

Supplementary information

Rome Foundation Working Team Report on overlap in disorders of gut–brain interaction

In the format provided by
the authors and unedited

SUPPLEMENTARY TABLE 1 | Detailed Summary of literature on DGBI overlap within and across anatomical regions

Authors (year)	Country	Participant age	DGBI overlap disorders and measure used to define	Study design	Study setting and recruitment	Participant characteristics (sample size, mean age and age range, sex) and findings	Measure used to assess risk and/or protective factor	Additional Details
DGBI Overlap <i>Within</i> Anatomical Regions								
Oesophageal DGBI Overlap								
Adult studies								
Bang et al (2015)¹	Korea	Adults in 20s	Rome III criteria	Military service-based cross-sectional study	8 different regiments of male soldiers from three different divisions of the Republic of Korea army from 1/2013 to 5/2013	N=967 participants, mean 21 years	Symptom Checklist-90-revised (SCL-90R)	Functional heartburn (FH) + Functional chest pain (FCP): 4 participants (0.4%), 2.2% of DGBI. FH + FCP + FD: 7 participants (0.7%), 3.9% of DGBI
Mudipalli et al (2007)²	United States	Adults	FCP (Rome II) Control patients without FCP	Clinic-based cross-sectional study	Consecutive patients referred to tertiary care center over a 2-year period with functional chest pain (FCP) of presumed oesophageal origin	N=100, 75 female, age 52 ±13 years old. N=69 responders (69%), 54 female	Demographics GI symptom questionnaire Oesophageal balloon testing and impedance planimetry	82% fulfilled criteria for other DGBI: dyspepsia (7%), dysphagia (7%) Oesophageal hypersensitivity in 78% patients with FCP
Rengarajan et al (2021)³	United States and France	Adults >18 years old	RH and FH (Rome IV)	Clinic-based cross-sectional study	Consecutive patients with oesophageal and extra-oesophageal symptoms suspicious for GERD refractory to PPI therapy	N=79 patients with functional oesophageal disorders FH: 60 patients (31 [51.6%] with overlap FH+RH) RH: 19 patients (10 [52.6%] with overlap RH+FH) NERD: 26 patients	Reflux diagnostic questionnaire, Hospital Anxiety and Depression Scales (HADS), Visceral sensitivity index (VSI) pH /impedance testing	Oesophageal acid burden similar in RH and FH, more reflux episodes with RH Similar anxiety/depression levels in RH and FH Portion of overlap with FD (33-44%) and IBS (13-27%) not statistically different Clinical, psychological, and functional profiles of overlap FH/RH similar to pure FH or RH Baseline impedance (MBNI) may help identify a true functional heartburn phenotype

Gastroduodenal DGBI Overlap								
Adult studies								
Yamawaki et al (2014) ⁴	Japan	Adults	EPS (Rome III) PDS (Rome III)	Clinic-based cross-sectional survey	Patients with FD: Nippon Medical School clinic patients HV: medical students/staff at Nippon Medical School	N=79 participants PDS: 65 patients (82.2%) EPS: 47 patients (59.4%) EPS+PDS overlap: N=33 patients (41.7%) HV: 44 patients	Glasgow Dyspepsia Severity Scale (GDSS) SF-8 HRQOL (Japanese version) Sodium acetate gastric emptying testing Pittsburgh Sleep Quality Index (PSQI; Japanese version)	No significant differences in GDSS, PSQI, SF-8 among the FD subtypes, all significantly different from HV T max and T1/2 significantly associated with GDSS in all FD subtypes
Nwokediuko et al (2012) ⁵	Nigeria	Adults	PDS (Rome III) EPS (Rome III) IBS (Rome III)	Clinic-based cross-sectional survey	Consecutive patients referred for endoscopy University of Nigeria Teaching Hospital Ituku Ozalla, Enugu, and Uzoma Specialty Clinic Trans Ekulu Engunu, Enugu State of Nigeria from 8/2010 to 5/2012	N= 428 patients presenting for endoscopic evaluation of upper GI symptoms Dyspepsia: 296 (69.1%) patients; 184 (62.2%) female FD: 192 patients (64.9%) EPS: 152 patients (79.2%) PDS: 62.5% EPS + PDS: 96 (50%)	Upper GI symptoms Demographics, lifestyle factors, employment status Medication use	Smoking, alcohol and NSAID use associated with EPS+PDS Concomitant IBS predictor of EPS and PDS separately, but not EPS+PDS

Fang et al (2015)⁶	Taiwan	Adults >20 years old	PDS (Rome III) EPS (Rome III)	Clinic-based cross-sectional survey	Consecutive patients referred for dyspeptic symptoms at outpatient clinics of National Taiwan University Hospital (NTUH) or Yun-Lin Branch from 1/2010 to 5/2012 HV: asymptomatic patients undergoing gastric cancer screening	N=2378 with dyspeptic symptoms FD: 491 patients PDS:353 (71.9%) EPS:298 (60.7%) EPS+PDS: 169 (34.4%) HV: 1031 asymptomatic individuals	Demographics, lifestyle factors, occupation, education Brief Symptom Rating Scale-5 (BSRS-5) EGD evaluation H. pylori testing (13C-urea, positive culture, or rapid urease test ±histology ±serology [2 of 3])	Coffee consumption inversely associated with FD and pure PDS, but not pure EPS or EPS+PDS Sleep disturbances associated with pure PDS, and EPS+PDS but not pure EPS Depression associated with pure PDS but not pure EPS or EPS+PDS. H. pylori infection only associated with pure PDS (not EPS, EPS+PDS) Trend towards more marked gastric atrophy, and CagA positive strains in pure PDS vs EPS or EPS+PDS
Zagari et al (2010)⁷	Italy	Adults ≥18 years old	FD (Rome II) Meal-related symptoms subgroup ("PDS") Epigastric pain subgroup ("EPS")	Population-based, random cross-sectional survey	Recruited from villages of Loiano and Monghidoro as part of the Multicentre Italian Study on Cholelithiasis (MICOL)	N=1033 participants (mean age 55.8 years, 51.1% male) Dyspepsia: 156 (17.3%) FD: 114/156 (73.1%); 11% prevalence in study population "PDS": 77 ^65.5% of FD), 7.4% prevalence "EPS": 55 (48.2% of FD) , 5.1% prevalence "EPS +PDS": 18 (15.8% of FD); 1.7% prevalence overall	Demographics, education level , occupation, marital status, weight, lifestyle factors, medication use GI symptom questionnaire EGD evaluation H pylori status	"EPS+PDS" statistically less than expected by chance (18 observed vs 37 expected) Unemployed and divorced risk factors for "EPS+PDS" Smoking risk factor for "EPS" but not "PDS" IBS associated with both "EPS" and "PDS"
Manabe et al (2010)⁸	Japan	Adults	PDS (Rome III) EPS (Rome III) Chronic idiopathic nausea (CIN)	Clinic-based cross-sectional survey	Consecutive patients presenting to Kawasaki Medical School Hospital or six affiliated general hospitals complaining of weekly symptoms from 8/2006 to 5/2008	N=364 participants FD: 198/364 (54.9%), 49.3% years, 57.1% female EPS: 161/198 (81.3%) PDS: 111/198 (56.1%) CIN:77/198 (38.9%) EPS+PDS: 80/198 (40.4%) EPS+CIN: 49/198 (24.7%) PDS+CIN: 64/198 (32.3%)	Demographics, lifestyle factors, BMI Upper GI symptom severity (7-point Likert)	Non-erosive reflux disease accounted for 52.0% (103/198) of all participants; Rome III classification could not be applied to 62.7% of the PDS group and 61.3% of the EPS group because the onset of symptoms< 6 months

Vakil et al (2013)⁹	Western Europe and Canada	Adults ≥18 years old	PDS (Rome III) EPS (Rome III) EPS+PDS (Rome III)	Clinic-based cross-sectional survey	Primary care patients presenting with "upper GI symptoms" at least 2x per week, part of Diamond study (NCT 00291746)	N=336 participants PDS: 36 (19%) EPS: 42 (22%) EPS+PDS: 81 (43%)	Demographics, lifestyle factors Reflux Disease Questionnaire (RDQ) EGD evaluation 48-hour pH testing	PDS, EPS, and EPS+PDS had similar upper GI symptoms overall; greater bloating, early satiety and central upper abdominal pain in EPS+PDS Similar duration of symptoms across all 3 FD subgroups Female sex and lower BMI increased OR of FD diagnosis vs. GERD
Hsu et al (2009)¹⁰	Taiwan	Adults ≥18 years old	FD (Rome III) PDS (Rome III) EPS (Rome III)	Clinic-based cross-sectional survey	Consecutive patients presenting to Lotung Poh-Ai Hospital, Yilan outpatient GI clinics with dyspepsia symptoms	FD: 187 participants; 72.1% female, 42.6±14.7 years EPS + PDS overlap (n=64, 34.2%) between EPS (n=157, 84.0%) and PDS (n=94, 50.3%)	Demographics Brief Symptom Rating Scale (BSRS) Maudsley personality inventory (short form)	PDS: higher psychopathological stress, including somatization, depression, phobia, neuroticism (univariate), and additional symptoms EPS not associated with psychopathology EPS+PDS: more severe psychopathology than either subgroup without overlapping
Wang et al (2008)¹¹	China	Adults ≥18 years old	FD (Rome III) PDS (Rome III) EPS (Rome III) IBS (Rome III)	Clinic-based cross-sectional survey	Consecutive patients presenting to general GI outpatient clinic at Sun Yatsen University affiliated hospital in Guangzhou, China	N=3014 participants; 52.8% female, 43.2±15.9 (range 18-97) years old FD: 608/3014 (20.2%) FD alone: 457/608 (75.1%); 15.2% prevalence FD+IBS overlap: 151/457 (33.0%); 5.0% prevalence	Dyspepsia and bowel symptom severity (6-point scale), bowel symptoms (6-point scale)	PDS alone: 223/608 (36.7%) EPS alone: 224/608 (26.8%) EPS+PDS: 161/608 (26.4%); overlap more common in IBS+FD than FD alone (P=0.02) Greater risk of IBS+FD overlap with post-prandial fullness symptoms (P=0.005)
Carbone et al (2020)¹²	Belgium	Adults	FD (Rome III and IV) EPS (Rome III and IV) PDS (Rome III and IV)	Clinic-based cross-sectional survey	Consecutive patients with dyspepsia referred for gastric emptying testing	N=168 participants (67% women, 44.9 ±1.2 years old) Rome III: PDS alone (29/96, 29%), EPS (9/96, 10%), overlapping EPS+PDS (58/96, 61%) Rome IV: PDS alone (70/96, 72.9%; EPS alone (9/96, 9.3%, EPS+PDS 17/96, 17.7%)	Demographics Meal-related dyspeptic symptoms at baseline and up to 4 hours after a meal Gastric emptying breath test	65% patients reported meal-related exacerbation of symptoms 70% Rome III pure PDS and EPS+PDS reported meal-related symptoms; 84% Rome IV pure PDS reported meal-related symptoms 72% Rome III EPS+PDS reported meal-related symptoms, 47% using Rome IV criteria

Vanheel et al (2017)¹³	Belgium	Adults	EPS (Rome III) PDS (Rome III)	Clinic-based cross-sectional survey	Consecutive FD patients recruited from the outpatient gastroenterology department at the University Hospitals Leuven	N=560 patients with FD (395 female, 41.8 ±0.7 years) PDS: 23% (89 female, 42 male) EPS 9% (34 female, 16 male) EPS+PDS overlap 68% (272 female, 107 male)	Rome III questionnaire to assess dyspepsia symptoms Demographics Gastric barostat testing to assess gastric sensitivity testing and accommodation Gastric emptying for solids using 14C octanoate breath testing	Findings in overall cohort: gastric hypersensitivity (37%), impaired gastric accommodation (37%), delayed gastric emptying (23%), no differences in distribution by Rome III subgroups EPS+PDS overlap group had higher T1/2 on gastric emptying vs. EPS group EPS+PDS overlap group gastric hypersensitivity associated with PDS symptom severity (P=0.03), EPS symptoms (P=0.02), and cumulative symptom score (P=0.02)
Van den Houte et al (2021)¹⁴	Belgium	Adults 18-70 years old	EPS (Rome III and IV) PDS (Rome III and IV)	Clinic-based cross-sectional study	Patients from 8 gastroenterology secondary care sites in Belgium	N=224 patients with FD (77% female, mean age 43.1 ±1, years old) Rome III: 25% PDS, 8% EPS, 67% overlap EPS+PDS Rome IV: 57% PDS, 8% EPS, 35% EPS+PDS	Demographics Dyspepsia symptom patterns	Postprandial fullness, early satiation, and bloating significantly more common in PDS and EPS+PDS groups vs. pure EPS Postprandial nausea more prevalent in EPS+PDS than pure PDS
Carbone et al (2015)¹⁵	Belgium	Adults 18-70 years old	EPS (Rome III) PDS (Rome III)	Clinic-based cross-sectional study	Consecutive ambulatory tertiary care patients presenting with dyspeptic symptoms	N=199 FD (77% female, 45.5±1.0 years) EPS: 16%, 66% female EPS+PDS: 51%, 71% female	Demographics Lifestyle factors Dyspepsia symptom patterns	Overlap EPS+PDS patients had greater post-prandial epigastric pain vs EPS; also higher postprandial nausea and bloating in the overlap group EPS+PDS overlapping group with exclusively postprandial, non-PDS symptoms (e.g., postprandial pain) were recategorized using adapted subdivision: "new PDS": 48%, "new EPS": 16%, "new overlapping EPS+PDS": 36%

Aono et al (2022) ¹⁶	Japan	Adults ages 20-75	EPS (Rome III and IV modification, Japanese version) PDS (Rome III and IV modification, Japanese version)	Multi-center, prospective observational study (UMIN 000041094)	Patients with dyspepsia symptoms seen at Hyogo College of Medicine and 8 related facilities from 4/2020 to 10/2020	N=205 patients with epigastric symptoms, 54.3 ±14.9 years old, 68.5% female Rome III: PDS 42/111 (37.8%), EPS 21/111 (18.9%), EPS+PDS overlap 48/111 (43.2%) Rome IV: PDS 71/111 (70.0%), EPS 21/111 (18.9%), EPS+PDS overlap 19/111 (17.1%)	Demographics and lifestyle factors <i>H. pylori</i> status Gastrointestinal symptom rating scale (GSRS) SF-8 HRQOL Hospital Anxiety and Depression Scale (HADS)	Decrease in EPS+PDS overlap from 43.2% (Rome III) to 17.1% (Rome IV) Abdominal pain score significantly higher in those classified as overlap in Rome III to PDS in Rome IV PDS change patients (Rome III to Rome IV) had significantly lower satiation rates, significantly higher acid reflux and abdominal pain scores vs. PDS stable patients
Cheng et al (2024) ¹⁷	China	Adults	EPS (Rome IV) PDS (Rome IV)	Clinic-based cross-sectional study (ChiCTR 180016661)	Rome IV FD patients enrolled from 12 hospitals from 7/2018 to 12/2018 Healthy volunteers	N=364 patients with FD, 242 female, 48.6 ±13.4 years EPS: 36 patients (9.9%), 21 female PDS: 125 patients (34.3%), 81 female EPS+PDS overlap: 203 (55.7%) patients, 140 female	Demographics, lifestyle factors Dyspepsia Symptom Scale Hospital Anxiety Depression Scales (HADS) Electrogastrography (gastric slow waves) Heart rate variability (autonomic function) Nutrient drink test (gastric satiety/accommodation) Post-drinking GI symptoms	Overlap group exhibited higher symptom score 30 minutes after drinking, higher anxiety/depression scores, and higher sympathovagal ratio than the pure EPS and PDS groups; PDS and overlap groups had reduced maximum tolerated volumes (MTV); P<0.05
Aziz et al (2019) ¹⁸	United States, Canada, United Kingdom	Adults	Rome IV Research Diagnostic Questionnaire	Internet cross-sectional health survey	Qualtrics global market survey in 2015 of adult general populations in study countries	N=131 participants fulfilling symptom criteria for Rome IV Functional Nausea and Vomiting Disorders (FNVD), 2.2% of surveyed population overall Chronic nausea and vomiting syndrome (CNVS): N=58 (1%) Cyclic vomiting syndrome (CVS): N=73 (1.2%)	Demographics, medications, health care visit Patient Health Questionnaire -12 (PHQ-12) somatic symptom severity Short Form-8 quality of life	FNVD overlap with FD in 81/131 (61.8%) 30/73 (41%) CVS patients endorsed occasional or regular cannabis use, 7/73 (9.5%) stated relief of symptoms with cannabis cessation (CVS-cannabis hyperemesis overlap); prevalence 0.1%

Josefsson et al (2022) ¹⁹	26 countries	Adults	Rome IV Research Diagnostic Questionnaire Rumination Questions (Rome IV diagnostic questions 32-34)	Internet cross-sectional health survey	Qualtrics global market survey in adult general populations (2000-3000 per country)	N=54,127 participants (51% male, 44.3 years old) Rumination syndrome: 1681 3.3% FD: 4537, ≈8.4% CVS: 780, ≈1.4% CVNS: 618, ≈1.1%	Patient Health Questionnaire-4 (PHQ-4; Psychological comorbidities) Healthcare utilization PROMIS Global-10 PHQ-15 (somatization)	Rumination + CVS overlap: 74, ≈0.14% Rumination +FD overlap: 451, ≈0.83% CVS+FD overlap: 376,≈ 0.69% CVS + CNVS overlap: 134, ≈0.25% CVNS + FD overlap: 361, ≈0.66%
Pediatric studies								
Turco et al. 2016 ²⁰	Italy	Median age: 10 years; range: 4.3–16.8 years	FD: Rome III criteria	Prospective observational study	Tertiary care clinic	N=100	Rome III questionnaire	17% had EPS, 47% had PDS, and 36% had overlap. The patients were followed for 6 months and they found that 38% of the PDS changed to EPS (19%) or to the overlap group (19%), while 41.2% of the EPS group changed to PDS (29.4%) and to the overlap group (11.8%). In the overlap group 30.6% transitioned to PDDS, and 19.4% to EPS.
Bowel DGBI Overlap								
Adult Studies								
Wong et al (2010) ²¹	United States	Adult >18 years old	IBS-C (Rome III) FC (Rome III)	Clinic-based, cross sectional survey (secondary analysis of larger study on risk factors for chronic constipation and impact on HRQOL and health care costs).	Group Health Members of Group Health Cooperative of Puget Sound (GHC), a healthcare maintenance organization from 9/1/2005 to 12/31/2005	N=1,100 participants with a clinical diagnosis of constipation (ICD-9CM 569.0X) IBS: 201 patients (78% female) FC: 231 patients (70% female) Controls: 1,700 patients (age and sex-matched)	Demographic questionnaires, SF-12 Health Survey, Patient Assessment of Constipation Quality of Life (PAC-QOL), Constipation Severity Scale (CSS), Brief Symptom Inventory (BSI). Measurements at baseline and 12 months follow-up	FC patients older, higher education level. 44.8% FC patients had abdominal pain. IBS-C worse CSS and PAC-QOL, worse psychological distress on BSI and greater SF-12 impairment. Removing diagnostic overlap exclusion: 89.5% of IBS-C also meet criteria for FC; 43.8% of FC meet IBS-C criteria Approximately 1/3 of participants at enrollment switch diagnoses at 12 months: IBS-C to FC (33%) and FC to IBS-C (32%)

Heidelbaugh et al (2015)²²	United States	Adults ≥18 years old	IBS-C (Rome III) CIC (Rome III);stratified into CIC-A (abdominal symptoms ≥1 weekly) or CIC-NA (no associated abdominal pain)	US population-based survey, cross-sectional online survey	Universal Survey Opinionsite, random cohort of 37,500 participants invited by email to participate	N= 10,030 participants IBS-C: 328 patients CIC: 552 patients [CIC-A: 363 (65.8%), CIC-NA: 189 (34.2%)]	31-question survey: symptom severity and bothersomeness, physician consultation, work/school productivity	All symptoms significantly more frequent in IBS-C vs. CIC (P<0.0001). Constipation extremely/very bothersome: IBS-C (72%)>CIC-A (62%) >CIC-NA (40%) ; P<0.01 all pairs. Other measured symptom bother: IBS-C and CIC-A > CIC-NA (significant). GI symptom effects on productivity (days/month): IBS-C (4.9) > CIC-A (3.2) >CIC-NA (1.2); P<0.001 all pairs
Rey et al (2014)²³	Spain	Adult >18 years old	IBS (Rome III) CC (Rome III) Non-painful CC (Rome III) Painful CC (Rome III CC with abdominal pain/discomfort 2-3 days per month, but not IBS-C) CC + IBS (participants meeting Rome criteria for both CC and IBS)	Population-based, random cross-sectional telephone survey	Spanish population, identified via national telephone directory, 6/2011	N=1500 participants; 762 (50.8%) female CC: 555 patients (37% interviewees); 288 (91%) with symptoms ≥6 mo.; overall prevalence 19.2%. Nonpainful CC: 209/288 (72.6%); 13.9% overall prevalence Painful CC: 30/288 (10.4%); 2.0% prevalence overall CC + IBS: 49/288 (17.0%); 23 IBS-C and 26 unsubtyped IBS; 3.3% overall prevalence Controls: nonconstipated participants	Sociodemographic questionnaire, quality of life in constipation-20 (CVE-20)	Participants with painful CC or CC+ IBS were younger, reported more constipation, more constipation symptoms vs. non-painful CC. Nonpainful CC more satisfied with laxative regimens than other subgroups. No significant differences in constipation-related QOL among nonpainful CC, painful CC, and CC + IBS.

Ford et al (2014)²⁴	Ontario, Canada	Adults >18 years old	IBS-C (Rome III) IBS-M (Rome III) IBS-D (Rome III) FDr (Rome III) CIC (Rome III)	Clinic-based cross-sectional survey	Consecutive, unselected patients with GI symptoms attending outpatient clinics at two hospitals in Hamilton, Ontario; 1/2012 to 12/2012	N=4224 consecutive patients; mean age 47.6 (16-93) years old; 2617 (62.0%) female IBS-C: 175 (11.3%) IBS-M: 509 (32.8%) IBS-D: 380 (24.5%) FDr: 95 (6.1%) CIC: 343 (22.1%)	Demographics and BMI Hospital Anxiety and Depression Score (HADS)	IBS-C vs. CIC: significantly younger, female, never married, more likely to report anxiety type symptoms, somatization-type behavior, greater individual constipation symptoms and bloating. Removing diagnostic mutual exclusivity exclusion: 513 with CIC, overlap with IBS-C in 18.1% Removing diagnostic mutual exclusivity exclusion: 615 with FDr, overlap with IBS-D in 27.6% IBS-D vs. FDr: significantly younger age, more females, more anxiety and somatization; trend toward lower BMI, higher education level; less loose, mushy, or watery stools, more bloating FDr: 50.5% did not report abdominal pain or discomfort at required frequency
Shekhar et al (2013)²⁵	United Kingdom	Adults >18 years old	IBS-C (Rome III) FC (Rome III)	Clinic-and community based case-control study	Outpatient Departments at University Hospitals of South Manchester (tertiary patients excluded), local general practices, community recruitment, existing departmental pool of volunteer patients	N=60 female participants IBS-C: 24 (aged 19-50) FC: 12 (aged 25-46) HV: 24 (aged 20-49), age and sex-matched	7- to 9-day baseline symptom diary (abdominal pain, bloating, bowel urgency; Bristol Stool Form Scale), Hospital Anxiety and Depression Scale (HADS), symptom measures hourly, Sitz Marker Study (5-day), rectal barostat testing platelet-depleted plasma (PDP) 5-HT concentrations (fasting and post-carbohydrate rich meal serotonin levels)	IBS-C vs FC: more abdominal pain and bloating, worse constipation 45% (5/11) FC and 69% (16/23) of IBS-C reported abdominal pain on more than one occasion on 7-day diary, no statistical difference in dairy reports of pain on >1 occasion, bowel-movement associated symptoms similar in both groups Greater post-prandial symptoms in IBS-C vs HV (not FC) No difference first sensation and stool sensation thresholds in IBS-C vs FC; lower pain threshold in IBS-C<FC<HV FC and IBS-C similarly delayed colic (P<0.01) and right segmental (P<0.01) transit vs HV Reduced PDP post-prandial serotonin levels in IBS-C , but similar meal response in FC and IBS-C

Koloski et al (2015)²⁶	Australia	Adults >18 years old	IBS-C (Rome III)	Population-based, random cross-sectional telephone survey	Postal survey (equal female: male) from New South Wales, Australia	N=3260 (53.8% female), mean age 54.3 (SD 15.6) years, 54.6% completed greater than high school level education FC: 206 (6.5%) IBS-C: 109 (3.5%)	Demographics, lifestyle factors, Hospital Anxiety and Depression Scale (HADS), SF-12 quality of life, health care seeking Latent class analysis (LCA)	FC vs. IBS-C: significantly older, less exercise (number of times, amount), higher SF-12 mental functioning, less health care visits in past 12 months LCA approach: one class predominantly FC (75%), with lower pain levels, more males. 2nd class mix of IBS-C and FC (56.7% and 43.3%, respectively)
Bouchoucha et al (2017)²⁷	France	Adults	IBS-C (Rome III) FC (Rome III)	Clinic-based cross-sectional survey	Consecutive, outpatients consulting at the Gastroenterology Clinic of the Anicenne Hospital (tertiary neurogastroenterology clinic) , referred by Center for Functional Gastrointestinal and Motility Disorders (CEFRED Centre d'Exploration Fonctionnelle et de Reeducation Digestive)	N=337 consecutive outpatients , 43.5 ±0.9 years old, 81% female	Diarrhea, constipation, bloating and abdominal pain symptoms (0-9 Likert), Bristol Stool Form Scale; Total and segmental colonic transit time (CTT) (radiopaque markers)	IBS-C vs FC: Greater frequency of female patients in IBS-C (87%) vs FC (74%), P=0.002 IBS-C with more severe constipation symptoms (P=0.002); similar stool form in both groups Total and segmental CTT similar in IBS-C and FC IBS associated with higher risk of bloating (P=0.013) and abdominal pain (P<0.001) ; Discriminant analysis: these two parameters correctly classify patients (71.2% overall; 73.7% IBS-C and 68.2% FC)
Drossman et al (2008)²⁸	United States and Canada	Adults > 18 years old	IBS -C (Rome II) IBS-D (Rome II) IBS-M (Rome II) IBS-Alternating (Rome II) Painful constipation (FC with pain ≥2 days per week); stratified to high pain constipation (HPC) and low pain constipation (LPC)	Follow-up surveys of participants in double-blinded randomized RCT (desipramine, R01 DK49334)	University of North Carolina and University of Toronto gastroenterology clinics	N=190 female participants, mean age 39.9 years, 85.7% white, mean education level 14.9 years, 52.4% married PC: 41 patients IBS-C: 80 patients IBS-A: 55 patients IBS-D: 55 patients	2-week diary cards (100mm VAS on abdominal pain or discomfort), stool frequency, stool consistency (BSFS) completed at randomization and 3, 6, 9, 12 months Sickness Impact Profile, healthcare utilization	PC vs IBS: higher pain scores (P=0.002), lower education (P=0.02), greater healthcare use and surgeries (P=0.05 to 0.003) PC similarities to IBS-C and IBS-A but different than IBS-D): stool frequency and consistency, bloating, laxative/antidiarrheal use, lower education Over 1 year, PC: higher pain scores vs IBS, stool frequency between IBS-C and IBS-A, stool consistency similar to IBS-A HPC and LPC: no difference in constipation, HPC switch to LPC over time, LPC pain cores stayed low

[illegible]

Adult studies								
de Bortoli et al (2016) ³²	Italy	Adults	ROME III, GERD-Q	Observational	Outpatient oesophageal centers	697 patients with heartburn, 65% GERD, 35% FH. IBS+GERD 33%, IBS+FH 77%	Structured interview based on questionnaires for GERD, IBS, anxiety, and depression, off-therapy upper-gastrointestinal (GI) endoscopy and 24 h MII-pH monitoring	IBS and anxiety were independent risk factors for FH in comparison with reflux-related heartburn in multivariate analysis.
Neumann et al. (2008) ³³	Germany	Adults	ROME III IBS and FD, NERD	Prospective observational study	Outpatient reflux clinics	71 patients, 33 NERD, NERD+IBS 63.6%, ERD+IBS 48%	Questionnaires, endoscopy	IBS and FD are common in the entire spectrum of GERD. IBS symptoms (bloating, abdominal pain, constipation and diarrhea) slightly more prevalent in NERD than in ERD and BE.
Futagami et al. (2013) ³⁴	Japan	Adults	ROME III FD & IBS, NERD	Prospective observational study	Tertiary care	139 patients 42.4% FD alone, 21.6% had FD+NERD, 19.4% FD+IBS, 16.5% FD+NERD+IBS, 10.1% IBS, and 8.6% NERD.	Questionnaires, endoscopy, (13)C-acetate breath test	Patients with FD+IBS overlap had more severe postprandial abdominal fullness, heartburn, and feeling of hunger than those with FD or IBS alone.
Noh et al. (2010) ³⁵	South Korea	Adults	ROME III FD & IBS, LA GERD	Prospective observational study	Health screening	2388 participants, FD 8.1%, IBS 10.1%, IBS+NERD 41.9%, IBS+RE 11.2%	Questionnaires, upper endoscopy	NERD overlapped more frequently with FD and IBS than RE. EPS was more prevalent than PDS in NERD. High somatization score and FD increased the OR for NERD in multiple regression analysis.
Pediatric studies								
Friesen et al. (2016) ³⁶	USA	Children age 8-17 years	Rome III, IBS, FD and symptoms of GERD	Retrospective review	Urban	100 patients, Mean age: 13 years 9 months, 76% female	Standardized questionnaires For GERD and overactive bladder syndrome (OBS)	Overlap IBS +FD = 33 %. At least one GERD symptom was present in 74 %of patients with 41 % reporting heartburn. Overlap syndromes/symptoms did not vary by FD subtype.
IBS and Upper DGBI Overlap								
Adult studies								
Kovács et al. (2022) ³⁷	Gibraltar	Adults	Rome IV criteria	Internet survey	2019-2020	888 individuals (IBS: 5.2%, FD: 9.9%, FD was present in 47.8% of IBS cases, and IBS present in 25% of FD cases.	Risk and protective factors using demographics, the Rome IV Diagnostic Questionnaire, clinical diagnosis history, healthcare utilization, and quality of life measured with PROMIS Global-10.	Women had higher prevalence rates for both conditions, with increased healthcare utilization and reduced quality of life in those meeting diagnostic criteria for both.

Loosen et al. (2022)³⁸	Germany	Adults	Disease database, physician diagnosed	Retrospective cohort study	2010-2019	65,569 patients; Mean age was 48.8 (SD: 18.4) years, 65.0% were female	Overlapping GI diagnoses before and after IBS diagnosis	High overlap between IBS and other GI diagnoses; 55% patients had ≥1 preexisting GI diagnosis within 12 months prior to IBS diagnosis. Most common overlapping diagnoses included intestinal infectious diseases (26%), gastritis/ duodenitis (21%), oesophageal disorders (15%), non-infectious enteritis/colitis (7.4%), functional dyspepsia (6%). 41% received one of these diagnosis within 12 months after IBS diagnosis.
Barberio et al. (2022)³⁹	UK	Adults	Rome IV criteria	Longitudinal observational study	Referral centers in UK	807 individuals. At study entry, 55.3% IBS+FD overlap.	Consultation behavior, treatments commenced, psychological health, IBS symptom severity, impact, depression scores	Risk factors for FD-IBS overlap include intensified healthcare use, severe IBS symptoms, chronic abdominal pain, and elevated risk of anxiety and depression.
Nam et al. (2021)⁴⁰	South Korea	Adults	Rome IV criteria	Prospective observational study	Nine tertiary referral centers in Korea	667 participants (334 healthy controls, 168 with FD-only, 37 with IBS-only, 128 (19.2%) with FD+IBS overlap.	Symptoms were assessed using questionnaires including GI symptom-related items and the Hospital Anxiety Depression Scale (HADS), with diagnoses based on Rome IV criteria, and the clinical characteristics of FD-IBS overlap were compared to FD-only or IBS-only groups.	In FD+IBS overlap, men complained of reflux symptom and loose/watery stools more than women ($P < 0.05$), whereas women showed more severe GI symptoms, especially epigastric pain/burning symptoms, and higher depression scores than men (all $P < 0.05$). Higher HADS scores with IBS+FD overlap.
Oshima et al. (2021)⁴¹	Japan	Adults	Rome III criteria	Online survey	Randomly assigned panelists in 2020.	5157 participants (FD: 8.5%, IBS: 16.6%, FD+IBS overlap: 4.0%).	Psychological symptoms (HADS), stress, physical distancing, worries about COVID-19	FD-IBS overlap was negatively affected by the COVID-19 pandemic, with FD-IBS overlap being a significant factor associated with symptom deterioration. Symptom deterioration experienced by 19% during COVID.
Nakov et al. (2020)⁴²	Bulgaria	Adults ages 18-65	Rome IV criteria	Internet survey	A population of social media users in Bulgaria	1896 individuals; mean age 35.5 years (SD 11.7), 73.1% females; (IBS: 20%, FD: 12.7%, FD+IBS overlap syndrome: 11.7%).	Sociodemographic factors, behavioral and lifestyle characteristics, gender, age, marital status, occupation, alcohol consumption, sexual problems, milk intolerance.	Prevalence of FD was 12.7% (39% PDS, 33% EPS, and 28% overlapping PDS+EPS). Patients with IBS ($p < 0.001$; OR: 127.88) significantly associated with FD prevalence. Gender ($p = 0.013$), milk intolerance ($p < 0.001$, OR: 1.65), urinary ($p = 0.035$) and sexual problems ($p < 0.001$, OR: 1.80) were associated with OS prevalence.

[illegible]

Schurman et al (2005) ⁴⁸	USA	Children age 8-18 years	Rome II, IBS and FD	Prospective cohort study	Urban	154 participants, Mean age: 11.8 +/- 2.5 years, 64% female, 86% White	Demographic questionnaire	FD comprising 35% by child report, 47% by parent report and 57% by physician evaluation. IBS was diagnosed in 30% by child report, 20% by parent report and 12% by physician evaluation. Both FD and IBS were met by 10% of child report, 10% by parent report and 30% by physician
Edwards et al. (2018) ⁴⁹	USA	Children age 8-17 years	Rome III and Rome IV, IBS and FD	Retrospective chart review	Urban	106 participants, mean age: 13.4 years, 70.8% female	Demographic questionnaire	Patients were significantly more likely to be diagnosed with FD (84.9% vs. 52.8%), IBS (69.8% vs. 34%), and FD/IBS overlap (58.5% vs. 17.9%) by Rome IV criteria, as compared to Rome III criteria
Karabult et al. (2013) ⁵⁰	Turkey	Children age 4-18 years	Rome III	Prospective cohort study	Tertiary care	345 total: 78 IBS (60.3% female) Mean age: 9.79 +/- 3.45 years, 214 healthy controls (49.5% female) Mean age: 9.49 +/- 3.49 years.	Demographic questionnaire	Prevalence of FD in IBS patients was 80.8%, or 63/78, significantly higher than the control group.
Schurman et al. (2017) ⁵¹	USA	Children age 8-17 years	Rome III	Retrospective cohort study	Tertiary care	250 children. Mean age: 13.25 +/- 2.78 years, 68% female.	Demographic questionnaires Factor analysis	FD demonstrated significant overlap with IBS (.42). No % or cases reported.
Colombo et al. (2021) ⁵²	USA	Children age 8-17 years	Rome III	Cross sectional	Tertiary care	260 children.	Demographic questionnaires DSDSC, BASC-3	39% of patients met Rome IV criteria for FD only and 8% met criteria for IBS only. 53% had both IBS and FD .Heartburn was present in 38% (27% FD, 35% IBS, and 46% of both IBS and FD ; p<0.01. They had more chest pain, bloating and sleep problems.
Helgeland et al. (2009) ⁵³	Norway	Children ages 4-15	Rome III, IBS +FD	Population based	Urban	124/142 (87%) at least 1 DGBI. Of those, Mean age: 9.4 +/- 9.4 years, 63% female	QPGS	66% met the criteria for 1, 29% for 2, and 5% for 3 diagnoses. IBS+FD = 1 patient. 1/124 (0.8%)
Friesen et al. (2016) ³⁶	USA	Children age 8-17 years	Rome III, IBS, FD and symptoms of GERD	Retrospective review	Urban	100 patients, Mean age: 13 years 9 months, 76% female	Standardized questionnaires For GERD and overactive bladder syndrome (OBS)	Overlap IBS +FD = 33 %. Overlap syndromes/symptoms did not vary by FD subtype.
Bowel DGBI and Fecal Incontinence (FI) Overlap								
Adult studies								
Sun et al. (2023) ⁵⁴	China	Adults	IBS, constipation, fecal incontinence (Rome IV)	Observational Study	Population	3145 healthy individuals, 10.5% FI (32.2% IBS+FI, 36.2% constipation+FI, 31.6% Isolated FI)	Rome IV criteria, online Groningen Defecation and Fecal Continence questionnaire	IBS (OR 12.5) and constipation (OR: 4.4) were the most significant factors contributing to FI. Among the patients with constipation-associated FI, 56.3% used anti-diarrhea medicine.

Goodoory et al (2023)⁵⁵	UK	Adults	IBS, fecal incontinence (Rome IV)	Cross-sectional study	UK national registry	1278 respondents, 758 with IBS, 202 (26.9%) with Rome IV FI, mean 47.2 yrs, 1086 (85%) female	Demographics, Rome IV questionnaire, Bristol Stool Form Scale, IBS-SSS, HADS, VSI, PHQ-15 (PHQ-12), WPAI:IBS, IBS-QOL, healthcare costs	Individuals with FI older, more likely to have IBS-D (47.0% vs 39.0%, p=0.008) and more severe IBS symptom scores, also higher depression, somatic symptom, and GI specific anxiety, and poorer HRQOL.
Simren et al (2017)⁵⁶	Sweden, US	Adults 18 to 65 years	IBS, fecal incontinence (Rome III)	Cross-sectional study	Academic tertiary referral clinics in US and Sweden	470 patients with IBS (304 US, 168 Sweden). 70 to 77% female, mean age 34±11 to 36±14 yrs. FI ≥ 1 day per month in 19.7% (US) and 13.7% (Sweden), with 29.8%-43.7% having less frequent FI	Demographic and disease-related information, IBS-SSS, IBS-QOL, HADS, BSI-18, WPAI:IBS, colorectal sensitivity (balloon distension), colorectal motility (radioopaque markers)	FI prevalence higher in older age; IBS patients with FI had overall worse IBS symptom severity, poorer HRQOL, psychological distress, and negative impact on work productivity. No associations with colorectal physiology.
Atarodi et al (2014)⁵⁷	UK	Adults	IBS (Rome III)	Cross-sectional study	Consecutive new and follow-up patients in tertiary referral clinic	500 patients with IBS (399 female), mean age 46 years 285 (57%) with FI	Demographics and clinical symptoms, IBS-SSS, IBS-QOL, HADS, FI questionnaire	FI severity: mild in 23.9%, moderate in 34.7%, severe in 31.9%; equal prevalence of FI in males/females; IBS-D highest (65.2%) but also in 37.9% IBS-C. Higher hx abdominal surgery and urinary incontinence with FI; 23.4% had no disclosed FI to provider, 30% use incontinence pads regularly
Hunt et al (2018)⁵⁸	US	Adults ages 18-82 years	IBS (Rome III and IV)	Cross-sectional study	Internet and local GI clinics	703 patients with IBS (506 female), mean 35 years. 60% reported FI in lifetime	Rome IV questionnaire, FI-SSS, FI-QoL, FFQ, VSI, IBS-QOL, GI-Cog	FI associated with worse HRQOL (statistical, not clinical significance). QOL predicted more by psychological variables (e.g., anxiety, catastrophizing) rather than physical symptoms
Meinds et al. (2017)⁵⁹	Netherlands	Adults	constipation, fecal incontinence (Rome III)	Observational study	Cross-section of the Dutch population	1259 respondents, 24.5% FC, 7.9% FI, 3.5% FC+FI	Rome III criteria, Groningen Defecation & Fecal Continence checklist	Constipation and/or FI are not always identified appropriately by patients. FC respondents were 2.7 times more likely to suffer from FI vs. non-constipated. 48.7% with FC, 35.0% with FI, and 38.6% with FC+FI qualified their bowel habits as either "good" or "very good". 49.4% of the respondents with FC and 48.0% with FI had not discussed their complaints.
Andy et al. (2016)⁶⁰	USA	Adults 50 and older	constipation, fecal incontinence, Combined Symptoms	Cross-Sectional Study	National Health and Nutrition Examination Survey (2005-2010)	3078 participants, Women (FI 11.2%, FC 11.8%, FI+FC 1.4%) Men (FI 8.7%, FC 4.6%, FI+FC 0.4%)	Hard stool consistency, stool frequency, loss of solid, liquid, or mucus stool	In adjusted models, women had greater odds of having constipation (OR 3.0) and FI (OR 1.4), and combined symptoms (OR = 4.6) than men. Shared risk factors included poor self-rated health and depression symptoms.

Sze et al (2013) ⁶¹	USA	Adult women	fecal Incontinence, Rome III constipation and IBS	Cross-Sectional Survey	Two gynecological outpatient clinics over 24 months	2319 women (FC 31%, FI 10%); 43% FI+FC)	4-item FI questionnaire, demographic and clinical history	constipated women were more likely to have FI vs. nonconstipated women [relative risk (RR) 1.60; prevalence of FI was strongly associated with the number of Rome III constipation symptoms (p<0.001).
Pelvic Floor Dysfunction and Bowel DGBI Overlap								
Adult studies								
Patcharatrakul et al (2011) ⁶²	Thailand	Adults	Rome II IBS, DD	Prospective observational study	Tertiary center	50 patients with DD (58% Rome II IBS)	Treating dyssynergic defecation patients with IBS by biofeedback therapy (BFT) improved both constipation and IBS symptoms.	IBS symptom disappearance was observed more frequently in patients with an improved defecation index compared with those with no improvement (P<0.05). High pretreatment constipation symptom score, high rectal sensory threshold, and a delayed colonic transit time portended poorer treatment outcomes.
Ahadi et al (2014) ⁶³	Iran	Adults/adolescents ages 15-75	Rome III IBS, DD	Prospective observational (nonrandomized, single blinded, semi experimental) study	Tertiary center	41 patients with DD (46.3% IBS)	Evaluation of defecation dynamics and balloon expulsion testing	IBS symptoms and anismus decreased significantly after BFT (P < 0.01). with similar results in non-IBS. Constipation symptoms (sensation of incomplete evacuation, difficult and painful defecation), defecation facilitative manual maneuver frequency, pelvic floor muscles resting amplitude and strain amplitude decreased and squeezing amplitude improved significantly after BFT in both IBS and non-IBS in both groups with and without IBS (P < 0.001). There were not significant differences between patients with and without IBS (P > 0.05) with respect to outcome.
Mulak et al (2010) ⁶⁴	Poland	Adults	Rome III IBS	Cross-sectional study	Tertiary center	66 patients with DD (41% DD)	Anorectal manometry and rectal distension test using water-perfused catheter and balloon	No significant differences in manometric parameters between IBS subgroups and the control group, except for pelvic floor dyssynergia (PFD). Lower rectal pain threshold observed particularly in IBS patients with diarrhea and mixed bowel habits (p < 0.01).
Nyam et al (1997) ⁶⁵	USA	Adults	Constipation, Slow-transit constipation (STC), pelvic floor dysfunction (PFD)	Cross-sectional survey	Tertiary center	74 patients with resistant constipation (70.3% STC only, 29.7% STC-PFD)	Colonic transit studies (marker or scintigraphic transit technique), tests of pelvic floor function	Physiologic evaluation reliably identified patients with severe chronic constipation who might benefit from surgery. No difference in the outcome of surgery in patients with STC alone vs. STC + pelvic floor dysfunction.

Glia et al (1998)⁶⁶	Sweden	Adults/adolescents ages 17-79	Constipation, slow-transit constipation (STC) and pelvic floor dysfunction (PFD)	Prospective observational study	Tertiary center	134 patients (112 females, median age 52); 20.9% STC, 23.9% PFD, 20.1% STC+PFD, 35.1% normal transit time and normal pelvic floor function	Anorectal manometry, electromyography (EMG), balloon expulsion test, colonic transit-time study, defecography	No diagnostic group differences in anal sphincter pressures. Rectal sensitivity to balloon distension was lower ($P < 0.05$) in patients with delayed transit. Paradoxical puborectalis contraction (PPC) was found on EMG in 42 patients (31%). The prevalence of PPC was higher ($P < 0.001$) in patients with PFD. Inability to evacuate the rectal balloon was reported by 37% of PFT and 12% with normal pelvic-floor function ($P < 0.001$).
Tanner et al (2021)⁶⁷	USA	Adults	Chronic constipation (CC), dyssynergic defecation (DD) and slow transit constipation (STC)	Prospective observational study	Motility center	230 patients (22% DD only, 55% STC only, 13% of both DD and STC)	High-resolution anorectal manometry (HR-ARM), Balloon expulsion testing (BET), whole gut transit scintigraphy (WGTS)	No symptoms suggestive of STC vs. DD; patients with STC and DD reported more severe constipation vs. normal transit and anorectal function. DD and STC evaluations needed to define pathophysiology of symptoms and help direct treatment in CC.
Shah et al (2014)⁶⁸	India	Adults ages 21-86	Rome III FC and IBS-C, Dyssynergic defecation (DD), Slow transit constipation (STC), Normal transit constipation (NTC)	Prospective observational study	Referral center	128 patients (23% had secondary constipation, 58% functional constipation (FC), and 19% constipation-predominant IBS (C-IBS). with primary constipation, 46 had NTC, 15 had STC, and 40 had DD.	Anorectal manometry (ARM), Balloon expulsion test, Colon transit study (CTS), Biofeedback therapy (BFT)	Patients with DD were more likely to have a history of finger evacuation, straining, incomplete evacuation, and sensation of anorectal obstruction compared to those without DD.
Goyal et al (2019)⁶⁹	India	Adults	Rome IV FD, IBS-C & Functional defecatory disorder (FDD)	Prospective observational study	Tertiary center	231 patients (57.1% FC and 42.9% IBS-C. FC group: 54.7% inadequate defecatory propulsion. IBS group: 89.4% dyssynergic defecation)	Anorectal manometry (ARM) and Balloon expulsion test (BET)	DD was diagnosed in 55.3% and 46.5% of FC and IBS-C patients, respectively. Rectal hyposensitivity was present in 60.6% of FC patients compared with 2% of IBS-C patients ($p < 0.001$).
Nullens et al (2012)⁷⁰	USA	Adults	Dyssynergic defecation (DD), slow transit constipation (STC)	Prospective observational study	Tertiary referral center	1411 patients (27.6% rectal evacuation disorder, healthy controls (HC)	ARM, BET, Colonic transit (geometric center) at 24 h and 48 h (GC24 and GC48), Ascending colon half-emptying time (AC t(1/2), Residual content in descending rectosigmoid colon and stool (DRS)	Both STC and DD were associated with lower GC24 and GC48 and slower AC t(1/2) than HC. GC48 differentiated DD from HC ($p < 0.001$) and DD from STC ($p = 0.007$). AC t(1/2) values differentiated HC from DD ($p = 0.006$) and STC ($p < 0.001$) and were associated with constipation (DD vs STC, $p = 0.007$). DRS at 48 h discriminated DD from STC (AUC=0.82) and stool content at 48 h, increasing the odds for DD over STC (OR per 5% in stool 2.4, 95% CI 1.1 to 5.5, $p = 0.03$).

Lv et al. (2023) ⁷¹	China	Adults	Rome IV FD, IBS-C, Dyssynergic defecation (DD), Slow transit constipation (STC)	Prospective observational study	Motility clinic	230 patients (64.8% IBS-C, 35.2% FC) DD: 85.2% IBS-C, 81% FC	High-resolution anorectal manometry (ARM), Colonic transit test using the Sitz marker study	IBS-C patients had a higher prevalence of delayed colonic transit compared to FC patients (36.63% vs 15.91%, P < 0.05).
Kaplan et al.(2022) ⁷²	Australia	Adults	Rome III IBS and FC	Prospective observational study	Tertiary referral neurogastroenterology Clinic	146 patients (62% FDD)	anorectal manometry (ARM), rectal sensory testing, and balloon expulsion time (BET)	Patients with four or more additional DGBIs experienced greater constipation severity compared to those with no additional DGBIs (P = 0.004).
General DGBI Overlap								
Adult studies								
Sperber et al. (2021) ⁷³	Multi-national (33 countries on 6 Continents)	Adults	22 DGBI (Rome III and IV)	Population-based cross-sectional study	Internet in 24 countries, personal interviews in 7 countries, and both in 2 countries	73,076 adult respondents (49.5% women)	Rome IV diagnostic questionnaire, Rome III IBS questions, and 80 items to identify variables associated with DGBI. At least 1 DGBI in 40.3% persons completing Internet surveys and 20.7% of persons completing the household surveys.	DGBI more prevalent in females than males, associated with lower QOL and more frequent doctor visits. Proportions of IBS were with Rome IV criteria vs. Rome III criteria, in the Internet survey (4.1% vs 10.1%) and household survey (1.5% vs 3.5%)
Aziz et al (2018) ⁷⁴	UK, US, Canada	Adults	Rome IV DGBI	Population-based cross-sectional study	Internet-based survey in 3 countries	5,931 of 6,300 general population adults from three English-speaking countries (2100 each from USA, Canada, and UK); 2,083 (35%) individuals met DGBI criteria, qualified for average of 1.5 DGBI diagnoses, and 742 of them (36%) qualified for DGBI diagnoses in ≥1 anatomic region.	Demographics, medication, surgical history, somatization, QOL, doctor-diagnosed organic GI disease, Rome IV DGBI	The presence of FGIDs in multiple regions was associated with increasing somatization, worse mental/physical QOL, more medical therapies, and a higher prevalence of abdominal surgeries; all P<0.001. Individuals with DGBIs in multiple regions had greater somatization and worse QOL than organic GI disease controls.
Pediatric studies								
Scarpato et al. (2018) ⁷⁵	Europe (multi-country)	Children age 4-18 years	Rome III	Prospective Multinational study	Urban population in the Mediterranean region	6602 students, Group A- age 4-10 (mean age: 7.7 +/- 1.9y). 7148 students Group B- age 11-18 (mean age: 13.8 +/- 2.1y)	Demographic questionnaire	There were significant variations in the prevalence of some DGBIs among different European countries. Group A: Prevalence of DGBIs was 20.7% (F, 46.5%). One DGBI was identified in 17.4% of the participants, a combination of 2 DGBIs was identified in 2.8%, 3 DGBIs were identified in 0.4%, and of 4 DGBIs were identified in 0.1%.Group B, prevalence of DGBIs was 26.6% (F, 55%), with a single DGBI recorded in 19.5% of the participants, 2 DGBIs in 6%, 3

								DGBIs in 1%, and 4 DGBIs in 0.1%.
Bouzos, et al. (2017)⁷⁶	Greece	Children ages 6-17 years	Rome III, IBS	Cross sectional	33 Schools, multiple cities	1588 children (51.8% females, mean age: 12.9±2.8 years)	QPGS (Rome III). Demographic questionnaires (children and family), exercise, hours of exposure to TV and bullying	A single DGBI was diagnosed in 19.3% of the participants, two DGBIs in 3.3%, three DGBIs in 0.4%, four in 0.3% and five in 0.1%. Overlap IBS/aerophagia 0.25%; IBS/abdominal migraine/aerophagia: 0.25%; IBS/abdominal migraine/aerophagia/CVS: 0.12%; IBS + AM + FD = 1 patients. 1/124 (0.8%); IBS/CVS/abdominal migraine/NRFI: 0.06%, IBS/aerophagia/NRFI/CVS: 0.06%; Increased physical exercise, male gender and higher parental educational level associated with decreased odds of any-DGBI. Prolonged TV-viewing, bullying at school, and larger families increased the likelihood of any DGBI.
Gulewitsch et al. (2013)⁷⁷	Germany	Children ages 6-10 years	Rome III	Cross sectional	Urban and rural	1537 participants. (51.1 % girls, 3.8% unknown), Mean age: 8.84 years +/- 1.25 years. 119 individuals or 7.7% fulfilled criteria for at least one DGBI.	Demographic questionnaires Strengths and Difficulties Questionnaire (SDQ) The parental version of the Children's Somatization Inventory (CSI) Children and parental response	4/119 (3.4%) had IBS+AM. DGBIs were strongly associated with somatization and emotional problems in community. Children with overlapping conditions had higher evidence of somatization, and more emotional and behavioral problems.
Helgeland et al. (2009)⁵³	Norway	Children ages 4-15	IBS, abdominal migraine (AM), aerophagia, cyclic vomiting syndrome (CVS), rumination, functional dyspepsia (Rome III)	Population based	Urban	124/142 (87%) at least 1 DGBI. Of those, Mean age: 9.4 +/- 9.4 years, 63% female	QPGS	66% met the criteria for 1, 29% for 2, and 5% for 3 diagnoses. IBS+AM = 10 patients. 10/124 (8.1%) 66% met the criteria for 1, 29% for 2, and 5% for 3 diagnoses. IBS + aerophagia = 12 patients. 12/124 (9.7%); AM + FC = 3 patients. 3/124 (2.4%); IBS + cyclic vomiting = 2 patients. 2/124 (1.6%); IBS + AM + aerophagia = 3 patients. 3/124 (2.4%); IBS + rumination syndrome = 1 patient. 1/124 (0.8%); IBS + AM + FD = 1 patients. 1/124 (0.8%); Aerophagia+FC+rumination = 1 patient. 1/124 (0.8%)

Abbreviations: HRQOL: health-related quality of life; IBS-C: irritable bowel syndrome with predominant constipation; FC: functional constipation; N: number of participants; SF-12: Short Form-12 health survey; P: P value; US: United States; CIC: chronic idiopathic constipation; CIC-A: chronic idiopathic constipation with abdominal symptoms; CIC-NA: chronic idiopathic constipation with no associated abdominal pain; CC: chronic constipation; IBS-M: irritable bowel syndrome with mixed bowel habits; IBS-D: irritable bowel syndrome with predominant diarrhea; FDr: functional diarrhea; HV: healthy volunteers; 5-HT: 5-hydroxytryptamine (serotonin); VAS: visual analogue scale; IBS-A: irritable bowel syndrome with alternating bowel habits; HPC: high pain constipation; PC: painful constipation; LPC: low pain constipation; PHQ-15: Patient Health Questionnaire-15; ; PHQ-12: Patient Health Questionnaire-12; HADS: Hospital Anxiety and Depression Scale; VSI: Visceral Sensitivity Index; WPAI: IBS: Work Productivity and Activity Impairment Questionnaire for IBS; BSI-18:

Brief Symptom Questionnaire-18; QPGS: Questionnaire on Pediatric Gastrointestinal Symptoms; Rome III PAGI-SYM: Patient Assessment of Upper GI Disorders Symptoms Questionnaire; PROMIS: Patient-Reported Outcomes Measurement Information System; EPS: epigastric pain syndrome; PDS: postprandial distress syndrome; T1/2: half emptying time; H. pylori: *Helicobacter pylori*; CagA: cytotoxicity-associated immunodominant antigen; FD: functional dyspepsia; CIN: chronic idiopathic nausea; EGD: esophagogastroduodenoscopy; BMI: body mass index; OR: odds ratio; GERD: gastro-oesophageal reflux; GI: gastroenterology; SF-8: Short Form-8 health survey; QOL: quality of life; IBS-QOL: IBS Quality of Life questionnaire; FI-SSS: Fecal Incontinence Symptom Severity Scale; FI-QoL: Fecal Incontinence Quality of Life; FFQ: Fear of Food Questionnaire; GI-Cog: Gastrointestinal Cognitions Questionnaire; FCP: functional chest pain; FH: functional heartburn; DGBI: functional gastrointestinal disorder; RH: reflux hypersensitivity; PPI: proton pump inhibitor; NERD: non-erosive reflux disease; ERD: erosive reflux disease; RE: reflux esophagitis; BE: Barrett's esophagus; MBNI: mean baseline nocturnal impedance; CI: confidence interval; 5-HTTLPR: serotonin-transporter-linked promoter region; ADRA2A: Adrenoceptor alpha 2A; CCK1R: type 1 cholecystokinin receptor; FI: fecal incontinence; DD: dyssynergic defecation; ARM: anorectal manometry; BET: balloon expulsion testing; CTS: colon transit study; NTC: normal transit constipation; STC: slow transit constipation; PFD: pelvic floor dysfunction. GC: geometric center; GC48: geometric center at 48 hours; AC: ascending colon

References – Supplementary table 1

- 1 Bang, C. S. *et al.* Functional Gastrointestinal Disorders in Young Military Men. *Gut Liver* **9**, 509-515, doi:10.5009/gnl14109 (2015).
- 2 Mudipalli, R. S., Remes-Troche, J. M., Andersen, L. & Rao, S. S. Functional chest pain: esophageal or overlapping functional disorder. *J Clin Gastroenterol* **41**, 264-269, doi:10.1097/01.mcg.0000225521.36160.1b (2007).
- 3 Rengarajan, A., Pomarat, M., Zerbib, F. & Gyawali, C. P. Overlap of functional heartburn and reflux hypersensitivity with proven gastroesophageal reflux disease. *Neurogastroenterol Motil* **33**, e14056, doi:10.1111/nmo.14056 (2021).
- 4 Yamawaki, H. *et al.* Impact of sleep disorders, quality of life and gastric emptying in distinct subtypes of functional dyspepsia in Japan. *J Neurogastroenterol Motil* **20**, 104-112, doi:10.5056/jnm.2014.20.1.104 (2014).
- 5 Nwokediuko, S. C., Ijoma, U. & Obienu, O. Functional dyspepsia: subtypes, risk factors, and overlap with irritable bowel syndrome in a population of african patients. *Gastroenterol Res Pract* **2012**, 562393, doi:10.1155/2012/562393 (2012).
- 6 Fang, Y. J. *et al.* Distinct aetiopathogenesis in subgroups of functional dyspepsia according to the Rome III criteria. *Gut* **64**, 1517-1528, doi:10.1136/gutjnl-2014-308114 (2015).
- 7 Zagari, R. M. *et al.* Epidemiology of functional dyspepsia and subgroups in the Italian general population: an endoscopic study. *Gastroenterology* **138**, 1302-1311, doi:10.1053/j.gastro.2009.12.057 (2010).
- 8 Manabe, N. *et al.* Clinical characteristics of Japanese dyspeptic patients: is the Rome III classification applicable? *Scand J Gastroenterol* **45**, 567-572, doi:10.3109/00365521003592663 (2010).
- 9 Vakil, N., Halling, K., Ohlsson, L. & Wernersson, B. Symptom overlap between postprandial distress and epigastric pain syndromes of the Rome III dyspepsia classification. *Am J Gastroenterol* **108**, 767-774, doi:10.1038/ajg.2013.89 (2013).
- 10 Hsu, Y. C. *et al.* Psychopathology and personality trait in subgroups of functional dyspepsia based on Rome III criteria. *Am J Gastroenterol* **104**, 2534-2542, doi:10.1038/ajg.2009.328 (2009).
- 11 Wang, A. *et al.* The clinical overlap between functional dyspepsia and irritable bowel syndrome based on Rome III criteria. *BMC Gastroenterol* **8**, 43, doi:10.1186/1471-230X-8-43 (2008).
- 12 Carbone, F., Vanuytsel, T. & Tack, J. Analysis of Postprandial Symptom Patterns in Subgroups of Patients With Rome III or Rome IV Functional Dyspepsia. *Clin Gastroenterol Hepatol* **18**, 838-846 e833, doi:10.1016/j.cgh.2019.07.053 (2020).

- 13 Vanheel, H. *et al.* Pathophysiological Abnormalities in Functional Dyspepsia Subgroups According to the Rome III Criteria. *Am J Gastroenterol* **112**, 132-140, doi:10.1038/ajg.2016.499 (2017).
- 14 Van den Houte, K. *et al.* Effects of Rome IV Definitions of Functional Dyspepsia Subgroups in Secondary Care. *Clin Gastroenterol Hepatol* **19**, 1620-1626, doi:10.1016/j.cgh.2020.06.043 (2021).
- 15 Carbone, F., Holvoet, L. & Tack, J. Rome III functional dyspepsia subdivision in PDS and EPS: recognizing postprandial symptoms reduces overlap. *Neurogastroenterol Motil* **27**, 1069-1074, doi:10.1111/nmo.12585 (2015).
- 16 Aono, S. *et al.* Epidemiology and Clinical Characteristics Based on the Rome III and IV Criteria of Japanese Patients with Functional Dyspepsia. *J Clin Med* **11**, doi:10.3390/jcm11092342 (2022).
- 17 Cheng, J. *et al.* The Overlap Subgroup of Functional Dyspepsia Exhibits More Severely Impaired Gastric and Autonomic Functions. *J Clin Gastroenterol* **58**, 31-38, doi:10.1097/MCG.0000000000001802 (2024).
- 18 Aziz, I. *et al.* Epidemiology, Clinical Characteristics, and Associations for Rome IV Functional Nausea and Vomiting Disorders in Adults. *Clin Gastroenterol Hepatol* **17**, 878-886, doi:10.1016/j.cgh.2018.05.020 (2019).
- 19 Josefsson, A. *et al.* Global Prevalence and Impact of Rumination Syndrome. *Gastroenterology* **162**, 731-742 e739, doi:10.1053/j.gastro.2021.11.008 (2022).
- 20 Turco, R. *et al.* Do Distinct Functional Dyspepsia Subtypes Exist in Children? *J Pediatr Gastroenterol Nutr* **62**, 387-392, doi:10.1097/MPG.0000000000000944 (2016).
- 21 Wong, R. K. *et al.* Inability of the Rome III criteria to distinguish functional constipation from constipation-subtype irritable bowel syndrome. *Am J Gastroenterol* **105**, 2228-2234, doi:10.1038/ajg.2010.200 (2010).
- 22 Heidelbaugh, J. J., Stelwagon, M., Miller, S. A., Shea, E. P. & Chey, W. D. The spectrum of constipation-predominant irritable bowel syndrome and chronic idiopathic constipation: US survey assessing symptoms, care seeking, and disease burden. *Am J Gastroenterol* **110**, 580-587, doi:10.1038/ajg.2015.67 (2015).
- 23 Rey, E., Balboa, A. & Mearin, F. Chronic constipation, irritable bowel syndrome with constipation and constipation with pain/discomfort: similarities and differences. *Am J Gastroenterol* **109**, 876-884, doi:10.1038/ajg.2014.18 (2014).
- 24 Ford, A. C. *et al.* Characteristics of functional bowel disorder patients: a cross-sectional survey using the Rome III criteria. *Aliment Pharmacol Ther* **39**, 312-321, doi:10.1111/apt.12573 (2014).
- 25 Shekhar, C. *et al.* Rome III functional constipation and irritable bowel syndrome with constipation are similar disorders within a spectrum of sensitization, regulated by serotonin. *Gastroenterology* **145**, 749-757; quiz e713-744, doi:10.1053/j.gastro.2013.07.014 (2013).
- 26 Koloski, N. A., Jones, M., Young, M. & Talley, N. J. Differentiation of functional constipation and constipation predominant irritable bowel syndrome based on Rome III criteria: a population-based study. *Aliment Pharmacol Ther* **41**, 856-866, doi:10.1111/apt.13149 (2015).
- 27 Bouchoucha, M. *et al.* Is-it possible to distinguish irritable bowel syndrome with constipation from functional constipation? *Tech Coloproctol* **21**, 125-132, doi:10.1007/s10151-016-1580-x (2017).
- 28 Drossman, D. A. *et al.* Further characterization of painful constipation (PC): clinical features over one year and comparison with IBS. *J Clin Gastroenterol* **42**, 1080-1088, doi:10.1097/mcg.0b013e31815146f9 (2008).
- 29 Singh, P. *et al.* Similarities in Clinical and Psychosocial Characteristics of Functional Diarrhea and Irritable Bowel Syndrome With Diarrhea. *Clin Gastroenterol Hepatol* **18**, 399-405 e391, doi:10.1016/j.cgh.2019.08.020 (2020).

- 30 Rajindrajith, S., Devanarayana, N. M. & Benninga, M. A. Constipation and Constipation-predominant Irritable Bowel Syndrome: A Comparative Study Using Rome III Criteria. *J Pediatr Gastroenterol Nutr* **64**, 679-684, doi:10.1097/MPG.0000000000001332 (2017).
- 31 Velasco-Benitez, C. A. *et al.* [Overlapping of functional gastrointestinal disorders in latinamerican schoolchildren and adolescents]. *Rev Chil Pediatr* **89**, 726-731, doi:10.4067/S0370-41062018005000808 (2018).
- 32 de Bortoli, N. *et al.* Functional Heartburn Overlaps With Irritable Bowel Syndrome More Often than GERD. *Am J Gastroenterol* **111**, 1711-1717, doi:10.1038/ajg.2016.432 (2016).
- 33 Neumann, H., Monkemuller, K., Kandulski, A. & Malfertheiner, P. Dyspepsia and IBS symptoms in patients with NERD, ERD and Barrett's esophagus. *Dig Dis* **26**, 243-247, doi:10.1159/000121354 (2008).
- 34 Futagami, S. *et al.* Impact of coexisting irritable bowel syndrome and non-erosive reflux disease on postprandial abdominal fullness and sleep disorders in functional dyspepsia. *J Nippon Med Sch* **80**, 362-370, doi:10.1272/jnms.80.362 (2013).
- 35 Noh, Y. W., Jung, H. K., Kim, S. E. & Jung, S. A. Overlap of Erosive and Non-erosive Reflux Diseases With Functional Gastrointestinal Disorders According to Rome III Criteria. *J Neurogastroenterol Motil* **16**, 148-156, doi:10.5056/jnm.2010.16.2.148 (2010).
- 36 Friesen, C. A., Rosen, J. M. & Schurman, J. V. Prevalence of overlap syndromes and symptoms in pediatric functional dyspepsia. *BMC Gastroenterol* **16**, 75, doi:10.1186/s12876-016-0495-3 (2016).
- 37 Kovacs, D. B., Szekely, A., Hubai, A. G. & Palsson, O. Prevalence, epidemiology and associated healthcare burden of Rome IV irritable bowel syndrome and functional dyspepsia in the adult population of Gibraltar. *BMJ Open Gastroenterol* **9**, doi:10.1136/bmjgast-2022-000979 (2022).
- 38 Loosen, S. H., Kostev, K., Jordens, M. S., Luedde, T. & Roderburg, C. Overlap between irritable bowel syndrome and common gastrointestinal diagnoses: a retrospective cohort study of 29,553 outpatients in Germany. *BMC Gastroenterol* **22**, 48, doi:10.1186/s12876-022-02118-y (2022).
- 39 Barberio, B. *et al.* Overlap of Rome IV Irritable Bowel Syndrome and Functional Dyspepsia and Effect on Natural History: A Longitudinal Follow-Up Study. *Clin Gastroenterol Hepatol* **20**, e89-e101, doi:10.1016/j.cgh.2021.04.011 (2022).
- 40 Nam, K. *et al.* Gender difference in the overlap of irritable bowel syndrome and functional dyspepsia: a prospective nationwide multicenter study in Korea. *J Gastroenterol* **56**, 537-546, doi:10.1007/s00535-021-01775-2 (2021).
- 41 Oshima, T. *et al.* Impacts of the COVID-19 pandemic on functional dyspepsia and irritable bowel syndrome: A population-based survey. *J Gastroenterol Hepatol* **36**, 1820-1827, doi:10.1111/jgh.15346 (2021).
- 42 Nakov, R. *et al.* Prevalence of Irritable Bowel Syndrome, Functional Dyspepsia and their Overlap in Bulgaria: a Population-Based Study. *J Gastrointestin Liver Dis* **29**, 329-338, doi:10.15403/jgld-2645 (2020).
- 43 von Wulffen, M. *et al.* Overlap of Irritable Bowel Syndrome and Functional Dyspepsia in the Clinical Setting: Prevalence and Risk Factors. *Dig Dis Sci* **64**, 480-486, doi:10.1007/s10620-018-5343-6 (2019).
- 44 Kim, S. Y. *et al.* Self-reported Sleep Impairment in Functional Dyspepsia and Irritable Bowel Syndrome. *J Neurogastroenterol Motil* **24**, 280-288, doi:10.5056/jnm17098 (2018).
- 45 Choi, Y. J. *et al.* Overlap between irritable bowel syndrome and functional dyspepsia including subtype analyses. *J Gastroenterol Hepatol* **32**, 1553-1561, doi:10.1111/jgh.13756 (2017).

- 46 Perveen, I., Rahman, M. M., Saha, M., Rahman, M. M. & Hasan, M. Q. Prevalence of irritable bowel syndrome and functional dyspepsia, overlapping symptoms, and associated factors in a general population of Bangladesh. *Indian J Gastroenterol* **33**, 265-273, doi:10.1007/s12664-014-0447-1 (2014).
- 47 Corsetti, M., Caenepeel, P., Fischler, B., Janssens, J. & Tack, J. Impact of coexisting irritable bowel syndrome on symptoms and pathophysiological mechanisms in functional dyspepsia. *Am J Gastroenterol* **99**, 1152-1159, doi:10.1111/j.1572-0241.2004.30040.x (2004).
- 48 Schurman, J. V. *et al.* Diagnosing functional abdominal pain with the Rome II criteria: parent, child, and clinician agreement. *J Pediatr Gastroenterol Nutr* **41**, 291-295, doi:10.1097/01.mpg.0000178438.64675.c4 (2005).
- 49 Edwards, T., Friesen, C. & Schurman, J. V. Classification of pediatric functional gastrointestinal disorders related to abdominal pain using Rome III vs. Rome IV criterions. *BMC Gastroenterol* **18**, 41, doi:10.1186/s12876-018-0769-z (2018).
- 50 Karabulut, G. S. *et al.* The Incidence of Irritable Bowel Syndrome in Children Using the Rome III Criteria and the Effect of Trimebutine Treatment. *J Neurogastroenterol Motil* **19**, 90-93, doi:10.5056/jnm.2013.19.1.90 (2013).
- 51 Schurman, J. V., Karazsia, B. T. & Friesen, C. A. Examination of competing diagnostic models of functional gastrointestinal disorders related to pain in children. *Neurogastroenterol Motil* **29**, doi:10.1111/nmo.13126 (2017).
- 52 Colombo, J. M., Deacy, A. D., Schurman, J. V. & Friesen, C. A. Heartburn in children and adolescents in the presence of functional dyspepsia and/or irritable bowel syndrome correlates with the presence of sleep disturbances, anxiety, and depression. *Medicine (Baltimore)* **100**, e25426, doi:10.1097/MD.00000000000025426 (2021).
- 53 Helgeland, H. *et al.* Diagnosing pediatric functional abdominal pain in children (4-15 years old) according to the Rome III Criteria: results from a Norwegian prospective study. *J Pediatr Gastroenterol Nutr* **49**, 309-315, doi:10.1097/MPG.0b013e31818de3ab (2009).
- 54 Sun, G. *et al.* Co-occurrence of fecal incontinence with constipation or irritable bowel syndrome indicates the need for personalized treatment. *Neurogastroenterol Motil* **35**, e14633, doi:10.1111/nmo.14633 (2023).
- 55 Goodoory, V. C., Ng, C. E., Black, C. J. & Ford, A. C. Prevalence and impact of faecal incontinence among individuals with Rome IV irritable bowel syndrome. *Aliment Pharmacol Ther* **57**, 1083-1092, doi:10.1111/apt.17465 (2023).
- 56 Simren, M. *et al.* Fecal incontinence in irritable bowel syndrome: Prevalence and associated factors in Swedish and American patients. *Neurogastroenterol Motil* **29**, doi:10.1111/nmo.12919 (2017).
- 57 Atarodi, S., Rafieian, S. & Whorwell, P. J. Faecal incontinence-the hidden scourge of irritable bowel syndrome: a cross-sectional study. *BMJ Open Gastroenterol* **1**, e000002, doi:10.1136/bmjgast-2014-000002 (2014).
- 58 Hunt, M. G., Wong, C., Aajmain, S. & Dawodu, I. Fecal incontinence in people with self-reported irritable bowel syndrome: Prevalence and quality of life. *J Psychosom Res* **113**, 45-51, doi:10.1016/j.jpsychores.2018.07.015 (2018).
- 59 Meinds, R. J., van Meegdenburg, M. M., Trzpis, M. & Broens, P. M. On the prevalence of constipation and fecal incontinence, and their co-occurrence, in the Netherlands. *Int J Colorectal Dis* **32**, 475-483, doi:10.1007/s00384-016-2722-3 (2017).
- 60 Andy, U. U. *et al.* Shared Risk Factors for Constipation, Fecal Incontinence, and Combined Symptoms in Older U.S. Adults. *J Am Geriatr Soc* **64**, e183-e188, doi:10.1111/jgs.14521 (2016).
- 61 Sze, E. H., Barker, C. D. & Hobbs, G. A cross-sectional survey of the relationship between fecal incontinence and constipation. *Int Urogynecol J* **24**, 61-65, doi:10.1007/s00192-012-1851-7 (2013).

- 62 Patcharatrakul, T. & Gonlachanvit, S. Outcome of biofeedback therapy in dyssynergic defecation patients with and without irritable bowel syndrome. *J Clin Gastroenterol* **45**, 593-598, doi:10.1097/MCG.0b013e31820c6001 (2011).
- 63 Ahadi, T. *et al.* The effect of biofeedback therapy on dyssynergic constipation in patients with or without Irritable Bowel Syndrome. *J Res Med Sci* **19**, 950-955 (2014).
- 64 Mulak, A. & Paradowski, L. Anorectal function and dyssynergic defecation in different subgroups of patients with irritable bowel syndrome. *Int J Colorectal Dis* **25**, 1011-1016, doi:10.1007/s00384-010-0950-5 (2010).
- 65 Nyam, D. C., Pemberton, J. H., Ilstrup, D. M. & Rath, D. M. Long-term results of surgery for chronic constipation. *Dis Colon Rectum* **40**, 273-279, doi:10.1007/BF02050415 (1997).
- 66 Glia, A., Lindberg, G., Nilsson, L. H., Mihocsa, L. & Akerlund, J. E. Constipation assessed on the basis of colorectal physiology. *Scand J Gastroenterol* **33**, 1273-1279, doi:10.1080/00365529850172359 (1998).
- 67 Tanner, S. *et al.* Prevalence and Clinical Characteristics of Dyssynergic Defecation and Slow Transit Constipation in Patients with Chronic Constipation. *J Clin Med* **10**, doi:10.3390/jcm10092027 (2021).
- 68 Shah, N. *et al.* Clinical and investigative assessment of constipation: a study from a referral center in western India. *Indian J Gastroenterol* **33**, 530-536, doi:10.1007/s12664-014-0505-8 (2014).
- 69 Goyal, O., Bansal, M. & Sood, A. Clinical and anorectal manometry profile of patients with functional constipation and constipation-predominant irritable bowel syndrome. *Indian J Gastroenterol* **38**, 211-219, doi:10.1007/s12664-019-00953-8 (2019).
- 70 Nullens, S. *et al.* Regional colon transit in patients with dys-synergic defaecation or slow transit in patients with constipation. *Gut* **61**, 1132-1139, doi:10.1136/gutjnl-2011-301181 (2012).
- 71 Lv, C. L. *et al.* Colorectal motility patterns and psychiatric traits in functional constipation and constipation-predominant irritable bowel syndrome: A study from China. *World J Gastroenterol* **29**, 5657-5667, doi:10.3748/wjg.v29.i41.5657 (2023).
- 72 Kaplan, A. I. *et al.* Experiencing multiple concurrent functional gastrointestinal disorders is associated with greater symptom severity and worse quality of life in chronic constipation and defecation disorders. *Neurogastroenterol Motil* **35**, e14524, doi:10.1111/nmo.14524 (2023).
- 73 Sperber, A. D. *et al.* Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology* **160**, 99-114 e113, doi:10.1053/j.gastro.2020.04.014 (2021).
- 74 Aziz, I. *et al.* The Prevalence and Impact of Overlapping Rome IV-Diagnosed Functional Gastrointestinal Disorders on Somatization, Quality of Life, and Healthcare Utilization: A Cross-Sectional General Population Study in Three Countries. *Am J Gastroenterol* **113**, 86-96, doi:10.1038/ajg.2017.421 (2018).
- 75 Scarpato, E. *et al.* Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents in the Mediterranean Region of Europe. *Clin Gastroenterol Hepatol* **16**, 870-876, doi:10.1016/j.cgh.2017.11.005 (2018).
- 76 Bouzios, I., Chouliaras, G., Chrousos, G. P., Roma, E. & Gemou-Engesaeth, V. Functional gastrointestinal disorders in Greek Children based on ROME III criteria: identifying the child at risk. *Neurogastroenterol Motil* **29**, doi:10.1111/nmo.12951 (2017).
- 77 Gulewitsch, M. D., Enck, P., Schwille-Kiuntke, J., Weimer, K. & Schlarb, A. A. Rome III criteria in parents' hands: pain-related functional gastrointestinal disorders in community children and associations with somatic complaints and mental health. *Eur J Gastroenterol Hepatol* **25**, 1223-1229, doi:10.1097/MEG.0b013e328364b55d (2013).

Supplementary Table 2 | Comprehensive overview of studies evaluating DGBI in individuals with organic GI disease in remission

Author, year	Country	Organic disease	DGBI (criteria)	Study design	Number with organic disease	Presence of DGBI in organic disease
Coeliac disease (CD)						
Adult studies						
Sainsbury et al, 2013 ¹	Worldwide	CD	IBS (Rome I-III)	Systematic review of 7 studies up to 2012	1388 with CD	38% overall: 22% for GFD-adherent, 47% for non GFD-adherent
Silvester et al, 2017 ²	USA	CD	IBS, FD, FAB (Rome III)	Single centre case series	85 with CD	At baseline, 6 months, 12 months following a GFD: FD, 27%-11%-8% IBS, 52%-32%-22% FAB, 9%-21%-16% Any of the above, 66%-58%-47%
Parker et al, 2022 ³	UK	CD	All DGBI (Rome IV)	Case-control (Cases were Coeliac UK members vs. general population controls)	863 with CD	GFD-adherent vs. non GFD-adherent: All DGBI, 51% vs. 75% FD, 5% vs. 14% IBS, 8% vs. 19% GFD-adherent vs. matched population controls: All DGBI, 52% vs. 35% IBS, 7.6% vs. 4.5% Proctalgia fugax, 10% vs. 5.4% No difference in oesophageal or gastroduodenal disorders
Pediatric Studies						
Turco et al, 2011 ⁴	Italy	CD	IBS, FD, FAP, FC, FAPD (Rome III)	Prospective 1 year follow up Case control	82 with CD	FAPD, 28% whilst on GFD vs. 8.9% controls IBS, 7.3% vs. 3.5% FD, 2% vs. 0% FAP, 4.8% vs. 3.5% FC, 18 vs. 1.8%

Saps et al, 2013 ⁵	USA	CD	IBS, FD, FAP, FAPD (Rome III)	Retrospective tertiary care cohort study	49 with CD	FAPD, 18.3% whilst on GFD vs. 8.3% controls IBS, 6.1% vs. 2.1% FD, 4.8% vs. 0% FAP, 6.3% vs. 1%
Saps et al, 2017 ⁶	USA and Italy	CD	IBS, FD, FAP, FAPD (Rome III)	Retrospective tertiary care cohort study	96 with CD	FAPD, 8% whilst on GFD vs. 8% siblings vs. 2% controls IBS, 6.2% vs. 4.1% vs. 1% FD, 0% vs. 1% vs. 0% FAP, 1% vs. 2% vs. 1%
Cristofori et al, 2021 ⁷	Italy	CD	IBS, FD, FAP, FC, FAPD (Rome IV)	Tertiary care case control study	417 with CD	FAPD 11.5% vs. 6.7% (RR 1.8, 95% CI 1.1 to 3) IBS, 7.2% (RR 2.3, 95% CI 1.1 to 4.6) Constipation 10.5% (RR 2.1, 95% CI 1.4 to 3.2)
Veeraraghavan et al, 2021 ⁸	USA	CD	IBS, FD, FAP, FC (Rome IV)	Retrospective chart review	616 with CD	Functional abdominal pain, 7% whilst on GFD IBS, 3%, Constipation, 20%
Inflammatory bowel disease (IBD)						
Adult studies						
Fairbrass et al, 2020. ⁹	Worldwide	IBD	IBS (Manning, Rome II-IV)	Systematic review of 27 studies between 2012-2020	3169 with IBD in remission (1825 with UC, 1050 with Crohn's disease)	Pooled prevalence of IBS in IBD in remission: All patients, 32.5% According to clinical disease activity indices, 33.6% Based on faecal calprotectin (<100mcg/g), 35.1% In endoscopic remission, 23.5% In histological remission, 25.8% Prevalence of IBS in UC in remission, 28.7% Prevalence of IBS in Crohn's disease in remission, 36.6%
Nigam et al, 2019 ¹⁰	UK	IBD	IBS, FC, FI (Rome IV)	Cross-sectional	61 with UC in remission	Any FBD, 41% IBS, 23% FC, 5%

						FI, 21%
Pediatric studies						
Zimmerman et al, 2013 ¹¹	USA	IBD	FAP (Rome III)	Prospective tertiary care study	174 with Crohn's disease in remission	FAP, 10.3%
Diederer et al, 2016 ¹²	Netherlands	IBD	IBS, FAP, FAPD (Rome III)	Cross-sectional study	123 with Crohn's disease (88 in clinical remission, 56 in biochemical remission). 61 UC (37 in clinical remission, 38 in biochemical remission) .	Clinical remission: IBS, 6.4% (in Crohn's disease, 4.5%; in UC, 10.8%) Biochemical remission: IBS, 16.1% (in Crohn's disease 16.7%; in UC, 10.8%) FAPD, 9.6% <i>IBS or FAP:</i> Clinical remission: 9.6% (in Crohn's disease, 8.0%; in UC, 13.5%) Biochemical remission: 22.6% (in Crohn's disease, 26.2%; in UC, 13.5%)
Watson et al, 2007 ¹³	USA	IBD	FAP, IBS, FD, FAPD (Rome III)	Cross sectional prospective study	81 with IBD in remission. 62 with Crohn's disease, 19 with UC.	IBD-FAPD, 26% (27% in Crohn's disease, 21% in UC)
Tran et al, 2021 ¹⁴	France	IBD	FAP, IBS, FAPD (Rome III)	National IBD network	102 with IBD in clinical remission. 75 with Crohn's disease, 19 UC, 8 unclassified.	At least one FGID, 22% IBD-FAPD, 17% IBS, 3.9%

Adult studies						
Klem et al, 2017 ²¹	Worldwide	Infectious enteritis	IBS (Rome I-III)	Systematic review of 45 studies (4 including children) up to 2015	21,421 with infectious enteritis	IBS within and beyond 12 months: Overall, 10.1% and 14.5% Bacterial, 13% and 12.9% Viral, 19.4% and 4.4% Protozoal, 6.9% and 53%
Futagami et al, 2015 ²²	Worldwide	Infectious enteritis	FD (Rome II-III, ICD-9 code)	Systematic review of 19 studies up to 2014	9517 with infectious enteritis	FD beyond 6 months, 9.55%
Wadhwa et al, 2016 ²³	USA	C.difficile infection	IBS (Rome III)	Cross-sectional	205 with C. difficile infection	IBS beyond 6 months, 25%
Gutierrez et al, 2015 ²⁴	USA	C.difficile infection	IBS, GERD, constipation, dyspepsia (not stated)	Retrospective case control study	891 military personnel with C. difficile infection	Functional gastrointestinal symptoms (IBS, GERD, constipation, dyspepsia) beyond 1 year, 14.1% after C-difficile vs. 6% in controls
Rahman et al, 2018 ²⁵	Bangladesh	Infectious enteritis	IBS, FD (Rome III)	Cross-sectional	345 with infectious enteritis (<i>Vibrio cholera</i> 39%, <i>E. coli</i> 33%, <i>Campylobacter</i> 9%)	At 12 month follow up: IBS, 16.5% FD, 7.4% Similar rates across the bacterial infections
Marasco et al, 2023 ²⁶	Worldwide	COVID-19	IBS, FD (Rome III-IV)	Systematic review of 10 studies up to 2022	1119 and 2763 with COVID-19 assessed for functional dyspepsia and IBS, respectively	Between 3 to 12 months: Post-COVID FD, 4% Post-COVID IBS, 12%
Pediatric Studies						
Saps et al, 2008 ²⁷	US and Italy	Infectious enteritis	IBS, FD, multiple FGIDs.	Multicenter tertiary care retrospective cohort study	44 with acute bacterial gastroenteritis (<i>Salmonella</i> 54%,	Abdominal pain/FGID:

			(Rome II)		<i>Campylobacter</i> 32%, and <i>Shigella</i> 14%) and 44 controls	36% in those exposed (87% had IBS and 24% FD) vs. 11% controls (RR 3.2, 95% CI 1.28-7.96).
Zhu et al, 2014 ²⁸	China	Infectious enteritis	IBS (Rome II)	Population based (schools) Cross-sectional study.	7,472 participants IBS: 808	Risk/Protective factors: IBS and young age (OR 0.94 95% CI 0.89-0.99) IBS and gastroenteritis during childhood (OR 1.29, 95% CI 1.00 – 1.63.).
Zhou et al. 2008 ²⁹	China	Infectious enteritis	IBS (Rome II)	Population based (schools) Cross-sectional study	51,956 students IBS: 10,490	Risk/Protective factors: IBS (OR 2.66 95% CI 2.46-2.89).
Saps et al, 2009 ³⁰	USA and Italy	Infectious enteritis	Multiple FGIDs. (Rome II)	Multicenter tertiary care retrospective cohort study.	44 children with acute gastroenteritis (secondary to rotavirus) and 44 controls.	AP-FGID, 16% exposed vs. 7% controls Prevalence of FGIDs following infection was 30% in year one, 9% in year two, and 12.5% in year three.
Thabane et al, 2010 ³¹	Canada	Infectious enteritis	IBS (Rome I)	Population based prospective cohort	305 with acute gastroenteritis (<i>E.coli</i> or <i>Campylobacter</i>) and 162 controls.	IBS cumulative incidence, 10.5% exposed vs. 2.5% controls (OR 4.6, 95% CI 1.6-13.3).

Cremon et al, 2014 ³²	Italy	Infectious enteritis	IBS, FD (Rome III)	Prospective controlled cohort study	Outbreak of <i>Salmonella</i> enteritis amongst 1811 individuals (randomly selected 250 exposed as children, 127 exposed as adults)	Among adults exposed as children: IBS, 35.3% exposed vs. 20.5% controls (OR 2.12, 95% CI 1.21-3.71) FD, 27.3% vs. 26% (OR 1.07, 95% 0.62 – 1.86) Prevalence in exposed and non-exposed as adults was the same.
Pensabane et al, 2015 ³³	Italy	Infectious enteritis	Multiple FGIDs (Rome III)	Prospective Cohort study.	32 with acute gastroenteritis (rotavirus 56.8%, salmonella 30%, adenovirus 6.6%, norovirus 3.3%, and <i>Giardia lamblia</i> 3.3%) and 32 controls.	All FGIDs following acute diarrhea: At 1 month: 40.6% exposed vs. 12.5% controls (RR 1.9) At 3 months: 53% vs. 15.6% (RR 2.2) At 6 months: 46.8% vs. 15.6% (RR 1.9) AP- FGIDs were more frequent at 6 months post-infection (28.1% exposed vs. 6.2% controls, RR = 1.7).
Schwille-Kiuntke J, 2015 ³⁴	Germany	Infectious enteritis	AP Questionnaire	Population based cross-sectional study.	643 with a history of <i>Salmonella</i> infection (50.1% male).	Abdominal pain, 31.7% exposed vs. 21.9% controls Headache 27.2% vs. 15.1%
Krajicek EJ et al, 2018 ³⁵	Australia	Infectious enteritis & non-GI	IBS (Rome I-II)	Case-control study.	1010 participants (509 outpatients with IBS, 501 matched controls)	Risk/Protective factors: Early childhood GI infections, 20% cases vs. 19% controls (OR 0.95 95% CI 0.62-1.45) Bronchitis, 43% vs. 25% (OR 1.73, 95% CI 1.20-2.51)

						Bronchitis and IBS after adjusting for antibiotic use ($p=0.01$).
Velasco-Benitez et al, 2019 ³⁶	Colombia	Non-GI infection	Multiple FGIDs (Rome III)	Prospective cohort study.	73 children with non-severe dengue episode and 62 controls	DGBI prevalence among exposed ranged from 14.9%-18.2% at 3-12 months follow-up. AP-DGBI prevalence following non-severe dengue episode: At 3 months: 8.5% exposed vs. 6.4% controls. At 6 months: 5.6% vs. 10% At 9 months: 0% vs. 3.7% At 12 months: 4.0% vs. 9.4%
Kesuma et al, 2019 ³⁷	Indonesia	Infectious enteritis	IBS (Rome III)	Population based cross sectional sample.	454 students IBS: 137 (50 <i>Blastocystis</i> spp) Non-IBS: 317 (20 <i>Blastocystis</i> spp).	<i>Blastocystis</i> spp. was more common amongst IBS than controls (36.5% vs. 28.6%, RR = 1.4; 95% CI = 0.8–2.7).
Carter et al. ³⁸ 2019	Wales, UK.	Infectious enteritis	IBS (Rome III)	Prospective population based cohort study.	205 with <i>Cryptosporidium</i>	Vomiting occurred significantly more frequently in children than adults Overall (inclusive of adults), 10% met IBS criteria. 23% had IBS-like symptoms 2.8% (children only) met all IBS criteria post-infection
Piriyakitphaibon V et al, 2022 ³⁹	Thailand	Infectious enteritis	Recurrent AP (ICD-10 code)	Retrospective tertiary care cohort study.	367 participants Recurrent AP: 94 Non-recurrent AP: 273	Recurrent AP, 36% exposed vs. 27.7% controls (OR 3.36, 95% CI 1.314–8.162) Risk factors: Mental health problems, 12.4% vs. 4.1% (OR 3.05, 95% CI 1.17–7.95)

						Abdominal pain lasting ≥ 7 days, 27.2% vs. 9.8% (OR 3.71, 95% CI 1.85–7.45) Change in stool frequency, 13.6% vs. 3.6% (OR 2.65, 95% CI 1.48–4.75)
Tan et al. ⁴⁰ 2018	Taiwan	Non GI infection	IBS (ICD-9 code)	Population-based retrospective cohort.	Infantile UTI (n=31,788) and non-UTI (n=127,152)	IBS, 1.9% exposed vs. 1.2% controls IBS was 1.52-fold higher (95% CI 1.38 - 1.67) compared with the non-UTI cohort (2.05 vs. 1.32 per 1000 person-years). Hazard ratio of IBS for boys (1.53; 95% CI 1.34 to 1.73) for girls (1.50; 95% CI 1.29 to 1.73).
Velasco Benitez et al. ⁴¹ 2019	Colombia	Non GI - Infection	Multiple FGIDs (Rome III)	Population based cross-sectional study.	4023 participants (Dengue: 301)	History of dengue had higher odds of having at least 1 FGID, OR 1.98 (95%CI 1.53-2.56, $p < 0.0001$) DGBI, 35.9% exposed vs. 22% controls
Farello G et al, 2021 ⁴²	Italy	COVID-19	Multiple FGID (Rome III)	Cross-sectional study.	407 participants	Compared to pre-pandemic prevalence rates: Rumination syndrome increased by 2.7 % (from 0%) IBS by 5% (from 3.8%) Abdominal migraine by 8.8% (from 5.1%) Functional abdominal pain by 2.8% (from 0.8%)
Stepan et al. ⁴³ 2022	Romania	COVID-19	IBS, FD, Abdominal migraine, FAP-NOS (not otherwise specified) (Rome IV)	Retrospective tertiary care cohort.	52 participants Pre-pandemic group, 18 Pandemic group, 34 (PCR +, 23, PCR -, 11)	COVID-19 positive pandemic group and IBS ($p = 0.04$). Significant associations of IBS ($p = 0.045$) and the urban environment ($p = 0.011$) were found with positive cases. IBS, 91.3% PCR (+) vs. 54.5% PCR (-)

						Abdominal migraine, 8.7% vs. 18.2%
						FD, 0% vs. 18.2%
						FAP-NOS, 0% vs. 9.1%

Abbreviations: CD, coeliac disease; IBD, inflammatory bowel disease; UC, ulcerative colitis; MC, microscopic colitis; PD, post-diverticulitis; C. difficile, *Clostridoides difficile*; GI, gastrointestinal; COVID-19, Coronavirus disease 2019; IBS, irritable bowel syndrome; FD, functional dyspepsia; FAB, functional abdominal bloating; DGBI, disorders of gut-brain interaction; FAP, functional abdominal pain; FAPD, functional abdominal pain; Fc, functional constipation; FI, faecal incontinence; ICD, international classification of diseases; GERD, gastro-oesophageal reflux disease; E.coli, *Escherichia coli*; AP, abdominal pain; UTI, urinary tract infection; PCR, polymerase chain reaction; GFD, gluten-free diet; CI, confidence interval; FBD, functional bowel disorder; GSRS-IBS, gastrointestinal symptom rating scale-IBS; FGID, functional gastrointestinal disorder; NOS, not otherwise specified.

References – Supplementary table 2

1. Sainsbury A, Sanders DS, Ford AC. Prevalence of irritable bowel syndrome-type symptoms in patients with celiac disease: a meta-analysis. *Clin Gastroenterol Hepatol.* 2013;11(4):359-365.e351.
2. Silvester JA, Graff LA, Rigaux L, et al. Symptoms of Functional Intestinal Disorders Are Common in Patients with Celiac Disease Following Transition to a Gluten-Free Diet. *Digestive Diseases and Sciences.* 2017;62(9):2449-2454.
3. Parker S, Palsson O, Sanders DS, et al. Functional Gastrointestinal Disorders and Associated Health Impairment in Individuals with Celiac Disease. *Clin Gastroenterol Hepatol.* 2022;20(6):1315-1325.e1314.
4. Turco R, Boccia G, Miele E, et al. The association of coeliac disease in childhood with functional gastrointestinal disorders: a prospective study in patients fulfilling Rome III criteria. *Aliment Pharmacol Ther.* 2011;34(7):783-789.
5. Saps M, Adams P, Bonilla S, Nichols-Vinueza D. Abdominal pain and functional gastrointestinal disorders in children with celiac disease. *J Pediatr.* 2013;162(3):505-509.
6. Saps M, Sansotta N, Bingham S, et al. Abdominal Pain-Associated Functional Gastrointestinal Disorder Prevalence in Children and Adolescents with Celiac Disease on Gluten-Free Diet: A Multinational Study. *J Pediatr.* 2017;182:150-154.
7. Cristofori F, Tripaldi M, Lorusso G, et al. Functional Abdominal Pain Disorders and Constipation in Children on Gluten-Free Diet. *Clin Gastroenterol Hepatol.* 2021;19(12):2551-2558.
8. Veeraraghavan G, Therrien A, Degroote M, et al. Non-responsive celiac disease in children on a gluten free diet. *World J Gastroenterol.* 2021;27(13):1311-1320.

9. Fairbrass KM, Costantino SJ, Gracie DJ, Ford AC. Prevalence of irritable bowel syndrome-type symptoms in patients with inflammatory bowel disease in remission: A systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2020;5:1053-1062.
10. Nigam GB, Limdi JK, Hamdy S, Vasant DH. The prevalence and burden of Rome IV functional colorectal disorders in ulcerative colitis. *Gut*. 2019;68 (Supplement 2):A203-204.
11. Zimmerman LA, Srinath AI, Goyal A, et al. The overlap of functional abdominal pain in pediatric Crohn's disease. *Inflamm Bowel Dis*. 2013;19(4):826-831.
12. Diederens K, Hoekman DR, Hummel TZ, et al. The prevalence of irritable bowel syndrome-type symptoms in paediatric inflammatory bowel disease, and the relationship with biochemical markers of disease activity. *Aliment Pharmacol Ther*. 2016;44(2):181-188.
13. Watson KL, Jr., Kim SC, Boyle BM, Saps M. Prevalence and Impact of Functional Abdominal Pain Disorders in Children With Inflammatory Bowel Diseases (IBD-FAPD). *J Pediatr Gastroenterol Nutr*. 2017;65(2):212-217.
14. Tran LC, Bridoux-Henno L, Gastineau S, et al. Functional abdominal pain disorders and patient- and parent-reported outcomes in children with inflammatory bowel disease in remission. *Dig Liver Dis*. 2021;53(10):1268-1275.
15. Limbri LF, Wilson TG, Oliver MR. Prevalence of irritable bowel syndrome and functional abdominal pain disorders in children with inflammatory bowel disease in remission. *JGH Open*. 2022;6(12):818-823.
16. Kamp EJ, Kane JS, Ford AC. Irritable bowel syndrome and microscopic colitis: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2016;14:659-668.
17. Kane JS, Irvine AJ, Derwa Y, Rotimi O, Ford AC. High prevalence of irritable bowel syndrome-type symptoms in microscopic colitis: Implications for treatment. *Therap Adv Gastroenterol*. 2018;11:1756284818783600.
18. Pagoldh J, Lundgren D, Suhr OB, Karling P. Irritable bowel syndrome-like symptoms in treated microscopic colitis patients compared with controls: A cross-sectional study. *Gastroenterol Rep (Oxf)*. 2020;8:374-380.
19. Cohen E, Fuller G, Bolus R, et al. Increased risk for irritable bowel syndrome after acute diverticulitis. *Clin Gastroenterol Hepatol*. 2013;11(12):1614-1619.
20. Carabotti M, Marasco G, Sbarigia C, et al. Site and duration of abdominal pain discriminate symptomatic uncomplicated diverticular disease from previous diverticulitis patients. *Intern Emerg Med*. 2024.
21. Klem F, Wadhwa A, Prokop LJ, et al. Prevalence, Risk Factors, and Outcomes of Irritable Bowel Syndrome After Infectious Enteritis: A Systematic Review and Meta-analysis. *Gastroenterology*. 2017;152(5):1042-1054.e1041.
22. Futagami S, Itoh T, Sakamoto C. Systematic review with meta-analysis: post-infectious functional dyspepsia. *Aliment Pharmacol Ther*. 2015;41(2):177-188.
23. Wadhwa A, Al Nahhas MF, Dierkhising RA, et al. High risk of post-infectious irritable bowel syndrome in patients with *Clostridium difficile* infection. *Aliment Pharmacol Ther*. 2016;44(6):576-582.
24. Gutiérrez RL, Riddle MS, Porter CK. Increased risk of functional gastrointestinal sequelae after *Clostridium difficile* infection among active duty United States military personnel (1998-2010). *Gastroenterology*. 2015;149(6):1408-1414.

25. Rahman MM, Ghoshal UC, Sultana S, et al. Long-Term Gastrointestinal Consequences are Frequent Following Sporadic Acute Infectious Diarrhea in a Tropical Country: A Prospective Cohort Study. *Am J Gastroenterol*. 2018;113(9):1363-1375.
26. Marasco G, Maida M, Cremon C, Barbaro MR, Stanghellini V, Barbara G. Meta-analysis: Post-COVID-19 functional dyspepsia and irritable bowel syndrome. *Aliment Pharmacol Ther*. 2023;58(1):6-15.
27. Saps M, Pensabene L, Di Martino L, et al. Post-infectious functional gastrointestinal disorders in children. *J Pediatr*. 2008;152(6):812-816, 816.e811.
28. Zhu X, Chen W, Zhu X, Shen Y. A cross-sectional study of risk factors for irritable bowel syndrome in children 8-13 years of age in suzhou, china. *Gastroenterol Res Pract*. 2014;2014:198461.
29. Zhou HQ, Li DG, Song YY, et al. [Risk factors of irritable bowel syndrome in adolescents in China]. *Zhonghua Er Ke Za Zhi*. 2008;46(2):136-138.
30. Saps M, Pensabene L, Turco R, Staiano A, Cupuro D, Di Lorenzo C. Rotavirus gastroenteritis: precursor of functional gastrointestinal disorders? *J Pediatr Gastroenterol Nutr*. 2009;49(5):580-583.
31. Thabane M, Simunovic M, Akhtar-Danesh N, et al. An outbreak of acute bacterial gastroenteritis is associated with an increased incidence of irritable bowel syndrome in children. *Am J Gastroenterol*. 2010;105(4):933-939.
32. Cremon C, Stanghellini V, Pallotti F, et al. Salmonella gastroenteritis during childhood is a risk factor for irritable bowel syndrome in adulthood. *Gastroenterology*. 2014;147(1):69-77.
33. Pensabene L, Talarico V, Concolino D, et al. Postinfectious functional gastrointestinal disorders in children: a multicenter prospective study. *J Pediatr*. 2015;166(4):903-907.e901.
34. Schwille-Kiuntke J, Unverdorben A, Weimer K, et al. Bacterial infections in childhood: A risk factor for gastrointestinal and other diseases? *United European Gastroenterol J*. 2015;3(1):31-38.
35. Krajicek EJ, Almazar AE, Larson JJ, Atkinson EJ, Talley NJ, Saito YA. Early Infections and the Risk of Irritable Bowel Syndrome: A Case-Control Study. *J Clin Gastroenterol*. 2018;52(10):896-901.
36. Velasco-Benítez CA, Ortiz-Rivera CJ. Post-infectious functional gastrointestinal disorders in children after a non-severe dengue episode without warning signs. *Biomedica*. 2019;39(Supl. 2):93-100.
37. Kesuma Y, Firmansyah A, Bardosono S, Sari IP, Kurniawan A. Blastocystis ST-1 is associated with Irritable Bowel Syndrome-diarrhoea (IBS-D) in Indonesian adolescences. *Parasite Epidemiol Control*. 2019;6:e00112.
38. Carter BL, Stiff RE, Elwin K, et al. Health sequelae of human cryptosporidiosis-a 12-month prospective follow-up study. *Eur J Clin Microbiol Infect Dis*. 2019;38(9):1709-1717.
39. Piriyaikitphaiboon V, Sirinam S, Noipayak P, Sirivichayakul C, Pornrattanarungsri S, Limkittikul K. Risk Factors for Recurrent Abdominal Pain in Children with Nonorganic Acute Abdominal Pain. *Pediatr Gastroenterol Hepatol Nutr*. 2022;25(2):129-137.
40. Tan TK, Saps M, Lin CL, Wei CC. Risks of irritable bowel syndrome in children with infantile urinary tract infection: a 13-year nationwide cohort study. *J Investig Med*. 2018;66(6):998-1003.
41. Velasco-Benítez CA O-RC. Is a history of dengue associated with the presence of Functional Gastrointestinal Disorders in Children? *Infectio*. 2019;23(2):161-166.

42. Farello G, Di Lucia A, Fioravanti B, Tambucci R, Stagi S, Gaudino R. Analysis of the impact of COVID-19 pandemic on functional gastrointestinal disorders among paediatric population. *Eur Rev Med Pharmacol Sci*. 2021;25(18):5836-5842.
43. Stepan MD, Cioboata R, Vintilescu Ş B, et al. Pediatric Functional Abdominal Pain Disorders following COVID-19. *Life (Basel)*. 2022;12(4).

Supplementary table 3 | Current literature addressing the treatment of DGBI symptoms in organic gastrointestinal disease in remission

	Celiac disease	Inflammatory bowel disease (IBD) and microscopic colitis (MC)	Post-diverticulitis	Post-infectious
Probiotics	A randomized, double-blind, placebo-controlled multicentre trial showed promising results with a probiotic mixture, with regards to symptom improvement and modification of gut microbiota, characterized by an increase in bifidobacteria. ¹	A meta-analysis of 22 RCTs did not identify any benefit of probiotics in IBD, but none of the trials recruited patients with symptoms of a DGBI, specifically. ²	No RCTs	No RCTs
Diet	Low FODMAP diet i) Small open-label pilot study in 25 patients showed a benefit with adjuvant low FODMAP diet.³ ii) A single-centre randomized controlled trial from Italy comprising 50 patients with celiac disease found that a short-term low FODMAP diet in addition to a GFD helped reduce gastrointestinal symptoms and improve mental well-being compared with a GFD alone.⁴	A RCT of low FODMAP diet in 52 patients with quiescent IBD with ongoing gastrointestinal symptoms showed a benefit of low FODMAP diet on both gastrointestinal symptoms and quality of life, compared with control dietary advice, but only examined the elimination phase of the diet. ⁷	No RCTs	No RCTs

	iii) Another randomized trial of 70 patients found a GFD/low FODMAP diet superior to GFD alone.⁵ Limitations are 4-week data comprising elimination phase only and concerns about combining two restrictive diets. Low Nickel diet i) A GFD can lead to higher loads of ingested alimentary Nickel and induce allergic contact mucositis. An observational study reported symptom improvement and histological remission in 20 patients with CD on a GFD, who then had a recrudescence of gastrointestinal symptoms with associated mucositis and dermatitis⁶. A low Nickel diet subsequently led to symptom resolution. Large confirmatory studies and RCTs are needed.			
Antispasmodics	No RCTs	No RCTs	No RCTs	No RCTs
Other peripherally acting GI drugs	No RCTs	i) Bile acid sequestrants (e.g., cholestyramine or colesevelam):	There is some evidence that mesalamine can	In a negative large placebo-controlled study of mesalazine in

		In one RCT of colesevelam in 26 patients with Crohn's disease with confirmed bile acid diarrhea response rates were higher, in terms of a reduction in number of liquid stools per day and improvement in stool consistency, with colesevelam compared with placebo. However, treatment was only for 4 weeks.⁸ ii) Anti-diarrhoeals (e.g., loperamide): In a RCT of loperamide in patients with Crohn's disease with chronic diarrhea, improvements in abdominal pain and diarrhea were significantly more likely with loperamide than placebo. However, treatment was for only 1 week.⁹ iii) Drugs acting on 5-HT receptors (e.g., ondansetron or ramosetron): In a 4-week RCT of ramosetron in patients with quiescent IBD but with IBS-D symptoms, improvements in overall IBS symptoms and bowel habit were significantly more likely with ramosetron than placebo. There was no significant difference in abdominal pain or discomfort between the groups.¹⁰ There have been no RCTs of drugs acting on 5-HT receptors in patients with MC with DGBI symptoms.	prevent the development of chronic symptoms after an episode of acute diverticulitis, although this is inconsistent.¹¹	patients with IBS-D, a subgroup of 13 patients fulfilling criteria for PI-IBS showed improvement with mesalazine with regards to average abdominal pain severity, average urgency score and average daily stool consistency, but the small sample size of this sub-analysis hampers firm conclusions.¹²
--	--	--	--	---

Gut-brain neuromodulators (e.g., tricyclic antidepressants)	No RCTs	i) In one retrospective case series, among 81 patients with IBD with ongoing gastrointestinal symptoms despite controlled inflammation, at least moderate improvement in symptoms occurred with initiation of a tricyclic antidepressant in 59.3% of patients.¹³ However, there have been no RCTs of tricyclic antidepressants in patients with IBD or MC with DGBI symptoms.	No RCTs	No RCTs
Gut-brain behavioral therapies (e.g., IBS-specific cognitive behavioral therapy, gut-directed hypnotherapy).	No RCTs	i) In one RCT mindfulness-based therapy led to an improvement in quality of life, compared with a waiting list control, in 38 patients with IBS-type symptoms. However, the effect on gastrointestinal symptoms was not examined.¹⁴ ii) In a meta-analysis of RCTs, there appeared to be short-term effects of gut-brain behavioral therapies on mood scores and quality of life in patients with IBD, but again effect on gastrointestinal symptoms was not studied, and most trials were not conducted in patients with a coexistent DGBI.¹⁵	No RCTs	No RCTs
Recommendations for clinical practice	Given the paucity of high-quality data, current recommendations for the treatment of DGBI symptoms in patients with organic disease in remission (e.g., through the use of dietary modifications, probiotics, antispasmodics, drugs acting on			

	5-HT receptors, anti-inflammatory drugs [i.e. mesalamine], gut-brain neuromodulators, and gut-brain behavioral therapies) would, therefore, have to be extrapolated from meta-analyses of RCTs in IBS. ¹⁶⁻²³
--	---

Abbreviations: FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; CD, coeliac disease; GFD, gluten-free diet; RCT, randomized controlled trial; DGBI, disorders of gut-brain interaction; IBS, irritable bowel syndrome; GI, gastrointestinal; 5-HT, 5-hydroxytryptamin; IBD, inflammatory bowel disease; MC, microscopic colitis; IBS-D, IBS with diarrhoea; PI-IBS, post-infection IBS.

REFERENCES - Supplementary Table 3

1. Francavilla R, Piccolo M, Francavilla A, et al. Clinical and Microbiological Effect of a Multispecies Probiotic Supplementation in Celiac Patients With Persistent IBS-type Symptoms: A Randomized, Double-Blind, Placebo-controlled, Multicenter Trial. *J Clin Gastroenterol*. 2019;53(3):e117-e125.
2. Derwa Y, Gracie DJ, Hamlin PJ, Ford AC. Systematic review with meta-analysis: The efficacy of probiotics in inflammatory bowel disease. *Aliment Pharmacol Ther*. 2017;46:389-400.
3. Trott N, Rej A, Coleman SH, Sanders DS. Adult celiac disease with persistent IBS-type symptoms: a pilot study of an adjuvant FODMAP diet. *Gastroenterol Hepatol Bed Bench*. 2021;14(4):304-310.
4. Roncoroni L, Bascuñán KA, Doneda L, et al. A low FODMAP gluten-free diet improves functional gastrointestinal disorders and overall mental health of celiac disease patients: A randomized controlled trial. *Nutrients*. 2018;10(8).
5. van Megen F, Skodje GI, Lergenmuller S, et al. A Low FODMAP Diet Reduces Symptoms in Treated Celiac Patients With Ongoing Symptoms-A Randomized Controlled Trial. *Clin Gastroenterol Hepatol*. 2022;20(10):2258-2266.e2253.
6. Borghini R, De Amicis N, Bella A, Greco N, Donato G, Picarelli A. Beneficial Effects of a Low-Nickel Diet on Relapsing IBS-Like and Extraintestinal Symptoms of Celiac Patients during a Proper Gluten-Free Diet: Nickel Allergic Contact Mucositis in Suspected Non-Responsive Celiac Disease. *Nutrients*. 2020;12(8).
7. Cox SR, Lindsay JO, Fromentin S, et al. Effects of low FODMAP diet on symptoms, fecal microbiome, and markers of inflammation in patients with quiescent inflammatory bowel disease in a randomized trial. *Gastroenterology*. 2020;158:176-188.e177.
8. Beigel F, Teich N, Howaldt S, et al. Colesevelam for the treatment of bile acid malabsorption-associated diarrhea in patients with Crohn's disease: A randomized, double-blind, placebo-controlled study. *J Crohn's Colitis*. 2014;8:1471-1479.
9. van Outryve M, Toussaint J. Loperamide oxide for the treatment of chronic diarrhoea in Crohn's disease. *J Int Med Res*. 1995;23:335-341.
10. Tomita T, Fukui H, Morishita D, et al. Efficacy of Serotonin Type 3 Receptor Antagonist Ramosetron on Diarrhea-Predominant Irritable Bowel Syndrome (IBS-D)-Like Symptoms in Patients with Quiescent Inflammatory Bowel Disease: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Clin Med*. 2022;11(23).

11. Stollman N, Magowan S, Shanahan F, Quigley EM. A randomized controlled study of mesalamine after acute diverticulitis: results of the DIVA trial. *J Clin Gastroenterol*. 2013;47(7):621-629.
12. Lam C, Tan W, Leighton M, et al. A mechanistic multicentre, parallel group, randomised placebo-controlled trial of mesalazine for the treatment of IBS with diarrhoea (IBS-D). *Gut*. 2016;65(1):91-99.
13. Iskandar HN, Cassell B, Kanuri N, et al. Tricyclic antidepressants for management of residual symptoms in inflammatory bowel disease. *J Clin Gastroenterol*. 2014;48(5):423-429.
14. Berrill JW, Sadlier M, Hood K, Green JT. Mindfulness-based therapy for inflammatory bowel disease patients with functional abdominal symptoms or high perceived stress levels. *Journal of Crohn's & colitis*. 2014;8(9):945-955.
15. Riggott C, Mikocka-Walus A, Gracie DJ, Ford AC. Efficacy of psychological therapies in people with inflammatory bowel disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2023.
16. Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. *Gut*. 2022;71(6):1117-1126.
17. Goodoory VC, Khasawneh M, Black CJ, Quigley EM, Moayyedi P, Ford AC. Efficacy of Probiotics in Irritable Bowel Syndrome: Systematic Review and Meta-analysis. *Gastroenterology*. 2023.
18. Ford AC, Talley NJ, Spiegel BM, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. *Bmj*. 2008;337:a2313.
19. Ford AC, Brandt LJ, Young C, Chey WD, Foxx-Orenstein AE, Moayyedi P. Efficacy of 5-HT₃ antagonists and 5-HT₄ agonists in irritable bowel syndrome: systematic review and meta-analysis. *Am J Gastroenterol*. 2009;104(7):1831-1843; quiz 1844.
20. Gunn D, Topan R, Barnard L, et al. Randomised, placebo-controlled trial and meta-analysis show benefit of ondansetron for irritable bowel syndrome with diarrhoea: The TRITON trial. *Aliment Pharmacol Ther*. 2023;57(11):1258-1271.
21. Goodoory VC, Tuteja AK, Black CJ, Ford AC. Systematic Review and Meta-analysis: Efficacy of Mesalamine in Irritable Bowel Syndrome. *Clin Gastroenterol Hepatol*. 2024;22(2):243-251.e245.
22. Ford AC, Lacy BE, Harris LA, Quigley EMM, Moayyedi P. Effect of Antidepressants and Psychological Therapies in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-Analysis. *Am J Gastroenterol*. 2019;114(1):21-39.
23. Black CJ, Thakur ER, Houghton LA, Quigley EMM, Moayyedi P, Ford AC. Efficacy of psychological therapies for irritable bowel syndrome: systematic review and network meta-analysis. *Gut*. 2020;69(8):1441-1451.

Supplementary Table 4 | Non-GI overlap with DGBI

Authors (year)	Country	DGBI and measure used to define	Overlapping condition and measure used to define	Study design	Study setting and recruitment	Participant characteristics (sample size, mean age and age range, sex)	Prevalence of overlapping condition
Headache							
Adult studies							
Jones et al, 2001 ¹	USA	<u>IBS</u> Rome II	<u>Headache</u> Self-reported	Cross sectional	Tertiary care	N=270 patients with IBS	51% reported CFS
Whitehead et al, 2002 ²	Worldwide	IBS	<u>Headache</u>	Systematic review			23-45%
Si et al, 2004 ³	China	<u>IBS</u> Rome II	<u>Headache</u> Self-reported	Cross sectional	Multi-center tertiary care	n=662 patients with IBS	29%
Whitehead et al, 2007 ⁴	USA	<u>IBS</u> ICD-9	<u>Headache</u> ICD-9	Cross sectional, healthcare database	Healthcare database - Group Health Cooperative of Puget Sound (GHC),	N=3,153 patients with IBS	25.91%
Pediatric studies							
Friesen et al, 2018 ⁵	USA	<u>IBS, FD, FAP</u> Rome IV	<u>Headache</u> Self reported	Cross sectional study	Tertiary Care	N= 235 (77.9% female ages 8-17yo) 86% FD; 58% IBS, 50% both IBS and FD	73.8% of FD (versus 45.2% of non-FD patients) 57.9% of IBS (versus 56.3% of non-IBS)
Devanarayana et al 2011 ⁶	Sri Lanka	<u>IBS, FD, FAP</u> Rome III	Demographic questionnaire	Cross sectional study	Randomly selected school children	N=2163 10- to 16-year-olds Mean age 13.4 years 270 (12.5%) had at least 1 abdominal pain-predominant FGD. 107 (4.9%) with IBS 54 (2.5%) with functional dyspepsia (FD) 96 (4.4%) with functional abdominal pain (FAP) 21 (1.0%) with functional abdominal migraine (AM)	36.7% with FGD had headaches as compared with 4% controls

Karabulut et al 2013 ⁷	Turkey	<u>IBS</u> Rome III	Demographic questionnaire	Prospective cohort	Tertiary care clinic	N=345 53% female (4-18 years) N=78 (22.6%) had Rome III IBS	41% in IBS vs 18.2% healthy controls (p< 0.0001)
Chumpitazi et al 2021 ⁸	USA	<u>Functional abdominal pain disorders (FAPD)</u> Rome III	Socio demographic questionnaire, Children's Somatic Symptom Inventory, Functional Disability Inventory (FDI),	Cross sectional	Children were identified from prior prospective studies.	N=406 (64.2% female, 7-17 years old) Median age = 10 years IBS: 284 patients FAP: 122 patients	172 (42%) headache
Zanchi et al 2021 ⁹	Italy	<u>FD, functional constipation, cyclic vomiting, FAP, or IBS</u> Rome III	The questionnaire was specifically developed for the study	Historic cohort follow-up study	outpatient clinic of the pediatric gastroenterology and the pediatric ward of the Institute for Maternal and Child Health IRCCS Burlo Garofolo of Trieste, Italy.	N=79 cases (50.6% female; age 2-17yo) N= 201 controls (61.2% female)	33% (26 out of 79) of DGBI patients reported headache or migraine versus 13% (26 out of 201) of healthy peers (p < 0.001).
Migraine							
Adult studies							
Cole et al, 2006 ¹⁰	USA	<u>IBS</u> ICD-9	<u>Migraine</u> ICD-9	Cross sectional	National health insurance database	N=97,593 with IBS	6%
Ladabaum et al, 2012 ¹¹	USA	<u>IBS</u> ICD-9	<u>Migraine</u> ICD-9	Cross sectional	Kaiser Permanente health insurance database	N=141,295 with IBS	36.7%
Lacy et al, 2019 ¹²	USA	<u>IBS</u> ICD codes	<u>Migraine</u> ICD-9	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	12.4% in the high count group 8.6% in the moderate count group 8.2% in the zero count group
Bin Abdulrahman et al, 2022 ¹³	Saudi Arabia	<u>IBS</u> Rome IV	<u>Migraine</u> Migraine severity questionnaire	Cross sectional	Nationwide survey	N=460 with IBS	55.2%
Wang et al, 2023 ¹⁴	USA	<u>IBS</u> Central	<u>Migraine</u> Central Sensitization Inventory	Cross sectional	Survey of patients in rural primary care practices	N=264 with IBS	74%

		Sensitization Inventory					
Pediatric studies							
Le Gal et al 2016 ¹⁵	Italy and France	<u>FD, IBS, or abdominal migraine (AM)</u> Rome III	<u>Migraine</u> International Classification of Headache	Case-control	Four European tertiary care hospitals	N=424 (46% female; mean age 10.5:8-13 years) vs 648 controls (40% female; mean age 11: range 7.9 to 13.1 years)	32% in DGBI group vs 18% in control group
Temporomandibular Joint Disorder							
Adult studies							
Jones et al, 2001 ¹	USA	<u>IBS</u> Rome II	<u>TMD</u> Self-reported diagnosis	Cross sectional	Tertiary care	N=270 patients with IBS	16% reported CFS
Whitehead et al, 2007 ⁴	USA	<u>IBS</u> ICD-9	<u>TMD</u> ICD-9	Cross-sectional	Healthcare database - Group Health Cooperative of Puget Sound (GHC),	N=3,153 patients with IBS	3.3%
Sanders et al, 2014 ¹⁶	USA	<u>IBS</u> Rome III	<u>TMD</u> ICD-9	Prospective cohort study	OPPERA study	N=74 respondents with IBS	9.16% incidence rate of first onset TMD in IBS
Gallotta et al, 2017 ¹⁷	Italy	<u>IBS</u> Rome III	<u>TMD</u> RDC/TMD criteria	Cross-sectional	Tertiary care clinic	N=91 patients with IBS	54.9%
Wang et al, 2023 ¹⁴	USA	<u>IBS</u> Central Sensitization Inventory	<u>TMD</u> Central Sensitization Inventory	Cross sectional	Survey of patients in rural primary care practices	N=264 with IBS	23.4%
Pediatric studies							
None							
Fibromyalgia							
Adult studies							
Veale et al (1991) ¹⁸	Ireland	<u>IBS</u> Clinical symptom criteria	<u>Fibromyalgia</u> self report	Cross-sectional	Patients recruited from GI clinic, rheumatology clinic.	N = 100 participants IBS: 20 patients	65%
Barton et al (1999) ¹⁹	United Kingdom	<u>IBS</u> Rome IV	<u>Fibromyalgia</u> American College of Rheumatology criteria	Cross-sectional	IBS patients recruited from a GI clinic.	N = 92 participants IBS: 46 patients (38 female, mean age 44 years [20-70 years])	28%
Sperber et al (1999) ²⁰	Israel	<u>IBS</u> Rome I&II	<u>Fibromyalgia</u> American College of	Cross-sectional	Patients recruited from a GI clinic.	N = 151 participants IBS: 79 patients	31.6%

			Rheumatology criteria				
Sperber et al (2000) ²¹	Israel	<u>IBS</u> Rome I	<u>Fibromyalgia</u> American College of Rheumatology criteria	Cross-sectional	Patients were recruited from a GI clinic.	N = 144 participants IBS: 75 patients	33.3%
Cole et al (2006) ¹⁰	USA	<u>IBS</u> ICD-9	<u>Fibromyalgia</u> medical or prescription claim	Retrospective	Patient and controls enrolled in a health insurance plan database	N = 124,995 participants IBS: 97,593 patients (72.2% female)	12.9%
Vandvik et al (2006) ²²	Norway	<u>IBS</u> Rome II	<u>Fibromyalgia</u> OPPHED questionnaire	Population-based cross-sectional	Norwegian county participants of public health survey	N=4,662 participants IBS:388 patients; (68% female)	5.15%
Wojczynski et al (2007) ²³	Sweden	<u>IBS</u> Rome II	<u>Fibromyalgia</u> American College of Rheumatology criteria	Population-based, nested case-control	Subset of the Swedish Twin Registry	N=29,616 individual twins,	11.3%
Ladabaum et al (2012) ¹¹	USA	<u>IBS</u> ICD-9	<u>Fibromyalgia</u> (ICD-9 codes)	Observational	IBS patients and controls enrolled in the Kaiser Permanente Northern California (HMO) database	N = 282,589 participants IBS: 141,295 patients (mean age 53 years, 73.6% female)	5.9%
Lacy et al (2019) ¹²	USA	<u>IBS</u> ICD-9 and CPT codes	<u>Fibromyalgia</u> (ICD-9 code)	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	15% in high-count group 10.1% in moderate-count group 8.5% in zero-count group
Settembre et al (2022) ²⁴	Italy	<u>FD: IBS</u> Rome IV	<u>Fibromyalgia</u> American College of Rheumatology criteria	Cross-sectional	Patients recruited from DGBI and FM clinics of a tertiary center	N = 102 participants DGBI: 53 patients IBS: 37 patients FD: 41 patients IBS and FD: 27 patients	45.3% DGBI (IBS and/or FD)
Wang et al, 2023 ¹⁴	USA	<u>IBS</u> Central Sensitization Inventory	<u>TMD</u> Central Sensitization Inventory	Cross sectional	Survey of patients in rural primary care practices	N=264 with IBS	52.5%
Pediatric studies							
None							

Musculoskeletal pain							
Adult studies							
Lee et al (1999) ²⁵	USA	IBS Rome criteria	Musculoskeletal pain self-report questionnaire	Cross- sectional	Two patient populations at a university center (Clinic population [CP] and Advertisement [AP]).	N = 657 participants CP: 342 patients AP: 315 patients	56% (AP) and 63.6% (CP) reported pain in the neck and shoulder
Locke et al (2000) ²⁶	USA	IBS Rome criteria	Musculoskeletal pain self-report questionnaire	Cross- sectional	Residents of Olmsted County were mailed a self-report questionnaire	N = 643 participants IBS: 11.8%	17.5% of participants with IBS who used analgesics had muscular ache and 20.5% had backaches
Tan et al (2003) ²⁷	Malaysia	IBS Rome I	Musculoskeletal pain self-report questionnaire	Observational	Medical school students	N = 533 IBS: 84 patients	23.2% had backaches
Vandvik et al (2004) ²⁸	Norway	IBS Rome II & III	Musculoskeletal pain The Subjective Health Complaint inventory	Prospective cohort	Patients at a general practice	N=1,448 participants IBS: 208 patients	22-49% had neck, back, leg, arm pain
Aggarwal et al (2006) ²⁹	United Kingdom	IBS Rome II	Somatic symptoms somatic symptom checklist)	Cross- sectional	Patients at a general medical practice	N=2,299 participants IBS: 211 patients,	37% reported somatic symptoms
Vandvik et al (2006) ²²	Norway	IBS Rome II	Somatic symptoms OPPHED questionnaire	Cross- sectional	Residents of Norwegian county	N = 4622 participants IBS: 388 patients (17.5%)	19.6% had pain in shoulder 15.2% in arms/hands, 12.4% in upper back, 17.5% in lower back, 16.8% in hips/legs/feet, 5.7% in other locations
Poitras et al (2008) ³⁰	Canada	IBS Rome II	Musculoskeletal Pain Questionnaire asking presence of symptoms	Case-control	Patients in GI clinic in a tertiary care university hospital	N=138 participants IBS: 71 patients	48% had joint pain 75% had back pain
Gulewitsch (2011) ³¹	Germany	IBS Rome III	Musculoskeletal Pain presence of pain > 3 months	Population- based, cross- sectional	University students	N=2,399 participants IBS: 425 patients	17.4% had backaches 4.5% had joint or limb aches
Ladabaum et al (2012) ¹¹	USA	IBS ICD-9	Somatic pain ICD-9 codes	Observational	IBS patients and non-IBS controls enrolled in the	N = 282,589 participants IBS: 141,295 patients	18.7% experienced chronic pain

					Kaiser Permanente Northern California (Health Maintenance Organization) database		
Fikree et al (2015) ³²	United Kingdom	<u>DGBI</u> Rome III	<u>Somatic symptoms</u> (PHQ-15)	Prospective case-control	New patients with GI symptoms at a general secondary care GI clinic	DGBI: 336 patients	11.9% of DGBI without joint hypermobility syndrome had chronic widespread pain
Schauer et al (2019) ³³	Germany	<u>IBS</u> Rome III	<u>Pain</u> Short form-12 questionnaire	Population-based cohort	Registry with random sample of German-speaking adults	N=4,194 participants IBS: 148 patients	64.5% reported general pain in general 47.1% reported back pain
Yanartas et al (2019) ³⁴	Turkey	<u>IBS</u> Rome IV	<u>Somatic Pain</u> Bradford Somatic Inventory	Cross-sectional	IBS patients from GI and internal medicine outpatient clinics	N=118 participants IBS: 51 patients	68.6% had neck and shoulder pain 47.1% had aches all over body 60.8% had leg pain
<i>Pediatric studies</i>							
Devanarayana et al, 2011 ⁶	Sri Lanka	<u>DGBI</u> Rome III	Demographic questionnaire	Cross sectional study	Randomly selected school children	N=2163 10- to 16-year-olds Mean age 13.4 years 270 (12.5%) had at least 1 abdominal pain-predominant FGD. 107 (4.9%) with IBS 54 (2.5%) with functional dyspepsia 96 (4.4%) with functional abdominal pain 21 (1.0%) with functional abdominal migraine	40.7% reported limb pain vs 5.7% controls
Karabulut et al, 2013 ⁷	Turkey	<u>IBS</u> Rome III	Demographic questionnaire	Prospective cohort	Tertiary care clinic	N=345 53% female (4-18 years) N=78 (22.6%) had Rome III IBS	41% back pain vs 9% healthy controls (p<0.0001),
Chumpitazi et al, 2021 ⁸	US	<u>IBS or FAP</u> (Rome III)	Socio demographic questionnaire, Children's Somatic Symptom Inventory, Behavior Assessment	Cross sectional	Children were identified from prior prospective studies.	N=406 (64.2% female, 7-17 years old) Median age = 10 years	33% muscle soreness 27% back pain 23% joint pain 21% extremity (arms and legs) pain

			System for Children-Second Edition, 14-day pain and stool diary, Functional Disability Inventory (FDI), Pediatric Health-Related Quality of Life 4.0 Generic Core Scales			IBS: 284 patients FAP: 122 patients	
Interstitial Cystitis							
Adult studies							
Whitehead et al, 2007 ⁴	USA	<u>IBS</u> ICD-9	<u>Interstitial cystitis</u> ICD-9	Cross sectional, Healthcare database	Healthcare database - Group Health Cooperative of Puget Sound (GHC),	N=3,153 patients with IBS	1.8%
Lacy et al, 2019 ¹²	USA	<u>IBS</u> ICD codes	<u>Interstitial cystitis</u> ICD-9	Cross sectional, Healthcare database	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	1.9% in the high count group 0.9% in the moderate count group 0.6% in the zero count group
Pediatric studies - Overactive bladder							
Friesen et al 2016 ³⁵	USA	<u>IBS, GERD, FD</u> (Rome III)	Standard medical history	Retrospective study	Retrospective chart review, Midwestern tertiary care children's hospital.	N=100 (66% female) Mean age: 13 years 9 months 8 to 17 years	44 % had at least one overactive bladder syndrome symptom 29 % reporting urinary urgency
Dyspareunia							
Adult studies							
Fass et al (1998) ³⁶	USA	<u>Non-ulcer dyspepsia</u> Clinical criteria <u>IBS</u> Manning criteria	<u>Dyspareunia</u> Sexual function questionnaire	Cross-sectional	University Functional Bowel Disorders clinic Healthy controls recruited by advertisement	N = 742 participants IBS-NP (IBS non patients): 41 participants IBS: 266 participants NUD: 85 participants IBS + NUD: 157 participants	30% of IBS-NP 9.3% IBS 3% of NUD 11.4% of NUD+IBS
Moore et al (2017) ³⁷	New Zealand	<u>IBS</u> Rome III	<u>Dyspareunia</u> self-report	Retrospective	Female patients from an IBS clinic	N = 160 participants (IBS, female)	12% IBS 47% IBS + endometriosis

Lacy et al (2019) ¹²	USA	IBS ICD-9-CM and CPT code	Dyspareunia Charlson-Quan comorbidity index	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	1.8%
Dysmenorrhea							
Adult studies							
Altman et al (2006) ³⁸	USA	IBS Clinical diagnosis	Dysmenorrhea and Premenstrual syndrome Clinical questionnaire	Retrospective	Most participants were recruited by community advertisement. 58 participants were recruited by mail through a health maintenance organization	N = 226 females participants with IBS	23%
Olafsdottir et al (2012) ³⁹	Iceland	Functional dyspepsia Bowel Disease questionnaire IBS Manning criteria in1996 and Rome III in 2006	Dysmenorrhea Clinical questionnaire	Longitudinal, population- based cohort	National registry	N = 1180 (1996) and 799 (2006) female participants	79% FD 10.5% (1996) and 25.7% (2006) Manning criteria positive IBS. 41.5% (1996) and 48.6% (2006) Manning criteria positive IBS
Yamamoto et al (2022) ⁴⁰	Japan	FD Rome III	Menstrual pain Clinical questionnaire	Prospective, cross- sectional	Female university students who completed a health examination	N = 4693 participants FD: 115 participants	21.7% light menstrual pain 41.7% sometimes heavy pain 27.8% heavy pain
Pediatric studies							
None							
Chronic pelvic pain							
Adult studies							
Walker et al (1996) ⁴¹	USA	IBS symptom-based criteria	Chronic Pelvic Pain Structured interview	Prospective	GI clinic patients	N = 60 female participants with IBS	35%
Pediatric studies							
None							
Insomnia							
Adult studies							
Ballou et al, 2018 ⁴²	USA	IBS Clinic diagnosis	Insomnia Insomnia severity index	Cross sectional	Tertiary care clinic survey	N=48	51%
Pediatric studies							

None							
Restless Legs Syndrome							
Adult studies							
Yun et al, 2012 ⁴³	Korea	<u>IBS</u> Rome II	<u>RLS</u> International Restless Legs Syndrome Study Group criteria	Cross sectional	Epidemiological cohort	N=373 with IBS	9.7%
Borji et al, 2012 ⁴⁴	Iran	<u>IBS</u> Rome III	<u>RLS</u> International Restless Legs Syndrome Study Group criteria	Cross sectional	Clinic based survey	N=225	25.3%
Wang et al, 2023 ¹⁴	USA	<u>IBS</u> Central Sensitization Inventory	<u>RLS</u> Central Sensitization Inventory	Cross sectional	Survey of patients in rural primary care practices	N=264 with IBS	19.2%
Pediatric studies							
None							
Sleep disturbance							
Adult studies							
Fass et al, 2000 ⁴⁵	USA	<u>IBS</u> Manning criteria	<u>Sleep disturbance</u> Clinical questionnaire	Cross sectional	UCLA tertiary care clinic	N=305 with IBS	50.2%
Fass et al, 2000 ⁴⁵	USA	<u>Functional dyspepsia</u> Clinical criteria	<u>Sleep disturbance</u> Clinical questionnaire	Cross sectional	UCLA tertiary care clinic	N=75 with FD	68.0%
Lacy et al, 2011 ⁴⁶	USA	<u>Functional dyspepsia</u> Rome III	<u>Sleep disturbance</u> Pittsburgh sleep quality index (PSQI)	Cross sectional	Dartmouth-Hitchcock Medical Center	N=121	43% reported trouble falling asleep 64% reported trouble staying asleep
Tang et al (2016) ⁴⁷	China	<u>Globus</u> -Globus Symptomology Questionnaire -Glasgow- Edinburgh Throat Scale	<u>Sleep disorders</u> Pittsburgh sleep quality index	Cross sectional	Guangzhou First People's Hospital and the Guangzhou Nansha Central Hospital (Both in Guangzhou, Guangdong Province, China)	n=3,006 respondents n=625 with Globus	23.7%
Ballou et al, 2018 ⁴²	USA	<u>IBS</u> Clinic diagnosis	<u>Sleep disturbance</u> PSQI	Cross sectional	Tertiary care clinic survey	N=48	72%
Wang et al, 2018 ⁴⁸	Worldwide	<u>IBS</u> Manning, Rome, and ICD	<u>Sleep disturbance</u> Definition varied by study	Systematic review and metaanalysis		K=36 N=63,620	37.6%

Pediatric studies							
Devanarayana et al 2011 ⁶	Sri Lanka	IBS, AM, FAP, FD Rome III	Demographic questionnaire	Cross sectional study	Randomly selected school children	N=2163 10- to 16-year-olds Mean age 13.4 years 270 (12.5%) had at least 1 abdominal pain-predominant FGD. 107 (4.9%) with IBS 54 (2.5%) with functional dyspepsia (FD) 96 (4.4%) with functional abdominal pain (FAP) 21 (1.0%) with functional abdominal migraine (AM)	47% DGBI vs 6% controls 61% IBS 52% AM 39% FAP 32% FD
Murphy et al 2021 ⁴⁹	US	FAP (Rome III)	Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance Short Form, API, FDI, Children's Somatic Symptom Inventory-24	Randomized control trial	Tertiary pediatric gastroenterology clinic in the Southeastern USA for evaluation of abdominal pain. .	N=278 (65% female; 11-17 years old) Mean age: 14.58 (SD=1.86)	45% with sleep disturbance - 19% mild - 18% moderate - 8% significant
Thompson 2023 ⁵⁰	USA	DGBI Rome IV	Sleep Disturbance Scale for Children, and the Behavior Assessment System for Children. Disorders	Retrospective study.	Tertiary care clinic	226 patients with pain predominant DGBI (72% female, ages 8-18)	Disorders of initiation and maintenance of sleep (DIMS; 40%)
Robbertz 2023 ⁵¹	Worldwide 9 countries	DGBI Rome III and IV	<u>Validated measures of sleep</u>	Systematic review	<i>Sample size of each study n>99</i> <i>Sleep Disorder prevalence</i>	Twenty-four articles with 110,864 participants	Patients with DGBIs reported more sleep problems than healthy peers, particularly those with IBS
Chronic Fatigue Syndrome							
Adult studies							
Jones et al, 2001 ¹	USA	IBS Rome II	CFS Self-reported	Cross sectional	Tertiary care	N=270 patients with IBS	14%

			diagnosis				
Van Oudenhove et al, 2011 ⁵²	Belgium	<u>Functional dyspepsia</u> Rome II	<u>CFS</u> 2-item screening questionnaire	Cross sectional	Tertiary care	N=259 with FD	39.4%
Densie et al, 2012 ⁵³	USA	<u>IBS</u> Rome II	<u>CFS</u> CDC-94 criteria	Cross sectional	Survey – Mid-Atlantic Twin Registry	N=240 participants with IBS	8.3%
Lacy et al, 2019 ¹²	USA	<u>IBS</u> ICD codes	<u>CFS</u> ICD-9	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	2.3% in the high count group 1.7% in the moderate count group 1.7% in the zero count group
Pediatric studies							
Karabulut et al 2013 ⁷	Turkey	<u>IBS</u> Rome III	Demographic questionnaire	Prospective cohort	Tertiary care clinic	345 53% female, 46.7% male Compared with healthy 214 49.5% female, 50.5% male 4-18 Mean age patients 9.5 ± 3.44	51.3% IBS vs 22% controls (p<0.0001).
Anxiety disorders							
Adult studies							
Chitkara et al, 2005 ⁵⁴	USA	<u>Aerophagia</u> Diagnostic code in medical record	<u>Anxiety</u> Diagnostic code in medical record	Cross sectional	Review of medical records from years 1996-2003; Mayo Clinic, Rochester	N=79	19%
Robertson et al 2008 ⁵⁵	United Kingdom	<u>Non-cardiac chest pain</u> Clinically defined	<u>Anxiety</u> HADS	Cross-sectional	Clinic-based	N=119 with non-cardiac chest pain	66%
Gale et al 2009 ⁵⁶	USA	<u>Globus</u> MMPI question “there seems to be a lump in my throat most of the time”	<u>Generalized anxiety disorder</u> Diagnostic interview scale (based on the DSM-III)	Cross-sectional	Vietnam veterans	N=4240 veterans n=271 with globus	25%

Hosseinzadeh et al, 2011 ⁵⁷	Iran	<u>Functional constipation</u> Rome III	<u>Anxiety</u> HADS Mini International Neuropsychiatric Interview (MINI)	Cross sectional	Tertiary care center	N=54	33.3% (HADS) 33.3% (MINI)
Foldes-Busque et al 2011 ⁵⁸	Canada	<u>Non-cardiac chest pain</u> Clinically defined	<u>Generalized anxiety disorder</u> Anxiety Disorders Interview Schedule for <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> (ADIS-IV)	Cross-sectional	Emergency department	N=771 with non-cardiac chest pain who presented to the ED	9%
Foldes-Busque et al 2011 ⁵⁸	Canada	<u>Non-cardiac chest pain</u> Clinically defined	<u>Panic disorder</u> Anxiety Disorders Interview Schedule for <i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i> (ADIS-IV)	Cross-sectional	Emergency department	N=771 with non-cardiac chest pain who presented to the ED	21%
Tang et al (2016) ⁴⁷	China	<u>Globus</u> Globus Symptomology Questionnaire – based on Rome III	<u>Anxiety</u> Zhung Self Rating Anxiety Scale	Cross sectional	Guangzhou First People's Hospital and the Guangzhou Nansha Central Hospital (Both in Guangzhou, Guangdong Province, China)	n=3,006 respondents n=625 with Globus	39.8%
Rommel et al (2016) ⁵⁹	Belgium	<u>Globus</u> Rome III	<u>Panic Disorder (PD)</u> : PHQ – Anxiety Module	cross-sectional	Clinic-based	N=58 patients with globus N=26 healthy controls	12%
Rommel et al (2016) ⁵⁹	Belgium	<u>Globus</u> Rome III	<u>Generalized Anxiety</u> PHQ – Anxiety Module	cross-sectional	Clinic-based	N=58 patients with globus N=26 healthy controls	9%
Lacy et al, 2019 ¹²	USA	<u>IBS</u> ICD codes	<u>Anxiety</u> ICD codes	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	20.4% High count group 15.5% Moderate count group 15.8% zero count group

Zamani et al, 2019 ⁶⁰	Worldwide	<u>Irritable Bowel Syndrome</u> Manning criteria, Rome criteria, and/or International Classification of Diseases (ICD) codes	<u>Anxiety</u> Validated measures or ICD codes	Systematic review and metaanalysis	Sample size of each study n>99 IBS Anxiety/depression prevalence	Anxiety symptoms: k=43 N=16,572 Anxiety disorders: k=20 n=375,534	Anxiety symptoms: 39.1% pooled prevalence (95% CI:32.4-45.8) Anxiety disorders: 23% (95% CI: 17.2-28.8)
Robertson et al, 2020 ⁶¹	Scotland	<u>Centrally mediated abdominal pain</u> Medical record review	<u>Anxiety</u> Medical record review; ICD codes	Cross sectional	Patients with CAPS with at least 1 hospital admission during the study time frame	N=18	38.9%
Hu et al, 2021 ⁶²	Worldwide	<u>Irritable Bowel Syndrome</u> Rome I-IV	<u>Anxiety</u> Validated measures	Systematic review and metaanalysis	Included studies with Rome confirmed IBS and anxiety/depression severity	k=9 n=not reported	IBS: 44% IBS-M: 37% IBS-C: 40% IBS-D: 37% IBS_U: 11%
Rengarajan et al, 2021 ⁶³	USA; France	<u>Functional Heartburn; Reflux hypersensitivity</u> Rome IV	<u>Anxiety</u> HADS	Cross-sectional	Tertiary care	N=79 with functional oesophageal disorders N=60 with FH n=19 with RH	58.6% in FH 63.2% in RH
Shiha et al, 2021 ⁶⁴	UK	<u>Functional Diarrhea</u> Rome IV	<u>Anxiety</u> HADS	Cross sectional	Sheffield Teaching Hospitals	N=147	21%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional Diarrhea</u> Rome IV	<u>Anxiety</u> HADS	Cross sectional	Patients registered with research groups	N=199	32.7%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional abdominal bloating and distension</u> Rome IV	<u>Anxiety</u> HADS	Cross sectional	Patients registered with research groups	N=130	38.5%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional constipation</u> Rome IV	<u>Anxiety</u> HADS	Cross sectional	Patients registered with research groups	N=76	44.7%
Esterita et al, 2021 ⁶⁶	China, Japan, Korea, Sweden, USA,	<u>Functional Dyspepsia</u> Rome III OR Rome IV	<u>Anxiety</u> Validated measures of anxiety	Systematic review	Studies were included if they measured anxiety and depression in FD	K=13 studies N=14,076	61.5% in refractory FD 23.3% in non-refractory FD

	Canada, Iran, Malaysia						
Shiha et al, 2021 ⁶⁴	UK	<u>Functional constipation</u> Rome IV	<u>Anxiety</u> HADS	Cross sectional	Sheffield Teaching Hospitals	N=102	19%
Thavamani et al, 2022 ⁶⁷	USA	<u>Cyclic vomiting</u> Diagnostic code in healthcare database	<u>Anxiety disorders</u> Diagnostic code in healthcare database	Cross sectional	Review of multi-institutional database	N=15,950 adults with CVS	37.5% Anxiety 5.7% Panic disorder
Pediatric studies							
Von Gontard et al, 2015 ⁶⁸	Germany	FD, IBS, FAP, FI (Rome III)	Child Behavior Checklist (CBCL)	Cross sectional study	Primary care clinic	N=951 (55.6% Male; 5.2 – 7.5 years old)	21.7%
Zanchi et al 2021 ⁹	Italy	FD, FC, cyclic vomiting, FAP, IBS (Rome III)	The questionnaire was specifically developed for the study	Historic cohort follow-up study Medical records were retrospectively reviewed.	outpatient clinic of the pediatric gastroenterology and the pediatric ward of the Institute for Maternal and Child Health IRCCS Burlo Garofolo of Trieste, Italy.	N=79 cases (50.6% female; age 2-17yo) N= 201 controls (61.2% female)	19% reported anxiety disorder (vs. 13% healthy controls)
Depression							
Adult studies							
Chitkara et al, 2005 ⁵⁴	USA	<u>Aerophagia</u> Diagnostic code in medical record	<u>Depression</u> Diagnostic code in medical record	Cross sectional	Review of medical records from years 1996-2003; Mayo Clinic, Rochester	N=79	12%
Robertson et al 2008 ⁵⁵	United Kingdom	<u>Non-cardiac chest pain</u>	<u>Depression</u> HADS	Cross-sectional	Clinic-based	N=119 with non-cardiac chest pain	32%
Gale et al 2009 ⁵⁶	USA	<u>Globus</u> Y/N “there seems to be a lump in my throat most of the time”	<u>Major depressive disorder</u> Diagnostic interview scale (based on the DSM-III)	Cross-sectional	Vietnam veterans	N=4240 veterans n=271 with globus	22%
Hosseinzadeh et al, 2011 ⁵⁷	Iran	<u>Functional constipation</u> Rome III	<u>Depression</u> HADS Mini International	Cross sectional	Tertiary care center	N=54	22.2% (HADS) 31.5% (MINI)

			Neuropsychiatric Interview (MINI)				
Foldes-Busque et al 2011 ⁵⁸	Canada	<u>Non-cardiac chest pain</u> Clinically defined	<u>Depression</u> Beck depression inventory	Cross-sectional	Emergency department	N=771 with non-cardiac chest pain who presented to the ED	6%
Tang et al (2016) ⁴⁷	China	<u>Globus</u> -Globus Symptomology Questionnaire -Glasgow-Edinburgh Throat Scale	<u>Depression</u> Zhung Self Rating depression Scale	Cross sectional	Guangzhou First People's Hospital and the Guangzhou Nansha Central Hospital (Both in Guangzhou, Guangdong Province, China)	n=3,006 respondents n=625 with Globus	31.2%
Rommel et al (2016) ⁵⁹	Belgium	<u>Globus</u> Rome III	<u>Depression</u> PHQ-9	Cross-sectional	Clinic-based,	N=58 patients with globus N=26 healthy individuals as controls	16%
Lacy et al, 2019 ¹²	USA	<u>IBS</u> ICD codes	<u>Depression</u> ICD codes	Retrospective	Truven Health Analytics MarketScan database	n=201,322 patients with IBS Divided into High, Moderate, and Zero tests/procedures within 2 years.	23.5% High count group 17.7% Moderate count group 17.5% zero count group
Zamani et al, 2019(19,25,84-86) ⁶⁰	Worldwide	<u>Irritable Bowel Syndrome</u> Manning,, Rome, and/or International Classification of Diseases (ICD) codes	<u>Depression</u> Validated measures or ICD codes	Systematic review and metaanalysis	Sample size of each study n>99 IBS Anxiety/depression prevalence	<u>Depression symptoms:</u> k=47 n=22,842 <u>Depressive disorders:</u> k=19 n=407,967	<u>Depression symptoms:</u> 28.8% (95% CI: 23.6-34) <u>Depressive disorders:</u> 23.3% (95% CI: 17.2-29.4)
Robertson et al, 2020 ⁶¹	Scotland	<u>Centrally mediated abdominal pain</u> Medical record review	<u>Depression</u> Medical record review; ICD codes	Cross sectional	Patients with CAPS with at least 1 hospital admission during the study time frame	N=18	88.9%
Rengarajan et al, 2021 ⁶³	USA; France	<u>Functional Heartburn;</u> <u>Reflux hypersensitivity</u> Rome IV	<u>Depression</u> HADS	Cross-sectional	Tertiary care	N=79 with functional oesophageal disorders N=60 with FH n=19 with RH	25% in FH 26.3% in RH
Esterita, 2021	China, Japan, Korea,	<u>Functional Dyspepsia</u> Rome III OR	<u>Depression</u> Validated measures of depression	Systematic review	Studies were included if they measured anxiety and depression in FD	K=13 studies N=14,076	63.3% in refractory FD 20.9% in non-refractory FD

	Sweden, USA, Canada, Iran, Malaysia	Rome IV					
Shiha et al, 2021 ⁶⁴	UK	<u>Functional constipation</u> Rome IV	<u>Depression</u> HADS	Cross sectional	Sheffield Teaching Hospitals	N=102	9.5%
Shiha et al, 2021 ⁶⁴	UK	<u>Functional Diarrhea</u> Rome IV	<u>Depression</u> HADS	Cross sectional	Sheffield Teaching Hospitals	N=147	11%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional Diarrhea</u> Rome IV	<u>Depression</u> HADS	Cross sectional	Patients registered with research groups	N=199	12.6%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional abdominal bloating and distension</u> Rome IV	<u>Depression</u> HADS	Cross sectional	Patients registered with research groups	N=130	15.4%
Goodoory et al, 2021 ⁶⁵	UK	<u>Functional constipation</u> Rome IV	<u>Depression</u> HADS	Cross sectional	Patients registered with research groups	N=76	10.5%%
Hu et al, 2021 ⁶²	Worldwide	<u>Irritable Bowel Syndrome</u> Rome I-IV	<u>Depression</u> Validated measures	Systematic review and metaanalysis	Included studies with Rome confirmed IBS and anxiety/depression severity	k=9 n=not reported	IBS: 36% IBS-M: 34% IBS-C: 38% IBS-D: 37% IBS_U: 22%
Thavamani et al, 2022 ⁶⁷	USA	<u>Cyclic vomiting</u> Diagnostic code in healthcare database	<u>Depression disorders</u> Diagnostic code in healthcare database	Cross sectional	Review of multi-institutional database	N=15,950 adults with CVS	33%
Pediatric studies							
Von Gontard et al, 2015 ⁶⁸	Germany	FD, IBS, FAP, FI (Rome III)	<u>Depression or anxiety</u> Child Behavior Checklist (CBCL)	Cross sectional study	Primary care clinic	N=951 (55.6% Male; 5.2 – 7.5 years old)	21.7%

[illegible]

Murray et al, 2019 ⁷¹	USA	<u>DGBI</u> Chart review	<u>ARFID</u> Chart review – DSM-5 criteria	Cross sectional	Retrospective chart review of patients presenting to tertiary care	N=410	6.3%
Atkins et al, 2023 ⁷²	USA	<u>DGBI</u> Chart review	<u>ARFID</u> Chart review – DSM-5 criteria	Cross sectional	Retrospective review of adult and children presenting to a neurogastroenterology clinic	N=539 410 adults and 129 children	23%
<i>Pediatric studies</i>							
Murray, 2022 ⁷³	USA	<u>DGBI</u> Chart review	<u>ARFID</u> Chart review – DSM-5 criteria	Cross sectional	Retrospective review of children presenting to a neurogastroenterology clinic	N=129 age 6 to 18 ; 57% female	8%
Atkins et al, 2023 ⁷²	USA	<u>DGBI</u> Chart review	<u>ARFID</u> Chart review – DSM-5 criteria	Cross sectional	Retrospective review of adult and children presenting to a neurogastroenterology clinic	N=539 410 adults and 129 children	25%
Kaul et al, 2024 ⁷⁴	USA	<u>FD and gastroparesis</u> Rome IV	<u>ARFID</u> NIAS, PARDI-ARQ	prospective longitudinal study	Tertiary care clinics	N=66 FD N=33 gastroparesis N=72 controls Median ag 15: range 10-17 years	48.1% 15% controls by NIAS 63.6% vs 9.7 controls by PARDI-AR- Q

*Studies in *italics* indicate systematic review and/or meta-analysis. In these cases, the studies included in those reviews are not included in this table

Abbreviations: AM - abdominal migraine, ARFID - Avoidant restrictive food intake disorder, CAPS - Centrally mediated abdominal pain
DGBI - disorder of gut brain interaction, FAP - functional abdominal pain, FC - functional constipation, FD - functional dyspepsia, FDr - functional diarrhea, FABD – functional abdominal bloating and distension, FH - functional heartburn, FI - fecal incontinence, GERD – Gastro-oesophageal reflux disease, IBS - irritable bowel syndrome, NUD - non-ulcer dyspepsia, RH - reflux hypersensitivity PROMIS - Patient-Reported Outcomes Measurement Information System, PTSD – post-traumatic stress disorder, ADIS - Anxiety Disorders Interview Schedule, ARQ – ARFID questionnaire, DSM - Diagnostic and Statistical Manual of Mental Disorders, HADS – Hospital Anxiety and Depression Scale, ICD - International Statistical Classification of Diseases, NIAS - Nine Item Avoidant/Restrictive Food Intake disorder screen, OPPHED - The Oppland and Hedmark Health Study.

References – Supplementary Table 4

1. Jones KR, Palsson OS, Levy RL, Feld AD, Longstreth GF, Bradshaw BH, Drossman DA. Comorbid disorders and symptoms in irritable bowel syndrome (IBS) compared to other gastroenterology patients. *Gastroenterology*. 2001 Apr;120(5):A66.
2. Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications? *Gastroenterology*. 2002 Apr;122(4):1140–1156. PMID: 11910364
3. Si JM, Wang LJ, Chen SJ, Sun LM, Dai N. Irritable bowel syndrome consultants in Zhejiang province: the symptoms pattern, predominant bowel habit subgroups and quality of life. *World J Gastroenterol*. 2004 Apr 1;10(7):1059–1064. PMCID: PMC4717100
4. Whitehead WE, Palsson OS, Levy RR, Feld AD, Turner M, Von Korff M. Comorbidity in irritable bowel syndrome. *Am J Gastroenterol*. 2007 Dec;102(12):2767–76.
5. Friesen C, Singh M, Singh V, Schurman JV. An observational study of headaches in children and adolescents with functional abdominal pain: Relationship to mucosal inflammation and gastrointestinal and somatic symptoms. *Medicine (Baltimore)*. 2018 Jul;97(30):e11395. PMCID: PMC6078717
6. Devanarayana NM, Mettananda S, Liyanarachchi C, Nanayakkara N, Mendis N, Perera N, Rajindrajith S. Abdominal pain-predominant functional gastrointestinal diseases in children and adolescents: prevalence, symptomatology, and association with emotional stress. *J Pediatr Gastroenterol Nutr*. 2011 Dec;53(6):659–665. PMID: 21697745
7. Karabulut GS, Beşer OF, Erginöz E, Kutlu T, Cokuğraş FÇ, Erkan T. The Incidence of Irritable Bowel Syndrome in Children Using the Rome III Criteria and the Effect of Trimebutine Treatment. *J Neurogastroenterol Motil*. 2013 Jan;19(1):90–93. PMCID: PMC3548133
8. Chumpitazi BP, Palermo TM, Hollier JM, Self MM, Czyzewski D, Weidler EM, Heitkemper M, Shulman RJ. Multisite Pain Is Highly Prevalent in Children with Functional Abdominal Pain Disorders and Is Associated with Increased Morbidity. *J Pediatr*. 2021 Sep;236:131–136. PMCID: PMC8403143

9. Zanchi C, Pintaldi S, Di Leo G, Ronfani L, Zamagni G, Viel M, Barbi E, Cozzi G. Fifteen-Years Follow-Up in a Cohort of Children with Functional Gastrointestinal Disorders: Prevalence and Risk Factors to Develop Neuropsychiatric Disorders and Other Comorbidities. *Children (Basel)*. 2021 Sep 24;8(10):838. PMID: PMC8534479
10. Cole JA, Rothman KJ, Cabral HJ, Zhang Y, Farraye FA. Migraine, fibromyalgia, and depression among people with IBS: a prevalence study. *BMC Gastroenterology*. 2006 Sep 28;6(1):26.
11. Ladabaum U, Boyd E, Zhao WK, Mannalithara A, Sharabidze A, Singh G, Chung E, Levin TR. Diagnosis, comorbidities, and management of irritable bowel syndrome in patients in a large health maintenance organization. *Clin Gastroenterol Hepatol*. 2012 Jan;10(1):37–45. PMID: PMC3242893
12. Lacy B, Ayyagari R, Guerin A, Lopez A, Shi S, Luo M. Factors associated with more frequent diagnostic tests and procedures in patients with irritable bowel syndrome. *Therap Adv Gastroenterol*. 2019;12:1756284818818326. PMID: PMC6317153
13. Bin Abdulrahman KA, Alenazi NS, Albishri SB, Alshehri FF. Association of Migraine and Irritable Bowel Syndrome in Saudi Arabia: A Nationwide Survey. *BioMed Research International*. Hindawi; 2022 Jan 18;2022:e8690562.
14. Wang XJ, Ebbert JO, Loftus CG, Rosedahl JK, Philpot LM. Comorbid extra-intestinal central sensitization conditions worsen irritable bowel syndrome in primary care patients. *Neurogastroenterol Motil*. 2023 Apr;35(4):e14546. PMID: 36807964
15. Le Gal J, Michel JF, Rinaldi VE, Spiri D, Moretti R, Bettati D, Romanello S, Berlese P, Lualdi R, Boizeau P, Viala J, Bellaiche M, Zuccotti GV, Crichiutti G, Alberti C, Titomanlio L. Association between functional gastrointestinal disorders and migraine in children and adolescents: a case-control study. *Lancet Gastroenterol Hepatol*. 2016 Oct;1(2):114–121. PMID: 28404068
16. Sanders AE, Slade GD, Bair E, Fillingim RB, Knott C, Dubner R, Greenspan JD, Maixner W, Ohrbach R. General health status and incidence of first-onset temporomandibular disorder: OPPERA prospective cohort study. *J Pain*. 2013 Dec;14(12 0):10.1016/j.jpain.2013.06.001. PMID: PMC3855662
17. Gallotta S, Bruno V, Catapano S, Mobilio N, Ciacchi C, Iovino P. High risk of temporomandibular disorder in irritable bowel syndrome: Is there a correlation with greater illness severity? *World J Gastroenterol*. 2017 Jan 7;23(1):103–109. PMID: PMC5221272
18. Veale D, Kavanagh G, Fielding JF, Fitzgerald O. Primary fibromyalgia and the irritable bowel syndrome: different expressions of a common pathogenetic process. *Br J Rheumatol*. 1991 Jun;30(3):220–222. PMID: 2049586

19. Barton A, Pal B, Whorwell PJ, Marshall D. Increased prevalence of sicca complex and fibromyalgia in patients with irritable bowel syndrome. *Am J Gastroenterol.* 1999 Jul;94(7):1898–1901. PMID: 10406256
20. Sperber AD, Atzmon Y, Neumann L, Weisberg I, Shalit Y, Abu-Shakrah M, Fich A, Buskila D. Fibromyalgia in the irritable bowel syndrome: studies of prevalence and clinical implications. *Am J Gastroenterol.* 1999 Dec;94(12):3541–6.
21. Sperber AD, Carmel S, Atzmon Y, Weisberg I, Shalit Y, Neumann L, Fich A, Friger M, Buskila D. Use of the Functional Bowel Disorder Severity Index (FBDSI) in a study of patients with the irritable bowel syndrome and fibromyalgia. *Am J Gastroenterol.* 2000 Apr;95(4):995–8.
22. Vandvik PO, Lydersen S, Farup PG. Prevalence, comorbidity and impact of irritable bowel syndrome in Norway. *Scand J Gastroenterol.* 2006 Jun;41(6):650–656. PMID: 16716962
23. Wojczynski MK, North KE, Pedersen NL, Sullivan PF. Irritable bowel syndrome: a co-twin control analysis. *Am J Gastroenterol.* 2007 Oct;102(10):2220–2229. PMID: 17897337
24. Settembre C, D’Antonio E, Moscato P, Loi G, Santonicola A, Iovino P. Association among Disorders of Gut-Brain Interaction (DGBI) and Fibromyalgia: A Prospective Study. *J Clin Med.* 2022 Feb 3;11(3):809. PMCID: PMC8836992
25. Lee OY, Fitzgerald LZ, Naliboff B, Schmulson M, Liu C, Fullerton S, Mayer EA, Chang L. Impact of advertisement and clinic populations in symptoms and perception of irritable bowel syndrome. *Aliment Pharmacol Ther.* 1999 Dec;13(12):1631–1638. PMID: 10594398
26. Locke GR, Zinsmeister AR, Talley NJ, Fett SL, Melton LJ. Risk factors for irritable bowel syndrome: role of analgesics and food sensitivities. *Am J Gastroenterol.* 2000 Jan;95(1):157–165. PMID: 10638576
27. Tan YM, Goh KL, Muhidayah R, Ooi CL, Salem O. Prevalence of irritable bowel syndrome in young adult Malaysians: a survey among medical students. *J Gastroenterol Hepatol.* 2003 Dec;18(12):1412–6.
28. Vandvik PO, Wilhelmsen I, Ihlebaek C, Farup PG. Comorbidity of irritable bowel syndrome in general practice: a striking feature with clinical implications. *Aliment Pharmacol Ther.* 2004 Nov 15;20(10):1195–203.
29. Aggarwal VR, McBeth J, Zakrzewska JM, Lunt M, Macfarlane GJ. The epidemiology of chronic syndromes that are frequently unexplained: do they have common associated factors? *International Journal of Epidemiology.* 2006 Apr 1;35(2):468–476.

30. Poitras P, Gougeon A, Binn M, Bouin M. Extra Digestive Manifestations of Irritable Bowel Syndrome: Intolerance to Drugs? *Dig Dis Sci*. 2008 Aug 1;53(8):2168–2176.
31. Gulewitsch MD, Enck P, Hautzinger M, Schlarb AA. Irritable bowel syndrome symptoms among German students: prevalence, characteristics, and associations to somatic complaints, sleep, quality of life, and childhood abdominal pain. *Eur J Gastroenterol Hepatol*. 2011 Apr;23(4):311–316. PMID: 21399505
32. Fikree A, Aktar R, Grahame R, Hakim AJ, Morris JK, Knowles CH, Aziz Q. Functional gastrointestinal disorders are associated with the joint hypermobility syndrome in secondary care: a case-control study. *Neurogastroenterol Motil*. 2015 Apr;27(4):569–579. PMID: 25817057
33. Schauer B, Grabe HJ, Ittermann T, Lerch MM, Weiss FU, Mönnikes H, Völzke H, Enck P, Schwille-Kiuntke J. Irritable bowel syndrome, mental health, and quality of life: Data from a population-based survey in Germany (SHIP-Trend-0). *Neurogastroenterol Motil*. 2019 Mar;31(3):e13511. PMID: 30444067
34. Yanartaş Ö, Kani HT, Kani AS, Akça ZND, Akça E, Ergün S, Tezcan N, Atug Ö, İmeryüz N, Sayar K. Depression and anxiety have unique contributions to somatic complaints in depression, irritable bowel syndrome and inflammatory bowel diseases. *Psychiatry and Clinical Psychopharmacology*. United Kingdom: Taylor & Francis; 2019;29(4):418–426.
35. Friesen CA, Rosen JM, Schurman JV. Prevalence of overlap syndromes and symptoms in pediatric functional dyspepsia. *BMC Gastroenterol*. 2016 Jul 25;16(1):75. PMCID: PMC4960818
36. Fass R, Fullerton S, Naliboff B, Hirsh T, Mayer EA. Sexual dysfunction in patients with irritable bowel syndrome and non-ulcer dyspepsia. *Digestion*. 1998;59(1):79–85. PMID: 9468103
37. Moore JS, Gibson PR, Perry RE, Burgell RE. Endometriosis in patients with irritable bowel syndrome: Specific symptomatic and demographic profile, and response to the low FODMAP diet. *Aust N Z J Obstet Gynaecol*. 2017 Apr;57(2):201–205. PMID: 28303579
38. Altman G, Cain KC, Motzer S, Jarrett M, Burr R, Heitkemper M. Increased symptoms in female IBS patients with dysmenorrhea and PMS. *Gastroenterol Nurs*. 2006;29(1):4–11. PMID: 16552294
39. Olafsdottir LB, Gudjonsson H, Jonsdottir HH, Björnsson E, Thjodleifsson B. Natural history of irritable bowel syndrome in women and dysmenorrhea: a 10-year follow-up study. *Gastroenterol Res Pract*. 2012;2012:534204. PMCID: PMC3312222

40. Yamamoto Y, Furukawa S, Watanabe J, Miyake T, Kato A, Kusumoto K, Takeshita E, Ikeda Y, Yamamoto N, Kohara K, Saheki S, Saeki Y, Hiasa Y. Association between menstrual pain and functional dyspepsia in a Japanese young population. *Neurogastroenterol Motil.* 2022 Aug;34(8):e14324. PMID: 35045210
41. Walker EA, Gelfand AN, Gelfand MD, Green C, Katon WJ. Chronic pelvic pain and gynecological symptoms in women with irritable bowel syndrome. *J Psychosom Obstet Gynaecol.* 1996 Mar;17(1):39–46. PMID: 8860885
42. Ballou S, Alhassan E, Hon E, Lembo C, Rangan V, Singh P, Hirsch W, Sommers T, Iturrino J, Nee J, Lembo A. Sleep Disturbances Are Commonly Reported Among Patients Presenting to a Gastroenterology Clinic. *Dig Dis Sci.* 2018;63(11):2983–2991. PMID: 30094624
43. Yun CH, Lee SK, Kim H, Park HK, Lee SH, Kim SJ, Shin C. Association between irritable bowel syndrome and restless legs syndrome in the general population. *J Sleep Res.* 2012 Oct;21(5):569–576. PMID: 22463600
44. Borji R, Fereshtehnejad SM, Vakili STT, Daryani NE, Ajdarkosh H. Association Between Irritable Bowel Syndrome and Restless Legs Syndrome: A Comparative Study With Control Group. *J Neurogastroenterol Motil.* 2012 Oct 31;18(4):426–433.
45. Fass R, Fullerton S, Tung S, Mayer EA. Sleep disturbances in clinic patients with functional bowel disorders. *Am J Gastroenterol.* 2000 May;95(5):1195–2000. PMID: 10811327
46. Lacy BE, Everhart K, Crowell MD. Functional dyspepsia is associated with sleep disorders. *Clin Gastroenterol Hepatol.* 2011 May;9(5):410–414. PMID: 21334461
47. Tang B, Cai HD, Xie HL, Chen DY, Jiang SM, Jia L. Epidemiology of globus symptoms and associated psychological factors in China. *J Dig Dis.* 2016 May;17(5):319–324. PMID: 27125332
48. Wang B, Duan R, Duan L. Prevalence of sleep disorder in irritable bowel syndrome: A systematic review with meta-analysis. *Saudi J Gastroenterol.* 2018;24(3):141.
49. Murphy LK, Palermo TM, Tham SW, Stone AL, Han GT, Bruehl S, Garber J, Walker LS. Comorbid Sleep Disturbance in Adolescents with Functional Abdominal Pain. *Behav Sleep Med.* 2021;19(4):471–480. PMCID: PMC8063352
50. Thompson P, Friesen HJ, Schurman JV, Colombo JM, Friesen CA. A Cross-Sectional Study of Sleep Disturbances in Children and Adolescents With Abdominal Pain-Associated Disorders of Gut-Brain Interaction. *Clin Pediatr (Phila).* 2023 Jul 17;99228231187226. PMID: 37461213

51. Robbertz AS, Shneider C, Cohen LL, Reed B. Sleep Problems in Pediatric Disorders of Gut-Brain Interaction: A Systematic Review. *J Pediatr Psychol*. 2023 Jul 29;jsad047. PMID: 37515755
52. Van Oudenhove L, Vandenberghe J, Vos R, Holvoet L, Tack J. Factors associated with co-morbid irritable bowel syndrome and chronic fatigue-like symptoms in functional dyspepsia. *Neurogastroenterol Motil*. 2011 Jun;23(6):524-e202. PMID: 21255194
53. Dansie EJ, Furberg H, Afari N, Buchwald D, Edwards K, Goldberg J, Schur E, Sullivan PF. Conditions Comorbid with Chronic Fatigue in a Population-Based Sample. *Psychosomatics*. 2012 Jan 1;53(1):44–50.
54. Chitkara DK, Bredenoord AJ, Rucker MJ, Talley NJ. Aerophagia in adults: a comparison with functional dyspepsia. *Alimentary Pharmacology & Therapeutics*. 2005;22(9):855–858.
55. Robertson N, Javed N, Samani NJ, Khunti K. Psychological morbidity and illness appraisals of patients with cardiac and non-cardiac chest pain attending a rapid access chest pain clinic: a longitudinal cohort study. *Heart*. 2008 Mar;94(3):e12. PMID: 17540685
56. Gale CR, Wilson JA, Deary IJ. Globus Sensation and Psychopathology in Men: The Vietnam Experience Study. *Psychosomatic Medicine*. 2009 Dec;71(9):1026–1031.
57. Hosseinzadeh ST, Poorsaadati S, Radkani B, Forootan M. Psychological disorders in patients with chronic constipation. *Gastroenterol Hepatol Bed Bench*. 2011;4(3):159–163. PMCID: PMC4017427
58. Foldes-Busque G, Marchand A, Chauny JM, Poitras J, Diodati J, Denis I, Lessard MJ, Pelland MÈ, Fleet R. Unexplained chest pain in the ED: could it be panic? *The American Journal of Emergency Medicine*. 2011 Sep 1;29(7):743–751.
59. Rommel N, Van Oudenhove L, Arts J, Caenepeel P, Tack J, Pauwels A. Esophageal Sensorimotor Function and Psychological Factors Each Contribute to Symptom Severity in Globus Patients. *Am J Gastroenterol*. 2016 Oct;111(10):1382–1388. PMID: 27481312
60. Zamani M, Alizadeh-Tabari S, Zamani V. Systematic review with meta-analysis: the prevalence of anxiety and depression in patients with irritable bowel syndrome. *Aliment Pharmacol Ther*. 2019;50(2):132–143. PMID: 31157418
61. Robertson AR. What Becomes of the Frequent Hospital Attenders with Centrally Mediated Gastrointestinal Pain Syndrome? *Visc Med*. 2020 Aug;36(4):312–317. PMCID: PMC7506295

62. Hu Z, Li M, Yao L, Wang Y, Wang E, Yuan J, Wang F, Yang K, Bian Z, Zhong LLD. The level and prevalence of depression and anxiety among patients with different subtypes of irritable bowel syndrome: a network meta-analysis. *BMC Gastroenterol. BioMed Central*; 2021 Dec;21(1):1–18.
63. Rengarajan A, Pomarat M, Zerbib F, Gyawali CP. Overlap of functional heartburn and reflux hypersensitivity with proven gastroesophageal reflux disease. *Neurogastroenterology & Motility*. 2021;33(6):e14056.
64. Shiha MG, Asghar Z, Thoufeeq M, Kurien M, Ball AJ, Rej A, Tai FWD, Afify S, Aziz I. Increased psychological distress and somatization in patients with irritable bowel syndrome compared with functional diarrhea or functional constipation, based on Rome IV criteria. *Neurogastroenterology & Motility*. 2021;33(10):e14121.
65. Goodoory VC, Houghton LA, Black CJ, Ford AC. Characteristics of, and natural history among, individuals with Rome IV functional bowel disorders. *Neurogastroenterol Motil*. 2021 Sep 16:e14268. PMID: 34532930
66. Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of Functional Dyspepsia with Depression and Anxiety: A Systematic Review. *J Gastrointest Liver Dis*. 2021 Jun 18;30(2):259–266. PMID: 33951117
67. Thavamani A, Umapathi KK, Velayuthan S, Sankararaman S. Burden of psychiatric disorders in patients with cyclic vomiting syndrome - Need for aggressive screening and early intervention. *Digestive and Liver Disease*. 2022 Feb 1;54(2):287–289.
68. von Gontard A, Moritz AM, Thome-Granz S, Equit M. Abdominal pain symptoms are associated with anxiety and depression in young children. *Acta Paediatr*. 2015 Nov;104(11):1156–1163. PMID: 26194632
69. Hendrix J, Ranganini D, Montero AM, Lockett C, Xu H, James-Stevenson T, Shin A. Early adverse life events and post-traumatic stress disorder in patients with constipation and suspected disordered defecation. *Neurogastroenterol Motil*. 2022 Mar;34(3):e14195. PMCID: PMC8715864
70. Shin A, Xu H, Imperiale TF. The Prevalence, Humanistic Burden, and Health Care Impact of Irritable Bowel Syndrome Among USA Veterans. *Clinical Gastroenterology and Hepatology*. 2023 Apr 1;21(4):1061-1069.e1.
71. Murray HB, Bailey AP, Keshishian AC, Silvernale CJ, Staller K, Eddy KT, Thomas JJ, Kuo B. Prevalence and Characteristics of Avoidant/Restrictive Food Intake Disorder in Adult Neurogastroenterology Patients. *Clin Gastroenterol Hepatol*. 2020 Aug;18(9):1995-2002.e1. PMID: 31669056

72. Atkins M, Zar-Kessler C, Madva EN, Staller K, Eddy KT, Thomas JJ, Kuo B, Burton Murray H. History of trying exclusion diets and association with avoidant/restrictive food intake disorder in neurogastroenterology patients: A retrospective chart review. *Neurogastroenterol Motil.* 2023 Mar;35(3):e14513. PMID: 36600490
73. Murray HB, Rao FU, Baker C, Silvernale CJ, Staller K, Harshman SG, Thomas JJ, Kuo B, Zar-Kessler C. Prevalence and Characteristics of Avoidant/Restrictive Food Intake Disorder in Pediatric Neurogastroenterology Patients. *J Pediatr Gastroenterol Nutr.* 2022 May 1;74(5):588–592. PMCID: PMC10126824
74. Kaul I, Burton-Murray H, Musaad S, Mirabile Y, Czyzewski D, van Tilburg MAL, Sher AC, Chumpitazi BP, Shulman RJ. Avoidant/restrictive food intake disorder prevalence is high in children with gastroparesis and functional dyspepsia. *Neurogastroenterol Motil.* 2024 Mar 7;e14777. PMID: 38454301