

**Study title:**

D1844R00004 LINGO

Irritable bowel syndrome Survey in gastroenterological adult outpatients in China

**Study period:**

2017Feb10 to 2017Sep30

**Objective:**

**Primary Objective**

To estimate the overall prevalence of IBS diagnosed using Rome III or IV criteria in GI adult outpatients in China.

**Main Secondary Objectives**

Secondary objectives of the observational study included as follows:

- 1) To estimate the distribution of sub-type of IBS diagnosed using Rome III or IV criteria in GI adult outpatients
- 2) To estimate the overall prevalence and distribution of sub-type of previously diagnosed IBS in GI adult outpatients
- 3) To estimate the overall prevalence and distribution of sub-type of IBS sufferers in GI adult patients without previous diagnosis
- 4) To estimate the overall prevalence and distribution of sub-type of IBS diagnosed using Rome III or IV criteria with previous IBS diagnosis
- 5) To identify demographic features of IBS and non-IBS outpatients
- 6) To identify lifestyle characteristics of IBS and non-IBS outpatients
- 7) To identify disease characteristics of IBS outpatients.
- 8) To assess the current treatment status of IBS outpatients
- 9) To estimate the overall prevalence and distribution of sub-type of IBS diagnosed by Rome III criteria in GI adult patients

- 10) To estimate the overall prevalence and distribution of sub-type of IBS diagnosed by Rome IV criteria in GI adult patients

**Study design:**

This was a multicenter, nationwide and cross-sectional study carried out in China, covering 30 sites and 3000 patients totally.

As the primary objective of this study was to estimate the prevalence of IBS in GI outpatients over whole China, a multi-stage, stratified, cluster random sampling method was utilized to select the sites and subjects.

We used all secondary and tertiary general hospitals in the hospital list as sampling pool. As for the ratio of tertiary to secondary general hospitals is approximately 1:4 in China, this study planned to select randomly 6 tertiary and 24 secondary hospitals. In each region, 1 tertiary hospital was selected; and the number of secondary hospital was decided proportionally according to the distribution of the secondary hospitals in each region. To adapt the representativeness of the data with the operational feasibility, we enlarged the sampling for 5 times in each region, so totally 30 tertiary and 120 secondary hospitals was randomly selected over the 6 geographic regions (north, northeast, east, south central, southwest and northwest). Among those, the research site was further selected based on GI department setup, willingness to participate in the study, capability and primary investigator's consideration. If the first sampling cannot provide enough hospitals to participate the study, alternative hospital(s) was selected through two options: a) similar hospitals from the same city, where the refused hospitals locate, were randomly selected for replacement; b) another random sampling in the region will be performed to replace the refused hospitals.

Within participated hospitals, subjects were enrolled consecutively from all the outpatients of GI department to minimize selection bias. "Consecutively" means that all eligible patients who are willing to participate in the study will be enrolled. As reported by 2014 China Health Statistical Yearbook, the total outpatients covered by tertiary and secondary hospitals are almost equal. Therefore, the enrolment of totally 3000 subjects was allocated to tertiary and secondary hospitals with a ratio of 1:1.

During the subject enrolment, the investigator firstly explained the purpose of the study to consecutive GI patients and written informed consents were obtained. Then qualified patients were given a questionnaire and finished it during waiting time. After receiving questionnaires, IBS diagnosis was made by investigators based on Rome III or Rome IV IBS diagnostic criteria. Subjects were identified as previously diagnosed IBS if they had been diagnosed with IBS previously by their clinicians whether they could be diagnosed IBS by Rome criteria or not. And subjects were classified as IBS sufferers without medical diagnosis if they satisfied Rome III or

Rome IV diagnostic criteria and had not received IBS diagnosis from physicians. Rome III criteria included: reports recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months, associated with two or more of the following three features: a. Improvement with defecation; b. Onset associated with a change in frequency of stool; or c. Onset associated with a change in form (appearance) of stool. Criterion must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis. Rome IV criteria included: reports recurrent abdominal pain at least 1 day/week in the last 3 months, associated with two or more of the following three features: a. symptom related with defecation; b. Onset associated with a change in frequency of stool; or c. Onset associated with a change in form (appearance) of stool. Criterion must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

Moreover, patients were defined as having IBS with constipation (IBS-C) if they experienced hard or lumpy stool  $\geq 25\%$  and loose (mushy) or watery stool  $< 25\%$  of bowel movements. Patients were defined having IBS with diarrhea (IBS-D) if they experienced loose (mushy) or watery stool  $\geq 25\%$  and hard or lumpy stool  $< 25\%$  of bowel movements. Patients experiencing hard or lumpy stool  $\geq 25\%$  and loose (mushy) or watery stool  $\geq 25\%$  of bowel movements were defined as Mixed IBS (IBS-M). And patients with insufficient abnormality of stool consistency to meet criteria for IBS-C, D, or M were defined as having unclassified IBS (Rome III criteria).

Rome IV diagnostic criteria for IBS subtype: Predominant bowel habits are based on stool form on days with at least one abnormal bowel movement. IBS-C:  $> 25\%$  of bowel movements with Bristol stool types 1 or 2 and  $< 25\%$  of bowel movements with Bristol stool types 6 or 7. IBS-D:  $> 25\%$  of bowel movements with Bristol stool types 6 or 7 and  $< 25\%$  of bowel movements with Bristol stool types 1 or 2. IBS-M:  $> 25\%$  of bowel movements with Bristol stool types 1 or 2 and  $> 25\%$  of bowel movements with Bristol stool types 6 or 7. IBS-U: Patients who meet diagnostic criteria for IBS but whose bowel habits cannot be accurately categorized into 1 of the 3 groups above should be categorized as having IBS-U.

For IBS patients, either ever-diagnosed or diagnosed with Rome III or IV criteria, investigators collected all the information on demographic features, lifestyle information, disease characteristics and treatment status. For non-IBS patients, only demographic information and lifestyle information were collected.

### **Study population:**

The subject population were the  $\geq 18$ -year consecutive outpatients in gastrointestinal department. The study design planned to enrol 3000 patients from 30 sites.

### **Inclusion Criteria:**

1. Provision of subject informed consent

2. Consecutive female and/or male GI outpatients aged 18 years and over

**Exclusion Criteria:**

1. Subject with a cognitive condition and unable to finish the questionnaire
2. Subject has an acute or chronic non-GI condition

**Statistical methods:**

The statistical analysis method for this study was primarily descriptive in nature.

Descriptive analysis was performed for primary endpoint and secondary endpoints. For continuous data, descriptive statistics was presented as number of patients (n), mean, standard deviation (SD), median, minimum and maximum. For categorical data, the frequency and percentage of patients in each category were presented. Counts that were zero were displayed as "0". Percentages were based on non-missing data unless otherwise specified.

In addition to the original prevalence, a weighted prevalence was calculated using the proportion of regional population number over total as the weight.

The relationship of IBS with demographic features and lifestyle characteristics was explored using risk factor analysis. Univariate and multivariate logistic regression model was utilized for this analysis.

**Results:**

During this study, 3000 eligible patients from 26 hospitals across China were enrolled, and finally all of them completed the study and were included in Full Analysis Set (FAS), which was defined as all enrolled patients who satisfied the inclusion and exclusion criteria.

**Primary Objective**

**Prevalence of IBS in GI adult outpatients in China** In the total 3000 GI adult outpatients, 499 (16.6%) patients were diagnosed as IBS by Rome III or Rome IV criteria (95% CI: 15.3% ~ 18.0%); 498 (16.6%) patients were diagnosed as IBS by Rome III criteria (95% CI: 15.3% ~ 17.9%); 187 (6.2%) patients were diagnosed as IBS by Rome IV criteria (95% CI: 5.4% ~ 7.1%); 186 (6.2%) patients were diagnosed as IBS by both Rome III and Rome IV criteria (95% CI: 5.3% ~ 7.1%); 312 (10.4%) patients were diagnosed as IBS by Rome III but not Rome IV criteria (95% CI: 9.3% ~ 11.5%); 1 (0.03%) patients were diagnosed as IBS by Rome IV but not Rome III criteria (95% CI: 0.0% ~ 0.1%).

**Subgroup analysis: By region of sites**

The percentages of IBS diagnosed by Rome III or Rome IV criteria were slightly higher in south central area (19.5%, 122/625), southwest area (20.0%, 88/439) and northwest area (17.9%, 67/375)

of China than that in north area (14.8%, 65/439), northeast area (14.8%, 83/560) and east area (13.2%, 74/562) of China. The distribution of IBS diagnosed by Rome III criteria by region was generally similar with the distribution of IBS diagnosed by Rome III or Rome IV. And then, the percentages of IBS diagnosed by Rome IV criteria were higher in southwest China (7.7%, 34/439), then in northeast China (6.8%, 38/560), south central China (6.6%, 41/625), northwest China (6.4%, 24/375), eastern China (5.3%, 30/562) and north China (4.6%, 20/439). Considering the differences among regions, the average (weighted using 1/6 as weights) prevalence for IBS diagnosed using Rome III/Rome IV, Rome III and Rome IV were 16.7%, 16.7% and 6.2%, respectively.

### **Secondary Objectives**

#### **1. Prevalence and distribution of sub-type of IBS diagnosed by Rome III criteria in GI adult outpatients**

In the study, 498 (16.6%) IBS patients were diagnosed by Rome III criteria (95% CI: 15.3% ~ 17.9%), including 80 IBS-C patients, 270 IBS-D patients, 75 IBS-M patients and 73 IBS-U patients. Among IBS patients diagnosed by Rome III criteria, the proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U were respectively 16.1%, 54.2%, 15.1% and 14.7%, with the highest proportion of sub-type IBS-D.

#### **Subgroup analysis: By region**

The proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U diagnosed by Rome III criteria were slightly different among the 6 regions of north, northeast, east, south central, southwest, northwest in China. In general, IBS-D patients were more than the other 3 IBS sub-type patients in each of the 6 regions of China. The proportion of IBS-D were slightly higher in east area (62.2%, 46/74), north area (60.0%, 39/65) and northwest area (58.2%, 39/67) of China than that in northeast area (55.4%, 46/83), southwest area (48.9%, 43/88) and south central area (47.1%, 57/121) of China. The proportion of IBS-C were slightly higher in south central area (22.3%, 27/121), northeast area (18.1%, 15/83) and northwest area (17.9%, 12/67) of China than in southwest area (13.6%, 12/88), east area (10.8%, 8/74) and north area (60.0%, 39/65) of China. The proportion of IBS-M were slightly higher in southwest area (21.6%, 19/88) and east area (17.6%, 13/74) of China than in northeast area (14.5%, 12/83), south central area (13.2%, 16/121), northwest area (11.9%, 8/67) and north area (10.8%, 7/65) of China. The proportion of IBS-U were slightly higher in north area (20.0%, 13/65), south central area (17.4%, 21/121) and southwest area (15.9%, 14/88) of China than in northeast area (12.0%, 10/83), northwest area (11.9%, 8/67) and east area (9.5%, 7/74) of China.

#### **Subgroup analysis: By hospital level**

The prevalence of IBS diagnosed by Rome III criteria between tertiary general hospitals (16.5%,

247/1500) and secondary general hospitals (16.7%, 251/1500) were generally similar. 247 IBS patients from tertiary general hospitals included 34 IBS-C patients, 140 IBS-D patients, 42 IBS-M patients and 31 IBS-U patients and the proportions were 13.8%, 56.7%, 17.0% and 12.6%, respectively. 251 IBS patients from secondary general hospitals included 46 IBS-C patients, 130 IBS-D patients, 33 IBS-M patients and 42 IBS-U patients and the proportions were 18.3%, 51.8%, 13.1% and 16.7%, respectively. The proportions of IBS-D and IBS-M were a little higher in tertiary general hospitals than in secondary general hospitals.

## **2. Prevalence and distribution of sub-type of IBS diagnosed by Rome IV criteria in GI adult outpatients**

In the study, 187 (6.2%) IBS patients were diagnosed by Rome IV criteria (95% CI: 5.4% ~ 7.1%), including 22 IBS-C patients, 124 IBS-D patients, 17 IBS-M patients and 24 IBS-U patients. Among IBS patients diagnosed by Rome IV criteria, the proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U were respectively 11.8%, 66.3%, 9.1% and 12.8%, with the highest proportion of sub-type IBS-D.

### **Subgroup Analysis: By Region**

The proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U diagnosed by Rome IV criteria were slightly different between the 6 regions of north, northeast, east, south central, southwest, northwest in China. More than half of the patients were diagnosed as IBS-D by Rome IV criteria in each of the 6 regions of China. The proportion of IBS-D were slightly higher in north area (90.0%, 18/20), northwest area (70.8%, 17/24) and northeast area (68.4%, 26/38) of China than in east area (63.3%, 19/30), southwest area (61.8%, 21/34) and south central area (56.1%, 23/41) of China. The proportion of IBS-C were slightly higher in south central area (17.1%, 7/41) and northeast area (15.8%, 6/38) of China than in north area (10.0%, 2/20), southwest area (8.8%, 3/34), northwest area (8.3%, 2/24) and east area (6.7%, 2/30) of China. The proportion of IBS-M were slightly higher in east area (16.7%, 5/30) of China than southwest area (11.8%, 4/34), south central area (9.8%, 4/41), northwest area (8.3%, 2/24) and northeast area (5.3%, 2/38) of China. The proportion of IBS-U were slightly higher in southwest area (17.6%, 6/34) and south central area (17.1%, 7/41) of China than in east area (13.3%, 4/30), northwest area (12.5%, 3/24) and northeast area (10.5%, 4/38) of China.

### **Subgroup Analysis: By Hospital Level**

The prevalence of IBS diagnosed by Rome IV criteria between tertiary general hospitals (6.3%, 95/1500) and secondary general hospitals (6.1%, 92/1500) were generally similar. 95 IBS patients from tertiary general hospitals included 7 IBS-C patients, 65 IBS-D patients, 13 IBS-M patients and 10 IBS-U patients and the proportions were 7.4%, 68.4%, 13.7% and 10.5%, respectively. 92 IBS

patients from secondary general hospitals included 15 IBS-C patients, 59 IBS-D patients, 4 IBS-M patients and 14 IBS-U patients and the proportions were 16.3%, 64.1%, 4.3% and 15.2%, respectively.

### **3. Prevalence and distribution of sub-type of IBS sufferers in GI adult outpatients without previous diagnosis**

There were 2959 GI adult outpatients without previously diagnosed IBS in this study, of which 470 (15.9%) patients were diagnosed as IBS by Rome III or Rome IV criteria (95% CI: 14.5% ~ 17.2%), 469 (15.8%) patients were diagnosed as IBS by Rome III criteria (95% CI: 14.5% ~ 17.2%), 173 (5.8%) patients were diagnosed as IBS by Rome IV criteria (95% CI: 5.0% ~ 6.7%). Among 469 IBS patients diagnosed by Rome III criteria, there were 77 (16.4%) IBS-C patients, 251 (53.5%) IBS-D patients, 71 (15.1%) IBS-M patients and 70 (14.9%) IBS-U patients. Among 173 IBS patients diagnosed by Rome IV criteria, there were 20 (11.6%) IBS-C patients, 115 (66.5%) IBS-D patients, 15 (8.7%) IBS-M patients and 23 (13.3%) IBS-U patients.

### **4. Prevalence and distribution of sub-type of previously diagnosed IBS in GI adult outpatients**

Among the total 3000 GI adult outpatients, 41 (1.4%) patients have been previously diagnosed as IBS in this study (95% CI: 0.9% ~ 1.8%). And 29 of them were diagnosed as IBS by Rome III criteria, including 3 IBS-C patients, 19 IBS-D patients, 4 IBS-M patients and 3 IBS-U patients; the proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U were 10.3%, 65.5%, 13.8% and 10.3%, respectively. 14 of them were diagnosed as IBS by Rome IV criteria, including 2 IBS-C patients, 9 IBS-D patients, 2 IBS-M patients and 1 IBS-U patient. The proportions of sub-types IBS-C, IBS-D, IBS-M and IBS-U were 14.3%, 64.3%, 14.3% and 7.1%, respectively.

#### **Subgroup Analysis: By Region**

Among the 41 patients who had been previously diagnosed as IBS, 10 patients were from east area and southwest area of China, with the proportion of 1.8% and 2.3% out of the overall GI outpatients in each area, respectively; 7 patients were from northeast area and south central area of China, with the proportion of 1.3% and 1.1% out of the overall GI outpatients in each area, respectively; 5 patients (1.3%) were from northwest area of China, and 2 patients (0.5%) were from north area of China.

#### **Subgroup Analysis: By Hospital Level**

In this study, 26 out of 41 previously diagnosed IBS patients were from tertiary general hospitals, which accounted for 1.7% over the total GI outpatients of tertiary general hospitals; the remaining 15 previously diagnosed IBS patients were from secondary general hospitals, which accounted for 1.0% over the total GI outpatients of secondary general hospitals. Among the 26 previously

diagnosed IBS patients from tertiary general hospitals, 18 patients who were diagnosed as IBS by Rome III criteria included 2 IBS-C patients, 12 IBS-D patients, 2 IBS-M patients and 2 IBS-U patients and the proportions were 11.1%, 66.7%, 11.1% and 11.1%, respectively; and 8 patients who were diagnosed as IBS by Rome IV criteria included 1 IBS-C patient, 6 IBS-D patients and 1 IBS-M patients and the proportions were 12.5%, 75.0% and 12.5%, respectively. Among the 15 previously diagnosed IBS patients from secondary general hospitals, 11 patients were diagnosed as IBS by Rome III criteria included 1 IBS-C patient, 7 IBS-D patients, 2 IBS-M patients and 1 IBS-U patients and the proportions were 9.1%, 63.6%, 18.2% and 9.1%, respectively; 6 patients were diagnosed as IBS by Rome IV criteria included 1 IBS-C patient, 3 IBS-D patients, 1 IBS-M patient and 1 IBS-U patient and the proportions were 16.7%, 50.0%, 16.7% and 16.7%, respectively.

#### **5. Prevalence and distribution of sub-type of IBS diagnosed by Rome III or Rome IV criteria with previous IBS diagnosis**

Totally, 29 (1.0%) IBS patients were diagnosed by Rome III or Rome IV criteria with previous IBS diagnosis in the study. And all the 29 patients were diagnosed as IBS by Rome III criteria; 14 of them were diagnosed as IBS by Rome IV criteria.

#### **6. Demographic features of IBS and non-IBS outpatients**

Overall, 3000 GI outpatients enrolled into current study were included in FAS, with the average age of  $46.3 \pm 14.78$  years, the average height of  $164.5 \pm 7.61$  cm, the average weight of  $62 \pm 11.29$  kg, the average BMI of  $22.8 \pm 3.35$  kg/m<sup>2</sup>, 44.6% (1339) male patients, 100% Asian patients, and the top three occupations of labourer (34.4%, 1032), white collar (25.5%, 764) and retired (19.6%, 589).

Among all of patients enrolled in this study, 499 GI adult outpatients were diagnosed with IBS by Rome III or Rome IV criteria, and the remaining 2501 were non-IBS patients. The average age of IBS patients ( $47.3 \pm 13.73$ ) was about 1.2 years older than non-IBS patients ( $46.1 \pm 14.97$ ). The mean value of height, weight and BMI were generally similar and the distribution of sex, race and occupation were generally balanced between IBS and non-IBS patients, with the exception that the labourers were a little more (37.1%, 185/499) and the students were a little fewer (0.8%, 4/499) in IBS patients than in non-IBS patients (33.9% of labourer and 2.9% of student).

Among 499 IBS patients diagnosed by Rome III or Rome IV criteria, the proportion of female patients was 55.3% (276/499), and was higher than that of male (44.7%, 223/499). And for occupation distribution of IBS, the proportion of labourers was the highest, with 37.1% (185/499), followed by white collar with 25.7% (128/499) and retired people with 18.0% (90/499), and the proportion of students was the lowest, with 0.8% (4/499).

#### **Subgroup Analysis: Demographic features of IBS Patients Diagnosed by Rome III but not**



## **Rome IV Criteria**

There were 312 IBS patients diagnosed by Rome III but not Rome IV criteria, with the age of  $46.9 \pm 14.04$  years, the average height of  $163.8 \pm 7.50$  cm, the average weight of  $61.3 \pm 11.29$  kg, the average BMI of  $22.8 \pm 3.32$  kg/m<sup>2</sup>, 43.6% (136) male patients, 100% Asian patients, and the top three occupation of labourer (36.5%, 114), white collar (23.7%, 74) and retired (18.6%, 58). Comparing with the IBS patients diagnosed by Rome IV criteria, the age was about 1 year younger in average in IBS patients diagnosed by Rome III but not Rome IV criteria. The mean value of height, weight and BMI were generally similar and the distribution of sex, race and occupation were generally balanced between the 2 groups IBS patients, with the exception that the white collars were a little fewer (23.7%, 74/312) and the unemployed were a little more (12.2%, 38/312) in IBS patients diagnosed by Rome III but not Rome IV criteria than in IBS patients diagnosed by Rome IV criteria (28.9% of white collar and 8.6% of unemployed).

## **Subgroup Analysis: Demographic features of patients with different sub-type IBS**

Among IBS patients diagnosed by Rome IV criteria in the study, there were 22 IBS-C patients, 124 IBS-D patients, 17 IBS-M patients and 24 IBS-U patients. Among the 4 sub-type IBS patients, the age was older in average in IBS-C patients ( $51.5 \pm 16.05$  years) and younger in IBS-M patients ( $43.9 \pm 114.04$  years) than the other 2 sub-type IBS patients; the height and weight were higher in IBS-D patients ( $165.4 \pm 7.29$  cm and  $63.0 \pm 10.64$  kg) than the other 3 sub-type IBS patients; the mean value of BMI was generally similar; the percentage of female was higher in IBS-C patients (72.7%) than the other 3 sub-type IBS patients in which the sex distribution were generally balanced. Among IBS patients diagnosed by Rome III but not Rome IV criteria in the study, there were 58 IBS-C patients, 147 IBS-D patients, 52 IBS-M patients and 55 IBS-U patients. Among the 4 sub-type IBS patients, the age was older in average in IBS-C patients ( $49.5 \pm 14.16$  years) than the other 3 sub-type IBS patients in which the average age were generally similar; the height and weight were higher in IBS-D patients ( $165.0 \pm 7.91$  cm and  $63.0 \pm 12.38$  kg) than the other 3 sub-type IBS patients; the mean value of BMI was generally similar; the percentage of female was lower in IBS-D patients (47.6%) than the other 3 sub-type IBS patients in which the proportion of female was all above 60%, and the highest was that in IBS-U patients (67.3%).

## **Subgroup Analysis: Demographic features of IBS and Non-IBS patients by region**

In north area, east area, south central area and southwest area of China, the average age of IBS patients was a little older than that of non-IBS patients; while in northeast and northwest area of China, IBS patients were a little younger than non-IBS patients. The percentage of female in IBS patients was a little higher than that in non-IBS patients in northeast and south central area of China; while in east and southwest area of China, the percentage of female in IBS patients was a little

lower than that in non-IBS patients; and the percentage of female was similar between IBS and non-IBS patients in north and northwest area of China. Height, weight and BMI were general similar between IBS and non-IBS patients in all the 6 regions.

## **7. Lifestyle characteristics of IBS and non-IBS outpatients**

### **Smoking History**

Overall, among the 3000 GI adult outpatients enrolled in this study, most patients never smoked (76.5%, 2296). Within the current smoker (17.4%, 522) and the former smoker (6.1%, 182), the average smoking duration and the average pack of cigarette consumed per month were  $24.3 \pm 13.64$  years and  $22.5 \pm 17.17$  packs. The smoking history between IBS (499) and non-IBS (2501) was generally similar. Either Rome III criteria or Rome IV criteria is used to diagnose IBS, the smoking history between IBS and non-IBS was still similar.

### **Alcohol History**

Overall, among the 3000 GI adult outpatients enrolled in this study, most patients never took alcohol (72.0%, 2159). Within the current drinker (20.3%, 609) and the former drinker (7.7%, 232), the top three types of alcohol intake were white spirits (67.4%, 567/841), beer (67.4%, 567/841), and wine (15.8%, 133/841); and 375 (44.6%) patients took alcohol equal or less than once a week; 276 (32.8%) patients took alcohol more than once a week but not every day; 190 (22.6%) patients took alcohol every day. The patients who have had drinking history were a little more and the frequency of alcohol intake was slightly higher in IBS patients than in non-IBS patients. Either Rome III criteria or Rome IV criteria is used to diagnose IBS, the frequency of alcohol intake was still slightly higher in both IBS groups than in non-IBS groups. The other information about alcohol history between IBS and non-IBS was generally similar.

### **Diet And Exercise Habit**

Overall, 3000 GI outpatients were enrolled into this study, with 80.7% (2420) diet regular patients, 9.4% (281) food allergy patients, 62.5% (1876) balanced diet patients, 28.2% (846) vegetables-based diet patients, 9.3% (278) meat-based diet patients. 1243 (41.4%) patients did exercise equal or more than once a week; 1139 (38.0%) patients did exercise occasionally; 618 (20.6%) patients never did exercise. The distribution of regular diet and the frequency of exercise habit were generally balanced between IBS and non-IBS patients, with the exception that food allergy patients were a little more (11.2%, 56/499) and the balanced diet patients were a little fewer (58.9%, 294/499) in IBS patients than in non-IBS patients (9.0% of food allergy patients and 63.3% of balanced diet patients). Either Rome III criteria or Rome IV criteria is used to diagnose IBS, there were more food allergy patients in both IBS groups than non-IBS groups. But balanced diet patients with IBS diagnosed using Rome III was less (58.8%, 293/498) than the other 3 groups.

## **Sleep Habit**

The average time from go to bed to fall asleep was  $33.8 \pm 36.67$  minutes in all 3000 GI outpatients. The average duration of on bed and actual sleep were  $8.126 \pm 1.2479$  minutes and  $7.273 \pm 1.3400$  minutes, respectively. The percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were 26.4% (793), 10.9% (327) and 18.9% (567), respectively. The average time from go to bed to fall asleep between IBS and non-IBS was generally similar; both the average duration of on bed and actual sleep were slightly shorter in IBS (8.017 and 7.045 hours) than non-IBS (8.148 and 7.319 hours). The percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were higher in IBS (29.9%, 14.6% and 23.4%) than in non-IBS (25.7%, 10.2% and 18.0%). Either Rome III criteria or Rome IV criteria is used to diagnose IBS, the average duration of on bed and actual sleep were slightly shorter in both IBS groups than non-IBS groups; the percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were higher in both IBS groups than in non-IBS groups.

### **Subgroup analysis: Lifestyle characteristics of IBS patients diagnosed by Rome III but not Rome IV**

Among the 312 IBS patients diagnosed by Rome III but not Rome IV criteria, most patients never smoked (77.2%, 241). Within the current smoker (16.7%, 52) and the former smoker (6.1%, 19), the average smoking duration and the average pack of cigarette consumed per month were  $22.9 \pm 11.35$  years and  $23.4 \pm 17.14$  packs. The smoking history between IBS patients diagnosed by Rome III but not Rome IV criteria and IBS patients diagnosed by Rome IV criteria was generally similar.

Among the 312 IBS patients diagnosed by Rome III but not Rome IV criteria, most patients never took alcohol (68.6%, 214). Within the current drinker (22.8%, 71) and the former drinker (8.7%, 27), the top three types of alcohol intake were white spirits (73.5%, 72/98), beer (64.3%, 63/98), and wine (14.3%, 14/98); and 40 (40.8%) patients took alcohol equal or less than once a week; 40 (40.8%) patients took alcohol more than once a week but not every day; 18 (18.4%) patients took alcohol every day. The patients who have had drinking history were a little more, the proportion of white spirits intake was a little higher, and the frequency of alcohol intake was slightly lower in IBS patients diagnosed by Rome III but not Rome IV criteria than in IBS patients diagnosed by Rome IV criteria.

Among the 312 IBS patients diagnosed by Rome III but not Rome IV criteria, with 78.8% (246) diet regular patients, 10.6% (33) food allergy patients, 55.4% (173) balanced diet patients, 33.3% (104) vegetables-based diet patients, 11.2% (35) meat-based diet patients. 121 (38.8%) patients did exercise equal or more than once a week; 116 (37.2%) patients did exercise occasionally; 75 (24.0%) patients never did exercise. The diet regular, food allergy and balanced diet patients were

a little fewer in IBS patients diagnosed by Rome III but not Rome IV criteria than in IBS patients diagnosed by Rome IV criteria. The frequency of exercise habit was also fewer in IBS patients diagnosed by Rome III but not Rome IV criteria than in IBS patients diagnosed by Rome IV criteria. The average time from go to bed to fall asleep was  $33.7 \pm 31.21$  minutes in the 312 IBS patients diagnosed by Rome III but not Rome IV criteria. The average duration of on bed and actual sleep were  $8.132 \pm 1.2005$  minutes and  $7.130 \pm 1.3810$  minutes, respectively. The percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were 29.8% (93), 14.4% (45) and 24.0% (75), respectively. The average time from go to bed to fall asleep between IBS patients diagnosed by Rome III but not Rome IV criteria and IBS patients diagnosed by Rome IV criteria was generally similar; both the average duration of on bed and actual sleep were slightly longer in IBS patients diagnosed by Rome III but not Rome IV criteria (8.132 and 7.130 hours) than IBS patients diagnosed by Rome IV criteria (7.824 and 6.902 hours). The percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep between IBS patients diagnosed by Rome III but not Rome IV criteria and IBS patients diagnosed by Rome IV criteria were generally similar.

#### **Subgroup Analysis: lifestyle characteristics of patients with different sub-type IBS**

There were 187 IBS patients diagnosed by Rome IV criteria in the study, including 22 IBS-C patients, 124 IBS-D patients, 17 IBS-M patients and 24 IBS-U patients. Among the 4 sub-type IBS patients, the smoking histories between different sub-type IBS patients were generally similar. The patients who never drank alcohol were a little more in IBS-C (77.3%) and IBS-U (83.3%) patients than the other two sub-type IBS patients (68.5% in IBS-D and 70.6% in IBS-M patients, respectively). The percentage of diet regular patients was a little higher in IBS-C patients (95.5%) than the other 3 sub-type IBS patients; the percentages of food allergy and balanced diet patients were a little lower in IBS-C patients (4.5% and 50.0%) than the other 3 sub-type IBS patients; the patients with exercise habit ( $\geq$  once per week) was more in IBS-D (42.7%) and IBS-M (47.1%) sub-type than that in IBS-C and IBS-U sub-type; the percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were a little higher in IBS-C patients (45.5%, 22.7% and 31.8%) than the other 3 sub-type IBS patients.

There were 312 IBS patients diagnosed by Rome III but not Rome IV criteria in the study, including 58 IBS-C patients, 147 IBS-D patients, 52 IBS-M patients and 55 IBS-U patients. Among the 4 sub-type IBS patients, the percentages of current/former smoker and drinker were a little lower in IBS-C patients (smoker: 15.5%; drinker: 20.7%) than the other 3 sub-type IBS patients. The percentage of diet regular patients was a little higher in IBS-U patients (83.6%) than the other 3 sub-type IBS patients; the percentages of food allergy and balanced diet patients were a little higher in IBS-M patients (19.2% and 67.3%) than the other 3 sub-type IBS patients; the patients with exercise habit

(≥ once per week) was more in IBS-D (39.5%) and IBS-M (53.8%) sub-type than that in IBS-C and IBS-U sub-type; the percentages of patients who had troubles to fall asleep, awaked early in the morning and had difficulties to maintain sleep were a little higher in IBS-C patients (41.4%, 17.2% and 31.0%) than the other 3 sub-type IBS patients.

### **Subgroup Analysis: Lifestyle characteristics of IBS and Non-IBS patients by region**

The percentage of current/former smoker in IBS patients was higher than that in non-IBS patients in east and southwest area of China; while the percentage of current/former smoker in IBS patients was lower than that in non-IBS patients in northeast China; and the percentage of current/former smoker was similar between IBS and non-IBS patients in the other 3 regions. The percentage of current/former drinker in IBS patients was higher than that in non-IBS patients in north, southwest and northwest area of China; while the percentage of current/former drinker was similar between IBS and non-IBS patients in the other 3 regions. Diet regular patients were a little fewer in IBS patients than in non-IBS patients in south central area of China; while the percentage of diet regular patients was similar between IBS and non-IBS patients in the other 5 regions. Food allergy patients were a little more in IBS patients than in non-IBS patients in northeast, south central and southwest area of China; while the percentage of food allergy patients was similar between IBS and non-IBS patients in the other 3 regions. Balanced diet patients were a little fewer in IBS patients than in non-IBS patients in north, east and northwest area of China; while the percentage of balanced diet patients was similar between IBS and non-IBS patients in the other 3 regions. The frequency of exercise habit was general similar between IBS and non-IBS patients in all the 6 regions. The average duration of actual sleep was slightly shorter in IBS patients than that in non-IBS patients in all the 6 regions.

### **8. Disease characteristics of IBS outpatients**

Overall, among 499 IBS patients diagnosed by Rome III or Rome IV criteria, 54.3% (271/499) had the history of GI disease, 14.2% (71/499) had the history of reflux disease, 9.2% (46/499) had received GI surgery, 5.8% (29/499) had been previously diagnosed as IBS, and 7.8% of patients (39/499) had been absent from work or school due to current disease during the past 90 days before attending the study, with the 14.2 days (SD: 25.17, range: 1-90) absent from work or school. For patients diagnosed with Rome IV criteria, the percentages of patients with GI Disease, previously diagnosed IBS, and reflux disease were slightly higher, and the percentage of patients with previously GI surgery was lower compared those diagnosed with Rome III criteria.

### **IBS Symptoms**

The percentages of patients who had abdominal pain or discomfort combined constipation, who had abdominal pain and bloating combined constipation, who had abdominal pain combined

constipation, or who had abdominal bloating combined constipation were all higher in IBS (15.8%, 6.0%, 8.2%, 12.6%) than in non-IBS (8.6%, 2.6%, 5.2%, 5.0%). The most common symptom of IBS patients was abdominal pain or discomfort combined constipation.

### **Medical History**

Among 499 IBS patients diagnosed by Rome III or Rome IV criteria, 293 (58.7%) patients had any other chronic medical disease beside IBS, the most common of which was gastrointestinal disorders, with 206 (41.3%) patients, primarily including chronic gastritis (18.4%), gastritis (6.2%), gastric ulcer (4.6%), gastritis erosive (3.4%), gastroesophageal reflux disease (2.2%), etc.; followed by vascular disorders, with 41 (8.2%) patients, primarily including hypertension (8.2%); again for infections and infestations, with 31 (6.2%) patients, etc.

### **9. Current treatment status of IBS outpatients**

Overall, among 499 IBS patients diagnosed by Rome III or Rome IV criteria, 20 (4.0%) patients had taken any drug treatment because of IBS; of which, the treatment was effective for 9 (45.0%) patients; 8 (40.0%) patients were satisfied with the treatment; the average cost of therapy per month was  $459.4 \pm 558.72$  ¥. The current treatment status was generally similar between IBS diagnosed by Rome III criteria and IBS diagnosed by Rome IV criteria.

### **10. The factors associated with IBS**

Logistic regression model was used to explore the factors that influence the occurrence of IBS, and single factor analysis results showed that the occupation of labourer would increase the probability of IBS occurrence, compared to white collar with the OR of 1.09; the occupation of student would decrease the probability of IBS occurrence, compared to white collar with the OR of 0.27; longer time of actual sleep and longer duration of on bed would decrease the probability of IBS occurrence, with the OR of 0.86 and 0.92, respectively; early awakening habit and difficulty in maintaining sleep would increase the probability of IBS occurrence with the OR of 1.52 and 1.40, respectively. Multiple-factor analysis results showed that length of actual sleep influence the occurrence of IBS, and longer time of actual sleep would decrease the probability of IBS occurrence.

### **Conclusion:**

1. The IBS prevalence rate using the Rome IV criteria was much lower than that with the Rome III criteria (6.2% vs 16.6%). Abdominal discomfort or bloating was commonly reported as the abdominal symptom in Chinese IBS patients which may explain the difference in the estimated prevalence rates using Rome III and Rome IV criteria.

2. The most prevalent sub-type was IBS-D in IBS patient with either Rome III criteria or Rome IV criteria, from either secondary or tertiary hospitals, as well as in each of the 6 regions of China.
3. Despite sampling a patient population seeking care at secondary and tertiary hospitals, the majority of IBS patients (94%) were undiagnosed, indicating the unmet need for a positive diagnosis of IBS in China.
4. Overall the demographic features were similar and the distribution of gender, race and occupation were balanced between IBS and non-IBS patients. There were more female IBS patients and more labourer patients in this study.
5. Compared with non-IBS patients, a greater proportion of IBS patients experienced sleep disorders (including trouble falling asleep, early awakening, and difficulty maintaining sleep). Having decreased time of actual sleep is likely to be associated with higher IBS occurrence. In addition, IBS patients also had more diet problems and alcohol intake problems than non-IBS patients.
6. Few IBS patients had received proper treatment and more than half patients were unsatisfied with current treatment.

**Publications:**

Not Applicable

