

# Irritable bowel syndrome in China: a review on the epidemiology, diagnosis, and management

Yi-Lin Liu<sup>1</sup>, Jin-Song Liu<sup>2</sup>

<sup>1</sup>The First Clinical Medical College of Nanchang University, Nanchang, Jiangxi 330006, China;

<sup>2</sup>Department of Gastroenterology, Wuhan Union Hospital of Tongji Medical College, Huazhong Science and Technology University, Wuhan, Hubei 430022, China.

## Abstract

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disease worldwide. Current guidelines of IBS are mostly based on the western populations and expected to vary in different communities. China has a large population and a vast literature is available on IBS. Due to linguistic variations in the literature, the studies are not widely known and their conclusions thus remain largely obscured to the western medical literature. In this article, we reviewed the published literatures on the investigations of IBS epidemiology, diagnosis, and management in the Chinese population and emphasized the different findings gleaned from the western publications. The detailed literature review will benefit understanding of and promote future study on IBS.

**Keywords:** Irritable bowel syndrome; Epidemiology; Diagnosis; Management; China

Irritable bowel syndrome (IBS) is a highly prevalent gastrointestinal functional disorder worldwide. The patients usually complain of abdominal pain, bloating, abdominal discomfort, and diarrhea/constipation, which severely impaired the patients' life quality. Currently, the Rome criteria are the mainly used guideline of IBS research and management. It is recognized that the sociocultural environment may influence the expression and interpretation of IBS, which may induce heterogeneity among different nations on IBS research and management. China has the largest IBS-afflicted population worldwide and a special cultural background. However, the studies on IBS in China are not well known worldwide because most of the publications are in the Chinese language. Therefore, it is necessary to review and introduce the Chinese literature to promote the research and management of IBS.

In this review, we collected the articles published on the topics of IBS epidemiology, pathogenesis, diagnosis, and management in the Chinese population/patients since 2010. All data were enrolled from the database of PubMed, Embase, Cochrane, and Wanfang.

## Epidemiology

As the results reported in most other areas, the prevalence of IBS in China varies between different regions and

populations. Also, the diagnostic criteria used in the investigation can change the positive diagnosis rate of IBS. In a previous review from China, the prevalence of IBS in the adult population was estimated to be 5% to 10% by using the Rome II or Manning criteria.<sup>[1]</sup> The prevalence of IBS varied among the different study subjects and study design. In a recent global survey, a large volume multicenter study in China, which involved 2914 adults from 10 cities, showed that the prevalence of IBS met Rome III and Rome IV criteria were 7.4% and 2.3% in an internet survey, and 3.8% and 1.4% in a household survey, respectively.<sup>[2]</sup> Two large volume single-center resident household surveys were conducted in the past decade. The survey from Hangzhou (China), which involved 1999 adults from five communities, suggested the IBS prevalence that met Rome III criteria was 5.9%.<sup>[3]</sup> The survey from Shanghai (China), which involved 18,000 adults, showed the prevalence of IBS that met Rome II criteria was 4.5%.<sup>[4]</sup> The prevalence varied in different age periods. In two surveys focusing on the student, the prevalence of IBS was significantly increased. In the IBS prevalence surveys using Rome III criteria, a school-based study showed that the prevalence of IBS in students aged 8 to 13 years was 10.8%.<sup>[5]</sup> Another survey in medical students, aged between 18 and 23 years, showed that the prevalence of IBS was 33.3%.<sup>[6]</sup> The results are still uncertain since they are from the single-center investiga-

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**Correspondence to:** Dr. Jin-Song Liu, Department of Gastroenterology, Wuhan Union Hospital of Tongji Medical College, Huazhong Science & Technology University, Wuhan, Hubei 430022, China  
E-Mail: jsliu@126.com

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tion and the sample is collected from a very limited group. The large population study from 7648 Shanghai adults showed that IBS prevalence was 12.7%.<sup>[7]</sup> The recent meta-analysis enrolled 76,763 subjects and showed that the general prevalence of IBS was 6.5%. Most studies showed that IBS-D (diarrhea-predominant IBS) or -M (mixed subtype IBS) were the predominant subtypes of IBS in China<sup>[8]</sup> [Table 1].

Several investigations have reported the risk factors associated with the IBS, including the diagnosis criteria, age, sex, food, history of gastrointestinal infection, education level, family income, psychological disorder, etc. The results were inconsistent except for psychological disorders and history of gastrointestinal infection. Two investigations found that the positive diagnosis rate using Rome III criteria was higher than Rome IV criteria<sup>[9,10]</sup> [Table 2]. The recent meta-analysis suggested that history of acute gastrointestinal infection, female, aged 39 to 50 years, food allergy, alcohol intake, and anxiety/depression were the significant risk factors. The education level or living area was not related to the IBS.<sup>[8]</sup>

**Diagnosis**

Rome criteria are commonly used in the diagnosis of IBS in China. In the Rome III criteria, the symptoms of IBS are defined as abdominal pain, discomfort, or bloating accompanied by the change of bowel habit, and the symptoms are relieved by defecation. In the newly published Rome IV criteria, the symptom of abdominal pain is required in the diagnosis and the symptoms could be relieved or exacerbated by defecation. The Rome IV criteria deleted the symptoms of bloating and discomfort in the diagnosis of IBS. On the other hand, in China, a significant number of patients only present symptoms of

bloating and/or discomfort, from which we can infer that the patients cannot be diagnosed as IBS based on the Rome IV criteria. In a sensitivity comparison of the Rome III/IV criteria on the diagnosis of IBS, the authors found that the diagnosis rates of IBS were 12.4% and 6.1%, respectively.<sup>[9]</sup> A similar study also found the positive diagnosis rate of IBS by Rome III criteria to be five times that of the Rome IV criteria.<sup>[10]</sup> All these studies suggested that the difference was mainly attributed to the condition that a significant number of patients only presented the symptoms of bloating. The symptomatology survey in Guangzhou reported the prevalence of chief complaint symptoms, including abdominal pain, abdominal discomfort, and bloating in Chinese IBS patients to be 35.8%, 25.1%, and 17.9%, respectively.<sup>[11]</sup> Based on the high prevalence of abdominal discomfort and bloating without abdominal pain in Chinese IBS patients, in the Chinese expert’s consensus on the diagnosis and treatment of IBS in China, the Rome III criteria were the apt candidate for use in the clinical operation and Rome IV criteria in scientific study.<sup>[12]</sup>

Symptoms’ overlap was commonly reported in Chinese IBS patients, which induced a high possibility of misdiagnosis and mistreatment. The survey in Guangdong showed that the position of symptoms was mainly located around the navel and upper abdomen, which were largely overlapped with the position of the symptoms of functional dyspepsia (FD). In the investigated subjects, ~20% of patients had the failed experience of proton pump inhibitor (PPI) treatment.<sup>[11]</sup> In a similar survey, which enrolled 302 patients with functional gastrointestinal diseases (FGID), the prevalence of patients with FD and IBS overlap was as high as 77%.<sup>[13]</sup> A recent multicenter investigation, which involved 735 cases of Rome III diagnosed IBS, found the prevalence of postprandial fullness, belching, and regurgitation to be 30.6%, 27.1%, and 21.8%, respectively. FD

**Table 1: Epidemiology finding of IBS in China.**

Authors	City/province	Area	Subject	Subject number	Diagnostic criteria	Prevalence	Male: Female	Predominant IBS subtype
Sperber <i>et al</i> <sup>[2]</sup>	Multicenter	Nationwide	Adults	2914	Rome III and Rome IV	Internet 7.4% (III) 2.3% (IV) Household 3.8% (III) 1.4% (IV)	NS	NS
Long <i>et al</i> <sup>[3]</sup>	Hangzhou/ Zhejiang	South-east	Adults	2115	Rome III	5.9%	51.3%:48.7%	IBS-D
Zhang <i>et al</i> <sup>[40]</sup>	Changzhou/ Jiangsu	East	Adults	2323	Rome III	7.6%	NS	NS
Xu <i>et al</i> <sup>[41]</sup>	Xi’an/Shaanxi	Northwest	Adults	752	Rome III	3.2% pure IBS, 1.4% overlap	15.1%:13.8%	NS
Shen <i>et al</i> <sup>[7]</sup>	Shanghai	East	Adults	7648	Rome III	13.1%	1%:0.92%	IBS-D
Shen <i>et al</i> <sup>[42]</sup>	Shanghai	East	Adults	11,569	Rome III	15.81%	1%:1.04%	NS
Zhao <i>et al</i> <sup>[4]</sup>	Multicenter	Nationwide	Adults	18,000	Rome II	4.6%	4.1%:5.0%	IBS-D
Zhu <i>et al</i> <sup>[5]</sup>	Suzhou/Jiangsu	East	Students	8000	Rome II	10.81%	10.3%:11.3%	NS
Liu <i>et al</i> <sup>[6]</sup>	Beijing	North	Medical students	767	Rome III	33.3%	80.8%:19.2%	IBS-M
Wang <i>et al</i> <sup>[43]</sup>	Inner Mongolia	North	Medical students	6105	Rome III	29.5%	31.3%:24.8%	IBS-D

The prevalence of IBS in the Chinese population is between 2.3% and 15.8%. Rome IV showed lower diagnosis sensitivity than Rome II and III. The medical students showed a dramatic increase. NS means there is no significant difference. IBS: Irritable bowel syndrome; IBS-D: Diarrhea-predominant IBS; IBS-M: mixed subtype IBS.

**Table 2: Risk factors related to the IBS in China.**

Authors	Age	Sex	Food	History of GI infection	Family income	Education level	Living area	Psychological disorders
Zhu <i>et al</i> <sup>[51]</sup>	Younger students had a higher risk	NS	Food allergy, fried food	Yes	NS	NS	NS	Psychological insults sustained in childhood
Liu <i>et al</i> <sup>[6]</sup>	Younger female had a higher risk	Females had a higher risk	NM	NM	NM	NS	NS	CTQ, SLSI, and PSQI were higher in IBS
Wang <i>et al</i> <sup>[43]</sup>	Older students had a higher risk	Females had a higher risk	Intended weight loss	NM	NS	NS	NS	Anxiety and depression were related to IBS
Long <i>et al</i> <sup>[3]</sup>	NS	NS	NS	NM	NS	NS	NM	Living stress and anxiety were related to IBS
Huang <i>et al</i> <sup>[44]</sup>	NS	Females had a higher rate of behavior disorder and food avoidance	NS	NM	NM	NM	NM	IBS-QOL was negatively correlated with a history of mental stress and being abused
Tang <i>et al</i> <sup>[45]</sup>	NM	Females had higher somatic symptoms and anxiety/depression score	NM	NM	NM	NM	NM	SAS and SDS scores were negatively correlated with IBS-QOL
Xu <i>et al</i> <sup>[41]</sup>	NS	NS	Alcohol consumption and smoking habit were related to IBS	NM	NM	NM	NS	Life events, childhood adversity, somatization, and hostility were related to IBS
Shen <i>et al</i> <sup>[7]</sup>	NM	Males had a higher prevalence of IBS-D. Females had a higher prevalence of IBS-C	Spicy food increases the prevalence of IBS. High protein diet was a protective factor	Yes	NM	NM	NM	Anxiety and insomnia were risk factors of IBS
Shen <i>et al</i> <sup>[42]</sup>	NM	Insomnia in females was higher than in males	NM	NM	NM	NM	NM	Insomnia was one of the risk factors of IBS

Female, food, history of gastrointestinal infection, and psychological disorder are the risk factors for Chinese IBS. NM means not mentioned in the study. NS means there is no significant difference. IBS: Irritable bowel syndrome; IBS-C: Constipation-predominant IBS; IBS-D: Diarrhea-predominant IBS; IBS-QOL: IBS quality of life. GI: Gastrointestinal; CTQ: child trauma questionnaire; SLSI: student-life stress inventory; PSQI: Pittsburgh sleep quality index; SAS: self-rating anxiety scale; SDS: self-rating depression scale.

(36.7%), belching disorders (27.1%), and functional heartburn (16.3%) were the three most frequent upper FGID in IBS patients.<sup>[14]</sup> The multicenter investigation from 11 Asian cities, which included Chinese patients, also reported the misuse of PPI in IBS to be 51%, which suggested the common-symptoms' overlap and thus that careful symptoms' distinguishing was required before the diagnosis of IBS in Asian patients.<sup>[15]</sup>

Alarm symptoms are commonly used in patients with symptoms of IBS to distinguish the potential organic disease (OD). In the Rome criteria, it is suggested that the diagnosis could be made based on the IBS symptoms after excluding the alarm symptoms. The related study is still very limited in the Chinese population. In a recent multicenter survey, the author reported a low prevalence of OD (3/90) in diagnoses of symptomatic IBS by endoscopy examination, which included two ileocecal valve inflammatory changes, one ulcerative proctitis, and two colon polyps. Being different from the findings in upper gastrointestinal FGID, which had a fairly high prevalence of OD in symptomatic diagnosed FGID, the result suggested that the prevalence of OD in symptomatic diagnosed IBS was low in patients younger than 47.5 years.<sup>[16]</sup>

Biomarker to increase the diagnose accuracy of IBS is commonly investigated in the Chinese population. The

study from Taiwan (China)<sup>[17]</sup> reported that fecal calprotectin and blood erythrocyte sedimentation rates were significantly higher in IBD patients than in the IBS patients and healthy control; this observation could be effectively used in the differential diagnosis. A survey in Beijing (China) compared the serum level of intestinal fatty acid-binding protein (I-FABP) in post-infection IBS, non-post-infection IBS, and healthy control. The result showed that I-FABP in post-infection IBS patients was significantly higher than in non-post-infection patients and healthy control. The increase of I-FABP only presents in the IBS-D subtype, which suggested that I-FABP was a potential biomarker for the diagnosis of post-infectious irritable bowel syndrome (PI-IBS).<sup>[18]</sup> Two well-designed studies investigated the small intestinal bacteria overgrowth (SIBO) in IBS. Zhao *et al*<sup>[19]</sup> reported that lactulose hydrogen breath test alone was not a valid method for SIBO diagnosis in IBS due to the high level of variation in oro-cecal transit time. To increase the accuracy of SIBO diagnosis, the combined scintigraphic measurement of oro-cecal transit was required. The study found that the patients with breath H<sub>2</sub> ≥ 5 ppm increase before the appearance of cecal contrast showed good clinical outcomes following antibiotic therapy. Yang *et al*<sup>[20]</sup> compared the microbial diversity and composition in the duodenal mucosa, duodenal fluid, rectal mucosa, and fresh feces using glucose hydrogen breath test for patients diagnosed with SIBO+ and SIBO- IBS-D. The result

showed that mucosal microbiota, rather than luminal bacteria, had more apparent dysbiosis in SIBO+ IBS-D patients than SIBO-, which suggested that rectal mucosa-associated microbiota might act as a potential predictor of SIBO in IBS-D patients.

## Management

### Diet

In western society, fermentable oligosaccharides, disaccharides and monosaccharides, and polyole (FODMAP) food are commonly believed to be the cause for the induction of IBS. On the other hand, in China, the food intake habit is completely different from that followed by the western society. Even within China, the habit also has a wide difference. A survey in Beijing (north of China) investigated 58 cases of Rome III criteria diagnosed IBS patients, who were mainly IBS-D subtype, and found that the top 10 incentives were cold food (66.7%), spicy food (61.1%), raw food (53.7%), greasy food (53.7%), dairy products (excluding yogurt) (37.0%), fruits (33.3%), alcohol (29.6%), leeks (24.1%), meat (22.2%), and yogurt (16.7%). During the onset of the symptoms, selectively excluding the food that caused bowel irritation could relieve the symptoms in 55.2% of patients.<sup>[21]</sup> Another study from Beijing showed that SIBO+ IBS-D patients had more fat intake compared with SIBO- IBS-D patients and healthy control. The fat intake was positively correlated with breath methane and the symptoms of abdominal pain.<sup>[22]</sup> The study in Fuzhou (south-east of China) found a higher food intolerance rate in IBS-D patients than in healthy control.<sup>[23]</sup> The population survey from Taiwan (south-east of China) suggested that alcohol drink could increase the risk of IBS 13 times.<sup>[24]</sup> Generally, studies conducted based on interviews with Chinese patients suggest that stimulating food, food intolerance, and food allergy are more important in the onset of IBS than FODMAP.

### Antispasmodics

Evidence for antispasmodics on the treatment of IBS is still poor due to the small size of the studies. The effect of antispasmodics on the IBS global symptoms score and the symptoms of bloating and diarrhea are uncertain. Recently, two large-size randomized control trials (RCTs) investigated the effect of antispasmodics on the treatment of IBS. In the single-center investigation that enrolled all four IBS subtypes patients, drotaverine hydrochloride significantly improved the abdominal pain score, stool frequency, and stool form.<sup>[25]</sup> The multicenter RCT by Zheng *et al*<sup>[26]</sup> reported that pinaverium bromide significantly improved the abdominal pain, stool frequency, and abdominal discomfort in IBS-D patients. The proportion of intention-to-treat for pinaverium bromide was significantly higher than that of placebo. No severe side effects were reported in the two investigations.

### Gut microbiota treatment

Both probiotics and fecal microbiota transplant (FMT) have been used in Chinese IBS treatment. Sun *et al*<sup>[27]</sup> used

the *Clostridium butyricum* to treat the IBS-D patients. The results showed that 4 weeks of *C. butyricum* treatment significantly improved the overall IBS-D symptoms, quality of life, and stool frequency than the placebo, with no more side effects. In an open-label trial, Fan *et al*<sup>[28]</sup> reported that combined *Bifidobacterium*, *Lactobacillus*, and *Enterococcus* capsules were beneficial for the IBS symptoms; these microbiota are thought to mainly contribute to the effect on abdominal pain and stool character. Huang *et al*<sup>[29]</sup> tried to use FMT to treat 19 cases of IBS-D, seven cases of constipation-predominant IBS (IBS-C), and four cases of mixed IBS. All the patients had failed to respond to the traditional medicine treatment. The fresh fecal matter of the healthy donor was injected into the ileum under the guide of an endoscope. The result showed that the IBS quality of life (IBS-QOL), IBS severity scoring system (IBS-SSS), gastrointestinal symptoms rating scale (GSRS), Hamilton anxiety rating scale (HAMA), and Hamilton depression rating scale (HAMD) scores at 1 month and 3 months after FMT were all significantly improved. No severe adverse event was noted except temporary low fever and increased frequency that happened in two patients and disappeared in 24 h without any medical treatment.

### Antibiotic

Rifaximin was commonly used in the treatment of IBS-D since this subtype had the highest prevalence in the Chinese population and acute gastrointestinal infection history played an important role in the IBS. The tendency of rifaximin to have a better effect on patients with SIBO+ was noted in more Chinese publications. Short-term rifaximin treatment on IBS-D was reported in several Chinese studies. Li *et al*<sup>[30]</sup> reported that 2 weeks of rifaximin significantly improved the IBS-SSS, severity of abdominal pain, bloating, abdominal discomfort, frequency of excretion, stool consistency, and IBS-QOL in patients with SIBO. On the other hand, in the patients without SIBO, rifaximin only showed effects on IBS-SSS, frequency of excretion, and IBS-QOL. In Zhao *et al*'s study, rifaximin also showed a better effect on the patients with SIBO than those without SIBO.<sup>[19]</sup> The question of whether SIBO can be used as the predictor of rifaximin is still controversial. Zhuang *et al*'s study<sup>[31]</sup> showed that rifaximin improved the abdominal pain, abdominal discomfort, abdominal distension, diarrhea, defecatory urgency, and incomplete evacuation in both SIBO+ and SIBO- IBS-D patients. The animal study by Jin *et al*<sup>[32]</sup> found that rifaximin decreased abdominal withdrawal reflex score, increased threshold, and reduced contractile response and intestinal permeability in a PI-IBS model by suppressing the expression of IL-12 and IL-17 and promoting the expression of the major tight junction (TJ) protein occludin which suggested that the effect of rifaximin on visceral hypersensitivity was via the inhibition of inflammation except for its antibacterial action.

### Secretagogues

Linaclotide and lubiprostone are secretagogues that are newly used in the treatment of IBS-C. National Medical Products Administration (NMPA) recently approved the use of linaclotide in Chinese clinical treatment. In phase 3

randomized trial, 12-week linaclotide treatment significantly improved the IBS degree of relief, spontaneous bowel movement/complete spontaneous bowel movement frequency, stool consistency, straining, abdominal pain, abdominal discomfort, and abdominal bloating compared with placebo. Diarrhea was the most common adverse event with low discontinuation rates.<sup>[33]</sup> The clinical trial of lubiprostone in Chinese IBS patients is still undergoing.

### Chinese medicine

As the origin of traditional Chinese medicine, herbal and acupuncture treatments are commonly used to alleviate the symptoms of IBS. Due to the completely different diagnostic criteria and assessment systems, the effect of Chinese medicine on IBS is not accepted. Currently, the RCT studies of Chinese medicine on IBS are only gradually developing. Several RCTs have reported the effect of Tongxiyaofang (TXYF) on IBS-D. Fan *et al*<sup>[34]</sup> reported that subjects given TXYF had significantly improved the abdominal pain, abdominal discomfort, and stool frequency than placebo and better effect on stool consistency than pinaverium. Chen *et al*'s study<sup>[35]</sup> also showed that TXYF had a better effect on IBS-SSS, stool frequency, and Bristol score than placebo with no more adverse event. The multicenter RCT by Tang *et al*<sup>[36]</sup> suggested that Tongxiening significantly improved IBS-SSS than the placebo with no more adverse event. The recent meta-analysis compared the Tongxiening/TXYF and other traditional medicine, including probiotics, pinaverium bromide, trimebutine, and oryzanol, on IBS-D. The result showed that TXYF improved the clinical effective rate and decreased the adverse events better than traditional medicine. Unfortunately, due to the different study designs, there is a meta-analysis report that the studies on TXYF showed significant heterogeneity. Although all the studies consistently suggested the effect of TXYF on the IBS-SSS, as for the individual symptoms were concerned, no significant effect was concluded.<sup>[37]</sup> Acupuncture is an important Chinese medicine for FGID. Recently, two well-designed RCTs reported the effect of acupuncture on IBS. The multicenter RCT conducted by Pei *et al*,<sup>[38]</sup> which enrolled 531 cases of IBS-C and -D patients, compared the effect of acupuncture and PEG 4000/pinaverium on the IBS-SSS. The result showed that acupuncture was more effective than PEG 4000 or pinaverium bromide for the treatment of IBS, with effects lasting up to 12 weeks. Zheng *et al*'s<sup>[39]</sup> RCT showed electroacupuncture and loperamide had a similar effect on the stool frequency and stool Bristol score in IBS-D.

### Conclusions

Since our last review on the Chinese IBS research in 2011 and the newly published Rome IV criteria, there has been a great development in the research of Chinese IBS. According to the studies, some different findings are shown between the Chinese and worldwide populations; these differences may reflect the differences prevailing between the Chinese and worldwide populations in relation to geography, culture, and environment. Investigations on pathophysiology mechanisms, reliable diagnosis criteria, and effective treatment methods in Chinese

IBS patients are required in the future. We hope that the findings will inspire future research in IBS.

### Conflicts of interest

None.

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