



ORIGINAL ARTICLE

Worldwide prevalence and burden of gastroparesis-like symptoms as defined by the United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) consensus on gastroparesis

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Abstract

Background/Objectives: The global epidemiology of gastroparesis is unknown. The European UEG and European Society for Neurogastroenterology and motility consensus defines Gastroparesis as a condition characterized by delayed gastric emptying in the absence of mechanical obstruction, with a symptom pattern of nausea and/or vomiting and overlapping postprandial distress syndrome (PDS). Real-world evidence of this gastroparesis-like symptom pattern is a crucial step in understanding the epidemiology of gastroparesis.

Methods: In the Rome Foundation Global Epidemiology Study, 54,127 respondents from 26 countries completed the Rome IV Diagnostic Questionnaire and variables associated with disorders of gut-brain interaction via Internet. We selected subjects with gastroparesis-like symptoms (GPLS) (nausea and/or vomiting ≥ 1 day/week and simultaneous PDS). Patients reporting organic gastrointestinal disease, or fulfilling

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criteria for self-induced vomiting, cyclic vomiting or cannabinoid hyperemesis syndrome were excluded. We determined prevalence, associated comorbidities, quality of life (QoL) (PROMIS Global-10), symptoms of anxiety and depression (PHQ-4), somatic symptoms (PHQ-12), and healthcare utilization.

Results: The global prevalence of GPLS was 0.9% overall and 1.3% among diabetic individuals. Subjects with GPLS showed frequent overlapping of epigastric pain syndrome and irritable bowel syndrome. Subjects with GPLS had significantly lower body mass index, QoL, more non-gastrointestinal somatic complaints, symptoms of anxiety and depression, higher medication usage and doctor visits in the overall and diabetic population, compared to subjects without these symptoms.

Conclusions: GPLS are common worldwide and more common in diabetic patients. The symptom complex is associated with multiple aspects of illness and an increased healthcare consumption.

KEYWORDS

gastroparesis, gastroparesis-like symptoms, prevalence

INTRODUCTION

Gastroparesis is a clinical syndrome characterized by delayed gastric emptying (GE) in the absence of mechanical obstruction.¹ Several symptoms have been reported in gastroparesis patients, including nausea and vomiting, post-prandial fullness, early satiety and bloating. The main causes of gastroparesis are idiopathic, diabetic and postsurgical.² This syndrome has been associated with decreased quality of life (QoL) and increased mortality.^{3,4} The epidemiology of gastroparesis is largely unknown and has only been addressed to some extent in studies from the US and the UK. The prevalence of diagnosed gastroparesis was estimated at 13.8 per 100,000 persons in the UK.⁵ Varied results have been reported in the US since the different ways prevalence data measured. A recent study, using a health insurance database, reported 267.7 per 100,000 adults.⁶ However, an estimate based on regression models for GE rates suggests that gastroparesis may affect up to 1.8% of the population.⁷

A diagnosis of gastroparesis requires identification of patients with the appropriate symptom pattern, followed by findings of delayed GE in the absence of mechanical obstruction.⁸ Although the correlation between symptoms and delayed GE is controversial, most large-scale studies have shown that patients with delayed GE for solids are more likely to report postprandial fullness, nausea and vomiting.⁹ Based on these observations, the European consensus on Gastroparesis defined gastroparesis as a condition characterized by delayed GE in the absence of mechanical obstruction, with a symptom pattern of nausea and vomiting, and overlapping postprandial distress syndrome (PDS).¹⁰ The combination of nausea, vomiting, early satiety, postprandial fullness, the two latter symptoms both part of PDS according to the Rome IV criteria,¹¹ have been described as “gastroparesis-like symptoms (GPLS)” in several publications.^{12,13}

Therefore, we used the database of Rome Foundation Global Epidemiology Study (RFGES) to estimate the global prevalence of

Key summary

What is already known about this subject?

- The European consensus on gastroparesis defines gastroparesis as a condition characterized by delayed gastric emptying in the absence of mechanical obstruction, with a symptom pattern of predominant nausea and vomiting with overlapping postprandial distress syndrome.
- The global epidemiology of gastroparesis is largely unknown and has only been addressed to some extent in studies from the United States and the United Kingdom.
- A recent study shows the prevalence of gastroparesis is 267.7 per 100,000 adults in the US. However, a population-based estimate suggests that up to 1.8% of the population is affected.

What are the new findings in your manuscript?

- The overall global prevalence of gastroparesis-like symptoms (GPLS) was 0.9% and 1.3% among diabetic individuals.
- Patients with GPLS showed high proportion of overlap with disorders of gut-brain interaction.
- Effects of GPLS included impaired quality of life, disruptive mood and anxiety states and burden of healthcare utilization.

GPLS, as well as the association with other GI symptoms, in diabetic and non-diabetic subjects in the general population. We also described its association with QoL, somatization, anxiety and depression, and aspects of healthcare utilization in the subjects with GPLS.

METHODS

Data sources

We analyzed data derived from RFGES. Results of this survey, reporting the prevalence and burden of Disorders of Gut-Brain Interaction (DGBI), were first published in 2021.¹⁴ The methodology of the RFGES is briefly summarized here. This multi-national epidemiological study was completed by 73,076 respondents in 33 countries. The survey contained the complete Adult Rome IV Diagnostic Questionnaire and an 80-item supplemental questionnaire on socio-demographic characteristics, medical and health history, comorbid symptoms and conditions, gastrointestinal infections, health care utilization, medications, childhood and current living conditions, psychosocial variables, diet, QoL, culture and religion. The item content of the entire global study questionnaire is showed in the supplementary material of the original article.¹⁴ The questionnaire was administered via an online internet survey or household door-to-door survey and completed by at least 2000 individuals with equal sex ratio and similar age distribution (40% for 18–39 years, 40% for 40–64 years, and 20% for above 65 years) in each country. Because of substantial differences in data collection methodology between the Internet and household methods in this study, we only analyzed the Internet survey data, which included 54,127 respondents in 26 countries (Argentina, Australia, Belgium, Brazil, Canada, China, Colombia, Egypt, France, Germany, Holland, Israel, Italy, Japan, Mexico, Poland, Romania, Russia, Singapore, South Africa, South Korea, Spain, Sweden, Turkey, United Kingdom and United States). All survey participants signed electronic informed consent form. Ethical review was completed in each country and the study was approved or exempted from ethics board oversight due to anonymization during the survey.

Factors used in the analyses

Case definition of subjects with GPLS

Using the Rome IV Diagnostic Questionnaire, we included individuals with symptoms of nausea and/or vomiting (at least 1 day per week) and fulfilling PDS criteria (presence of postprandial fullness and/or early satiety, at least 2–3 days per week) for more than 6 months. Patients who self-reported a relevant organic gastrointestinal disease, such as celiac disease, inflammatory bowel disease, cancer, peptic ulcer, or fulfilled criteria for self-induced vomiting, cyclic vomiting syndrome or cannabinoid-hyperemesis syndrome were excluded.

Demographics and comorbidities

Study variables included participant demographics: age, sex, body mass index (BMI), and living settings including urban and rural communities (communities with <2500 inhabitants). We extracted

comorbidities, including diabetes and DGBI, including functional heartburn, functional chest pain, reflux hypersensitivity, functional dysphagia, epigastric pain syndrome (EPS), chronic nausea and vomiting syndrome (CNVS), rumination syndrome, and irritable bowel syndrome (IBS).

Quality of life and mood and anxiety states

The survey comprised different questionnaires. Patient-Reported Outcomes Measurement Information System (PROMIS Global-10), which includes physical and mental health component scores, was used to evaluate QoL. The Patient Health Questionnaire-4 (PHQ-4), which includes Patient Health Questionnaire-2 (PHQ-2) for depression and Generalized Anxiety Disorder-2 (GAD-2) for anxiety, was used for anxiety and depression status.¹⁵ Scale scores ≥ 3 of the PHQ-2 and the GAD-2 were used to define probable cases of depression or anxiety, respectively.¹⁵ The Patient Health Questionnaire-12 (PHQ-12) score was used as a measure for non-gastrointestinal symptom severity (or somatization).¹⁶

Health care utilization

Health care utilization was quantified by assessing general health care utilization, including general practitioner or specialist visits, number of surgeries, medication usage and access to healthcare.

Statistical analysis

The prevalence of GPLS was calculated as a percentage of all participants and the subgroups. We calculated country-specific prevalence rates for GPLS and prevalence rates for GPLS in both diabetic and non-diabetic subjects. Global pooled prevalence rates were calculated using Yang's meta-prevalence method¹⁷ which combines separate population survey prevalence estimates into an overall meta-prevalence estimate. Prevalence was reported as a percentage with 95% Confidence Intervals. Age- and sex-specific overall prevalence of GPLS were described. Participants who had GPLS were divided into two groups depending on whether they had diabetes or not. Subgroups of patients with GPLS were characterized by appropriate descriptive statistics (means, standard deviations, and percentages). Descriptive analyses of overlap in selected DGBI and GPLS, QoL (PROMS Global-10), anxiety and depression state (PHQ-4), somatization (PHQ-12), and health consumption, were conducted. All data are reported as mean or percent followed by 95% confidence intervals (CI). The statistical significance level used was 0.05. To compare two groups, categorical variables were compared using Pearson's chi-squared tests if the expected counts were greater than or equal to 5 in at least 80% of the cell otherwise Fishers exact test was performed and continuous variables were compared using 2 sample T-tests.

RESULTS

Prevalence of GPLS

Among 54,127 respondents (49.1% female, 7.2% with diabetes, mean age 44.3 years) reflecting the global population, 467 participants (0.9%) reported GPLS with a mean age of 39.0 ± 13.6 years, including 308 (66%) women and 159 (34%) men. Of these, 50 subjects had diabetes. Baseline characteristics of subjects with and without GPLS are shown in Table 1. The prevalence rates of GPLS among the surveyed countries ranged from 0.2% (0.0%–0.4%) in Japan to 1.7% (1.1%–2.2%) in the United States (Figure 1). The overall prevalence of GPLS was 0.9% (0.8%–0.9%), with a significantly higher prevalence among women (1.2% [1.0%–1.3%]) compared to men (0.6% [0.5%–0.7%]) (OR = 2.02, 95% CI 1.67–2.45, $p < 0.01$). When considering prevalence in different age groups, GPLS were present in 1.1% (1.0%–1.3%) in the range of 18–39 years, 0.8% (0.7%–0.9%) in the range of 40–64 years and 0.3% (0.2%–0.4%) in 65 years or older. When looking into the urban-rural disparity, the odds of having GPLS was 1.43 higher in rural communities than among those in urban areas, but this difference was not statistically significant (95% CI 0.53–3.88, $p = 0.48$).

In non-diabetic individuals, the prevalence of GPLS was 0.8% (0.8%–0.9%). The prevalence among females was also higher than males in non-diabetic individuals, 1.1% (1.0%–1.2%) and 0.6% (0.5%–0.6%), respectively (OR = 1.99, 95% CI 1.62–2.44, $p < 0.01$). The highest prevalence was seen in the United States (1.4%) and the lowest prevalence was found in Japan (0.3%) and Singapore (0.3%) (Figure 2).

Among individuals with diabetes mellitus the overall prevalence was 1.3% (0.9%–1.6%), ranging broadly from 0.0% to 4.5%. The highest prevalence was demonstrated in China (4.5%). None of the diabetic patients in Japan ($N = 111$), Spain ($N = 183$) or Romania ($N = 108$) reported GPLS (Figure 3). The prevalence in diabetic women was almost threefold compared to diabetic men, 2.2% (1.4%–2.9%) versus 0.8% (0.4%–1.1%), respectively (OR = 2.82, 95% CI 1.59–5.02, $p < 0.01$).

GPLS and other DGBI

We studied the overlap of GPLS with other DGBI. Patients with GPLS showed 47.8% overlap with EPS and 44.1% overlap with IBS, including IBS with constipation (14.8%), IBS with diarrhea (10.1%), IBS mixed type (18.0%) and unspecified IBS (1.3%). Among subjects with GPLS, the prevalence of CNVS, functional heartburn, functional chest pain, reflux hypersensitivity, functional dysphagia, and rumination syndrome were 38.5%, 16.9%, 4.9%, 17.1%, 40.9% and 11.8%, respectively. All of these were significantly more common in patients with versus without GPLS (all $p < 0.01$). Comparing diabetics with non-diabetics, IBS was more common in non-diabetic subjects ($p < 0.01$), but with no significant difference among the other DGBI. The overlap between DGBI and GPLS in diabetic, non-diabetic subjects or overall is shown in Table 2.

Burden of GPLS

A summary of results related to the burden of GPLS is shown in Table 3. Mean BMI in the subjects with GPLS was significantly lower than in subjects without symptoms. Compared to control subjects, patients with GPLS reported statistically significant lower scores in physical health QoL (mean PROMIS Global-10: Physical Health component score) and in mental health QoL (mean PROMIS Global-10: Mental Health component score). The average score for subjects with GPLS on PHQ-12 measuring the severity of non-gastrointestinal bodily symptoms (or somatization) was 11.3 ± 4.3 , compared to 5.4 ± 3.8 in subjects without GPLS ($p < 0.01$). For anxiety and depression, patients with GPLS also had significantly higher mean PHQ-4 scores. Up to 55.2% of subjects with GPLS had a score of ≥ 3 on the GAD-2 and 54.6% had a score of ≥ 3 on the PHQ-2, suggestive of anxiety and depression, compared to 17.2% and 17.0% respectively in the control group (both $p < 0.01$).

Regarding health care utilization, the odds ratio for at least one doctor visit was 2.72 (95% CI 1.50–4.93, $p < 0.01$) in the symptomatic group, compared to those without GPLS. Access to medical care was rated as easy by most of the subjects, with only 18.0%

TABLE 1 Baseline characteristics of subjects with and without gastroparesis-like symptoms (GPLS)

Sex/Age	Without gastroparesis-like symptoms N (%)			With gastroparesis-like symptoms N (%)		
	Overall (n = 53,660)	With diabetes (n = 3834)	Without diabetes (n = 49,826)	Overall (n = 467)	With diabetes (n = 50)	Without diabetes (n = 417)
Male	27,390 (51.0)	2430 (63.4)	24,960 (50.1)	159 (34.0)	19 (38.0)	140 (33.6)
Female	26,270 (49.0)	1404 (36.6)	24,866 (49.9)	308 (66.0)	31 (62.0)	277 (66.4)
Age 18–39	22,743 (42.4)	563 (14.7)	22,180 (44.5)	260 (55.7)	18 (36.0)	242 (58.0)
Age 40–64	22,102 (41.2)	1819 (47.4)	20,283 (40.7)	179 (38.3)	23 (46.0)	156 (37.4)
Age ≥ 65	8815 (16.4)	1452 (37.9)	7363 (14.8)	28 (6.0)	9 (18.0)	19 (4.6)

Prevalance of gastroparesis-like symptoms by country

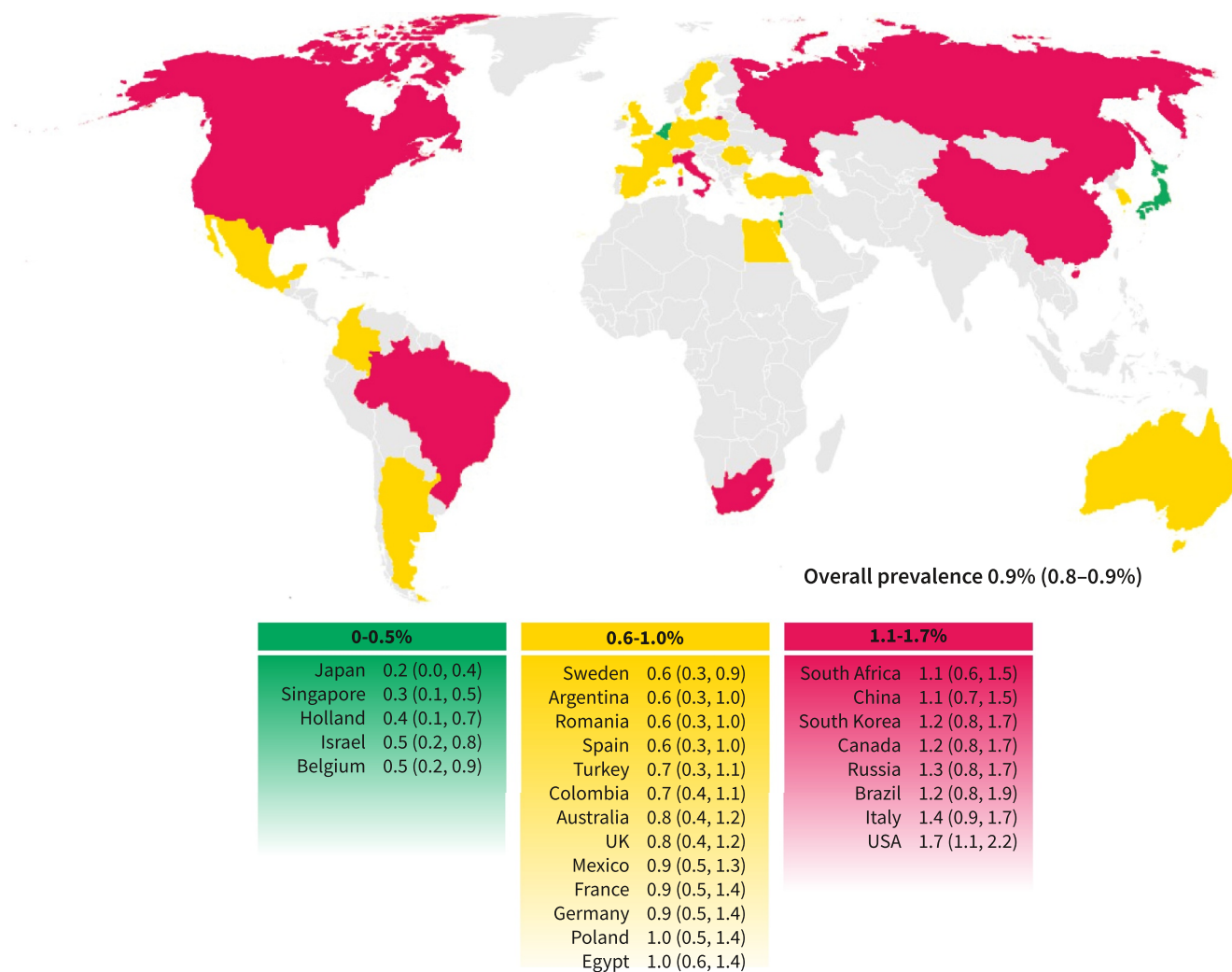


FIGURE 1 Prevalence of gastroparesis-like symptoms (% and 95% CI) in the general population in each country

self-reporting inadequate availability of medical care. On average, subjects with GPLS took 3.2 ± 2.3 types of medication for gastrointestinal symptoms or mood disorders, compared to 1.1 ± 1.6 types in control group ($p < 0.01$) and reported undergoing a mean of 0.5 ± 0.7 abdominal surgical procedures, including appendectomy, cholecystectomy, partial intestinal resection or hysterectomy, which was significantly higher than the 0.3 ± 0.6 procedures in subjects without GPLS ($p < 0.01$). The average use of medicines and history of abdominal surgeries in diabetic patients with GPLS was higher than in non-diabetic subjects with 3.6 ± 2.5 types of medication and 0.8 ± 0.9 abdominal surgical interventions, when compared to 3.1 ± 2.3 types and 0.5 ± 0.7 times in non-diabetes (both $p < 0.01$) (Table 3). The percentage of each answer for questionnaires regarding the burden of GPLS in different groups is shown in Table S1.

When assessing the impact and health care utilization of GPLS in diabetic subjects, we found similar results. Diabetic individuals with GPLS had a significantly lower BMI, lower QoL scores for physical

QoL and mental QoL, higher PHQ-12 and PHQ-4 scores compared to those without symptoms. The odds ratio for at least one doctor visit was 3.21 (95% CI 1.83–5.64, $p < 0.01$) in the symptomatic group, compared to those without GPLS. The number of medications and surgeries was significantly higher (Table 4).

DISCUSSION

To our knowledge, this is the first worldwide population-based study providing data on the epidemiology and impact of GPLS, using data from systematic internet surveys in 26 countries on six continents, although the original paper from RFGES had reported the global prevalence of PDS alone was 6.1% and CNVS alone was 0.9%.¹⁴ Our findings provide a first step in bridging a major knowledge gap on the epidemiology of this symptomatic group. Moreover, country-specific rates of GPLS in our study could be used to improve strategies to recognize this condition and provide guidance to its management.

Prevalence of gastroparesis-like symptoms in non-diabetics by country

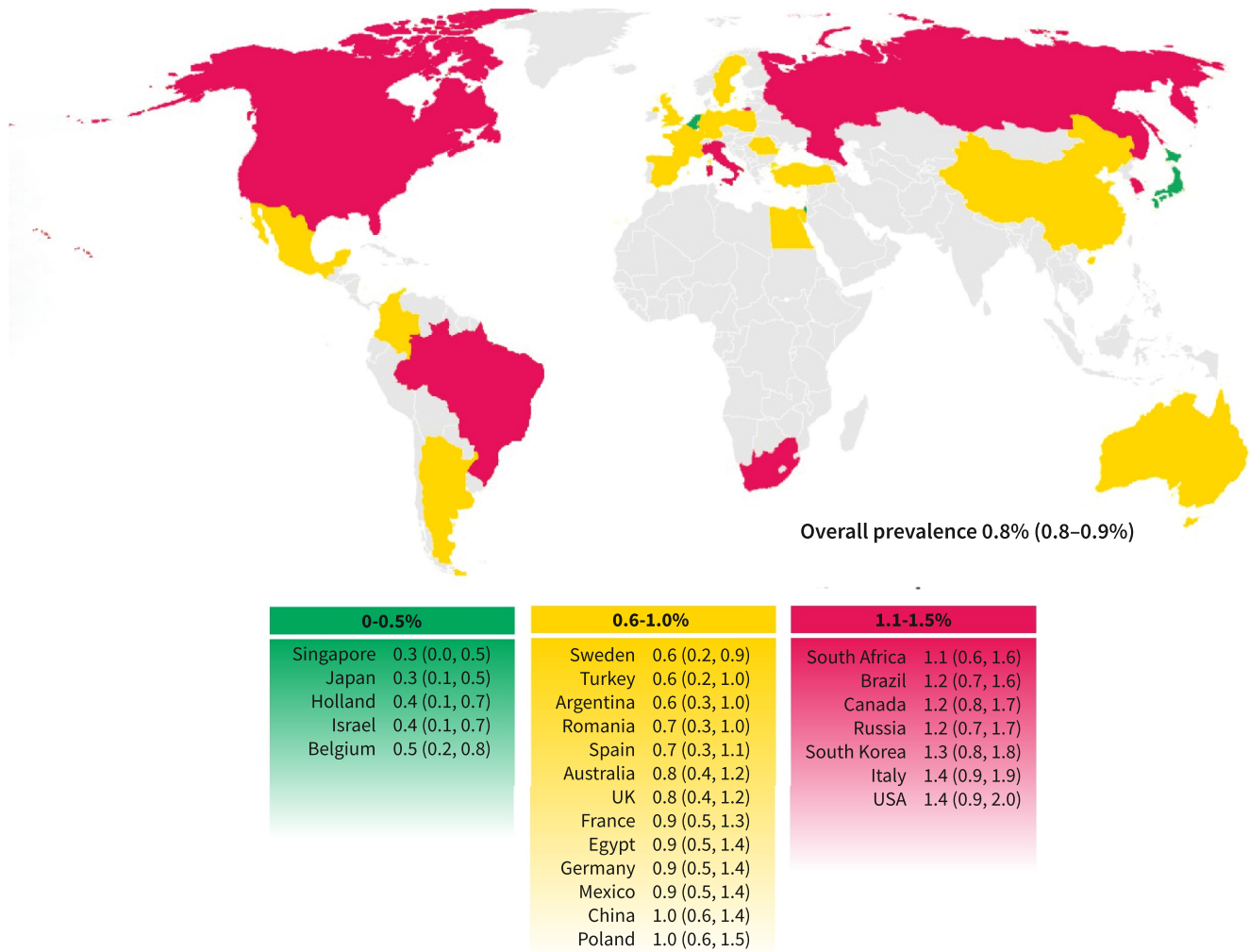


FIGURE 2 Prevalence of gastroparesis-like symptoms (% and 95% CI) in the non-diabetic subjects in each country

In line with our hypothesis, the prevalence of GPLS was substantially higher than the prevalence of gastroparesis as previously determined from medical records. This is not surprising since not all patients with GPLS have had a GE test or have documented delayed GE, and many patients do not seek medical attention for their symptoms.^{5,18,19} A previous study in Olmsted County using both GI disease questionnaires and regression models, suggested that delayed GE was present in 1.8% of community subjects, which is close to our current estimate of GPLS in the US population (1.7%).⁷ The female to male ratio for the global prevalence of GPLS in our study was 2, which is also similar with the prevalence of gastroparesis from the medical records in the UK, reported at near twofold in women compared to men, and from the insurance database in the US, stated more than twice as common in female.^{5,20} The prevalence of gastroparesis in diabetes mellitus patients varies widely in past research. Our study also found that the prevalence of GPLS in diabetes showed considerable variation between countries. A relative low prevalence of GPLS in diabetes was observed in some countries

with high diabetes prevalence, such as Mexico and Poland. Whether this reflects the prevalence of diabetic gastrointestinal complications in different countries, a different proportion of type 2 diabetics within the diabetes population, or whether this is driven by geographic variations in symptom profiles of gastroparesis will require additional studies. If we focus on the US population, the prevalence (3.7%) in our study is consistent with prior research, as it lies between the previously reported 4.6% prevalence in type 1 diabetes and 1.3% in type 2 diabetes.¹⁹ Contrary to previous research of gastroparesis from medical records, in our study, prevalence of GPLS decreased with age.⁵ A possible explanation is that gastroenterologists may not refer young patients for a GE study, while our epidemiological studies address all age categories. It is also worth noting that various GI symptoms, such as abdominal pain and bloating, were included in the previous studies on GP which may also affect the epidemiology findings.

We also found that individuals with GPLS commonly have overlapping symptoms compatible with EPS and IBS. Previous studies

Prevalence of gastroparesis-like symptoms in diabetics by country

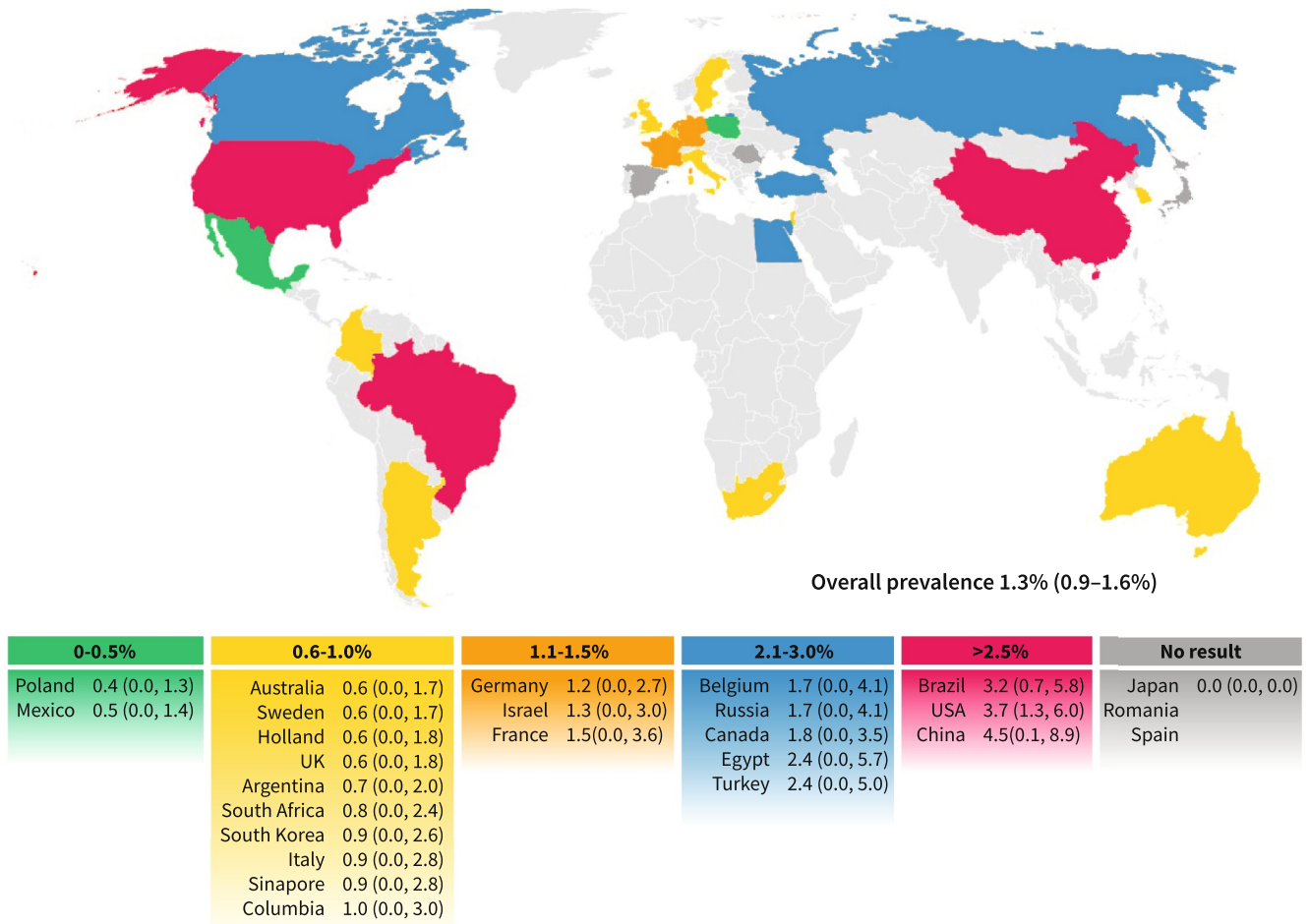


FIGURE 3 Prevalence of gastroparesis-like symptoms (% and 95% CI) in the diabetic subjects in each country

have shown that patients with gastroparesis are more likely to have slow transit constipation and delayed small bowel transit.^{21,22} FD is comprised of PDS and EPS.¹¹ As we included PDS in the definition of GPLS, and overlapping EPS and PDS is common, it should come as no surprise that co-existing EPS was common in this population.²³ Furthermore, nausea has been reported as one of the independent risk factors for IBS-FD overlap among IBS patients and PDS was also associated with IBS-FD overlap among FD patients.²⁴ These findings may help explain the substantial overlap between the GPLS and IBS. Since nausea and/or vomiting are considered the key symptom of GPLS, 38.5% patients with GPLS fit ROME IV criteria of CNVS. However, other gastrointestinal symptoms which can change clinical management need to be considered when making a diagnosis of CNVS. Moreover, in our study, patients with rumination syndrome were included in the GPLS group. Clinically, rumination may be confused with gastroparesis. The overlap with rumination in our study (11.8%) is higher than the 3.3% reported in a previous study, using ROME III diagnostic criteria,²³ probably related to changes in the diagnostic criteria. Furthermore, approximately one third of patients with GPLS exhibited features of functional dysphagia. One

possible explanation is that gastroesophageal reflux disease is a common co-morbidity in gastroparesis.²³ Patients with reflux disease symptoms are more likely to experience nonobstructive dysphagia.

This study also documented the considerable impact and burden of GPLS. Although it is not substantiated in the literature that gastroparesis may cause weight loss, we found that patients with GPLS, in particular those with diabetes, had lower BMI than subjects without symptoms. While the difference in BMI may be statistically significant when comparing individuals with GPLS to those without symptoms in the overall population, the difference is not clinically relevant as the mean BMI is very similar (25.4 ± 6.9 vs. 25.6 ± 5.4 kg/m²) and the difference is likely caused by the large sample. Multiple studies have shown that gastroparesis is associated with an increased healthcare burden and a notably reduced health-related QoL. We found both physical and mental QoL impairment in individuals with GPLS. These findings are consistent with a recent study, which demonstrated that physical and mental QoL assessed by the SF-36 were impaired in 41% and 26% of gastroparesis patients, respectively, and up to 50% had impaired QoL according to PAGI-QoL.³ Additionally, subjects with

TABLE 2 The number of patients diagnosed with DGBIs in the group of 467 subjects with gastroparesis-like symptoms

DGBIs	With gastroparesis-like symptoms N (%)				Without gastroparesis-like symptoms N (%)				
	Overall	With diabetes	Without diabetes	*p-value	Overall	With diabetes	Without diabetes	**p-value	*p-value
Functional heartburn	79 (16.9)	12 (24.0)	67 (16.1)	0.16	534 (1.0)	62 (1.6)	472 (0.9)	<0.01	<0.01
Functional chest pain	23 (4.9)	3 (6.0)	20 (4.8)	0.73	718 (1.3)	66 (1.7)	652 (1.3)	0.03	<0.01
Reflux hypersensitivity	80 (17.1)	11 (22.0)	69 (16.5)	0.33	375 (0.7)	47 (1.2)	328 (0.7)	<0.01	<0.01
Functional dysphagia	191 (40.9)	15 (30.0)	176 (42.2)	0.10	1521 (2.8)	159 (4.1)	1362 (2.7)	<0.01	<0.01
EPS	223 (47.8)	23 (46.0)	200 (48.0)	0.79	1083 (2.0)	109 (2.8)	974 (2.0)	<0.01	<0.01
Rumination syndrome	55 (11.8)	7 (14.0)	48 (11.5)	0.61	1456 (2.7)	115 (3.0)	1341 (2.7)	0.26	<0.01
CNVS	180 (38.5)	22 (44.0)	158 (37.9)	0.40	323 (0.6)	27 (0.7)	296 (0.6)	0.395	<0.01
Rome-IV IBS	206 (44.1)	12 (24.0)	194 (46.5)	<0.01	1989 (3.7)	174 (4.5)	1815 (3.6)	<0.01	<0.01
IBS-C	69 (14.8)	3 (6.0)	66 (15.8)	0.09	643 (1.2)	48 (1.3)	595 (1.2)	0.75	<0.01
IBS-D	47 (10.1)	5 (10.0)	42 (10.1)	0.99	582 (1.1)	55 (1.4)	527 (1.1)	0.03	<0.01
IBS-M	84 (18.0)	4 (8.0)	80 (19.2)	0.05	628 (1.2)	61 (1.6)	567 (1.1)	0.01	<0.01
IBS-U	6 (1.3)	0	6 (1.4)	1.00	136 (0.3)	10 (0.3)	126 (0.3)	0.92	<0.01

Abbreviations: CNVS, Chronic nausea and vomiting syndrome; DGBI, disorders of gut-brain interaction; EPS, epigastric pain syndrome; IBS, irritable bowel syndrome; IBS-C, IBS subtype constipation; IBS-D, IBS subtype diarrhea; IBS-M, IBS mixed; IBS-U, IBS unidentified subtype.

*p-value for the Chi-Square test of association between gastroparesis-like symptoms and DGBI.

**p-value for the Chi-Square test of association between diabetes and DGBI.

TABLE 3 Summary of the impact of gastroparesis-like symptoms

Variables	With gastroparesis-like symptoms mean (SD)				Without gastroparesis-like symptoms mean (SD)				
	Overall	With diabetes	Without diabetes	**p-value	Overall	With diabetes	Without diabetes	**p-value	*p-value
BMI	25.4 (6.9)	25.5 (5.9)	25.3 (7.0)	<0.01	25.6 (5.4)	29.3 (6.1)	25.3 (5.2)	<0.01	<0.01
PHQ-12 somatic symptom scale score	11.3 (4.3)	10.0 (4.2)	11.4 (4.3)	<0.01	5.4 (3.8)	5.8 (4.0)	5.3 (3.8)	<0.01	<0.01
PROMIS Global-10: Physical health component score	11.2 (2.7)	11.4 (3.0)	11.2 (2.7)	<0.01	14.5 (2.7)	13.4 (2.8)	14.6 (2.7)	<0.01	<0.01
PROMIS Global-10: Mental health component score	10.9 (3.6)	12.0 (3.7)	10.7 (3.6)	<0.01	13.6 (3.3)	13.3 (3.2)	13.6 (3.3)	<0.01	<0.01
Patient Health Questionnaire-4 (PHQ-4)	6.3 (3.5)	5.4 (3.6)	6.4 (3.5)	<0.01	2.7 (2.9)	2.7 (3.0)	2.7 (2.9)	<0.01	<0.01
Total surgery	0.5 (0.7)	0.8 (0.9)	0.5 (0.7)	<0.01	0.3 (0.6)	0.5 (0.8)	0.3 (0.6)	<0.01	<0.01
Total medications	3.2 (2.3)	3.6 (2.5)	3.1 (2.3)	<0.01	1.1 (1.6)	1.6 (1.9)	1.1 (1.5)	<0.01	<0.01

*p-value of association between gastroparesis-like symptoms and different variables (with gastroparesis-like symptoms vs. without gastroparesis-like symptoms).

**p-value of association between diabetes and different variables (diabetic vs. non-diabetic).

GPLS constitute an added burden to the healthcare system due to multiple somatic symptoms, frequent doctor visits and use of multiple medications, which also holds true for diabetics.

In a recent study by the Gastroparesis Clinical Research Consortium, patients with FD and gastroparesis at tertiary hospitals are not distinguishable based on clinical symptoms and pathologic features.²⁵ The nature of and distinction between gastroparesis versus

FD is likely to remain an issue in the near future. Our study has focused on "GPLS" based on the European consensus on gastroparesis.¹⁰ While delayed GE is found in up to 35% of patients with FD,⁹ by focusing on nausea and vomiting a separate patient group is identified as these are not considered cardinal symptoms of FD.

There are several limitations to this study. First, while we investigated the prevalence of GPLS, we have no information on the

TABLE 4 Summary of the impact of gastroparesis-like symptoms in the diabetic population

Variables	Overall	With gastroparesis-like symptoms	Without gastroparesis-like symptoms	p-value
BMI	29.2 (6.1)	25.5 (5.9)	29.3 (6.1)	<0.01
PHQ-12 somatic symptom scale score	5.8 (4.1)	10.0 (4.2)	5.8 (4.0)	<0.01
PROMIS Global-10: Physical health component score	13.4 (2.8)	11.4 (3.0)	13.4 (2.8)	<0.01
PROMIS Global-10: Mental health component score	13.3 (3.2)	12.0 (3.7)	13.3 (3.2)	<0.01
Patient Health Questionnaire-4 (PHQ-4)	2.7 (3.0)	5.4 (3.6)	2.7 (3.0)	<0.01
Total surgery	0.5 (0.8)	0.8 (0.9)	0.5 (0.8)	<0.01
Total medications	1.6 (1.9)	3.6 (2.5)	1.6 (1.9)	<0.01

true prevalence of gastroparesis since this would require measurement of GE in a large community sample on a multinational scale. However, to advance epidemiological insights, GE testing can be applied in population samples with GPLS and combined with the current epidemiological assessment, as they may reveal the true epidemiology of gastroparesis. Second, the diagnosis of diabetes was based on patient self-report. We were not able to determine the type of diabetes mellitus as this was not addressed in the global survey questionnaire. Hence, we cannot evaluate the prevalence of GPLS in subjects with Type 1 and 2 diabetes mellitus. Finally, we cannot exclude the possibility that a few subjects had underlying or co-existent organic disease, although patients who self-reported a chronic organic disease or abdominal surgery history were disqualified from the DGBI group, thus making this limitation less substantial.

In summary, GPLS are common worldwide and more common in subjects with diabetes. GPLS. The presence of GPLS is associated with multiple aspects of illness and an increased healthcare consumption.

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CONFLICT OF INTEREST

The authors disclose no conflicts.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

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