Original Article

The comparative efficacy and safety of 9 traditional Chinese medicines combined with standard quadruple therapy for *Helicobacter pylori*-associated gastritis: a systematic review and network meta-analysis

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Background: There are 9 traditional Chinese medicines (TCMs) combined with standard quadruple (SQ) available for the treatment of *Helicobacter pylori* (Hp)-associated gastritis, but their relative efficacy and best options in clinical decision making are unknown due to a lack of high-quality head-to-head randomized controlled trials (RCTs). This study aimed to explore which formulas are the most effective and/or safest for Hp-associated gastritis.

Methods: We performed a search of electronic databases including PubMed, Web of Science, Cochrane Library, Embase, Chinese databases and South Korean database from inception to March 2022 to identify all relevant RCTs on the comparison between TCM combined with SQ and SQ for Hp-associated gastritis. Efficacy outcomes were the eradication rate of Hp and therapeutic response rate, and safety outcome was incidence of adverse reactions. Publication bias was assessed quantitatively using Egger's regression analysis and qualitatively using trim-and-fill method. Quality assessment was performed using Cochrane Risk of Bias, version 2 (ROB 2) tool. The Bayesian methods were applied to compare each treatment.

Results: A total of 55 trials with 6,187 patients were involved. The experimental group included 9 TCMs combined with SQ. The control group was SQ. The pair-wise meta-analysis demonstrated that compared with control group, 8 TCMs combined with SQ could statistically improve the eradication rate of Hp in patients with gastritis, 9 TCMs combined with SQ could significantly improve the therapeutic response rate. Additionally, Banxia Xiexin decoction combined with SQ (BXS) could statistically decrease the incidence of adverse reactions. The network meta-analysis results showed that BXS, Xiangsha Liujunzi combined with SQ (XSS), and Huangqi Jianzhong decoction combined with SQ (HQS) was the best measures to effectively eradicate Hp, enhance therapeutic effect, and decrease adverse reactions, respectively. The results of trim-and-fill method indicated that the results were stable and less affected by publication bias.

Conclusions: Compared with SQ, TCM combined with SQ generally has a better clinical effect and higher safety in patients with Hp-associated gastritis. BXS, XSS, and HQS are recommended based on the patient's condition and needs in clinical practice. Further high-quality double-blinded RCTs are warranted to validate the conclusions.

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Keywords: Traditional Chinese medicine; *Helicobacter pylori*; gastritis; network meta-analysis

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Introduction

Helicobacter pylori (Hp) can persist for decades in the stomach environment, where it damages the gastric mucosa (1). Infection of Hp induces various human digestive system diseases, such as dyspepsia, chronic gastritis, gastroduodenal ulcer disease, gastric carcinoma, and mucosa-associated lymphoid tissue lymphoma (2). Hp-induced gastritis is a chronic inflammatory reaction of the gastric mucosa, usually accompanied by pathological changes such as atrophy and intestinal metaplasia (3,4). Hp infection has been identified as one of the identified risk factors for gastric cancer (5).

Currently, over 50% of the global population are infected with Hp, and its prevalence is higher in developing countries (6). In the case of failure of the triple therapy or high antibiotic resistance, quadruple therapy(Triple therapy plus bismuth) becomes the treatment of choice (7). With the increasing resistance of Hp to antibiotic regimens, all regimens recommended worldwide in treatment guidelines as first-line and rescue therapies continue to face failures in approximately 10–30% of patients (8). China is currently facing the challenges posed by critically high infection, side effects, intestinal flora imbalance, high recurrence rate (9). Therefore, it is imperative to modify therapeutic strategy. Recently, many clinical and pharmacological trials have shown that traditional Chinese medicines (TCM) has a tremendous therapeutic effect on Hp (10-13). Meta-analysis has revealed that Banxia Xiexin decoction showed more effects in inhibiting Hp and improving Hp-related inflammation (14). TCM combined with quadruple therapy has been recognized to improve Hp eradication (15). It has become a new option for treating Hp-induced gastritis. Due to the difference of drug compositions, effective concentration, individual characteristics, psychological state, etc., the efficacy outcomes of the eradication rate of Hp and therapeutic response rate and safety outcome of incidence of adverse reactions differ among various TCMs combined with standard quadruple (SQ). To date, a systematic review and meta-analysis evaluating the efficacy of TCMs in eradicating Hp infection has not been published (16). The differences among different TCMs combined with SQ and the most effective drug combination have not been confirmed.

It is critical to compare the effectiveness and safety of different TCMs combined with quadruple therapy and to determine which regimen is preferred. In this study, RCTs of SQ combined with TCM in the experimental group and SQ in the control group were selected for analysis. We aimed to compare and rank the efficacy and safety of the abovementioned TCMs combined with SQ therapy in patients with Hp-associated gastritis, which measured outcomes of various drug combinations, such as the eradication rate of Hp, therapeutic response rate, and incidence of adverse reactions through a network meta-analysis to provide evidence-based medicine evidence for clinical drug use. We present the following article in accordance with the PRISMA-NMA reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5421/rc).

Highlight box

Key findings

- Banxia Xiexin decoction combined with standard quadruple is the most effective to eradicte Hp; Xiangshang Liujunzi combined with standard quadruple is the most effective to improve symptoms; and Huangqi Jianzhong decoction is the safest to decrease adverse reactions.

What is known and what is new?

- The combination of 9 TCMs and standard quadruple therapy is currently available for the treatment of Hp-associated gastritis in clinical application. However, no high-quality head-to-head RCTs exist to identify their relative efficacy and optimal regimens.
- This study compared the relative efficacy of 9 combinations and identified the most effective and safest regimen for patients with Hp- associated gastritis.

What is the implication, and what should change now?

- Clinicians should consider comprehensively the effect, safety, accessibility, affordability of drugs and physical state of the patients to make prescription. Further well-designed and high quality RCTs are needed to validate the conclusions of this study.

Methods

Protocol

A protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO, www.crd.york.ac.uk/prospero/). The registration number is CRD42022329348.

Eligibility criteria

Two authors (Zhixian Bao and Guobing Wu) independently selected RCTs that met the following conditions: (I) Participants: adults (>18 years age) diagnosed with gastritis who were positive for Hp infection according to 1 or more of the diagnostic methods, which included 13C or 14C breath tests, rapid urease tests, serology tests, and histopathology tests; No history of taking antibiotics, proton pump inhibitors (PPIs), bismuth, H2 receptor antagonists or nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks; No severe heart and lung diseases, mental diseases or malignant tumors; No other bacterial or viral infection; No participation in other drug trials in the past 3 months; Not pregnant or lactating; No relevant drug contraindications. (II) Interventions: TCM combined with SQ. TCM included Banxia Xiexin decoction, Huanglian Wendan decoction, Huangqi Jianzhong decoction, Huopu Xialing Decoction, Lianpuyin, Xiangsha Liujunzi, Weifuchun, Weisu granule, and Jinghua Weikang, with no limit applied to the duration, dosage, and the order of administration. The duration of SQ was 10 or 14 days. The intervention could not add other Chinese or Western medicine, acupuncture, massage, or other traditional Chinese treatment modalities. (III) Comparison: SQ (PPI + 2 antibiotics + bismuth agent). PPIs include omeprazole, Rabeprazole, pantoprazole and tinidazole; antibiotics include amoxicillin, claricid and furazolidone; bismuth agents include colloidal bismuth pectin, compound bismuth aluminate tablets, bismuth potassium citrate; The dosage of these drugs correspond with guideline recommendations. (IV) Outcomes: eradication rate of Hp, therapeutic response rate, the incidence of adverse reactions.

We defined eradication of Hp as negative results of 13C or 14C breath test 4 weeks or 1 month after the end of the total experiment. The therapeutic response rate was calculated according to the improvement of clinical symptoms after the entire course of treatment: Obvious effect: abdominal pain, abdominal distension, nausea, vomiting, and other symptoms disappeared completely; Effective: the symptoms had partially disappeared; Ineffective: no significant change in symptoms. The therapeutic response rate = (number of obvious effect + number of effective)/total number of participants ×100%. The incidence of adverse reactions was described as the occurrence of adverse reactions in patients during the treatment.

We excluded the following literature: (I) that including similar or duplicate data (the study with the complete data was selected from a series of studies conducted by the same team); (II) no expected outcome; (III) review, case study, nursing summary, conference abstract, and so on; (IV) animal or *in vitro* experiments.

Literature retrieval strategy

We searched the databases of PubMed, Web of Science, Cochrane Library, Embase, Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Wanfang Data, Chinese Biomedical Medicine (CBM), Taiwan Scholar Journal Database (TWS), Hong Kong University library, The Chinese University of Hong Kong Library, Run Run Shaw Libirary - City University of Hong Kong, Lee Shau Kee Library - The Hong Kong University of Science and Technology, Hong Kong Baptist University Library, Pao Yue - Kong Library - The Hong Kong Polytechnic University, The Education University of Hong Kong Library, and RISS (South Korea) and manually searched journals and magazines to obtain related literature of which the publication time was from inception to March 2022. The reference list of all selected articles was independently screened to identify additional studies that had been missed in the initial search. We combined theme words and free words for the search (Appendix 1). Languages were limited to English and Chinese. Two independent authors performed the initial retrieval, and any discrepancy was resolved through mutual discussion or communication with another author. We did not need to contact any authors as the full texts were all available, and data could be extracted from the articles.

Study selection and data extraction

Two authors (Zhixian Bao and Guobing Wu) independently screened the literature and extracted data, followed by cross-checking. Any discrepancy was resolved through

mutual discussion or communication with another author (Jie Du). The literature screening process was as follows: a manual re-check was performed after the automatic re-check to exclude duplicate literature; literature was selected according to the inclusion and exclusion criteria after reading the title and abstract; full texts were read to determine the final literature to be involved.

Relevant data were extracted: (I) literature characteristics: first author, publication year, region, type of study, sample size, baseline participant characteristics, component of TCMs, details of the intervention measures, treatment process, duration of treatment type; (II) outcome data: definition of the outcome, the number of adverse events in the experimental group and control group, the number of patients based on primary random assignment, not the actual study completion. The intention-to-treat protocol was conducted to collect and analyze study outcomes; (III) methodological details: all relevant information on randomization, distribution concealment, blindness, and lost follow-up.

In the geometry of the networks of drug comparisons, a node represented each TCM combined with quadruple therapy and directly randomized comparisons between drugs were linked by the lines between the nodes. The width of the line represents the number of studies with drug comparisons connected by the line.

Quality assessment

Two authors (Zhixian Bao and Guobing Wu) independently used the Cochrane Risk of Bias, version 2 (ROB 2) tool to perform a quality assessment of the included studies. Any disagreement was resolved through negotiation with a third reviewer (Jie Du). The tool includes 5 fields (bias due to randomization, bias due to deviations from intended intervention, bias due to missing data, bias due to outcome measurement, bias due to selection of reported result), overall risk of bias and weight. The risk of bias for each area is classified into three levels: "low risk", "some concerns", and "high risk" based on the reviewers' responses to the signal questions. If the bias risk assessment results in all fields are "low risk", then the overall bias risk is "low risk"; If the bias risk assessment result of some fields is "some concerns" and there is no "high risk", then the overall bias risk is "some concerns"; As long as the evaluation result of bias risk in one area is "high risk", the overall bias risk is "high risk". The weights are based on the sample size.

Statistical analysis

The software programs R (The R Foundation for Statistical Computing, Vienna, Austria) and RevMan 5.4 (The Nordic Cochrane Center, Denmark) was used to conduct all outcomes for pair-wise meta-analysis and network meta-analysis. Odds ratio (OR) and 95% confidence interval (CI) were calculated because only dichotomous outcomes were involved. A P value <0.05 indicated statistical significance. Heterogeneity was evaluated among studies using I^2 statistics with a value of >50% indicating significant heterogeneity. If there was no or low heterogeneity, pair-wise meta-analysis and network meta-analysis were directly performed; otherwise, the source of heterogeneity was further analyzed. After excluding the influence of apparent clinical heterogeneity, a random-effect model was used for meta-analysis. If there was significant clinical heterogeneity, subgroup analysis, sensitivity analysis, or descriptive analysis were performed. There was no need for inconsistency testing because there was no closed loop. The potential scale reduction factor (PSRF) was calculated to evaluate convergence based on the Brooks-Gelman-Rubin method. The closer the PSRF value was to 1, the higher convergence the model reached. We also conducted the rank probability and surface under the cumulative ranking curve (SUCRA) rank to identify the superiority of intervention.

Publication bias

Publication bias was assessed quantitatively using Egger's regression analysis. A P value <0.05 was considered publication bias. When publication bias existed, the effect of publication bias on the results was evaluated using the trim-and-fill method. The statistically consistent significance of results before and after the trim-and-fill method indicated that the results were stable and less affected by publication bias.

Sensitivity analyses

Sensitivity analysis was evaluated by comparing statistical significance before and after excluding each article to identify the source of heterogeneity in the pairwise comparisons. If the statistical significance of the outcomes before and after such exclusion changed, it indicated that the results were not robust, and the researchers proceeded to read the full text to identify the source of heterogeneity.

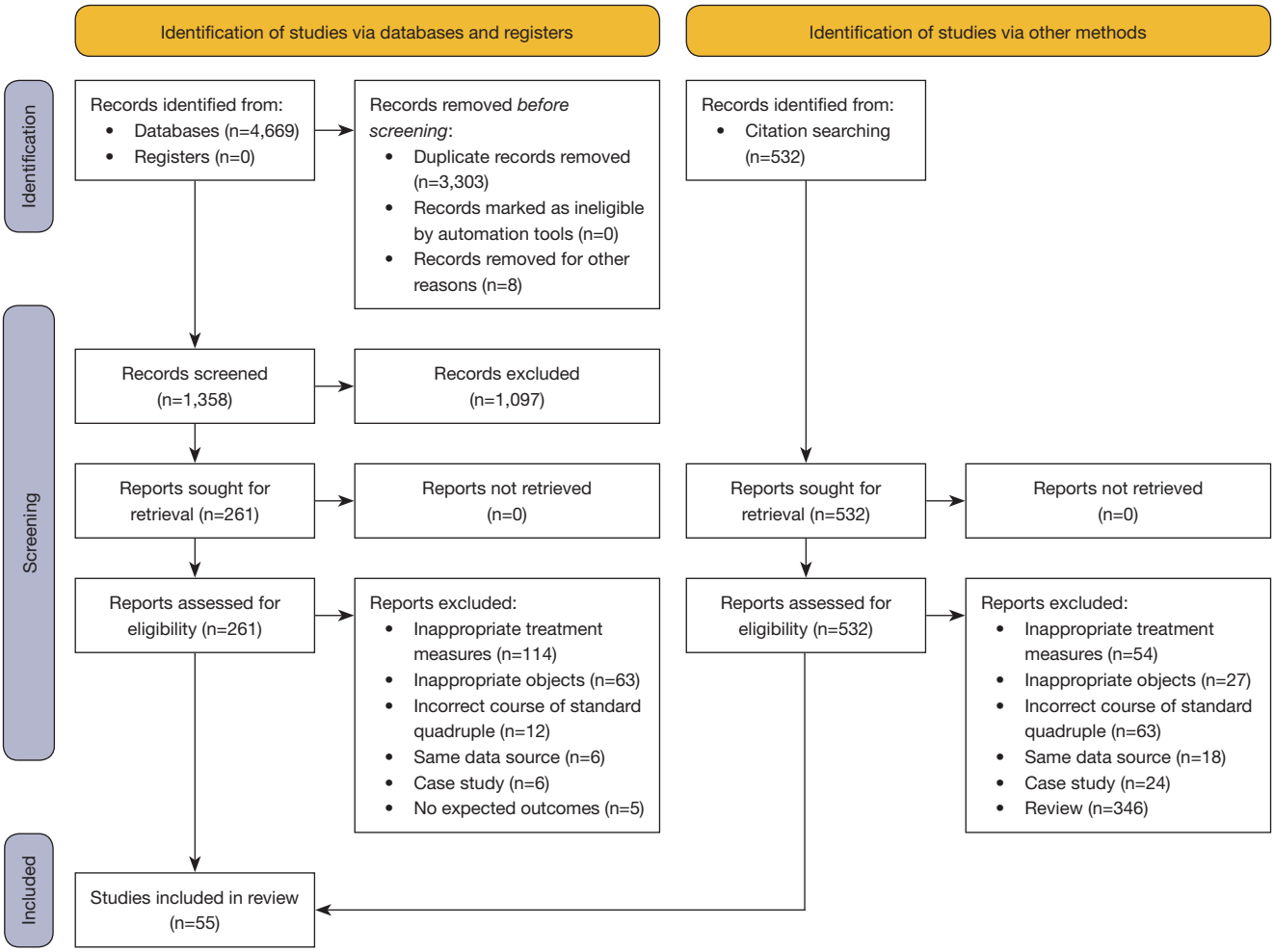

Figure 1 Flow chart of trial identification and selection.

Results

Characteristics of included studies and quality assessment

Our search yielded 5,201 studies, and 55 were eventually involved, with a total of 6,187 participants (the specific literature screening process is shown in *Figure 1*). The details of the included studies are summarized in *Table 1*. No English-language articles met the selection criteria, and only Chinese literature was involved, with a publication time range of 2013 to 2021. We screened the literature and summed up 9 kinds of TCM combined with SQ therapy for Hp-associated gastritis: Banxia Xiexin decoction combined with SQ (BXS) with 1,176 patients from 12 trials, Huanglian Wendan decoction combined with SQ (HLS) with 344 patients from 4 trials, Huangqi Jianzhong decoction combined with SQ (HQS) with 240 patients from 4 trials, Huopu Xialing decoction combined with SQ (HPS) with 476 patients from 4 trials, Lianpuyin combined with SQ (LPS) with 940 patients from 9 trials, Xiangsha Liujunzi combined with SQ (XSS) with 92 patients from 2 trials, Weifuchun combined with SQ (WFS) with 579 patients from 5 trials, Weisu granule combined with SQ (WSS) with 312 patients from 3 trials, and Jinghua Weikang combined with SQ (JHS) with 2,005 patients from 12 trials. All patients were in the mean age range (18–72 years), male gender (52.3%). In addition, 4 articles by Zeng (17), Zhang (32), Yang (51), and Li (30) showed that TCM combined with SQ extended the duration of PPIs; 2 articles by Ling (22) and Wang (26) showed that TCM combination extended the duration of PPIs and bismuth agents.

Among the included studies, 21 studies reported random number tables, 17 studies adopted allocation methods based

Table 1 Characteristics of studies included in comparison

Trials	TCM	Sample size (E/C)	Age (E/C) (mean ± SD, years)	Gender (E/C)		Interventions (E/C)	Period (days)		Outcomes	Balance report of baseline
				Male	Female		TCM	SQ		
Zeng (17) 2021	BX	40	35.1±3.9	25	15	BX + OME + BPC + AMO + CLA	28	14	(a) (b)	P>0.05
		40	34.4±3.5	26	14	OME + BPC + AMO + CLA				
Ding *et al.* (18) 2017	BX	60	45.31±2.61	23	36	BX + RAB + CBP + AMO + CLA	14	14	(b) (c)	P>0.05
		60	44.85±2.46	24	35	RAB + CBP + AMO + CLA				
Hou *et al.* (19) 2021	BX	40	41.68±10.29	22	18	BX + OME + BPC + CLA + AMO	14	14	(a) (b) (c)	P>0.05
		40	42.13±10.34	23	17	OME + BPC + CLA + AMO				
Huang *et al.* (20) 2018	BX	88	46.78±13.362	34	54	BX + OME + BPC + AMO + FUR	14	14	(b)	P>0.05
		88	42.22±12.188	36	52	OME + BPC + AMO + FUR				
Li (21) 2019	BX	20	52.6±10.5	11	9	BX + OME + BPC + AMO + CLA	28	14	(b)	No estimate
		20	52.2±10.3	12	8	OME + BPC + AMO + CLA				
Ling (22) 2021	BX	46	45.5±4.5	24	22	BX + RAB + CBP + AMO + CLA	14	14	(a) (b) (c)	P>0.05
		46	45.8±4.6	25	21	RAB + CBP + AMO + CLA				
Liu (23) 2021	BX	43	50.12±5.58	25	18	BX + AMO + CLA + CBP + PAN	28	14	(a)	No estimate
		43	49.85±5.64	26	17	AMO + CLA + CBP + PAN				
Ma *et al.* (24) 2021	BX	54	51.3±5.9	28	26	BX + PAN + BPC + AMO + CLA	14	14	(a) (b) (c)	P>0.05
		54	51.3±5. 9	30	24	PAN + BPC + AMO + CLA				
Qie *et al.* (25) 2021	BX	49	31.7±1.2	26	23	BX + AMO + CLA + RAB + CBP	28	14	(a) (b)	P>0.05
		49	31.6±1.3	25	24	AMO + CLA + RAB + CBP				
Wang (26) 2019	BX	60	52.17±10.34	32	28	BX + OME + AMO + CLA + BPC	28	14	(a) (b) (c)	P>0.05
		60	52.55±10.49	33	27	OME + AMO + CLA + BPC				
Zhao *et al.* (27) 2020	BX	58	50.81±11.92	30	28	BX + RAB + AMO + CLA + BPC	14	14	(a) (b) (c)	P>0.05
		58	47.97±14.01	32	26	RAB + AMO + CLA + BPC				
Zhang (28) 2020	BX	30	49.03±10.44	14	16	BX + RAB + CBA + AMO + CLA	84	14	(a) (b) (c)	P>0.05
		30	48.70±10.72	16	14	RAB + CBA + AMO + CLA				
He *et al.* (29) 2021	HL	55	42.83±4.38	26	29	HL + BPC + CLA + AMO + RAB	14	14	(a) (b)	P>0.05
		55	42.78±4.35	28	27	BPC + CLA + AMO + RAB				
Li *et al.* (30) 2017	HL	41	39.21±4.54	24	17	HL + OME + CBP + TIN + CLA	14	14	(a) (b)	No estimate
		41	39.80±4.33	23	18	OME + CBP + TIN + CLA				
Sun (31) 2019	HL	41	44.51±9.42	20	21	HL + RAB + BPC + CLA + MET	14	14	(a) (c)	P>0.05
		41	43.15 ±10.32	23	18	RAB + BPC + CLA + MET				
Zhang *et al.* (32) 2017	HL	35	42.14±10.10	20	15	HL + RAB + CLA + MET + CBP	28	10	(a) (b)	P>0.05
		35	39.95±11.04	18	17	RAB + CLA + MET + CBP				
Chen *et al.* (33) 2020	HQ	40	36.06±12.72	19	21	HQ + RAB + CLA + AMO + BIS	14	14	(a) (b) (c)	P>0.05
		40	35.62±11.34	21	19	RAB + CLA + AMO + BIS				

Table 1 (*continued*)

Table 1 (*continued*)

Trials	TCM	Sample size (E/C)	Age (E/C) (mean ± SD, years)	Gender (E/C)		Interventions (E/C)	Period (days)		Outcomes	Balance report of baseline
				Male	Female		TCM	SQ		
Hu (34) 2021	HQ	38	41.56±4.45	20	18	HQ + AMO + OME + CLA + BPC	28	14	(a) (b) (c)	P>0.05
		38	42.11±4.56	19	19	AMO + OME + CLA + BPC				
Wang (35) 2021	HQ	52	42.8±4.5	24	28	HQ + AMO + CBP + CLA + RAB	14	14	(a) (b)	P>0.05
		52	42.8±4.5	23	29	AMO + CBP + CLA + RAB				
Yang *et al.* (36) 2021	HQ	30	48.3±3.2	17	13	HQ + OME + CLA + AMO + CBP	no estimate	14	(a) (b)	P>0.05
		30	50.6±2.8	16	14	OME + CLA + AMO + CBP				
Cai *et al.* (37) 2018	HP	83	59.14±8.99	43	40	HP + PAN + AMO + FUR + CBP	14	14	(a) (b)	P>0.05
		83	58.42±8.65	46	37	PAN + AMO + FUR + CBP				
Huang (38) 2019	HP	42	52.7±11.3	22	20	HP + ESO + BPC + TIN + CLA	14	14	(a) (b)	P>0.05
		45	53.1±11.6	22	23	ESO + BPC + TIN + CLA				
Xie *et al.* (39) 2018	HP	59	44.7±2.4	32	27	HP + PAN + CBA + CLA + AMO	14	14	(a) (b)	P>0.05
		59	44.2±2.7	30	29	PAN + CBA + CLA + AMO				
Zhang *et al.* (40) 2016	HP	53	51.24±3.12	32	21	HP + PAN + CBA + CLA + AMO	14	14	(a) (b) (c)	P>0.05
		52	52.36±2.48	31	21	PAN + CBA + CLA + AMO				
Duan (41) 2021	LP	50	45.2±2.6	28	22	LP + AMO + RAB + CLA + CBP	no estimate	14	(a) (b)	P>0.05
		50	43.5±2.4	29	21	AMO + RAB + CLA + CBP				
Huang *et al.* (42) 2020	LP	51	42.83±1.47	38	13	LP + RAB + CLA + AMO + CBP	14	14	(a)	P>0.05
		51	42.49±1.21	40	11	RAB + CLA + AMO + CBP				
Li (43) 2018	LP	50	45.4±5.5	26	24	LP + RAB + AMO + CLA + CBP	14	14	(a) (b)	P>0.05
		50	45.5±5.5	26	24	RAB + AMO + CLA + CBP				
Liu *et al.* (44) 2021	LP	60	51.1±8.2	31	29	LP + RAB + AMO + CLA + BPC	14	14	(a) (b) (c)	P>0.05
		60	49.8±7.8	32	28	RAB + AMO + CLA + BPC				
Su *et al.* (45) 2018	LP	20	32.21±10.26	12	8	LP + CBP + CLA + AMO + RAB	14	14	(b)	P>0.05
		20	32.52±10.39	13	7	CBP + CLA + AMO + RAB				
Tian *et al.* (46) 2015	LP	80	25–64	43	36	LP + RAB + AMO + CLA + CBP	14	14	(a) (b)	P>0.05
		40	22–65	22	17	RAB + AMO + CLA + CBP				
Wang *et al.* (47) 2019	LP	100	41.55±1.09	50	50	LP + RAB + AMO + CLA + CBP	14	14	(b)	P>0.05
		100	42.23±1.92	51	49	RAB + AMO + CLA + CBP				
Li (48) 2019	LP	41	21–60	25	16	LP + AMO + CBP + LAN + CLA	14	14	(a) (b)	P>0.05
		41	22–61	24	17	AMO + CBP + LAN + CLA				
Shui (49) 2018	LP	38	41.09±2.18	22	16	LP + AMO + CLA + RAB + CBP	14	14	(a) (b)	P>0.05
		38	40.21±2.59	21	17	AMO + CLA + RAB + CBP				
Wang (50) 2018	XS	30	59.12±2.76	16	14	XS + AMO + LEV + OME + CBP	14	14	(a) (b)	P>0.05
		30	58.65±3.25	17	13	AMO + LEV + OME + CBP				

Table 1 (*continued*)

Table 1 (*continued*)

Trials	TCM	Sample size (E/C)	Age (E/C) (mean ± SD, years)	Gender (E/C)		Interventions (E/C)	Period (days)		Outcomes	Balance report of baseline
				Male	Female		TCM	SQ		
Yang *et al.* (51) 2020	XS	16	58.74±4.13	9	7	XS + BPC + OME + AMO + CLA	42	14	(b)	P>0.05
		16	58.18±4.39	8	8	BPC + OME + AMO + CLA				
Deng (52) 2018	WF	40	54.35±2.07	16	24	WF + OME + BPC + AMO + CLA	14	14	(a) (b)	P>0.05
		40	54.21±2.03	17	23	OME + BPC + AMO + CLA				
He *et al.* (53) 2017	WF	99	41.19±11.64	51	48	WF + ESO + CBP + AMO + CLA	14	14	(a) (b) (c)	P>0.05
		97	41.73±11.48	52	45	ESO + CBP + AMO + CLA				
Tang *et al.* (54) 2017	WF	70	48.8±6.5	39	31	WF + RAB + BPC + AMO + CLA	14	14	(a) (b) (c)	P>0.05
		70	48.7±6.3	38	32	RAB + BPC + AMO + CLA				
Zang (55) 2020	WF	33	49.35±6.37	19	14	WF + LAN + CBP + AMO + CLA	365	14	(a) (b) (c)	P>0.05
		32	48.34±7.31	18	14	LAN + CBP + AMO + CLA				
Zhang *et al.* (56) 2019	WF	49	57.66±2. 20	26	23	WF + ESO + CBP + AMO + CLA	14	14	(b)	P>0.05
		49	57.26±2. 45	24	25	ESO + CBP + AMO + CLA				
Chen (57) 2021	WS	48	47.18±2.75	24	24	WS + ILA + CBP + CLA + ORN	14	14	(a) (b) (c)	P>0.05
		48	47.32±2.68	26	22	ILA + CBP + CLA + ORN				
Huang *et al.* (58) 2021	WS	50	45.11±5. 79	25	25	WS + RAB + BIS + AMO + CLA	14	14	(a) (b) (c)	P>0.05
		50	45.38±6. 64	23	27	RAB + BIS + AMO + CLA				
Qi (59) 2021	WS	58	45.23±6.12	36	22	WS + OME + BPC + AMO + CLI	14	14	(a) (b) (c)	P>0.05
		58	46.75±7.24	39	19	OME + BPC + AMO + CLI				
Hang (60) 2020	JH	30	41.10±11.70	13	17	JH + CBP + AMO + CLA + PAN	14	14	(b)	P>0.05
		30	41.30±11.67	14	16	CBP + AMO + CLA + PAN				
Huang *et al.* (61) 2016	JH	55	45.8±4.2	32	23	JH + CBA + AMO + CLA + ESO	28	14	(a) (b) (c)	P>0.05
		55	48.2±4.9	35	20	CBA + AMO + CLA + ESO				
Li *et al.* (62) 2020	JH	104	48.9±9.0	57	47	JH + AMO + CLA + RAB + BPC	14	14	(a) (c)	P>0.05
		104	48.6±9.2	58	46	AMO + CLA + RAB + BPC				
Tang *et al.* (63) 2018	JH	60	46.72±12.23	28	32	JH + CBP + ESO + AMO + FUR	14	14	(a) (b)	P>0.05
		50	45.28±13.35	23	27	CBP + ESO + AMO + FUR				
Wang *et al.* (64) 2020	JH	39	42.34±10.67	15	20	JH + BPC + AMO + CLA + OME	14	14	(a) (b) (c)	P>0.05
		38	43.17±12.33	16	19	BPC + AMO + CLA + OME				
Wu *et al.* (65) 2013	JH	120	19 –68	76	44	JH + BPC + AMO + CLA + OME	28	14	(a) (b) (c)	P>0.05
		120	20–65	80	40	BPC + AMO + CLA + OME				
Zhang *et al.* (66) 2018	JH	60	20–72	22	38	JH + RAB + AMO + FUR + BPC	14	14	(a) (b)	P>0.05
		60	18–70	26	34	RAB + AMO + FUR + BPC				
Zheng (67) 2020	JH	35	41.000±11.664	14	19	JH + BPC + AMO + CLA + OME	14	14	(a) (c)	P>0.05
		35	40.294±22.379	16	18	BPC + AMO + CLA + OME				

Table 1 (*continued*)

Table 1 (*continued*)

Trials	TCM	Sample size (E/C)	Age (E/C) (mean ± SD, years)	Gender (E/C)		Interventions (E/C)	Period (days)		Outcomes	Balance report of baseline
				Male	Female		TCM	SQ		
Zhang (68) 2018	JH	59	45.02±6.743	31	28	JH + BPC + AMO + FUR + ESO	14	14	(a) (b) (c)	P>0.05
		57	43.79±8.938	30	27	BPC + AMO + FUR + ESO				
Chen (69) 2018	JH	32	48.50±14.08	15	17	JH + BPC + TIN + CLA + RAB	14	14	(a) (c)	P>0.05
		31	48.32±11.71	14	17	BPC + TIN + CLA + RAB				
Li *et al.* (70) 2018	JH	347	46.02±11.93	154	193	JH + CBP + AMO + FUR + OME	14	10	(a) (c)	P>0.05
		124	44.90±12.30	57	67	CBP + AMO + FUR + OME				
Luo *et al.* (71) 2018	JH	270	50.33±8.98	110	160	JH + BPC + AMO + FUR + ESO	14	10	(a) (c)	P>0.05
		90	50.00±10.00	37	53	BPC + AMO + FUR + ESO				

(a) Eradication rate of Hp; (b) Therapeutic response rate; (c) Incidence of adverse reactions. TCM, traditional Chinese medicine; E, experimental group; C, control group; SQ, standard quadruple; BX, Banxiaxiexin decoction; HL, Huanglian Wendan decoction; HQ, Huangqi Jianzhong decoction; HP, Huopu Xialing decoction; LP, Lianpuyin; XS, Xiangsha Liujunzi decoction; WF, Weifuchun; WS, Weisu granule; JH, Jinghua Weikang; OME, omeprazole; BPC, bismuth potassium citrate; AMO, amoxicillin; CLA, claricid; RAB, Rabeprazole; CBP, colloidal bismuth pectin; FUR, furazolidone; PAN, pantoprazole; CBA, compound bismuth aluminate tablets; TIN, tinidazole; Hp, *Helicobacter pylori*.

on different visit orders or treatment regimens, and the rest just mentioned "randomly allocated", and no specific randomization methods were elaborated. There were 4 studies that described allocation concealment; 39 studies mentioned that participants were not blinded; 3 studies described blinding of outcome assessment. The effect of loss of follow-up was estimated correctly and made no difference to the outcomes in 4 studies; 4 studies estimated the effect of loss of follow-up inappropriately, and the remaining studies reported no loss of follow-up. There was no selective reporting in all 55 studies. The rest did not describe any relative information (*Figure 2*). Overall, the quality of the included literature was relatively poor, which may affect the reliability and extrapolation of the article results.

Eradication rate of Hp

Network graphs are displayed in *Figure 3*. There were 49 studies involving 9 kinds of integrated Chinese and Western medicine interventions, all of which were direct comparisons. The results showed that the maximum number of studies included in the comparison between JHS and quadruple therapy was 12, the number of studies comparing BXS, HLS, HQS, HPS, LPS, XSS, WFS, and WSS with quadruple therapy, respectively, was 10, 4, 4, 4, 7, 1, 4, and 3. A total of 5,540 participants were enrolled (3,018 in the experimental group and 2,522 in the control group).

The results of the Bayesian network meta-analysis in *Table 2* show that the Hp eradication rates of 2 TCMs combined with SQ (BXS: OR =1.628, 95% CI: 1.157–2.147; LPS: OR =1.516, 95% CI: 1.017–2.056) were higher than those of SQ alone. The Hp eradication rate of JHS (OR =0.654, 95% CI: 0.385–0.950) was lower than that of SQ. The Hp eradication rates of both HLS (OR =0.060, 95% CI: 0.939–0.809) and HQS (OR =–0.394, 95% CI: –1.286 to 0.444) were lower than HPS, the Hp eradication rates of BXS (OR =0.109, 95% CI: –0.621 to 0.802), HLS (OR =–0.286, 95% CI: –1.084 to 0.468), HQS (OR =–0.629, 95% CI: –1.430 to 0.137) and HPS (OR =–0.234, 95% CI: –1.060 to 0.583) were lower than LPS, the Hp eradication rates of HQS (OR =–0.007, 95% CI: –0.824 to 0.816) were lower than those of WFS, the Hp eradication rates of HLS (OR =–0.190, 95% CI: –1.163 to 0.796), HQS (OR =–0.518, 95% CI: –1.476 to 0.426), HPS (OR =–0.122, 95% CI: –1.176 to 0.887), and WFS (OR =–0.521, 95% CI: –1.524 to 0.473) were lower than those of WSS, the Hp eradication rates of both HQS (OR =0.252, 95% CI: –0.414 to 0.858) and WFS (OR =0.232, 95% CI: –0.404 to 0.990) were lower than those of JHS. The result of rank probability in *Figure 4A* shows that BXS had the highest probability (0.85) of becoming the best intervention to improve the Hp eradication rate for patients with Hp-associated gastritis, followed by LPS (0.78), WWS (0.70),

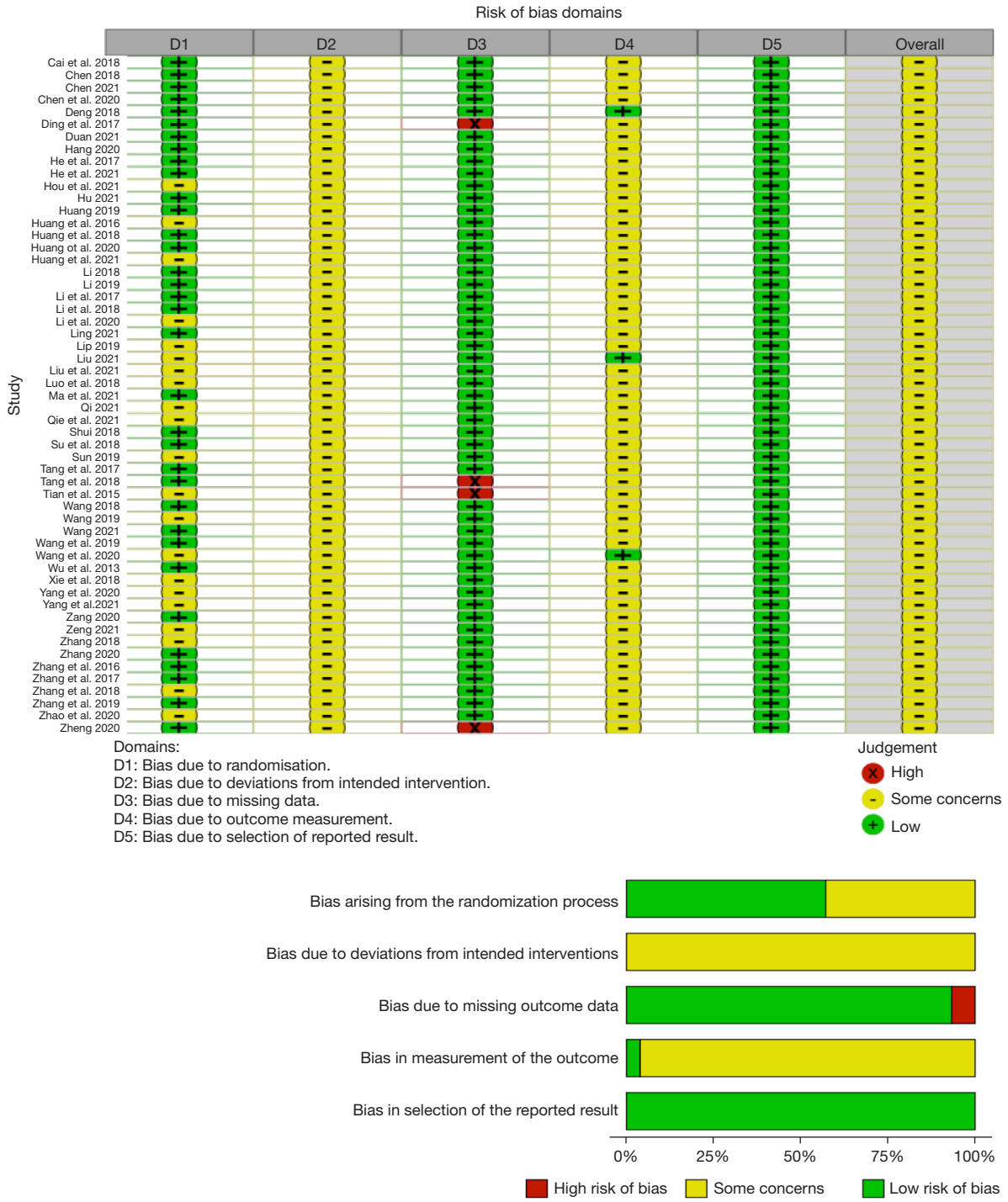

Figure 2 Risk of bias summary and risk of bias graph.

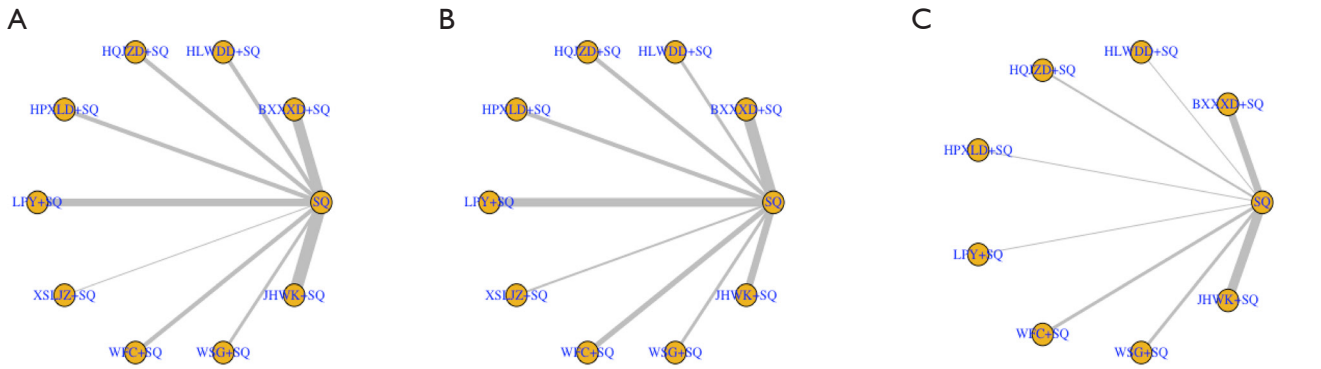

Figure 3 Network plot for safety. (A) Eradication rate of Hp; (B) therapeutic response rate; (C) incidence of adverse reactions. Hp, *Helicobacter pylori*.

Table 2 Comparison of Hp eradication rate

Comparator	Intervention [odds ratios (95% CI)]								
	BXS	HLS	HQS	HPS	LPS	XSS	WFS	WSS	JHS
HLS	0.383 (−0.365, 1.170)								
HQS	0.733 (−0.003, 1.513)	0.331 (−0.482, 1.179)							
HPS	0.338 (−0.519, 1.150)	−0.060* (−0.939, 0.809)	−0.394* (−1.286, 0.444)						
LPS	0.109* (−0.621, 0.802)	−0.286* (−1.084, 0.468)	−0.629* (−1.430, 0.137)	−0.234* (−1.060, 0.583)					
XSS	0.542 (−0.828, 1.861)	0.155 (−1.227, 1.539)	−0.166 (−1.593, 1.132)	0.216 (−1.171, 1.617)	0.434 (−0.907, 1.758)				
WFS	0.738 (−0.079, 1.519)	0.336 (−0.549, 1.191)	−0.007* (−0.824, 0.816)	0.384 (−0.464, 1.311)	0.631 (−0.158, 1.406)	0.185 (−1.136, 1.577)			
WSS	0.209 (−0.695, 1.124)	−0.190* (−1.163, 0.796)	−0.518* (−1.476, 0.426)	−0.122* (−1.176, 0.887)	0.105 (−0.808, 1.037)	−0.330 (−1.806, 1.175)	−0.521* (−1.524, 0.473)		
JHS	0.968 (0.403, 1.542)	0.576 (−0.083,1.232)	0.252* (−0.414, 0.858)	0.641 (−0.071, 1.365)	0.865 (0.292 1.450)	0.414 (−0.818, 1.730)	0.232* (−0.404, 0.990)	0.760 (−0.051, 1.568)	
SQ	1.628* (1.157, 2.147)	1.230 (0.656, 1.849)	0.898 (0.302, 1.480)	1.292 (0.637, 1.955)	1.516* (1.017, 2.056)	1.076 (−0.125, 2.360)	0.886 (0.320, 1.540)	1.413 (0.661, 2.198)	0.654* (0.385, 0.950)

*, represents statistically significant superiority/inferiority of the intervention over the comparator. Hp, *Helicobacter pylori*. BXS, Banxiaxiexin decoction; HLS, Huanglian Wendan decoction; HQS, Huangqi Jianzhong decoction; HPS, Huopu Xialing decoction; LPS, Lianpuyin; XSS, Xiangsha Liujunzi; WFS, Weifuchun; WSS, Weisu granule; JHS, Jinghua Weikang; SQ, standard quadruple.

HPS (0.63), HLS (0.59), XSS (0.50), WFS (0.368), HQS (0.367), JHS (0.21), then SQ (0.0051).

Therapeutic response rate

Network graphs are demonstrated in *Figure 3B*. There were 47 studies involving 9 kinds of integrated Chinese and Western medicine interventions, all of which were direct comparisons. The results showed that the maximum number of studies included in the comparison between BXS and quadruple therapy was 11, the number of studies comparing HLS, HQS, HPS, LPS, XSS, WFS, WSS, and

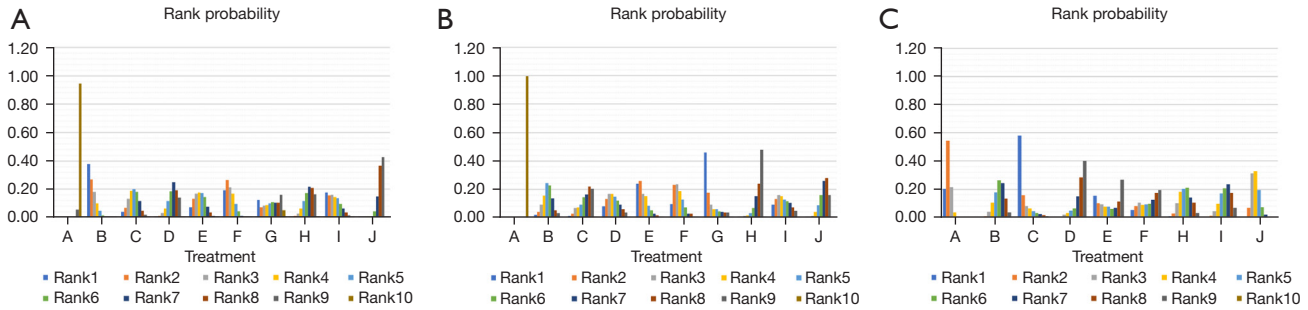

Figure 4 The result of rank probability. (A) Eradication rate of Hp; (B) therapeutic response rate; (C) incidence of adverse reactions. A, SQ; B: Banxiaxiexin decoction + SQ; C, Huanglian Wendan decoction + SQ; D, Huangqi Jianzhong decoction + SQ; E, Huopu Xialing decoction + SQ; F, Lianpuyin + SQ; G, Xiangsha Liujunzi + SQ; H, Weifuchun + SQ; I, Weisu granule + SQ; J, Jinghua Weikang + SQ. Hp, *Helicobacter pylori*; SQ, standard quadruple.

Table 3 Comparison of therapeutic response rate

Comparator	Intervention [odds ratios (95% CI)]								
	BXS	HLS	HQS	HPS	LPS	XSS	WFS	WSS	JHS
HLS	0.256 (–0.647, 1.102)								
HQS	–0.134* (–1.042, 0.760)	–0.369* (–1.525, 0.661)							
HPS	–0.475* (–1.374, 0.386)	–0.705* (–1.853, 0.353)	–0.314* (–1.434, 0.751)						
LPS	–0.279* (–0.952, 0.371)	–0.532* (–1.481, 0.472)	–0.154* (–1.113, 0.806)	0.201 (–0.806, 1.137)					
XSS	–0.657* (–2.315, 0.747)	–0.915* (–2.718, 0.644)	–0.536 (–2.309, 1.036)	–0.191 (–1.892, 1.354)	–0.385 (–2.048, 1.043)				
WFS	0.496 (–0.147, 1.182)	0.243 (–0.670, 1.212)	0.639 (–0.361, 1.668)	0.980 (0.033, 1.953)	0.787 (0.058, 1.505)	1.157 (–0.233, 2.831)			
WSS	–0.091* (–1.022, 0.826)	–0.346* (–1.515, 0.805)	0.051 (–1.144, 1.229)	0.394 (–0.792, 1.551)	0.194 (–0.827, 1.138)	0.565 (–1.127, 2.297)	–0.599* (–1.621, 0.388)		
JHS	0.309* (–0.305, 0.899)	0.052* (–0.798, 0.940)	0.427 (–0.447, 1.368)	0.778 (–0.145, 1.730)	0.581 (–0.069, 1.279)	0.960 (–0.408, 2.676)	–0.196* (–0.874, 0.495)	0.384 (–0.534, 1.345)	
SQ	1.476* (1.088, 1.898)	1.229 (0.475, 2.026)	1.613 (0.845, 2.450)	1.956* (1.179, 2.781)	1.769* (1.260, 2.304)	2.130 (0.819, 3.749)	0.976 (0.440, 1.523)	1.567 (0.757, 2.447)	1.169 (0.751, 1.638)

* represents statistically significant superiority/inferiority of the intervention over the comparator. BXS, Banxiaxiexin decoction; HLS, Huanglian Wendan decoction; HQS, Huangqi Jianzhong decoction; HPS, Huopu Xialing decoction; LPS, Lianpuyin; XSS, Xiangsha Liujunzi; WFS, Weifuchun; WSS, Weisu granule; JHS, Jinghua Weikang; SQ, standard quadruple.

JHS with quadruple therapy, respectively, was 3, 4, 4, 8, 2, 5, 3, and 7. A total of 4,734 participants were enrolled (2,395 in the experimental group and 2,339 in the control group).

The results of the Bayesian network meta-analysis in *Table 3* show that the therapeutic response rates of 3 TCMs combined with SQ (BXS: OR =1.476, 95% CI: 1.088–1.898; HPS: OR =1.956, 95% CI: 1.179–2.781; LPS: OR =1.769, 95% CI: 1.260–2.304) were higher than those of SQ alone. The therapeutic response rate of BXS was lower than that of HQS (OR =–0.134, 95% CI: –1.042 to 0.760), HPS (OR =–0.475, 95% CI: –1.374 to 0.386), LPS (OR =–0.279, 95% CI: –0.952 to 0.371), XSS (OR =–0.657, 95% CI:

Table 4 Comparison of incidence of adverse reactions

Comparator	Intervention [odds ratios (95% CI)]							
	BXS	HLS	HQS	HPS	LPS	WFS	WSS	JHS
HLS	−1.293* (−3.244, 0.553)							
HQS	0.418 (−0.870, 1.803)	1.722 (−0.403, 3.985)						
HPS	−0.011 (−2.653, 3.635)	1.247 (−1.718, 5.208)	−0.431 (−3.309, 3.291)					
LPS	0.072 (−1.749, 2.396)	1.377 (−1.033, 4.220)	−0.327 (−2.552, 2.173)	0.118 (−3.849, 3.486)				
WFS	−0.179* (−1.192, 0.900)	1.102 (−0.805, 3.145)	−0.597* (−2.077 0.816)	−0.107 (−3.834, 2.460)	−0.263 (−2.578, 1.704)			
WSS	0.0438 (−0.990, 1.106)	1.322 (−0.595, 3.351)	−0.376 (−1.891, 1.038)	0.111 (−3.678, 2.698)	−0.034 (−2.398, 1.907)	0.240 (−0.960, 1.330)		
JHS	−0.505* (−1.277, 0.278)	0.798 (−1.027, 2.653)	−0.918* (−2.261 0.318)	−0.451 (−4.101, 2.117)	−0.560 (−2.799, 1.204)	−0.313* (−1.312, 0.531)	−0.550* (−1.511, 0.357)	
SQ	−0.953* (−1.627, −0.298)	0.322 (−1.396, 2.156)	−1.370* (−2.632, −0.203)	−0.904 (−4.589, 1.591)	−0.772* (−1.640, −0.018)	0.772 (0.018, 1.640)	−1.004* (−1.834, −0.219)	−0.459* (−0.890, −0.037)

* represents statistically significant superiority/inferiority of the intervention over the comparator. BXS, Banxiaxiexin decoction; HLS, Huanglian Wendan decoction; HQS, Huangqi Jianzhong decoction; HPS, Huopu Xialing decoction; LPS, Lianpuyin; WFS, Weifuchun; WSS, Weisu granule; JHS, Jinghua Weikang; SQ, standard quadruple.

−2.315 to 0.747), WSS (OR =−0.091, 95% CI: −1.022 to 0.826), and JHS (OR =0.309, 95% CI: −0.305 to 0.899). The therapeutic response rate of HLS was lower than that of HQS (OR =−0.369, 95% CI: −1.525 to 0.661), HPS (OR =−0.705, 95% CI: −1.853 to 0.353), LPS (OR =−0.532, 95% CI: −1.481 to 0.472), XSS (OR =−0.915, 95% CI: −2.718 to 0.644), WSS (OR =−0.346, 95% CI: −1.515 to 0.805), and JHS (OR =0.052, 95% CI: −0,798 to 0.940). The therapeutic response rate of HQS was lower than that of HPS (OR =−0.314, 95% CI: −1.434 to 0.751) and LPS (OR =−0.154, 95% CI: −1.113 to 0.806), and the therapeutic response rate of WFS was lower than that of WSS (OR =−0.599, 95% CI: −1.621 to 0.388) and JHS (OR =−0.196, 95% CI: −0.874 to 0.495). The results of rank probability in *Figure 4B* show that XSS had the highest probability (0.81) of becoming the best intervention to improve the therapeutic response rate for patients with Hp-associated gastritis, followed by HPS (0.80), LPS (0.73), HQS (0.62), WSS (0.59), BXS (0.53), HLS (0.38), JHS (0.32), WFS (0.22), and SQ alone (0.0001).

Incidence of adverse reactions

The network graphs are displayed in *Figure 3C*. There were 27 studies involving 8 kinds of integrated Chinese and Western medicine interventions other than WSS combined quadruple therapy, all of which were direct comparisons. The results showed that the maximum number of studies included in the comparison of JHS and quadruple therapy was 9, the number of studies comparing BXS, HLS, HQS, HPS, LPS, WFS, and WSS with quadruple therapy, respectively, was 7, 1, 2, 1, 1, 3, and 3. A total of 3,587 participants were enrolled (1,999 in the experimental group and 1,588 in the control group).

The results of the Bayesian network meta-analysis (*Table 4*) showed that the incidence of adverse reactions of 5 TCMs combined with SQ (BXS: OR =−0.953, 95% CI: −1.627 to −0.298; HQS: OR =−1.370, 95% CI: −2.632 to −0.203; LPS: OR =−0.772, 95% CI: −1.640 to −0.018; WSS: OR =−1.004, 95% CI: −1.834 to −0.219; JHS: OR =−0.459, 95% CI: −0.890 to −0.037) were lower than those of SQ alone, the incidence of adverse reactions of BXS (OR =−1.293, 95% CI: −3.244 to 0.553) was lower than that of HLS; the incidences of adverse reactions of BXS (OR =−0.179, 95% CI: −1.192 to 0.900) and HQS (OR =−0.597, 95% CI: −2.077 to 0.816) were lower than that of WFS; the incidences of adverse reactions of BXS (OR =−0.505, 95% CI: −1.277 to 0.278), HQS (OR =−0.918, 95% CI: −2.261 to

0.318), WFS (OR =–0.313, 95% CI: –1.312 to 0.531), and WSS (OR =–0.550, 95% CI: –1.511 to 0.357) were lower than that of JHS. The results of rank probability (*Figure 4C*) showed that HQS had the lowest probability (0.20) of becoming the worst intervention to reduce the incidence of adverse reactions for patients with Hp-associated gastritis, followed by WSS (0.34), BXS (0.36), LPS (0.37), HPS (0.43), WFS (0.45), JHS (0.64), HLS (0.85), and SQ alone (0.87).

Sensitivity analysis

The sensitivity analysis results indicated that except for the incidence of adverse reactions in WSS, the remaining outcome indicators were robust and reliable. Due to the high heterogeneity of WSS (I^2=52%, P=0.12), we identified that the study of Huang *et al.* (58) was the source of heterogeneity by excluding each article in the sensitivity analysis. The difference in gender ratio among the trials might account for the high heterogeneity after reviewing the full text. The result indicated that WSS (OR =0.24, 95% CI: 0.10–0.56) could significantly reduce the incidence of adverse reactions in patients with gastritis after the exclusion of Huang *et al.*'s study.

Publication bias

Egger's test results were insignificant in the analysis: the therapeutic response rate in BXS (t=0.41, P=0.6930). Egger's test results were significant in both analyses: the Hp eradication rate in BXS (t=2.97, P=0.0179), the eradication rate of Hp in JHS (t=2.63, P=0.0252). The statistically consistent significance of results before and after the trim-and-fill method in the Hp eradication rate of BXS and JHS meant that the results were stable and less affected by publication bias. In summary, all outcomes analyzed were robust and reliable.

Discussion

Hp was found and isolated by the Australian scientists J. Robin Warren and Barry J. Marshall in 1983 (72). It is classified as a class I carcinogen by the World Health Organization (WHO) in 1994 (73). The vast majority of Hp-induced gastritis remains completely asymptomatic for a long time, despite the presence of Hp inducing chronic inflammation over many decades (74). With the increasing and broad application of antibacterial drugs, antibiotic resistance of Hp is becoming a severe problem in clinical practice. Many studies have shown the anti-bacterial activity of TCM against Hp *in vitro* and *in vivo* (75,76). Researches show that Banxia Xiexin decoction and single Chinese herbal drugs have intense bacteriostatic action on Hp resistant strains *in vitro* (77-79). Meta-analyses have demonstrated that Huangqi Jianzhong decoction plus conventional medicine is more effective in improving the Hp eradication rate than Western medicine alone for treating chronic gastritis (80), Huanglian Wendan decoction and Weifuchun could effectively treat Hp-related gastric diseases (81,82). Jinghua Weikang has been shown to have an inhibitory effect on gastric inflammation induced by Hp and to exert a protective effect against gastric injury via inhibition of inflammation reactions (83). Meanwhile, Huopu Xialing decoction, Lianpuyin, Liujunzi decoction, Weifuchun, and Weisu granule also have an inhibitory effect on gastric inflammation and promote gastric mucosal repair.

This study aimed to evaluate the efficacy and safety of different TCMs combined with SQ and to explore which formula is the most effective for Hp-associated gastritis. In terms of eradication rate of Hp, compared with the simple quadruple therapy, BXS and LPS both helped to eradicate Hp, and BXS was the best treatment for Hp eradication. If poor availability or other reasons prevent its clinical application, LPS is an alternative. If a patient is diagnosed with Hp-associated gastritis by a medical professional, but does not show significant gastritis-related symptoms or other discomfort, and the physician determines that the patient's primary treatment goal is to eradicate Hp in order to treat the gastritis caused by Hp, the use of BXS or LPS is more effective than the commonly used quadruple therapy to eradicate Hp. BXS is optimal regimen. In terms of Hp eradication rate, compared with the simple quadruple therapy, BXS and LPS both helped to eradicate Hp, and BXS was the best treatment for Hp eradication. In terms of therapeutic response rate, HPS and LPS are the top 2 best treatment measures. If a patient is diagnosed with Hp-related gastritis and has significant gastritis-related symptoms, such as epigastric pressure, nausea, vomiting, belching, loss of appetite, or gastrointestinal bleeding, and the physician determines that the patient's treatment is focused on eliminating or relieving symptoms, with Hp eradication as a secondary treatment, the clinician is recommended to use the HPS. LPS is the alternative for the abovementioned. In terms of safety, HQS and WSS are the top 2 options. If the patient is diagnosed with HP-related gastritis, but the patient is weak or has other conditions

that require increased focus on drug safety, clinicians are recommended to use HQS, with WSS as an alternative. In conclusion, no treatment regimen is completely without any drawbacks, and the one that works best according to different outcomes is variable. For example, Lianpuyin is more effective in both eradicating Hp and improving symptoms, but its safety is less satisfactory. Therefore, in the course of clinical treatment, physicians should choose the type of herbal formula combined with Western medicine that is appropriate for the patient's actual physical state.

The following limitations exist in this paper: (I) some of the included studies did not clearly indicate whether reasonable allocation concealment and blinding were used, which may have an impact on the quality evaluation results of the literature; (II) the overall quality of the included literature was poor, which affects the truthfulness of extrapolation of study findings; (III) there were few studies describing the incidence of adverse reactions as an outcome, which makes the findings biased; (IV) some of the studies were somewhat heterogeneous, which mainly related to the addition or subtraction of components in TCM prescriptions.

In this study, we conducted a network meta-analysis and investigated the efficacy and safety of TCM combined with quadruple therapy in eradicating Hp. The conclusion indicated that compared with quadruple therapy alone, some TCMs combined with quadruple therapy can effectively eradicate Hp, eliminate the symptoms, and reduce adverse reactions. In summary, clinicians need to readjust their mindset to include TCM as an option when prescribing, and it is important to choose the appropriate TCM according to the patient's gastritis condition and needs, which requires clinicians to be well versed in the knowledge of TCM. This requires that managers must strengthen the training of physicians in TCM and raise the threshold of TCM knowledge test results at the time of entry. For subsequent research in TCM, clinical practice research should be as important and rigorous as theoretical research. In clinical practice research, investigators should pay attention to pre-experimental protocol design and quality control, and strictly comply with the design process of RCTs, so that the quality of the trials is higher and the guidance significance for future clinical trials is enhanced. Not only the effect of the TCM should be reported, but also the safety of the TCM should be emphasized in the process of data collection, which facilitates the comprehensive evaluation of TCM. Policy makers should attach great importance to the development of treatment guidelines to produce standardized and authoritative guidelines to guide the future application of TCM. This will actively prevent various physicians from adding or subtracting ingredients to TCM based on their own experience. However, further strictly designed randomized double-blind controlled trials are required to verify these conclusions.

Conclusions

BXS is the most likely to be the best intervention to improve the Hp eradication rate in patients with HP-associated gastritis, followed by LPS. XSS is the most likely to be the best intervention to improve the therapeutic response rate for patients with Hp-associated gastritis, followed by HPS. HQS is the most likely to be the best intervention to reduce the incidence of adverse reactions for patients with Hp-associated gastritis, followed by WSS. However, in real clinical practice, the effect, safety, accessibility, affordability of drugs and physical state of the patients should be should be taken into account comprehensively, rather than focusing on only one or some aspect, which is not conducive to the prognosis of patients. Due to the commonly poor quality of the included studies, the conclusions need to be verified by rigorously designed randomized controlled trials.

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Footnote

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