

# Psychosocial factors associated with health-related quality of life in patients with chronic disease: Results of a cross-sectional survey

Chronic Illness

1–15

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## Abstract

**Objective:** The impact of various psychosocial factors (sense of coherence, illness perception, patient enablement, self-efficacy, health literacy, personality) is not fully understood across a wide range of chronic diseases, and in particular in patients with multimorbidity. As such, this study assessed the key psychosocial factors associated with impaired health-related quality of life (HRQoL) in patients with one or more chronic diseases based on cross-sectional data collected in Flanders (Belgium).

**Methods:** Cross-sectional data on 544 chronically ill patients were analysed. Multiple linear regression models were built to analyze the key psychosocial factors associated with HRQoL (EQ-5D-5L<sub>index</sub> as dependent factor).

**Results:** Overall, the strongest independently associated factor with HRQoL was illness perceptions ( $\beta = -0.52$ ,  $P < 0.001$ ). In addition, sense of coherence ( $\beta = 0.14$ ,  $P < 0.05$ ) was independently positively associated with HRQoL. Moreover, after stratification for multimorbidity, the negative association of illness perceptions with HRQoL was stronger when multimorbidity is present compared to when it is absent ( $\beta = -0.62$ ,  $P < 0.001$  vs  $\beta = -0.38$ ,  $P < 0.001$ ).

**Conclusions:** This study revealed interesting associations of the modifiable psychosocial factors of illness perceptions and sense of coherence with HRQoL in a population of chronically ill

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persons. Given that the burden of chronic diseases will rise in the next decades, designing and implementing interventions that enhance these psychosocial abilities of patients, especially illness perceptions in multimorbid patients, is needed in order to reduce the burden of chronic diseases in terms of impaired HRQoL.

## Keywords

Chronic disease, multimorbidity, health-related quality of life, EQ-5D, psychosocial factors, illness perception, sense of coherence

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## Introduction

The twenty-first century is characterized by an increased predominance of chronic diseases, currently affecting billions of people worldwide.<sup>1</sup> In 2019, chronic diseases accounted for 74% of deaths globally, with a significant fraction of the diseases being preventable.<sup>2</sup> In general, chronic diseases lead to reduced physical, emotional and social functioning, higher risk of depression and anxiety, and reduced health-related quality of life (HRQoL).<sup>3–5</sup> The latter has been the subject of research during the last decades due to the absence of an adequate cure for several chronic diseases and hence the shift from cure to care.<sup>6</sup> HRQoL is a subjective measure of overall well-being and reflects how a medical condition, its symptoms, and treatment are perceived by a patient.<sup>6,7</sup>

A recent systematic review provided a large amount of evidence on the substantial reduction in HRQoL in patients with chronic diseases.<sup>5</sup> Indeed, the impact of chronic diseases on HRQoL has been addressed by numerous studies, however a better understanding of the influence of important associated factors is lacking. Although several sociodemographic (e.g., age, gender), clinical (e.g., comorbidity), and environmental factors (e.g., perceived support) have been found to be associated with HRQoL in specific chronic diseases,<sup>8–12</sup> the impact of various psychosocial factors (e.g., sense of coherence, illness perception, patient enablement, self-efficacy, health literacy, personality) is not fully understood across

a wide range of chronic diseases, and in particular in patients with multimorbidity (i.e., the co-existence of multiple chronic conditions). New insights, especially derived from multivariate models, are important when designing evidence-based interventions to improve HRQoL in chronically ill patients.

The aim of this study is to assess the key psychosocial factors associated with impaired HRQoL in patients with one or more chronic diseases based on cross-sectional data collected in Flanders (Belgium). These results can then be used to guide health care providers in their clinical practice on the one hand and to inform policy makers in preventing and reducing burden of disease in the population on the other hand.

## Methods

### Study design

Data from a questionnaire-based, cross-sectional study (QAPICHE study, which is an acronym for “quality of life in patients with chronic disease”) conducted in Flanders (Belgium) were used. The aim of the QAPICHE study is to provide insight in HRQoL outcomes and their predictors in patients with chronic diseases in the context of a primary care setting. Detailed information on the methodology has been published previously.<sup>13</sup> The study was approved by the Ethical Committee of the Ghent University Hospital, Belgium (reference number: B670201939629) and is registered on [clinicaltrials.gov](https://clinicaltrials.gov), ID: NCT03925805.

## Participants

Inclusion criteria were being an adult ( $\geq 18$  years) and being diagnosed with at least one of the following chronic diseases: cardiometabolic disorders, mental disorders, and/or musculoskeletal disorders. Patients with insufficient understanding of Dutch to complete the questionnaire were excluded. As such, a total of 544 persons, recruited between June 2019 and June 2021, participated in the study. 287 of them (52.8%) were recruited via 56 general practitioners and the remaining 257 persons (47.2%) were recruited via 18 officially recognized Flemish patient organizations.

## Measures

*Sociodemographic factors.* The following sociodemographic variables were collected: age, sex (male, female), and educational attainment. The latter was classified into low (lower secondary education or less), intermediate (higher secondary education), and high (higher education), according to the International Standard Classification of Education (ISCED).<sup>14</sup>

*Multimorbidity.* Participants had to indicate on a list of 24 chronic conditions whether they had suffered from a certain disease with the responses “yes” (only filled in for the conditions that have been confirmed by a doctor or for which the participant is taking prescribed drugs) or “no”. Defining multimorbidity as the presence of two or more chronic diseases at the same time in one individual is not universally accepted, especially when highly prevalent conditions (e.g., hypertension, osteoporosis) are included as these result in higher prevalence rates.<sup>15</sup> Therefore, a cut-off value of  $\geq 3$  concurrent diseases was used to define multimorbidity, using the simple count method.<sup>16</sup>

*Health-related quality of life.* HRQoL was measured using the EQ-5D-5L, which is composed of two parts: a descriptive system and a visual analogue scale (VAS). The former covers five dimensions

(mobility, self-care, usual activities, pain/discomfort, anxiety/depression) defined by five severity levels (no problems, slight problems, moderate problems, severe problems, extreme problems/unable to) from which a single index score or utility score can be calculated, ranging between 0 (representing death) and 1 (representing perfect health) and with negative values for health states perceived worse than death.<sup>17</sup> Recently, an EQ-5D-5L value set has been developed based on health states preferences from the general population of Belgium.<sup>18</sup> Possible index values range between  $-0.532$  and 1. The EQ-VAS measures respondents' self-rated health on a 0 (worst imaginable health) to 100 (best imaginable health) scale.

*Personality traits.* Personality traits were measured using the Big Five Inventory (BFI-10), which allows a quick assessment of a person's degree of extraversion, agreeableness, conscientiousness, emotional stability, and intellect/openness.<sup>19</sup> The instrument consists of 10 items where each item is scored on a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree).

*Sense of coherence.* Sense of coherence was measured using the brief Antonovsky's Sense of Coherence Scale (SOC-13), which examines the meaningfulness, comprehensibility and manageability of a situation or disease using 13 items.<sup>20</sup> Responses range from 1 (never or very seldom) to 7 (very often). SOC scores range from 13 to 91, and a higher score indicates higher SOC.

*Self-efficacy.* The General Self-Efficacy Scale (GSES)<sup>21,22</sup> assessed optimistic self-beliefs to cope with a variety of difficult demands in life. Total scores range between 10 and 40, with higher scores indicating more self-efficacy.

*Health literacy.* A short scale of the European Health Literacy Survey (HLS-EU-Q6)<sup>23</sup> addresses difficulties in accessing, understanding, appraising, and applying information in tasks concerning decision-making in health care, disease prevention, and health promotion.<sup>23</sup>

**Table 1.** Characteristics of the study participants (n = 544).

	% (N)
<b>Age, mean (SD)</b>	58.6 (15.8)
18 – 44 years	19.3% (105/543)
45 – 54 years	18.2% (99/543)
55 – 64 years	22.8% (124/543)
≥ 65 years	39.6% (215/543)
<b>Sex</b>	
Female	67.1% (365/544)
Male	32.9% (179/544)
<b>Education</b>	
Low	28.4% (154/542)
Intermediate	32.5% (176/542)
High	39.1% (212/542)
<b>Employment status</b>	
Employed	20.1% (109/541)
Unemployed	5.7% (31/541)
Student	1.3% (7/541)
Disability	26.4% (143/541)
Pensioner	44.9% (243/541)
Other	1.5% (8/541)
<b>Civil status</b>	
Single	18.4% (100/543)
Married or legally cohabiting	66.5% (361/543)
Divorced	8.7% (47/543)
Widow(er)	6.4% (35/543)
<b>Disease type</b>	
Cardiovascular disease	58.8% (317/539)
Mental disease	27.1% (146/539)
Musculoskeletal disease	70.1% (378/539)
Diabetes	27.1% (146/539)
Other	70.3% (379/539)
<b>Multimorbidity</b>	
Yes	63.4% (341/538)
No	36.6% (197/538)
<b>Anxiety/depression, mean (SD)</b>	
HADS-A <sup>1</sup>	7.5 (4.9)
HADS-D <sup>1</sup>	6.9 (4.8)
<b>Self-efficacy, mean (SD)</b>	
GSES <sup>2</sup>	28.6 (5.8)
<b>Sense of coherence, mean (SD)</b>	
SOC-13 <sup>3</sup>	58.2 (14.9)
<b>Personality traits, mean (SD)</b>	
BFI extraversion <sup>4</sup>	3.4 (0.9)
BFI agreeableness <sup>4</sup>	3.9 (0.7)
BFI conscientiousness <sup>4</sup>	4.0 (0.8)
BFI neuroticism <sup>4</sup>	3.2 (1.0)
BFI openness <sup>4</sup>	3.3 (1.0)

(continued)

Table 1. Continued

	% (N)
<b>Health literacy</b> (HLS-EU-Q6 <sup>5</sup> ), mean (SD)	2.8 (0.5)
<b>Social support</b> (F-SozU <sup>6</sup> ), mean (SD)	22.5 (5.7)
<b>Illness perception</b> (IPQ-B <sup>7</sup> ), mean (SD)	5.7 (1.7)
<b>Empowerment</b> (PEI <sup>8</sup> ), mean (SD)	3.9 (3.5)

<sup>1</sup>Maximum score of 21, with higher scores indicating higher levels of anxiety and depression.

<sup>2</sup>Maximum score of 40, with higher scores indicating more self-efficacy.

<sup>3</sup>Maximum score of 91, with higher scores indicating higher sense of coherence.

<sup>4</sup>Maximum score of 5, with higher scores indicating higher levels of that specific personality domain.

<sup>5</sup>Maximum score of 4, with higher scores indicating better health literacy.

<sup>6</sup>Maximum score of 30, with higher scores indicating higher perceived and received social support.

<sup>7</sup>Maximum score of 10, with higher scores indicating a more threatening view of the illness.

<sup>8</sup>Maximum score of 12, with higher scores indicating better empowerment.

Responses are reported from 1 (very difficult) to 4 (very easy). The overall scale score varies between 1 and 4, with higher scores indicating better health literacy.

*Patient enablement.* The Patient Enablement Instrument (PEI) focuses on the impact of a clinical consultation in primary care on a patient's ability to understand and cope with the disease.<sup>24</sup> The PEI consists of six questions that are scored on a three-point scale. Total scores range between 0 and 12, with higher scores indicating higher enablement. Patient enablement will be used as a proxy for patient empowerment.

*Social support.* Social support was measured using the six-item shortened version of the Social Support Questionnaire (F-SozU).<sup>25,26</sup> Responses are rated on a five-point Likert scale, ranging from 1 (does not apply) to 5 (exactly applicable). The total score ranges from 0 to 30, with higher values representing higher perceived and received social support.

*Anxiety/depression.* The Hospital Anxiety and Depression Scale (HADS)<sup>27</sup> is a 14-item brief instrument to determine presence of anxiety (HADS-A) and depressive states (HADS-D), each consisting of seven items.<sup>27,28</sup> A maximum score of 21 can be achieved per scale. The higher the overall score, the higher the levels of anxiety and depression.

*Illness perceptions.* The brief Illness Perception Questionnaire (IPQ-B) assesses

patients' cognitive and emotional representations of their illness.<sup>29,30</sup> The questionnaire uses a scale from 0 to 10 to assess cognitive illness representations (item 1-5), emotional representations (item 6 and 8), and illness comprehensibility (item 7). A higher overall score reflects a more threatening view of the illness.

### Statistical analysis

Statistics were undertaken using IBM SPSS statistical software (version 27.0). First, descriptive analyses were performed. For continuous variables, mean and standard deviations are shown, for categorical variables, percentages are used.

After checking the assumptions, multiple linear regression models were built assessing the key psychosocial factors associated with HRQoL (EQ-5D-5L<sub>index</sub> as dependent factor). Based on the literature and univariate regressions, the following candidate variables were selected: personality traits, sense of coherence, self-efficacy, health literacy, empowerment, social support, anxiety/depression, and illness perceptions. Next, age, sex, education, and multimorbidity were entered in the model as potential confounders. Collinearity diagnostics (Variance Inflation Factor and Tolerance) were checked. Fitness of the model was evaluated by inspecting adjusted R<sup>2</sup>. A p-value smaller than 0.05 was considered as statistically significant.

## Results

### Sample characteristics

Data on 544 chronically ill patients were available for analysis. The EQ-5D-5L was completed by 502 participants (92.3%). Descriptive statistics are outlined in Table 1. The mean age was 58.6 years ( $SD=15.8$ ) and 67.1% were women. Low education was reported by 28.4% of respondents and 39.1% was highly educated. The majority were married or cohabiting (66.5%). 44.9% were retired, 26.4% were on disability or illness leave, and 20.1% were employed. Approximately 16.5% had one chronic disease. Multimorbidity occurred in 63.4% of the participants.

### EQ-5D-5L outcomes

The EQ-5D dimensions were recoded into two categories: no problems reported and any problems reported. The majority of participants reported problems of pain/discomfort (80.5%), followed by problems of usual activities (65.3%), mobility (57.4%), anxiety/depression (48.2%), and self-care (26.9%) (Table 2). Patients with multimorbidity reported the highest frequency of problems while patients with only one chronic disease reported the lowest frequency of problems (Figure 1). Patients with negative illness perceptions and low levels of empowerment, self-efficacy, social support, sense of coherence, and health literacy had worse outcomes on all dimensions compared to those with high levels on these psychosocial traits (Appendix 1). Results for the personality factors were less pronounced, except for neuroticism: patients with a high degree of neuroticism had worse outcomes on all the dimensions compared to those with a low degree of neuroticism.

The mean EQ-VAS for the total sample was 60.3 (Table 2). Patients with multimorbidity reported a significantly lower EQ-VAS score compared to patients with two chronic diseases (55.8 vs 65.8,  $P < 0.001$ ) or with one chronic disease (55.8 vs 70.6,  $P < 0.001$ ).

The mean EQ-5D-5L index value for the total sample was 0.64 (Table 2). Full health (i.e., a utility of 1) was reported by 12.4% of the patients. The lowest utility seen was  $-0.48$ , rated by one respondent only. Participants with multimorbidity reported a significantly lower mean EQ-5D-5L index score compared to participants with two chronic diseases (0.57 vs 0.75,  $P < 0.001$ ) or with one chronic disease (0.57 vs 0.80,  $P < 0.001$ ).

### Psychosocial factors

Median splits were performed to transform continuous psychosocial factors into categorical variables with “high” and “low” groups.<sup>31</sup> Overall, we observed that the majority of respondents had negative illness perceptions (50.7%) and low levels of empowerment (51.9%), self-efficacy (52.2%), social support (51.4%), sense of coherence (52.0%), health literacy (52.6%), extraversion (53.2%), agreeableness (69.6%), conscientiousness (57.4%), neuroticism (52.0%), and openness (63.8%). In total, 27% and 24% of respondents had a probable anxiety (HADS-A) or depressive disorder (HADS-D), respectively. Scale scores of the psychosocial factors are shown in Table 1.

### Psychosocial factors associated with EQ-5D-5L index

Univariate analysis of associations with HRQoL are outlined in Table 3. Negative illness perceptions, anxiety/depression, neuroticism, and low levels of empowerment, self-efficacy, social support, sense of coherence, and health literacy were significantly ( $P < 0.001$ ) associated with impaired HRQoL, after adjusting for age, gender, education. In a number of cases, associations were stronger in multimorbid patients suggesting stratification for multimorbidity.

Results of the multivariable regression model are outlined in Table 4. When adjusted for age, sex, and education, the model explained

**Table 2.** Distribution of EQ-5D-5L according to gender, age, and multimorbidity status.

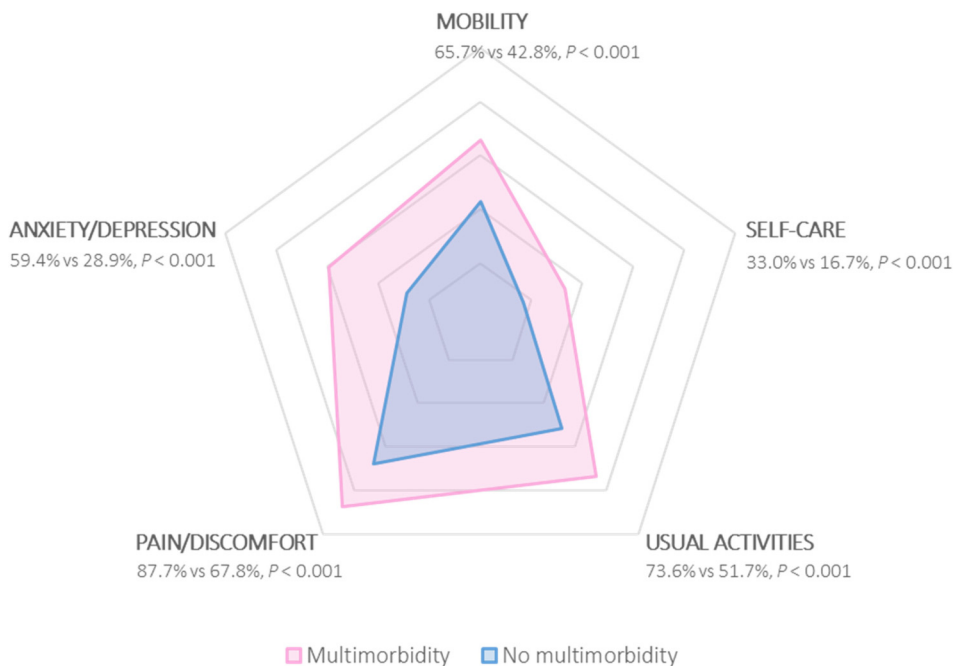
	Total (n = 502)	Men (n = 162)	Women (n = 340)	18-44 year (n = 102)	45-54 year (n = 96)	55-64 year (n = 115)	≥65 year (n = 188)	1 chronic disease (n = 84)	2 chronic diseases (n = 96)	≥ 3 chronic diseases (n = 318)
<b>EQ-5D-5L index,</b> mean (SD)	0.64 (0.31)	0.77 (0.28)	0.58 (0.31)	0.57 (0.32)	0.53 (0.31)	0.64 (0.29)	0.74 (0.29)	0.80 (0.22)	0.75 (0.23)	0.57 (0.32)
<b>EQ-VAS, mean (SD)</b>	60.3 (18.8)	67.8 (18.1)	56.8 (18.0)	55.0 (17.7)	51.9 (18.4)	60.4 (18.1)	67.4 (17.2)	70.6 (14.3)	65.8 (16.7)	55.8 (18.8)
<b>MOBILITY</b>										
No problems	42.6%	56.8%	35.9%	44.1%	30.2%	41.7%	48.9%	60.7%	54.2%	34.3%
Slight problems	21.9%	17.3%	24.1%	21.6%	33.3%	20.9%	17.0%	25.0%	19.8%	22.0%
Moderate problems	23.3%	14.8%	27.4%	26.5%	26.0%	20.9%	21.8%	8.3%	18.8%	28.3%
Severe problems	9.4%	7.4%	10.3%	6.9%	9.4%	15.7%	6.4%	3.6%	6.3%	11.9%
Extreme problems/ unable to	2.8%	3.7%	2.4%	1.0%	1.0%	0.9%	5.9%	2.4%	1.0%	3.5%
<b>SELF-CARE</b>										
No problems	73.1%	85.2%	67.4%	68.6%	64.6%	75.7%	78.2%	83.3%	83.3%	67.0%
Slight problems	15.5%	4.3%	20.9%	16.7%	24.0%	16.5%	10.1%	9.5%	10.4%	18.9%
Moderate problems	7.4%	5.6%	8.2%	10.8%	10.4%	4.3%	5.9%	3.6%	5.2%	9.1%
Severe problems	2.6%	2.5%	2.6%	2.0%	1.0%	3.5%	3.2%	2.4%	NA	3.5%
Extreme problems/ unable to	1.4%	2.5%	0.9%	2.0%	NA	NA	2.7%	1.2%	1.0%	1.6%
<b>USUAL</b>										
<b>ACTIVITIES</b>										
No problems	34.7%	61.7%	21.8%	21.6%	12.5%	30.4%	55.9%	51.2%	45.8%	26.4%
Slight problems	23.1%	16.0%	26.5%	25.5%	25.0%	27.0%	18.6%	26.2%	21.9%	22.6%
Moderate problems	23.9%	13.6%	28.8%	27.5%	35.4%	25.2%	14.9%	14.3%	19.8%	28.0%
Severe problems	14.3%	4.9%	18.8%	20.6%	21.9%	13.9%	7.4%	7.1%	10.4%	17.6%
Extreme problems/ unable to	4.0%	3.7%	4.1%	4.9%	5.2%	3.5%	3.2%	1.2%	2.1%	5.3%
<b>PAIN/</b>										
<b>DISCOMFORT</b>										

(continued)

Table 2. Continued

	Total (n = 502)	Men (n = 162)	Women (n = 340)	18–44 year (n = 102)	45–54 year (n = 96)	55–64 year (n = 115)	≥65 year (n = 188)	1 chronic disease (n = 84)	2 chronic diseases (n = 96)	≥ 3 chronic diseases (n = 318)
No problems	19.5%	35.2%	12.1%	15.7%	9.4%	18.3%	27.7%	38.1%	27.1%	12.3%
Slight problems	23.9%	31.5%	20.3%	23.5%	12.5%	20.0%	32.4%	29.8%	33.3%	18.9%
Moderate problems	27.5%	17.9%	32.1%	27.5%	33.3%	33.0%	21.3%	19.0%	24.0%	31.1%
Severe problems	25.7%	14.8%	30.9%	29.4%	40.6%	24.3%	16.5%	13.1%	14.6%	32.7%
Extreme problems/ unable to ANXIETY/	3.4%	0.6%	4.7%	3.9%	4.2%	4.3%	2.1%	NA	1.0%	5.0%
<b>DEPRESSION</b>										
No problems	51.8%	66.0%	45.0%	26.5%	35.4%	55.7%	71.3%	67.9%	74.0%	40.6%
Slight problems	25.7%	22.2%	27.4%	34.3%	32.3%	25.2%	18.1%	27.4%	12.5%	29.2%
Moderate problems	14.9%	9.9%	17.4%	24.5%	19.8%	12.2%	9.0%	4.8%	8.3%	19.8%
Severe problems	6.2%	1.2%	8.5%	11.8%	9.4%	6.1%	1.6%	NA	5.2%	8.2%
Extreme problems/ unable to	1.4%	0.6%	1.8%	2.9%	3.1%	0.9%	0%	NA	NA	2.2%





**Figure 1.** Reported problems on the EQ-5D-5L dimensions, by multimorbidity status. The further away from the origin, the more problems reported.

52% of the variance in the dependent variable HRQoL. Multicollinearity (Tolerance < 0.4, Variance Inflation Factor > 2.5) was observed for HADS-A and HADS-D. High correlations of both HADS scales with the EQ-5D were observed (because they include related constructs), leaving them both out of the model. The most important independently associated factor with HRQoL was illness perceptions ( $\beta = -0.52$ ,  $P < 0.001$ ): the lower the HRQoL, the more negative illness perceptions (or vice versa). On the contrary, sense of coherence ( $\beta = 0.14$ ,  $P < 0.05$ ) was independently positively associated with HRQoL: the higher HRQoL, the more sense of coherence (or vice versa). Another important associated factor, which was non-psychosocial, was multimorbidity ( $\beta = -0.14$ ,  $P < 0.001$ ).

After stratifying the model for multimorbidity (to account for effect modification of multimorbidity), the negative association of illness perceptions with HRQoL was even stronger when

multimorbidity is present compared to when it is absent ( $\beta = -0.62$ ,  $P < 0.001$  vs  $\beta = -0.38$ ,  $P < 0.001$ ). Furthermore, sense of coherence was significantly associated with HRQoL in patients with 1 of 2 single conditions ( $\beta = 0.19$ ,  $P < 0.05$ ), but not in the multimorbidity model.

## Discussion

In general, the results of this study again confirm that people suffering from at least one chronic disease have a significant lower HRQoL than their healthy peers. Indeed, the average EQ-5D index value (0.64) and EQ-VAS (60.3) scores in this sample were significant lower than the national Belgian population norms of 0.84 (EQ-5D index) and 76.1 (EQ-VAS) for the same age group.<sup>32</sup> Likewise, the prevalence of reporting problems on all EQ-5D dimensions was higher in this sample compared to the Belgian reference scores for the same age group: 81% vs 63% for pain/discomfort, 65%

**Table 3.** Univariate analysis.

	Overall				Multimorbidity absent		Multimorbidity present	
	B	P value <sup>1</sup>	P value <sup>2</sup>	P value <sup>3</sup>	B	P value <sup>2</sup>	B	P value <sup>2</sup>
<b>Empowerment</b>	0.03	<0.001*	<0.001*	<0.001*	0.02	<0.001*	0.04	<0.001*
<i>Interaction with multimorbidity</i>	0.01	0.053	<0.05*					
<b>HADS anxiety</b>	-0.04	<0.001*	<0.001*	<0.001*	-0.02	<0.001*	-0.04	<0.001*
<i>Interaction with multimorbidity</i>	-0.02	<0.01*	<0.001*					
<b>HADS depression</b>	-0.04	<0.001*	<0.001*	<0.001*	-0.04	<0.001*	-0.04	<0.001*
<i>Interaction with multimorbidity</i>	-0.00	0.646	0.495					
<b>Illness perception</b>	-0.12	<0.001*	<0.001*	<0.001*	-0.08	<0.001*	-0.14	<0.001*
<i>Interaction with multimorbidity</i>	-0.06	<0.001*	<0.001*					
<b>Self-efficacy</b>	0.03	<0.001*	<0.001*	<0.001*	0.02	<0.001*	0.02	<0.001*
<i>Interaction with multimorbidity</i>	0.01	0.271	0.325					
<b>Social support</b>	0.02	<0.001*	<0.001*	<0.001*	0.01	<0.001*	0.02	<0.001*
<i>Interaction with multimorbidity</i>	0.00	0.405	0.316					
<b>Sense of coherence</b>	0.01	<0.001*	<0.001*	<0.001*	0.01	<0.001*	0.01	<0.001*
<i>Interaction with multimorbidity</i>	0.00	<0.05*	<0.01*					
<b>BFI extraversion</b>	-0.00	0.948	0.503	0.575	-0.01	0.907	0.00	0.561
<i>Interaction with multimorbidity</i>	0.01	0.699	0.924					
<b>BFI agreeableness</b>	0.03	0.210	0.126	0.226	0.01	0.510	0.02	0.395
<i>Interaction with multimorbidity</i>	0.00	0.922	0.987					
<b>BFI conscientiousness</b>	0.02	0.312	0.299	0.712	0.03	0.107	-0.00	0.766
<i>Interaction with multimorbidity</i>	-0.03	0.397	0.167					
<b>BFI neuroticism</b>	-0.11	<0.001*	<0.001*	<0.001*	-0.07	<0.05*	-0.10	<0.001*
<i>Interaction with multimorbidity</i>	-0.03	0.315	0.122					
<b>BFI openness</b>	0.01	0.641	0.630	0.452	-0.01	0.764	0.02	0.282
<i>Interaction with multimorbidity</i>	0.04	0.220	0.251					
<b>Health literacy</b>	0.11	<0.001*	<0.001*	<0.05*	0.08	<0.05*	0.09	<0.05*
<i>Interaction with multimorbidity</i>	0.00	0.944	0.984					

\* Significant level set at 0.05.

<sup>1</sup>Unadjusted.

<sup>2</sup>Adjusted for age, gender, and education.

<sup>3</sup>Adjusted for age, gender, education, and multimorbidity.

**Table 4.** Results from the multivariable regression model.

	Overall model		Multimorbidity absent		Multimorbidity present	
	$\beta$	P value	$\beta$	P value	$\beta$	P value
Age	-0.08	0.064	-0.11	0.116	-0.08	0.180
Gender (men)	0.02	0.577	0.13	0.071	0.01	0.909
Education (low)	-0.02	0.563	0.04	0.561	-0.05	0.395
Education (intermediate)	-0.06	0.098	-0.09	0.208	-0.07	0.196
Multimorbidity	-0.14	<0.001*				
Empowerment	0.07	0.066	0.10	0.176	0.08	0.130
Illness perception	-0.52	<0.001*	-0.38	<0.001*	-0.62	<0.001*
Self-efficacy	0.06	0.202	0.08	0.356	0.05	0.462
Social support	0.07	0.089	0.09	0.220	0.09	0.104
Sense of coherence	0.14	<0.05*	0.19	<0.05*	0.08	0.344
BFI extraversion	-0.05	0.168	-0.10	0.122	-0.04	0.455
BFI agreeableness	-0.03	0.358	-0.05	0.464	-0.04	0.394
BFI conscientiousness	-0.03	0.477	0.07	0.305	-0.06	0.227
BFI neuroticism	0.02	0.637	0.05	0.548	0.00	0.936
BFI openness	-0.04	0.250	-0.08	0.225	-0.07	0.165
Health literacy	-0.03	0.429	0.10	0.162	-0.08	0.124
<b>Adjusted R<sup>2</sup></b>	<b>0.52</b>		<b>0.45</b>		<b>0.48</b>	

\* Significant level set at 0.05.

vs 20% for usual activities, 57% vs 21% for mobility, 48% vs 31% for anxiety/depression, and 27% vs 5% for self-care.<sup>32</sup> Next, and also in line with the literature, this study has shown that multimorbidity is significantly associated with poor HRQoL in adults.<sup>33,34</sup> In detail, pain/discomfort was generally the most affected domain because this domain puts the greatest limitation on people's lives.<sup>33,35</sup>

Furthermore, this study showed that two modifiable psychosocial factors are associated with HRQoL in chronically ill patients. In the complete group of chronically ill patients, patients' illness perceptions and sense of coherence were significantly associated with HRQoL. These results indicate that promoting the protective effects of these inner resources are crucial, especially when the goal is to strengthen chronic disease self-management and to improve HRQoL. As such, the study results are useful for clinicians, public health professionals, researchers, and policy makers in their efforts to improve the overall well-being of chronically ill patients.

As expected, having negative illness perceptions was significantly associated with worse HRQoL – more specifically, it was identified as the most strongly associated factor. Indeed, previous studies showed that chronically ill patients with more negative beliefs about the effect and outcomes (i.e., causes, consequences, treatment, timeline) of their illness and with stronger emotional reactions to the illness had worse HRQoL, higher psychological distress, medication non-adherence, and higher use of health care services.<sup>36–41</sup> In addition, this study found that the negative association of illness perceptions was more important in patients with multimorbidity. This may be explained by the fact that illness perceptions formed by multimorbid patients may differ from those with a single condition due to higher treatment burden from multimorbidity and synergies and antagonisms between conditions and disease management strategies.<sup>42</sup>

Another associated factor was sense of coherence. Previous studies also highlighted the role of sense of coherence as a significant predictor

of HRQoL: the higher a person's sense of coherence, the better his/her HRQoL, resulting from effectively coping with life stressors.<sup>43-45</sup> It is also found that sense of coherence may function as a protective mediator for HRQoL dimensions in the process of psychological adaptation to a disease.<sup>43</sup> However, the association of sense of coherence with HRQoL was no longer present in the multimorbidity model, leaving illness perceptions as the only significant independent variable. A possible explanation could be that even high levels of sense of coherence cannot improve HRQoL in people with high levels of multimorbidity.

Although the univariate models showed significant associations between the other psychosocial factors and HRQoL, these factors did not maintain their significance in the multivariate models. These results show that illness perceptions and sense of coherence are the two main psychosocial factors that overshadow the others, and are therefore the most important to target.

Based on these study results, several recommendations can be made. A first step is to increase awareness of the importance of illness perceptions on patients' reported outcomes among general practitioners, preventing patients from having maladaptive illness perceptions which is of particular importance in multimorbid patients. In addition, patients' illness perceptions as well as sense of coherence are potentially modifiable, therefore screening for patients with low levels of these psychosocial traits and implementing interventions may be promising methods to enhance HRQoL in chronically ill patients. The latter should include interventions that beneficially change the illness perceptions of patients, especially multimorbid patients, towards a more positive emotional response, referred to as "cognitive reappraisal". Short psychological interventions, for example cognitive behaviour therapy, might foster more positive illness perceptions such as perceived personal control over illness.<sup>41</sup> In return, perceived controllability is related to active coping and empowerment, eventually resulting in better well-being outcomes.<sup>46</sup> Among multimorbid patients, interventions

should focus on increasing patients' knowledge regarding their diseases and informing them about the different disease management regimes. In order to strengthen patients' sense of coherence, one study suggests that interventions based on empowerment can fuel the strategies to support people to deal with challenges that come with the self-management of diseases. As a consequence, patients will experience stress as less threatening, by coping with it more efficiently.<sup>20</sup> Strategies to reinforce empowerment as such, by focussing on self-management, can also include cognitive behavioural therapy components such as psycho-education, cognitive reframing, goal planning, and process evaluation.<sup>47</sup>

To correctly interpret the results discussed above, some strengths and limitations need to be addressed. First, this study has a cross-sectional design. As such, no causality can be assumed, limiting interpretation of identified associations. Second, the voluntary response procedure is vulnerable to sampling bias due to a high non-response rate, resulting in an unrepresentative population.<sup>48</sup> For example, there was an overrepresentation of women, older individuals, and individuals with higher educational levels in our sample because these people are more prone to return postal questionnaires.<sup>49,50</sup> However, a representative sample population is less important when looking at associations. Third, the actual health status of patients may be underestimated due to selective non-response effects.<sup>51,52</sup> Consequently, those patients unwilling to complete the questionnaire are potentially those with worse health, and thus worse HRQoL. Additionally, it is important to mention that the outbreak of the COVID-19 pandemic occurred during the datacollection process. As such, pandemic-related stress may have worsened the HRQoL of those patients who were included during the pandemic. Analyzing the pre-pandemic ( $N=203$ ) and pandemic data ( $N=299$ ) revealed that the COVID-19 pandemic may had negative effects on patients' HRQoL in terms of EQ-5D index values (0.72 vs 0.59,  $P < 0.001$ ) and EQ-VAS scores (65.4 vs 56.8,  $P < 0.001$ ) – however caution is needed as both

groups are not fully comparable due to sociodemographic differences. Besides these limitations, important strengths of this research should be addressed as well. A strength of this study is the use of objective medical diagnoses for half of the patients (those recruited via general practitioners), which limits the risk of self-reported bias. However, we assume that the disease status of patients recruited via officially recognized patients organizations are reliable as well. Another strength is the inclusion of international, validated instruments to assess HRQoL and its determinants. A strength regarding the latter is the inclusion of a wide range of possible influencing psychosocial factors. Furthermore, the sample size includes participants from all age categories ( $\geq 18$  years) while many studies focus on older populations, since chronic diseases are more prevalent in the elderly.<sup>53,54</sup> A final strength is that a high variance of HRQoL could be explained by our regression model.

## Conclusion

This study revealed interesting associations of the modifiable psychosocial factors of illness perceptions and sense of coherence with HRQoL in a population of chronically ill persons. Given that the burden of chronic diseases will rise in the next decades, designing and implementing interventions that enhance these psychosocial abilities of patients, especially illness perceptions in multimorbid patients, is needed in order to reduce the burden of chronic diseases in terms of impaired HRQoL.

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