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Small Intestinal Bacterial Overgrowth in Irritable Bowel Syndrome: Systematic Review and Meta-analysis

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See related article, Spiegel B et al, on page 1944 in *Gastroenterology*.

BACKGROUND & AIMS: Small intestinal bacterial overgrowth (SIBO) has been proposed as an etiologic factor in irritable bowel syndrome (IBS), but evidence is conflicting. We conducted a systematic review and meta-analysis of the prevalence of SIBO in IBS. **METHODS:** MEDLINE and EMBASE were searched up to November 2008. Case series and case-control studies applying diagnostic tests for SIBO in unselected adults meeting diagnostic criteria for IBS were eligible. Prevalence of a positive test for SIBO was extracted and pooled for all studies, and compared between cases and controls using an odds ratio and 95% confidence interval (CI). **RESULTS:** Twelve studies were identified containing 1921 subjects meeting criteria for IBS. Pooled prevalence of a positive lactulose or glucose hydrogen breath test was 54% (95% CI, 32%–76%) and 31% (95% CI, 14%–50%), respectively, with statistically significant heterogeneity between study results. Prevalence of a positive jejunal aspirate and culture was 4% (95% CI, 2%–9%). The pooled odds ratio for any positive test for SIBO in cases compared with healthy asymptomatic controls was 3.45 (95% CI, 0.9–12.7) or 4.7 (95% CI, 1.7–12.95), depending on the criteria used to define a positive test, with statistically significant heterogeneity for both. **CONCLUSIONS: Prevalence of SIBO in individuals meeting diagnostic criteria for IBS was highest with breath testing. The prevalence in cases with IBS compared with controls varied according to criteria used to define a positive test. The role of testing for SIBO in individuals with suspected IBS remains unclear.**

Irritable bowel syndrome (IBS) is a chronic relapsing and remitting disorder of the gastrointestinal (GI) tract. The condition is characterized by abdominal pain or discomfort in association with an alteration in bowel habit.[1] The exact cause of IBS remains unknown, although the prevailing hypothesis is that there are abnormalities in the brain–gut axis. Proposed central mechanisms include abnormalities of pain processing,[2,3] somatization,[4] and maladaptive coping.[5] Potential peripheral causes include abnormal motility,[6,7] dysregulated intestinal immunity,[8] low-grade inflammation and altered GI permeability after enteric infection,[9,10] and imbalances in intestinal flora.[11]

Bloating is reported by up to 80% of IBS sufferers,[12,13] and often is exacerbated by food.[14] Although data are conflicting, some studies report increased intestinal gas on abdominal radiograph in IBS,[15,16] particularly in the small intestine.[16] Increased hydrogen production after the administration of fermentable substrate has been shown in IBS subjects compared with healthy controls,[17] and total excretion of hydrogen also may be increased in IBS.[18] It has been proposed that the unifying explanation for increased hydrogen production, and therefore symptoms such as bloating in a proportion of individuals assumed to have IBS, is colonization of the proximal small bowel by fermenting bacteria, as occurs in small intestinal bacterial overgrowth (SIBO).

There is some evidence to support this hypothesis. A group of researchers in the United States showed a prevalence of presumed SIBO in individuals with symptoms suggestive of IBS of almost 80%, using lactulose hydrogen breath testing.[19] After treatment of presumed SIBO with antibiotics in a proportion of these individuals, symptoms including abdominal pain, bloating, and diarrhea improved. These findings led the same group of researchers to conduct a randomized controlled trial of rifaxamin, a nonabsorbable antibiotic, in subjects with IBS.[20] This led to a significant improvement in global IBS symptoms and a reduction in bloating scores after completion of therapy, compared with individuals who received placebo.

However, a recent large study from the United States that also used lactulose hydrogen breath testing to diagnose SIBO did not replicate these findings.[21] In addition, direct aspiration and culture of jejunal secretions is considered the gold standard for the diagnosis of SIBO, but only one study has used this approach to date.[22] This failed to show a significant difference in the prevalence of SIBO in cases meeting diagnostic criteria for IBS compared with healthy asymptomatic controls from the general population. Therefore, there is controversy surrounding the proposed etiologic role of SIBO in IBS. We performed a systematic review and meta-analysis in an attempt to examine this issue in more detail.

Methods

Search Strategy and Study Selection

A search of the medical literature was conducted using MEDLINE (January 1950 to November 2008) and EMBASE (January 1980 to November 2008). Studies on irritable bowel syndrome were identified with the terms *irritable bowel syndrome* and *functional diseases*, *colon* (both as Medical Subject Headings and free text terms), and *IBS* and *functional* adj5 *bowel* (as free

Abbreviations used in this paper: CI, confidence interval; GI, gastrointestinal; IBS, irritable bowel syndrome; PPI, proton pump inhibitor; SIBO, small intestinal bacterial overgrowth.

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Table 1. Eligibility Criteria

Adults (90% of participants aged >16 y) with a presumed diagnosis of IBS (either according to a physician's opinion, questionnaire, or meeting specific diagnostic criteria[a])
Case series or case-control design
Participants not specially selected
Tests for SIBO applied to all patients and results recorded[b]
>90 subjects included

[a]Manning et al,[23] Kruis et al[26] score, or Rome I,[24] II,[25] or III[1] criteria. [b]Lactulose, glucose, xylose, or sucrose hydrogen breath tests, or jejunal aspirate and culture (or any combination of these).

text terms). These were combined using the set operator AND with studies identified with the terms: *breath tests*, *intestinal diseases*, *bacteria*, *small intestine*, *malabsorption syndromes*, *bacterial infections*, *intestine*, *lactulose*, *glucose*, *xylose*, and *sucrose* (both as Medical Subject Heading terms and free text terms), and the following free text terms: *bacterial overgrowth*, *lactulose hydrogen*, *glucose hydrogen*, *xylose hydrogen*, and *sucrose hydrogen*.

There were no language restrictions and abstracts of the articles identified were assessed for appropriateness to the study question, and all potentially relevant articles were obtained and evaluated in detail. Conference proceedings between 2000 and 2008 were searched by hand to identify eligible studies published only in abstract form. Bibliographies of all identified relevant studies were used to perform a recursive search of the literature.

Case series and case-control studies recruiting unselected adult subjects meeting diagnostic criteria for IBS and applying tests for SIBO to all enrolled individuals were eligible for inclusion. Diagnostic criteria for IBS included a physician's opinion, questionnaire data, or specific symptom-based criteria, including the Manning et al[23] and Rome criteria,[1,24,25] or the Kruis et al[26] scoring system. These could be supplemented by results of GI investigations, if individual studies performed these. We considered lactulose, glucose, xylose, and sucrose hydrogen breath testing, and jejunal aspirate and culture as valid methods of assessing for SIBO. Small studies lead to problems with accuracy when estimating the pooled effect in a meta-analysis because the outcome of interest is rare.[27] We therefore made an a priori decision that studies were eligible for inclusion only if they contained 90 individuals or more. Detailed eligibility criteria for study inclusion are provided in Table 1. Articles were assessed independently by 2 reviewers according to the prospectively defined eligibility criteria.

Data Extraction

All data were extracted by 2 reviewers onto a Microsoft Excel spreadsheet (XP Professional Edition; Microsoft Corp, Redmond, WA), and discrepancies were resolved by consensus. For case series the number of individuals with a positive test for SIBO was expressed as a proportion of the total number of cases meeting diagnostic criteria for IBS. In case-control studies this was performed for both cases and non-IBS controls. In addition, the following clinical data were extracted for each study: country of origin and setting (primary, secondary, or tertiary care), number of centers, test used to detect SIBO and criteria used to define a positive test, diagnostic criteria used to define IBS, source of controls (for case-control studies), and whether studies excluded individuals using antibiotics or proton pump inhibitors (PPIs) before enrolment.

Data Synthesis and Statistical Analysis

The proportion of individuals meeting diagnostic criteria for IBS with a positive test for SIBO was combined for both case series and case-control studies, subgrouped according to the test used, to give a pooled prevalence in all individuals meeting diagnostic criteria for IBS. In addition, for case-control studies data were pooled for both cases and controls, and the prevalence of a positive test for SIBO, regardless of the type of test used, was compared between the 2 groups with an odds ratio and 95% confidence interval (CI). We planned to conduct sensitivity analyses according to geographic region, study setting (primary care, secondary care, tertiary care), diagnostic criteria used to define IBS, and, for case-control studies, according to whether the assessors were blinded to the symptom status of the subject to examine whether this had any effect on the prevalence or odds of SIBO and to explore reasons for any heterogeneity observed.

Data were pooled using a random effects model[28] to give more conservative estimates. StatsDirect version 2.4.4 (StatsDirect, Ltd, Cheshire, England) was used to generate Forest plots of pooled prevalences and pooled odds ratios with 95% CIs. We assessed for evidence of heterogeneity using the I^2 statistic,[29] and for publication bias by applying the Egger test to funnel plots.[30]

Results

The search strategy identified 9517 potentially relevant citations (Figure 1). Of these, 17 appeared to be relevant to the study question and were retrieved for further evaluation. Five were ineligible for various reasons, leaving 12 studies containing 2247 subjects, 1921 (85.5%) of whom met diagnostic criteria for IBS.[19,21,22,31–39] Six were case-control studies,[21,22,32,33,37,38] using either healthy members of the general population or healthy relatives as controls. Only one of the case-control studies stated specifically that assessors interpreting the results of diagnostic tests for SIBO were blinded to the symptom status of the subjects.[21] Detailed study characteristics, including the criteria used in each study to define the presence of SIBO, are provided in Table 2. Six of the studies excluded individuals who had used

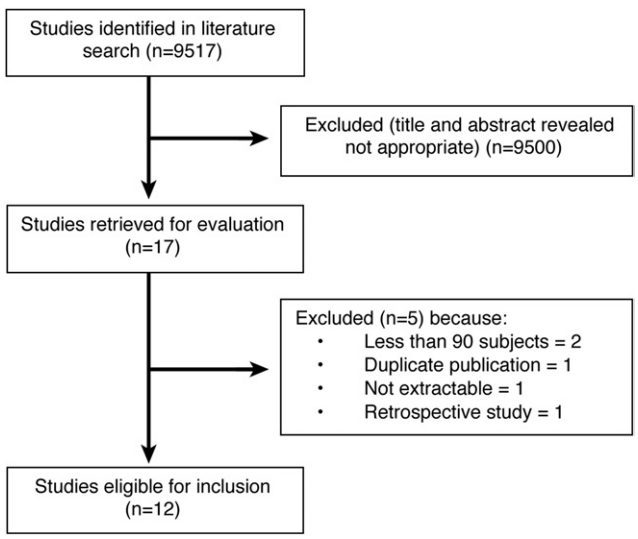

Figure 1. Flow diagram of assessment of studies identified in the systematic review.

Table 2. Characteristics of Included Studies

Study	Type of study	Country and setting	Prior antibiotic use allowed	Diagnostic tests applied for SIBO	Criteria used to define SIBO	Sample size	Number of subjects meeting diagnostic criteria for IBS	Number of subjects with IBS with a positive test (%)
Pimentel et al,[19] 2000	Case series	United States, tertiary care	Not stated	Lactulose hydrogen breath test	2 distinct peaks of hydrogen production, hydrogen production <90 min after lactulose ingestion, or an increase in hydrogen concentration of >20 ppm over baseline	202	202	157 (78)
Nucera et al,[36] 2005	Case series	Italy, tertiary care	None within prior 2 months	Lactulose hydrogen breath test	2 distinct peaks of hydrogen production >10 ppm above baseline, or hydrogen production <90 min after lactulose ingestion	98	98	64 (65)
Madrid et al,[34] 2007	Case series	Chile, tertiary care	Not stated	Lactulose hydrogen breath test	An increase in hydrogen concentration of >20 ppm over baseline	225	225	172 (76)
Parodi et al,[37] 2007	Case-control	Italy, unclear	Not stated	Lactulose hydrogen breath test	Not specified	162	132	66 (50)
Bratten et al,[21] 2008	Case-control	United States, tertiary care	None within prior 1 month	Lactulose hydrogen breath test	2 distinct peaks of hydrogen production >12 ppm above basal value with decrease of ≥5 ppm before second peak, an increase in hydrogen concentration <90 min after lactulose ingestion, or an increase in hydrogen concentration of >20 ppm over baseline	214[a]	180	121 (67) or 25 (14)[b]
Carrara et al,[31] 2008	Case series	Italy, secondary care	None within prior 2 weeks	Lactulose hydrogen breath test	An increase in hydrogen concentration of >20 ppm over baseline <90 min after lactulose ingestion	127	127	55 (43)
Lupascu et al,[33] 2005	Case-control	Italy, tertiary care	None within prior 2 months	Glucose hydrogen breath test	An increase in hydrogen concentration of >20 ppm over baseline	167	65	20 (31)
McCallum et al,[39] 2005	Case series	United States, tertiary care	Not stated	Glucose hydrogen breath test	An increase in hydrogen or methane production resulting in an absolute value >20 ppm	143	143	55 (38.5)
Majewski and McCallum,[35] 2007	Case series	United States, tertiary care	Not stated	Glucose hydrogen breath test	Peak of hydrogen or methane production of >20 ppm (if baseline <10 ppm), or >12 ppm (if baseline >10 ppm)	204	204	93 (46)
Rana et al,[38] 2008	Case-control	India, secondary care	None within prior 1 month	Glucose hydrogen breath test	An increase in hydrogen concentration of ≥12 ppm above baseline	325	225	25 (11)

Table 2. Continued

Study	Type of study	Country and setting	Prior antibiotic use allowed	Diagnostic tests applied for SIBO	Criteria used to define SIBO	Sample size	Number of subjects meeting diagnostic criteria for IBS	Number of subjects with IBS with a positive test (%)
Posserud et al,[22] 2007	Case-control	Sweden, tertiary care	None within prior 2 weeks	Jejunal aspirate and culture[c]	$\geq 10^5$ colony-forming units of colonic bacteria per milliliter, or a bacterial count (including noncolonic bacteria) ≥95th centile of that in healthy controls	204	162	70 (43) or 7 (4)[b]
Grover et al,[32] 2008	Case-control	United States, tertiary care	Not stated	Sucrose hydrogen breath test	Baseline hydrogen concentration of ≥20 ppm, an increase in hydrogen or methane concentration of ≥12 ppm above baseline ≤60 min after sucrose ingestion, or a peak of ≥12 ppm above baseline >60 min after ingestion followed by a second peak of ≥20 ppm above baseline after a gap of ≥15 min from the first peak	192	158	52 (33)

[a]The study by Bratten et al[21] contained 264 subjects, but 50 of these were methane-producers and were excluded from further reporting of breath test results in the original study.
[b]Prevalence according to the criteria used to define a positive test that gave the highest and lowest prevalence of SIBO.
[c]The study by Posserud et al[22] also used lactulose and glucose hydrogen breath testing, but in fewer than 90 subjects.

antibiotics within the past 2 weeks to 2 months.[21,22,31,33,36,38] Despite the fact that many of the studies used more than one criteria to define a positive test result, only 2 studies reported the prevalence according to the different criteria separately.[21,22] One study that used lactulose hydrogen breath testing reported that the prevalence was highest when an increase in breath hydrogen concentration within 90 minutes of lactulose ingestion was used to define SIBO, and lowest when a dual peak of breath hydrogen production was used.[21] Another study examining the yield of jejunal aspirate and culture in suspected IBS reported the lowest prevalence when 10^5 or more colony-forming units of colonic bacteria per milliliter was used to define a positive test, and the highest prevalence when a bacterial count, including noncolonic bacteria, that was in the 95th or higher centile of the count in healthy controls was used.[22] We conducted sensitivity analyses with the data from these 2 studies included according to the criteria used to define a positive test that gave either the highest or lowest prevalence of SIBO. Because of the small number of studies identified it was not possible to conduct the majority of our a priori sensitivity analyses, with the exception of the prevalence of a positive test for SIBO in suspected IBS according to the diagnostic test used.

Prevalence of a Positive Lactulose Hydrogen Breath Test in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome

Six studies reported prevalence of a positive lactulose hydrogen breath test in 964 subjects.[19,21,31,34,36,37] Five studies used the Rome II criteria to define IBS,[21,31,34,36,37] whereas the sixth study used the Rome I criteria.[19] Three of the studies were conducted in Italy,[31,36,37] 2 in the United States,[19,21] and 1 in Chile.[34] If the criteria that gave the lowest prevalence of SIBO in the study by Bratten et al[21] were used then the prevalence of a positive lactulose hydrogen breath test in individual studies ranged from 14% to 78%, with a pooled prevalence in subjects meeting diagnostic criteria for IBS of 54% (95% CI, 32%–76%) (Figure 2). If the criteria that gave the highest prevalence of a positive test for SIBO in the Bratten et al[21] study were used then the prevalence in individual studies ranged from 43% to 78%, with a pooled prevalence of 64% (95% CI, 52%–75%). There was statistically significant heterogeneity detected between study

Figure 2. Prevalence of a positive lactulose hydrogen breath test in subjects meeting diagnostic criteria for IBS.

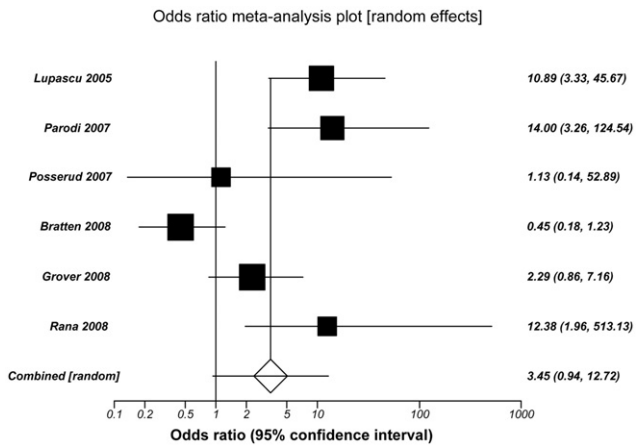

Figure 3. Odds of a positive test for SIBO in subjects meeting diagnostic criteria for IBS compared with healthy controls using criteria that gave the lowest prevalence of a positive test.

results in both cases (I^2 = 98% and 92.5%, respectively; $P < .001$ for both).

Prevalence of a Positive Glucose Hydrogen Breath Test in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome

Four studies reported on the prevalence of a positive glucose hydrogen breath test in 637 subjects meeting Rome II criteria for IBS.[33,35,38,39] The studies were conducted in India,[38] Italy,[33] and the United States.[35,39] The prevalence of a positive glucose hydrogen breath test in individual studies varied between 11% and 46%, with a pooled prevalence of 31% (95% CI, 14%–50%). Again, there was statistically significant heterogeneity detected between study results (I^2 = 96%; $P < .001$).

Prevalence of a Positive Sucrose Hydrogen Breath Test in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome

Only one study conducted in the United States used sucrose hydrogen breath testing in 158 subjects with Rome II IBS.[32] The prevalence of a positive test in subjects meeting diagnostic criteria for IBS was 33% (95% CI, 26%–41%).

Prevalence of Positive Jejunal Aspirate and Culture in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome

A Swedish study used jejunal aspirate and culture to detect possible SIBO in 162 individuals with Rome II IBS.[22] The prevalence of a positive test was only 4% (95% CI, 2%–9%) when 10^5 or more colony-forming units of colonic bacteria per milliliter were used to define SIBO. When a lower bacterial count, including noncolonic bacteria, of the 95th or higher centile of the count in healthy controls was used the prevalence was 43% (95% CI, 35.5%–51%).

Prevalence of Small Intestinal Bacterial Overgrowth in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome Compared With Healthy Controls

There were 6 case-control studies, containing 1248 subjects, 922 (74%) of whom met diagnostic criteria for IBS.[21,22,32,33,37,38] All 6 studies used the Rome II criteria to define IBS. Two studies used lactulose hydrogen breath testing,[21,37] 2 studies used glucose hydrogen breath testing,[33,38] 1 study used sucrose hydrogen breath testing,[32] and 1 study used jejunal aspirate and culture.[22] Controls were members of the general population in 5 studies,[21,22,32,37,38] and healthy first-degree relatives in the sixth study.[33] If the criteria that gave the lowest prevalence of a positive test in the Bratten et al[21] and Posserud et al[22] studies were used there were 195 (21%) of 922 subjects meeting Rome II criteria for IBS testing positive for SIBO, compared with 23 (7%) of 326 healthy controls without symptoms suggestive of IBS. The odds of a positive test for SIBO in individuals meeting diagnostic criteria for IBS compared with controls was 3.45 (95% CI, 0.9–12.7) (Figure 3), with statistically significant heterogeneity between trial results (I^2 = 84%; $P < .001$), but no evidence of funnel plot symmetry (Egger test, $P = .32$). If the criteria that gave the highest prevalence of a positive test in the Bratten et al[21] and Posserud et al[22] studies were used there were 354 (38%) of 922 subjects meeting Rome II criteria for IBS testing positive for SIBO, compared with 40 (12%) of 326 healthy controls without symptoms suggestive of IBS. The odds of a positive test for SIBO in individuals meeting diagnostic criteria for IBS compared with controls was 4.7 (95% CI, 1.7–12.95) (Figure 4), again with statistically significant heterogeneity between trial results (I^2 = 78%; $P = .003$), and evidence of funnel plot asymmetry (Egger test, $P = .04$).

Effect of Proton Pump Inhibitor Use on the Prevalence of Small Intestinal Bacterial Overgrowth in Subjects Meeting Diagnostic Criteria for Irritable Bowel Syndrome

Three studies containing 445 subjects with symptoms suggestive of IBS reported data on PPI use,[35,36,39] 2 studies stated that they had excluded those individuals who had used PPIs within the past 2 months,[31,38] and only 1 study stated that it had not controlled for PPI use.[22] In the remaining studies this issue was unclear. There were 70 (33%) of 212 individuals with a positive test for SIBO who were prescribed a PPI, compared with 69 (30%) of 233 individuals testing negative. The odds ratio for PPI use in those with a positive test for SIBO was 1.4 (95% CI, 0.9–2.1).

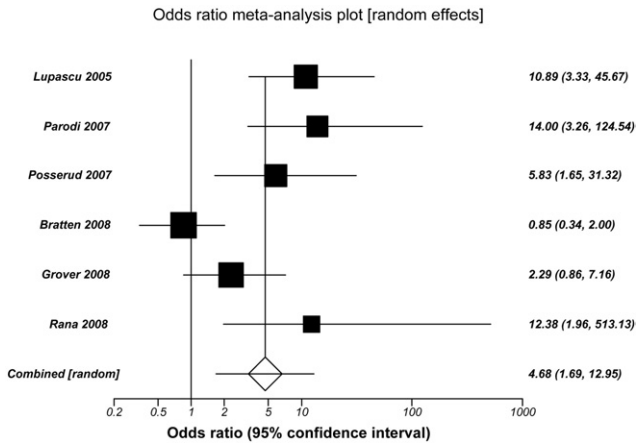

Figure 4. Odds of a positive test for SIBO in subjects meeting diagnostic criteria for IBS compared with healthy controls using criteria that gave the highest prevalence of a positive test.

Discussion

This study has shown a prevalence of SIBO in subjects meeting diagnostic criteria for IBS of between 4% and 64%, depending on the type of test used and the criteria used to define a positive test result. However, there was significant heterogeneity when data from studies that used the same type of test were combined. In addition, when jejunal aspirate and culture was used, the current gold standard test for the detection of SIBO, with a cut-off level of 10^5 or more colony-forming units of colonic bacteria per milliliter used to define the presence of SIBO, the prevalence of a positive test in individuals with symptoms suggestive of IBS decreased to only 4%. When the prevalence of a positive test for SIBO was compared between cases with symptoms suggestive of IBS and healthy asymptomatic controls, regardless of the test used, there was a 3- to 5-fold increase in the odds of a positive test result in individuals meeting diagnostic criteria for IBS, although this was not statistically significant when the criteria that gave the lowest prevalence of a positive test for SIBO in the studies by Bratten et al[21] and Posserud et al[22] were used. In addition, there was significant heterogeneity between studies, and when data were pooled using the criteria that gave the highest prevalence of a positive test for SIBO, the funnel plot asymmetry suggested publication bias, or other small study effects. There remains, therefore, uncertainty concerning the utility of testing for SIBO in IBS.

Strengths of our study include the exhaustive literature search, rigorous statistical methods, and pooling of data to allow synthesis of all the available published evidence to allow us to examine the yield of testing for SIBO in IBS, as well as our extraction of data to estimate the effect of PPI use on the prevalence of a positive test result for SIBO. Weaknesses of the study, as with any systematic review and meta-analysis, arise from the available evidence. A majority of studies were based in tertiary care, which may limit the generalizability of the findings to subjects with symptoms suggestive of IBS in routine clinical practice. There were only very limited data reporting on the yield of jejunal aspirate and culture, the current gold standard for diagnosing SIBO. In addition, case-control studies are subject to spectrum bias because the study design often omits mild cases that are difficult to diagnose, and this leads to an overestimation of the diagnostic performance of the test being examined, compared with studies using a clinical cohort.[40] Because 6 of the 12 studies included in this systematic review were case-control studies this should be kept in mind when interpreting the results. Because only one of these case-control studies stated that assessors were blinded to the symptom status of the subject there is the possibility that the prevalence of a positive test for SIBO may have been overestimated in cases meeting diagnostic criteria for IBS compared with controls. The quality of the studies included also has implications for the results of a systematic review and meta-analysis. There are published recommendations for the evaluation of study quality in systematic reviews of diagnostic test accuracy, in which the index test underevaluation is compared with a current reference standard,[41,42] but there are none in existence for the studies included in this type of systematic review and meta-analysis. An informal quality assessment of eligible studies in this review revealed that 8 of the 12 studies stated explicitly that they were prospective and recruited consecutive patients, and all used either the Rome I or II criteria to define the presence of IBS, considered to be the gold standard for making the diagnosis of IBS by experts in the field at the time they were conducted. Finally, there was significant heterogeneity, which could not be explained by the limited sensitivity analyses we were able to conduct, and some evidence of publication bias, suggesting that the prevalence of a positive test for SIBO in individuals meeting diagnostic criteria for IBS may have been overestimated.

The uncertainty in the yield of testing for SIBO in IBS that we have observed could be caused by problems with the accuracy of available methods for confirming the diagnosis. Whether jejunal aspirate and culture should be viewed as the gold standard is controversial. There is concern that SIBO involving the distal small intestine will not be detected if this method is used because it only samples the duodenum or upper jejunum, and that there are species of bacteria that are, as yet, not able to be cultivated using conventional culture-based techniques. These issues limit the sensitivity of jejunal aspirate and culture to detect SIBO. Breath tests also are problematic. When glucose is used as the fermentable substrate it is absorbed rapidly in the proximal small intestine, and therefore may lack sensitivity for the diagnosis of SIBO for similar reasons to jejunal sampling. Lactulose is digested poorly, and is therefore more likely to identify SIBO of the distal small bowel. However, there are issues with the ability of all available breath tests to discriminate between a premature increase in breath hydrogen caused by true SIBO from that arising as a result of rapid intestinal transit time, and therefore specificity also is suboptimal.

Another possible explanation for the lack of any definite utility of testing for SIBO in IBS is that the 2 conditions are not linked causally. The proposed mechanism of abnormal GI flora causing excessive intestinal gas production, leading to bloating in IBS, is itself controversial. There are some studies that have evaluated intestinal gas on abdominal radiograph or computed tomography,[14–16] but the results are conflicting, and there does not appear to be a definite correlation between the amount of gas observed and the presence of bloating. A recent review of this subject concluded that excessive gas production may lead to abdominal bloating in some sufferers, but that this was unlikely to explain the symptom in the majority of IBS patients.[43] Other studies have shown no difference in the overall gas content of the gut in subjects with IBS compared with healthy controls,[44,45] and this has led some investigators to propose that intestinal gas volumes in subjects with IBS are normal, but rather it is the handling of this gas that is abnormal.[44] If excessive gas production arising from SIBO leading to bloating is the framework for understanding IBS, this fails to take into account many of the other proposed mechanisms for IBS. Although SIBO could account for why some individuals with IBS experience an improvement in symptoms after a course of antibiotics, it would not explain why symptoms in IBS appear to improve with other nonpharmacologic treatments such as hypnotherapy and cognitive behavioral therapy.[46] The benefit of antibiotics could arise as a result of the high placebo response rate of IBS to therapy in randomized controlled trials.

There appeared to be an association between SIBO and IBS in many of the studies we identified, but this was not consistent and there remains the possibility of confounding by another factor. Recently, it has been proposed that the apparent association between SIBO and IBS may be caused by concurrent use of PPIs.[47] This could arise because individuals reporting GI

symptoms are likely to be prescribed PPIs empirically as a therapeutic measure. The resultant inhibition of gastric acid secretion then could render an individual more susceptible to bacterial colonization of the upper small intestine,[48] and therefore SIBO. Unfortunately, only 3 of the studies we identified reported data concerning rates of PPI use in involved subjects,[35,36,39] and although the proportion using PPIs, and the odds ratio for PPI use, were somewhat higher in those meeting diagnostic criteria for IBS with a positive breath test result than those without, the difference was not statistically significant. If PPI use is indeed causing an apparent increase in SIBO in individuals with IBS it may be that antibiotics, such as rifaximin, are treating this deleterious effect of PPI therapy successfully.

Unfortunately, the pooling of data from studies identified by this systematic review and meta-analysis do not allow us to resolve these unanswered questions. To address these uncertainties we need researchers in the future to either control for PPI use or exclude PPI users altogether from prevalence studies of SIBO in IBS. In addition, we require more data validating the current available tests for confirming the presence of SIBO before their utility in IBS can be determined. In summary, this systematic review and meta-analysis has shown conflicting evidence for the yield of tests for SIBO in individuals meeting diagnostic criteria for IBS compared with healthy individuals from the general population, with the prevalence varying according to the criteria used to define a positive test. Additional evidence examining this subject is required before the routine exclusion of SIBO in individuals with suspected IBS can be recommended in usual clinical practice.

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Reprint requests

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Conflicts of interest

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