Original research

Prevalence of irritable bowel syndrome and functional dyspepsia after acute gastroenteritis: systematic review and meta-analysis

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ABSTRACT

Objective Disorders of gut-brain interaction may arise after acute gastroenteritis. Data on the influence of pathogen type on the risk of postinfection IBS (PI-IBS), as on postinfection functional dyspepsia (PI-FD), are limited. We conducted a systematic review and meta-analysis to determine prevalence of PI-IBS or PI-FD after acute gastroenteritis.

Design We included observational studies recruiting ≥50 adults and reporting prevalence of IBS or FD after acute gastroenteritis with ≥3-month follow-up. A random effects model was used to estimate prevalence and ORs with 95% CIs.

Results In total, 47 studies (28 170 subjects) were eligible. Overall prevalence of PI-IBS and PI-FD were 14.5% and 12.7%, respectively. IBS persisted in 39.8% of subjects in the long-term (>5 years follow-up) after diagnosis. Individuals experiencing acute gastroenteritis had a significantly higher odds of IBS (OR 4.3) and FD (OR 3.0) than non-exposed controls. PI-IBS was most associated with parasites (prevalence 30.1%), but in only two studies, followed by bacteria (18.3%) and viruses (10.7%). In available studies, *Campylobacter* was associated with the highest PI-IBS prevalence (20.7%) whereas Proteobacteria and SARS-CoV-2 yielded the highest odds for PI-IBS (both OR 5.4). Prevalence of PI-FD was 10.0% for SARS-CoV-2 and 13.6% for bacteria (Enterobacteriaceae 19.4%).

Conclusion In a large systematic review and meta-analysis, 14.5% of individuals experiencing acute gastroenteritis developed PI-IBS and 12.7% PI-FD, with greater than fourfold increased odds for IBS and threefold for FD. Proinflammatory microbes, including Proteobacteria and subcategories, and SARS-CoV-2, may be associated with the development of PI-IBS and PI-FD.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A well-established body of evidence shows that acute infectious gastroenteritis is a risk factor for the development of disorders of gut-brain interaction (DGBI), and specific subgroups of DGBI have a clear postinfection origin, including postinfection IBS (PI-IBS) and postinfection functional dyspepsia (PI-FD).

⇒ Although there have been prior systematic assessments of this issue, data on the influence of pathogen type on PI-IBS are limited, and there have been few studies to date examining the prevalence of PI-FD.

WHAT THIS STUDY ADDS

⇒ This updated systematic review and meta-analysis included 47 studies and 28 170 individuals, 14.5% of people experiencing acute gastroenteritis developed PI-IBS and 12.7% developed PI-FD, with a nearly fourfold increased odds for IBS and threefold for FD, respectively.

⇒ Persistence rates of PI-IBS were considerable (52.3% of subjects at 1–4 years follow-up and 39.8% of subjects at >5 years follow-up).

⇒ Based on available studies, aggressive and proinflammatory microbial taxa, including Proteobacteria and subcategories (eg, Enterobacteriaceae), and SARS-CoV-2, may be associated with increased risk of developing PI-IBS and PI-FD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In this updated analysis, we found a slight increase in prevalence of PI-IBS and PI-FD compared with previous data.

⇒ Generally, as acute gastroenteritis is a common disorder worldwide, our findings may be relevant for public health, and physicians should pay heed if their patients present with a recent episode of infectious gastroenteritis.

⇒ Moreover, physicians should be aware that some microbes with proinflammatory characteristics may be associated with PI-IBS or PI-FD.

INTRODUCTION

Functional gastrointestinal diseases, renamed as disorders of gut-brain interaction (DGBI) according to the Rome IV criteria in 2016, are among the most common digestive disorders worldwide.[1 2] The most prevalent DGBI include IBS, with a prevalence ranging from nearly 4% to 11%,[3 4] and functional dyspepsia (FD), with a prevalence of 7%, worldwide.[4] These disorders have a considerable impact on health services and society, being associated with

high morbidity and loss of working hours, impaired quality of life and economic expenditure.[5] Despite their prevalence, their pathophysiology remains poorly understood. Several pathways, including genetic predisposition, altered GI motility, visceral hypersensitivity, alterations of the brain-gut axis, low-grade immune activation, increased intestinal permeability and impairment of gut microbiome, are potentially involved.[6]

Consolidated evidence shows that acute infectious gastroenteritis represents a common risk factor for the development of DGBI.[7–9] Specific subgroups of DGBI have a clear postinfection (PI) origin, including PI-IBS, defined as the development of IBS after an episode of acute gastroenteritis,[10–12] and PI-FD, defined as onset of a symptom complex characterised by epigastric pain, bloating, early satiety, fullness, epigastric burning, belching, nausea and vomiting, following an acute gastroenteritis. The most common pathogens implicated in the development of PI-IBS and PI-FD are represented by viruses (including norovirus, rotavirus, SARS-CoV-2), bacteria (*Campylobacter*, *Salmonella*, *Escherichia coli*, *Shigella*, *Clostridioides difficile*)[13–16] and protozoa (*Giardia*).[17 18] In general, protozoal or bacterial acute gastroenteritis tend to have a stronger association with the development of PI-IBS or PI-FD than viral infections.[7 9 19]

The prevalence of PI-IBS was 17% in a prior meta-analysis of 34 studies,[20] while the prevalence of PI-FD has been reported by only a few studies.[9] Despite the available data, it is still difficult to provide a clear and contemporaneous picture of the epidemiology of PI-IBS and PI-FD for several reasons. First, different factors could influence their prevalence, including the causative pathogen, the country and the method (clinical evaluation or microbiological diagnosis) and timing of assessment.[21] Moreover, most available prevalence data come from studies based on the Rome I, II and III criteria.[7] The introduction of Rome IV in 2016 has altered the criteria of DGBI, resulting in a decrease in IBS prevalence,[22] due to a requirement for more frequent symptoms.[23] Also, data systematic assessments of the persistence of PI-IBS and PI-FD after initial diagnosis are lacking. Finally, comprehensive data on the prevalence of PI-FD remain limited. For these reasons, we aimed to carry out a contemporaneous systematic review and meta-analysis of studies evaluating the prevalence of PI-IBS and PI-FD.

METHODS

This study was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (online supplemental table 1).[24]

Selection criteria

We considered eligible observational studies recruiting ≥50 adults (aged ≥15 years) with documented acute gastroenteritis; laboratory proven, clinically suspected or self-reported. Studies had to report the proportion of subjects reporting symptoms compatible with PI-IBS or PI-FD at least 3 months after the episode of acute gastroenteritis. Although some included studies refer to this as the incidence of PI-IBS or PI-FD, we used the term prevalence, given that not all studies excluded the presence of symptoms of IBS or FD prior to infection, and even in studies that did exclude this, participants could be at risk of recall bias. We reduced the usual 6-month threshold from the infection episode for the diagnosis of IBS or FD,[1] as the Rome Foundation has recently recommended clinical diagnostic criteria to enable the diagnosis of DGBI after a shorter symptom duration of at least 8 weeks, if the relevant symptom-based criteria are met and other organic conditions have been ruled out.[2] Diagnosis of IBS was based on Manning, Rome I, II, III or IV criteria and FD based on Rome I, II, III or IV criteria. We excluded case reports, abstracts and studies without prevalence data.

Information sources, search strategy and study selection

To identify potentially eligible studies, we searched PubMed, Scopus and ISI Web of Science systematically and without language restrictions up to 15 October 2023. The complete search string is available in online supplemental material. Moreover, the bibliographies of selected papers were hand searched to provide additional references. Three investigators (SP, MM and LHE) assessed titles and abstracts of all studies independently to exclude studies that did not meet the eligibility criteria. Conflicts in study selection were resolved by consulting a third reviewer (GI).

Data extraction

Details on data extraction are available in online supplemental material.[14 15 25–29]

Quality assessment and risk of bias

Details on quality assessment [30] and risk of bias are available in online supplemental material.

Data synthesis and statistical analysis

Details on data synthesis and statistical analysis[31 32 33] are available in online supplemental material.

RESULTS

Study selection and characteristics of included studies

The search strategy generated 5462 citations after removal of duplicates. From these, 75 appeared to be relevant and were retrieved for further assessment. In total, 47 studies, including a total of 28 170 subjects, were eligible and were included in the final analysis (figure 1).[10 14–16 18 19 25–29 34–69] Of these, 46 studies (21 679 subjects) reported prevalence of PI-IBS and 13 studies (6491 subjects) reported prevalence of PI-FD, respectively. Characteristics of included studies are provided in online supplemental tables 2,3. Thirty-four studies only reported prevalence of PI-IBS,[10 15 16 18 27 29 34–39 41 44–54 56–63 67 69] 1 study only PI-FD[42] and 12 studies both PI-IBS and PI-FD.[14 19 25 26 28 40 43 55 64–66 68] Most studies were conducted in a single country, except for 2 studies, 1 conducted in both Bangladesh and India, and the other in 14 different countries.[26 43] Subjects were recruited in 27 different countries, but mostly in Europe and North America. Agreement between investigators for assessment of study eligibility was excellent (κ statistic=0.86). Sixteen studies were judged as high-quality, with the remaining studies classified as fair-quality (online supplemental tables 4,5). Analyses according to overlap between PI-IBS and PI-FD and according to different iterations of the Rome criteria are provided in the online supplemental material.

Pooled prevalence of PI-IBS

The overall prevalence of PI-IBS is summarised in figure 2 and table 1. Based on 46 studies and 14 446 subjects, the pooled prevalence was 14.5% (95% CI 11.2% to 18.1%) with high heterogeneity (I^2=97.1%, p<0.0001).[10 14–16 18 19 25–29 34–41 43–69] When subgrouping according to geographical location, the highest prevalence of PI-IBS was observed in North America (12 studies, 4921 subjects, 18.9%; 95% CI 11.1% to 28.1%; I^2=98.1%, p<0.0001),[16 35–38 40 48–50 56 65 66] followed by Europe (19 studies, 6453 individuals, 15.0%; 95% CI 9.8% to 21.1%;

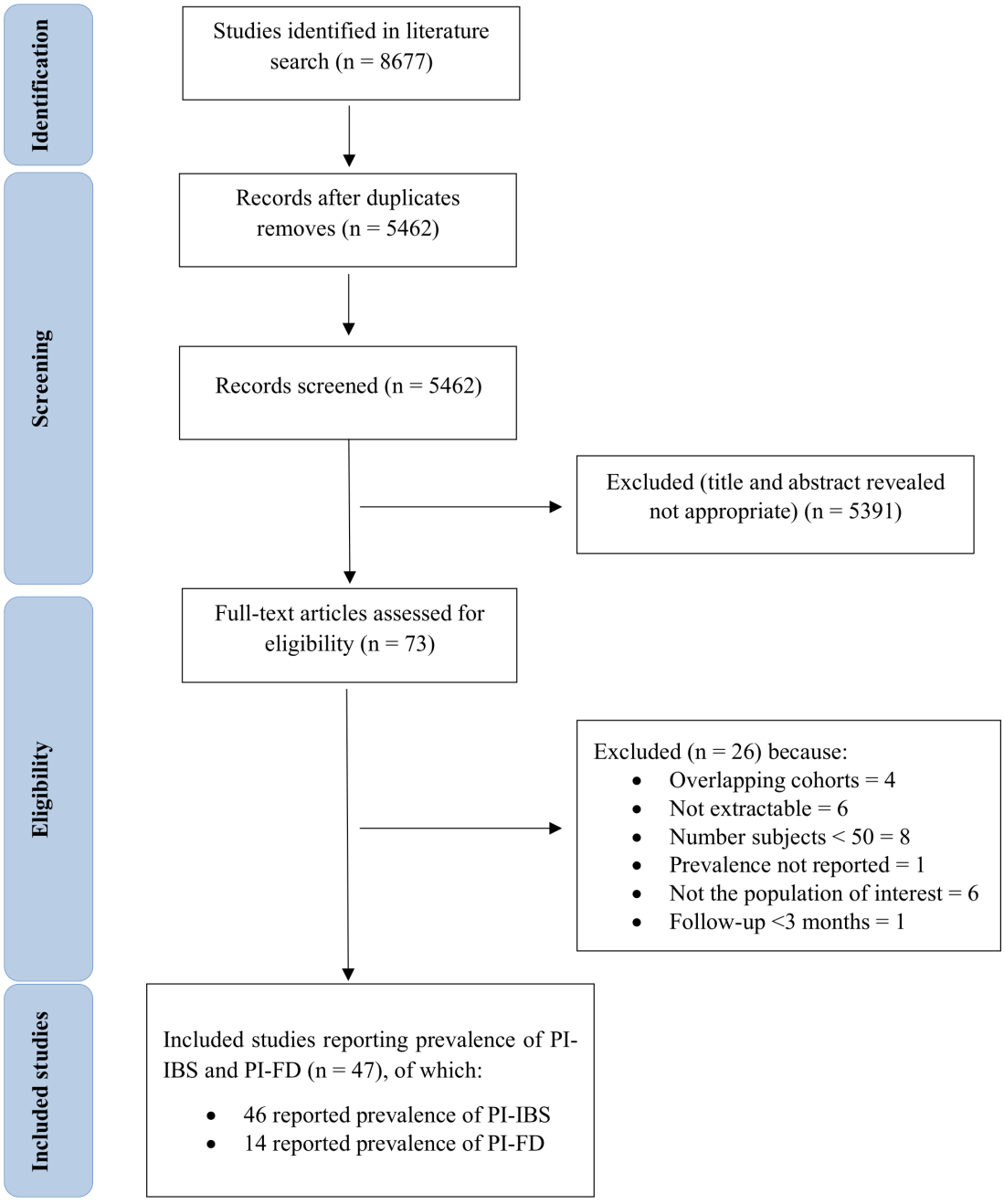

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the search process. PI, postinfection; FD, functional dyspepsia.

I^2=97.5%, p<0.0001).[10 14 18 25 27 34 39 45 47 51–53 55 57 61 63 64 68 69] Fourteen studies (1092 subjects) reported extractable data for IBS subtype.[10 14 16 26 28 35 39 40 43 45 54 59 68 69] IBS with diarrhoea (IBS-D) was the most frequent type (46.1% of subjects), followed by IBS with mixed bowel habits (IBS-M) (38.5%), while constipation-predominant IBS (10.0%) and unsubtyped IBS (5.4%) were less common. When data from 22 case-control studies were pooled, the OR for IBS in individuals with a history of acute gastroenteritis versus controls was 4.3 (95% CI 3.1 to 5.9) with moderate heterogeneity (I^2=68.3%; p<0.0001) but without funnel plot asymmetry (Egger test, p=0.54).[10 15 19 25 26 28 29 43 44 47–50 53 55 57 60 62 65 67–69]

Given a strict application of the Rome IV diagnostic criteria for IBS requires a symptom duration of 6 months, studies that only reported data 3 months after the infection were excluded.[38 39 44 45] However, both the pooled prevalence (14.8%, 95% CI 11.3% to 18.8%; I^2=97.2%, p<0.0001) and the pooled OR (4.2, 95% CI 3.1 to 5.8; I^2=68.6%, p<0.0001, Egger test p=0.7) of PI-IBS remained almost unchanged compared with the main analysis.

Further sensitivity analyses were carried out including studies that recruited subjects with laboratory confirmed infection (27 studies, 7940 subjects) with similar results (prevalence 14.6%; 95% CI 10.4% to 19.5%, I^2=96.9%, p<0.0001).[15 16 19 25–27 29 34 35 38–41 43 44 46 47 51–53 55 56 59–61 63 68] Prevalence of PI-IBS was calculated excluding two studies that did not report on whether IBS symptoms predated infection,[37 68] but again with a similar prevalence (14.2%; 95% CI 11.4% to 17.2%, I^2=95.5%, p<0.0001). The prevalence of PI-IBS was lower (12.4%; 95% CI 9.1% to 16.1%) when we conducted a sensitivity analysis excluding nine studies that surveyed individuals at

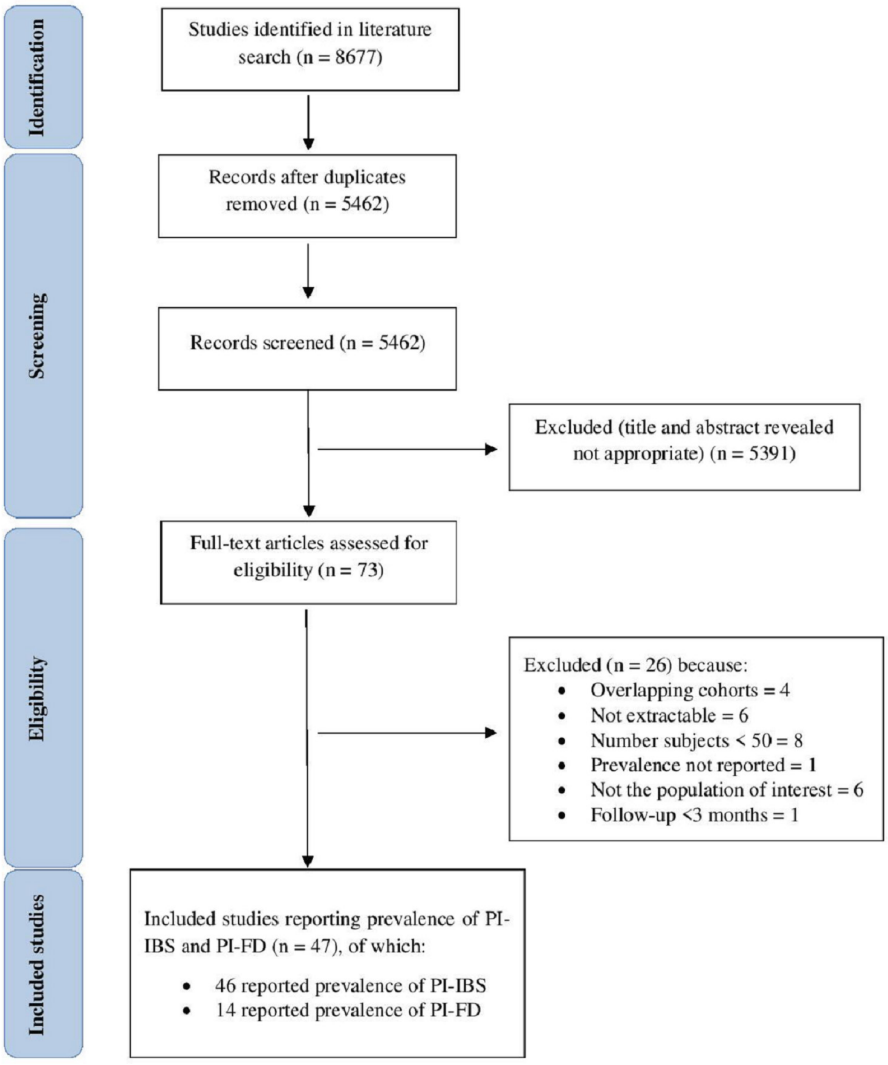

Figure 2 Pooled prevalence of PI-IBS after acute gastroenteritis. PI, postinfection.

different time-points after infection, with significant heterogeneity (I^2=96.6%, p<0.0001).[16 35 36 40 41 49 56 62 67] When only high-quality studies (17 studies, 5603 subjects, online supplemental tables 4,5) were evaluated,[15 19 25 26 28 37 40 43 44 47–49 55 60 67 68] the prevalence of PI-IBS was 12.9% (95% CI 6.5% to 21.1%, I^2=98.5%, p<0.0001), while the OR for PI-IBS was 4.5 (95%

Table 1 Prevalence of PI-IBS in overall studies and at subgroup analyses (stratified for IBS diagnostic criteria, study population origin, method of acute gastroenteritis diagnosis and quality of included studies)

Subgroups	Events/Total exposed	Prevalence of PI-IBS (%)	95% CI	I^2 (%)	P value for χ^2
Overall	2290/14 446	14.5	11.2% to 18.1%	97.1	<0.0001
IBS diagnostic criteria					
Rome I	658/3197	15.3	8.8% to 23.1%	96.3	<0.0001
Rome II	252/2373	11.4	9.3% to 13.6%	57.0	0.0065
Rome III	1050/5091	20.0	12.0% to 29.5%	98.3	<0.0001
Rome IV	330/3785	10.7	6.0% to 15.8%	95.4	<0.0001
Geographical location					
Europe	1009/6453	15.0	9.8% to 21.1%	97.5	<0.0001
North America	979/4921	18.9	11.1% to 28.1%	98.1	<0.0001
Middle East	70/602	11.8	9.4% to 14.5%	0.0	0.64
Asia	218/2035	10.9	7.0% to 15.6%	89.4	<0.0001
Study quality					
High quality	1038/5603	12.9	6.5% to 21.1%	98.5	<0.0001
Fair quality	1252/8842	15.3	12.2% to 18.7%	94.4	<0.0001

PI, postinfection.

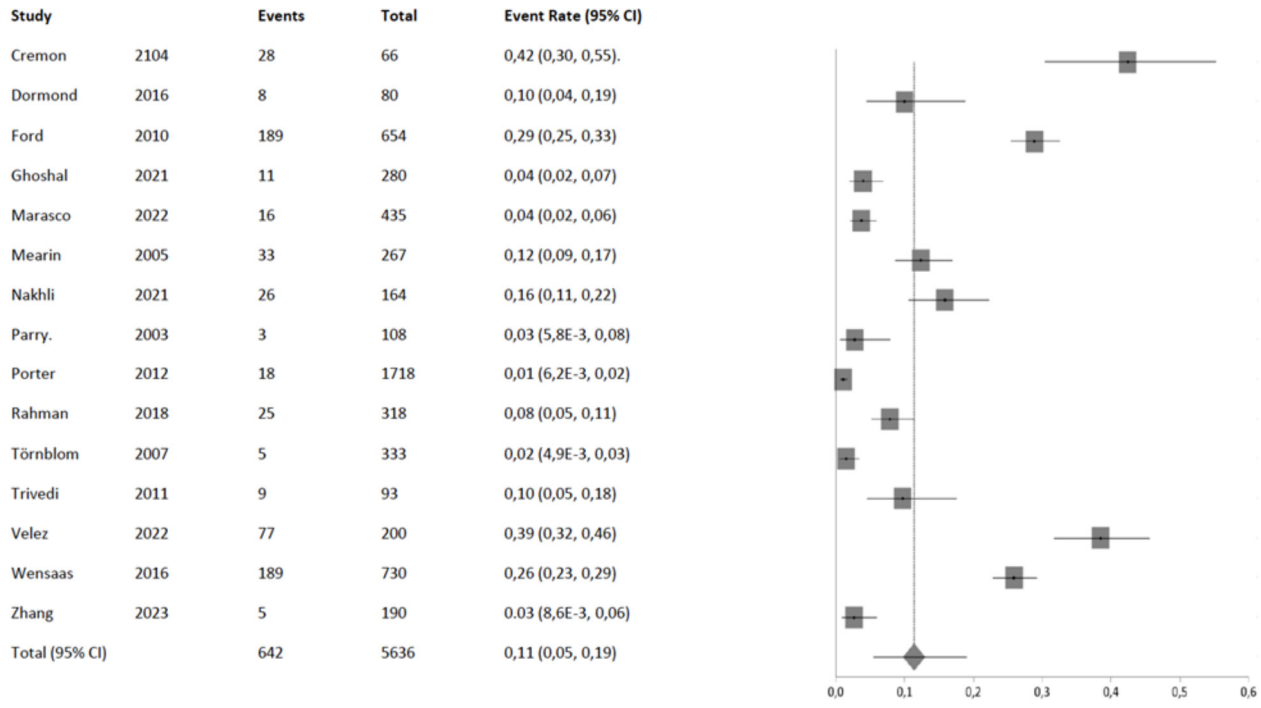

Figure 3 Pooled prevalence of postinfection functional dyspepsia after acute gastroenteritis.

CI 2.9 to 7.2; I^2=47%, p=0.04, Egger test: p=0.27) in 11 studies (online supplemental tables 4,5).[15 25 26 28 43 44 47–49 55 60]

Pooled prevalence of PI-FD

The pooled prevalence of PI-FD is reported in figure 3 and table 2. Based on 13 studies containing 5636 individuals, the pooled prevalence was 12.7% (95% CI 6.6% to 20.4%; I^2=97.6%, p<0.0001).[14 19 25 26 28 40 42 43 55 64–66 68] All included studies reported prevalence of PI-FD for 6 months or more after the infection. As for PI-IBS, the highest prevalence of PI-FD was observed when North American studies, including 1191 subjects (26.1%; 95% CI 16.7% to 36.8%) with high heterogeneity (I^2=92.1%, p<0.0001) were pooled.[25 40 42 65 66] Only four studies (99 subjects) reported extractable data for PI-FD subtype.[26 28 40 43] Specifically, we found that the postprandial distress syndrome was the most frequent subtype (54.6%), followed by the epigastric pain syndrome (25.2%), while overlap of both was less common (20.2%). When data from nine case-control studies were pooled,[19 25 26 28 42 43 55 65 68] individuals exposed to acute gastroenteritis had threefold increased odds of developing FD as compared with controls (OR 3.0; 95% CI 1.9 to 4.8), with moderate heterogeneity (I^2=61.4%; p=0.008).

The prevalence of PI-FD was 10.2% (95% CI 3.6% to 19.6%; I^2=97.5%, p<0.0001) when only studies with confirmed gastroenteritis were included (8 studies, 2344 subjects).[19 25 26 28 40 55 64 68] When a further sensitivity analysis was carried out excluding the study that did not rule out presence of FD before infection,[68] the prevalence of PI-FD was similar (11.7%; 95% CI 5.6% to 19.7%; I^2=97.4%, p<0.0001). The prevalence of PI-FD was slightly higher (13.5%; 95% CI 6.6% to 22.4%; I^2=97.8%, p<0.0001) when the study that surveyed subjects at different time-points after infection was excluded.[40] Finally, in 9 high-quality studies, including 2558 individuals (online supplemental tables 4,5), prevalence of PI-FD was 10.9% (95% CI 5.0% to

Table 2 Prevalence of PI-FD in overall studies and at subgroup analyses (stratified for FD diagnostic criteria, study population origin, method of acute gastroenteritis diagnosis and quality of included studies)

Subgroups	Events/Total exposed	Prevalence of PI-FD (%)	95% CI	I^2 (%)	P value for χ^2
Overall	616/3838	12.7	6.6% to 20.4%	97.6	<0.0001
FD diagnostic criteria					
Rome II	239/1455	9.5	1.4% to 23.5%	98.0	<0.0001
Rome III	253/1394	17.3	5.4% to 34.0%	97.8	<0.0001
Rome IV	124/989	12.5	1.8% to 30.7%	98.0	<0.0001
Geographical location					
Europe	258/1504	13.8	3.4% to 29.6%	98.0	<0.0001
North America	309/1191	26.1	16.7% to 36.9%	92.1	<0.0001
Asia	41/788	4.9	2.3% to 8.2%	73.6	0.0227
Study quality					
High quality	336/2558	10.9	5.0% to 18.7%	96.7	<0.0001
Fair quality	280/1280	16.8	2.8% to 39.2%	98.6	<0.0001

PI-FD, postinfection functional dyspepsia.

18.7%, I^2=96.7%, p<0.0001)[14 19 25 26 28 40 43 55 68] and the OR for PI-FD was 3.3 (95% CI 1.8 to 6.1; I^2=58.7%, p=0.02), when pooling data from 7 studies (online supplemental tables 4,5).[19 25 26 28 43 55 68]

Persistence of PI-IBS and PI-FD over time

After an initial diagnosis of PI-IBS, IBS persisted in 49.8% (100 of 201) of subjects at 6–11 months follow-up in five studies (95% CI 42.9% to 56.6%, I^2=0%, p=0.93),[15 34 48 59 60] in 52.3% of subjects (125 of 239) at 1–4 years follow-up in three studies (95% CI 39.2% to 65.2%, I^2=0, p=0.19)[48 70 71] and in 39.8% of subjects (187 of 471) at >5 years follow-up in four studies (95% CI 33.5% to 46.2%, I^2=32.1%, p=0.22).[70 72 73]

The pooled persistence of FD could not be assessed with available data.

Risk factors for PI-IBS and PI-FD

We were able to assess risk factors for IBS in included studies. Several factors, relating to the patient history or to the features of the initial GI infection, increased the risk of PI-IBS, including: female sex (OR 1.59, 95% CI 1.24 to 2.04),[10 15 16 18 25 27 35 39 41 45 46 51 54 56 58–60] history of anxiety (OR 3.58, 95% CI 2.07 to 6.19),[16 52 54] duration of diarrhoea >3 weeks (OR 2.58, 95% CI 1.45 to 4.60)[18 35 51] and hospitalisation (OR 1.65, 95% CI 1.21 to 2.23).[16 25 35] Other subject and infection characteristics were not significantly associated with increased or decreased risk of PI-IBS, including: age >35 years (OR 0.91, 95% CI 0.58 to 1.41),[15 18 59] depression (OR 2.21, 95% CI 0.70 to 6.94),[16 52 54] use of antibiotics (OR 1.06, 95% CI 0.74 to 1.52),[25 27 35 56 58] bloody stools (OR 1.30, 95% CI 0.98 to 1.73)[16 18 35 56 58] and fever (OR 1.24, 95% CI 0.79 to 1.96).[16 18 25 35 41 46 54 58]

The assessment of risk factors for FD was not possible with the available studies.

Prevalence and odds of PI-IBS according to the infectious agent

Prevalence of PI-IBS was 10.7% (95% CI 6.3% to 16.0%; I^2=95.5%, p<0.0001) for viral infections in 13 studies of 3585 individuals,[10 19 26 27 36 37 40 41 43 44 53 59 66] 18.3% for bacterial infections (95% CI 14.3% to 22.6%, I^2=94.7%, p<0.0001) in 20 studies of 7050 subjects[14–16 25 28 29 34 35 39 46 49 51 52 54–56 58 61 63 67] and 30.1% (95% CI 4.5% to 66.1%; I^2=97.3%, p<0.0001) for parasitic infections in 2 studies with 779 subjects (online supplemental figures 1–3 and table 3).[60 68] The ORs for PI-IBS in individuals with a history of acute gastroenteritis versus controls were, respectively, 4.8 for bacteria (95% CI 2.8 to 8.1) with moderate heterogeneity (I^2=63.8%, p=0.011),[15 25 28 29 49 55 67] 6.2 for viruses (95% CI 1.6 to 24.9) with high heterogeneity (I^2=82.7%, p<0.0001)[10 19 26 43 44 53] and 5.5 for parasites (95% CI 4.4 to 6.9) without heterogeneity (I^2=0%, p=0.7252).[60 68]

The prevalence of PI-IBS was 17.2% after Proteobacteria infection in 18 studies (95% CI 13.5% to 21.2%; I^2=92.4%, p<0.0001),[14 15 25 28 29 34 35 39 46 51 52 54–56 58 61 63 67] and 16.2% after Enterobacteriaceae infection in 10 studies (95% CI 11.6% to 21.5%; I^2=85.1%, p<0.0001).[14 15 25 28 29 34 46 54 58 67] The highest prevalence of PI-IBS was observed after *Campylobacter* infection (20.7%; 95% CI 13.7% to 28.6%; I^2=95.9%, p<0.0001), as reported in six studies.[35 39 52 56 61 63] The OR for developing PI-IBS was 5.4 for Proteobacteria (95% CI 2.5 to 11.9, I^2=69.7%, p=0.0056)[15 25 28 29 55 67] and 4.3 for Enterobacteriaceae (95% CI 1.5 to 12.7, I^2=69.9%, p=0.0189).[15 25 29 67] When only subjects with SARS-CoV-2 infection were evaluated, the prevalence of PI-IBS, as reported in 12 studies and 3407 subjects, was 9.8% (95% CI 5.7% to 15.0%, I^2=95.3%, p<0.0001).[19 26 27 36 37 40 41 43 44 53 59 66] When data from case-control studies were pooled, individuals with a history of SARS-CoV-2 infection had a fivefold increased risk of developing PI-IBS compared with controls (OR 5.4; 95% CI 1.2 to 24.7, I^2=78.7%, p=0.0009).[19 26 43 44 53]

Prevalence and odds of PI-FD according to the infectious agent

Prevalence of PI-FD was 13.6% (95% CI 4.8% to 26.0%, I^2=94.2%, p<0.0001) for bacterial infections (4 studies, 759 individuals)[14 25 28 55] and 10.0% (95% CI 2.3% to 23.6%; I^2=97.5%, p<0.0001) for SARS-CoV-2 infection (5 studies, 1269 subjects)[19 26 40 43 66] (online supplemental figures 4,5, and table 3). The prevalence of FD was higher than the overall pooled prevalence after Enterobacteriaceae infections (19.4%; 95% CI 5.9% to 38.3%; I^2=93.3%, p<0.0001) in three studies.[14 25 28] No data were available for parasites and other viruses besides SARS-CoV-2. In case-control studies, the odds for FD were non-significant for both bacteria (three studies, OR 3.8; 95% CI 0.98 to 14.68, I^2=69.5%, p=0.06)[25 28 55] and SARS-CoV-2 (three studies, OR 2.4, 95% CI 0.7 to 8.3, I^2=44.1%, p=0.17).[19 26 43]

Prevalence of PI-IBS or PI-FD during longitudinal follow-up

This subanalysis is available in online supplemental material.

Overlap between PI-IBS and PI-FD

This subanalysis is available in online supplemental material.

Prevalence of PI-IBS or PI-FD based on Rome criteria

The prevalence of PI-IBS diagnosed with Rome I criteria was 15.3% (95% CI 8.8% to 23.1%, I^2=96.3%, p<0.0001) in eight

Table 3 Subgroup analysis of PI-IBS and PI-FD based on the infectious agent

Taxa	Events/Total exposed	Prevalence (%)	95% CI	I^2 (%)	P value for χ^2	OR	95% CI	I^2 (%)	P value for χ^2
PI-IBS									
Bacteria	1375/7050	18.3	14.3% to 22.6%	94.7	<0.0001	4.8	2.8 to 8.1	63.8	0.011
Viruses	312/3585	10.7	6.3% to 16.0%	95.5	<0.0001	6.2	1.6 to 24.9	82.7	<0.0001
Parasites	349/779	30.1	4.4% to 66.1%	97.3	<0.0001	5.5	4.4 to 6.9	0.0	0.7252
PI-FD									
Bacteria	89/759	13.6	4.8% to 26.0%	94.2	<0.0001	3.8	1.0 to 14.7	69.5	0.0376
Viruses (SARS-CoV-2)	135/1269	10.5	2.3% to 23.6%	97.5	<0.0001	2.4	0.7 to 8.3	44.1	0.1669

PI-FD, postinfection functional dyspepsia.

studies (n=3197 subjects),[14 38 39 45 48 49 52 63] as detailed in table 1. In the 12 studies (n=2373 subjects)[15 29 46 50 51 55 60–62 64 65 67] that used the Rome II criteria, the prevalence of PI-IBS was 11.4% (95% CI 9.3% to 13.6%, I^2=57.7%, p=0.0065). The highest prevalence of PI-IBS (20.0%, 95% CI 12.0% to 29.5%; I^2=98.3%, p<0.0001) was observed in 14 studies (n=5091 subjects) that applied the Rome III criteria,[10 16 19 25 28 34 35 43 47 54 56 68 69] while in the 12 studies (n=3785 subjects)[18 26 27 36 37 40 41 44 53 58 59 66] that used the Rome IV criteria it was 10.7% (95% CI 6.4% to 15.8%; I^2=95.4%, p<0.0001).

As detailed in table 2, the prevalence of PI-FD diagnosed with Rome II criteria was 9.5% (95% CI 1.4% to 23.5%; I^2=98%, p<0.0001) in 5 studies and 1455 subjects,[14 42 55 64 65] while it was 17.3% (95% CI 5.4% to 34.0%; I^2=97.8%, p<0.0001) when FD was defined according to Rome III criteria (4 studies, 1394 subjects)[25 28 43 68] and 12.5% (1.8% to 30.1%; I^2=98%, p<0.0001) in 4 studies that used the Rome IV criteria (n=989 subjects).[19 26 40 66]

DISCUSSION

The pathophysiology of DGBI is poorly understood, and these disorders are traditionally perceived by healthcare professionals as being mostly psychological and less 'valid' diseases,[74] with a potential risk of underestimating patients' expectations and complaints.[75] However, a well-established body of evidence supports a PI origin for a subset of patients with DGBI.[8 76] We carried out a systematic review and meta-analysis to update prevalence of PI-IBS and PI-FD, pooling together data from 47 studies and 28 170 subjects. We also performed subgroup analyses according to the microbial taxa responsible for the acute gastroenteritis, the length of follow-up from the infection episode and the criteria used for diagnosis, and assessed the persistence of PI-IBS over time after the initial diagnosis.

In our study, the overall prevalence of PI-IBS was 14.5%, and that of PI-FD was 12.7%. Our findings differ slightly from those observed in previous meta-analyses, where, the overall prevalence of PI-IBS ranged from 17% in 2019[20] and 11.5% in 2017,[7] while the observed prevalence for PI-FD was 9.5% in 2014.[9] The discrepancy between our results and previous experiences can be explained by several factors. Our eligibility criteria differ from those of the meta-analysis by Svendsen *et al*,[20] which included studies with <50 subjects and with a pre-existing diagnosis of IBS, while we included larger cohorts of individuals, most of which had not a previous diagnosis of IBS, except for one study that was excluded in a sensitivity analysis. This approach, together with the unprecedented inclusion of studies using Rome IV criteria (that are stricter than previous iterations), may have reduced the observed prevalence of PI-IBS in our study. Moreover, our study provided a considerable update of data compared with previous meta-analyses from 2017[7] and 2014,[9] as 18 of the 47 studies that we included (38%) were published after 2017. The appearance of SARS-CoV-2 could also explain the discrepancies, although a recent meta-analysis reported a 12% prevalence for IBS and 4% for FD after COVID-19,[77] suggesting that other infections may have contributed to this increase in prevalence. In case-control studies, individuals with a history of acute gastroenteritis had a fourfold higher odds of developing IBS and a nearly threefold higher odds of developing FD than controls, confirming previous data.[7 9] Beyond this prevalence analysis, we were also able to evaluate the persistence of symptoms in affected individuals after initial diagnosis, and observed chronicity of PI-IBS in the long term, as it persisted in more than half of diagnosed subjects at 1–5 years follow-up and in nearly 40% of them during longer follow-up. To our knowledge, this question has not been addressed in previous meta-analyses.

Our results are relevant for healthcare systems, as acute gastroenteritis is estimated to affect 179 million subjects/year worldwide[78 79] and infections may contribute to a considerable proportion of IBS cases.[80 81] Further observational studies are unlikely to change the fact that acute enteric infection can lead to the development of de novo GI symptoms compatible with either IBS or FD. This suggests that the mechanisms underlying the development of such symptoms are where future research efforts should be directed. Nevertheless, our findings are important conceptually, as they support the gradual switch in envisioning DGBI from functional to organic disorders, as microbial factors may be considered equally as important to neuroimmune interactions.[82]

When possible, based on available studies, we also evaluated the prevalence and odds of developing PI-IBS or PI-FD according to the microbial causative agents of acute gastroenteritis. As previously reported,[7] parasites were most commonly associated with PI-IBS, with a prevalence of nearly 30% and a greater than fivefold increased odds compared with controls in available studies. This observation has several possible biological explanations, as parasitic infections can elicit the immune system,[83 84] meaning they can trigger the immune pathways that underlie IBS,[82] and are also detrimental for the gut microbiome.[85] However, this finding should be taken with caution, as it derives from a subanalysis of only two studies. In our study, nearly 18% of individuals who experienced a bacterial acute gastroenteritis developed IBS, with a nearly fivefold increased odds compared with controls. Gram-negative bacteria were mainly responsible for the development of PI-IBS, as the highest prevalence was observed after *Campylobacter* infection, while Proteobacteria and Enterobacteriaceae provided the highest odds, among bacteria, for developing the disease.

These results arise only from a subgroup analysis, which has limitations. However, it is also true that they reflect the functional characteristics of these bacterial taxa, which have a considerable proinflammatory potential[86–88] and are increased in patients with IBS.[89] Moreover, *Campylobacter jejuni* leads to a marked impairment of the gut microbiome and altered recovery after the infection in patients with PI-IBS.[90] Viruses had the lowest impact on PI-IBS, with a prevalence of almost 11%, but with a sixfold increased odds, that derived mainly from case-control studies of subjects with previous SARS-CoV-2 infection, who had a nearly fivefold higher odds of developing IBS than controls. These data differ from a previous meta-analysis where 19% and 4% of subjects developed PI-IBS after a viral infection, respectively, within and beyond 12 months from the infectious event.[7] This discrepancy can be explained by the different number of cohorts; 5 in the previous meta-analysis, compared with 13 in our analysis, due mainly to studies reporting IBS after SARS-CoV-2 infection.[7]

The prevalence of PI-FD after bacterial and SARS-CoV-2 infections were, respectively, 13.6% and 10.5%, slightly lower than observed for IBS. Interestingly, Enterobacteriaceae yielded a 19% prevalence suggesting that most aggressive strains can also increase the risk of FD. However, when analysing case-control studies assessing bacterial and SARS-CoV-2 infections, the ORs were not significant in any case, probably due to the lower number of studies. No data on the impact of parasites on FD were available.

We also identified other risk factors significantly associated with the development of PI-IBS, including patient-related factors, such as female sex and history of anxiety, and infection-related

factors, that is, diarrhoea >3 weeks and hospitalisation. Our findings fit with the known higher prevalence of IBS in females and in subjects with psychological comorbidities,[6] and by the previous evidence that associates PI-IBS with the clinical severity of gastroenteritis.[7]

In our meta-analysis, the prevalence of PI-IBS appeared relatively stable in the first 12 months after the acute gastroenteritis episode, but with a considerable increase up to 25.5% in individuals followed up for >12 months. The prevalence of PI-FD varied similarly. Both IBS and FD are multifactorial diseases, and several other factors, including dietary shifts or stressful events, can emerge after the microbiome disruption and the immune triggering, and contribute to the pathogenesis of the disease. However, the longer the time distance between the episode of acute gastroenteritis and the diagnosis of IBS or FD, the weaker the pathophysiological correlation with the infection. Finally, the prevalence of PI-IBS and PI-FD varied according to different Rome criteria. In our study, the lowest prevalence of PI-IBS was observed with the Rome IV criteria, which are stricter than their predecessors, while the Rome III criteria, which are more inclusive and sensitive, were associated with the highest prevalence of both PI-IBS and PI-FD.[91 92] Our findings confirm previous data,[88] although we did not observe a significant difference between the two prevalence rates, possibly due to the heterogeneity of different cohorts. The heterogeneity of cohorts, as well as the considerable number of new studies in our meta-analysis may also explain the slight differences in prevalence of IBS subtypes between our study and previous meta-analyses. For example, Klem *et al* found a higher prevalence of IBS-M than IBS-D (46% (95% CI 31% to 62%) vs 40% (95% CI 25% to 57%), respectively),[7] whereas in our study the prevalence of IBS-D was 46.1%, compared with 38.5% for IBS-M.

With 47 studies and 28 170 subjects, this is the largest meta-analysis to evaluate the prevalence of PI-IBS and PI-FD after acute gastroenteritis, to our knowledge, to date. We have updated previous meta-analyses on PI-IBS and PI-FD after 4 years[20] and 8 years,[9] respectively, also adding data concerning previously unknown microbes, such as SARS-CoV-2. However, our study has some limitations. First, we found moderate to high heterogeneity in most of our analyses. This may be partly explained by differences in study design, definitions of IBS and FD, sample sizes and length of follow-up of eligible studies. We tried to mitigate this by defining precise eligibility criteria and performing multiple subgroup analyses, and most studies were of high quality. However, the degree of heterogeneity was not lessened in many of our sensitivity analyses, although this is similar to the heterogeneity observed in the previous meta-analysis by Klem *et al*.[7] Second, most studies included in our analysis came from Western populations, with limited data available from areas with a high prevalence of acute gastroenteritis, such as the Asia-Pacific region and Africa.[86] Another limitation is the lack of microbiological evidence of gastroenteritis in several studies, which prevented a clear assessment of the microbial strains involved in PI-IBS and PI-FD. Finally, we have only limited data on specific pathogens, such as parasites.

In conclusion, our findings provide an update to the epidemiology of PI-IBS and PI-FD and of the likelihood of developing them after acute gastroenteritis, together with an unprecedented evaluation of IBS persistence over time after initial diagnosis that suggests a stable chronicisation of the disease in affected individuals. Moreover, our data suggest that infections from proinflammatory taxa, that is, Proteobacteria, and SARS-CoV-2, may be associated with PI-IBS and PI-FD.

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REFERENCES

1 Drossman DA, Hasler WL. Rome IV-functional GI disorders: disorders of gut-brain interaction. *Gastroenterology* 2016;150:1257–61.
2 Drossman DA, Tack J. Rome foundation clinical diagnostic criteria for disorders of gut-brain interaction. *Gastroenterology* 2022;162:675–9.
3 Mearin F, Lacy BE, Chang L, *et al*. Bowel disorders. *Gastroenterology* 2016;150:1393–407.
4 Sperber AD, Bangdiwala SI, Drossman DA, *et al*. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome foundation global study. *Gastroenterology* 2021;160:99–114.
5 Agarwal N, Spiegel BMR. The effect of irritable bowel syndrome on health-related quality of life and health care expenditures. *Gastroenterol Clin North Am* 2011;40:11–9.

6 Ford AC, Sperber AD, Corsetti M, *et al*. Irritable bowel syndrome. *The Lancet* 2020;396:1675–88.
7 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;152:1042–54.
8 Barbara G, Grover M, Bercik P, *et al*. Rome foundation working team report on post-infection irritable bowel syndrome. *Gastroenterology* 2019;156:46–58.
9 Futagami S, Itoh T, Sakamoto C. Systematic review with meta-analysis: post-infectious functional dyspepsia. *Aliment Pharmacol Ther* 2015;41:177–88.
10 Zanini B, Ricci C, Bandera F, *et al*. Incidence of post-infectious irritable bowel syndrome and functional intestinal disorders following a water-borne viral gastroenteritis outbreak. *Am J Gastroenterol* 2012;107:891–9.
11 Oshima T, Siah KTH, Yoshimoto T, *et al*. Impacts of the COVID-19 pandemic on functional dyspepsia and irritable bowel syndrome: a population-based survey. *J Gastroenterol Hepatol* 2021;36:1820–7.
12 Saps M, Pensabene L, Turco R, *et al*. Rotavirus gastroenteritis: precursor of functional gastrointestinal disorders *J Pediatr Gastroenterol Nutr* 2009;49:580–3.
13 Scallan Walter EJ, Crim SM, Bruce BB, *et al*. Postinfectious irritable bowel syndrome after campylobacter infection. *Am J Gastroenterol* 2019;114:1649–56.
14 Mearin F, Pérez-Oliveras M, Perelló A, *et al*. Dyspepsia and irritable bowel syndrome after a salmonella gastroenteritis outbreak: one-year follow-up cohort study. *Gastroenterology* 2005;129:98–104.
15 Ji S, Park H, Lee D, *et al*. Post-infectious irritable bowel syndrome in patients with shigella infection. *J Gastroenterol Hepatol* 2005;20:381–6.
16 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;44:576–82.
17 Hanevik K, Dizdar V, Langeland N, *et al*. Development of functional gastrointestinal disorders after giardia lamblia infection. *BMC Gastroenterol* 2009;9:27.
18 España-Cueto S, Oliveira-Souto I, Salvador F, *et al*. Post-infectious irritable bowel syndrome following a diagnosis of traveller's diarrhoea: a comprehensive characterization of clinical and laboratory parameters. *J Travel Med* 2023;30:taad030.
19 Zhang D, Chen C, Xie Y, *et al*. Post-infection functional gastrointestinal disorders following coronavirus Disease-19: a prospective follow-up cohort study. *BMC Infect Dis* 2023;23:422.
20 Svendsen AT, Bytzer P, Engsbro AL. Systematic review with meta-analyses: does the pathogen matter in post-infectious irritable bowel syndrome *Scand J Gastroenterol* 2019;54:546–62.
21 Berumen A, Edwinson AL, Grover M. Post-infection irritable bowel syndrome. *Gastroenterol Clin North Am* 2021;50:445–61.
22 Oka P, Parr H, Barberio B, *et al*. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020;5:908–17.
23 Goodoory VC, Craig OF, Gracie DJ, *et al*. Prognosis of patients with Rome IV-defined versus physician-diagnosed irritable bowel syndrome: longitudinal follow-up study. *Neurogastroenterology Motil* 2022;34.
24 Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;71.
25 Cremon C, Stanghellini V, Pallotti F, *et al*. Salmonella gastroenteritis during childhood is a risk factor for irritable bowel syndrome in adulthood. *Gastroenterology* 2014;147:69–77.
26 Marasco G, Cremon C, Barbaro MR, *et al*. Post COVID-19 irritable bowel syndrome. *Gut* 2022.
27 Nazarewska A, Lewandowski K, Kaniewska M, *et al*. Irritable bowel syndrome following COVID-19: an underestimated consequence of SARS -Cov-2 infection. *Pol Arch Intern Med* 2022;132:16323.
28 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;113:1363–75.
29 Youn YH, Kim HC, Lim HC, *et al*. Long-term clinical course of post-infectious irritable bowel syndrome after Shigellosis: A 10-year follow-up study. *J Neurogastroenterol Motil* 2016;22:490–6.
30 G W. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis, Available: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
31 Higgins JPT, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
32 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
33 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:bmj.d4002.
34 Andresen V, Löwe B, Broicher W, *et al*. Post-infectious irritable bowel syndrome (PI-IBS) after infection with shiga-like toxin-producing escherichia coli (STEC) O104:H4: A cohort study with prospective follow-up. *United European Gastroenterol J* 2016;4:121–31.
35 Berumen A, Lennon R, Breen-Lyles M, *et al*. Characteristics and risk factors of post-infection irritable bowel syndrome after campylobacter enteritis. *Clin Gastroenterol Hepatol* 2021;19:1855–63.
36 Blackett JW, Li J, Jodorkovsky D, *et al*. Prevalence and risk factors for gastrointestinal symptoms after recovery from COVID-19. *Neurogastroenterol Motil* 2022;34:e14251.
37 Blackett JW, Wainberg M, Elkind MSV, *et al*. Potential long coronavirus disease 2019 gastrointestinal symptoms 6 months after coronavirus infection are associated with mental health symptoms. *Gastroenterology* 2022;162:648–50.
38 Borgaonkar MR, Ford DC, Marshall JK, *et al*. The incidence of irritable bowel syndrome among community subjects with previous acute enteric infection. *Dig Dis Sci* 2006;51:1026–32.
39 Dunlop SP, Jenkins D, Neal KR, *et al*. Relative importance of enterochromaffin cell hyperplasia, anxiety, and depression in postinfectious IBS. *Gastroenterology* 2003;125:1651–9.
40 Ebrahim Nakhli R, Shanker A, Sarosiek I, *et al*. Gastrointestinal symptoms and the severity of COVID-19: disorders of gut-brain interaction are an outcome. *Neurogastroenterology Motil* 2022;34.
41 Farsi F, Zonooz SR, Ebrahimi Z, *et al*. The incidence of post-infectious irritable bowel syndrome, anxiety, and depression in Iranian patients with coronavirus disease 2019 pandemic: a cross-sectional study. *Turk J Gastroenterol* 2022;33:1033–42.
42 Ford AC, Thabane M, Collins SM, *et al*. Prevalence of uninvestigated dyspepsia 8 years after a large waterborne outbreak of bacterial dysentery: a cohort study. *Gastroenterology* 2010;138:1727–36; .
43 Ghoshal UC, Ghoshal U, Rahman MM, *et al*. Post-infection functional gastrointestinal disorders following coronavirus disease-19: a case-control study. *J Gastroenterol Hepatol* 2022;37:489–98.
44 Golla R, Vuyyuru S, Kante B, *et al*. Long-term gastrointestinal sequelae following COVID-19: a prospective follow-up cohort study. *Clin Gastroenterol Hepatol* 2023;21:789–96.
45 Gwee KA, Leong YL, Graham C, *et al*. The role of psychological and biological factors in postinfective gut dysfunction. *Gut* 1999;44:400–6.
46 Koh S-J, Lee DH, Lee SH, *et al*. Incidence and risk factors of irritable bowel syndrome in community subjects with culture-proven bacterial gastroenteritis. *Korean J Gastroenterol* 2012;60:13–8.
47 Kowalcyk BK, Smeets HM, Succop PA, *et al*. Relative risk of irritable bowel syndrome following acute gastroenteritis and associated risk factors. *Epidemiol Infect* 2014;142:1259–68.
48 Marshall JK, Thabane M, Borgaonkar MR, *et al*. Postinfectious irritable bowel syndrome after a food-borne outbreak of acute gastroenteritis attributed to a viral pathogen. *Clin Gastroenterol Hepatol* 2007;5:457–60.
49 Marshall JK, Thabane M, Garg AX, *et al*. Incidence and epidemiology of irritable bowel syndrome after a large waterborne outbreak of bacterial dysentery. *Gastroenterology* 2006;131:445–50; .
50 Nair P, Okhuysen PC, Jiang Z-D, *et al*. Persistent abdominal symptoms in US adults after short-term stay in Mexico. *J Travel Med* 2014;21:153–8.
51 Neal KR, Hebden J, Spiller R. Prevalence of gastrointestinal symptoms six months after bacterial gastroenteritis and risk factors for development of the irritable bowel syndrome: postal survey of patients. *BMJ* 1997;314:779–82.
52 Nielsen HL, Engberg J, Ejlertsen T, *et al*. Psychometric scores and persistence of irritable bowel after campylobacter concisus infection. *Scand J Gastroenterol* 2014;49:545–51.
53 Noviello D, Costantino A, Muscatello A, *et al*. Functional gastrointestinal and Somatoform symptoms five months after SARS-Cov-2 infection: a controlled cohort study. *Neurogastroenterol Motil* 2022;34:e14187.
54 Parida PK, Mishra D, Pati GK, *et al*. A prospective study on incidence, risk factors, and validation of a risk score for post-infection irritable bowel syndrome in Coastal Eastern India. *Indian J Gastroenterol* 2019;38:134–42.
55 Parry SD, Stansfield R, Jelley D, *et al*. Does bacterial gastroenteritis predispose people to functional gastrointestinal disorders? A prospective, community-based, case-control study. *Am J Gastroenterol* 2003;98:1970–5.
56 Peters S, Pascoe B, Wu Z, *et al*. Campylobacter Jejuni genotypes are associated with post-infection irritable bowel syndrome in humans. *Commun Biol* 2021;4:1015.
57 Pitzurra R, Fried M, Rogler G, *et al*. Irritable bowel syndrome among a cohort of European travelers to resource-limited destinations. *J Travel Med* 2011;18:250–6.
58 Sharifi M, Safarpour AR, Barati-Boldaji R, *et al*. Post-infectious irritable bowel syndrome after an epidemic of gastroenteritis in south of Iran. *Middle East J Dig Dis* 2022;14:304–9.
59 Siyal M, Abbas Z, Ashraf J, *et al*. Incidence and predisposing factors for de novo post-COVID-19 irritable bowel syndrome. *Eur J Gastroenterol Hepatol* 2023;35:59–63.
60 Soyturk M, Akpinar H, Gurler O, *et al*. Irritable bowel syndrome in persons who acquired trichinellosis. *Am J Gastroenterol* 2007;102:1064–9.
61 Spence MJ, Moss-Morris R. The cognitive behavioural model of irritable bowel syndrome: a prospective investigation of patients with gastroenteritis. *Gut* 2007;56:1066–71.
62 Stermer E, Lubezky A, Potasman I, *et al*. Is traveler's diarrhea a significant risk factor for the development of irritable bowel syndrome? A prospective study. *Clin Infect Dis* 2006;43:898–901.

63 Thornley JP, Jenkins D, Neal K, *et al*. Relationship of campylobacter toxigenicity in vitro to the development of postinfectious irritable bowel syndrome. *J Infect Dis* 2001;184:606–9.
64 Törnblom H, Holmvall P, Svenungsson B, *et al*. Gastrointestinal symptoms after infectious diarrhea: a five-year follow-up in a Swedish cohort of adults. *Clin Gastroenterol Hepatol* 2007;5:461–4.
65 Trivedi KH, Schlett CD, Tribble DR, *et al*. The impact of post-infectious functional gastrointestinal disorders and symptoms on the health-related quality of life of US military personnel returning from deployment to the Middle East. *Dig Dis Sci* 2011;56:3602–9.
66 Vélez C, Paz M, Silvernale C, *et al*. Factors associated with chronic de novo post-coronavirus disease gastrointestinal disorders in a metropolitan US County. *Clin Gastroenterol Hepatol* 2022;20:e1488–92.
67 Wang LH, Fang XC, Pan GZ. Bacillary dysentery as a causative factor of irritable bowel syndrome and its pathogenesis. *Gut* 2004;53:1096–101.
68 Wensaas KA, Hanevik K, Hausken T, *et al*. Postinfectious and sporadic functional gastrointestinal disorders have different prevalences and rates of overlap: results from a controlled cohort study 3 years after acute Giardiasis. *Neurogastroenterol Motil* 2016;28:1561–9.
69 Wouters MM, Van Wanrooy S, Nguyen A, *et al*. Psychological comorbidity increases the risk for postinfectious IBS partly by enhanced susceptibility to develop infectious gastroenteritis. *Gut* 2016;65:1279–88.
70 Jung IS, Kim HS, Park H, *et al*. The clinical course of postinfectious irritable bowel syndrome: a five-year follow-up study. *J Clin Gastroenterol* 2009;43:534–40.
71 Marshall JK, Thabane M, Garg AX, *et al*. Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery. *Gut* 2010;59:605–11.
72 Neal KR, Barker L, Spiller RC. Prognosis in post-infective irritable bowel syndrome: a six year follow up study. *Gut* 2002;51:410–3.
73 Litleskare S, Rortveit G, Eide GE, *et al*. Prevalence of irritable bowel syndrome and chronic fatigue 10 years after giardia infection. *Clin Gastroenterol Hepatol* 2018;16:1064–72.
74 Bradley S, Alderson S, Ford AC, *et al*. General practitioners' perceptions of irritable bowel syndrome: a Q-methodological study. *Fam Pract* 2018;35:74–9.
75 Mearin F, Sans M, Balboa A. Relevance and needs of irritable bowel syndrome (IBS): comparison with inflammatory bowel disease (IBD). *Gastroenterol Hepatol* 2022;45:789–98.
76 Tang HY, Jiang AJ, Wang XY, *et al*. Uncovering the pathophysiology of irritable bowel syndrome by exploring the gut-brain axis: a narrative review. *Ann Transl Med* 2021;9:1187.
77 Marasco G, Maida M, Cremon C, *et al*. Meta-analysis: post-COVID-19 functional dyspepsia and irritable bowel syndrome. *Aliment Pharmacol Ther* 2023;58:6–15.
78 Grytdal SP, DeBess E, Lee LE, *et al*. Incidence of norovirus and other viral pathogens that cause acute gastroenteritis (AGE) among Kaiser permanente member populations in the United States, 2012-2013. *PLoS One* 2016;11:e0148395.
79 Schmidt MA, Groom HC, Rawlings AM, *et al*. Incidence, etiology, and healthcare utilization for acute gastroenteritis in the community, United States. *Emerg Infect Dis* 2022;28:2234–42.
80 Riddle MS, Welsh M, Porter CK, *et al*. The epidemiology of irritable bowel syndrome in the US military: findings from the millennium cohort study. *Am J Gastroenterol* 2016;111:93–104.
81 Barbara G, Stanghellini V, Cremon C, *et al*. Almost all irritable bowel syndromes are post-infectious and respond to probiotics: controversial issues. *Dig Dis* 2007;25:245–8.
82 Vanuytsel T, Bercik P, Boeckxstaens G. Understanding neuroimmune interactions in disorders of gut-brain interaction: from functional to immune-mediated disorders. *Gut* 2023;72:787–98.
83 Ianiro G, Iorio A, Porcari S, *et al*. How the gut parasitome affects human health. *Therap Adv Gastroenterol* 2022;15:17562848221091524.
84 Gamsjäger L, Cirone KM, Schluessel S, *et al*. Host innate immune responses and microbiome profile of neonatal calves challenged with cryptosporidium parvum and the effect of bovine colostrum supplementation. *Front Cell Infect Microbiol* 2023;13:1165312.
85 McGregor BA, Razmjou E, Hooshyar H, *et al*. A shotgun metagenomic analysis of the fecal microbiome in humans infected with giardia duodenalis. *Parasit Vectors* 2023;16:239.
86 Zeng MY, Inohara N, Nuñez G. Mechanisms of inflammation-driven bacterial dysbiosis in the gut. *Mucosal Immunol* 2017;10:18–26.
87 Shin NR, Whon TW, Bae JW. Proteobacteria: microbial signature of dysbiosis in gut microbiota. *Trends Biotechnol* 2015;33:496–503.
88 Litvak Y, Byndloss MX, Tsolis RM, *et al*. Dysbiotic proteobacteria expansion: a microbial signature of epithelial dysfunction. *Curr Opin Microbiol* 2017;39:1–6.
89 Pittayanon R, Lau JT, Yuan Y, *et al*. Gut microbiota in patients with irritable bowel syndrome-a systematic review. *Gastroenterology* 2019;157:97–108.
90 Jalanka J, Gunn D, Singh G, *et al*. Postinfective bowel dysfunction following campylobacter enteritis is characterised by reduced microbiota diversity and impaired microbiota recovery. *Gut* 2023;72:451–9.
91 Tack J, Talley NJ, Camilleri M, *et al*. Functional gastroduodenal disorders. *Gastroenterology* 2006;130:1466–79.
92 Stanghellini V, Chan FKL, Hasler WL, *et al*. Gastroduodenal disorders. *Gastroenterology* 2016;150:1380–92.