Health-Related Quality of Life and Functional Capacity Outcomes Post Transcatheter Aortic Valve Replacement (TAVR): A Systematic Review and Meta-Analysis

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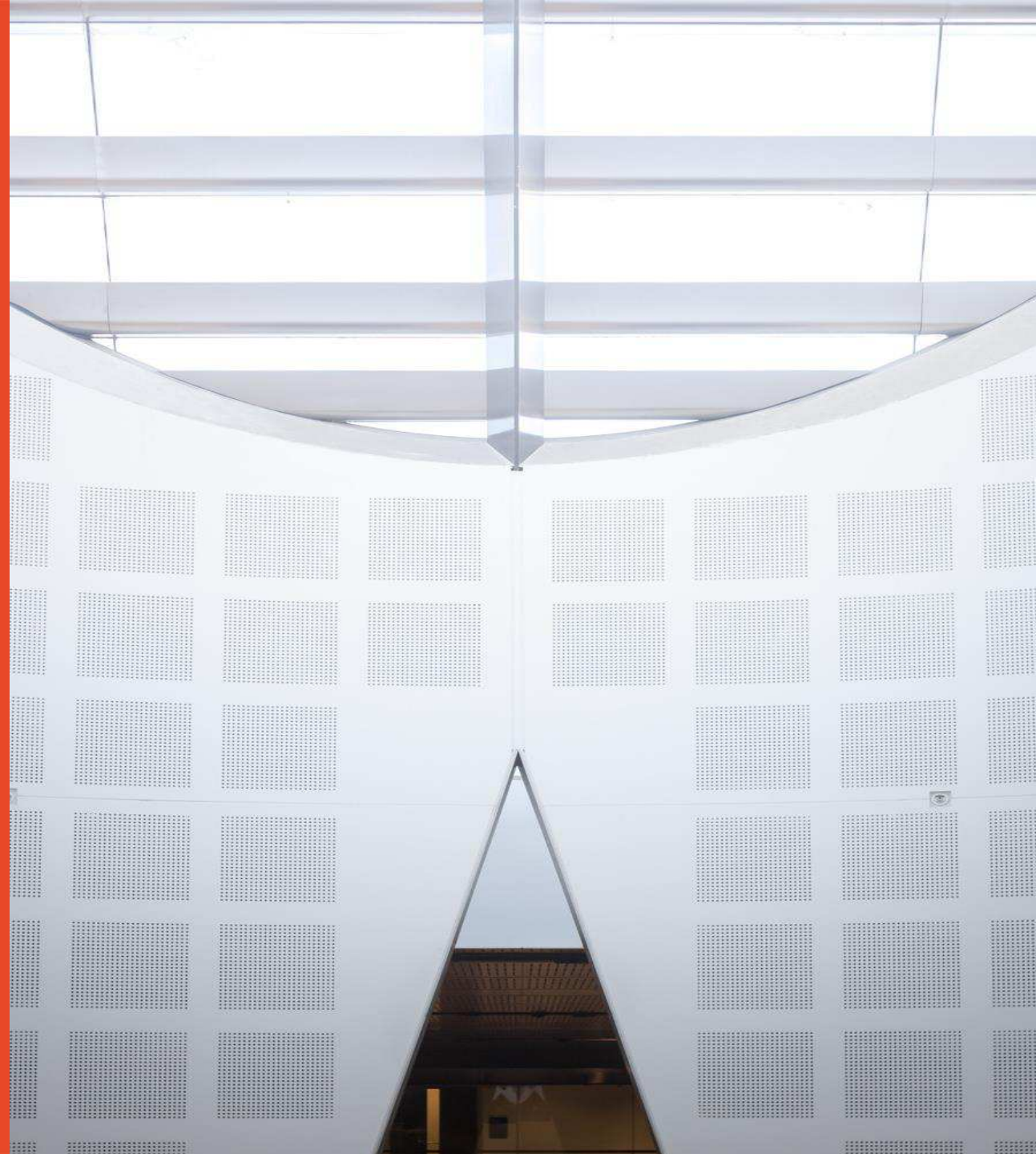
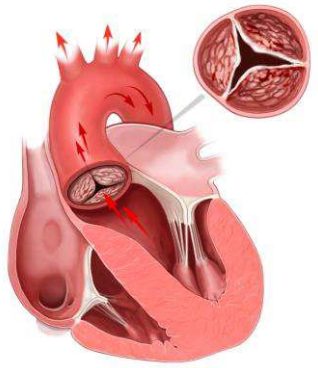


Background

Aortic stenosis (AS) is one of the most common heart valve diseases globally

- AS is the narrowing of the aortic valve opening, impeding delivery of blood from the heart to the body.
- Prevalence of AS increases with age (almost 10% in 80-89 year olds)[1].
- Symptoms of AS include angina, syncope, and those of heart failure (primarily dyspnoea).
- AS will eventually lead to death if treatment not provided.

  The PARTNER trial – Cohort B, reported a mortality rate of 50.7% within one year[2].



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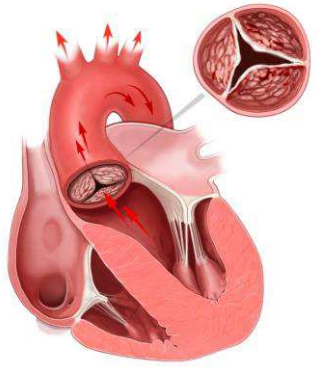
Background

Traditional treatment for severe AS is surgical valve replacement (SAVR), or medical treatment alone in high-risk patients

- With SAVR, patients >80yrs old mortality increases sharply[3].
- Older, higher-risk surgical patients can often be predisposed to a delayed recovery period, increased complications and cognitive decline post operatively (SAVR).
- Conservative management associated with a poor prognosis amongst high-risk, severe AS patients.
- A new approach to Aortic Valve Replacement was required.



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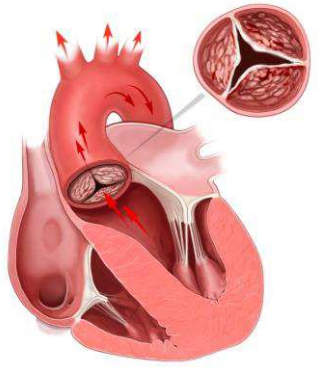
Background

An effective contemporary treatment alternative to SAVR for high-risk patients is TAVR (Transcatheter Aortic Valve Replacement)

- Minimally invasive, percutaneous insertion of a bio-prosthetic valve directly in position of the native stenosed aortic valve (femoral approach common)
- Reduced procedural time – usually 1-2 hours, less anaesthetic, smaller wounds, less pain and shorter recovery time
- Compared to SAVR, TAVR patients have lower mortality in the short term (1yr 14.2% TAVR vs 19.1% SAVR) and equivalent mortality at 5 years[4,5].



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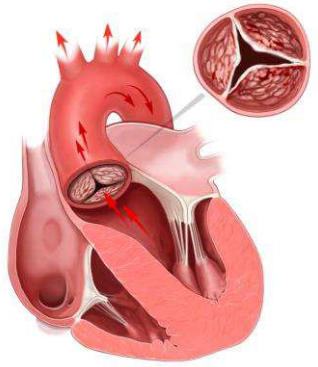
Background

Knowledge Gaps in Cardiovascular Care of the Older Adult Population

- Recent TAVR vs SAVR studies focused on mortality rate and post operative complication outcomes.
- Older patients may place greater value on functional capacity and quality of life outcomes, than longevity[6].
- Since initial TAVR in 2002 >150,000 cases worldwide[7].
- Limited comprehensive evidence in TAVR, for key patient outcomes such as quality of life, physical function, and maintenance of independence.



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Health-Related Quality of Life (HRQoL) and Functional Capacity Outcomes Post Transcatheter Aortic Valve Replacement (TAVR): A Systematic Review and Meta-Analysis

Methods

Aim: to perform a systematic search and meta-analysis to describe changes in functional capacity and HRQoL outcomes for TAVR patients.

Keywords: Transcatheter * Aortic Valve * Quality of Life * Functional Assessment * ADL

Inclusion Criteria:

1) included **TAVR patients**

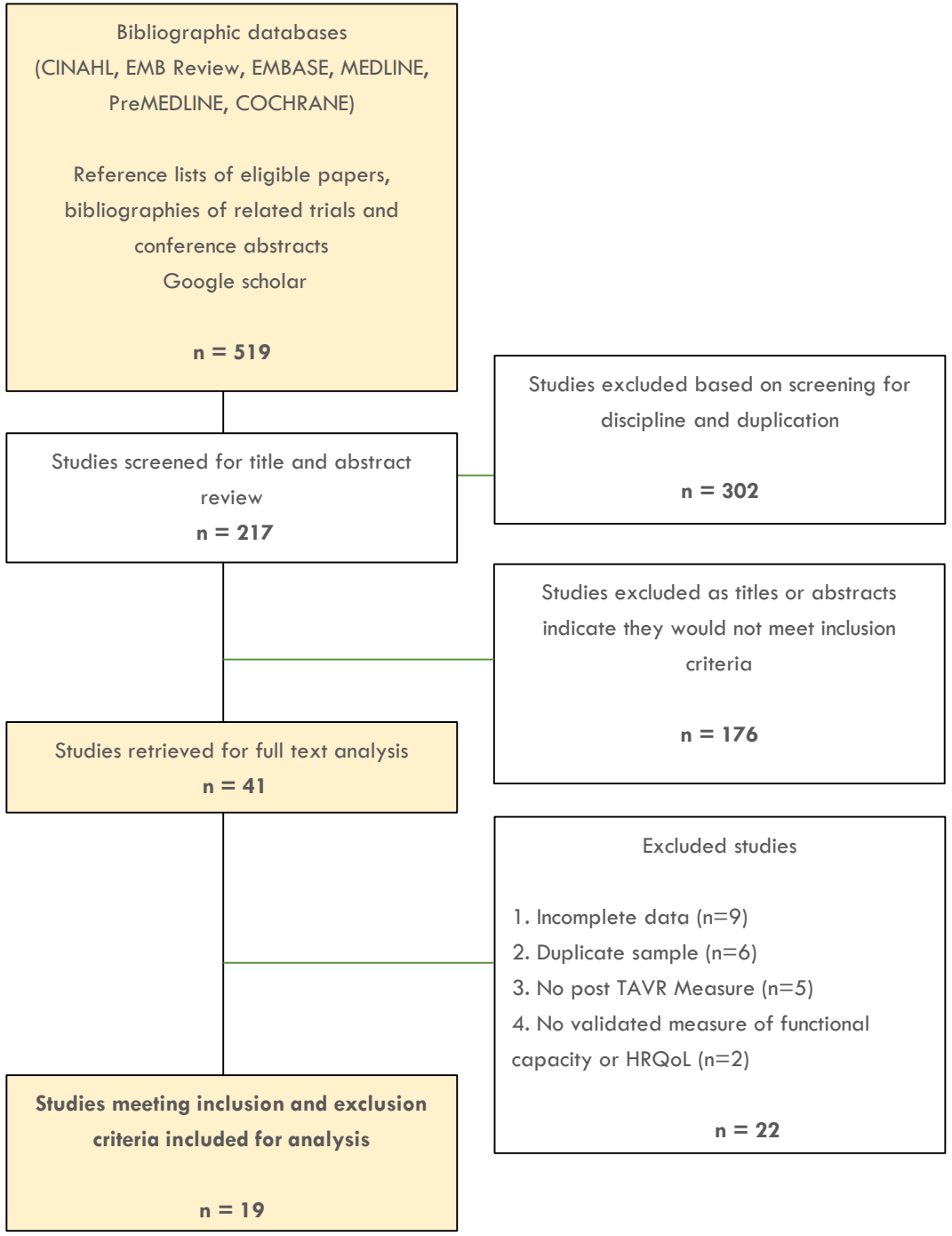
2) reported **at least one measure of functional capacity** (objective or self-reported) and/or **quality of life**

3) reported the measure(s) both **pre and post TAVR**

(minimum 1m and up to 12m post)

4) used **validated and reliable tools** for assessing functional capacity and/or quality of life, in patients with **cardiovascular disease**

Search Strategy



Results

Study Characteristics (n=19)

- **6 were multi-centre** and **13 were single site**
- **13 were observational, 5 RCT's** and **1 registry**
- Europe (n=13), the Middle East (n=1), North America (n=5) and Australasia (n=1).
- Total sample was **2645 patients,** with study sample size ranging from n=36 to n=484.
- Participants had a **mean age of 81.7±2.1** years (78–86 years) and **52%±8.8 were females**
- A **range of measures of functional capacity and HRQoL** were used. 5 studies used 6MWT and 3 used DASI, 9 used SF12/36, 6 used EQ5D, and lastly 3 used MLHFQ and 4 KCCQ.

Results

Study Measures

Measure	Description	Range / Values	Clinically Meaningful Difference
SF36/SF12	36-Item / 12-Item Short Form Health Survey	**The Mental Component Summary (MCS) and the Physical Component Summary (PCS).** The score ranges 0-100, increasing values represent better HRQOL	≥2.5 points
EQ5D-Index (Utilities)	EuroQoL 5D, generic HRQoL index instrument	A single **index value obtained by combining and weighting these various dimensions of HRQoL.** The score ranges from 0.0–1.0, higher value represents increased HRQoL.	≥0.074 points
EQ5D-VAS	EuroQoL Visual Analogue Scale, rating health state	Respondents **rate their present health status using a scale** from 0 – 100, increasing values represent better HRQoL	≥8 points
MLHFQ	Minnesota Living With Heart Failure Questionnaire	Scoring system works inversely to the other tools, with a range 0 to 105, **decreasing values represent better HRQoL**	≤5 points
KCCQ-OS	The Kansas City Cardiomyopathy Questionnaire, overall summary.	Scores for each subscale and overall score, range from 0 to 100, **increasing values represent better HRQoL**	≥20 points
6MWT	Six-minute walk test, objective measure of physically capacity	**Distance measured in total metres achieved over six-minutes.** Increasing distance represents better physical walking capacity	≥50 metres
DASI	Duke Activity Status Index, functional capacity of patients with cardiovascular disease	**Each item is weighted by its known metabolic cost** and weights of positive terms, which are combined to provide a single score. The score ranges 0 to 58.2, increasing values represent better HRQoL	≥4 points

Results

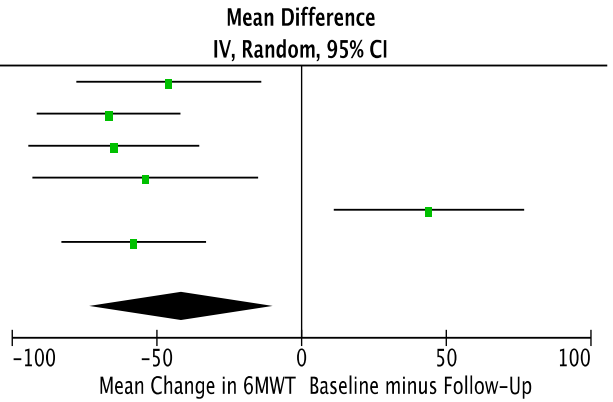
Functional Capacity improved significantly as measured by the 6-minute walk test (6MWT) and a clinically meaningful increase in ability to perform daily physical-based tasks (Duke Activity Status Index (DASI)

A **mean increase of 41.48m in 6MWT** (CI 9.69-73.28, p=0.01) and a **5.42 points mean increase was reported with DASI** (CI 3.16-7.68) p=<0.01).

	Baseline			Follow-Up				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bagur et al. (2011)	165.9	77.6	46	211.8	78.7	46	16.5%	-45.90 [-77.84, -13.96]
DeLarochellière et al. (2015) (anemia)	167.8	120.5	242	234.5	122.1	148	17.6%	-66.70 [-91.55, -41.85]
DeLarochellière et al. (2015) (no anemia)	220.5	116.5	137	285.4	112.2	98	16.9%	-64.90 [-94.46, -35.34]
Gotzmann et al. (2012)	213	131	112	267	165	112	15.2%	-54.00 [-93.02, -14.98]
Green et al. (2013) (fast walkers)	240	96	133	196	148	103	16.3%	44.00 [11.09, 76.91]
Green et al. (2013) (slow walkers)	72	34	133	130	126	103	17.6%	-58.00 [-83.01, -32.99]
Total (95% CI)			**803**			**610**	**100.0%**	**-41.48 [-73.28, -9.69]**

Heterogeneity: $Tau^2 = 1333.58$; $Chi^2 = 34.00$, df = 5 ($P < 0.00001$); $I^2 = 85\%$

Test for overall effect: Z = 2.56 (P = 0.01)



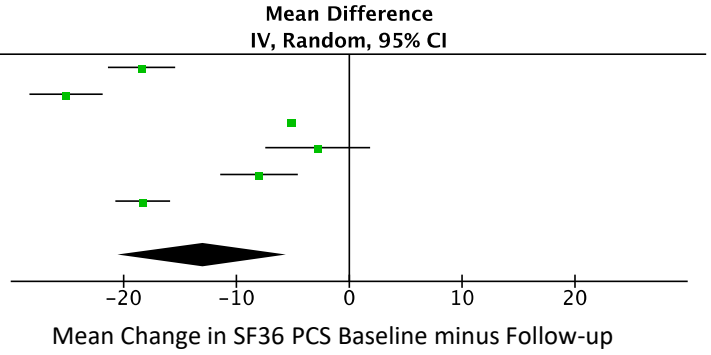
Results

HRQoL improved significantly and demonstrated a clinically meaningful difference post TAVR.

Short Form Health Surveys had similar increases in both for the **Physical Component Summary Score** (PCS), a **mean increase of 12.98 points,** (SF36) (CI 5.48-20.49, p=<0.01) and **by10.14 points** (SF12) (CI 4.20-16.09, p=<0.01) at follow-up. Mental Component Summary Score (MCS) improved slightly less but still significantly (SF36 a mean increase of 5.43 points (CI 0.88-9.99, p=<0.01) and SF12 by 5.95 points (CI 2.80-9.09, p=<0.01).

	Baseline			Follow-Up				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bekeredjia et al. (2010)	28.4	10	80	46.8	9.2	80	16.7%	-18.40 [-21.38, -15.42]
Georgiadou et al. (2011)	21.6	5.1	36	46.7	7.5	28	16.6%	-25.10 [-28.34, -21.86]
Krane et al. (2012)	31.8	0.9	106	36.9	1.1	106	17.2%	-5.10 [-5.37, -4.83]
Orvin et al. (2014)	35.3	9.5	36	38.1	10.6	36	16.1%	-2.80 [-7.45, 1.85]
Stortecky et al. (2012)	31.5	9	62	39.5	10	56	16.6%	-8.00 [-11.45, -4.55]
Taramasso et al. (2012)	31.9	8.8	100	50.2	8.7	100	16.9%	-18.30 [-20.73, -15.87]
Total (95% CI)			**420**			**406**	**100.0%**	**-12.98 [-20.49, -5.48]**

Heterogeneity: $Tau^2 = 85.44$; $Chi^2 = 331.45$, df = 5 (P < 0.00001); $I^2 = 98\%$
Test for overall effect: Z = 3.39 (P = 0.0007)



Mean Change in SF36 PCS Baseline minus Follow-up

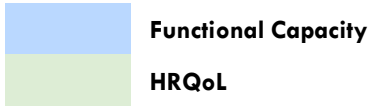
Results

HRQoL improvements were seen irrespective of the measure used and whether it was general or cardiac specific.

Cardiac-specific HRQoL as measured by the **MLFHQ improved with a decrease of 21.30 points** (CI 27.13-15.46), p=<0.01, which was clinically meaningful and the **KCCQ with a mean increase of 15.97 points** (CI 7.64-24.30), p=<0.01 post TAVR. In the more general **EQ5D questionnaire** statistically significant increases were seen in both elements, **the utilities score with a mean difference increase of 0.05 points**, (CI 0.01-0.10), p=0.03 and the **VAS a 13.81 point increase** (CI 9.28-18.34), p=<0.01, the latter being clinically meaningful.

Results Interpretation

Measure	Change	Post TAVR
6MWT	↑	>40m exercise capacity
DASI	↑	Personal Care, Walking, Housework, Recreational Activities
SF PCS	↑	Walking, Physical Capability, Accomplish More Activities
SF MCS	↑	Calmer, Desire to Engage in Activities, Less Worn Out, Decreased Anxiety
MLHFQ & KCCQ	↑	Improved HF symptoms, Exercise Capacity, More Control, Personal Care, Less Fatigue, Improved Social Interaction
EQ5D	↑	Walking, Personal Care, Overall General Health



Results

A high level of cross study heterogeneity was present.

For functional capacity analysis this ranged from I2 = 59% (DASI) to I2 = 85% (6MWT). Similar heterogeneity ranges were found in HRQoL outcome measures, with the lowest I2 = 55% (EQ5D utilities) to I2 = 98% (SF36 PCS component). The high levels of heterogeneity may reflect the range of studies included, with the **majority being single centre studies observational studies (68%)** compared with multi-site trials.

Discussion

- Post TAVR, patients had **significant improvement in functional capacity** of the 6-minute walk test and a meaningful increase in ability to perform daily physical-based tasks.
- **HRQoL improved consistently following TAVR** regardless of measure used.
- TAVR resulted in clinically meaningful increases in both the physical and mental HRQoL composite scores, however, **physical scores overall had greater improvements**.

Conclusion

- TAVR represents not only an increasingly viable but directly beneficial option for high-risk, severe AS patients.