Health Status after Transcatheter vs. Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis at Low Surgical Risk

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Disclosures

- The PARTNER 3 trial (NCT 02675114) and quality-of-life substudy was supported by a research grant from Edwards LifeSciences.

- Within the past 12 months, I have had a financial interest, arrangement or affiliation with the organizations listed below:
  - Edwards LifeSciences: Consulting fees
  - Boston Scientific Corp: Research grant support; Advisory board

Background

- The PARTNER 3 and Evolut Low Risk trials have demonstrated that transfemoral TAVR is both safe and effective when compared with SAVR in patients with severe aortic stenosis at low surgical risk

- While prior studies have demonstrated improved early health status with transfemoral TAVR compared with SAVR in **intermediate and high-risk** patients, there is little evidence of any late health status benefit with TAVR

- Whether treatment of a lower risk population might demonstrate a sustained health status benefit of TAVR vs. SAVR is unknown

Study Objectives

- To compare health status outcomes among patients with severe AS at low surgical risk treated with either TAVR or SAVR

- To identify factors associated with any differential health status benefits of TAVR vs. SAVR at 1 year

Methods:
Study Design

- Patients with severe AS determined to be at low-surgical risk (STS < 4%) were randomized 1:1 to transfemoral TAVR with the SAPIEN-3 balloon expandable valve or SAVR at 71 sites

- Key Exclusion Criteria
  - Bicuspid aortic valve
  - Severe untreated coronary artery disease
  - Unfavorable anatomy for transfemoral TAVR
  - Significant frailty
  - Severe renal or lung disease

- Measures of health status were collected at baseline, 1 month, 6 months and 1 year with plans for on-going annual assessment through 10 years

Methods:
Health Status Measures

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Instrument	*Description/Role*
Kansas City Cardiomyopathy Questionnaire (KCCQ)	• Heart Failure-specific • Domains: Symptoms, Physical Limitations, Quality of Life, Social Limitations • Scores: 0-100 (higher = better) • KCCQ-Overall Summary Score (KCCQ-OS) - Δ 5, 10, 20 points = small, moderate, large clinical change

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SF-36	• General physical and mental health • Scores standardized such that mean = 50 with SD 10 (higher = better) • Minimal Clinically Important Difference ~ 2 points

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SF-36	• General physical and mental health • Scores standardized such that mean = 50 with SD 10 (higher = better) • Minimal Clinically Important Difference ~ 2 points
EQ-5D (EuroQOL)	• Generic instrument for assessment of utilities • Scores: 0-1 (0 = death; 1 = perfect health)

Statistical Analysis

- **Primary Endpoint:** KCCQ-OS Score through 12 months
- **Analytic Population**: as-treated patients with any available baseline health status assessment
- Scores between treatment groups compared using longitudinal random-effects growth curve models at each time point with adjustment for age, sex, baseline health status and treatment assignment
- Categorical analyses performed to incorporate both survival and health status
- Pre-specified subgroups examined with interaction terms
  - Age, sex, STS risk score, atrial fibrillation, LVEF, and NYHA Class

Baseline Characteristics

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Characteristic	TAVR N = 494	SAVR N = 449	P-Value
Age	73.3 yrs	73.6 yrs	0.47
Male	67.4%	71.3%	0.20
STS Risk Score	1.9	1.9	0.23
Coronary Artery Disease	27.6%	27.6%	0.99
Peripheral Arterial Disease	6.9%	7.4%	0.80
Prior Stroke	3.4%	5.1%	0.26
COPD	5.1%	6.0%	0.57
Atrial Fibrillation	15.6%	18.8%	0.23
Ejection Fraction	65.7%	66.2%	0.43
Mean AV Gradient	49 mmHg	48 mmHg	0.20

Baseline Health Status

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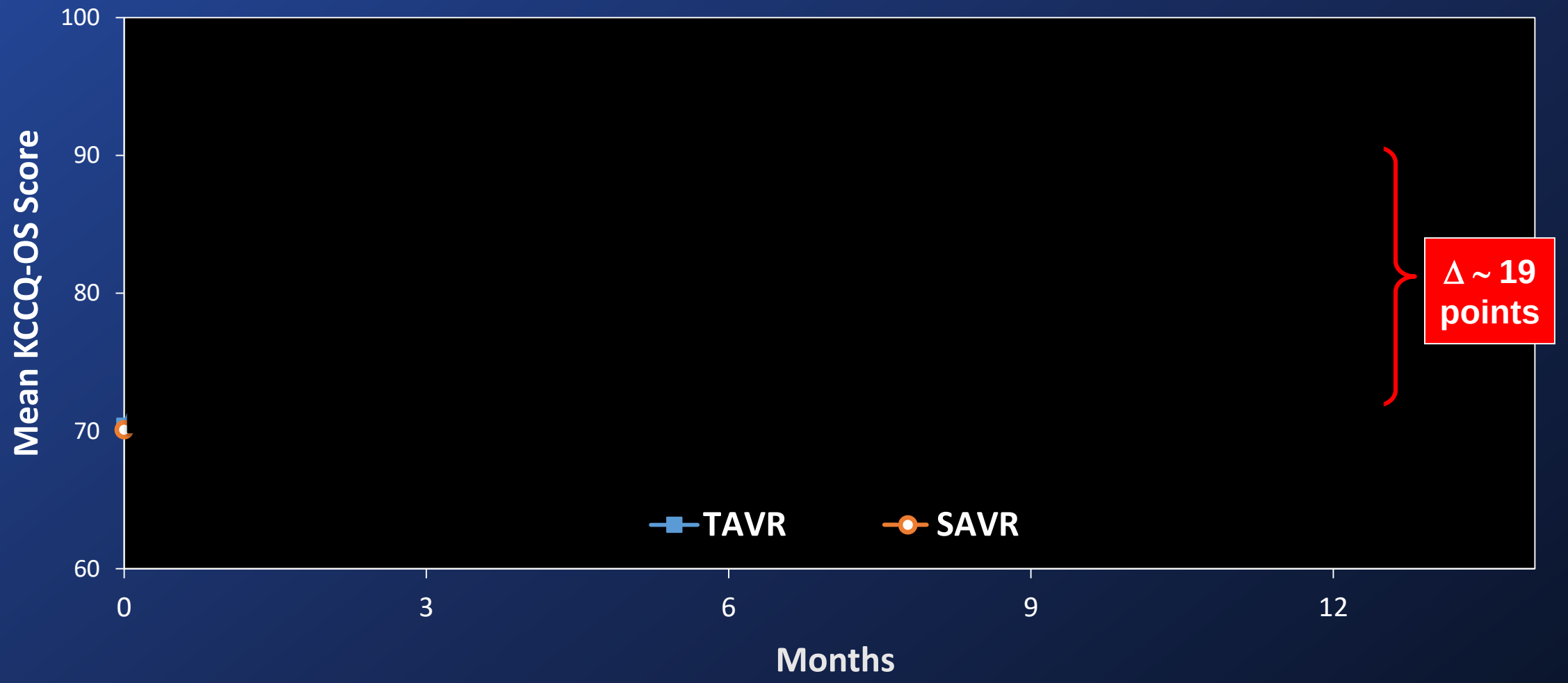
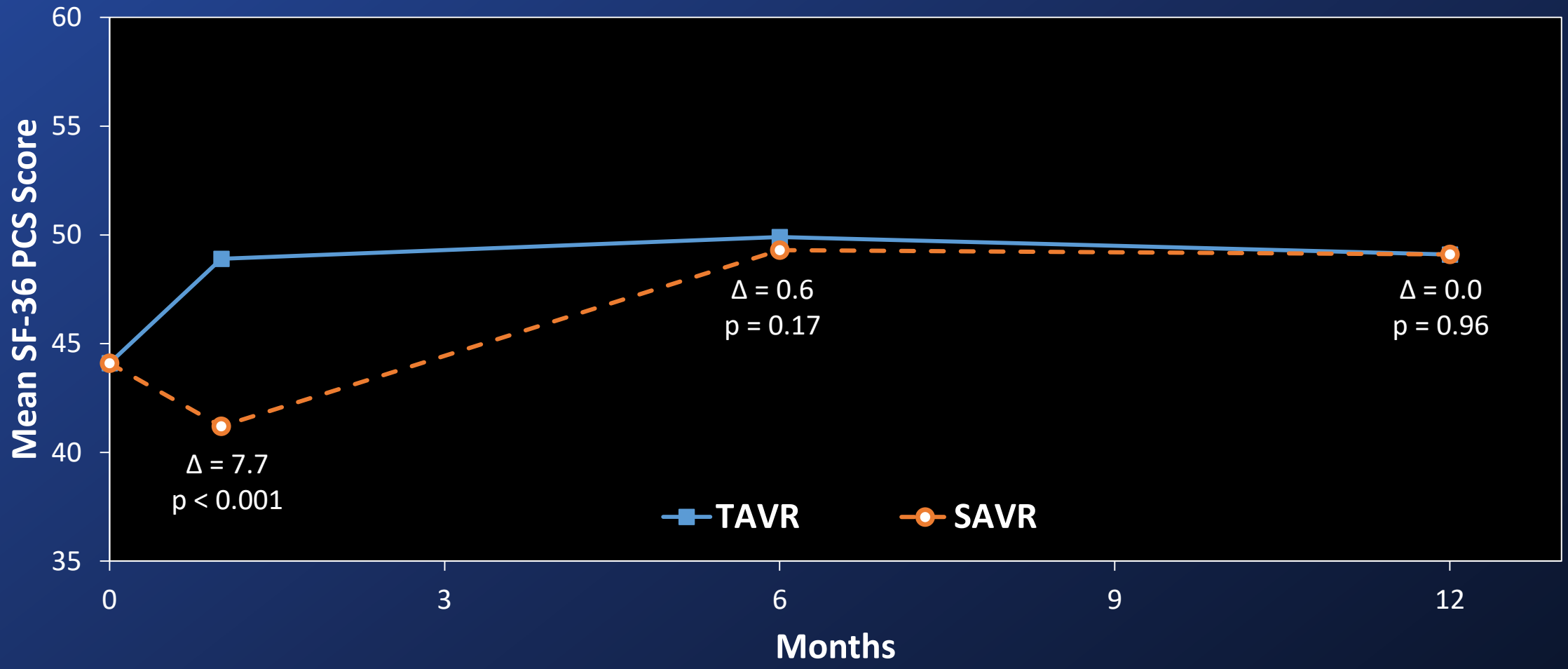
Characteristic	TAVR N = 494	SAVR N = 449	P-Value
KCCQ Overall Summary	70.4 ± 19.4	70.1 ± 20.9	0.83
KCCQ Physical Limitation	76.6 ± 19.8	76.9 ± 20.6	0.81
KCCQ Quality of Life	58.1 ± 24.4	58.2 ± 25.8	0.96
SF-36 Physical Summary	44.1 ± 9.2	44.1 ± 9.0	0.96
SF-36 Mental Summary	52.5 ± 9.1	51.3 ± 10.0	0.05
EQ-5D Utilities	0.83 ± 0.11	0.83 ± 0.13	0.59

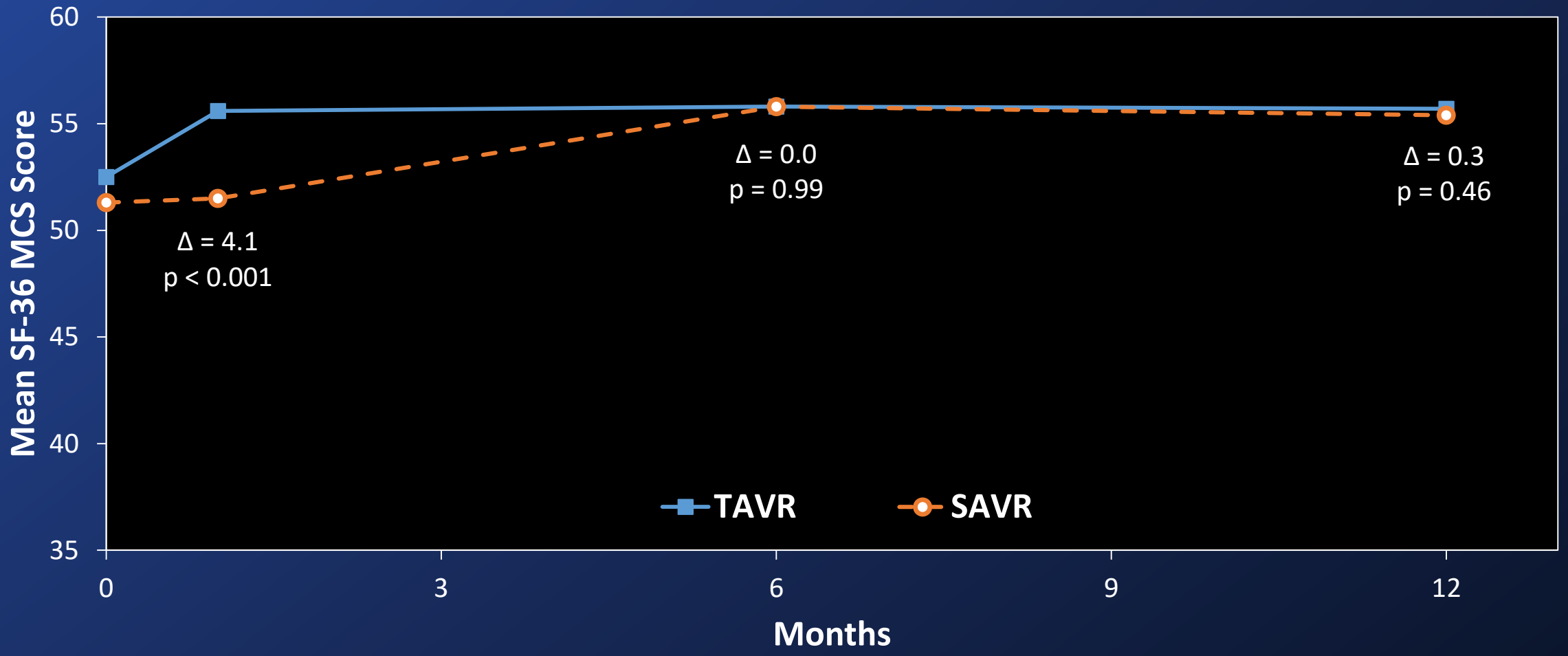
Primary Endpoint: KCCQ-Overall Summary



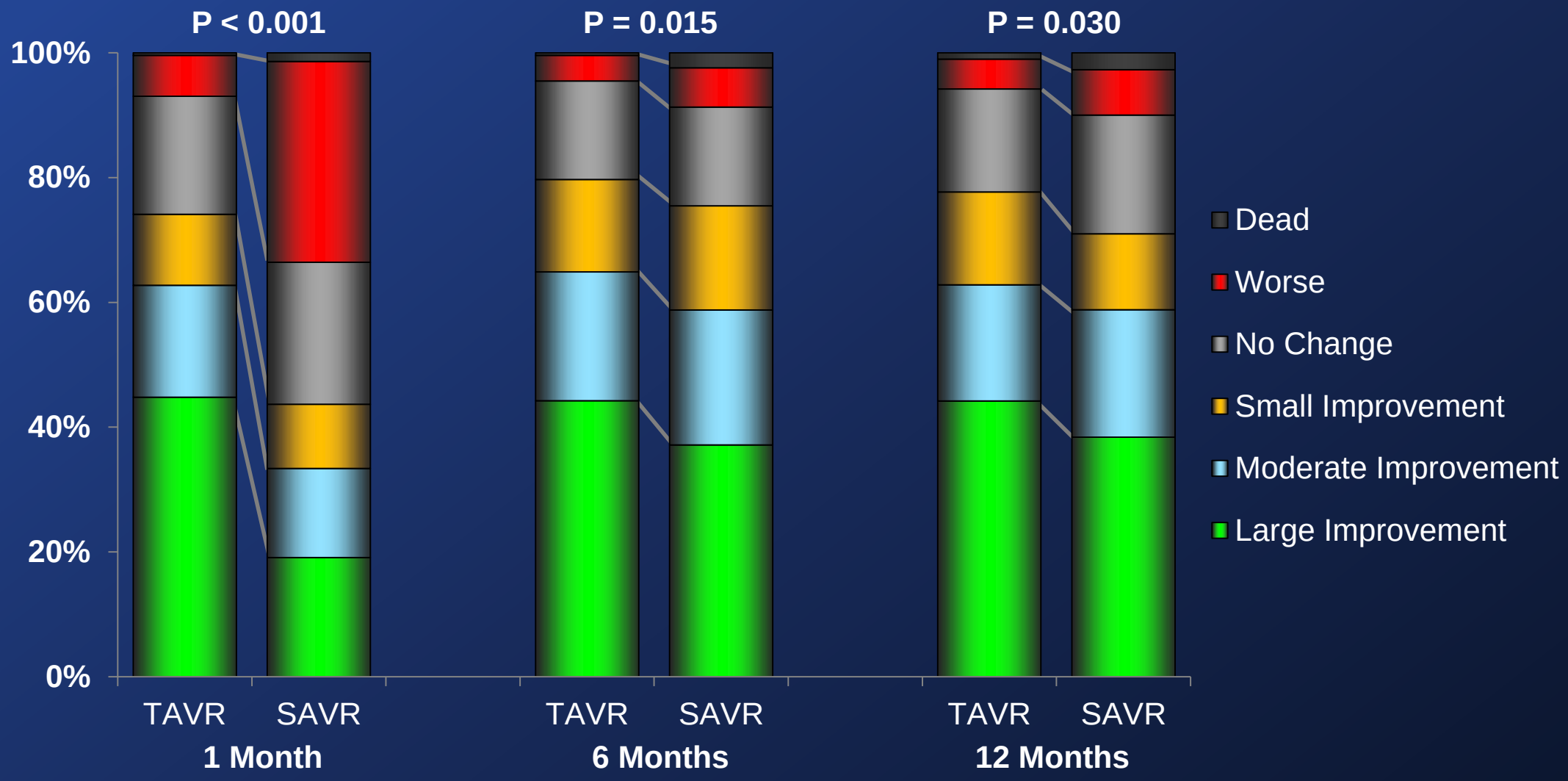
SF-36 Physical Summary Score



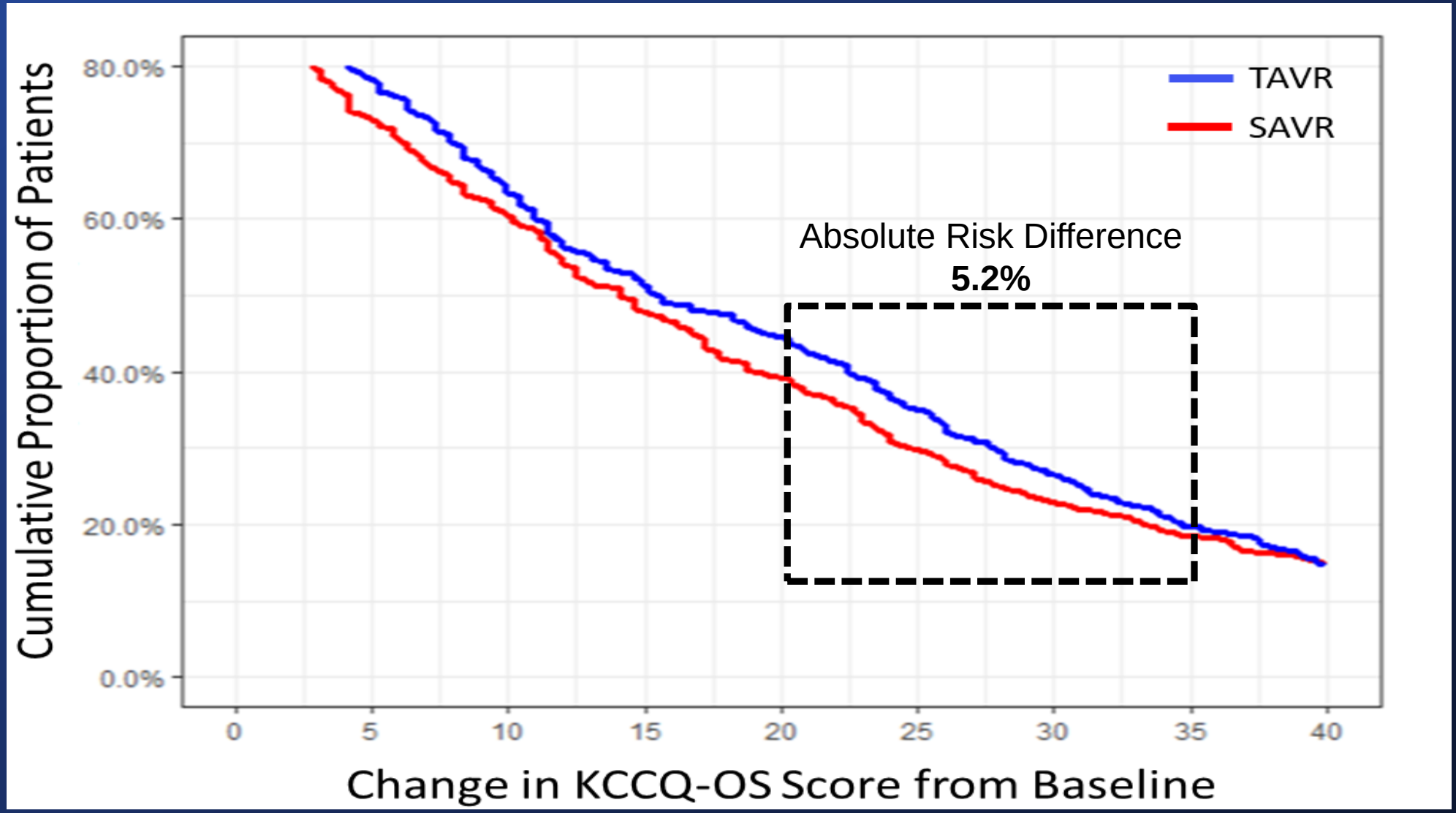
SF-36 Mental Summary Score



Categorical Analysis:
Survival and Health Status (KCCQ-OS) Combined



Cumulative Response Curves at 12 Months



Subgroup Analyses:
Difference in KCCQ-OS at 12 months

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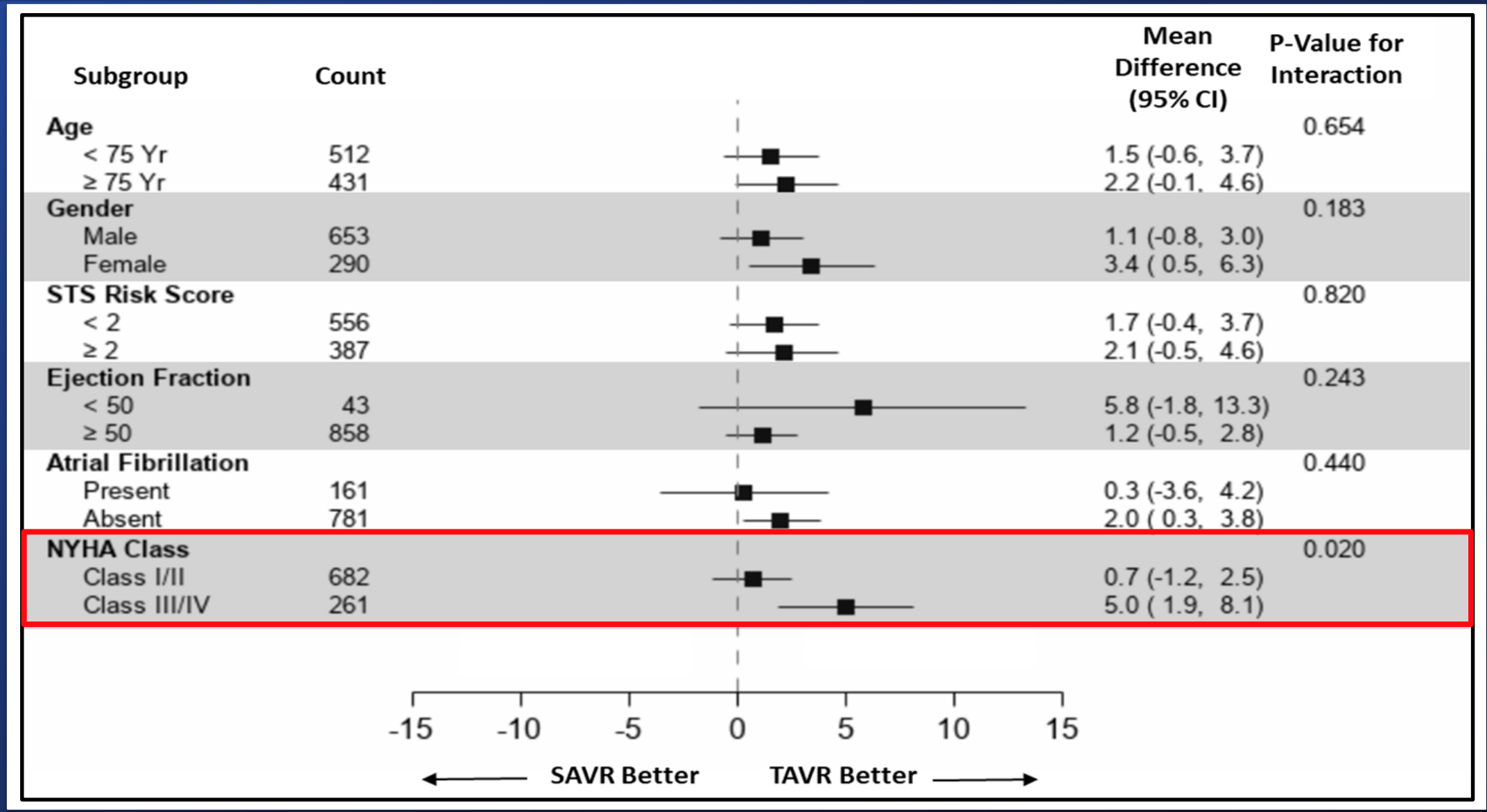
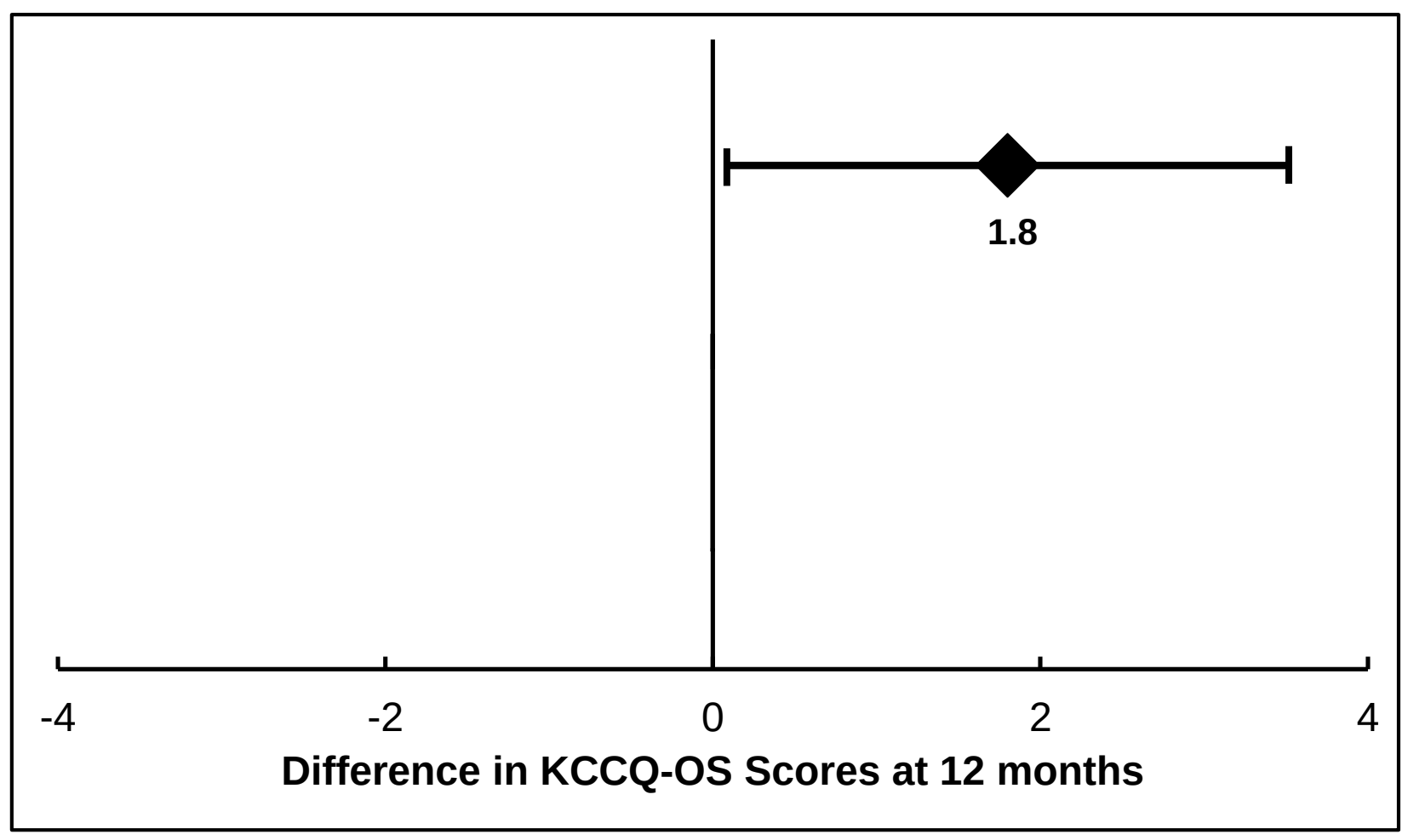


Exploratory Analysis:
Effect of Peri-Procedural Complications

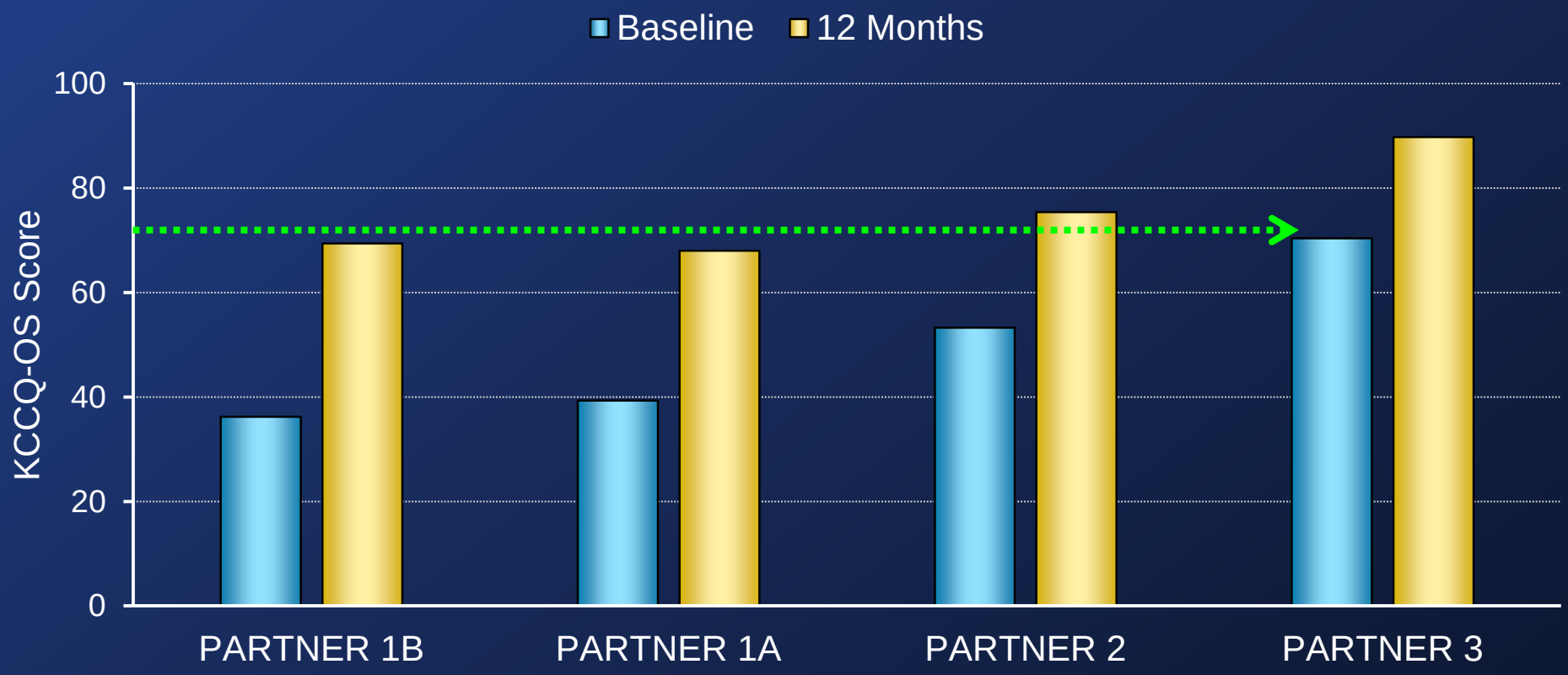


Limitations

- Results may not be generalizable to other types of TAVR prostheses, alternative access routes or other patients excluded from PARTNER 3 trial
- Trial was unblinded, which could have led to provider or subject bias regarding expectations of treatment outcome
- Durability of health status differences between the cohorts beyond 1 year is unknown

Summary

- Among patients with severe AS at low surgical risk, both TAVR and SAVR resulted in substantial health status benefits at 12 months despite most patients having NYHA class I or II symptoms at baseline



Summary

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- When compared with SAVR, TAVR was associated with significantly improved disease-specific health status not only at 1 month, but also at 6 and 12 months

- Although the late health status benefit of TAVR was numerically small, it represents a subset of individual patients who derived substantially greater health status benefit from TAVR than SAVR
  - *NNT = 19 to achieve a ≥ 20 point difference in 1 year KCCQ-OS*

- Exploratory analyses suggest that differences in peri-procedural complication rates also accounted for a modest proportion of the late health status benefits associated with TAVR

Conclusions

- Taken together with the clinical outcomes of the PARTNER 3 trial, these findings further support the use of TAVR in patients with severe AS at low surgical risk

- Longer term follow up is necessary (and on-going) to determine whether the health status benefits of TAVR at 1 year are durable

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JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Baron SJ, Magnuson EA, Lu M, Wang K, Chinnakondepalli K, Mack M, Thourani VH, Kodali S, Makkar R, Herrmann HC, Kapadia S, Babaliaros V, Williams M, Kereiakes D, Zajarias A, Alu MC, Webb JC, Smith CR, Leon MB, Cohen DJ on behalf of the PARTNER 3 Investigators. Health status after transcatheter vs. surgical aortic valve replacement in low-risk patients with aortic stenosis.
J Am Coll Cardiol 2019. *In Press.*

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Back-Up Slides

Substantial Improvement

Improvement in KCCQ-OS ≥ 20 points

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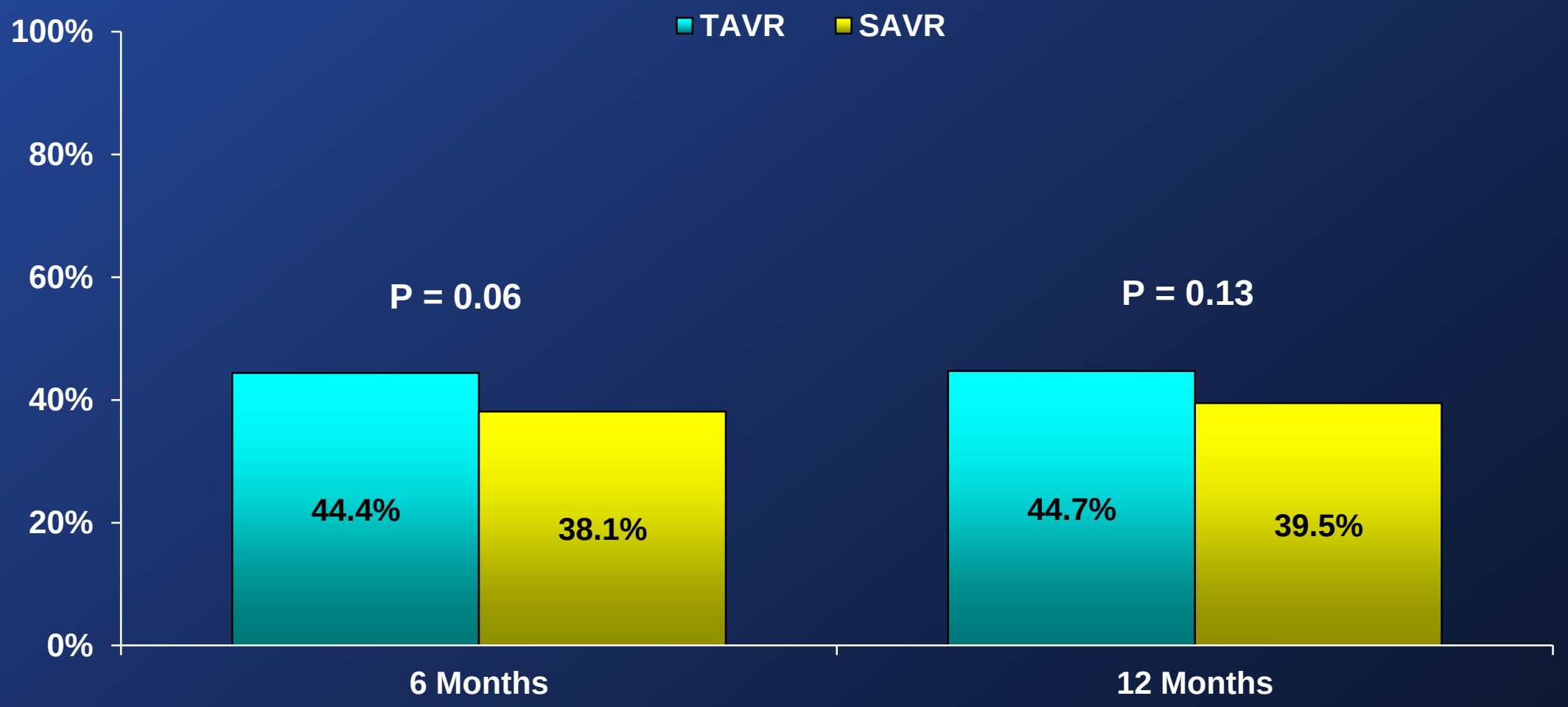

Excellent Outcome

Alive with KCCQ-OS ≥ 75 and No Decline in KCCQ-OS > 10 points

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