

# Body constitutions of traditional Chinese medicine caused a significant effect on irritable bowel syndrome

۲

Kuo-Fan Liao<sup>a,b</sup>, Han-Ying Tsai<sup>c</sup>, Cheng-Fong Chen<sup>d,e,f</sup>, Teh-Fu Hsu<sup>g,h</sup>, Chun-Yi Hsu<sup>c</sup>, Ta-Kai Ho<sup>c</sup>, Ding-Hao Liu<sup>i,j</sup>, Chung-Lan Kao<sup>i,j,k</sup>, Chien-Ying Wang<sup>k,I,m,n,\*</sup>, Ai-Ru Hsieh<sup>o,\*</sup>

<sup>a</sup>Department of Traditional Chinese Medicine, Feng Yuan Hospital, Ministry of Health and Welfare, Taipei, Taiwan, ROC; <sup>b</sup>Institute of Public Health, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>c</sup>Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; <sup>d</sup>Department of Exercise and Health Sciences, University of Taipei, Taipei, Taiwan, ROC; <sup>e</sup>Department of Orthopaedics and Traumatology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; <sup>f</sup>Department of Surgery, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>g</sup>Department of Emergency Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>h</sup>Institute of Clinical Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>b</sup>Cepartment of Physical Medicine and Rehabilitation, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; <sup>k</sup>School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; <sup>b</sup>Department of Critical Care Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; <sup>m</sup>Division of Trauma, Department of Emergency Medicine, Taipei, Taiwan, ROC; <sup>o</sup>Department of Exercise and Health Sciences, University of Taipei, Taiwan, ROC; <sup>o</sup>Department of Statistics, Tamkang University, New Taipei City, Taiwan, ROC

### Abstract

**Background:** According to the theory of traditional Chinese medicine (TCM), all types of body constitutions, except for the Gentleness (ie, the control group in our study), have disease susceptibility and affect the disease development process. This study attempted to investigate the relationship between TCM body constitutions and irritable bowel syndrome (IBS).

**Methods:** This cross-sectional study was based on Taiwan Biobank (TWB) and collected clinical data from 13 941 subjects aged 30 to 70. The results of the study showed that subjects with Yang-deficiency (N = 3161 subjects, odds ratio [OR] = 2.654, 95% CI = 1.740-3.910), Ying-deficiency (N = 3331 subjects, OR = 1.096, 95% CI = 0.627-1.782) or Stasis (N = 2335 subjects, OR = 1.680, 95% CI = 0.654-3.520) were more likely to have IBS.

**Results:** If the subjects with two or more TCM body constitutions: Yang-deficiency + Ying-deficiency (OR = 3.948, 95% CI = 2.742–5.560), Yang-deficiency + Stasis (OR = 2.312, 95% CI = 1.170-4.112), Ying-deficiency + Stasis (OR = 1.851, 95% CI = 0.828-3.567), or Yang-deficiency + Ying-deficiency + Stasis (OR = 3.826, 95% CI = 2.954-4.932) were also prone to IBS. **Conclusion:** These results confirmed the high correlation between TCM body constitutions and IBS. Because the current treatment for IBS is not entirely satisfactory, integrated traditional Chinese and Western medicine might provide patients with an alterna-

tive treatment option to alleviate IBS.

Keywords: Body constitution; Irritable bowel syndrome; Taiwan Biobank; Traditional Chinese medicine

# **1. INTRODUCTION**

Irritable bowel syndrome (IBS) is a gastrointestinal tract disease characterized by recurrent abdominal pain or gastrointestinal

Journal of Chinese Medical Association. (2024) 87: 558-566.

Received June 13, 2023; accepted December 3, 2023.

discomfort combined with changes in the frequency of bowel movements or changes in the shape of stools.<sup>1</sup> In addition to gastrointestinal symptoms, IBS often occurs in combination with other symptoms such as dizziness, headache, noncardiac chest pain, back pain, chronic fatigue syndrome, fibromyalgia, painful intercourse, frequent urination, major depression, anxiety, and somatization disorder.<sup>2</sup> IBS is the most common clinical gastrointestinal disorder, accounting for about 15% of the population in Western countries and about 20% of the population in China.<sup>3</sup> Although not all patients with IBS seek medical help, IBS patients make up a large percentage of gastroenterology or other medical visits.<sup>4</sup> In the United States, the annual medical costs associated with IBS are estimated to exceed \$1 billion directly.<sup>5</sup>

The etiology of IBS remains uncertain.<sup>6</sup> Despite numerous studies, they have been contradictory, and no abnormalities specific to this disease have been identified. In the past, the focus of IBS had been on the altered dynamics of the gastrointestinal tract and the hypersensitivity of the visceral organs.<sup>7,8</sup> ۲

<sup>\*</sup> Address correspondence. Dr. Ai-Ru Hsieh, Department of Statistics, Tamkang University, 151, Yingzhuan Road, New Taipei City 251, Taiwan, ROC. E-mail address: airudropbox@gmail.com (A.-R. Hsieh); Dr. Chien-Ying Wang, Department of Critical Care Medicine, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei112, Taiwan, ROC. E-mail address: wangcy@ vghtpe.gov.tw (C.-Y. Wang).

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

doi: 10.1097/JCMA.000000000001083

Copyright © 2024, the Chinese Medical Association. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/ by-nc-nd/4.0/)

Nowadays, many studies link IBS to inflammatory responses, changes in fecal flora, bacterial overgrowth, and gut-brain interactions.9-12 The role of food sensitivities needs to be considered, and the presence of a genetic predisposition is also being investigated.<sup>13,14</sup> Treatment for IBS includes lifestyle changes, dietary changes, and medication.<sup>15</sup> Dietary changes include eliminating off-gassing foods and avoiding lactose and gluten.<sup>16-18</sup> However, for patients with IBS who have limited success with lifestyle and dietary changes, gastroenterologists recommend medication.<sup>1</sup> For patients with constipation, gastroenterologists use osmotic laxatives; patients with abdominal pain are prescribed antispasmodic agents; and patients with known stressors are treated with antidepressants.<sup>19-21</sup> For patients with diarrhea, gastroenterologists prescribe antidiarrheal medications.<sup>22</sup> Although several options exist to treat IBS, the results are not satisfactory for all patients. According to one study, nearly 43% of patients with IBS have an unmet need for treatment.<sup>23</sup> As a result, more and more patients are seeking alternative therapies, such as traditional Chinese medicine (TCM), to treat IBS symptoms.<sup>24,25</sup>

Several articles have been published on the treatment of IBS in TCM.  $^{\rm 26\text{-}28}$ 

At the same time, many studies examine the differences in TCM body constitution between individuals, suggesting that doctors need to use different treatment modalities depending on the individual's TCM body constitution.<sup>29-31</sup> According to a study on the theory of body constitution in TCM, the body constitution of a person is related to gender, age, mental state, and living environment, which in turn determines the susceptibility to disease and the course of disease development.<sup>32</sup> The theory of body constitution in TCM originates from the Yellow Emperor's Canon of Medicine, written more than 2000 years ago. It summarized the characteristics of the patient's whole body and the imbalance of the body and mind from the Ying-Yang, Exterior-Interior, Cold-Heat, and Deficiency- Excess of the disease and the patient's Qi, Blood, Body Fluids, and Internal Organs.<sup>32</sup> TCM body constitution emphasizes the specificity and individuality of each patient. Therefore, treating diseases in TCM is not only to alleviate the discomfort caused by symptoms but also to restore the balance and harmony of the patient's overall physical and psychological condition.<sup>29,31,33</sup> This study was based on the Body Constitutions Questionnaire (BCQ) and the Taiwan Biobank (TWB). BCQ could determine the physical and psychological deviations of each patient in the past month and assess whether the patient has the TCM body constitution of Yangdeficiency (BCQ+), Ying-deficiency (BCQ-), Stasis (BCQs), or Gentleness.<sup>34–36</sup> Therefore, the physiological characteristics of patients are affected differently by different TCM body constitutions, and the susceptibility of patients to disease and the degree of disease progression are also different.<sup>32</sup>

Modern medicine usually adopts a reactive approach to treating disease, that is, diagnosis and treatment are carried out after the onset of the disease. However, TCM emphasizes the concept of "treating diseases that have not yet occurred" and believes that a person is healthy only when their body and mind are in balance and harmony; an unhealthy body and mind are prone to have an imbalanced body constitution, and an imbalanced body constitution is susceptible to disease and will affect the subsequent development of the disease.<sup>29</sup> The TCM body constitution could be used clinically to help physicians determine a person's susceptibility to certain diseases, such as IBS, and it could also be used to predict a patient's prognosis for the disease.<sup>34</sup> There are no relevant studies on the association between TCM body constitution and IBS. Therefore, we decided to conduct this study to investigate the association between BCQ+, BCQ-, Stasis, and IBS in the hope that TCM could play a key role in preventing and treating IBS in the future.

# 2. METHODS

#### 2.1.1. Study design and participants

This cross-sectional study included 13 941 subjects aged 30 to 70 years who participated in TWB (https://www.twbiobank. org.tw, https://www.biobank.org.tw), the world's only Chinese intergenerational tracking, vertically integrated examination, and data release human biobank, which began in 2012. The TWB is a human biobank promoted by the Taiwanese government, which integrates information on participants' lifestyles, environmental factors, TCM body constitution, clinical medicine, and biomarkers, to establish a local research database in Taiwan.<sup>37,38</sup> Taiwanese scholars have published several studies using the TWB database, including many studies on chronic diseases, and the results have clinical reference value.<sup>39-43</sup> The recruitment of subjects by the TWB is strictly regulated and conducted in full compliance with the guidelines. In addition, this study was approved by the Institutional Review Board of Taipei Veterans General Hospital.

#### 2.2. Measurements

The TWB collected phenotypic data from subjects by completing health-related questionnaires. In detail, after participating in the TWB study, subjects would undergo general physical examinations and interviews with trained researchers regarding their lifestyles, dietary habits, living environment, family history, and BCQ of TCM. The objective analysis of the TCM body constitution in this study was conducted using the BCQ developed by Dr. Su's research team in Taiwan. The BCQ focuses on the subjects' physical condition in the last month. The BCQ consists of 44 questions, each with five options to choose from: 0 (not at all), 25 (slightly), 50 (moderately), 75 (very), and 100 (most severely). There are 19 questions related to Yang-deficiency (BCQ+): 3, 5, 8, 9, 15, 16, 17, 22, 23, 24, 28, 31, 33, 36, 37, 41, 42, 43, 44; 19 questions related to Yingdeficiency (BCQ-): 2, 4, 8, 10, 11, 16, 18, 20, 23, 26, 29, 30, 31, 32, 35, 37, 38, 39, 40; and 16 questions related to Stasis (BCQs): 1, 4, 5, 6, 7, 12, 13, 14, 16, 17, 19, 20, 21, 25, 27, 34. According to the five-point Likert Scale, each question is scored 1 to 5 points, and the three body constitutions scales are summed up separately, with Yang-deficiency (BCQ+)  $\leq$  31 points, Ying-deficiency (BCQ-) ≤30 points, and Stasis (BCQs) ≤27 points. Anyone to three body constitutions might be present. If the subject does not meet any of the body constitution criteria, the subject is considered to be Gentleness (i.e., the control group in this study). In addition, according to the literature, the Cronbach's  $\alpha$  and intraclass correlation coefficient (ICC) of BCQ for Yang-deficiency, Ying-deficiency, and Stasis constitution were 0.88 and 0.91, 0.85 and 0.91, and 0.88 and 0.91, respectively.<sup>34-36,44,45</sup>

Yang symbolizes the dynamic, energic, and valuable characteristics of the body.<sup>34</sup> An insufficiency of Yang often results in feelings of coldness, lethargy, and reduced vitality levels.<sup>34</sup> Yin is the element that provides nourishment, cooling, and moisture. Yin deficit often causes a shortfall in these attributes, resulting in dryness and elevated temperature.<sup>45</sup> Stasis refers to the condition when there is a disruption in the smooth flow and operation of the body's system due to the stagnation or obstruction of Qi (energy) or Blood.<sup>45</sup>

#### 2.3. Statistical analysis

The demographic and clinical variables analyzed in our study included three body constitutions of TCM (ie, BCQ+, BCQ-, BCQs, Gentleness), age, gender, education, employment, body mass index, drug allergy, depression, headache, migraine, cervicalgia, low back pain, arthritis, alcohol consumption, smoking, exercise, tea, coffee, vegetarian, nutritional supplements, white

Liao et al.

blood cell (WBC) count, total bilirubin, albumin, Aspartate transaminase (AST), and  $\alpha$ -fetoprotein.

The continuous variables were shown as mean  $\pm$  SD, and categorical variables were shown as values and percentages. An independent *t* test was used to assess the correlation of continuous variables. Pearson chi-square test was used for categorical variables to determine the relationships. Finally, a multivariate logistic regression analysis was performed to test whether TCM body constitutions could be associated with IBS.

All statistical analyses were performed using R version 4.1.1. A multiple logistic regression analysis was performed using the "glm" function in R. Statistical significance was claimed when two-sided p values were <0.05.

# 3. RESULTS

The study included 13 941 subjects (IBS individuals: 372), including 8667 females (62.17%) and 5274 males (37.83%) aged 30 to 70 years (mean age: 48.51 years, SD = 10.7 years). Among them, 3161 (22.67%) were BCQ+ (mean ± SD = 45.4±10.35), 3331 (23.89%) were BCQ- (mean age= 46.59 years, SD = 10.47 years), 2335 (16.75%) were BCQs (mean age = 44.93 years, SD = 10.11 years), and 9459 (67.85%) were Gentleness (mean age: 49.58 years, SD = 10.63 years). Table 1 showed that the mean age of those with Gentleness was higher than those with BCQ+, BCQ-, and BCQs. Among the female subjects, there were more Gentleness subjects than those with BCO+, BCQ-, and BCQs. Patients with BCQ+ and IBS had a higher proportion of depression (p = 0.006), cervicalgia (p =0.011), and low back pain (p = 0.018) than those with BCQ+ but no IBS (Table 1). Patients with BCQ- and IBS had higher proportions of depression (p = 0.010), cervicalgia (p = 0.032), low back pain (p = 0.002), and arthritis (p = 0.038) than participants with BCQ- but without IBS (Table 1). The proportion of drug allergy (p < 0.001), depression (p < 0.001), headache (p = 0.003), migraine (p = 0.005), and arthritis (p < 0.001) was higher in patients with Gentleness and IBS than in participants with Gentleness but no IBS (Table 1). Participants with BCQ+, BCQ-, or BCQs without IBS had higher WBC counts than those with BCQ+, BCQ-, or BCQs with IBS (p < 0.001; p < 0.001; p= 0.005, Table 2). In albumin (p = 0.036; p = 0.001), AST (p = 0.005), Table 2). 0.036; p = 0.016), and  $\alpha$ -fetoprotein (p = 0.018; p = 0.001), the values were higher in participants with BCQ+ or BCQs with IBS than in participants without IBS (Table 2).

The proportion of patients with BCQ+ and IBS who did not exercise or were nonvegetarians was significantly higher than those who exercised regularly or were vegetarians (p = 0.006; p = 0.004, Table 3). In patients with BCQ- and IBS, the proportion of those who did not drink tea or were nonvegetarians was significantly higher than those who did not drink tea or were vegetarians (p = 0.029; p = 0.005, Table 3). The proportion of patients with Gentleness and IBS who did not drink tea or take nutritional supplements regularly was significantly higher than that of participants who did drink tea or took nutritional supplements regularly (p = 0.016; p = 0.007, Table 3).

A total of 372 (2.67%) patients with IBS were included in this study. Table 4 shows the prevalence of IBS in each TCM body constitution. BCQ+ (5.7%), BCQ- (4.9%), and BCQs (5.3%) were significantly higher than those without BCQ+ (1.8%), BCQ- (2.0%), and BCQs (2.1%).

The results of this study's multiple logistic regression model calculated the odds ratio (OR) between TCM constitution and IBS (Table 5). Model 1 was for a patient with BCQ+, and its OR was 2.654 (95% CI = 1.740-3.910); Model 2 was for a patient with BCQ-, and its OR was 1.096 (95% CI = 0.627-1.782); Model 3 was for a patient with BCQs, and its OR was 1.68

(95% CI = 0.654-3.520); Model 4 was for a patient BCQ+ and BCQ-, and the OR was 3.948 (95% CI = 2.742-5.560); Model 5 was for a patient with BCQ+ and BCQs, and the OR was 2.312 (95% CI = 1.170-4.112); Model 6 was a patient with BCQ- and BCQs, and the OR was 1.851 (95% CI = 0.828-3.567); Model 7 was a patient with BCQ+, BCQ-, and BCQs, and the OR was 3.826 (95% CI = 2.954-4.932) (Table 5).

# 4. DISCUSSION

( )

This study is the first to investigate the relationship between different TCM body constitutions and IBS, including single TCM body constitutions: BCQ+, BCQ-, BCQs, and combined TCM body constitutions: BCQ+ + BCQ-, BCQ+ + BCQs, BCQ- + BCQs, BCQ++ BCQ- + BCQs. We observed that an imbalanced TCM body constitution is a risk factor for IBS, increasing the likelihood of the patient developing IBS by 1.096 to 3.948 times.

There are two common and objective BCQ widely used in TCM: the Constitution in Chinese Medicine Questionnaire (CCMQ), developed in China, and the BCQ in Taiwan.<sup>34-36,44-46</sup> Although the objective testing tools for TCM body constitutions in China and Taiwan are very similar; after all, their lifestyles and cultures are different.<sup>47</sup> In this study, the reliability and validity of the BCQ, a Taiwanese TCM body constitution research tool that has been validated in many studies, was used to classify patients with IBS.<sup>35,48-50</sup> Our study found significant differences in depression, somatic comorbidities, hematology tests, and biochemistry examinations among individuals with imbalanced TCM body constitutions.31,51,52 In addition, our study also found that personal health behavior and dietary characteristics influenced the imbalance of TCM body constitutions.<sup>53–55</sup> It was also worth noting that our study found that drug allergy, depression, somatic comorbidities, and nutritional characteristics of patients with IBS were significantly different from those of subjects with non-IBS in the Gentleness constitution. It was reasonable to speculate that the BCQ in TWB is a cumulative score calculation. The scores of BCQ+, BCQ-, and BCQs questionnaires were at the margin of attainment for these patients who had a Gentleness constitution but suffered from IBS

On the other hand, most modern medical studies have confirmed that demographic characteristics such as lifestyle and psychological factors are risk factors for IBS.56,57 Age, female, married, functional dyspepsia (FD), and gastroesophageal reflux disease (GERD) have been reported to be strongly associated with the prevalence of IBS, especially in women.56-60 Women have a higher rate of IBS than men, which may be related to visceral sensitivity, central nervous system pain management, psychological characteristics, and the specific effects of estrogen and progesterone on bowel function.<sup>61</sup> In addition, people with psychological disorders have a higher incidence of IBS, which may be related to the gut-brain axis and changes in gut microbes.62 Compared with younger patients, the coping ability of older patients increases with age, which may also be closely related to IBS.63 In TCM, bad lifestyle and dietary habits could cause deviations in the patient's body constitution; for example, people with BCQs are usually characterized by smoking, irregular sleep-wake rhythms, and less activity.64 Past studies have shown that a good lifestyle could improve symptoms of IBS and productivity and quality of life for patients with IBS.65,66

Previous studies have shown that age, gender, consumption of irritating foods, and some psychiatric disorders, including anxiety and depression, could contribute to the development of IBS.<sup>67–69</sup> Many patients with IBS also have intestinal comorbidities and/

	-bueV	deficiency (N – 21	161)a	Vina.d	laficiancy (N – 25	231\b		., tacie (N – 2335)°		Gen	Hanace (N – 0/F
		uelicielicy (N = 2)		n-filli		2/100					
	-	BS		B	S		B	S		B	6
		No			No			No			No
	Yes N = 180 (5.7)	N = 2981 (94.3)		Yes N = 164 (4.9)	N = 3167 (95.1)		Yes N = 124 (5.3)	N = 2211 (94.7)		Yes N = 162 (1.7)	N = 9297 (98.3)
<b>Characteristics</b>	Z	(%)	þ	N	(%	d	N	(%	d	N (S	(%
Age	$46.39 \pm 9.81$	$45.41 \pm 10.38$	0.158 <sup>d</sup>	$46.82 \pm 9.59$	$46.58 \pm 10.51$	0.642 <sup>d</sup>	$45.94 \pm 9.44$	$44.87 \pm 10.15$	0.179 <sup>d</sup>	$49.38 \pm 10.02$	$49.59 \pm 10.64$
Sex			0.113			1.000			0.162		
Male	52 (28.9)	698 (23.4)		47 (28.7)	899 (28.4)		35 (28.2)	495 (22.4)		80 (49.4)	3992 (42.9)
Female	128 (71.1)	2283 (76.6)		117 (71.3)	2268 (71.6)		89 (71.8)	1716 (77.6)		82 (50.6)	5305 (57.1)
Education level			0.447			0.078			0.408		
Junior high or below	9 (5)	242 (8.1)		8 (4.8)	327 (10.3)		6 (4.8)	182 (8.2)		16 (9.9)	1186 (12.8)
Senior high (vocational)	58 (32.2)	867 (29.1)		53 (32.3)	949 (30.0)		39 (31.5)	649 (29.4)		45 (27.8)	2893 (31.1)
College or above	113 (62.8)	1870 (62.7)		103 (62.8)	1889 (59.7)		79 (63.7)	1378 (62.4)		101 (62.4)	5209 (56.1)
Employment			0.319			0.444			0.366		
Yes	132 (73.3)	2062 (69.5)		116 (70.7)	2131 (67.5)		93 (75.0)	1556 (70.8)		100 (62.5)	6036 (65.3)
No	48 (26.7)	904 (30.5)		48 (29.3)	1024 (32.5)		31 (25.0)	642 (29.2)		60 (37.5)	3208 (34.7)
Body mass index	$23.36 \pm 3.76$	$23.63 \pm 3.89$	0.204	$23.53 \pm 3.79$	$24.00 \pm 3.92$	$0.054^d$	$23.82 \pm 3.84$	$24.15 \pm 4.15$	0.342 <sup>d</sup>	$23.78 \pm 3.04$	$24.25 \pm 3.52$
Drug allergies	22 (12.2)	347 (11.6)	0.907	21 (12.8)	348 (11.0)	0.552	16 (12.9)	247 (11.2)	0.654	26 (16.0)	679 (7.3)
Depression	21 (11.7)	184 (6.2)	0.006	18 (11.0)	182 (5.7)	0.010	14 (11.3)	150 (6.8)	0.084	17 (10.5)	208 (2.2)
Headache	94 (52.2)	1394 (46.8)	0.178	87 (53.0)	1424 (45.0)	0.051	70 (56.5)	1137 (51.4)	0.318	46 (28.4)	1746 (18.8)
Migraine	13 (7.2)	163 (5.5)	0.407	11 (6.7)	167 (5.3)	0.536	10 (8.1)	137 (6.2)	0.520	8 (4.9)	158 (1.7)
Cervicalgia	126 (70.0)	1794 (60.2)	0.011	110 (67.1)	1846 (58.3)	0.032	90 (72.6)	1446 (65.4)	0.123	58 (35.8)	2769 (29.8)
Low back pain	114 (63.3)	1609 (54.0)	0.018	104 (63.4)	1599 (50.5)	0.002	72 (58.1)	1230 (55.6)	0.661	52 (32.1)	2443 (26.3)
Arthritis	15 (8.3)	171 (5.7)	0.202	17 (10.4)	191 (6.0)	0.038	8 (6.5)	132 (6.0)	0.980	16 (9.9)	358 (3.9)

# Original Article. (2024) 87:5

www.ejcma.org

Table 1

561

<sup>4</sup>vang-deficiency. 656 (only Yang-deficiency) + 637 (Yang-deficiency + Ying-deficiency) + 284 (Yang-deficiency + Stasis). <sup>4</sup>Ving-deficiency. 854 (only Ying-deficiency) + 637 (Yang-deficiency + Ying-deficiency + 256 (Ying-deficiency + Stasis) + 1584 (Yang-deficiency + Ying-deficiency + Stasis). <sup>5</sup>Stasis: 211 (only Stasis) + 284 (Yang-deficiency + Stasis) + 256 (Ying-deficiency + Stasis) + 1584 (Yang-deficiency + Ying-deficiency + Stasis). <sup>6</sup>Idependent *t* test.

IBS = irritable bowel syndrome; TCM = traditional Chinese medicine.

۲

J Chin Med Assoc

۲

0.514

0.054° <0.001 <0.003 0.003 0.005 0.116 0.115 <0.001

0.642<sup>d</sup> 0.118

þ

6

0.241

۲

Relationship between TCM body constitutions, hematology test, biochemistry examination (N = 13 941) Table 2

۲

Liao et al.

	Yang-	deficiency (N = 3	161) <sup>a</sup>	- Ying-	deficiency (N = 33 sc	331) <sup>b</sup>		stasis (N = 2335)° sc		Gen	tleness (N = 9456 c	
	- - - - - - - - 	N0 1 - 2081		2 Voc	N0 N1 - 2167		a Sov	N0 N = 2211		2 00 00	N0 N - 0207	
	N = 180 (5.7)	N = 2301 (94.3)		nes N = 164 (4.9)	u = 5107 (95.1)		N = 124 (5.3)	u = 22 II (94.7)		nes N = 162 (1.7)	N = 3237 (98.3)	
<b>Characteristics</b>	Mean	1 ± SD	d	Mean	i ± SD	d	Mean	I ± SD	d	Mean	± SD	d
WBC count (10 <sup>3</sup> /µL)	$5.38 \pm 1.40$	$5.80 \pm 1.43$	<0.001	$5.41 \pm 1.38$	$5.86 \pm 1.45$	<0.001	$5.53 \pm 1.48$	$5.88 \pm 1.44$	0.005	$5.79 \pm 1.43$	$5.83 \pm 1.41$	0.999
Total bilirubin (mg/dL)	$0.69 \pm 0.32$	$0.64 \pm 0.29$	0.119	$0.67 \pm 0.27$	$0.66 \pm 0.28$	0.561	$0.69 \pm 0.30$	$0.63 \pm 0.27$	0.020	$0.68 \pm 0.29$	$0.68 \pm 0.28$	0.561
Albumin (g/dL)	$4.56 \pm 0.25$	$4.53 \pm 0.26$	0.036	$4.57 \pm 0.25$	$4.54 \pm 0.24$	0.065	$4.59 \pm 0.24$	$4.52 \pm 0.27$	0.001	$4.60 \pm 0.26$	$4.56 \pm 0.24$	0.065
6AST (U/L)	$21.89 \pm 5.81$	$20.98 \pm 5.57$	0.036	$21.88 \pm 5.72$	$21.25 \pm 5.58$	0.173	$22.35 \pm 6.31$	$20.96 \pm 5.49$	0.016	$23.47 \pm 5.66$	$21.97 \pm 5.57$	0.173
lpha-Fetoprotein (ng/mL)	$2.99 \pm 1.01$	$2.83 \pm 0.97$	0.018	$2.98 \pm 1.00$	$2.87 \pm 0.98$	0.078	$3.06 \pm 0.97$	$2.83 \pm 0.97$	0.001	$2.91 \pm 0.88$	$2.92 \pm 0.98$	0.078
6ACT concernation	I oldofiwi	TOM Standard Louis	ido locacitibout	incoo modicino. MIDO	Incode of the state of the stat							

<sup>6</sup>AST = aspartate transaminase; IBS = irritable bowel syndrome; TCM = traditional Chinese medicine; WBC = white blood cell. <sup>4</sup>Yang-deficiency; 656 (only Yang-deficiency) + 637 (Yang-deficiency + Ying-deficiency) + 284(Yang-deficiency + Stasis), + 1584 (Yang-deficiency + Ying-deficiency + Stasis). <sup>4</sup>Ying-deficiency; 854 (only Ying-deficiency) + 637 (Yang-deficiency + Ying-deficiency + 248, Yang-deficiency + Ying-deficiency + Stasis). <sup>5</sup>Stasis: 211 (only Stasis) + 284 (Yang-deficiency + Stasis) + 1584 (Yang-deficiency + Stasis).

# Table 3

Relationship between TCM body constitutions, with lifestyles (N = 13 941)

۲

	3	ig-uciliation (in -	3101)"	1		1100				20		
		IBS			IBS			IBS			IBS	
	Yes N = 180 (5.7)	No N = 2981 (94.3)	I	Yes N = 164 (4.9)	No N = 3167 (95.1)		Yes N = 124 (5.3)	No N = 2211 (94.7)		Yes N = 162 (1.7)	No N = 9297 (98.3)	
Characteristics		N (%)	d	2	1 (%)	d		1 (%)	d		1 (%)	d
Personal health behav	iors											
Alcohol	11 (6.1)	133 (4.5)	0.397	9 (5.5)	167 (5.3)	0.356	9 (7.3)	111 (5.0)	0.374	9 (5.6)	530 (5.7)	0.997
Cigarette	13 (52.0)	223 (53.6)	0.899	10 (43.5)	278 (52.9)	0.521	9 (45.0)	194 (59.5)	0.394	6 (24.0)	685 (39.5)	0.234
Exercise	75 (41.7)	942 (31.6)	0.006	66 (40.2)	1077 (34.0)	0.120	41 (33.1)	637 (28.8)	0.361	84 (51.9)	4242 (45.6)	0.134
Dietary characteristics												
Tea	50 (27.8)	1001 (33.6)	0.128	42 (25.6)	1083 (34.2)	0.029	37 (29.8)	781 (35.3)	0.251	42 (25.9)	3289 (35.4)	0.016
Coffee	65 (36.1)	1161 (38.9)	0.497	64 (39.0)	1212 (38.3)	0.911	51 (41.1)	874 (39.5)	0.795	58 (35.8)	3271 (35.2)	0.936
Vegetarian	18 (10.0)	136 (4.6)	0.004	15 (9.1)	124 (3.9)	0.005	10 (8.1)	93 (4.2)	0.088	10 (6.2)	490 (5.3)	0.828
Nutritional	62 (34.4)	835 (28.0)	0.171	61 (37.2)	905 (28.6)	0.058	46 (37.1)	618 (28.0)	0.063	67 (41.4)	2821 (30.3)	0.007
supplement												

J Chin Med Assoc

www.ejcma.org

# Table 4

Relationship between TCM body constitutions and IBS

		Yang-deficiency			Ying-deficiency			Stasis	
	Yes N = 3161	No N = 10 780		Yes N = 3331	No N = 10 610		Yes N = 2335	No N = 11 606	
Characteristics		N (%)	p		N (%)	p		N (%)	р
IBS			<0.001			<0.001			< 0.001
Yes No	180 (5.7) 2981 (94.3)	192 (1.8) 10 588 (98.2)		164 (4.9) 3167 (95.1)	208 (2.0) 10 402 (98.0)		124 (5.3) 2211 (94.7)	248 (2.1) 11 358 (97.9)	

IBS = irritable bowel syndrome; TCM = traditional Chinese medicine.

# Table 5

------

Multiple logistic regression of IBS symptoms for different types of TCM body constitutions

IBS, OR (95% CI)		
	OR (95% CI)	р
Intercept	0.017 (0.015-0.020)	<2e-16
Model 1	2.654 (1.740-3.910)	2.10E-06
Model 2	1.096 (0.627-1.782)	0.7296
Model 3	1.680 (0.654-3.520)	0.2188
Model 4	3.948 (2.742-5.560)	2.26E-14
Model 5	2.312 (1.170-4.112)	0.0083
Model 6	1.851 (0.828-3.567)	0.0941
Model 7	3.826 (2.954-4.932)	<2e-16

Model 1: only Yang-deficiency; Model 2: only Ying-deficiency; Model 3: only Stasis; Model 4: Yangdeficiency + Ying-deficiency; Model 5: Yang-deficiency + Stasis; Model 6: Ying-deficiency + Stasis; Model 7: Yang-deficiency + Ying-deficiency + Stasis.

IBS = irritable bowel syndrome; OR = odds ratio; TCM = traditional Chinese medicine

or extraintestinal comorbidities, such as FD, GERD, fibromyalgia, chronic fatigue syndromes, and chronic pelvic pain.<sup>70</sup> The same study also showed that one or more comorbidities were associated with more significant medical needs, poorer prognosis, and higher levels of anxiety and depression. In this context, we also investigated the relationship between drug allergy, depression, comorbidities, hematology test, biochemistry examination, personal health behaviors, dietary characteristics and IBS to verify the differences in TCM body constitutions in IBS patients. According to TCM theory, body constitution is related to body structure, physiological function, and psychological state, and a dynamic balance between Ying and Yang is necessary to maintain health.<sup>32</sup> Yang is the "energy" that regulates the function of the body's organs, ensures the balance of body fluids, and maintains temperature; Ying is the "substance" that includes blood, fluids, and nutrients needed by organs and tissues.<sup>71</sup> Even if there is no disease, an imbalance of Ying-Yang in the body will be classified as one of two significant types of deficiency: Yang-deficiency or Ying-deficiency.<sup>49</sup> People with low physiological energy are Yang-deficiency, and those with fluid deficiency are Ying-deficiency.<sup>49</sup> When the Ying and Yang activities in the body are obstructed, the TCM body constitution is Stasis.<sup>36</sup> According to TCM, Yang-deficiency patients often have cold limbs and a pale complexion because they lack the energy needed for whole-body circulation. Li et al<sup>72</sup> established a rat model of Yang-deficiency-IBS by mechanical and chemical colon irritants. They found that changes in the intestinal immune system affect the brain-gut axis and alter gastrointestinal function, which could explain the correlation between Yang-deficiency and IBS.72 Patients with Ying-deficiency tend to have dry and hot skin due to lack of fluid, often manifesting as dry cough, little tears, intestinal heat, and constipation.73 Patients with Stasis

www.ejcma.org

often have celiac disease, inflammatory bowel disease, IBS, and obesity due to poor blood circulation in the body as well as damage to the mucus layer of the digestive tract and changes in permeability.<sup>74</sup> However, these pathological and physiological mechanisms between Yang-deficiency, Ying-deficiency, and Stasis and IBS still need to be further investigated.

Western medicine treats IBS differently depending on the symptoms and severity. Treatments include cognitive behavioral therapy, hypnotherapy, antispasmodics, tricyclic antidepressants, ispaghula, 5-HT3 antagonists, 5-HT4 agonists, and selective serotonin reuptake inhibitors to improve overall symptoms in patients with IBS.75 In recent years, more and more patients with IBS have turned to TCM after the ineffective treatment of Western medicine.76 TCM believes that the patient's body is unique and that treatment should be based on the overall body condition, paying attention to all the patient's symptoms and understanding the body constitutions so that appropriate treatment and preventive measures could be provided.<sup>29,77</sup> In TCM, different body constitutions are treated with Chinese herbal medicines or acupuncture points, which are adjusted according to the individual's clinical performance. For example, Yang-deficiency patients often feel cold and have a decrease in subcutaneous fat; Ying-deficiency patients often have dry mouth, dry eyes, hot flashes, constipation, decreased urine output, and insomnia; and Stasis patients often have metabolic diseases such as obesity and diabetes.<sup>29,64,78-80</sup> Xiao et al<sup>81</sup> summarized clinical randomized controlled trials from 1998 to 2013. They concluded that, in general, Chinese herbal medicines could modulate neurotransmitters and hormones of the intestinal nervous system, regulate smooth muscle movement in the gastrointestinal tract, modulate the hypothalamic-pituitary-adrenal axis, reduce intestinal inflammation, and restore intestinal flora.81

TCM provides a comprehensive method for addressing IBS, a disorder characterized by symptoms such as stomach discomfort, bloating, diarrhea, and constipation.24 TCM has specific therapy methods for addressing IBS associated with Yang deficit, Yin deficiency, and Stasis.<sup>82</sup> Yang-deficiency in the setting of IBS might present as peripheral vasoconstriction, a tendency to seek warmth, diarrhea, and lethargy.83 Herbs with thermogenic properties that enhance the function of the Spleen and Stomach, such as Fu Zi (Aconite) and Gan Jiang (Dried Ginger), are often used.<sup>87</sup> Yin deficit may cause symptoms such as dry mouth, constipation, and a feeling of heat, particularly in the afternoon or evening.48 Herbs such as Sheng Di Huang (Rehmannia) and Mai Men Dong (Ophiopogon) are utilized to eliminate heat and replenish yin.<sup>84</sup> Stasis denotes the state of Qi (energy) or Blood being stagnant, resulting in symptoms such as persistent, piercing abdominal discomfort, swelling, and even dark-colored feces.<sup>85</sup> Commonly used herbs, such as Dan Shen (Salvia) and Chuan Xiong (Ligusticum), enhance blood circulation and alleviate Stasis.85 Patients should prioritize discussing their use of TCM with their healthcare practitioner, particularly if they are also receiving conventional

 $( \bullet )$ 

#### Liao et al.

therapies for IBS.<sup>86</sup> Due to the diverse range of causes and symptoms associated with IBS, a complete strategy that incorporates stress management, dietary adjustments, and lifestyle modifications in conjunction with TCM might provide holistic treatment.<sup>81</sup>

BCQ reflects individual health status and health trends regarding physiological differences, life course, psychological status, and adaptive stress to the natural and social environment. Our study demonstrated that Yang-deficiency, Ying-deficiency, and Stasis correlate with IBS. From the perspective of preventive medicine, the future focus will change from passive symptom treatment to active disease prevention. As patients with IBS are not fully satisfied with the efficacy of Western medicine, integrated Chinese and Western medical treatment might be the future trend. Individualized treatment should be provided to patients with different TCM body constitutions to improve and alleviate the symptoms of IBS.

Clinical trial design and analysis frequently depend on underlying assumptions that, if ignored, can significantly impact the results. Sensitivity analysis is essential for evaluating these potential effects. Additional exploration into TCM has yielded noteworthy impacts on IBS. We intend to conduct an analysis, both with and without adjustments for baseline characteristics, while examining various thresholds or definitions for outcome assessment.

In conclusion, participants with BCQ+, BCQ-, or BCQs were prone to IBS. In the future, we could provide different health education and precise treatment for patients with IBS with different TCM body constitutions in a preventive medicine approach to alleviate the discomfort of patients. We recommend that patients with IBS receive not only conventional treatment from Western medicine but also TCM to stop the vicious cycle and reduce the discomfort caused by the disease.

### ACKNOWLEDGMENTS

This research was funded by the Ministry of Science and Technology (MOST 110-2314-B-032-001 and 112-2314-B-032-001) and Taipei Veterans General Hospital (V112C-215) in Taiwan.

We acknowledge the staff at Taiwan Biobank for their hard work in collecting and distributing the data. We thank the Big Data Center, Taipei Veterans General Hospital, Medical Scholarship Foundation in memory of Professor Albert Ly-Young Shen, and Tamkang University of Taiwan.

#### REFERENCES

- 1. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG clinical guideline: management of irritable bowel syndrome. *Am J Gastroenterol* 2021;116:17–44.
- 2. Huysmans E, Leemans L, Beckwée D, Nijs J, Ickmans K, Moens M, et al. The relationship between cognitive and emotional factors and healthcare and medication use in people experiencing pain: a systematic review. *J Clin Med* 2020;9:2486.
- Häuser W, Marschall U, Layer P, Grobe T. The prevalence, comorbidity, management and costs of irritable bowel syndrome: an observational study using routine health insurance data. *Dtsch Arztebl Int* 2019;116:463–70.
- 4. Polster AV, Palsson OS, Törnblom H, Öhman L, Sperber AD, Whitehead WE, et al. Subgroups of IBS patients are characterized by specific, reproducible profiles of GI and non-GI symptoms and report differences in healthcare utilization: a population-based study. *Neurogastroenterol Motil* 2019;31:e13483.
- Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018. *Gastroenterology* 2019;156:254–72. e11.

- 6. Ng QX, Soh AYS, Loke W, Lim DY, Yeo W-S. The role of inflammation in irritable bowel syndrome (IBS). J Inflamm Res 2018;11:345–9.
- Simrén M, Castedal M, Svedlund J, Abrahamsson H, Björnsson E. Abnormal propagation pattern of duodenal pressure waves in the irritable bowel syndrome (IBS). *Dig Dis Sci* 2000;45:2151–61.
- 8. Nozu T, Kudaira M, Kitamori S, Uehara A. Repetitive rectal painful distention induces rectal hypersensitivity in patients with irritable bowel syndrome. *J Gastroenterol* 2006;41:217–22.
- Liebregts T, Adam B, Bredack C, Röth A, Heinzel S, Lester S, et al. Immune activation in patients with irritable bowel syndrome. *Gastroenterology* 2007;132:913–20.
- Jeffery IB, O'toole PW, Öhman L, Claesson MJ, Deane J, Quigley EM, et al. An irritable bowel syndrome subtype defined by species-specific alterations in faecal microbiota. *Gut* 2012;61:997–1006.
- Lupascu A, Gabrielli M, Lauritano EC, Scarpellini E, Santoliquido A, Cammarota G, et al. Hydrogen glucose breath test to detect small intestinal bacterial overgrowth: a prevalence case-control study in irritable bowel syndrome. *Aliment Pharmacol Ther* 2005;22:1157–60.
- 12. Camilleri M. Diagnosis and treatment of irritable bowel syndrome: a review. *JAMA* 2021;325:865–77.
- 13. Monsbakken KW, Vandvik PO, Farup PG. Perceived food intolerance in subjects with irritable bowel syndrome–etiology, prevalence and consequences. *Eur J Clin Nutr* 2006;60:667–72.
- Lembo A, Zaman M, Jones M, Talley NJ. Influence of genetics on irritable bowel syndrome, gastro-oesophageal reflux and dyspepsia: a twin study. *Aliment Pharmacol Ther* 2007;25:1343–50.
- Drossman DA, Thompson WG. The irritable bowel syndrome: review and a graduated multicomponent treatment approach. *Ann Intern Med* 1992;116(12\_Part\_1):1009–16.
- Zhu Y, Zheng X, Cong Y, Chu H, Fried M, Dai N, et al. Bloating and distention in irritable bowel syndrome: the role of gas production and visceral sensation after lactose ingestion in a population with lactase deficiency. *Am J Gastroenterol* 2013;108:1516–25.
- 17. Yang J, Deng Y, Chu H, Cong Y, Zhao J, Pohl D, et al. Prevalence and presentation of lactose intolerance and effects on dairy product intake in healthy subjects and patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2013;11:262–8.e1.
- Vazquez–Roque MI, Camilleri M, Smyrk T, Murray JA, Marietta E, O'Neill J, et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. *Gastroenterology* 2013;144:903–11.e3.
- Chapman R, Stanghellini V, Geraint M, Halphen M. Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. *Am J Gastroenterol* 2013;108:1508–15.
- Zheng L, Lai Y, Lu W, Li B, Fan H, Yan Z, et al. Pinaverium reduces symptoms of irritable bowel syndrome in a multicenter, randomized, controlled trial. *Clin Gastroenterol Hepatol* 2015;13:1285–92.e1.
- Clouse RE, Lustman P, Geisman R, Alpers D. Antidepressant therapy in 138 patients with irritable bowel syndrome: a five-year clinical experience. *Aliment Pharmacol Ther* 1994;8:409–16.
- Brandt LJ, Chey WD, Foxx-Orenstein AE, Quigley EM, Schiller LR, Schoenfeld PS, et al. An evidence-based systematic review on the management of irritable bowel syndrome. Am J Gastroenterol 2009;104:S8–35.
- 23. Basilisco G, Barbara G, Bellini M, Cataudella G, D'Alba L, et al; Group ISoNMS. Patient dissatisfaction with medical therapy for chronic constipation or irritable bowel syndrome with constipation: analysis of N-of-1 prospective trials in 81 patients. *Aliment Pharmacol Ther* 2020;51:629–36.
- 24. Yan J, Miao ZW, Lu J, Ge F, Yu LH, Shang WB, et al. Acupuncture plus Chinese herbal medicine for irritable bowel syndrome with diarrhea: a systematic review and meta-analysis. *Evid Based Comp Alternat Med* 2019;2019:7680963.
- 25. Wu IX, Wong CH, Ho RS, Cheung WK, Ford AC, Wu JC, et al. Acupuncture and related therapies for treating irritable bowel syndrome: overview of systematic reviews and network meta-analysis. *Therap Adv Gastroenterol* 2019;12:1756284818820438.
- Bensoussan A, Talley NJ, Hing M, Menzies R, Guo A, Ngu M. Treatment of irritable bowel syndrome with Chinese herbal medicine: a randomized controlled trial. *JAMA* 1998;280:1585–9.
- Leung WK, Wu JC, Liang S, Chan L, Chan FK, Xie H, et al. Treatment of diarrhea-predominant irritable bowel syndrome with traditional Chinese herbal medicine: a randomized placebo-controlled trial. *Am J Gastroenterol* 2006;101:1574–80.

564

www.ejcma.org

( )

**(** 

- Li DY, Dai YK, Zhang YZ, Huang MX, Rl Li, Ou-Yang J, et al. Systematic review and meta-analysis of traditional Chinese medicine in the treatment of constipation-predominant irritable bowel syndrome. *PLoS One* 2017;12:e0189491.
- 29. Li L, Yao H, Wang J, Li Y, Wang Q. The role of Chinese medicine in health maintenance and disease prevention: application of constitution theory. *Am J Chin Med* 2019;47:495–506.
- 30. Wong W, Lam CLK, Wong VT, Yang ZM, Ziea ET, Kwan AKL. Validation of the constitution in Chinese medicine questionnaire: does the traditional Chinese medicine concept of body constitution exist? *Evid Based Comp Alternat Med* 2013;2013:481491.
- 31. Wang J, Wang Q, Li L, Li Y, Zhang H, Zheng L, et al. Phlegm-dampness constitution: genomics, susceptibility, adjustment and treatment with traditional Chinese medicine. *Am J Chin Med* 2013;41:253–62.
- Sun Y, Zhao Y, Xue SA, Chen J. The theory development of traditional Chinese medicine constitution: a review. J Tradit Chin Med 2018;5:16–28.
- 33. Xue L, Qi W, Zeqiang J, Zhuqing L, Mengxing Z, Peiying Y, et al. Clinical research linking Traditional Chinese Medicine constitution types with diseases: a literature review of 1639 observational studies. *J Tradit Chin Med* 2020;40:690–702.
- 34. Su YC, Chen LL, Lin JD, Lin JS, Huang YC, Lai JS. BCQ+: a body constitution questionnaire to assess Yang-Xu: part I: establishment of a first final version through a Delphi process. *Forsch Komplement Med* (2006) 2008;15:327–34.
- 35. Lin JS, Chen LL, Lin JD, Chang CH, Huang CH, Mayer PK, et al. BCQ-: a Body constitution questionnaire to assess Yin-Xu: Part II: evaluation of reliability and validity. *Comp Med Res* 2012;19:285–92.
- Lin JD, Lin JS, Chen LL, Chang CH, Huang YC, Su YC. BCQs: a body constitution questionnaire to assess stasis in traditional Chinese medicine. *Eur J Integr Med* 2012;4:e379–91.
- 37. Chen CH, Yang JH, Chiang CW, Hsiung CN, Wu PE, Chang LC, et al. Population structure of Han Chinese in the modern Taiwanese population based on 10,000 participants in the Taiwan Biobank project. *Hum Mol Genet* 2016;25:5321–31.
- Fan CT, Lin JC, Lee CH. Taiwan Biobank: a project aiming to aid Taiwan's transition into a biomedical island. *Pharmacogenomics* 2008;9:235–46.
- 39. Chiu TH, Huang YC, Chiu H, Wu PY, Chiou HYC, Huang JC, et al. Comparison of various obesity-related indices for identification of metabolic syndrome: a population-based study from Taiwan biobank. *Diagnostics* 2020;10:1081.
- Huang YH, Liao SF, Khor SS, Lin YJ, Chen HY, Chang YH, et al. Largescale genome-wide association study identifies HLA class II variants associated with chronic HBV infection: a study from Taiwan Biobank. *Aliment Pharmacol Ther* 2020;52:682–91.
- 41. Lin E, Kuo PH, Lin WY, Liu YL, Yang AC, Tsai SJ. An association study in the Taiwan Biobank elicits three novel candidates for cognitive aging in old adults: NCAM1, TTC12 and ZBTB20. *Aging* 2021;13:18769–88.
- 42. Hsueh KC, Nfor ON, Hsu SY, Yang SF, Liaw YP. Type 2 diabetes, PNPLA3 rs738409 polymorphism, and the risk of liver cirrhosis: analysis of Taiwan Biobank. *Front Genet* 2022;13:822700.
- Chen CH, Lee JI, Jhan JH, Lee YC, Geng JH, Chen SC, et al. Secondhand smoke increases the risk of developing kidney stone disease. *Sci Rep* 2021;11:17694.
- 44. Chen LL, Lin JS, Lin JD, Chang CH, Kuo HW, Liang WM, et al. BCQ+: a body constitution questionnaire to assess Yang-Xu: part II: evaluation of reliability and validity. *Forsch Komplement Med* (2006) 2009;16:20–7.
- 45. Lin JD, Chen LL, Lin JS, Chang CH, Huang YC, Su YC. BCQ: a body constitution questionnaire to assess Yin-Xu part I: establishment of a provisional version through a Delphi process. *Forsch Komplement Med* (2006) 2012;19:234–41.
- 46. Qi W. Classification and diagnosis basis of nine basic constitutions in Chinese medicine. *Tradit Chin Med* 2005;28:1.
- Wong W, Lam CLK, Su YC, Lin SJS, Ziea ETC, Wong VT, et al. Measuring body constitution: validation of the body constitution questionnaire (BCQ) in Hong Kong. *Complement Ther Med* 2014;22:670–82.
- Lee S, Park J, Lee H, Kim K. Development and validation of Yindeficiency questionnaire. Am J Chin Med 2007;35:11–20.
- 49. Langevin HM, Badger GJ, Povolny BK, Davis RT, Johnston AC, Sherman KJ, et al. Yin scores and yang scores: a new method for quantitative diagnostic evaluation in traditional Chinese medicine research. *J Altern Complement Med* 2004;10:389–95; discussion 387.

(

www.ejcma.org

Kim H, Kim J. Reliability and validity of a cold-heat

J Chin Med Assoc

- Ryu H, Lee H, Kim H, Kim J. Reliability and validity of a cold-heat pattern questionnaire for traditional Chinese medicine. J Altern Complement Med 2010;16:663–7.
- 51. Chen SL, Liu YT, Hsueh KC, Tang PL. Body constitution of traditional Chinese medicine caused a significant effect on depression in adult women. *Complement Ther Clin Pract* 2021;42:101288.
- 52. Lai NS, Lu MC, Chang HH, Lo HC, Hsu CW, Huang KY, et al. Association of traditional Chinese medicine body constitution and health-related quality of life in female patients with systemic lupus ery-thematosus: a cross-sectional study. *Evid-Based Complement Alter Med* 2021;2021:1–11.
- 53. Bai Q, Chuang Y, Zhao Y, Wang Y, Ge P, Xu Y, et al. The correlation between demographical and lifestyle factors and traditional Chinese medicine constitution among Macau elderly individuals. *Evid -Based Complement Alter Med* 2021;2021:1–9.
- 54. Xu Z, Chen Y, Yu D, Feng D, Tang C, Li T, et al. Optimal exercise intensity and volume to impact rats with Traditional Chinese Medicine phlegm-dampness constitution. *Sports Med health sci* 2021;3:28–33.
- 55. Shi M, Liu Z, Xu M, Chen J, Lin B, Yu Y, et al. Relationship between life habits and constitution types of Chinese medicine in the senile living at home in Beijing downtown. *Chin J Integr Med* 2016;36:564–9.
- Talley NJ, Zinsmeister AR, Melton III LJ. Irritable bowel syndrome in a community: symptom subgroups, risk factors, and health care utilization. Am J Epidemiol 1995;142:76–83.
- 57. Yilmaz S, Dursun M, Ertem M, Canoruc F, Turhanoğlu A. The epidemiological aspects of irritable bowel syndrome in Southeastern Anatolia: a stratified randomised community-based study. *Int J Clin Pract* 2005;59:361–9.
- Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol* 2012;10:712–21.e4.
- 59. Jung HK, Halder S, McNally M, Locke Iii G, Schleck C, Zinsmeister A, et al. Overlap of gastro-oesophageal reflux disease and irritable bowel syndrome: prevalence and risk factors in the general population. *Aliment Pharmacol Ther* 2007;26:453–61.
- Wang A, Liao X, Xiong L, Peng S, Xiao Y, Liu S, et al. The clinical overlap between functional dyspepsia and irritable bowel syndrome based on Rome III criteria. *BMC Gastroenterol* 2008;8:1–7.
- Chang L, Heitkemper MM. Gender differences in irritable bowel syndrome. Gastroenterology 2002;123:1686–701.
- Mudyanadzo TA, Hauzaree C, Yerokhina O, Architha NN, Ashqar HM. Irritable bowel syndrome and depression: a shared pathogenesis. *Cureus* 2018;10:e3178.
- Karevold E, Ystrom E, Coplan RJ, Sanson AV, Mathiesen KS. A prospective longitudinal study of shyness from infancy to adolescence: stability, age-related changes, and prediction of socio-emotional functioning. J Abnorm Child Psychol 2012;40:1167–77.
- Yao H, Mo S, Wang J, Li Y, Wang CZ, Wan JY, et al. Genome-wide DNA methylation profiles of phlegm-dampness constitution. *Cell Physiol Biochem* 2018;45:1999–2008.
- Lustyk KM, Jarrett ME, Bennett JC, Heitkemper MM. Does a physically active lifestyle improve symptoms in women with irritable bowel syndrome? *Gastroenterol Nurs* 2001;24:129–37.
- Okami Y, Kato T, Nin G, Harada K, Aoi W, Wada S, et al. Lifestyle and psychological factors related to irritable bowel syndrome in nursing and medical school students. J Gastroenterol 2011;46:1403–10.
- Locke III G, Yawn B, Wollan P, Melton III L, Lydick E, Talley N. Incidence of a clinical diagnosis of the irritable bowel syndrome in a United States population. *Aliment Pharmacol Ther* 2004;19:1025–31.
- Eswaran S, Tack J, Chey WD. Food: the forgotten factor in the irritable bowel syndrome. *Gastroenterol Clin North Am* 2011;40:141–62.
- Qin HY, Cheng CW, Tang XD, Bian ZX. Impact of psychological stress on irritable bowel syndrome. World J Gastroenterol 2014;20:14126–31.
- Riedl A, Schmidtmann M, Stengel A, Goebel M, Wisser AS, Klapp BF, et al. Somatic comorbidities of irritable bowel syndrome: a systematic analysis. J Psychosom Res 2008;64:573–82.
- Chen LL, Su YC. Health promotion for deficient constitution in Chinese medicine. *Hu li za zhi* 2007;54:16–20.
- 72. Li Y, Su X, Wu P, Wang J, Guo Y, Zhu J, et al. Proteomics analysis of IBS-D with spleen and kidney yang deficiency. *J Tradit Chin Med* 2017;4:39–49.
- Shen M, Cui Y, Hu M, Xu L. Quantifying traditional Chinese medicine patterns using modern test theory: an example of functional constipation. BMC Complement Altern Med 2017;17:1–8.

#### Liao et al.

- 74. Park J, Choi TJ, Kang KS, Choi S-H. The interrelationships between intestinal permeability and phlegm syndrome and therapeutic potential of some medicinal herbs. *Biomolecules* 2021;11:284.
- 75. Spiller R, Aziz Q, Creed F, Emmanuel A, Houghton L, Hungin P, et al; Clinical Services Committee of The British Society of Gastroenterology. Guidelines on the irritable bowel syndrome: mechanisms and practical management. *Gut* 2007;56:1770–98.
- Spanier JA, Howden CW, Jones MP. A systematic review of alternative therapies in the irritable bowel syndrome. *Arch Intern Med* 2003;163:265–74.
- Weeks J. Chinese TCM renaissance and the global movement for integrative health and medicine. J Altern Complement Med 2017;23:79–81.
- Heli L, Li Z, Zhiqiang C, Huijuan J, Lei J. Physical and mental health conditions of young college students with different Traditional Chinese Medicine constitutions in Zhejiang Province of China. J Tradit Chin Med 2015;35:703–8.
- 79. Yu X, Sun S, Guo Y, Liu Y, Yang D, Li G, et al. Citri Reticulatae Pericarpium (Chenpi): botany, ethnopharmacology, phytochemistry, and pharmacology of a frequently used traditional Chinese medicine. J Ethnopharmacol 2018;220:265–82.
- Um SB, Yeom H, Kim NH, Kim HC, Lee HK, Suh I. Association between dry eye symptoms and suicidal ideation in a Korean adult population. *PLoS One* 2018;13:e0199131.

- 81. Xiao HT, Zhong L, Tsang SW, Lin ZS, Bian ZX. Traditional Chinese medicine formulas for irritable bowel syndrome: from ancient wisdoms to scientific understandings. *Am J Chin Med* 2015;43:1–23.
- 82. Jiang M, Yang J, Zhang C, Liu B, Chan K, Cao H, et al. Clinical studies with traditional Chinese medicine in the past decade and future research and development. *Planta Med* 2010;76:2048–64.
- 83. Zhu J, Liu S, Guo Y, Hou L, Su X, Li Y, et al. A new model of diarrhea with spleen-kidney yang deficiency syndrome. *Evid-Based Complement Alter Med* 2018;2018:4280343.
- Jiang TT, Li JC. Review on the systems biology research of Yindeficiency-heat syndrome in traditional Chinese medicine. *Anat Rec* 2023;306:2939–44.
- Zhang BH, Gao R, Li ZH, Li BS, Wang FY, Tang XD. Treatment of irritable bowel syndrome by Chinese medicine and pharmacy: an analysis of data mining on experiences of experts. *Chin J Integr Med* 2013;33:757–60.
- Manheimer E, Wieland SL, Cheng K, Li SM, Shen X, Berman BM, et al. Acupuncture for irritable bowel syndrome: systematic review and metaanalysis. Am J Gastroenterol 2012;107:835–47.
- Zhou Y, Xu B. New insights into molecular mechanisms of "Cold or Hot" nature of food: When East meets West. Food Res Intern 2021;144:1100361.