CARDIOLOGY & CARDIOTHORACIC SURGERY CASE STUDIES

Steven Duff, MD

Hassan Rajjoub, MD

OBJECTIVES

- Identify inclusion and exclusion criteria for TAVR Candidacy.
- Understand exclusion for CABG in patients with previous pneumonectomy.
- Evaluate clinical picture for urgency for CABG.
- Review diagnosis, preoperative work up, surgery and post operative care for AVR.

- 80 yr old male admitted Licking with DOE, increasing prior 3 weeks
  - ECG – NSR poss old septal infarct, nonspecific T-wave abnormality
  - Troponin I - 2616, 2418, 2776
  - Echo – Reduced EF of 25%
- PMH: Left pneumonectomy, prostate cancer with radiation, HTN, CVA with no residual – Daily Plavix

L. J.
11-19-1938

- LEFT HEART CATHETERIZATION
  TRIPLE VESSEL DISEASE – EF
  TRANSFER TO RMH

WORK-UP

- Chest CT: left mediastinal shift with cardiac structures adherent to lateral chest wall
  - Making exposure and cannulation difficult
- Poor pulmonary function: FEV1: 1L
- STS risk: > 6

CT CHEST

PROCEDURE

- Referred for high risk PCI to LAD & OBM

- 48 yr old male w/ no significant PMH, had not seen a doctor in several years, admitted to Licking after syncopal episode at work
  - ECG - SR w/ incomplete RBBB
  - Troponin I - 16, 36, 51
  - Echo - Bicuspid aortic valve with severe stenosis with mean gradient 42 mm/Hg EF – 62%
- Taken to cath lab to define his coronary anatomy

J. A.
4-15-71

LEFT HEART CATHETERIZATION

LM – NO DISEASE

LAD, CIRC, RCA – MINOR IRREGULARITIES

TRANSFER TO RMH

WORK UP

- Received Plavix load prior to catheterization; need for wash out
- Mandible x-rays with dental caries and referred to oral surgeon
- Required 4 extractions
- Discharged home to heal and plans to readmit for AVR

MANDIBULAR X-RAY

PROCEDURE

- Pericardial AVR
- Month Follow-Up
  - Doing well
  - Repeat TTE: mean gradient 5

- 75 yr old female presents to ED with 4-5 day hx of intermittent chest pain, worse on day of admission
  - PMH: breast lumpectomy with axillary node dissection and radiation in 2014, HTN, Dyslipidemia, newly diagnosed AF RVR this admission
  - ECG – NSR w/ non-specific changes
  - Troponin I – 1300, 1375
  - Decision made to emergently take her to cath lab, Brilinta given

J. T.
5-16-1943

LEFT HEART CATHETERIZATION

TRIPLE VESSEL DISEASE
TRANSFER TO RMH

WORK-UP

- Received to RMH around midnight
- Ongoing chest pain and taken to catheterization lab for IABP

PROCEDURE

- Urgent CABG
- Month Follow up
  - Doing well

- 56 yr old female admitted w/ c/o chest pain. PMH includes CAD w/ PCI to RCA in 2013, HTN, hyperlipidemia, former smoker, and GERD.
  - ECG – NSR, inferior infarct age undetermined, no ischemic changes
  - Troponin I – negative X3
  - Lexiscan 2 months prior showed no evidence of ischemia

B. G.
1-1-63

NUCLEAR SCAN

LEFT HEART CATHETERIZATION

EXTENSIVE CAD

TRANSFER TO RMH

- 31 yr old male w/ 4 day history of nausea, HA, lightheadedness, subjective fever, diaphoresis, dry cough. Significant leukocytosis of 25.7K w/ left shift and history of polysubstance abuse of IV methamphetamines along with smoking.
  - Echo – Mod aortic valve regurgitation. Aortic valve vegetation, non-rheumatic tricuspid valve with nod regurgitation, RVSP 30mmHg. Tricuspid valve vegetation.

T. T.
7-24-87

ECHO

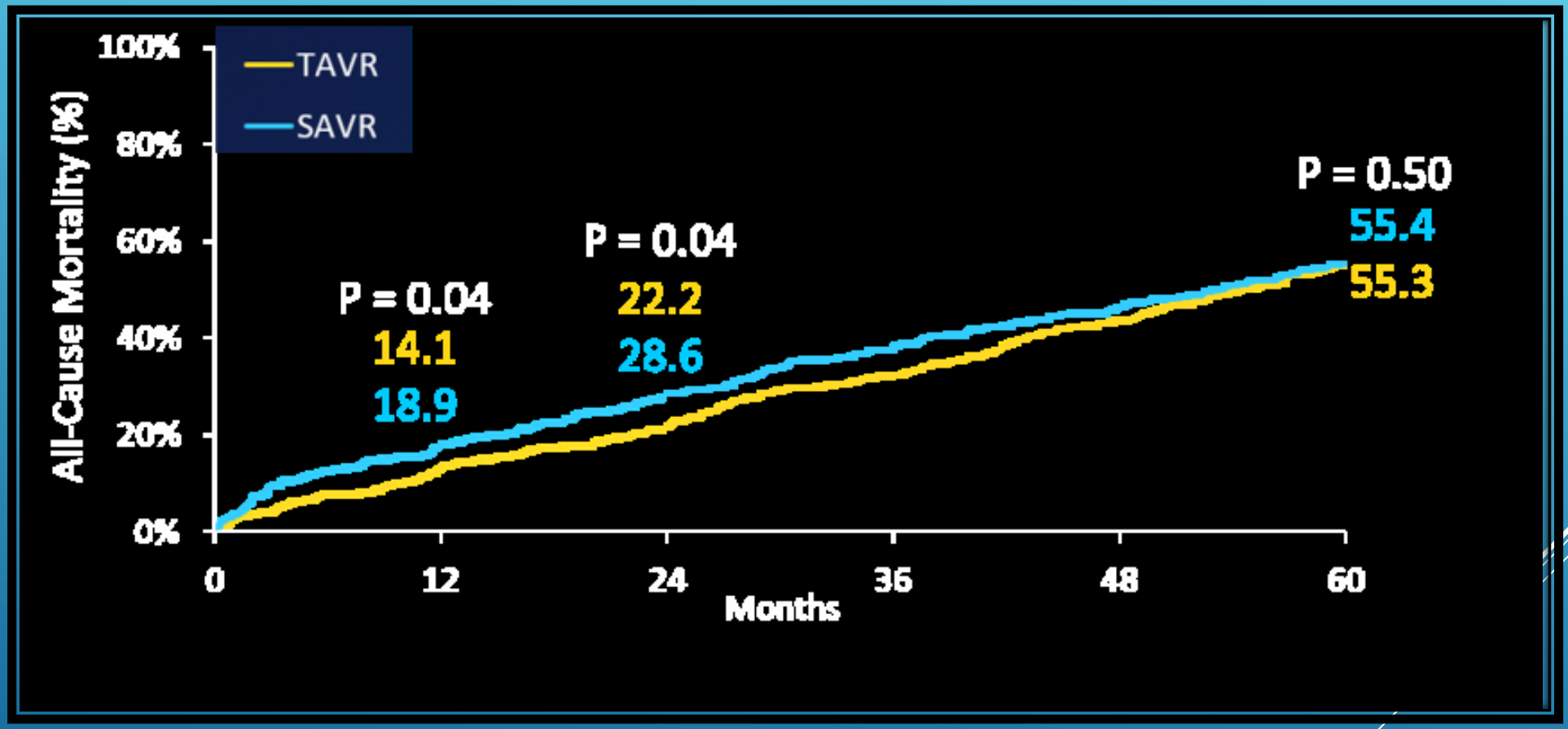
TRANSFERRED TO GRANT

TAVR

Michael J. Reardon, MD, FACC
Houston Methodist DeBakey Heart & Vascular Institute, Houston, TX
For the Evolut Low Risk Trial Investigators

PRIMARY RESULTS FROM THE EVOLUT LOW RISK TRIAL

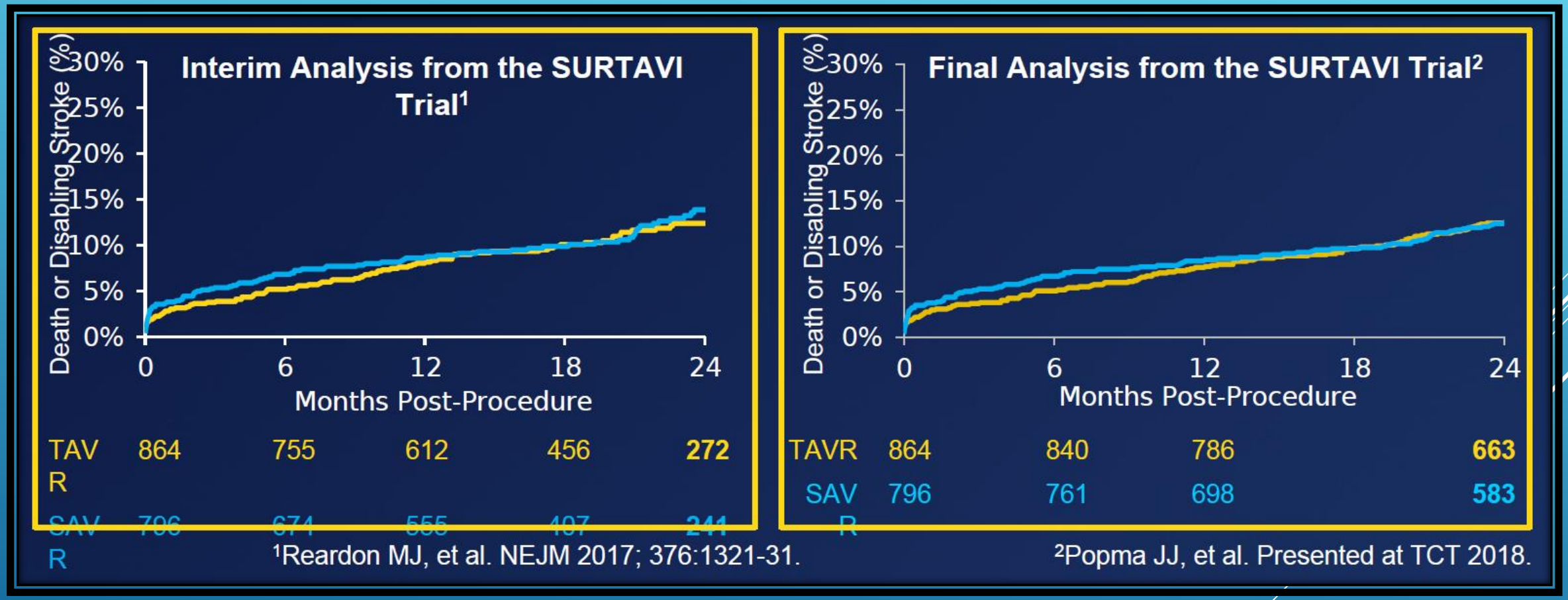
- We performed a series of randomized controlled trials in patients with severe aortic stenosis across a spectrum of surgical risk.
- In high-risk patients, TAVR was superior to SAVR for the primary endpoint to 2 years[1] and similar at



1Reardon et al. J Am Coll Cardiol 2015; 66: 113-21; 2Gleason, et al. J Am Coll Cardiol 2018; 72:

BACKGROUND

- The SURTAVI intermediate risk trial showed noninferiority at interim analysis.
- The final analysis of the SURTAVI Trial confirmed the early Bayesian results, showing TAVR noninferior to SAVR.



BACKGROUND

To assess the safety and efficacy of TAVR with the Evolut self-expanding supra-annular valve compared with surgical AVR in patients with a low predicted risk of 30-day surgical mortality.

OBJECTIVE

Principal Investigators: Jeffrey Popma, Michael Reardon

Executive Committee: Jeffrey Popma, Michael Reardon, G. Michael Deeb, Steven Yakubov

Steering Committee: David Adams, Stan Chetcuti, G. Michael Deeb, John Forrest, Thomas Gleason, John Heiser, William Mehri, Mubashir Mumtaz, Daniel O'Hair, Nicolo Piazza, Joshua Rovin, Michael Reardon, Paul Sorajja, Didier Tchétché, Paul Teirstein, Antony Walton, Steven Yakubov, George Zorn III

Screening Committee: G. Michael Deeb (Chair), Thomas Gleason, Jeffrey Popma, Michael Reardon,Steven Yakubov

Echo Core Laboratory: Jae Oh, Mayo Clinic, Rochester, MN

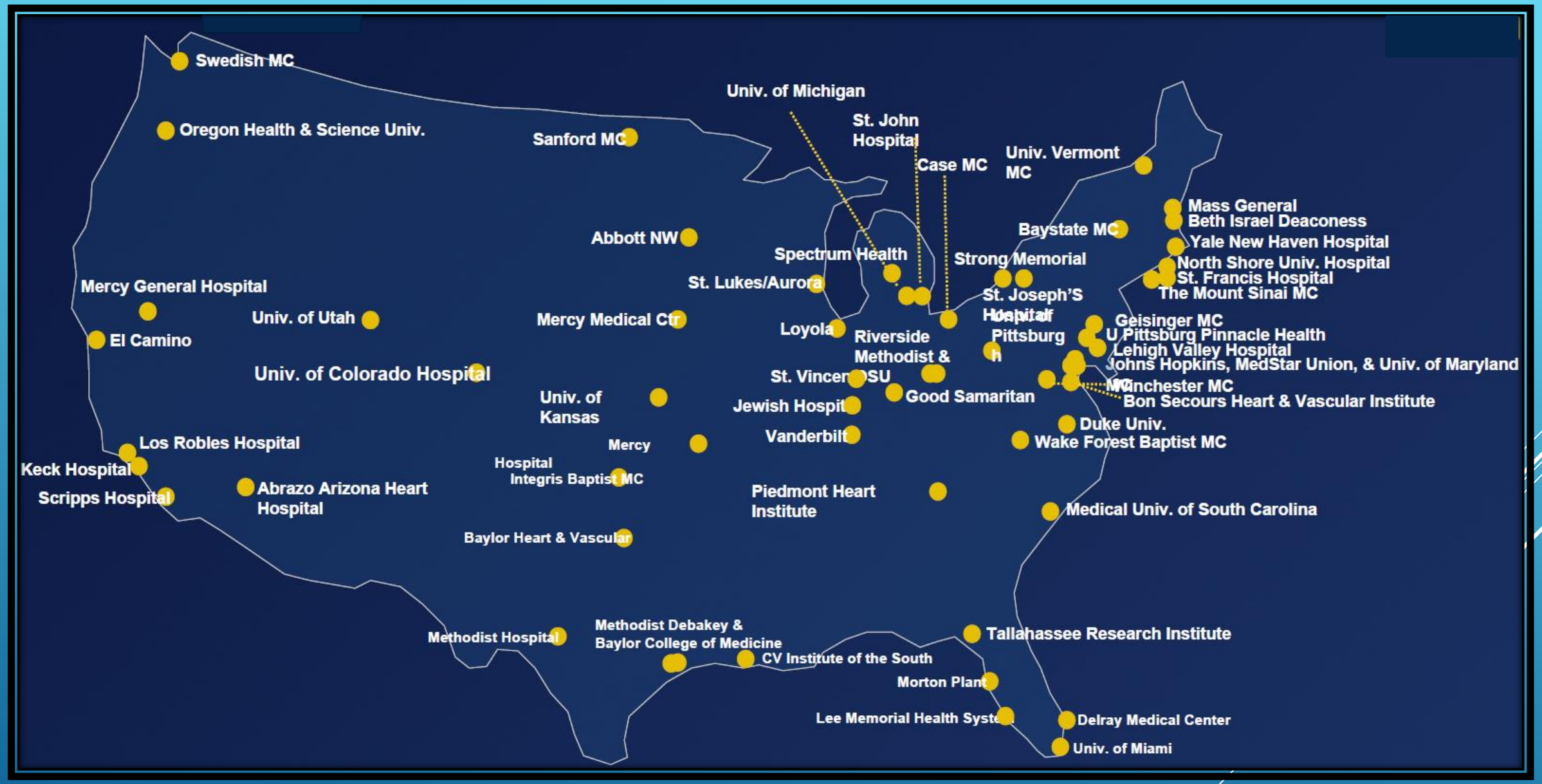
Data & Safety Monitoring Board: Baim Institute for Clinical Research; David Faxon (Chair), William Holman, John Lopez, Scott Kasner, John Orav

Clinical Events Committee: Baim Institute for Clinical Research; Claudia Hochberg (Chair), Cliff Berger, Torin Fitton, Sergio Waxman, Scott Bortman, Carey Kimmelstiel, David Grossman, Manish Chauhan, Jeffrey Veluz, Robert Rodriguez, Sanjay Samy, Gregory Smaroff, Jonathan Waks, Daniel Kramer

Statistical Design and Analyses: Andrew Mugglin, Paradigm Biostatistics, LLC

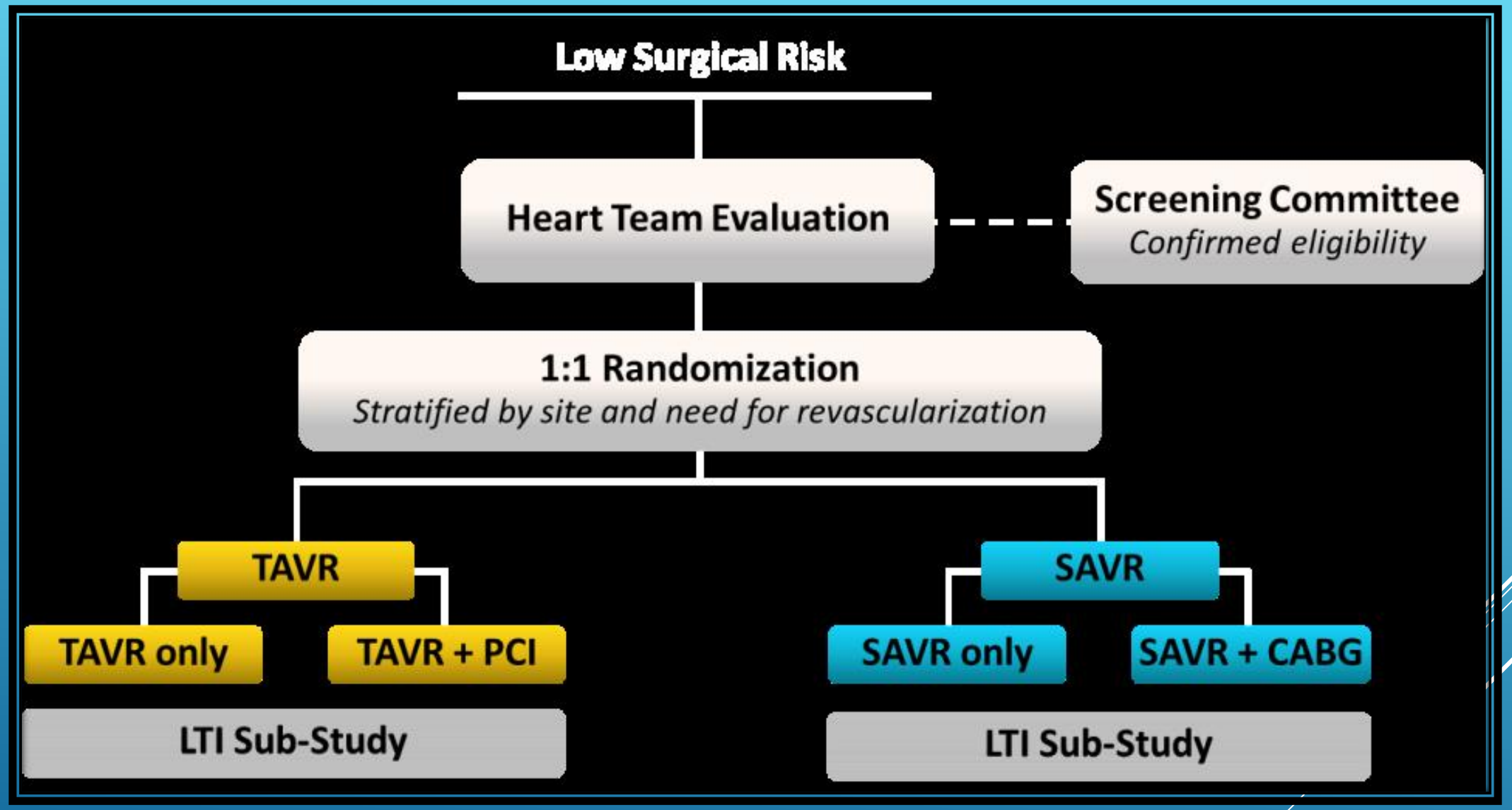
Sponsor: Medtronic

STUDY ADMINISTRATION



PARTICIPATING SITES IN THE UNITED STATES

AUSTRALIA, CANADA, EUROPE, JAPAN AND NEW ZEALAND



STUDY DESIGN

STUDY ENDPOINTS

Primary Safety and Effectiveness Endpoint

All-cause mortality or disabling stroke at 2 years

Hierarchical Powered Secondary Endpoints

Noninferiority

- Mean gradient at 1 year
- EOA at 1 year
- Change in NYHA class from baseline to 1 yr
- Change in KCCQ score from baseline to 1 yr.

Superiority

- Mean gradient at 1 yr.
- EOA at 1 yr.
- Change in KCCQ score from baseline to

Other Secondary Endpoints

- 30-day safety composite of
  - All-cause mortality
  - Disabling stroke
  - Life threatening bleeding
  - Major vascular complications
  - Stage 2 or 3 acute kidney injury
- New pacemaker implantation at 30 days
- Heart failure rehospitalization at 1 yr.
- Aortic-valve reintervention at 1 yr.
- Moderate/severe AR at 1 yr.
- All stroke at 1 yr.

KEY INCLUSION CRITERIA

Symptomatic severe AS1:

- Aortic valve area ≤1.0 cm^2 (or aortic valve area index <0.6 cm2/m2), **OR** mean gradient ≥40 mmHg **OR** Vmax ≥4 m/sec at rest

Asymptomatic very severe AS1:

- Aortic valve area ≤1.0 cm^2 (or aortic valve area index <0.6 cm2/m2), **AND** Vmax ≥5 m/sec or mean gradient ≥ 60 mmHg at rest
- Aortic valve area of ≤1.0 cm2 (or aortic valve area index of ≤0.6 cm2/m2), **AND** a mean gradient ≥40 mmHg or Vmax ≥4.0 m/sec by transthoracic echocardiography at rest, **AND** an exercise tolerance test that demonstrates limited exercise capacity, abnormal BP response, or arrhythmia
- Aortic valve area of ≤1.0 cm2 (or aortic valve area index of ≤0.6 cm2/m2), AND mean gradient ≥40 mmHg, OR Vmax ≥4.0 m/sec by transthoracic echocardiography at rest, AND LVEF<50%.

A predicted risk of 30-day mortality <3% per multidisciplinary local heart team assessment.

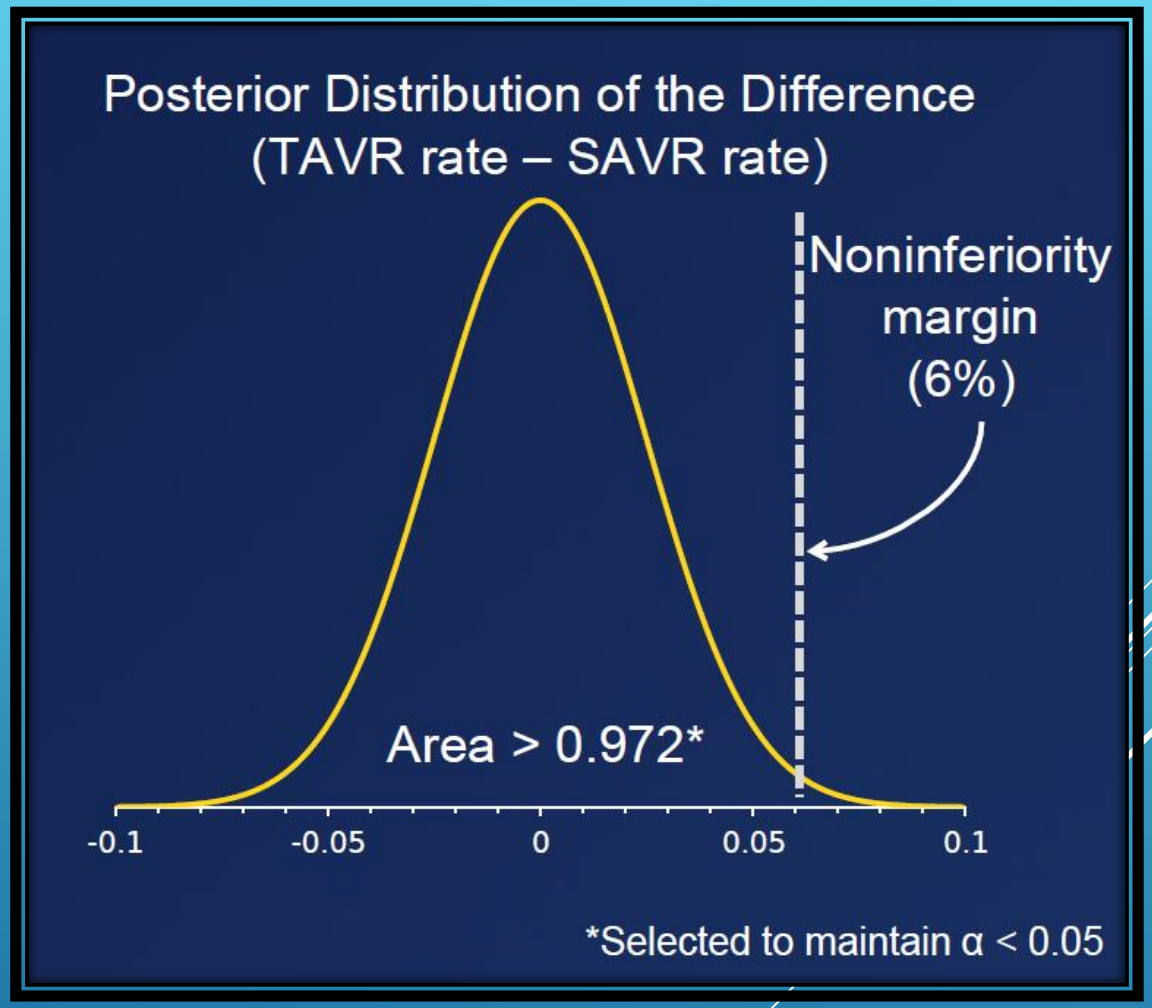
KEY EXCLUSION CRITERIA

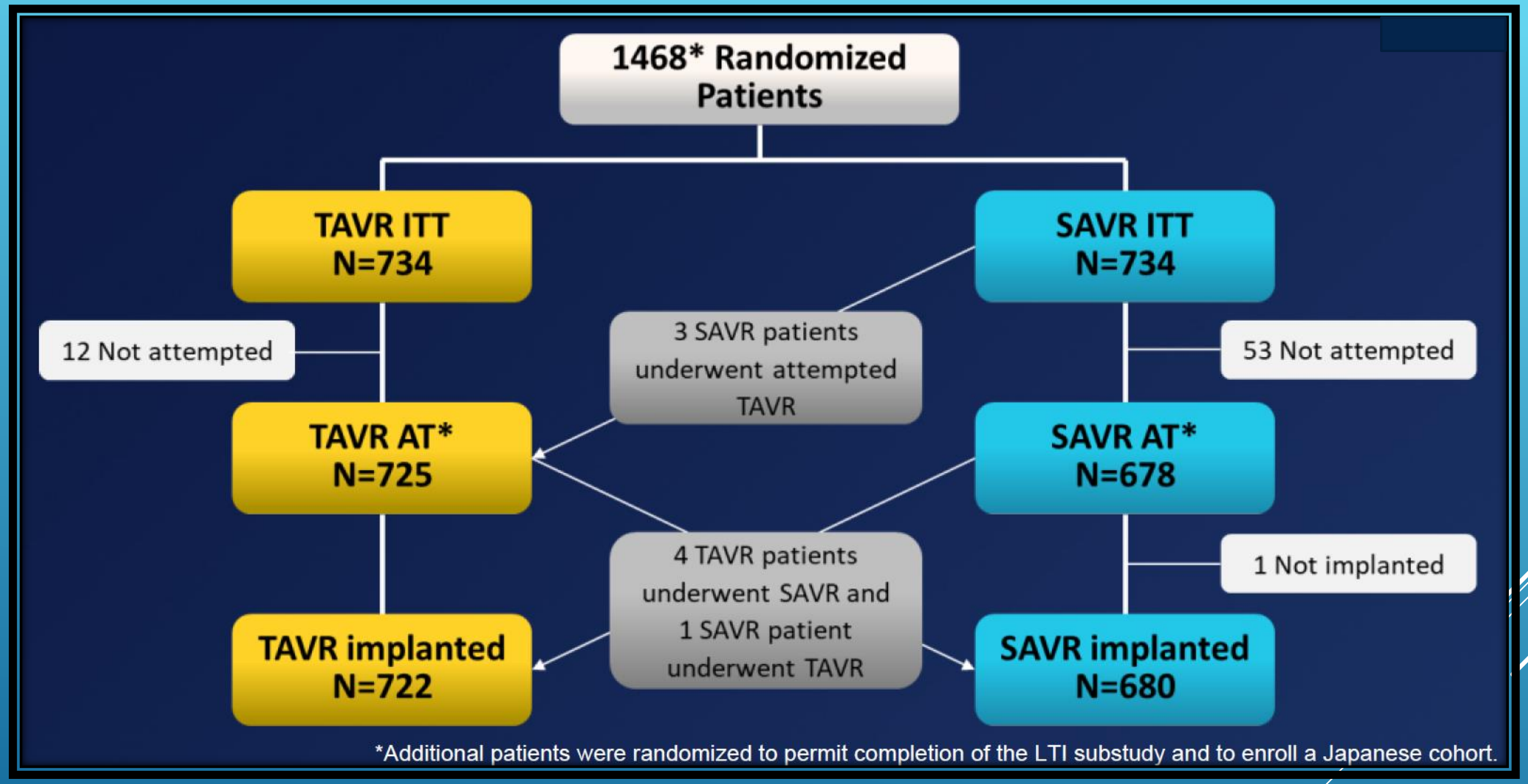
- Contraindication for placement of a bioprosthetic valve
- Multivessel coronary artery disease with SYNTAX score >22
- Bicuspid aortic valve verified by imaging
- Hypersensitivity or contraindication to all anticoagulation/ antiplatelet regimens
- Any PCI or peripheral intervention within 30 days prior to randomization
- Symptomatic carotid or vertebral artery disease or successful treatment of carotid stenosis within 10 weeks of Heart Team assessment
- Recent (within 2 months) cerebrovascular accident or transient ischemic attack
- Acute MI within 30 days
- Severe liver, lung or renal disease
- Unsuitable anatomy including native aortic annulus <18 mm or >30 mm
- Severe mitral or tricuspid regurgitation

STATISTICAL METHODS

NONINFERIORITY TESTING OF THE PRIMARY ENDPOINT

- This was a randomized, multinational, noninferiority trial.
- The Bayesian adaptive design prespecified an "early-win" interim analysis when 850 patients reached 1-year follow-up.
- The estimated sample size was 1200 patients.
- The 2-year primary analysis cohort comprised all patients with an attempted implant procedure (as-treated).
- The prespecified criteria for success was





PATIENT FLOW

STUDY TIMELINE AND VALVES STUDIED

2016	2017	2018

First Patient Randomized
Mar. 28, 2016

*Last Patient Randomized
Nov. 27, 2018

CoreValve 31 mm

Evolut R: 23, 26, 29 | Added Evolut R 34 mm

Evolut PRO: 23, 26, 29 mm

Primary Endpoint Assessment Dec. 27, 2018

CoreValve 31 = 3.6%	Evolut R = 74.1%	Evolut PRO =22.3%

Vascular access
§ 99% transfemoral
§ 0.6% subclavian
§ 0.4% direct aortic

RESULTS

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
Age, years	74.1 ± 5.8	73.6 ± 5.9
Female sex	36.0	33.8
Body surface area, m2	2.0 ± 0.2	2.0 ± 0.2
STS PROM, %	1.9 ± 0.7	1.9 ± 0.7
NYHA Class III or IV	25.1	28.5
Hypertension	84.8	82.6
Chronic lung disease (COPD)	15.0	18.0
Cerebrovascular disease	10.2	11.8
Peripheral arterial disease	7.5	8.3

There are no significant differences between groups.

BASELINE CHARACTERISTICS

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
SYNTAX Score	1.9 ± 3.7	2.1 ± 3.9
Permanent pacemaker, CRT or ICD	3.2	3.8
Prior CABG	2.5	2.1
Previous PCI	14.2	12.8
Previous myocardial infarction	6.6	4.9
Atrial fibrillation/flutter	15.4	14.5
Aortic valve gradient, mm Hg	47.0 ± 12.1	46.6 ± 12.2
Aortic Valve area, cm2	0.8 ± 0.2	0.8 ± 0.2
Left ventricular ejection fraction, %	61.7 ± 7.9	61.9 ± 7.7

There are no significant differences between groups.

BASELINE CARDIAC RISK FACTORS

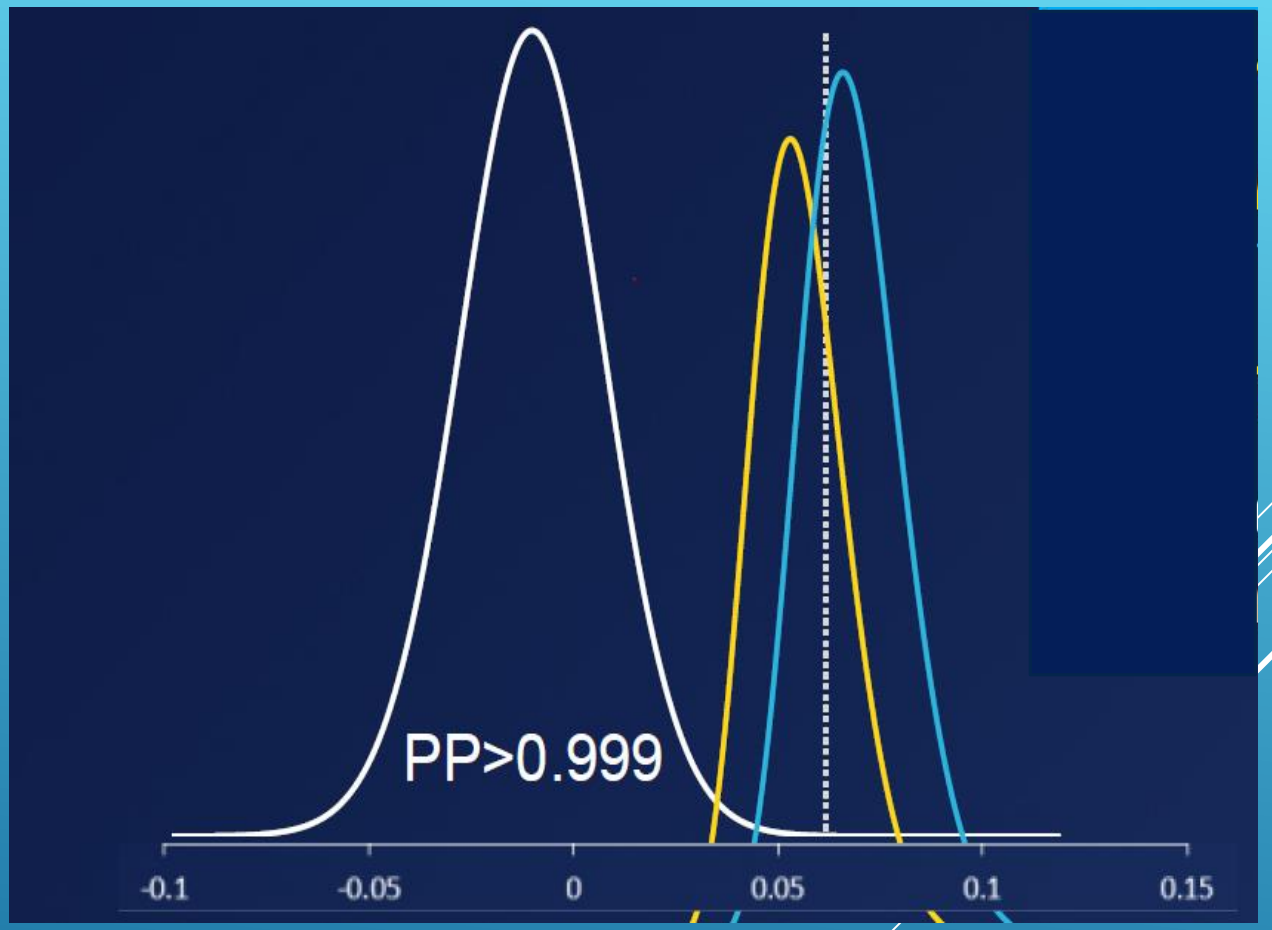
TAVR PROCEDURAL DATA

%	TAVR (N=724)
General Anesthesia	56.9
Iliofemoral access	99.0
Embolic protection device used	1.2
Pre-TAVR balloon dilation	34.9
Post-TAVR balloon dilation	31.3
More than 1 valve used	1.2
Partial or complete repositioning of the valve (Evolut/PRO only)	37.3
Staged or concomitant PCI performed	6.9

All-Cause Mortality or Disabling Stroke at 2 Years

Primary Endpoint Met
TAVR is noninferior to SAVR

TAVR 5.3%SAVR 6.7%
Posterior probability of Noninferiority >0.999



TAVR –SAVR difference = -1.4% (95% BCI; -4.9, 2.1)

PRIMARY ENDPOINT

All Noninferiority and Superiority Endpoints Met

	TAVR	SAVR	Difference TAVR-SAVR	Posterior Probability
Noninferiority (margin)			**(90% BCI)**	
Mean gradient at 12 mo. (5mmHg)	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.1, -2.1)	>0.999
Mean EOA at 12 months (0.1 cm2)	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	>0.999
Mean NYHA class change (12 months –Baseline) (0.375)	0.9 ± 0.7	1.0 ± 0.7	-0.1 (-0.2, 0.0)	>0.999
Mean KCCQ change (12 months –Baseline) (5)	22.2 ± 20.3	20.9 ± 21.0	1.3 (-1.2, 3.8)	>0.999
Superiority			**(95% BCI)**	
Mean gradient at 12 months, mmHg	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.2, -2.0)	>0.999
Mean EOA at 12 months, cm2	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	>0.999
Mean KCCQ change (30 Days–	20.0 ± 21.1	9.1 ± 22.3	10.9 (8.6,	>0.999

HIERARCHICAL SECONDARY ENDPOINTS

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety endpoint*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)
Aortic valve reintervention	0.4	0.4	(-0.8, 0.7)

* Significantly favors TAVR; * Significantly favors SAVR

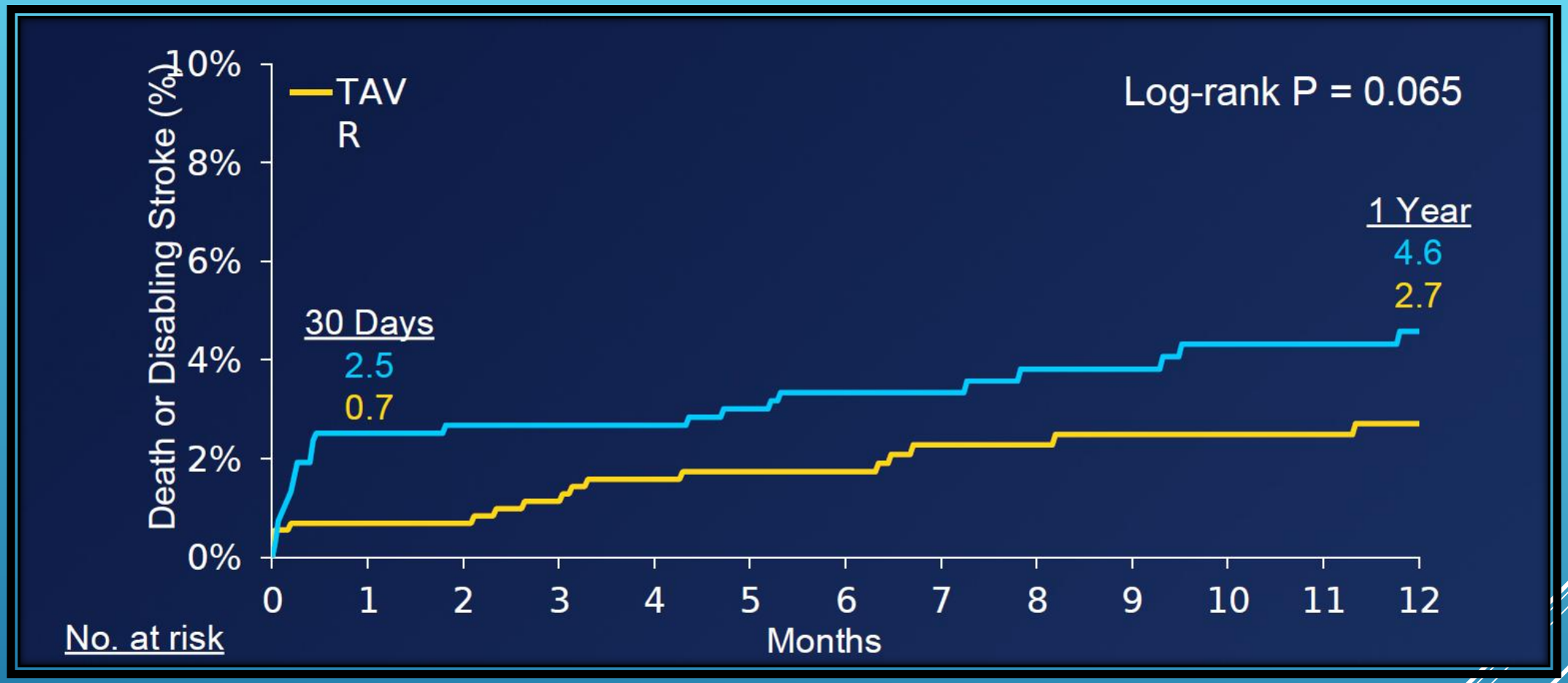
BCI = Bayesian credible interval

CLINICAL OUTCOMES AT 30 DAYS

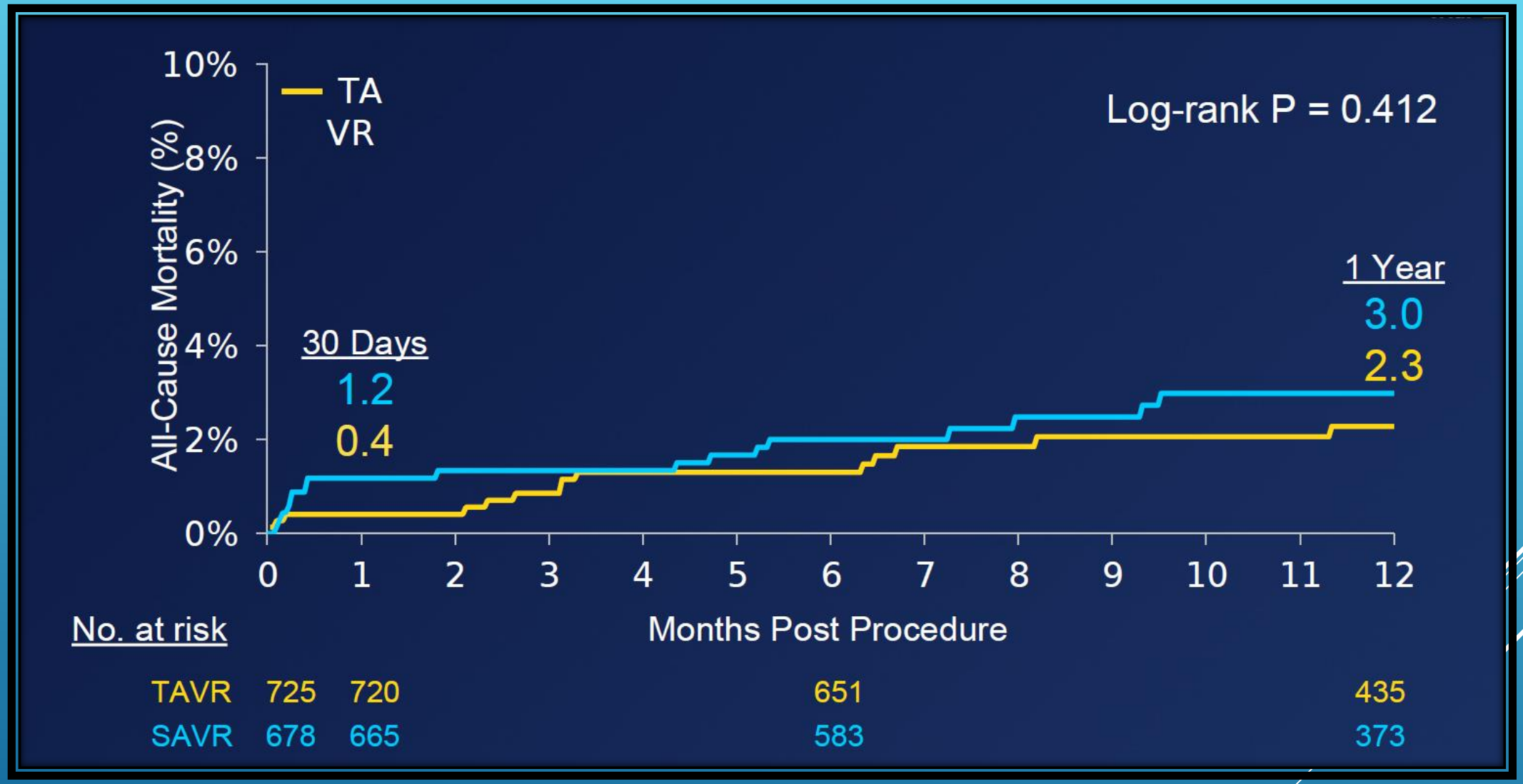
Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
All-cause mortality or disabling stroke	2.9	4.6	**(-4.0, 0.4)**
All-cause mortality	2.4	3.0	**(-2.6, 1.3)**
Cardiovascular mortality	1.7	2.6	**(-2.7, 0.7)**
All stroke	4.1	4.3	**(-2.4, 1.9)**
Disabling stroke*	0.8	2.4	(-3.1, -0.3)
Transient ischemia attack	1.7	1.8	**(-1.6, 1.3)**
Myocardial infarction	1.7	1.6	**(-1.3, 1.5)**
Endocarditis	0.2	0.4	**(-0.9, 0.5)**
Valve thrombosis	0.2	0.3	**(-0.9, 0.5)**
Aortic valve reintervention	0.7	0.6	**(-1.0, 0.9)**
Heart failure hospitalization*	**3.2**	**6.5**	**(-5.9, -1.0)**

**** Significantly favors TAVR***

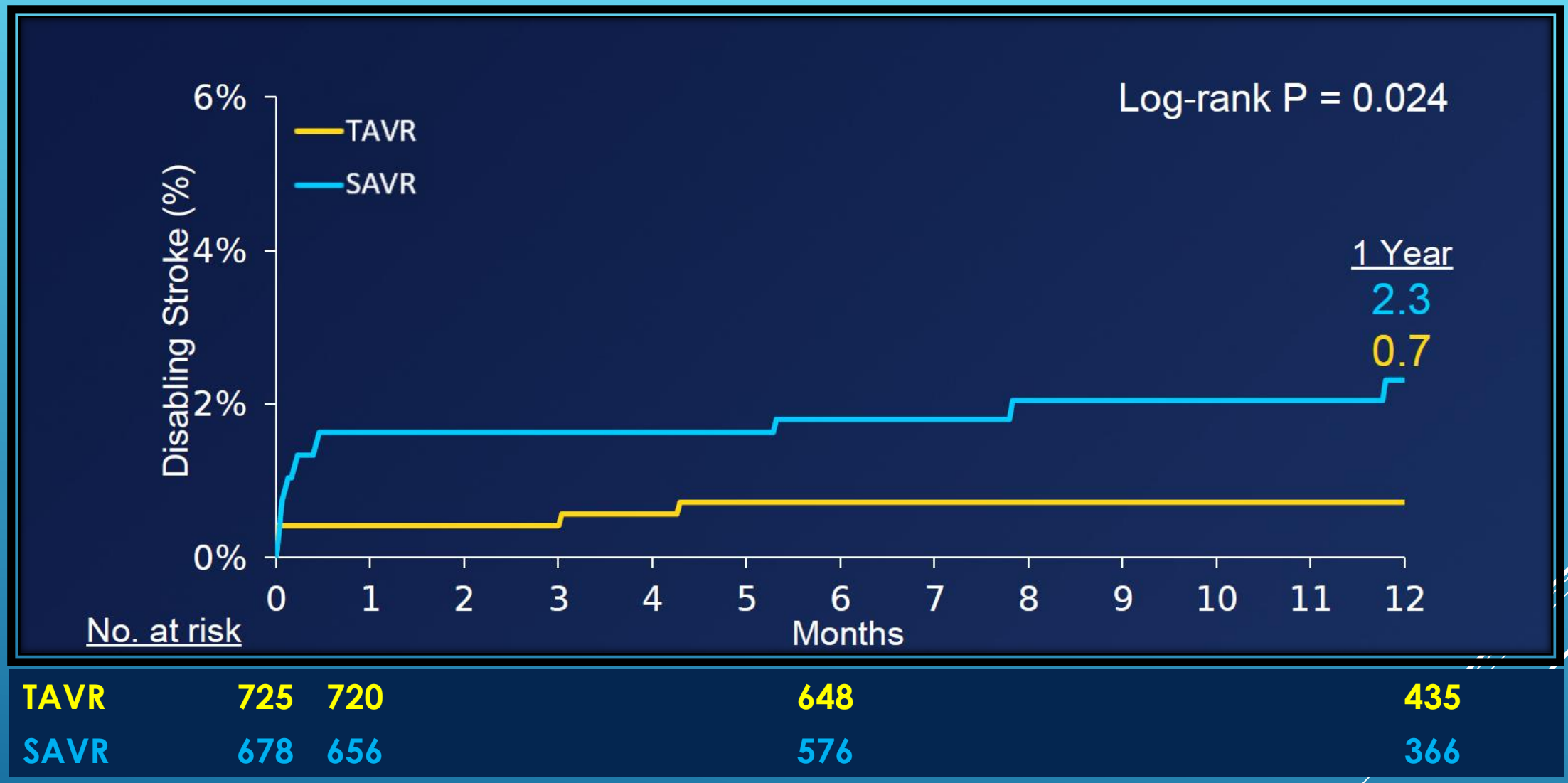
CLINICAL OUTCOMES AT 1 YEAR



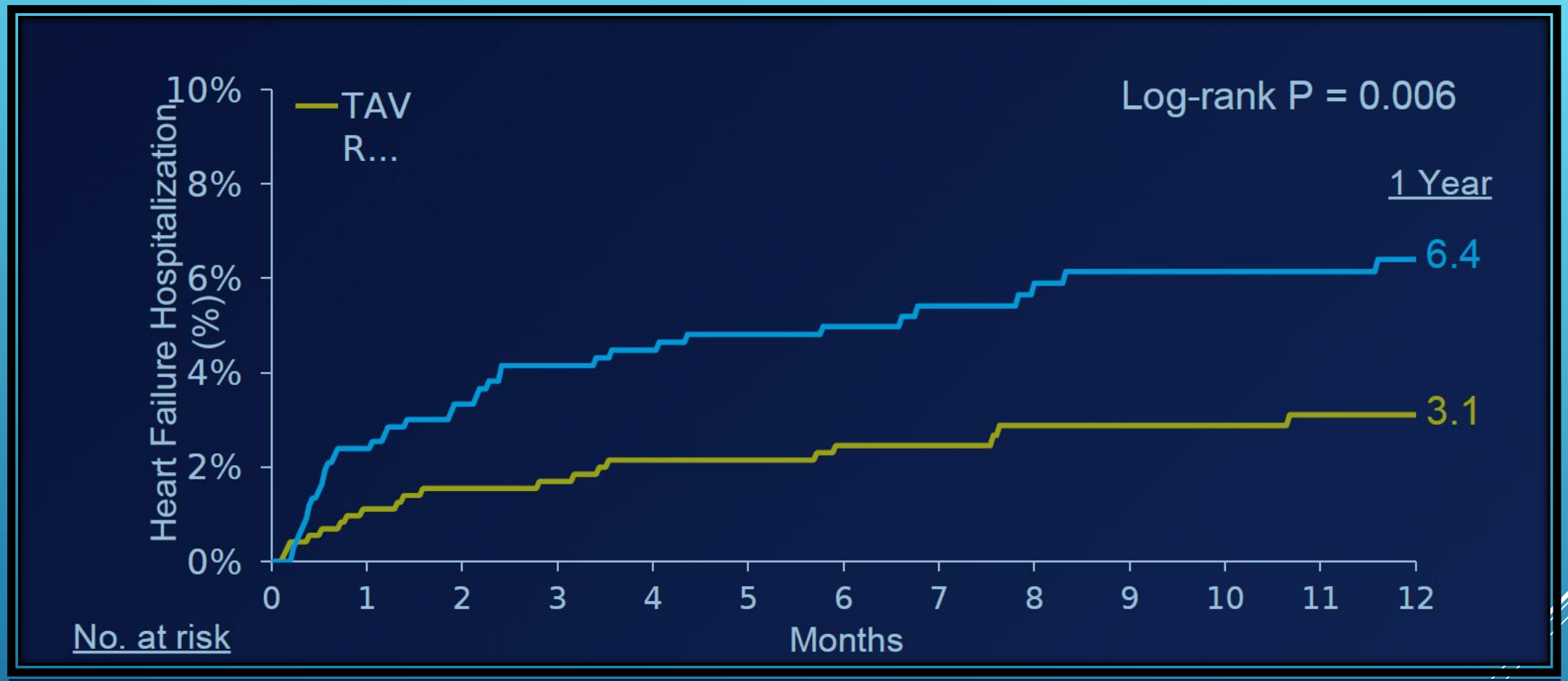
K-M ALL-CAUSE MORTALITY OR DISABLING STROKE AT 1 YR.



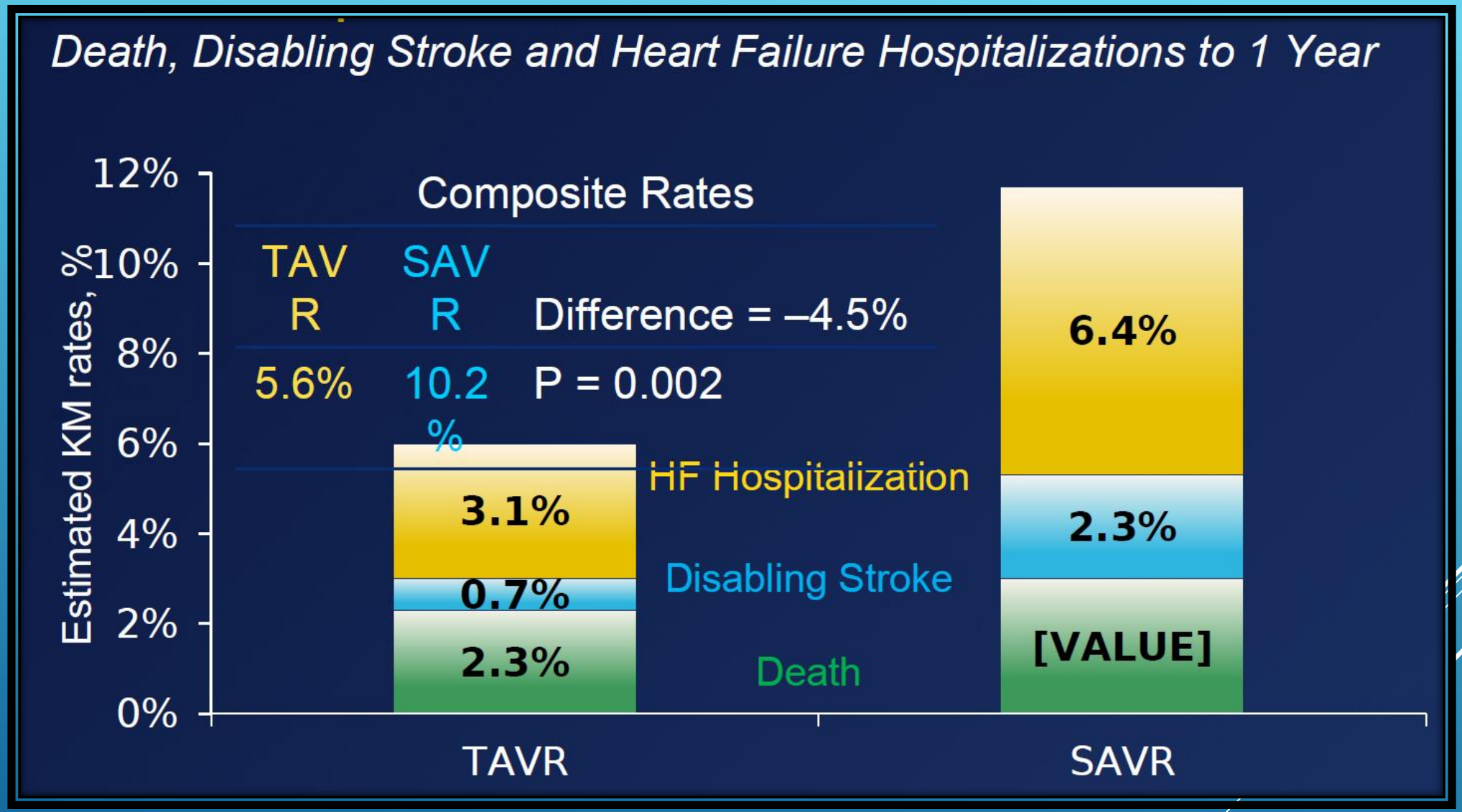
K-M RATES OF ALL-CAUSE MORTALITY AT 1 YEAR



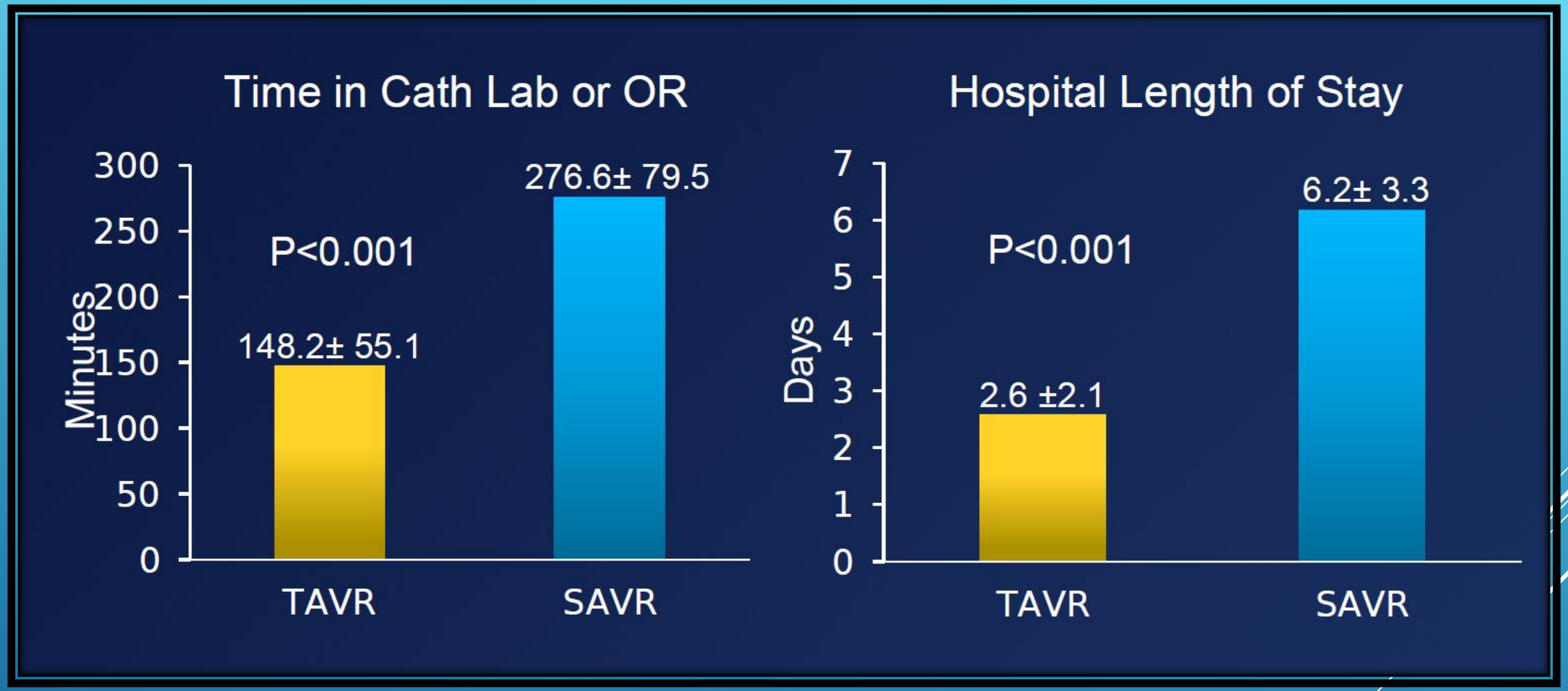
K-M DISABLING STROKE AT 1 YEAR



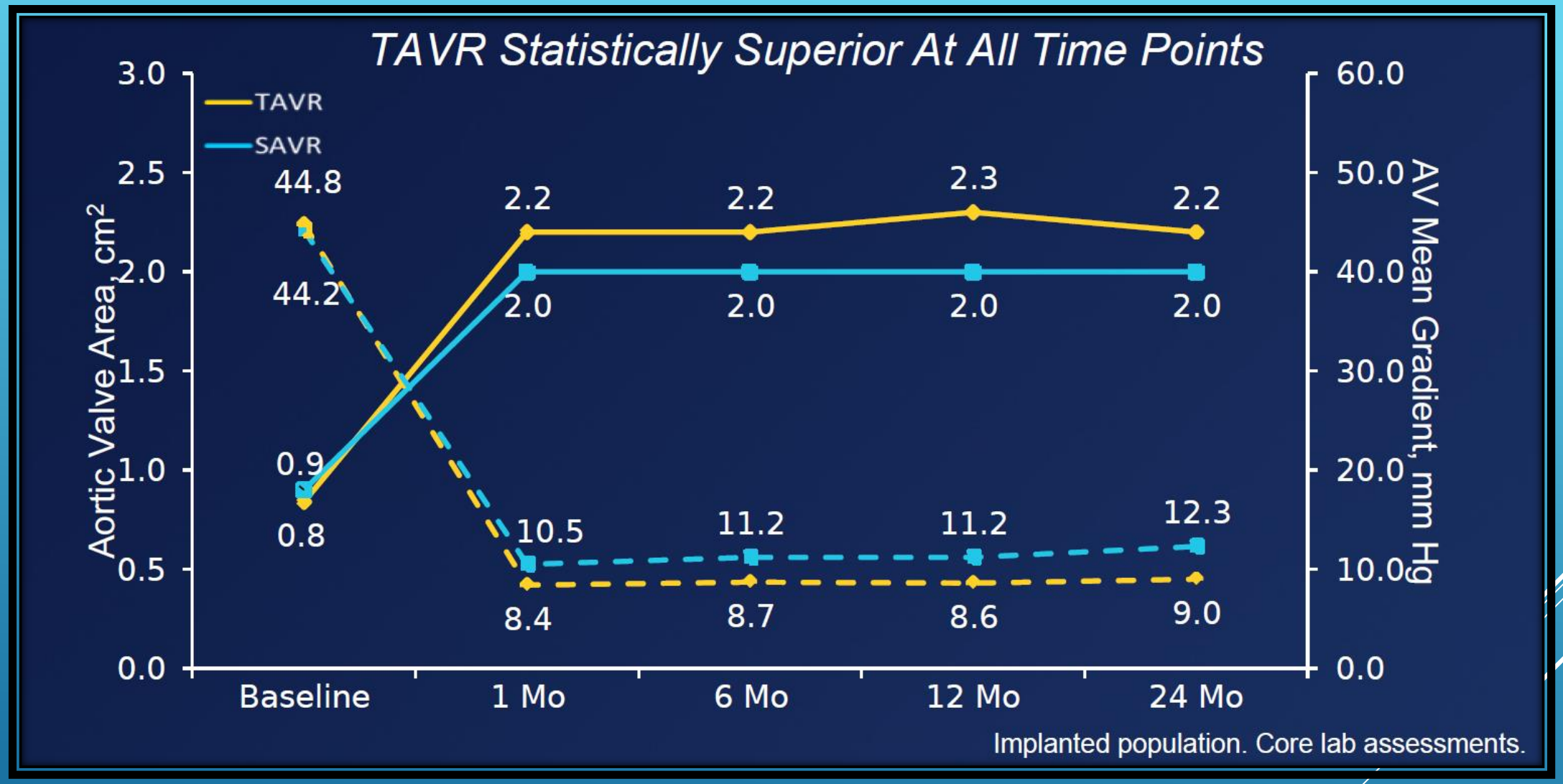
K-M HEART FAILURE HOSPITALIZATION AT 1 YEAR



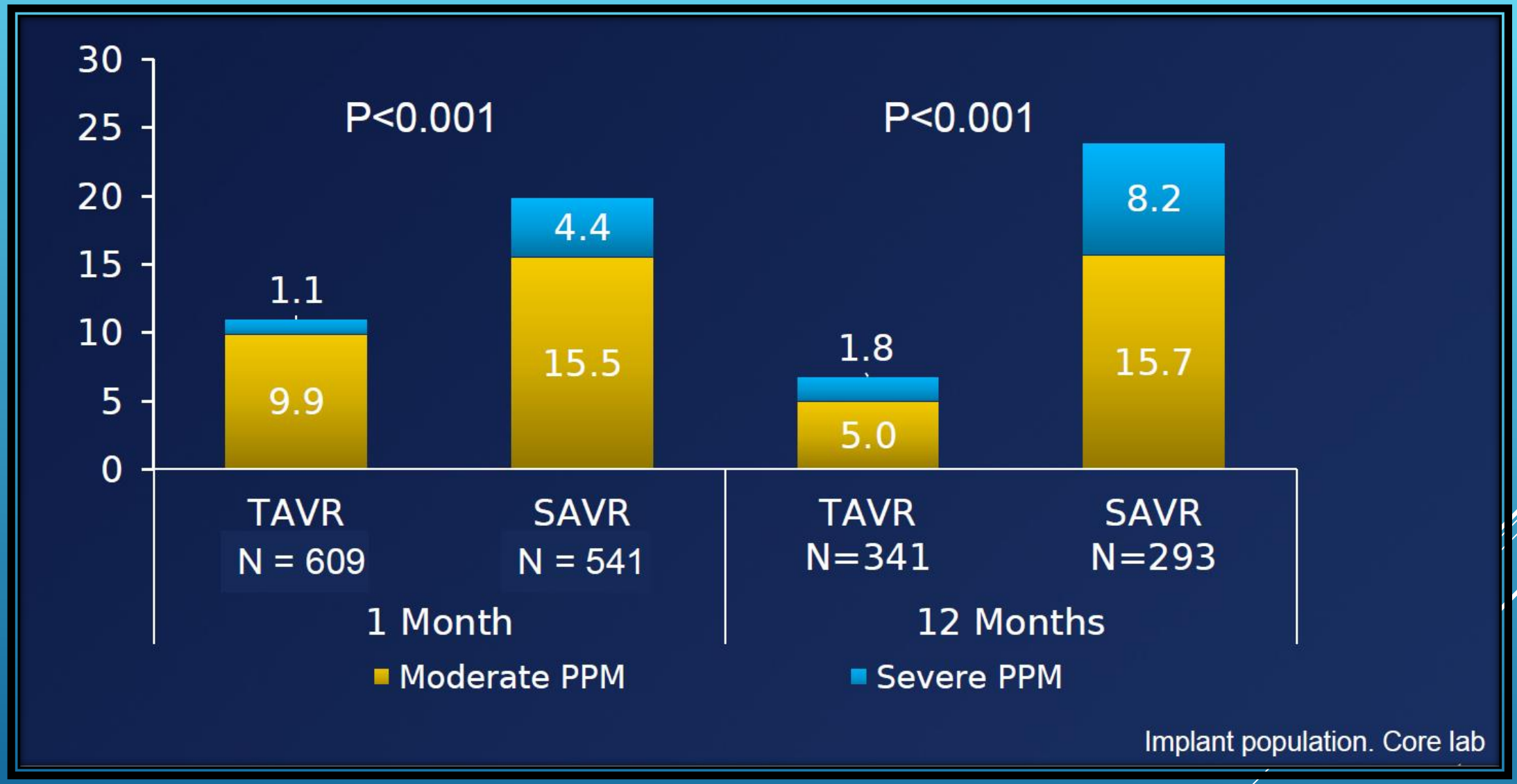
CLINICAL IMPLICATIONS



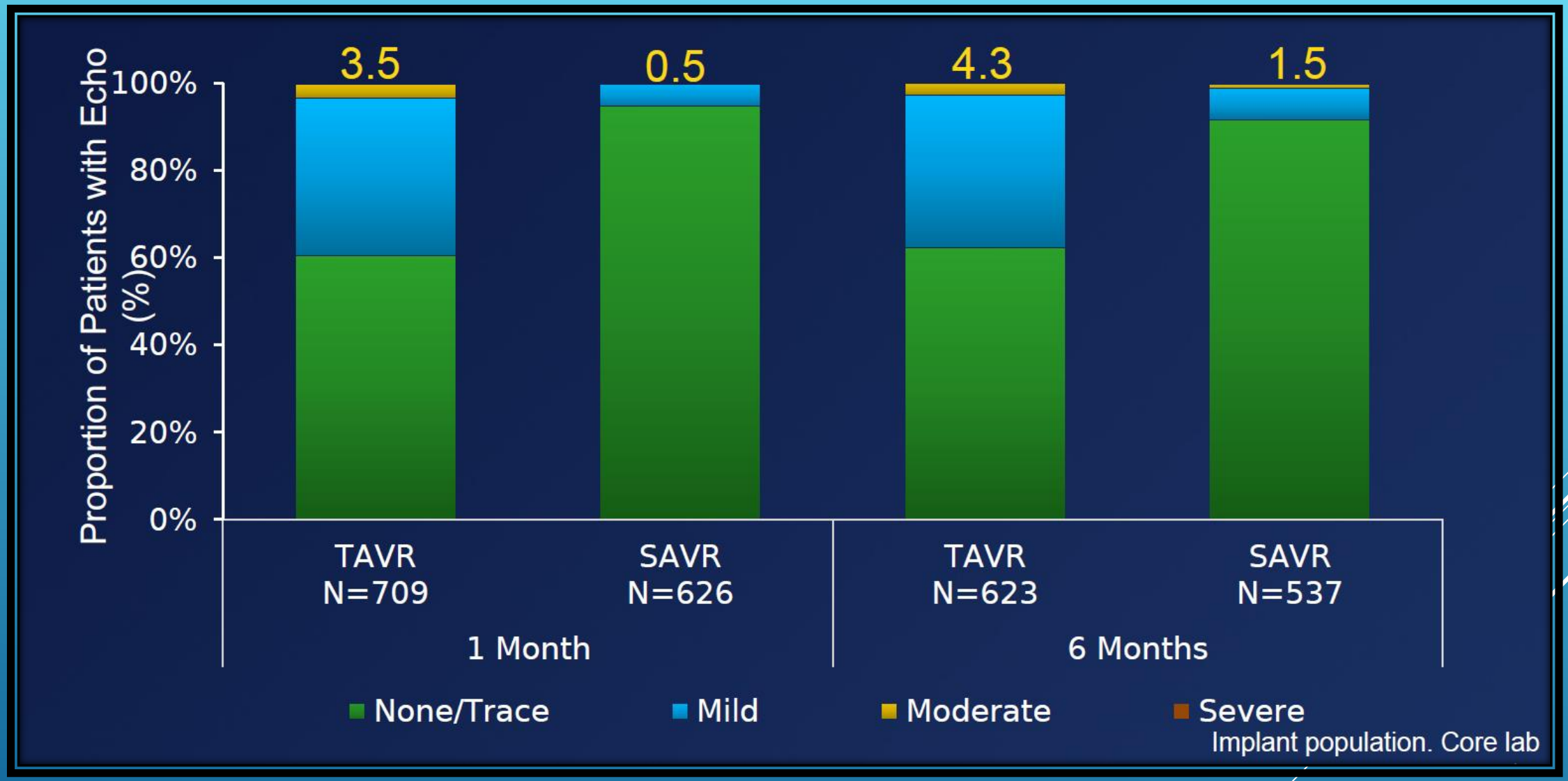
PROCEDURAL TIME AND LENGTH OF STAY



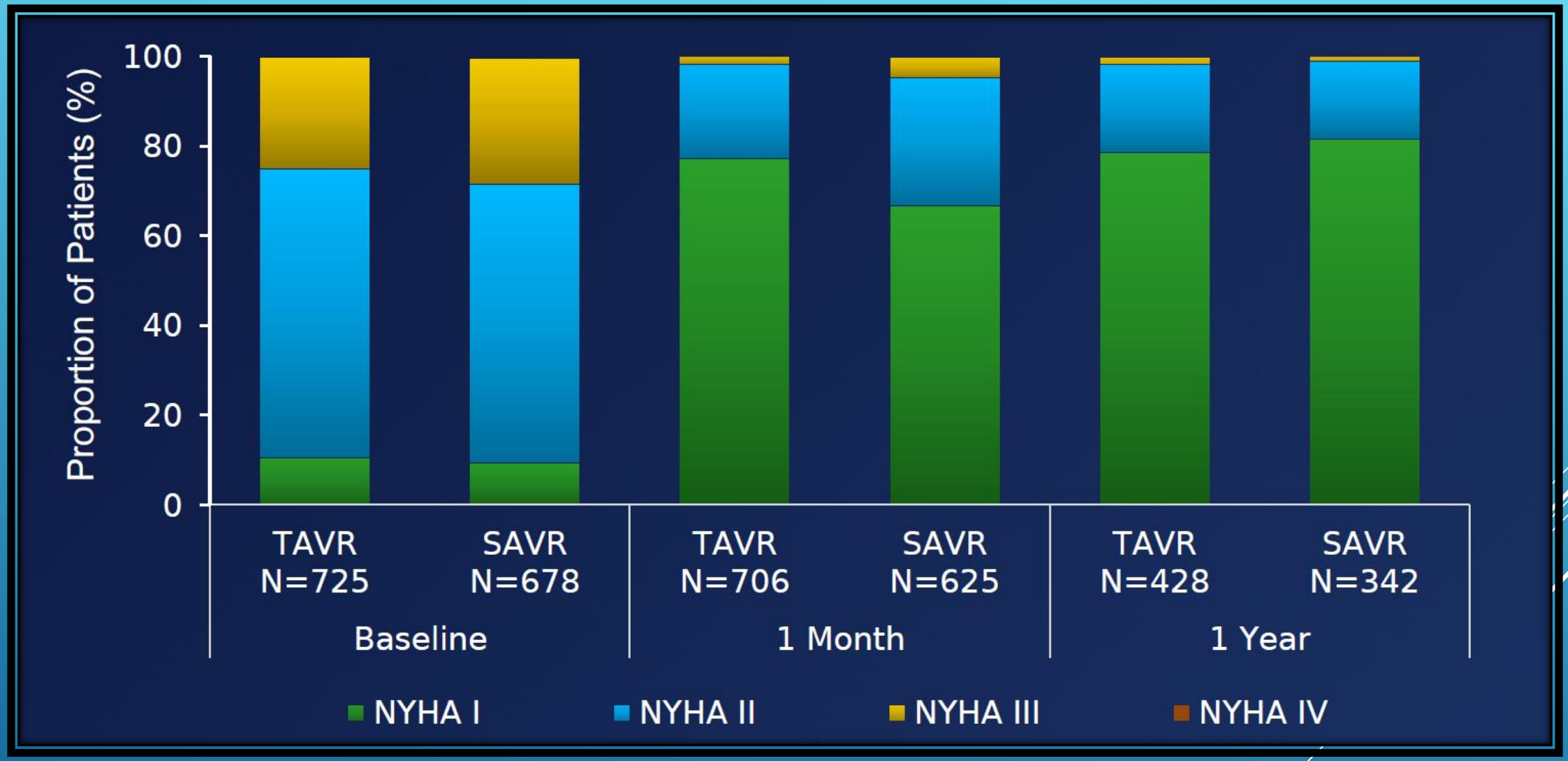
VALVE HEMODYNAMICS



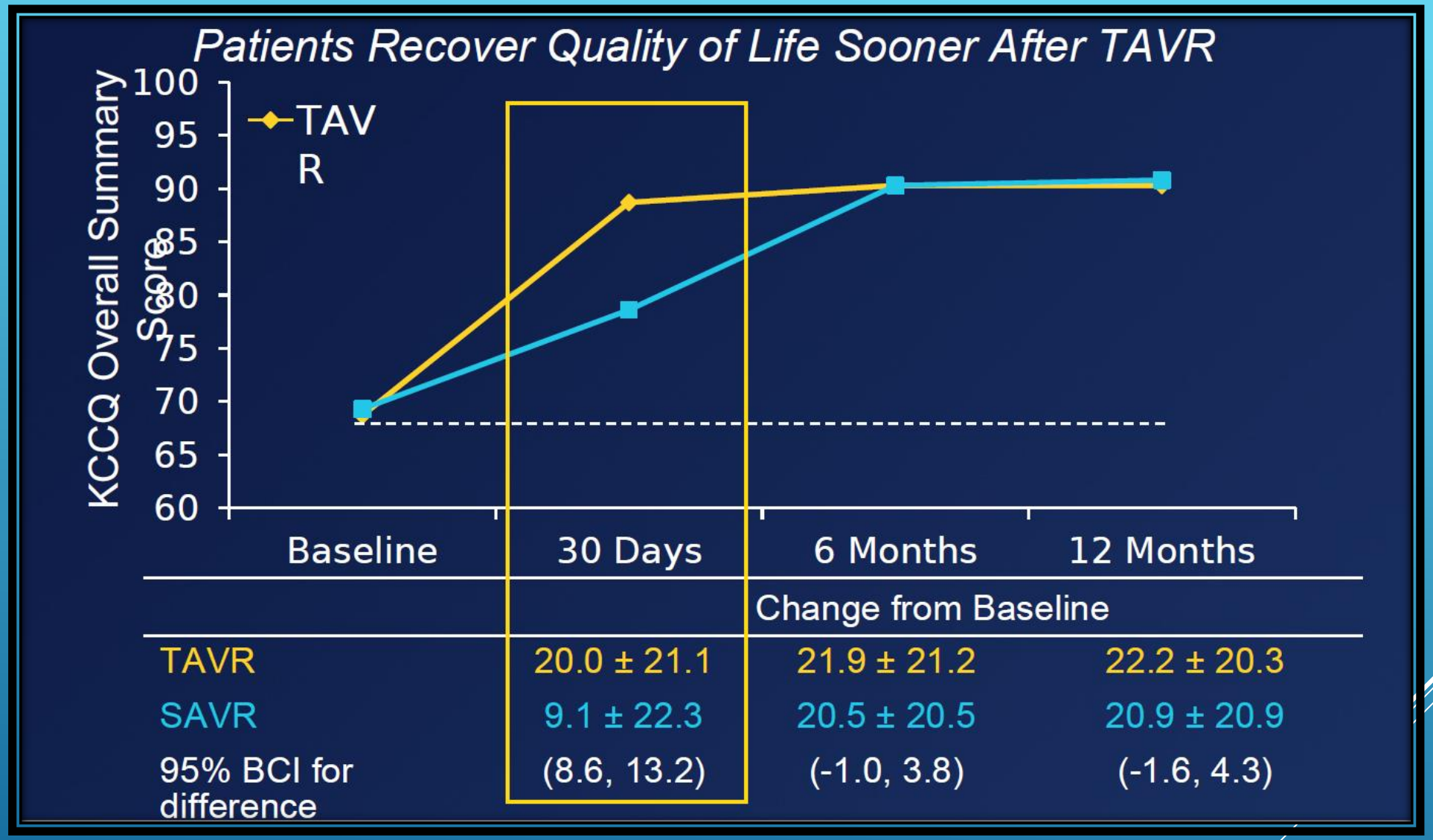
PROSTHESIS-PATIENT MISMATCH



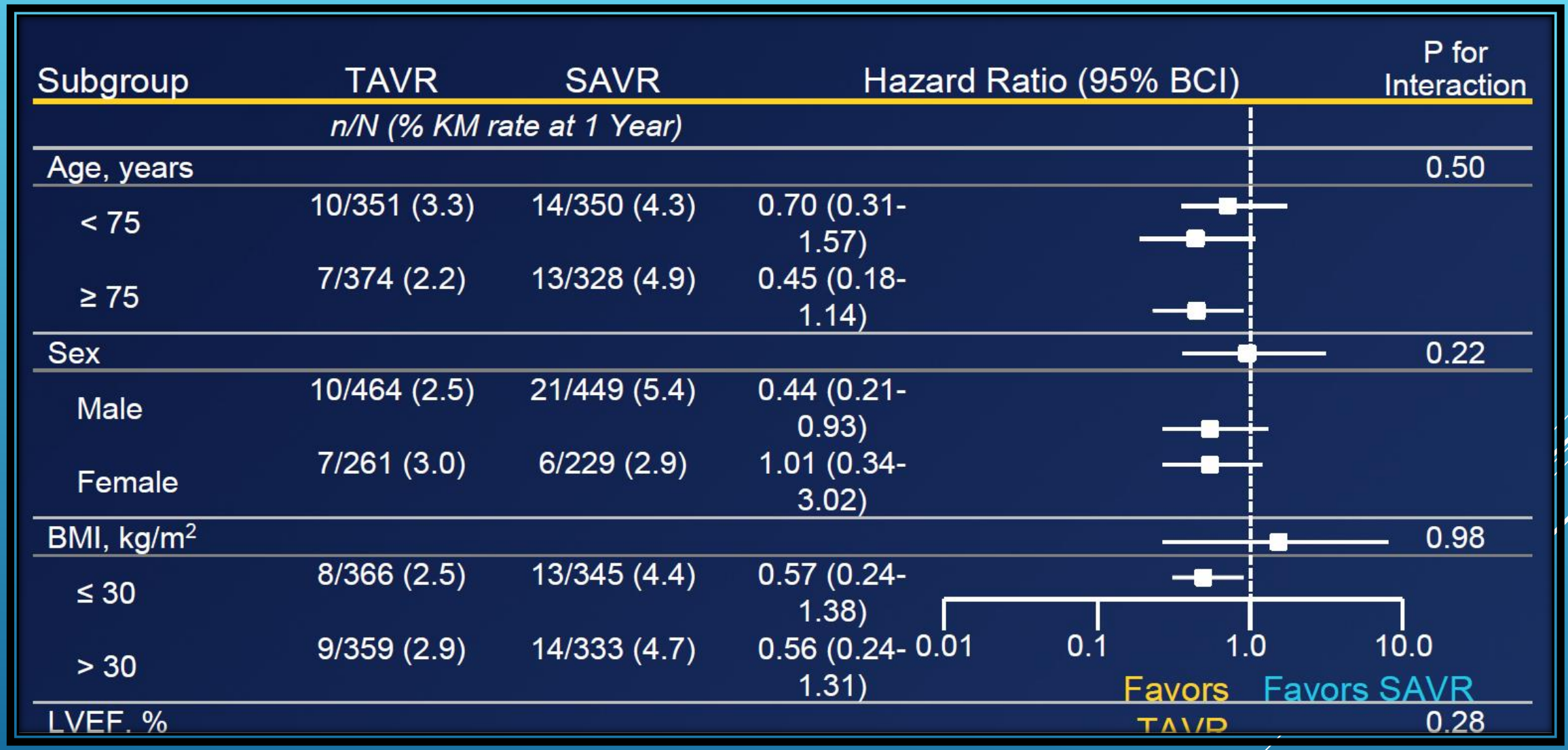
TOTAL AORTIC VALVE REGURGITATION



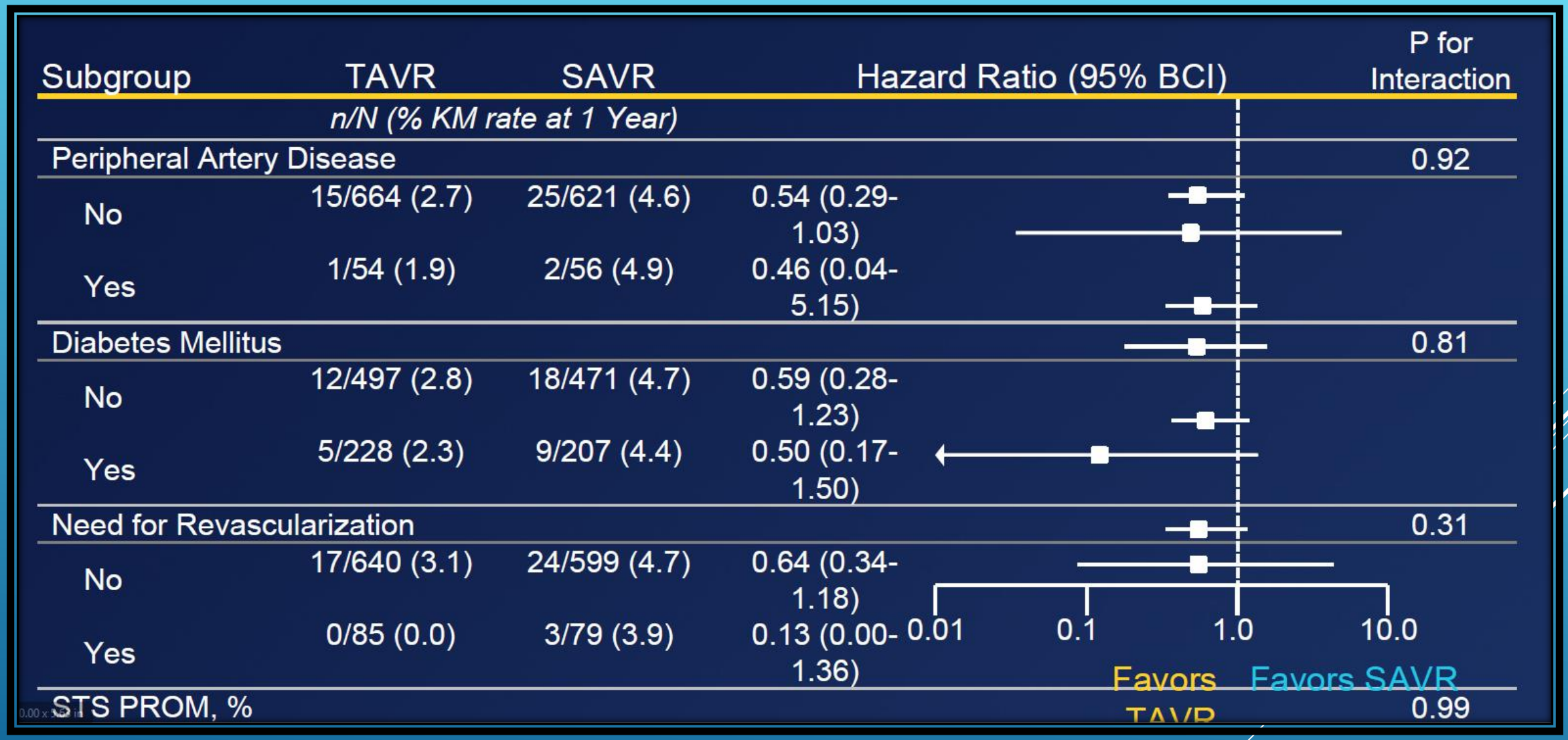
NYHA FUNCTIONAL CLASS



KCCQ SUMMARY SCORE



SUBGROUP ANALYSIS FOR DEATH OR DISABLING STROKE AT 1 YEAR



SUBGROUP ANALYSIS FOR DEATH OR DISABLING STROKE AT 1 YEAR

SUMMARY

- TAVR with self-expanding supra-annular valves was noninferior to surgery for the primary endpoint of death or disabling stroke at 2 years in patients with severe aortic stenosis at low surgical risk.
- At 30 days, TAVR showed a better safety and recovery profile than surgery, with less death or disabling stroke, less disabling stroke, shorter length of stay and better QOL while SAVR had fewer pacemakers implanted and less residual AR.
- At 1 year, both groups had excellent survival. TAVR showed fewer disabling strokes and heart failure rehospitalization with superior hemodynamics manifest by lower gradients, larger EOAs and less PPM.

CONCLUSION

TAVR may be a preferred strategy to surgery in patients with severe aortic stenosis at low risk of surgical mortality.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn, III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*