

Detailed inclusion and exclusion criteria

Inclusion criteria: (1) the presence of irritable bowel syndrome (IBS) symptoms that met the Rome IV criteria, *i.e.*, recurrent abdominal pain occurring, on average, at least 1 day a week in the last 3 months and associated with 2 or more of the following criteria: defecation, a change in stool frequency, or a change in the form (appearance) of the stool (criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis); (2) aged 18 years old or older; (3) patients visited the gastroenterology clinics and completed colonoscopy; and (4) a routine blood examination, routine fecal examination, and fecal occult blood test were performed within the last 6 months (otherwise, eligible patients were required to finish these tests).

Exclusion criteria: (1) other diagnosed diseases that can explain patients' IBS symptoms, such as known celiac disease, inflammatory bowel disease (IBD), infectious colitis, non-IBD and noninfectious colitis, terminal ileitis, parasitic infection, microscopic colitis, lactose intolerance, bile acid malabsorption, intestinal tuberculosis, ischemic enteritis, radiation colitis, Bechet's disease, and malignant tumor including colorectal cancer, carcinoid and lymphoma, etc.; (2) metabolic diseases (uncontrolled thyroid diseases and diabetes); (3) severe neurological and psychiatric disorders, such as severe depression with high suicidal tendency, alcohol or substance abuse or dependence, history of mental illness, etc., which may impede the normal conduct of the trial; (4) severe and unstable extraintestinal conditions (such as heart, liver, kidney, respiratory and other important organ dysfunction) may require urgent treatment immediately or at any time; (5) who had undergone major abdominal surgery, whose normal anatomical structure and physiological functions of the gastrointestinal tract are altered significantly, which can fully explain the gastrointestinal symptoms. It should be noted that simple appendectomy, cholecystectomy, or endoscopic treatment (including polypectomy, mucosal resection and submucosal dissection) are not considered exclusion criteria; (6) pregnancy, possible pregnancy or lactation; (7) colonoscopy was performed in the past 6 months;

(8) currently taking large doses of anti-anxiety/anti-depressant drugs (exceeding the upper limit of conventional doses) or enteric sensitive antibiotics; (9) malignancy diagnosed to be in an active state within the last year of enrollment (excluding completely resected localized basal cell or squamous cell carcinoma of the skin); or (10) refusal to take part in the study.

Supplementary Table 1 Colonoscopy findings in suspected irritable bowel syndrome patients and healthy examiners, *n* (%)

Colonoscopy findings	Suspected IBS (<i>n</i> =730)	Healthy examiners (<i>n</i> = 725)	<i>P</i> value
Ulcerative colitis	8 (1.10)	0 (0)	0.008
Non-IBD and noninfectious colitis	42 (5.75)	27 (3.72)	0.069
CRC	11 (1.51)	1 (0.14)	0.004
Terminal ileitis	18 (2.47)	7 (0.97)	0.028
Total organic diseases	76 (10.41)	34 (4.69)	< 0.001

CRC: Colorectal cancer; IBD: Inflammatory bowel disease; IBS: Irritable bowel syndrome.