

# What is the burden of illness in patients with reflux disease in South Africa?

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## ABSTRACT

**Objectives:** To describe the impact of heartburn on patients' Health-Related Quality of Life (HRQL) in South Africa.

**Design:** Survey of patient-reported outcomes and physician-assessed symptoms. **Setting:** South African, major referral gastroenterology clinic. **Subjects:** Consecutive patients with predominant symptoms of heartburn. **Outcome measures:** Patients completed the Afrikaans versions of the Gastrointestinal Symptom Rating Scale (GSRS), the Quality of Life in Reflux and Dyspepsia questionnaire (QOLRAD) and the Short Form Health-36 (SF-36). Physician-assessed frequency and severity of heartburn during the previous 7 days were also recorded. **Results:** 125 patients with symptoms of heartburn (age: M=46.0 [ $\pm$ 12 years]; females= 74%, 87% mixed race) completed the Afrikaans translation of GSRS, the QOLRAD and the Short-Form-36 (SF-36). Patients were bothered most by symptoms of reflux (mean GSRS score of 4.9, on a scale of 1 [not bothered] to 7 [very bothered]), indigestion (4.0) and abdominal pain (4.0). As a result of their symptoms, important reflux related aspects of life, such as problems with food and drink (3.5), emotional distress (3.6), impaired vitality (3.7), sleep disturbance (3.8) and impaired physical/social functioning (4.3) were experienced (QOLRAD scores where 1 represents the most severe impact on daily functioning and 7 no impact). Overall HRQL measured by the SF-36 was poor across all domains and was significantly lower compared to the UK general population. **Conclusions:** There is consistent evidence that GERD symptoms substantially impair all aspects of HRQL in this mixed race South African population referred to this central clinic.

**Keywords:** Burden of illness, Heartburn, Health-Related Quality of Life, South Africa

## INTRODUCTION

Gastroesophageal reflux disease (GERD) is characterized either by symptoms alone, without verifiable erosion in the esophagus (non-erosive gastroesophageal reflux disease, NERD) or by esophageal mucosal damage related to abnormal reflux of gastric contents into the esophagus. Its most common manifestations, regardless if it is NERD or GERD, are heartburn and/or acid regurgitation.<sup>1</sup> Symptoms can also be associated with a number of extra-esophageal conditions, including asthma, chest pain, sleep disturbance and otolaryngologic disorders. GERD is one of the most common diseases in western countries with an increasing incidence and prevalence in recent decades, that may partly be explained by the attention dedicated to its study.<sup>2-5</sup> Up to 40% of the adult Western population is affected by GERD<sup>6</sup>, not all of whom seek help from their general practitioner.<sup>7</sup> Nevertheless, heartburn and acid regurgitation

are among the most common reasons for consultation in general practice.<sup>7,8</sup>

A number of well-controlled clinical studies have been conducted in South Africa recently, providing evidence that GERD sufferers are seeking care and can be successfully treated.<sup>9-12</sup> However, it is unclear what the exact prevalence of GERD is in South Africa. A recent review suggested that GERD may be less frequent in the sub-Saharan African region than in the Western world, but pointed also out the possible reasons for underreporting such as: patients may not present to hospitals; endoscopic services may be inadequate; and the average life expectancy in sub-Saharan Africa is much lower than in industrialized countries.<sup>13</sup>

The impact of GERD on patients' health-related quality of life (HRQL) is of particular concern because it is generally diagnosed on the basis of patient-reported symptoms alone.<sup>14,15</sup> This is because the majority of patients who seek the assistance of a general practitioner for symptoms of GERD lack signs of esophageal mucosal injury<sup>16</sup> and, in any case, endoscopy is rarely available in primary care, where GERD diagnosis and treatment most often takes place.

Although the impact of GERD on HRQL in Europe and North America is well documented<sup>14,17,18</sup> these studies use different

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methodologies in different countries, making international comparisons of the impact of GERD problematic. A series of studies were therefore undertaken using a standardized methodology to assess the impact of heartburn on patients' HRQL in South Africa, Italy, Spain, Germany, Poland and Hungary. This paper reports the results of the study that used translations of validated generic and disease-specific instruments to measure patient-reported outcomes in South Africa.

## PATIENTS and METHODS

### Patient population

Patients with current or previously verified predominant symptoms of heartburn were eligible for entry into the study. Heartburn was defined as a 'burning feeling rising from the stomach or lower part of the chest up towards the neck'. Exclusion criteria included concurrent diagnosis of Irritable Bowel Syndrome or peptic ulcer disease, a major psychiatric illness or dementia, or any other significant medical or surgical disease. Patients treated for peptic ulcer with anti-secretory or anti-*Helicobacter pylori* therapy and were referred for follow-up endoscopy, or those using acetyl salicylic acid (ASA) or other nonsteroidal anti-inflammatory drugs (NSAIDs) daily were also excluded. Patients had to be able to complete the patient-reported outcome instruments themselves, as no proxy assessment or interpreter was allowed. The study was conducted between September 2002 and September 2003 in one centre, at a major referral gastroenterology clinic. Good Clinical Practice was followed (written informed consent was obtained from the patient, and the study protocol and consent form was approved by independent local Ethics in accordance with the revised Declaration of Helsinki) and the patients were free to discontinue participation in the study at any time.

### Demographic and clinical characteristics

Patient demographics (age, sex, race, family and employment status), medical history (including history of gastrointestinal disease) and frequency of heartburn symptoms were recorded. In addition, investigators assessed the severity of patients' symptoms using a four-graded scale (0= none: no symptoms; 1= mild: awareness of sign or symptom, but easily tolerated; 2= moderate: discomfort sufficient to cause interference with normal activities; 3= severe: incapacitating with inability to perform normal activities). All data were reported in a paper case report form.

### The impact of gastrointestinal symptoms on HRQL

HRQL can be measured with generic or disease-specific questionnaires.<sup>19</sup> Generic instruments are comprehensive and allow comparison of HRQL across diseases, treatments and populations. Disease-specific instruments, which capture details about specific symptoms, are more sensitive than generic instruments, and are therefore more responsive to treatment and other changes over time.<sup>19</sup>

Patients completed four instruments: the Gastrointestinal Symptom Rating Scale (GSRS)<sup>20</sup>; the heartburn version of Quality of Life in Reflux and Dyspepsia (QOLRAD) questionnaire<sup>21</sup>, which has excellent psychometric characteristics in clinical trials<sup>22,23</sup>; and the Short-Form Health 36 (SF-36).<sup>24</sup> All instruments have been tested in terms of validity and reliability.<sup>21,25</sup>

They were translated into Afrikaans by MAPI research institute<sup>26</sup> and linguistically validated according to international guidelines.<sup>27</sup>

GSRS is a disease-specific instrument comprising 15 items combined into five symptom clusters, three (reflux, abdominal pain, indigestion) relevant to GERD and two (diarrhoea and constipation) representing other gastrointestinal symptoms. It uses a seven-point Likert-type scale from 1 (absence of bothersome symptoms) to 7 (very bothersome symptoms). Its reliability and validity are well documented<sup>20</sup> and norm values for a general population are available in some countries.<sup>28</sup> An Afrikaans translation of GSRS was psychometrically validated in the same study population.<sup>29</sup>

The other disease-specific instrument, the heartburn version of QOLRAD includes 25 items combined into five dimensions: emotional distress, sleep disturbance, vitality, food/drink problems and physical/social functioning. The questions are rated on a seven-point Likert scale in which, in the reverse of GSRS, lower values indicate a more severe impact on daily functioning. QOLRAD has been extensively documented in international studies in patients with heartburn with regard to reliability, validity and responsiveness to treatment.<sup>18,21</sup> Its factor structure has been replicated in several translations.<sup>30</sup> The Afrikaans translation of QOLRAD was psychometrically validated in this study population.<sup>29</sup>

SF-36 is an extensively used generic HRQL questionnaire, its 36 items clustered in eight dimensions: bodily pain, general health, mental health, physical functioning, emotional role, physical role, social functioning and vitality. Item scores for each dimension are coded, summed and transformed into a scale from 0 (worst measurable health state) to 100 (best measurable health state). This study used the Afrikaans acute version of SF-36, which covers a one-week recall period. The reliability and validity of SF-36 is well documented in many languages.<sup>31</sup> The mean scores of heartburn patients in each domain of the SF-36 were compared to previously determined United Kingdom norm values.<sup>32</sup> Afrikaans norm values to the knowledge of the authors are not available.

The patient, using paper and pencil, completed all questionnaires. All study personnel were trained to instruct the patients in a standardized way in order to minimize bias and enhance compliance.

### Statistical methods

Statistics were calculated with SAS version 8.02.<sup>33</sup> Pearson correlation coefficients were used to assess convergent and discriminant validity, and p-values were adjusted for multiplicity (Bonferroni: 0.05/165).<sup>34</sup> If data was missing from one or more assessment, the mean of the completed items in the same dimension was used, provided that more than 50% of the items in that dimension had been completed.<sup>35</sup> Missing values were less than 5% and patients in that group were not significantly different from the rest of the study population.

## RESULTS

### Demographic and clinical characteristics

A total of 125 patients entered the study. Their demographic and clinical characteristics are shown in Table 1. The age of the study population ranged from 18 to 78 with a mean age of 46

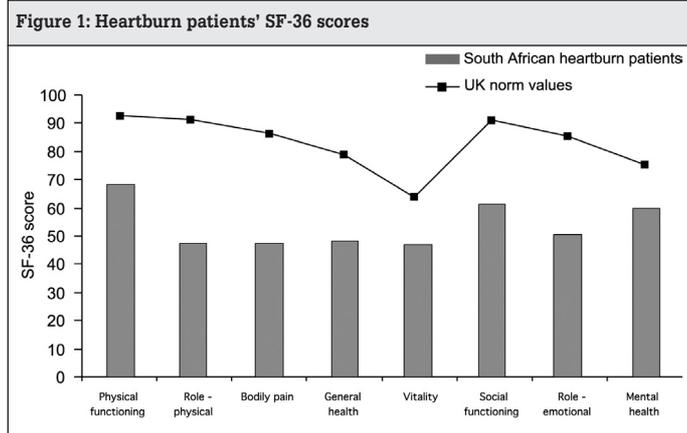
Table 1. Patient demographics and clinical data (N=125).		
Variables		
Age:	Mean (SD) years	46.0 (12.3)
Sex:	Female	74.4
Race:	Mixed	87.2
Marital status:	Married	55.2
Employment status:	Full-time employed	40.0
	Part-time employed	5.6
	Unemployed	16.0
	Homemaker, Student, Early retirement, Retired	36.0
Duration of current episode:	< 1 month	24.8
	1-6 months	41.6
	> 6 months	33.6
Duration of disease:	< 1 year	8.8
	1-5 years	48.0
	> 5 years	43.2
Severity of symptoms, last 7 days:	Mild	11.2
	Moderate	27.2
	Severe	61.6
Frequency of symptoms, last 7 days:	1-2 days	18.4
	3-4 days	28.0
	≥5 days	53.6
Previous peptic ulcer and/or ulcerative reflux esophagitis:	Yes	32.8
Doctor visit because of emotional problems during the past 5 years:	Yes	25.6

(±12.3) years and 74% were female. Over half were married (55%) and most were of mixed race (87%). The majority were either employed full-time (40%) or described as a homemaker/student/retired (36%). Most patients (91%) had experienced heartburn symptoms for over a year and in two thirds (66%), the duration of the current episode was 6 months or less. Over half of patients (54%) had experienced symptoms on five or more occasions in the previous 7 days. Most patients (62%) described their symptoms as being severe during this period.

### The impact of gastrointestinal symptoms on HRQL

Gastrointestinal Symptom Rating Scale and Quality of Life in Reflux and Dyspepsia

Patients with heartburn were most bothered by the GSRS symptom clusters related to GERD: reflux (GSRS score of 4.9 on a scale of 1 [not bothered] to 7 [very bothered]), indigestion



(GSRS = 4.0) and abdominal pain (GSRS = 4.0). These symptoms were reflected in all five dimensions of QOLRAD, with patients experiencing food and drink problems (QOLRAD score of 3.5 on a scale of 1 to 7, where 1 is most severe), emotional distress (3.6), impaired vitality (3.7), sleep disturbance (3.8) and impaired physical/social functioning (4.3).

### Short Form-36

Scores for the individual domains of SF-36 are shown in Figure 1. The lowest scores (<50) were reported for physical role, bodily pain, general health, and vitality. A five score difference between the domains of the studied population and the general norm values are considered to be clinically relevant<sup>36</sup>, that was the case in all domains compared to the UK norm scores.

### Correlations between patient-reported outcome instruments

The relevant symptom clusters of GSRS symptom scale (reflux, abdominal pain, and indigestion) were significantly correlated (p<0.0003) with all five dimensions of the QOLRAD, the disease-specific HRQL measure (Table 2). As expected, the strongest correlations were found with re-

Table 2. Correlation coefficients (Pearson) between GSRS, QOLRAD and SF-36 domains, and physician-assessed frequency and severity of symptoms					
Instruments	GSRS Reflux	GSRS Abdominal pain	GSRS Indigestion	GSRS Diarrhoea	GSRS Constipation
SF-36 Bodily pain	-0.27	-0.40	-0.39	-0.32	-0.35
SF-36 General Health	-0.17	-0.30	-0.32	-0.20	-0.24
SF-36 Mental Health	-0.31	-0.36	-0.31	-0.23	-0.36
SF-36 Physical functioning	-0.11	-0.27	-0.27	-0.29	-0.10
SF-36 Role - Emotional	-0.13	-0.17	-0.26	-0.20	-0.20
SF-36 Role - Physical	-0.18	-0.27	-0.30	-0.19	-0.22
SF-36 Social Functioning	-0.27	-0.23	-0.32	-0.26	-0.28
SF-36 Vitality	-0.29	-0.39	-0.38	-0.18	-0.38
QOLRAD Emotional distress	-0.61	-0.57	-0.55	-0.27	-0.47
QOLRAD Food/drink problems	-0.55	-0.52	-0.49	-0.39	-0.48
QOLRAD Physical/social functioning	-0.56	-0.54	-0.50	-0.35	-0.45
QOLRAD Sleep disturbance	-0.64	-0.54	-0.54	-0.33	-0.47
QOLRAD Vitality	-0.60	-0.60	-0.55	-0.37	-0.48
Physician-assessed symptoms	0.55	0.44	0.36	0.17	0.29
Frequency of heartburn symptoms	0.75	0.51	0.42	0.24	0.38
Severity of heartburn symptoms					

Notes: Correlation coefficients in bold are statistically significant p<0.0003.

flux related symptoms (reflux, abdominal pain and indigestion). The correlation between the GRS abdominal pain and indigestion and the generic measure SF-36 were also significant in the domains of bodily pain, general health, mental health and vitality dimensions ( $p < 0.0003$ ). GRS assessment of reflux symptoms only significantly impacted mental health of the SF-36.

Correlations between patient-reported outcomes and physician-rated symptom assessments

Finally, physician-assessed severity and frequency of heartburn symptoms correlated significantly with the three GERD-related GRS domains (reflux, abdominal pain and indigestion). Of the remaining GRS domains, the only significant correlation was between constipation and physician-assessed severity of symptoms.

## DISCUSSION

This study demonstrates that the burden of illness in patients with predominant symptoms of heartburn is substantial in the South African, primarily mixed race Afrikaans speaking population studied, as measured by disease-specific and generic HRQL instruments. As expected patients reported that their most bothersome symptoms were reflux, indigestion and abdominal pain, in that order. It should be noted that this study was conducted in a single, major referral gastroenterology centre, and therefore the results are particular to patients with mixed race referred for gastroenterological investigation. As no published South African HRQL data is available on GERD patients, it is difficult to compare our findings with previous research. Future studies should look at patients recruited from several clinics, both gastroenterology and general practices and with various demographic background.

Because of their heartburn symptoms, patients reported that they could not eat and drink as they liked, their vitality was impaired, they were emotionally distressed, their physical/social functioning was impaired and they were bothered by sleep disturbance due to nocturnal heartburn. The emotional distress of the patient population due to heartburn was further emphasized by the fact that 26% reported visiting a doctor because of an emotional problem during the past five years.

Although norm values are not available for the South African population, these SF-36 scores, when compared to the UK<sup>32</sup> or Western European data<sup>37,38</sup>, indicate a severe impairment in health status. Patients accomplished less, were limited in their work and activities and felt more tired than the general UK population as measured by the SF-36. It should also be emphasized that the difference between the studied GERD population and the UK norms was considerably larger than five score units, that is considered to be clinically significant. Poor HRQL compared to normative values have been shown in a series of studies, and the impairment is generally largest with regard to bodily pain, vitality and emotional well-being.<sup>17</sup> The impact of GERD on overall HRQL measured in this study is in agreement with recent studies.<sup>15,39</sup> In general, patients with heartburn experience worse pain, social functioning and emotional wellbeing than those with diabetes, hypertension and acute coronary events.<sup>40</sup> These aspects of patients' lives

are impaired whether or not heartburn is associated with erosive esophageal lesions.<sup>4,17,41</sup> A recent study corroborates that the severity of gastrointestinal symptoms is the most important factor in affecting health status.<sup>42</sup> Similarly, Irvine concluded that besides disease severity, anxiety and comorbid conditions are also strongly related to impaired HRQL.<sup>43</sup>

The conclusion that reflux, indigestion and abdominal pain are the most bothersome symptoms of GERD is supported also by previous studies.<sup>17,18,44</sup> The impact of GERD on sleep disturbance seen in these patients is the focus of considerable research<sup>45-47</sup>, but remains poorly recognized in primary care. The HRQL effects of GERD, including emotional distress, may account for the relatively high prevalence of anxiety and depression seen in other studies.<sup>48</sup> However, with effective symptom resolution patients lives are restored to the level observed in the general population.<sup>15</sup> In addition, previous research has shown that both the severity and the frequency of symptoms increase the likelihood to consult<sup>49</sup> and that when symptoms are sufficiently treated well-being is restored.<sup>18,44,50-52</sup>

Primary care physicians, are largely unaware of the associated burden of esophageal and extra-esophageal complications, and the pain and distress it can cause<sup>53</sup>, despite the recent interest in the substantial impact of GERD on patients' HRQL. This is particularly pertinent, given that effective treatment the one starting with the most effective acid suppression, i.e. a step down regimen, with proton pump inhibitors, for example, leads to significant improvements in HRQL.<sup>45,50,54</sup> This is also more cost-effective in maintaining quality of life.<sup>55,56</sup> For instance, esomeprazole 20 mg once daily (either continuous or on-demand) was significantly and clinically superior to ranitidine 150 mg twice daily in maintaining quality of life and achieving an optimal level of patient satisfaction.<sup>54</sup> According to a recent expert review, PPI therapy should be initiated regardless of whether the heartburn symptoms are associated with esophagitis or not.<sup>4</sup> In addition to the patient's perspective HRQL is one of the major endpoints in medical research that will help provide more selective treatment regimens for patients.<sup>57</sup> Current treatment guidelines discuss this issue in more detail.<sup>2,58</sup>

In conclusion, both generic and disease-specific patient-reported instruments provided clear and consistent evidence that patients with heartburn are bothered and incapacitated by their symptoms, and that their HRQL is impaired as a result. Continuing education of primary care and specialist physicians is required to mitigate the impact of this widespread and under-treated condition.

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