, 0 (0).

# TAVR UNLOAD

**TABLE 2** Primary and Secondary Clinical Endpoints

| Pairwise Comparison Endpoint | TAVR Win, % (n = 89) | CASS Win, % (n = 89) | Win Ratio (95% CI) | P Value[a] |
|---|---|---|---|---|
| **At longest follow-up** | | | | |
| Hierarchical composite endpoint (events and KCCQ) | 47.6 | 36.3 | 1.31 (0.91-1.88) | 0.14 |
| Hierarchical composite endpoint (events) | 35.7 | 30.9 | 1.15 (0.76-1.76) | 0.51 |
| **At 1-y follow-up** | | | | |
| Hierarchical composite endpoint (events and KCCQ) | 48.0 | 30.9 | 1.55 (1.04-2.31) | 0.032 |
| Hierarchical composite endpoint (events) | 31.1 | 22.3 | 1.39 (0.82-2.35) | 0.22 |

| Time-to-Event Endpoint | n (%) | Event Rate[b] | n (%) | Event Rate[b] | HR (95% CI) | P Value[c] |
|---|---|---|---|---|---|---|
| **At longest follow-up** | | | | | | |
| Major adverse cardiovascular and cerebrovascular events | 46 (51.7) | 33.0 | 51 (57.3) | 41.6 | 0.83 (0.56-1.24) | 0.37 |
| All-cause death | 35 (39.3) | 18.6 | 35 (39.3) | 19.4 | 0.98 (0.61-1.56) | 0.92 |
| Any stroke | 2 (2.2) | 1.1 | 6 (6.7) | 3.4 | 0.32 (0.06-1.58) | 0.16 |
| Disease-related hospitalizations or HFH equivalents | 34 (38.2) | 24.4 | 40 (44.9) | 31.7 | 0.80 (0.51-1.27) | 0.35 |
| **At 1-y follow-up** | | | | | | |
| Major adverse cardiovascular and cerebrovascular events | 26 (29.2) | 29.7 | 33 (37.1) | 38.8 | 0.75 (0.45-1.26) | 0.27 |
| All-cause death | 8 (9.0) | 9.3 | 12 (13.5) | 14.3 | 0.60 (0.25-1.48) | 0.26 |
| Any stroke | 1 (1.1) | 1.1 | 4 (4.5) | 5.1 | 0.23 (0.03-2.09) | 0.16 |
| Disease-related hospitalizations or HFH equivalents | 24 (27.0) | 27.5 | 28 (31.5) | 33.9 | 0.83 (0.48-1.43) | 0.49 |

TAVR UNLOAD. JACC. 2024, 0 (0).

# Upcoming Trials

- PROGRESS
  - TAVR with Edwards balloon expandable valve vs. deferral in moderate aortic stenosis
- EXPAND II
  - TAVR with Medtronic Pro+ or FX vs. GDMT in moderate aortic stenosis
- Early vs deferred AVR in moderate AS and MR
  - Enrolling in Switzerland

- EASY-AS
  - Asymptomatic severe AS randomized to AVR for GDMT in the UK, Australia, New Zealand

# THANK YOU