COAPT TRIAL

Health Status after Transcatheter Mitral-Valve Repair in Patients with Heart Failure and Secondary Mitral Regurgitation: Results from the COAPT Trial

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On behalf of the COAPT Investigators

COAPT (NCT01626079) is funded by Abbott

Disclosures

- The COAPT trial was sponsored by Abbott and designed collaboratively by the principal investigators and the sponsor.
- The health status analysis was conducted independently at Saint Luke's Mid America Heart Institute (Kansas City, Missouri).

- I have no disclosures other than support from a Career Development Grant Award (K23 HL116799) from the NIH/NHLBI.

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Background

- The 2 major goals in treating heart failure are to prolong survival and to improve health status (i.e., patients' symptoms, functional limitations, and quality of life)
- Recently, the COAPT trial demonstrated that treatment of patients with symptomatic heart failure and secondary (functional) MR with transcatheter mitral valve repair (TMVr) using MitraClip resulted in improved survival and fewer heart failure hospitalizations
- To fully define the benefits of TMVr, it is important to understand its impact on health status as well

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Objectives

1. To compare the early and late health status outcomes of TMVr versus standard care
2. To examine whether the health status benefit of TMVr differs according to patient factors
3. To explore the impact of differences in mortality on the health status benefits of TMVr

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Study Design

- Multicenter, open-label RCT in patients with heart failure and 3+ or 4+ secondary MR who remained symptomatic despite maximally-tolerated GDMT
- Enrollment between December 2012 and June 2017 at 78 sites in the US and Canada
- Follow-up through 2 years, with a minimum of 1 year of follow-up in all patients
- Crossover not permitted before 2 years

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Study Measures

- Patient-reported health status assessed at baseline and 1, 6, 12, and 24 months
  - Kansas City Cardiomyopathy Questionnaire
    - Scores 0-100; higher=better; MCID=5 points
  - SF-36 Physical and Mental Summary Scores
    - Higher=better; population mean 50 SD 10; MCID=2.5 points

- Primary outcome: KCCQ-overall summary score (KCCQ-OS) over 24 months

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Statistical Analysis

- Health status over 24 months compared between groups using piecewise linear regression
  - Differs from the NEJM analysis in which patients who died of HF had their KCCQ score imputed to the worst observed value
- Subgroups explored with interaction terms
  - Age, sex, COPD, cause of cardiomyopathy (ischemic vs. nonischemic), LV end diastolic volume index, effective regurgitant orifice (ERO), walk speed, ADL dependency
- Categorical analyses performed in order to integrate survival and health status
- Sensitivity analysis jointly modeled health status and survival using a Bayesian approach

Stone GW et al. N Engl J Med. 2018;379(24):2307-2318.

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Patient Characteristics

	TMVr (n=302)	Standard Care (n=309)
Age, years	71.7 ± 11.8	72.7 ± 10.6
Male	66.6%	61.8%
Ejection fraction, %	31.3 ± 9.1	31.2 ± 9.6
Diabetes mellitus	35.1%	39.5%
Creatinine, mg/dL	1.8 ± 1.2	1.8 ± 1.4
Atrial fibrillation	55.6%	50.8%
Chronic lung disease	23.5%	23.0%
Ischemic cardiomyopathy	60.9%	60.6%

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Baseline Health Status

	TMVr (n=302)	Standard Care (n=309)
KCCQ		
Overall Summary	53.2 ± 22.8	51.6 ± 23.3
Physical Limitations	58.3 ± 24.5	55.7 ± 26.0
Symptoms	60.3 ± 24.9	58.9 ± 24.7
Quality of Life	45.2 ± 25.6	44.7 ± 25.8
Social Limitation	49.5 ± 29.2	46.8 ± 30.4
SF-36		
Physical Summary	33.0 ± 9.0	32.6 ± 10.0
Mental Summary	46.7 ± 12.7	45.4 ± 13.0

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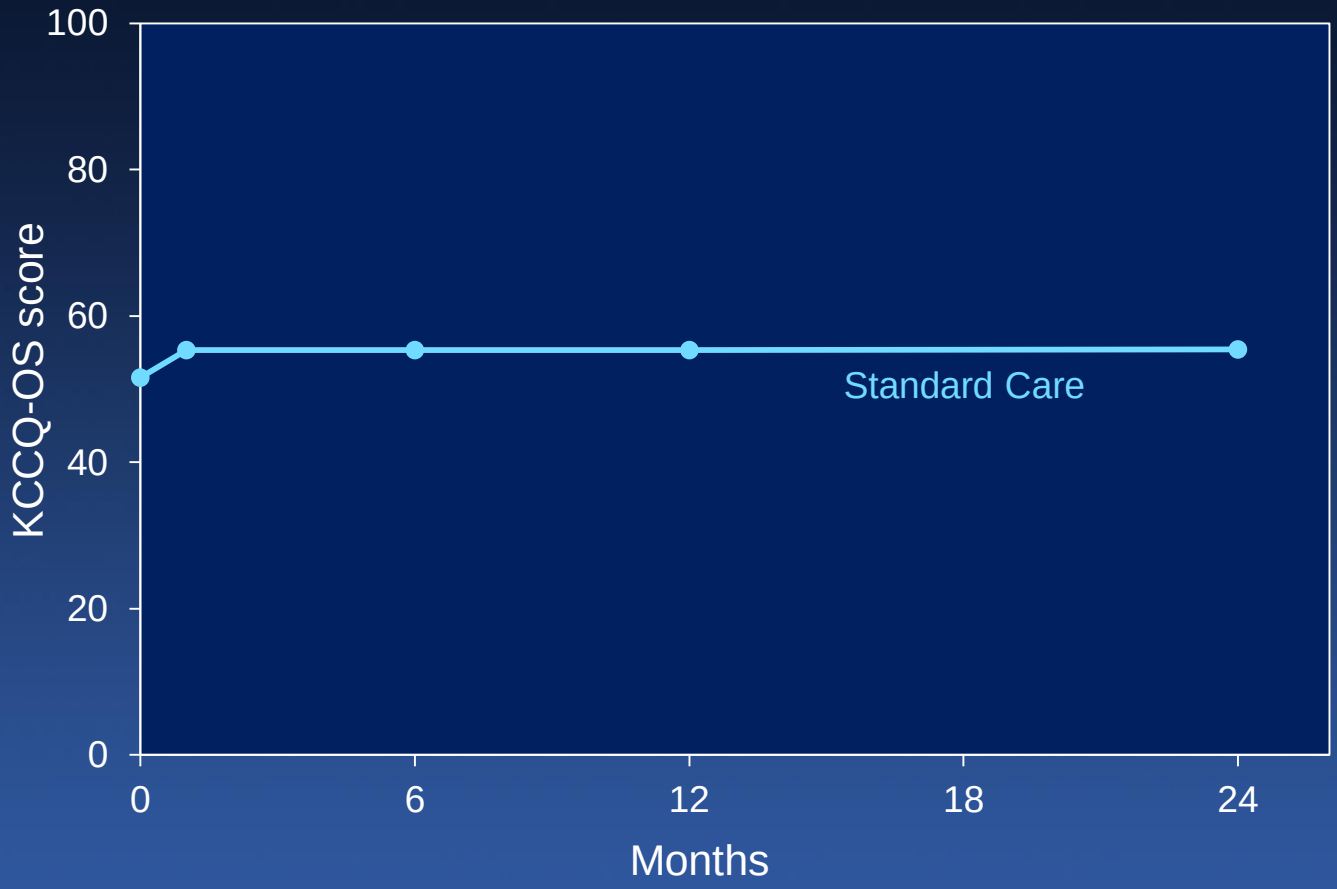
Primary Outcome: KCCQ-OS



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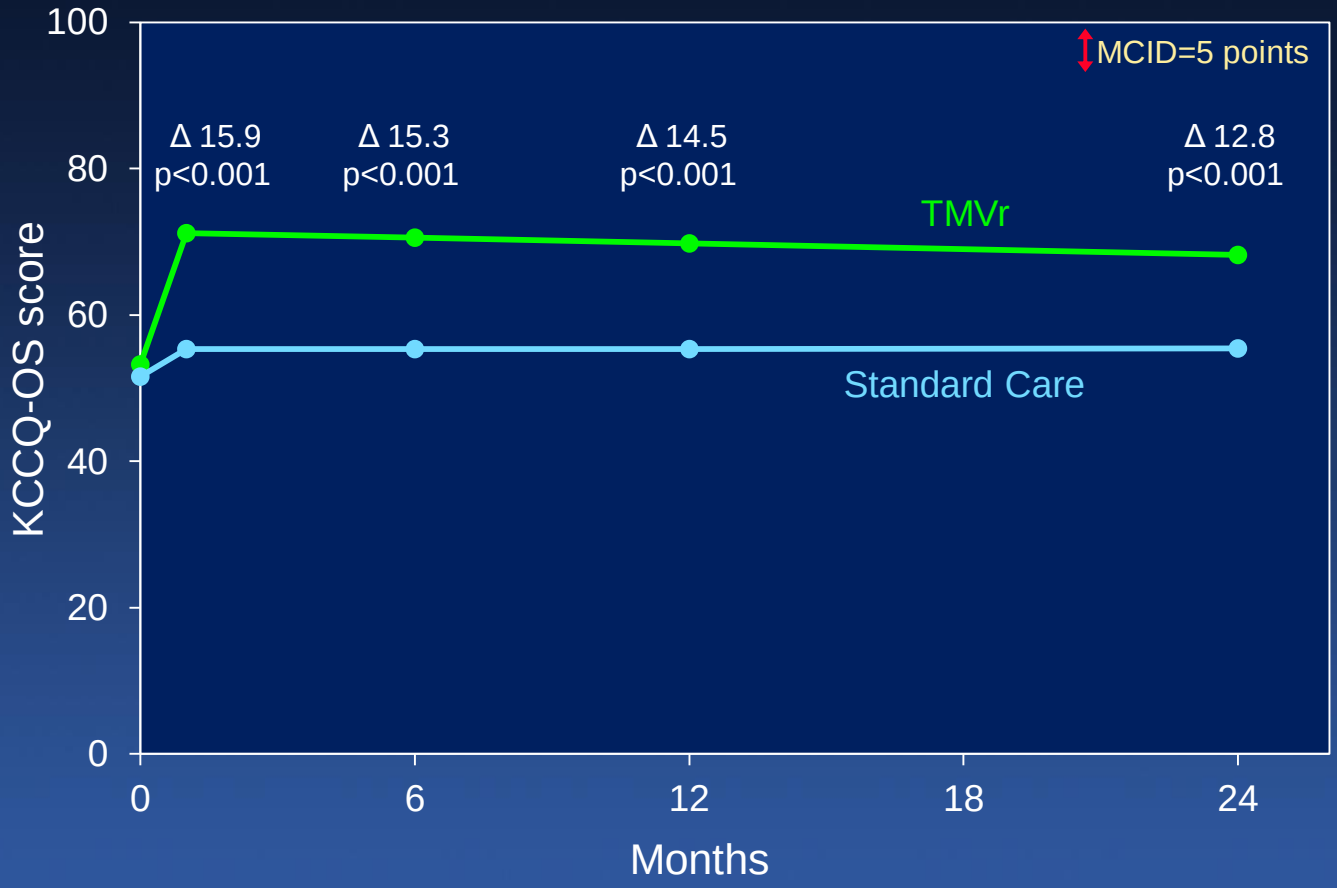
Primary Outcome: KCCQ-OS



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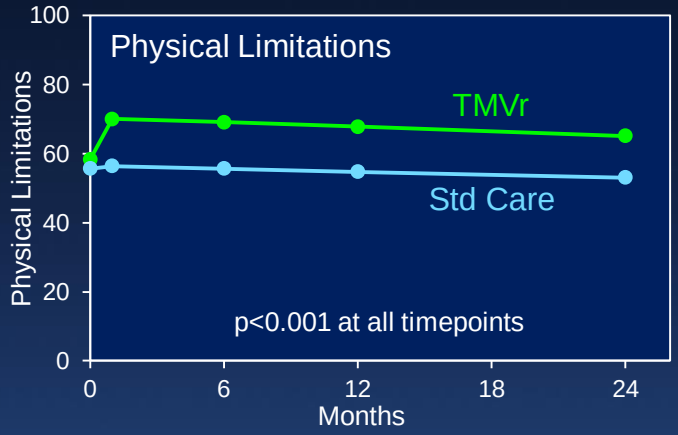
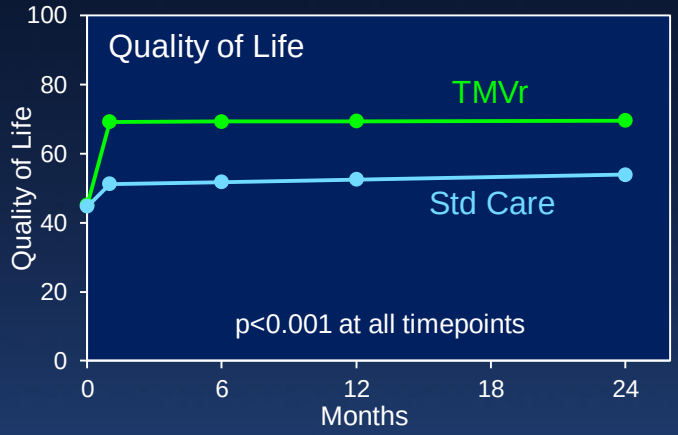
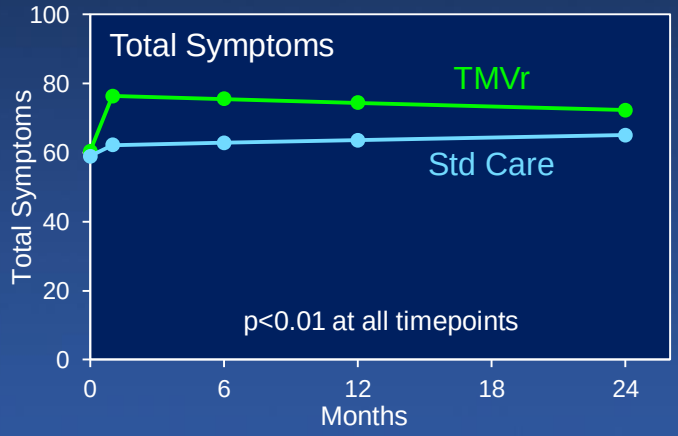
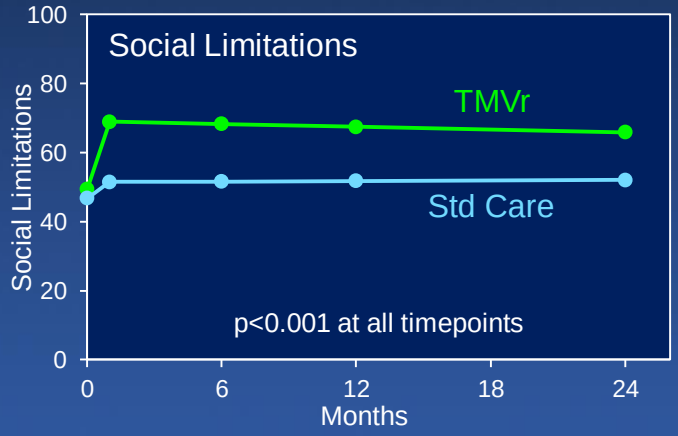
KCCQ Domains









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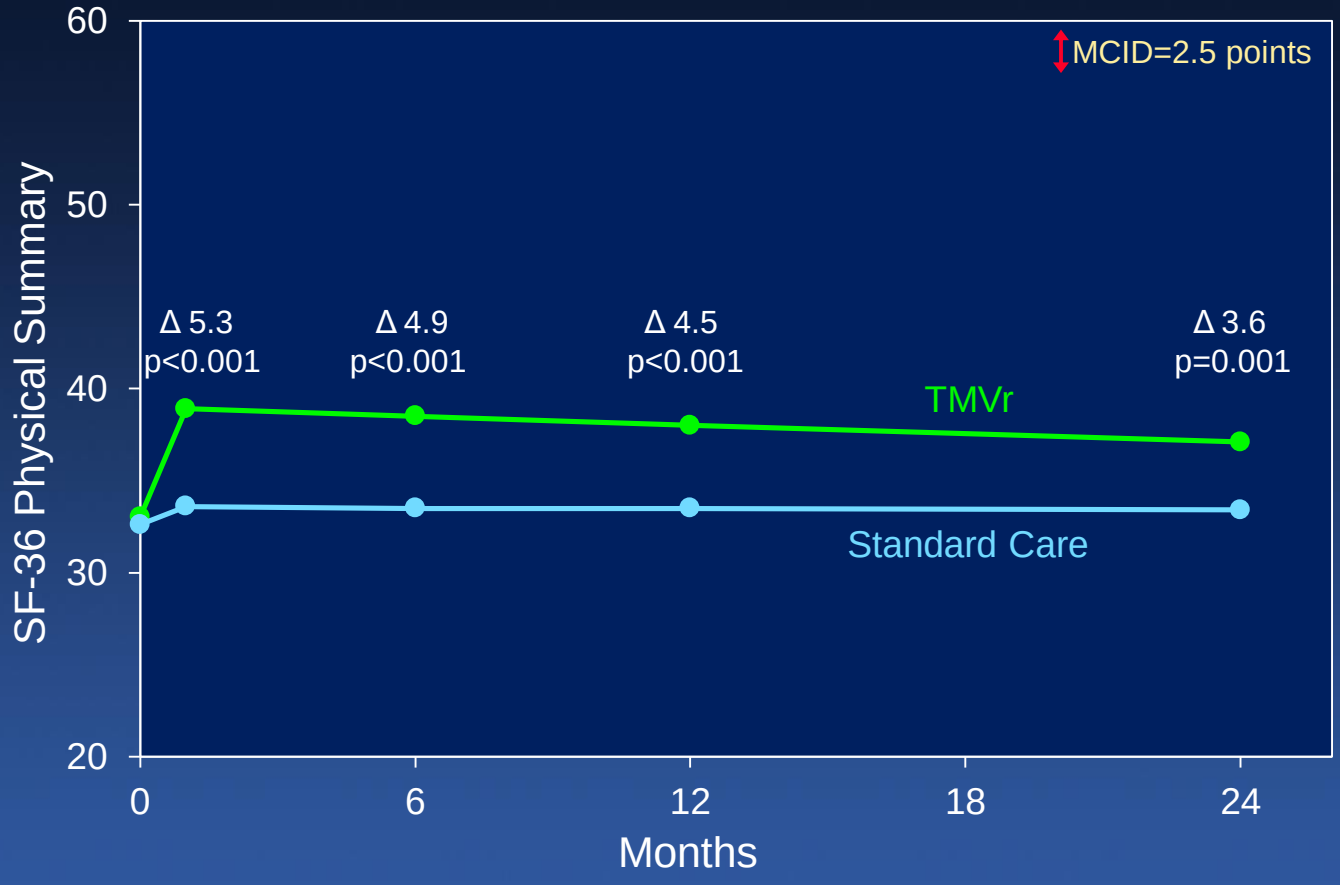
SF-36 Physical Summary



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SF-36 Mental Summary

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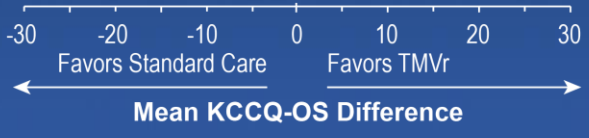
Subgroup Analyses

Category	n	Mean Difference (95% CI)	Interaction P-Value
Age			0.24
<74 years	297	14.7 (9.6, 19.8)	
≥74 years	317	14.1 (9.0, 19.2)	
Sex			0.67
Male	393	15.3 (10.8, 19.8)	
Female	221	12.8 (6.8, 18.8)	
COPD			0.33
Yes	143	14.0 (6.3, 21.8)	
No	471	14.4 (10.3, 18.5)	
Cardiomyopathy			0.02
Ischemic	373	18.3 (13.6, 22.9)	
Nonischemic	241	8.4 (2.7, 14.1)	
LVEDV Index			0.27
<94 mL/m²	269	14.3 (8.9, 19.7)	
≥94 mL/m²	298	15.3 (10.1, 20.4)	
ERO			0.64
<0.4 cm²	325	14.7 (9.8, 19.6)	
≥0.4 cm²	266	15.3 (9.8, 20.9)	
Walk Speed			0.90
<0.8 m/s	268	14.9 (9.3, 20.5)	
≥0.8 m/s	343	13.5 (8.9, 18.1)	
ADL Dependency			0.80
Yes	107	17.6 (8.6, 26.6)	
No	505	13.4 (9.6, 17.3)	



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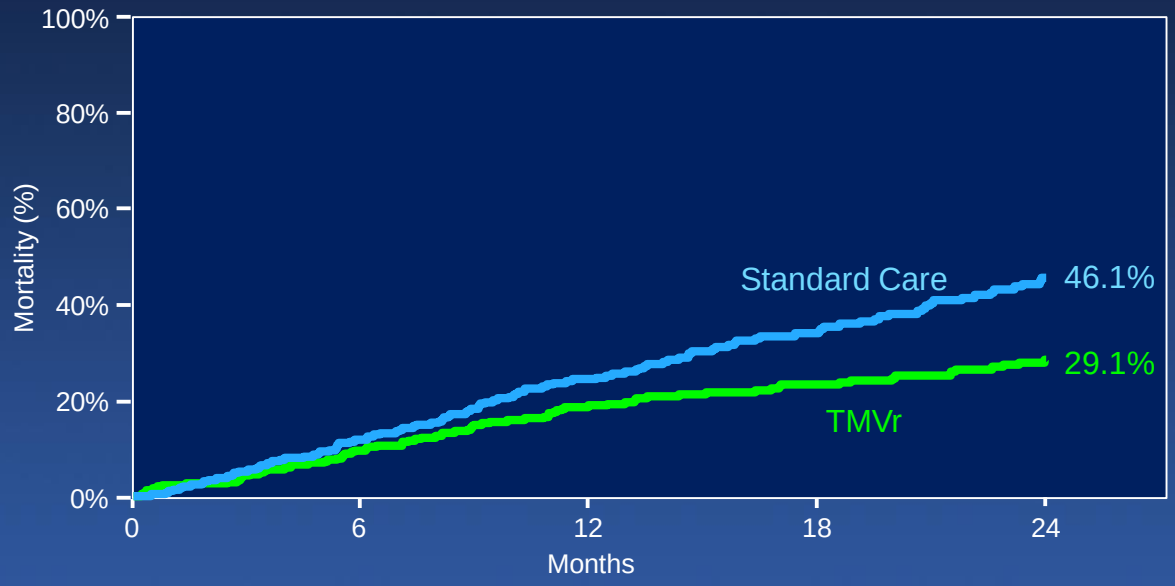
Challenges in Health Status Assessment

Impact of Differential Mortality

Health status can only be assessed in survivors, but those with worse health status are more likely to die



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Challenges in Health Status Assessment

Impact of Differential Mortality

- Strategies to address this challenge:
  - Categorical analyses that integrate survival and health status
  - Jointly modeling health status and mortality, which allows us to understand the expected health status benefit of TMVr assuming the patient survives

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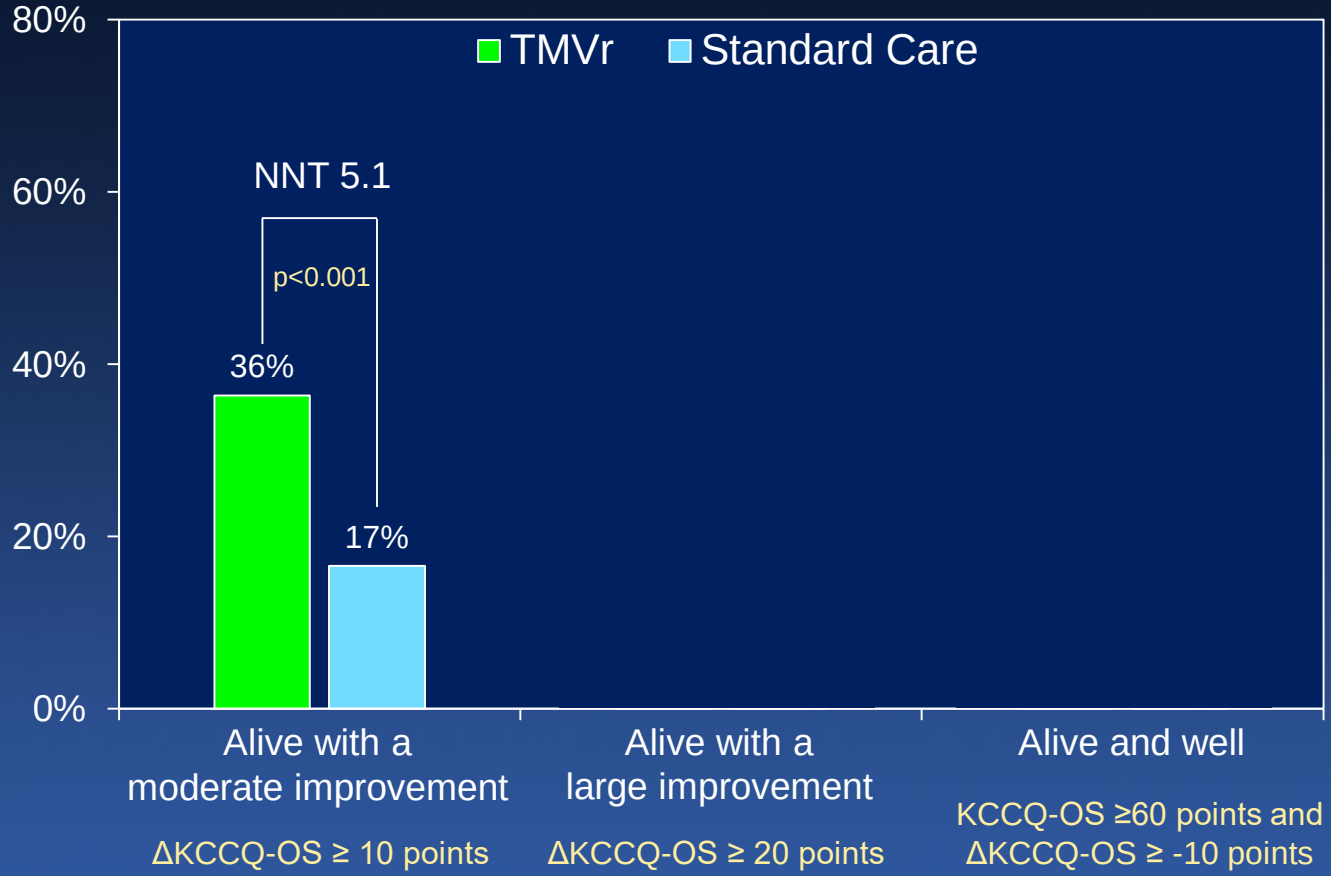
Categorical Outcomes at 24 Months



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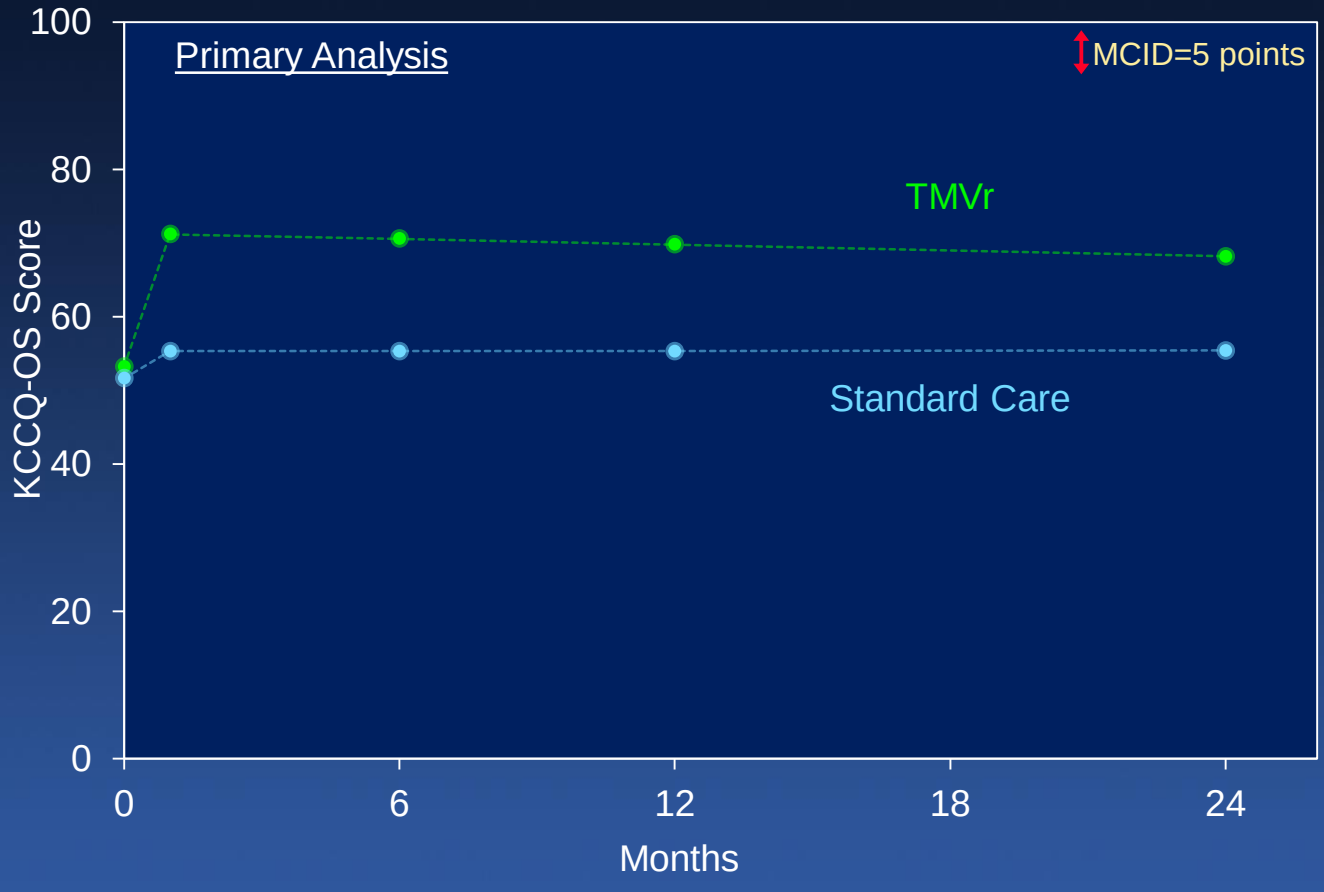
Joint Model Results: KCCQ-OS



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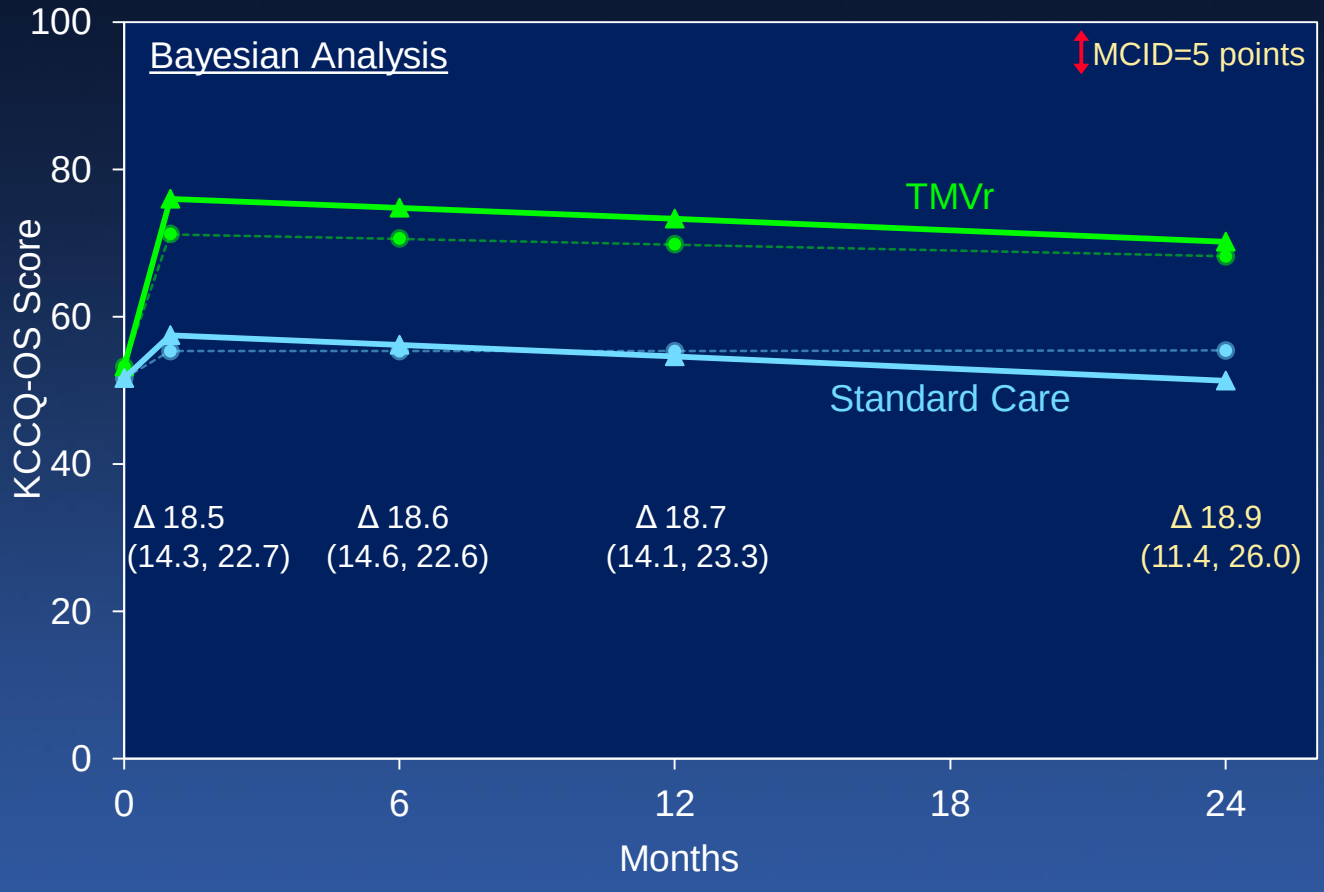
Joint Model Results: KCCQ-OS



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Limitations

- Non-blinded study/possibility of placebo effect
- Durability of the health status results beyond 24 months is unknown
- The health status results may not be generalizable beyond the strict inclusion/ exclusion criteria of the COAPT trial and outside of experienced centers and operators

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Summary

- In patients with heart failure and 3+ or 4+ secondary MR, TMVr with MitraClip provided substantial benefits in terms of symptoms, functional status, and quality of life
- The difference in health status between groups was moderately large, fully evident by 1 month, and generally sustained through 24 months
- The health status benefit of TMVr was also consistent across most key subgroups

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Conclusion

Considering the previously reported benefits of TMVr on survival and heart failure hospitalization, these health status results further support the use of MitraClip for patients with heart failure and 3+ or 4+ secondary MR who remain symptomatic despite maximally-tolerated GDMT

Acknowledgments

- HETA/Outcomes group at MAHI: David Cohen, Khaja Chinnakondepalli, Kaijun Wang, Elizabeth Magnuson, Suzanne Baron, John Spertus
- COAPT PIs and investigators: William Abraham, JoAnn Lindenfeld, Michael Mack, Gregg Stone, Saibal Kar, D. Scott Lim, Jacob Mishell, and others
- Abbott team: Julie Prillinger, Scott Goates
- COAPT patients

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. ■, NO. ■, 2019

PUBLISHED BY ELSEVIER

Health Status After Transcatheter Mitral-Valve Repair in Heart Failure and Secondary Mitral Regurgitation

COAPT Trial

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ABSTRACT

BACKGROUND In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, transcatheter mitral valve repair (TMVr) led to reduced heart failure (HF) hospitalizations and improved survival in patients with symptomatic HF and 3+ to 4+ secondary mitral regurgitation (MR) on maximally-tolerated medical therapy. Given the advanced age and comorbidities of these patients, improvement in health status is also an important treatment goal.

Back-up slides

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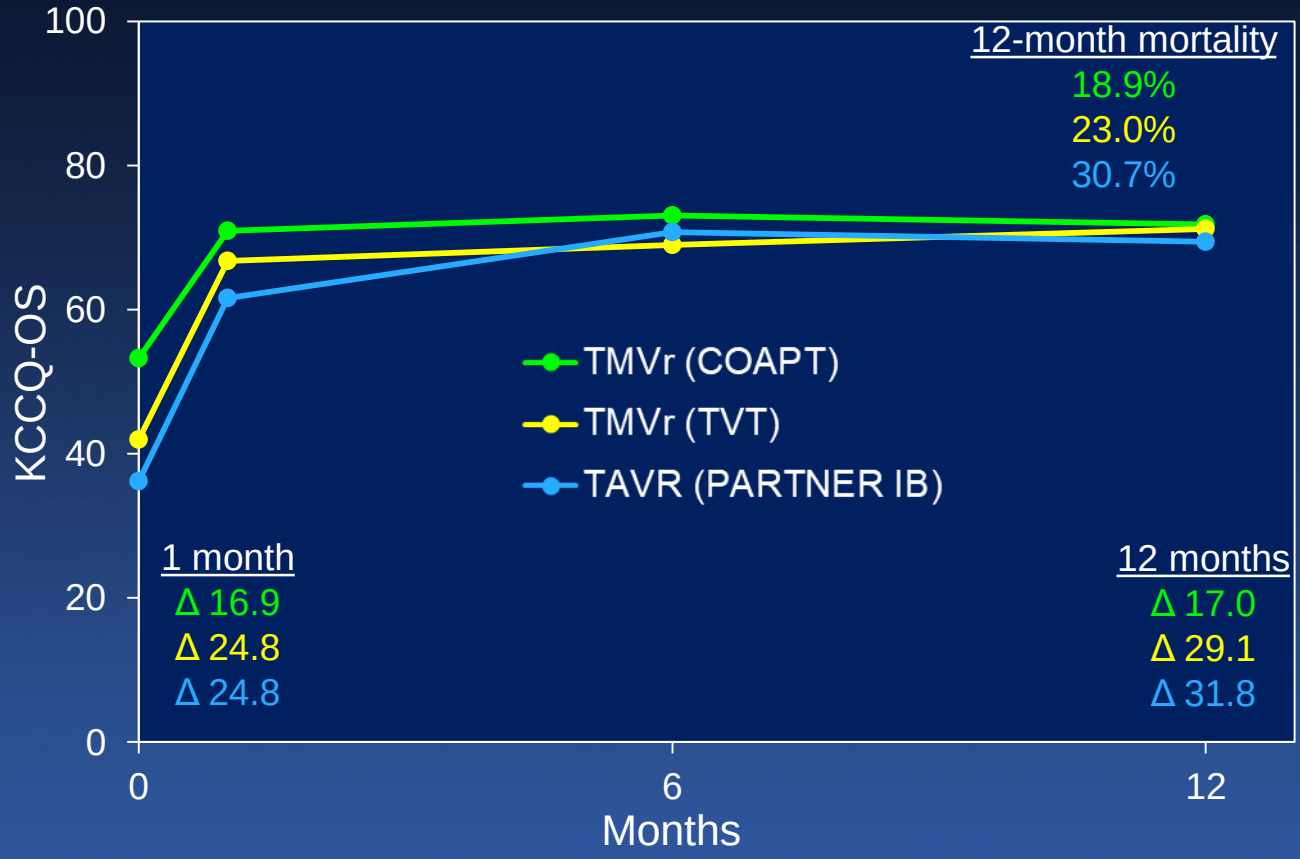
Health Status in COAPT in Perspective



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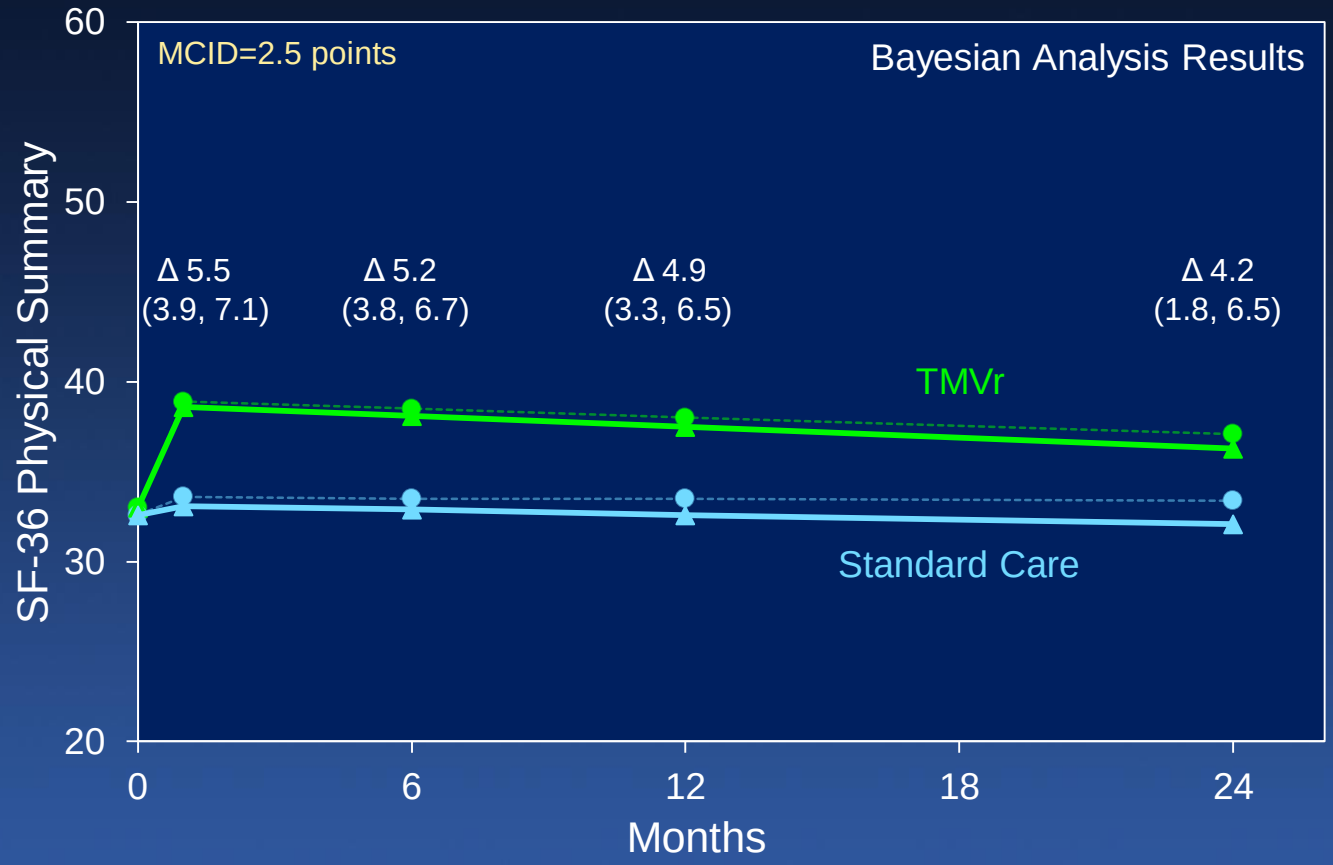
SF-36 Physical Summary



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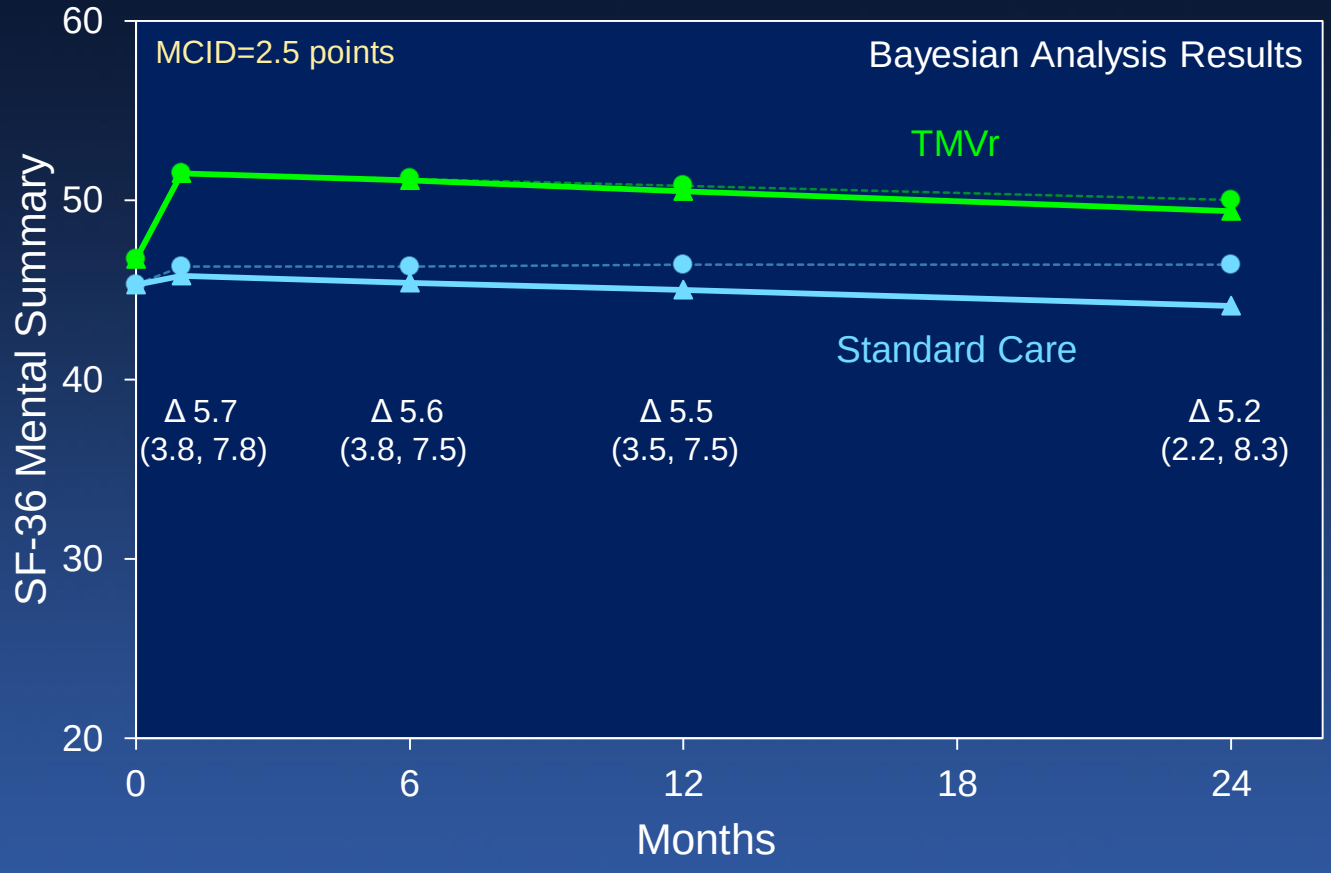
SF-36 Mental Summary



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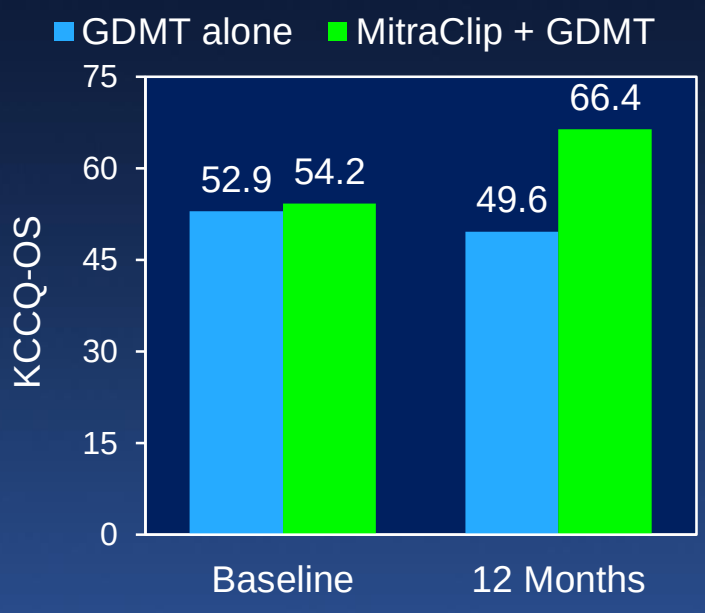
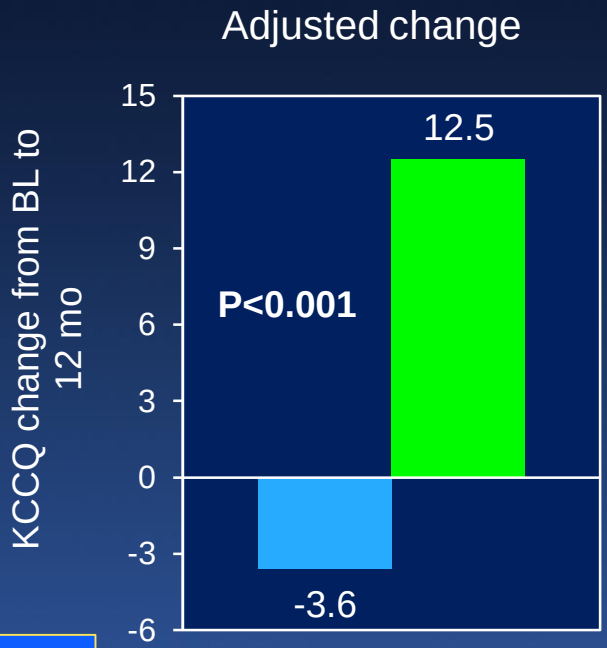
KCCQ from Baseline to 12 Months

Main COAPT analysis





KCCQ scores for patients who died of heart failure were imputed as the worst observed KCCQ score

Stone GW et al. N Engl J Med. 2018;379(24):2307-2318.

TVT Health Status Results

Factors associated with 30-day KCCQ-OS after TMVr		
	Estimate (95% CI)	**P-value**
Baseline KCCQ-OS (per 10-points)	3.9 (3.6 to 4.2)	<0.001
Age (per 5-years)	-0.5 (-1.0 to -0.0)	0.030
Hemoglobin (per 1 g/dL)	0.6 (0.1 to 1.1)	0.018
Atrial fibrillation or flutter	-2.2 (-3.7 to -0.6)	0.007
Severe chronic lung disease	-3.9 (-6.2 to -1.5)	0.001
Home oxygen use	-2.7 (-4.9 to -0.4)	0.021
Permanent pacemaker	-2.1 (-3.7 to -0.4)	0.013
Prior CABG	2.0 (0.3 to 3.7)	0.022

Factors in the model that were not significantly associated with QOL (p>0.05): sex, race, BSA, prior MI, PCI, PAD, LV EF, prior stroke, current smoker, diabetes, GFR, current dialysis, moderate/severe aortic insufficiency, moderate/severe tricuspid insufficiency, acuity of case

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KCCQ Domain	Mean Between Group Difference (95% CI)	P-value
Physical Limitations		
1 month	13.7 (9.9, 17.5)	<0.001
6 months	13.3 (9.8, 16.9)	<0.001
12 months	12.9 (9.1, 16.8)	<0.001
24 months	12.1 (6.3, 18.0)	<0.001
Total Symptoms		
1 month	14.2 (10.6, 17.8)	<0.001
6 months	12.7 (9.4, 15.9)	<0.001
12 months	10.9 (7.4, 14.3)	<0.001
24 months	7.3 (2.1, 12.5)	0.006
Quality of Life		
1 month	18.0 (14.0, 22.0)	<0.001
6 months	17.5 (13.8, 21.2)	<0.001
12 months	16.9 (12.9, 20.9)	<0.001
24 months	15.7 (9.6, 21.8)	<0.001
Social Limitation		
1 month	17.5 (12.8, 22.2)	<0.001
6 months	16.7 (12.4, 21.0)	<0.001
12 months	15.8 (11.1, 20.4)	<0.001
24 months	13.9 (6.8, 20.9)	<0.001

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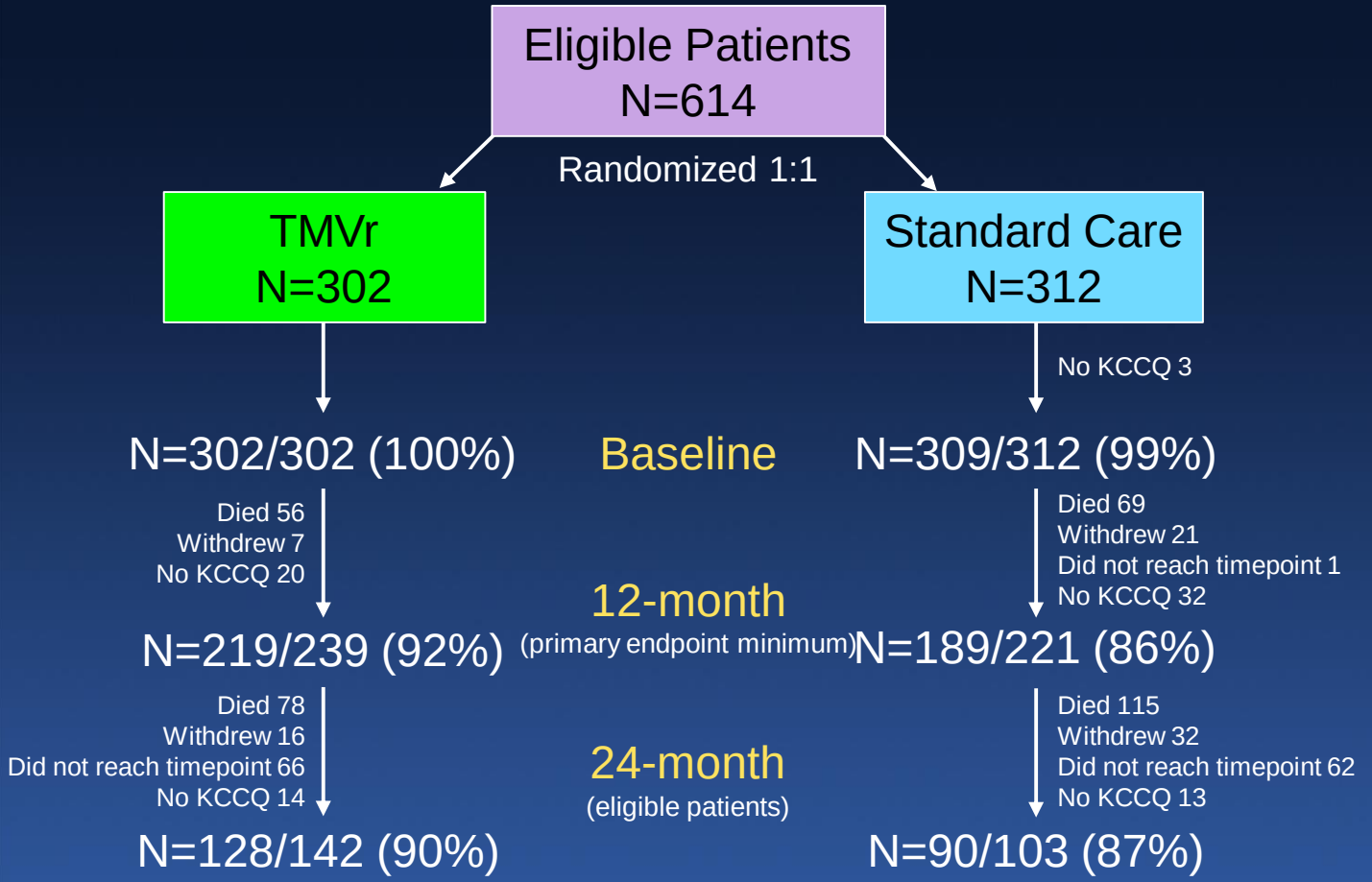
Eligible Patients
N=614
Randomized 1:1
TMVr
N=302
Standard Care
N=312
No KCCQ 3
N=302/302 (100%)
Baseline
N=309/312 (99%)
Died 56
Withdrew 7
No KCCQ 20
Died 69
Withdrew 21
Did not reach timepoint 1
No KCCQ 32
12-month
(primary endpoint minimum)
N=219/239 (92%)
N=189/221 (86%)
Died 78
Withdrew 16
Did not reach timepoint 66
No KCCQ 14
Died 115
Withdrew 32
Did not reach timepoint 62
No KCCQ 13
24-month
(eligible patients)
N=128/142 (90%)
N=90/103 (87%)

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Key Inclusion/Exclusion Criteria

Key Inclusion Criteria

1. LVEF 20%-50% and LVESD ≤70 mm
2. NYHA II-IVa despite maximally-tolerated GDMT and CRT (if indicated)
3. Not appropriate for mitral valve surgery by local heart team assessment

Key Exclusion Criteria

1. ACC/AHA stage D HF, hemodynamic instability, or cardiogenic shock
2. Untreated CAD requiring revascularization
3. COPD requiring continuous home oxygen or chronic oral steroid use
4. Severe pulmonary hypertension or right ventricular dysfunction
5. Life expectancy <12 months due to non-cardiac conditions