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Health related quality of life in patients with Barrett's Esophagus: A Systematic Review

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Abstract

Background & Aims—Barrett's esophagus (BE) affects approximately 10% of patients with chronic gastroesophageal reflux disease (GERD). Patients with BE are at risk for reduced health-related quality of life (HRQoL) associated with GERD, in addition to the potential psychosocial stress of carrying a diagnosis of a premalignant condition with a risk of esophageal adenocarcinoma (EAC). We sought to systematically review the published literature on HRQoL of patients with BE.

Methods—We searched PubMed, PsycINFO, and CINAHL for relevant clinical trials using a defined search strategy. We also manually searched relevant scientific meeting abstracts and related articles in bibliographies. Eligible articles were case series, cohort studies, or clinical trials that included one or more measures of HRQoL and/or quantitatively assessed burden of disease in patients with BE. Effect sizes were calculated when possible.

Results—Our initial search identified 95 articles. After 2 physician review, 25 articles met inclusion criteria. Data demonstrate that BE is associated with a significant decrement in HRQoL as measured by both generic and disease-targeted instruments. In addition, patients with BE are at risk for psychological consequences such as depression, anxiety and stress, which may be related to their increased risk of EAC. Compared to subjects with GERD alone or the general population, a diagnosis of BE also leads to increased healthcare utilization and spending.

Conclusions—Barrett's esophagus compromises multiple facets of patients' quality of life. Physicians and researchers should incorporate patient reported outcomes data including HRQoL measures when treating or studying patients with Barrett's esophagus.

Keywords

Barrett's esophagus; GERD; quality of life; systematic review; health-related quality of life; disease-targeted quality of life; QOLRAD; SF-36

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Introduction

Barrett's esophagus (BE), originally described by Norman Barrett¹ and later defined by Allison and Johnstone², is a metaplastic change of the esophageal mucosa in which the normal squamous epithelium is replaced by intestinalized columnar cells. Barrett's esophagus is associated with chronic gastroesophageal reflux disease (GERD) and carries an increased risk of the development of esophageal adenocarcinoma³⁻⁵.

Gastroesophageal reflux is a common condition affecting 10 to 20% of Americans on a regular basis⁶, and is associated with a number of symptoms including heartburn, chest pain, acid regurgitation as well as the "extra-esophageal" manifestations of asthma, chronic cough, and hoarseness. Nocturnal reflux symptoms can impact sleep and therefore affect daytime alertness and productivity⁷. Barrett's esophagus is less prevalent than GERD, with an estimated population prevalence of 1-2%⁸⁻¹⁰. Amongst patients with reflux symptoms however, the prevalence of BE has been reported to be as high as 18% and patients with BE often share similar symptoms as those with GERD^{8, 11}. Because of the frequency of the above symptoms and the related impact on lifestyle (e.g. alteration of sleep and eating patterns), persons with GERD and BE may experience a reduction in their HRQoL compared to the general population.

Research in patient reported outcomes is a burgeoning field. Healthcare-related quality of life (HRQoL), for instance, helps to focus attention on a patient's experience with a particular disease and to highlight the importance of treatment, particularly when decrements in HRQoL are present. Health-related quality of life can be quantified with both generic and disease-targeted instruments. Generic measures allow researchers to compare quality of life across different disease states and with healthy controls. Disease-targeted measures are especially useful when evaluating new treatments for specific disorders, as generic instruments may be inadequately sensitive to detect improvements in domains specific to that disease. In addition to generic and disease-targeted measures of HRQoL, measurements of "utility" also quantify changes in quality of life precipitated by disease and therapy, and can be used in cost-effectiveness analyses. A more detailed description of the specific HRQoL measures reported in this review is included in Table 1, and further information of HRQoL assessment in gastrointestinal disease has been published¹²⁻¹⁵.

While the wealth of published data on HRQoL in GERD patients has been recently reviewed by multiple authors¹⁶⁻²⁰, comparatively little has been published on HRQoL in patients with a diagnosis of Barrett's esophagus and to our knowledge, this topic has not previously been systematically reviewed. Our hypothesis was that patients with BE are burdened by decreases in HRQoL from GERD symptoms, as well as a possible decrement associated with carrying a pre-malignant condition. Therefore, we performed a systematic review of the published data on HRQoL in subjects with BE.

Methods

Two members of the study team (SDC and QKL) searched the PubMed search engine of MEDLINE-indexed literature from the National Center for Biotechnology Information (<http://www.pubmed.gov>) as well as the Cumulative Index to Nursing & Allied Health Literature (CINAHL) database, and the psychiatric literature database "PsycINFO" through September, 2008.

To identify relevant articles, we used the medical subject heading (MeSH) search terms "Barrett esophagus" (which included articles published using the spelling "oesophagus") and "quality of life", as well as the terms, "Barrett's esophagus", "Barrett esophagus", "Barrett's", "intestinal metaplasia" combined with the terms "quality of life", "QoL", "HRQoL", "SF-36", "QOLRAD", "GIQLI", "burden", and "economic impact". We also searched the MeSH term

“GERD” with the MeSH term “quality of life” in addition to the term “Barrett’s esophagus”. In addition, we searched a subset of journals specializing in quality of life (*Quality of Life Research*, *Quality Review Bulletin*, *Qualitative Health Research*, *Health and Quality of Life Outcomes*, *Quality & Safety in Health Care*, *Journal for Healthcare Quality*, *Quality in Health Care*, *American Journal of Medical Quality*, and *the International Journal for Quality in Health Care*) for “Barrett’s esophagus.” We subsequently assessed the bibliographies of all identified relevant articles (as well as reviews and letters to the editor) to identify data missed on the initial literature search. We also hand searched abstracts from the published proceedings of the 2003–2008 national meetings of the American College of Gastroenterology and the American Gastroenterological Association. We limited our search to original studies on human adults published after 1970, available in English.

Studies eligible for inclusion met the following criteria:

1. The study was a case series, cross-sectional study, cohort study, or clinical trial,
2. The study included a one or more quantitative measures of quality of life, and/or a quantitative assessment of the burden of disease (e.g. financial or psychological burden), and
3. The study presented data specifically on patients with Barrett’s esophagus.

We excluded individual case reports, reviews, summaries, comments and letters without new clinical information. We also excluded cost-effectiveness studies or decision analyses unless new quality of life data were presented. We excluded retrospective post-intervention studies, and included interventional studies only if pre-operative HRQoL data were presented.

The reviewers (SDC and QKL) independently searched the literature using the pre-defined strategy, and assessed abstracts to determine whether they were eligible for inclusion. If there was disagreement or a discrepancy, the full article was reviewed to arrive at consensus. Data from relevant studies (e.g. SF-36 scores) were extracted into tables and reviewed by all authors. This methodology conformed to published guidelines for conducting systematic reviews^{21, 22}.

When sufficient data were reported, effect sizes (ES) were calculated using a construct-anchored approach.^{23, 24} An ES of ≥ 0.5 is generally recognized as a clinically-relevant difference.²⁵ Since we were primarily interested in a cross-sectional assessment of HRQoL in BE, effect sizes were computed based on changes between groups (e.g. BE vs. controls) using the following equation:

$$ES = \frac{(HRQoL_{\text{group1}} - HRQoL_{\text{group2}})}{SD_{\text{group1}}}$$

Because of the heterogeneity of the measurements used in the studies reviewed, meta-analytical techniques could not be used to combine results across all studies. Furthermore, even within studies utilizing the same measure (e.g. SF-36, QOLRAD), meta-analytic techniques could not be used due to variable study methodology (case-control vs. cohort), differential reporting of measures (summary scores vs. subscale scores), and differences in study populations (BE as a subset of GERD vs. BE alone).

Results

Quality of Life Measures

The studies reported in this review utilize a variety of quality of life measures including the Medical Outcomes Study SF-36^{26, 27}, the Gastrointestinal Quality of Life Index (GIQLI)²⁸, the Quality of Life in Reflux and Dyspepsia questionnaire (QOLRAD)²⁹, the Gastroesophageal Reflux Health-Related Quality of Life instrument (GERD-HRQL)³⁰, health state utilities¹², and quantitative measures of psychologic symptoms, including the Hopkins Symptom Checklist (SCL-90)³¹, and the Hospital Anxiety and Depression Scale (HADS)³². Table 1 describes the individual measures in detail and provides a simplified interpretation key.

Search results

The initial PubMed, CINAHL, and PsycINFO search resulted in 82 studies. The bibliography review identified an additional 6 studies, and the subspecialty society meeting abstract search identified an additional 7 studies, rendering a total of 95. Of these studies, 70 were excluded because they were not relevant (e.g. a trial in which BE patients were excluded), did not use quantitative measures of HRQoL, or did so only after an intervention in the context of a retrospective trial (e.g. post-esophagectomy). A total of 25 studies were included in the final review (see Figure 1).

Five studies assessed BE patients with the SF-36, while three studies reported QOLRAD results, and two reported GIQLI results. Four studies evaluated utility measures in patients with BE. We also included 8 studies that did not use traditional QOL instruments, but quantitatively assessed impact (psychological, financial, social, etc.) or burden of disease by other measures. Nine studies included patients with BE as a subset of patients with GERD symptoms, or *a priori* compared BE patients to GERD patients. The remaining 15 studies included only patients diagnosed with Barrett's esophagus.

Generic quality of life

The largest study, the ProGERD study, included patients with GERD and BE from Germany, Austria and Switzerland, who were part of a prospective multi-center cohort study of GERD patients on proton pump inhibitor (PPI) therapy³³. The trial included over 6,200 patients, 702 of whom had a diagnosis of BE (11% of cohort). At baseline, the mean SF-36 summary scores of study patients were lower than general population norms. In comparison to the GERD only patients, BE patients had a statistically significant decrease in the mean physical summary score (42.6 ± 8.9 vs. 43.5 ± 8.8 for non-erosive GERD) and an increase in the mean mental summary score (46.2 ± 11.7 vs. 43.9 ± 11.9 for non-erosive GERD). However, the authors commented that while statistically significant, these differences may not be clinically relevant. Indeed, the ES for the inter-group score differences were lower than 0.5, indicating minimal clinical relevance. Gerson, Eloubeidi, and Lippmann also reported lower SF-36 scores compared to the general population^{34–37}. In Eloubeidi et. al, ES for SF-36 subscale scores were large (0.6 – 1.6), when BE patients were compared to age and gender matched controls³⁷. See Table 2, Figure 2.

Disease-targeted quality of life

One study assessed GIQLI scores in patients with BE undergoing laparoscopic Nissen fundoplication. Pre-operative GIQLI scores of 96.8 ± 9.3 (mean \pm SD) were reported, indicating reduced HRQoL compared to healthy individuals (122.6 ± 8.5)³⁸. Another, smaller study in BE patients reported a similar mean baseline GIQLI score of 94.2 ± 17.4 ³⁹.

The already-mentioned Pro-GERD study used QOLRAD to assess 702 BE patients, and found that at baseline, the mean overall score was 4.6 ± 1.3 , similar to the GERD cohort without BE (ES = 0). The QOLRAD component scores were similar to the GERD cohort as well. Of interest, following PPI therapy 82% of BE patients experienced a clinically relevant improvement of 0.5 or more points, and 68% had a change of 1.0 or greater³³. Fisher et. al also assessed QOLRAD scores in a small BE cohort, and reported a mean total score of 6.8 ± 1.5 (mean \pm SD), which is higher than other studies⁴⁰. Scores were also reported for subscales on food and drink (5.8 ± 1.25), emotional distress (6.1 ± 1.15), sleep disturbance (6.2 ± 1.15), physical and social functioning (6.6 ± 1.54), and vitality (6.0 ± 1.22). High ES for these values (1.1 – 1.9) indicates that in this study, BE patients had substantially better HRQoL than controls based on the QOLRAD. See Table 3, Figure 3.

Health state utility

Gerson et. al assessed time trade-off utilities in BE patients for the continuum of disease including nondysplastic BE (utility = 0.91), BE with low grade dysplasia (0.85), BE with high grade dysplasia (0.77), and BE with adenocarcinoma of the esophagus (0.67)³⁵. Hur et. al used the SG technique in a similar study, and reported utilities for nondysplastic BE (0.95), intensive endoscopic surveillance for high grade dysplasia (0.90), and post-esophagectomy for high grade dysplasia with subsequent dysphagia (0.92)⁴¹. Gerson et. al conducted a study of BE patients on and off PPI therapy, and found that time trade-off and SG utilities decreased off therapy as expected (0.92 to 0.90 and 0.95 to 0.93 respectively)⁴². Fisher et. al studied “holistic scenario” utilities using the VAS method for 16 different treatment trajectories of BE patients ranging from standard endoscopic surveillance (0.8) to BE with cancer diagnosis and death during esophagectomy (0) (Table 4)⁴⁰.

Relationship between quality of life and symptoms

Gerson and colleagues assessed quality of life in BE patients both on and off PPI therapy using the GERD HRQL⁴³. The investigators reported significantly lower (i.e. better) GERD-HRQL scores for BE patients on PPI therapy compared with those off PPI therapy (mean 2.9 vs. 18.8). None of the included studies used a both symptom severity measure and a HRQoL measure, so as to better evaluate the contribution of GERD symptoms to HRQoL.

Burden of Endoscopic Surveillance

The impact of surveillance endoscopy on HRQoL in the Barrett’s population has been investigated. Kruijshaar et. al studied 180 patients with BE (the majority of whom had experienced more than 2 prior endoscopies) using a questionnaire that included the HADS⁴⁴. Overall, 59% of BE patients found endoscopy “burdensome,” with 47% reporting throat ache post-procedure, and 14% reporting the procedure itself was painful. Patients reported significantly increased levels of depression, anxiety, and distress during the week prior to their endoscopy compared with the week after. Those who interpreted their risk of esophageal cancer to be high had correspondingly higher levels of procedural discomfort and tended to find endoscopy more burdensome.

Financial burden

A study of West Virginia’s Medicaid reimbursement for claims related to Barrett’s esophagus found that the statewide cost of illness for Barrett’s esophagus tripled during a 3-year period from 1995 to 1999. The cost of treating BE was reported to be over \$1,200 per patient per year, with pharmacy costs accounting for the majority of the cost. Compared with patients with GERD alone and the general Medicaid population, costs for BE patients were 21% and 62% higher, respectively⁴⁵. A similar study in a Veterans Administration Hospital population from 1999 found that outpatient costs for treating BE were \$1,241 per patient per year (1997 dollars)

⁴⁶. Medications (63%) and endoscopic procedures (31%) accounted for the majority of this cost, with proton pump inhibitors accounting for roughly 2/3 of the medication cost. Interestingly, the authors reported that the medication costs for BE patients (\$65/month) were greater than those of patients with diabetes at the same facility (\$63/month). A cost analysis from the German ProGERD cohort reported the total direct and indirect costs per BE patient per year were €680/year, approximately twice that of GERD patients.⁴⁷ The majority of BE costs in this study were also due to medications (71%). Also of note was that roughly 4% of BE patients reported missing work days due to their diagnosis.

Another study assessed the impact of a diagnosis of BE on life and health insurance. The authors of this study found that a diagnosis of BE was associated with a mean increase in life insurance premiums of 177%⁴⁸. In addition, when asked about health insurance with BE as a preexisting condition, only half of the queried companies responded. Of those who responded, 2/10 companies refused to provide insurance, and 8/10 demanded additional medical information or an additional health assessment prior to providing a quote.

There are likely other unknown indirect costs associated with Barrett's esophagus, but these studies provide evidence of a sizeable increase in costs associated with BE compared to GERD.

Cancer risk perception

Several studies assessed patient perceptions of cancer risk in those with BE. A study of 92 U.S. patients with BE undergoing endoscopic surveillance found that 68% of patients overestimated their 1-year risk of developing esophageal cancer, and 38% overestimated their lifetime cancer risk⁴⁹. A subsequent European study found that 20% of BE patients overestimated their numerical 1-year cancer risk from Barrett's esophagus⁵⁰.

Gerson et. al assessed time trade-off values in patients with mostly nondysplastic BE, assessing trade-off of cancer risk. Lower mean time trade-off values were reported for esophageal cancer (0.67 +/-0.19) and dysplasia (LGD 0.85+/-0.12 or HGD 0.77+/-0.14), than for the nondysplastic state (0.91 +/- 0.13) (see Table 4).

Other investigators assessed fear of recurrence of cancer, worry of cancer, and levels of anxiety and depression in patients with early neoplasia who were treated with endoscopic therapy vs. surgical treatment, using the Worry of Cancer Scale (WOCS) and the HADS⁵¹. The authors reported significantly more fear of recurrence in the endoscopy group compared to the surgery group based on the WOCS, but nonsignificant differences between groups with the HADS. Of note, in this study all patients had minimal depression or anxiety at baseline (with scores <7 on the HADS).

A more recent study evaluated HRQoL in patients undergoing radiofrequency ablation for BE-dysplasia at baseline and 12 months following therapy, comparing those with persistent dysplasia to those with eradication of dysplasia⁵². Those with eradication of dysplasia demonstrated significantly less worry, less stress, and less sleep disturbance compared to those with persistent dysplasia, indicating that successful treatment of dysplasia can lead to improvement in certain components of HRQoL.

We found no studies that addressed fear of recurrence or cancer risk concomitantly with a generic or disease-targeted HRQoL measure, so it is not possible to evaluate the extent that cancer risk impacts the HRQoL decrement in Barrett's esophagus.

Labeling Effect

A "labeling effect" occurs when the receipt of a disease diagnosis negatively impacts the quality of life of the patient. This effect has been demonstrated in hypertension and hepatitis C, as well

as other diseases.^{53, 54} Since BE is a premalignant condition, there is a significant risk for this particular variety of HRQoL decrement. While we found no studies directly comparing HRQoL in diagnosed to undiagnosed groups in BE patients, one group reported that a theoretical labeling effect corresponding to a decrement in utility of 10% or more would render endoscopic screening for esophageal cancer cost-ineffective⁵⁵. Future studies are needed to measure the labeling effect in BE.

Psychological distress

In a study of BE patients with low-grade (LGD) and high-grade (HGD) dysplasia, both groups reported moderate generalized “worry” regarding their diagnosis (41 and 48 out of 100 on a VAS, respectively), and mild levels of depression (4 and 15/100) and amount of stress (11 and 17/100)⁵². A second study assessed the HRQoL in patients with BE using the SCL-90³⁶. This study showed that BE patients, in contrast to GERD patients, had higher (i.e. worse) scores in the depression domain. Men with BE were found to have higher scores on multiple psychological domains including anxiety, hostility, somatization, obsessive-compulsive, and paranoia. Another study of BE patients undergoing endoscopic surveillance found that the BE patients had higher anxiety scores than the general population at multiple time points on the HADS⁵⁶.

Quality of life following an intervention

Two prospective studies of laparoscopic fundoplication reported both pre-operative and postoperative HRQoL data. Kamolz et. al reported GIQLI scores post-operatively (121.9 +/- 8.2, mean +/- SD) that were improved significantly compared to pre-operative scores (96.8 +/- 9.3), and were comparable to those of healthy controls³⁸. A second study reported post-operative GIQLI scores of 113 ± 9.3 compared to 94.2 ± 17.4 pre-operatively³⁹. A study of treatment of dysplasia in BE with radiofrequency ablation demonstrated that improvement in HRQoL was dependent on whether the treatment was curative⁵². As reported above, multiple studies have demonstrated improved HRQoL on acid-suppressive therapy^{33, 43}.

Discussion

Barrett’s esophagus affects millions in the US and yet there are few data on HRQoL in this disorder. Despite the fact that the absolute risk of EAC is small⁵⁷ and that several cohort studies have failed to demonstrate a lower life expectancy for those with BE^{58, 59}, patients with BE tend to overestimate their cancer risk⁴⁹. Patients may feel psychologically burdened by the threat of developing EAC, which could negatively affect their overall quality of life. Though addressed in few studies, there is evidence that a diagnosis of BE it is associated with an increased risk of disease-related psychological distress. There is also evidence that patients with BE who develop dysplasia may experience further decrease in quality of life, particularly psychological distress and worry, which can be mitigated by successful treatment. In addition to the cancer risk and psychological burden, patients with BE experience increased healthcare utilization and cost of illness because of their diagnosis. It is generally recommended that patients with BE undergo surveillance upper endoscopy at intervals of every 3 years or shorter depending on their level of dysplasia. At least in one study, many BE patients found endoscopy burdensome. In addition, BE patients participating in an endoscopic screening program will have a higher cumulative chance of procedural complications with repeated (albeit low risk) esophagogastroduodenoscopy. This increased healthcare utilization leads to increased costs to patients and 3rd party payers as well.

The measured generic and disease-targeted HRQoL of BE patients appears to be comparable to that of GERD patients. In the largest study that used the SF-36 and QOLRAD measures (the ProGERD study), BE patients were a subset of GERD patients, and therefore presumably had

similar symptoms. A significant limitation of such studies is that BE and GERD overlap, and therefore it is difficult to separate each condition's impact on HRQoL. In fact, some studies have shown that patients with BE may experience fewer symptoms than GERD patients^{60, 61}. The reason for this phenomenon is not entirely clear, but it may be that the Barrett's epithelium is less sensitive to acid refluxate. Some BE patients might be expected to have improved HRQoL compared to GERD patients, particularly if symptoms are minimal. Furthermore, symptomless BE patients would be less likely to seek medical attention, and therefore, may go undiagnosed. Such patients would likely have similar HRQoL to that of the general population.

It also should be noted that HRQoL decrements from psychological distress due to BE are dependent on how BE patients understand their cancer risk. This understanding is dependent on how the condition is explained to them by their physician. Unfortunately, the extent of cancer risk comprehension is difficult to measure and control for. Additional studies that control for symptom severity are needed to assess for the relative importance of BE-specific, non-GERD symptom-related factors such as cancer risk. Additionally, the potential impact of more sensitive surveillance methods, such as the newer imaging techniques, on HRQoL, is unclear. Presumably any decrement in HRQoL due to psychological stress from cancer risk may be partially ameliorated by better risk stratification.

As with all systematic reviews, though we followed a rigorous *a priori* search strategy, it is possible that we missed articles pertaining to HRQoL in BE. We also may have missed relevant studies since we restricted our search to English language publications. In many of the papers we reviewed, BE patients represented a subset of the studied cohort of GERD patients, and therefore it is possible that the BE patients studied (for the most part, those with reflux symptoms) were not necessarily representative of the whole population of BE. In addition, interpretation of data from HRQoL questionnaires can be complicated by issues of multiple testing, particularly when comparing results from instruments with numerous subdomains. Also, we report HRQoL measures developed for GERD. While these may be appropriate tools with which to measure the BE population, such measures have not been validated specifically in BE patients, and a disease-targeted quality of life measure does not exist for Barrett's. Therefore, it is possible that these measures do not completely capture the extent of HRQoL perturbations in this population. Due to the heterogeneity of patient populations, study methodology, and measurement tools (10 different quantitative measures of HRQoL or psychological distress were used amongst the 25 studies), we were unable to pool data from different studies or assess for publication bias, which likely would have strengthened our conclusions.

Nevertheless, the studies highlight the spectrum of changes in quality of life seen in BE. A diagnosis of Barrett's esophagus has an impact on a variety of domains of quality of life, increases healthcare and other costs, affects healthcare utilization and health behavior, and carries the potential for morbidity (see figure 4). Future studies are needed to clarify the extent to which cancer risk and symptoms influence quality of life for patients with Barrett's esophagus, and to what extent these effects can be mitigated with appropriate physician counseling and therapy targeted at symptom relief. In the interim, providers caring for subjects with BE should be aware of the implications of the diagnosis with respect to quality of life and psychological effects, and be vigilant for any adverse effects after the diagnosis is made.

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Abbreviations

BE	Barrett's esophagus
CINAHL	Cumulative Index to Nursing & Allied Health Literature
EAC	Esophageal adenocarcinoma
GERD	Gastroesophageal reflux disease
GERD HRQL	Gastroesophageal reflux disease health related quality of life instrument
GIQLI	Gastrointestinal quality of life index
HADS	Hospital anxiety and depression scale
HGD	High grade dysplasia
HRQoL	Health-related quality of life
LGD	Low grade dysplasia
MeSH	Medical subheading
PPI	proton pump inhibitor
QOLRAD	Quality of life in reflux and dyspepsia questionnaire
SCL-90	Symptom checklist-90
SF-36	Short form-36
SG	Standard gamble
TTO	Time tradeoff
VAS	Visual analog scale
WOCS	Worry of cancer scale

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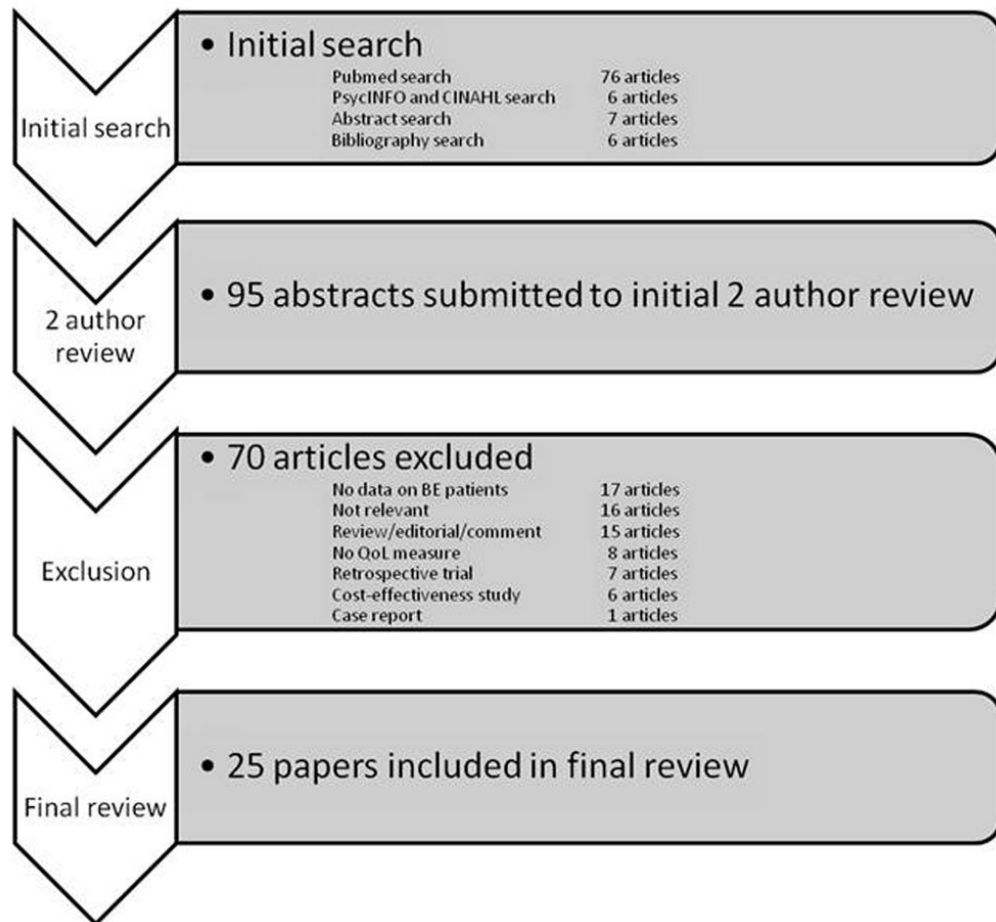


Figure 1.
Search strategy for systematic review

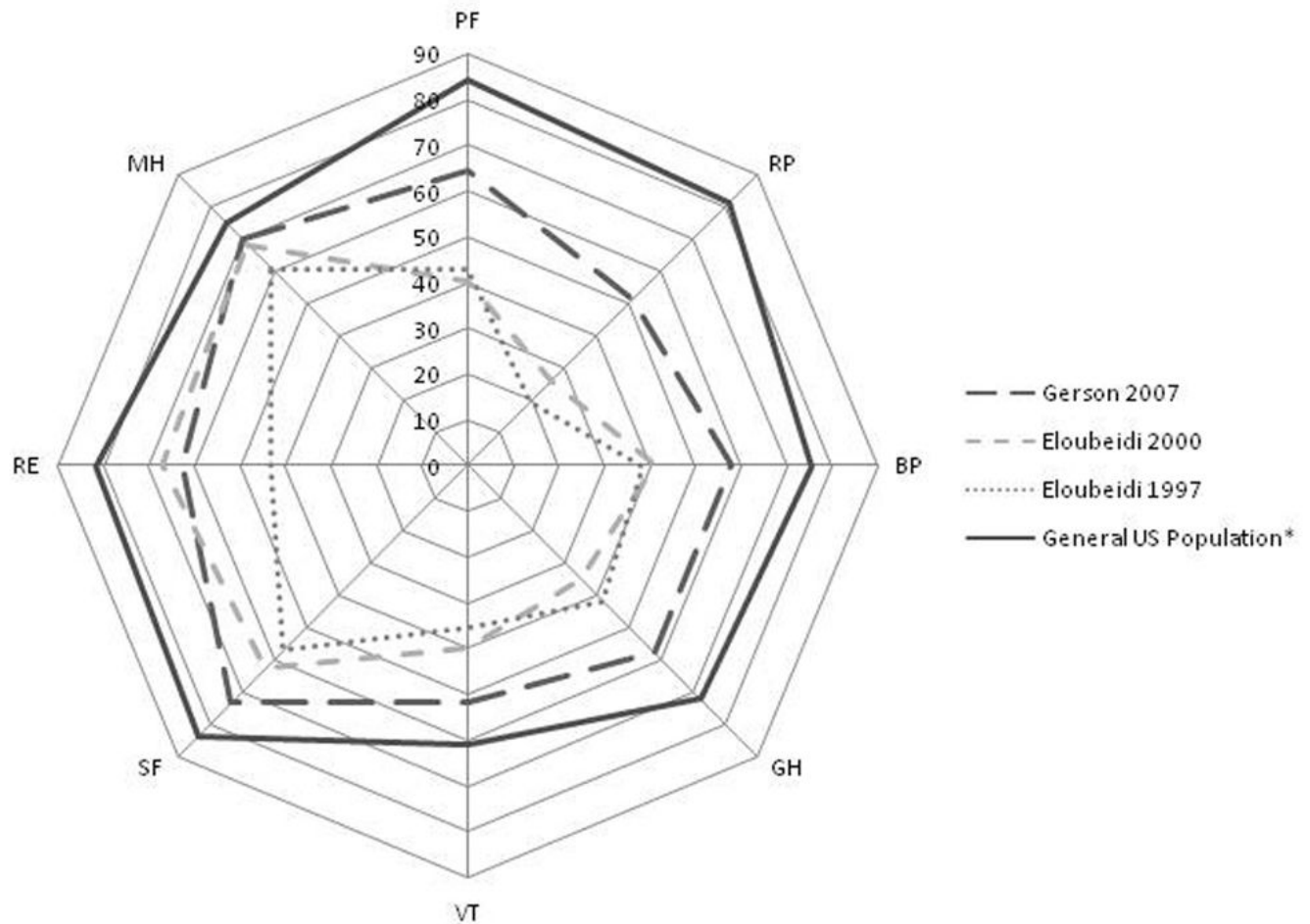


Figure 2.

Pilot graph of Medical Outcomes Short Form-36 (SF-36) subdomain scores measuring generic quality of life in patients with Barrett's esophagus compared to a healthy control population. Lower scores on the SF-36 (i.e. towards center of graph) indicate worsened quality of life.

PF: Physical Functioning; RP: Role Limitations-Physical; BP: Bodily Pain; GH: General Health; VT: Vitality; SF: Social Functioning; RE: Role Limitations-Emotional; MH: Mental Health

*Control data from Ware⁶⁴

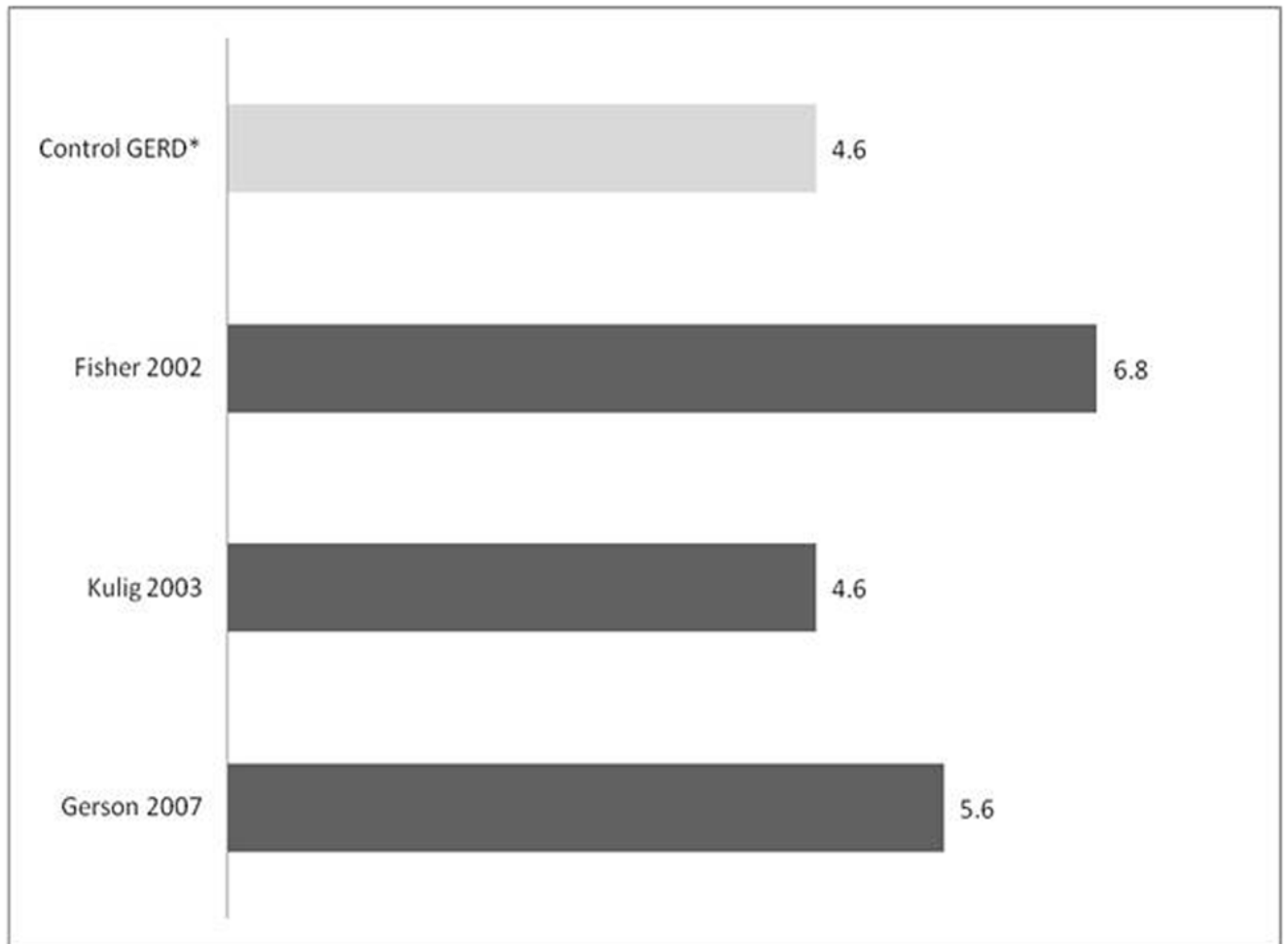


Figure 3. Total scores on the Quality of Life in Reflux and Dyspepsia questionnaire (QOLRAD) measuring disease-targeted quality of life in patients with Barrett's Esophagus compared to patients with gastroesophageal reflux disease
*Control GERD data from Kulig et. al ³³

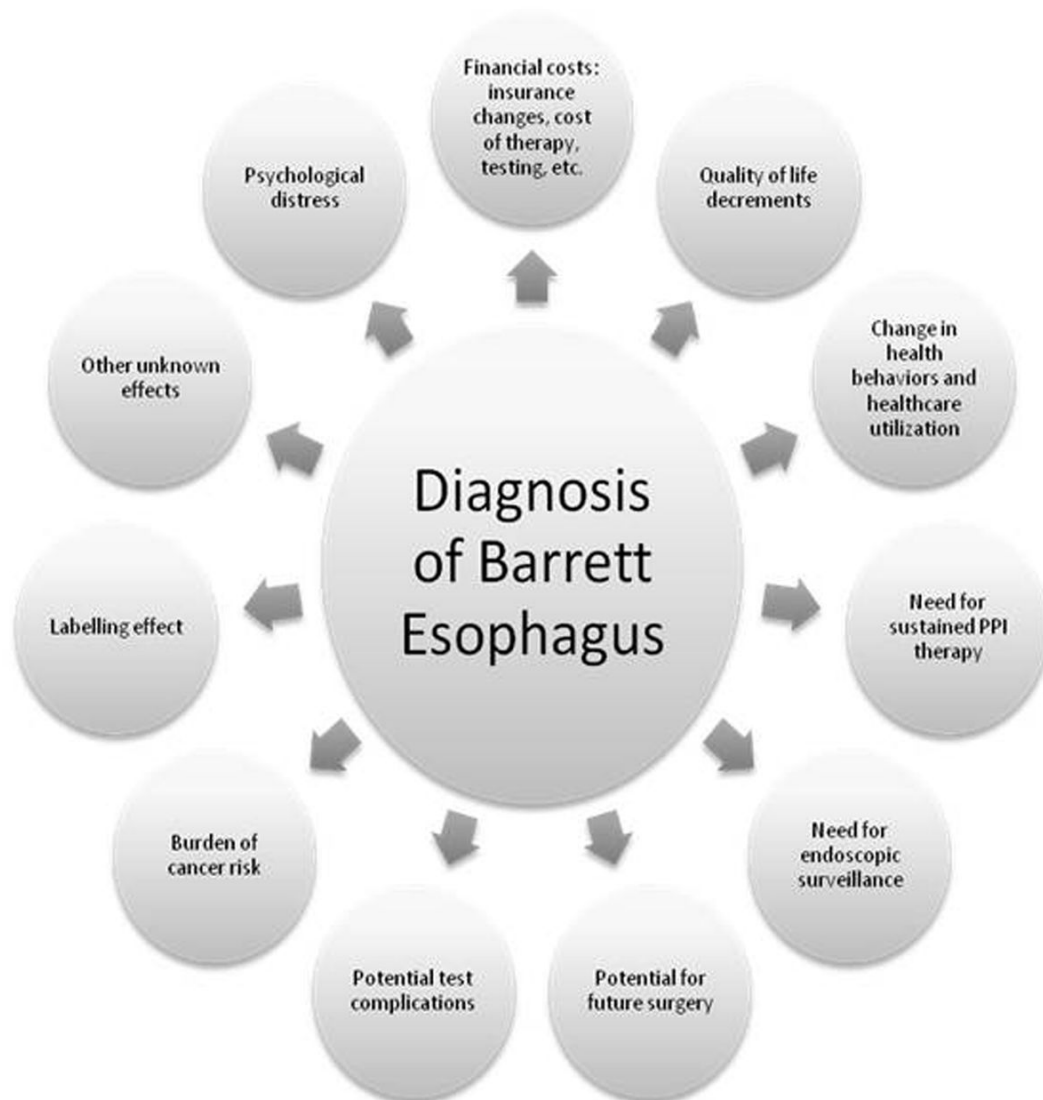


Figure 4.
Impact of diagnosing Barrett Esophagus.
Modified from Dellon et. al *Gastrointest Endosc* 2007 Jan;65(1):31–5.

Table 1

Quantitative measures of quality of life

Measure (ref)	#Q	Components/subscales	Scoring	Comments	Simplified Interpretation
SF-36 ²⁶ , 62	36	<p>2. Summary scores</p> <ul style="list-style-type: none"> Mental Component Summary (MCS) Physical Component Summary (PCS) <p>8. Subscales</p> <ul style="list-style-type: none"> Physical Function (PF) Role Limitations-Physical (RP) Bodily Pain (BP) General Health (GH) Vitality (VT) Social Functioning (SF) Role Limitations-Emotional (RE) Mental Health (MH) 	<ul style="list-style-type: none"> Scores range from 0–100 on each subscale and summary score Higher scores indicate better quality of life Score is standardized to the general population with a mean of 50, SD of 10 A 3-point difference is considered clinically meaningful 	This is a widely used measure of generic quality of life that has been validated in multiple disease states, and allows comparisons between diseases.	
GIQLI ²⁸	36	<p>4 Domains</p> <ul style="list-style-type: none"> physical well-being gastrointestinal symptoms social well-being emotional well-being 	<ul style="list-style-type: none"> Questions are multiple-choice, graded on a 0–4 scale Higher scores indicate less severe symptoms and improved HRQoL Final score is the sum of the question responses (max = 144) 	This measure assesses the effect of gastrointestinal symptoms including reflux on quality of life. It is a system-specific measure developed in Germany that has been used in multiple gastrointestinal disease states.	
QOLRAD ²⁹	25	<p>1. Summary score</p> <ul style="list-style-type: none"> Total score <p>5. Subscales</p> <ul style="list-style-type: none"> Food and Drink Emotional Distress Sleep Disturbance 	<ul style="list-style-type: none"> Responses to questions are graded on a 7-point Likert scale Higher scores indicate better HRQoL Total score is mean of subscale scores 	This measure was specifically designed for use in patients with heartburn symptoms	

Measure (ref)	#Q	Components/subscales	Scoring	Comments	Simplified Interpretation
		<ul style="list-style-type: none"> Physical and Social Functioning Vitality 			
GERD-HRQL ³⁰	10	<p>4 Domains</p> <ul style="list-style-type: none"> Intensity and frequency of heartburn Difficulty swallowing Bloating Burden of GERD medication 	<ul style="list-style-type: none"> Answers are graded on a 1–5 scale Higher scores correspond to more severe symptoms and worsened HRQoL Maximum total score is 50 	Often used as a patient reported gauge of severity of symptoms. This measure has been found to be reliable and valid in a wide range of patient groups	
Health State Utility ¹²	1	n/a	<ul style="list-style-type: none"> Patients are asked to give a value to life with a given disease state Scores range from 0 to 1, where 0 ≈ death and 1 ≈ perfect health Techniques: <ul style="list-style-type: none"> -Standard Gamble (SG): Patients are asked how much of a chance of death they would be willing to risk to be free of disease -Time Tradeoff: Patients are asked how much of their lifespan they would trade away to be free of a given disease state -Visual Analog Scales (VAS): Used to rate different disease states on a continuum from death to perfect health 	Utilities allow comparisons between diseases and provide data for use in cost effectiveness studies and decision analyses. For a given disease state, SG values tend to be highest (because of patients' aversion to risk) and VAS tend to yield the lowest numbers. Therefore, values generated using different techniques cannot be directly compared.	
SCL-90 ^{31, 63}	90	<p>9 dimensions of symptoms</p> <ul style="list-style-type: none"> Depression Anxiety Hostility Obsessive-compulsiveness Interpersonal sensitivity 	<ul style="list-style-type: none"> Questions are multiple-choice, graded on a 0–4 scale Higher scores correspond to increased distress related to each item Results expressed as <i>t</i> scores with a population mean of 50 and a SD of 10 A <i>t</i> score at or above the 90th percentile indicates a high level 	This is a widely used measure of psychological distress. It is relatively easy to use and takes fewer than 20 minutes to complete. It has been used to measure the full spectrum of psychiatric symptoms in a variety of disease states.	

Measure (ref)	#Q	Components/subscales	Scoring	Comments	Simplified Interpretation
HADS ³²	14	<ul style="list-style-type: none"> • Phobic anxiety • Somatization • Paranoid ideation • Psychosis <p>2 components</p> <ul style="list-style-type: none"> • Depression • Anxiety 	<ul style="list-style-type: none"> • 7 questions each for anxiety and depression graded on a 0–3 scale • Scores range from 0–21 on each component • Higher scores correlate with worsened symptoms • Scores of: <7: minimal depression/anxiety • 7–8: possible depression/anxiety • 10–11: probable depression/anxiety • 14/15: severe depression/anxiety 	<p>Developed to measure anxiety and depression in a population of patients seen in a general medical clinic. Easy to complete and score, and has been validated in multiple populations. Often used to assess hospital-related emotional distress.</p>	

Measures: SF-36: medical outcomes study short form-36; GIQLI: Gastrointestinal Quality of Life Index; QOLRAD: Quality of Life in Reflux and Dyspepsia Questionnaire; GERD-HRQL: Gastroesophageal Reflux Disease Health Related Quality of Life Instrument; SCL-90: Hopkins Symptom Checklist-90; HADS: Hospital Anxiety and Depression Score.

Abbreviations: SD: Standard Deviation; #Q: number of questions in instrument

Table 2
Studies reporting results of SF-36 in patients with Barrett’s esophagus

Author ^{ref}	Year	n	SF-36 summary scores (mean [SD])	SF-36 subdomain scores (mean[SD])	Comparison	Effect size				
Gerson ³⁵	2007	60	n/a	Physical Function (PF)	64.4 [30.7]	n/a	n/a			
				Role Limitations-Physical (RP)	50.9 [43.8]					
				Bodily Pain (BP)	57.7 [24.8]					
				General Health (GH)	57.7 [24.8]					
				Vitality (VT)	51.9 [24.4]					
				Social Functioning (SF)	73.3 [28.3]					
				Role Limitations-Emotional (RE)	62.6 [43.3]					
Mental Health (MH)	69.8 [21.2]									
Kulig ³³	2003	702	PCS MCS	n/a						
				NERD PCS	43.5 [8.8]		-0.1			
				NERD MCS	43.9 [11.9]		0.2			
				ERD PCS	43.1 [9.0]		-0.1			
ERD MCS	45.0 [12.0]		0.1							
Eloubeidi ³⁴	2000	107	n/a	* Physical Function (PF)	40 (18–65)	n/a	n/a			
				Role Limitations-Physical (RP)	26 (0–38)					
				Bodily Pain (BP)	41 (31–62)					
				General Health (GH)	35 (20–50)					
				Vitality (VT)	40 (20–55)					
				Social Functioning (SF)	63 (38–88)					
				Role Limitations-Emotional (RE)	67 (0–100)					
				Mental Health (MH)	68 (52–84)					
				Eloubeidi ³⁷	1997	25	n/a	Age/gender matched controls		
								Physical Function (PF)	42.9 [28.5]	PF
Role Limitations-Physical (RP)	19.8 [34.6]	RP	76.0 [36.7]					-1.6		
Bodily Pain (BP)	38.5 [24.5]	BP	68.5 [26.1]					-1.2		
General Health (GH)	41.8 [26.9]	GH	66.6 [23.3]					-0.9		
Vitality (VT)	35.4 [21.8]	VT	63.0 [21.4]					-1.3		

Author ^{ref}	Year	n	SF-36 summary scores (mean [SD])	SF-36 subdomain scores (mean[SD])	Comparison	Effect size
Lippmann ³⁶	2008	167		Social Functioning (SF) Role Limitations-Emotional (RE) Mental Health (MH)	SF RE MH	-1.1 -0.8 -0.7
			n/a		<u>GERD</u> Male PCS Female PCS	n/a

* values are median (interquartile range); Abbreviations: n/a = not available or not reported; SF-36 = medical outcomes study short form-36; GERD = gastroesophageal reflux disease; NERD = non-erosive reflux disease; ERD = erosive reflux disease.

Effect size calculated by $(HRQoL_{group1} - HRQoL_{group2})/SD_{group1}$

Table 3 Studies reporting results of the Quality of Life in Reflux and Dyspepsia Questionnaire (QOLRAD) in patients with Barrett's esophagus

Author ^{ref}	Year	n	QOLRAD total score (mean[SD])	QOLRAD component score (mean[SD])	Comparison	Effect size		
Gerson ³⁵	2007	60	5.6 [1.5]	food and drink	n/a	n/a		
				emotional distress	5.4 [1.6]			
				sleep disturbance	5.7 [1.7]			
				physical/social functioning	5.4 [1.7]			
Kulig ³³	2003	702	4.6 [1.3]	n/a	NERD total score	4.6 [1.3]		
					ERD total score	4.6 [1.3]	0	
Fisher ⁴⁰	2002	15	n/a	Gender-matched control population*				
				food and drink	5.8 [1.3]	food and drink	3.8 [1.6]	1.5
				emotional distress	6.1 [1.2]	emotional distress	4.5 [1.6]	1.3
				sleep disturbance	6.2 [1.2]	sleep disturbance	4.7 [1.6]	1.3
				physical/social functioning	6.6 [1.5]	physical/social functioning	4.9 [1.6]	1.1
				vitality	6.0 [1.2]	vitality	3.7 [1.6]	1.9

Abbreviations: n/a: not available or not reported; NERD: non-erosive reflux disease; ERD: erosive reflux disease

* previously published cohort of patients with upper GI symptoms who were referred for endoscopy

Table 4
Studies assessing utility in Barrett's esophagus and associated health states

Author (ref)	Year	n	Measure	Results (mean[SD])
Gerson ³⁵	2007	60	VAS, TTO	Nondysplastic BE 0.91 [0.13]
				BE with LGD 0.85 [0.12]
				BE with HGD 0.77 [0.14]
				BE with EAC 0.67 [0.19]
Hur ⁴¹	2006	20	SG	Nondysplastic BE 0.95 [0.07]
				Post-esophagectomy for HGD with dysphagia 0.92 [0.08]
				Post-PDT for HGD w/recurrence uncertainty 0.93 [0.11]
				Post-PDT for HGD w/recurrence uncertainty & dysphagia 0.91 [0.12]
				Intensive endoscopic surveillance for HGD 0.90 [0.14]
Gerson ⁴²	2005	40	VAS on meds [*]	69 [19]
			VAS off meds [*]	55 [21]
			time trade-off on meds	0.92 [0.08]
			time trade-off off meds	0.90 [0.12]
			SG on meds	0.95 [0.05]
			SG off meds	0.93 [0.07]
Fisher ⁴⁰	2002	15	VAS [†]	16 "holistic scenarios"
				BE surveillance 8 [8-10]
				BE surveillance & future complication of endoscopy requiring surgery 7 [5-8]
				BE surveillance & future complication of endoscopy requiring hospitalization 5 [4-8]
				BE surveillance & a future complication of endoscopy leading to death in 10y 4 [0-7]
				BE surveillance & future complication of endoscopy leading to death in 4y 3 [0-5]
				BE/LGD surveillance 5 [3-8]
				BE/LGD & a future complication of endoscopy requiring surgery 5 [5-8]
				BE/LGD & a future complication of endoscopy leading to death 3 [0-6]
				BE/LGD & future EAC dx requiring esophagectomy 5 [3-7]
	BE/LGD & future EAC dx, esophagectomy w/surgical complication & death 2 [0-5]			

Author (ref)	Year	n	Measure	Results (mean[SD])
			BE/LGD & complication of endoscopy, & EAC dx & esophagectomy	5 [3.5-5]
			BE/LGD & future complication of endoscopy & EAC dx & death during surgery	2 [0-5]
			BE with HGD requiring esophagectomy w/post-op dysphagia	4 [3-5]
			BE with HGD requiring esophagectomy & death during surgery	1 [0-2]
			BE/LGD & EAC dx requiring esophagectomy without cure leading to death	2 [0-3]
			BE/LGD & EAC dx requiring esophagectomy & death during surgery	0 [0-2]

* results are out of 100 point scale

† results are out of 10 point scale in medians [inter-quartile range]

Abbreviations: VAS = visual analog scale; SG = paper standard gamble; BE = Barrett's esophagus; LGD: low grade dysplasia; HGD: high grade dysplasia; EAC: esophageal adenocarcinoma; Dx: diagnosis; PDT: photodynamic therapy