



Integrated Chinese herbal medicine with Western Medicine versus Western Medicine in the effectiveness of primary hypertension treatment: A systematic review and meta-analysis of randomized controlled trials



Shadi A.D. Mohammed^{a,c,1}, Liu Hanxing^{a,1}, Lu Fang^a, Adnan Mohammed Algradi^b, Mohammed Alradhi^d, Mohammed Safi^e, Liu Shumin^{a,*}

^a Heilongjiang University of Chinese Medicine, Harbin, 150040, Heilongjiang, China

^b Key Laboratory of Chinese Materia Medica, Ministry of Education of Heilongjiang University of Chinese Medicine, Harbin, 150040, Heilongjiang, China

^c School of Pharmacy, Lebanese International University, 18644, Sana'a, Yemen

^d Department of Urology, Affiliated Hospital of Qingdao Binhai University, Qingdao, Shandong, China

^e Department of Respiratory Diseases, Shandong Second Provincial General Hospital, Shandong University, Shandong, China

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ABSTRACT

Ethnopharmacological relevance: Integrated Chinese herbal medicine (CHM) and Western Medicine (WM) treatments have been used for primary hypertension (PHTN) patients in China. Currently, there are many randomized control trials (RCTs) published regarding the effect of CHM and WM on PHTN, which indicated that combining Chinese with WM was effective and safe for PHTN when compared with WM alone, but the quality of evidence was insufficient, and there is no clear information and summary are available for these RCTs assessing the effectiveness of CHM with WM versus WM in patients with PHTN.

Objectives: This systematic study and meta-analysis aimed to evaluate the effectiveness and safety of CHM combined with WM in comparison with WM in reducing systolic and diastolic blood pressure for patients with PHTN.

Methods: The information of this study was searched from electronic databases (PubMed, COCHRANE, EMBASE, Ovid, CNKI, VIP, Wanfang, and CBM). The markedly effective and effective terms were according to Guiding Principles for Clinical Research of New Chinese Medicines. Two investigators independently reviewed each trial. The Cochrane risk of bias assessment tool was used for quality assessment, and RevMan 5.4 was used for meta-analysis.

Results: In this study, a total of 29 studies that included 2623 patients were recorded. The study results displayed that the clinical effectiveness in the treatment of hypertension patients from the integrated medicines was considerably higher than that with WM alone, clinical effective (RR 1.23, 95% CI [1.17, 1.30], $P < 0.00001$), and markedly effective (ME) in the patients (RR 1.66, 95% CI [1.52, 1.80], and $P < 0.00001$). Random effect in SBP (MD 7.91 mmHg, [6.00, 983], $P < 0.00001$) and DBP (MD 5.46 mmHg, [3.88, 6.43], $P < 0.00001$), a subgroup analysis was carried out based on the type of intervention, duration of treatment, and CHM formulas that showed significance. Furthermore, no severe side effects were reported, and no patients stopped treatment or withdrawal due to any severe adverse events.

Conclusion: Compared to WM alone, the therapeutic effectiveness of CHM combined with WM is significantly improved in the treatment of hypertension. Additionally, CHM with WM may safely and efficiently lower systolic blood pressure (SBP) and diastolic blood pressure (DBP) in individuals with PHTN. However, rigorous randomized controlled trials with a large sample, high quality, long duration of treatment, and follow-up are recommended to strengthen this clinical evidence.

* Corresponding author.

E-mail address: keji-liu@163.com (L. Shumin).

¹ These authors have contributed equally to this work.

Abbreviations

PHTN	Primary hypertension
CHM	Chinese herbal medicine
WM	Western Medicine
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
CNKI	China National Knowledge Infrastructure
RCTs	Randomized Controlled Trials
RR	Risk Ratio
MD	Mean Difference
VIP Database	China Science Journal Database
CBM	China Biomedical Literature Database
ME	markedly effective
CCB	Calcium Channel Blocker
ACEI	Angiotensin-converting enzyme Inhibitor
ARB	Angiotensin II Receptor Blocker
ACC/AHA	American College of Cardiology (ACC)/American Heart Association
ISH	International Society of Hypertension
ESC/ESH	European Society of Hypertension/European Society of Cardiology

1. Introduction

Primary hypertension is a clinical syndrome characterized by elevated SBP and DBP ($\geq 140/90$ mmHg), which is regarded as one of the leading causes of high mortality as well as cardiovascular and renal morbidity (James et al., 2014; Unger et al., 2020; Williams et al., 2018; Zhang and Moran, 2017). According to the World Health Organization (WHO), approximately one billion people have hypertension worldwide, and only less than one-fifth of them are under control (WHO, 2021), while more than three hundred million hypertension patients in China (Huang et al., 2016). It is reported that approximately seven million deaths are due to hypertension yearly (Chobanian et al., 2003). A meta-analysis of 61 studies that included almost one million adults found that people between 40 and 70 years, with blood pressure ranging from 115/75 to 185/115, had a double chance of developing cardiovascular disease when increase SBP by 20 mmHg and DBP by 10 mmHg (Lewington S et al., 2002). Furthermore, the Asian population survey results displayed that the risk of stroke and fatal myocardial infarction increased by 53% and 31%, respectively, for each increase in SBP (10 mmHg) (Joint Committee for Guideline, 2019).

From the last decades, diuretics, long-acting calcium channel blockers (CCB), Angiotensin-Converting Enzyme Inhibitors (ACEI), Angiotensin II Receptor Blockers (ARB), and Beta-Blockers have been used as the first-line medications in the management of hypertension (Joint Committee for Guideline, 2019; Unger et al., 2020; Whelton et al., 2018; Williams et al., 2018). However, many adverse reactions, including headache, dizziness, orthostatic hypotension, sexual dysfunction, etc., limit the clinical application of antihypertensive drugs (Yach et al., 2004). Furthermore, in 2016, blood pressure regulation was also suboptimal, with just 39% of hypertensive patients meeting the therapeutic goal of blood pressure less than 140/90 mmHg (Redon et al., 2016). Consequently, there are numerous scientific researches carried out to find an alternative or complementary therapies such as integrative medicine, traditional Chinese treatment, diet therapy, lifestyle therapy, and so on (Chen et al., 2012; Cramer, 2016; hua et al., 2018; Ozemek et al., 2018; Ozemek et al., 2020; Xu and Chen, 2008).

In China, around 20% of hypertension patients have been treated using traditional Chinese medication, and several studies have shown that CHM may successfully lower systolic and diastolic blood pressure and reduce complications (Huang et al., 2016; Ren et al., 2020).

Recently, CHM (Modified Tianma Gouteng, Banxia Baizhu Tianma, and Modified Qiju Dihuang decoction) has been used as adjuvant therapy with WM for patients with PHTN and they are enhancing the antihypertensive effect without increasing adverse effects (Gu et al., 2015; Shen and Jin, 2015; Tai et al., 2020; Wang, 2016). While many systematic reviews of single formulas of CHM and WM for the treatment of hypertension reported some benefits from this combination (Tai et al., 2020; Wang et al., 2013; Xiong et al., 2012, 2019a), and there are many RCTs of single formulas using a combination of CHM with WM compared to WM to treat hypertension and showed this combination has a better therapeutic effect, no clear information and summary was provided for RCTs comparing the efficacy and harmful effects of CHM with WM to WM. Therefore, this the first systematic review and meta-analysis of randomized controlled trials were reported the different formulas of CHM and their RCTs with WM compared to WM for the treatment of hypertension between 2010 and 2020 in order to assess the safety and effectiveness of integrated CHM with WM in comparison of WM treating PHTN.

2. Methods

This systematic review and meta-analysis were undertaken under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009). This review was registered in PROSPERO, and the registration number for this systematic review and meta-analyses is CRD42020223500.

2.1. Search strategies for the identification studies

The literature of this study was published in English and Chinese and systematically retrieved from eight electronic databases, including PubMed, Cochrane Central Register of Controlled Trials, EMBASE, Ovid, China Knowledge Resource Integrated Database (CNKI), China Science and Technology Journal Database (VIP), Wanfang Data, and Chinese Biomedical Literature Database (CBM) between January 2010 and November 15, 2020. The key search words were: ("Primary Hypertension" OR "Hypertension" OR "Essential Hypertension" OR "High Blood Pressure" OR "yuan fa xinggaoxueya" OR "gaoxueya" OR "gaoxueyabing") AND ("Traditional Chinese medicine" OR "Chinese medicine" OR "Chinese patent medicine" OR "Chinese herbal medicine") AND ("Randomized Controlled Trial" OR "sui ji dui zhao" OR "sui ji"). The search strategy for each database (MeSH term) was detailed in Supplementary Material (S1).

The Endnote 9 software and manual checking have been used to remove duplicates. Two reviewers (Shadi A.D. Mohammed and Liu Hanxing) individually examined the studies' titles and abstracts obtained via an initial search. According to our last designed eligibility standards criteria, we excluded abstracts that did not meet our standards, while the abstracts with insufficient details about the eligibility standards criteria requirements were further screened. Full texts of the residual studies were also independently identified by the same reviewers, and any difference of opinion was decided by a third author (Lu Fang).

2.2. Study selection

2.2.1. Patients

Studies were included in this systematic review and meta-analyses a) Are conducted only in patients with PHTN b) Met the eligibility standards criteria.

2.2.2. Interventions

The experimental group used WM and traditional Chinese drugs without considering the dosage form and drug administration time. The comparison of this study is as follows: (1) Combined CHM and CCB vs. CCB/With or without Placebo, (2) Combined CHM and ACEI vs. ACEI/

With or without Placebo, (3) Combined CHM and ARB vs. ARB/With or without Placebo, (4) Combined CHM and diuretic vs. diuretic/With or without Placebo. (5) Combined CHM with a combination of antihypertensive drugs vs. a combination of antihypertensive medications/with or without placebo.

2.2.3. Control group

The Control group was antihypertensive drugs such as Diuretic, ACEI, ARB, CCB, B-blocker alone, or a combination of antihypertensive medications, with or without a placebo.

2.2.4. Outcomes

While the primary outcome was effectiveness. Secondary outcomes, SBP, DBP, and adverse reaction.

The clinical effectiveness includes two terms (Markedly effective and Effective) according to Guiding Principles for Clinical Research of New Chinese Medicines (Zheng, 2002) as follows: (A) Markedly effective; 1) Diastolic blood pressure decreased by more than 10 mmHg and reached the normal range; 2) Diastolic blood pressure has not decreased to normal, but has decreased by 20 mmHg or more; (B) Effective; 1) Diastolic blood pressure decreased less than 10 mmHg, but reached the normal range; 2) Diastolic blood pressure decreased by 10–19 mmHg compared to before treatment, but did not reach the normal range; 3) Systolic blood pressure decreased by more than 30mmhg compared with that before treatment. One of them is required. (C) Ineffective. Those who fail to meet the above standards.)

2.2.5. Study type

In a randomized controlled trial of integrated CHM with WM in treating PHTN, Only Trials in Chinese and English language will be included in this study.

2.3. Eligibility standards

2.3.1. Exclusion criteria

The study should be excluded if any of the following items occur: (a) Those were not randomized control trials. (b) CHM with WM as an active intervention in the experimental group and WM in the control group are not the same (c) Study of CHM with WM with hypertension in non-human subjects or *in vitro* studies. (d) Patients diagnosed with secondary hypertension, such as pheochromocytoma, Cushing syndrome renal hypertension, primary aldosteronism, and abdominal aortic banding, as well as hypertension patients with another disease (e.g., diabetes mellitus and coronary artery disease), or another type of hypertension, e.g. (Gestational hypertension and isolated systolic hypertension) (e) Acupuncture, massage, qigong, Tai Chi, Baduanjin, cupping, blood-letting treatment, yoga, and other complementary and alternative medicine interventions were used in either the experimental or control groups. (f) Insufficient data could be extracted for statistical (BP data according to international standard, clinical effect, and name of hypertension drugs). (g) A systematic review, meta-analysis, case reports, abstract-only publications, conferences, author responses, and books.

There are no restrictions on gender, age, race, and duration of treatment.

2.4. Data extraction

Data extraction: Based on eligibility standards criteria, the two researchers (Shadi A. D. Mohammed and Liu Hanxing) selected the literature and extracted the data independently. We will contact the authors for missing or unclear data. If we do not get a response, we either measure the data or exclude it. (Xiong et al., 2019b). In cross-checking the data extraction table, the disagreement or consultation is solved by consensus with the third author (Lu Fang). We used An Excel spreadsheet to record the following data: (a) Basic information study ID (author, years), (b) Methods: study design and size of the sample. (c)

Participant demographic details: age, gender, duration of disease, the measurement of hypertension before treatment, and diagnostic criteria for hypertension. (d) Interventions: the type of drugs used in the experimental group, the type of medications used in the control group, and the length of treatment. (e) Results: primary outcomes (clinical effectiveness), secondary outcomes (Hypertension in both groups and adverse drug reactions), withdrawal with reasons, and screening results. Data extraction was demonstrated in detail in Supplementary Material (S2).

2.5. Assessment of risk of bias (ROB)

We assessed these trials' methodological quality by the risk of bias tool recommended by the Cochrane Handbook. According to the ROB evaluation standard in the ROB assessment tool of the Cochrane manual, two reviewers independently conduct the evaluation. (Shadi A. D. Mohammed, Liu Hanxing) evaluated the included studies methodological quality using RevMan 5.4. Quality evaluated for the following seven aspects: (1) random sequence generation; (2) concealment of allocation; (3) blinding of patients and personnel; (4) blinding of assessor; (5) incomplete outcome data addressed; (6) selective reporting; (7) other bias. The authors' judgment for each item is as follows; low, high, and unclear risk of bias. All differences were resolved by consultation among the reviewers or discussion with a third author (Lu Fang).

2.6. Data analysis and synthesis

We used Review Manager (RevMan) software, Version 5.4.1 (The Cochrane Collaboration), for data analysis and synthesis. Continuous outcomes were presented as mean difference (MD) between experimental and control groups with 95% CI. For dichotomous data, they were presented as Risk Ratio (RR) with 95% CI. The primary and secondary outcome indicators were meta-analyzed using a random-effects model, with heterogeneity evaluated using the I² statistic. Strong heterogeneity was defined as I² values greater than 75%. (Abdulazeez et al., 2021). A subgroup and sensitivity analysis were used to assess the probable source of heterogeneity and the result's strength. Subgroup analyses that pre-specified was according the type of intervention (to classify WM for improving SBP and DBP, this classification (CCB, ACEI, ARB, and combination intervention medications may indicate the source of heterogeneity), and post-hoc subgroups were baseline duration of treatment (due several studies report contradictory results related to treatment duration, we performed the average duration of treatment among all studies, which may indicate the source of heterogeneity), and CHM formulas (in the studies variety of different Chinese medicine prescriptions, to control this heterogeneity, and achieve more accurate results we use subgroup analysis of the same CHM drug prescriptions). To evaluate the robustness and reproducibility of the results, we do a sensitivity analysis. Sensitivity analysis assesses the effect of overall results by eliminating specific low-quality studies and focuses on the features or types of research, such as methodologic quality. In this study, SBP and DBP were presented as mean difference (MD), while clinical treatment and duration of treatment less and more 7 weeks as Risk Ratio (RR).

3. Results

3.1. Literature screening

According to our search strategy in 8 electronic databases, 4340 trials were identified. Among them, 2285 records were removed using Endnote 9 and manually checked because of duplicates. After we were going through the titles and abstracts, we excluded 1476 papers for the following reasons: In animals or *in vitro* studies (47), blood pressure data not reported(13), hypertension With another disease(776), No Abstract (1), Other intervention “other type of hypertension, Quality of life,

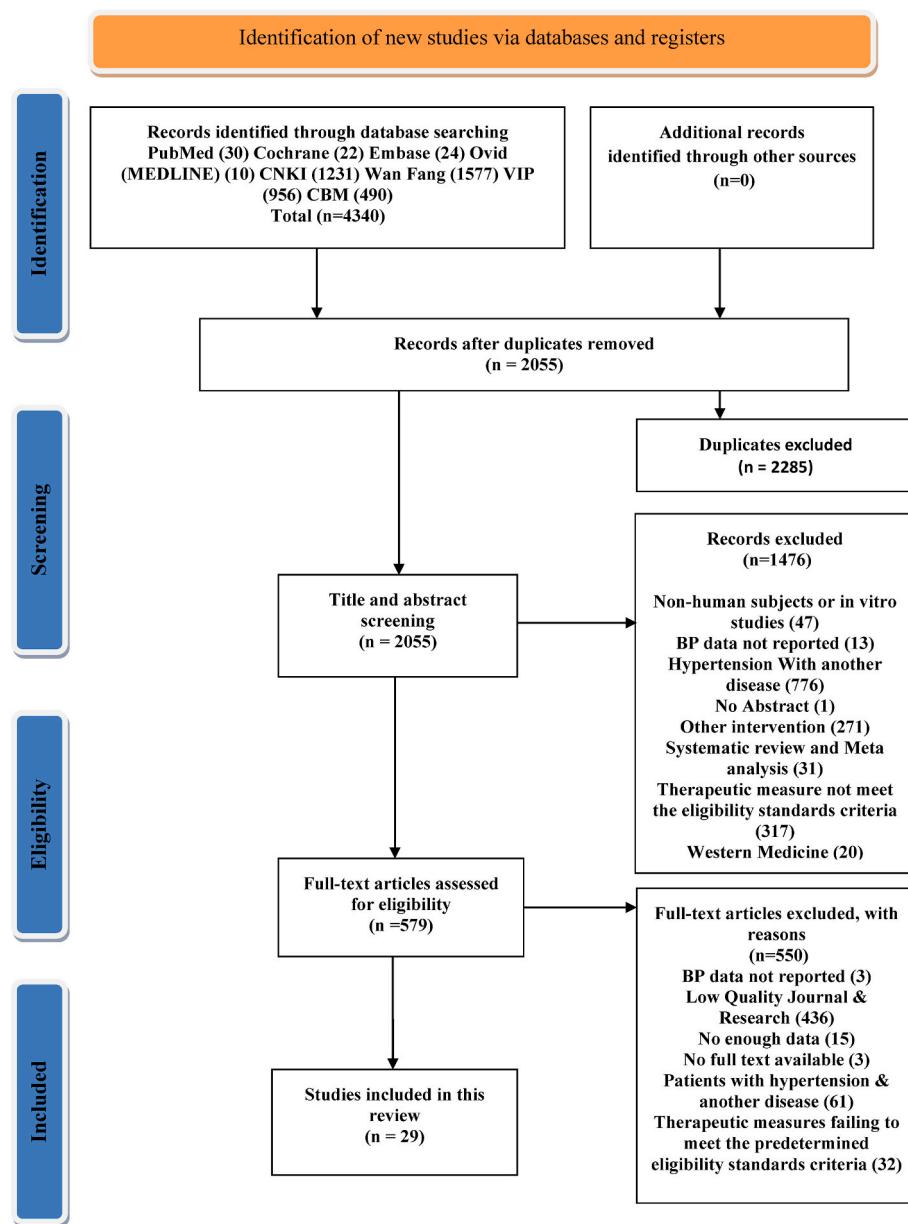


Fig. 1. Flow diagram of study selection and identification (PRISMA).

nursing" (271), Other types of studies such as Systematic Review and Meta-analysis(31), Therapeutic measure in control or experimental group did not meet the eligibility standards criteria (317), WM(20). After browsing the full text of the remaining 579 articles, we excluded 550 records for reasons (Blood Pressure data not reported(3), Low-Quality Journal & Research according to " 2020 China Science and Technology Core Journal Catalogue (Natural Science Volume)([China Institute of Science and Technology Information, 2020](#)), An overview of Chinese Core Journals 2017) edition([Zhu, 2018](#)), and Chinese Science Citation Database, CSCD Core journal list ([National Science Library, 2019](#))" (436), No enough data(15), No full text available(3), Patients with hypertension & another disease(61), Therapeutic measures in control or experimental group failing to meet the predetermined eligibility standards criteria (32). In the end, 29 articles that met the eligibility standards criteria were included in this study. [Fig. 1](#) shows the process of study selection.

3.2. Characteristics of included studies

The enrolled 29 articles were published between January 2010 and November 15, 2020. All 29 studies included were randomized clinical trials conducted in China, 28 published in Chinese, and one published in English. All trials related to comparing the experimental group (CHM with WM) and control group (WM). The type and dosage of antihypertensive drugs in the experimental group were the same as in the control group. In total, 2623 patients were classified randomly into a CHM with WM and WM groups. They were all from China, including 1504 males and 1119 females. The participants' average ages ranged from (59.1 ± 7.8) years. Five trials ([Du, 2014](#); [Gong et al., 2018](#); [Man, 2014](#); [Pan et al., 2012](#); [Xu, 2016](#)) did not report disease duration, but the other 23 papers average disease duration (8.7 ± 4.1) . All trials could be accessible in full texts. The duration of treatment continued between 2 and 12 weeks, six trials duration of treatment for three months([Duan, 2013](#); [Gong et al., 2018](#); [Ran, 2013](#); [Wang et al., 2018](#); [Yang et al., 2014](#); [Zhao and Jiang, 2015](#))(6/29, 21%), eight trials duration of treatment two months ([Bian, 2016](#); [Jiang and Zhu, 2010](#); [Man, 2014](#); [Pan et al., 2012](#); [Shen and Jin,](#)

Table 1

Basic characteristics of the included studies.

References	Simple Size (M/F)	Age (Years)	Diagnosis Standard	Duration Of Disease	Hypertension Classification	Experimental Group	Control Group	Treatment Duration	Adverse Reactions
Bian (2016)	67/67	E: 56.6 E: 43/ 24 C: 41/ 26	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 10.0 ± 2.5 C: 10.6 ± 2.2	Not reported	Tianma Gouteng decoction, one dose, qd & C	L-Amlodipine Besylate, 2.5 mg, qd	8 weeks	Not observed
Cao et al. (2018)	30/30	E: 57.5 E: 20/ 10 C: 18/ 12	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 6.7 ± 4.3 C: 7.4 ± 5.1	E: Level 1, 13 Level 2, 17 C: Level 1, 11 Level 2, 19	Jianpi Tongluo granules, half dose, bid & C	Amlodipine Besylate, 5 mg, qd. Benazepril 10 mg daily.	4 weeks	Not observed
Du (2014)	50/50	E: 62.6 E: 18/ 32 C: 20/ 30	"Chinese Guidelines for the Management of Hypertension 2010)"	Not reported	Not reported	Tianma Gouteng decoction, one dose, tid & C	L-Amlodipine Besylate, 2.5 mg, qd	4 weeks	E: Two patients of stomach discomfort and diarrhea, one patient of skin allergy C: One patient of gingival hyperplasia, two patients of palpitations, three patients of facial flushing, one patient of ankle edema
Duan (2013)	30/30	E: 65.5 E: 16/ 14 C: 15/ 15	1999 "WHO/ISH Hypertension Treatment Guidelines"	T: 0.1–10.0	E: Level 1, 10 Level 2, 10 C: Level 1, 8 Level 2, 22	Jiawei Wendan decoction, half dose, bid & C	Amlodipine Besylate, 5 mg, qd	12 weeks	Not reported
Fu (2017)	30/30	E: 83.6 E: 15/ 15 C: 13/ 17	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 21.5 ± 3.1 C: 20.8 ± 4.2	E: Level 2, 26 Level 3, 4 C: Level 2, 25 Level 3, 5	Modified Tianma Gouteng decoction, one-third dose, tid & C	Nifedipine Controlled Release tablets, 30 mg, qd, and Irbesartan, 150 mg, qd, and Hydrochlorothiazide, 12.5 mg, qd	4 weeks	E: One patient of skin rash C: One patient of ankle edema
Gong et al. (2018)	40/40	E: 56.3 E: 24/ 16 C: 23/ 17	"Chinese Guidelines for the Management of Hypertension 2005)"	Not reported	Not reported	Shuanghua Zhixuan decoction, half dose, bid & C	L-Amlodipine Besylate, 2.5 mg, qd	12 weeks	Not observed
Gu et al. (2015)	30/30	E: 51.9 E: 16/ 14 C: 15/ 15	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 6.3 ± 2.2 C: 7.2 ± 1.7	Not reported	Modified Qiju Dihuang decoction, half dose, bid & C	Amlodipine, 5 mg, qd	4 weeks	Not reported
Huo (2016)	38/38	E: 45.6 E: 22/ 16 C: 24/ 14	1999 "WHO/ISH Hypertension Treatment Guidelines"	E: 4.2 ± 1.5 C: 4.6 ± 1.4	Not reported	Modified Xuefu Zhuyu decoction, one dose, bid & C	Lacidipine, 2 mg, bid.	4 weeks	Not reported
Jiang and Zhu (2010)	52/52	T: 72.0 T: 73/ 31	1978 "WHO/ISH Hypertension Treatment Guidelines"	T: 0.5–18.0	T: Level 1, 24 Level 2, 53 Level 3, 27	Shihu Yangyin decoction, half dose, bid & C	Felodipine Sustained Release tablets, 5 mg, qd	8 weeks	E: One patient of head swelling and headache, one patient of flushing, one patient of lower limb edema, one patient of polyuria C: Four patients of head swelling and headache, two patients of flushing, three patients of lower limb edema, two patients of polyuria, one patient of fatigue
Li (2013)	34/34	E: 56.7 E: 20/ 14 C: 22/ 12	"2004 China Guidelines for Prevention and Treatment of Hypertension (Practical Edition)"	E: 10.6 ± 6.4 C: 11.2 ± 5.8	E: Level 1, 14 Level 2, 20 C: Level 1, 16 Level 2, 18	An Nao pills, one pill, bid & C	L-Amlodipine Besylate, 2.5 mg, qd.	4 weeks	E: One patient of fatigue C: Two patients of headache, one patient of flushed face, one patient of fatigue

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Table 1 (continued)

References	Simple Size (M/F)	Age (Years)	Diagnosis Standard	Duration Of Disease	Hypertension Classification	Experimental Group	Control Group	Treatment Duration	Adverse Reactions
Liang and Lin (2014)	60/60 E: 35/ 25 C: 37/ 23	E: 54.5 ± 6.5 C: 53.8 ± 6.9	"Chinese Guidelines for the Management of Hypertension 2005"	E: 4.5 ± 2.0 C: 3.7 ± 2.4	Not reported	Tianma Gouteng decoction, one dose, qd & C	Amlodipine Besylate capsules, 5 mg, qd	4 weeks	Not reported
Man (2014)	45/40 E: 25/ 20 C: 20/ 20	E: 73.3 ± 11.2 C: 71.9 ± 8.8	"Interpretation of Cardiovascular Disease Diagnosis and Treatment Guidelines"	Not reported	E: Level 1, 10 Level 2, 20 Level 3, 15 C: Level 1, 10 Level 2, 17 Level 3, 13	Songling Xuemaikang capsules, 1.5 g, tid & C	Irbesartan, 150 mg, qd	8 weeks	Not reported
Miu and Hu (2012)	34/34 E: 22/ 12 C: 21/ 13	E: 56.9 ± 9.2 C: 56.3 ± 8.8	1999 "WHO/ISH Hypertension Treatment Guidelines"	E: 10.6 ± 6.4 C: 11.2 ± 5.8	E: Level 1, 14 Level 2, 20 C: Level 1, 16 Level 2, 18	Pinggan Qianyang granules, one dose, bid & C	Losartan, 50 mg, qd.	4 weeks	E: One of dizziness and fatigue C: Two patients of dizziness and fatigue, one patient of headache, one patient of lower limb soreness
Ning (2014)	40/38 E: 21/ 19 C: 18/ 20	E: 59.2 ± 7.5 C: 58.9 ± 6.4	"Chinese Guidelines for the Management of Hypertension 2010"	E: 9.3 ± 3.1 C: 10.6 ± 2.9	Not reported	Zhen Jian granules, two doses, bid & C	Amlodipine Besylate, 5 mg, qd	4 weeks	Not reported
Pan et al. (2012)	30/30 E: 15/ 15 C: 14/ 16	E: 52.6 ± 12.3 C: 68.1 ± 6.7	"Guiding Principles for Clinical Research of New Chinese Medicines"	Not reported	Not reported	Sheyao Shiliangcha decoction, one dose, bid & C	Candesartan Cilexetil tablets, 8 mg, qd	8 weeks	Not observed
Pang (2013)	30/26 E: 21/9 C: 19/7	E: 63.4 ± 6.6 C: 62.8 ± 6.5	"Chinese Guidelines for the Management of Hypertension 2010"	E: 7.1 ± 2.8 C: 7.3 ± 2.6	Not reported	Modified Banxia Baizhu Tianma decoction, half dose, bid & C	Enalapril, 5 mg, bid, and Nifedipine Sustained Release tablets, 10 mg, bid	4 weeks	Not reported
Ran (2013)	40/40 E: 31/9 C: 30/ 10	E: 52.4 ± 4.7 C: 53.6 ± 5.0	"Chinese Guidelines for the Management of Hypertension 2010"	E: 7.9 ± 4.0 C: 9.2 ± 4.1	Not reported	Bushen Jiangya decoction, half dose, bid & C	Benazepril Hydrochloride tablets, 10 mg, qd. Amlodipine 5 mg daily.	12 weeks	E: Three patients of headache, two patients of cough, five patients of edema, two patients of facial flushing, one patient of nausea and vomiting, six patients of dry mouth C: Two patients of headache, four patients of cough, three patients of edema, one patient of facial flushing, one patient of nausea and vomiting, five patients of dry mouth
Shen and Jin (2015)	30/30 E: 21/9 C: 23/7	E: 55.1 ± 12.1 C: 54.3 ± 11.4	"Chinese Guidelines for the Management of Hypertension 2010"	E: 9.0 ± 2.5 C: 8.3 ± 2.4	Not reported	Banxia Baizhu Tianma decoction, half dose, bid & C	Irbesartan, 150 mg, qd, and Hydrochlorothiazide, 12.5 mg, qd	8 weeks	Not reported
Wang et al. (2018)	40/40 E: 21/ 19 C: 22/ 18	E: 69.8 ± 5.9 C: 69.4 ± 5.8	"Chinese Guidelines for the Management of Hypertension 2010"	E: 12.4 ± 11.6 C: 11.8 ± 10.6 Level 3, 11 C: Level 1, 11 Level 2, 19 Level 3, 10	E: Level 1, 10 Level 2, 19 Level 3, 11 C: Level 1, 11 Level 2, 19 Level 3, 10	Tianma Sanqi decoction, one dose, qd & C	L-Amlodipine, 2.5 mg, qd	12 weeks	Not reported
Wang et al. (2019)	45/45 E: 19/ 26 C: 21/ 26	E: 52.4 ± 7.1 C: 52.9 ± 6.6	"Chinese Guidelines for the Management of Hypertension 2010"	E: 4.3 ± 2.4 C: 4.1 ± 2.7	E: Level 1, 17 Level 2, 28 C: Level 1, 19 Level 2, 26	Pinggan Ziyan Tongyu decoction, one-third dose, tid & C	Amlodipine Besylate, 5 mg, qd	2 weeks	E: One patient of mild diarrhea C: Two patients of palpitation, one patient of insomnia, one patient of loss of appetite
							Telmisartan, 40 mg, qd	8 weeks	Not reported

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Table 1 (continued)

References	Simple Size (M/F)	Age (Years)	Diagnosis Standard	Duration Of Disease	Hypertension Classification	Experimental Group	Control Group	Treatment Duration	Adverse Reactions
Wang, Y. et al. (2015)	47/47 E: 30/ 17 C: 29/ 18	E: 50.7 ± 3.6 C: 50.2 ± 4.6	"Guiding Principles for Clinical Research of New Chinese Medicines"	E: 6.4 ± 1.4 C: 6.2 ± 1.5	E: Level 1, 32 Level 2, 10 Level 3, 5 C: Level 1, 35 Level 2, 8 Level 3, 4	Zini Yuntongping decoction, half dose, bid & C			
Wang (2016)	42/40 E: 23/ 19 C: 25/ 15	E: 63.2 ± 8.5 C: 63.5 ± 8.4	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 7.6 ± 2.5 C: 7.4 ± 2.7	E: Level 1, 15 Level 2, 20 Level 3, 7 C: Level 1, 14 Level 2, 17 Level 3, 9	Modified Tianma Gouteng decoction, one dose, bid & C	Perindopril, 4 mg, qd	4 weeks	E: One patient of headache C: Two patients of headache, one patient of fatigue, one patient of sleep disturbance
Wu (2011)	30/30 E: 7/23 C: 8/22	E: 58.6 ± 10.1 C: 58.5 ± 10.3	"Chinese Guidelines for the Management of Hypertension 2005)"	E: 8.1 ± 5.8 C: 8.7 ± 7.9	Not reported	Denglao Zhejue Jiuwei granules, one dose, bid & C	Amlodipine Besylate, 5 mg, qd	8 weeks	C: Two patients had discomfort such as flushing and edema of lower limbs
Xu (2016)	30/30 E: 19/ 11 C: 20/ 10	E: 62.4 ± 9.0 C: 63.8 ± 7.4	"Chinese Guidelines for the Management of Hypertension 2010)"	Not reported	Not reported	Huatan Quyu decoction, one dose, bid & C	Enalapril Folic Acid tablets, 10 mg/0.8 mg, qd	8 weeks	Not reported
Yang et al. (2014)	60/60 E: 35/ 25 C: 31/ 29	E: 61.6 ± 7.5 C: 57.2 ± 6.2	"Chinese Guidelines for the Management of Hypertension 2005)"	E: 7.0 ± 1.3 C: 6.0 ± 1.0	Not reported	Zhong Yao decoction, half dose, bid & C	Nifedipine Sustained Release tablets, 10 mg, qd	12 weeks	Not reported
Zhang (2010)	55/50 E: 33/ 22 C: 33/ 17	E: 55.0 C: 56.0	1999 "WHO/ISH Hypertension Treatment Guidelines"	E: 4.0–28.0 C: 3.0–29.0	E: Level 1, 22 Level 2, 23 Level 3, 10 C: Level 1, 20 Level 2, 21 Level 3, 9	Zini Qingnao Jiangya decoction, half dose, bid & C	Nifedipine Sustained Release tablets, 10 mg, bid, and Enalapril, 5 mg, bid	4 weeks	Not reported
Zhao and Jiang (2015)	78/78 T: 89/ 67	T: 65.3 ± 12.5	1999 "WHO/ISH Hypertension Treatment Guidelines"	T: 9.7 ± 3.6	Not reported	Modified Tianma Gouteng decoction, half dose, bid & C	Captopril, 25 mg, tid	4 weeks	Not reported
Zheng and Yao (2016)	64/63 E: 32/ 32 C: 32/ 31	E: 53.5 C: 52.7	"Chinese Guidelines for the Management of Hypertension 2010)"	E: 6.5 C: 5.9	Not reported	Zini Jiangya decoction, one dose, bid & C	Ramipril, 2.5 mg, qd	4 weeks	Not reported
Zhou, Han and Xu (Zhou et al., 2015)	120/ 120 T: 144/ 96	T: 35.0 ± 6.0	"Chinese Guidelines for the Management of Hypertension 2005)"	T: 0.1–2.0	Not reported	Pinggan Jianpi decoction, half dose, bid & C	Amlodipine Besylate, 5 mg, qd	12 weeks	Not reported

E, Experimental Group; C, Control Group; T:Total; M, male; F, female; qd, once daily; bid, twice daily; tid, three times daily; BP, blood pressure.

2015; Wang, Y. et al., 2015; Wu, 2011; Xu, 2016) (8/29, 28%), fourteen trials duration of treatment for one month(Cao et al., 2018; Du, 2014; Fu, 2017; Gu et al., 2015; Huo, 2016; Li, 2013; Liang and Lin, 2014; Miu and Hu, 2012; Ning, 2014; Pang, 2013; Wang, 2016; Zhang, 2010; Zhao and Jiang, 2015; Zheng and Yao, 2016)(14/29, 48%), and one trials duration of treatment for two weeks(Wang et al., 2019). Most of them lasted two months (14/29, 48%). The basic characteristics of all 29 included randomized control trials are summarized in Table 1, and the CHM in included studies are summarized in Table 2.

Five different diagnostic criteria of hypertension were used in include trials as follow: Chinese Guidelines for the Management of Hypertension" 2010, 2005"(Chinese Hypertension League (CHL), 2006; Liu, 2010), ISH/WHO "1999,1978"(Wu, 1999), Chinese Guidelines for Hypertension Prevention and Treatment(Chinese Hypertension League (CHL), 2004), Interpretation of Cardiovascular Disease Diagnosis and Treatment Guidelines(Zhao and Hu, 2004), and Guiding Principles for Clinical Research of New Chinese Medicines(Zheng, 2002). Fourteen trials (Bian, 2016; Cao et al., 2018; Du, 2014; Fu, 2017; Gu et al., 2015;

Ning, 2014; Pang, 2013; Ran, 2013; Shen and Jin, 2015; Wang et al., 2018, 2019; Wang, 2016; Xu, 2016; Zheng and Yao, 2016) used Chinese Guidelines for the Management of Hypertension 2010), five trials (Duan, 2013; Huo, 2016; Miu and Hu, 2012; Zhang, 2010; Zhao and Jiang, 2015) used 1999 WHO/ISH, one trail (Jiang and Zhu, 2010)used 1978 WHO/ISH, five trials (Gong et al., 2018; Liang and Lin, 2014; Wu, 2011; Yang et al., 2014; Zhou et al., 2015) used Chinese Guidelines for the Management of Hypertension-2005, two trials(Pan et al., 2012; Wang, Y. et al., 2015) used Guiding Principles for Clinical Research of New Chinese Medicines, one trial (Li, 2013) used 2004 China Guidelines for Prevention and Treatment of Hypertension (Practical Edition), and one trial (Man, 2014) used Interpretation of Cardiovascular Disease Diagnosis and Treatment Guidelines.

The primary outcome was reported clinical effectiveness mentioned for all patients in this study according to Guideline Principles for Clinical Research of New Chinese Medicines in China(Zheng, 2002) markedly effective, effective, and ineffective Table 3. The secondary outcome, mentioned in details SBP and DBP before and after treatment of both the

Table 2

CHM in the included studies.

References	Formula	Composition of formula
Bian (2016)	Tianma Gouteng decoction	Shells of <i>Haliotis diversicolor</i> Reeve 20 g, Tuber of <i>Gastrodia elata</i> Blume 15 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 15 g, Bark of <i>Eucommia ulmoides</i> Oliv. 15 g, Cane of <i>Polygonum multiflorum</i> Thunb. 15 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 15 g, <i>Leonurus japonicus</i> Houtt. 15 g, The part of the sclerotium with pine roots of <i>Poria cocos</i> (Schw.) Wolf 15 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 10 g, Root of <i>Scutellaria baicalensis</i> Georgi 10 g
Cao et al. (2018)	Jianpi Tongluo granules	Root of <i>Astragalus membranaceus</i> (Fisch.) Bunge 15 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 15 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 10 g, Dry body of <i>Pheretima aspergillum</i> (E.Perrier) 12 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 12 g, Flower of <i>Carthamus tinctorius</i> L. 10 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 10 g
Du (2014)	Tianma Gouteng decoction	Tuber of <i>Gastrodia elata</i> Blume 15 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 20 g, Shells of <i>Haliotis diversicolor</i> Reeve 30 g, Root of <i>Scutellaria baicalensis</i> Georgi 15 g, Bark of <i>Eucommia ulmoides</i> Oliv. 20 g, Root of <i>Achyranthes bidentata</i> Blume 15 g, Cane of <i>Polygonum multiflorum</i> Thunb. 25 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 15 g, Root of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 15 g, Root of <i>Paeonia lactiflora</i> Pall. 15 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 15 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 5 g
Duan (2013)	Jiawei Wendan decoction	Dried ripe peel of <i>Citrus reticulata</i> Blanco 10 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 10 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 10 g, Dry young fruit of <i>Citrus × aurantium</i> L. 10 g, Dry middle layer of stalk of <i>Bambusa tuldaoides</i> Munro 10 g, Processed products of <i>Glycyrrhiza uralensis</i> Fisch. 6 g, Rhizome of <i>Zingiber officinale</i> Roscoe 6 g, Dry ripe fruit of <i>Ziziphus jujuba</i> Mill. two pieces, Processed products of <i>Polygonum hydropiper</i> L., <i>Artemisia annua</i> L., and <i>Xanthium sibiricum</i> Patrin ex Widder 10 g, Mature seeds of <i>Raphanus sativus</i> L. 10 g, Ripe fruit of <i>Amomum villosum</i> Lour. 10 g, Mature seeds of <i>Cassia obtusifolia</i> L. 10 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 10 g, Rhizome of <i>Cyperus rotundus</i> L. 10 g
Fu (2017)	Modified Tianma Gouteng decoction	Tuber of <i>Gastrodia elata</i> Blume 30 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 30 g, Bark of <i>Eucommia ulmoides</i> Oliv. 12 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 12 g, Processed products of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 30 g, Dry ripe pulp of <i>Cornus officinalis</i> Siebold & Zucc. 15 g, Root of <i>Scutellaria baicalensis</i> Georgi 12 g, Dried ears of <i>Prunella vulgaris</i> L. 30 g, Roots and rhizomes of <i>Gentiana scabra</i> Bunge 15 g, Root of <i>Achyranthes bidentata</i> Blume 15 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 30 g, Dry body of <i>Pheretima aspergillum</i> (E.Perrier) 15 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 30 g, Cane of <i>Polygonum multiflorum</i> Thunb. 12 g, The part of the sclerotium with pine roots of <i>Poria cocos</i> (Schw.) Wolf 12 g
Gong et al. (2018)	Shuanghua Zhixuan decoction	Root of <i>Astragalus membranaceus</i> (Fisch.) Bunge 30 g, Ripe fruit of <i>Lycium barbarum</i> L. 20 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 15 g, Ripe fruit of <i>Crataegus pinnatifida</i> Bunge 15 g, Root of <i>Angelica sinensis</i> (Oliv.) Diels 10 g, Processed products of <i>Atractylodes macrocephala</i> Koidz. 10 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Root of <i>Paeonia lactiflora</i> Pall. 10 g, Mature seeds of <i>Raphanus sativus</i> L. 10 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 10 g, Flower of <i>Carthamus tinctorius</i> L. 5 g
Gu et al. (2015)	Modified Qiju Dihuang decoction	Dry flower head of <i>Chrysanthemum morifolium</i> Ramat. 12 g, Ripe fruit of <i>Lycium barbarum</i> L. 15 g, Processed products of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 10 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 15 g, Rhizome of <i>Dioscorea opposita</i> Thunb. 15 g, Dry ripe pulp of <i>Cornus officinalis</i> Siebold & Zucc. 12 g, Root bark of <i>Paeonia suffruticosa</i> Andrews 12 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 12 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 12 g, Root of <i>Achyranthes bidentata</i> Blume 12 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Oxide mineral spinel magnetite 30 g
Huo (2016)	Modified Xuefu Zhuyu decoction	Root of <i>Angelica sinensis</i> (Oliv.) Diels 9 g, Roots and rhizomes of <i>Panax ginseng</i> C.A.Mey. 9 g, Mature seeds of <i>Prunus persica</i> (L.) Batsch 9 g, Flower of <i>Carthamus tinctorius</i> L. 9 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 9 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 9 g, Processed products of <i>Arisaema amurense</i> Maxim. 6 g, Dry outer peel of <i>Citrus reticulata</i> Blanco 6 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 6 g, Root of <i>Paeonia lactiflora</i> Pall. 6 g, Dry young fruit of <i>Citrus × aurantium</i> L. 6 g, Rhizome of <i>Acorus tatarinowii</i> Schott 6 g, Roots and rhizomes of <i>Rheum palmatum</i> L. 3 g, Dry middle layer of stalk of <i>Bambusa tuldaoides</i> Munro 3 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 3 g, Root of <i>Bupleurum chinense</i> DC. 3 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 3 g
Jiang and Zhu (2010)	Shihu Yangyin decoction	Stem of <i>Dendrobium officinale</i> Kimura & Migo 15 g, Root of <i>Ophiopogon japonicus</i> (Thunb.) Ker Gawl. 15 g, Root of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 15 g
Li (2013)	An Nao pills	Bovis Calculus Artificatus (Made from beef gall powder, cholic acid, hyodeoxycholic acid, taurine, bilirubin, cholesterol, trace elements, etc.) 15 g, Dried bile of <i>Sus scrofa domestica</i> Brisson. 200 g, Sulfide mineral cinnabar 55 g, Processed products of the fresh branches and leaves of <i>Cinnamomum camphora</i> (L.) J.Presl 35 g, Horn of <i>Bubalus bubalis</i> Linnaeus 200 g, Pearls of <i>Hyriopsis cumingii</i> (Lea) 50 g, Root of <i>Scutellaria baicalensis</i> Georgi 150 g, Rhizome of <i>Coptis chinensis</i> Franch. 150 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 150 g, Sulfide minerals Realgar 95 g, Root of <i>Curcuma longa</i> L. 150 g, Sulfate mineral gypsum 120 g, Oxide mineral corundum family hematite 65 g, Shells of <i>Hyriopsis cumingii</i> (Lea) 80 g, <i>Mentha haplocalyx</i> Briq. 15 g
Liang and Lin (2014)	Tianma Gouteng decoction	Shells of <i>Haliotis diversicolor</i> Reeve 20 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, The part of the sclerotium with pine roots of <i>Poria cocos</i> (Schw.) Wolf 15 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 15 g, <i>Leonurus japonicus</i> Houtt. 15 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 15 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Root of <i>Scutellaria baicalensis</i> Georgi 10 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 10 g, Bark of <i>Eucommia ulmoides</i> Oliv. 10 g, Cane of <i>Polygonum multiflorum</i> Thunb. 10 g
Man (2014)	Songling Xuemaikang capsules	Fresh Pine Leaves, Root of <i>Pueraria lobata</i> (Willd.) Ohwi, Processed products of the pearls of <i>Hyriopsis cumingii</i> (Lea) Tuber of <i>Gastrodia elata</i> Blume 12 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 10 g, Root of <i>Achyranthes bidentata</i> Blume 10 g, Shells of <i>Haliotis diversicolor</i> Reeve 20 g, Shells of <i>Ostrea gigas</i> Thunberg 30 g
Miu and Hu (2012)	Pinggan Qianyang granules	<i>Bidens Pilosa</i> L., Winged branches or winged appendages of <i>Euonymus alatus</i> (Thunb.) Siebold, Root of <i>Scrophularia ningpoensis</i> Hemsl., Dry ripe pulp of <i>Cornus officinalis</i> Siebold & Zucc., Root of <i>Stephania tetrandra</i> S.Moore, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam.
Ning (2014)	Zhen Jian granules	Leaf of <i>Chimonanthus Salicifolius</i> S. Y. Hu, Processed products of <i>Atractylodes macrocephala</i> Koidz., Dry bark, branch bark and root bark of <i>Magnolia officinalis</i> Rehder & E.H.Wilson, Ripe fruit of <i>Crataegus pinnatifida</i> Bunge, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam., Mature seeds of <i>Cassia obtusifolia</i> L., Dry young fruit of <i>Citrus × aurantium</i> L.
Pan et al. (2012)	Sheyao Shiliangcha decoction	Tuber of <i>Gastrodia elata</i> Blume 10 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 10 g, Root of <i>Pueraria lobata</i> (Willd.) Ohwi 10 g, Processed products of <i>Atractylodes macrocephala</i> Koidz. 15 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 15 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 20 g, Dried ripe peel of <i>Citrus reticulata</i> Blanco 6 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 6 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 6 g, Ripe fruit of <i>Crataegus pinnatifida</i> Bunge 12 g
Pang (2013)	Modified Banxia Baizhu Tianma decoction	Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 30 g, Dry ripe fruit of <i>Ligustrum lucidum</i> W.T.Aiton 15 g, <i>Eclipta prostrata</i> (L.) L. 15 g, Rhizome of <i>Curculigo orchioides</i> Gaertn. 12 g, Leaf of <i>Epimedium sagittatum</i> (Siebold & Zucc.) Maxim. 15 g,
Ran (2013)	Bushen Jiangya decoction	(continued on next page)

Table 2 (continued)

References	Formula	Composition of formula
Shen and Jin (2015)	Banxia Baizhu Tianma decoction	<i>Leonurus japonicus</i> Houtt. 15 g, Tuber of <i>Alisma plantago-aquatica</i> subsp. <i>orientale</i> (Sam.) Sam. 15 g, <i>Siegesbeckia orientalis</i> L. 15 g, Root bark of <i>Lycium chinense</i> Mill. 30 g, Bark of <i>Eucommia ulmoides</i> Oliv. 15g Tuber of <i>Pinellia ternata</i> (Thunb.) Makino 10 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Processed products of <i>Atractylodes macrocephala</i> Koidz. 20 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 10 g, Dry outer peel of <i>Citrus reticulata</i> Blanco 10 g, Cane of <i>Polygonum multiflorum</i> Thunb. 10 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 6 g
Wang et al. (2018)	Tianma Sanqi decoction	Flower of <i>Panax notoginseng</i> (Burkll) F.H.Chen 6 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Stem of <i>Dendrobium officinale</i> Kimura & Migo 6 g
Wang et al. (2019)	Pinggan Ziyin Tongyu decoction	Tuber of <i>Gastrodia elata</i> Blume 20 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 20 g, Shells of <i>Haliotis diversicolor</i> Reeve 20 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 20 g, Root of <i>Scutellaria baicalensis</i> Georgi 15 g, Rhizome of <i>Coptis chinensis</i> Franch. 10 g, Root of <i>Pueraria lobata</i> (Willd.) Ohwi 15 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 20 g, Bark of <i>Eucommia ulmoides</i> Oliv. 20 g, Root of <i>Paeonia lactiflora</i> Pall. 20 g, Root of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 20 g, Ripe fruit of <i>Lycium barbarum</i> L. 20 g, Dry ripe fruit of <i>Ligustrum lucidum</i> W.T.Aiton 20 g, Mature seeds of <i>Ziziphus jujuba</i> var. <i>spinosa</i> (Bunge) Hu ex H.F.Chow 15 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 20 g, Dry body of <i>Pheretima aspergillum</i> (E.Perrier) 20 g, Root of <i>Angelica sinensis</i> (Oliv.) Diels 20 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 20 g, <i>Leonurus japonicus</i> Houtt. 20 g
Wang, Y. et al. (2015)	Zini Yuntongping decoction	Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, Root of <i>Angelica sinensis</i> (Oliv.) Diels 15 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 15 g, Tuber of <i>Gastrodia elata</i> Blume 12 g, Rhizome of <i>Polygonatum kingianum</i> Collett & Hemsl. 12 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 20 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 10 g, Flower of <i>Carthamus tinctorius</i> L. 10 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 10 g, Dry ripe fruit of <i>Tribulus terrestris</i> L. 10 g, Dry flower head of <i>Chrysanthemum morifolium</i> Ramat. 10 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 10 g, Root of <i>Angelica dahurica</i> (Hoffm.) Benth. & Hook.f. ex Franch. & Sav. 6 g, Rhizome of <i>Atractylodes lancea</i> (Thunb.) DC. 20 g, Oxide mineral spinel magnetite 30 g, Shells of <i>Hyriopsis cumingii</i> (Lea) 30 g
Wang (2016)	Modified Tianma Gouteng decoction	Tuber of <i>Gastrodia elata</i> Blume 9 g, Root of <i>Scutellaria baicalensis</i> Georgi 9 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 9 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 9 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 9 g, <i>Leonurus japonicus</i> Houtt. 9 g, Cane of <i>Polygonum multiflorum</i> Thunb. 9 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, Root of <i>Achyranthes bidentata</i> Blume 15 g, Shells of <i>Haliotis diversicolor</i> Reeve 15 g, Bark of <i>Eucommia ulmoides</i> Oliv. 15 g
Wu (2011)	Denglao Zhejue Jiuwei granules	Root of <i>Astragalus membranaceus</i> (Fisch.) Bunge 30 g, Oxide mineral corundum family hematite 30 g, Root of <i>Codonopsis pilosula</i> (Franch.) Nannf. 15 g, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf 15 g, Dried ripe peel of <i>Citrus reticulata</i> Blanco 6 g, Processed products of <i>Pinellia ternata</i> (Thunb.) Makino 12 g, Mature seeds of <i>Cassia obtusifolia</i> L. 24 g, Processed products of <i>Atractylodes macrocephala</i> Koidz. 10 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 3 g
Xu (2016)	Huatan Quyu decoction	Tuber of <i>Pinellia ternata</i> (Thunb.) Makino 12 g, Roots and rhizomes of <i>Glycyrrhiza uralensis</i> Fisch. 6 g, Ripe fruit of <i>Crataegus pinnatifida</i> Bunge 30 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 15 g, Processed products of <i>Poria cocos</i> (Schw.) Wolf 15 g, Dried ripe peel of <i>Citrus reticulata</i> Blanco 12 g, Processed products of <i>Atractylodes macrocephala</i> Koidz. 15 g, Flower of <i>Carthamus tinctorius</i> L. 9 g, Rhizome of <i>Conioselinum anthriscoides</i> 'Chuanxiong' 12 g
Yang et al. (2014)	Zhong Yao decoction	Processed products of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 30 g, Dry ripe pulp of <i>Coriurus officinalis</i> Siebold & Zucc. 15 g, Rhizome of <i>Dioscorea opposita</i> Thunb. 15 g, Ripe fruit of <i>Lycium barbarum</i> L. 10 g, Mature seeds of <i>Cuscuta chinensis</i> Lam. 10 g, Carapace and plastron of <i>Chinemys reevesii</i> (Gray) 10 g, Horn of <i>Cervus elaphus</i> Linnaeus 10 g, Root of <i>Cyathula officinalis</i> K.C.Kuan 15 g
Zhang (2010)	Zini Qingnao Jiangya decoction	Tuber of <i>Gastrodia elata</i> Blume 15 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, Shells of <i>Haliotis diversicolor</i> Reeve 30 g, Dried ears of <i>Prunella vulgaris</i> L. 15 g, Dry ripe fruit of <i>Tribulus terrestris</i> L. 20 g, Dry flower head of <i>Chrysanthemum morifolium</i> Ramat. 15 g, Root of <i>Paeonia lactiflora</i> Pall. 15 g, Root of <i>Rehmannia glutinosa</i> (Gaertn.) DC. 15 g, Root of <i>Achyranthes bidentata</i> Blume 30 g
Zhao and Jiang (2015)	Modified Tianma Gouteng decoction	Tuber of <i>Gastrodia elata</i> Blume 15 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 15 g, Processed products of <i>Paeonia lactiflora</i> Pall. 15 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 15 g, Shells of <i>Haliotis diversicolor</i> Reeve 15 g, Bark of <i>Eucommia ulmoides</i> Oliv. 15 g, Root of <i>Achyranthes bidentata</i> Blume 15 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 15 g, The part of the sclerotium with pine roots of <i>Poria cocos</i> (Schw.) Wolf 10 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 10 g, <i>Leonurus japonicus</i> Houtt. 10 g
Zheng and Yao (2016) Zhou et al. (2015)	Zini Jiangya decoction Pinggan Jianpi decoction	Dried ears of <i>Prunella vulgaris</i> L. 10 g, Tuber of <i>Gastrodia elata</i> Blume 10 g, Mature kernel of <i>Gardenia jasminoides</i> J.Ellis 10 g, Bark of <i>Eucommia ulmoides</i> Oliv. 10 g, Root of <i>Achyranthes bidentata</i> Blume 10 g, Root of <i>Scutellaria baicalensis</i> Georgi 10 g, Stems with leaves of <i>Taxillus chinensis</i> (DC.) Danser 10 g, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil. 12 g, Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge 12 g, Shells of <i>Haliotis diversicolor</i> Reeve 20 g Tuber of <i>Gastrodia elata</i> Blume, Hooked stem of <i>Uncaria rhynchophylla</i> (Miq.) Miq. ex Havil., Root of <i>Pueraria lobata</i> (Willd.) Ohwi, Dry ripe fruit of <i>Tribulus terrestris</i> L., Root of <i>Paeonia lactiflora</i> Pall., Roots and rhizomes of <i>Salvia miltiorrhiza</i> Bunge, Root of <i>Astragalus membranaceus</i> (Fisch.) Bunge, Dry sclerotia of <i>Poria cocos</i> (Schw.) Wolf, The part of the sclerotium with pine roots of <i>Poria cocos</i> (Schw.) Wolf, Cane of <i>Polygonum multiflorum</i> Thunb.

CHM with WM group (experimental group) and WM group (control group), **Table 4**, and the adverse reaction, 4 studies(Bian, 2016; Cao et al., 2018; Gong et al., 2018; Pan et al., 2012) no observed any adverse reactions, but in eight studies, there are adverse reactions in the experimental group (Du, 2014; Fu, 2017; Jiang and Zhu, 2010; Li, 2013; Miu and Hu, 2012; Ran, 2013; Wang et al., 2019; Wang, 2016), and in nine studies of control group there are adverse reactions (Du, 2014; Fu, 2017; Jiang and Zhu, 2010; Li, 2013; Miu and Hu, 2012; Ran, 2013; Wang et al., 2019; Wang, 2016; Wu, 2011), others sixteen studies no mentioned the adverse effects. The adverse reactions summarize in detail in **Table 1**.

3.3. Risk of bias (ROB) assessment

The data from these trials were extracted independently by the two investigators. They used the Cochrane tool in RevMan 5.4.1 to evaluate the risk of bias (ROB). All 29 studies were mentioned as randomized controlled studies in this systematic review. Twelve trials (Bian, 2016; Cao et al., 2018; Du, 2014; Fu, 2017; Gong et al., 2018; Gu et al., 2015; Ran, 2013; Shen and Jin, 2015; Wang, 2016; Wu, 2011; Yang et al., 2014; Zhao and Jiang, 2015) used random sequence generation. Allocation concealment is only mentioned in two trials(Fu, 2017; Wu, 2011). However, no details were identified in the domains of blinding of participants, personnel, and outcome assessors. None of all 29 trials missed outcome data, and no withdrawal in the trials was reported. All studies included in this systematic review have been shown to be at low risk of

biased reporting. All studies have reported their predefined primary results, and the results of all studies are correctly reported. There were no other possible causes of bias found. (Risk of bias ROB summaries are presented in Fig. 2 (a) and (b).

3.4. Effectiveness analyses

3.4.1. Clinical effectiveness

In this study, all trials mentioned the clinical effectiveness of blood pressure for every patient in the experimental and control groups Table 3. The therapeutic effect in the experimental group was 750 patients markedly effective, 479 patients are effective, and 92 patients ineffective, while the control group's therapeutic effect was 446 patients markedly effective, 529 patients effective, and 327 patients ineffective. The total effective in experimental group 1229 patients ($1229/1321 = 93.04\%$), but in the control group the total effective 975 patients ($975/1302 = 74.88\%$). We selected a random effect model to evaluate clinical effectiveness. The clinical effect of integrated CHM with WM in hypertension treatment is significantly improved compared to WM alone. ($RR = 1.23$; 95% CI [1.17, 1.30]; $P < 0.00001$; $I^2 = 62\%$). Fig. 3 (A).

For those markedly effective patients who achieved the therapeutic goal in the treatment of PHTN, CHM effectiveness combined with WM was significantly higher than WM alone. ($RR = 1.66$; 95% CI [1.52, 1.80]; $P = 0.55$; $I^2 = 0\%$). The results have shown that combination therapy is superior to WM alone in clinical effect and achieving blood pressure targets. Fig. 3 (B)

3.4.2. Blood pressure systolic and diastolic

In this study, all 29 trials reported the treatment effects on blood pressure, measured by SBP and DBP, including 2623 patients (CHM with WM group 1321 patients, WM group 1302 patients). We use the random effect model in SBP (MD 7.91, [6.00, 983], $P < 0.00001$) Fig. 4(A) and DBP (MD 5.46, [3.88, 6.43], $P < 0.00001$) Fig. 4(B), we found that SBP and DBP all of which were extremely heterogeneous, and we performed a subgroup analysis and sensitivity analysis. This subgroup was performed according to control group, then we selected a random effect model, and classify WM that affect SBP in control group into four classes as follow CCB, ACEI, ARB, and combination intervention, CCB; (MD = 5.58, 95% CI [4.59, 6.58], $P = 0.47$; $I^2 = 0\%$); ACEI; (MD = 8.52, CI 95% [6.08, 10.97], $P = 0.41$), ARB; (MD = 6.73, 95% CI [0.66, 12.79], $P = 0.009$), and combination intervention; (MD = 8.03, [5.86, 10.19], $P = 0.72$; $I^2 = 0\%$) Fig. 5(A). Also, WM that affect DBP was divided as for SBP, CCB; (MD = 5.13, 95% CI [3.60, 6.67], $P = 0.0002$), ACEI; (MD = 5.33, 95% CI [1.78, 8.88], $P = 0.07$), ARB; (MD = 4.89, 95% CI [3.10, 6.68], $P = 0.96$), and combination intervention; (MD = 4.80, [2.31, 7.29], $P = 0.04$; $I^2 = 60\%$) Fig. 5 (B).

Sensitivity analysis was performed in these subgroup analysis in these subgroups CCB (Hu, 2016; Liang and Lin, 2014; Ning, 2014; Yang et al., 2014), in ACEI (Zheng and Yao, 2016), in ARB (Wang, Y. et al., 2015), and in combination intervention (Zhang, 2010), in these studies due to high risks of bias, different of age between the patients, difference in disease duration, and difference in male and female in experimental and control group, for that these studies may have been the source of heterogeneity in SBP and DBP due to methodological quality. After excluding these publications, the 95% confidence intervals were quite constant and overlapped significantly, suggesting that the meta-analysis findings were largely stable. Fig. 6(A) and (B).

Furthermore, we conduct subgroup analysis according to the duration of treatment of SBP and DBP (less than 7 weeks and more than 7 weeks). In SBP the type of outcome <7 weeks (MD = 7.44, 95% CI [6.07, 8.81], $P = 0.61$; $I^2 = 0\%$), and >7 weeks (MD = 5.77, 95% CI [4.38, 7.17], $P = 0.05$; $I^2 = 45\%$) Fig. 7 (A). And in DBP the type of outcome <7 weeks (MD = 3.82, 95% CI [1.97, 5.68], $P = 0.002$; $I^2 = 65\%$), and >7 weeks (MD = 5.07, CI 95% CI [3.71, 6.43], $P = 0.001$; $I^2 = 66\%$), Fig. 7 (B). Besides, we performed the risk ratio in patients less than 7 weeks ($RR = 1.23$; 95% CI [1.17, 1.30]; $P < 0.28$; $I^2 = 21\%$) Fig. 8 (A), and in

more than 7 weeks ($RR = 1.23$; 95% CI [1.13, 1.34]; $P < 0.00001$; $I^2 = 74\%$). Fig. 8 (B)

Sensitivity analysis was performed in these subgroup analyses either in SBP or DBP in less than 7 weeks, and these studies may have been the source of heterogeneity (Hu, 2016; Liang and Lin, 2014; Ning, 2014; Zheng and Yao, 2016), and in the more than 7 weeks these studies (Bian, 2016; Wang, Y. et al., 2015; Yang et al., 2014) in these studies due to high risks of bias, the difference in age between the patients, the difference in disease duration, and different hypertension classification stages between patients in the experimental and control group, that is may be affect heterogeneity due to methodological quality in these studies. The 95% CI was little changed and overlapped after these studies were removed, showing that the meta-analysis results were mostly stable. Fig. 9(A) and (B).

Also, subgroup analysis according to the same CHM prescriptions formula was used to investigate the causes of heterogeneity (Xiong et al., 2019b) Table 5.

3.5. Adverse reaction

In this study, 4 studies (Bian, 2016; Cao et al., 2018; Gong et al., 2018; Pan et al., 2012) no observed any adverse reactions, but in eight studies, there were adverse reactions in the experimental group (Du, 2014; Fu, 2017; Jiang and Zhu, 2010; Li, 2013; Miu and Hu, 2012; Ran, 2013; Wang et al., 2019; Wang, 2016), and in 9 studies of control group there are adverse reactions (Du, 2014; Fu, 2017; Jiang and Zhu, 2010; Li, 2013; Miu and Hu, 2012; Ran, 2013; Wang et al., 2019; Wang, 2016; Wu, 2011), others sixteen studies no mentioned the adverse effects. There were 2623 patients whose blood pressures were measured. We finally collected all the cases (100%) with complete data no patient stopped treatment or withdrawal. The CHM with WM group (experimental group) had 31 patients with side effects, and the WM group (control group) had 55 patients with side effects. The adverse effects reported in CHM and WM groups were; gastrointestinal discomfort, diarrhea, skin rash, headache, flushing, limb edema, polyuria, dizziness, fatigue, cough, nausea, vomiting, dry mouth, and mild diarrhea. WM group adverse effects included; gingival hyperplasia, palpitations, facial flushing, ankle edema, headache, polyuria, fatigue, cough, nausea, vomiting, palpitation, sleep disturbance, and lower limb soreness. During the treatment duration, no patients stopped the treatment due to the adverse reaction; all the adverse reactions mentioned were not severe, and all disappeared after symptomatic treatment. The adverse effect summarizes in detail in Table 1.

3.6. Publication bias

The publication bias was investigated, and the outcomes were analyzed by funnel plot for; clinical effect in all patients (A), markedly effective (B), SBP according to the type of intervention (C), DBP according to type of intervention (D), SBP according to the duration of treatment (E), DBP according to the duration of treatment (F), RR less than 7 weeks (G), RR more than 7 weeks (H). In this systematic review, the funnel plot was asymmetric, indicating a mild publication bias. Fig. 10.

4. Discussion

4.1. Summary of evidence

Reducing BP to the average level, reversing cardiovascular risk factors, maintaining target organs, and reducing mortality and cardiovascular complications is the primary therapeutic goal in treating hypertension (Lawes et al., 2008; Weber et al., 2014; Williams et al., 2018). According to the different global medical guidelines on the management of hypertension, including 2017 ACC/AHA, 2020 ISH, and 2018 ESC/ESH that the main objective of the antihypertensive

Table 3

Comparison on clinical efficacies between CHM with WM versus WM.

Author	Total clinical effectiveness rate % (Experimental group) % (Control group)	Experimental group (CHM with WM)				Control group (WM)			
		Markedly effective	Effective	Ineffective	Total	Markedly effective	Effective	Ineffective	Total
Bian (2016)	89.6 (39/21/7) 71.6 (27/21/19)	39	21	7	67	27	21	19	67
Cao et al. (2018)	96.7 (14/15/1) 76.7 (11/12/7)	14	15	1	30	11	12	7	30
Du (2014)	92.0 (30/16/4) 68.0 (19/15/16)	30	16	4	50	19	15	16	50
Duan (2013)	100.0 (17/13/0) 96.7 (2/27/1)	17	13	0	30	2	27	1	30
Fu (2017)	87.0 (15/11/4) 50.0 (7/8/15)	15	11	4	30	7	8	15	30
Gong et al. (2018)	87.5 (12/23/5) 67.5 (7/20/13)	12	23	5	40	7	20	13	40
Gu et al. (2015)	93.3 (17/11/2) 73.3 (10/12/8)	17	11	2	30	10	12	8	30
Huo (2016)	97.4 (21/16/1) 84.2 (14/18/6)	21	16	1	38	14	18	6	38
Jiang and Zhu (2010)	92.3 (32/16/4) 80.8 (25/17/10)	32	16	4	52	25	17	10	52
Li (2013)	94.0 (25/7/2) 82.0 (10/18/6)	25	7	2	34	10	18	6	34
Liang and Lin (2014)	95.0 (45/12/3) 76.7 (32/14/14)	45	12	3	60	32	14	14	60
Man (2014)	95.6 (25/18/2) 80.0 (18/14/8)	25	18	2	45	18	14	8	40
Miu and Hu (2012)	94.1 (25/7/2) 82.4 (10/18/6)	25	7	2	34	10	18	6	34
Ning (2014)	87.5 (16/19/5) 60.5 (10/13/15)	16	19	5	40	10	13	15	38
Pan et al. (2012)	93.3 (11/17/2) 70.0 (5/16/9)	11	17	2	30	5	16	9	30
Pang (2013)	96.7 (23/6/1) 88.5 (13/10/3)	23	6	1	30	13	10	3	26
Ran (2013)	87.5 (20/15/5) 37.5 (8/7/25)	20	15	5	40	8	7	25	40
Shen and Jin (2015)	90.0 (17/10/3) 63.3 (10/9/11)	17	10	3	30	10	9	11	30
Wang et al. (2018)	85.0 (24/10/6) 62.5 (18/11/11)	24	10	6	40	18	11	11	40
Wang et al. (2019)	93.3 (15/27/3) 64.5 (6/23/16)	15	27	3	45	6	23	16	45
Wang, Y. et al. (2015)	93.6 (23/21/3) 76.6 (12/24/11)	23	21	3	47	12	24	11	47
Wang (2016)	97.6 (39/2/1) 80.0 (23/9/8)	39	2	1	42	23	9	8	40
Wu (2011)	96.7 (10/19/1) 70.0 (1/20/9)	10	19	1	30	1	20	9	30
Xu (2016)	93.3 (15/13/2) 66.7 (9/11/10)	15	13	2	30	9	11	10	30
Yang et al. (2014)	95.0 (35/22/3) 73.3 (26/18/16)	35	22	3	60	26	18	16	60
Zhang (2010)	87.3 (17/31/7) 62.0 (8/23/19)	17	31	7	55	8	23	19	50
Zhao and Jiang (2015)	91.0 (39/32/7) 80.8 (22/41/15)	39	32	7	78	22	41	15	78
Zheng and Yao (2016)	96.8 (49/13/2) 71.4 (33/12/18)	49	13	2	64	33	12	18	63
Zhou et al. (2015)	96.7 (80/36/4) 91.7 (50/60/10)	80	36	4	120	50	60	10	120

medications was to decrease blood pressure (the optimal blood pressure target for patients <65 years < 130/80, but for patients >65 years the target <140/90) in patients with hypertension to protect the patients from the cardiovascular morbidity and mortality. (Mann, 2020; Unger et al., 2020; Whelton et al., 2018; Williams et al., 2018). In China, there are many CHM single formulations used as adjuvant therapy with WM for treating patients with PHTN, and their integrated treatments were more effective and safer when compared with WM treatments alone (Tai et al., 2020; Wang et al., 2017; Wang, P. et al., 2015). This systematic review and meta-analysis were conducted to evaluate the effectiveness and safety of integrated CHM with WM in decreasing systolic and

diastolic blood pressure for patients with PHTN. In this systematic study, 29 RCTs, including 2623 patients with PHTN treated with CHM with WM, were included and compared with WM.

The clinical effect of all experimental groups displayed significance, and the patients achieved blood pressure therapeutic goals. Furthermore, this study reported the clinical outcome for every patient, and all the 29 studies of the experimental group demonstrated a high therapeutic effect. The 1229 patients (93.04%) displayed effectiveness and achieved the target blood pressure goal, while only 92 patients (6.96%) were ineffective. But in the control group, the total effective 975 patients (975/1302 = 74.88%), and 327 patients were ineffective (327/1302 =

Table 4

SBP and DBP before and after treatments.

Author	Pre-treatment SBP(mmHg)	Post treatment SBP(mmHg)	Pre-treatment DBP(mmHg)	Post treatment DBP(mmHg)
Bian (2016)	E: 148.0 ± 24.0 C: 150.0 ± 22.0	E: 120.0 ± 15.0 C: 130.0 ± 16.0	E: 101.0 ± 10.0 C: 98.0 ± 10.0	E: 80.0 ± 5.0 C: 87.0 ± 6.0
Cao et al. (2018)	E: 165.2 ± 9.9 C: 163.4 ± 9.2	E: 123.6 ± 8.7 C: 129.4 ± 8.7	E: 95.3 ± 8.6 C: 94.9 ± 8.6	E: 84.8 ± 6.9 C: 89.8 ± 7.2
Du (2014)	E: 149.6 ± 14.5 C: 152.8 ± 12.3	E: 130.0 ± 10.7 C: 136.8 ± 13.6	E: 94.0 ± 10.0 C: 91.2 ± 10.8	E: 83.5 ± 9.1 C: 82.9 ± 10.7
Duan (2013)	E: 155.1 ± 5.7 C: 155.6 ± 7.8	E: 122.2 ± 4.1 C: 127.4 ± 4.4	E: 82.8 ± 8.8 C: 86.2 ± 7.6	E: 73.2 ± 3.8 C: 79.5 ± 4.1
Fu (2017)	E: 169.4 ± 5.8 C: 170.9 ± 6.3	E: 138.7 ± 8.8 C: 146.3 ± 13.0	E: 80.9 ± 7.8 C: 81.4 ± 7.6	E: 67.1 ± 4.1 C: 68.4 ± 7.3
Gong et al. (2018)	E: 158.2 ± 8.6 C: 157.3 ± 9.3	E: 129.7 ± 6.5 C: 132.8 ± 6.8	E: 96.9 ± 5.3 C: 97.1 ± 6.2	E: 80.1 ± 6.1 C: 85.3 ± 5.9
Gu et al. (2015)	E: 167.9 ± 5.3 C: 166.7 ± 6.7	E: 119.5 ± 6.3 C: 125.6 ± 7.4	E: 99.0 ± 4.9 C: 98.0 ± 5.8	E: 75.5 ± 5.4 C: 81.0 ± 5.6
Huo (2016)	E: 158.7 ± 8.3 C: 157.4 ± 9.3	E: 125.2 ± 6.4 C: 139.3 ± 7.3	E: 94.4 ± 6.1 C: 94.6 ± 7.1	E: 76.8 ± 5.4 C: 83.4 ± 8.3
Jiang and Zhu (2010)	E: 159.1 ± 10.5 C: 158.1 ± 10.0	E: 138.9 ± 11.1 C: 143.5 ± 11.3	E: 97.7 ± 4.3 C: 97.2 ± 4.8	E: 85.5 ± 5.6 C: 89.4 ± 5.5
Li (2013)	E: 168.5 ± 12.2 C: 167.6 ± 12.6	E: 123.6 ± 8.3 C: 132.6 ± 8.4	E: 108.3 ± 8.5 C: 107.6 ± 8.7	E: 77.5 ± 6.3 C: 84.5 ± 6.6
Liang and Lin (2014)	E: 159.5 ± 6.5 C: 158.9 ± 5.9	E: 135.1 ± 2.6 C: 146.7 ± 3.5	E: 85.9 ± 5.6 C: 94.4 ± 5.7	E: 71.9 ± 4.1 C: 82.1 ± 4.0
Man (2014)	E: 173.1 ± 10.5 C: 174.8 ± 11.3	E: 134.8 ± 8.5 C: 138.3 ± 9.1	E: 95.3 ± 6.9 C: 98.2 ± 8.1	E: 79.4 ± 6.2 C: 87.4 ± 4.5
Miu and Hu (2012)	E: 167.5 ± 12.3 C: 166.7 ± 12.8	E: 122.6 ± 8.4 C: 134.3 ± 8.9	E: 107.3 ± 8.6 C: 109.2 ± 6.3	E: 78.5 ± 6.2 C: 85.4 ± 4.5
Ning (2014)	E: 157.1 ± 10.1 C: 158.4 ± 7.5	E: 143.5 ± 7.9 C: 142.9 ± 6.5	E: 93.7 ± 4.5 C: 94.3 ± 4.5	E: 82.3 ± 5.6 C: 84.9 ± 4.3
Pan et al. (2012)	E: 160.3 ± 9.6 C: 159.2 ± 10.6	E: 130.7 ± 8.4 C: 135.8 ± 10.1	E: 97.2 ± 6.0 C: 97.3 ± 6.7	E: 80.8 ± 6.0 C: 85.5 ± 6.9
Pang (2013)	E: 163.0 ± 13.2 C: 164.0 ± 15.5	E: 131.0 ± 4.6 C: 139.0 ± 5.1	E: 92.0 ± 10.5 C: 94.0 ± 10.2	E: 80.0 ± 9.6 C: 86.0 ± 8.1
Ran (2013)	E: 160.2 ± 8.2 C: 162.1 ± 9.1	E: 118.9 ± 9.4 C: 132.1 ± 17.5	E: 97.2 ± 6.2 C: 99.2 ± 5.9	E: 69.8 ± 7.6 C: 77.1 ± 10.9
Shen and Jin (2015)	E: 148.5 ± 8.0 C: 149.1 ± 8.1	E: 129.4 ± 6.8 C: 138.3 ± 6.9	E: 97.3 ± 4.6 C: 98.1 ± 4.5	E: 81.3 ± 3.2 C: 89.5 ± 3.5
Wang et al. (2018)	E: 145.1 ± 6.8 C: 145.3 ± 7.2	E: 123.5 ± 4.4 C: 130.1 ± 3.9	E: 80.4 ± 8.5 C: 78.7 ± 9.6	E: 72.6 ± 6.3 C: 71.6 ± 7.6
Wang et al. (2019)	E: 160.8 ± 5.5 C: 159.8 ± 6.1	E: 123.7 ± 7.0 C: 130.0 ± 8.2	E: 99.3 ± 6.3 C: 98.6 ± 6.7	E: 81.2 ± 3.5 C: 85.9 ± 4.5
Wang, Y. et al. (2015)	E: 163.5 ± 12.6 C: 160.4 ± 11.7	E: 125.4 ± 9.1 C: 137.2 ± 10.0	E: 97.2 ± 10.7 C: 96.2 ± 9.9	E: 82.3 ± 5.1 C: 87.6 ± 6.3
Wang (2016)	E: 165.6 ± 20.4 C: 164.6 ± 19.4	E: 128.8 ± 8.4 C: 131.5 ± 9.3	E: 97.6 ± 9.6 C: 98.5 ± 9.6	E: 76.6 ± 7.4 C: 81.9 ± 8.5
Wu (2011)	E: 156.8 ± 6.7 C: 156.7 ± 6.8	E: 122.9 ± 4.5 C: 126.4 ± 5.2	E: 79.1 ± 4.6 C: 78.1 ± 6.3	E: 68.2 ± 2.9 C: 69.5 ± 4.4
Xu (2016)	E: 150.5 ± 6.0 C: 149.2 ± 4.5	E: 132.2 ± 7.0 C: 140.1 ± 5.9	E: 88.7 ± 4.6 C: 87.5 ± 4.3	E: 75.2 ± 5.7 C: 82.0 ± 5.0
Yang et al. (2014)	E: 166.3 ± 14.3 C: 162.5 ± 13.5	E: 124.6 ± 10.1 C: 135.7 ± 11.2	E: 102.5 ± 9.1 C: 98.1 ± 8.2	E: 73.6 ± 6.5 C: 84.5 ± 7.1
Zhang (2010)	E: 159.2 ± 13.0 C: 160.4 ± 13.8	E: 140.8 ± 13.3 C: 149.0 ± 14.1	E: 88.4 ± 8.0 C: 90.3 ± 7.5	E: 80.4 ± 6.5 C: 81.1 ± 6.1
Zhao and Jiang (2015)	E: 168.7 ± 12.4 C: 168.0 ± 21.3	E: 134.3 ± 11.9 C: 142.4 ± 15.4	E: 102.3 ± 11.3 C: 101.5 ± 23.5	E: 87.2 ± 14.6 C: 88.3 ± 15.5
Zheng and Yao (2016)	E: 166.0 ± 7.2 C: 159.5 ± 6.2	E: 134.3 ± 2.9 C: 146.0 ± 3.5	E: 91.1 ± 5.9 C: 93.4 ± 5.7	E: 71.2 ± 3.7 C: 82.9 ± 3.9
Zhou et al. (2015)	E: 164.2 ± 7.6 C: 165.3 ± 8.0	E: 126.9 ± 8.9 C: 132.7 ± 10.3	E: 98.6 ± 6.1 C: 97.8 ± 5.4	E: 80.6 ± 8.3 C: 87.6 ± 9.2

Abbreviation: E, Experimental Group; C, Control Group; DBP, diastolic blood pressure; SBP, systolic blood pressure; mmHg, millimetres of mercury.

25.115%). The overall result in this study indicated that the combination of CHM with WM significantly reduced SBP by 7.91 mmHg and DBP by 5.16 mmHg. According to a study that mentioned blood pressure levels in the 130–139 SBP, and DBP 85–89 mmHg range are related with a more than two-fold increase in relative risk of cardiovascular disease when compared to blood pressure levels below 120/80 mmHg, also the benefits of lowering BP, which was associated with reductions in stroke incidence by 35–40%, myocardial infarction by 20–25%, and heart failure by 50%. (Xiong et al., 2019a). In this study, although the decreasing blood pressure effect is limited, it did have an important clinical significance and reflected the cardiovascular protective effects

of combination of CHM with WM for patients with PHTN. However, more convincing evidence is required to confirm these conclusions due to the inconsistent results between the studies and significant heterogeneity.

While we conducted a subgroup analysis of the SBP and DBP outcomes based on the type of intervention, which revealed that grouping variables may have been the cause of SBP and DBP heterogeneity, the stability of the data was then assessed using a sensitivity analysis after the combining of the studies, the heterogeneity was high. However, after subgroup analysis based on the type of intervention, the heterogeneity was reduced to some extent, among them the I^2 of subgroups CCB, ACEI,

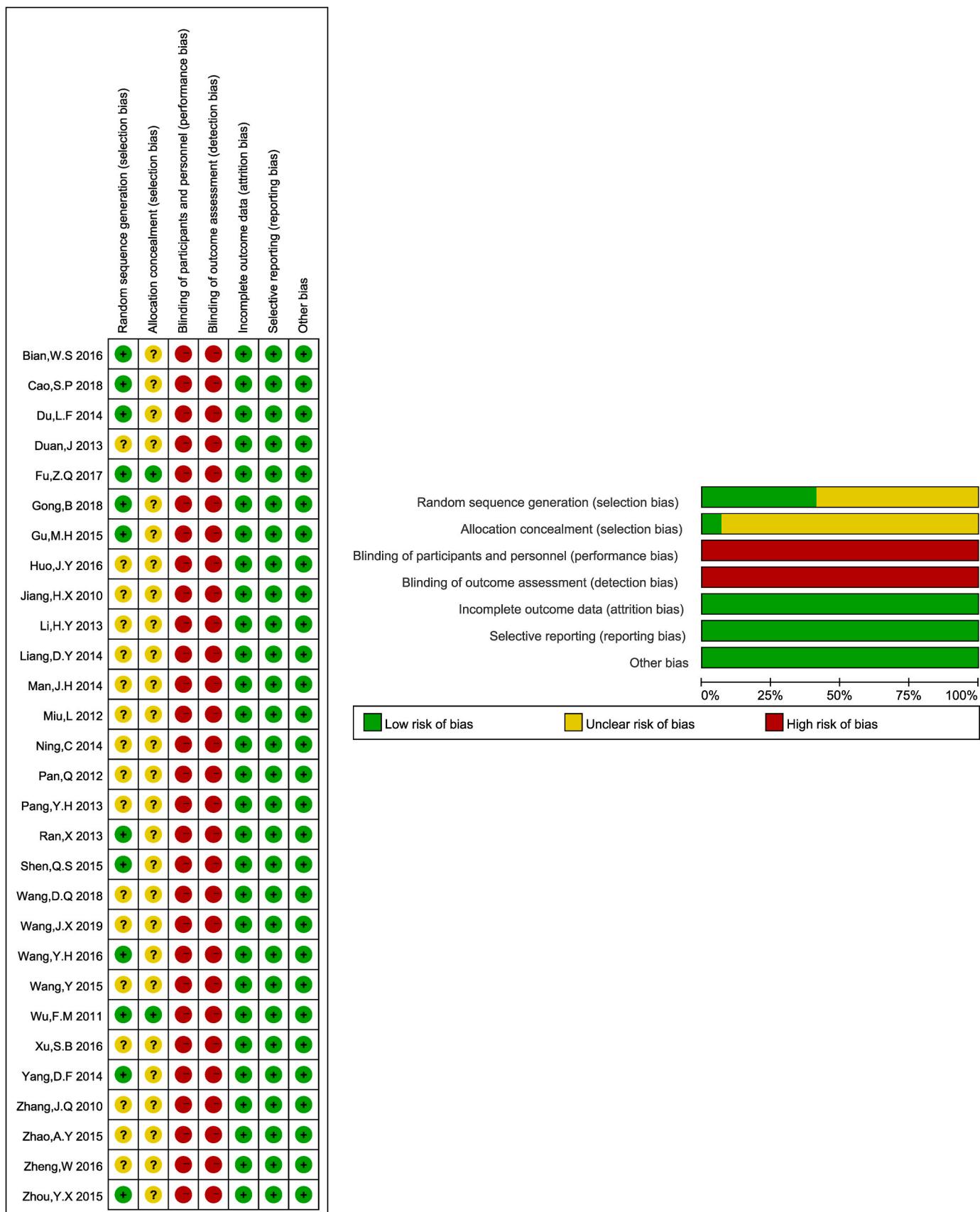
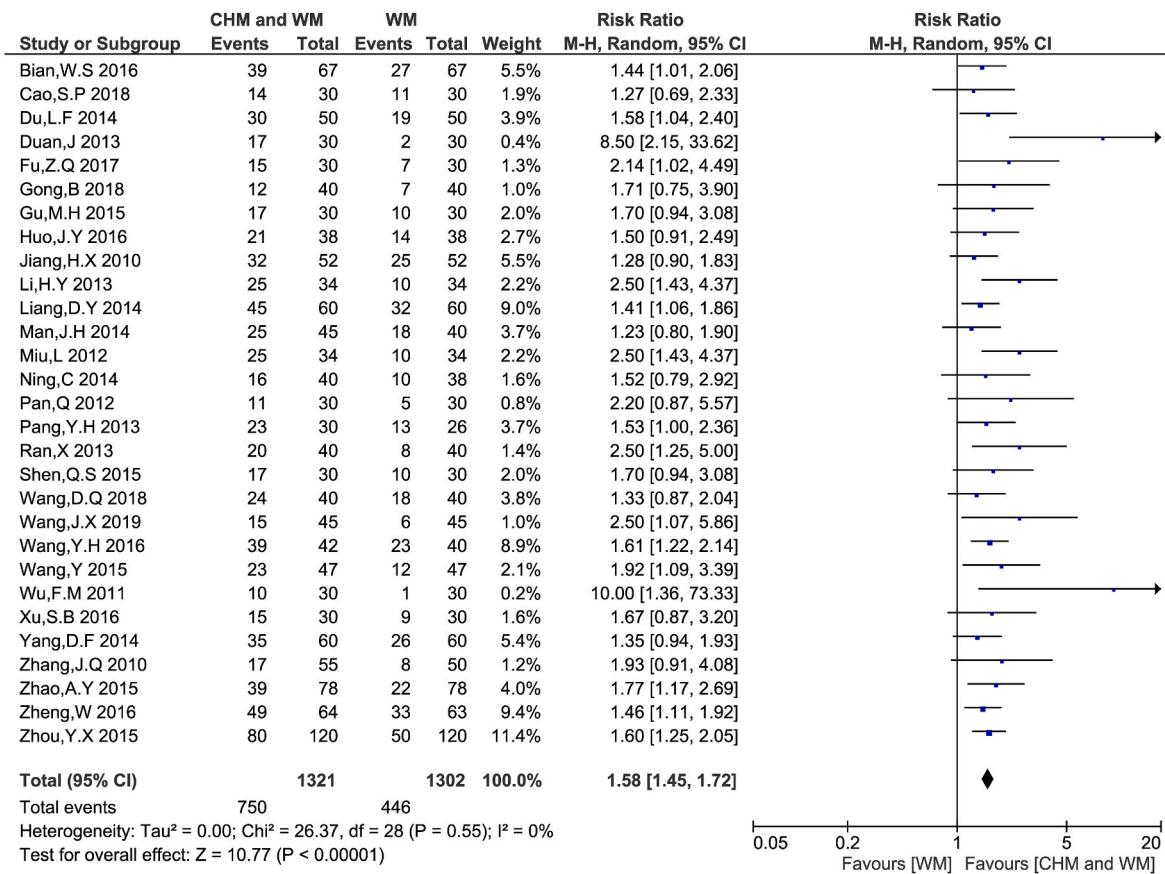
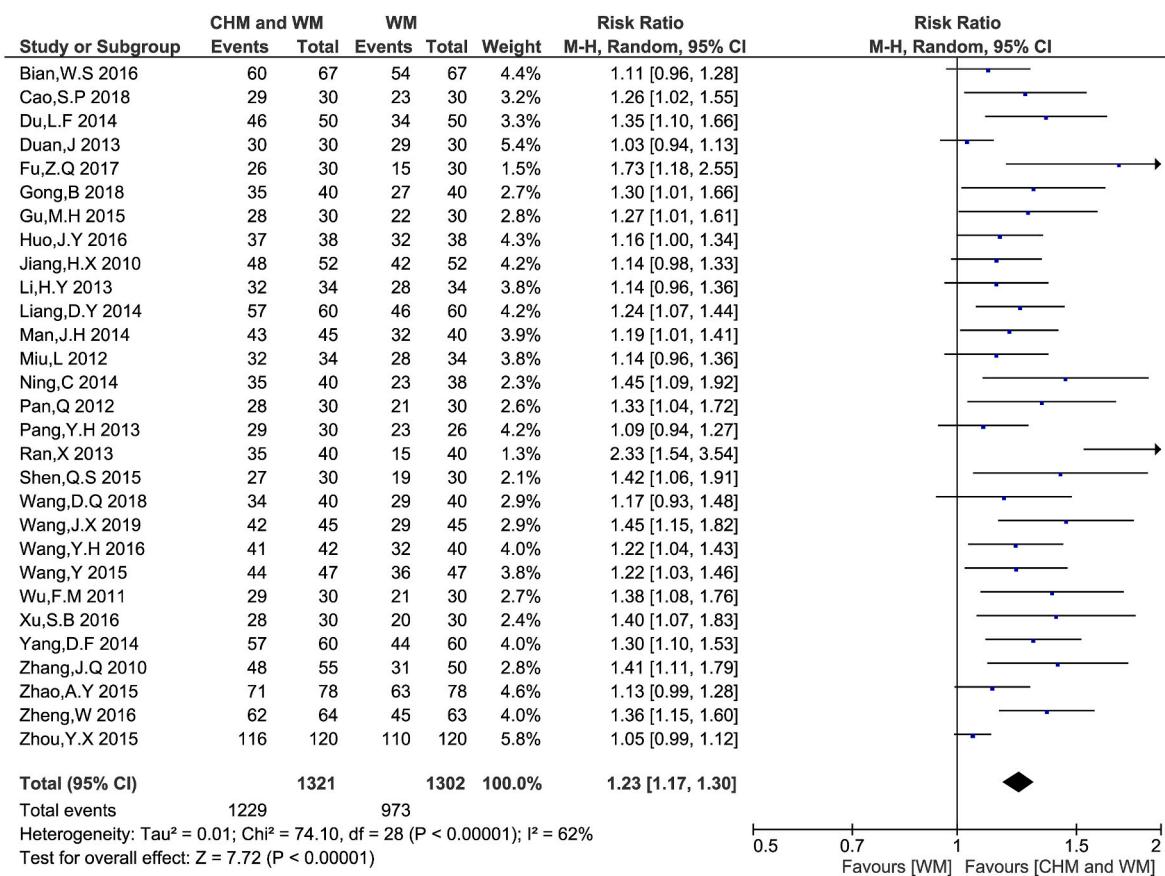


Fig. 2. (a) Risk of Bias(ROB) + low risk; – high risk; ? unclear risk; (b) Risk of bias summary.

**Fig. 3.** Forest plot Clinical Effects CHM combined with WM and WM (A), Markedly Effective (B).

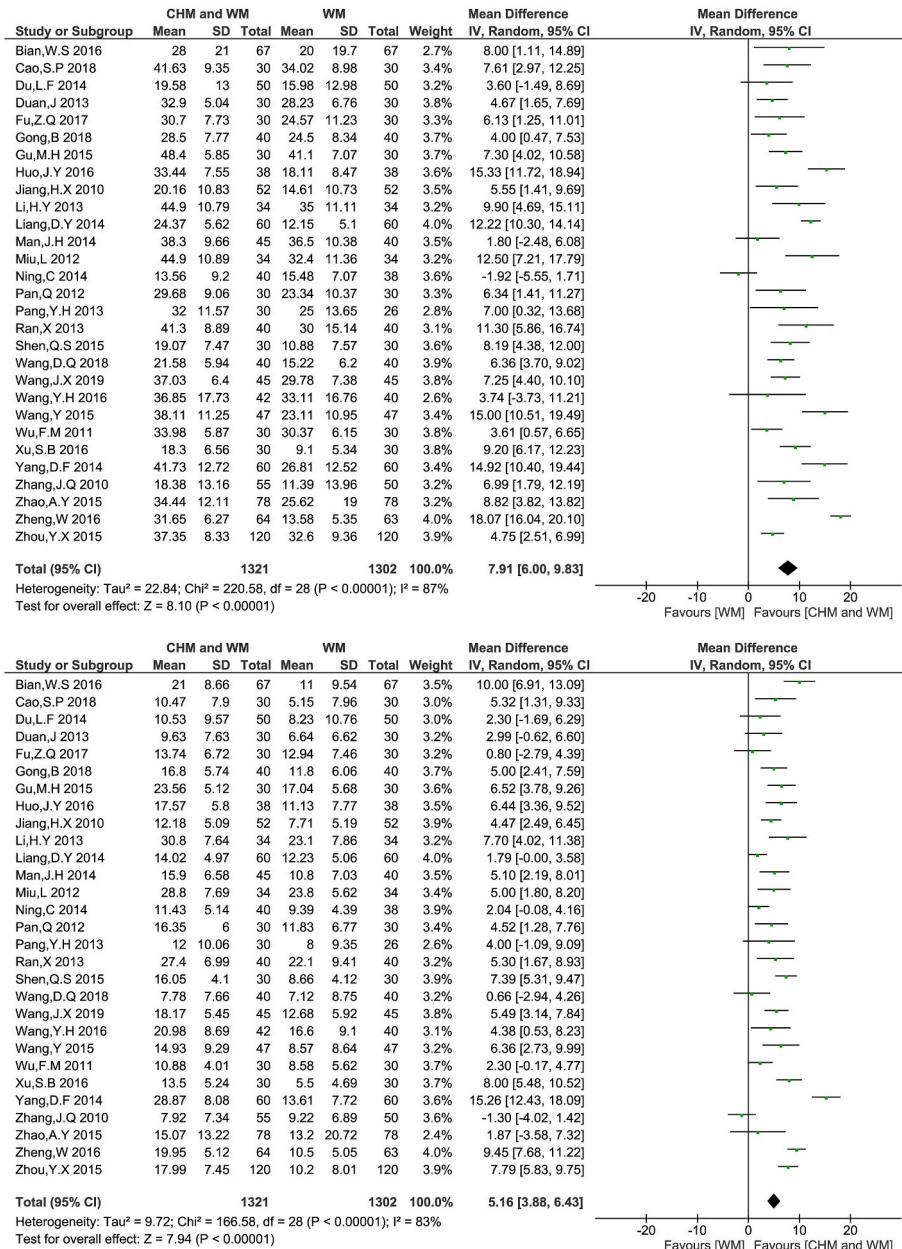


Fig. 4. Random effect model SBP(A); DBP (B).

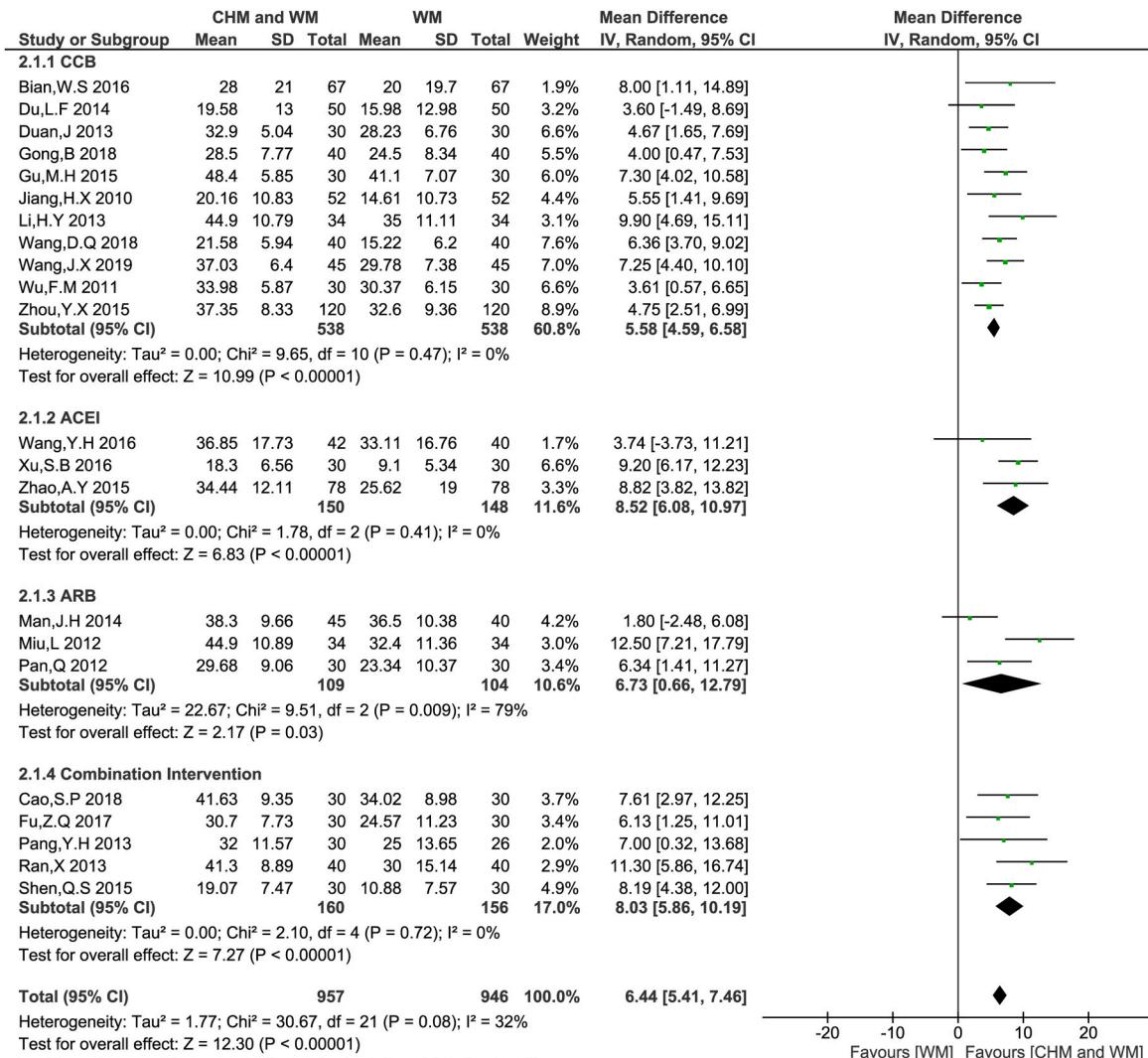


Fig. 5. Forest plot subgroup comparison according to the type of intervention between CHM combined with WM and WM alone, SBP (A); DBP (B).

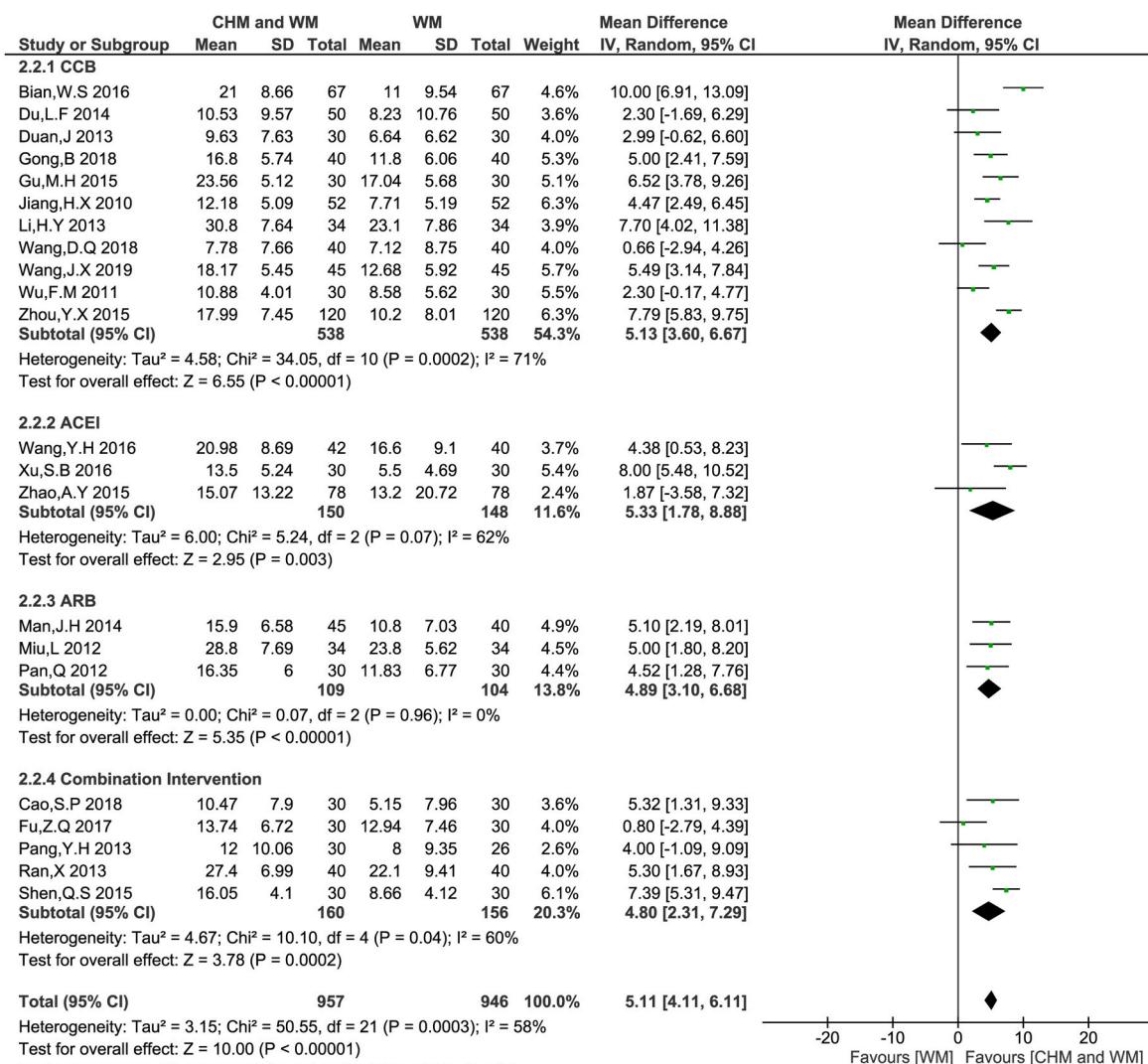


Fig. 5. (continued).

and combination intervention were decreased significantly in SBP, and ARB of DBP, indicating that type of intervention may be the source of heterogeneity. Many studies reported that based on these subgroups, there is a benefit in reducing blood pressure(hua et al., 2018; hui et al., 2016; Wu et al., 2014). In this study, the results of SBP subgroup analysis and DBP subgroup analysis by type of intervention showed that, when compared to WM alone, combined application of CHM with WM based on CCB, ACEI, and combination intervention could significantly reduce systolic blood pressure, but there was no significant difference in DBP results, maybe due methodological quality of the included studies was quit low.

In another subgroup analysis, duration of treatment, the heterogeneity was large after combining the studies; however, after subgroup analysis based on treatment duration, the heterogeneity was reduced to some extent; among them, the I^2 of subgroups less than seven weeks was significantly reduced in SBP, indicating that the treatment duration of each study may be the source of heterogeneity. Many studies reported contradictory results in the treatment duration of blood pressure (Canoy et al., 2022; Sheppard et al., 2020). The result showed those who take CHM with WM for less than 7 weeks have a better effect than WM, but there is no difference in the more than 7 weeks subgroup; additionally, we conduct the risk ratio in patients for less than 7 weeks and more than 7 weeks, which shows that for less than 7 weeks, the patient's treatment is highly significant, but there is no difference in the long-term

treatment. We conclude there is no difference with long-term therapy.

Moreover, subgroup analysis according to the CHM prescription formula, a previous study of the combination of Tianma Gouteng decoction formula and nifedipine showed a better effect in the treatment of hypertension(Tai et al., 2020). In this study, the Tianma Gouteng decoction formula subgroup has significantly decreased SBP by 8.30 mmHg 338 and DBP by 4.68 mmHg but identified significant heterogeneity suggesting the poor methodological quality of original research studies. The second group of Modified Tianma Gouteng decoction in the last study showed effectively improved the clinical effect and reduce the level of blood pressure in elderly patients(Donge and JUAN, 2020). In this study Modified Tianma Gouteng decoction formula significantly decreased SBP by 6.78 mmHg 339 and DBP by 2.35 mmHg, furthermore showed no heterogeneity. However, because only one study was enrolled for the remaining 23 formulas, more evidence are needed in future research.

In addition, this study results showed that the adverse reaction reported only from nine trials (9/29, 31%), and 712 patients (712/2623, 27.14%) showed no severe side effects, while 334 patients there were not observed any side effects (334/3632, 12.73%). Besides that, no patients stopped treatment or withdrawal due to any severe adverse events, indicating that the completion rate of all studies was 100%. In brief, combined CHM with WM is clinically effective and safe in achieving blood pressure therapeutic goals, especially those who used

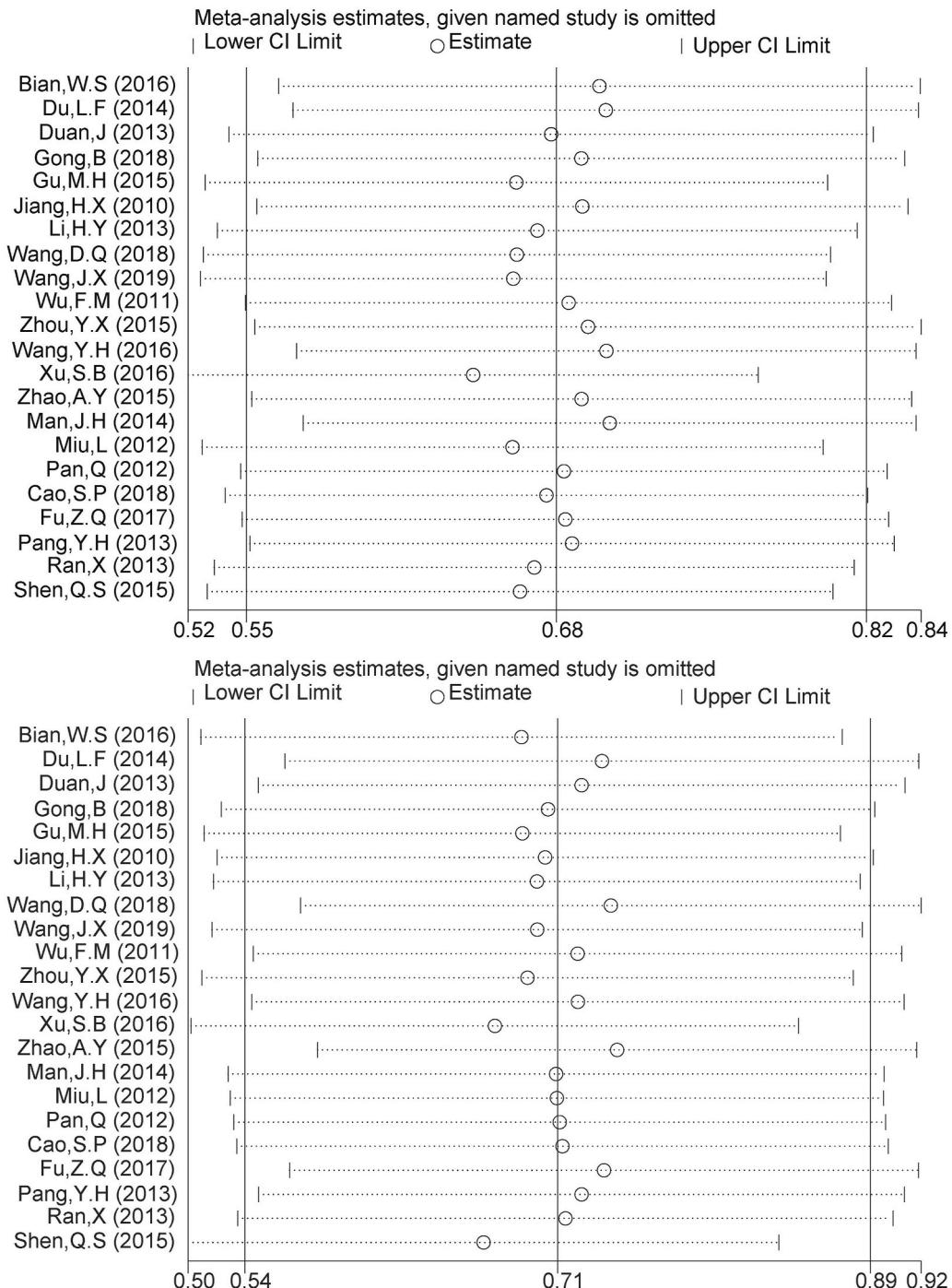


Fig. 6. Sensitivity analysis according to the type of intervention SBP(A) and DBP (B).

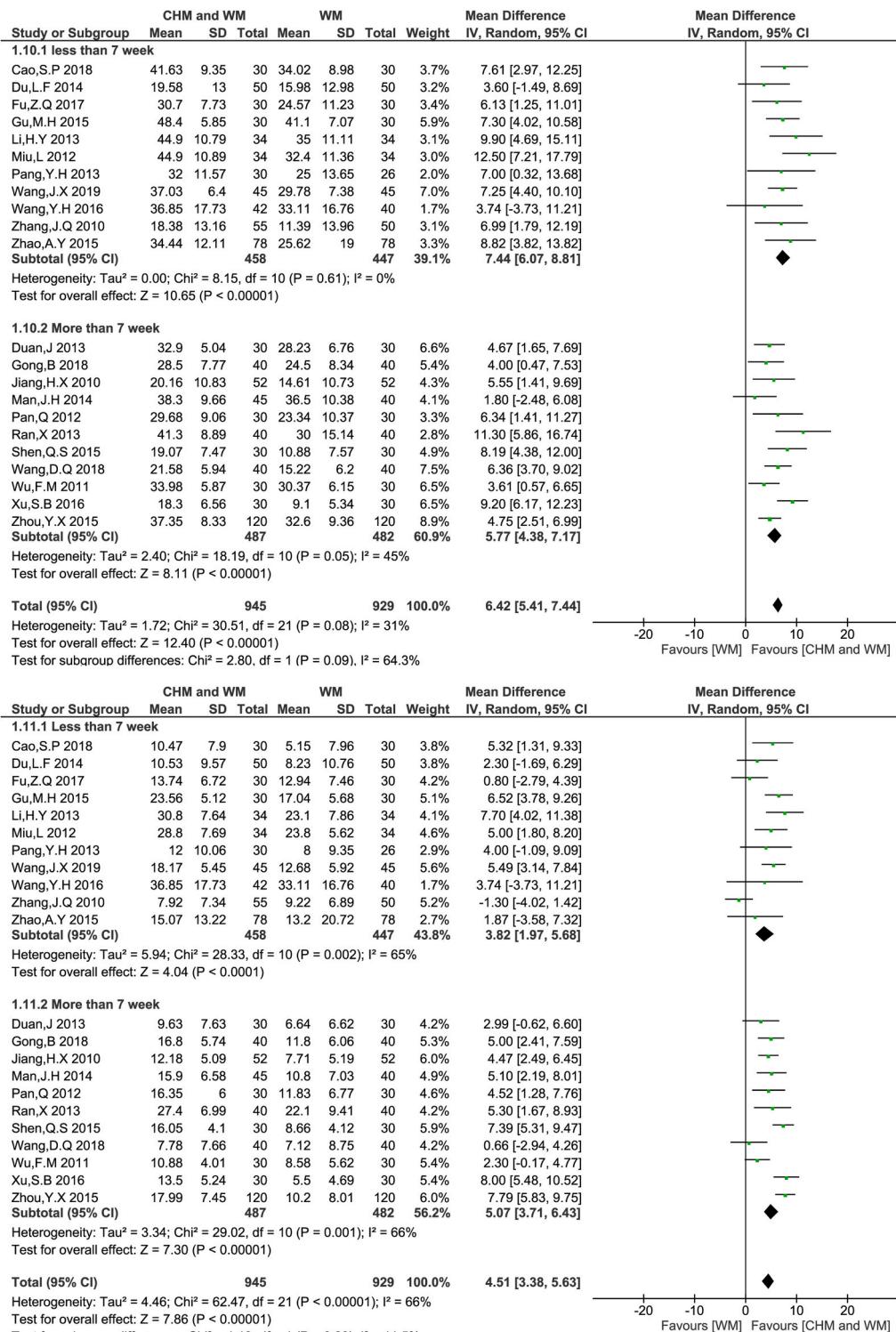


Fig. 7. Forest plot according to the duration of treatment of SBP less and more than 7 weeks(A) DBP less and more than 7 weeks (B).

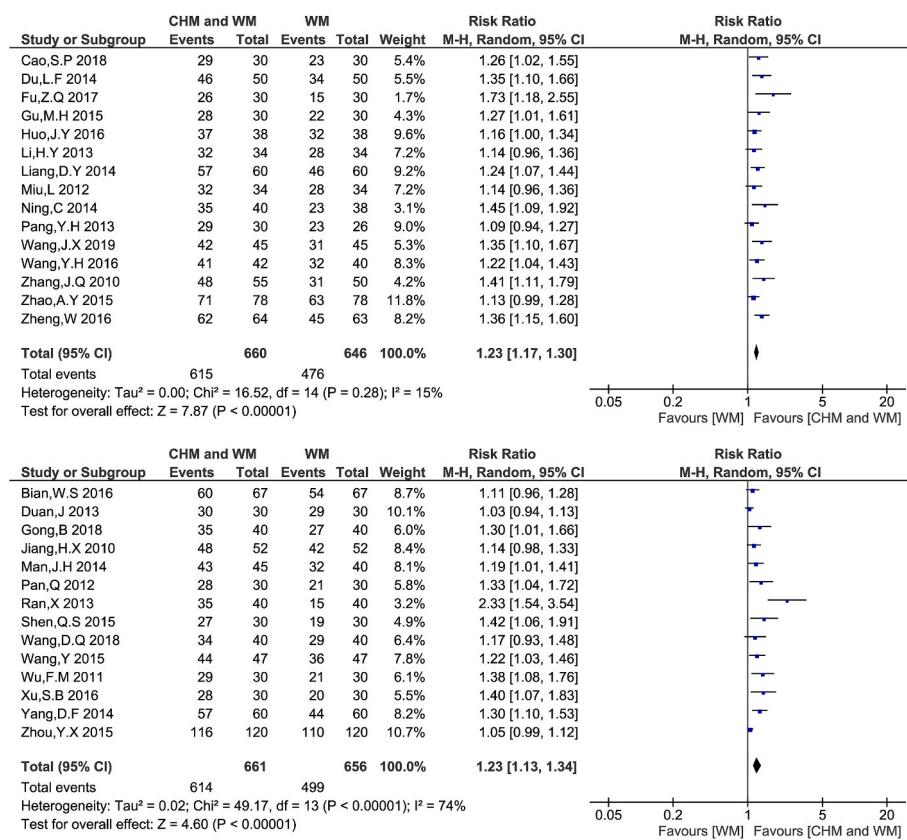


Fig. 8. Risk ratio duration of treatment in patients less than 7 weeks (A) and more than 7 weeks(B).

this combination CHM with WM in less than 7 weeks of therapy.

4.2. Limitations

This study has the following limitations. First, the included trials methodological quality was assessed to be generally low based on the Cochrane handbook. Although all studies are randomized control trials, only 12 trials demonstrated random sequence, and two trials reported allocation concealment. None of them reported blinding of participants and personnel. Also, no trial blinded the outcome assessors, and all 29 studies included in the current meta-analysis were not placebo control studies. Therefore, evidence supporting combining CHM with WM in treating patients with PHTN was indecisive. Second, we only searched for literature published in Chinese and English, the majority of the 29 studies are Chinese studies, and we did not search in other Asian countries databases where CHM research may be published, so some publication bias exists. Third, in this systematic review, we did not consider the differences in blood pressure stages, disease duration, and patient's age, influencing blood pressure results. Fourth, information recording the effectiveness of CHM and WM on the incidence of cardiovascular and cerebrovascular events and the mortality rate is lacking, and most of the included studies had a limited duration of treatment. Therefore, we cannot determine the long-term protective effect of

integrated medicines. Fifth, conclusions on CHM with WM adverse effects are also uncertain, as only thirteen studies have reported evidence of adverse reactions. Sixth, CHM has a variety of active ingredients, and different doses are utilized, which affect blood pressure results.

4.3. Suggestions for clinical research

Although the study finding shows that the integrated CHM with WM could be safe and effective in treating PHTN, most studies with poor methodological quality and high heterogeneity. Consequently, the evidence for safety and effectiveness was inadequate; therefore, caution should be given to interpreting existing evidence and possible outcomes. Our suggestions further studies are required to determine the safety and effectiveness of combining CHM with WM to treat PHTN. Furthermore, in order to confirm the effectiveness of their integrated medication, the most rigorous randomized controlled trials (large sample, High quality, long duration of treatment, a long-term follow-up to observe the long-term effect, and adverse effects monitored strictly) are required.

5. Conclusion

In summary, this systematic review provides evidence that the integrated CHM with WM could improve the clinical effectiveness, SBP,

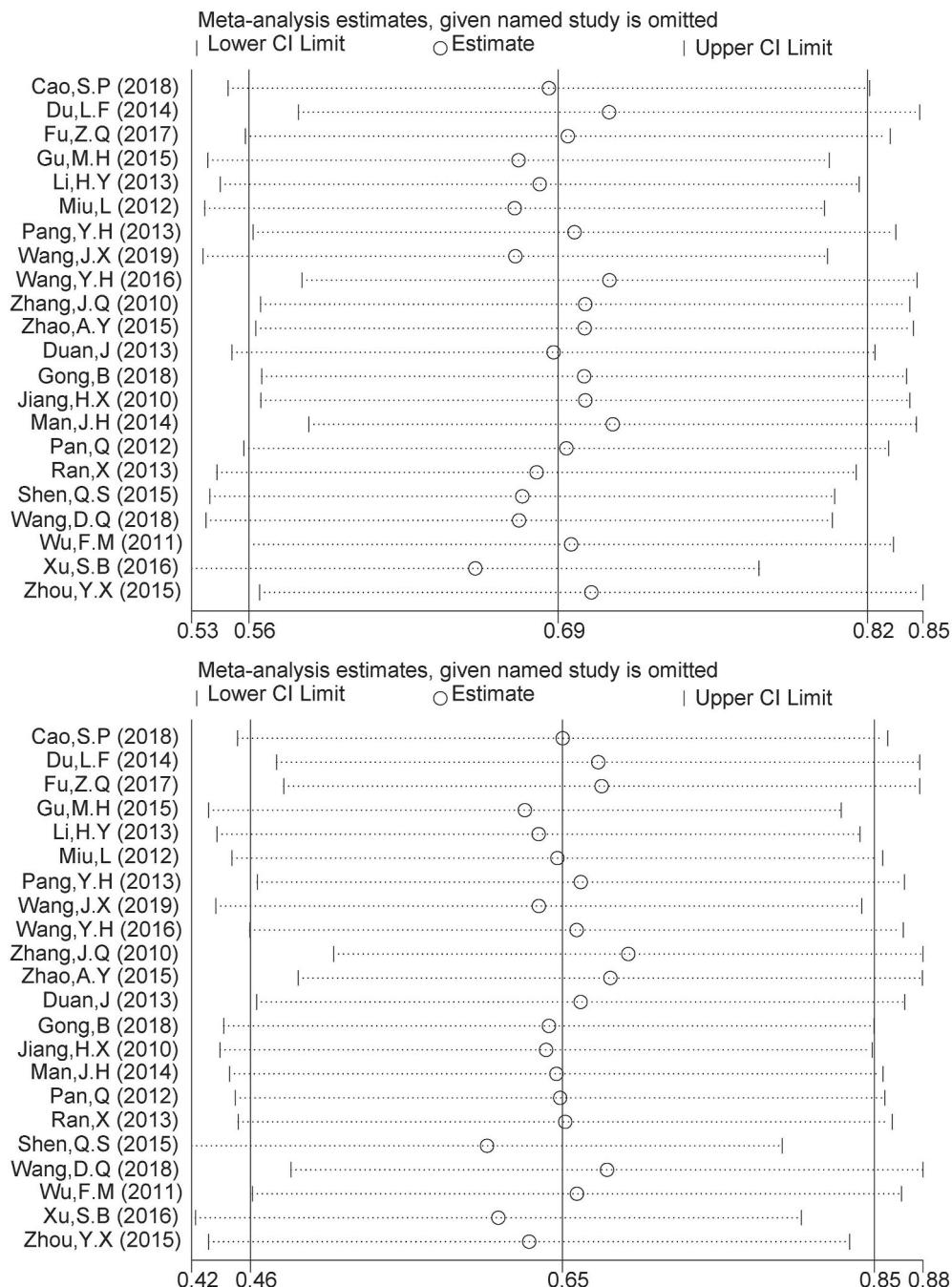


Fig. 9. Sensitivity analysis SBP in less and more than 7 weeks (A), DBP in less and more than 7 weeks (B).

Table 5
Subgroup effect of CHM on blood pressure.

CHM Formula	Number of studies using the same CHM formula	Number of Patients in each studies	Outcomes	
			SBP (mmHg)	DBP (mmHg)
Tianma Gouteng decoction [Bian (2016); Du (2014); Liang and Lin (2014)]	3	(134; 100; 120) T: 354	MD: 8.30 [2.40, 14.20]; P = 0.006; I ² = 81%	MD: 4.68 [-0.68, 10.03]; P = 0.09; I ² = 90%
Modified Tianma Gouteng decoction [Fu (2017); Wang (2016); Zhao and Jiang (2015)]	3	(60; 82; 156) T: 298	MD: 6.78 [3.61, 9.94]; P < 0.0001; I ² = 0%	MD: 2.35 [-0.02, 4.72]; P = 0.05; I ² = 0%
Jianpi Tongluo granules [Cao et al. (2018)]	1	T: 60	MD: 7.61 [2.97, 12.25]; P < 0.001	MD: 5.32 [1.31, 9.33]; P = 0.009
Jiawei Wendan decoction [Duan (2013)]	1	T: 60	MD: 4.67 [1.65, 7.69]; P < 0.002	MD: 2.99 [-0.62, 6.60]; P = 0.10
Shuanghua Zhixuan decoction [Gong et al. (2018)]	1	T: 80	MD: 4.00 [0.47, 7.53]; P < 0.03	MD: 5.00 [2.41, 7.59]; P = 0.0002
Modified Qiju Dihuang decoction [Gu et al. (2015)]	1	T: 60	MD: 7.30 [4.02, 10.58]; P < 0.0001	MD: 6.52 [3.78, 92.6]; P < 0.00001
Modified Xuefu Zhuyu decoction [Huo (2016)]	1	T: 76	MD: 15.33 [11.77, 18.49]; P < 0.0001	MD: 6.44 [3.36, 9.52]; P < 0.0001
Shihu Yangyin decoction [Jiang and Zhu (2010)]	1	T: 104	MD: 5.55 [1.41, 9.69]; P = 0.009	MD: 4.47 [2.49, 6.45]; P < 0.00001
An Nao pills [Li (2013)]	1	T: 68	MD: 9.90 [4.69, 15.11]; P = 0.0002	MD: 7.70 [4.02, 11.38]; P < 0.0001
Songling Xuemaikang capsules [Man (2014)]	1	T: 85	MD: 1.80 [-2.48, 6.08]; P = 0.41	MD: 5.10 [2.19, 8.01]; P = 0.0006
Pinggan Qianyang granules [Miu and Hu (2012)]	1	T: 68	MD: 12.50 [7.21, 17.79]; P < 0.00001	MD: 5.00 [1.80, 8.20]; P = 0.002
Zhen Jian granules [Ning (2014)]	1	T: 78	MD: 1.92 [-5.55, 1.71]; P < 0.30	MD: 2.04 [-0.08, 4.16]; P = 0.06
Sheyao Shiliangcha decoction [Pan et al. (2012)]	1	T: 60	MD: 6.34 [1.41, 11.27]; P = 0.01	MD: 4.52 [1.28, 7.76]; P = 0.006
Modified Banxia Baizhu Tianma decoction [Pang (2013)]	1	T: 56	MD: 7.00 [0.32, 13.68]; P = 0.04	MD: 4.00 [-1.09, 9.09]; P = 0.12
Bushen Jiangya decoction [Ran (2013)]	1	T: 80	MD: 11.30 [5.86, 16.74]; P < 0.0001	MD: 5.30 [1.67, 8.93]; P = 0.004
Banxia Baizhu Tianma decoction [Shen and Jin (2015)]	1	T: 60	MD: 8.19 [4.38, 12.00]; P < 0.0001	MD: 7.39 [5.31, 9.47]; P < 0.00001
Tianma Sanqi decoction [Wang et al. (2018)]	1	T: 80	MD: 6.36 [3.70, 9.02]; P < 0.00001	MD: 0.66 [-2.94, 4.26]; P = 0.72
Pinggan Ziyin Tongyu decoction [Wang et al. (2019)]	1	T: 90	MD: 7.25 [4.40, 10.10]; P < 0.00001	MD: 5.49 [3.14, 7.84]; P < 0.00001
Zini Yuntongping decoction [Wang, Y. et al., 2015]	1	T: 94	MD: 15.00 [10.51, 19.49]; P < 0.00001	MD: 6.36 [2.73, 9.99]; P = 0.0006
Denglao Zhejue Jiuwei granules [Wu (2011)]	1	T: 60	MD: 3.61 [0.57, 6.65]; P = 0.02	MD: 2.30 [-0.17, 4.77]; P = 0.07
Huatan Quyu decoction [Xu (2016)]	1	T: 60	MD: 9.20 [6.17, 12.23]; P < 0.00001	MD: 8.00 [5.48, 10.52]; P < 0.00001
Zhong Yao decoction [Yang et al. (2014)]	1	T: 120	MD: 14.92 [10.40, 19.44]; P < 0.00001	MD: 15.26 [12.43, 18.09]; P < 0.00001
Zini Qingnao Jiangya decoction [Zhang (2010)]	1	T: 105	MD: 6.99 [1.79, 12.19]; P = 0.008	MD: 1.3 [-4.02, 1.42]; P = 0.35
Zini Jiangya decoction [Zheng and Yao (2016)]	1	T: 127	MD: 18.07 [16.04, 20.10]; P < 0.00001	MD: 9.45 [7.68, 11.22]; P < 0.00001
Pinggan Jianpi decoction [Zhou et al. (2015)]	1	T: 240	MD: 4.75 [2.51, 6.99]; P < 0.0001	MD: 7.79 [5.83, 9.75]; P < 0.00001

Abbreviation: T, Total; SBP, systolic blood pressure; DBP, diastolic blood pressure; MD, mean difference.

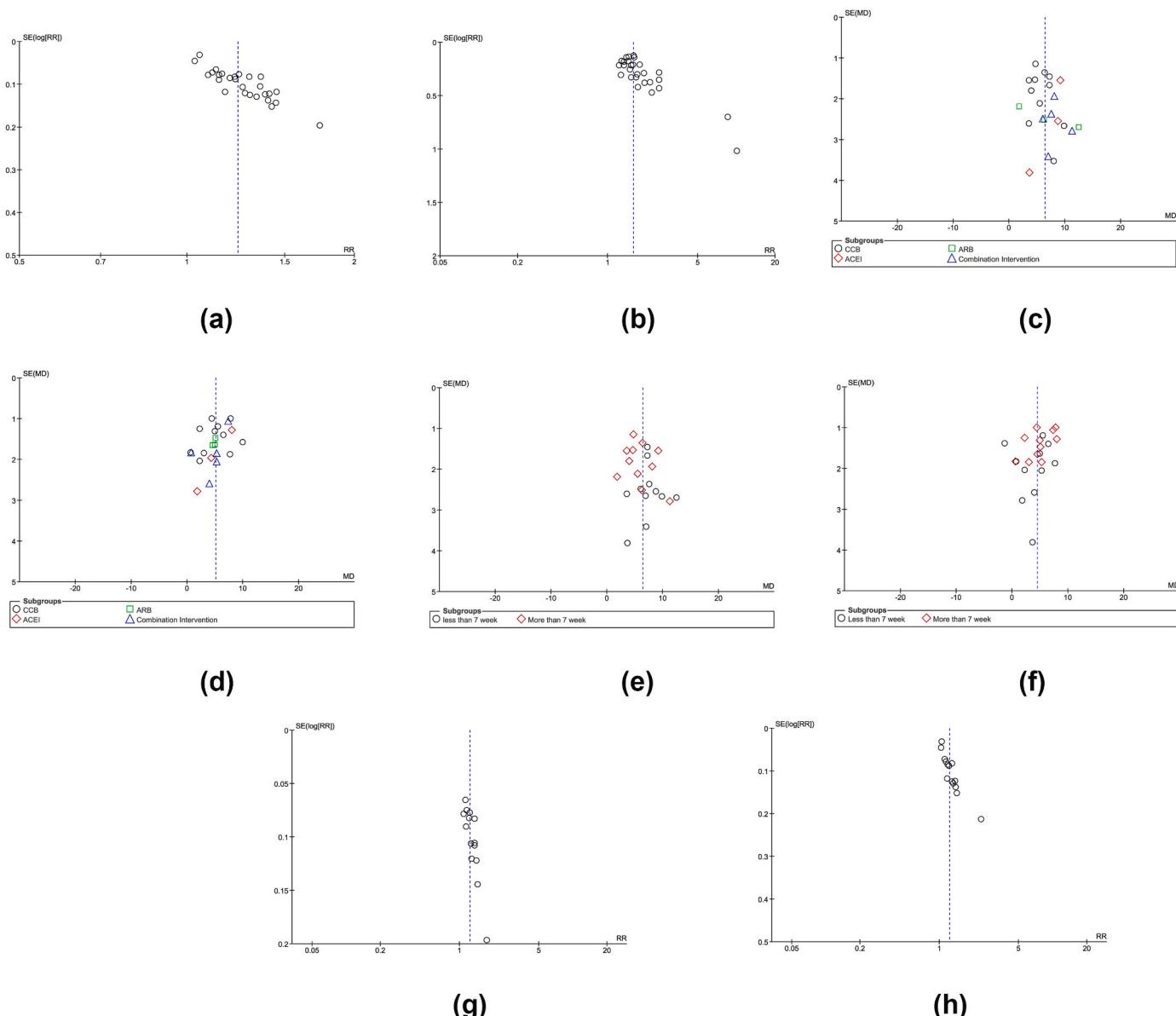


Fig. 10. Funnel plot clinical effect in all patients (A), markedly effective (B), SBP according to type of intervention (C), DBP according to the type of intervention (D), SBP according to the duration of treatment (E), DBP according to the duration of treatment (F), RR less than 7 weeks (G), RR more than 7 weeks (H).

and DBP in patients with PHTN better than using WM alone. In treatment duration less than 7 weeks, combination therapy CHM with WM improves SBP and DBP better than WM alone, but there is no significant difference in more than 7 weeks. Moreover, no patient stopped treatment or withdrawal due to severe adverse effects, indicating that combining CHM with WM could be safe in treating hypertension. Due to some methodological limitations and heterogeneity in included trials, these findings should be interpreted with caution. Further strict RCTs with a large sample, high quality, long duration of treatment, and follow-up are recommended to strengthen this clinical evidence.

Registration and protocol

We registered this systematic and meta-analysis review in PROSPERO, the registration number CRD42020223500.

Support

Non-financial support for this systematic review and meta-analyses.

CRediT authorship contribution statement

Shadi A.D. Mohammed: designed and conceived this study, Formal analysis, The revision process was performed. **Liu Hanxing:** designed and conceived this study, Formal analysis. **Lu Fang:** The disagreement was resolved by discussion. **Adnan Mohammed Algradi:** The revision process was performed, All authors approved the final version of the submitted manuscript. **Mohammed Alradhi:** Formal analysis, The revision process was performed. **Mohammed Safi:** Formal analysis, The revision process was performed. **Liu Shumin:** designed and conceived this study.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jep.2022.115703>.

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