

# The use of HeartQoL in patients with coronary heart disease: Association with risk factors and European reference values. The EUROASPIRE IV study of the European Society of Cardiology

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## Abstract

**Background:** HeartQoL is a recently developed core health-related quality of life instrument for patients with coronary heart disease. The current study aims to investigate its association with patients' coronary risk profile and to provide reference values for patients with coronary heart disease across Europe.

**Design:** Analyses are based on the EUROASPIRE IV (EUROpean Action on Secondary and Primary prevention through Intervention to Reduce Events) cross-sectional survey.

**Methods:** Patients with a diagnosis of coronary heart disease were examined and interviewed six months to three years after their coronary event. The HeartQoL questionnaire was completed by 7261 coronary heart disease patients. Reference values were calculated and the association with the coronary risk profile was assessed.

**Results:** Significantly worse outcomes were observed in higher-risk patient groups. Both metabolic and behavioural risk factors were associated with worse HeartQoL outcomes. Further, the HeartQoL scores decreased as the number of risk factors increased. The mean global reference values in males were  $2.27 \pm 0.65$  (<60 years),  $2.30 \pm 0.61$  (between 60 and 69 years) and  $2.19 \pm 0.64$  ( $\geq 70$  years). Likewise, in females, the respective global HeartQoL reference values were  $2.02 \pm 0.67$ ,  $2.01 \pm 0.66$  and  $1.83 \pm 0.70$ . The ceiling effect in males was 11.4%, 10.4% and 7.4% for the three age classes respectively, whereas in females the ceiling effect was 5.2%, 3.5% and 1.9%, respectively.

**Conclusion:** HeartQoL scores were associated with patients' coronary risk profile. The reference values may help other researchers to interpret HeartQoL scores. Further research should focus on the minimal important difference needed to evaluate the effect of therapies and lifestyle changes.

## Keywords

Health-related quality of life, coronary heart disease, patient reported outcome

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## Introduction

Coronary heart disease (CHD) is associated with a substantial physical and mental burden.<sup>1</sup> Patients are likely to have an impaired health-related quality of life (HRQL) due to pain, anxiety, and functional and social limitations. Over the last few decades, the assessment of patient reported outcomes has become increasingly important, as highlighted by the Institute of Medicine, the European Medicines Agency, and the UK National Health Service.<sup>2–4</sup>

Various instruments, such as generic instruments for use across different patient groups and disease-specific instruments for use in particular diagnostic groups, are available to assess HRQL. Both types of measures cover multiple areas, including social functioning, physical functioning and mental functioning. Generic instruments are applicable in any given population (healthy individuals as well as patients with specific pathologies), whereas disease-specific instruments are only applicable in a particular patient group, do not allow for comparison across patient groups and tend to be more sensitive to small changes.<sup>5</sup> The best-known generic tools are the SF-36 (36-items Short Form) and EQ-5D (EuroQoL 5-dimensions) questionnaires.<sup>6,7</sup> The HeartQoL is a recently developed core HRQL instrument for patients with CHD for making between-diagnosis comparisons possible and to assess the change in HRQL after treatment; it has been validated in patients with angina, myocardial infarction (MI) and ischaemic heart failure.<sup>8,9</sup> It has the advantage over other existing CHD tools (e.g. the Seattle Angina Questionnaire (SAQ) for angina patients; and the Minnesota Living with Heart Failure (MLHF) questionnaire for patients with heart failure) of allowing for between-diagnosis comparisons of HRQL.<sup>10,11</sup>

HRQL outcomes are known to be associated with the patients' characteristics, their coronary risk profile and their long-term cardiovascular prognosis.<sup>12–14</sup> The aim of the present study was to establish HeartQoL reference values for patients with CHD across Europe and to investigate the association with their coronary risk profile using information from the EUROASPIRE IV (EUROpean Action on Secondary and Primary prevention through Intervention to Reduce Events) survey.

## Methods

### *Study population and data collection*

Analyses are based on the EUROASPIRE IV cross-sectional survey (2012–2013), which included 24 European countries: Belgium, Bosnia Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, France, Germany, Greece, Ireland, Latvia, Lithuania, Netherlands, Poland, Romania, Russian Federation,

Serbia, Slovenia, Spain, Sweden, Turkey, Ukraine and the United Kingdom. More detailed information about the study has been reported previously.<sup>15</sup> Patients eligible for inclusion were men or women aged  $\geq 18$  years and  $< 80$  years at the time of identification who were interviewed six months to three years following hospitalization for a first or recurrent coronary event, that is, the recruiting event. Such events could include elective or emergency coronary artery bypass graft surgery (CABG), elective or emergency percutaneous coronary intervention (PCI), first or recurrent acute MI and acute myocardial ischaemia. Personal and demographic details as well as medical and cardiovascular history and reported lifestyle and risk factor management were assessed. A physical examination assessing weight, height, waist circumference, blood pressure, heart rate, breath carbon monoxide, serum total cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides, plasma glucose and HbA1c was performed. Furthermore, the patients were asked about their current risk factors such as smoking, physical activity and weight as well as about any associated lifestyle changes since the recruiting event. Physical activity levels were assessed using the validated International Physical Activity Questionnaire (IPAQ).<sup>16</sup> Since the IPAQ is known to have some problems with over reporting the physical activity status, a single question on physical activity levels was added to the questionnaire. Patients were also asked to complete the validated HeartQoL questionnaire,<sup>8</sup> comprising 14 items with four answer categories ranging from 'not bothered by' to 'bothered a lot by'. Global (all items), physical (10 items) and emotional (four items) scores, calculated as the mean of the item scores, can be computed, with scores ranging between 0 (lowest HRQL) and 3 (best HRQL) (Figure 1). The psychometric characteristics of the HeartQoL questionnaire have been previously assessed with good reliability and validity for most of the translations, with the exception of Bosnia Herzegovina; Bosnian scores are therefore not included in the current analyses.<sup>8,17</sup>

The most recent European guidelines on cardiovascular prevention were used to set the risk factor targets.<sup>18</sup> These are: blood pressure  $\geq 140/90$  mmHg ( $\geq 140/80$  mmHg in patients with diabetes); low-density lipoprotein (LDL)-cholesterol  $\geq 1.8$  mmol/l; and HbA1c  $\geq 7\%$  in diabetic patients. As no targets for total cholesterol or fasting glucose were set in the current guidelines, we used the following targets based on the previous guidelines: total cholesterol  $\geq 4.5$  mmol/l and fasting glucose  $\geq 6.1$  mmol/l.<sup>19</sup> Central obesity was defined as a waist circumference  $> 102$  cm and  $> 88$  cm for men and women, respectively; and overweight and obesity were defined as a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> and  $\geq 30$  kg/m<sup>2</sup>, respectively.

**Thank you for addressing these questions that will give us an understanding of how your heart problem has affected you.**

We would like to know how your heart problem has bothered you and how you have been feeling **DURING THE LAST 4 WEEKS.**

	Please check the box that most applies to you			
First, in the last 4 weeks, have you been bothered by having to:	No	A little	Some	A lot
	3	2	1	0
1. Walk indoors on level ground?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Garden, vacuum, or carry groceries?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Climb a hill or a flight of stairs without stopping?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Walk more than 100 yards at a brisk pace?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Lift or move heavy objects?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Now, in the last 4 weeks, have you been bothered by:</b>				
	Please check the box that most applies to you			
6. Feeling short of breath?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Being physically restricted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Feeling tired, fatigued, low on energy?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. Not feeling relaxed and free of tension?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. Feeling depressed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Being frustrated?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. Being worried?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13. Being limited in doing sports or exercise?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14. Working around the house or yard?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Thank you</b>				

**Figure 1.** HeartQoL instrument used to assess patients' global, physical and emotional HeartQoL score.

### Statistical analyses

Descriptive analyses for males and females were reported separately (mean  $\pm$  SD or  $n$  + %). To assess the association with the risk profile, generalized linear mixed models were used in order to account for the clustering of patients within countries. Baseline adjustments for age, gender and educational level were performed. Additional adjustments were made for recruiting diagnosis, diabetes, history of stroke and recurring coronary events. Statistical significance was defined as  $p < 0.05$ . All analyses were performed with IBM SPSS statistical software (version 21.0).

To calculate the reference values, HeartQoL scores were stratified by gender, age group (<60 years;  $\geq 60$  years and <70 years;  $\geq 70$  years), diabetes and educational level (primary education: primary school or less; secondary education: secondary school completed, high school completed or intermediate between

secondary level completed; high education: university/college degree or equivalent). Mean (SD) and median (interquartile range) values were calculated and the 10th and 90th percentiles and the ceiling percentage are reported. No research has yet focused on the clinically important difference for HeartQoL. One-half of a standard deviation has been shown to be representative of the minimal important difference (MID) in several HRQL instruments.<sup>20</sup> The MID can be seen as the smallest difference in score of importance to patients and clinicians.

### Results

#### Patient characteristics

HeartQoL information was available for 7261 patients (90.8%). The main patient characteristics are provided in Table 1. The mean age was 64.1 (SD = 9.6) years;

**Table 1.** Patient characteristics at the time of interview (N = 7261).

	All (N = 7261)	Men (n = 5526)	Women (n = 1735)
Age in years, mean (SD)	64.09 (9.59)	63.37 (9.66)	66.40 (9.00)
Age categories			
<60 years	32.0% (2325/7261)	34.8% (1921/5526)	23.3% (404/1735)
60–69 years	37.5% (2722/7261)	37.5% (2070/5526)	37.6% (652/1735)
≥70 years	30.5% (2214/7261)	27.8% (1535/5526)	39.1% (679/1735)
Education			
Primary education	17.0% (1225/7205)	15.9% (871/5482)	20.5% (354/1723)
Secondary education	60.3% (4342/7205)	59.7% (3274/5482)	62.0% (1068/1723)
High education	22.7% (1638/7205)	24.4% (1337/5482)	17.5% (301/1723)
Diabetes	26.8% (1936/7225)	25.8% (1418/5500)	30.0% (518/1725)
Raised fasting glucose, ≥6.1 mmol/l	85.6% (1426/1665)	85.8% (1048/1222)	85.3% (378/443)
Raised HbA1c, ≥7%	47.7% (885/1854)	46.2% (626/1355)	51.9% (259/499)
Central obesity	58.9% (4218/7157)	53.8% (2932/5452)	75.4% (1286/1705)
Body mass index			
Normal	17.8% (1287/7237)	16.9% (930/5509)	20.7% (357/1728)
Overweight	44.2% (3196/7237)	46.9% (2585/5509)	35.4% (611/1728)
Obese	38.1% (2754/7237)	36.2% (1994/5509)	44.0% (760/1728)
Current smoker	15.7% (1138/7261)	17.1% (944/5526)	11.2% (194/1735)
Self-reported physical activity			
No physical activity	8.2% (588/7162)	7.6% (413/5458)	10.3% (175/1704)
Only light physical activity in most weeks	51.4% (3681/7162)	49.1% (2682/5458)	58.6% (999/1704)
<20 min, 3×/week	19.9% (1428/7162)	20.7% (1132/5458)	17.4% (296/1704)
≥20 min, 3×/week	20.5% (1465/7162)	22.6% (1231/5458)	13.7% (234/1704)
IPAQ			
Low	19.7% (1145/5820)	18.0% (806/4469)	25.1% (339/1351)
Moderate	38.5% (2242/5820)	38.5% (1720/4469)	38.6% (522/1351)
High	41.8% (2433/5820)	43.5% (1943/4469)	36.3% (490/1351)
Raised total cholesterol, ≥4.5 mmol/l	38.5% (2692/6987)	35.5% (1890/5330)	48.4% (802/1657)
On lipid lowering medication	87.3% (6311/7230)	87.8% (4830/5502)	85.7% (1481/1728)
Raised total cholesterol in treated patients	34.1% (2074/6084)	31.0% (1446/4668)	44.4% (628/1416)
Raised LDL-cholesterol, ≥1.8 mmol/l	80.1% (5407/6752)	78.7% (4045/5142)	84.6% (1362/1610)
Raised LDL-cholesterol, ≥2.5 mmol/l	41.6% (2810/6752)	39.3% (2023/5142)	48.9% (787/1610)
Raised LDL-cholesterol, ≥1.8 mmol/l, in treated patients	78.5% (4615/5882)	77.1% (3471/4503)	83.0% (1144/1379)
Raised blood pressure, ≥140/90 mmHg <sup>a</sup>	41.6% (3003/7221)	41.3% (2270/5493)	42.4% (733/1728)
On blood pressure lowering medication	95.3% (6887/7230)	95.1% (5233/5502)	95.7% (1654/1728)
Raised blood pressure in treated patients	41.8% (2866/6851)	41.5% (2160/5202)	42.8% (706/1649)

<sup>a</sup>140/80 mmHg if diabetes.

IPAQ: International Physical Activity Questionnaire; LDL: low-density lipoprotein

76.1% were male; 17.0% had a low education level and 22.7% were highly educated.

### HeartQoL scores and coronary risk

Generalized linear mixed models analyses indicated differences in scores between the different patient groups, with significantly worse HeartQoL outcomes in higher

risk patient groups (Table 2).

a. Non-modifiable risk factors: significantly lower scores were observed in females, older patients, and primary education level patients. However, with the exception of gender (global and physical HeartQoL), none of the age or education level differences met or exceeded the MID.

**Table 2.** Association between coronary risk profile and HeartQoL scores (mean (SD)).

	Global HeartQoL	HeartQoL physical	HeartQoL emotional
<b>Non-modifiable risk factors</b>			
Gender			
Male (n = 5526)	2.26 (0.64)	2.22 (0.7)	2.36 (0.69)
Female (n = 1735)	1.94 (0.68)	1.89 (0.75)	2.08 (0.78)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>
Age			
<60 years (n = 2325)	2.22 (0.66) <sup>†</sup>	2.22 (0.71)	2.23 (0.76)
60–69 years (n = 2722)	2.23 (0.64)	2.19 (0.71)	2.35 (0.69) <sup>†</sup>
≥70 years (n = 2214)	2.08 (0.68)	2.00 (0.76)	2.30 (0.73)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> = 0.029</b>	<b>p<sup>b</sup> = 0.021</b>	<b>p<sup>b</sup> &lt; 0.001</b>
Educational level			
Primary (n = 1225)	2.04 (0.70)	1.98 (0.78)	2.19 (0.78)
Secondary (n = 4342)	2.19 (0.66)	2.14 (0.72)	2.32 (0.71)
High (n = 1638)	2.27 (0.63)	2.25 (0.69)	2.31 (0.70)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> = 0.001</b>	<b>p<sup>b</sup> = 0.010</b>
<b>Metabolic risk factors</b>			
Diabetes			
No (n = 5289)	2.24 (0.64)	2.21 (0.70)	2.32 (0.71)
Yes (n = 1936)	2.03 (0.69)	1.95 (0.77)	2.23 (0.75)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> = 0.297</b>
Raised HbA1c in diabetes patients			
No (n = 969)	2.10 (0.70)	2.03 (0.77)	2.28 (0.73)
Yes (n = 885)	1.97 (0.67)	1.89 (0.75)	2.18 (0.76)
	<b>p<sup>a</sup> = 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> = 0.041</b>
	<b>p<sup>b</sup> = 0.160</b>	<b>p<sup>b</sup> = 0.119</b>	<b>p<sup>b</sup> = 0.673</b>
Raised blood pressure in treated patients			
No (n = 3985)	2.20 (0.65)	2.16 (0.71)	2.31 (0.72)
Yes (n = 2866)	2.13 (0.67)	2.09 (0.75)	2.28 (0.73)
	<b>p<sup>a</sup> = 0.040</b>	<b>p<sup>a</sup> = 0.025</b>	<b>p<sup>a</sup> = 0.359</b>
	<b>p<sup>b</sup> = 0.100</b>	<b>p<sup>b</sup> = 0.061</b>	<b>p<sup>b</sup> = 0.621</b>
Raised LDL-cholesterol in treated patients			
No (n = 1267)	2.20 (0.65)	2.15 (0.72)	2.33 (0.70)
Yes (n = 4615)	2.22 (0.65)	2.18 (0.71)	2.32 (0.72)
	<b>p<sup>a</sup> = 0.001</b>	<b>p<sup>a</sup> = 0.001</b>	<b>p<sup>a</sup> = 0.024</b>
	<b>p<sup>b</sup> = 0.505</b>	<b>p<sup>b</sup> = 0.794</b>	<b>p<sup>b</sup> = 0.153</b>
Central obesity			
No (n = 2939)	2.31 (0.62)	2.30 (0.67)	2.34 (0.71)
Yes (n = 4218)	2.10 (0.67)	2.03 (0.75)	2.27 (0.73)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> = 0.016</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> = 0.196</b>
Body mass index			
Normal (n = 1287)	2.23 (0.65) <sup>†</sup>	2.21 (0.70) <sup>†</sup>	2.30 (0.74)

(continued)

Table 2. Continued

	Global HeartQoL	HeartQoL physical	HeartQoL emotional
Overweight (n = 3196)	2.26 (0.64)	2.22 (0.70)	2.34 (0.71)
Obese (n = 2754)	2.08 (0.68)	2.01 (0.75)	2.24 (0.74)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> = 0.006</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> = 0.174</b>
<b>Behavioural risk factors</b>			
Smoking status at interview			
Still smoking – no cessation attempt (n = 263)	2.17 (0.72) <sup>†‡</sup>	2.17 (0.76) <sup>†</sup>	2.18 (0.84)
Still smoking – cessation attempt (n = 797)	2.14 (0.68)	2.12 (0.73)	2.19 (0.78)
Prior smoker <sup>†</sup> (n = 1126)	2.27 (0.62)	2.24 (0.68)	2.33 (0.69)
Never smoker (n = 2376)	2.14 (0.67)	2.09 (0.74)	2.27 (0.73)
	<b>p<sup>a</sup> = 0.003</b>	<b>p<sup>a</sup> = 0.036</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> = 0.030</b>	<b>p<sup>b</sup> = 0.030</b>	<b>p<sup>b</sup> = 0.133</b>
Physical activity			
No physical activity (n = 588)	1.70 (0.76)	1.59 (0.84)	1.98 (0.87)
Only light physical activity in most weeks (n = 3681)	2.08 (0.65)	2.02 (0.72)	2.23 (0.74)
<20 min, 3×/week (n = 1428)	2.36 (0.57)	2.34 (0.62)	2.39 (0.66)
≥20 min, 3×/week (n = 1465)	2.48 (0.52)	2.47 (0.57)	2.50 (0.61)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>
IPAQ			
Low (n = 1145)	1.87 (0.74)	1.78 (0.82)	2.10 (0.82)
Moderate (n = 2242)	2.20 (0.62)	2.16 (0.69)	2.32 (0.71)
High (n = 2433)	2.34 (0.60)	2.32 (0.65)	2.38 (0.67)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>
Attempt to increase physical activity			
Yes (n = 4417)	2.27 (0.62)	2.24 (0.68)	2.36 (0.69)
No (n = 2740)	2.05 (0.70)	1.99 (0.77)	2.19 (0.77)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> = 0.045</b>
Change in physical activity according to IPAQ classes			
Change in physical activity + low IPAQ (n = 491)	1.98 (0.70)	1.9 (0.78)	2.20 (0.77)
No change in physical activity + low IPAQ (n = 625)	1.78 (0.77)	1.69 (0.85)	2.01 (0.85)
Change in physical activity + moderate/high IPAQ (n = 3104)	2.33 (0.59)	2.31 (0.64)	2.40 (0.66)
No change in physical activity + moderate/high IPAQ (n = 1531)	2.16 (0.65)	2.12 (0.71)	2.26 (0.73)
	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> &lt; 0.001</b>
	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>	<b>p<sup>b</sup> &lt; 0.001</b>
Weight change between recruiting diagnosis and interview			
≥5% weight loss (n = 1222)	2.11 (0.67)	2.06 (0.75)	2.25 (0.74)
–5% < weight change < +5% (n = 3002)	2.20 (0.65)	2.15 (0.72)	2.31 (0.73)
≥5% weight gain (n = 685)	2.19 (0.68)	2.16 (0.74)	2.26 (0.75)
	<b>p<sup>a</sup> = 0.004</b>	<b>p<sup>a</sup> &lt; 0.001</b>	<b>p<sup>a</sup> = 0.439</b>
	<b>p<sup>b</sup> = 0.152</b>	<b>p<sup>b</sup> = 0.115</b>	<b>p<sup>b</sup> = 0.550</b>

Analyses based on multilevel linear regression.

<sup>a</sup>p-value adjusted for age, gender, educational level.

<sup>b</sup>p-value adjusted for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke, recurring coronary events.

If overall significance, post hoc analyses were performed and showed significance between different categories, with the exception of † no significant difference with next group, and ‡ no significant difference between first and last group.

LDL: low-density lipoprotein; IPAQ: International Physical Activity Questionnaire

- b. Metabolic risk factors: diabetes, obesity and central obesity were associated with worse HeartQoL outcomes whereas there was no association of HeartQoL with raised HbA1c in patients with diabetes, nor with raised blood pressure or raised cholesterol in medically treated patients after full correction of the model. None of the metabolic risk factor differences met or exceeded the MID.
- c. Behavioural risk factors: HeartQoL scores were associated with better outcomes in prior smokers, in those who reported higher physical activity levels, and in those who had attempted to increase their physical activity level since their recruiting event. The latter two seem to reinforce one another, with the best outcome being seen in highly active patients who have made an attempt to increase their physical activity level, and the worst outcome in insufficiently active patients who had not made any attempt to increase their physical activity level. Finally, weight change was not associated with HeartQoL scores. The physical activity variables (both the single question, as well as the IPAQ and the combination of physical activity changes and IPAQ) met or exceeded the MID, with the lower physical activity categories having clinically relevant worse global and physical HeartQoL scores compared with the higher activity levels.
- d. Number of risk factors: worse HeartQoL scores were seen as the number of risk factors increased with the lowest HeartQoL scores in patients with  $\geq 3$  risk factors; the difference between the global and physical scores in patients with 0 or 1 risk factors and those with  $\geq 3$  risk factors exceeded the MID (Table 3).

### HeartQoL scores

The mean global HeartQoL score was 2.2 (SD = 0.66), while the mean physical and emotional subscale scores were 2.1 (SD = 0.73) and 2.3 (SD = 0.72), respectively. The HeartQoL global scale and subscale scores followed a typical HRQL distribution, with global scale and both subscale scores skewed to the left. The mean country-specific global HeartQoL scores, adjusted for age and gender, are shown in Figure 2, with scores of  $>2.4$  in Spain and Greece and mean scores  $<2.0$  in Turkey, France, Croatia, Poland, Bulgaria and Lithuania. The difference between the five countries with the worst global scores (Lithuania, Bulgaria, Poland, Croatia and France) and the five countries (Spain, Greece, Latvia, Sweden and the Netherlands) with the best global scores exceeded the MID.

### HeartQoL reference data

Reference values are given for CHD patients stratified by gender and age in Table 4. No floor effect was observed, though a ceiling effect was seen on all scales. Better scores are seen in males and younger patients, resulting in higher ceiling effects. The difference in mean global scores (2.26 and 1.94) and physical scores (2.22 and 1.89) between males and females approached the MID. Particularly in the 60–69-year-old age group, the MID was reached between males and females on all scales.

HeartQoL scores were further stratified by diabetes and educational level. Patients with diabetes scored worse than those without diabetes; however, the MID was not reached. Within diabetic patients however, the MID was reached between males and females on all three scales.

Likewise, lower educated patients scored worse than highly educated patients; however, again, the MID was not reached. In lower educated patients, the MID between males and females was well exceeded on all scales. The same was true for the global scale in highly educated patients.

Furthermore, mean item scores are provided: the highest mean was found on item 1 in both males (2.7) and females (2.5) and the lowest mean was found on item 5, again in both males (2.0) and females (1.7). Four items (2, 3, 4 and 5) exceeded the MID between males and females. Amongst the males, only item 5 had a mean score  $<2.0$ ; whereas among females, nine items had mean scores  $<2.0$  (items 2, 3, 4, 5, 7, 8, 12, 13 and 14).

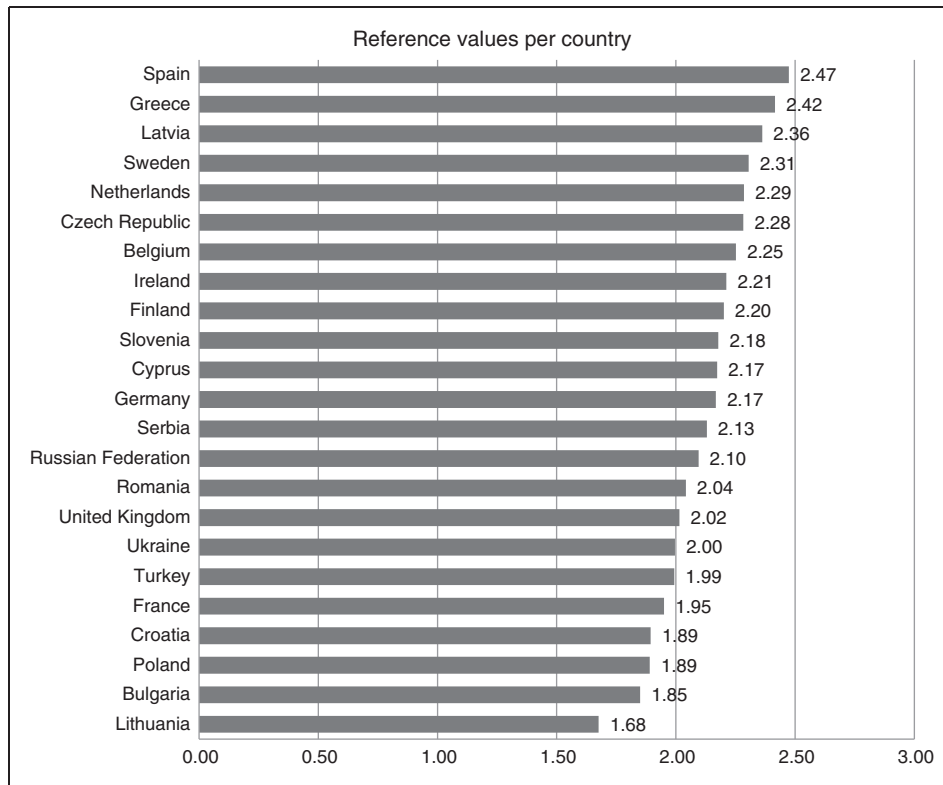
### Discussion

The aim of this study was to investigate the association between HeartQoL scores in CHD patients and their

**Table 3.** HeartQoL adjusted means (SE) in relation to the number of risk factors.

Number of risk factors	Global HeartQoL	HeartQoL physical	HeartQoL emotional
0 ( <i>n</i> = 856)	2.06 (0.072)	2.04 (0.079)	2.13 (0.081)
1 ( <i>n</i> = 1876)	1.93 (0.058)	1.86 (0.064)	2.10 (0.066)
2 ( <i>n</i> = 1756)	1.78 (0.056)	1.69 (0.062)	2.01 (0.063)
$\geq 3$ ( <i>n</i> = 1017)	1.60 (0.061)	1.48 (0.067)	1.90 (0.069)
	<b><math>p^a &lt; 0.001</math></b>	<b><math>p^a &lt; 0.001</math></b>	<b><math>p^a = 0.002</math></b>

<sup>a</sup>*p*-value adjusted for age, gender, educational level, recruiting diagnosis, diabetes, history of stroke and recurring coronary events. Risk factors included are: raised blood pressure, raised low-density lipoprotein cholesterol, current smoking, low physical activity and central obesity.



**Figure 2.** Global HeartQoL reference values per country, adjusted for age and gender.

coronary risk profile and to establish HeartQoL reference values for patients with CHD across Europe using data from the EUROASPIRE IV study, which included HeartQoL information from 7261 European patients with CHD. The patients included in the study had a typical coronary profile and, as in the EUROASPIRE III survey, a worse risk factor profile was associated with poor HRQL values, with an increase in number of risk factors being associated with worse HeartQoL outcomes.<sup>13,14</sup>

HeartQoL was associated with non-modifiable demographic risk factors such as gender, age and educational level. Substantiating previously reported findings in the general population as well as in CHD patients, worse HeartQoL outcomes were found in female patients.<sup>14,21,22</sup> Some suggest that women tend to over report their problems during interviews because women verbalize better than men,<sup>23</sup> others argue that women perceive symptoms in a different way,<sup>24,25</sup> also, higher depression rates and a lower sense of coherence and social status are referred to as possible reasons for worse HRQL outcomes in females.<sup>26–28</sup> Similarly to the general population, worse HeartQoL scores were seen with increasing age due to the natural aging process (deterioration of both physical and mental abilities).<sup>29</sup> A lower educational level, which has a direct relation to the expected income level, health habits, comorbidities,

access to health care facilities and a more adverse cardiovascular risk factor profile, was also associated with worse HRQL outcomes.<sup>30–33</sup>

Consistent with previous studies, patients with adverse metabolic risk factors such as diabetes, obesity and central obesity also performed worse on the HeartQoL questionnaire although no association was seen with the emotional component.<sup>22,34,35</sup> Finally, behavioural risk factors such as smoking and low levels of physical activity were associated with worse outcomes.<sup>36–42</sup> In general, self-reported behavioural changes since the recruiting event were associated with favourable outcomes. However, no association was seen with changes in weight. In CHD and other chronic disease patients, weight changes can occur for various reasons. Sometimes, a reduction in weight is a result of well-thought-out lifestyle changes that can result in better HRQL outcomes; however, patients often lose weight unintentionally as a result of their disease not resulting in improved HRQL scores.

In addition to statistical significance, the clinical significance was considered. Based on the theory of one-half of a standard deviation as clinically important difference, only the differences between genders, physical activity levels and the accumulation of risk factor were relevant. The other significant differences were smaller and might be of less clinical



Table 4. Age and gender specific reference data.

	Male (mean (SD))			Female (mean (SD))			
	<60 years (n = 1921)	60–69 years (n = 2070)	≥70 years (n = 1535)	All ages	<60 years (n = 404)	60–69 years (n = 652)	≥70 years (n = 679)
HeartQoL global							
Means (SD)	2.26 (0.64)	2.30 (0.61)	2.19 (0.64)	1.94 (0.68)	2.02 (0.67)	2.01 (0.66)	1.83 (0.70)
Median (p25–p75)	2.43 (1.86–2.79)	2.46 (1.93–2.79)	2.29 (1.79–2.71)	2 (1.43–2.5)	2.11 (1.57–2.57)	2.14 (1.64–2.50)	1.93 (1.536–2.36)
p10	1.36	1.43	1.29	0.93	1.07	1.00	0.86
p90	2.93	3.00	2.93	2.79	2.86	2.79	2.71
% floor effect	0.2%	0.1%	0.2%	0.3%	0.2%	0.2%	0.7%
% ceiling effect	9.9%	10.4%	7.4%	3.3%	5.2%	3.5%	1.9%
HeartQoL physical							
Mean (SD)	2.22 (0.7)	2.26 (0.68)	2.11 (0.73)	1.89 (0.75)	2.01 (0.73)	1.96 (0.73)	1.75 (0.77)
Median (p25–p75)	2.4 (1.8–2.8)	2.4 (1.9–2.8)	2.3 (1.6–2.7)	2 (1.4–2.5)	2.10 (1.53–2.6)	2.1 (1.5–2.5)	1.80 (1.20–2.40)
p10	1.20	1.20	1.10	0.70	1.00	0.80	0.60
p90	3.00	3.00	2.90	2.80	2.90	2.80	2.70
% floor effect	0.4%	0.3%	0.7%	0.9%	0.5%	0.9%	1.2%
% ceiling effect	13.6%	14.1%	9.9%	4.3%	6.7%	5.2%	2.1%
HeartQoL emotional							
Mean (SD)	2.36 (0.69)	2.41 (0.66)	2.41 (0.66)	2.08 (0.78)	2.06 (0.80)	2.14 (0.74)	2.05 (0.81)
Median (p25–p75)	2.5 (2–3)	2.5 (2–3)	2.75 (2–3)	2.25 (1.5–2.75)	2.00 (1.56–2.75)	2.25 (1.75–2.75)	2.25 (1.5–2.75)
p10	1.25	1.50	1.50	1.00	1.00	1.00	1.00
p90	3.00	3.00	3.00	3.00	3.00	3.00	3.00
% floor effect	1.0%	0.8%	0.7%	2.2%	3.0%	1.4%	2.7%
% ceiling effect	31.9%	33.7%	33.4%	20.1%	18.8%	21.2%	19.9%
Diabetes							
HeartQoL global	2.13 (0.67)	2.18 (0.66)	2.05 (0.68)	1.78 (0.67)	1.85 (0.63)	1.84 (0.66)	1.70 (0.70)
HeartQoL physical	2.05 (0.75)	2.09 (0.75)	1.94 (0.77)	1.69 (0.75)	1.78 (0.69)	1.75 (0.74)	1.59 (0.77)
HeartQoL emotional	2.31 (0.72)	2.39 (0.66)	2.33 (0.73)	2.01 (0.80)	2.00 (0.82)	2.07 (0.75)	1.96 (0.83)
No diabetes							
HeartQoL global	2.31 (0.62)	2.36 (0.59)	2.25 (0.61)	2.01 (0.68)	2.08 (0.67)	2.09 (0.64)	1.90 (0.69)
HeartQoL physical	2.28 (0.68)	2.33 (0.64)	2.17 (0.7)	1.97 (0.74)	2.08 (0.73)	2.05 (0.71)	1.82 (0.76)
HeartQoL emotional	2.38 (0.69)	2.42 (0.65)	2.44 (0.63)	2.12 (0.77)	2.07 (0.79)	2.17 (0.74)	2.09 (0.79)
Education							
Primary							
HeartQoL global	2.16 (0.67)	2.20 (0.69)	2.13 (0.67)	1.75 (0.69)	1.74 (0.71)	1.88 (0.66)	1.66 (0.70)
HeartQoL physical	2.11 (0.74)	2.15 (0.74)	2.03 (0.76)	1.68 (0.78)	1.72 (0.78)	1.84 (0.73)	1.54 (0.79)
HeartQoL emotional	2.3 (0.74)	2.32 (0.75)	2.36 (0.69)	1.93 (0.83)	1.79 (0.84)	1.97 (0.82)	1.95 (0.84)

(continued)

Table 4. Continued

	Male (mean (SD))			Female (mean (SD))				
		<60 years (n = 1921)	60–69 years (n = 2070)	≥70 years (n = 1535)	All ages	<60 years (n = 404)	60–69 years (n = 652)	≥70 years (n = 679)
	All ages							
Secondary								
HeartQoL global	2.26 (0.63)	2.24 (0.66)	2.31 (0.60)	2.20 (0.64)	1.99 (0.68)	2.05 (0.65)	2.05 (0.65)	1.90 (0.70)
HeartQoL physical	2.21 (0.70)	2.24 (0.70)	2.26 (0.67)	2.10 (0.73)	1.93 (0.74)	2.04 (0.71)	2.04 (0.71)	1.82 (0.75)
HeartQoL emotional	2.38 (0.69)	2.26 (0.75)	2.46 (0.62)	2.44 (0.65)	2.14 (0.77)	2.08 (0.79)	2.08 (0.79)	2.12 (0.8)
High								
HeartQoL global	2.33 (0.60)	2.38 (0.60)	2.33 (0.61)	2.26 (0.59)	2.01 (0.67)	2.12 (0.69)	2.07 (0.61)	1.85 (0.70)
HeartQoL physical	2.32 (0.66)	2.40 (0.64)	2.32 (0.67)	2.20 (0.66)	1.98 (0.73)	2.09 (0.74)	2.07 (0.68)	1.81 (0.75)
HeartQoL emotional	2.37 (0.68)	2.34 (0.69)	2.36 (0.68)	2.42 (0.66)	2.07 (0.75)	2.19 (0.74)	2.08 (0.71)	1.97 (0.78)
HeartQoL item scores								
1. Walk indoors on level ground	2.69 (0.71)	2.72 (0.68)	2.72 (0.68)	2.61 (0.78)	2.54 (0.81)	2.62 (0.74)	2.58 (0.79)	2.46 (0.86)
2. Garden, vacuum, or carry groceries	2.40 (0.88)	2.48 (0.83)	2.43 (0.85)	2.27 (0.95)	2.00 (1.00)	2.15 (0.91)	2.06 (0.99)	1.84 (1.05)
3. Climb a hill or a flight of stairs without stopping	2.11 (1.01)	2.17 (1.00)	2.15 (0.98)	1.96 (1.04)	1.64 (1.07)	1.84 (1.03)	1.72 (1.07)	1.46 (1.08)
4. Walk more than 100 metres at a brisk pace	2.10 (1.05)	2.20 (1.01)	2.15 (1.03)	1.90 (1.10)	1.71 (1.12)	1.90 (1.06)	1.84 (1.10)	1.47 (1.12)
5. Lift or move heavy objects	1.96 (1.05)	2.04 (1.04)	2.01 (1.02)	1.79 (1.08)	1.50 (1.09)	1.67 (1.05)	1.56 (1.09)	1.34 (1.10)
6. Feeling short of breath	2.34 (0.85)	2.34 (0.86)	2.37 (0.83)	2.29 (0.87)	2.04 (0.94)	2.04 (0.95)	2.13 (0.91)	1.95 (0.96)
7. Being physically restricted	2.21 (0.90)	2.24 (0.90)	2.24 (0.88)	2.12 (0.93)	1.92 (0.96)	2.03 (0.89)	1.98 (0.94)	1.80 (1.01)
8. Feeling tired, fatigued, low on energy	2.08 (0.90)	2.06 (0.92)	2.11 (0.88)	2.04 (0.89)	1.73 (0.94)	1.74 (0.97)	1.80 (0.91)	1.67 (0.96)
9. Not feeling relaxed and free of tension	2.29 (0.83)	2.19 (0.88)	2.32 (0.80)	2.35 (0.79)	2.01 (0.90)	2.02 (0.87)	2.05 (0.90)	1.95 (0.93)
10. Feeling depressed	2.49 (0.78)	2.41 (0.84)	2.53 (0.74)	2.53 (0.76)	2.19 (0.93)	2.14 (0.95)	2.24 (0.88)	2.16 (0.96)
11. Being frustrated	2.45 (0.81)	2.34 (0.87)	2.51 (0.76)	2.49 (0.78)	2.21 (0.91)	2.15 (0.95)	2.25 (0.86)	2.20 (0.94)
12. Being worried	2.23 (0.86)	2.15 (0.90)	2.28 (0.83)	2.27 (0.84)	1.94 (0.94)	1.92 (0.95)	2.01 (0.91)	1.87 (0.96)
13. Being limited in doing sports or exercise	2.03 (1.01)	2.08 (1.00)	2.09 (0.99)	1.92 (1.05)	1.78 (1.08)	1.89 (1.01)	1.85 (1.06)	1.64 (1.12)
14. Working around the house or yard	2.27 (0.93)	2.31 (0.92)	2.31 (0.92)	2.18 (0.96)	1.99 (1.02)	2.17 (0.96)	2.04 (1.01)	1.84 (1.04)

importance. Future studies should investigate the clinically meaningful difference in HeartQoL scores in order to make correct statements about the utility of the instrument to distinguish between patient characteristics.

Next, reference values were calculated. This study is the first to provide HeartQoL reference values for coronary patients. These values can be useful for other researchers in interpreting HeartQoL scores and assessing whether their study population scores lower or higher on the HeartQoL questionnaire than the EUROASPIRE IV dataset. Reference values were generated, stratifying by gender, age group, educational level and diabetes status since these variables are known to be associated with HRQL. Clinically relevant differences between males and females were found in the total sample, as well as in diabetic patients and lower educated patients. The most relevant differences mainly occurred on the global and physical scale and in the 60–69-year-old age class. The level to which the participating centres were representative of their country could be questioned, hence within this study only overall European reference values are considered.

Our research has some important limitations. First, EUROASPIRE IV is a cross-sectional study and the lifestyle changes made since the recruiting event were self-reported. The patients included in the survey were mainly identified from academic hospitals situated in selected geographical areas and therefore do not constitute a representative sample of all CHD patients in each country. Also, clinically important differences for HeartQoL have not yet been studied, therefore one-half of a standard deviation was used as MID.<sup>20</sup>

In summary, these HeartQoL reference values can be used in clinical practice across Europe. Similar to other instruments, HeartQoL scores were associated with patients' coronary risk profile. Clinically relevant differences were seen between males and females, especially in diabetic patients and less educated patients, and between higher and lower physical activity levels. Also, the number of risk factors showed important differences in the HeartQoL score. However, further research should focus on the HeartQoL MID, since the current MID values are based on other HRQL instruments or on theoretical observations and must be substantiated by empirical data. This will help to evaluate the effect of therapies and lifestyle changes on HeartQoL scores.

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