The Prevalence and Burden of Disorders of Gut-Brain Interaction (DGBI) before versus after the COVID-19 Pandemic

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Ethics

Before data collection started, the study was reviewed by the Institutional Review Board (IRB) at the University of North Carolina (Chapel Hill, NC, USA), and the University of Sheffield (Sheffield, UK). It was deemed IRB exempt because all study participants were anonymous to the investigators. All authors had access to the study data and reviewed and approved the final manuscript.

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ABSTRACT

Background & Aims: COVID-19 infection may increase the risk of developing Disorders of Gut-Brain Interaction (DGBI). However, the extent of this effect on a population level is poorly understood. We performed a two-country survey to address this issue.

Methods: A population-based Internet survey with pre-defined demographic quotas was conducted across the UK and USA in 2017 (pre-pandemic, n=4050) and repeated in 2023 (post-pandemic, n=4002). The surveys included the Rome IV diagnostic questionnaire, and questions about non-gastrointestinal somatic symptoms, anxiety and depression, quality of life, and healthcare utilization. The 2023 survey also included questions regarding COVID-19 infection and illness history.

Results: The overall DGBI prevalence, i.e., meeting diagnostic criteria for at least one DGBI, has significantly increased from the pre- to post- pandemic era (38.3% vs. 42.6%, OR 1.20, 95% C.I 1.09-1.31), with similar findings independently noted in the UK and USA. The rise in DGBI was observed within the esophageal (8.8% vs. 10.1%, OR 1.16), gastroduodenal (11.9% vs. 16.4%, OR 1.45), and bowel domains (30.1% vs. 32.5%, OR 1.12). The two most widely investigated DGBI showed large post-pandemic prevalence increases, with functional dyspepsia rising from 8.3% to 11.9% (OR 1.48) and irritable bowel syndrome from 4.7% to 6.0% (OR 1.31).

In multivariable analysis, factors significantly associated with having DGBI in the post-pandemic era included younger age, female sex, anxiety, depression, medium-to-high somatic symptom severity, increasing number of COVID-19 infections, experiencing abdominal pain or diarrhea during COVID-19 infection, and suffering with long-COVID.

Individuals with DGBI in the post-pandemic era, in particular those with long-COVID, reported reduced quality of life and higher mood disturbances, somatic symptom reporting and healthcare use than individuals with DGBI in the pre-pandemic era.

Conclusion: The population prevalence and burden of DGBI have increased following the COVID-19 pandemic. Healthcare services and research funding bodies need to adapt to this post-COVID rise in DGBI and address how to best manage this patient group.

INTRODUCTION

Disorders of gut-brain interaction (DGBI) are clusters of chronic gastrointestinal symptoms that occur in the absence of organic or structural disease.[1] In total, there are more than 30 DGBI which can be centrally-mediated or arise from any region within the gastrointestinal tract, including the esophagus, gastroduodenum, bowel, biliary, and anorectum. The Rome Foundation Global Epidemiological Survey (RFGES) conducted in 2017 found that 40% of adults across the globe fulfill symptom-based criteria for at least one DGBI and incur considerable health impairment, healthcare utilization and reduced quality of life.[2]

However, the prevalence and burden of DGBI, as demonstrated by the RFGES, was determined a few years before the outbreak of the SARS-COV-2 (i.e. COVID-19) pandemic. There has been increasing recognition of the enteropathic nature of COVID-19 which, through binding to angiotensin converting enzyme 2 receptors on gut epithelial cells, can lead to acute gastrointestinal symptoms.[3] A systematic review and meta-analysis of 78 798 patients positive for COVID-19 reported that the most frequent gastrointestinal manifestations during an infective episode were diarrhea (16.5%), nausea and vomiting (9.7%), and abdominal pain (4.5%).[4] Following an acute bout, 1-in-10 people continue to suffer with lingering gastrointestinal symptoms (as part of the spectrum of long-COVID), with many reporting severe symptoms.[5,6] Indeed, abdominal pain and gastrointestinal issues are amongst the five most common symptoms of long-COVID.[7] A recent meta-analysis concluded the prevalence of post-COVID-19 IBS and functional dyspepsia to be 12% and 4%, respectively, and higher than non-infected controls.[8] These findings are akin to the well-recognized entity of post-infection DGBI (e.g. post-infection IBS or functional dyspepsia) which also arise in approximately 1-in-10 people following an outbreak of either a viral, bacterial, or protozoal infection.[9] Risk factors for post-infection DGBI include female sex, younger age, psychological distress during or before acute gastroenteritis, and severity of the acute episode.[9,10]

We hypothesized that the population prevalence and burden of DGBI has increased following the COVID-19 pandemic compared with pre-pandemic estimates. An ideal method to investigate whether there has been such a change would be to undertake a like-for-like epidemiological survey before and after the COVID-19 pandemic, with comparable demographic characteristics and use of the same diagnostic questionnaire. However, this has not previously been performed and served the purpose of our current study, especially as we have proprietary access to the unique RFGES dataset from 2017 and the capability to repeat the survey in 2023. Alongside recognized associations for DGBI (i.e. female sex, younger age, mood disturbances, somatic symptom reporting), we also hypothesized that

COVID-infection related factors (e.g. number and severity of infections, vaccination status) might influence the development of DGBI in the post-pandemic era.[9-12]

METHODS

Study Design and Participant Recruitment

Qualtrics Inc, a global market survey company, was commissioned in the year 2017 to provide a nationally representative general population sample of adults in 26 countries for the RFGES, with the aim of determining the global prevalence and impact of DGBI.[2] Quota-based sampling was used to generate demographically balanced and population-representative samples for each country with regards to age (40% aged 19-39 years, 40% aged 40-64 years, and 20% aged 65 years and over) and sex (50% male:50% female split).

For the purpose of the current study we specifically extracted and analyzed the UK and USA dataset from the RFGES, of which there were almost 2000 people from each country.[2] In the year 2023, we commissioned Qualtrics Inc. to re-sample ~2000 people each from the general populations of the UK and USA, using the same demographic quotas as the RFGES, but also adding COVID-related questions. This provided us with very similar two-country survey samples collected with identical methodology at two different time points, with different participants on both occasions, which enabled us to compare the prevalence and burden of DGBI before and after the COVID-19 pandemic.

Questionnaires

At both time points the study questionnaires included the entire Rome IV Adult Diagnostic Questionnaire,[13] and questions about the participants' sociodemographic characteristics, history of medical diagnoses (including celiac disease, inflammatory bowel disease, GI cancer), concerns regarding bowel habit, and healthcare utilization (doctor visits and medications). They also included the Patient Health Questionnaire-12 (PHQ-12) to assess non-gastrointestinal somatic symptoms,[14] the Patient Health Questionnaire-4 (PHQ-4) for anxiety and depression,[15] and the PROMIS Global-10 Questionnaire that measures the physical and mental health aspects of a person's overall quality of life.[16]

The 2023 survey also included questions for a history of test-confirmed COVID-19 infections, the number of such infection instances, the presence of gastrointestinal symptoms during COVID-19 infection (i.e. abdominal pain, vomiting, diarrhea), ongoing symptoms related to COVID-19 infection (i.e. long COVID), and COVID-19 vaccination status.

Statistical analysis

SPSS version 27.0 was used to analyze the questionnaire data with p-values of <0.05 deemed significant. There were no missing data points as the online questionnaire required

participants to complete each question before continuing. Categorical variables were summarized by descriptive statistics including total numbers and percentages, with comparisons between groups performed using the chi-square test. Odds ratios (OR) with 95% confidence intervals (95% CI) were presented as appropriate. The mean and standard deviation of continuous variables were calculated, with differences between independent groups assessed using the unpaired Student's t test. For the post-pandemic dataset, we performed binary logistic regression to identify independent factors associated with DGBI.

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RESULTS

Baseline characteristics

A total of 4050 individuals from the UK (n=2027) and USA (n=2023) completed the survey in the year 2017 (pre-pandemic), while a total of 4002 individuals from the UK (n=2002) and the USA (n=2000) completed the survey in the year 2023 (post-pandemic).

The sex and age group distributions of participants were almost identical between the 2017 and 2023 survey samples due to quota-based sampling: 49.8% vs. 50.0% females, 39.7% vs. 39.9% of ages 18-39 years, 40.1% vs. 40.2% of ages 40-64 years, and 20.2% vs. 20.0% of age 65 and older. This was similar across the UK and USA; see **supplementary table.**

Prevalence of DGBI before vs. after the COVID-19 Pandemic

As reported in **table 1**, the overall prevalence of DGBI increased from 38.3% pre-pandemic to 42.6% in the post-pandemic era (OR 1.20, 95% C.I 1.09-1.31). This rise was independently seen in the UK (36.7% to 41.2%, OR 1.21, 95% C.I 1.07-1.38) and in the USA (39.9% to 44.0%, OR 1.18, 95% C.I 1.04-1.34); **figure 1**. The increase in DGBI prevalence after the COVID-19 pandemic was consistent in both sexes separately, and in all age groups. In males, the prevalence of DGBI increased from 32.2% to 36.9% (p=0.002), whilst in females it increased from 44.4% to 48.3% (p=0.01). The rise in DGBI prevalence after the pandemic in the different age groups was: 45.0% vs. 49.6% in ages 18-34 years, 43.7% vs. 45.7% in ages 35-49 years, 36.6% vs. 42.5% in ages 50-64 years, and 24.8% vs. 28.6% for those of ages 65 years and over.

A rise in DGBI was observed within the esophageal domain (8.8% vs. 10.1%, OR 1.16, 95% CI 1.00-1.35), accounted for by an increase in functional dysphagia (4.7% vs. 5.7%, OR 1.23, 95% C.I 1.01-1.50) but not the other esophageal DGBI.

The biggest rise in DGBI was observed within the gastroduodenal domain (11.9% vs. 16.4%, OR 1.45, 95% 1.28-1.65), which was independently noted in the UK (10.2% vs. 13.2%, OR 1.34, 95% C.I 1.11-1.63) and in the USA (13.6% vs. 19.6%, OR 1.55, 95% C.I. 1.31-1.83). The rise of gastroduodenal DGBI was mainly accounted for by an increase in prevalence of functional dyspepsia (8.3% vs. 11.9%, OR 1.48, **figure 2**), and seen in the UK (6.6% vs. 9.3%, OR 1.45) and the USA (10.1% vs. 14.5%, OR 1.50)**.** Within the functional dyspepsia category, postprandial distress syndrome increased from 7.1% to 10.4% (OR, 1.53) and epigastric pain syndrome from 3.2% to 4.2% (OR 1.33)**.** Other notable rises include chronic

nausea and vomiting syndrome (1.4% to 2.0%, OR 1.47) and cyclic vomiting syndrome (1.1% to 1.8%, OR 1.69).

There was also a significant increase in DGBI in the bowel domain (30.1% vs. 32.5%, OR 1.12, 95% C.I 1.02-1.23), in the UK (29.4% vs. 32.7%, OR 1.17) and the USA (30.8% vs. 32.4%, OR 1.08). Irritable bowel syndrome increased from 4.7% to 6.0% (OR 1.31, 95% C.I 1.08-1.60, **figure 2**), with rises seen in the UK (4.0% vs. 5.5%, OR 1.40) and USA (5.3% vs. 6.6%, OR 1.25). Increases were seen also in functional bloating and distension (2.7% vs. 3.6%, OR 1.34).

There were no significant pre- to post-pandemic differences in the anorectal domain.

Burden of DGBI before vs. after the COVID-19 pandemic

At both survey time points, individuals with DGBI had a higher prevalence of anxiety, depression, medium-to-high somatic symptoms, reduced quality of life, greater medication use, more frequent GI healthcare visits and concerns regarding bowel habit (**table 2**) compared to others in the samples.

Compared to those with DGBI in the pre-pandemic era, individuals with DGBI in the year 2023 had poorer psychological and life functioning on average, higher levels of anxiety, depression and somatic symptom scores, and reduced quality of life scores (all p-values <0.001). The post-pandemic DGBI cohort also had more frequent use of GI medications, anxiolytics, antidepressants, and were generally more concerned regarding their bowel habit **(table 2)**.

COVID-19 related history

Of the 4002 individuals who comprised the post-pandemic cohort, 1974 (49.3%) reported having been diagnosed with COVID-19; most of these had COVID once (n=1276), with 520 having had COVID twice, 157 three or more times, and 21 were unsure how often they had the illness.

Of the 1974 individuals who had been diagnosed with COVID, 616 (31.2%) reported diarrhea during their infection, 539 (27.3%) had abdominal pain, 616 (31.2%) had diarrhea, and 413 (20.9%) had vomiting. The presence of long COVID (i.e., current lingering COVID-related symptoms from a past COVID-19 infection) was reported by 317 individuals, which was 16.1% of the 1974 people with COVID history, and 7.9% of the entire 4002 people who completed the post-pandemic questionnaire. Finally, 3098 (77.4%) of 4002 reported that they had been vaccinated, at least once, against COVID-19.

Factors associated with DGBI in the post-pandemic cohort

On binary multivariable regression analysis, factors independently associated with having any DGBI in the post-pandemic era included younger age (OR 1.01, 95% CI 1.00-1.02), female sex (OR 1.51, 95% CI 1.24-1.84), anxiety (OR 1.33, 95% CI 1.00-1.77), depression (OR 1.48, 95% CI 1.11-1.97), medium-to-high somatic symptoms (OR 2.24, OR 1.78-2.81) increasing number of COVID-19 infections (OR 1.21, 95% C.I 1.04-1.42), experiencing abdominal pain (OR 1.56, 95% CI 1.17-2.07) or diarrhea (OR 1.31, 95% CI 1.00-1.71) during an acute COVID-19 infection, and long-COVID (OR 1.38, 95% CI 1.04-1.83). The presence of vomiting during an acute COVID-19 infection was not associated with DGBI (OR 0.81, 95% CI 0.61-1.09) and neither was vaccination status (OR 1.12, 95% CI 0.86-1.44).

Illness burden amongst those with long-COVID DGBI

Finally, we assessed differences amongst individuals in the post-pandemic cohort who had DGBI, with and without a history of long-COVID **(table 3).** This revealed that individuals with DGBI and long-COVID had a greater illness burden and poorer life functioning than those with DGBI and no long-COVID, as demonstrated by higher anxiety, depression and somatic symptom scores, reduced quality of life, more frequent use of GI medications, more healthcare visits, and more concern regarding their bowel habit.

DISCUSSION

To our knowledge, this large population-based study is the first to investigate the overall prevalence and burden of DGBI before and after the COVID-19 pandemic within two countries. It reveals a broad and significant rise in DGBI after COVID-19 in the adult population, as seen in the combined and independent samples of the UK and USA, amongst both sexes, and across all adult age groups. The most notable increase was seen in DGBI arising from the gastroduodenal domain, in particular functional dyspepsia. An increase in IBS, which is the most commonly recognized DGBI within routine clinical practice, was also observed. In multivariable analysis, factors independently associated with having DGBI in the post-pandemic era included younger age, female sex, anxiety, depression, somatic symptoms, increasing number of COVID-19 infections, experiencing abdominal pain or diarrhea during COVID-19 infection, and suffering with long-COVID. Individuals with DGBI in the post-pandemic era, in particular those suffering with long-COVID, demonstrate a greater illness burden and healthcare utilization than those with DGBI before the pandemic.

These findings support our *a priori* hypotheses, which we formulated based on the growing evidence reporting gastrointestinal manifestations during an acute episode of COVID-19 and subsequent development of post-COVID functional dyspepsia and IBS.[4,8] These concepts align to the well-recognized model of post-infection DGBI following outbreaks of infective enteritis.[9,17] However, such outbreaks are generally confined to a community or municipality, and do not change the prevalence of DGBI on a larger population scale. In contrast, COVID-19 has been a global pandemic, with most of the world population exposed or infected. We hypothesized that this event would result in a rise in post-COVID DGBI at a general population level. Having undertaken the RFGES in 2017, we decided to replicate the study in 2023 within the UK and USA, by using the same methodology and demographic recruitment processes across both time points. Notably, the rates of DGBI from the 2017 dataset were consistent with previously published data from a survey conducted in 2015 within the USA using the same methodology.[18] This provides confidence in a reliable research methodology and supports our hypothesis that the increase in DGBI observed in the post-pandemic era is likely attributable to COVID-19. The inclusion of all DGBI in this survey, as opposed to only functional dyspepsia and IBS, is a further strength of the study. While the latter tend to receive the most attention in the literature, all DGBI are associated with illness burden, reduced quality of life, and healthcare utilization.[2] Finally, we minimized selection bias for both the RFGES and the post-pandemic survey by presenting the studies to prospective participants as a general health study as opposed to specifically mentioning GI- or COVID-

related issues. Both surveys also had multiple built-in quality-assurance measures to exclude poor-quality responders and minimize the risk of missing data or incorrect values.

However, there are appreciable limitations. First, these are cross-sectional datasets and, importantly, for the post-pandemic dataset we have no longitudinal data to assess whether post-COVID DGBI regresses over time. For example, following outbreaks of infective enteritis, the overall risk of developing IBS within the first 12 months is four times higher in exposed patients versus unexposed controls.[9] However, after 12 months, the relative risk of having IBS is twice as high in exposed versus unexposed individuals suggesting that, in a subset of patients, the symptoms of post-infectious IBS disappear over time. Indeed, after a viral enteric infection there is no difference in the prevalence of IBS at 12 months.[9] Whether such findings can be extrapolated to post-COVID DGBI is unknown although given that the virus is still present and society is susceptible to repeat infections then arguably the latest DGBI prevalence rates may remain stable. Second, this study was undertaken in adults and data in the pediatric population is relatively sparse. An Italian study reported that the prevalence of DGBI increased in the pediatric population at the peak of the lockdown period, with functional dyspepsia increasing from 0.6% to 1.3%, IBS increasing from 3% to 8.8%, abdominal migraine from 5.1% to 13.9%, and functional abdominal pain from 0.8% to 3.6%.[19] However, that study used the Rome III criteria, did not evaluate the burden of all DGBI, and there was no data after the pandemic.[19] Third, while mood disturbances were common and associated with DGBI, we cannot determine the direction of causality. For example, the emergence of the COVID-19 pandemic has created an environment where many determinants of poor mental health are exacerbated, with levels of anxiety and major depressive disorders increasing across the globe.[20] Previous studies have shown that in one-third of DGBI cases the mood disturbance preceded gut symptoms, while in two-third of cases gut symptoms preceded mood disturbances, but our study was not geared to explore this.[21] Fourth, we observed an increase in functional vomiting disorders but surprisingly not cannabinoid hyperemesis syndrome, despite its rise in emergency departments.[22] This may reflect the Rome IV diagnostic criteria requiring symptom improvement after cannabis cessation, which is challenging to prove and can lead to under-estimation. Fifth, our study used self-reported data and we did not have access to medical records nor could we perform clinical investigations. Reassuringly, most people who have symptoms compatible with a DGBI do not have organic disease and, in our dataset, those who reported a doctor diagnosis of celiac disease, inflammatory bowel disease or GI cancer were excluded from having a DGBI.[23,24] It is also plausible that those who reported long-COVID with DGBI may have had pre-existing DGBI, and were prone to recall bias, although this should not detract from the data showing they now have the highest illness burden. This aligns with an

observational cohort study demonstrating increased prevalence, persistence and severity of somatic symptoms post-COVID-19 infection.[25] Finally, our results may not be generalizable to countries with different healthcare systems, social constructs, and COVID-19 infection rates.

There has been a rise in general bodily symptoms and diagnoses following COVID-19 compared with pre-pandemic estimates. A retrospective review of electronic health records found an increase in 15 of 21 diagnostic categories, including gut symptoms of diarrhea and vomiting.[26] Our study supports this observation but in greater detail from a DGBI perspective, which will have important clinical and research implications. DGBI have traditionally been viewed as challenging to manage and generally underfunded by national research bodies, despite their societal impact in terms of prevalence, impaired work productivity and reduced quality of life.[2] Following the publication of the RFGES dataset from 2017 there have been increasing calls for greater provision of service to manage these frequently encountered patients.[2] Our latest study highlights that the problem has amplified, in that individuals with DGBI in the post-pandemic era, in particular those with long-COVID with DGBI, have greater symptom burden and healthcare utilization compared with pre-pandemic levels. Long-COVID is associated with substantial multimorbidity - including DGBI - and these latter gut symptoms will need to be accounted for within healthcare services. There are no specific guidelines on how to best manage long-COVID with DGBI although it might be speculated that therapies will align to general societal recommendations for the management of IBS and functional dyspepsia.[27,28] Interestingly, there is a paucity of randomized controlled trials in post-infection DGBI and this is a general area of unmet need.[29] As DGBI may be linked with perturbations along the microbiome-gut-brain axis it would be of interest to study the pathophysiology of long-COVID with DGBI and the clinical and mechanistic role of diet, anti-inflammatory drugs, antispasmodics, probiotics, neuromodulators and behavioral interventions in this setting.[29]

In summary, this two-country population-based survey shows that there has been a rise in the prevalence and burden of DGBI following the COVID-19 pandemic. Healthcare services and research funding bodies should prepare for the increase in post-COVID and long-COVID with DGBI, and address optimal management for this patient group.

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Table 1: The prevalence of DGBI before and after the COVID-19 pandemic

	Pre-pandemic (year 2017, n=4050)	Post-pandemic (year 2023, n=4002)	Odd ratio (OR, 95% CI)	P-value
Any DGBI	1550 (38.3%)	1704 (42.6%)	1.20 (1.09-1.31)	<0.0001
Esophageal disorders				
Functional heartburn	103 (2.5%)	110 (2.7%)	1.08 (0.83-1.42)	0.57
Functional chest pain	68 (1.7%)	81 (2.0%)	1.21 (0.87-1.68)	0.25
Reflux hypersensitivity	74 (1.8%)	68 (1.7%)	0.94 (0.67-1.30)	0.66
Globus	32 (0.8%)	33 (0.8%)	1.04 (0.64-1.70)	0.86
Functional dysphagia	189 (4.7%)	227 (5.7%)	1.23 (1.01-1.50)	0.04
Any esophageal disorder	357 (8.8%)	404 (10.1%)	1.16 (1.00-1.35)	0.05
Gastroduodenal disorders				
Functional dyspepsia	338 (8.3%)	475 (11.9%)	1.48 (1.28-1.71)	<0.0001
Postprandial distress syndrome	287 (7.1%)	418 (10.4%)	1.53 (1.31-1.79)	<0.0001
Epigastric pain syndrome	130 (3.2%)	169 (4.2%)	1.33 (1.05-1.68)	0.02
Belching disorder	49 (1.2%)	40 (1.0%)	0.82 (0.54-1.26)	0.37
Rumination syndrome	136 (3.4%)	167 (4.2%)	1.25 (0.99-1.58)	0.06
Chronic nausea and vomiting disorder	56 (1.4%)	81 (2.0%)	1.47 (1.05-2.08)	0.03
Cyclical vomiting syndrome	44 (1.1%)	73 (1.8%)	1.69 (1.16-2.47)	0.01
Cannabinoid hyperemesis syndrome	18 (0.4%)	16 (0.4%)	0.90 (0.46-1.77)	0.78
Any gastroduodenal disorders	481 (11.9%)	655 (16.4%)	1.45 (1.28-1.65)	<0.0001
Biliary disorders				
Functional biliary pain	2 (0.0%)	7 (0.2%)	3.55 (0.74-17.1)	0.11
Bowel disorders				
Irritable bowel syndrome (IBS)	189 (4.7%)	242 (6.0%)	1.31 (1.08-1.60)	0.01

Functional constipation	351 (8.7%)	360 (9.0%)	1.04 (0.89-1.22)	0.60
Functional diarrhea	193 (4.8%)	219 (5.5%)	1.16 (0.95-1.41)	0.15
Opioid induced constipation	92 (2.3%)	64 (1.6%)	0.70 (0.51-0.97)	0.03
Functional bloating/distension	109 (2.7%)	143 (3.6%)	1.34 (1.04-1.73)	0.02
Unspecified functional bowel disorder	309 (7.6%)	300 (7.5%)	0.98 (0.93-1.16)	0.82
Any bowel disorder	1220 (30.1%)	1302 (32.5%)	1.12 (1.02-1.23)	0.02
Anorectal disorders				
Fecal incontinence	126 (3.1%)	125 (3.1%)	1.00 (0.78-1.29)	0.98
Levator Ani syndrome	57 (1.4%)	77 (1.9%)	1.37 (0.97-1.94)	0.07
Proctalgia fugax	221 (5.5%)	214 (5.3%)	0.98 (0.81-1.19)	0.83
Any anorectal disorder	347 (8.6%)	364 (9.1%)	1.07 (0.92-1.25)	0.40

Note - Centrally mediated pain syndrome is not included in the table as there was only a single case found in the samples at each time point.

Table 2: Characteristics of individuals with or without DGBI (in the pre- and post-pandemic era)

	Pre-pandemic (year 2017)		Post-pandemic (year 2023)		
	No DGBI (n=2500)	DGBI[a] (n=1550)	No DGBI (n=2298)	DGBI[b] (n=1704)	P-value comparing DGBI positive groups (pre[a]- vs. post[b]-pandemic)
Mean age (SD)	49.8 (16.8)	44.8 (15.5)	49.2 (17.4)	44.3 (16.1)	0.41
Female	1122 (45%)	895 (58%)	1035 (45%)	965 (57%)	0.52
Anxiety (PHQ-4 subscale ≥3)	275 (11%)	487 (31.4%)	396 (17.2%)	669 (39.3%)	<0.0001
Depression (PHQ-4 subscale ≥3)	243 (9.7%)	455 (29.4%)	386 (16.8%)	646 (37.9%)	<0.0001
Medium/high somatic symptom severity (PHQ-12, ≥8)	332 (13.3%)	634 (40.9%)	458 (19.9%)	856 (50.2%)	<0.0001
PROMIS-10 PCS (SD)	15.6 (2.7)	13.4 (3.0)	14.9 (2.7)	12.9 (3.0)	<0.0001
PROMIS-10 MCS (SD)	14.8 (3.4)	12.6 (3.7)	13.4 (3.6)	11.4 (3.7)	<0.0001
Laxatives	132 (5.3%)	252 (16.3%)	150 (6.5%)	274 (16.1%)	0.89
Anti-diarrheals	84 (3.4%)	127 (8.2%)	120 (5.2%)	169 (9.9%)	0.09
Anti-emetics	59 (2.4%)	117 (7.5%)	113 (4.9%)	191 (11.2%)	<0.0001
Acid-suppressive drugs	357 (14.3%)	529 (34.1%)	460 (20.0%)	643 (37.7%)	0.03
Prescribed analgesia	319 (12.8%)	411 (26.5%)	369 (16.1%)	396 (23.2%)	0.03
Non-prescribed analgesia	328 (13.1%)	400 (25.8%)	431 (18.8%)	573 (33.6%)	<0.0001
Analgesia	584 (23.4%)	693 (44.7%)	700 (30.5%)	805 (47.2%)	0.15
Antispasmodics	106 (4.2%)	167 (10.8%)	135 (5.9%)	236 (13.8%)	0.01
Anxiolytics	226 (9.0%)	380 (24.5%)	338 (14.7%)	506 (29.7%)	0.001
Anti-depressants	273 (10.9%)	415 (26.8%)	352 (15.3%)	520 (30.5%)	0.02
Sedatives	195 (7.8%)	289 (18.6%)	269 (11.7%)	364 (21.4%)	0.05
GI-related healthcare visits	436 (17.4%)	607 (39.2%)	439 (19.1%)	648 (38.0%)	0.51
Concern regarding bowel habit					
Not at all	1890 (75.6%)	590 (38.1%)	1420 (61.8%)	488 (28.6%)	
Somewhat	494 (19.8%)	780 (50.3%)	720 (31.3%)	910 (53.4%)	<0.0001
Very concerned	116 (4.6%)	180 (11.6%)	158 (6.9%)	306 (18.0%)	

PCS, physical component score; MCS, mental component score.

Note: There was a significant difference in all variables (p<0.0001) between those with DGBI vs. without DGBI, in both 2017 and in 2023.

Table 3: Characteristics of individuals in the post-pandemic era with DGBI +/- long COVID

	DGBI without long COVID n=1507	DGBI with long COVID n=197	P-value
Mean age (SD)	44.3 (16.3)	44.7 (14.4)	0.76
Female	835 (55.4%)	130 (66.0%)	0.005
Anxiety (PHQ-4 ≥3 subscale)	565 (37.5%)	104 (52.8%)	<0.0001
Depression (PHQ-4 subscale ≥3)	549 (36.4%)	97 (49.2%)	<0.0001
Medium/high somatic symptom severity (PHQ-12, ≥8)	729 (48.4%)	127 (64.5%)	<0.0001
PROMIS-10 PCS (SD)	13.1 (2.9)	11.7 (2.9)	<0.0001
PROMIS-10 MCS (SD)	11.5 (3.8)	10.3 (3.3)	<0.0001
Laxatives	238 (15.8%)	36 (18.3%)	0.37
Anti-diarrheals	140 (9.3%)	29 (14.7%)	0.02
Anti-emetics	160 (10.6%)	31 (15.7%)	0.03
Acid-suppressive drugs	561 (37.2%)	82 (41.6%)	0.23
Analgesia	700 (46.4%)	105 (53.3%)	0.07
Antispasmodics	208 (13.8%)	28 (14.2%)	0.88
Anxiolytics	421 (27.9%)	85 (43.1%)	<0.0001
Anti-depressants	430 (28.5%)	90 (45.7%)	<0.0001
Sedatives	311 (20.6%)	53 (26.9%)	0.04
GI-related healthcare visits	545 (36.2%)	103 (52.3%)	<0.0001
Concern regarding bowel habit Not at all Somewhat Very concerned	 445 (29.5%) 805 (53.4%) 257 (17.1%)	 43 (21.8%) 105 (53.3%) 49 (24.9%)	 0.01

PCS, physical component score; MCS, mental component score

Figure 1: The prevalence of DGBI in the UK and USA, before and after the pandemic

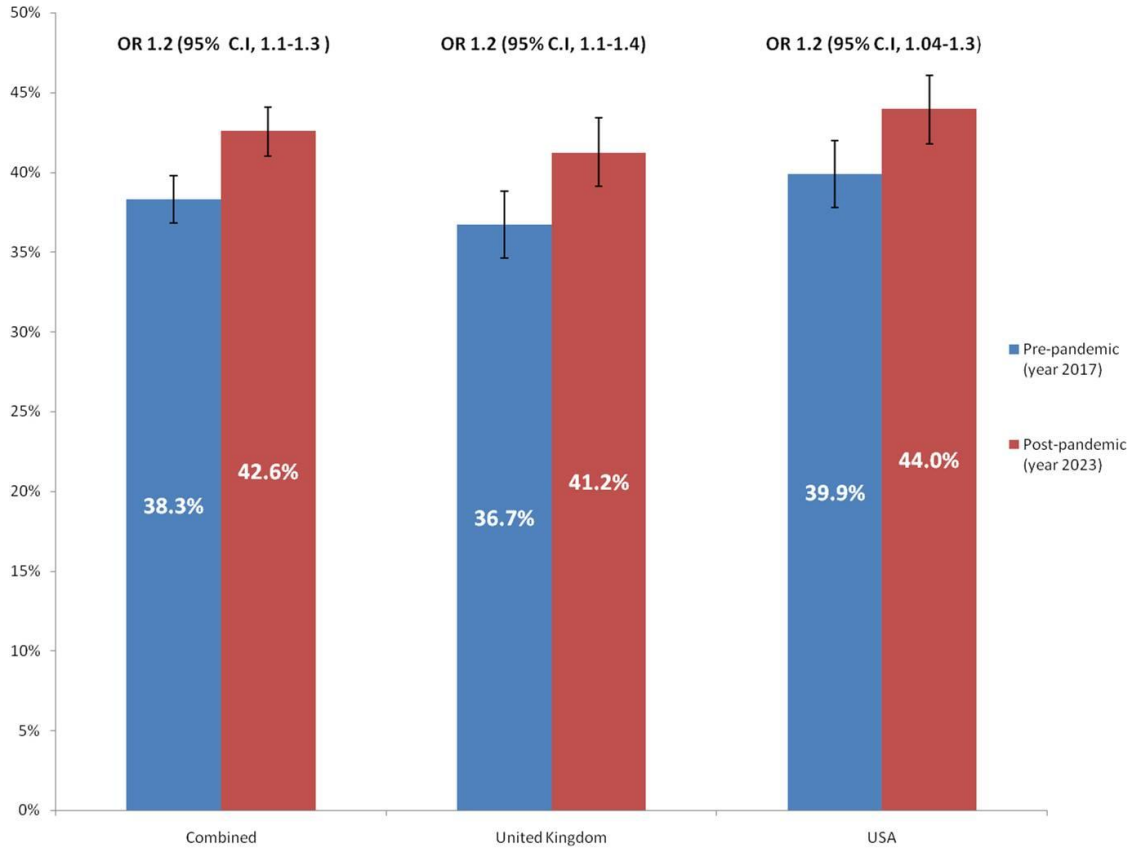

Figure 2: The prevalence of functional dyspepsia and IBS, before and after the pandemic