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Review

# Overview of systematic reviews with meta-analyses on Chinese herbal medicine in stroke management

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ABSTRACT

*Objectives:* Chinese herbal medicine (CHM) has been used to improve stroke recovery together with conventional medicine in an integrative fashion, but its effectiveness and safety remain controversial. We aim to summarize the clinical evidence on the effectiveness and safety of CHM for post-stroke management. We performed a comprehensive synthesis of clinical evidence on the add-on effect of CHM in the treatment of stroke patient receiving routine stroke care.
*Design:* We conducted an overview of systematic reviews with meta-analyses to evaluate the evidence on the effect of CHM together with conventional medicine intervention in stroke recovery.
*Methods:* A literature search of four international and three Chinese databases from inception to November 2017 was performed. We included systematic reviews summarizing the treatment effects of CHM plus conventional medicine intervention versus conventional medicine intervention. Methodological quality of included systematic reviews was assessed using the Methodological Quality of Systematic Reviews Instrument.
*Results:* Fourteen systematic reviews with good methodology were included, which consisted of 271 randomized controlled trials and 24,434 total subjects. Meta-analyses revealed that five CHMs had significant beneficial effect on neurological improvement when used with conventional treatment: Xingnaojing injection [Pooled weighted mean difference (WMD): −3.78 (−4.75, −2.81)], Panax notoginseng saponins [Pooled WMD: −5.06 (−5.70, −4.42)], Xiaoxuming decoction [Pooled WMD: -1.86 (−3.25, −0.48)], Qingkailing injection [Pooled WMD: −5.60 (−8.50, −2.70)], and Shuxuetong [Pooled WMD: −5.86 (−6.93, −4.86)]. In addition, Panax notoginseng saponins injection combined with conventional medicine intervention significantly reduced mortality [Pooled odds ratio: 0.32 (0.17, 0.59)]. None of these CHM was associated with increased risk of adverse events.
*Conclusions:* We found several CHM providing additional benefits for stroke recovery when used together with conventional medicine treatment. Further high quality research is needed to verify the efficacy and safety of integrating CHM and conventional medicine in stroke management.


## 1. Introduction

Stroke is a common cerebrovascular disease due to interruption or reduction of blood supply to the brain from leaking of a blood vessel (hemorrhagic stroke) or blockage of artery (ischemic stroke) [1], and is the second leading cause of death worldwide [2]. The incidence of stroke increases with age [3], with an annual age-adjusted incidence rate ranging from 41 to 316 per 100,000 population worldwide [4]. More importantly, the World Health Organization (WHO) estimates that stroke is the third leading cause of disease burden worldwide. Stroke is responsible for 139,874 Disability-adjusted life-years (DALYs) in thousands dollars, or 5.2% of total DALYs in the world according to WHO global and regional DALY estimates for 2000–2015 [5]. Functional effects caused by stroke can last a lifetime [6]. Survivors could become permanently disabled or require institutional care after stroke [7]. The treatment approach of pharmacological treatment in post-stroke management is to prevent and manage

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comorbidities [8]. Nevertheless, to date, there are limited pharmacological treatment options to improve post-stroke recovery despite numerous clinical trials [9,10].

In Asian countries, Chinese Medicine (CM) can be an alternative and complementary approach for stroke management [11–14]. Chinese herbal medicine (CHM) is commonly used together with conventional medicine intervention in stroke rehabilitation, usually in an integrative fashion [15–18]. Evidence-based medicine has been applied in CHM studies; yet clinical trials have been criticized for the lack of scientific rigour despite guideline recommendations [19–22].

Systematic reviews (SRs) with meta-analysis have also been conducted to examine the relative benefits or harms of CHM together with conventional medicine intervention in the treatment of stroke over the years. An overview of SRs with meta-analyses on CHM in stroke management can provide a concise summary of results from SRs, and is essential for overcoming the knowledge gaps by composing, appraising, and summarizing all critical information from individual SRs. This study aims to provide an overview of the effectiveness and safety of different CHM for post-stroke management. With a comprehensive synthesis of clinical evidence on the add-on effect of CHM in routine stroke care, this study will provide support to evaluate the effectiveness of CHM in combination with conventional medicine intervention in stroke management.

## 2. Methods

### 2.1. Search strategy

A literature search of online databases [MEDLINE, EMBASE, Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effect (DARE)] and Chinese databases [Chinese Biomedical Databases (CBM), Wan Fang Digital journals and Taiwan Periodical Literature Databases] from inception to November 2017 was performed. Specialized search filter for reviews was used for MEDLINE and EMBASE [23,24]. Detailed searching strategies were reported in Fig. 1 and Appendix A.

### 2.2. Eligibility criteria (Inclusion and exclusion criteria)

#### 2.2.1. Types of studies

We included SRs with meta-analysis of randomized controlled trials (RCTs) and quasi-randomized controlled trials in this

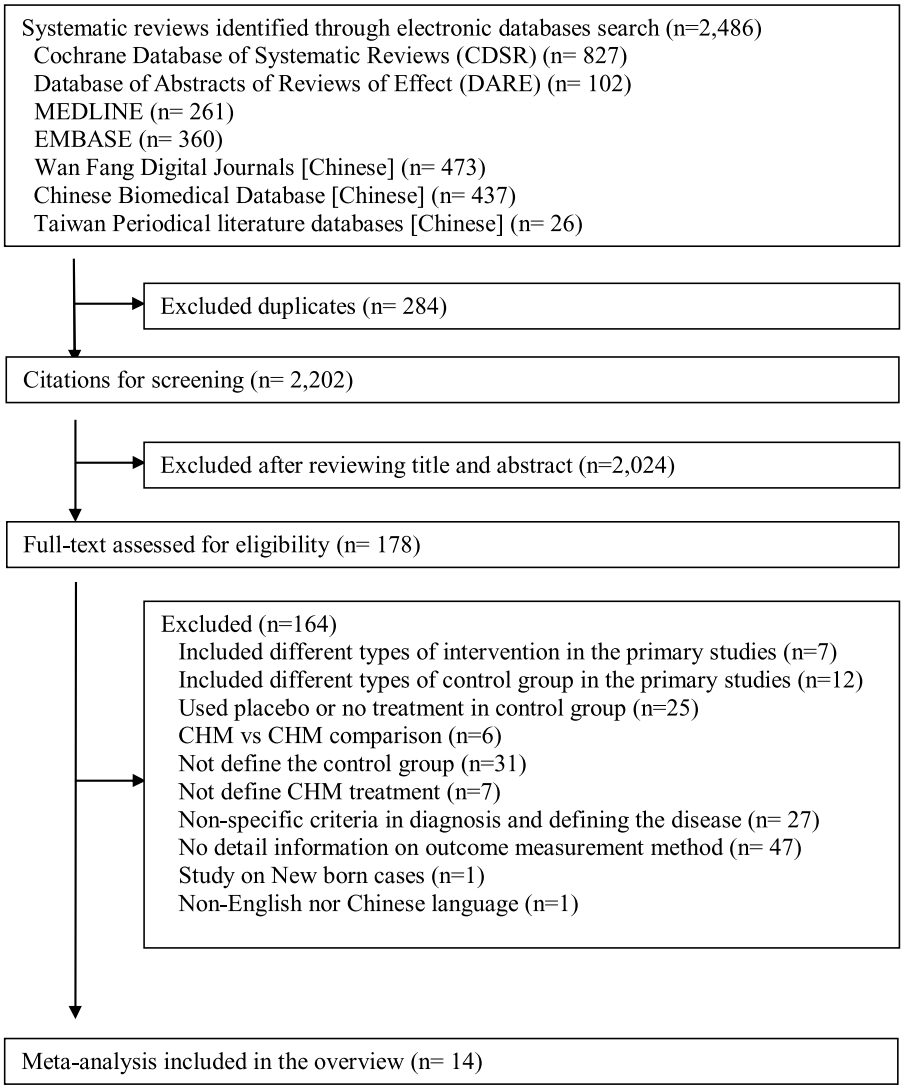


**Fig. 1.** Flowchart of literature selection on meta-analyses of Chinese herbal medicines for stroke.

overview. RCTs are trials that group patients by simple random methods such as computers, random numbers, tossing, and dice. Quasi-randomized controlled trials are trials that are grouped in a semi-random manner, such as a substitution order, a single medical record number, and a single-double on admission day. We excluded SRs with meta-analysis of observational studies, which included case-control studies, cross-sectional studies, longitudinal studies, and cohort studies. We used the Cochrane Collaboration definition for systematic review, that is a form of publication that searches, identifies, appraises, and collates all empirical evidence according to the pre-specified eligibility criteria to answer the objectives or specific research questions, using systematic methods to minimize risk of bias [25].

*2.2.2. Subjects*

We included patients diagnosed with any type of stroke by World Health Organization stroke criteria [26] (ischemic stroke, acute ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, acute stroke, progressive cerebral infarction, acute cerebral infarction, cerebral hemorrhage, and cerebral ischemic stroke), or American Stroke Association criteria [27] (Ischemic, hemorrhagic, transient ischemic). The subjects in the included reviews were not limited by gender, age, course of the disease, and treatment duration.

*2.2.3. Intervention and control*

We included peer-reviewed full articles published in English and Chinese language. Subjects were using conventional medicine intervention or conventional medicine intervention in addition to CHM. CHM is defined as herbal medications included in the 'Pharmacopoeia of People's Republic of China 2015, vol I' [28]. We included all formulation of CHM interventions regardless of the types of dosage forms (e.g. oral, parenteral, or others) used for management of all types of stroke. Conventional medicine intervention was defined by American Stroke Association and European Stroke Organization [29,30]. Conventional care and traditional Chinese patent medicine can be used in both treatment and control arms as a routine stroke care in China.

*2.3. Selection of systematic reviews*

*2.3.1. Data extraction*

We extracted the following data from full-text articles: i) basic characteristics of the SRs, searching date of the study, number of included studies, total number of patients and bibliographic information; ii) detail information on study design and patient, intervention, control and outcomes; iii) meta-analysis results of the including pooled effects of each comparison for each outcome; and iv) results of methodological quality assessment.

2.3.2. Quality assessment of systematic reviews

Methodological quality of SRs was assessed using Assessing the Methodological Quality of Systematic Reviews (AMSTAR) [31]. The judgments were given in 11 items as "Yes", "No", "cannot answer" or "not applicable" based on the information provided. The detail description of AMSTAR is provided in Table 1. Two researchers conducted literature selection, data extraction and methodological quality assessment independently. Any disagreement was discussed with consensus. A third reviewer assessed unresolved discrepancy when necessary.

*2.3.2. Data analyses*

The CHM treatments were assessed at SRs level. The pool effect estimates were extracted from each meta-analyses. We extracted pooled relative risk (RR) or pooled odds ratio (OR) for dichotomous outcomes, and pooled weighted mean difference (WMD) for continuous outcomes with 95% confidence interval (CI). For publication bias, funnel plot results would be reported if it was being mentioned in the included SRs. Heterogeneity across RCTs was reported by describing $I^2$ values reported in included meta-analysis; $I^2$ values of 0–25%, 26–50%, and above 50% represented low, medium and high heterogeneity, respectively [32].

## 3. Outcome

We evaluated all possible clinical evidence in the use of CHM along with conventional medicine intervention for stroke management. Neurological function and mortality were the two major

**Table 1**
Methodological quality of included meta-analyses on Chinese herbal medicine for stroke management.

| First author and year of publication | AMSTAR item | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| Cao, 2008 [51] | Y | Y | Y | Y | Y | Y | Y | Y | Y | N | Y |
| Cheng, 2012 [50] | N | NR | Y | Y | N | N | Y | Y | N | Y | Y |
| Fu, 2013 [HYPERLINK \l "Ref49" \o " [49] D.L. Fu, L. Lu, W. Zhu, J.H. Li, H.Q. Li, A.J. Liu, C. Xie, G.Q. Zheng, Xiaoxuming decoction for acute ischemic stroke: A systematic review and meta-analysis, Journal of Ethnopharmacology, 148 (2013) 1-13." 49] | N | Y | Y | Y | N | Y | Y | Y | Y | Y | Y |
| Han, 2013 [48] | N | Y | Y | N | N | N | Y | Y | N | N | N |
| Hao, 2012 [47] | N | Y | Y | Y | N | Y | Y | Y | Y | Y | Y |
| Li, 2017 [38] | Y | Y | N | Y | N | Y | Y | Y | N | Y | N |
| Ma, 2017 [40] | N | N | N | NR | N | N | Y | N | N | Y | N |
| Peng, 2014 [46] | N | Y | Y | N | N | N | Y | Y | N | Y | Y |
| Wang, 2017 [39] | N | N | N | Y | N | Y | Y | Y | N | Y | N |
| Wu, 2005 [45] | N | NR | Y | Y | N | Y | Y | Y | Y | N | N |
| Wu, 2014 [44] | N | Y | Y | N | N | Y | Y | N | Y | N | N |
| Yu, 2009 [43] | N | NR | Y | Y | N | N | Y | Y | Y | Y | N |
| Zhang, 2012 [42] | N | Y | Y | N | N | Y | Y | Y | Y | N | N |
| Zhang, 2017 [41] | N | N | N | NR | N | N | N | N | N | N | N |
| # of Yes | 2 | 8 | 10 | 8 | 1 | 8 | 13 | 11 | 7 | 8 | 5 |
| (%) | (14.3) | (57.1) | (71.4) | (57.1) | (7.1) | (57.1) | (92.9) | (78.6) | (50.0) | (57.1) | (35.7) |

Keys: N, no; Y, yes (meta-analysis fulfilling the criteria); NR, not reported; # of Yes, number of yes; AMSTAR item: 1. Was an 'a priori' design provided? 2. Was there duplicate study selection and data extraction? 3. Was a comprehensive literature search performed? 4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? 5. Was a list of studies (included and excluded) provided? 6. Were the characteristics of the included studies provided? 7. Was the scientific quality of the included studies assessed and documented? 8. Was the scientific quality of the included studies used appropriately in formulating conclusions? 9. Were the methods used to combine the findings of studies appropriate? 10. Was the likelihood of publication bias assessed? 11. Was the conflict of interest included?

outcomes for evaluating the effectiveness of CHM. The primary clinical outcomes were neurological function improvement and mortality reduction. Neurological function was assessed at the end of treatment course by the National Institutes of Health Stroke Scale (NIHSS) [33,34], Scandinavian Stroke Scale (SSS) [35] and Chinese Stroke Scale (CSS) [36], or Modified Edinburgh-Scandinavian Stroke Scale (MESSS) [37]. Mortality was reported after 2 weeks of therapeutic course and was assessed by the number of deaths in the participants. We also reported on other outcomes, including adverse events, change of activity of daily living, physical and cognitive disability were also reported in this paper.

## 4. Results

### 4.1. Study characteristics

A total of 2,486 citations were retrieved from the electronic databases, among which 14 SRs [38–51] fulfilled the inclusion criteria. These eligible SRs were published between 2005–2017. The characteristics of included SRs have been summarized in Table B. Among 13 (92.9%) SRs [38,40–51] that provided a date on literature search, 10 (71.4%) SRs [38,40–42,44,46–50] were conducted after 2010, with the most recent search conducted in November 2016 [40]. The percentage of male participants ranged from 58.6%–62.1% (from three SRs [38,44,48]). The reported age of participants ranged from 24–92 years (from eleven SRs [38,39,42–45,47–51]). The duration of stroke onset ranged from 30 minutes to 3 months (from seven SRs [38–40,47–50]). The treatment duration ranged from 8 hours to 120 days (from 12 SRs [38,39,42–51]). Regarding stroke types, 11 (78.6%) SRs [38–42,45,47–51] focused on ischemic stroke or cerebral infarction. Only one SR (7.1%) [43] summarized the evidence on cerebral hemorrhage. Two SRs (14.3%) [44,46] summarized evidence on all types of stroke.

### 4.2. Details of CHMs

Of 14 SRs, 10 CHMs, which included Dengzhan Xixin, Xingnaojing, Yiqi Huoxue, Shuxuetong, Panax notoginseng saponins, Qingkailing, Danshen, Buyang Huanwu, Xiaoxuming, and Dengzhanhua, were included in our evaluation.

Dengzhan Xixin

Dengzhan Xixin is extracted by Erigeron breviscapus originally growing in southwest of China. It is comprised with active ingredient, caffeic acid ester fraction and scutellarin [52–54]. It could activate blood circulation to remove stasis, inhibiting platelet aggregation and reducing blood viscosity [55]. It is widely used in China for treating ischemic stroke, coronary heart disease, and other cardio-cerebral vascular diseases.

Xingnaojing

Xingnaojing is derived from traditional Chinese emergency medication, An-Gong-Niu-Huang pill, which consists of artificial musk, synthetic borneol, Curcuma aromatic Salisb, and Gardenia jasminoides J.Ellis [56]. Xingnaojing reduce brain injury and enhance functional recovery in animal studies [57–60]. It is used to treat nervous system disorder in China.

Yiqi Huozue

Yiqi Huoxue is composed of Astragalus, Chuanxiong, Salvia, Radix Paeoniae Alba, and safflower. It is prepared as oral or injection formulation. It can reduce C-reactive protein level and to inhibit inflammatory response. It is used for reducing blood viscosity, improving blood circulation in cerebral, and promoting nerve and tissue reparation after cerebral ischemic injury.

Shuxuetong

Shuxuetong is composed of leech and earthworm. It is an injection formulation. It can enhance blood circulation to remove stasis and obstruction for ischemic stroke. In addition, it can regulate lipid metabolism and blood coagulation.

Panax notoginseng saponins

Panax notoginseng saponins is also called Chinese ginseng or tienchi ginseng. It is comprised with active ingredient, Dencichine, chemical name ß-N-oxalyl-L-α, ß-diaminopropionic acid, which produces hemostatic effect. It could induce platelet release of hemostatic active substances such as arachidonic acid, platelet factor III and $Ca^2$, and finally showed procoagulant effect, and its influence intensity was proportional to the blood concentration [61].

Qingkailing

Qingkailing is derived from a traditional Chinese medicine, Angongniuhuang pills in 1970s. Qingkailing injection composed of Calculus Bovis, Radix Scutellariae Baicalensis, Flos Lonicerae, Fructus gardeniae, and Cornu Bubali [62]. It helps in regulating immunity, and enhancing the absorption of intracranial hematoma [63]. It is used to treat cerebrovascular disease [64].

Danshen

Danshen consist of 15 biologically active substances [65]. It has been used in oral or injection formulation. Danshen agents help in dilating heart and brain vessels, suppressing the aggregation of platelets, and removing blood stasis [66]. It is used in the treatment of acute ischemic stroke, cardiovascular diseases and other systemic disorders [67].

Buyang Huanwu

Buyang Huanwu includes seven kinds of Chinese medicine. It is believed to promote the regeneration of peripheral nerves [68], improve recovery of neurological function, and repair the injured blood vessels and lesion tissues [69]. Buyang Huanwu is used in different stages of ischemic stroke.

Xiaoxuming

Xiaoxuming has been using for treating stroke in China since Tang Dynasty. This Chinese medicine consists of 12 herbs which helps in alleviating blood brain barrier disruption and, protecting neurovascular unit and mitochondria from cerebral injury due to cerebral ischemia and reperfusion in animal studies [70–72].

Dengzhanhua

Dengzhanhua is derived from Erigeron Breviscapus. It contains with active components of Dengzhanhua injection are Scutellarin and Pyromeconic acid [73,74]. It inhibits platelet 5-HT release and platelet destruction [75]. Dengzhanhua renders brain oedema and neutrophil infiltration after cerebral ischemia reperfusion [76]. It is mainly used for acute ischemic stroke [77].

The details of CHM and conventional medicine intervention are reported in Table 2. CHM were used as an add-on therapy to conventional care in the included SRs. Conventional medicine intervention included use of drugs, such as antiplatelet agents, anticoagulants, fibrinogen-depleting agents, and volume expansion and vasodilators, neuroprotective agents, and traditional Chinese patent medicine such as Danshen injection [78], and snake venom [79]. Conventional care also included treatment for stroke related complications, such as brain edema, seizures, dysphagia, pneumonia, voiding dysfunction and urinary tract infections, and deep vein thrombosis.

### 4.3. Methodological quality of included SRs

All SRs [38–51] performed comprehensive literature search and evaluated the scientific quality of the included studies (Table A). Twelve (85.7%) SRs [38–40,42,43,45–51] assessed and documented risk of bias among included studies. Eight (57.1%) SRs [38,42,44,46–49,51] had at least 2 independent data extractors to select study and extract data; search for grey literature [38,39,43,45,47,49–51]; and reported the characteristics of included studies [38,39,42,44,45,47,49,51]. Eight (57.1%) SRs [38–

**Table 2**
Characteristics of included meta-analyses on Chinese herbal medicine for stroke management.

| First author and year of publication | Included study design | Search period | Type of disease | No. of studies (No. of patients) | Nature of Chinese herbal medicine interventions | Nature of control interventions | Outcomes reported |
|---|---|---|---|---|---|---|---|
| Cao, 2008 [51] | RCT or quasi-RCT | 2007 | Ischemic stroke (Cerebral infarction) | 9 (723) | Dengzhanhua injection+ conventional medicine intervention[a] vs conventional medicine intervention[a] | Mannitol, antibiotics | Neurological improvement |
| Cheng, 2012 [50] | RCT | 2011 | Ischemic stroke | 7 (545) | Qingkailing injection + conventional medicine intervention vs conventional medicine intervention | Mannitol, Dextran, Nimodipine, Aspirin | Scores of neurological deficit, mortality, scores of neurological deficit, inflammation factor, revival of coma |
| Fu, 2013 [49] | RCT | 2012 | Ischemic stroke | 8 (601) | Xiaoxuming decoction + conventional medicine intervention[b] vs conventional medicine intervention[b] | Antiplatelet agents, anticoagulants, fibrinogen-depleting agents, volume expansion, vasodilators | Modified Rankin Scale scores, neurological deficit scores, the clinical effective rate |
| Han, 2013 [48] | RCT or quasi-RCT | 2012 | Ischemic stroke | 28 (2385) | Therapy of supplementing qi and activating blood + conventional medicine intervention vs conventional medicine intervention | Thrombolytic, fibrinolytic, anticoagulants, antiplatelet agents | Clinical efficacy, activities of daily living, recovery, neurologic impairment assessment, plasma viscosity |
| Hao, 2012 [47] | RCT | 2012 | Ischemic stroke | 19 (1580) | Buyang Huanwu decoction + conventional medicine intervention[c] vs conventional medicine intervention[c] | Antiplatelet agents, anticoagulants, fibrinogen-depleting agents, volume expansion, vasodilators | Total effective rate for acute ischemic stroke, scores of neurological deficit |
| Li, 2017 [38] | RCT | 2016 | Ischemic stroke | 25 (2714) | Dengzhanxixin + conventional medicine intervention vs conventional medicine intervention | Fibrinolytic agents, antiplatelet agents, anticoagulants | Activities of daily living, Modified Rankin Scale scores, neurological deficit scores, quality of life, mortality |
| Ma, 2017 [40] | RCT | 2016 | Ischemic stroke (Cerebral infarction) | 53 (4915) | Xingnaojing injection + conventional medicine intervention vs conventional medicine intervention | Thrombolysis, antihypertensive drug, anticoagulants | Overall response rate, neurological deficit score, blood lipid, hemorheology, infarction size |
| Peng, 2014 [46] | RCT | 2013 | Stroke | 13 (1714) | Xingnaojing injection + CHM/ conventional medicine intervention vs CHM/ conventional medicine intervention | Citicoline, Piracetam, Mannitol statins, antiplatelet agents, and Danshen injection | Effective rate, neurological deficit scores, inflammation factor |
| Wang, 2017 [39] | RCT | NA | Ischemic stroke (Cerebral infarction) | 23 (2291) | Dengzhanxixin injection + conventional medicine intervention vs conventional medicine | Antiplatelet agents, anticoagulants, neuroprotective drugs, neurotrophy agents, dehydrating agents, diuretic, antihypertensive drug, hypoglycemic drugs, antihyperlipidemics | Neurological deficit scores, quality of life, response rates |
| Wu, 2005 [45] | RCT or quasi-RCT | 2003 | Ischemic stroke | 3 (304) | Compound Danshen injection + conventional medicine intervention vs conventional medicine intervention | Snake venom, saline, and glucose | Effective rates of Improvement in neuronal damage and/or functional impairment |
| Wu, 2014 [44] | RCT | 2013 | Stroke | 13 (1110) | Qingkailing conventional medicine intervention vs conventional medicine intervention | Cerebral hemorrhage (hemostatics, drugs lowering intracranial pressure, antihypertensive drug, antibiotics, brain cell activators); cerebral infarction (vasodilators, antihyperlipidemics, brain cell activators) | Acute cerebral hemorrhage, acute cerebral infarction, neurological damage, recovery of awareness, whole blood viscosity coefficient |
| Yu, 2009 [43] | RCT or quasi-RCT | 2008 | Cerebral hemorrhage | 21 (1759) | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention[d] | Mannitol, Furosemide, glycerol, fructose, human blood protein | Hemorrhage, mortality, effectiveness, neurological deficits, cerebral hematoma volume and the volume of cerebral edema, cerebral hemorrhage |
| Zhang, 2012 [42] | RCT or quasi-RCT | 2012 | Ischemic stroke (Cerebral infarction) | 11 (972) | Shuxuetong + conventional medicine intervention[e] vs conventional medicine intervention[e] | Aspirin, Salvia, fibrinolytic, Ozagrel, Mannitol, enteric-coated Aspirin, Ginkgo biloba, Mannitol, Edaravone, low molecular weight Heparin, Citicoline | Total effective rate, neurological deficit scores |
| Zhang, 2017 [41] | RCT | 2015 | Ischemic stroke | 36 (2821) | Yiqi Huoxue + conventional medicine intervention vs conventional medicine intervention | Thrombolysis, antiplatelet agents, anticoagulants, neurotrophy agents, antihypertensive drug, antihyperlipidemics | Neurological deficit scores, plasma viscosity, cholesterol level |

CHM denotes the inclusion of all types of Chinese herbal medicines.
Keys: CHM, Chinese herbal medicine; RCT, randomized controlled trial.
[a] Mannitol, management of blood glucose, blood pressure, and antibiotics, no thrombolytic therapy vs applied.
[b] General supportive care mainly include: A. airway, ventilatory support and supplemental oxygen B. cardia monitoring and treatment C. temperature D. blood pressure E. blood sugar and F. nutrition; 2. Specialized care mainly include a variety of measures to improve cerebral blood circulation (such as antiplatelet agents, anticoagulants, fibrinogen-depleting agents, and volume expansion and vasodilators, except thrombolytic agents) and neuroprotective agents; 3. Treatment of acute complications which

40,43,46,47,49,50] assessed the likelihood of publication bias. Five (35.7%) SRs [46,47,49–51] stated the conflict of interest for both included primary studies as well as the SRs. Only one (7.1%) SR [51] provided the protocol for the SR and provided a list of included and excluded studies.

### 4.4. Outcome measures

The types of outcomes measures used across the SRs were summarized in Table 3. Twelve (85.7%) SRs [38–47,49,50] provided meta-analytic results on neurological deficit scores. Three (21.4%) SRs [38,43,50] reported meta-analytic results on mortality.

### 4.5. Outcomes

#### 4.5.1. Neurological deficit

*4.5.1.1. Stroke (ischemic stroke and cerebral hemorrhage) patients.* One SR [46] evaluated the evidence of CHM in combination with conventional medicine intervention. Xingnaojing plus conventional medicine intervention demonstrated statistically significant improvement in neurological deficit score compared to conventional medicine intervention, but with high heterogeneity (Pooled WMD= -3.78, 95% CI= -4.75 to -2.81, 6 RCTs, $I^2$ = 54%)

*4.5.1.2. Cerebral hemorrhage patients.* Two SRs [43,44] summarized the evidence on CHM in combination with conventional medicine intervention for reducing neurological deficit in cerebral hemorrhage patients. Only one SR [43] had low heterogeneity. Panax notoginseng saponins in combination with conventional medicine intervention also demonstrated statistically significant improvement in neurological function versus conventional medicine intervention (Pooled WMD= -5.06, 95% CI= -5.70 to -4.42, 11 RCTs, $I^2$ = 8%).

*4.5.1.3. Ischemic stroke patients.* Ten SRs [38–42,44,45,47,49,50] reviewed various CHM with conventional medicine intervention versus conventional medicine intervention for improving neurological function in ischemic stroke patients.

Seven CHM, including Xiaoxuming [49], Qingkailing [44,50], Buyang Huanwu [47], Shuxuetong [42], Dengzhan Xixin [38,39], Xingnaojing [40], and Yiqi Huoxue [41], combined with individual conventional medicine intervention showed statistically significant improvement in neurological deficit as compared to the use of conventional medicine intervention alone. Two SRs [42,44] had larger effect size (more than 5 pooled weighted mean difference) and moderate heterogeneity than the rest of seven SRs [38–41,47,49,50]. Qingkailing in combination with conventional medicine intervention demonstrated statistically significant improvement in neurological function versus conventional medicine intervention with medium heterogeneity (Pooled WMD= -5.60, 95% CI= -8.50 to -2.70, 2 RCTs, $I^2$ = 41%). Shuxuetong in combination with conventional medicine intervention also demonstrated statistically significant improvement in neurological function versus conventional medicine intervention with medium heterogeneity (Pooled WMD= -5.86, 95% CI= -6.93 to -4.86, 7 RCTs, $I^2$ = 33%). Two SRs [40,47] reviewed the effects of Buyang Huanwu and Xingnaojing. However, the clinical benefits could not be determined due to high heterogeneity (with $I^2$ values above 50%) of included studies.

#### 4.5.2. Mortality rate reduction

*4.5.2.1. Cerebral hemorrhage patients.* One SR [43] summarized Panax notoginseng saponins plus conventional medicine intervention versus conventional medicine intervention for the reduction of mortality rate for 14–40 days treatment duration in patient with cerebral hemorrhage. Meta-analysis showed that Panax notoginseng saponins in combining with conventional medicine intervention reduced the intracerebral hemorrhage mortality rate with low heterogeneity (Pooled OR = 0.32, 95% CI = 0.17 to 0.59, 7 RCTs, $I^2$ = 0%).

Ischemic stroke patients

Two SRs [38,50] reported that Qingkailing, and Dengzhan Xixin plus conventional medicine intervention comparing conventional medicine intervention did not show additional benefit in reducing mortality in patients with ischemic stroke. The pooled RR for Qingkailing was 0.39 with moderate heterogeneity (Pooled RR = 0.39, 95% CI = 0.10 to 1.55, 2 RCTs, $I^2$ = 46%) and the pooled RR for Dengzhan Xixin was 0.27 although with low heterogeneity (Pooled RR = 0.27, 95% CI = 0.05 to 1.63, 2 RCTs, $I^2$ = 0%)

#### 4.5.3. Other outcomes

Three SRs [38,39,48] reviewed CHM plus conventional medicine intervention versus conventional medicine intervention on functional disability improvement measured by Barthel Index (BI) of Activities of Daily Living. Two CHM, Panax notoginseng saponins injection and therapy of supplementing qi and activating blood, plus conventional medicine intervention has significant benefit in improving functional disability in patient with stroke, cerebral hemorrhage and acute ischemic stroke respectively and which far exceeded the Minimal clinically important different (MCID) for the BI when used within a stroke population [80]. Other reported outcomes measured by Tumor Narcotic Factor alpha level, hematoma volume, plasma viscosity, and Traditional Chinese Medicine syndrome were listed in the Appendix B.

#### 4.5.4. Adverse events (AE)

Safety data was inadequately reported from SRs. Four SRs [43,44,47,49] found that the included studies made no mention of AE. Two SRs [40,41] did not report adverse event. Five SRs [39,42,45,46,50] reported a wide range of AE from both intervention groups, including skin purpura, flushing, nausea and

mainly include: A. brain edema and elevated intracranial pressure B. seizures C. dysphagia D. pneumonia E. voiding dysfunction and urinary tract infections and F. deep vein thrombosis.

[c] General supportive care mainly include: A. airway, ventilatory support and supplemental oxygen B. cardia monitoring and treatment C. temperature D. blood pressure E. blood sugar and F. nutrition; 2. Specialized care mainly include a variety of measures improve cerebral blood circulation (such as antiplatelet agents, anticoagulants, fibrinogen-depleting agents, and volume expansion and vasodilators, except thrombolytic agents) and neuroprotective agents; 3. Treatment of acute complications which mainly include: A. brain edema and elevated intracranial pressure B. seizures C. dysphagia D. pneumonia E. voiding dysfunction and urinary tract infections and F. deep vein thrombosis.

[d] General supportive care (airway, ventilatory support and supplemental oxygen, prevent infection) 2. Control blood pressure (Lowering the intracranial pressure, blood pressure control) 3. Lower down intracranial pressure (Mannitol, furosemide, glycerol, fructose, human blood protein).

[e] Lowering the intracranial pressure, cerebral edema, aspirin, Salvia, fibrinolytic, control blood pressure, control intracranial pressure protection and symptomatic treatment, ozagrel, mannitol, generation of plasma, TMP, enteric-coated aspirin, ginkgo biloba, mannitol, edaravone, symptomatic and supportive, dehydration, expansion, anti-platelet aggregation, Neurology nutraceutical brain protective agents, free radical scavenging, control blood sugar, low molecular weight heparin, citicoline, low molecular weight heparin, conventional supportive care, glucose, saline.

**Table 3**
Chinese herbal medicine in stroke management.

Improvement in neurological deficit

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95%CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| **Chinese herbal medicine in stroke management: overview of meta-analyses results in stroke** | | | | | |
| Peng, 2014 [46] | Xingnaojing injection + CHM/ conventional medicine intervention vs CHM/ conventional medicine intervention | NIHSS [33,34], Scandinavian Stroke Scale (SSS) [35] and Chinese Stroke Scale (CSS) [36] for 14 days after stroke | 6 (703) | Pooled WMD: -3.78 (-4.75, -2.81) | 54% |
| **Chinese herbal medicine in stroke management: overview of meta-analyses results in cerebral hemorrhage** | | | | | |
| Wu, 2014 [44] | Qingkailing conventional medicine intervention vs conventional medicine intervention | CSS [36] | 1 (60) | MD: -4.08 (-8.00, -0.16) | NA |
| Yu, 2009 [43] | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention[d] | CSS [36] or NIHSS [33,34] | 11 (845) | Pooled WMD: -5.06 (-5.70, -4.42) | 8% |
| Chinese herbal medicine in stroke management: overview of meta-analyses results in ischemic stroke | | | | | |
| Cheng, 2012 [50] | Qingkailing injection + conventional medicine intervention vs conventional medicine intervention | Modified Edinburgh-Scandinavian Stroke Scale (MESSS) [37] | 3 (272) | Pooled WMD: -3.49 (-4.70, -2.28) | 0% |
| Fu, 2013 [49] | Xiaoxuming decoction + conventional medicine intervention[b] vs conventional medicine intervention[b] | NIHSS [33,34] | 3 (186) | Pooled WMD: -1.86 (-3.25, -0.48) | 10% |
| Hao, 2012 [47] | Buyang Huanwu decoction + conventional medicine intervention[c] vs conventional medicine intervention[c] | MESSS [37] or CSS [36] | 9 (786) | Pooled WMD: -4.65 (-6.57, -2.72) | 84% |
| Li, 2017 [38] | Dengzhanxixin+conventional medicine intervention vs conventional medicine intervention | Neurological Function Deficit Score (NFDS) | 7 (612) | Pooled WMD: -3.99 (-5.68, -2.30) | 77% |
| Li, 2017 [38] | Dengzhanxixin+conventional medicine intervention vs conventional medicine intervention | NIHSS | 5 (463) | Pooled WMD: -1.67 (-2.59, -0.76) | 69% |
| Ma, 2017 [40] | Xingnaojing injection + conventional medicine intervention vs conventional medicine intervention | CSS | 18 (1625) | Pooled WMD: -5.72 (-6.94, -4.50) | 87% |
| Ma, 2017 [40] | Xingnaojing injection + conventional medicine intervention vs conventional medicine intervention | NIHSS | 12 (1273) | Pooled WMD: -3.44 (-4.52, -2.36) | 92% |
| Wang, 2017 [39] | Dengzhanxixin injection + conventional medicine intervention vs conventional medicine | NIHSS | 5 (289) | Pooled WMD: -2.11 (-2.73, -1.48) | 0% |
| Wang, 2017 [39] | Dengzhanxixin injection + conventional medicine intervention vs conventional medicine | Nerve Deficiency Scale (NDS) | 5 (310) | Pooled WMD: -2.86 (-3.87, -1.86) | 31% |
| Wu, 2014 [44] | Qingkailing conventional medicine intervention vs conventional medicine intervention | CSS [36] | 2 (141) | Pooled WMD: -5.60 (-8.50, -2.70) | 41% |
| Zhang, 2012 [42] | Shuxuetong + conventional medicine interventione vs conventional medicin[e] intervention[e] | CSS [36] at 14/15 days after 2 wk of treatment | 7 (740) | Pooled WMD: -5.86 (-6.93, -4.86) | 33% |
| Zhang, 2017 [41] | Yiqi Huoxue + conventional medicine intervention vs conventional medicine intervention | CSS [36] | 26 (2410) | Pooled WMD: -4.59 (-5.67, -3.52) | 96% |

Improvement in neural functional damage

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| **Chinese herbal medicine in stroke management: overview of meta-analyses results in ischemic stroke** | | | | | |
| Cheng, 2012 [50] | Qingkailing injection + conventional medicine intervention vs conventional medicine intervention | MESSS [37] (Define as Cure, Significant improvement, and Improvement) | 7 (545) | Pooled RR: 1.12 (1.04, 1.19) | 44% |
| Wu, 2005 [45] | Compound Danshen injection + conventional medicine intervention vs conventional medicine intervention | MESSS [37] or CSS [36] (Define as Cure, Significant improvement, and Improvement) | 2 (234) | Pooled RR: 1.03 (0.98, 1.08) | 0% |
| Wu, 2005 [45] | Compound Danshen dropping pill + conventional medicine intervention vs conventional medicine intervention | MESSS [37] or CSS [36] (Define as Cure, Significant improvement, and Improvement) | 1 (70) | RR: 1.25 (1.00, 1.56) | NA |
| Wu, 2005 [45] | Compound Danshen injection/ dropping pill + conventional medicine intervention vs conventional medicine intervention | MESSS [37] or CSS [36] (Define as Cure, Significant improvement, and Improvement) | 3 (304) | Pooled RR: 1.07 (1.01, 1.14) | 52% |

Mortality rate reduction

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|

**Table 3** (*Continued*)

| Mortality rate reduction | | | | | |
|---|---|---|---|---|---|
| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
| **Chinese herbal medicine in stroke management: overview of meta-analyses results in cerebral hemorrhage** | | | | | |
| Yu, 2009 [43] | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention[d] | Intracerebral hemorrhage mortality rate | 7 (597) | Pooled OR: 0.32 (0.17, 0.59) | 0% |
| **Chinese herbal medicine in stroke management: overview of meta-analyses results in ischemic stroke** | | | | | |
| Cheng, 2012 [50] | Qingkailing injection + conventional medicine intervention vs conventional medicine intervention | Death assessed at the end of 2-wk therapeutic course/ 1 month after stroke onset | 2 (105) | Pooled RR: 0.39 (0.10, 1.55) | 46% |
| Li, 2017 [38] | Dengzhan Xixin + conventional medicine intervention vs conventional medicine intervention | Death within 14 days | 2 (184) | Pooled RR: 0.27 (0.05, 1.63) | 0% |

dyspepsia, eruption, rash, dizziness, drowsiness, fibrinogen decrease, alanine transaminase increase, thrombocytopenia. There was no difference between CHM plus conventional medicine intervention and conventional medicine intervention for adverse events. None of these SRs showed that CHM usage would increase the risk of AE. No life-threatening adverse effects were noted in all these SRs.

## 5. Discussion

This overview summarizes the findings from SRs with meta-analysis to provide evidence for clinicians to identify treatment alternatives with CHM in post-stroke management. The evidence compiled by this overview indicated that five CHM [42–44,46,49], namely Xiaoxuming, Xingnaojing, Qingkailing, Panax notoginseng saponins, and Shuxuetong, in combining conventional medicine intervention, were safe and effective in treating patients with stroke. The results of our study provide clinical evidence on the add-on effect of CHMs in routine stroke care. These CHMs produce different therapeutic effects in stroke management. Xiaoxuming protects against blood-brain barrier disruption and neurological injury due to cerebral ischemia and reperfusion [70]; Xingnaojing has shown to reduce brain injury and enhance functional recovery post stroke in both animal and human studies [50,81,82]; Qingkailing is commonly used in combination with western medicine for the treatment of cerebral hemorrhage and cerebral edema. Panax notoginseng saponins reduce cerebral edema [83] and cell damage [84–86]; Shuxuetong produce anti-coagulant and anti-platelet aggregation effects. It inhibits thrombosis and thrombolysis and reduces the scope of cerebral ischemia.

Our study is unique because we provided an overview on CHM for stroke management, rather than focused on a single intervention. Multiple RCTs and reviews have been published examining the potential relative benefits or harms of a particular CHM together with conventional medicine intervention in the treatment of stroke in different stages over the years. Some CHM, including Buyang Huanwu [87–97], Erigeron Breviscapus (Dengzhan Xixin) [98–100], Ginkgo Biloba extract [101,102], Ligustrazine [103,104], Qingkailing [105–108], and Salvia Miltiorrhiza Ligustrazine Injection [110], in combining with conventional medicine intervention, were reported to be effective in improving neurological function in patients after stroke in SRs with meta-analysis. However, some of these SRs did not state precise interventions [50,92,93,98,99,103], comparisons [47,88,90,91,100–102,104–106], or outcomes [87,89,95–97,108,109]. These SRs had unclear eligibility criteria for searching for studies [87,88,90,97–99,102,103,105,108] and uncertainty of data collection from included studies in the review process [47,89,91–93,95,96,100,101,104,106,107,109]. The results of these studies indicate that uncertainties relating to CHM on post-stroke management are not well studied. Our study provides an opportunity to overcome the gaps by composing, appraising, and summarizing all relevant SRs into an overview.

Our investigation has broader implications for applying integrated Western- Chinese medicine care model for stroke. Conventional medicine intervention had not been shown to improve neurological function significantly after stroke. CHM can be an alternative and complementary approach for stroke management. Through the application of overview of SRs for evaluating the effectiveness and safety of CHM on post-stroke management, we identified the treatment benefit of CHM [42–44,46,49] (Xiaoxuming, Xingnaojing, Qingkailing, Panax notoginseng saponins, and Shuxuetong) in addition to conventional medicine intervention in neurological deficit improvement with stroke by validated measures.

The current SRs had several limitations, including small number of eligible RCTs, lack of methodological details, and insufficient reporting of trials. The included SRs were not reported optimally. Study characteristics, risk of bias of individual studies including publication and selection bias, and funding sources were not completely reported in the SRs. Furthermore, many of the original RCTs are of poor quality [100]. The evidence on the efficacy, safety and quality of CHMs is insufficient to meet the applicable standards [14]. Researchers should follow CONSORT statement for reporting of trials. Reporting information, including characteristics, risk of bias assessment, and outcome measures, should also be standardized to facilitate comparison across SRs. There is room for improvement in methodological quality of the SRs. Researchers should follow PRISMA and AMSTAR tool for reporting SRs. Diagnosis criteria, interventions, outcome measures should be reported in greater details to enhance the explicitly and reliability of the SRs. The scope of reviews on stroke management needs to reflect the current practice accordingly to international guidelines [111,112] in diagnosis, and management with conventional medicine intervention.

There is insufficient safety information on the maximum dose and treatment duration of individual CHM. In our overview of SRs, only 3 SRs reported the mortality rate after intervention. There was limited clinical study assess the mortality rate after the use of CHM intervention in stroke management. Therefore, there was little evidence of the effect of CHM in the reduction of mortality in combining with conventional medicine intervention. Researchers should conduct comprehensive evaluation on the safety of the medicine on both clinical and research level.

## 6. Conclusions

CHM could provide additional benefit in addition to conventional medicine intervention for stroke management. However, this finding requires verification in rigorous RCTs. Further high quality research is needed to verify the efficacy and safety of CHM in addition to conventional medicine intervention on stroke management.

## Author contributions statement

Contribute equally to this paper. Study concept and design. Acquisition of data. Analysis and interpretation of data. Drafting of the manuscript. Critical revision of the manuscript for important intellectual content. Administrative, technical, or material support. All authors reviewed the manuscript.

## Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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## Appendix A. Other reported outcomes

**Chinese herbal medicine in stroke management:overview ofmeta-analysesresults in stroke**

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| ***Effective rate*** | | | | | |
| Peng, 2014[46] | Xingnaojing injection + CHM/ conventional medicine intervention vs CHM/ conventional medicine intervention | Effective rate defined by NIHSS[33,34], SSS[35] & CSS[36], and the general neurological status[113] | 6 (839) | Pooled OR: 3.25 (2.30, 4.59) | 0% |
| Wu, 2014[44] | Qingkailing + conventional medicine intervention vs conventional medicine intervention | Effective rate defined by MESSS[37]<br>Effective rate = (number of recovered patients + number of patients with significant progress + number of patients with progress)/ total number x 100% | 4 (410) | Pooled RR: 1.34 (1.2, 1.50) | 0% |
| ***Improvement in inflammatory factor*** | | | | | |
| Peng, 2014[46] | Xingnaojing injection + CHM/ conventional medicine intervention vs CHM/ conventional medicine intervention | TNF-αlevel in serum for 14 days after stroke | 3 (258) | Pooled SMD: −3.21 (−5.19, −1.23) | 96% |

**Chinese herbal medicine in stroke management:overview ofmeta-analysesresults in cerebral hemorrhage**

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| ***Decrease of cerebral hematoma volume*** | | | | | |
| Yu, 2009[43] | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention [d] | Overall cerebral hematoma volume | 10 (773) | Pooled WMD: −5.82 (−7.46, −4.18) | 89% |
| ***Cerebral edema volume*** | | | | | |
| Yu, 2009[43] | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention[d] | Cerebral hemorrhage and cerebral hematoma volume | 2 (102) | Pooled WMD: −11.49 (−14.72, −8.26) | 0% |
| ***Improvement in activities of daily living (assessing the degree of disability)*** | | | | | |
| Yu, 2009[43] | Panax notoginseng saponins injection + conventional medicine intervention[d] vs conventional medicine intervention[d] | BI[114,115] | 4 (192) | Pooled WMD: 11.55 (8.96, 14.13) | 30% |

**Chinese herbal medicine in stroke management:overview ofmeta-analysesresults in cerebral hemorrhage (continuous)**

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| ***Effectiveness*** | | | | | |
| Wu, 2014[44] | Qingkailing + conventional medicine intervention vs conventional medicine intervention | Effective rate defined by MESSS[37]<br>Effective rate = (number of recovered patients + number of patients with significant progress + number of patients with progress)/ total number x 100% | 4 (338) | Pooled RR: 1.17 (1.08, 1.26) | 23% |
| ***Degree of absorption of cerebral hematoma*** | | | | | |
| Wu, 2014[44] | Qingkailing + conventional medicine intervention vs conventional medicine intervention | Hematoma size and absorption rate (v=1/2 x L x S x the slice) The absorption rate of the hematoma = (before treatment - after)/treatment before x 100% | 2 (116) | Pooled WMD: −3.73 (−4.30, −3.16) | 0% |

**Chinese herbal medicine in stroke management:overview ofmeta-analysesresults in acute ischemic stroke**

| First author and year of publication | Comparison | Outcome assessment method | No. of studies (No. of patients) | Pooled results (95% CI) | Heterogeneity $I^2$ (%) |
|---|---|---|---|---|---|
| ***Effectiveness*** | | | | | |
| Wu, 2014[44] | Qingkailing + conventional medicine intervention vs conventional medicine intervention | Effective rate defined by MESSS[37]<br>Effective rate = (number of recovered patients + number of patients with significant progress + number of patients with progress)/ total number x 100% | 5 (362) | Pooled RR: 1.27 (1.14, 1.42) | 0% |
| ***Effectiveness (effective rate)*** | | | | | |
| Fu, 2013[49] | Xiaoxuming decoction + conventional medicine intervention[b] vs conventional medicine intervention[b] | Effective rate defined by MESSS[37] of nervous functional deficits and disability degree<br>Effective define as clinical cure, markedly effective, effective, ineffective | 7 (531) | Pooled RR: 1.17 (1.09, 1.26) | 0% |
| Hao, 2012[47] | Buyang Huanwu decoction + conventional medicine intervention[c] vs conventional medicine intervention[c] | Effective rate defined by MESSS[37] of nervous functional deficits and disability degree<br>Effective define as Cure, Significant improvement, and Improvement | 17 (1444) | Pooled RR: 1.18 (1.12, 1.24) | 36% |
| ***Effectiveness(recovery rate)*** | | | | | |
| Han, 2013[48] | Therapy of supplementing qi and activating blood + conventional medicine intervention vs conventional medicine intervention | Recovery rate defined by MESSS[37] | 24 (2223) | Pooled RR: 4.24 (2.26, 5.51) | 0% |
| ***Improvement in activity of daily living (assessing the degree of disability)*** | | | | | |
| Han, 2013[48] | Therapy of supplementing qi and activating blood + conventional medicine intervention vs conventional medicine intervention | BI[114] | 5 (487) | Pooled WMD: 12.79 (4.29, 21.29) | 88% |
| Li, 2017[38] | Dengzhan Xixin + conventional medicine intervention vs conventional medicine intervention | BI[114] | 5 (346) | Pooled WMD: 10.20 (8.16, 12.25) | 34% |
| Wang, 2017 [39] | Dengzhanxixin injection + conventional medicine intervention vs conventional medicine | BI[114] | 3 (280) | Pooled WMD: 9.48 (8.34, 10.63) | 2% |
| ***Inflammation factor*** | | | | | |
| Cheng, 2012 [50] | Qingkailing injection + conventional medicine intervention vs conventional medicine intervention | TNF-a | 2 (153) | Pooled WMD: −5.56 (−9.23, −1.90) | 96% |
| ***Improvement in plasma viscosity*** | | | | | |
| Han, 2013[48] | Therapy of supplementing qi and activating blood + conventional medicine intervention vs conventional medicine intervention | Plasma viscosity | 7 (582) | Pooled WMD: −0.54 (−0.90, −0.17) | 96% |
| Zhang, 2017 [41] | Yiqi Huoxue + conventional medicine intervention vs conventional medicine intervention | Plasma viscosity | 7 (661) | Pooled WMD: −0.26 (−0.34, −0.19) | 92% |

| Chinese herbal medicine in stroke management:overview ofmeta-analysesresults in acute ischemic stroke (continuous) | | | | | |
|---|---|---|---|---|---|
| **First author and year of publication** | **Comparison** | **Outcome assessment method** | **No. of studies (No. of patients)** | **Pooled results (95% CI)** | **Heterogeneity $I^2$ (%)** |
| ***Improvement in the effectiveness of Traditional Chinese Medicine syndromes (TCMs)*** | | | | | |
| Han, 2013[48] | Therapy of supplementing qi and activating blood + conventional medicine intervention vs conventional medicine intervention | TCMs | 4 (293) | Pooled WMD: −5.23 (−8.53, −1.93) | 83% |
| **Chinese Herbal Medicine in stroke management:Overview ofMeta-AnalysesResults in Acute cerebral infarction** | | | | | |
| **First author and year of publication** | **Comparison** | **Outcome assessment method** | **No. of studies (No. of patients)** | **Pooled results (95% CI)** | **Heterogeneity $I^2$ (%)** |
| ***Marked neurologic improvement*** | | | | | |
| Cao, 2008[51] | Dengzhanhua injection + conventional medicine intervention[a] vs conventional medicine intervention[a] | Neurologic dysfunction (moter/ cognition deficit) or NIHSS[33,34]. The proportion of patients with at least 45% neurologic improvement | 9 (723) | Pooled RR: 1.53 (1.36, 1.72) | 0% |
| ***Effectiveness*** | | | | | |
| Wang, 2017 [39] | Dengzhanxixin injection + conventional medicine intervention vs conventional medicine | Effective rate defined by Neurological Deficit Score [#] Effective (cure, significant improvement, and improvement) | 16 (1,501) | Pooled RR: 1.20 (1.15, 1.25) | 0% |
| Zhang, 2012 [42] | Shuxuetong + conventional medicine intervention[e] vs conventional medicine intervention [e] | Effective rate defined by Neurological Deficit Score [#] Effective (cure, significant improvement, and improvement) | 11 (972) | Pooled OR: 4.46 (3.02, 6.59) | 0% |

## Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.aimed.2018.11.002.

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