Title: Prevalence and Burden of Disorders of Gut-Brain Interaction Among UK Medical Students

Article type: Original Article

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Acknowledgment: Not applicable

Financing: Not applicable

Conflict of interest statement by authors: None

Compliance with ethical standards: Ethical approval was obtained from the University of Sheffield. Ref 044371

Authors Contribution Statement: LCB and IA conceived the study, contributed to the study design, collected data, analyzed the data, and wrote the initial manuscript. All authors had access to the study data, revised the manuscript, and approved the final version of the article. IA is guarantor of the article.

Manuscript word count: 3352

Abstract word count: 250

Number of Figures and Tables: 4 tables and 2 figures

Personal, Professional, and Institutional Social Network accounts.

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Discussion Points: How frequently do medical students experience gastrointestinal and associated symptoms?

Dates
Submission: 11/10/2023
Revisions:12/06/2023
Responses: 12/12/2023
Acceptance: 03/22/2024
Publication: 03/25/2024

Editors
Associate Editor/Editor: Francisco J. Bonilla-Escobar
Student Editors: Hang-Long (Ron) Li, Carlos de la Cruz-de la Cruz
Copyeditor:
Proofreader:
Layout Editor:

ABSTRACT.

Background: Disorders of Gut-Brain Interaction (DGBI) affect 40% of the general population and are associated with substantial health impairment. Medical students reportedly have among the highest rates of DGBI, although data is mainly confined to studies from Asia and Africa. We addressed this issue within a UK-based university.

Methods: An anonymous, online general health survey was completed by 378 of 1621 medical students. Demographic data, medical history, and gastrointestinal symptoms were collected, the latter using a modified Rome IV questionnaire to determine the presence of DGBI symptoms over the last 3 months. Additional validated questionnaires screened for somatisation, psychological distress, eating disorders, quality of life, and burnout.

Results: DGBI were present in 76% (n=289/378), of which two-of-three had multiple affected sites. The most frequent DGBI were gastroduodenal (57%), followed by bowel (49%), oesophageal (29%), and anorectal (26%) disorders. Approximately 50% of students with DGBI experienced painful gastrointestinal symptoms at least one day/week.

Students with DGBI, compared to those without, had significantly higher anxiety and depression scores, increased somatic symptom reporting, reduced mental and physical quality of life, poorer eating habits, and more frequent medication use (p-values, all <0.05). They were also at significantly higher risk of burnout, through study exhaustion and disengagement. The greatest health impairment was seen in those with multiple, painful, DGBI. Only 23% and 5% of students with DGBI had consulted a primary care provider and gastroenterologist, respectively, for their gastrointestinal symptoms.

Conclusion: Medical students commonly experience DGBI and associated health burden, yet infrequently seek help. Greater awareness may lead to increased support, improved health status, and better study engagement.

Key Words: Disorders of Gut-Brain Interaction; Functional Gastrointestinal Disorders; Medical students; Psychological distress; Burnout

INTRODUCTION.

Disorders of Gut Brain Interaction (DGBI), formerly known as functional gastrointestinal disorders, are defined as chronic gastrointestinal symptoms in the absence of organic gastrointestinal disease to explain the symptoms (i.e. no evidence of infection, inflammatory diseases, ulcers, or cancer).[1] The pathophysiology of DGBI is not fully known but can be best understood based on the biopsychosocial model of illness, and relates to any combination of visceral hypersensitivity, motility disturbances, alterations in mucosal and immune function, gut microbiota, and central nervous system processing. [1] Whilst irritable bowel syndrome (IBS) and functional dyspepsia are the most commonly recognized DGBI, there are a total of 22 DGBI which can arise from any of the following six anatomical regions within the gastrointestinal (GI) tract; the oesophagus, gastroduodenum, bowel, biliary, centrally mediated, and anorectum.

A recent global epidemiological study reported that over 40% of adults fulfill symptom-based criteria for a DGBI and incur considerable physical and mental health impairment, high healthcare utilization, decreased work productivity, and reduced quality of life.[2] Furthermore, one-in-three individuals with DGBI in the general population have multiple anatomical regions affected, which is associated with even greater health impairment.[3] Finally, eating disorders are common in patients with DGBI attending tertiary care medical centres, although their prevalence among people with DGBI within the community is unknown.[4]

There is data to suggest that medical students have amongst the highest rates of DGBI, with prevalence rates exceeding those reported within the general population (**supplementary table**). This, in part, may be explained by medical students across the globe experiencing high levels of stress, anxiety, depression, and burnout,[5,6] which could lead to gut symptoms through the bi-directional communication between the brain-gut axis. As shown in **supplementary table** the prevalence of IBS in medical students ranges from 4.8-61.7% (compared to 3.8% in the global adult population),[2] while the prevalence of functional dyspepsia ranges from 0.66-34.8% (compared to 7.2% globally).[2] However, most of this literature comes from Asia and Africa, and predominantly focuses on IBS and functional dyspepsia as opposed to all other DGBI, and with limited information on the general overall burden of DGBI amongst this cohort. As such, the present study aimed to determine the prevalence and burden of DGBI amongst medical students in the United Kingdom (UK).

METHODS

Following internal university assessment and ethical approval (ref 044371), this cross-sectional study was conducted at the University of Sheffield medical school during the academic year 2022-2023. Individuals currently enrolled within the medical school were invited in November 2022 to complete an online survey (using Google forms platform) regarding general physical and mental health. Completing and submitting the online survey was deemed as informed consent. The study was anonymous as no personal identification details were recorded (i.e. name, date of birth, university registration number, e-mail address). No financial incentives were provided. The following questionnaires were completed:

1. Demographics – age, gender, ethnicity, sexual orientation, year of study, and any substance use (i.e. tobacco, cannabis, alcohol, illicit drugs).

2. Medical history - this included any previous organic gastrointestinal diagnosis (i.e. inflammatory bowel disease, eosinophilic esophagitis, coeliac disease, gastrointestinal cancers), anxiety, depression, eating disorders, COVID-19 infection, and gastrointestinal surgery.

Individuals were also asked whether they took any of the following medications more than once per week – laxatives, anti-diarrhoeals, antiemetics, antispasmodics, acid-suppressive drugs, non-opioid/opioid painkillers, and medication for anxiety and/or depression.

3. Healthcare utilisation – individuals were asked if they had sought healthcare from their primary health care provider, a mental health specialist, or a gastroenterologist since starting at university.

4. Modified version of the Rome IV diagnostic questionnaire for DGBI[7] – in the interest of minimising this 86 point questionnaire, we selected 17 questions that specifically enquired for the presence of the following gastrointestinal symptoms: a) feeling of a lump or something stuck in the throat, b) pain in the middle of your chest, c) heartburn, d) food sticking in your chest after swallowing or going down slowly, e) felt so full after a regular sized meal, f) unable to finish a regular sized meal because you felt too full, g) pain or burning in your upper abdomen, h) nausea, i) vomiting, j) food coming back up into your mouth after you swallowed it, k) belching, l) pain in your lower abdomen, m) bloating or noticed your belly looks unusually large, n) constipation (i.e. hard stools or going several days without having a bowel movement), o) diarrhoea (i.e. watery mushy stools, or have many bowel movements in a day), p) accidental leakage of stool, and q) aching, pain or pressure in the rectum when you were not having a bowel movement.

Individuals were asked to record how frequently they experienced the above symptoms in the last 3 months, with the following options available - never, less than 2-3 days a month, 1 day a week, 2-3 days a week, most days, everyday, or multiple times per day. For DGBI to be considered then, in most instances, the relevant symptoms had to be present at least 1 day per week e.g. for functional dyspepsia, nausea and vomiting syndromes, IBS (abdominal pain and altered bowel habit), and functional bloating. However, for the other DGBI to be considered, the symptom frequencies were at least 1 day per month for functional anorectal

disorders, at least 2-3 days per month for faecal incontinence or rumination, at least 2-3 days per week for functional chest pain/heartburn/constipation/diarrhoea, and most days for belching.

Based on these answers - and in the absence of known organic GI disease - we were able to consider 17 DGBI across 4 anatomical regions (oesophagus, gastroduodenal, bowel and anorectal), with gallbladder disorders and centrally mediated disorders of gastrointestinal pain excluded due to their rarity in epidemiological studies.[2] In addition, some umbrella disorders were used instead of individual disorders, e.g. functional nausea and vomiting disorders was used to encompass chronic nausea vomiting syndrome, cyclic vomiting syndrome, and cannabinoid hyperemesis syndrome.

We further sub-divided DGBI into painful or non-painful, based on whether individuals experienced painful symptoms from any gastrointestinal organ domain at least one day per week.

5. SCOFF questionnaire[8] – this is a validated 5-question self-report screening tool for eating disorders, frequently used within primary care in the UK.[9] The validated cut-off of two or more positive responses was used to determine the presence of an eating disorder.[9]

6. Patient Health Questionnaire (PHQ)-12 somatisation score[10] – this validated questionnaire asks how "bothered" individuals have been by twelve non-GI somatic symptoms over the past 4 weeks. Each answer ranges from 0 (not bothered at all) to 2 (bothered a lot). Thus, a higher score indicates a higher level of somatisation, with the combined total ranging from 0-24. In addition, the number of affected somatic sites can be assessed, with a range of 0-12.

7. Hospital Anxiety and Depression Scale (HADS) questionnaire[11] - this validated questionnaire comprises 14 questions, with the results subsequently divided into two subscales for anxiety and depression score. A score of 11 or more in each subscale was considered to be evidence of clinical anxiety or depression, respectively.[11]

8. Short Form (SF)-8 questionnaire[12] – this validated 8-item questionnaire is used in epidemiological studies to assess general health related quality of life (QOL) over the past 4 weeks. The 8 items can be aggregated to form a physical component score (PCS) and mental component score (MCS), ranging from 0-100. A low MCS or PCS represents poorer QOL, whilst a high score represents better QOL.

9. Oldenburg Burnout Inventory (OLBI)[13] – this validated questionnaire assesses burnout, specifically in relation to work, across the two dimensions of OLBI-exhaustion and OLBI-disengagement. A higher score indicates a higher rate of burnout, with each subscale score ranging from 8-32. The questionnaire was adapted to make it more applicable to this study population, i.e. each time the word "work" appears in the questionnaire it was replaced by "work/ study".

Statistical analysis

Statistical analysis was conducted using IBM SPSS version 28 (SPSS Inc, Chicago, Illinois, United States). The level of significant was set at a *P*-value of <0.05.

Categorical variables were summarised using descriptive statistics and compared using chi-squared test, or Fisher's exact test, as necessary. In addition, odds ratios (OR) with 95% confidence intervals (CI) were calculated for some categorical variables between those with and without symptoms compatible with DGBI, and separately between those with painful and non-painful DGBIs. Continuous variables were summarised through the use of mean and standard deviation, with between-group comparison obtained through the use of an independent samples t-test. Finally, bivariate correlation was used to examine the strength and direction of the relationship between continuous variables

RESULTS.

Prevalence of DGBI

The online survey was disseminated to 1621 medical students of whom 378 completed, giving a response rate of 23%. The mean age of respondents was 21 years (SD 2.5), with 73% being female, and 70% of white ethnicity.

The prevalence of having at least one DGBI over the last 3 months amongst medical student respondents was 76% (n=289), with almost half affected by DGBI across multiple anatomical regions (see **Figure 1**). Prevalence of all individual DGBIs studied are displayed in **Table 1.** Amongst the entire cohort, the most frequently met diagnostic criteria for DGBI were gastroduodenal (n=214, 57%), followed by bowel (n=184, 49%), oesophageal (n=110, 29%), and anorectal (n=98, 26%) disorders. IBS and functional dyspepsia affected 17% and 28% of the cohort respectively, while other common DGBI included functional nausea and vomiting (37%), belching disorders (26%), anorectal disorders (25%), functional bloating (23%), functional chest pain (16%), globus (15%), and functional dysphagia (11%).

Comparison of Medical Students with DGBI vs. no-DGBI

Table 2 compares the DGBI cohort against those with no-DGBI. There was no difference in mean age or year of study, including when stratified into pre-clinical and clinical students. However, medical students with DGBI were over twice as likely to be female than those without (77% vs. 61%, OR 2.1, 95% CI 1.3-3.6). There was no difference between the two cohorts regarding self-reported smoking status, alcohol use or illicit drug use. However, a high number of individuals reported consuming alcohol in both groups (over 70%), although no quantification regarding frequency or amount of alcohol was obtained.

Medical students with DGBI were significantly more likely than those without DGBI to have previously been diagnosed with anxiety (28% vs. 12%, p=0.003) and depression (23% vs. 10%, p=0.01). They were also significantly more likely to use at least one type of GI medication (15% vs. 1%, p<0.001), and non-opioid painkillers (30% vs. 9%, p<0.001), compared to those without DGBI. Whilst those with DGBI were more likely to have sought healthcare at university for their gastrointestinal symptoms, this was still relatively low, with only 23% consulting a primary care provider, 33% a mental health specialist, and 5% a gastroenterologist.

In accordance with the SCOFF questionnaire, medical students with DGBI were almost three times more likely than those without DGBI to have an eating disorder (30% vs. 14%, p=0.002). They also had significantly worse mean somatisation scores (6.3 vs. 3.5, p<0.001), more somatic sites affected (4.9 vs. 2.9, p<0.001), and worse mean anxiety (9.0 vs. 6.5, p<0.001) and depression (4.2 vs. 2.9, p<0.002) scores. Finally, those with DGBI reported significantly worse quality of life and higher levels of burnout, regarding both study disengagement and exhaustion, than those without DGBI.

Multiple DGBI

Amongst those with at least one DGBI, almost 2-in-3 (63%) of individuals had multiple affected anatomical sites, and 12% had all 4 anatomical regions affected. The possible overlaps between anatomical regions are displayed **in Figure 2,** whilst **Table 3** demonstrates the correlation between increasing number of DGBIs and worsening quality of life (i.e. negative correlation), and greater burnout, somatisation, anxiety and depression scores (i.e. positive correlation).

Comparison of painful vs. non-painful DGBI

Table 4 compares the painful DGBI cohort against those with non-painful DGBI. We defined painful DGBI as having pain at least one day per week from any anatomical GI region; this case definition was met by 51% (n=147/289) of those with DGBI. Amongst those with painful DGBI, 58% (n=85) had one painful anatomical site, 27% (n=39) had two, 14% (n=20) had three and 2% (n=3) had painful DGBI across all 4 anatomical sites.

Individuals with painful DGBIs, and in particular those with multiple painful sites, were significantly more likely to have higher levels of anxiety, depression, somatisation, eating disorders, burnout, and reduced quality of life. They also reported significantly higher use of anti-spasmodic medications, acid suppressive drugs and non-opioid pain killers. While those with painful DGBI were significantly more likely to seek a healthcare provider, this was still relatively infrequent with 33% having seen a primary care provider, 46% a mental health specialist, and only 8% having seen a gastroenterologist.

DISCUSSION.

To our knowledge, this is the first study to examine the prevalence and burden of DGBI amongst UK medical students. We found that 76% of UK medical students who completed this anonymous online survey had symptoms compatible with a Rome IV DGBI, which is much higher than the reported prevalence of 37% amongst the UK general adult population.[2] Furthermore, almost two-thirds of medical students with DGBI had multiple affected anatomical sites, and over half experienced painful gastrointestinal symptoms at least once per week. The presence of DGBI was associated with psychological distress, somatic symptom reporting, eating disorders, burnout, and reduced quality of life, yet medical students infrequently seek help for their symptoms, even when painful.

The general health burden of DGBI as seen in medical students aligns with that reported for the general population, although it appears to be of a greater severity. For example, over 50% of medical students with DGBI experience frequent painful symptoms - which in itself correlated with increased physical and mental distress – in comparison to 26% of UK adults with DGBI having painful DGBI.[14] Many of the risk factors for painful DGBI (e.g. female sex, gastroenteritis, abuse, stress, poor sleep, obesity, psychological disorders, and somatic symptoms) were explored and apparent within our medical student cohort.[15] Protective factors against painful DGBI in adults include social support and optimism, [15] yet rates of healthcare utilisation or support for DGBI symptoms were low amongst medical students. For instance, less than a quarter of those with DGBI, and only a third of those with painful DGBI, had consulted a primary care provider regarding their GI symptoms. This supports previous findings that medical students have low rates of healthcare consultation for DGBI symptoms[16-18] although reasons for this remain unclear. Possible fear of repercussions regarding training progression and general stigma surrounding ill-health can prevent medical students from seeking help for their physical and mental health.[19,20] DGBI are also under-taught within medical education which might lead to a lack of awareness of these disorders amongst medical students.[21]

A high proportion of medical students with DGBI had associated psychological distress, burnout (i.e. study exhaustion and disengagement) and eating disorders. These factors have been reported in DGBI within the general population, but are arguably more prevalent within medical students given the extensive demands placed upon them from a relatively young age.[5,6] Medicine has traditionally been considered as a highly demanding and stressful course, with a competitive admission process followed by frequent and rigorous examinations over a 5 to 6 year period.[5,6] Moreover, students face additional pressures to conduct research, publish in scientific journals, teach, build management and leadership skills and win prizes in order to choose the speciality of their choice. Additional stressors over this time-period include relationships, financial difficulties and housing issues, all of which have been heightened by the COVID-19 pandemic.[5,6] Hence, it is not surprising that high levels of psychiatric illness, burnout and substance use are being reported by medical students across the globe.[5,6] A recent study found that 29% of medical students respondents were given a mental health diagnosis whilst at medical school, and 82% could be classified as 'disengaged' and 85% 'exhausted' using the Oldenburg Burnout Scale.[22] In England and Wales, over 80% of medical students have high levels of burnout,[22,23] whilst a global systematic review and meta-analysis reported that medical students have a higher burden of burnout than age-matched peers.[24] An association between burnout and IBS has

been reported,[25,26] which our study builds upon by highlighting the relationship between burnout and overall DGBI amongst medical students. Similarly, there is association between eating disorders and DGBI,[4] and a global systematic review found medical students have higher rates of eating disorders than the general adult population.[27] In summary, the combination of DGBI and its associated health impairment may lead to reduced academic performance, increased dropout, and potential long-term consequences for patient safety. Medical schools should therefore become familiar with the high prevalence and burden of DGBI, openly raise awareness of these conditions, and sign-post students to seek help via appropriate channels. Future research studies should look into interventions suggested for DGBI but specifically within medical students (e.g. diet, lifestyle, exercise, antispasmodics, psychological support etc). Hopefully, these measures will not just positively impact upon medical students as they progress to doctors, but also for patients and the healthcare system as a whole.

There are limitations to this study. First, the cross-sectional study design identifying an association between DGBI and other co-morbidities does not infer causality. Second, it was conducted at only one university, and may not be representative of medical students at other UK institutions. Moving forward, it raises interest to conduct further studies of DGBI in medical students elsewhere, but also among junior doctors in whom a high prevalence of stress and burnout, leading to career disengagement and reduced patient quality of care, is increasingly being recognised.[28] Third, there was no comparative control group, either from another course within the university or the general population. However, the prevalence of DGBI within medical students reported in this UK study, and that from India, far exceed those reported within their respective general populations.[2,29] The study from India also reported DGBI to be significantly more common in medical students than its humanities students.[29] Fourth, the low response rate of 23% (n=378/1621) may mean that the reported prevalence of DGBI as 76% (n=289/378) is not reflective of the prevalence of DGBI amongst the entire cohort of medical students at the university. However, we aimed to reduce potential selection bias by promoting the study as an evaluation of physical and mental health, as opposed to specifically mentioning gastrointestinal symptoms. Nevertheless, the results could be extrapolated to calculate the minimum possible prevalence of DGBI for the entire population of medical students at the university, i.e. if all the non-responders were presumed to lack any symptoms compatible with DGBI, the minimum prevalence of DGBI in this cohort would be 18% (n=289/1621). This equates to almost 1-in-5 medical students and still suggests a high prevalence. Fifth, the predominance responders to the survey were female (73%), although the female to male ratio in the medical school is almost 1:1, again adding to potential selection bias. Sixth, we did not use the Rome IV diagnostic questionnaire in its entirety, as it encompasses 86 questions with a complex scoring algorithm, but rather selected 17 pertinent questions that captured the spectrum of gastrointestinal symptoms followed by using clinically relevant frequency cut-offs to determine the presence of DGBI and also painful DGBI. Further, the Rome diagnostic criteria require symptoms to be active over the last 3 months but to have started at least 6 months prior. The latter we did not enquire for and might therefore have over-estimated the prevalence of Rome IV DGBI, although the frequent presence of symptoms, in particular those that are painful, is nevertheless of concern. Seventh, the use of an anonymous study questionnaire meant that results could not be corroborated through clinical notes, nor could investigations be done. As such, some of the reported symptoms may have been due to underlying organic disease, although this is unlikely in individuals of a relatively young age reporting chronic symptoms. Finally, the most common DGBI in this study was

functional nausea and vomiting disorders, with a prevalence of 37%, which is much higher than the global prevalence of around 1.0% in the 18-39 age group.[2] This marked difference may be due to a high rate of alcohol use in the study population, with 78% of medical students drinking alcohol, although we did not quantify individuals' drinking habits. Previous research suggests that UK medical students have high rates of alcohol misuse.[30] Therefore, for some individuals in this study, the symptoms of functional nausea and vomiting disorders may have instead been caused by alcohol consumption.

In conclusion, DGBI are common and burdensome among UK medical students, yet they infrequently seek help for their symptoms, even when painful. Increased awareness of DGBI amongst medical students may lead to improved support, health status, and study engagement.

SUMMARY - ACCELERATING TRANSLATION

Disorders of gut-brain interaction (DGBI) are chronic gastrointestinal symptoms that occur in the absence of organic disease. In this UK based study, the prevalence of symptoms compatible with DGBI amongst medical students at Sheffield University was 76%, of whom two-of-three had multiple affected anatomical sites. Approximately 50% of medical students reported experiencing pain from a GI region at least once per week. The presence of DGBI (in particular, multiple painful DGBI) was associated with anxiety, depression, somatisation, eating disorders, reduced quality of life, and burnout through study disengagement and exhaustion. Medical students with DGBI had low healthcare utilisation relative to their symptom burden. Our findings will help increase awareness of DGBI amongst medical students and may lead to improved support, health status, and study engagement.

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FIGURES AND TABLES.

Figure 1. The number of anatomical regions affected by DGBIs amongst 378 medical students

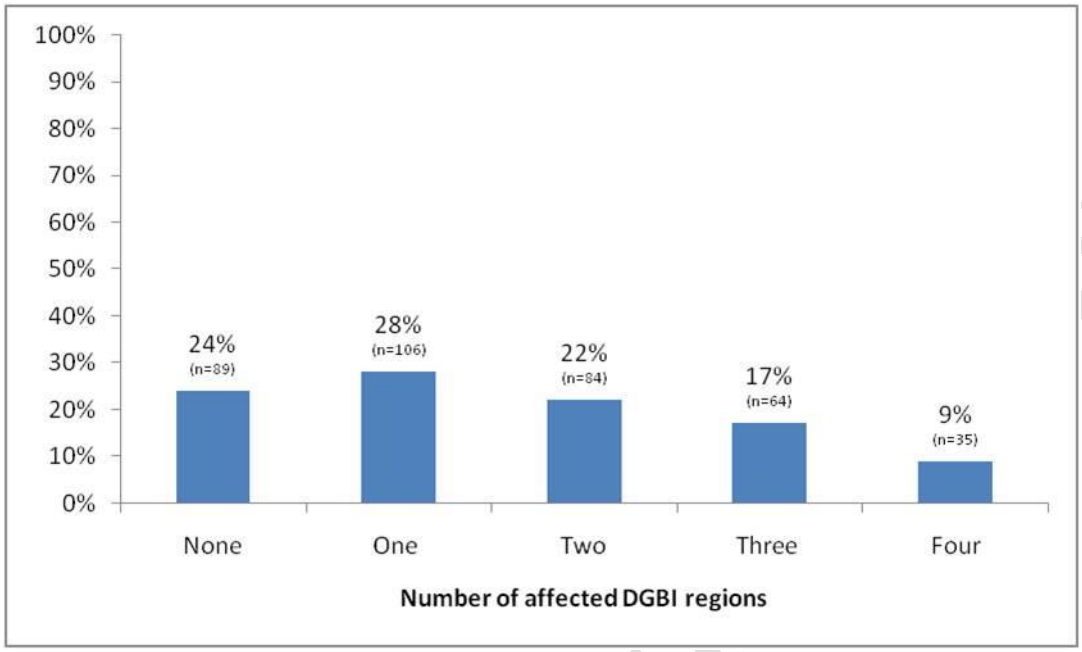

Figure 2. *Venn diagram showing the overlap between anatomical regions in those medical students with DGBI (n=289)*

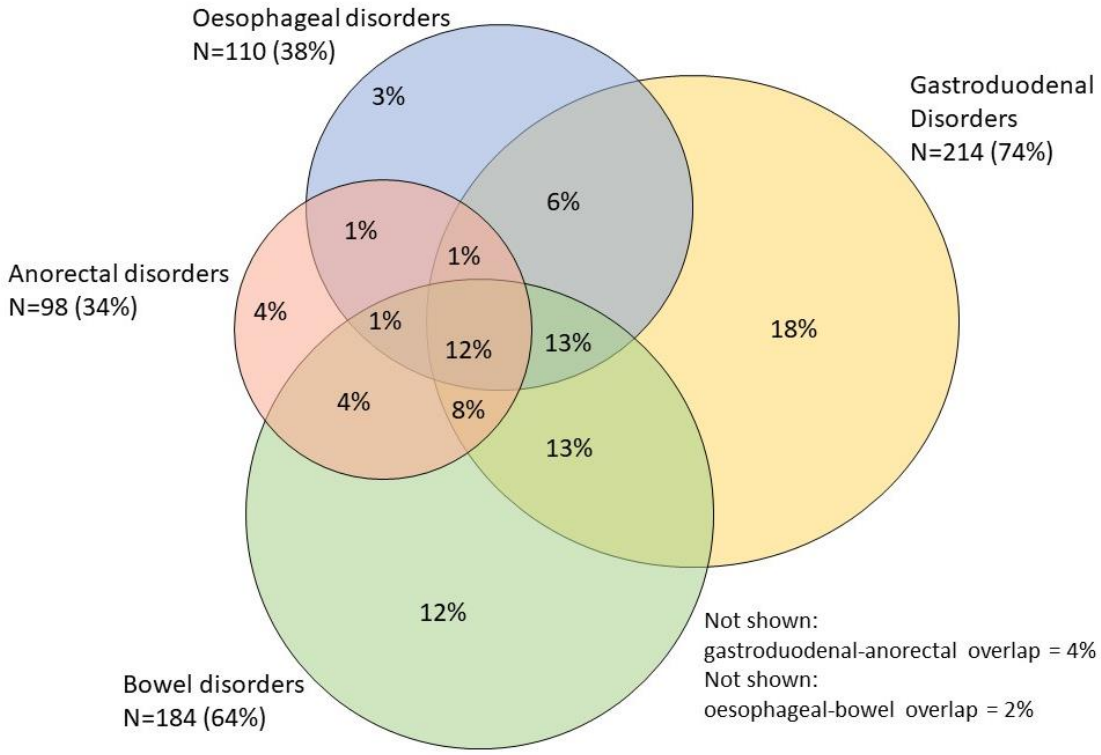

Table 1. Prevalence of specific DGBI diagnoses amongst medical students (n=378)

Anatomical region	Disorder of Gut-Brain Interaction	N (%)
Oesophageal (n=110, 29%)	Globus	57 (15%)
	Functional chest pain	61 (16%)
	Functional heartburn	35 (9%)
	Functional dysphagia	40 (11%)
Gastroduodenal (n=214, 57%)	Functional dyspepsia (FD)	106 (28%)
	Post prandial distress syndrome (PDS)	78 (21%)
	Epigastric pain syndrome (EPS)	45 (12%)
	Functional nausea and vomiting disorders	141 (37%)
	Rumination syndrome	26 (7%)
	Belching disorders	98 (26%)
Bowel (n=184, 49%)	Irritable bowel syndrome (IBS)	63 (17%)
	Functional constipation	16 (4%)
	Functional diarrhoea	14 (4%)
	Unspecified bowel disorder	3 (1%)
	Functional bloating	88 (23%)
Anorectal (n=98, 26%)	Faecal incontinence	12 (3%)
	Functional anorectal disorders	93 (25%)

Note: Functional nausea and vomiting disorders includes chronic nausea vomiting syndrome, cyclic vomiting syndrome, cannabinoid hyperemesis syndrome. Functional anorectal pain disorders include levator ani syndrome and proctalgia fugax.

Table 2. Characteristics of medical students with and without Rome IV DGBI

	Symptoms not compatible with a Rome IV DGBI (N=89)	Symptoms compatible with Rome IV DGBI (N=289)	P value	Odds ratio (95% CI)
Demographics:				
Mean age in years (SD)	20.6 (2.5)	20.8 (2.5)	0.69	--
Mean year of study (SD)	2.6 (1.5)	2.6 (1.5)	0.93	--
Pre-clinical	47 (53%)	167 (58%)	0.41	1.2 (0.8-2.0)
Female	54 (61%)	222 (77%)	0.003	2.1 (1.3-3.6)
Heterosexual	77 (87%)	201 (70%)	0.002	0.4 (0.2-0.7)
White	53 (60%)	212 (73%)	0.013	1.9 (1.1-3.1)
Drink Alcohol	66 (74%)	239 (83%)	0.074	1.7 (0.9-2.9)
Smoke Tobacco	5 (6%)	14 (5%)	0.78	0.9 (0.3-2.4)
Use Cannabis/ Marijuana	5 (6%)	17 (6%)	0.93	1.1 (0.4-2.9)
Use other illicit drugs	2 (2%)	16 (6%)	0.26	2.5 (0.6-11.3)
Past medical history:				
Anxiety	11 (12%)	81 (28%)	0.003	2.8 (1.4-5.5)
Depression	9 (10%)	65 (23%)	0.01	2.6 (1.2-5.4)
Eating disorder	3 (3%)	18 (6%)	0.43	1.9 (0.5-6.6)
COVID-19 infection	45 (51%)	197 (68%)	0.002	2.1 (1.3-3.4)
Any abdominal surgery	7 (8%)	20 (7%)	0.76	0.9 (0.4-2.1)
Medication use:				
Any GI medication	1 (1%)	42 (15%)	<.001	15.0 (2.0-110.3)
Constipation	0 (0%)	9 (3%)	0.12	0.8 (0.7-0.8)
Diarrhoea	0 (0%)	9 (3%)	0.12	0.8 (0.7-0.8)
Nausea	0 (0%)	7 (2%)	0.21	0.8 (0.7-0.8)
Antispasmodics	0 (0%)	9 (3%)	0.12	0.8 (0.7-0.8)
Stomach acid	1 (1%)	24 (8%)	0.02	8.0 (1.1-59.8)
Non-opioid painkillers	8 (9%)	87 (30%)	<.001	4.4 (2.0-9.4)
Opioid painkillers	0 (0%)	3 (1%)	1.000	0.8 (0.7-0.8)
Anxiolytics/ antidepressants	6 (7%)	41 (14%)	0.06	2.3 (0.9-5.6)
Healthcare utilisation:				
Primary care	8 (9%)	66 (23%)	0.004	3.0 (1.4-6.5)
Gastroenterologist	5 (6%)	15 (5%)	0.79	0.9 (0.3-2.6)
Mental health	19 (21%)	98 (34%)	0.03	1.9 (1.1-3.3)
Burden of DGBIs:				
Eating Disorder (SCOFF ≥2)	12 (14%)	87 (30%)	0.002	2.8 (1.4-5.3)
HADS-Anxiety ≥ 11	14 (16%)	101 (35%)	<.001	2.9 (1.5-5.3)
HADS-Depression ≥ 11	3 (3%)	21 (7%)	0.19	2.2 (0.7-7.7)
Burden of DGBI, Mean (SD)				
PHQ-12 score	3.5 (2.9)	6.3 (3.6)	<.001	--
Number of PHQ-12 sites	2.9 (2.1)	4.9 (2.5)	<.001	--
SF-8 PCS QOL	83.1 (1.45)	73.8 (18.5)	<.001	--
SF-8 MCS QOL	72.1 (21.1)	61.9 (20.0)	<.001	--
HADS-Anxiety score	6.5 (4.0)	9.0 (4.3)	<.001	--
HADS-Depression score	2.9 (3.1)	4.2 (3.5)	<.002	--
OLBI-Disengagement score	17.0 (4.0)	18.2 (4.0)	0.01	--
OLBI-Exhaustion score	19.3 (4.1)	21.5 (4.1)	<.001	--

N (%) *unless otherwise indicated*

Table 3 Relationship between psychological distress and number of anatomical sites affected by DGBIs

	Number of anatomical sites affected by DGBIs	
Variable	**Correlation**	**P value**
SF-8 MCS QOL	-0.397	<.001
SF-8 PCS QOL	-0.389	<.001
OLBI-Disengagement score	0.245	<.001
OLBI-Exhaustion score	0.314	<.001
PHQ-12 somatic score	0.528	<.001
Number of PHQ-12 sites	0.526	<.001
HADS-Anxiety score	0.461	<.001
HADS-Depression score	0.293	<.001

Table 4: Comparison between medical students with and without painful DGBI

Cohort with DGBI n=289	Non-painful DGBIs (n=142)	Painful DGBIs (n=147)	P value	Odds ratio (95% CI)	
Demographics					
Mean age in years (SD)	20.5 (2.6)	21.0 (2.4)	0.06	--	
Mean year of study (SD)	2.4 (1.6)	2.8 (1.4)	0.05	--	
Pre-clinical	87 (61%)	80 (54%)	0.24	0.8 (0.5-1.2)	
Female	99 (70%)	123 (84%)	0.005	2.2 (1.3-3.9)	
Heterosexual	105 (74%)	96 (65%)	0.11	0.7 (0.4-1.1)	
White	96 (68%)	116 (79%)	0.03	2.8 (1.1-3.0)	
Past medical history					
Anxiety	23 (16%)	58 (40%)	<.001	3.4 (1.9-5.9)	
Depression	15 (11%)	50 (34%)	<.001	4.4 (2.3-8.2)	
Eating disorder	3 (2%)	15 (10%)	0.004	5.2 (1.5-18.6)	
COVID-19 Infection	95 (67%)	102 (69%)	0.65	1.1 (0.7-1.8)	
Any abdominal surgery	9 (6%)	11 (8%)	0.70	1.2 (0.5-3.0)	
Medication use					
Any I medication	12 (9%)	30 (20%)	0.004	2.8 (1.4-5.7)	
Constipation	4 (3%)	5 (3%)	1.00	1.2 (0.3-4.6)	
Diarrhoea	3 (2%)	6 (4%)	0.50	2.0 (0.5-8.0)	
Nausea	2 (1%)	5 (3%)	0.45	2.5 (0.5-12.9)	
Antispasmodics	1 (1%)	8 (5%)	0.04	8.1 (1.0-65.7)	
Stomach acid	6 (4%)	18 (12%)	0.01	3.2 (1.2-8.2)	
Non-opioid painkillers	34 (24%)	53 (36%)	0.03	1.8 (1.1-3.0)	
Opioid painkillers	1 (1%)	2 (1%)	1.00	1.9 (0.2-21.7)	
Anxiolytic/ antidepressants	10 (7%)	31 (21%)	<.001	3.5 (1.7-7.5)	
Healthcare utilisation at university					
Primary care	17 (12%)	49 (33%)	<.001	3.7 (2.0-6.8)	
Gastroenterologist	4 (3%)	11 (8%)	0.07	2.8 (0.9-9.0)	
Mental health	30 (20%)	68 (46%)	<.001	3.2 (1.9-5.4)	
Burden of DGBIs:					
Eating Disorder (SCOFF ≥2)	33 (23%)	54 (37%)	0.01	1.9 (1.1-3.2)	
HADS-Anxiety ≥ 11	31 (22%)	70 (48%)	<.001	3.3 (1.9-5.4)	
HADS-Depression ≥ 11	6 (4%)	15 (10%)	0.05	2.6 (1.0-6.8)	
Burden of DGBIs: Mean (SD)				**Number of painful DGBI sites**	
				Correlation	**P value**
PHQ-12 somatic score	4.9 (2.9)	7.5 (3.8)	<.001	0.446	<.001
Number of PHQ-12 sites	4.0 (2.2)	5.8 (2.5)	<.001	0.432	<.001
SF-8 PCS QOL	79.8 (14.6)	68.1 (20.0)	<.001	-0.322	<.001
SF-8 MCS QOL	69.1 (17.6)	55.0 (19.8)	<.001	-0.348	<.001
HADS-Anxiety score	7.7 (3.9)	10.3 (4.3)	<.001	0.414	<.001
HADS-Depression score	3.6 (3.1)	4.8 (3.7)	0.003	0.245	<.001
OLBI-Disengagement score	17.6 (3.7)	18.8 (4.1)	0.01	0.184	0.002
OLBI-Exhaustion score	21.0 (4.1)	22.1 (4.0)	0.02	0.192	<.001

N (%) unless otherwise indicated