

World Journal of *Gastroenterology*

World J Gastroenterol 2017 November 14; 23(42): 7495-7652



**EDITORIAL**

- 7495 Current and emerging pharmacological therapy for non-alcoholic fatty liver disease

Eshraghian A

REVIEW

- 7505 Intestinal epithelium, intraepithelial lymphocytes and the gut microbiota - Key players in the pathogenesis of celiac disease

Cukrowska B, Sowińska A, Bierla JB, Czarnowska E, Rybak A, Grzybowska-Chlebowczyk U

ORIGINAL ARTICLE**Basic Study**

- 7519 Pregnane X receptor and constitutive androstane receptor modulate differently CYP3A-mediated metabolism in early- and late-stage cholestasis

Gabbia D, Dalla Pozza A, Albertoni L, Lazzari R, Zigiotta G, Carrara M, Baldo V, Baldovin T, Floreani A, De Martin S

- 7531 Induction of precocious intestinal maturation in T-cell deficient athymic neonatal rats

Arévalo Sureda E, Gidlund C, Weström B, Prykhodko O

- 7541 Nuclear heat shock protein 110 expression is associated with poor prognosis and hyperthermo-chemotherapy resistance in gastric cancer patients with peritoneal metastasis

Kimura A, Ogata K, Altan B, Yokobori T, Mochiki E, Yanai M, Kogure N, Yanoma T, Suzuki M, Bai T, Kuwano H

- 7551 Combined treatment of pancreatic cancer xenograft with ⁹⁰Y-ITGA6B4-mediated radioimmunotherapy and PI3K/mTOR inhibitor

Aung W, Tsuji AB, Sudo H, Sugyo A, Ukai Y, Kouda K, Kurosawa Y, Furukawa T, Saga T, Higashi T

- 7563 Effects of Hemp seed soft capsule on colonic ion transport in rats

Lu XF, Jia MD, Zhang SS, Zhao LQ

- 7572 Novel D-galactosamine-induced cynomolgus monkey model of acute liver failure

Feng L, Cai L, He GL, Weng J, Li Y, Pan MX, Jiang ZS, Peng Q, Gao Y

- 7584 Diversity of bacterial lactase genes in intestinal contents of mice with antibiotics-induced diarrhea

Long CX, He L, Guo YF, Liu YW, Xiao NQ, Tan ZJ

- 7594 Potential rat model of anxiety-like gastric hypersensitivity induced by sequential stress

Jing FC, Zhang J, Feng C, Nian YY, Wang JH, Hu H, Yang BD, Sun XM, Zheng JY, Yin XR

Retrospective Cohort Study

- 7609 Post-colonoscopy colorectal cancer rate in the era of high-definition colonoscopy

Iwatate M, Kitagawa T, Katayama Y, Tokutomi N, Ban S, Hattori S, Hasuike N, Sano W, Sano Y, Tamano M

- 7618 Right- and left-sided colorectal cancers respond differently to traditional Chinese medicine

Liu SS, Shi Q, Li HJ, Yang W, Han SS, Zong SQ, Li W, Hou FG

Observational Study

- 7626 Hepatitis B virus outreach to immigrant population in Greater Boston Area: Key to improving hepatitis B knowledge

Djoufack R, Cheon SSY, Mohamed A, Faye F, Diouf K, Colvin R, Morrill J, Duffy-Keane AM, Perumalswami P, Jourdain G, Fusco DN

- 7635 Predictors of healthcare-seeking behavior among Chinese patients with irritable bowel syndrome

Fan W, Xu D, Chang M, Zhu L, Fei G, Li X, Fang X

SYSTEMATIC REVIEWS

- 7644 Vaccinations in immunosuppressive-dependent pediatric inflammatory bowel disease

Nguyen HT, Minar P, Jackson K, Fulkerson PC

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Zhao-Shan Niu, MD, Associate Professor, Laboratory of Micromorphology, School of Basic Medicine, Medical Department of Qingdao University, Qingdao 266071, Shandong Province, China

AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 1375 experts in gastroenterology and hepatology from 68 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

INDEXING/ABSTRACTING

World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents[®]/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch[®]), Journal Citation Reports[®], Index Medicus, MEDLINE, PubMed, PubMed Central and Directory of Open Access Journals. The 2017 edition of Journal Citation Reports[®] cites the 2016 impact factor for *WJG* as 3.365 (5-year impact factor: 3.176), ranking *WJG* as 29th among 79 journals in gastroenterology and hepatology (quartile in category Q2).

FLYLEAF

I-IX Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: Xiang Li
Responsible Electronic Editor: Yan-Jie Ma
Proofing Editor-in-Chief: Lian-Sheng Ma

Responsible Science Editor: Ze-Mao Gong
Proofing Editorial Office Director: Jin-Lei Wang

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Damian Garcia-Olmo, MD, PhD, Doctor, Professor, Surgeon, Department of Surgery, Universidad Autonoma de Madrid; Department of General Surgery, Fundacion Jimenez Diaz University Hospital, Madrid 28040, Spain

Stephen C Strom, PhD, Professor, Department of Laboratory Medicine, Division of Pathology, Karolinska Institutet, Stockholm 141-86, Sweden

Andrzej S Tarnawski, MD, PhD, DSc (Med), Professor of Medicine, Chief Gastroenterology, VA Long Beach Health Care System, University of California, Irvine, CA, 5901 E. Seventh Str., Long Beach,

CA 90822, United States

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjgnet.com/1007-9327/editorialboard.htm>

EDITORIAL OFFICE
Jin-Lei Wang, Director
Yuan Qi, Vice Director
Ze-Mao Gong, Vice Director
World Journal of Gastroenterology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>

<http://www.wjgnet.com>

PUBLICATION DATE
November 14, 2017

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
Full instructions are available online at <http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Observational Study

Predictors of healthcare-seeking behavior among Chinese patients with irritable bowel syndrome

Wenjuan Fan, Dong Xu, Min Chang, Liming Zhu, Guijun Fei, Xiaoqing Li, Xiucai Fang

Wenjuan Fan, Dong Xu, Min Chang, Liming Zhu, Guijun Fei, Xiaoqing Li, Xiucai Fang, Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

Dong Xu, Department of Gastroenterology, The First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, Fujian Province, China

ORCID number: Wenjuan Fan (0000-0002-2927-9266); Dong Xu (0000-0002-6690-7049); Min Chang (0000-0003-3963-6455); Liming Zhu (0000-0002-8710-8780); Guijun Fei (0000-0001-6517-9695); Xiaoqing Li (0000-0003-1334-1544); Xiucai Fang (0000-0002-5600-8779).

Author contributions: Fan W collected the data and wrote the manuscript; Xu D and Chang M collected the data; Zhu L, Fei G and Li X consulted with the patients; Fang X designed the study, consulted with the patients and critically revised the manuscript; all authors had final approval of the article.

Supported by the Program of International S&T Cooperation, No. 2014DFA31850; Project of the National Key Technologies R&D Program in the 11th Five Year Plan period, No. 2007BAI04B01; and National High-tech R&D Program ("863" Program, 2010AA023007), China.

Institutional review board statement: The observational study was approved by the Ethics Committee of Peking Union Medical College Hospital.

Informed consent statement: Parts of study participants provided informed written consent prior to study enrollment and other patients orally consented to participate the study after informed.

Conflict-of-interest statement: The authors of the manuscript have no conflicts of interest to disclose.

Data sharing statement: We have submitted an article "Analysis of symptomatic characteristics of patients with irritable bowel syndrome in China" with the same database to Chinese Journal of General Practitioners, which has been published on 2017, 16(9): 668-671.

Open-Access: This article is an open-access article which was

selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Xiucai Fang, MD, Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, #1, Shuaifuyuan, Dongcheng District, Beijing 100730, China. fangxiucai2@aliyun.com

Telephone: +86-10-69156892

Fax: +86-10-69151963

Received: August 2, 2017

Peer-review started: August 4, 2017

First decision: August 30, 2017

Revised: September 13, 2017

Accepted: October 18, 2017

Article in press: October 19, 2017

Published online: November 14, 2017

Abstract

AIM

To analyze predictors of healthcare-seeking behavior among Chinese patients with irritable bowel syndrome (IBS) and their satisfaction with medical care.

METHODS

Participating patients met IBS Rome III criteria (excluding those with organic diseases) and were enrolled in an IBS database in a tertiary university hospital. Participants completed IBS questionnaires in face-to-face interviews. The questionnaires covered intestinal and extra-intestinal symptoms, medical consultations, colonoscopy,

medications, and self-reported response to medications during the whole disease course and in the past year. Univariate associations and multivariate logistic regression were used to identify predictors for frequent healthcare-seeking behavior (≥ 3 times/year), frequent colonoscopies (≥ 2 times/year), long-term medications, and poor satisfaction with medical care.

RESULTS

In total, 516 patients (293 males, 223 females) were included. Participants' average age was 43.2 ± 11.8 years. Before study enrollment, 55.2% had received medical consultations for IBS symptoms. Ordinary abdominal pain/discomfort (non-defecation) was an independent predictor for healthcare-seeking behavior (OR = 2.07, 95%CI: 1.31-3.27). Frequent colonoscopies were reported by 14.7% of patients (3.1 ± 1.4 times per year). Sensation of incomplete evacuation was an independent predictor for frequent colonoscopies (OR = 2.76, 95%CI: 1.35-5.67). During the whole disease course, 89% of patients took medications for IBS symptoms, and 14.7% reported they were satisfied with medical care. Patients with anxiety were more likely to report dissatisfaction with medical care (OR = 2.08, 95%CI: 1.20-3.59). In the past year, patients with severe (OR = 1.74, 95%CI: 1.06-2.82) and persistent (OR = 1.66, 95%CI: 1.01-2.72) IBS symptoms sought medical care more frequently.

CONCLUSION

Chinese patients with IBS present high rates of frequent healthcare-seeking behavior, colonoscopies, and medications, and low satisfaction with medical care. Intestinal symptoms are major predictors for healthcare-seeking behavior.

Key words: Irritable bowel syndrome; Colonoscopy; Healthcare seeking; Treatment; Outcomes

© **The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: The prevalence of irritable bowel syndrome (IBS) in the general Chinese population is about 6.5%. Many patients are dissatisfied with the efficacy of traditional IBS treatments. Data about healthcare-seeking behavior among these patients in China are lacking. We analyzed a database of patients with IBS from Peking Union Medical College Hospital to identify predictors for healthcare-seeking behavior and satisfaction with medical care among this population. We found high rates of frequent healthcare-seeking behavior, colonoscopies, and medications, and low satisfaction with medical care. Intestinal symptoms were major predictors for healthcare-seeking behavior. Anxiety influenced satisfaction with medical care.

Fan W, Xu D, Chang M, Zhu L, Fei G, Li X, Fang X. Predictors of healthcare-seeking behavior among Chinese patients with irritable bowel syndrome. *World J Gastroenterol* 2017; 23(42): 7635-7643 Available from: URL: <http://www.wjgnet.com>

[com/1007-9327/full/v23/i42/7635.htm](http://dx.doi.org/10.3748/wjg.v23.i42.7635) DOI: <http://dx.doi.org/10.3748/wjg.v23.i42.7635>

INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional bowel disorder with a global prevalence of 11%^[1]. A meta-analysis found the pooled prevalence of IBS in a Chinese community was 6.5%^[2]. Rome III criteria indicate IBS is characterized by persistent or recurrent abdominal pain or discomfort associated with altered bowel habits, and patients with IBS report lower quality of life^[3]. In the United States, IBS is associated with an annual economic burden of more than 20 billion dollars (direct and indirect healthcare costs)^[4]. Data from Korea in 2008 showed the annual average National Health Insurance costs for IBS per person were USD64.1, the cost for outpatient care was USD43.7, and that for inpatient care was USD1087.9^[5]. A Chinese study focused on medical costs showed that IBS accounted for 3.3% of the total healthcare budget for the entire Chinese nation^[6]. Data from Western countries indicated intestinal symptoms (including increasing pain severity and duration) were independently associated with seeking healthcare for IBS^[7], and frequent consulters were more likely to have coexisting anxiety or depression^[8]. In France, 71.9% of patients consulted their general physicians, 45.9% consulted gastroenterologists, and 8% had been hospitalized for IBS^[9]. An epidemiological study in China demonstrated that 22.4%^[10] of patients with IBS symptoms sought healthcare, but there were no detailed data revealing the predictors for healthcare-seeking behavior among patients with IBS in China.

The pathogenesis of IBS is unclear, and its diagnosis depends on Rome diagnostic criteria. However, in France, 67% of patients who met Rome II criteria underwent additional investigations to determine etiologies^[9]. The therapeutic goals of IBS are to alleviate intestinal symptoms, reduce episodes, and improve quality of life. Nevertheless, many patients with IBS are dissatisfied with the efficacy of traditional treatment options and undergo frequent consultations, referrals, multiple medications, and even unnecessary abdominal or pelvic surgeries^[11]. The present study aimed to provide evidence for IBS management strategies through a database analysis of patients with IBS from Peking Union Medical College Hospital (PUMCH).

MATERIALS AND METHODS

Participants

Participants were consecutive patients with IBS enrolled in a gastroenterology clinic at PUMCH (a tertiary university hospital) from June 2009 to February 2016. Eligible patients were aged 18-65 years. All patients met Rome III diagnostic and subtype criteria^[12], including recurrent

abdominal pain or discomfort at least 3 d/mo in the last 3 mo associated with two or more of these features: (1) improvement with defecation; (2) onset associated with a change in the frequency of stools; and (3) onset associated with a change in the form of stools. Criteria were fulfilled in the last 3 mo with symptom onset at least 6 months before diagnosis. Patients with organic gastrointestinal diseases and metabolic diseases were excluded based on the results of routine tests for blood, urine, stool; liver, kidney, and thyroid function; measurements of carcinoembryonic antigen, erythrocyte sedimentation rate and C-reactive protein; and abdominal ultrasound and colonoscopy in the past year. Eligible patients needed to be able to complete the questionnaires. After being informed about the study, some participating patients provided informed written consent and others provided oral consent to participate before study enrollment. This study was approved by the PUMCH Ethics Committee (S-234).

Methods

IBS symptom questionnaires were administered by well-trained investigators in face-to-face interviews. Information collected included demographic data, IBS disease course, frequency and severity of IBS symptoms, defecation-related symptoms, extra-intestinal symptoms, examination results in the past year, and psychological and sleeping status and management. Symptom score for IBS with diarrhea (IBS-D) was calculated according to Zhu *et al.*^[3], with a total possible score of 15 that reflected the frequency and severity of abdominal pain/discomfort, frequency of bowel movements during symptom onset, and improvement of abdominal pain/discomfort with defecation. We defined mild symptoms as a symptom score ≤ 8 , moderate symptoms as 9–10, and severe symptoms as > 10 , based on symptom score percentiles and the severity and frequency of abdominal pain, number of other symptoms, health-related quality of life, and healthcare use^[13]. In this questionnaire, ordinary abdominal pain/discomfort referred to abdominal pain/discomfort during non-defecation, whereas persistent symptoms referred to having IBS symptom onset every day.

Patients with difficulty falling asleep, light sleep/dreaminess, sleeping time < 6 h, or early awakening in the past 3 mo were defined as having sleeping disorders. The Hamilton anxiety (HAMA) and Hamilton depression (HAMD) scales were used to evaluate patients' psychological status by specially trained professionals through conversation and observation^[14].

The validated simplified Chinese version of the IBS-Quality of Life (IBS-QOL) instrument was completed by patients and transformed to scores according to the instructions provided^[3,15]. Healthcare-seeking conditions consisted of healthcare-seeking behavior throughout the whole disease course and the past year, medical costs, treatment efficacy evaluation, and satisfaction with medical care as reported by patients. Medical

costs were converted and presented as USD, based on the average exchange rate during 2009–2015 from the National Bureau of Statistics of China (USD1 = CNY6.4195).

Statistical analysis

All analyses were performed using SPSS version 19.0 (IBM Corporation, Somers, NY, United States). Parametric data were presented as mean \pm SD. Nonparametric data were presented as median (interquartile range). Comparisons among the two groups were made by Student's *t*-tests for parametric data. The Mann-Whitney *U* test was used to compare nonparametric data between the two groups. Chi-square tests were used for categorical variables. Spearman's test was performed to assess nonparametric correlations between two quantitative variables. Univariate associations were identified by χ^2 tests. Variables that were significant in the chi-square tests were included in a multivariate logistic regression model to identify independent predictors for healthcare-seeking behavior among patients with IBS. *P* < 0.05 was considered statistically significant.

RESULTS

Demographic data

Data for 516 patients with IBS were included in the final analysis. Patients' average age was 43.2 ± 11.8 years, and the sample included 56.8% males and 43.2% females. The median IBS disease course was 6.5 (8) years; 30.8% of patients had a disease course ≥ 10 years, and 12.0% ≥ 20 years.

IBS-D, IBS with constipation (IBS-C) and mixed IBS (IBS-M) accounted for 94.4%, 3.5%, and 2.1% of patients, respectively. We did not include patients with unsubtyped IBS. The average symptom score for IBS-D was 9.4 ± 1.6 ; 26.2% had mild symptoms, 51.7% moderate symptoms, and 22.1% severe symptoms. In addition, 58.1% of patients had coexisting sleeping disorders, with a median duration of 3.5 (9) years. A total of 362 patients (70.2%) completed HAMA and HAMD assessment. The average HAMA score was 16.2 ± 7.3 and the average HAMD score was 13.2 ± 6.1 . We found that 62.1% of patients had coexisting anxiety, of which 49.6% were moderate to severe. In addition, 29% of patients had coexisting depression, with 14.2% being moderate to severe. The average IBS-QOL score was 71.7 ± 17.9 , and there was no significant difference between males and females (73.0 ± 17.7 vs 71.0 ± 19.1 , *P* = 0.22).

Healthcare-seeking behavior among patients with IBS

During the whole disease course, 285 patients (55.2%) had sought healthcare at least once for IBS symptoms (current consultation not included). These patients were defined as the consulter group. In the past year this figure increased to 79.3%, with an average number of visits of 4.5 ± 6.2 . The majority of patients

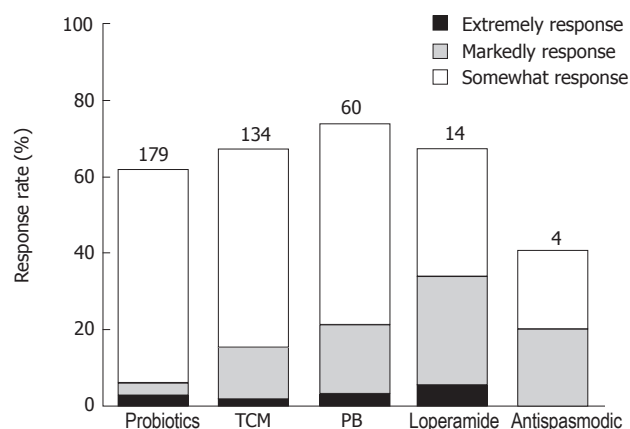


Figure 1 Patients with irritable bowel syndrome with diarrhea reported effective rate in the past year. Number on top of the column referred to number of patients who used that kind of drug. TCM: Traditional Chinese medicine; PB: Pinaverium bromide.

(79.3%) consulted with tertiary hospitals; primary/secondary care accounted for 20.7% of consultations. In addition, most patients (97.9%) consulted with gastroenterologists; 8.6% also consulted with other departments including general physicians (9.5%), traditional Chinese medicine practitioners (6.8%), and gynecologists (4.6%).

In the past year, 49.1% of patients had more than three consultations. Patients with anxiety and depression underwent more consultations than patients without [anxiety, 3.0 (3.5) vs 2.0 (2.8), $P = 0.005$; depression, 3.0 (4.0) vs 2.0 (2.9), $P = 0.001$]. The number of consultations for patients with IBS in the past year was positively correlated with symptom score ($r = 0.271$, $P < 0.001$) but negatively correlated with IBS-QOL score ($r = -0.228$, $P < 0.001$).

Colonoscopies: During the whole disease course, 41.9% of patients underwent colonoscopies (average 1.7 ± 1.3); 76 patients (14.7%) underwent at least two colonoscopies, with the maximum being 10 (over 6 years). In the past year, 64.9% of patients underwent colonoscopies (average 1.1 ± 0.3); 19 patients (3.7%) had colonoscopies at least twice (maximum of three).

Medications and efficacy: In total, 89% of patients with IBS had taken medications during the whole disease course, with 54.7% reporting intermittent use and 16.9% long-term use. Consulters were more likely to take medications than non-consulters (93.7% vs 83.1%, $P < 0.001$). In the past year, the rate of medication was 88.8% and 14.8% of patients took more than three kinds of medications. Common medications used by patients with IBS-D were probiotics, traditional Chinese medicines, pinaverium bromide, loperamide, and traditional antispasmodics. Probiotics were most commonly used (52.2%), followed by traditional Chinese medicine (41.3%) (Table 1). Patient-reported medication response rates in the past year were over 50%. Although the overall response rate for pinaverium bromide was

Table 1 Irritable bowel syndrome with diarrhea patients reported medication use ($n = 487$) n (%)

Medications	The whole disease course	The past year
Probiotics	240 (49.3)	254 (52.2)
Traditional Chinese Medicine	195 (40.0)	201 (41.3)
Pinaverium bromide	49 (10.1)	82 (16.8)
Loperamide	19 (3.9)	21 (4.3)
Traditional antispasmodic	11 (2.3)	10 (2.1)

Data were presented as number and percentage of patients who used medications.

73.1% and probiotics was 61.2%, "somewhat response" for the two medications was reported by 52.4% and 55.9%, respectively (Figure 1). Common medications used by those with IBS-C included traditional Chinese medicine, enemas, and prokinetics.

Medical costs and overall satisfaction with medical care

Total direct medical costs estimated per patient per year for the whole disease course and for the past year were USD691.8 \pm 1067.2 and USD762.7 \pm 1146.0, respectively, with a maximum amount of USD7788.8. Degree of satisfaction with medical care was reported as complete satisfaction for 11.4% of patients, satisfaction for 31.8%, and dissatisfaction for 56.8%. Non-consulters reported a higher overall satisfaction rate (including complete satisfaction and satisfaction) than consulters (58.9% vs 30.5%, $P < 0.001$).

Variables influencing healthcare-seeking behavior and satisfaction

Univariate analysis: We investigated predictors for consultation, frequent consultations (≥ 3 times/year), frequent colonoscopies (≥ 2 times/year), long-term medications, multiple medications (≥ 3 kinds), and dissatisfaction with medical care in the whole disease course and the past year. Consulters were more likely to present with ordinary abdominal pain/discomfort, persistent symptoms, anxiety, and depression in the whole disease course. In the past year, consulters were more likely to have loose stools (Bristol Stool Form Scale type 6) and weight loss (Table 2). In addition, among frequent consulters over the whole disease course, the percentages of females, severe symptoms, weight loss, and coexisting functional dyspepsia (FD) were higher than among patients with < 3 consultations/year. In the past year, variables influencing healthcare-seeking behavior included severe symptoms, ordinary abdominal pain/discomfort, persistent symptoms, weight loss, and FD (Table 3). During the whole disease course, more females than males reported frequent colonoscopies (52.6% vs 38.6%, $P = 0.047$), sensation of incomplete evacuation (84.2% vs 65%, $P = 0.003$), and coexisting pain in other parts of the body (50% vs 33.6%, $P = 0.018$).

Table 2 Factors with significant difference between consulted and non-consulted patients with irritable bowel syndrome *n* (%)

	Consulters	Non-consulters	OR (95%CI)
During the whole disease course	<i>n</i> = 285	<i>n</i> = 231	
Ordinary abdominal pain/discomfort	174 (61.1)	101 (43.7)	2.02 (1.43-2.92)
Persistent symptoms	104 (36.5)	60 (26.0)	1.64 (1.12-2.40)
Disease course \geq 7 yr	121 (42.5)	77 (33.3)	1.48 (1.03-2.12)
Co-existed with GERD	157 (55.1)	107 (46.3)	1.42 (1.00-2.01)
Sleeping disorder	179 (62.8)	121 (52.4)	1.54 (1.08-2.18)
Anxiety ¹	128 (67.4)	98 (57.0)	1.56 (1.02-2.38)
Depression ¹	64 (33.7)	41 (23.8)	1.62 (1.02-2.58)
In the past year	<i>n</i> = 409	<i>n</i> = 107	
Mental labor	199 (48.7)	33 (30.8)	2.13 (1.35-3.35)
Severe abdominal pain	68 (16.6)	27 (25.2)	0.59 (0.36-0.98)
Loose stool	312 (83.6)	70 (72.9)	1.70 (1.07-2.69)
Weight loss	119 (29.1)	17 (15.9)	2.17 (1.24-3.81)

¹The number of consulters and non-consulters were 190 and 172. IBS: Irritable bowel syndrome; GERD: Gastroesophageal reflux disease; OR: Odds ratio.

Table 3 Factors with significant difference between frequent and infrequent consulters in patients with irritable bowel syndrome *n* (%)

	Frequent consulters	Infrequent consulters	OR (95%CI)
During the whole disease course	<i>n</i> = 136	<i>n</i> = 149	
Female	76 (55.9)	65 (43.6)	0.55 (0.35-0.86)
Severe symptoms	39 (28.7)	24 (16.1)	1.93 (1.08-3.45)
Weight loss	45 (33.1)	26 (17.4)	2.34 (1.35-4.07)
Co-existed with FD	94 (69.1)	79 (53)	1.98 (1.22-3.22)
In the past year	<i>n</i> = 201	<i>n</i> = 208	
Severe symptoms	62 (30.8)	24 (11.5)	3.42 (2.03-5.75)
Ordinary abdominal pain/discomfort	123 (61.2)	97 (46.6)	1.8 (1.22-2.67)
Persistent symptoms	80 (39.8)	48 (23.1)	2.20 (1.44-3.38)
Weight loss	71 (35.3)	48 (23.1)	1.82 (1.18-2.81)
Co-existed with FD	131 (65.2)	114 (54.8)	1.54 (1.04-2.30)

Data were presented as *n* (%). χ^2 test. FD: Functional dyspepsia; OR: Odds ratio; CI: Confidence interval.

Table 4 Factors with significant difference of medication behaviors in patients with irritable bowel syndrome in the past year *n* (%)

	Long-term medication (<i>n</i> = 88)	Intermittent medication (<i>n</i> = 370)	OR (95%CI)	Medications \geq 3 kinds (<i>n</i> = 68)	Medications < 3 kinds (<i>n</i> = 390)	OR (95%CI)
Mental labor	26 (29.5)	169 (45.7)	0.59 (0.30-0.82)			
Severe symptoms	33 (37.5)	73 (19.7)	2.44 (1.48-4.03)			
Persistent symptoms	45 (51.1)	107 (28.9)	2.57 (1.60-4.13)	33 (48.5)	119 (30.5)	2.15 (1.27-3.62)
Weight loss	40 (45.5)	86 (23.2)	2.75 (1.70-4.47)	28 (41.2)	98 (25.1)	2.09 (1.22-3.56)
Anxiety ¹	46 (79.3)	163 (61.3)	2.42 (1.23-4.79)	40 (78.4)	169 (61.9)	1.87 (1.11-3.15)
Depression ¹	24 (41.4)	75 (28.2)	1.80 (1.00-3.23)			
Co-exist with FD				49 (72.1)	232 (59.5)	1.76 (1.00-3.10)

¹The number of long-term medication and intermittent medication were 58 and 266. χ^2 test. IBS: Irritable bowel syndrome; FD: Functional dyspepsia; OR: Odds ratio.

Table 4 lists differences between patients with long-term medications and intermittent medications, multiple medications (\geq 3 kinds) and fewer than three kinds of medications. Patients with persistent symptoms, weight loss, and anxiety were more likely to take long-term and multiple medications.

Comparison of degree of satisfaction with medical care in the whole disease course and in the past year showed that IBS symptoms, weight loss, sleeping disorders, and psychological disorders influenced

patient-reported satisfaction rates (Table 5).

Multivariate analysis: We entered the above influencing factors into a multivariate logistic regression model, and found ordinary (not pre-defecation) abdominal pain/discomfort was an independent predictor for consultation in the whole disease course. Severe symptoms and persistent symptoms were independent predictors for frequent consultations in the past year. In the whole disease course, frequent colonoscopies were associated

Table 5 Factors with significant difference between irritable bowel syndrome patients with satisfaction and dissatisfaction to medical care *n* (%)

	Satisfaction	Dissatisfaction	OR (95%CI)
During the whole disease course	<i>n</i> = 293	<i>n</i> = 223	
Severe symptoms	76 (25.9)	38 (17.0)	1.71 (1.10-2.64)
Ordinary abdominal pain/discomfort	179 (61.1)	96 (43.0)	2.08 (1.46-2.96)
Persistent symptoms	112 (38.2)	52 (23.3)	2.04 (1.38-3.01)
Mucous stool	196 (66.9)	129 (57.8)	1.47 (1.03-2.11)
Weight loss	90 (30.7)	46 (20.6)	1.71 (1.13-2.57)
Co-existed with GERD	162 (55.3)	102 (45.7)	1.47 (1.03-2.08)
Co-existed with sleeping disorder	189 (64.5)	111 (49.8)	1.83 (1.29-2.62)
Anxiety ¹	145 (72.5)	81 (50.0)	2.64 (1.70-4.08)
Depression ¹	73 (36.5)	32 (19.8)	2.34 (1.44-3.78)
In the past year	<i>n</i> = 255	<i>n</i> = 261	
Severe symptoms	69 (27.1)	45 (17.2)	1.69 (1.11-2.58)
Ordinary abdominal pain/discomfort	155 (60.8)	120 (46.0)	1.66 (1.17-2.34)
Persistent symptoms	98 (38.4)	66 (25.3)	1.73 (1.19-2.52)
Mucous stool	172 (67.5)	153 (58.6)	1.46 (1.02-2.10)
Weight loss	81 (31.8)	55 (21.1)	1.65 (1.11-2.45)
Anxiety ¹	125 (72.7)	101 (53.2)	2.34 (1.51-3.64)
Depression ¹	61 (35.5)	44 (23.2)	1.82 (1.15-2.89)

¹The number of satisfaction and dissatisfaction were 172 and 190. χ^2 test. IBS: Irritable bowel syndrome; GERD: Gastroesophageal reflux disease; OR: Odds ratio.

with sensation of incomplete evacuation. In the past year, long-term medications were associated with persistent symptoms and weight loss. In the whole disease course, coexisting anxiety was the strongest independent predictor for dissatisfaction with medical care (Table 6).

DISCUSSION

In the present study, we analyzed clinical medical care data for patients with IBS from a tertiary hospital, and found that IBS-D was most common in China. Most patients consulted with gastroenterologists in tertiary hospitals, and there was a high rate of colonoscopies. In patients with IBS-D, the most commonly used medications were probiotics. Conventional treatments were reported as partially effective, and patient-reported satisfaction rates were low. Ordinary abdominal pain/discomfort, severe and persistent symptoms, weight loss, and anxiety were independent predictors for healthcare-seeking behavior and satisfaction with medical care.

In our study, patients with IBS showed a long disease course, with 30% of patients having IBS for more than 10 years, which highlighted the importance of accurate diagnosis and effective management^[16]. Most of our participants had IBS-D, with 5.5% having IBS-C/IBS-M; these rates are much lower than domestic epidemiological data^[10]. This might be attributed to the fact that we enrolled patients with typical IBS symptoms, and suggests patients with IBS-D

Table 6 Multivariate analysis of factors associated with healthcare seeking behaviors and satisfaction to medical care in patients with irritable bowel syndrome

	Adjusted OR (95%CI)
Consultation in the whole disease course	
Ordinary abdominal pain/discomfort	2.07 (1.31-3.27)
Consultation in the past year	
Mental labor	2.19 (1.35-3.55)
Weight loss	2.17 (1.22-3.89)
Frequent consultations in the whole disease course	
Severe symptoms	1.88 (1.12-3.15)
Weight loss	1.94 (1.09-3.47)
Frequent consultations in the past year	
Severe symptoms	1.74 (1.06-2.82)
Persistent symptoms	1.66 (1.01-2.72)
Frequent colonoscopies in the whole disease course	
Sensation of incomplete evacuation	2.76 (1.35-5.67)
Co-existed pain in other parts of the body	1.92 (1.07-3.45)
Long-term medication in the past year	
Persistent symptoms	2.02 (1.07-3.81)
Weight loss	2.58 (1.38-4.82)
Dissatisfaction with medical care in the whole disease course	
Ordinary abdominal pain/discomfort	1.99 (1.24-3.18)
Weight loss	1.73 (1.01-2.95)
Anxiety	2.08 (1.20-3.59)

Logistic regression analysis. IBS: Irritable bowel syndrome; OR: Odds ratio.

might be more likely to seek healthcare. In the whole disease course, the consultation rate for IBS symptoms (55.2%) was similar to that in Taiwan (47%)^[17] and the United States (46%)^[18], but was lower than in Australia (73%)^[18]. Chinese patients with IBS mostly consulted with tertiary hospitals (78.9%) and gastroenterologists (97.9%), which differs from Western countries^[9,19] and may be related to a lack of well-established referral systems. A small number of patients consulted with other departments because of coexisting headache and urogenital symptoms^[20].

The Rome III IBS diagnostic criteria emphasize improvement of abdominal pain/discomfort after defecation. However, our data showed more than half of participating patients presented with ordinary abdominal pain/discomfort (non-defecation). In addition, ordinary abdominal pain/discomfort was an independent predictor for healthcare seeking among patients with IBS. Previous published papers indicated the severity^[7,16,21], frequency^[21], and duration^[7] of abdominal pain were predictors for seeking healthcare among patients with IBS. We demonstrated that the number of visits was positively correlated with intestinal symptom scores, and patients with severe symptoms and weight loss were more likely to frequently seek healthcare. In the past year, predictors for frequent consultations included persistent symptoms. Weight loss was one of the alarm features for patients with IBS^[22] with a reported prevalence of 21%, which might be associated with

FD (especially postprandial distress syndrome^[23] and psychological disorders^[24]). The reported prevalence of gastrointestinal malignancies in the population with unintentional weight loss was 6%–38%^[25]. Patients with IBS were more worried about having serious diseases than healthy controls^[26], and 21% of healthcare seekers reported “fear that abdominal symptoms relate to cancer or other illness” as the most important reason for seeking healthcare^[27]. Usually, patients attributed their symptoms to organic etiologies such as intestinal infection or ulcers^[28]. Fear of organic diseases prompted frequent consultations^[29].

A previous study in Hong Kong^[30] showed a higher degree of anxiety was an independent factor associated with healthcare-seeking behavior in IBS, but that study did not show the exact degree of anxiety and odds ratios. Despite intestinal symptoms, we found patients with anxiety and depression had more visits. During the whole disease course, anxiety and depression were more common among consulters than non-consulters. However, multifactor analysis indicated that anxiety and depression were not independent predictors for healthcare-seeking behavior.

Before study enrollment, 64.9% of patients underwent colonoscopies and 14.7% of patients had colonoscopies at least twice. In an American cohort study, the detection rate of structural lesions of the colon in non-IBS-C patients fulfilling Rome II criteria without alarm features was similar to healthy controls^[31]. Akhtar *et al.* reviewed medical records of patients with IBS who underwent colonoscopies because of new gastrointestinal symptoms 15 years after diagnosis, and found that there was no difference in the prevalence of organic colonic lesions with non-IBS controls^[32]. The newly established Rome IV criteria recommend appropriate diagnostic testing only if alarm symptoms are present^[13]. The American College of Gastroenterology recommends colonoscopy should be performed in patients with IBS who have alarm features and in those aged over 50 years^[22]. In China, the high colonoscopy rate may be associated with the increasing incidence of colorectal cancer^[33] and the relatively low cost of examination. We demonstrated that the sensation of incomplete evacuation and pain in other parts of the body were independent predictors for frequent colonoscopies.

In total, 88% of patients had taken medications in the past year, and 14.8% had taken more than three kinds of medications. Probiotics were the most commonly used drugs. Despite multiple studies confirming the efficacy of probiotics in treating IBS^[34,35], our results displayed a markedly low response rate and they are not the most commonly used drugs in Western countries. Most other investigated drugs were partially effective, which was similar to a study in the United States that showed only 19%, 18%, 15%, and 10% of patients with IBS reported medical therapy was completely effective in relieving constipation, diarrhea, abdominal pain, and bloating, respectively^[11]. Psychological evaluations at enrollment showed a

high prevalence of anxiety and depression, although few patients reported use of antidepressants or psychotherapy. Interestingly, 83.1% of non-consulters had taken medications, which might partially account for the low response rate. In the past year, patients with persistent symptoms and weight loss were more likely to take long-term medications.

IBS severely influenced patients' quality of life and caused considerable financial burden. In Germany^[36], total costs for IBS were €994.97 per patient per year, 37% of which was for medications; in the past year, one in 15 patients was hospitalized for IBS. In the present study, average direct costs were estimated at USD762.7 per patient in the past year. Even so, the patient-reported rate of complete satisfaction was 11.4%, which was close to United States data (14%)^[11] and indicates dissatisfaction with current treatment is a global issue. In addition, 41.1% of non-consulters reported dissatisfaction with medical care, which suggests they were unsatisfied with over-the-counter drugs. Coexisting anxiety was the strongest predictor for poor satisfaction with medical care, followed by ordinary abdominal pain/discomfort. The latter suggests that the pathogenesis of ordinary abdominal pain/discomfort differs from pre-defecation abdominal pain/discomfort, and may need higher level treatment (*e.g.*, centrally acting drugs).

There were some limitations in this study. First, we set strict inclusion criteria for patients with IBS, which excluded patients with light, atypical symptoms, and fewer examinations. In addition, some patients did not complete HAMA and HAMD evaluations. Patient-reported healthcare-seeking behavior was retrospective and we did not know whether their medications were prescription or over-the-counter medicines. Finally, our study was a single-center study and might not be representative of the overall situation in China.

In conclusion, Chinese patients with IBS were dominated by those with IBS-D. Patients most commonly consulted with tertiary hospitals and gastroenterologists, and there was a high rate of colonoscopies. Most conventional treatments were only partially effective and patients reported low satisfaction rates. Intestinal symptoms influenced healthcare-seeking behavior among patients with IBS from different levels, and coexisting anxiety was the strongest predictor for dissatisfaction with medical care.

ARTICLE HIGHLIGHTS

Research background

Irritable bowel syndrome (IBS) is a chronic recurrent functional bowel disorder which impairs patients' quality of life. Patients with IBS report poor treatment response and satisfaction rates for traditional treatments and undergo frequent consultations and referrals. In China, data for predictors of healthcare-seeking behavior and satisfaction with medical care are lacking. Studies regarding predictors for healthcare-seeking behavior among patients with IBS may provide evidence for IBS management strategies in this region.

Research motivation

The present study comprehensively summarized the characteristics of

healthcare-seeking behavior, medical costs, and satisfaction with care among Chinese patients with IBS. The authors also investigated predictors for frequent consultations, frequent colonoscopies, dissatisfaction with medical care, and long-term and multiple medications among Chinese patients with IBS. The authors' study provides a basis for future studies on healthcare-seeking behavior among patients with IBS, and may provide management guidance for clinicians.

Research objectives

The main objectives of this study were to investigate the characteristics of healthcare-seeking behavior, medical costs, and satisfaction with care among Chinese patients with IBS, and determine predictors for frequent consultations, frequent colonoscopies, dissatisfaction with medical care, and long-term and multiple medications in this population.

Research methods

The authors enrolled patients with IBS who met Rome III diagnostic criteria and excluded organic diseases in a tertiary gastroenterology clinic from 2009 to 2016. Patients were administered IBS questionnaires in face-to-face interviews, which included intestinal and extra-intestinal symptoms, medical consultations and management. Data were collected and analyzed with SPSS version 19.0 software. Patients were divided into frequent consulters and infrequent consulters; frequent colonoscopies and infrequent colonoscopies; long-term medications and intermittent medications; medications ≥ 3 kinds and medications < 3 kinds; satisfaction with medical care and dissatisfaction with medical care. Univariate analysis was conducted with χ^2 test to detect factors with significant differences between groups and the significant different factors above were entered into a multivariate logistic regression model to determine independent predictors for their healthcare-seeking behavior.

Research results

The authors found Chinese IBS patient present high rates of frequent healthcare-seeking behavior, colonoscopies, medications and low satisfaction with medical care. Abdominal pain/discomfort during non-defecation period (ordinary abdominal pain/discomfort) instead of pre-defecation abdominal pain/discomfort was the independent predictor for their healthcare-seeking behavior. Sensation of incomplete evacuation was the independent predictor for frequent colonoscopies. Patients with anxiety were more likely to report "dissatisfaction to medical care". In the past year, patients with severe and persistent IBS symptoms sought medical care frequently. How to educate patients and obtain reasonable utilization of medical resources need to be solved.

Research conclusions

The results demonstrated that most patients with IBS were partially responsive to traditional treatment. Intestinal symptoms were major predictors for healthcare-seeking behavior, and patients with anxiety were more likely to be dissatisfied with medical care. The authors' results provided guidance for Chinese IBS management. Doctors should pay attention to patients with specific symptoms such as ordinary abdominal pain/discomfort and anxiety.

Research perspectives

From the study, The authors learned that patients with IBS tended to undergo frequent consultations and investigations. Physicians should give patients sufficient explanations and pay attention to their psychological status. Future researches might emphasize the reasons of low effective rate of routine treatments and investigate the efficacy of psychological treatment through prospective studies.

ACKNOWLEDGMENTS

The authors thank Shaomei Han from Department of Epidemiology and Statistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and School of Basic Medicine, Peking Union Medical College for her statistical support.

REFERENCES

- 1 **Lovell RM**, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol* 2012; **10**: 712-721.e4 [PMID: 22426087 DOI: 10.1016/j.cgh.2012.02.029]
- 2 **Zhang L**, Duan L, Liu Y, Leng Y, Zhang H, Liu Z, Wang K. [A meta-analysis of the prevalence and risk factors of irritable bowel syndrome in Chinese community]. *Zhonghua Neiye Zazhi* 2014; **53**: 969-975 [PMID: 25623565 DOI: 10.3760/cma.j.issn.0578-1426.2014.12.011]
- 3 **Zhu L**, Huang D, Shi L, Liang L, Xu T, Chang M, Chen W, Wu D, Zhang F, Fang X. Intestinal symptoms and psychological factors jointly affect quality of life of patients with irritable bowel syndrome with diarrhea. *Health Qual Life Outcomes* 2015; **13**: 49 [PMID: 25925746 DOI: 10.1186/s12955-015-0243-3]
- 4 **Everhart JE**, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. *Gastroenterology* 2009; **136**: 741-754 [PMID: 19166855 DOI: 10.1053/j.gastro.2009.01.015]
- 5 **Jung HK**, Kim YH, Park JY, Jang BH, Park SY, Nam MH, Choi MG. Estimating the burden of irritable bowel syndrome: analysis of a nationwide Korean database. *J Neurogastroenterol Motil* 2014; **20**: 242-252 [PMID: 24840377 DOI: 10.5056/jnm.2014.20.2.242]
- 6 **Zhang F**, Xiang W, Li CY, Li SC. Economic burden of irritable bowel syndrome in China. *World J Gastroenterol* 2016; **22**: 10450-10460 [PMID: 28058026 DOI: 10.3748/WJG.V22.I47.10450]
- 7 **Talley NJ**, Boyce PM, Jones M. Predictors of health care seeking for irritable bowel syndrome: a population based study. *Gut* 1997; **41**: 394-398 [PMID: 9378398]
- 8 **Koloski NA**, Talley NJ, Boyce PM. Predictors of health care seeking for irritable bowel syndrome and nonulcer dyspepsia: a critical review of the literature on symptom and psychosocial factors. *Am J Gastroenterol* 2001; **96**: 1340-1349 [PMID: 11374666 DOI: 10.1111/j.1572-0241.2001.03789.x]
- 9 **Dapigny M**, Bellanger J, Bonaz B, Bruley des Varannes S, Bueno L, Coffin B, Ducrotté P, Flourie B, Lémann M, Lepicard A, Reigneau O. Irritable bowel syndrome in France: a common, debilitating and costly disorder. *Eur J Gastroenterol Hepatol* 2004; **16**: 995-1001 [PMID: 15371923]
- 10 **Xiong LS**, Chen MH, Chen HX, Xu AG, Wang WA, Hu PJ. [A population-based epidemiologic study of irritable bowel syndrome in Guangdong province]. *Zhonghua Yixue Zazhi* 2004; **84**: 278-281 [PMID: 15059507]
- 11 **Hulisz D**. The burden of illness of irritable bowel syndrome: current challenges and hope for the future. *J Manag Care Pharm* 2004; **10**: 299-309 [PMID: 15298528 DOI: 10.1853/jmcp.2004.10.4.299]
- 12 **Longstreth GF**, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; **130**: 1480-1491 [PMID: 16678561 DOI: 10.1053/j.gastro.2005.11.061]
- 13 **Drossman DA**. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. *Gastroenterology* 2016; Epub ahead of print [PMID: 27144617 DOI: 10.1053/j.gastro.2016.02.032]
- 14 **Hamilton M**. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960; **23**: 56-62 [PMID: 14399272]
- 15 **Huang D**, Liang L, Fang X, Xin H, Zhu L, Shi L, Yao F, Sun X, Zhang F, Ke M. Effect of psychological factors on quality of life in patients with irritable bowel syndrome with diarrhea. *Zhongguo Xiaohua Zazhi* 2015; **9**: 599-605
- 16 **Kwan AC**, Hu WH, Chan YK, Yeung YW, Lai TS, Yuen H. Prevalence of irritable bowel syndrome in Hong Kong. *J Gastroenterol Hepatol* 2002; **17**: 1180-1186 [PMID: 12453277]
- 17 **Lu CL**, Chen CY, Lang HC, Luo JC, Wang SS, Chang FY, Lee SD. Current patterns of irritable bowel syndrome in Taiwan: the Rome II questionnaire on a Chinese population. *Aliment Pharmacol Ther* 2003; **18**: 1159-1169 [PMID: 14653836]
- 18 **Ron Y**. Irritable bowel syndrome: epidemiology and diagnosis. *Isr Med Assoc J* 2003; **5**: 201-202 [PMID: 12725144]
- 19 **Wilson S**, Roberts L, Roalfe A, Bridge P, Singh S. Prevalence of irritable bowel syndrome: a community survey. *Br J Gen Pract* 2004; **54**: 495-502 [PMID: 15239910]

- 20 **Song J**, Wang Q, Wang C. Symptom features of irritable bowel syndrome complicated with depression. *Zhongguo Xiaohua Zazhi* 2015; **35**: 590-594 [DOI: 10.3760/cma.j.issn.0254-1432.2015.09.006]
- 21 **Koloski NA**, Talley NJ, Huskic SS, Boyce PM. Predictors of conventional and alternative health care seeking for irritable bowel syndrome and functional dyspepsia. *Aliment Pharmacol Ther* 2003; **17**: 841-851 [PMID: 12641507]
- 22 **American College of Gastroenterology Task Force on Irritable Bowel Syndrome**, Brandt LJ, Chey WD, Foxx-Orenstein AE, Schiller LR, Schoenfeld PS, Spiegel BM, Talley NJ, Quigley EM. An evidence-based position statement on the management of irritable bowel syndrome. *Am J Gastroenterol* 2009; **104** Suppl 1: S1-S35 [PMID: 19521341 DOI: 10.1038/ajg.2008.122]
- 23 **Bilbao-Garay J**, Barba R, Losa-García JE, Martín H, García de Casasola G, Castilla V, González-Anglada I, Espinosa A, Guijarro C. Assessing clinical probability of organic disease in patients with involuntary weight loss: a simple score. *Eur J Intern Med* 2002; **13**: 240-245 [PMID: 12067819]
- 24 **Eslick GD**, Howell SC, Talley NJ. Dysmotility Symptoms Are Independently Associated With Weight Change: A Population-based Study of Australian Adults. *J Neurogastroenterol Motil* 2015; **21**: 603-611 [PMID: 26424045 DOI: 10.5056/jnm14124]
- 25 **Abu-Freha N**, Lior Y, Shoher S, Novack V, Fich A, Rosenthal A, Etzion O. The yield of endoscopic investigation for unintentional weight loss. *Eur J Gastroenterol Hepatol* 2017; **29**: 602-607 [PMID: 28350752 DOI: 10.1097/MEG.0000000000000824]
- 26 **Faresjö Å**, Grodzinsky E, Hallert C, Timpka T. Patients with irritable bowel syndrome are more burdened by co-morbidity and worry about serious diseases than healthy controls--eight years follow-up of IBS patients in primary care. *BMC Public Health* 2013; **13**: 832 [PMID: 24025070 DOI: 10.1186/1471-2458-13-832]
- 27 **Williams RE**, Black CL, Kim HY, Andrews EB, Mangel AW, Buda JJ, Cook SF. Determinants of healthcare-seeking behaviour among subjects with irritable bowel syndrome. *Aliment Pharmacol Ther* 2006; **23**: 1667-1675 [PMID: 16696818 DOI: 10.1111/j.1365-2036.2006.02928.x]
- 28 **Björkman I**, Simrén M, Ringström G, Jakobsson Ung E. Patients' experiences of healthcare encounters in severe irritable bowel syndrome: an analysis based on narrative and feminist theory. *J Clin Nurs* 2016; **25**: 2967-2978 [PMID: 27218818 DOI: 10.1111/jocn.13400]
- 29 **Gralnek IM**. Health care utilization and economic issues in irritable bowel syndrome. *Eur J Surg Suppl* 1998; (**583**): 73-76 [PMID: 10027677]
- 30 **Hu WH**, Wong WM, Lam CL, Lam KF, Hui WM, Lai KC, Xia HX, Lam SK, Wong BC. Anxiety but not depression determines health care-seeking behaviour in Chinese patients with dyspepsia and irritable bowel syndrome: a population-based study. *Aliment Pharmacol Ther* 2002; **16**: 2081-2088 [PMID: 12452941]
- 31 **Chey WD**, Nojkov B, Rubenstein JH, Dobhan RR, Greenston JK, Cash BD. The yield of colonoscopy in patients with non-constipated irritable bowel syndrome: results from a prospective, controlled US trial. *Am J Gastroenterol* 2010; **105**: 859-865 [PMID: 20179696 DOI: 10.1038/ajg.2010.55]
- 32 **Akhtar AJ**, Shaheen MA, Zha J. Organic colonic lesions in patients with irritable bowel syndrome (IBS). *Med Sci Monit* 2006; **12**: CR363-CR367 [PMID: 16940928]
- 33 **Chen W**, Zheng R, Zeng H, Zhang S. The incidence and mortality of major cancers in China, 2012. *Chin J Cancer* 2016; **35**: 73 [PMID: 27484217 DOI: 10.1186/s40880-016-0137-8]
- 34 **Didari T**, Mozaffari S, Nikfar S, Abdollahi M. Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis. *World J Gastroenterol* 2015; **21**: 3072-3084 [PMID: 25780308 DOI: 10.3748/wjg.v21.i10.3072]
- 35 **Hungin AP**, Mulligan C, Pot B, Whorwell P, Agréus L, Fracasso P, Lionis C, Mendive J, Philippart de Foy JM, Rubin G, Winchester C, de Wit N; European Society for Primary Care Gastroenterology. Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice -- an evidence-based international guide. *Aliment Pharmacol Ther* 2013; **38**: 864-886 [PMID: 23981066 DOI: 10.1111/apt.12460]
- 36 **Müller-Lissner SA**, Pirk O. Irritable bowel syndrome in Germany. A cost of illness study. *Eur J Gastroenterol Hepatol* 2002; **14**: 1325-1329 [PMID: 12468953]

P- Reviewer: Chiba T, Ducrotte P, Dumitrascu DL, Rodrigo L

S- Editor: Gong ZM **L- Editor:** A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>



ISSN 1007-9327

