Correlates of gastroenterology health-services utilization among patients with gastroesophageal reflux disease: a large database analysis

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Abstract

Background: Gastroesophageal reflux disease (GERD) is associated with high utilization of health care services. Diagnostic tests usually are not required to establish GERD diagnosis, but endoscopy is recommended for patients with alarm symptoms such as dysphagia and unintentional weight loss, and those whose symptoms are not relieved by proton pump inhibitors (PPIs) therapy. Evidence on the correlates of utilization of gastroenterology health services among GERD patients is limited. The study aim was to examine associations of patient and physician’s characteristics with high utilization of gastroenterology services.

Methods: In a cross-sectional study using the database of the second largest integrated care organization in Israel, data of all adult GERD patients (N = 75,219) in 2012–2015 were analyzed. High utilization of services was assessed using two dependent variables analyzed separately: undergoing two or more gastroscopies or having six or more visits to a gastroenterology consultant during the study-period.

Results: Overall, 11,261 (15.0%) patients had two or more gastroscopies and 23,703 (31.5%) had six or more visits to a gastroenterology consultant. The likelihood of high utilization of gastroscopy increased with age; in immigrants from the Former Soviet Union versus patients who were born in Israel; residents of Jerusalem, the south, the north and Haifa districts versus the center district; in patients with high PPI purchases, and in patients who belonged to clinics in which the physician-manger had no board certification. The correlates were similar for visits to a gastroenterology consultant.

Conclusions: Patient and physician’s characteristics were related to high utilization of gastroenterology services among GERD patients. The associations with age and country of birth might reflect more severe disease. The regional differences warrant further research and interventions at the district level. Training in gastroenterology of primary care physicians without a board certification is warranted.

Keywords: Gastroscopy, Gastroenterology health services, Gastroesophageal reflux disease, Primary care, Physicians’ board certification

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Background

Gastroesophageal reflux disease (GERD) is common worldwide [1]. Complications of GERD include erosive esophagitis (EE), Barrett’s esophagus (BE) [2] and esophageal adenocarcinoma [3]. Diagnostic tests usually are not required to establish GERD diagnosis [3], but endoscopy is recommended for patients with alarm symptoms such as dysphagia, unintentional weight loss and anemia, and those whose symptoms are not relieved by proton pump inhibitors (PPIs) therapy [3, 4].

GERD negatively affects quality of life and causes substantial economic burden to the health care system and reduced work productivity, especially in patients with severe and frequent symptoms [5–8]. The economic burden attributed to GERD is driven by consultations costs, diagnostic tests and medications [9–11]. Most studies on utilization of health care services among GERD patients assessed general services such as hospitalizations, emergency department visits and physician visits [5, 6, 8, 12], mostly according to intensity and severity of symptoms [5–8], with limited or no adjustment for patient’s characteristics (such as demographics and comorbidity) or physician’s characteristics [5, 6, 8]. Only few studies assessed utilization of gastroenterology health services among GERD patients [10, 13]. A study on repeated upper endoscopy in the Veterans Health Administration included 14,284 patients with reflux [13], indicated that 54.2 and 31.5% of the repeated endoscopy in this group were classified as probable and possible overuse, respectively, while only 14.3% likely represented appropriate use. Understanding the correlates of high utilization of gastroenterology health services among GERD patients may be the first step towards efficient, cost-saving and safe treatment. Accordingly, the aim of the current study was to examine associations of patient and physician’s characteristics with high utilization of gastroenterology services (outpatient visits to gastroenterology consultant and gastroscopy) among patients with GERD.

Table 1 Utilization of gastroscopy (two tests or more) according to patient and physician’s characteristics (Continued)

| Variable | ≥2 gastroscopies | 0–1 gastroscopies | P value |
|----------|------------------|-------------------|--------|
| | N = 11,261 | N = 63,958 | |
| Medical director | 4440 (39.6) | 26,189 (41.1) | |
| Other | 2493 (22.2) | 15,250 (23.9) | 0.001 |
| Primary care physician seniority | | | |
| Low (0–8 years) | 5830 (51.8) | 31,984 (50.0) | |
| High (9–43 years) | 5429 (48.2) | 31,970 (50.0) | |

Data presented are numbers and percentages in parenthesis
Df degrees of freedom, PPIs proton pump inhibitors, SES socioeconomic status
Missing data: Residential district (205 patients); SES (3733 patients)
Table 2  Unadjusted and adjusted associations of patient and physician’s characteristics with high utilization of gastroscopy

| Variable                          | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value* |
|----------------------------------|-------------------------|---------|----------------------|---------|
| Sex, females vs. males           | 1.06 (1.02–1.11)        | 0.003   | 0.99 (0.95–1.04)     | 0.7     |
| Age, years                       | Df = 5                  | < 0.001 | Df = 5              | < 0.001 |
| 19–34                            | Reference               |         | Reference            |         |
| 35–44                            | 1.53 (1.39–1.69)        | < 0.001 | 1.33 (1.20–1.47)     | < 0.001 |
| 45–54                            | 2.62 (2.40–2.86)        | < 0.001 | 2.03 (1.85–2.23)     | < 0.001 |
| 55–64                            | 3.32 (3.05–3.62)        | < 0.001 | 2.30 (2.09–2.52)     | < 0.001 |
| 65–74                            | 3.57 (3.27–3.90)        | < 0.001 | 2.22 (2.01–2.46)     | < 0.001 |
| 75+                              | 2.85 (2.58–3.14)        | < 0.001 | 1.55 (1.38–1.74)     | < 0.001 |
| Country of birth                 | Df = 4                  | < 0.001 | Df = 4              | < 0.001 |
| Israel                           | Reference               |         | Reference            |         |
| Former Soviet Union              | 1.92 (1.83–2.01)        | < 0.001 | 1.39 (1.32–1.46)     | < 0.001 |
| Asia/North Africa                | 1.30 (1.19–1.42)        | < 0.001 | 1.01 (0.92–1.12)     | 0.8     |
| Europe/Americas                  | 1.21 (1.12–1.31)        | < 0.001 | 0.92 (0.84–1.00)     | 0.05    |
| Other/ unknown                   | 1.34 (1.20–1.51)        | < 0.001 | 1.02 (0.90–1.16)     | 0.7     |
| Residential district             | Df = 5                  | < 0.001 | Df = 5              | < 0.001 |
| Center                           | Reference               |         | Reference            |         |
| Jerusalem                        | 2.00 (1.82–2.19)        | < 0.001 | 2.27 (2.02–2.54)     | < 0.001 |
| North                            | 1.51 (1.40–1.64)        | < 0.001 | 1.49 (1.36–1.63)     | < 0.001 |
| Haifa                            | 1.51 (1.40–1.62)        | < 0.001 | 1.44 (1.32–1.57)     | < 0.001 |
| Tel Aviv                         | 0.74 (0.69–0.80)        | < 0.001 | 0.73 (0.68–0.78)     | < 0.001 |
| South                            | 2.38 (2.25–2.52)        | < 0.001 | 2.43 (2.26–2.61)     | < 0.001 |
| SES of place of residence        |                         |         |                      |         |
| Middle/High (5–10)               | Reference               |         | Reference            |         |
| Low (1–4)                        | 1.28 (1.21–1.35)        | < 0.001 | 1.04 (0.97–1.12)     | 0.25    |
| Background diseases              |                         |         |                      |         |
| Heart disease (reference = no)   | 1.51 (1.44–1.59)        | < 0.001 | 1.12 (1.05–1.18)     | < 0.001 |
| Hypertension (reference = no)    | 1.71 (1.64–1.78)        | < 0.001 | 1.01 (0.96–1.06)     | 0.7     |
| Diabetes (reference = no)        | 1.62 (1.54–1.71)        | < 0.001 | 1.14 (1.07–1.21)     | < 0.001 |
| Number of PPIs purchases         |                         |         |                      |         |
| Low (0–8)                        | Reference               |         | Reference            |         |
| High (9+)                        | 2.83 (2.71–2.95)        | < 0.001 | 2.43 (2.31–2.54)     | < 0.001 |
| Primary care physician board     |                         |         |                      |         |
| certification                     | Df = 3                  | < 0.001 | Df = 3              | < 0.001 |
| Family medicine                  | Reference               |         | Reference            |         |
| None                             | 1.20 (1.14–1.26)        | < 0.001 | 0.94 (0.88–1.00)     | 0.03    |
| Internal medicine                | 1.09 (1.03–1.15)        | 0.003   | 1.02 (0.96–1.08)     | 0.6     |
| Other                            | 1.22 (1.06–1.40)        | 0.005   | 1.14 (0.98–1.32)     | 0.09    |
| Board certification of the clinic|                         |         |                      |         |
| physician-manager                | Df = 4                  | < 0.001 | Df = 4              | < 0.001 |
| Family medicine                  | Reference               |         | Reference            |         |
| None                             | 1.77 (1.63–1.91)        | < 0.001 | 1.27 (1.16–1.39)     | < 0.001 |
| Internal medicine                | 0.95 (0.88–1.03)        | 0.2     | 0.95 (0.87–1.03)     | 0.2     |
| Medical director                 | 1.01 (0.95–1.07)        | 0.7     | 0.90 (0.83–0.97)     | 0.004   |
| Other                            | 0.91 (0.85–0.98)        | 0.009   | 1.05 (0.96–1.14)     | 0.3     |
Table 2 Unadjusted and adjusted associations of patient and physician’s characteristics with high utilization of gastroscopy (Continued)

| Variable                        | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value* |
|--------------------------------|------------------------|---------|----------------------|---------|
| Primary care physician seniority |                        |         |                      |         |
| Low (0–8 years)                 | Reference              |         | Reference            |         |
| High (9–43 years)               | 0.93 (0.90–0.97)       | 0.001   | 0.99 (0.94–1.04)     | 0.7     |

CI confidence interval, Df degrees of freedom, OR odds ratio, PPIs proton pump inhibitors, SES socioeconomic status

Methods

Study design and population

A cross-sectional study was conducted using the computerized databases of Maccabi Healthcare Services (MHS), the second largest integrated care organization in Israel. MHS currently has over 2 million members, comprising about 25% of Israel’s population. Data of all patients aged more than 18 years with GERD between January 1, 2012 and December 31, 2015, were analyzed. Patients with GERD were identified using physician’s diagnosis code of the International Classification of Diseases, 9th edition (ICD-9) for GERD (530.81) or MHS corresponding codes (Y14968 code for esophageal reflux, gastroesophageal reflux disease, GERD, and reflux esophageal).

The dependent variables

High utilization of gastroenterology services was defined as: 1) undergoing two or more gastroscopies; and 2) six or more (upper tertile) visits to gastroenterology consultant, during the four-year study period. The diagnosis of uncomplicated GERD usually does not require gastroscopy [4]. In the study sample, 42.6% of GERD patients underwent at least one diagnostic gastroscopy during the study period: 27.7% underwent one gastroscopy and 15.0% underwent two or more gastroscopies. Accordingly, we considered that undergoing two or more gastroscopies during the study period as high utilization of gastroscopy.

The independent variables

The selection of the independent variables was based on our hypothesis that characteristics of both patients (e.g., age, comorbidity), and physicians (e.g., board certification), are related to utilization of these services. This was stimulated by previous studies on associations of demographic and clinical factors with health care utilization [6, 12, 14, 15].

Patient’s characteristics

Data were obtained on age (in years, categorized as 19–34, 35–44, 45–54, 55–64, 65–74, 75+), sex, residential district and country of birth (grouped as Israel, Former Soviet Union [FSU], Europe/Americas, Asia/North Africa and other/unknown). Socioeconomic status (SES) of the town of residence defined by the Central Bureau of Statistic [16] was used as a proxy of SES. Patients who lived in towns with SES ranks of 1–4 and 5–10 were classified as living in low and middle/high SES communities, respectively. MHS registries were used to determine the presence of diabetes mellitus [17], hypertension [18] and cardiovascular disease [19]. Information was obtained on purchasing PPIs; patients were classified as high users if they had above the median number (eight) of PPIs purchases in the study sample.

Characteristics of primary care physicians

A primary care clinic can include several physicians who treat patients, and a manger (mostly one of the primary care physicians in the clinic). We extracted information on both the treating primary care physician and the physician-manager of the clinic. Data were obtained regarding the physician’s board certification (none, family medicine, internal medicine, medical director and other) and physician’s seniority (categorized as having above the median number of seniority years versus having the median or less of seniority years).

Statistical analysis

Differences between patients with high utilization of gastroscopy (undergoing two or more tests) and those who one or no gastroscopy, in demographic and clinical characteristics were assessed using the chi-square test. Multivariable analysis was performed using logistic regression models. Similar analyses were performed for the dependent variable high utilization of visits to a gastroenterology consultant (six or more). Unadjusted and adjusted odds ratios (and 95% confidence intervals) for each independent variable were obtained from logistic regression models. Statistical significance was set at P < 0.05. Data were analyzed using SPSS version 25 (IBM, New York, United States).

Results

We identified 75,219 patients (57.1% females) with GERD with a mean age of 53.1 years (standard deviation 15.9). Additional demographic characteristics are presented in Additional file 1: Table S1. Overall, 11,261 (15.0%) underwent two or more gastroscopies and 23,703 (31.5%) had six or more visits to a specialist in gastroenterology.
Factors associated with high utilization of gastroscopy (two or more tests)
The percentage of patients aged 55 years or older was higher in those who had two gastroscopies or more than in patients who had 0–1 gastroscopies. The group of high utilization of gastroscopy included also higher percentages of patients who were born in the FSU, residents of Jerusalem and the south districts; and patients with heart disease, diabetes mellitus, hypertension and high PPIs purchases compared to the group who performed 0–1 gastroscopies. The percentage of physician-managers who did not have a board certification was higher in the high utilization group (Table 1).

A multivariable analysis showed that compared to patients aged 19–34 years, the likelihood of high utilization of gastroscopy significantly increased with age. Patients who were born in FSU had 1.39-fold increased likelihood for high utilization of gastroscopy than those who were born in Israel. Compared to residents of the center district, residents of Jerusalem and the south districts had more than 2-fold higher likelihood for gastroscopy high utilization and patients who lived in Haifa and north districts had ~1.50-fold increased likelihood. Patients with high number of PPIs purchases had 2.43-fold higher likelihood for gastroscopy high utilization compared to patients who had less PPIs purchases. Having a clinic physician-manager without a board certification was associated with 1.27-fold higher likelihood of gastroscopy utilization compared to having a physician-manager with board certification in family medicine (Table 2).

Factors associated with having six or more visits to a gastroenterology consultant
A higher percentage of females and older patients was found among those with high number (six or more) of visits to a gastroenterology consultant than in patients who had less visits. The former group included also higher percentages of patients who were born in Asia/North Africa and who had a high number of PPIs purchases (Table 3).
| Variable | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value* |
|----------|------------------------|---------|----------------------|---------|
| Sex, females vs. males | 1.32 (1.28–1.36) | < 0.001 | 1.43 (1.38–1.48) | < 0.001 |
| Age, years | DF = 5 | | | |
| 19–34 | Reference | | | |
| 35–44 | 1.04 (0.98–1.10) | 0.2 | 1.00 (0.94–1.06) | 0.9 |
| 45–54 | 1.14 (1.07–1.21) | < 0.001 | 0.96 (0.90–1.02) | 0.2 |
| 55–64 | 1.61 (1.52–1.70) | < 0.001 | 1.12 (1.05–1.19) | 0.001 |
| 65–74 | 2.42 (2.29–2.56) | < 0.001 | 1.39 (1.30–1.49) | < 0.001 |
| 75+ | 3.88 (3.63–4.14) | < 0.001 | 1.81 (1.66–1.96) | < 0.001 |
| Country of birth | DF = 4 | | | |
| Israel | Reference | | | |
| Former Soviet Union | 1.04 (0.99–1.08) | 0.054 | 0.77 (0.74–0.81) | < 0.001 |
| Asia/North Africa | 1.79 (1.68–1.91) | < 0.001 | 1.21 (1.13–1.30) | < 0.001 |
| Europe/Americas | 1.45 (1.36–1.53) | < 0.001 | 0.92 (0.86–0.98) | 0.01 |
| Other/unknown | 1.43 (1.31–1.56) | < 0.001 | 0.99 (0.90–1.09) | 0.9 |
| Residential district | DF = 5 | | | |
| Center | Reference | | | |
| Jerusalem | 2.23 (2.07–2.41) | < 0.001 | 2.10 (1.92–2.30) | < 0.001 |
| North | 0.95 (0.89–1.01) | 0.09 | 0.81 (0.75–0.88) | < 0.001 |
| Haifa | 0.84 (0.79–0.89) | < 0.001 | 0.80 (0.74–0.86) | < 0.001 |
| Tel Aviv | 1.05 (1.01–1.09) | 0.009 | 0.99 (0.94–1.05) | 0.8 |
| South | 1.31 (1.24–1.37) | < 0.001 | 1.24 (1.17–1.31) | < 0.001 |
| SES of place of residence | | | | |
| Middle/High (5–10) | Reference | | | |
| Low (1–4) | 1.33 (1.27–1.38) | < 0.001 | 0.85 (0.80–0.89) | < 0.001 |
| Background diseases | | | | |
| Heart disease (reference = no) | 3.10 (2.98–3.23) | < 0.001 | 2.28 (2.18–2.39) | < 0.001 |
| Hypertension (reference = no) | 1.99 (1.93–2.06) | < 0.001 | 1.24 (1.19–1.29) | < 0.001 |
| Diabetes (reference = no) | 2.00 (1.92–2.09) | < 0.001 | 1.28 (1.22–1.35) | < 0.001 |
| Number of PPIs purchases | | | | |
| Low (0–8) | Reference | | | |
| High (9+) | 1.94 (1.88–2.00) | < 0.001 | 1.47 (1.42–1.53) | < 0.001 |
| Primary care physician board certification | DF = 3 | < 0.001 | DF = 3 | < 0.001 |
| Family medicine | Reference | | | |
| None | 0.99 (0.95–1.03) | 0.5 | 0.95 (0.90–0.99) | 0.01 |
| Internal medicine | 0.97 (0.93–1.01) | 0.2 | 0.99 (0.94–1.04) | 0.7 |
| Other | 0.97 (0.87–1.09) | 0.6 | 0.99 (0.88–1.12) | 0.9 |
| Board certification of the clinic physician-manager | DF = 4 | < 0.001 | DF = 4 | < 0.001 |
| Family medicine | Reference | | | |
| None | 1.33 (1.24–1.41) | < 0.001 | 1.47 (1.37–1.59) | < 0.001 |
| Internal medicine | 0.90 (0.85–0.96) | 0.001 | 0.94 (0.88–1.00) | 0.05 |
| Medical Director | 0.94 (0.90–0.99) | 0.01 | 0.99 (0.94–1.05) | 0.8 |
| Other | 0.90 (0.86–0.95) | < 0.001 | 0.96 (0.90–1.02) | 0.2 |
The strength of these associations was mostly attenuated in multivariable model (Table 4).

**Discussion**

We found that the utilization of gastroscopy and/or visits to a gastroenterology consultant by GERD patients increased with age. There was a higher utilization by patients in the peripheral districts than in the center of Israel; by patients born in the FSU than in those born in Israel; by patients with heart disease, diabetes and hypertension; and by patients of primary care clinics headed by non-board certified physicians.

The finding that utilization increased with patients’ age is probably explained by physicians’ concerns of GERD complications such as EE, BE, and esophageal cancer that increase with age [20–23]. However, this is an unlikely explanation for the observed higher utilization of gastroenterology services by patients from the periphery compared with those from the center of Israel. Regional differences in the severity and complications of GERD are not expected. Therefore, these differences probably reflect variation in referral policy across districts and warrant further exploration. A study from the United States on repeated upper endoscopy in general, showed similar regional differences, even after controlling for diagnostic codes of gastroesophageal illnesses [14].

Patients born in the FSU and in Asia and North Africa utilized gastroscopy more than patients who were born in Israel. This might be due to differences in the severity of GERD and/or its complications. Indeed, it has been shown that Israelis born in FSU and Israelis who emigrated from Asian countries (mostly west Asia) display higher risk for gastroesophageal adenocarcinoma than persons born in Israel [24]. Ethnic differences in esophageal pathology in patients undergoing endoscopy were also reported in the United States [25–28].

The association between the number of PPIs purchases and utilization of services is probably due to the intensity of GERD symptoms [8]. It is consistent with the observation by Mody et al. [29] that twice-daily PPIs use was associated with higher health services utilization and costs than once-daily use. The association of having heart disease, diabetes, hypertension and high number with visits to a gastroenterology consultant might be attributed to medical surveillance. The association with heart disease might be related to GERD symptoms involving chest pain in some patients. PPIs failure is common among diabetic patients [15] and this might explain the positive association of diabetes and utilization of services.

While health care utilization patterns and resulting costs are affected by the severity of GERD symptoms [5] and comorbidity, we also found that physician’s education and training have a role in the management of the disease. In the Israeli system, referrals such as gastroscopy require approval of the physician-manager. Therefore, additional education or training of physician-managers who do not have a formal board certification in areas of family medicine/gastroenterology might be warranted to improve care and reduce cost related to GERD management.

The main strength of our study is its use of multi-year data of a large sample of adult GERD patients, who were identified by their diagnostic code. The code of GERD was partially validated by the purchases of PPIs by most patients at least once during the study period. However, the use of data from medical records of MHS database over a four-year study period has limitations. Differences might exist between physicians in documenting medical information. Information on the indications of gastroscopy and the results of the tests are lacking and we cannot determine whether the referrals were clinically appropriate or represented overuse of services. Therefore, our findings refer to correlates with high utilization of gastroenterology services rather than overuse.

**Conclusions**

Both patient and physician’s characteristics play a role in high utilization of gastroenterology health services among GERD patients. The relationships with age and country of birth might reflect more severe disease in older people and some ethnic groups. The regional differences warrant further research and interventions at the district level. Training in gastroenterology of primary care physicians without a board certification is warranted.

**Additional file**

**Additional file 1:** Table S1. Characteristics of patients with GERD (N = 75,219), 2012–2015. (DOCX 15 kb)

**Abbreviations**

BE: Barrett’s esophagus; FSU: Former Soviet Union; GERD: Gastroesophageal reflux disease; ICD-9: The International Classification of Diseases, 9th edition;
MHS: Maccabi healthcare services; PPIs: Proton pump inhibitors; SES: Socioeconomic status

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Authors’ contributions
KM, GH, ABT, TZB designed the study and obtained funding. KM, RK, GH, ABT contributed in data collection. RK and SG were responsible for data management. KM, SG, WN participated in statistical analysis. WN, KM wrote the first draft of the manuscript. All authors contributed to interpretation of the data and approved the final manuscript.

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Availability of data and materials
Individual level data from this study cannot be made publically available due to legal and ethical restrictions.

Ethics approval and consent to participate
The Helsinki committee of Bayit Bavel Medical Center of MHS (number 47/2014) and the ethics committee of Tel Aviv University approved the study protocol. Since this was a retrospective study in which we used coded (anonymized) administrative data from medical records, the Helsinki committee granted exemption from informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References
1. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63:87–101.
2. Ronkainen J, Talley NJ, Johansson SE, Lind T, Vieth M, Agreus L, Aro P. Erosive esophagitis is a risk factor for Barrett’s esophagus: a community-based follow-up study. Am J Gastroenterol. 2011;106:1946–52.
3. Hunt R, Armstrong D, Kellner P, Atifene M, Bane A, Bhatia S, Chen MH, Choi MG, Melo AC, Fock KM, et al. World gastroenterology organisation global guidelines: GERD global perspective on gastroesophageal reflux disease. J Clin Gastroenterol. 2013;47:67–78.
4. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol. 2013;108:308–28 quiz 329.
5. Toghanian S, Wahlqvist P, Johnson DA, Bolge SC, Lijjas B. The burden of disrupting gastroesophageal reflux disease: a database study in US and European cohorts. Clin Drug Investig. 2010;30:167–78.
6. Wahlqvist P, Karlsson M, Johnson D, Carlsson I, Bolge SC, Wallander MA. Relationship between symptom load of gastroesophageal reflux disease and health-related quality of life, work productivity, resource utilization and concomitant diseases: survey of a US cohort. Alliment Pharmacol Ther. 2008;27:960–70.
7. des Varannes SB, Lofman HG, Karlsson M, Wahlqvist P, Ruth M, Furstenau ML, Despiegel N, Stalhammar NO. Cost and burden of gastroesophageal reflux disease among patients with persistent symptoms despite proton pump inhibitor therapy: an observational study in France. BMC Gastroenterol. 2013;13:39. https://doi.org/10.1186/1471-230X-13-39.
8. Toghanian S, Johnson DA, Stalhammar NO, Zerbib F. Burden of gastro-esophageal reflux disease in patients with persistent and intense symptoms despite proton pump inhibitor therapy: a post hoc analysis of the 2007 national health and wellness survey. Clin Drug Invest. 2011;31:703–15.
9. Brook RA, Wahlqvist P, Kleinman NL, Wallander MA, Campbell SM, Smeeding JE. Cost of gastro-oesophageal reflux disease to the employer: a perspective from the United States. Aliment Pharmacol Ther. 2007;26:889–98.
10. Kim KM, Cho YK, Bae SJ, Kim DS, Shim KN, Kim JH, Jung SW, Kim N. Prevalence of gastroesophageal reflux disease in Korea and associated health-care utilization: a national population-based study. J Gastroenterol Hepatol. 2012;27:741–5.
11. Rubenstein JH, Chen JW. Epidemiology of gastroesophageal reflux disease. Gastroenterol Clin North Am. 2014;43:1.
12. Gosselin A, Luo R, Lohoue H, Toy E, Lewis B, Crawley J, Dub MS. The impact of proton pump inhibitor compliance on health-care resource utilization and costs in patients with gastroesophageal reflux disease. Value Health. 2009;12:34–9.
13. Rubenstein JH, Pohl H, Adams MA, Kerr E, Hollerman R, Vigan S, Dominitz JA, Inadomi JM, Provenzale D, Francis J, Saini SD. Overuse of repeat upper endoscopy in the veterans health administration: a retrospective analysis. Am J Gastroenterol. 2011;106:1678–85.
14. Gawron AJ, Cole G, Hu N, Thompson WK, Fang J, Sameor M. Regional variability of repeat esophagogastroduodenoscopy use in the national veteran population. Dig Dis Sci. 2017;62:3303–10.
15. Hershovici T, Jha LK, Gadam R, Cui HY, Gerson L, Thomson S, Fass R. The relationship between type 2 diabetes mellitus and failure to proton pump inhibitor treatment in gastroesophageal reflux disease. J Clin Gastroenterol. 2012;46:62–8.
16. Israel Central Bureau of Statistics. Characterization and classification of geographic units by the socio-economic level of the population 2008. 2013. 17. Heymann AD, Chodick G, Shalev V, Kokia E. The implementation of managed care for diabetes using medical informatics in a large preferred provider organization. Diabetes Res Clin Pract. 2006;74:210–4.
18. Weitzman D, Chodick G, Shalev V, Grossman C, Grossman E. Prevalence and factors associated with resistant hypertension in a large health maintenance organization in Israel. Hypertension. 2014;64:501–7.
19. Shalev V, Chodick G, Gorel I, Silber H, Kokia E, Heymann AD. The use of an automated patient registry to manage and monitor cardiovascular conditions and related outcomes in a large health organization. Int J Cardiol. 2011;152:345–9.
20. Johnson DA, Fennerty MB. Heartburn severity underestimates erosive esophagitis severity in elderly patients with gastroesophageal reflux disease. Gastroenterology. 2004;126:660–4.
21. Richter JE. Gastroesophageal reflux disease in the older patient: presentation, treatment, and complications. Am J Gastroenterol. 2000;95:368–73.
22. Spechler SJ, Barrett esophagus and risk of esophageal cancer: a clinical review. JAMA. 2013;310:627–36.
23. Pohl H, Wrobel K, Bojarski C, Voderholzer W, Sonnenberg A, Rosch T, Baumgart DC. Risk factors in the development of esophageal adenocarcinoma. Am J Gastroenterol. 2013;108:200–7.
24. Levi Z, Kark JD, Shammis A, Derennai E, Tsar D, Keinan-Boker L, Liphshitz I, Niv Y, Furman M, Afek A. Body mass index and socioeconomic status measured in adolescence, country of origin, and the incidence of gastroesophageal adenocarcinoma in a cohort of 1 million men. Cancer. 2013;119:4086–93.
25. Sharma P, Wani S, Romero Y, Johnson D, Hamilton F. Racial and geographic issues in gastroesophageal reflux disease. Am J Gastroenterol. 2008;103:2669–80.
26. Want SB, Rastogi A, Barisal A, Hall S, Mathur S, Sharma P. Symptom profiles and endoscopic findings in African-American patients with gastroesophageal reflux disease (GERD). Gastroendoscopy. 2007;32:161.
27. Nguyen TH, Thrift AP, Ramsey D, Green L, Shaib YH, Graham DY, El-Serag HB. Risk factors for Barrett’s esophagus compared between African Americans and non-Hispanic whites. Am J Gastroenterol. 2014;109:1780–8.
28. Spechler SJ, Jain SK, Tendler DA, Parker RA. Racial differences in the frequency of symptoms and complications of gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2002;16:795–800.
29. Mody R, Eisenberg D, Hou L, Kamat S, Singer J, Gerson LB. Comparison of health care resource utilization and costs among patients with GERD on once-daily or twice-daily proton pump inhibitor therapy. Clinicoecon Outcomes Res. 2013;5:161–9.

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