

A Systematic Review of Integrated Traditional Chinese and Western Medicine for Managing Irritable Bowel Syndrome

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Abstract: Traditional Chinese medicine (TCM) has been commonly used by Chinese practitioners to treat irritable bowel syndrome (IBS). However, the effectiveness of combining TCM with Western medicine in managing IBS has not been evaluated systematically. In this study, we evaluated the clinical effectiveness of combining TCM and Western medicine in the treatment of IBS via meta-analyses. We reviewed 72 eligible randomized controlled trials from January 2009 to December 2013 investigating the effectiveness of integrated TCM and Western medicine in the management of IBS. In the meta-analyses, the relative risks (RRs) and 95% confidence interval (95%CI) were calculated using raw data from each study, and low heterogeneity was detected. When compared to the Western medicine treatment alone, our result showed TCM combined with Western interventions significantly improved IBS global symptoms (RR, 1.21; 95%CI: 1.18–1.24). Additionally, there was no significant difference in therapeutic effects of the integrated approach in the meta-analyses involving the various IBS subtypes. Likewise, both Chinese proprietary herbal medicine plus conventional treatment and compound herbal preparations plus conventional treatment showed similar and statistically significant effects on global improvement compared with western treatment alone, with RRs of 1.22 (95%CI: 1.14–1.30) and 1.22 (95%CI: 1.18–1.27), respectively. These results demonstrated that treating IBS with integrated traditional Chinese and Western medicines showed better effectiveness than conventional Western medicine alone. Although

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due to the quality of the included studies, our results might possess a high risk of bias. TCM, particularly Chinese proprietary medicine, with the benefits of low-cost, easy to use, and good palatability, would be an attractive option to be used in conjunction with conventional Western medicine to manage IBS patients.

Keywords: Traditional Chinese Medicine; Integrated TCM and Western Medicine; Irritable Bowel Syndrome; Effectiveness; Systematic Review; Meta-Analysis.

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic or recurrent abdominal pain or discomfort, which is associated with disturbed defecation in the absence of morphological changes and biochemical abnormalities (Longstreth *et al.*, 2006; Chang and Talley, 2010). Based on the Rome III diagnostic criteria (Longstreth *et al.*, 2006), according to different bowel behaviors and IBS subtypes, they are presented as IBS-D (diarrhea-predominant), IBS-C (constipation-predominant), IBS-M (mixed), and unspecified IBS (IBS-U) (Brandt *et al.*, 2009). It is a common disease which affects about 5–20% of the population worldwide, depending upon the diagnostic criteria applied (Liu and Hou, 2011). For example, in two of the major cities in China, the prevalence of IBS was estimated to be 7.26% (Manning criteria) or 0.82% (Rome criteria) in Beijing (Pan *et al.*, 2000) and 11.5% (Manning criteria) or 5.67% (Rome criteria) in Guangdong (Xiong *et al.*, 2004). Besides suffering from the clinical symptoms and obvious negative impact on health-related quality of life, patients with this disorder would also require increased consumption of medical resources and shoulder a considerable economic burden (Quigley *et al.*, 2006; Nellesen *et al.*, 2013).

Despite the variety of approaches for symptom relief and quality of life improvement that have been used by clinicians and patients, symptoms of IBS are often recurrent and resistant to therapy. Many IBS sufferers, especially Chinese, who are not completely satisfied with the treatment outcomes, have turned to traditional Chinese medicine (TCM) for a remedy (Yoon *et al.*, 2011; Wen *et al.*, 2013). As a therapeutic discipline, TCM is derived and developed from the traditional Chinese physician's considerable clinical practice and experience over many centuries (Shergis *et al.*, 2013; Liu *et al.*, 2014b). In China, TCM is regularly used to treat IBS patients in either Western medicine hospitals or TCM hospitals. In the management of IBS, significant clinical therapeutic effects have been reported, with a number of TCM herbal mixtures specifically formulated based on the patients' symptoms (Wang *et al.*, 2008).

In China, TCM has been routinely used alongside Western or allopathic Medicine in the healthcare system (Gu *et al.*, 2013; Zhao *et al.*, 2014). In the new version of the Chinese National Essential Medicines List issued by the Ministry of Health in 2013, there are a total of 520 kinds of medicines including 203 Chinese proprietary medicines. Compared with the last version released in 2009 (that included 102 varieties of Chinese medicine out of a total of 307 drugs), 101 new Chinese patent medicines were added as essential medicines.

The proportion of increase of Chinese medicine in the new National Essential Medicines List really signals the intention of the Chinese Ministry of Health of putting more emphasis on using both Chinese and Western medicine to meet the demands for essential medicines.

Referring back to the management of IBS, studies have shown that TCM practitioners have accumulated rich experience and used different herbal products or concoctions in treating the main symptoms of IBS (Tang, 2009). In fact, the combination of TCM with Western medicine has been used for a long time in the treatment of IBS by Chinese practitioners (Zhang *et al.*, 2013), however, their effectiveness has not been adequately evaluated. With the increasing constraint in health care resources and demands for accountability in health resource usage, the effectiveness of using TCM in the management of IBS needs to be systematically reviewed. The information obtained would allow for assessment of the value of extra cost involved in adding TCM to the management of IBS. In our present study, treatment of IBS by TCM combined with Western medicine has been evaluated systematically. This would provide the basis for further investigation, as well as making evidence-based recommendations regarding integrated TCM and Western medicine treatment. The objective of our study was to evaluate the clinical effectiveness of the combination of TCM and Western medicine in the treatment of IBS by systematically combining the results from retrieved studies via a meta-analysis, and to recommend a future role for the use of TCM in IBS management.

Methods

Literature Search Strategy

We searched PubMed, the Chinese publications in China National Knowledge Infrastructure (CNKI) and the Wanfang Database for articles from January 2009 to December 2013. The search terms used were “IBS” and “integrated TCM and Western medicine”, or “IBS” and “combination of traditional Chinese and Western treatment”. Furthermore, we also conducted a manual search for additional publications from the reference sections of the retrieved articles. No language restriction was applied.

Study Selection Criteria

Randomized controlled trials that investigated the effectiveness of integrated TCM and Western medicine (treatment group) compared with Western medicine (control group) in the management of IBS were included. The drugs in the control group could be Western medicines, while TCM plus the same Western medicine was used in the treatment group. All the medicines had to be administered orally.

Exclusion criteria were: (a) The drugs used in the control group were TCM or placebo; (b) different Western medicines were used in the treatment group and the control group; (c) drugs were not orally administered; (d) conference papers or master thesis not officially published; and (e) the same data was published in different journals. For the last category, only the latest publication would be considered.

Data Extraction and Analysis

Data were collected independently by the reviewers. Any concerns about inclusion or exclusion criteria of a study were resolved by discussion among the reviewers. Data extracted from the studies included effectiveness, year of publication, clinical type of IBS, diagnostic criteria, types of Chinese medicines and Western medicines used, duration of treatment, and follow-up.

The relative risks (RRs) and 95% confidence interval (95%CI) were calculated using raw data derived from each study. Statistical analyses were carried out using Review Manager Software 5.2 (RevMan 5.2), which was the Cochrane Collaboration's program for preparing and maintaining Cochrane reviews. Meta-analysis was performed with random effects model or fixed effect model according to the level of heterogeneity when the treatment group was compared with the control group.

Assessment of Trial Quality

The quality of each study was assessed by RevMan 5.2. Publication bias analysis was evaluated via funnel plot.

Results

Results of Literature Search

A total of 108 potentially eligible publications were identified by the electronic search with 4 extra articles identified from manual search of the reference lists of retrieved articles. After culling, 72 articles involving 6,395 patients with IBS met the selection criteria and were included in this analysis. Figure 1 shows a flow diagram of the literature search and study selection process. All the included studies were carried out in China and published in Chinese.

Study Characteristics

Characteristics of the 72 included studies are shown in Table 1. The majority of the trials used Rome criteria for the diagnosis of IBS, while three trials used Chinese National criteria. Among the 72 included studies, 29 trials enrolled patients with IBS-D, 8 trials enrolled those with IBS-C, 1 trial enrolled patients with IBS-M, and the remaining 34 studies did not specify the type of IBS of the participants.

Of the 72 studies, 8 Chinese proprietary medicines were used in 12 studies, compound herbal preparations were prescribed in the remaining 60 studies with herbal formulae or modified formulae based on syndrome differentiation according to practitioners' clinical experience. These Chinese proprietary medicines included different forms (oral liquid, capsule, powder, or granules), while compound herbal preparations were of decoction formulation. Among the 12 studies which used Chinese proprietary herbal medicines,

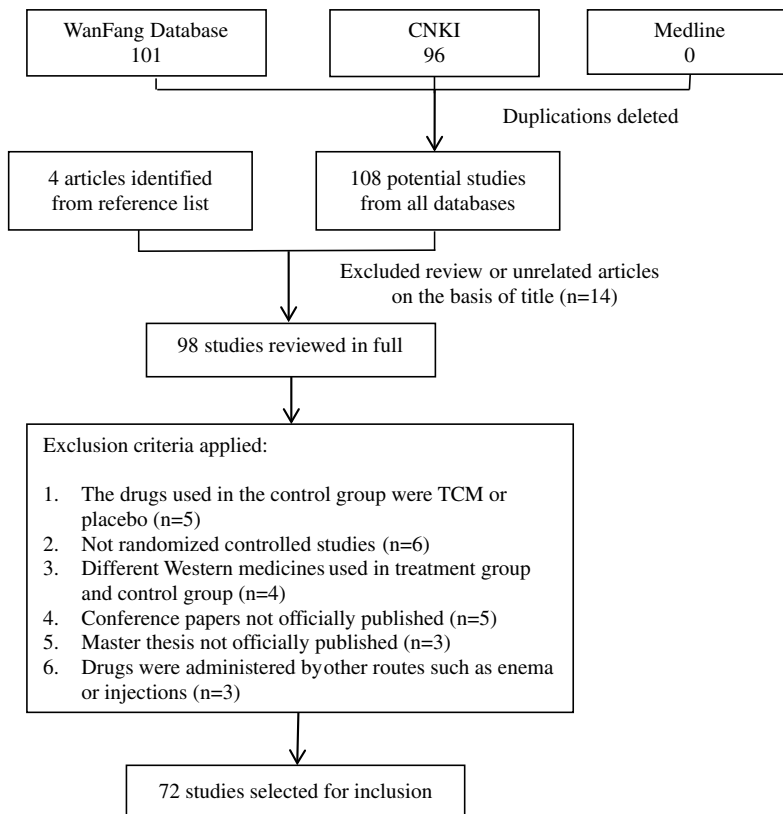


Figure 1. Flow diagram of the study selection process.

5 trials tested Gushen Changan combined with Western medicines for the treatment of IBS-D, while the other 7 used different Chinese proprietary medicines for various IBS subtypes. The control interventions of Western medicines were antispasmodics, antidiarrheals, antidepressants, prokinetics, bulking agents, and probiotics; or a combination of these drugs according to the patient's symptoms.

The duration of treatment was 4 weeks in 48 studies, 1 week in 1 study, 2 weeks in 5 studies, 2–4 weeks in 2 studies, 5–8 weeks in 14 studies, while the longest period of treatment was 12 weeks in 2 studies.

Risk of Bias Assessment

Among the 72 randomized controlled studies, 4 studies used a random number table to generate the allocation sequence (Wu, 2009; Chen, 2012; Li, 2012b; Xiong, 2013), and three grouped according to the patients' treatment order (Fan, 2009; Li, 2010, 2012a), while the remaining 65 studies did not describe the sequence generation method in detail. None of the studies reported blindness or an adequate concealed allocation method of randomization. Only one study reported the withdrawal information (Li, 2012b). Using the

Table 1. Characteristics of Studies Included in the Analysis

Study	IBS Type	Diagnostic Criteria	Chinese Medicine	Western Medicine	Duration (wk)	Follow-Up (wk)
Wang and Zhu, 2009	IBS-C	Rome III	Liuwei Anxiao casple	Mosapride, Oryzanol, VB1	4	NA
Sun and Zhao, 2009	IBS-D	Rome II	Tongxie YaoFang modified decoction	Trimebutine, Bifidobacterium	4	NA
Liu <i>et al.</i> , 2011	IBS-C	Rome II	Individualized HM standard formula	Mosapride	4	NA
Xu and Wang, 2011	IBS-C	Rome III	Simo Tang oral solution	Mosapride, Bifidobacterium	4	NA
Liu <i>et al.</i> , 2009a	IBS-C	Rome III	Jianpi Liqi decoction	Trimebutine	8	NA
Fan, 2009	IBS-C	Rome II	Runchangshu modified decoction	VB1, VB6, VC, Cisapride	6	NA
Liao, 2010	IBS-C	Rome II	Maziren decoction	Mosapride	4	24
Wang and Ji, 2009	IBS	Rome II	Tiaohe Ganpi recipe	Oryzanol, Doxepin, Cisapride, Diphenoxylate	4	NA
Wu and Zheng, 2010	IBS	Chinese National criteria	Tongxie YaoFang modified decoction	Pinaverium Bromide, Loperamide, Domperidone, Antidepressant	4	NA
Wu <i>et al.</i> , 2010	IBS	Rome II	Anshen Ningchang modified decoction	Trimebutine	4	NA
Wang, 2009a	IBS-D	Rome II	Gushen Changan capsule	Alverine	4	NA
Lu and Yan, 2012	IBS-D	Rome III	Gushen Changan capsule	Bifidobacterium	4	NA
Weng <i>et al.</i> , 2009	IBS	Rome III	Addition Sini San	Pinaverium Bromide	4	NA
An and Shi, 2009	IBS	Rome II	TCM syndrome — differentiation therapy	Pinaverium Bromide	6	NA
Ou, 2009	IBS	Rome II	Modified Xiaoyao San	Flupentixol and Melitracen	4	NA
Xiong, 2013	IBS	Rome II	Tongxie YaoFang modified decoction	Symptomic drugs	4	NA
Li, 2012a	IBS	Rome II	TCM syndrome — differentiation therapy	Symptomic drugs	4	NA
Zeng, 2009	IBS	Rome II	Jianpi Tiaochang decoction	Bifidobigen	4	12
Ye <i>et al.</i> , 2012	IBS	Rome III	Liuwei Muxiang capsule	Itopride, Oryzanol	4	NA
Zheng, 2013a	IBS	Chinese National criteria	Modified Liujuanzi decoction	Diphenoxylate, Colloidal Bismuth, Cisapride	1	NA
Li, 2010	IBS	Rome II	Individualized HM standard formula	Pinaverium Bromide	8	NA
Yan, 2009	IBS	Rome III	TCM syndrome — differentiation therapy	Pinaverium Bromide	4	NA

Table 1. (Continued)

Study	IBS Type	Diagnostic Criteria	Chinese Medicine	Western Medicine	Duration (wk)	Follow-Up (wk)
Zhao, 2009	IBS	Chinese National criteria	Modified Xiaoyao San	Nifedipine, Oryzanol	8	NA
Yin and Dong, 2010	IBS	Rome III	TCM syndrome — differentiation therapy	Bifidobacterium, Pinaverium Bromide, Polyduosan	4	NA
Cao and Ren, 2010	IBS	Rome II	Individualized HM standard formula	Smecta, Bifidobacterium	4	NA
Zhou <i>et al.</i> , 2012	IBS	Rome III	Shugan Liji and Jianpi Huashi or Runchang Tongbian recipe	Pinaverium Bromide, Phenolphthalein	4	NA
Hao, 2011	IBS	Rome III	Modified Tongxie YaoFang and Sini San decoction	Nifedipine, Trimebutine	4	NA
Yang, 2012	IBS	Rome II	Individualized HM standard formula	Smecta, Bifidobacterium	4	52
Hong, 2010	IBS	Rome II	Individualized HM standard formula	Pinaverium Bromide, Smecta	4	NA
Ji, 2010	IBS-D	Rome II	Modified Shenling Baizhu San	Pinaverium Bromide, Oryzanol	3	NA
Liu <i>et al.</i> , 2009b	IBS-D	Rome II	Wuling San and Tongxie Yaofang modified decoction	Sucralfate, Pinaverium Bromide, Loperamide, Domperidone	4	NA
Zhen, 2009	IBS-D	Rome II	Zhenren Yangzhang decoction and Shengma Gegen decoction	Smecta	2	NA
Sun, 2013	IBS-D	Rome II	Tongxie YaoFang modified decoction	Anisodamine, Diphenoxylate, Bifidobacterium	4	NA
Wu, 2009	IBS-D	Rome II	Shenling Baizhu San decoction	Pinaverium Bromide, Oryzanol	4	NA
Miao, 2013	IBS-D	Rome II	Individualized HM standard formula	Pinaverium Bromide	4	NA
Su, 2011	IBS-D	Rome II	Modified Tongxie YaoFang and Shenling Baizhu San decoction	Trimebutin	6	NA
Pang <i>et al.</i> , 2011	IBS-D	Rome II	Tiaogan Fupi decoction	Smecta	8	NA
He, 2010	IBS-D	Rome II	Tongxie YaoFang modified decoction	Pinaverium Bromide, Bifidobacterium	4	NA
Tong and Cai, 2012	IBS-D	Rome III	Individualized HM standard formula	Trimebutin	4	12
Chen, 2013	IBS-D	Rome II	Shugan Yipi decoction	Doxepin, Polyzym	4	NA
Leng, 2009	IBS-D	Rome II	TCM syndrome — differentiation therapy	Trimebutine	6	NA

Table 1. (Continued)

Study	IBS Type	Diagnostic Criteria	Chinese Medicine	Western Medicine	Duration (wk)	Follow-Up (wk)
Zhang <i>et al.</i> , 2009	IBS-D	Rome II	TCM syndrome — differentiation therapy	Pinaverium Bromide	4	NA
Li, 2012b	IBS-D	Rome III	Tongxie YaoFang and Sini San modified decoction	Bifidobacterium, Trimebutine	4	52
Du, 2012	IBS-D	Rome II	Shugan Yipi decoction	Doxepin, Polyzym	8	NA
Zhang, 2012	IBS-D	Rome II	Tongxie YaoFang decoction	Berberine, Smecta, Oryzanol	4	12
Wang, 2009b	IBS-D	Rome II	Tongxie YaoFang modified decoction	Pinaverium Bromide	4	NA
Xie and Chen, 2009	IBS-D	Rome II	Individualized HM standard formula	Pinaverium Bromide	12	NA
Zhu, 2012	IBS-D	Rome III	Gushen Changan capsule	Bifidobacterium	4	NA
Ren and Jiang, 2011	IBS-D	Rome III	Gushen Changan capsule	Trimebutine Bifidobacterium	2	NA
Song, 2013	IBS	Rome II	XiaoJian Zhong decoction	Pinaverium Bromide	5	NA
Jiang, 2009	IBS-C	Rome II	Runchang Shu recipe	VB1, VB6, VC, Cisapride	6	NA
Li and Wang, 2009	IBS-D	Rome II	Shugan Jianpi decoction	Trimebutine	8	NA
Zeng and Yan, 2012	IBS-D	Rome II	Tongxie YaoFang modified decoction	Pinaverium Bromide	4	NA
Liu and Yang, 2009	IBS	Rome II	Tongxie YaoFang modified decoction	Pinaverium Bromide	4	NA
Yi <i>et al.</i> , 2009	IBS	Rome II	Yiji Ning decoction	Symptomatic drugs	4	NA
Liu and Xu, 2011	IBS-C	Rome III	Modified Mazi Renwan	Pinaverium Bromide	4	NA
Chen, 2012	IBS	Rome II	Tongxie YaoFang modified decoction	Symptomatic drugs	4	NA
Liu <i>et al.</i> , 2011	IBS-M	Rome III	Shugan Liqi Jianpi decoction	Trimebutine, Flupentixol and Melitracen	4	NA
Zeng, 2011	IBS-D	Rome III	Shgan Jianpi recipe	Trimebutine, Clostridium Butyricum	2	NA
Zheng, 2013b	IBS	Rome II	Yigan Fupi decoction	Trimebutine, Bifidobacterium, Pan-creatin Enteric-coated capsule drugs	4	NA
Wang, 2011	IBS	Rome III	Shugan Jianpi decoction	Pinaverium Bromide, symptomatic drugs	4	NA
Wei <i>et al.</i> , 2010	IBS	Rome II	Xiaoyao San decoction	Trimebutine	4	12
Xiong, 2011	IBS	Rome II	TCM syndrome — differentiation therapy	Pinaverium Bromide, Loperamide	2–4	12

Table 1. (Continued)

Study	IBS Type	Diagnostic Criteria	Chinese Medicine	Western Medicine	Duration (wk)	Follow-Up (wk)
Lv, 2012	IBS	Rome II	TCM syndrome — differentiation therapy	Trimebutine, Oryzanol	4	NA
Yu <i>et al.</i> , 2011	IBS	Rome II	Chaihu Shugan San decoction	Bifidobacterium	2	NA
Cheng, 2010	IBS-D	Rome III	Sishen Wan modified decoction	Bifidobacterium, Pinaverium Bromide	12	24
Shen <i>et al.</i> , 2012	IBS	Rome III	Zhizhu Kuanzhong capsule	Trimebutine	4	NA
Li, 2012	IBS	Rome II	Individualized HM formula	Trimebutine	4	NA
Huang, 2011	IBS	Rome III	Shugan Jieyu capsule	Pinaverium Bromide	4	NA
Huang <i>et al.</i> , 2011	IBS-D	Rome III	Zhenqi Fuzheng powder	Bifidobacterium	8	12
Chen, 2011	IBS	Rome III	Shenling Baizhu granules	Trimebutine	6	NA
Yu and Lao, 2012	IBS-D	Rome III	Gushen Changan capsule	Berberine	2	NA

Notes: IBS: Irritable bowel syndrome; IBS-D: diarrhea-predominant subtype of IBS; IBS-C: constipation-predominant subtype of IBS; IBS-M: mixed subtype of IBS; TCM: traditional Chinese Medicine; HM: herbal medicines; NA: not reported.

general methodological quality assessment from the *Cochrane Handbook*, these studies might possess high risk of bias.

Effectiveness of Combination of TCM and Western Medicine

Global Symptoms of IBS

All studies reported outcomes of the global improvement of symptoms, and the total effective rate was calculated with effective patients divided by the total number of cases (i.e., using the Intention-to-Treat analysis). Evaluation criteria was based on “Clinical Research Guidelines for New Chinese Herbal Drug” (Zheng, 2002), “Irritable bowel syndrome diagnosis and treatment of Integrative Medicine program (draft)” (Chen *et al.*, 2005), or “Diagnostic basis of clinical disease and criteria for recovery and improvement” (Sun, 2002).

Among the 72 studies, 71 reported that the patients in the treatment group showed a statistically significant improvement in symptoms compared with control group after treatment. By contrast, only one study demonstrated an insignificant improvement in symptoms. The RRs for each study and all studies combined for the combination of TCM and Western medicine vs. Western medicine alone are shown in Fig. 2. In the random-effects meta-analysis of all included studies, low heterogeneity ($\tau^2 = 0.00$; $\chi^2 = 76.44$, $p = 0.31$; $I^2 = 7\%$) was detected. When compared to the Western medicine treatment, our meta-analysis showed TCM combined with Western medicine interventions significantly improved global symptoms of IBS (RR, 1.21; 95%CI: 1.18–1.24).

Subtype Analysis — Effectiveness in Various IBS Subtypes

We examined the effectiveness of integrated TCM and Western medicine by different IBS subtypes. As shown in Fig. 3, the results of meta-analysis showed that compared to Western medicine treatment alone, the integrated approach was more effective in the treatment of IBS-D in the 29 trials that enrolled patients with IBS-D (RR, 1.19; 95%CI: 1.15–1.24). Again, low level of heterogeneity ($\tau^2 = 0.00$; $\chi^2 = 33.01$, $p = 0.24$; $I^2 = 15\%$) was detected. Similarly, 8 IBS-C trials also demonstrated that integrated TCM and Western medicine was therapeutically more effective than Western medicine alone (RR, 1.23; 95%CI: 1.13–1.33) (Fig. 4). Only one study treated IBS-M and reported that the effective rate of treatment group was 95.0%, which control group was 77.5% (Liu *et al.*, 2011). There was significant difference between two groups ($p < 0.05$).

The remaining 34 studies did not specify the type of IBS in the participants and showed that the total effective rate was higher in the treatment groups compared to control groups (RR, 1.22; 95%CI: 1.18–1.27) (Fig. 5). The effects were similar to the global improvement of symptoms of all the studies.

Subgroup Analysis — Chinese Proprietary Medicines vs. Chinese Herbal Decoctions

For the subgroup analysis, we examined the possible different efficacies between Chinese proprietary herbal medicines and compound herbal preparations. We found that both

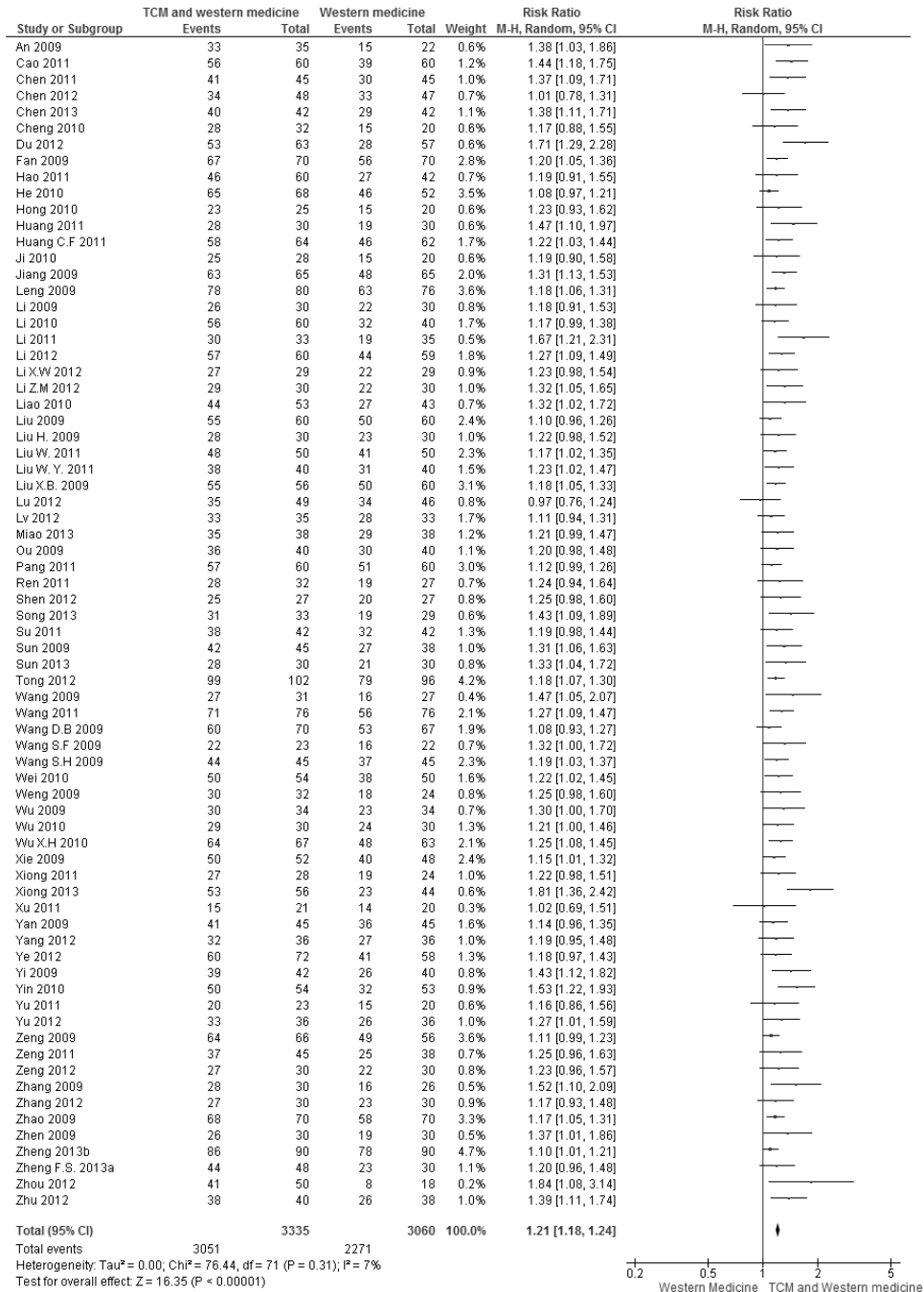


Figure 2. Comparison of TCM plus Western medicine and Western medicine for all studies.

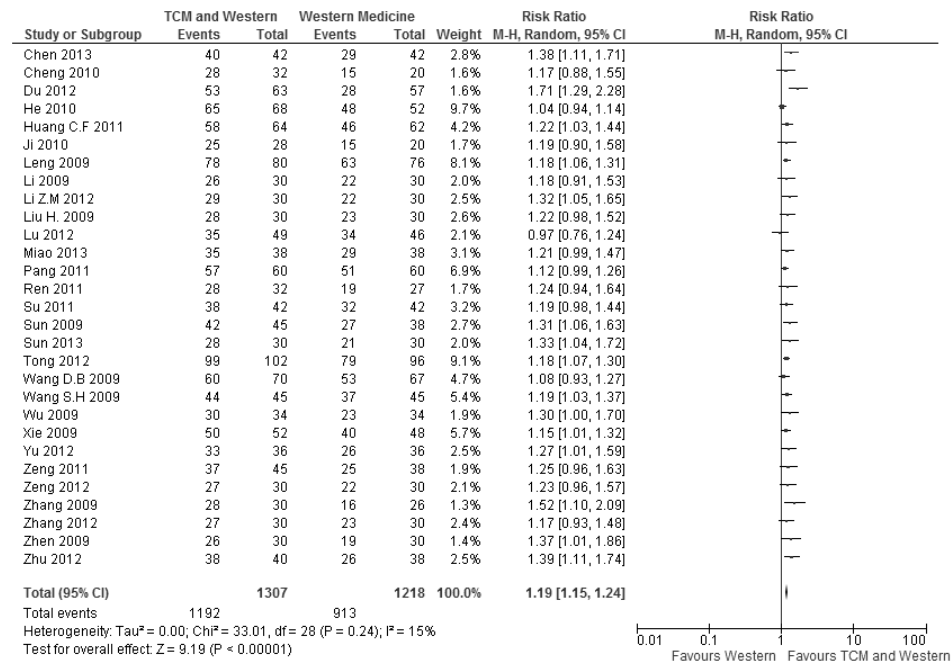


Figure 3. Comparison of TCM plus Western medicine and Western medicine in treatment of IBS-D patients.

Chinese proprietary herbal medicine plus Western medicine treatment and compound herbal preparations plus Western medicine treatment showed similar and statistically significant effects on global improvement compared with Western medicine treatment alone. RRs were 1.22 (95%CI: 1.14–1.30) and 1.22 (95%CI: 1.18–1.27), respectively. There was little heterogeneity ($\tau^2 = 0.00$; $\chi^2 = 11.74$, $p = 0.38$; $I^2 = 6\%$) in Chinese proprietary herbal medicine plus conventional treatment trials, and medium heterogeneity ($\tau^2 = 0.01$; $\chi^2 = 121.78$, $p < 0.00001$; $I^2 = 52\%$) in compound herbal preparations plus conventional treatment trials. Meta-analysis results are shown in Figs. 6 and 7. However, the number of included articles was small; therefore, further studies and analysis should be performed in future to confirm this observation.

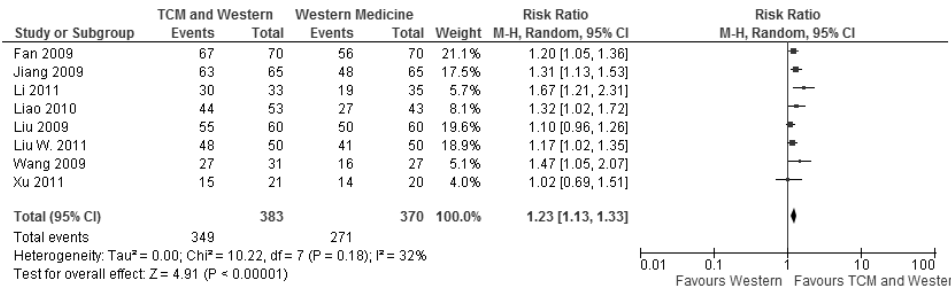


Figure 4. Comparison of TCM plus Western medicine and Western medicine in treatment of IBS-C patients.

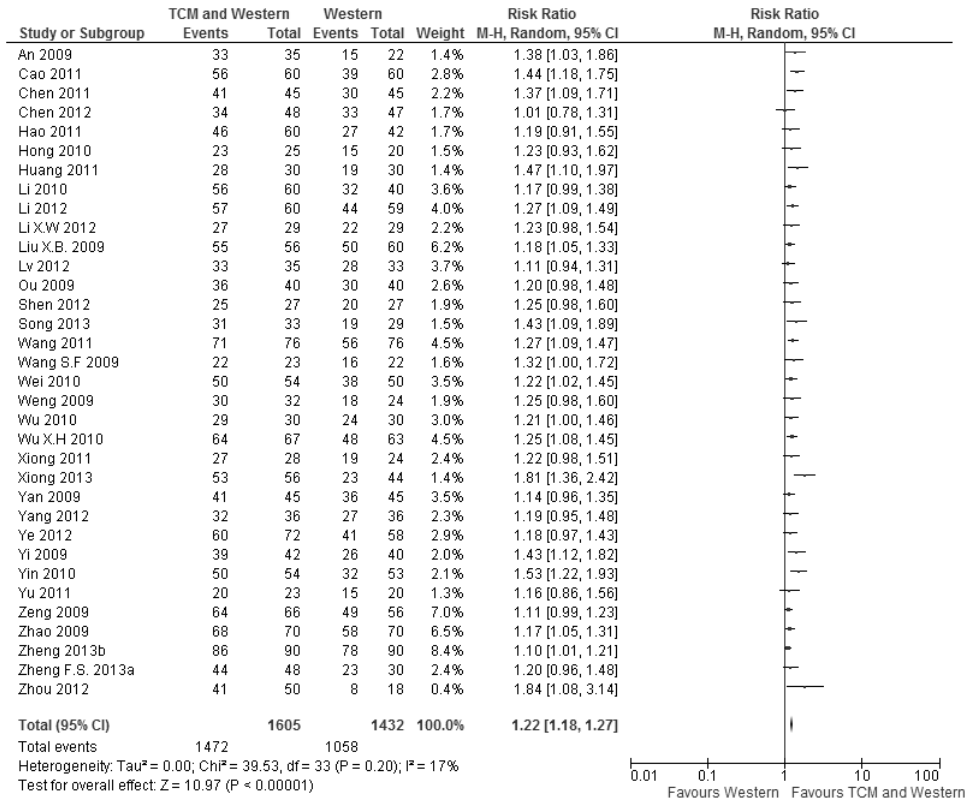


Figure 5. Comparison of TCM plus Western medicine and Western medicine for studies not specify the type of IBS.

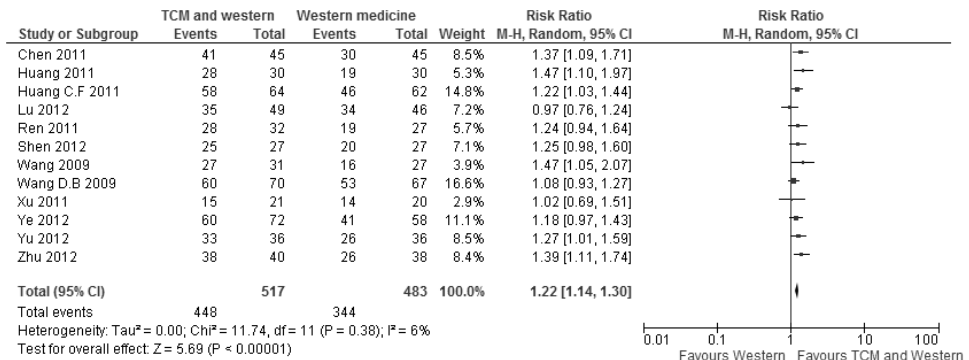


Figure 6. Comparison of Chinese proprietary herbal medicine plus Western medicine and Western medicine.

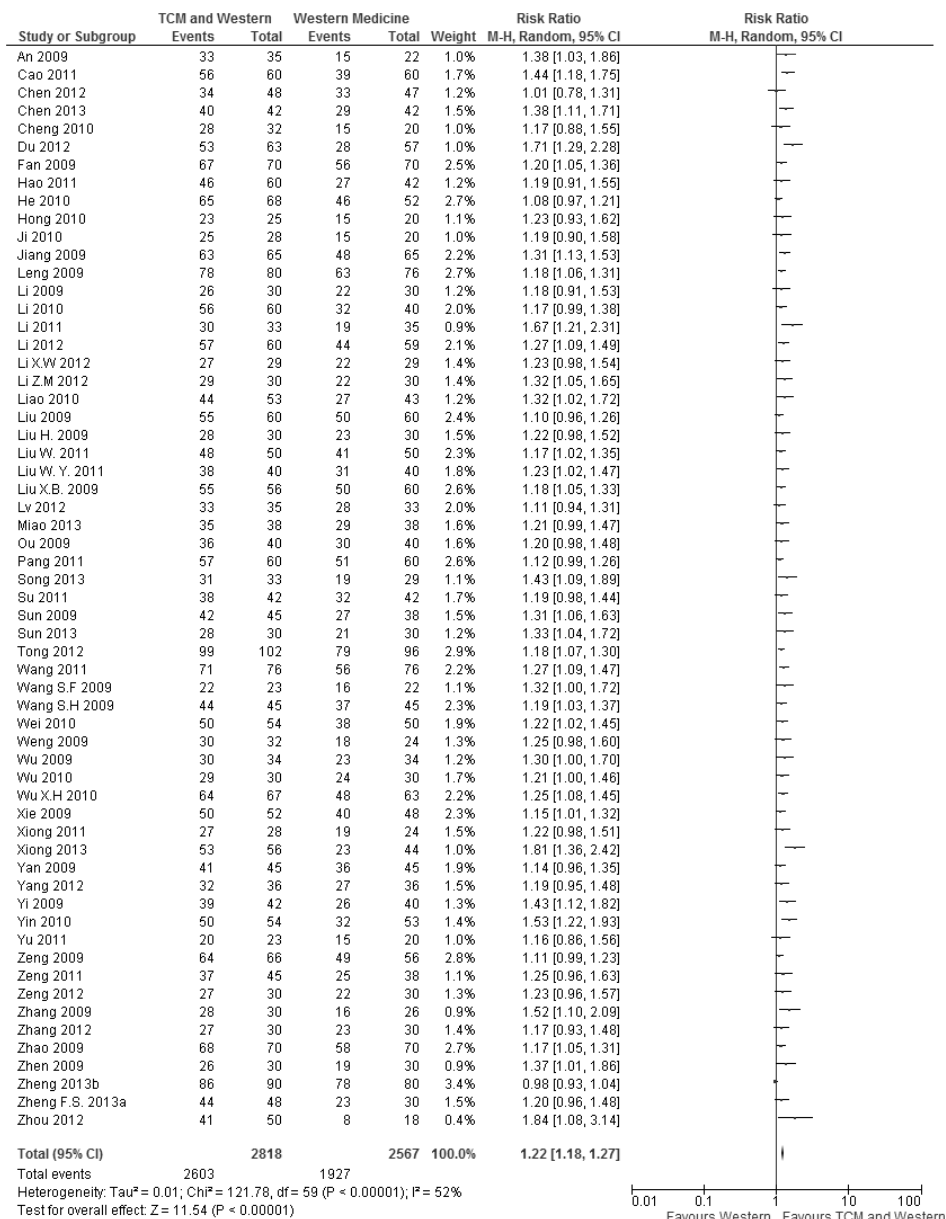


Figure 7. Comparison of compound herbal preparations plus Western medicine and Western medicine.

Follow-Up and Adverse Events

The additional outcome measures were number and type of adverse events reported in six studies (Fan, 2009; Jiang, 2009; Wang, 2009a; Ren and Jiang, 2011; Chen, 2012; Xiong, 2013). These included allergic reaction, headache, nausea, diarrhea, fatigue, and loss of

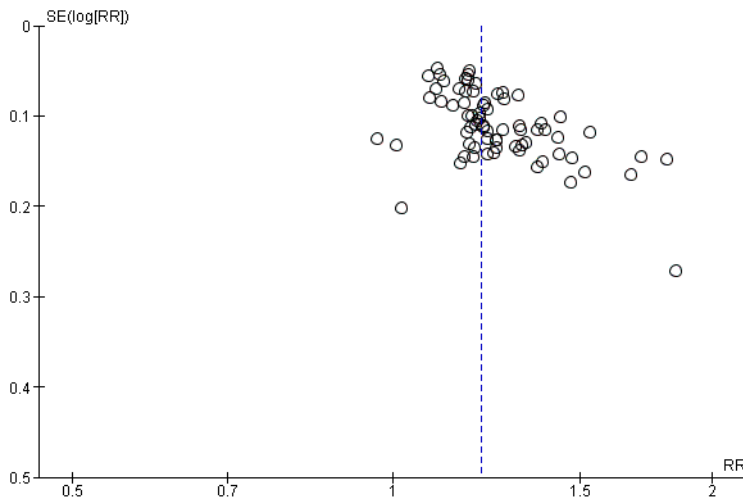


Figure 8. Funnel plot of comparison of TCM plus Western medicine and Western medicine for all studies.

appetite, which occurred both in the treatment and control groups in similar proportion. No serious adverse events were reported from the integrative therapies or Western medicines, with only tolerable minor side effects which disappeared without special treatment. Another 11 studies reported that no side effects occurred during the trial period.

Ten trials reported follow-up assessment ranging from three months to one year after the treatment. Of these studies, seven reported lower recurrence rates in the treatment group compared to the control group (Zeng, 2009; Zhao, 2009; Cheng, 2010; Wei *et al.*, 2010; Li, 2012b; Yang, 2012; Zhang, 2012). No trials reported any cost-effectiveness information.

Publication Bias Analysis

The funnel plot indicated an asymmetry (Fig. 8), which could either be interpreted as there being no studies which showed the integrated approach in IBS management to be inferior to Western medicine treatment alone, or studies with negative results were not published.

Discussion

Although IBS is a common disease, there is still no universally accepted satisfactory treatment. Patients with IBS often have absenteeism, reduced health-related quality of life, more frequent physician visits, and greater medication use. All these negative effects of IBS naturally impose great social and economic burden on the patients and society (Quigley *et al.*, 2006; Ringel *et al.*, 2009; Nellesen *et al.*, 2013). Hence, more effective treatments for IBS are needed to relieve symptoms, improve health-related quality of life, and reduce health care utilization.

Due to the wide range of the symptoms that may be experienced, the available conventional pharmacological approaches are mainly targeted at symptomatic relief, such as

treatments with antispasmodics for abdominal pain, antidiarrheals for diarrhea, antidepressants for depression and anxiety, and prokinetics and bulking agents for constipation (Longstreth *et al.*, 2006; Brandt *et al.*, 2009). However, the use of these multiple medications has been limited by side effects, expensive drug costs, and high recurrence rate. The low levels of satisfaction with the treatment of these conventional medicines, in recent years, have caused an increasing number of patients and practitioners turning to alternative medicine for symptom reduction, particularly Chinese herbal medicines or integrated Chinese and Western medicine for remedy (Rahimi and Abdollahi, 2012; Grundmann and Yoon, 2014; Liu *et al.*, 2014a).

In this respect, clinical trials have shown that TCM therapies or TCM combined with Western medicine might offer better symptom improvement to some patients with IBS. Among these trials, a number of Chinese proprietary medicines were used more frequently according to syndrome subtypes (Li *et al.*, 2013). Although a previous review of herbal medicine alone showed a beneficial effect on IBS symptoms (Shi *et al.*, 2008), review of combination therapy (herbal medicine and conventional drugs) in IBS has not provided conclusive evidence of its efficacy, due to small study sample sizes and methodological flaws (Liu *et al.*, 2006). Consequently, the real efficacy of combination therapy involving TCM for IBS is still unclear.

Our meta-analysis evaluated the evidence for the clinical effectiveness of the combination of TCM and Western medicine in the treatment of IBS. To our knowledge, no other similar review was available. In the present study, a total of 72 randomized controlled trials were included for our meta-analysis. We found that TCM combined with Western interventions significantly improved global symptoms of IBS. At the same time, the relapse rate was lower, and no serious adverse events were reported. Additionally, there was no significant difference in therapeutic effects of the integrated approach in the meta-analyses involving the various IBS subtypes (IBS-D, IBS-C, not specify the type of IBS). Similarly, Chinese proprietary herbal medicine plus conventional treatment and compound herbal preparations plus conventional treatment showed similar and statistically significant effects on global improvement compared with Western treatment alone. Evaluating the global improvement of symptoms of all the studies, different subtypes and subgroups, our results demonstrated that the therapeutic effect for relieving IBS symptoms was enhanced by the combination therapy. This may be due to the synergic actions of TCM plus Western medicine. However, further studies investigating the potential mechanisms of pharmacological action in well-designed clinical trials are warranted to elucidate this.

The most striking finding in this review was the assessment of the similar therapeutic effect of Chinese proprietary medicine and compound herbal decoctions. Chinese proprietary medicines, usually formulated as tablets or capsules for convenience or better palatability, can make up for poor adherence of herbal formulae that require boiling the different herbs. Therefore, it is different from decoction which can be modified based on different syndrome, and its application is usually only for patients with specified syndrome. However, in our meta-analysis, 8 Chinese proprietary medicines that supposedly would be suitable for different patients' syndrome types, such as Senling Baizhu granules, Liuwei Anxiao capsules, Shenqi Fuzheng powder, and Gushen Changan capsules, were used in

12 studies. The result suggests that Chinese proprietary herbal medicines may have similar treatment effect on all IBS subtypes. This would potentially facilitate the use of Chinese proprietary medicine in the management of IBS as not all Chinese proprietary medicine may be readily available, especially outside China. However, due to small study number and sample sizes, further large and rigorous trials are needed to confirm this promising treatment option.

From the public health perspective, in the new National Essential Medicines List issued by the Ministry of Health of China, 203 kinds of Chinese proprietary medicines were selected to meet the most fundamental health needs of the population as essential medicines. To be included into the National Essential Medicines List, a drug should be able to satisfy health care needs and in appropriate dosage forms for administration as well as at a price the public can afford. Globally, there is a paucity of evidence to substantiate the clinical efficacy of TCM for inclusion into the National Essential Medicines List. The results from our meta-analysis showed that the combination of TCM in the essential medicine is beneficial for IBS patients, and can therefore provide an example to justify the inclusion of TCM in the essential medicine list.

However, several limitations of this study should be noted. First, the quality of the included trials was relatively poor. Second, the treatment duration was different across studies, and there was a lack of follow-up in most studies to assess long-term outcomes. Third, the assessment of side effects and recurrent episodes was not detailed and not available from nearly all included studies. Together, these may potentially introduce bias in favor of TCM plus conventional interventions. Furthermore, publication bias should be taken into consideration in this meta-analysis as studies with negative results may not be published or terminated. Finally, we must acknowledge the potential effect of the inability to obtain unpublished literature.

Conclusions

In summary, the results of this meta-analysis provided the evidence that treating IBS with integrated traditional Chinese and Western medicine showed better effectiveness than conventional Western medicine alone. Our results also showed similar efficacy between Chinese proprietary medicine and herbal decoctions. Chinese proprietary medicine, being low-cost, easy to use, and having good palatability, can make up for poor adherence of Chinese herbal medicine. Therefore, it would be more beneficial and acceptable for IBS patients. The integration of these therapies may provide IBS patients with better treatment outcomes. However, due to the aforementioned limitations, our current data are insufficient to recommend this as first-line treatment. Further multi-center large-scale randomized controlled studies are required to assess the long-term effectiveness and safety of TCM for treatment of IBS.

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