# Evaluation of the GERD Impact Scale, an international, validated patient questionnaire, in daily practice. Results of the ALEGRIA study

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## Abstract

***Background and study aims :*** **Gastroesophageal reflux disease (GERD) is a common chronic disease that is primarily diagnosed based on symptom severity and frequency. This study gathered epidemiological data in a population of GERD patients and evaluated the added-value of the GERD Impact Scale (GIS), a novel, validated patient questionnaire, as a tool for initial and long-term patient management.**

***Patients and methods :*** **This observational study recruited patients (296 study centers) with symptomatic GERD and a history of erosive, or reflux, esophagitis. Symptoms were assessed by GIS and physician-subject interview and recorded at baseline (visit 1), at 4–6 weeks (visit 2) and 8–14 weeks (visit 3) ; also recorded at each visit was the physician's assessment of GERD severity and treatment changes. Analyses were performed on an intent-to-treat basis.**

***Results*** **: Subjects (n=1919 ; mean age, 55 years) were 54% female. Lifestyle characteristics included stress (~70% of subjects), mean daily consumption of five cups of caffeine-containing beverages (~70%), alcohol consumption of approximately nine units per week (~50%) and smoking/ex-smoker (41%). Proton pump inhibitors were prescribed in 99% of cases : mainly esomeprazole (82%), with a median dose of 40 mg. Prescribed therapy was changed (mainly dosage levels) between visits in ~60% of subjects. The severity of GERD symptoms and GIS scores decreased substantially throughout the study. Mean GIS scores correlated positively with increasing GERD severity and clinical judgment at all visits. Physicians reported that the GIS helped them define the appropriate treatment for the patient and to evaluate the patient's response to treatment in 81% of cases.**

***Conclusions*** **: This study demonstrates the added-value and usefulness of the patient self-assessment GIS as a management tool for GERD.** (Acta gastroenterol. belg., **2009**, 72, **3-8**).

## 1. Introduction

Gastroesophageal reflux disease (GERD) is estimated to affect 10–20% of the general population in the Western world, and is a common cause of health care seeking in the primary care setting (1,2). GERD occurs when movement of gastric contents into the esophagus causes troublesome symptoms (such as heartburn and regurgitation) and/or complications (3). Such symptoms may lead to sleep disturbance (4) and a decrease in the patient's quality of life (QoL) including a lack of vitality and limitations in food and drink intake. Night-time heartburn and sleep complaints are associated with excessive gastroesophageal reflux (5). Feelings of poor physical and mental health interfere with the patient's ability to function normally on a daily basis (6,7) and are likely to impair their performance at work (6,8-10).

In many patients, GERD is a chronic, relapsing disease that required a long-term management strategy. In up to half of all cases, GERD is associated with erosive, or reflux according to the Montreal definition, esophagitis (11). However, individuals with GERD suffer significant pain and discomfort whether or not esophagitis is present, and the resulting impairment in QoL is not dependent on endoscopic findings (7,12). Thus, international guidelines recommend that GERD should be diagnosed and managed on the basis of symptom frequency and severity (3,13-15). Although the symptoms of GERD are experienced by the patient, assessments of symptom severity have traditionally been carried out by the physician. However, the agreement between patients and physicians in their assessments of severity of reflux symptoms seems poor, particularly before treatment and for more severe symptoms (16).

The lack of physician-patient agreement in the assessment of symptoms has far-reaching implications. In day-to-day clinical practice, both the decision to offer the patient treatment and the type of treatment offered are determined by the physician's initial assessment of symptoms. Poor physician-patient agreement prior to therapy may be an obstacle to the appropriate management of GERD and this may contribute to widespread treatment dissatisfaction experienced by patients (17). Conversely, studies have shown that the benefits of good physician-patient communication are likely to extend beyond more accurate symptom assessment to improved patient health outcomes, satisfaction, well-being and trust (18-22).

When supported by appropriate instruments, patients may be the most faithful reporters of their own symptoms and this could allow a move towards giving greater weighting to patients' own reports (3). In this regard, a novel patient questionnaire, the GERD Impact Scale (GIS), may be of use. This validated questionnaire was designed to aid physicians in the identification of an appropriate treatment and to evaluate the patient's response to treatment. The GIS was developed from an initial systematic literature review, followed by patient

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focus groups and primary care physician and patient cognitive interviews (23). The GIS has demonstrated good psychometric properties in newly diagnosed GERD patients and those already receiving treatment, and has been shown to be a valid and reliable tool for use in clinical practice to identify instances of need for more effective therapy in subjects with a confirmed diagnosis of reflux disease (23).

As part of the ALEGRIA (A real Life Evaluation of GERD Impact of symptom Assessment in Belgium) study (Study ID : NIS-GBE-NEX-2006/1 ; ClinicalTrials.gov Identifier : NCT00545883), which was designed to gather epidemiological data in a primary care population of GERD patients with a history of erosive esophagitis, we therefore evaluated symptom control and impact on daily life, from a patient's perspective, using the GIS. A secondary objective was to evaluate the added value of the GIS in terms of aiding the physician's determination of the appropriate treatment and evaluation of treatment response. The study was non-interventional, being designed and conducted to ensure that the physician's decision regarding assigning patients to a particular therapeutic strategy was followed according to standard clinical practice.

## 2. Patients & Methods

### 2.1. *Patients*

A total of 2001 patients were included in this study from 296 study centers in Belgium. The study was conducted between 5 May 2006 and 5 June 2007.

The patient population included in the study fulfilled the following inclusion criteria : willing and able to sign the informed consent form and comply with the requirements of this study, at the discretion of the primary care physician or gastroenterologist ; male or female, aged $\geq$ 18 years ; undergoing treatment for GERD according to current practice (24) and according to the summary of product characteristics of the prescribed treatment ; suffering from Los Angeles grade A-D erosive esophagitis (25) and not currently treated with a proton pump inhibitor (PPI), for whom the physician has decided to initiate or change the treatment for GERD. Excluded were females of childbearing potential who were not using a reliable form of contraception, and pregnant or nursing women.

Three visits were planned in this study. At the first visit (day 1), demographic and baseline data (age, gender, GERD history, current GERD symptoms, clinical judgment and prescribed treatment) were recorded after obtaining the subjects' informed consent. At the next two visits (week 4-6 [Visit 2] and week 8-14 [Visit 3], respectively), GERD symptoms, clinical judgment and changes in treatment were recorded. At each visit, the patient was also asked to complete the GIS, as outlined below. All procedures were in accordance with routine clinical practice and not study-related except for the completion of the GIS.

The study was performed in accordance with the Declaration of Helsinki, all applicable legislation and received all necessary ethical approval.

### 2.2. *GERD Impact Scale (GIS)*

In this study, both the Dutch and French versions of the GIS were used. The GIS is composed of nine questions (Table 1) and uses a four-graded Likert scale for answers : i.e. *daily*, *often*, *sometimes*, and *never*. The recall period for the questions was the seven days preceding study visits. The nine questions cover three dimensions : upper GI symptoms (questions 1a, 1b and 1d), other acid-related GI symptoms (questions 1c and 1e) and the impact of the symptoms on the patient's daily lives (questions 2, 3, 4 and 5).

A mean score was calculated for each dimension, generating a number between 1 and 4. In addition, the pre–post changes from Visit 1 to Visit 2 and Visit 2 to Visit 3 were also calculated within each severity level.

### 2.3. *Demographics, lifestyle factors, and clinical characteristics*

Demographics, lifestyle factors, duration of GERD, history of GERD treatment, and results of endoscopy (performed prior to study entry) were documented at Visit 1. The following lifestyle factors were assessed using a simple checklist : alcohol use (units per week) ; smoking ; ex-smoker ; caffeine intake (units per week) ; stress ; other (description specified).

Type and extent of esophageal tissue damage was classified according to the Los Angeles classification system (25).

Table 1. — **Questions of the GERD Impact Scale (GIS)**

| |
|---|
| 1. How often have you had the following symptoms : |
| a. Pain in your chest or behind the breastbone ? |
| b. Burning sensation in your chest or behind the breastbone ? |
| c. Regurgitation or acid taste in your mouth ? |
| d. Pain or burning in your upper stomach ? |
| e. Sore throat or hoarseness that is related to your heartburn or acid reflux ? |
| 2. How often have you had difficulty getting a good night's sleep because of your symptoms ? |
| 3. How often have your symptoms prevented you from eating or drinking any of the foods you like ? |
| 4. How frequently have your symptoms kept you from being fully productive in your job or daily activities ? |
| 5. How often do you take additional medication other than what the physician told you to take (Maalox, Gaviscon, Rennies etc.) ? |

### 2.4. *GERD symptoms and clinical judgment*

At each visit, the following GERD symptoms were assessed by the physician : heartburn ; acid regurgitation ; dysphagia ; and epigastric pain. The severity of symptoms was graded on a four-point scale (*none*, *mild*, *moderate*, or *severe*). The physician was also asked to give an overall judgment of the patient's GERD-related symptoms at each visit. This was done in response to the question, "Based on your routine clinical judgment, how would you rate the patient's severity of GERD-related symptoms ?" using a three-point scale (*mild*, *moderate*, or *severe*).

### 2.5. *Physician's judgment of the usefulness of the GIS*

At the end of the study, the physician was asked to make a judgment on the usefulness of the GIS in response to the question, "Does the GIS facilitate the choice of appropriate treatment for your GERD patient and to evaluate the response to this treatment ?" Two response options were provided : *yes* and *no*.

### 2.6. *Data analysis*

All data obtained in this study were generally summarized with descriptive statistics for the intent-to-treat population (i.e. all patients for whom Visit 2 occurred). Analysis of the added value of the GIS was achieved by correlating the mean GIS scores with the GERD symptom scores assessed by the physician, the physician's clinical judgment, endoscopic findings (Los Angeles classification), and the physician's judgment of the usefulness of the GIS using Spearman's correlation coefficients.

## 3. Results

### 3.1. *Patient demographics, lifestyle factors and clinical characteristics*

A total of 2001 subjects were enrolled in the study, of whom 1919 were included in the intent-to-treat population (Table 2). Patients were typically female (54%) with a mean age of 55 years (range, 18–95 years) and mean bodyweight of 75 kg (range, 40–152 kg). Lifestyle factors included : stress (approximately 70% of patients) ; consumption of a daily average of five cups of caffeine-containing beverages for approximately 70% of patients ; 50% recorded mean weekly consumption of approximately nine units of alcohol ; and 41% of patients were smokers or ex-smokers. Other relevant factors recorded for 5% of patients included use of non-steroidal inflammatory drugs (NSAIDs), intake of spicy or unhealthy food, and psychological problems.

In terms of clinical characteristics (Table 3), the mean duration of GERD symptoms was 3.5 years (range, 0–66 years) and the majority of patients had Los Angeles grade A or B esophagitis (91.5%).

Table 2. — **Demographic and lifestyle characteristics (intent-to-treat population, n = 1919)**

| | |
|---|---|
| Women, n (%) | 1034 (54) |
| Mean age, years (± SD) | 54.9 ± 16.2 |
| Mean bodyweight, kg (± SD) | 75.0 ± 14.1 |
| Stress, n (%) | 1260 (66) |
| Caffeine consumers, n (%) | 1395 (73) |
| Mean consumption, cups/day (± SD) | 4.7 ± 3.7 |
| Alcohol consumption | 879 (46) |
| Mean consumption, units/week (± SD)[a] | 9.2 ± 12.4 |
| Smoker, n (%) | 443 (23) |
| Ex-smoker, n (%) | 349 (18) |

[a]Unit of alcohol equivalent to 300 mL beer, 125 mL wine or 25 mL liqor.

Table 3. — **Clinical characteristics (intent-to-treat population, n = 1919)**

| | |
|---|---|
| Los Angeles classification of erosive esophagitis, n (%) | |
| Grade A | 1238 (64.5) |
| Grade B | 510 (27) |
| Grade C | 119 (6) |
| Grade D | 42 (2) |
| Missing | 10 (0.5) |
| Mean duration of GERD, years (± SD) | 3.5 ± 5.7 |
| Previous GERD therapy, n (%)[a] | |
| Antacids | 492 (26) |
| $H_2$-receptor antagonists | 455 (24) |
| Proton pump inhibitors (empiric therapy) | 292 (15) |
| Proton pump inhibitors (after endoscopy) | 574 (30) |
| None | 486 (25) |

[a]Multiple responses possible.
GERD, gastroesophageal reflux disease.

### 3.2. *GERD treatment*

Most patients had previously received treatment for their GERD symptoms, most commonly with a PPI (15% had received empiric PPI therapy and 30% received PPI therapy after endoscopy).

At study entry (Visit 1), PPIs were prescribed in 99% of patients ; the main PPI was esomeprazole (82%) with a median daily dose of 40 mg. Prescribed therapy was subsequently revised in approximately 60% of subjects between Visit 1 and 2 and 15% of subjects between Visit 2 and 3. In the vast majority of cases, only the dose was altered. The nature of therapy changed in most patients from "acute treatment (full dose)" (79% of patients) at visit 1 to "maintenance treatment (half dose)" (96% of patients) at visit 3.

### 3.3. *GERD symptoms recorded by interview and the clinician's judgment of their severity*

Heartburn, acid regurgitation and epigastric pain were each reported for approximately 90% of patients at Visit 1, while approximately 70% of patients had dysphagia (Fig. 1). At Visit 1, 46% of patients complained of moderate heartburn ; at Visit 2, 45% complained of mild heartburn and at Visit 3, 59% had no heartburn. Acid regurgitation decreased from 44% with moderate symptoms at Visit 1 to mild (46.2%) and no symptoms at

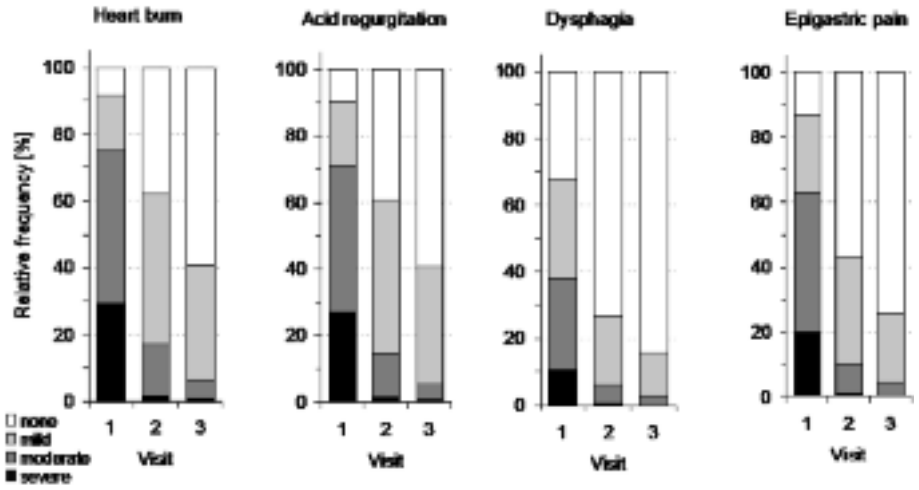


Fig. 1. — Severity of GERD symptoms, as assessed by physician interview.
Visit 1, n = 1919 ; Visit 2, n = 1916 ; Visit 3, n = 1879. Adjusted relative frequencies are shown.

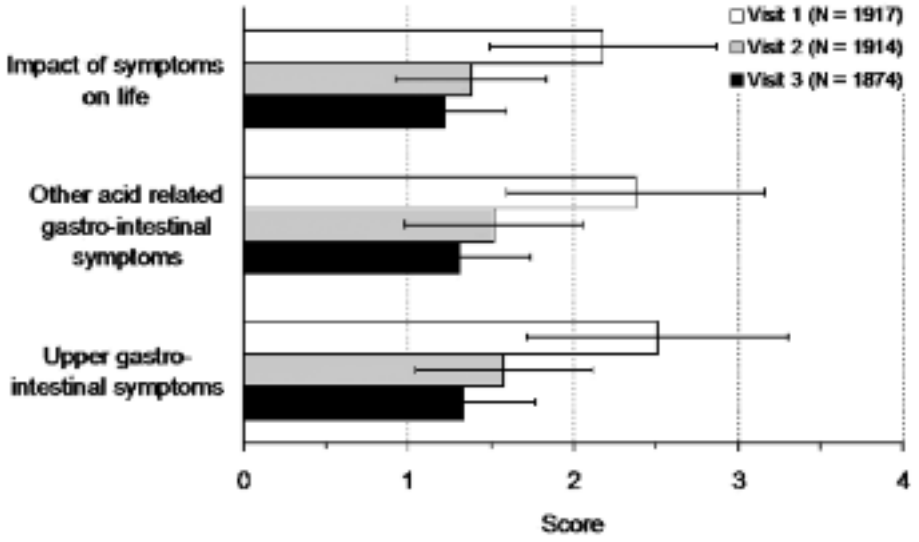


Fig. 2. — Mean scores for the three dimensions of the GERD Impact Scale, by visit

Visits 2 and 3, respectively. Moderate epigastric pain was reported in around half of patients (43%) at Visit 1, but by Visits 2 and 3 the majority of patients reported no pain (57% and 74%, respectively). Approximately 30% of patients reported having no, mild or moderate dysphagia, respectively, at Visit 1, but by Visits 2 and 3, absence of dysphagia was reported by 73% and 84%, respectively.

The physician's assessment of GERD severity was associated with the patient's answers during the interview. During the observation period, the percentage of patients with moderate or severe GERD decreased substantially : at Visit 1, approximately 90% of patients suffered from moderate or severe GERD ; this decreased to 30% and 15% at Visits 2 and 3, respectively.

### 3.4. *GERD symptoms and their impact on the patient's daily activities, as recorded by the GIS*

The mean scores of the three dimensions covered by the GIS improved substantially during the course of the study (Fig. 2). This was also the case when the mean scores were baseline adjusted. Mean (± SD) scores for the impact of symptoms on daily activities domain were $2.2 \pm 0.7$, $1.4 \pm 0.5$ and $1.2 \pm 0.4$ at Visits 1, 2 and 3, respectively. Other acid-related GI symptoms domain mean scores were $2.4 \pm 0.8$, $1.5 \pm 0.5$ and $1.3 \pm 0.4$ at these time points. Upper GI symptoms domain mean scores were $2.5 \pm 0.8$, $1.6 \pm 0.5$ and $1.3 \pm 0.4$ at Visits 1, 2 and 3, respectively.

Table 4. — **Correlation (Spearman's correlation coefficients) of GERD Impact Scale (GIS) mean-scores with clinical judgments, endoscopy and usefulness of GIS (intent-to-treat population)**

| | Clinical judgment | | | | | | Endoscopy[a] | | GIS usefulness[b] | |
|---|---|---|---|---|---|---|---|---|---|---|
| GIS dimension | Visit 1 n = 1914 | P-value | Visit 2 n = 1911 | P-value | Visit 3 n = 1869 | P-value | Visit 1 n = 1907 | P-value | Visit 1 n = 1897 | P-value |
| Upper GI symptoms | 0.47 | < 0.0001 | 0.45 | < 0.0001 | 0.35 | < 0.0001 | 0.13 | < 0.0001 | -0.02 | 0.30 |
| Other acid related GI symptoms | 0.40 | < 0.0001 | 0.43 | < 0.0001 | 0.31 | < 0.0001 | 0.11 | < 0.0001 | -0.07 | 0.0046 |
| Impact of symptoms on life | 0.45 | < 0.0001 | 0.40 | < 0.0001 | 0.35 | < 0.0001 | 0.13 | < 0.0001 | -0.06 | 0.0052 |

[a]Before study entry.
[b]At study end (Visit 3).
GI, gastrointestinal.

3.5. *Physician's evaluation of the usefulness of the GIS and correlations with clinical judgment and endoscopy*

At study end, the majority of physicians reported that the GIS had facilitated treatment decisions and helped to evaluate the patient's response to treatment in 81% of cases. The Mean GIS mean-scores obtained at Visit 1 increased slightly with increasing degree of esophagitis on prior endoscopy. There was also a trend for higher GIS mean-scores and increasing severity of GERD, according to clinical judgment. Correlation analyses revealed that the GIS mean-scores significantly correlated with the physician's clinical judgment at all visits (Table 4). The correlation with endoscopy findings was also positive but less pronounced, and no correlation was found between the GIS mean-scores and the physician's judgment of the usefulness of the GIS, which shows that the GIS score appears to be useful, regardless of the severity of the patient's disease.

Further analysis showed that the patients who had a change in GERD treatment at visit 2 (20 patients increased PPI dose, 1037 patients decreased and 703 patients had no change) showed a better improvement in GIS mean-scores between visits 1 and 2, compared to patients without change in GERD treatment. At visit 3 (4 patients increased dose, 183 patients decreased and 1561 patients had no change), the improvement was similar in both groups. However, there was no real correlation in GIS scores between patients who did not change PPI treatment at visits 2 or 3, those who increased and those who decreased the dose.

## 4. Discussion

The primary objective of this non-interventional study was to gather epidemiological data in a population of GERD patients. This was achieved in approximately 2000 patients from 296 study centers in Belgium. The data gathered revealed that stress, caffeine consumption and smoking were present in a high proportion of patients. The patient's treatment history was recorded and symptom assessment by interview revealed that the majority of patients suffered from heartburn, acid regurgitation, epigastric pain and dysphagia. Our study shows only weak correlation between symptoms and last endoscopic grade of esophagitis. Symptoms improved markedly over one or two months of treatment. Our study reports these data for the first time in Belgium and confirms previous reports from other countries. The particular weakness of the correlation between GIS and endoscopic score in the present study may also be linked to the fact that the majority of the patients had a same grade of endoscopic score (grade A and B), meaning that the population was rather homogenous from this point of view.

The secondary objective of this study was to evaluate the added value of the GIS, a novel, validated, self-administered patient questionnaire for the initial and long-term management of GERD patients. Whether it is by clinician interview or patient self-assessment by questionnaire, symptom assessment must support the use of specific treatment and lead to improved patient outcomes if it is to be useful (26). The present study shows that the patients' assessment of their symptoms using the GIS correlated with the current method of symptom assessment, i.e. the physician's clinical judgment. This significant correlation highlights a supplementary element for the validation of the GIS and the fact that this correlation is low shows that GIS has an added value over clinical judgement and endoscopy, suggesting that it should be used in routine clinical practise.

During the course of the observation period the patients' symptoms improved, as assessed by both clinician-interview and GIS scores, and this appeared to parallel the changes in treatment between visits. As a patient-reported outcome, the GIS gives an "objective" measurement of symptoms and their impact, thus allowing a physician to compare scores between two visits and so helping the physician make the appropriate decision in patient management. This study did not investigate whether the GIS was instrumental in identifying the need for therapy change, but for the vast majority of patients (81%) the physicians did state that the GIS helped them to assess the patients' symptoms, identify the appropriate treatment and to evaluate the patient's response to treatment at visit 2 and 3. As such, the GIS proved to be a useful management tool.

Symptom assessment is the most important factor for both the diagnosis and identification of appropriate therapeutic strategies and also for monitoring the

patient's response to the choice of therapy (14,27). This is particularly the case because in the majority of patients with GERD, it is the impact of symptoms on daily life which is the main burden of the disease (28).

A recent systematic review of the literature concluded that there is a need for a new evaluative tool for the assessment of GERD symptoms and their response to therapy (29). The benefits of using a standardized questionnaire over physician-patient interview are that it facilitates a quantitative assessment of subject responses (26). Due to the subjective nature of symptoms it has been reported that patient self-reporting is more appropriate than assessment by a clinician (3) and although symptom diaries are generally considered to be the 'gold standard', they are not without their weaknesses and well-designed questionnaires with an appropriate recall period may be sufficient (27).

In addition to providing a way for the patient to easily describe the symptom burden that is often difficult to verbalise, the impact of these symptoms on the patient's life are also evaluated by the GIS. This enables the patient to provide information to their physician on how GERD may be disrupting their sleep, work, physical activity and social life. This may otherwise be overlooked if the physician fails to ask and the patient does not volunteer it.

In conclusion, this real life study has shown that the GIS might be a useful tool in aiding physicians identify the appropriate treatment and to evaluate the patient's response to GERD therapy.

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