


## ORIGINAL ARTICLE

# Barrett Esophagus: Quality of life and factors associated with illness perception

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## Abstract

**Background:** Health-related Quality of life (HRQoL) in patients with Barrett's esophagus (BE), a premalignant condition, may be influenced by gastroesophageal reflux disease (GERD) symptoms and the risk of developing esophageal adenocarcinoma.

**Methods:** We aim to investigate HRQoL in non-dysplastic Barrett Esophagus (NDBE) patients, identify factors associated with a **negative illness perception** of the diagnosis BE and compare outcomes between patients treated in a specialized BE center with non-expert centers. In this multi-center cross-sectional study, HRQoL of NDBE patients were assessed using the Short Form 36, Hospital Anxiety and Depression Scale, Cancer worry Scale, and Reflux Disease Questionnaire. A multivariable, linear regression analysis was conducted to assess factors associated with **illness perception (Illness perception scale)** of the BE diagnosis. Outcome parameters of patients from expert centers were compared to non-expert centers.

**Results:** A total of 859 NDBE patients (**mean age 63.6% and 74.5% male**), of which 640 from BE expert centers were included. BE patients scored similar or higher

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means (i.e. better) on generic HRQoL in comparison with a Dutch norm population. The multivariable regression model showed that cancer worry, GERD symptoms, signs of anxiety and depression, and female gender were associated with a **negative illness perception** of BE. GERD symptoms were reported in the minority (22.4%) of BE patients. Levels of anxiety symptoms were comparable to a Dutch norm population (mean 3.7 vs. 3.9  $p$  0.183) and lower for depression symptoms (mean 6.8 vs. 7.6  $p$  < 0.001). Overall, there were no differences found on outcomes between expert centers and non-expert centers.

**Conclusion:** NDBE patients scored similar or better on generic HRQoL, anxiety and depression than an age and gender matched norm population. The presence of cancer worry, gastrointestinal symptoms, anxiety and depression, and female gender are factors associated with a **negative illness perception** of the diagnosis BE.

#### KEYWORDS

Barrett esophagus, cancer worry, esophageal cancer, GERD, **illness perception**, quality of life

## INTRODUCTION

The prevalence of gastroesophageal reflux disease (GERD) in Western countries has increased over the past few decades and is one of the most encountered conditions in primary care practice, with an estimated prevalence of between 18% and 27% in the USA and 9%–26% in Europe.<sup>1</sup> The diagnosis of GERD is associated with a 10%–15% risk of Barrett's esophagus (BE), involving a metaplastic transformation of the lower esophageal lining from squamous to intestinal type epithelium.<sup>2</sup> Current guidelines recommend endoscopic surveillance for patients with non-dysplastic Barrett's esophagus (NDBE) every 2–5 years.<sup>3,4</sup> Among those with BE (with or without GERD symptoms), 0.2%–0.5% will develop esophageal adenocarcinoma (EAC).<sup>5</sup> Previous studies have shown it is difficult for patients to accurately estimate this cancer risk.<sup>6–8</sup> These perceptions on developing EAC may affect patients' HRQoL. HRQoL is generally considered encompassing patients' physical-, psychological-, and social functioning, which can be affected by both the disease and treatment.<sup>9</sup> Our recent study, performed in a Dutch single center, showed decreased HRQoL in those patients who overestimated their cancer risk.<sup>6</sup> Most BE patients reported a HRQoL compared to a general Dutch population, this in contrast to the results on HRQoL in previous studies.<sup>10</sup> Many of these studies are underpowered, single center or cannot be reliably compared with current patient pathways.<sup>14</sup>

Several factors (e.g. fear of cancer, anxiety, trust in physicians, sense of control, gastrointestinal (GI) symptoms) were perceived as influencing HRQoL according to BE patients. None of the previously performed quantitative studies measuring HRQoL in BE patients sufficiently reflected these perceptions of HRQoL.<sup>11</sup> Quantitative data confirm associations between decreased HRQoL and fear of cancer, anxiety, and GI symptoms<sup>7,10,12</sup>. A more recent study on the prevalence of factors influencing HRQoL in patients receiving surveillance of their BE showed GERD symptom severity was associated

#### Key summary

##### Summarize the established knowledge on this subject

- Patients with Barrett Esophagus have worse generic HRQoL than the general population.
- Symptom control is an important factor in maximizing HRQoL.
- Patients with Barretts Esophagus are at increased risk for psychological sequelae such as depression and anxiety.

##### What are the significant and/or new findings of this study?

- In contrast to previous publications, generic HRQoL was similar or better compared with an age and gender matched reference population.
- Interestingly, Barrett patients reported lower depression symptoms in comparison with the Dutch general population. The anxiety scores were comparable to the Dutch general population.
- **Negative illness perception** of the diagnosis Barrett Esophagus was associated with female gender, having more cancer worry, experiencing more GI symptoms and symptoms of anxiety and depression.
- There were no differences found on HRQoL outcomes between the expert centers and non- expert centers.

with EAC cancer worry, anxiety and depression.<sup>7</sup> **However, it is not known what factors are associated with negative illness perception by patients with the diagnosis BE. Illness perceptions are a representation of patients' beliefs and expectations about an illness or somatic symptoms. These perceptions have been found to be**

**important determinants of behavior and have been associated with a number of important outcomes, such as treatment adherence and increased healthcare use.**<sup>13</sup>

Patients with BE are at risk for psychological consequences such as depression and anxiety. A recent German study showed high numeracy rates of depression (14.2%) and anxiety (9.9%), those were about 3–5 times higher in the study sample than in the general population. Rates of BE-related reflux and pain symptoms showed the strongest association with higher levels of depressive and anxiety symptoms. Though, absence of information on patients' disease characteristics limited generalizability of these results.<sup>14</sup>

There is an increasing shift of care for BE patients to specialized BE centers. A previous review suggested delivering a focused BE-specific service for all BE patients.<sup>15</sup> However, it is not clear if patients are experiencing better HRQoL-outcomes in hospitals specialized in Barrett surveillance and treatment. In this multicenter study, we aim to assess the generic and disease specific QoL in NDBE patients, identify factors associated with **negative illness perception** of the diagnosis BE and compare outcomes between patients treated in a specialized BE center with non-expert centers. This may lead to a better understanding of the impact of the factors influencing HRQoL, which could be the start of a person-centered approach for measuring HRQoL in patients with BE.

## MATERIALS AND METHODS

**We performed a cross-sectional multi-center study, which was conducted between October 2019 and August 2021.** Due to the COVID-19 pandemic, inclusion was interrupted between January 2021 and July 2021. **For the collection of the data patients completed a self-administered questionnaire.**

### Patients

For this study, we analyzed the data collected from **five expert centers** for surveillance and endoscopic treatment of BE in the Netherlands (including two academic centers). BE expert-centers were defined according to the ESGE Barrett guideline (with dedicated gastroenterologist and nurse practitioners).<sup>3</sup> In addition, three non-expert centers for BE (of which one academic center) were included. All patients included in the endoscopic surveillance programs of the participating centers were asked to participate in the study. The inclusion criteria were (1) proven macroscopic and histologic BE, (2) aged 18–80 years (3) able to read, understand and complete the Dutch informed consent form and the study questionnaires. Patients were excluded if there was (1) a history of BE endoscopic treatment or a surgical esophageal resection, and (2) presence of low- or high-grade dysplasia or EAC in BE histology.

Patients were invited to participate with a postal invitation. Non-responsive patients received a one-time postal reminder after 4 weeks. All subjects gave written informed consent in accordance

with the Declaration of Helsinki. The protocol was approved by the Medical Ethical Committee United (MEC-U) with reference W19.068. Subsequently, all institutional review boards of the participating hospitals approved the protocol.

### Questionnaires

Patients were asked to fill out demographic and clinical items (age, gender, marital status, employment status, educational level, knowledge of the diagnosis BE, use of medication treating GERD, and comorbidity). Generic HRQoL was measured with the Short Form 36 (SF-36). This widely used questionnaire has been validated for measuring generic QoL in multiple disease states.<sup>16,17</sup> Scores on the SF-36 range from 0 to 100 on each dimension (**physical functioning, social functioning, physical role functioning, emotional role functioning, vitality, bodily pain, mental health and general health**), with higher scores indicating better HRQoL. To compare data from our sample and Dutch normative data, the sample was age and gender standardized and based on a general Dutch population in the age of 61–70.<sup>18</sup>

Cancer worry was measured using the Cancer Worry Scale (CWS).<sup>19</sup> Scores range from 6 to 24, with a higher score indicating more cancer worry. Based on a previous Dutch validation study, we divided patients into three categories: no cancer worry (score <6), low level of cancer worry (score 7–9), and high level of cancer worry (score ≥10).<sup>20</sup>

To measure symptoms of anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) was utilized.<sup>21</sup> Patient results were obtained by summing up each subscale (**anxiety and depression**), yielding values from 0 to 21. To compare to a general Dutch population, data of 1901 individuals were used including 48.8% men with a mean age of 61.3 (SD 2.3). A cut-off score of >8 was used, indicating moderate to severe signs of anxiety and/or depression.<sup>22</sup>

The presence of GERD symptoms was measured using the Reflux Disease Questionnaire (RDQ).<sup>23–26</sup> The mean of all three dimensions (**dyspepsia, regurgitation, and heartburn**) gives a total score ranging from 0 to 5. Where a score of 0 represents nil symptoms, a score of 1–2 mild symptoms, and 3–5 severe symptoms of GERD.<sup>27</sup>

Cognitive and emotional **perceptions** of BE were assessed with the Brief Illness Perception Questionnaire (B-IPQ).<sup>28–30</sup> **The B-IPQ uses a nine single-item scale approach, and each item is scored on a 0–10 scale. Five of the items assess cognitive illness perceptions, two items assess emotional perceptions (e.g. sense of control and worry) and one item assesses illness comprehensibility (understanding of the diagnosis).** A higher score reflects a more threatening perception of the illness.

### Statistical analysis

Continuous sociodemographic data are presented with means and standard deviation. Categorical variables are summarized with

frequency and percentages. The eight domains of the SF-36 score were converted to standard scores based on the scores of an age and gender matched representative reference sample of the Dutch population.<sup>18</sup> Standard scores were calculated by dividing the difference between the patients' SF-36 score and the mean score of the matched reference population by the SDs of the reference population. A standard score thus indicates how many SDs the observed SF-36 score falls below or above the score of the reference population. Consequently, scores of the reference population are set at 0. A mean standard score of 0.20 is considered to indicate a small deviation from the reference population, since it resembles the effect size calculation.<sup>31</sup> Mean standard scores of 0.20, 0.50 and 0.80 are considered to indicate small, moderate and large deviations from the reference population, respectively. To evaluate factors associated with a **negative illness perception** of the diagnoses Barrett (B-IPQ) a regression analysis was used. All variables were univariate tested on a significant correlation with **BE illness perception**. Variables with  $P < 0.2$  in the univariable analyses were included in a multivariable model and R-squared was computed. To avoid multicollinearity, a correlation of the independent variables of less than 0.8 was accepted. For comparison of continuous variables between the BE expert centers and non-expert centers the student's t-test or Mann Whitney U (depending on normality) and for categorical variables a Chi-square test was used.  $P < 0.05$  is considered statistically significant. Data were analyzed using the IBM Statistical Package for Social Sciences (SPSS), version 25.

## RESULTS

A total of 1731 BE patients were invited to participate, of whom 859 (49.6%) signed **informed** consent and completed the questionnaires. The mean age of BE patients was 63.6 years (SD = 13.4). Most patients were male (74.5%), married or cohabitating (81.5%), working (45.8%), and completed secondary or post-secondary education (74.3%). An overview with all demographic and clinical baseline characteristics is shown in Table 1. Most baseline characteristics showed no significant differences between the BE centers and non-expert centers. However, participants in the non-expert centers reported significantly more comorbidities (two in the expert centers (0–14) versus three (0–11) in the non-expert centers).

### Generic HRQoL

The participants treated in non-expert centers reported significantly lower scores on mental health ( $p.004$ ), representing more psychological distress and less well-being. In addition, they scored lower on the vitality domain, however this was not significant ( $p.051$ ).

Overall, BE patients had similar or higher mean scores on SF36 subscales than the Dutch reference population (Figure 1). The domains mental health, bodily pain, role functioning, and physical functioning showed a moderate but significant deviation with the reference population.

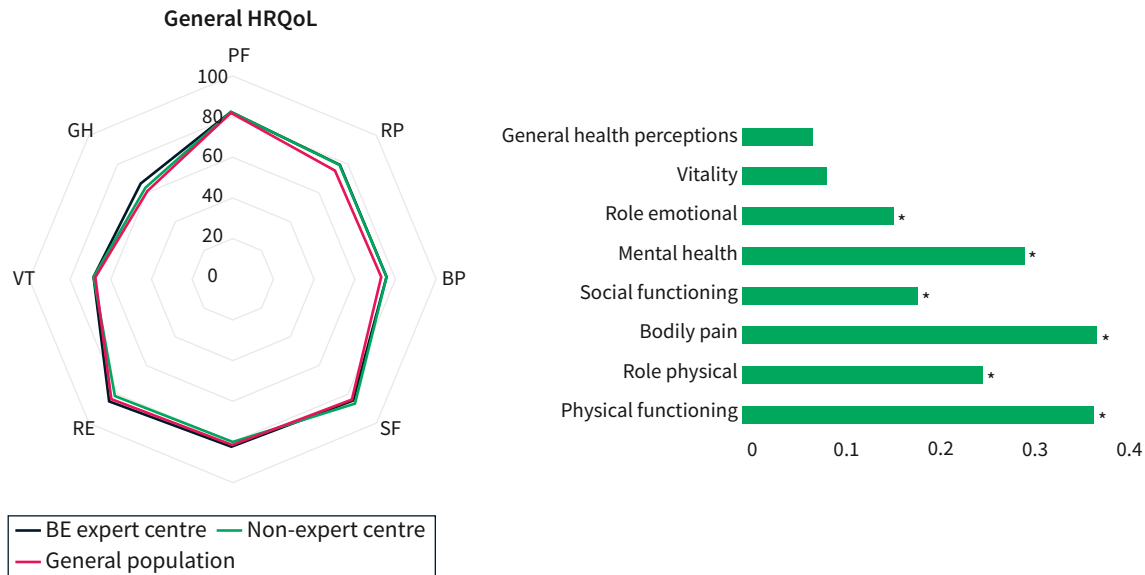
**TABLE 1** Baseline characteristics

	All patients $n = 859$	BE expert centers $n = 640$	Non-expert centers $n = 219$	$P$
Male gender, $N$ (%)	640 (74.5)	555 (74.4)	85 (75.2)	0.851
Age in years, <i>mean</i> (SD)	63.6 (10.4)	63.9 (9.1)	64.5 (7.9)	0.192
Marital status, $N$ (%)				0.121
No relationship	72 (8.4)	63 (8.5)	9 (8.0)	
Married/living together	698 (81.5)	614 (82.5)	84(75.0)	
Divorced	46 (5.4)	36 (4.8)	10 (8.9)	
Widow/widower	39 (4.6)	30 (4.0)	9 (8.0)	
Education, <sup>a</sup> $N$ (%)				0.408
< High school	219 (25.7)	186 (25.1)	33 (30.0)	
High school	363 (42.6)	322 (43.4)	41 (37.3)	
Bachelor/University	270 (31.7)	234 (31.5)	36 (32.7)	
Employment status, $N$ (%)				0.192
Employed	340 (40.2)	300 (40.8)	40 (36.0)	
Unemployed	82 (9.7)	66 (9.0)	16 (14.4)	
Retired	377 (44.6)	326(44.4)	51 (45.9)	
Other	47 (5.6)	43 (5.9)	4 (3.6)	
Total comorbidity, <i>median</i> (range)	2 (0–14)	2 (0–14)	3 (0–11)	0.026

Note: BE expert centers represent five different hospitals and the Non-expert centers represent three different hospitals.

Abbreviation: BE, Barrett Esophagus.

<sup>a</sup>3 missing values.



**FIGURE 1** Health-related quality of life (HRQoL) scores for patients with Barrett Esophagus (BE). Standard scores of >0 indicate better HRQoL than a general Dutch population. Scores of 0.2, 0.5 and 0.8 indicate respectively a small, moderate, or large deviation from the reference population \* $P < 0.005$

### GERD symptoms

Overall, 92.4% of BE patients stated that they were using PPI as prescribed by their physician. Most patients experienced no GERD symptoms (77.6%), only 2.8% of patients reported severe GI symptoms. BE patients in the non-expert centers reported more symptoms of heartburn, however this was not significant ( $X^2(2) = 5.529, p.063$ ) (Table 2).

### Cancer worry

With a mean value of 9.14, BE patients reported low scores of cancer worry. As Table 3 shows, only 18.7% of patients scored lower than 6, indicating no cancer worry. 414 BE patients (48.8%) reported a low level of cancer worry, and 32.5% of the BE population reported a high level (>10) of cancer worry. This was not significantly different between the participating hospitals.

### Anxiety and depression

Moderate to severe signs of a depression were found in 113 BE patients (13.2%). Additionally, 16.3% of patients reported moderate to severe signs of an anxiety disorder. Barrett patients reported lower means for depression (representing less signs of a depression) compared to the Dutch general population (mean 6.8 vs. 7.6  $p < 0.000$ ). The anxiety scores were comparable to the Dutch general population (mean 3.7 vs. 3.9  $p.183$ ). There were no significant differences between the participating hospitals.

### Factors associated with illness perception

Overall, values of cognitive and emotional perception of BE were low, representing a non-threatening perception of illness. No significant differences on BE **illness perception** were found between the BE expert centers and non-expert centers. Most patients stated a minimal effect on their life (3.00), moderate personal control over illness (4.78), good beliefs about the effectiveness of treatment (3.47); and little experience of symptoms (2.75). Only high values were found on timeline, a scale representing the expected duration of the illness (8.97). BE patients stated a minimal emotional representation of BE, an item questioning: How much does Barrett affect you emotionally? (e.g. does it make you angry, scared, upset or depressed) (2.12). Furthermore, concern about Barrett's was low (3.00) and there was a good understanding of the illness (3.77).

Regression analysis was used to determine the factors associated with **illness perception** of the diagnosis BE. As Table 4 shows, a **negative illness perception** of BE is associated with cancer worry, GI symptoms, signs of anxiety and depression, and female gender.

### DISCUSSION

The present multi-center study in NDBE patients was designed to investigate factors associated with a **negative illness perception** of the diagnosis BE. Overall, values of cognitive and emotional perceptions of BE were low, representing a non-threatening perception of Barrett's. The results of this study show that a **negative illness perception** of the diagnosis BE is associated with the female gender and more cancer worry, GI symptoms and symptoms of anxiety and depression.

**TABLE 2** GERD symptoms

	All BE patients	BE expert centers	Non-expert centers	P
Dyspepsia				0.481
None	674 (78.7)	590 (79.3)	84 (75.0)	
Mild	144 (16.8)	123 (16.5)	21 (18.8)	
Severe	38 (4.4)	31 (4.2)	7 (6.3)	
Regurgitation				0.517
None	604 (70.4)	529 (74.9)	75 (72.1)	
Mild	199 (23.2)	168 (22.6)	31 (27.4)	
Severe	55 (6.4)	48 (6.4)	7 (6.2)	
Heartburn				0.063
None	665 (77.7)	584 (78.5)	81 (72.3)	
Mild	156 (18.2)	134 (18.0)	22 (19.6)	
Severe	35 (4.1)	26 (3.5)	9 (8.0)	
Total				0.182
None	666 (77.6)	583 (78.3)	83 (76.9)	
Mild	168 (19.6)	144 (19.3)	24 (21.2)	
Severe	24 (2.8)	18 (2.4)	6 (5.3)	

Note: Gastro esophageal reflux disease symptoms measured with the Reflux Disease Questionnaire. Values are represented with mean (SD). Abbreviation: BE, Barrett Esophagus.

**TABLE 3** Cancer worry

	All patients	BE expert centers	Non-expert centers	P
Total cancer worry mean (SD)	9.14 (2.92)	8.98 (2.84)	9.14 (2.70)	0.938
No cancer worry	159 (18.7)	141 (19.1)	18 (16.1)	
Low cancer worry	414 (48.8)	360 (48.8)	54 (48.2)	
High cancer worry	276 (32.5)	236 (32.0)	40 (35.7)	
Positive history of cancer		93 (12.5)	18 (15.9)	0.309
Positive family history with cancer		197 (26.5)	20 (17.7)	0.044

Note: Cancer worry measured with the Cancer worry scale (CWS) Values are represented with n (%).

**TABLE 4** Factors associated with a negative illness perception

Variables	B	95%	R square	$\beta$	t	P
Cancer worry	0.990	0.769–1.211	0.260 <sup>a</sup>	0.290	8.796	<0.000
GI symptoms	4.332	3.404–5.240	0.388 <sup>b</sup>	0.302	9.246	<0.000
Symptoms of anxiety and depression	0.493	0.383–0.603	0.452 <sup>c</sup>	0.290	8.776	<0.000
Gender	1.617	0.0048–3.186	0.456 <sup>d</sup>	0.061	2.024	<0.043

Note: Table 4: Regression Coefficients for identification of factors associated with negative illness perceptions of the diagnosis Barrett Esophagus.

<sup>a</sup>Independent variable: (Constant), Total\_CWS.

<sup>b</sup>Independent variables: (Constant), Total\_CWS, totalRDQ.

<sup>c</sup>Independent variables: (Constant), Total\_CWS, totalRDQ, TotalHADS.

<sup>d</sup>Independent variables: (Constant), Total\_CWS, totalRDQ, TotalHADS, geslacht.

The present study shows comparable or higher generic HRQoL compared to a Dutch reference population.<sup>18</sup> This finding suggests a minimal influence on generic HRQoL by the diagnosis of BE. This

coincides with our earlier observations in focus-groups interviews<sup>32</sup> and a single center questionnaire study,<sup>6</sup> which showed Dutch BE patients experience a good HRQoL. Nevertheless, this finding



contradicts previous studies, which have concluded that patients with BE reported decreased HRQoL on the SF-36, compared to norm reference data. A more recent study in the UK showed NDBE patients had significantly lower scores across all domains of the SF-36 compared to a healthy cohort.<sup>7</sup> This study used propensity scores matching for age, gender and comorbidities. There are two probable causes for these differences in previous studies. Firstly, it could be argued that these results were due to the presence of GERD symptoms. BE patients in our study reported low values on GERD symptoms. A previous study in NDBE patients showed that experiencing moderate to severe GERD symptoms decreased HRQoL.<sup>33</sup> Secondly, Britton et al. compared GERD HRQoL with a younger and healthy population (e.g. mean age 50.3 and no comorbidities). The present study compared the data to a reflection of a general population in the age of 61–70 years with 50% experiencing one or more chronic conditions. **In addition, sub-analyses in the age group 40–61 and >70 years similar results were found with comparable or higher HRQoL than the reference population.**

As our regression model shows, cancer worry is an important factor associated with a **negative illness perception** of BE. Only 18.7% of NDBE patients in the present study scored lower than 6, indicating no cancer worry. Nearly half of the BE population (32.5%) reported a high level (>10) of cancer worry. These findings are inconsistent with that of Britton et al. who found 69.5% levels of >10 on the CWS.<sup>7</sup>

Reporting higher levels of GI symptoms was associated with a **negative illness perception** of BE. However, patients reported good symptom control, representing with only 2.8% of patients reported severe GI symptoms. **In accordance with the present result, the study of Britton et al.<sup>7</sup> demonstrated 10% moderate to severe acid regurgitation in comparison with the 6.4% found in the present study. The number of moderate to severe symptoms of heartburn were comparable between the expert centers in the Netherlands and an expert center in the UK (3.5% vs. 2.2%<sup>7</sup>). These comparison of data must be interpreted with caution because different instruments were used.** GERD has been associated with functional deficiencies, such as sleeping difficulties, reduced ability to consume food, impaired sex life, thus affecting quality of life and increasing the risk for a comorbid mental disorder.<sup>34,35</sup> Appropriately adjusted medical treatment is essential for reducing GERD related symptoms. In addition, we suggest physicians to create an approachable and low threshold contact opportunity for BE patients to discuss flare ups of symptoms.

Most BE patients in the present study reported no symptoms of anxiety (81.7%) or depression (84.9%). In comparison with one Chinese<sup>12</sup> and two studies from the UK<sup>7,36</sup> the present population scored lower on the incidence of abnormal or borderline signs of depression (17.3%,<sup>12</sup> 19%,<sup>7</sup> 14%<sup>36</sup> vs. 13.2%) or symptoms of anxiety (25.2%,<sup>12</sup> 31%,<sup>7</sup> 39%<sup>36</sup> vs. 16.3%). This difference in results may be explained by several cultural differences, especially when considering that the HADS norm data of several reference populations between countries differ. Hanschmidt et al.<sup>14</sup> found levels of depression and anxiety 3–5 times higher in the study sample than in the general

population. This rather contradictory result may be due the lack of information on patients' disease characteristics on the presence of BE dysplasia or EAC in that specific study. Another possible explanation for this is that Hansschmidt reported high presence of GERD symptoms. In general, increased anxiety levels, but not depression levels, are associated with greater severity of GERD symptoms such as retrosternal pain and retrosternal burning.<sup>37</sup>

Female gender is known as a risk factor for experiencing more functional gastrointestinal diseases. The Rome Foundation Global Study on the Prevalence and Burden of Functional Gastrointestinal Disorders,<sup>38</sup> reported functional dysphagia as the most prevalent esophageal disorder. The rates for functional heartburn, reflux hypersensitivity, and esophageal chest pain were substantially lower. All esophageal disorders were more prevalent among women. Although reflux esophagitis is predominant in men (5:1 ratio for men: women), symptomatic GERD exhibits a female preponderance and this difference becomes more apparent during the perimenopausal period.<sup>39</sup> As known individuals with GERD symptoms have a decrement in their QoL, these scores are similar to patients with inflammatory bowel disease.<sup>40</sup> Beside experiencing more GERD symptoms, women have a higher risk for developing an anxiety disorder or depression. Anxiety disorders were more prevalent in Dutch women than in men (annual prevalence in 2020 age 60–65 years 16.6% in men vs. 35.3% in women) and women are almost twice as likely to ever develop a depressive disorder compared to men (24.3% vs. 13.1%).<sup>41,42</sup> A recent study in BE patients showed that, women were more likely to be screened positive for depressive or generalized anxiety disorder.<sup>14</sup> These data underline the importance of accurate treatment and counseling to women with BE and functional esophageal disorders.

A secondary objective of the study was to compare outcomes on HRQoL between patients who undergo surveillance in a BE expert center with non-expert centers. In the current study, there were no differences found between the eight centers in **experiencing illness perceptions** and associated symptoms. Only the patients in the non-expert centers scored worse on mental health. Since this difference has not been found on the BE specific questionnaires, it is probably not related to the diagnosis BE or the BE care patients received. There is an increasing shift of care for BE patients to specialized BE centers. A previous review suggested delivering a focused BE-specific service for all BE patients. It concluded follow-up for BE patients appears inconsistent and often inadequate to meet patients' needs and expectations.<sup>15</sup> In our study, BE patients stated a good understanding of the diagnosis BE. **Patients in the expert centers perceived they were not better informed, despite the presence of BE dedicated physicians and nurses working in those centers. There is no uniform procedure in the participating hospitals for informing patients. In general, patients are informed by telephone or short outpatient clinic visit about the results of their gastroscopy.**

Our data did not present patient-reported experience measures (PREMs). PREMs report information on patients' perceptions of their experience receiving care. In contrast to PROMs, PREMs do not look at the outcomes of care but the impact of the process of the care on

the patient's experience for example, communication and timeliness of assistance.<sup>43</sup> We believe that it is beneficial to evaluate care through patient experiences. Previous qualitative studies found trust and communication with the physician as important factors influencing quality of life in BE patients.<sup>44–46</sup>

Our multi-center study also has several limitations. The inclusion period of this study was interrupted due to the COVID-19 pandemic. This was a deliberate choice to minimize the influence of the pandemic as much as possible. Inclusion started again when most of the restrictive measures had been lifted. Secondary analysis of our data showed no differences on all primary and secondary outcomes between patients included before or during the pandemic. Secondly, despite the multi-center design of the study, data may not be representative for the BE population worldwide. Differences could be expected due to differences in the health care system as well as cultural differences. In addition, the response rate was only 49.6%. As this was a self-administered anonym questionnaire study, we could not compare baseline characteristics between responders and non-responders. Considering the percentage of included males and the average age of 63.6 years a good representation of a Barrett population is provided.<sup>47</sup> Finally, a possible deficiency in the method of this study is the fact that not all factors that are considered important according to BE patients were included. Namely, trust in physicians, burden of endoscopy, sleeping difficulties, diet and lifestyle, were not included in the questionnaires. Therefore, factors influencing the outcome may have been missed in the regression model.

In conclusion, overall HRQoL in a multi-center BE population was comparable with an age and gender matched Dutch reference population. The presence of cancer worry, GI symptoms, anxiety and depression and female gender are associated with a **negative illness perception** of the diagnosis BE. There were no differences found on HRQoL outcomes between the expert centers with dedicated gastroenterologist and nurse practitioners and non- expert centers. We recommend that physicians offer an easy and approachable contact opportunity for BE patients to discuss symptom flares or fear of cancer.

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#### CONFLICT OF INTEREST

The authors declare no commercial, financial or potential personal conflicts of interest.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### ETHICAL APPROVAL

The protocol was approved by the Medical Ethical Committee United (MEC-U) with reference W19.068.

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