



Do You Know What Quality of Life Means for Your Patients with Heart Failure?

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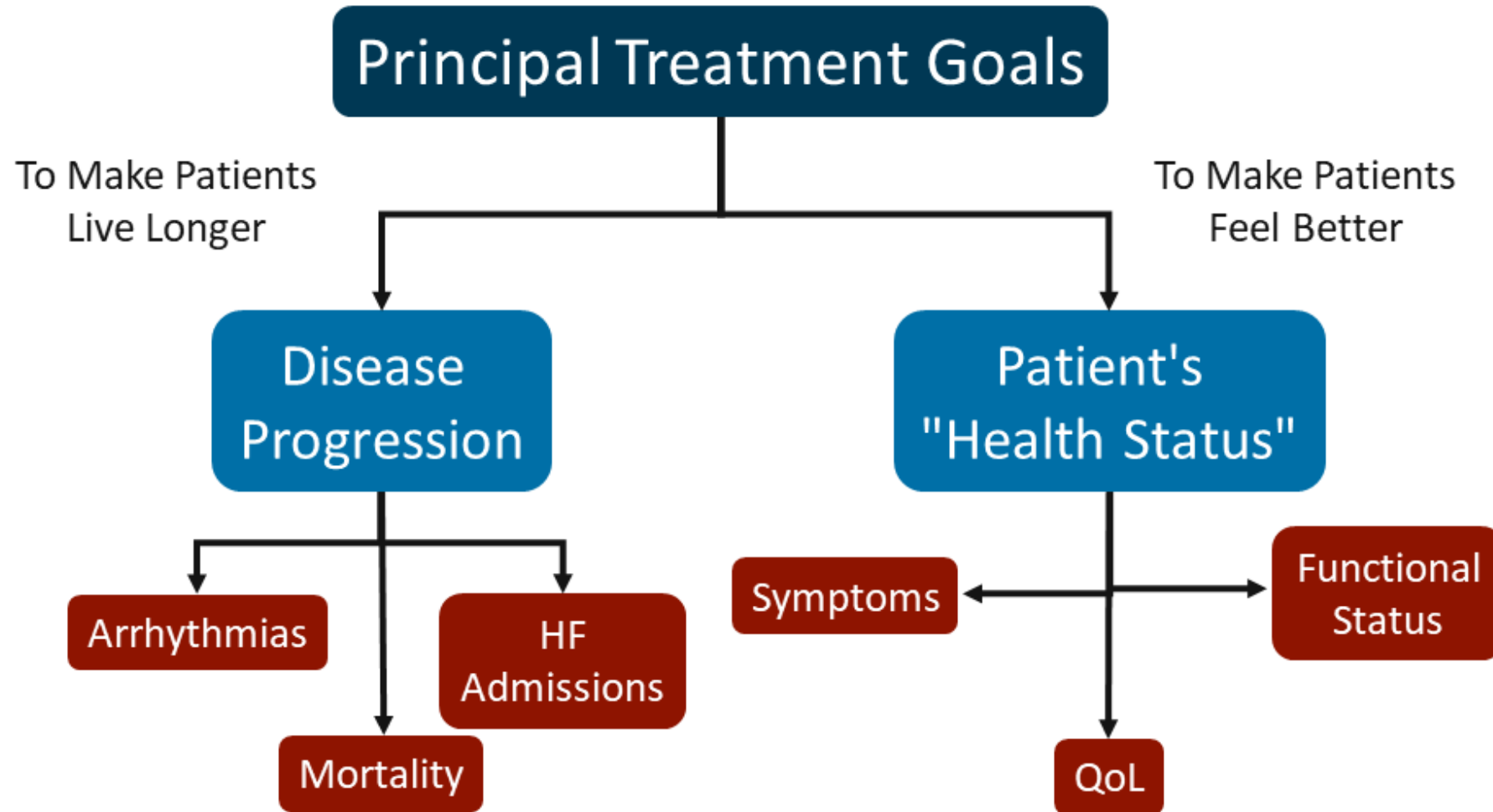
Speaker Disclosure

Dr. Jonathan Howlett

- **Relationships with commercial interests:**
 - **Grants/Research Support:** AstraZeneca, Merck, Servier, Pfizer, Novartis, Medtronic, Bayer
 - **Speakers Bureau/Honoraria:** Bayer, Servier, Boehringer Ingelheim, Novartis
 - **Consulting Fees:** General Electric, Government of Canada & Alberta, Novo Nordisk, AstraZeneca, Merck, Servier, Pfizer, Novartis, St Jude, Bayer
 - **Medical Advisory Board:** Cardiol



Treatment Goals for HF



Ponikowski P, et al. *Eur Heart J*. 2016;37:2129-2200; Yancy C, et al. *Circulation*. 2017;136:e137-e161; Pokharel Y, et al. *JAMA Cardiol*. 2017;2:1315-1321.

Selected therapies: Effect on HR QoL and 6 MWT in patients with HFrEF

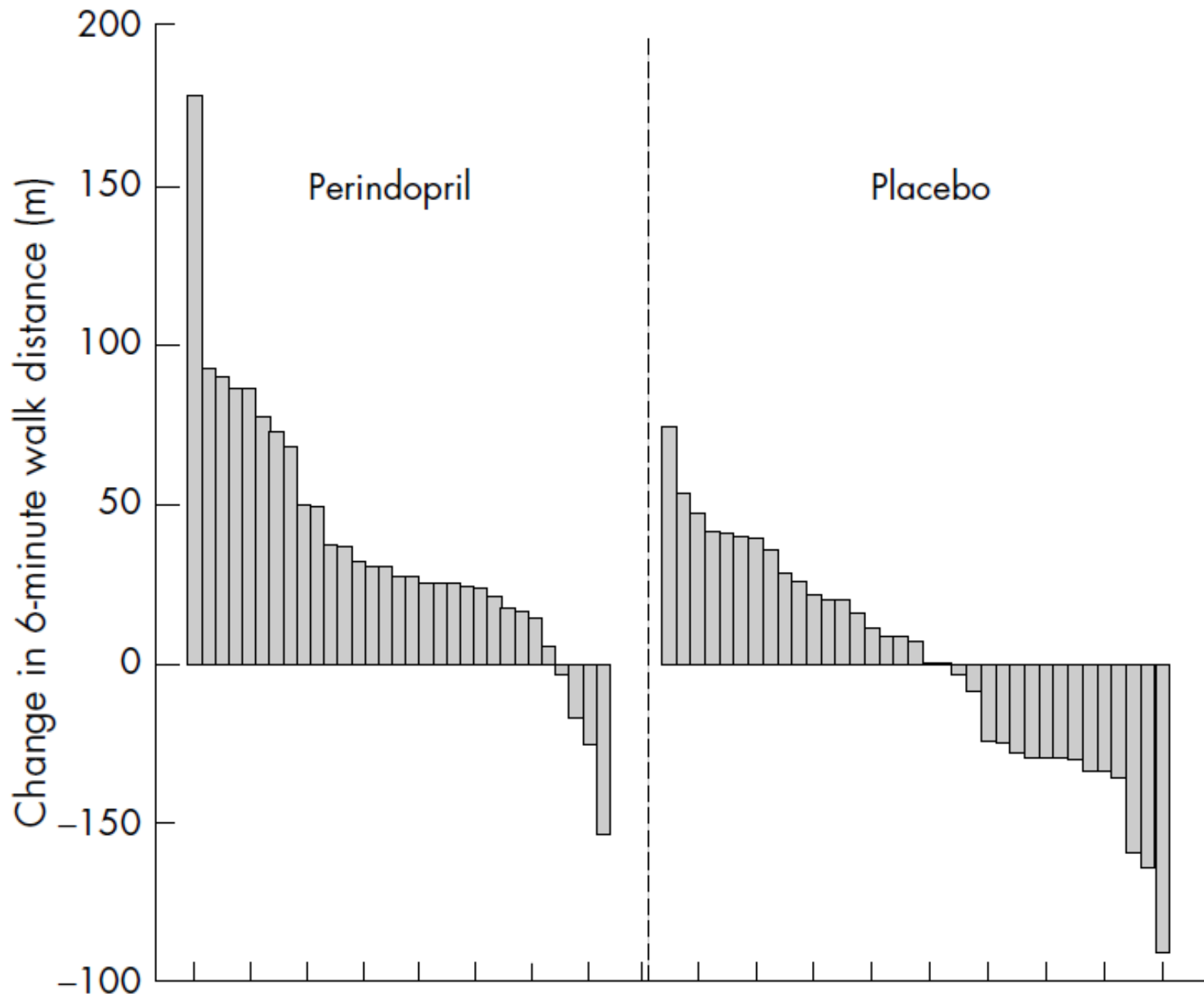
Therapy	Improved outcomes?	Improved symptoms?	Improved 6MWT?	Improved HRQoL?
ACE/ ARB	++	++		
Beta blockers	+++	++		
ARNi	+++	++		
MRA	+++	+		
SGLTi	+++	++		
Ivabradine	+	+++		
Hydralazine	+	+++		
Digoxin	+	++		
Vericiguat	+	+/-		
CRT	+++	++++		

J. Al

Study

Woodley
Waagstein
CIBIS-1
Fisher
ANZ
Bristow-1
Bristow-2
Packer
Metra
MERIT-HF
Eichhorn
Olsen
Krum
Colucci
Goldstein
Hulsman
Terzi
Hon
Witchitz
Cohn
Cice
Brehm
Blenkov
Sanderson-M
Sanderson-C

Overall (95% CI)
Random effects m



Weighted mean difference % Weight

-19.00 (-58.35, 20.35)	8.6
0.00 (-34.46, 34.46)	10.4
89.00 (-16.96, 194.96)	1.5
10.00 (-5.81, 25.81)	22.2
22.00 (-10.87, 54.87)	11.0
-60.00 (-124.66, 4.66)	3.8
0.00 (-36.35, 36.35)	9.6
2.00 (-49.53, 53.53)	5.6
-43.00 (-94.53, 8.53)	5.6
-10.00 (-26.66, 6.66)	21.5

r p= 0.730 heterogeneity p=0.117
eter p=0.492 heterogeneity p=0.140

beta-blockers had no effect on 6-min walk distance.

Selected therapies: Effect on HR QoL and 6 MWT in patients with HFrEF

Therapy	Improved outcomes?	Improved symptoms?	Improved 6MWT?
ACE/ ARB	++	++	+
Beta blockers	+++	++	No
ARNi	+++	++	?+
MRA	+++	+/-	No
SGLTi	+++	++	
Ivabradine	+	+++	
Hydralazine	+	+++	
Digoxin	+	++	
Vericiguat	+	+/-	
CRT	+++	++++	

Important inconsistencies

HF is associated with a high patient burden, and poorer HRQoL than other chronic diseases (including cancer)

HF signs and symptoms^{1,2} can **reduce mobility and impair daily functioning**³



Dyspnea



Fatigue



Trouble sleeping



Cough



Ascites



Swelling



Fluid retention



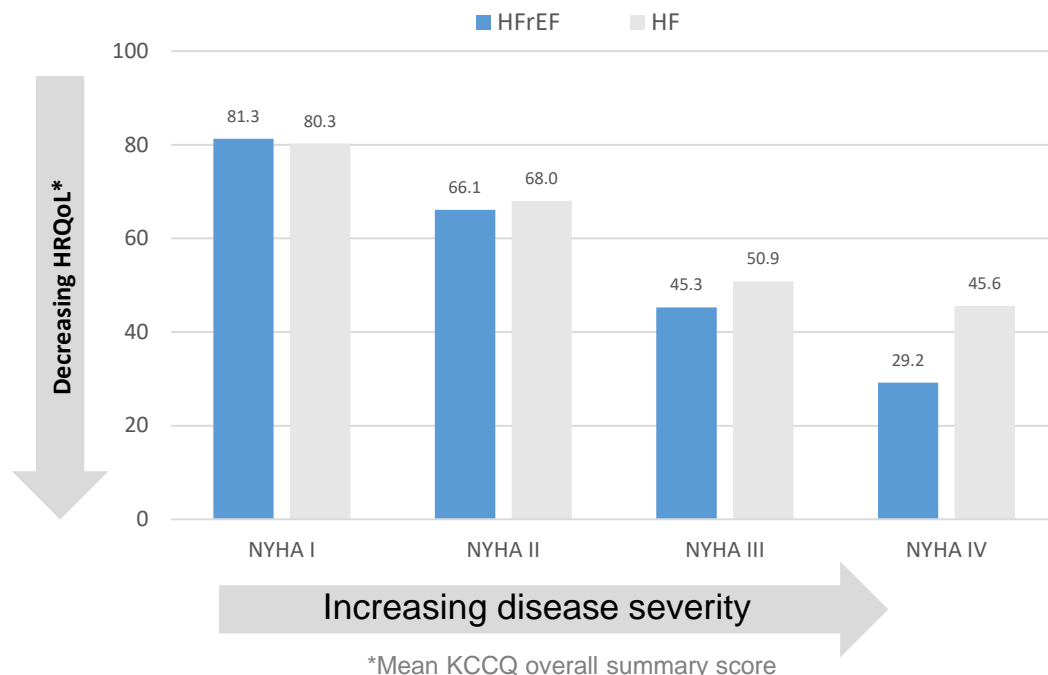
Pulmonary oedema



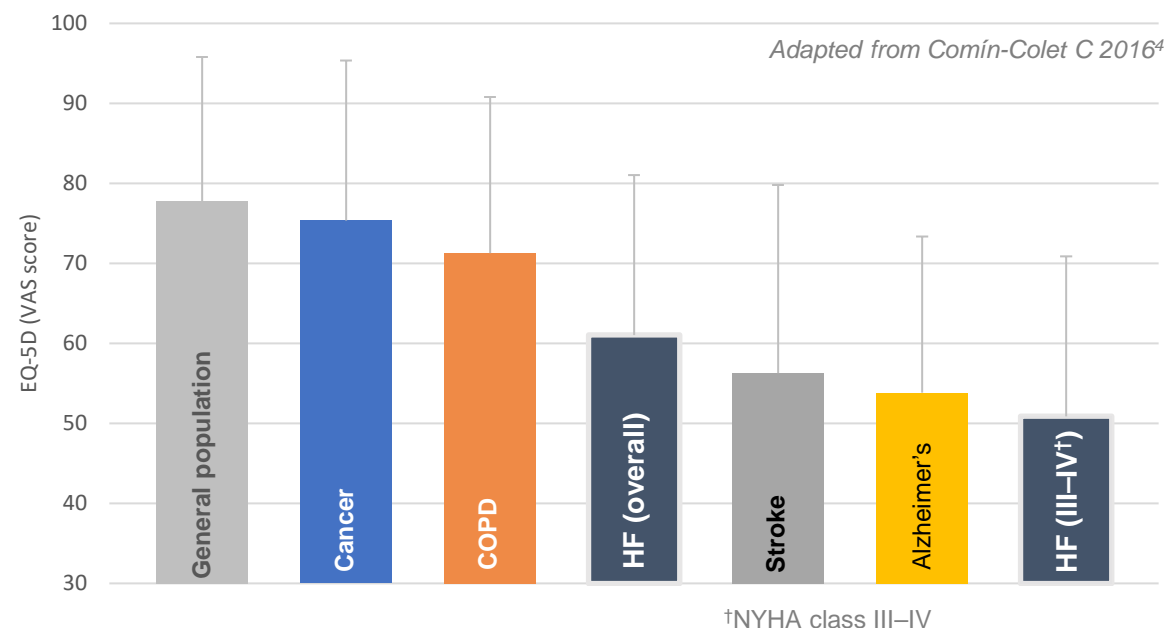
Loss of appetite

The impact of HF symptoms can cause a **significant reduction in HRQoL**,³ and more severe HF is associated with a **greater humanistic burden**³

HRQoL deteriorates with HF disease severity³

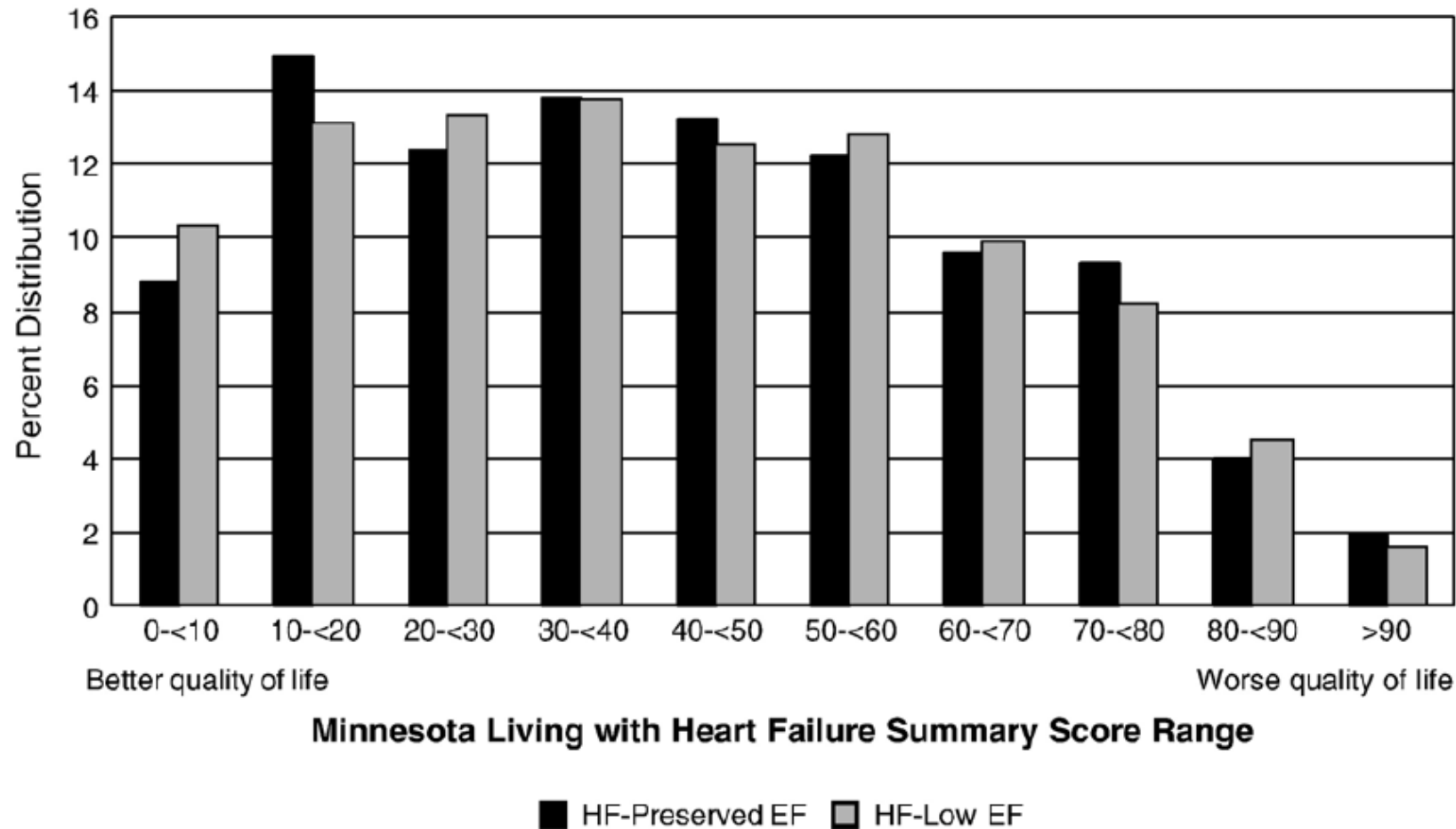


Patients with HF, especially those with severe symptoms, report poorer HRQoL vs. other chronic diseases⁴



¹NHLBI; ²AHA; ³Giles L 2019; ⁴Comín-Colet C 2016.

HFR- QOL does not discriminate by EF



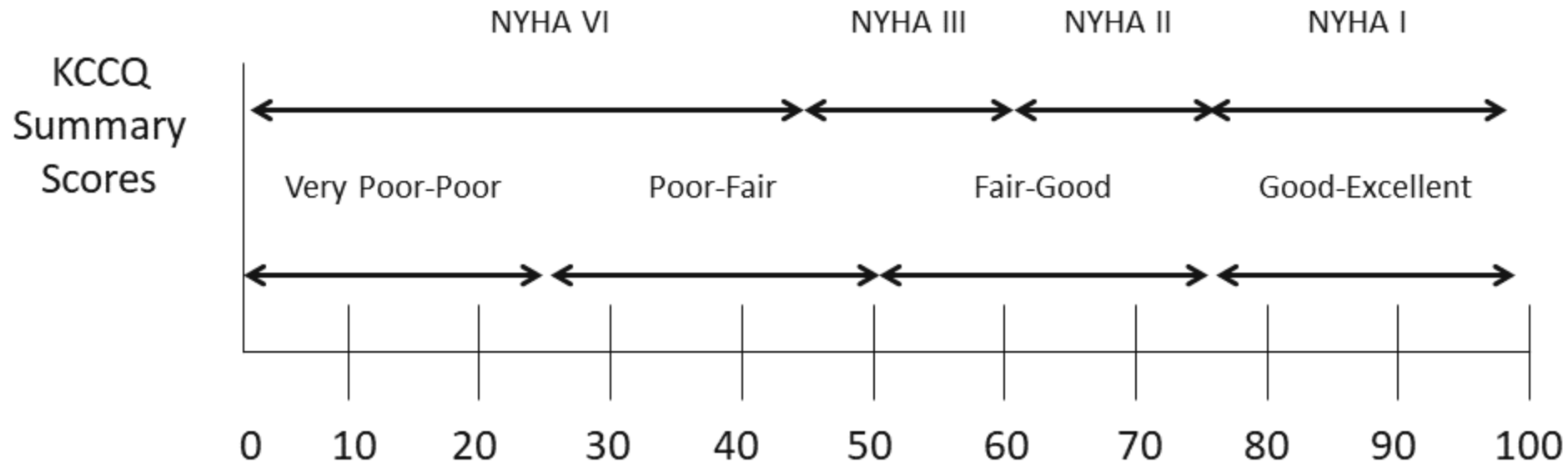
The KCCQ

- 23/12 items that measure 5 clinically relevant domains^[a,b]
 - Physical limitation
 - Symptoms: frequency, severity, and change over time
 - Social limitation
 - Self-efficacy
 - QoL
- Represents the patient's perspective of their HF
- Available in over > 95 translations; licensing available
- Has established validity, reliability, and responsiveness^[a,c]
- Qualified by the US FDA's CDRH and CDER as a clinical outcome assessment^[d,e]

a. Green CP, et al. *J Am Coll Cardiol*. 2000;35:1245-1255; b. Spertus JA, et al. *Circ Cardiovasc Qual Outcomes*. 2015;8:469-476; c. Luo N, et al. *Eur J Heart Fail*. 2018;21:63-70; d. US FDA; e. US FDA.

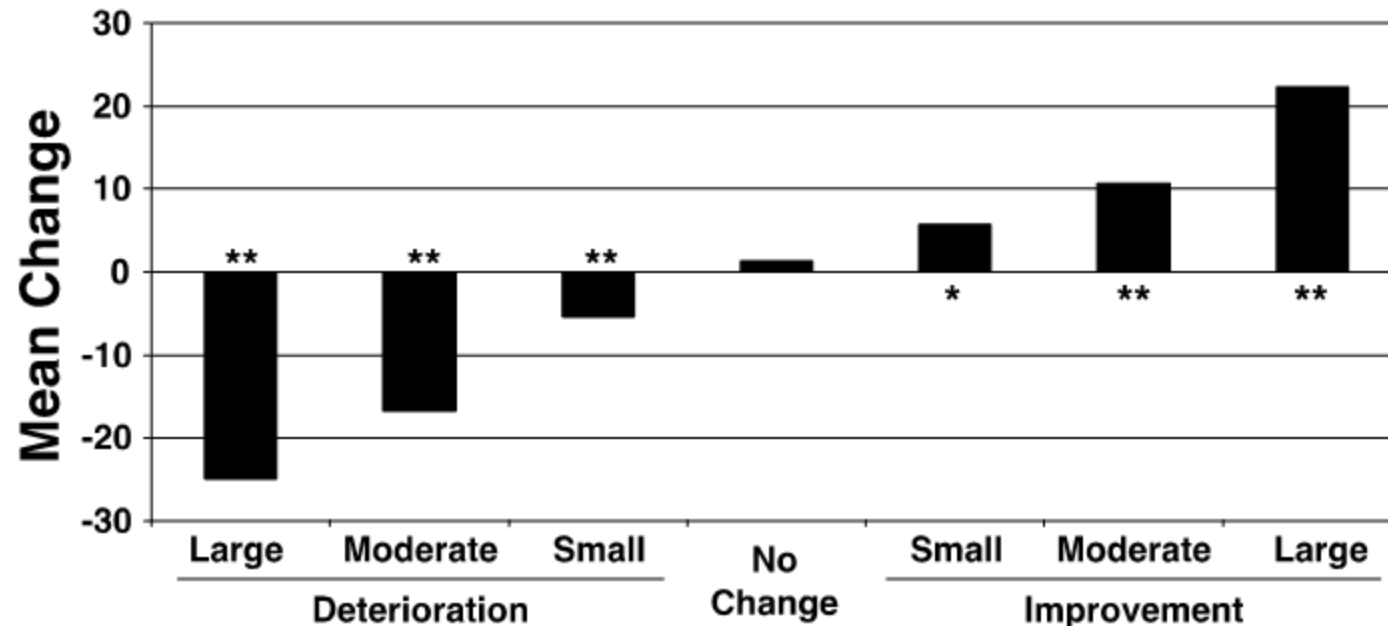
Converting the KCCQ Into Clinical Terms

- Evaluation of patients (N = 505) with HFrEF (LVEF < 40%)
- The association between KCCQ summary score (range, 0 to 100; higher scores indicate better health status) and NYHA, as well as other clinical and outcome measures, was evaluated



Changes in KCCQ Overall Summary By Clinical Change

- Prospective, 14-center cohort of 476 outpatients with HF
- Changes in 7 HF measures were compared with clinically observed change
 - KCCQ; SF-12; NYHA FC; 6MWT; BNP
- The KCCQ most accurately reflected clinical change in patients with HF



Clinically Important Improvement

- Small = 5 points
- Moderate = 10 points
- Large = 20 points

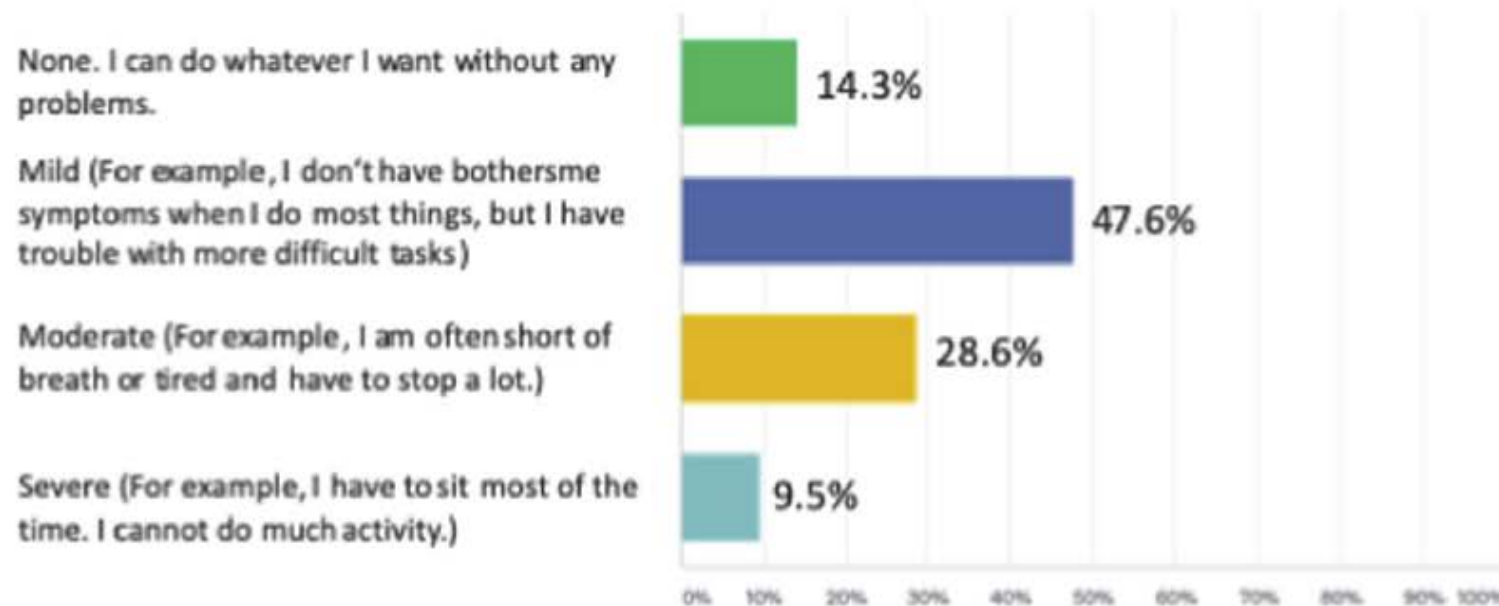
* $P < .05$ as compared with stable patients; ** $P < .001$
Spertus J, et al. *Am Heart J*. 2005;150:707-715.

QOL plays an important role in patient choice

FIGURE 2 Patient-Reported Severity of Heart Failure Symptoms or Disability

Q1: How would you describe your heart failure symptoms or disability?

Answered: 42 Skipped: 0



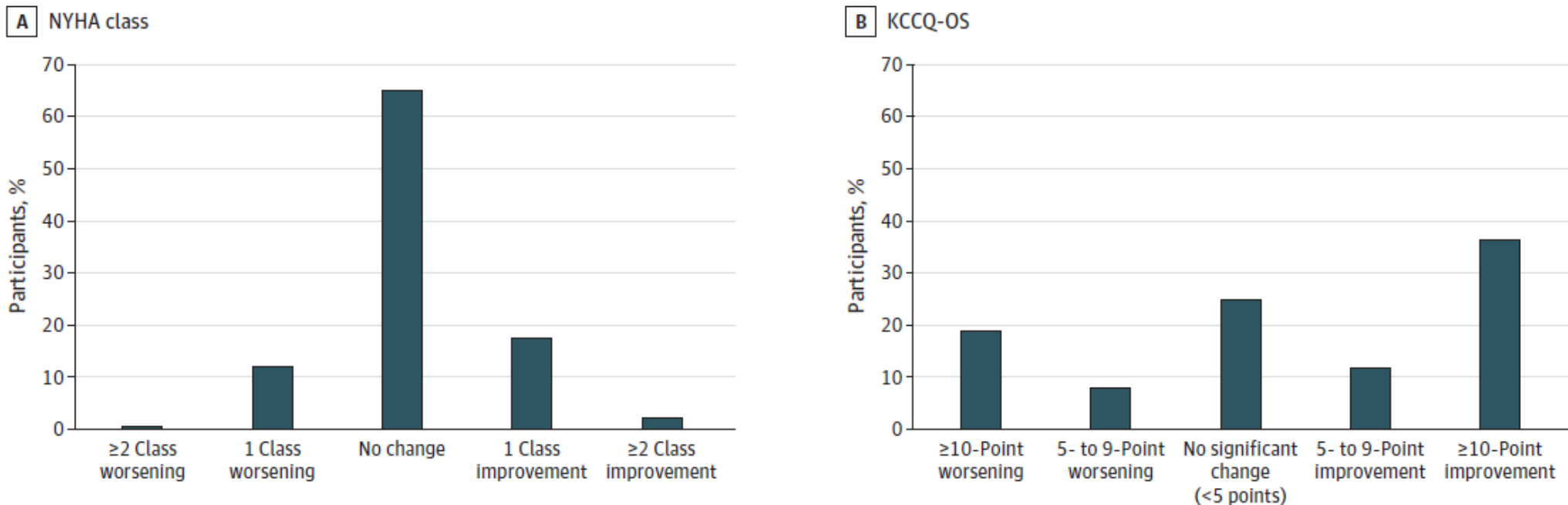
Powered by  SurveyMonkey

Comparison of New York Heart Association Class and Patient-Reported Outcomes for Heart Failure With Reduced Ejection Fraction

Stephen J. Greene, MD; Javed Butler, MD, MPH, MBA; John A. Spertus, MD, MPH; Anne S. Hellkamp, MS; Muthiah Vaduganathan, MD, MPH; Adam D. DeVore, MD, MHS; Nancy M. Albert, PhD; Carol I. Duffy, DO; J. Herbert Patterson, PharmD; Laine Thomas, PhD; Fredonia B. Williams, EdD; Adrian F. Hernandez, MD, MHS; Gregg C. Fonarow, MD

- 2872 patients in CHAMP registry with 12 month follow up
- NYHA Class, KCCQ, EQ-5D compared in terms of change from baseline and clinical outcomes

Figure 1. Change From Baseline to 12-Month Follow-up in New York Heart Association (NYHA) Class and Kansas City Cardiomyopathy Questionnaire Overall Summary Score (KCCQ-OS)

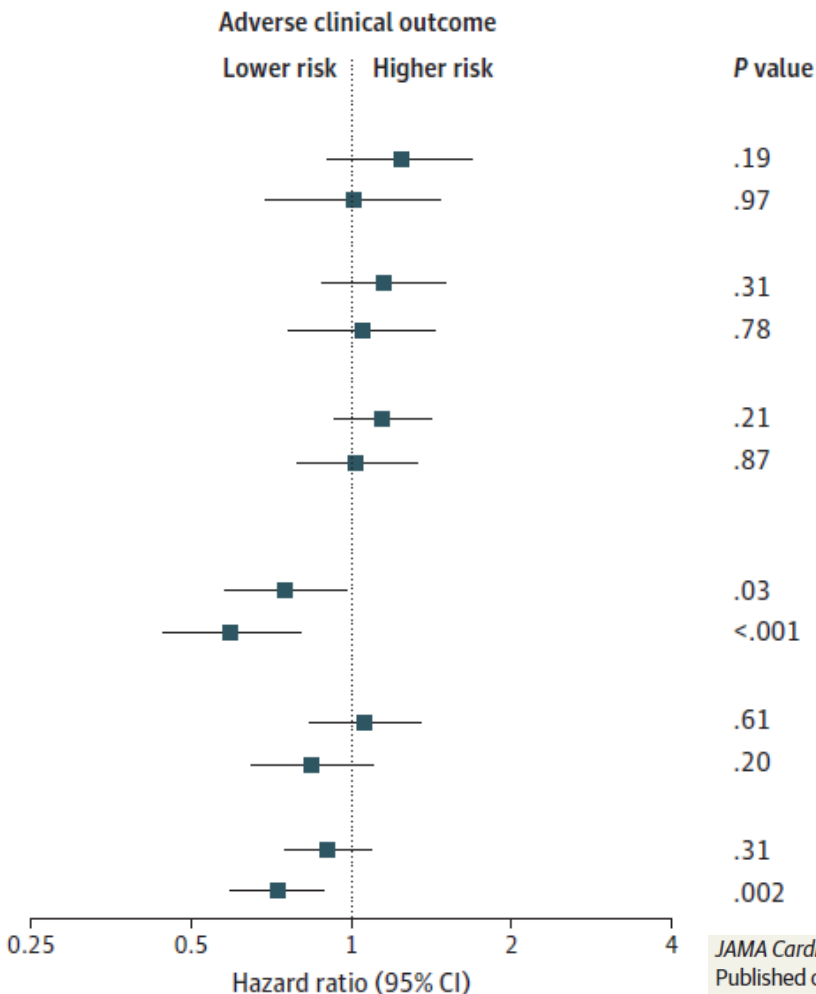


JAMA Cardiol. doi:10.1001/jamacardio.2021.0372
Published online March 24, 2021.

KCCQ more sensitive and predictive than NYHA over time

Figure 2. Associations Between Change in New York Heart Association (NYHA) Class and Kansas City Cardiomyopathy Questionnaire Overall Summary Score (KCCQ-OS) With Clinical Outcomes Among Patients With Heart Failure (HF) With Reduced Ejection in Contemporary US Outpatient Practice

NYHA class: any improvement	Improvement vs no improvement hazard ratio (95% CI)
Death	
Unadjusted	1.23 (0.90-1.69)
Adjusted	1.01 (0.69-1.47)
HF hospitalization	
Unadjusted	1.15 (0.88-1.50)
Adjusted	1.05 (0.76-1.43)
Death or HF hospitalization	
Unadjusted	1.14 (0.93-1.41)
Adjusted	1.02 (0.79-1.32)
KCCQ-OS: ≥5-point improvement	
Death	
Unadjusted	0.75 (0.58-0.98)
Adjusted	0.59 (0.44-0.80)
HF hospitalization	
Unadjusted	1.06 (0.84-1.36)
Adjusted	0.84 (0.65-1.10)
Death or HF hospitalization	
Unadjusted	0.90 (0.75-1.10)
Adjusted	0.73 (0.59-0.89)



**NOT PREDICTIVE
OF OUTCOMES**

**PREDICTIVE OF
OUTCOMES**



ESC

European Society
of Cardiology

European Heart Journal (2020) 00, 1–12
doi:10.1093/eurheartj/ehaa943

CLINICAL RESEARCH

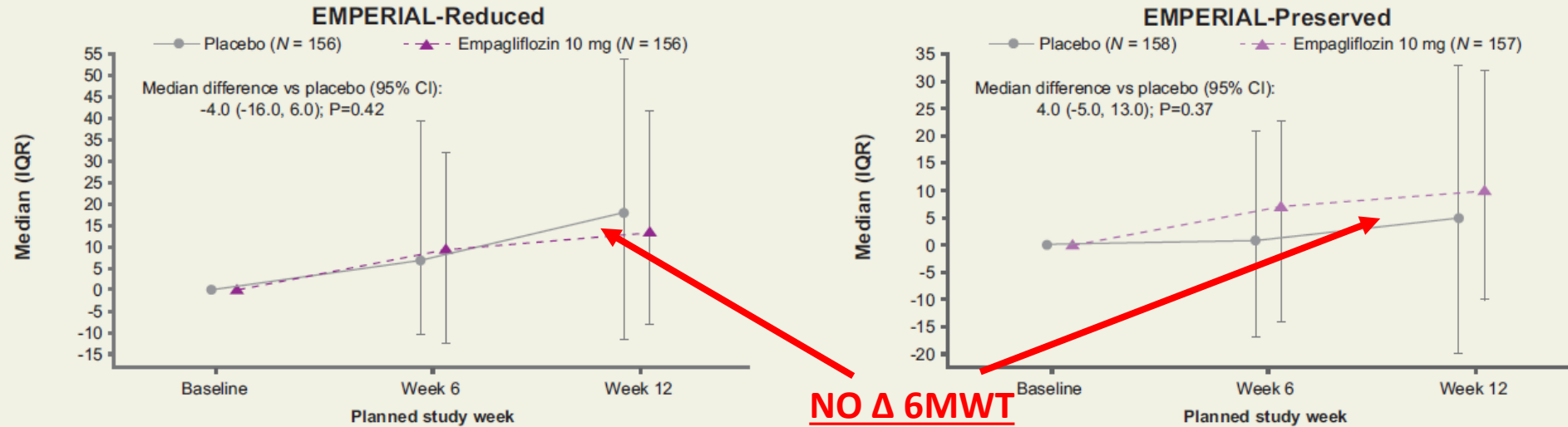
Heart failure

Effect of empagliflozin on exercise ability and symptoms in heart failure patients with reduced and preserved ejection fraction, with and without type 2 diabetes

William T. Abraham^{1*}, JoAnn Lindenfeld², Piotr Ponikowski³,
Piergiuseppe Agostoni ^{4,5}, Javed Butler⁶, Akshay S. Desai⁷,
Gerasimos Filippatos ^{8,9}, Jacek Gniot ¹⁰, Michael Fu¹¹, Lars Gullestad^{12,13,14,15},
Jonathan G. Howlett ¹⁶, Stephen J. Nicholls¹⁷, Josep Redon¹⁸,
Isabelle Schenkenberger¹⁹, José Silva-Cardoso²⁰, Stefan Störk ²¹,
Jerzy Krzysztof Wranicz²², Gianluigi Savarese ²³, Martina Brueckmann^{24,25},
Waheed Jamal ²⁴, Matias Nordaby ²⁴, Barbara Peil²⁶, Ivana Ritter ²⁴,
Anastasia Ustyugova²⁴, Cordula Zeller ²⁷, Afshin Salsali²⁸, and
Stefan D. Anker ²⁹

EMPERIAL: 6MWT vs. KCCQ

Primary endpoint: 6MWT change from baseline to Week 12 (metres)

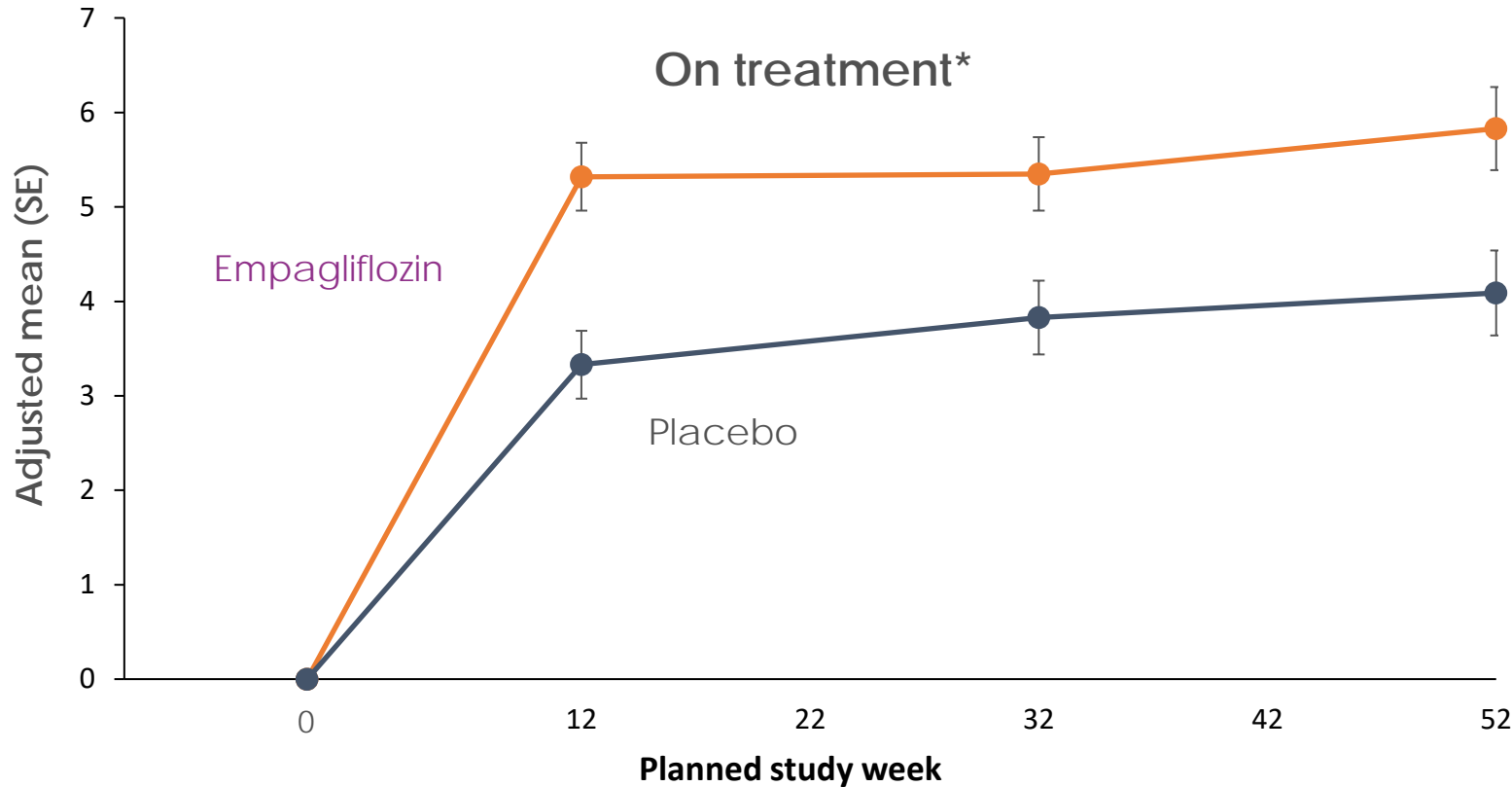


	Median change from baseline to Week 12 (IQR)		Median difference (95% CI)	Median difference (95% CI)
	Empagliflozin 10 mg	Placebo		
KCCQ-TSS				
EMPERIAL-Reduced	7.29 (-2.60, 18.75)	3.65 (-6.25, 13.54)	3.13 (0.00, 7.29)	
EMPERIAL-Preserved	4.17 (-3.13, 16.67)	2.08 (-6.25, 20.83)	2.08 (-2.08, 6.25)	

But Signal for QOL!

EMPEROR – REDUCED

Quality of life: KCCQ-CSS at 52 weeks



Change from baseline (95% CI)
at Week 52

Empagliflozin: 5.8 ± 0.4
Placebo: 4.1 ± 0.4

Absolute difference

1.7

(95% CI 0.5, 3)

$p=0.0058$

N with data at visit

Placebo	1701	1688	1505	1151
Empagliflozin	1734	1720	1561	1176

All models include covariates age, baseline eGFR, region, baseline diabetes status, sex and baseline LVEF

*No imputation for death

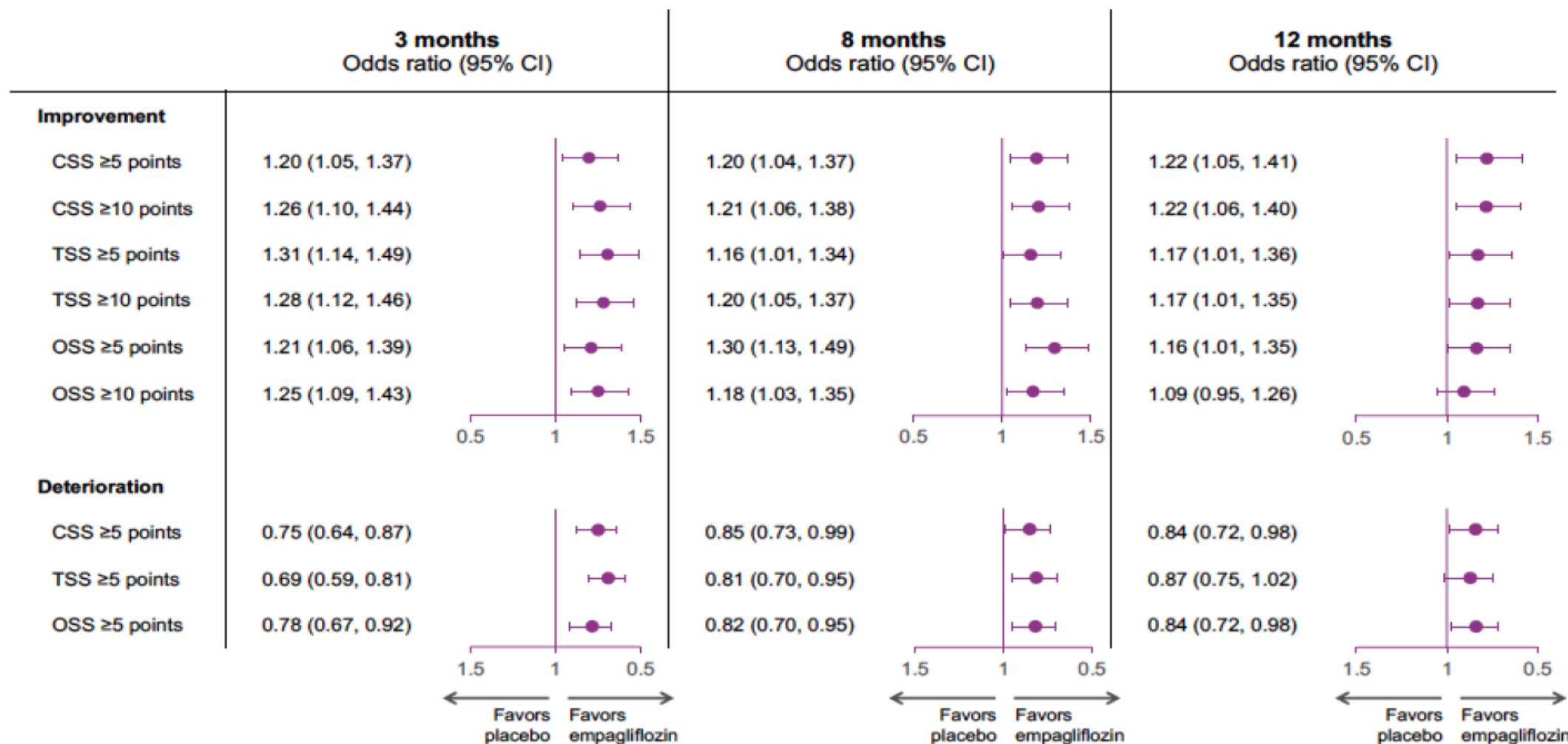
CV, cardiovascular; eGFR, estimated glomerular filtration rate; HHF, hospitalisation for heart failure, KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire clinical summary score

LVEF, left ventricular ejection fraction

Packer M *et al.* N Engl J Med 2020. DOI:10.1056/NEJMoa2022190; Data on file.

Empagliflozin effect on KCCQ during trial: *Responder analysis*

Consistently higher likelihood of improvement and lower likelihood of deterioration



Selected therapies: Effect on HR QoL and 6 MWT in patients with HFrEF

Therapy	Improved outcomes?	Improved symptoms?	Improved 6MWT?
ACE/ ARB	++	++	+
Beta blockers	+++	++	No
ARNi	+++	++	?+
MRA	+++	+/-	No
SGLTi	+++	++	No
Ivabradine	+	+++	++
Hydralazine	+	+++	+++
Digoxin	+	++	++
Vericiguat	+	+/-	N/A
CRT	+++	++++	+++

Selected therapies: Effect on HR QoL and 6 MWT in patients with HFrEF

Therapy	Improved outcomes?	Improved symptoms?	Improved 6MWT?	Improved HRQoL?
ACE/ ARB	++	++	+	+
Beta blockers	+++	++	No	+
ARNi	+++	++	?+	++
MRA	+++	+/-	No	Mixed
SGLTi	+++	++	No	+++
Ivabradine	+	+++	++	+++
Hydralazine	+	+++	+++	++
Digoxin	+	++	++	++
Vericiguat	+	+/-	N/A	+/-
CRT	+++	++++	+++	++++

KCCQ changes with heart failure interventions

Intervention	Study	KCCQ Improvement	Citation
Empagliflozin	EMPEROR-Reduced	+1.64 (TSS), +1.35 (CSS), +1.30 (OSS) at 8 months +1.69 (TSS), +1.61 (CSS), +1.52 (OSS) at 12 months ↑≥5 points (CSS) in 52% (vs 48% placebo) at 8 months ↑≥5 points (CSS) in 51% (vs 48% placebo) at 12 months	
Dapagliflozin			Kosiborod 2019
Exercise			Flynn 2019
Ivabradine			Ekman 2011
Sacubitril/Valsartan	PIONEER-HF	+1.6 (CSS) at 8 months ↑≥5 points (OSS) in 35% (vs 33% enalapril)	McMurray 2014 Lewis 2017

**This equates to NNT of:
14-22 for moderate or large
improvement in QOL for SGLT2
inhibitors
Evidence within 3 months**

Quality of Life in HF

- Key outcome for patients
- Consistently indicative of disease state
- More sensitive to change than NYHA Class
- More predictive of outcomes than all other status indicators
- Regulatory agencies will consider for drug approval
- Can be performed ONLINE or in WAITING ROOM
 - Easy to score
- BUT....

They will NOT improve your golf game.....



“Did you win?”