Year in Review:
Valvular and Structural Intervention

David J. Cohen, M.D., M.Sc.

Director of Clinical and Outcomes Research
Cardiovascular Research Foundation, New York, NY

Director of Academic Affairs
St. Francis Hospital, Roslyn NY

TCT-AP 2023: 12 minutes

Disclosures

Grant Support/Drugs

- MyoKardia/BMS

Grant Support/Devices

- Edwards Lifesciences
- Boston Scientific
- Corvia
- I-Rhythm

- Abbott Vascular
- CathWorks
- Phillips
- Zoll/Therox

Consulting/Advisory Boards

- Medtronic
- Boston Scientific
- Corvia

- Edwards Lifesciences
- Abbott Vascular
- Impulse Dynamics

David Cohen's Top Three

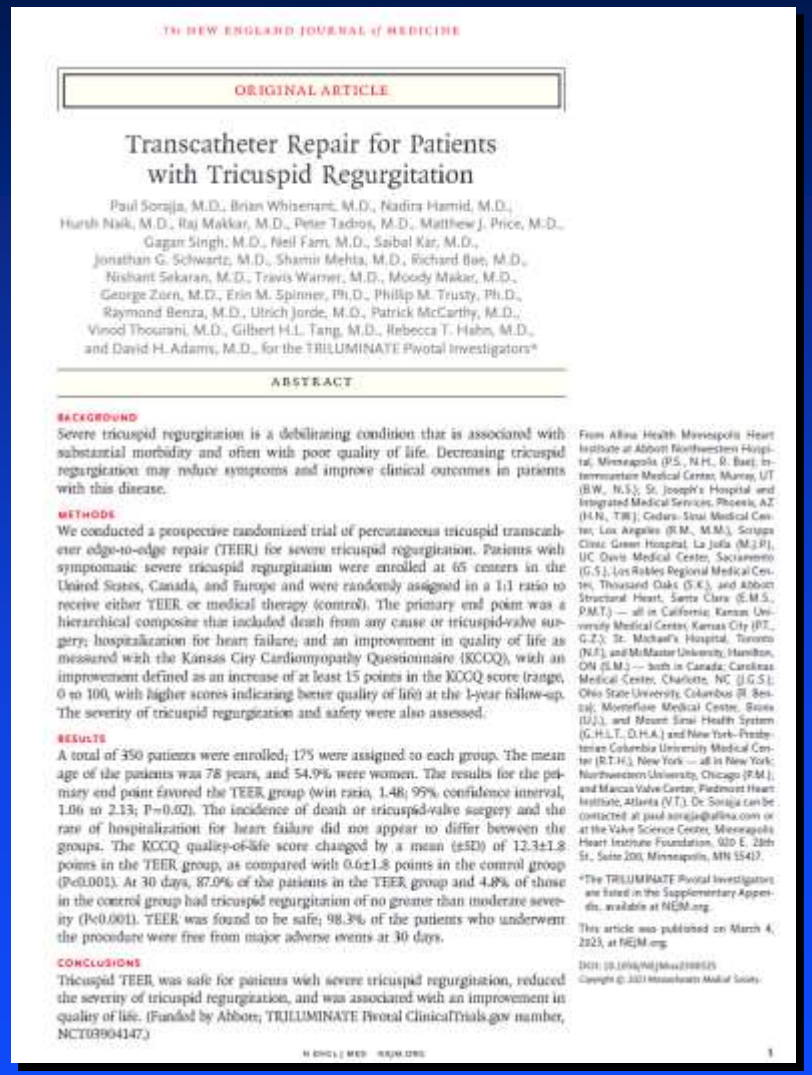
#1

- TRILUMINATE

TRILUMINATE: Background

- Tricuspid regurgitation is present in ~5% of patients over age 65 and is associated with poor quality of life and increased mortality
- Treatment generally limited to diuretics to improve quality of life
- Except in conjunction with surgery for left-sided valve dz, TV surgery is rarely performed in the US, because of poor outcomes (operative mortality ~8%) and high rates of complications (perm. pacer 10-15%)
- Numerous devices have been developed for treatment of TR, but no studies have compared outcomes with standard medical therapy

TRILUMINATE: Study Design



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Repair for Patients with Tricuspid Regurgitation

Paul Sorajja, M.D., Brian Whisenant, M.D., Nadira Hamid, M.D., Hursh Naik, M.D., Raj Makkar, M.D., Peter Tadros, M.D., Matthew J. Price, M.D., Gagan Singh, M.D., Neil Fam, M.D., Saibal Kar, M.D., Jonathan G. Schwartz, M.D., Shamir Mehta, M.D., Richard Bae, M.D., Nishant Sekaran, M.D., Travis Warner, M.D., Moody Makar, M.D., George Zorn, M.D., Erin M. Spinner, Ph.D., Phillip M. Trusty, Ph.D., Raymond Benza, M.D., Ulrich Jorde, M.D., Patrick McCarthy, M.D., Vinod Thourani, M.D., Gilbert H.L. Tang, M.D., Rebecca T. Hahn, M.D., and David H. Adams, M.D., for the TRILUMINATE Pivotal Investigators*

ABSTRACT

BACKGROUND

Severe tricuspid regurgitation is a debilitating condition that is associated with substantial morbidity and often with poor quality of life. Decreasing tricuspid regurgitation may reduce symptoms and improve clinical outcomes in patients with this disease.

METHODS

We conducted a prospective randomized trial of percutaneous tricuspid transcatheter edge-to-edge repair (TEER) for severe tricuspid regurgitation. Patients with symptomatic severe tricuspid regurgitation were enrolled at 65 centers in the United States, Canada, and Europe and were randomly assigned in a 1:1 ratio to receive either TEER or medical therapy (control). The primary end point was a hierarchical composite that included death from any cause or tricuspid-valve surgery; hospitalization for heart failure; and an improvement in quality of life as measured with the Kansas City Cardiomyopathy Questionnaire (KCCQ), with an improvement defined as an increase of at least 15 points in the KCCQ score (range, 0 to 100, with higher scores indicating better quality of life) at the 1-year follow-up. The severity of tricuspid regurgitation and safety were also assessed.

RESULTS

A total of 350 patients were enrolled; 175 were assigned to each group. The mean age of the patients was 78 years, and 54.9% were women. The results for the primary end point favored the TEER group (win ratio, 1.48; 95% confidence interval, 1.06 to 2.13; P=0.02). The incidence of death or tricuspid-valve surgery and the rate of hospitalization for heart failure did not appear to differ between the groups. The KCCQ quality-of-life score changed by a mean (±SD) of 12.3±1.8 points in the TEER group, as compared with 0.6±1.8 points in the control group (P<0.001). At 30 days, 87.0% of the patients in the TEER group and 4.8% of those in the control group had tricuspid regurgitation of no greater than moderate severity (P<0.001). TEER was found to be safe; 98.3% of the patients who underwent the procedure were free from major adverse events at 30 days.

CONCLUSIONS

Tricuspid TEER was safe for patients with severe tricuspid regurgitation, reduced the severity of tricuspid regurgitation, and was associated with an improvement in quality of life. (Funded by Abbott; TRILUMINATE Pivotal ClinicalTrials.gov number, NCT03904147.)

From Allina Health Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis (P.S., N.H., R. Bae); Intermountain Medical Center, Murray, UT (B.W., N.S.); St. Joseph's Hospital and Integrated Medical Services, Phoenix, AZ (H.N., T.W.); Cedars-Sinai Medical Center, Los Angeles (R.M., M.M.), Scripps Clinic Green Hospital, La Jolla (M.J.P.), UC Davis Medical Center, Sacramento (G.S.), Los Robles Regional Medical Center, Thousand Oaks (S.K.), and Abbott Structural Heart, Santa Clara (E.M.S., P.M.T.) — all in California; Kansas University Medical Center, Kansas City (P.T., G.Z.); St. Michael's Hospital, Toronto (N.F.), and McMaster University, Hamilton, ON (G.H.L.) — both in Canada; Carolinas Medical Center, Charlotte, NC (J.G.S.); Ohio State University, Columbus (R. Benza); Montefiore Medical Center, Bronx (U.J.), and Mount Sinai Health System (G.H.L.T., D.H.A.) and New York–Presbyterian Columbia University Medical Center (R.T.H.), New York — all in New York; Northwestern University, Chicago (P.M.); and Marcus Valve Center, Piedmont Heart Institute, Atlanta (V.T.). Dr. Sorajja can be contacted at paul.sorajja@allina.com or at the Valve Science Center, Minneapolis Heart Institute Foundation, 920 E. 28th St., Suite 200, Minneapolis, MN 55407.

*The TRILUMINATE Pivotal Investigators are listed in the Supplementary Appendix, available at NEJM.org.

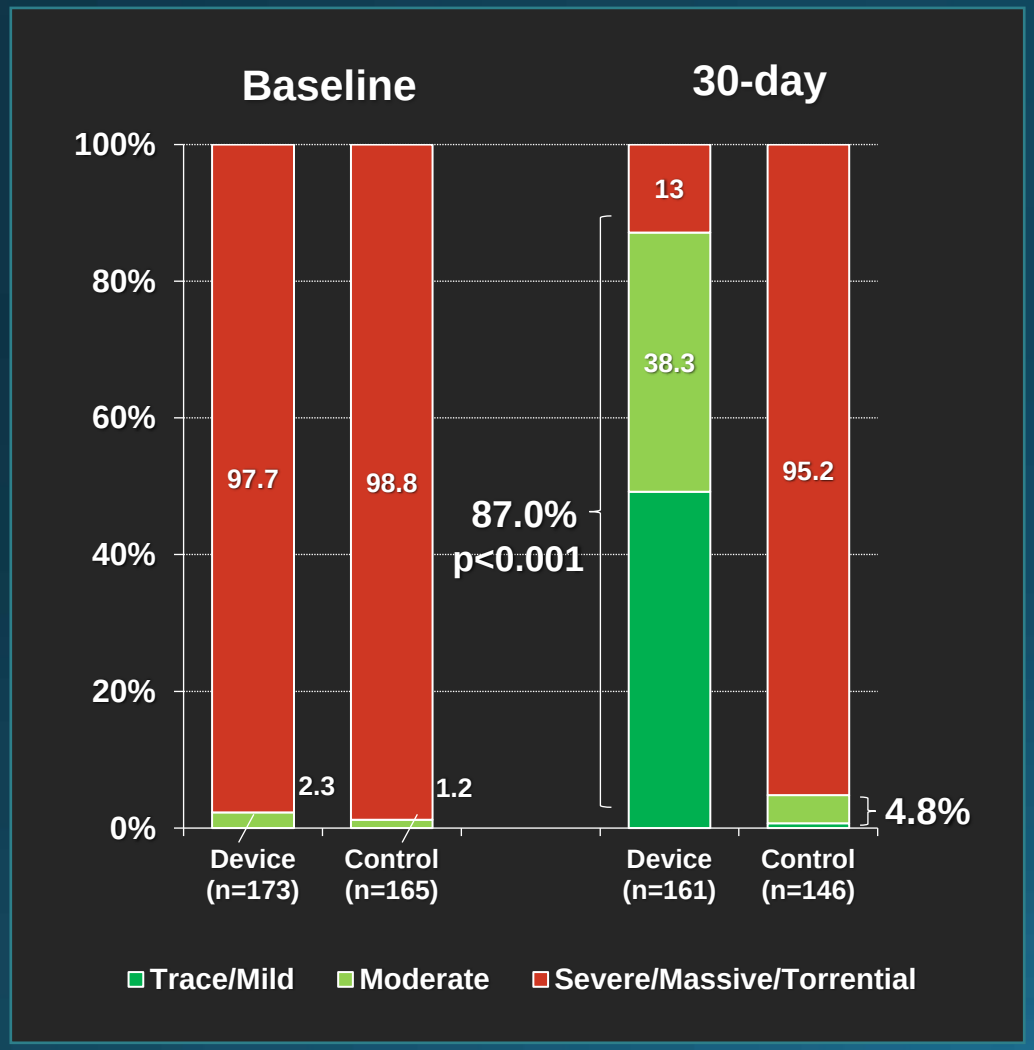
This article was published on March 4, 2023, at NEJM.org.

DOI: 10.1056/NEJMoa2300525

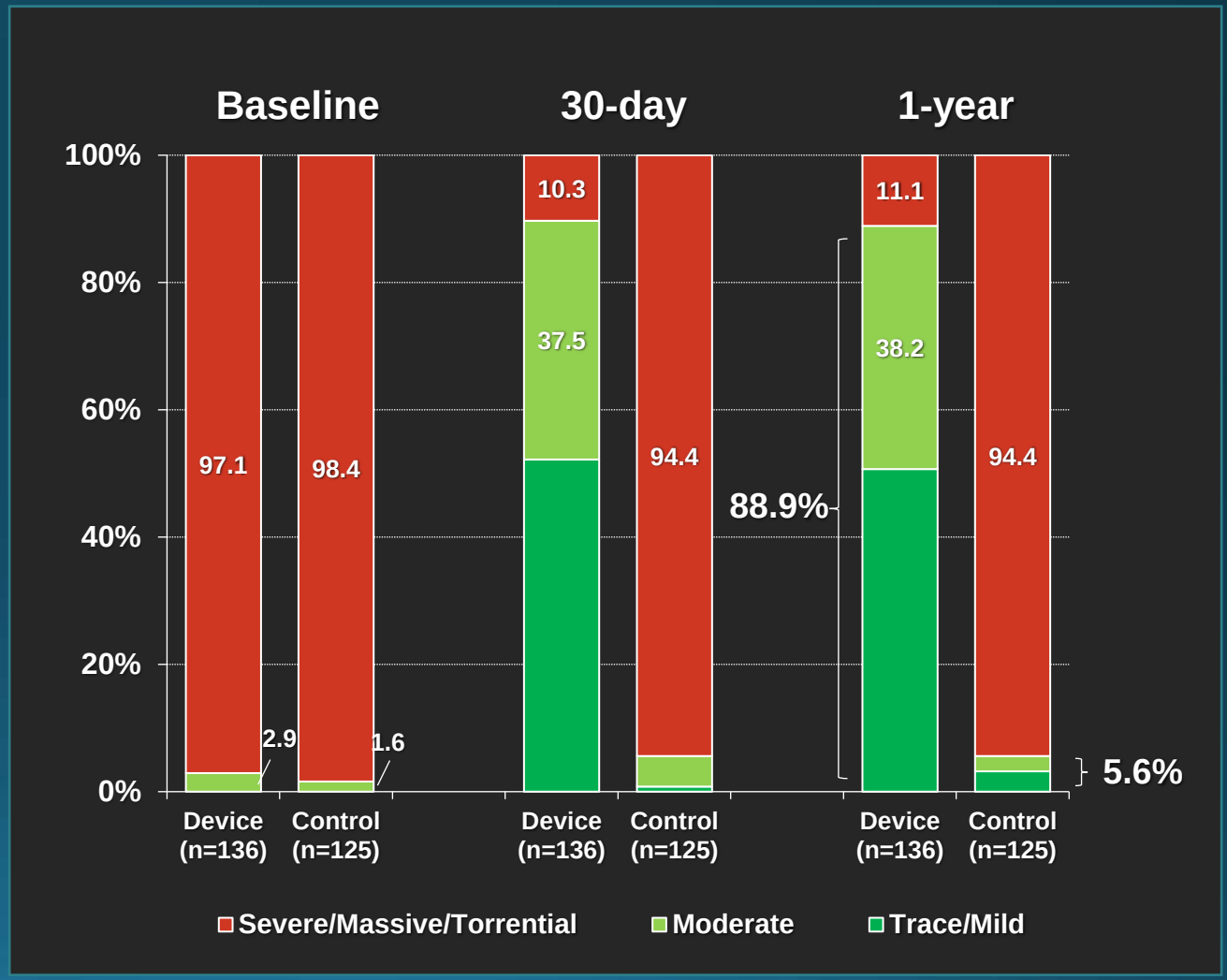
- 350 patients with severe, symptomatic TR and at least intermediate risk for surgery
- Exclusion criteria
  - LVEF < 20%
  - Need for other valve surgery
  - Severe pulmonary HTN

  Criteria designed to identify a population expected to benefit from TV repair
- Randomized to TV repair using TriClip G4 system or continued medical therapy
- Primary endpoint: Ordinal composite of death, TV surgery, HF hospitalization, KCCQ improvement <15 points at 1 year

Change in TR Severity

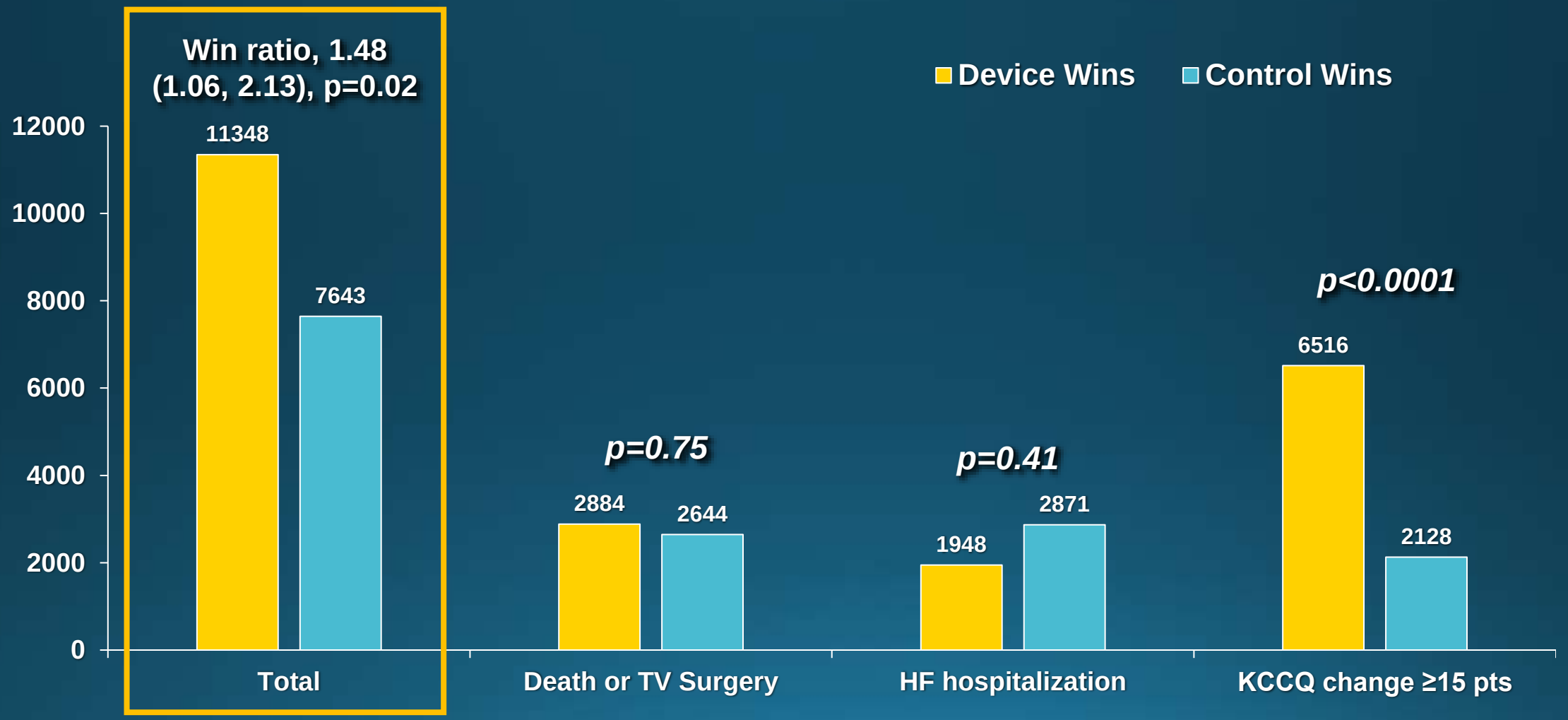


Complete Case Analysis



Sorajja P, et al. NEJM 2023

Primary Endpoint

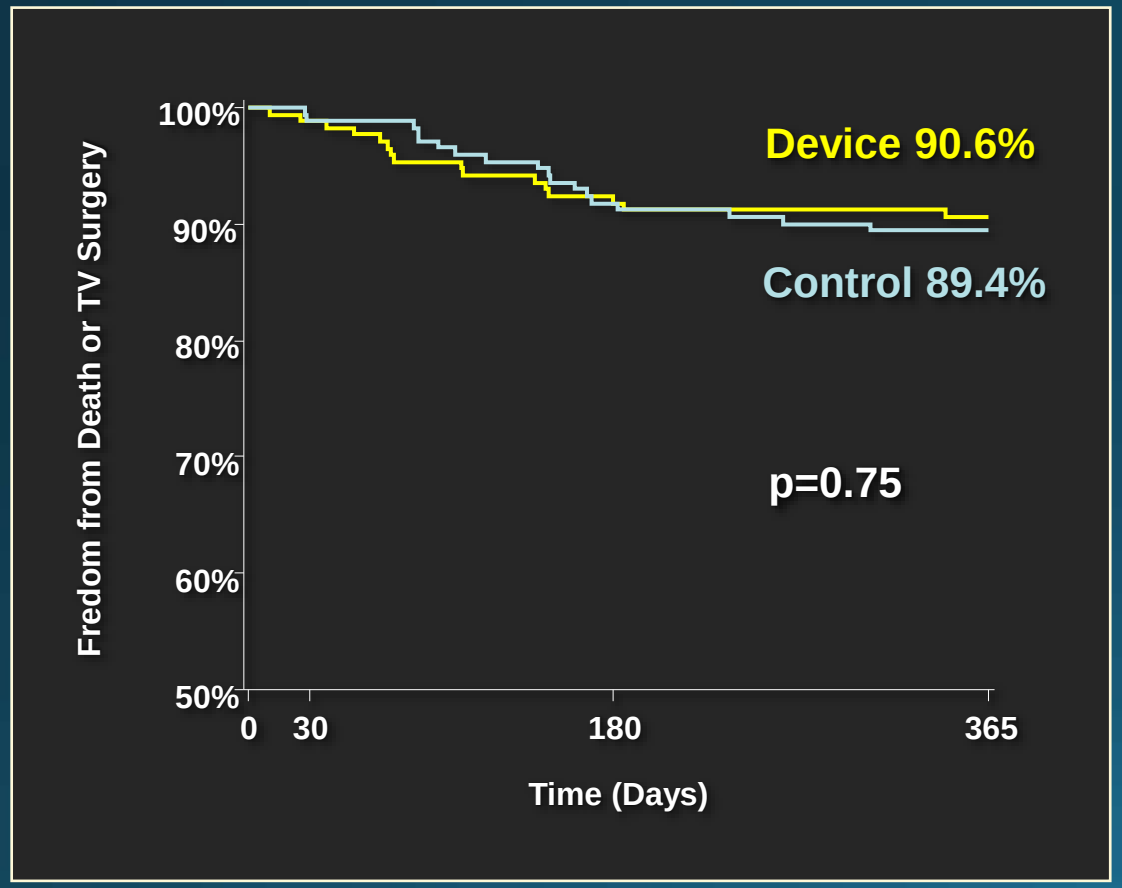


Sorajja P, et al. NEJM 2023

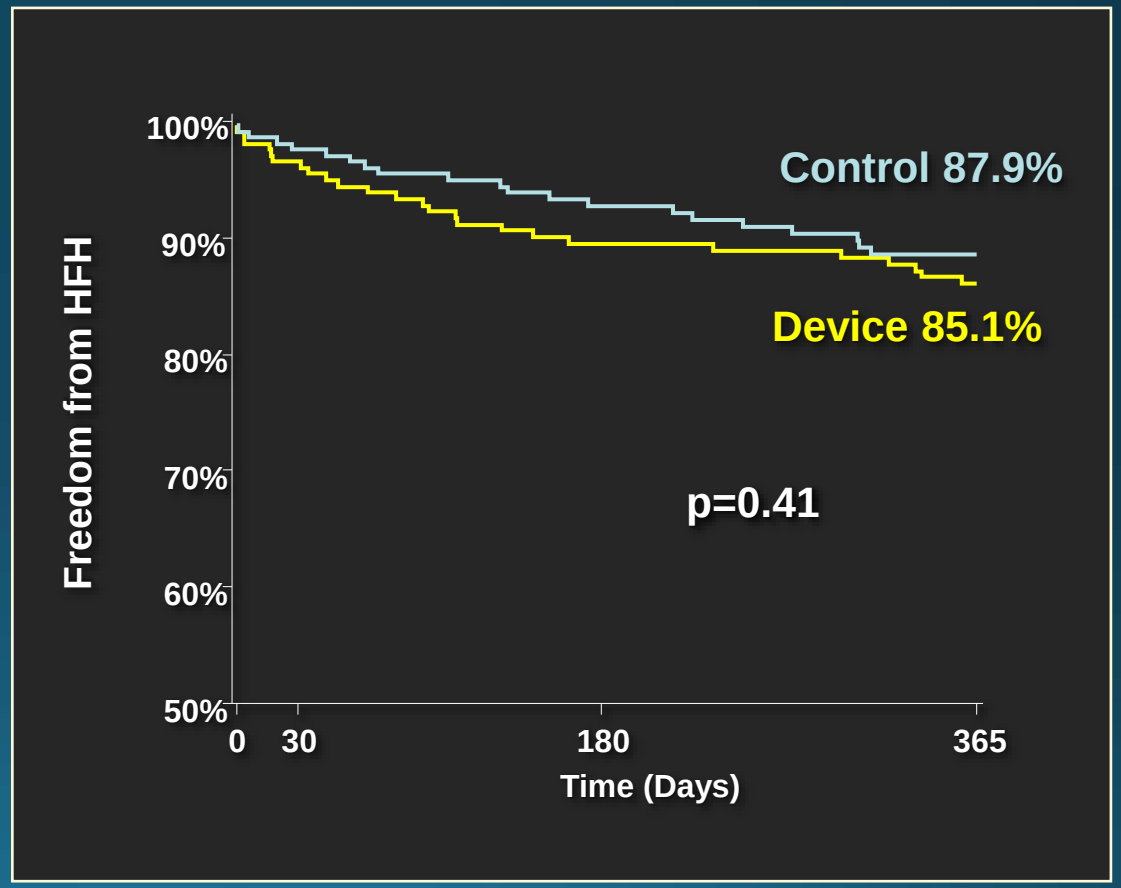
Endpoint Components

TRILUMINATE™ PIVOTAL TRIAL

Death or TV Surgery



HF Hospitalization (HFH)



Sorajja P, et al. NEJM 2023

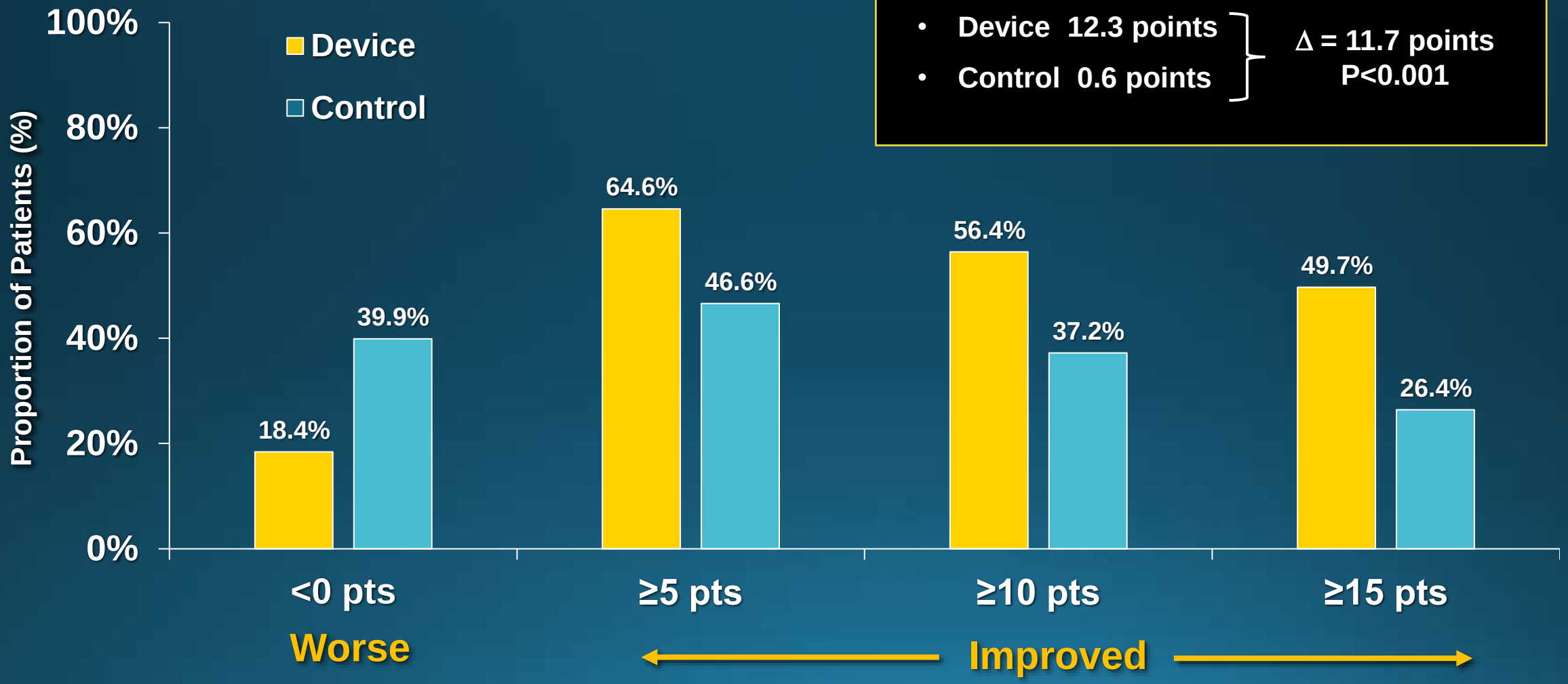
Quality of Life: Change in KCCQ-OS

TRILUMINATE™ PIVOTAL TRIAL

Mean Change in KCCQ

- Device 12.3 points
- Control 0.6 points

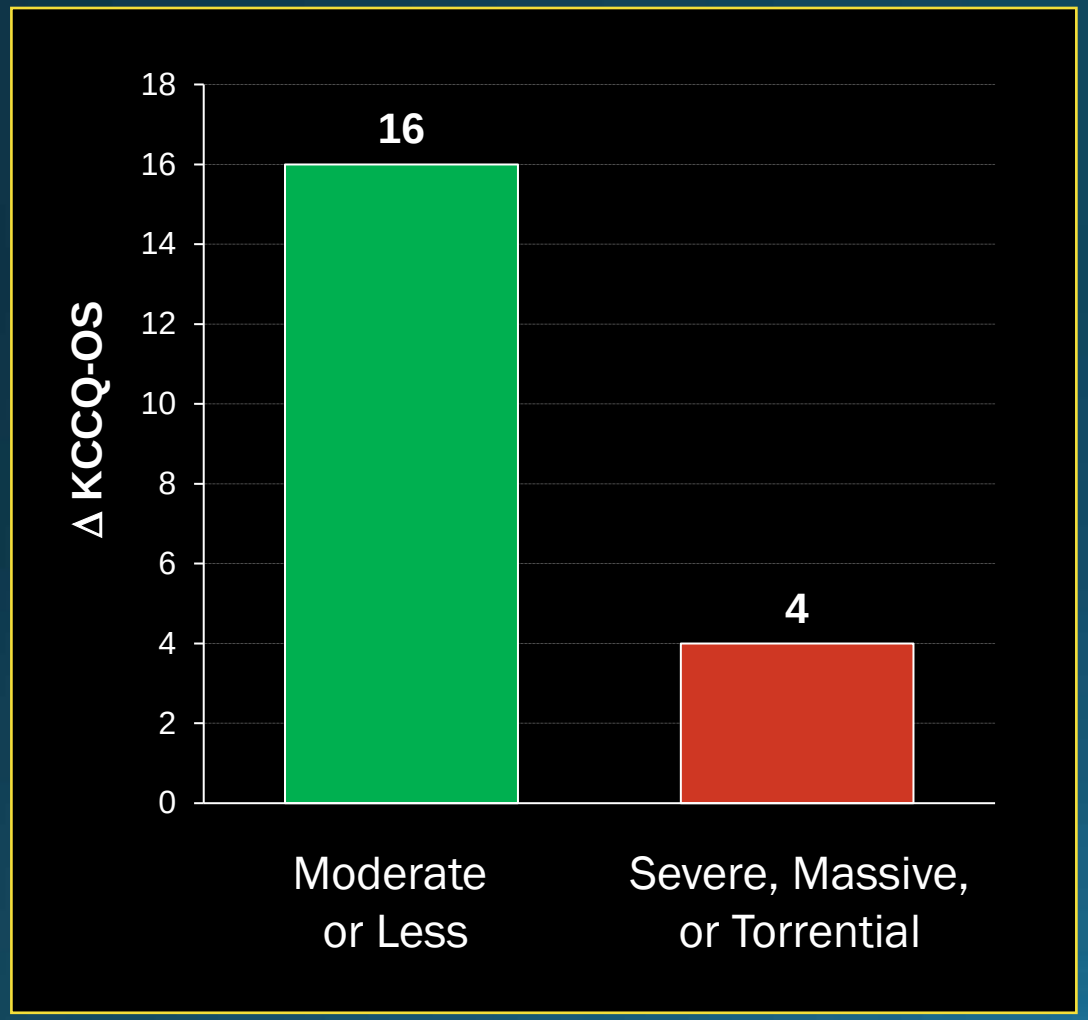
Δ = 11.7 points
P<0.001



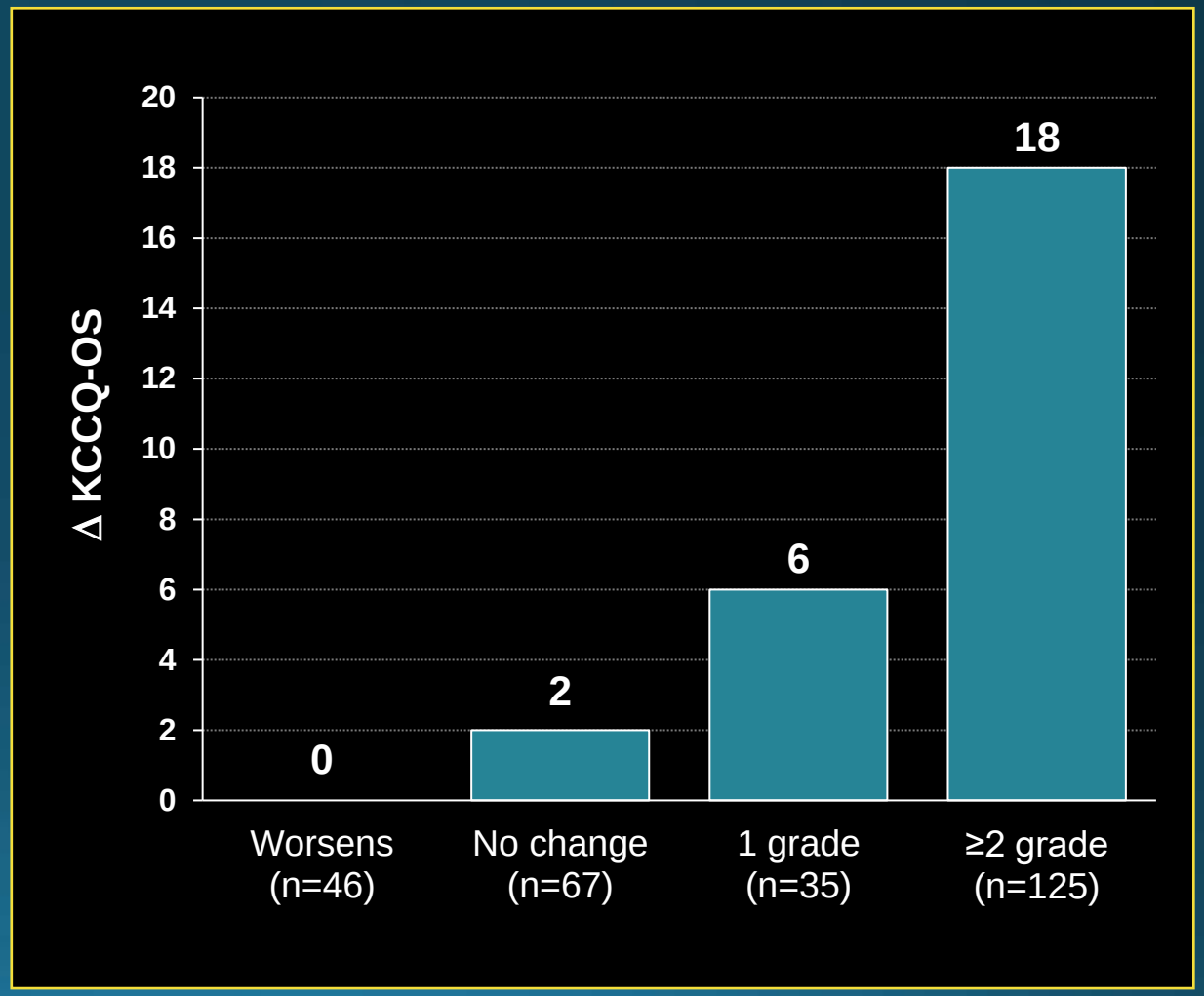
Sorajja P, et al. NEJM 2023

Relationship between TR and QOL

Residual TR grade at 1-yr



Change in TR, baseline to 1-yr



Sorajja P, et al. NEJM 2023

Key Insights

- Study met primary endpoint, but benefit driven entirely by QOL → ? Will this be sufficient for approval and reimbursement
  - Older patients value QOL benefit even more than survival
- Lack of impact on clinical endpoints (esp. HFH) somewhat surprising
  - Most pts had atrial TR → Event rates much lower than in COAPT
  - Should we be focusing on patients with LV dysfunction, pulmonary HTN, etc?
  - Is QOL benefit all placebo?
- Dose response relationship between TR reduction and QOL improvement strongly suggestive of true benefit
- Await results of other ongoing trials (TRISCEND II, CLASP-TR) to see if there is greater impact on clinical events

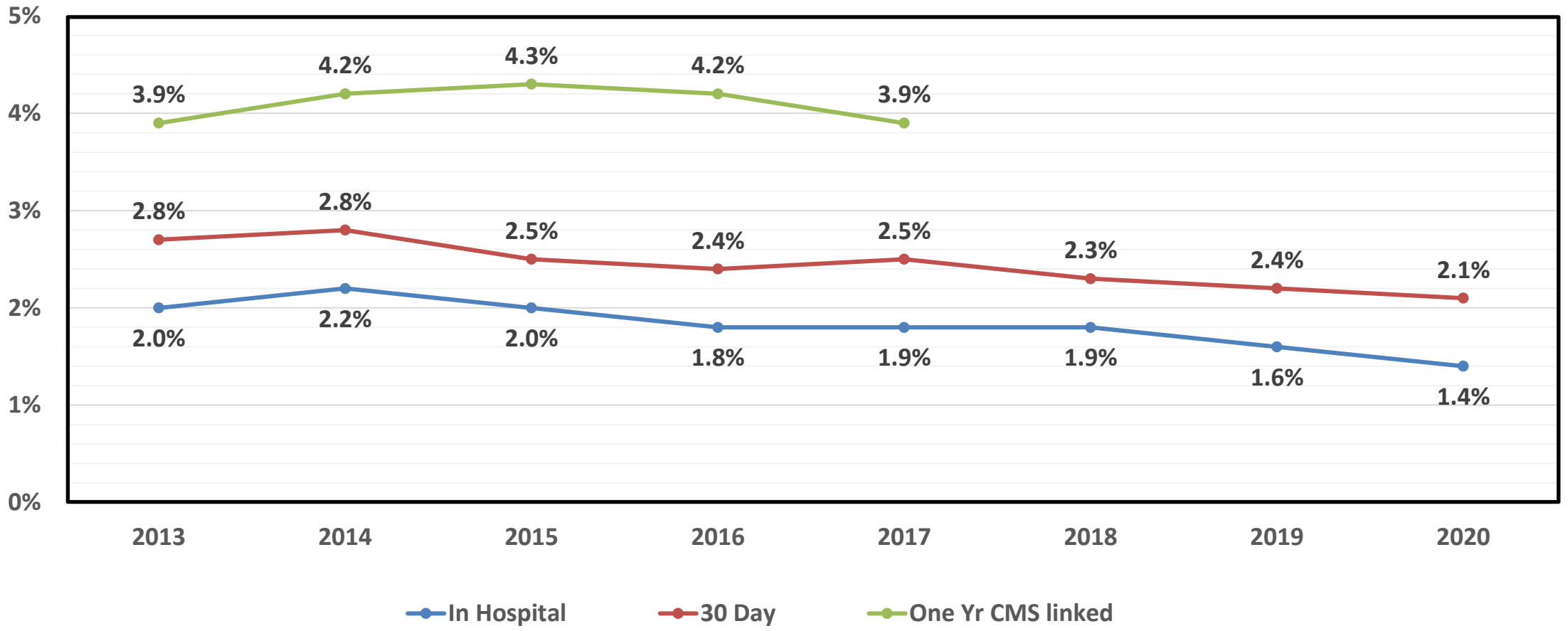
David Cohen's

Top Three

2

- PROTECTED-TAVR

TVT Registry: TAVR-Related Stroke

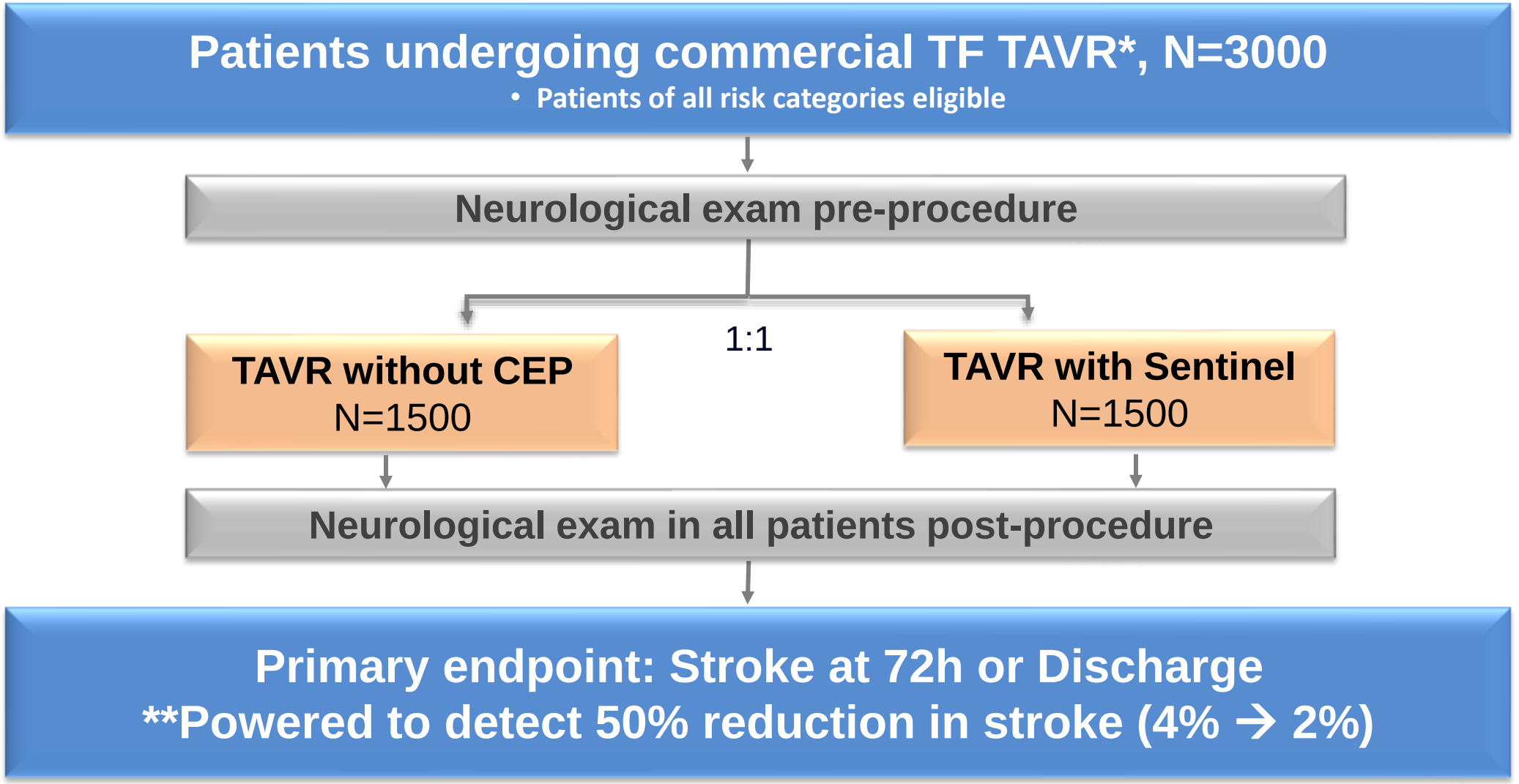


STS National Database™
Trusted. Transformed. Real-Time.

NCDR®
NATIONAL CARDIOVASCULAR DATA REGISTRY

PROTECTED TAVR

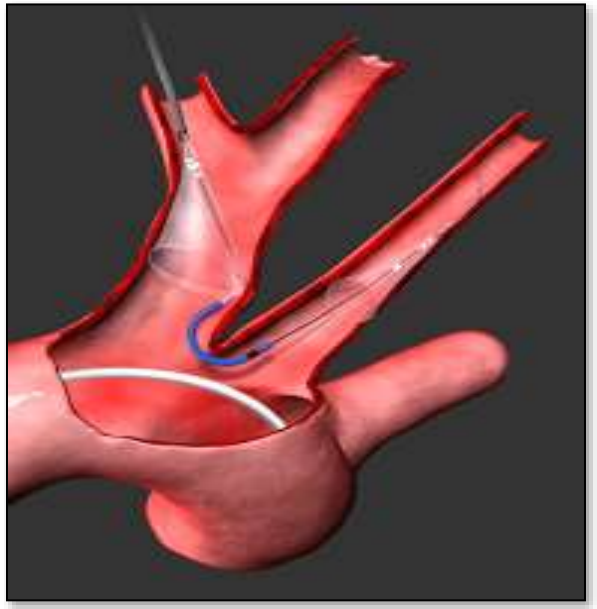
Trial Design



Kapadia SR, et al. N Engl J Med 2022; 387:1253-1263

SENTINEL Device

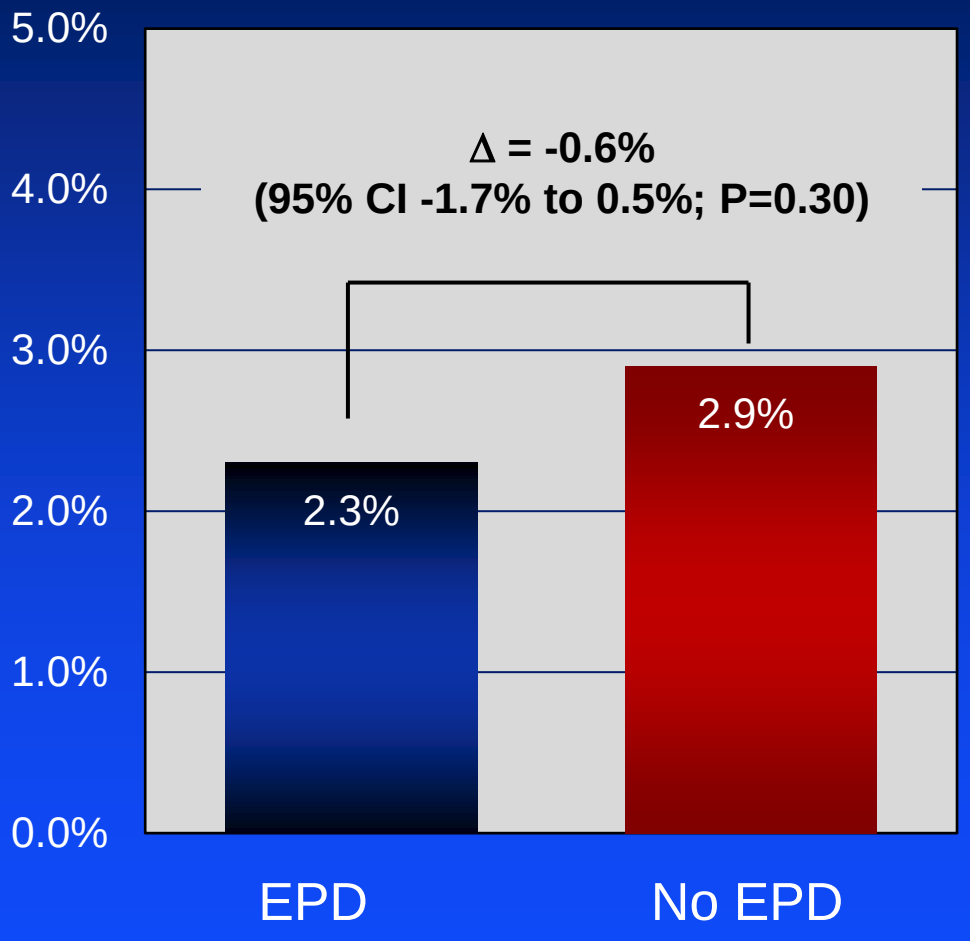
- Two independent polyurethane filters (pore size 140 µm) deployed in the right brachiocephalic trunk and left common carotid artery



- Delivered through 6Fr sheath via right radial artery

PROTECTED TAVR: Results

Primary Endpoint: Stroke at 72 hrs



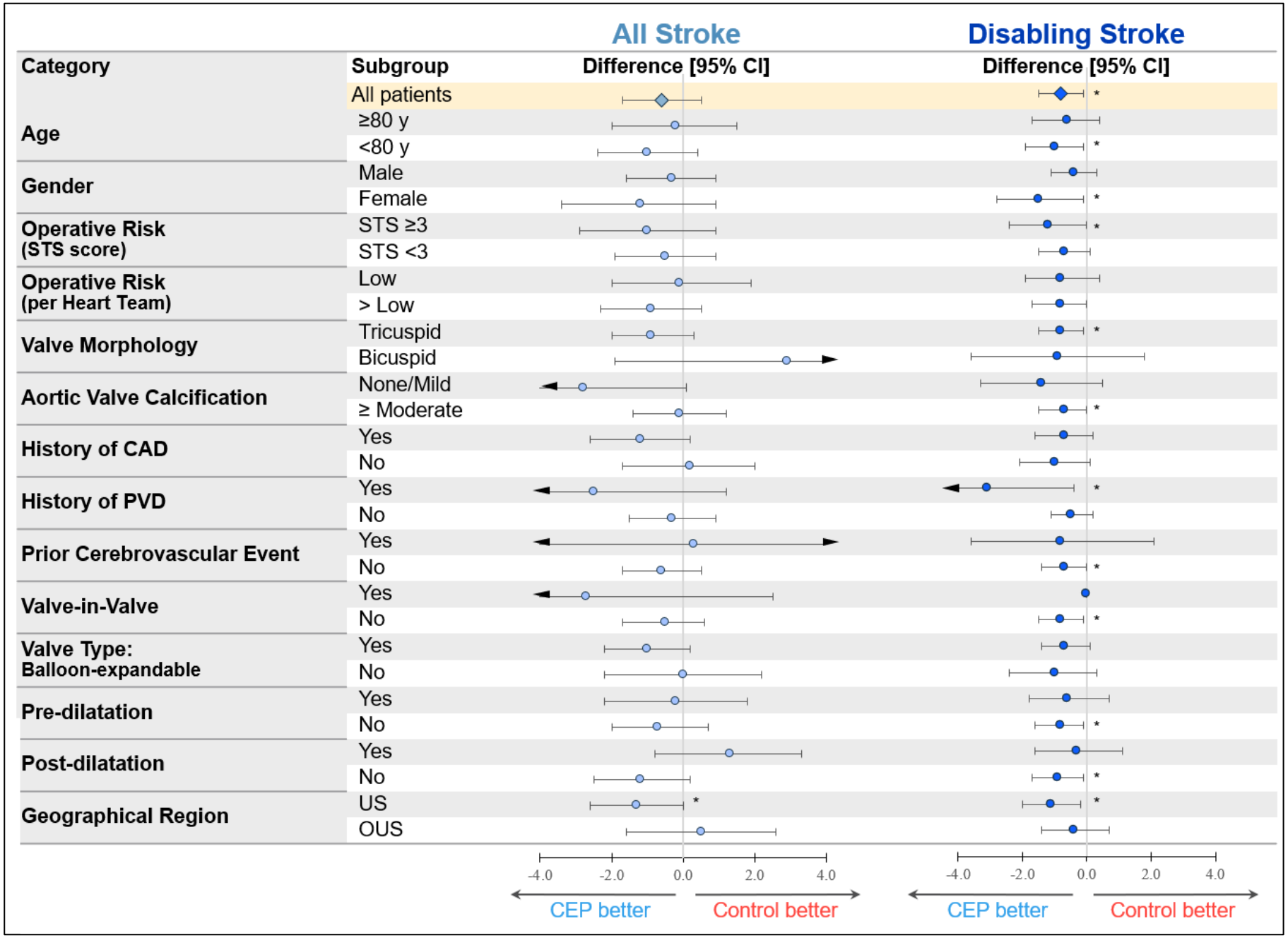
Prespecified Secondary Endpoints

	EPD	No EPD	P-Value
Disabling Stroke	0.5%	1.3%	0.02
Non-Disabling Stroke	1.7%	1.5%	NS
TIA	0.1%	0.1%	NS
Stroke, TIA, or Delirium	3.1%	3.7%	NS
Death	0.5%	0.3%	NS
AKI	0.5%	0.5%	NS

Kapadia SR, et al. N Engl J Med 2022; 387:1253-1263

PROTECTED TAVR:

Subgroup Analyses



Key Insights

- Despite high rates of recovery of embolic debris, there is no evidence that CEP with the Sentinel device reduces overall rates of stroke with TAVR → Debris retrieval should not be considered a valid surrogate for benefit of CEP
- In light of previous studies, suggestion that CEP converts major strokes into minor strokes is mechanistically and biologically plausible → await PROTECT-TAVI (n=7000) results
- Given these results and lack of consistent predictors of disabling stroke, there are only 2 rational strategies to using CEP in TAVR in 2023– *everyone or no one*

David Cohen's Top Three

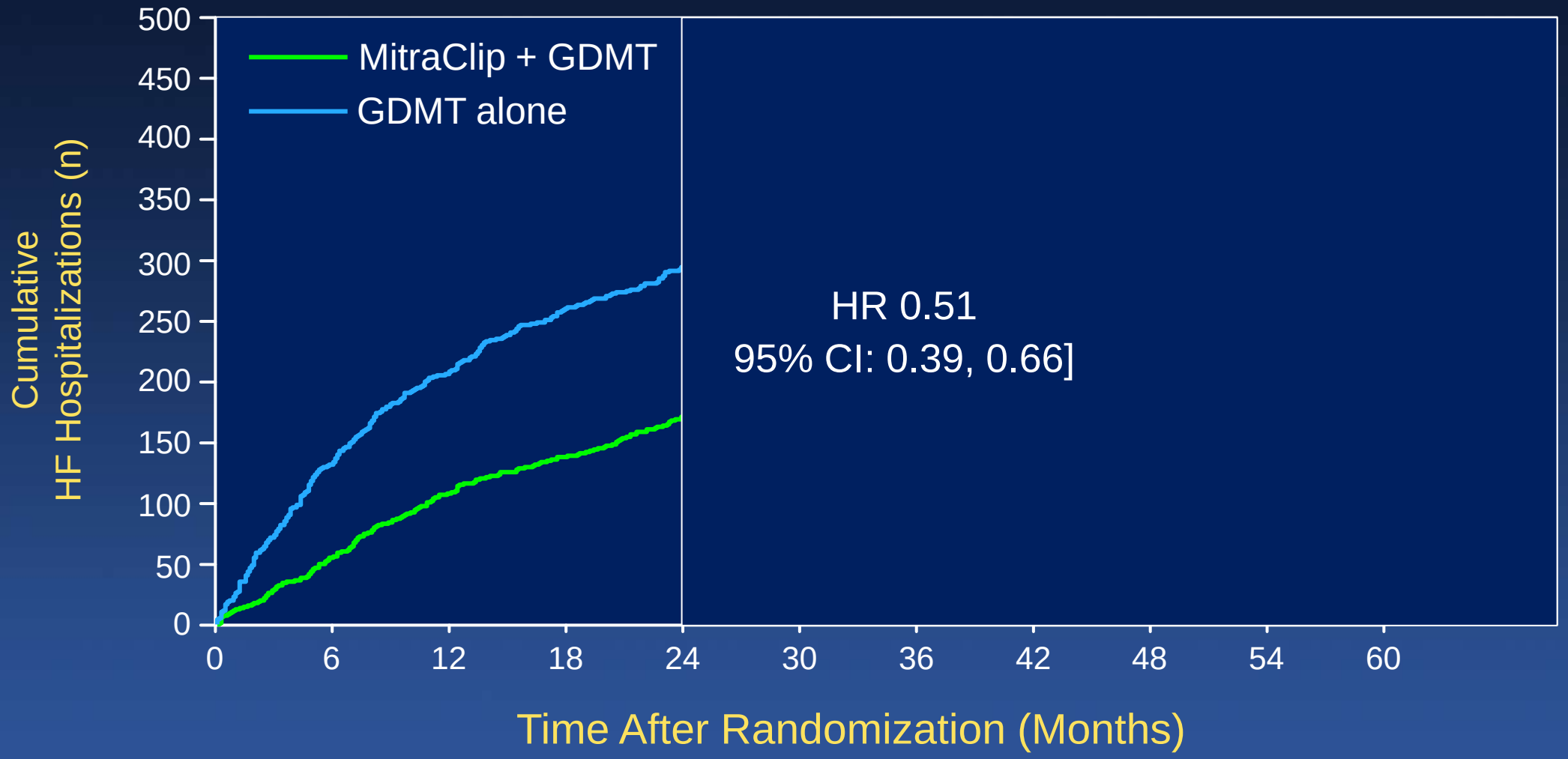
3

- COAPT 5-Year Outcomes

Primary Results at 2 Years

- 614 pts with heart failure and severe secondary mitral regurgitation randomized to MitraClip + GDMT vs. GDMT alone
- Primary results demonstrated significant reductions in HF hospitalization and all-cause mortality as well as substantial improvement in KCCQ through 2-year follow-up
- Clinical and echocardiographic follow-up continued through 5 years
- Control patients allowed to cross over to MitraClip after 2 years if they continued to meet eligibility criteria→ performed in 67 pts (45% of eligible)

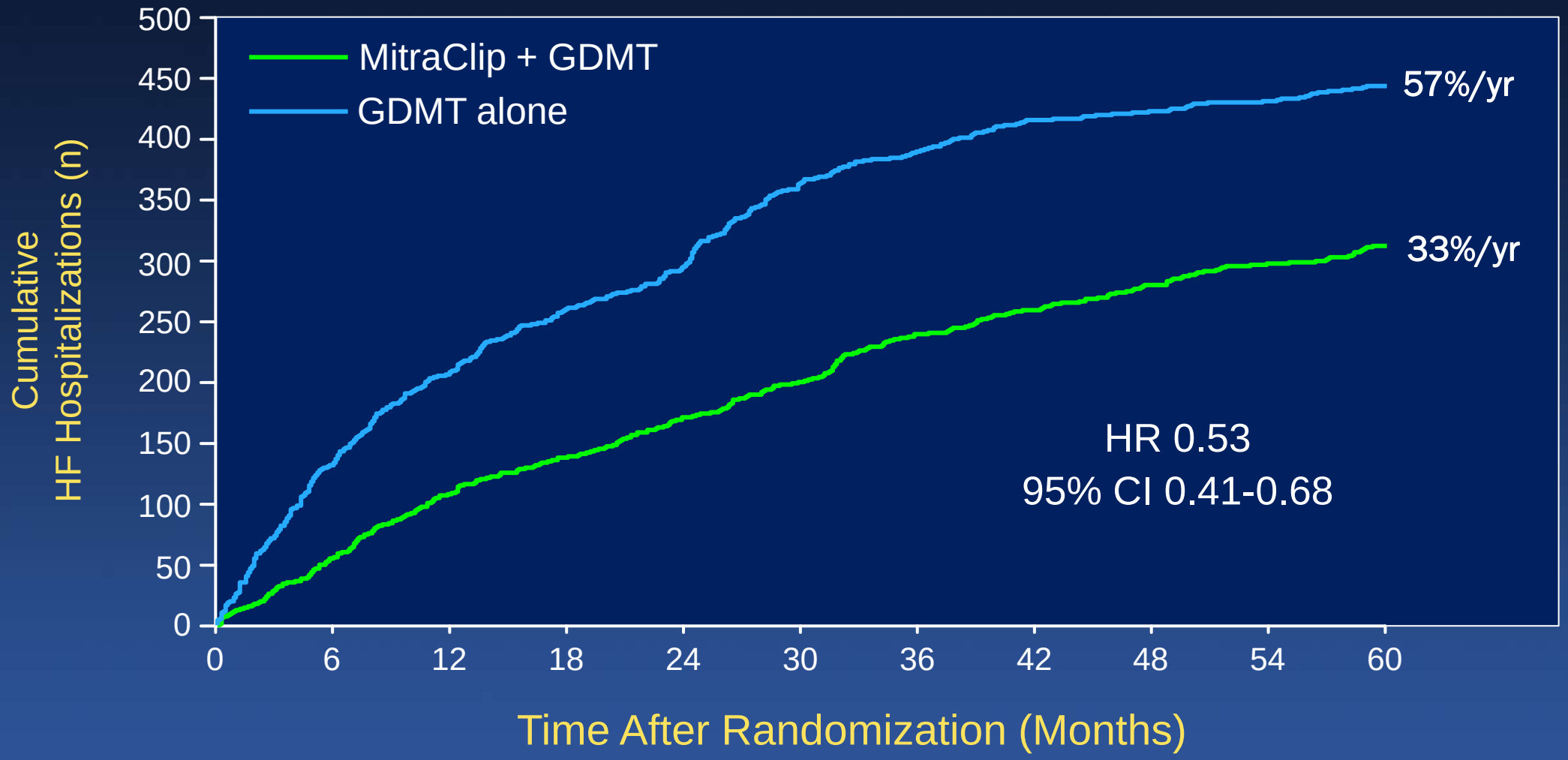
Primary Effectiveness: All HF Hospitalizations



Stone GW, et al. N Engl J Med 2023

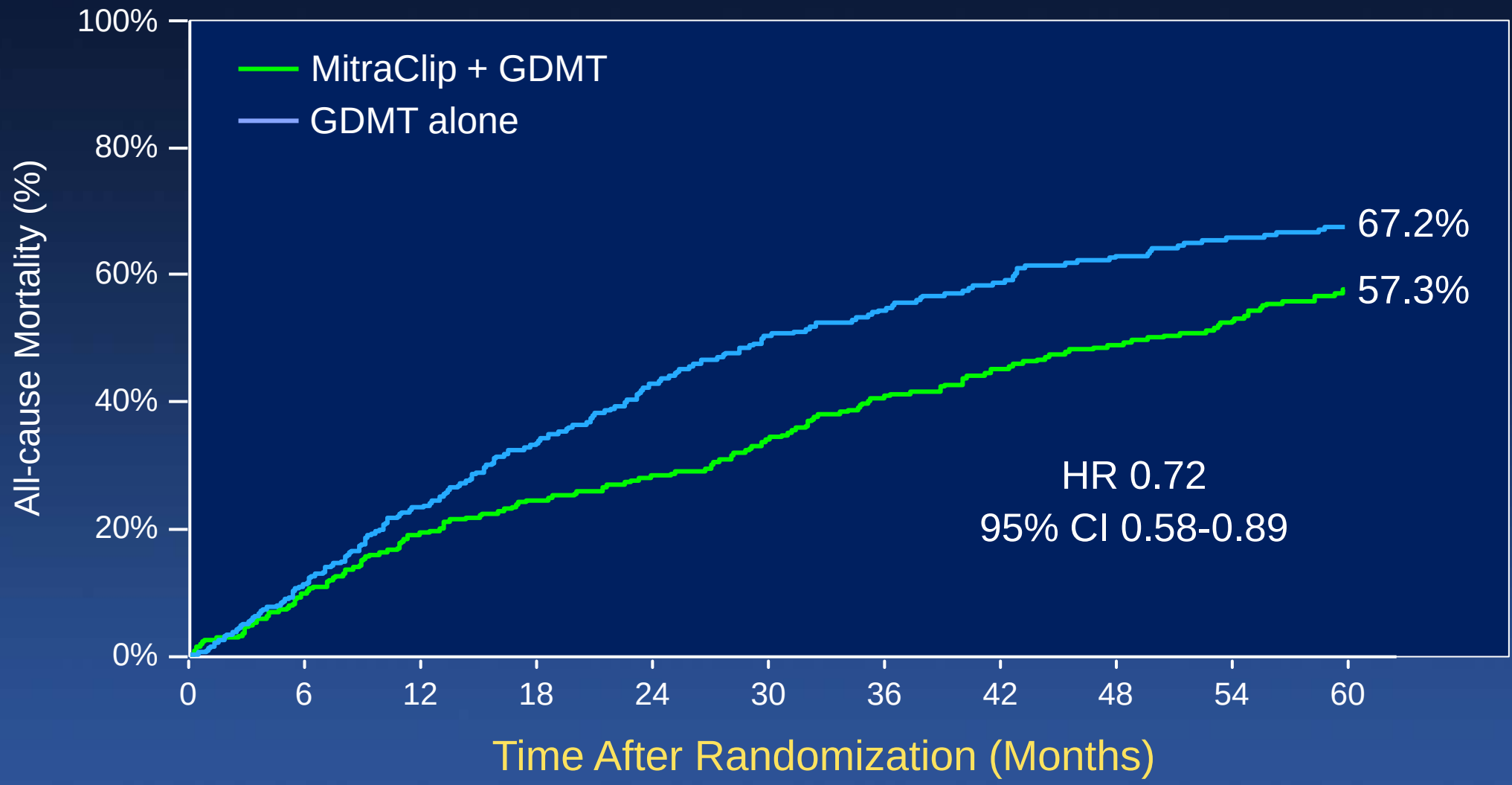
COAPT TRIAL

Primary Effectiveness: All HF Hospitalizations



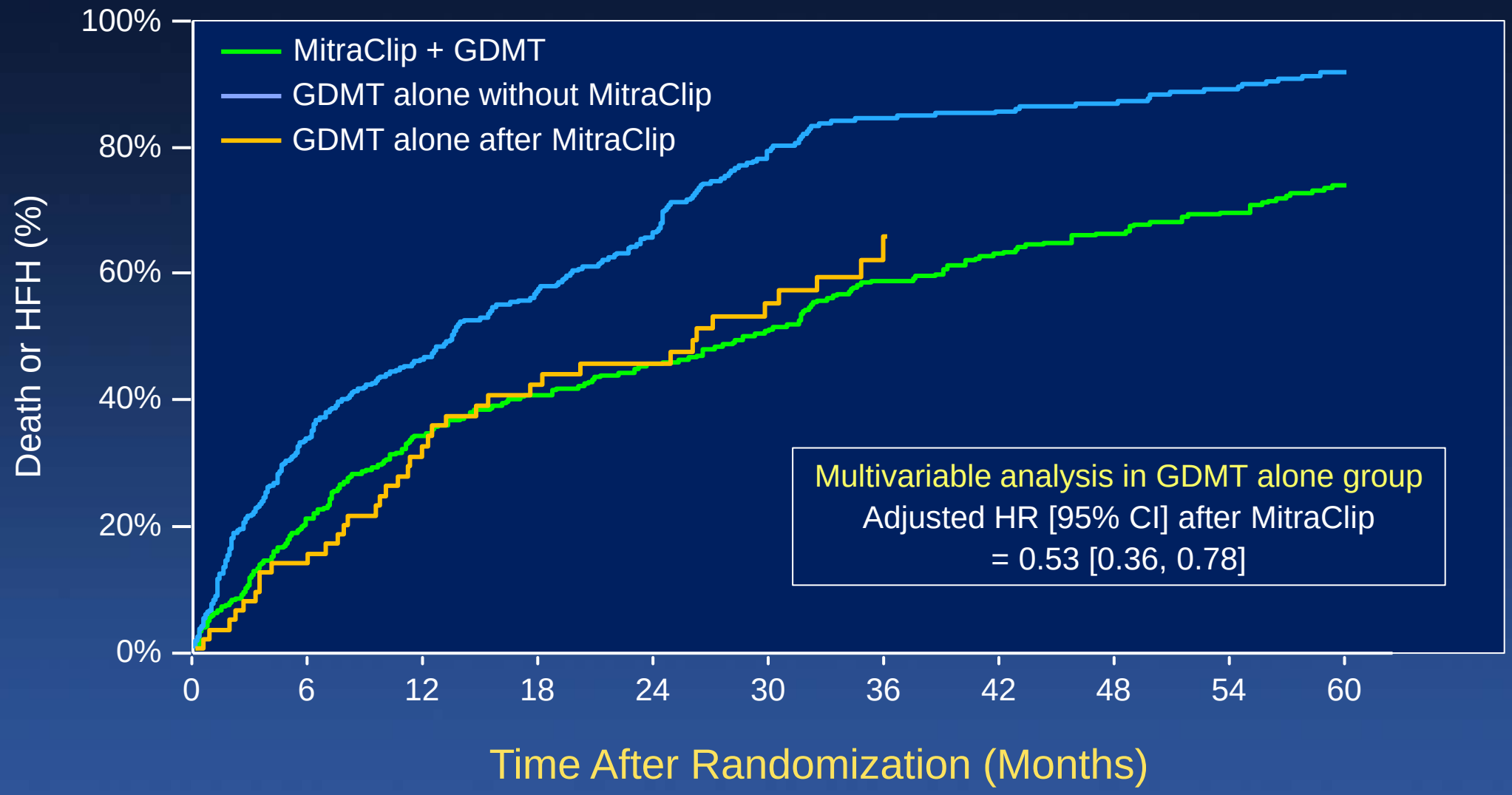
Stone GW, et al. N Engl J Med 2023

All-Cause Mortality



Stone GW, et al. N Engl J Med 2023

Death or HF Hospitalization with or without Crossover



Stone GW, et al. N Engl J Med 2023

COAPT TRIAL

Conclusions and Implications

- In pts with heart failure and severe SMR, TEER with the MitraClip demonstrated durable MR reduction and reductions in HFH and all-cause mortality through 5-year f/u
- Treatment effects were reduced after 2-3 years, in large part due to MitraClip treatment in 44.9% of control group pts surviving to 2 years
- Among qualifying patients, the benefits of late TEER were similar to those of initial TEER
- However, since more than half of all control pts did not survive 2-years, these findings suggest that early TEER for suitable pts should be preferred

Honorable Mention

Trial/Study	Target Population	Comparison	Key Finding
REDUCE-LAP II	HFpEF	Corvia Intertrial Shunt vs. Sham	8 mm interatrial shunt (Corvia) did not lead to improved clinical outcomes or QOL compared with sham control → suggestion of benefit in pts without exercise-induced pulm. HTN

Honorable Mention

Trial/Study	Target Population	Comparison	Key Finding
REDUCE-LAP II	HFpEF	Corvia Intertrial Shunt vs. Sham	8 mm interatrial shunt (Corvia) did not lead to improved clinical outcomes or QOL compared with sham control → suggestion of benefit in pts without exercise-induced pulm. HTN
CLASP-2D	Degenerative MR and High Surgical Risk	Pascal vs. MitraClip	6 month clinical outcomes similar with PASCAL vs. MitraClip. MR reduction slightly more durable with PASCAL (? mechanism)

Honorable Mention

Trial/Study	Target Population	Comparison	Key Finding
REDUCE-LAP II	HFpEF	Corvia Intertrial Shunt vs. Sham	8 mm interatrial shunt (Corvia) did not lead to improved clinical outcomes or QOL compared with sham control → suggestion of benefit in pts without exercise-induced pulm. HTN
CLASP-2D	Degenerative MR and High Surgical Risk	Pascal vs. MitraClip	6 month clinical outcomes similar with PASCAL vs. MitraClip. MR reduction slightly more durable with PASCAL (? mechanism)
Simard/Alkhouli (TVT reg.)	Severe MR with Cardiogenic Shock	MitraClip vs. Failed MitraClip	TVT registry study→ comparison of successful vs. failed TEER demonstrated improved 1-yr mortality with successful procedure

Final Thoughts

- Research in structural and valvular heart disease remains vibrant in 2023
- Most randomized trials are occurring in the US, driven largely by the regulatory and reimbursement environment
- Although the 10 years were dominated by treatment of AS, the next 10 years are likely to be the decade of the tricuspid valve → we have a lot to learn!