

Quality of Life in heart failure Insights from the G-CHF study

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Truncated slide set with published results

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Objectives

HF and health-related quality of life (HRQL) in the Global Congestive Heart Failure (G-CHF) study:

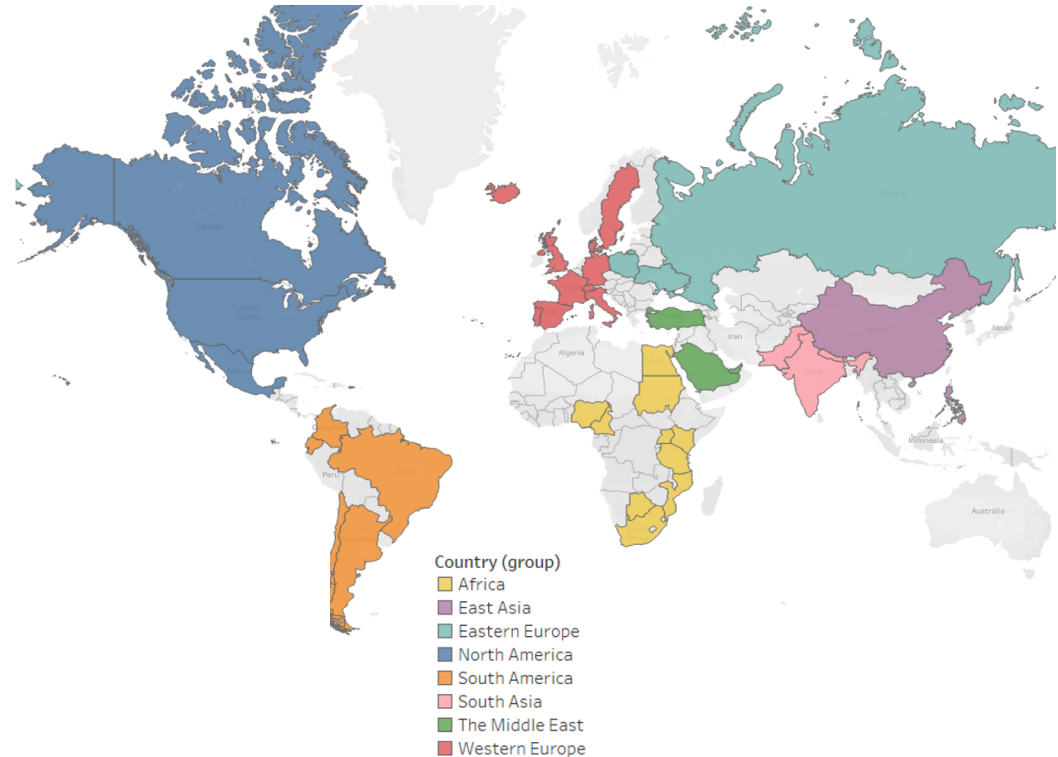
1. Global variations in HRQL and associations with clinical outcomes
2. Determinants of HRQL in HF patients across different income levels

Epidemiology of HF

- 26 millions live with HF worldwide
- Mortality rates remain high despite treatment advances
- HF characteristics, treatment, and outcomes have been well described in Western-, and high-income countries
- Less data allowing for direct comparison of HF patients across different global regions and income levels

The Global Congestive Heart Failure (G-CHF) Study

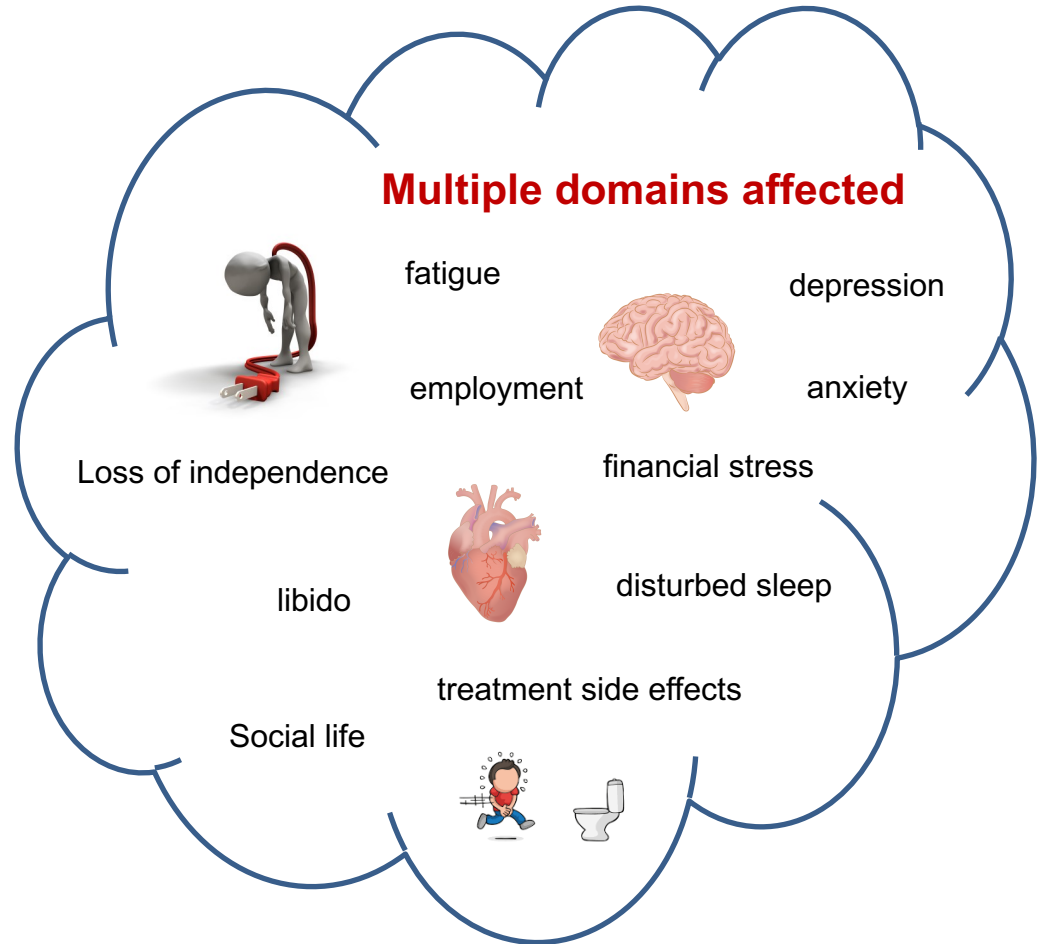
- >23,000 adult patients with a clinical diagnosis of HF
- 40 countries, 8 regions
- Wide inclusion criteria, 1/3rd inpatients
- Enrollment: 2017 – 2020
- Median follow-up 1.8 years, planned up to 5 years
- Sub-study with detailed characterization of ~5,000 patients



Heart failure definition and implications

“Heart failure is a multidimensional **clinical syndrome** caused by structural and/or functional impairment of ventricular filling or ejection of blood”

Heart failure is typically **manifested by** dyspnea, fatigue, exertional intolerance, and fluid retention



Health-related quality (HRQL) of life in heart failure

- Poor HRQL is common in patients with HF
- HRQL predicts mortality and HF hospitalizations

We do not know:

- If self-reported HRQL differ in different geographic regions and across different income levels
- the association of HRQL with clinical outcomes outside Western-, and high-income countries
- The determinants of HRQL in different settings

Heart failure management goals



European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

ACC/AHA/HFSA FOCUSED UPDATE

2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

Canadian Journal of Cardiology 33 (2017) 1342–1433

Society Guidelines

2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure



- ✓ Improving survival & reducing disease progression
- ✓ Control symptoms
- ✓ **Improve functional capacity and (health-related) quality of life**



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Patient reported outcomes in clinical trials

- supported by regulatory agencies

Health and Quality of Life Outcomes



Guidelines

Open Access

Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance

U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research*¹, U.S. Department of Health and Human Services FDA Center for Biologics Evaluation and Research*² and U.S. Department of Health and Human Services FDA Center for Devices and Radiological Health*³



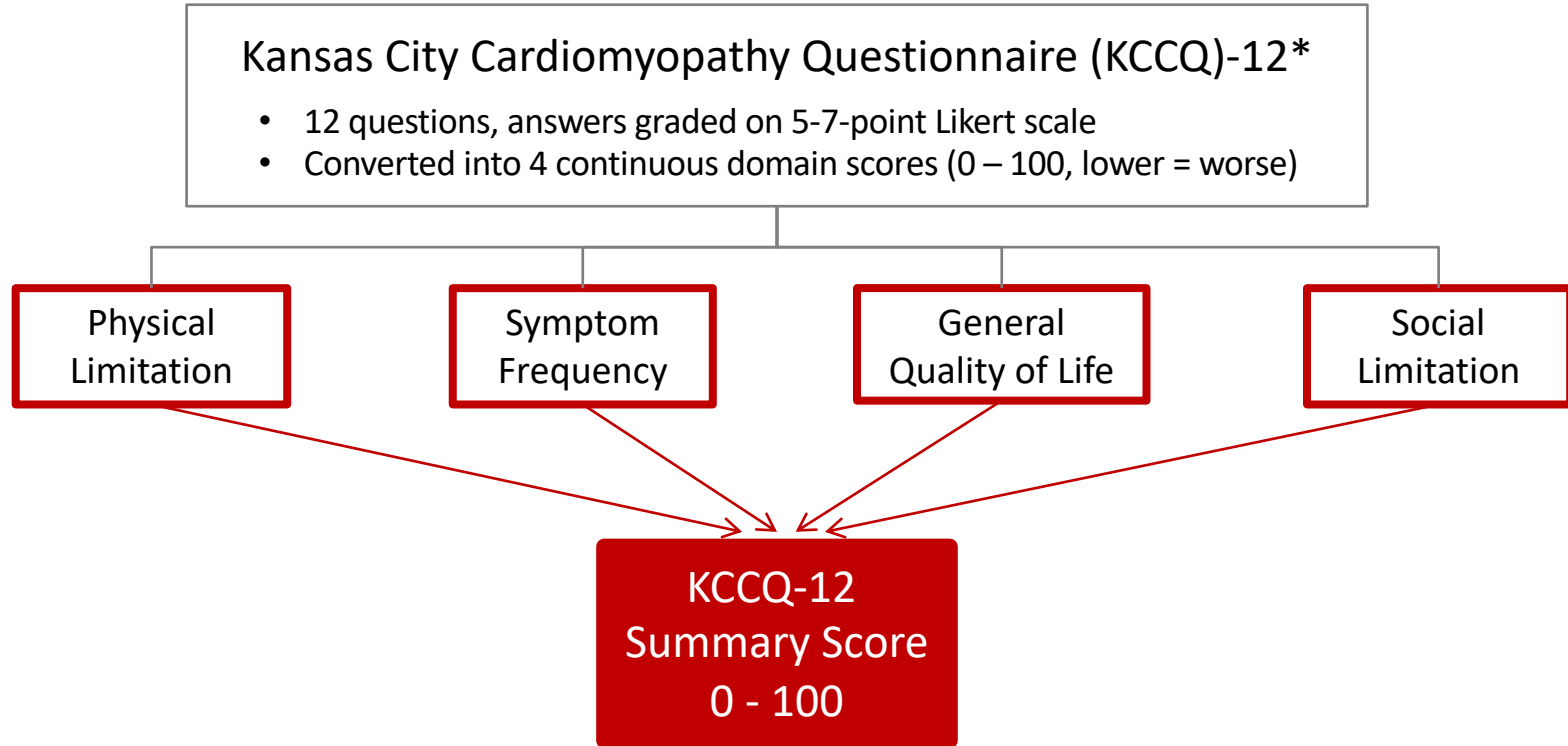
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Definition of HRQL

“An individual patient’s perception of their **overall well-being** in the **context of** their perceived disease burden, symptom status and function, social status, goals of life, culture, value systems and expectations”

- Assessment and quantification by standardized instrument with validated psychometric properties
- ***Generic or Disease specific***

Health-related Quality of life (HRQL) assessment



Kansas City Cardiomyopathy Questionnaire – 12

Domain 1: Physical limitation

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	Extremely Limited	Quite a bit Limited	Moderately Limited	Slightly Limited	Not at all Limited	Limited for other reasons or did not do the activity
a. Showering/bathing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Walking 1 block on level ground	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Hurrying or jogging (as if to catch a bus)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	1	2	3	4	5	6

Kansas City Cardiomyopathy Questionnaire – 12

Domain 2: Symptom Frequency

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
1	2	3	4	5

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
1	2	3	4	5	6	7

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
1	2	3	4	5	6	7

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
1	2	3	4	5

Kansas City Cardiomyopathy Questionnaire – 12

Domain 3: General Quality of Life

6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely**
limited my enjoyment
of life

☐

1

It has limited my
enjoyment of life
quite a bit

☐

2

It has **moderately**
limited my enjoyment
of life

☐

3

It has **slightly**
limited my enjoyment
of life

☐

4

It has **not limited**
my enjoyment
of life at all

☐

5

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all
satisfied

☐

1

Mostly
dissatisfied

☐

2

Somewhat
satisfied

☐

3

Mostly
satisfied

☐

4

Completely
satisfied

☐

5

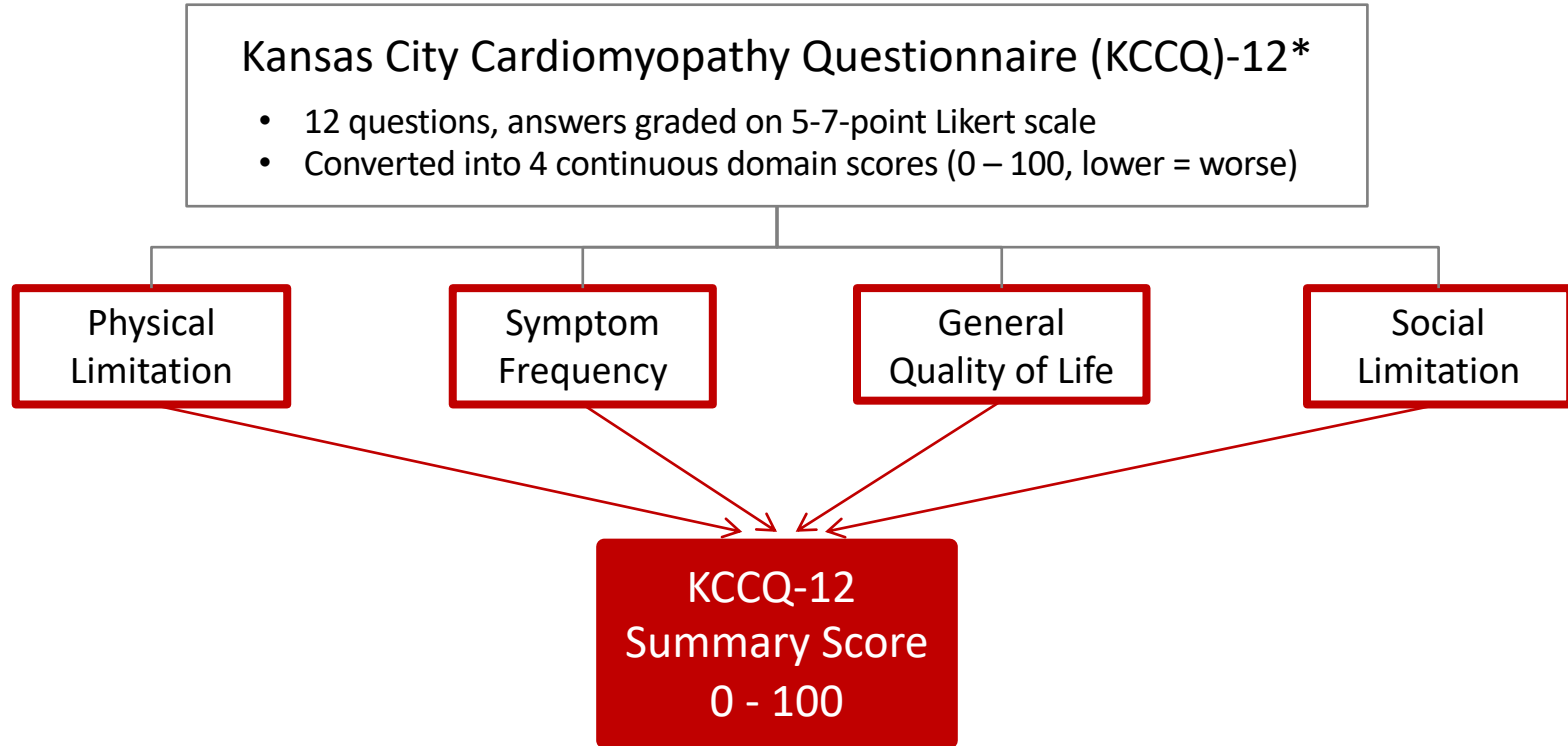
Kansas City Cardiomyopathy Questionnaire – 12

Domain 4: Social Limitation

8. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Activity	Severely Limited	Limited quite a bit	Moderately limited	Slightly limited	Did not limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Working or doing household chores	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Visiting family or friends out of your home	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	1	2	3	4	5	6

Health-related Quality of life (HRQL) assessment



KCCQ-12-SS categorization

TABLE 1 Clinical Correlates of Changes in KCCQ Scores				
	Change in 6-Min Walk Test (m)	Change in Vo₂ (ml/kg/min)	OR for Mortality/Hospitalization (%)	OR for Mortality (%)
Small change (5 points)	112	2.5	11	9
Moderate to large change (10 points)	225	5	23	19
Large to very large change (20 points)	450	10	52	42
KCCQ = Kansas City Cardiomyopathy Questionnaire; OR = odds ratio.				

Score	classification
0 to 24	Very Poor
25 to 49	Poor to Fair
50 to 74	Fair to Good
75 – 100	Good to Excellent

Objectives

HF and health related quality of life (HRQL) in the Global Congestive Heart Failure (G-CHF) study:

1. Global variations in HRQL and associations with clinical outcomes
2. Determinants of HRQL in HF patients across different income levels

Study Objectives

To examine differences in HRQL in HF in 8 geographic regions

To evaluate associations between HRQL and clinical outcomes in patients with HF

1. Overall
2. By geographic region
3. By NYHA class (I&II vs. III&IV)
4. By reduced and preserved EF ($\geq 40\%$ vs. $< 40\%$)

Methods

Design: Prospective, median follow-up time 1.6 years

Population: Baseline G-CHF population with KCCQ-12 completed, n=23 292 (99.5%)

HRQL metric: KCCQ-12 summary score

Outcomes

1 ^{ary} All-cause Death	n = 4,460 (19.2%)
2 ^{ary} HF hospitalization	n = 3,885 (16.7%)
2 ^{ary} Death or first HF hospitalization	n = 6,949 (29.8%)

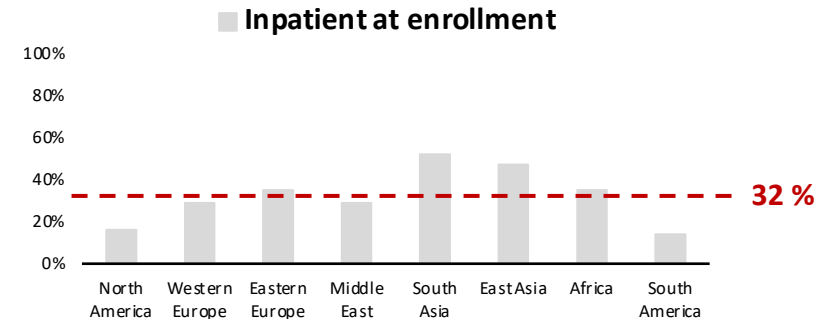
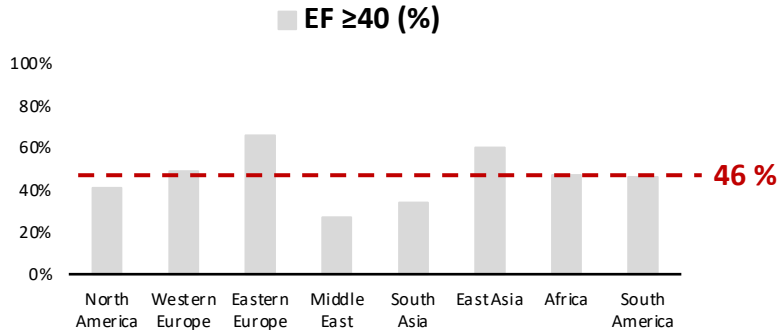
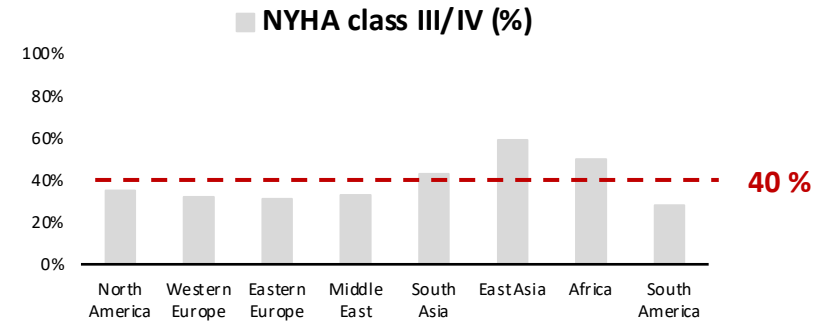
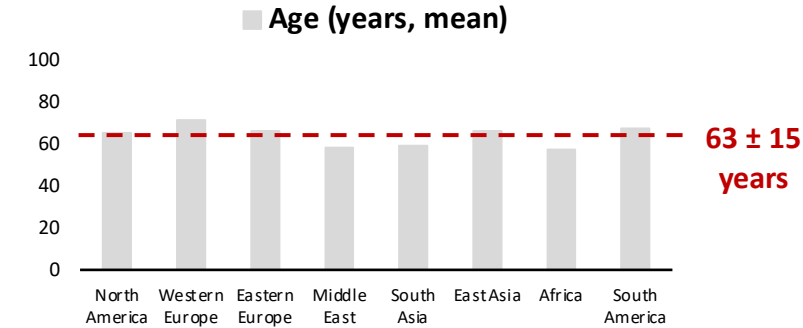
Statistical Approach

- KCCQ-12-SS analyzed as continuous variable (score 0-100) and grouped into 4 25-point categories
- Generalized linear models for adjusted KCCQ-12-SS and outcome rates
- Multivariable Cox proportional hazard regression models to evaluate associations between KCCQ-12-SS and 1^{ary} and 2^{ary} outcomes
 - by 10-unit decrements and by 4 group-categories
- Adjusted for 15 baseline variables;
 - Sex, age, geographic region, history of diabetes, history of COPD
 - Treatment (beta blockers, RAS blockers)
 - Inpatient at enrolment, BMI, systolic blood pressure, left ventricular ejection fraction, right ventricular function and valvular dysfunction
 - Urban living location, education



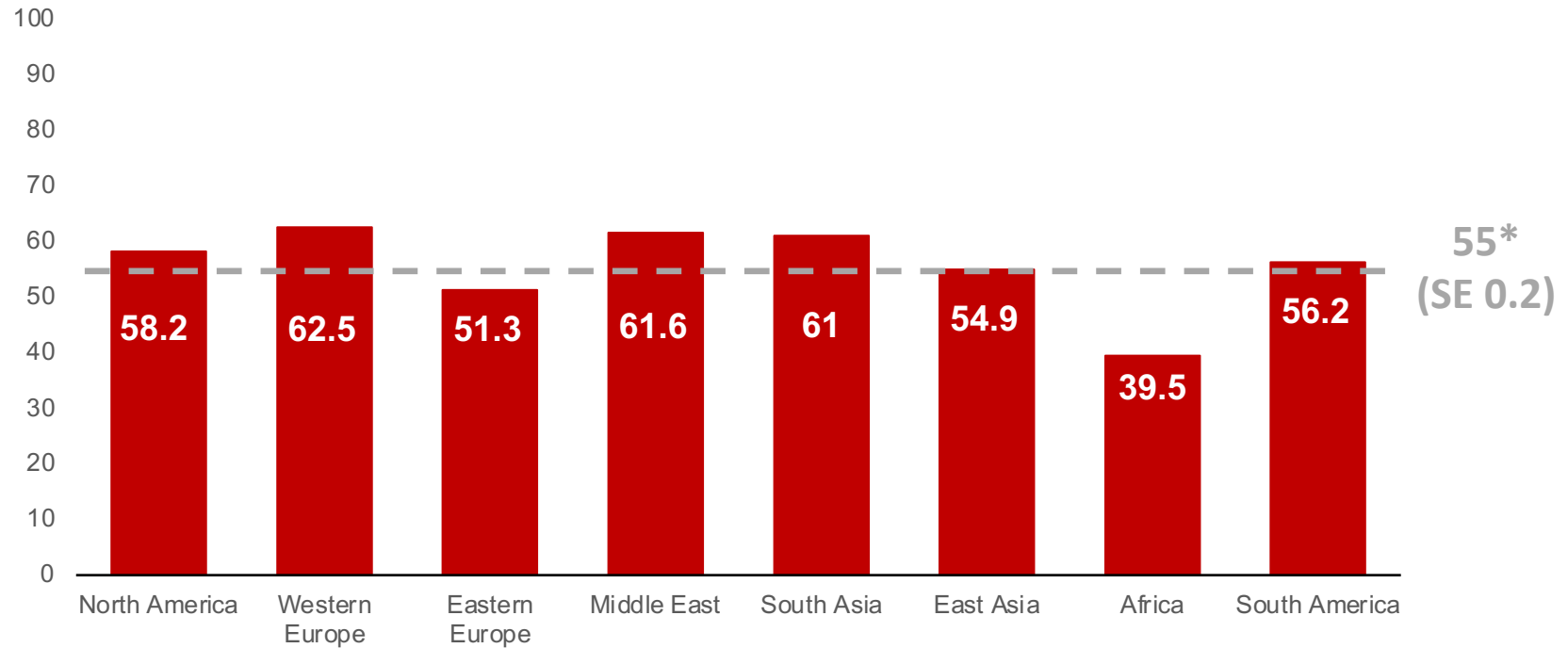
Baseline characteristics

N=23085, women 30-40% except in Africa (54%)



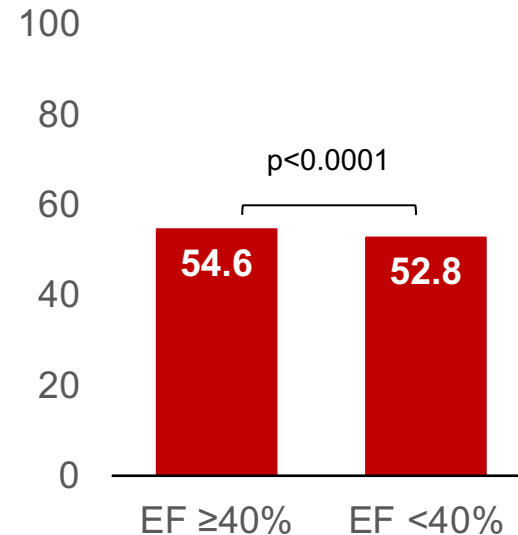
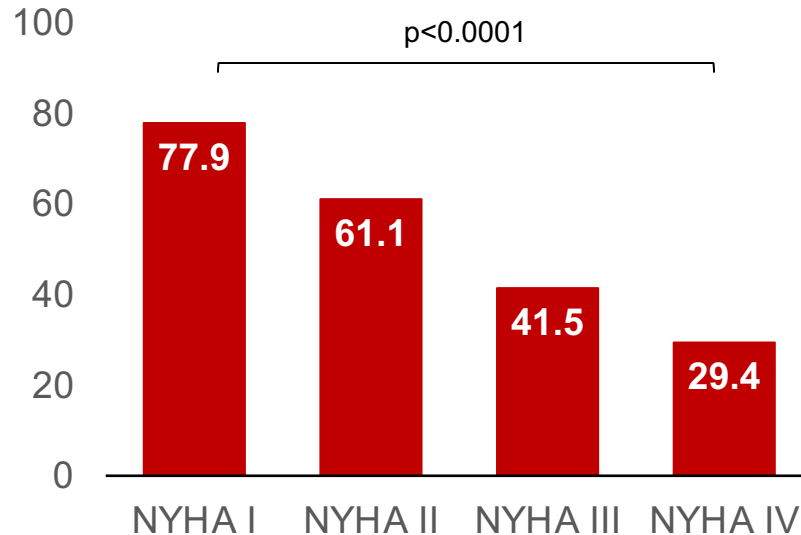
*Adjusted for age, sex, EF and inpatient/outpatient

Adjusted mean* KCCQ-12-SS overall and by geographic region N=23293, women 30-40% except in Africa (54%)



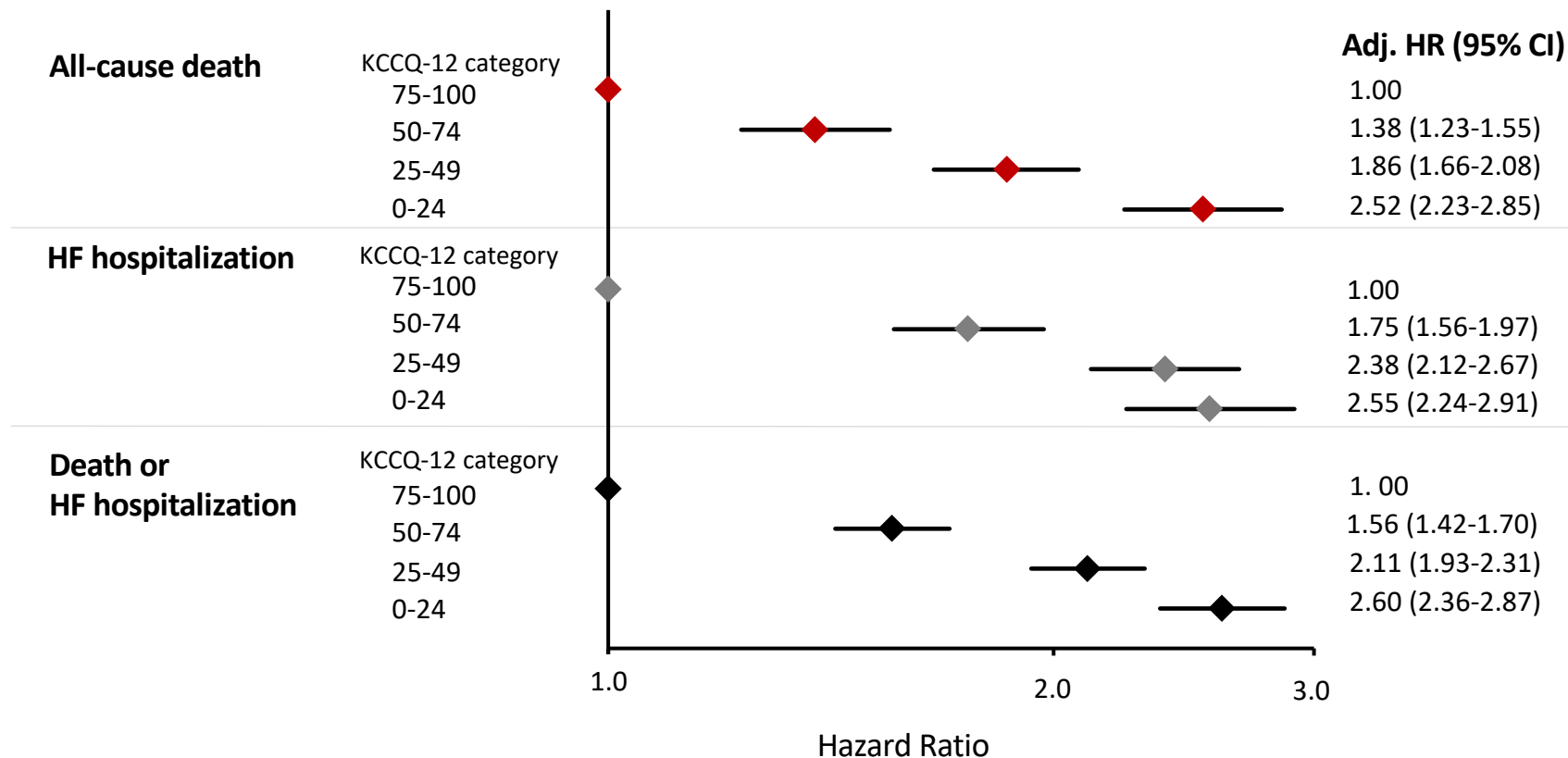
*Adjusted for age, sex, EF and inpatient/outpatient

Adjusted KCCQ-12-SS in subgroups by NYHA symptoms class and in EF \geq vs. $<40\%$

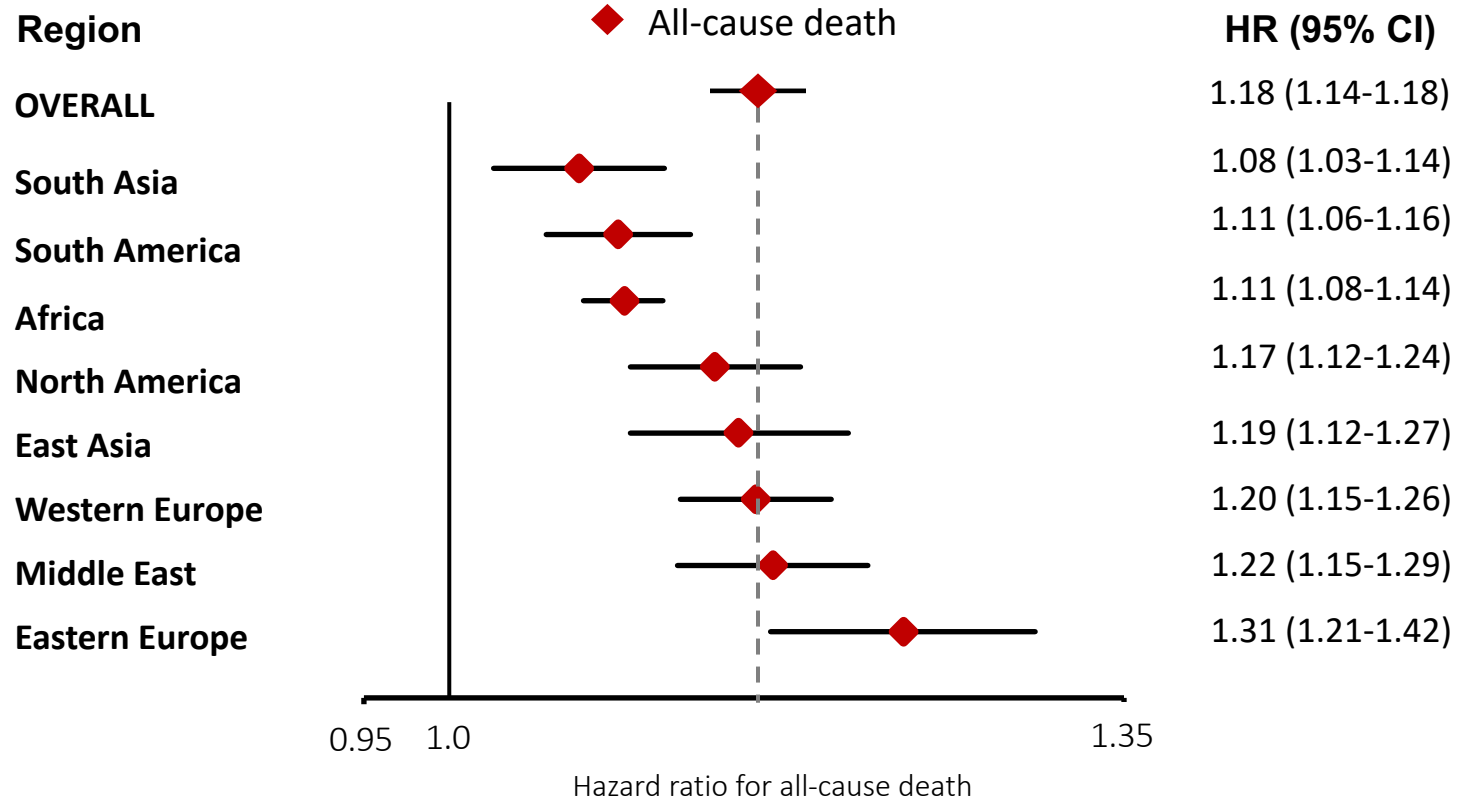


KCCQ-12 summary score predicts death and HF hospitalization

◆ All-cause death ◆ HF hospitalization ◆ Death or HF hospitalization

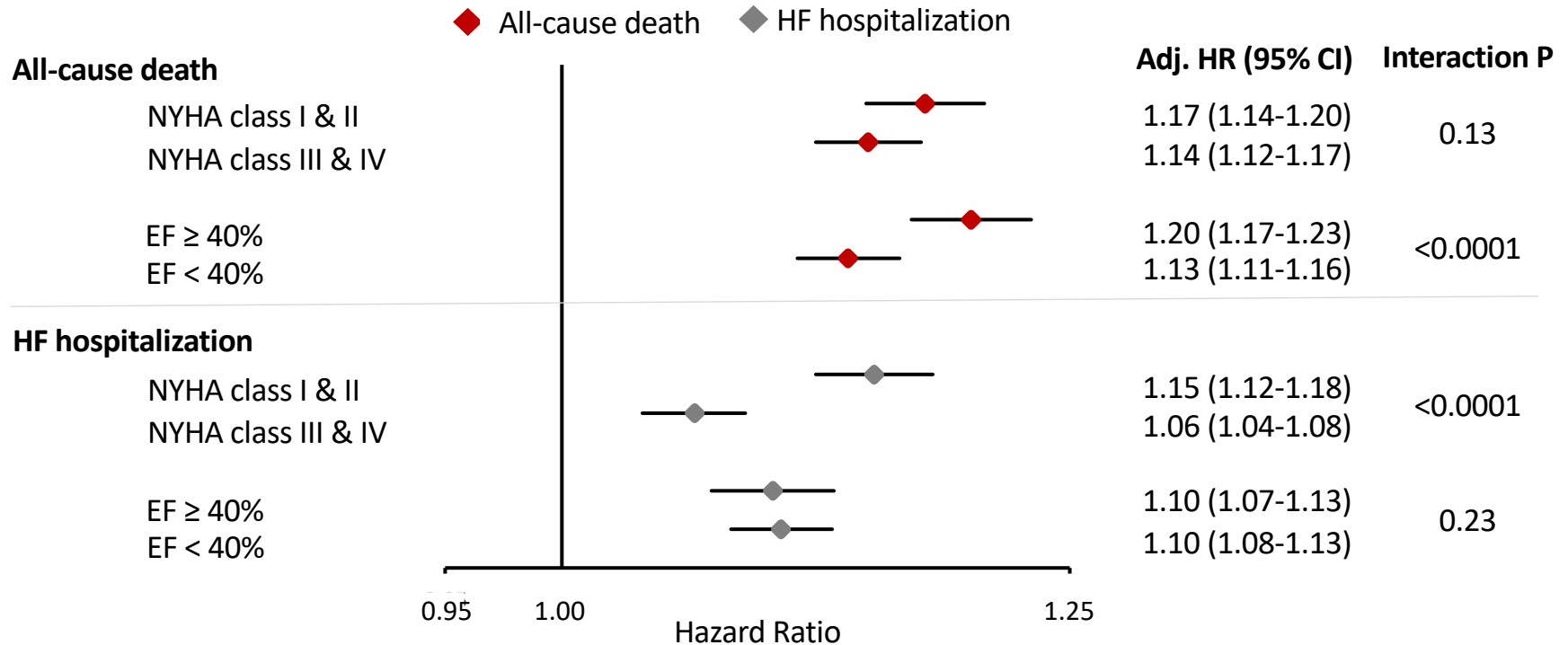


Regional variations in risk of death per 10-unit decrements in KCCQ-12 summary score

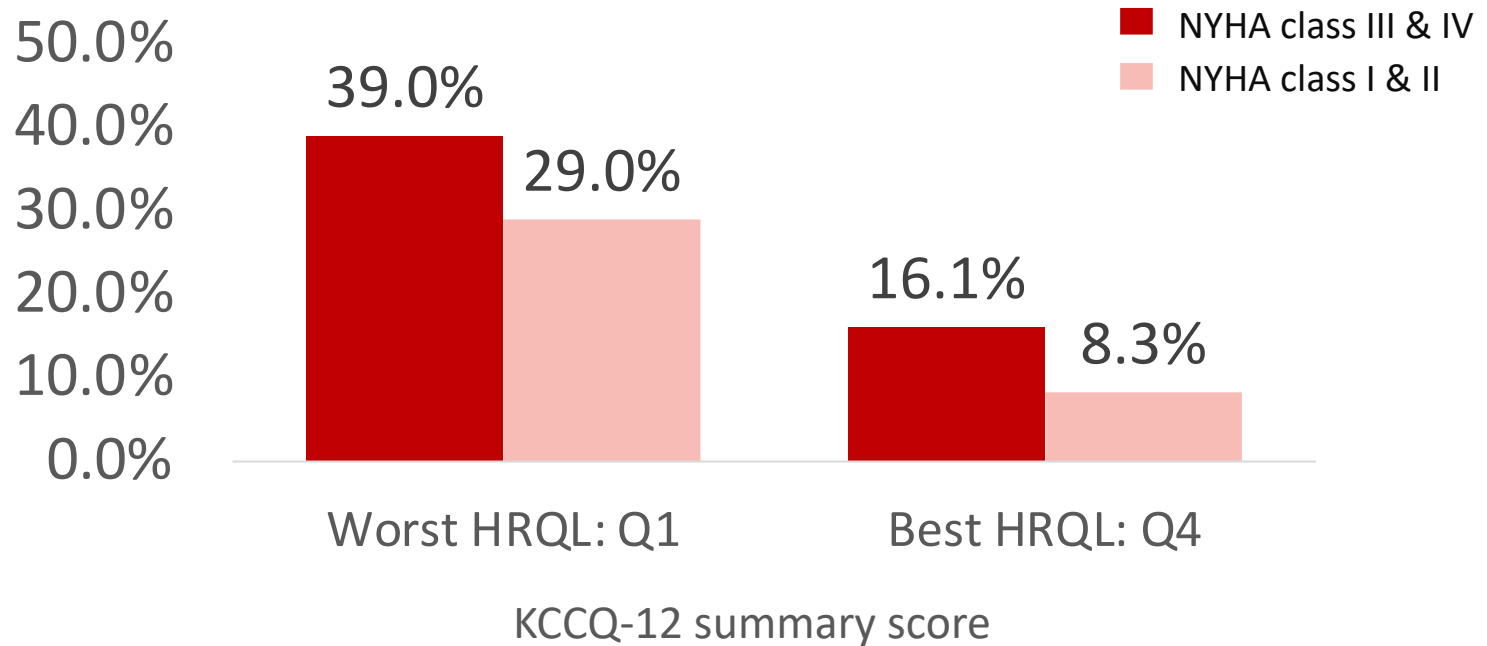


Overall heterogeneity highly significant ($P < 0.0001$)

Variations in the associations between KCCQ-12 score and risk of outcomes by 10-unit decrements according to symptom severity and EF



Age- & sex-standardized mortality rates by physician judged symptom class and by self-rated health status



Interim Conclusions

In the G-CHF study, with patients from 40 countries, incl. 9 African countries, we see:

- Considerable variations in self-reported HRQL in different geographic regions
- Poor HRQL is a strong predictor of mortality and HF hospitalization
 - In all world regions
 - In mildly and more severe symptomatic HF
 - Among those with preserved and reduced EF
- The importance of HRQL for predicting mortality varies between the regions - weakest in South Asia and strongest in Eastern Europe

Remaining gaps in knowledge

It is not known whether disparities in HRQL across geographic regions are explained by:

- Heterogeneity in disease severity at presentation?
- Other social and demographic characteristics?
- Cultural aspects influencing how patients perceive their HRQL and answer to health status questionnaires?

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HF and health-related quality of life (HRQL) in the Global Congestive Heart Failure (G-CHF) study:

1. Global variations in HRQL and associations with clinical outcomes
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➤ Analysis ongoing, stay tuned!

Implications and future directions

- HRQL is an inexpensive and simple prognostic marker that is useful in characterizing symptom severity and prognosis in all patients with HF
- HRQL covers multiple domains of HF patient's health status and adds value on top of commonly used prognostic markers in HF
- It should be a priority to make HRQL evaluation a part of routine clinical practice
- Mechanisms for the difference in strength of prediction of mortality between regions remains to be understood

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Thank you!

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