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Systematic review: natural history of irritable bowel syndrome

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SUMMARY

Background: The natural history of irritable bowel syndrome is unclear, including the likelihood that these patients will be diagnosed with an alternative organic or functional gastrointestinal disorder. Understanding the stability of an irritable bowel syndrome diagnosis may limit repeated diagnostic evaluation among these patients.

Methods: The inclusion criteria included observational longitudinal studies of clinic-based samples of adult patients with irritable bowel syndrome. Only studies published in the English language in full manuscript form were included. Literature searches, selection and review of eligible articles, and data abstraction were performed in a duplicate, independent manner.

Results: Fourteen studies met study selection criteria. In six studies with relevant information, 2–5% of irritable bowel syndrome patients were diagnosed with an alternative organic GI disorder after 6 months to 6 years of follow-up. Long-term follow-up indicated that 2–18% of patients developed worse irritable bowel syndrome symptoms, approximately 30–50% of patients had unchanged symptoms, and the rest either improved or had symptoms disappear. Prior surgery (one study), higher somatic scores (one study), higher baseline anxiety (two studies), depression scores (one study) were predictive of worsening of symptoms during long-term follow-up.

Conclusions: Irritable bowel syndrome, a chronic disorder, is a stable diagnosis. Once initial investigations are negative, fewer than 5% are diagnosed with an alternative organic GI disorder. Repeated diagnostic evaluations of patients with recurrent or persistent symptoms similar to their baseline symptoms are not warranted.

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic relapsing condition that is diagnosed with symptom-based criteria.[1] Most patients with IBS undergo exhaustive diagnostic evaluations to rule out other organic GI disorders before physicians and/or patients accept this diagnosis.[2] The natural history of IBS has been described as a chronic course with intermittent flares.[1] Thus, this natural history lends itself to repeated diagnostic evaluations at considerable expense while exposing the patient to procedure-related complications.

The natural history of IBS, including the stability of a symptom-based IBS diagnosis and the frequency and duration of symptomatic IBS flares, is poorly documented. Previous studies[3, 4] estimate the likelihood of diagnosing an alternative organic GI disorder during prolonged follow-up of IBS patients. Previous studies[5] also suggest that some patients with IBS transition into other functional GI disorders. In order to minimize repeated expensive and potentially morbid diagnostic evaluations in these patients, it is important to

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determine the stability of an IBS diagnosis and the frequency that IBS transitions to alternative functional GI disorders. Therefore, knowledge of the natural history of IBS is relevant to primary care providers, gastroenterologists and health care policy makers. Although a previous systematic review[6] discussed the clinical course and prognostic determinants of IBS, it did not provide a detailed account of the stability of an IBS diagnosis, the frequency of transition to alternative functional GI disorders, or the frequency and duration of symptomatic IBS flares. The current report provides an updated systematic review with new publications and with a detailed evaluation of the natural history of IBS.

Therefore, this systematic review of published literature encompasses the following objectives: (i) to determine the stability of the IBS diagnosis (i.e. to determine the likelihood that an alternative organic GI disorder would be diagnosed after an initial diagnosis of IBS); (ii) to determine the likelihood that IBS patients would transition to alternative functional GI disorders; (iii) to characterize the frequency and duration of symptomatic flares of IBS; (iv) to identify limitations in the current research; and (v) to identify areas for future research.

MATERIALS AND METHODS

Literature search

A computer-assisted search using the OVID interface to MEDLINE and EMBASE was conducted to identify potentially relevant published papers. A search of the MEDLINE database from 1966 to present was performed using the exploded (exp) medical subject heading (MeSH) terms (exp irritable bowel syndrome) AND (exp incidence OR exp prevalence OR exp epidemiology OR exp natural history OR exp clinical course OR exp prognosis). An identical search of the biomedical and pharmaceutical EMBASE database from 1990 to 2003 was also performed. The results in all searches were limited to human studies published in the English language. Manual searches of reference lists from potentially relevant papers were also performed to identify any additional studies that may have been missed using the computer-assisted strategy.

Study selection criteria

Two investigators (H.E., P.P.) independently reviewed the titles and abstracts of all citations identified by the literature search. Potentially relevant studies were retrieved and the selection criteria applied. The inclusion criteria were (i) longitudinal studies of clinic-based samples of adult patients; (ii) IBS had to be defined according to either conventional definitions or some operational definition documented by the investigators; (iii) total number of the inception cohort had to be available; (iv) total number of subjects available at the end of follow-up was reported; (v) the study was observational; and (vi) published in the English language in full manuscript form. The exclusion criteria included: (i) therapy trials; and (ii) cross sectional studies with no follow-up. Population-based studies were not included because patients in these studies did not uniformly have a physician-based diagnosis of IBS.

Data extraction and data analysis

The eligible articles were reviewed in a duplicate, independent manner by two investigators (H.E., P.P.). Agreement on selection of studies was 100%. Data abstraction on predesigned forms was also performed in a duplicate, independent fashion by the two investigators. Agreement between investigators was >90% and disagreement in data extraction was resolved by consensus. For studies regarding the stability of the IBS diagnosis, the incidence of alternative organic GI disorder diagnoses, timing of diagnosis, and type of alternative organic GI disorder was extracted. For studies about the progression of IBS diagnosis to another functional GI disorder, the incidence of alternative functional GI disorders, the timing of diagnosis of alternative functional GI disorder, and type of alternative functional GI disorder was extracted. For studies about the frequency of flares of IBS, the frequency of IBS flares and the duration of IBS flares were extracted. If data were available, we calculated the proportions of patients with IBS who developed alternate organic disease, or functional disorder during follow-up, and the proportion of patients with IBS who become asymptomatic at the end of follow-up. Drop out rates were presented or calculated from the available data. We also specifically abstracted the study design (retrospective/prospective), duration of follow-up, demographic features of the study population and determinants of outcomes (if any). The data was presented in a tabular and graphic format.

RESULTS

Characteristics of selected studies

Searching the MEDLINE database yielded 539 articles in the in the titles search; the EMBASE database yielded 372 articles. There were several articles found in more than one search, and a net total of 22 articles were found. The titles and abstracts of these 22 articles were reviewed by two authors (H.E., P.P.).

The literature search identified 14 relevant studies that met our initial criteria[3, 4, 7–18]. (Table 1) These included 10 studies identified in the previously published review[6] in addition to three studies excluded by that review,[11, 12, 17] and one recent study.[14] One additional study[19] was not abstracted because it examined the same cohort of an earlier study.[4] All studies were clinic-based: seven prospective[7, 10, 12, 15–18] and seven retrospective.[3, 4, 8, 9, 11, 13, 14] Chaudhary *et al.*[8] published the earliest study in 1962 and Keefer *et al.*[14] published the most recent article in 2002. The studies were conducted in four countries. Most studies ($n = 8$) were conducted in the UK,[7–11, 13, 16, 18] and four studies were conducted in the United States.[3, 7, 14, 15, 17]

The prospective studies were generally smaller in sample size ($n = 20$–104) as compared with retrospective studies ($n = 75$–163). Also, the follow-up was less complete in prospective (47–100%) than in retrospective studies (four of seven had >80% follow-up).[3, 4, 8, 11, 13] Women comprised the majority of study subjects (36–100%) in most studies. Most studies employed some definition for IBS that combined abdominal pain with altered bowel movements,[3, 7, 9, 10, 12, 13, 16, 18] although three studies might have included patients without abdominal pain.[8, 11, 18] Only five studies categorized patients with IBS as diarrhoea-dominant, constipation-dominant or alternating; these particular studies were published after 1983.[3, 4, 10, 12, 17] Many of the studies listed sigmoidoscopy ($n = 7$) and barium enema ($n = 5$) as part of the IBS definition.[4, 7, 8, 11–13, 18] Ten studies recorded the duration of IBS symptoms prior to the onset of follow-up. Generally, these studies included patients with chronic IBS symptoms (few weeks to 20 years) with four studies having patients with >10 years of IBS symptoms. The primary outcome of most studies was the persistence or resolution of the presumed IBS symptoms.

Likelihood of diagnosing an alternative organic GI disorder after an initial IBS diagnosis

The development of alternative or consequent organic diseases was specifically addressed in six of 14 studies (Table 2).[3, 4, 11, 13, 16, 18] The proportion of patients developing organic diseases after baseline investigation ranged between 2 and 9% of those who completed follow-up and 1.4–9% of the original cohort when followed for up to 30 years. When follow-up is limited to 6 months to 6 years after original IBS diagnosis, only 2–5% of IBS patients were diagnosed with an alternative organic GI disorder during follow-up. In the studies that reported organic disease development, five of six reported baseline investigations[4, 11, 13, 18] that consisted of sigmoidoscopy (four studies), barium enema (five studies), and/or blood work including haemoglobin, ESR (three studies). In these studies, the proportions of patients developing alternative organic disease also ranged between 2 and 5%.

In the first of these studies,[18] only one patient (2%) developed a gastric ulcer, and none of the patients reported weight loss or hospitalization during an average follow-up of 12 months. In the second and largest of these four studies,[11] six (3.7%) of 163 patients had a new gastrointestinal diagnosis during the follow-up: adenocarcinoma of the stomach (two patients) <1 and 4 years after initial consultations; adenocarcinoma of the colon (two patients) found 2 and 6 years respectively, after initial investigation; ulcerative colitis (one patient) developed 5 years after the onset of symptoms and 3 years after normal sigmoidsocopy; and pancreatic steatorrhoea developed in the final patient who declined further investigations. In the third study,[13] four patients (5%) developed alternative organic diagnoses over a follow-up of 6 years: one patient was diagnosed with gastric ulcers, one was discovered to have jejunal diverticulum with possible bacterial overgrowth, and the remaining two patients had thyroid dysfunction. The fourth study,[4] reported that five patients (4.5%) were considered diagnostic failures: one patient died of bronchogenic carcinoma 6 months after IBS diagnosis and autopsy revealed chronic pancreatitis; another died of pancreatic cancer 18 months after IBS diagnosis. The remaining three patients had symptomatic gallbladder stones, kidney stones, or thyrotoxicosis during follow-up.

Lastly, the study by Owen *et al.*[3] was the one that reported the highest proportion of organic diagnoses

Table 1. Descriptive details of 14 studies examining the natural history of IBS that were identified in this systematic review

First author (reference)	Design	*n*	Age (years)	% Of females	Type of IBS	Definition of IBS	Baseline investigation	Duration of IBS symptoms before start of follow-up
Chaudhary, UK[8]	Retrospective	130	20–60	66% (86/130)	NA	Spastic colon group: pain of colonic origin was present, bowel habit was variable; alternating constipation and diarrhoea Painless diarrhoea group: patients w/o pain	Sigmoidoscopy, BE	25% had history >10 years, 37% had symptoms from 1 to 10 years
Waller, UK[18]	Prospective	74	Most were <40	41% (30/74)	NA	Abdominal pain and altered bowel habit for which no organic cause was found. Diarrhoea or alternating diarrhoea and constipation w/o abdominal pain	Sigmoidoscopy, BE, ESR, haemoglobin	32 (64%) had symptoms from 1 to 9 years 7 (14%) had symptoms for 10 years or more Remaining 11 patients (22%) had symptoms for <1 year
Hawkins, UK[11]	Retrospective	163	13–76	61% (100/163)		Chronic (>6-week duration), diarrhoea without an organic cause	Sigmoidoscopy, BE, blood tests	NA
Holmes, UK[13]	Retrospective	91	22–86 Mean 57	49% (45/91)	NA	Recurrent abdominal pain associated with a disturbance of bowel rhythm (constipation or diarrhoea), or mucus through rectum	Sigmoidoscopy BE, FOBT, blood test, ESR	NA
Hillman, New Zealand[12]	Prospective	30	16–60	100% (30/30)	Diarrhoea ($n = 6$), Constipation ($n = 14$), Alternating ($n = 10$)	Altered bowel habit and abdominal pain	sigmoidoscopy, and labs	NA
Svendsen, Denmark[4]	Retrospective	112	18+	76% (85/112)	Diarrhoea ($n = 28$), constipation ($n = 84$)	Alternating bowel habits, distension, rumbling for months w/o organic explanation	GI-made diagnosis, BE	2 years
Harvey, UK[10]	Prospective	104	16–81	56% (58/104)	39% diarrhoea, 36% constipation, 25% alternating	Manning Criteria	Blood count, liver enzymes, thyroid function and physical exam	6 months–2 years 62 >2 years 28 (6 months–2 years) 24 <6 months
Prior, UK[16]	Prospective	80; 41 (51%) with IBS	18–68	100%	NA	Abdominal pain >1 month, distension and alteration of bowel habits	No IBD; no gastric surgery	NA
Blewett, UK[7]	Prospective	70	18–65	66% (46/70)	NA	Altered bowel habit and abdominal pain related to defecation and bloating	GI-made diagnosis, Sigmoidoscopy	46 months in those with symptoms, 59 months in rest

Fowlie, UK[9]	Retrospective	75	Mean 39	36% (27/75)	NA	Altered bowel habit abdominal pain and abdominal distension	No rectal bleeding	Mean duration of symptoms = 50 months
Owens, United States[3]	Retrospective	112	Median 41 Range 20–64	68% (76/112)	IBS-diarrhoea	Rome criteria, abdominal pain with altered defecation, abdominal distension, or both	Proctoscopy in 65%, BE in 79%	12 patients (11%) had symptoms for 1–4 weeks; 30 patients had symptoms for 1–12 months; and 60 patients (54%) had symptoms >1 year
Lembo, United States[15]	Prospective	20	18–60	50% (10/20)		Rome criteria Recent-onset-IBS and Longstanding-IBS	GI-made diagnosis	>5 years
Stevens, United States[17]	Prospective	25	22–73 mean 44	68% (17/25)	Constipation-predominant ($n = 6$), diarrhoea-predominant ($n = 6$), and mixed ($n = 12$)	Criteria by Latimer *et al.*	GI-made diagnosis, blood work	15.5 years
Keefer, United States[14]	Retrospective	13	Mean 50	62% (8/13)	NA	Rome criteria	NA	14.7 years

IBS, irritable bowel syndrome; BE, barium enema; NA, not available; FOBT, foecal occult blood test; ESR, erythrocyte sedimentation rate.

(10 patients or 9%). However in that study, only one patient (0.9%) developed gastric ulcer that was detected after a relatively short time (2 years) and therefore was felt to be related to the initial diagnosis of IBS. Eight of the nine remaining patients developed alternative organic GI disorders more than 12 years after the original IBS diagnosis: chronic pancreatitis ($n = 2$; 17 and 30 years later), gastrointestinal cancer ($n = 4$; 13–30 years later), small bowel obstruction ($n = 2$; 2 and 12 years later), and gastric ulcer ($n = 1$;12 years later). Thus, it is unlikely that the original IBS diagnosis was a mis-diagnosis of an underlying organic GI disorder.

Given the relatively small number of patients developing organic disease in each study, proper examination of risk factors for developing alternative organic disease could not be performed.

Likelihood that IBS patients transition to an alternative functional GI disorder

No study meeting our inclusion criteria directly addressed the development of other functional gut disorders (e.g. chronic constipation, functional dyspepsia). One study observed that most patients who retained symptoms had the same nature of symptoms (Table 2).[18] In that prospective study conducted in the UK and published in 1969, an analysis performed at the end of 12-month follow-up revealed that of patients who retained symptoms (88% of the initial 50 patients), all but one had a constant nature of symptoms. In the same study, an analysis was also conducted at the end of 31-month follow-up that showed 81% of available symptomatic patients retained the same nature of symptoms. This single study did not address development of other functional GI disorders.

Frequency and duration of symptomatic flares of IBS

All studies reported on symptoms of IBS at the end of follow-up (Table 2). The reported proportion of patients with the complete disappearance of symptoms ranged between 12 and 38% in the five studies that reported on symptom-free patients.[8, 10, 13, 16–18] The median follow-up duration in these studies was 2 years. A sixth study[3] reported that 29% of patients did have IBS-related visits during a median follow-up of 12 years. In general, there was no significant correlation between the proportion of those with complete disappearance of

Table 2. The outcomes reported in 14 studies examining the natural history of IBS. These are the same studies described in Table 1

First author (reference)	Duration of follow-up	% With complete follow-up	Primary outcome of the study	Organic diseases	Functional gut diseases	Predictors of outcomes
Chaudhary[8]	32: <1 year 63: 1–3 years 31: >3 years	126/130 = 97%	47/126 (37%) symptom-free Mild 73/126 (58%) Severe 6/126 (5%)	NA	NA	NA
Waller[18]	12–31 months	50/74 = 68% Excluded four for comorbid conditions, four incomplete investigations, and 16 who defaulted	18 (36%)improved 25 (50%)unchanged 1 (2%)worsened 6 (12%)symptom-free In 27 patients with 31 months f/u 2 (7%) relapsed 1 (4%) remained in remission 2 (7%) lost their symptoms Rest unchanged (81%)	One (2%) developed gastric ulcer. No weight loss, or hospitalization for IBS symptoms. One attempted suicide	At the end of 12-month f/u, nature of symptoms remained constant in all but one patient. After 31 months f/u, again the nature of the symptoms remained constant	NA
Hawkins[11]	2–20 years	150 (92%) 7 died unrelated 6 untraceable	Diarrhoea ceased in 63 patients (38.5%), intermittent or occasional in 47 patients (28.8%) and persistent in 34 (20.8%)	6 patients (3.7%) developed: stomach cancer (2), colon cancer (2), ulcerative colitis (1), and pancreatic steatorrhoea (1). Lactase def in 8% (of 22 with persistent diarrhoea who were tested)	NA	NA
Holmes[13]	6 years	77/91 = 85% 7 died 4 had an alternative diagnosis 3 could not be traced	44/77 (57%) still had IBS symptoms and 29/77 (38%) had no bowel problems (symptom-free)	4/77 (5%) had: Gastric ulcer (1), jejunal diverticulae (1), thyroid dysfunction (2)	NA	NA
Hillman[12]	2–3 years	14/30 = 47%	Symptoms were generally less severe although they persisted in all but one patient. The clinical severity scores of 7 (50%) improved, 5 (36%) were unchanged and 2 (14%) were worse	NA	NA	Higher somatic scores at baseline predicts persistence of IBS symptoms
Svendsen[4]	5–7 years	90/112 = 80% 17 died (15 unrelated) 3 diagnostic failures, 1 emigration, 1 unknown	Of the 90 living: 46 (51%) IBS-related symptoms improved during f/u. 44 (49%) unchanged or worsened	5/110 (4.5%) had gall bladder stones, kidney stones, and thyrotoxicosis; 2 died (chronic pancreatitis, pancreatic cancer)	NA	Only predictor of a poor prognosis (IBS troubles unchanged/worsened) was abdominal surgery before the diagnosis. Not age, gender, IBS treatment, diet, or IBS type
Harvey[10]	5 years	Excluding those who left the area, the overall follow-up was 97/104 (93%)	66 patients (68%) had either no symptoms at all or minor symptoms. 14 (14%) were moderately troubled by symptoms and still needed treatment. 17 (18%) felt worse	NA	NA	NA

Prior[16]	12 months	71/80 = 89%, of those 37 (52%) had IBS. 9 could not be traced	24 (65%) of patients with IBS were symptomatic compared with 11 (32%) without IBS symptoms	3/37 (8%) with IBS had a gynecologic diagnosis (endometriosis in 2 and PID in one) after EUA and laparoscopy. C/w 15/34 (44%) w/o IBS	NA	NA
Blewett[7]	6–17 months	62/70 = 87%	At f/u 32 (52%) had good outcome as defined by a Bowel Symptom Scale (BSS), which allows patients to report current symptoms on a scale of 1–6 'Good outcome' is a report of 3–1.	NA	NA	The following were not predictive of poor outcome IBS: age, gender, early response to treatment, duration of symptoms, psychological diagnoses, or initial response to therapy.
Fowlie[9]	5 years	43/59 = 73% 3 died unrelated 13 could not be traced 16 did not respond	28 (65%) reported 'improved'. 13 (30%) reported 'unchanged', and 2 (5%) said 'worse'	NA	NA	Persistence of IBS symptoms: higher baseline anxiety scores. Worse: women, diarrhoea, >2 years symptoms at baseline. Best: men, short illness, constipation, preceded by a diarrhoeal episode
Owens[3]	Median 29 years (range = 1–32 years)	25 (22%) lost to f/u after median of 11 years (12 moved away and 13 lost to f/u for unknown reasons)	32/112 (29%) made no IBS-related visits	10 (9%) patients developed chronic pancreatitis, gastrointestinal cancer, small-bowel obstruction and gastric ulcers after a median 15 years (2–30) after IBS diagnosis	NA	Less frequent visits for IBS was associated with notation in the chart of psychosocial history, presence of precipitating factors, discussion of diagnosis and treatment with patients
Lembo[15]	18 months for R-IBS and 19 months for L-IBS patients	100%	60% of R-IBS vs. 46% of L-IBS patients indicated that their symptoms had improved	NA	NA	NA
Stevens[17]	2 months	100%	48% symptom-free, rest symptomatic	NA	NA	Anxiety and depression (non significant correlates to IBS symptoms)
Keefer[14]	1 year	10/13 = 77%	80% improved one year after participating in relaxation-response meditation treatment	NA	NA	No difference in IBS symptoms related to length of history, or gender. Better outcome in the painless diarrhoea, and past h/o dysentery

IBS, irritable bowel syndrome; NA, not available.

symptoms and the duration of follow-up or the duration of IBS symptoms. Four studies[4, 9, 12, 18] reported on the proportion of patients with unchanged symptoms (30–50%) and patients whose symptoms had worsened (2–18%). None of the studies had details about the frequency and duration of IBS flares.

Only seven studies examined the determinants of recurrence or persistence of symptoms.[3, 4, 7, 9, 12, 14, 17] These are listed in detail in Table 2. Prior surgery (one study), higher somatic scores (one study), higher baseline anxiety (two studies), depression scores (one study) were predictive of worse outcomes in those studies. While one study reported constipation-predominant IBS,[9] another found painless diarrhoea[14] as a favourable prognostic indicator. One study reported short duration (<2 years) of IBS symptoms to be a predictor of better prognosis.[15] Multivariate analyses were not conducted in any of the studies.

DISCUSSION

This systematic review indicates that the diagnosis of IBS is relatively stable after an initial baseline evaluation. In studies that reported a baseline workup, only 2–5% of patients developed alternative organic diagnosis during follow-up. In several studies, approximately a third of all patients diagnosed initially with IBS reported complete disappearance of their symptoms during a median follow-up period of 2 years. However, there was no information on the number and duration of IBS flares. Finally, the reviewed studies did not provide an answer to the transition of IBS into other functional gut disorders such as chronic constipation and functional dyspepsia.

A previous systematic review by Janssen *et al.* focused mainly on the natural history of IBS symptoms, but that review did not specifically address the main question examined in our review: the likelihood of diagnosing an alternative organic GI disorder during follow-up. Furthermore, our updated review includes multiple studies that were not included in Janssen's review.[10, 11, 13, 16] Also, we did not include population-based studies,[5, 20, 21] which were part of the Janssen review. These studies identified patients with IBS using symptom questionnaires and further investigations were usually not conducted. As the primary goal is to examine the occurrence of organic GI disease in patients diagnosed with IBS, we have reviewed only clinic-based studies. These studies provide information on initial diagnostic work-up, definition of IBS diagnosis, additional investigation (e.g. sigmoidoscopy, barium enema) during follow-up, and diagnosis of alternative organic disorders.

Our major finding is the relatively low likelihood (2–5%) that patients with well-documented IBS will be diagnosed with an alternative organic disorder that accounts for their gastrointestinal symptoms during long-term follow-up. This is reassuring for patients and providers and argues against repeated diagnostic work-ups to look for organic disease. However, most of the studies in this review pertained to patients referred to gastroenterology clinics who underwent extensive investigation including sigmoidoscopy, colonoscopy and/or barium enema, and stool studies. Patients with abnormalities in these tests were not included in the follow-up. Therefore, the stability of the IBS diagnosis cannot be generalized outside of this setting. In the future, it would be beneficial to perform long-term follow-up studies of IBS patients diagnosed in primary care clinics after a more focused and limited diagnostic work-up.

Gastric ulcer, gastric cancer and thyroid abnormalities were the most frequently reported alternative organic disorders that were identified during follow-up of patients with IBS. Most of the studies were performed in the UK during the 1960s and 1970s. The incidence of gastric (and duodenal) ulcers has been declining steadily over the past three decades because of the falling prevalence of *Helicobacter pylori* infection.[22] Therefore, it is unclear if this finding is relevant to patients seen in the 21st century. Based on this data, clinicians might consider a thyroid stimulating hormone levels as part of the initial work-up of patients with IBS. Other organic diagnoses that were reported in IBS patients included chronic pancreatitis, pancreatic cancer and gallstones, but these were too infrequent to warrant specific recommendations. Importantly, we did not include studies that examined organic diseases in therapeutic trials, or case reports of possible side effects of medications.[23]

The review indicates that IBS symptoms persist in the majority of patients over a period of several years, but a substantial minority of IBS patients become symptom-free within 2 years. Approximately two-thirds of patients either retain the original symptom severity or worsen. One study indicated the character of symptoms remain the same in those who retain these symptoms.[12] Unfortunately, our review also identified a relative

dearth of information on important features of the clinical course of IBS such as the number, duration, or risk factors of symptomatic IBS flares. One UK study[24] evaluated 122 patients with active IBS flares for 12 weeks. During follow-up, patients reported active IBS symptoms during 50% of days, reported that they experienced a mean of 12 distinct 'episodes' of active IBS symptoms during this period and that the maximum duration of each individual 'episode' was 5 days.

Although there is a notion that functional GI disorders are a continuum with possibly shared pathophysiology and risk factors, this review indicates a dearth of data to support this concept. One population-based study,[5] a random sample of 835 residents of Olmsted Co, Minnesota, who responded to mailed questionnaires were remailed the same questionnaire 12–20 months later (83% response rate). The age- and sex-adjusted prevalence rates for IBS were not significantly different from the first mailing. Among the 582 subjects free of IBS on the first survey, 9% developed symptoms, while 38% of the 108 who initially had IBS did not meet the criteria during follow-up. Similar onset and disappearance rates were observed for the other main symptom categories (chronic diarrhoea, chronic constipation and dyspepsia). The substantial turnover with constant prevalence implied transition between these disorders. However, in this review in which IBS has a physician-based diagnosis (unlike the population based study described above),[5] no study was conducted with the main goal of examining the possible transition between IBS and other functional bowel disorders. Such information is important to clinicians because if we know that patients with IBS transition to chronic constipation or functional dyspepsia then this may limit future diagnostic work-up. This information can also be important in counselling and reassuring patients with these symptoms.

This review is limited because we attempted to obtain information from studies that were not primarily designed to address our questions. We resorted to a systematic review with data extraction because of our *a priori* knowledge of the paucity of relevant literature. We also did not include abstracts in this review as we felt that the details required to answer our questions would not be provided in most abstracts. We did not employ a score for methodological quality of the studies because there is no standard validated scale for this purpose.

Ideal natural history studies of IBS patients might fit the following criteria: (i) prospective; (ii) all patients would undergo an appropriate diagnostic evaluation to rule out alternative organic GI disorders at study entry; (iii) patients re-evaluated on a regular schedule (e.g. quarterly or bi-annually); (iv) patients would complete validated questionnaires about IBS symptom frequency and duration, quality of life and utilization of health care resources; and (v) patients would be followed for prolonged periods (e.g. up to 10 years). This may be an idealized study that would be difficult to complete, but it would provide definitive answers about the natural history of IBS.

In summary, this review indicates that IBS is a stable diagnosis after an appropriate diagnostic work-up to rule out alternative organic disorders. Given the chronic nature of IBS in most patients, repeated testing should be avoided for patients with recurrent or persistent symptoms that are similar to their baseline symptoms. This review also verifies that there is a paucity of data about the frequency and duration of IBS flares and a paucity of data about transition of IBS to other functional GI disorders. Future studies of well-characterized cohorts of IBS patients are needed to address these questions.

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