

## Additional files

### Contents

<b>Additional file 1 Search strategies for literature review</b> .....	2
<b>Additional file 2 The reporting rates of 42 questions based on the CONSORT-CHM Formulas 2017 (n=3,265)</b> .....	4
<b>Additional file 3 PRISMA flow diagram of included and excluded studies</b> .....	9
<b>Additional file 4 Baseline characteristics of included studies (n=3,265)</b> .....	10
<b>Additional file 5 The diseases classified with ICD-11 MMS involved in this review</b> .....	12
<b>Additional file 6 The information about dosage forms and administration routes of CHM formulas</b> .....	12
<b>Additional file 7 Safety assessment of the included studies (n=1,284)</b> .....	13
<b>Additional file 8 Reporting details of 42 sub-questions among 3,265 studies</b> .....	14
<b>Additional file 9 Reporting difference between three types of CHM formulas</b> .....	15
<b>Additional file 10 Discussion about major results</b> .....	16

## Additional file 1 Search strategies for literature review

### 1. Ovid

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Set	Search term
1	random\$.tw.
2	factorial\$.tw.
3	(crossover\$ or cross over\$ or cross-over\$).tw.
4	placebo\$.tw.
5	single blind.mp.
6	double blind.mp.
7	triple blind.mp.
8	(singl\$ adj blind\$).tw.
9	(double\$ adj blind\$).tw.
10	(tripl\$ adj blind\$).tw.
11	assign\$.tw.
12	allocat\$.tw.
13	randomized controlled trial/
14	or/1-13
15	((single#entity or single) adj3 (component or drug\$ or herb\$)).mp.
16	(compound prescription\$ or herbal mixture or Fufang).mp.
17	(Chinese Medicine Patent Prescription or proprietary Chinese medicines).mp.
18	(Chinese patent adj3 (medicine or drug\$)).mp.
19	(Chinese adj3 (patent or proprietary) adj3 (medicine or drug\$)).mp.
20	(Chinese adj2 (patent or proprietary) adj2 (medicine or drug\$ or prescription\$)).mp.
21	or/15-20
22	14 and 21
23	limit 22 to yr="2018 -Current" [Limit not valid in DARE; records were retained]

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DARE: Database of Abstracts of Reviews of Effects

### 2. VIP database

(M=临床试验+M=随机+M=对照+M=随机试验+M=随机对照试验+M=临床研究+M=半随机) AND (中医药+M=草药+M=中药+M=复方+M=汤剂+M=中成药+M=注射剂+M=加减方+M=外用中药) AND 年份: 2018-2022

### 3. Wanfang database

(题名: (临床试验 or 随机 or 对照 or 随机试验 or 随机对照试验 or 临床研究 or 半随机)) and (题名或关键词:(中医药 or 草药 or 中药 or 复方 or 汤剂 or 中成药 or 注射剂 or 加减方 or 外用中药)) and Date:2018-2022

#### 4. CNKI database

(SU="临床试验" or SU="随机" or SU="对照" or SU="随机试验" or SU="随机对照试验" or SU="临床研究" or SU="半随机")  
AND (SU="中医药" or SU="草药" or SU="中药" or SU="复方" or SU="汤剂" or SU="中成药" or SU="注射剂" or SU="加减方" or SU="外用中药") AND (发表时间: 2018-01-01-2022-06-08)

#### 5. CBM database

((("中医药"[标题] OR "草药"[标题] OR "中药"[标题] OR "复方"[标题] OR "汤剂"[标题] OR "中成药"[标题] OR "注射剂"[标题] OR "加减方"[标题] OR "外用中药"[标题]) OR ("中医药"[摘要] OR "草药"[摘要] OR "中药"[摘要] OR "复方"[摘要] OR "汤剂"[摘要] OR "中成药"[摘要] OR "注射剂"[摘要] OR "加减方"[摘要] OR "外用中药"[摘要])) AND ("临床试验"[标题] OR "随机"[标题] OR "对照"[标题] OR "随机试验"[标题] OR "随机对照试验"[标题] OR "临床研究"[标题] OR "半随机"[标题])) AND 2018-2022[日期]

**Additional file 2 The reporting rates of 42 questions based on the CONSORT-CHM Formulas 2017 (n=3,265)**

<b>Section/topic</b>	<b>Extension items</b>	<b>Sub-questions for assessment</b>	<b>Reporting rate* (%)</b>
<b>Title, abstract, and keywords</b>	1a. Statement of whether the trial targets a TCM Pattern, a Western medicine–defined disease, or a Western medicine–defined disease with a specific TCM Pattern, if applicable.	<i>Q1. Whether it reported that the trial targeted a specific TCM Pattern in “Title”?</i>	48.2
	1b. Illustration of the name and form of the formula used, and the TCM Pattern applied, if applicable	<i>Q2. Whether the name of the CHM formula was reported in “Abstract”?</i>	67.0
		<i>Q3. Whether the dosage form of the CHM formula was reported in “Abstract”?</i>	39.7
		<i>Q4. Whether the TCM Pattern was reported in “Abstract”?</i>	55.8
	1c. Determination of appropriate keywords, including “Chinese herbal medicine formula” and “randomized controlled trial”	<i>Q5. Whether the “Chinese herbal medicine formula” was presented in “Key word”?</i>	8.4
		<i>Q6. Whether “randomized controlled trials” was presented in “Key words”?</i>	8.3
<b>Introduction Background and objectives</b>	2a. Statement with biomedical science approaches and/or TCM approaches	<i>Q7. Whether the TCM background and explanation of the disease or the TCM Pattern was reported in “Background”?</i>	23.7
		<i>Q8. Whether the biomedical science explanation and/or TCM rationale about the CHM formula were reported in “Background”?</i>	21.8
	2b. Statement of whether the formula targets a Western medicine–defined disease, a TCM Pattern, or a Western medicine–defined disease with a specific TCM Pattern	<i>Q9. Whether the objective or hypotheses focused on the CHM formula in treatment of a Western medicine-defined disease, a TCM Pattern, or a Western medicine-defined disease with a specific TCM Pattern?</i>	41.6

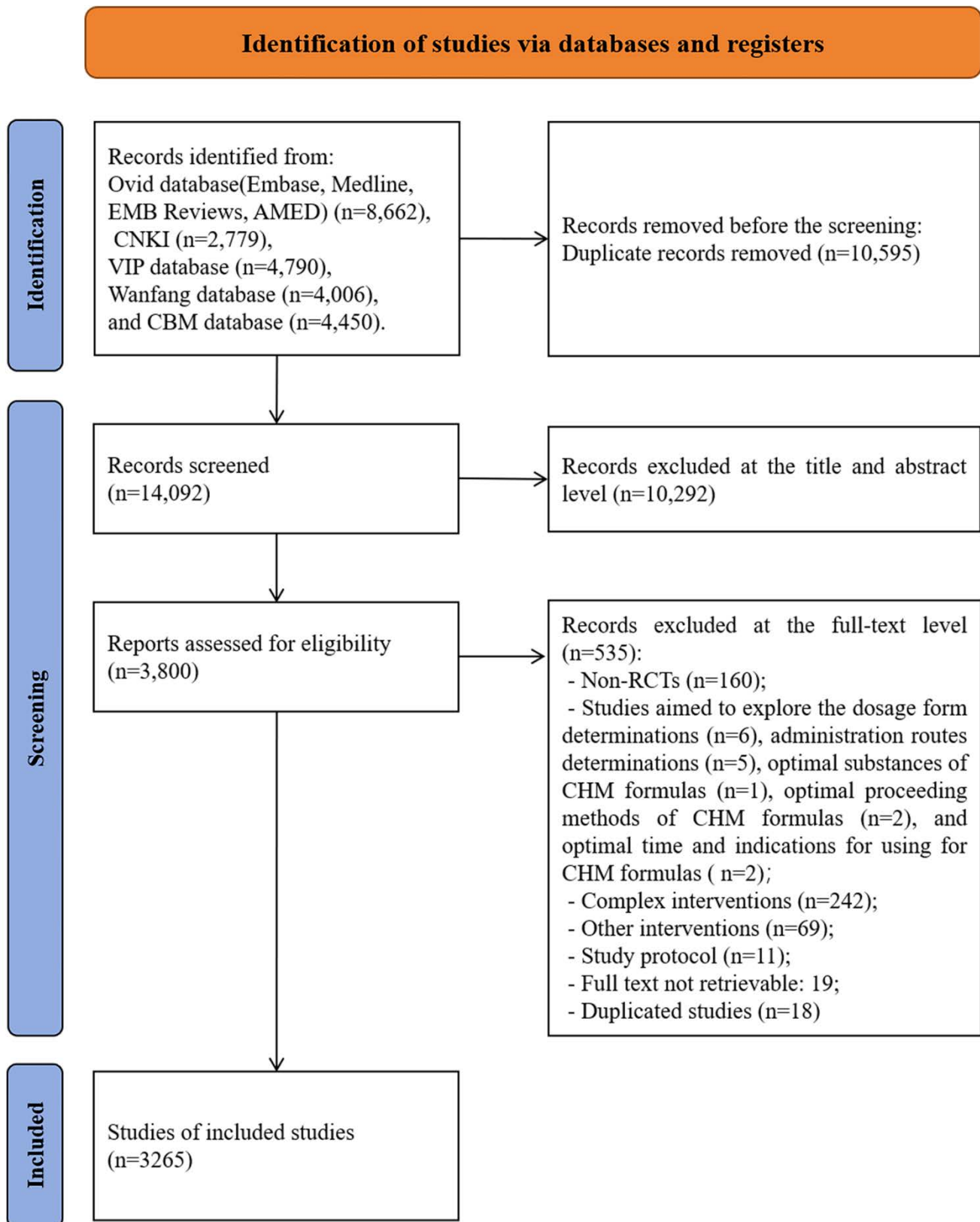
<p><b>Methods</b></p> <p><b>Participants</b></p>	<p>4a. Statement of whether participants with a specific TCM Pattern were recruited, in terms of 1) diagnostic criteria and 2) inclusion and exclusion criteria. All criteria used should be universally recognized, or reference given to where detailed explanation can be found.</p>	<p><i>Q10. Whether the participants with a specific TCM Pattern were recruited, in terms of 1) diagnostic criteria and 2) inclusion and exclusion criteria, and whether all criteria used were universally recognized, or reference given to where detailed explanation can be found in "Methods"?</i></p>	<p>95.4</p>
<p><b>Interventions</b></p> <p><b>5a. For fixed CHM formulas</b></p>	<p>5a-1. Name, source, and dosage form (e.g., decoctions, granules, powders)</p>	<p><i>Q11. Whether the name of the CHM formula was reported in "Methods"?</i></p>	<p>78.8</p>
		<p><i>Q12. Whether the source of the CHM formula was reported in "methods"?</i></p>	<p>24.7</p>
		<p><i>Q13. Whether the dosage form of the CHM formula was reported in "methods"?</i></p>	<p>58.7</p>
	<p>5a-2. Name, source, processing method, and dosage of each medical substance. Names of substances should be presented in at least 2 languages: Chinese (Pinyin), Latin, or English. Names of the parts of the substances used should be specified.</p>	<p><i>Q14. Whether the name of each medical substance was reported in "Methods"?</i></p>	<p>86.1</p>
		<p><i>Q15. Whether the source of each medical substance was reported in "Methods"?</i></p>	<p>16.3</p>
		<p><i>Q16. Whether the processing method of each medical substance was reported in "Methods"?</i></p>	<p>56.3</p>
		<p><i>Q17. Whether the dosage of each medical substance was reported in "Methods"?</i></p>	<p>79.2</p>
	<p>5a-3. Authentication method of each ingredient and how, when, where, and by whom it was conducted; statement of whether any voucher specimen was retained, and if so, where they were kept and whether they are accessible</p>	<p><i>Q18. Whether the Authentication method of each ingredient was reported in "Methods"?</i></p>	<p>0.0</p>
	<p>5a-4. Principles, rationale, and interpretation of forming the formula</p>	<p><i>Q19. Whether the principles, rationale, and interpretation of forming the formula were reported?</i></p>	<p>83.8</p>

	5a-5. Reference(s) as to the efficacy of the formula, if any	<i>Q20. Whether the reference(s) as to the efficacy of the formula was presented?</i>	59.5
	5a-6. Pharmacologic study results of the formula, if any	<i>Q21. Whether the pharmacologic study results of the formula were presented?</i>	41.4
	5a-7. Production method of the formula, if any	<i>Q22. Whether the production method of the formula was reported?</i>	80.7
	5a-8. Quality control of each ingredient and of the product of the formula, if any. This would include any quantitative and/or qualitative testing method(s); when, where, how, and by whom these tests were conducted; whether the original data and samples were kept, and, if so, whether they are accessible.	<i>Q23. Whether the quality control of each ingredient and of the product of the formula was conducted?</i>	0.1
	5a-9. Safety assessment of the formula, including tests for heavy metals and toxic elements, pesticide residues, microbial limit, and acute/chronic toxicity, if any. If yes, it should be stated when, where, how, and by whom these tests were conducted; if the original data and samples were kept; and, if so, whether they are accessible.	<i>Q24. Whether the safety assessment of the formula was conducted?</i>	0.0
	5a-10. Dosage of the formula, and how the dosage was determined	<i>Q25. Whether the dosage of the formula was reported?</i>	79.0
		<i>Q26. Whether the treatment duration of the CHM formulas was reported in "Methods"?</i>	89.5
	5a-11. Administration route (e.g., oral, external)	<i>Q27. Whether the Administration route of the CHM formula was reported in "Methods"?</i>	93.9
<b>5b. For individualized CHM formulas</b>	5b-1. See recommendations 5a 1–11	<i>See Q11 to Q27.</i>	
	5b-2. Additional information: how, when, and by whom the formula was modified	<i>Q28. For trials with individualized CHM formulas, whether it reported how, when, and by whom the CHM formula was modified in "Methods"?</i>	68.8

<b>5c. For patent proprietary CHM formulas</b>	5c-1. Reference to publicly available materials, such as pharmacopeia, for the details about the composition, dosage, efficacy, safety, and quality control of the formula	<i>Q29. For trials with patent proprietary CHM formulas, whether the composition and dosage were reported in "Methods"?</i>	78.1
	5c-2. Illustration of the details of the formula, namely 1) the proprietary product name (i.e., brand name), 2) name of manufacturer, 3) lot number, 4) production date and expiry date, 5) name and percentage of added materials, and 6) whether any additional quality control measures were conducted	<i>Q30. For trials with patent proprietary CHM formulas, whether the efficacy was reported in "Methods"?</i>	79.5
		<i>Q31. For trials with patent proprietary CHM formulas, whether the safety or quality control was reported in "Methods"?</i>	75.4
		<i>Q32. For trials with patent proprietary CHM formulas, whether the proprietary product name (i.e., brand name), name of the manufacturer, and lot number were reported in "Methods"?</i>	75.8
		<i>Q33. For trials with patent proprietary CHM formulas, whether the production date and expiry date were reported in "Methods"?</i>	75.8
	5c-3. Statement of whether the patent proprietary formula used in the trial is for a condition that is identical to the publicly available reference	<i>Q34. For trials with patent proprietary CHM formulas, whether the patent proprietary formula used in the trial is for a condition that is identical to the publicly available reference was stated?</i>	45.6
<b>5d. Control groups Placebo control</b>	5d-1. Name and amount of each ingredient	<i>Q35. For trials with placebo control, whether the name and amount of each ingredient of the placebo were reported in "Methods"?</i>	35.9
	5d-2. Description of the similarity of placebo with the intervention (e.g., color, smell, taste, appearance, packaging)	<i>Q36. For trials with placebo control, whether the similarity of placebo with the intervention (e.g., color, smell, taste, appearance, packaging) was reported in "Methods"?</i>	55.1
	5d-3. Quality control and safety assessment, if any	<i>Q37. For trials with placebo control, whether the quality control and safety assessment of the placebo were reported in "Methods"?</i>	15.3

	5d-4. Administration route, regimen, and dosage	<i>Q38. For trials with placebo control, whether the administration route, regimen, and dosage of the placebo were reported in "Methods"?</i>	66.1
	5d-5. Production information: where, when, how, and by whom the placebo was produced	<i>Q39. For trials with placebo control, whether the production information of the placebo was reported, including where, when, how, and by whom the placebo was produced?</i>	56.8
<b>Outcomes</b>	Illustration of outcome measures with Pattern in detail	<i>Q40. Whether the outcome measures included TCM indicators in "Outcome"?</i>	44.9
<b>Discussion Generalizability</b>	Discussion of how the formula works on different TCM Patterns or diseases	<i>Q41. Whether any discussion of how the formula works on different TCM Patterns or diseases was reported in "Discussion" ?</i>	2.3
<b>Interpretation</b>	Interpretation with TCM theory	<i>Q42. Whether any interpretation with TCM theory was reported in "Discussion"?</i>	74.9

\* The reporting rate of each sub-question was calculated with the formula: Reporting rate =  $n_i / (N - n_j) \times 100\%$ . Specifically, the "n<sub>i</sub>" is the number of "Fully reported" while the "N" is the total included RCTs, and the "n<sub>j</sub>" is the number of "not applicable".



**Additional file 4 Baseline characteristics of included studies (n=3,265)**

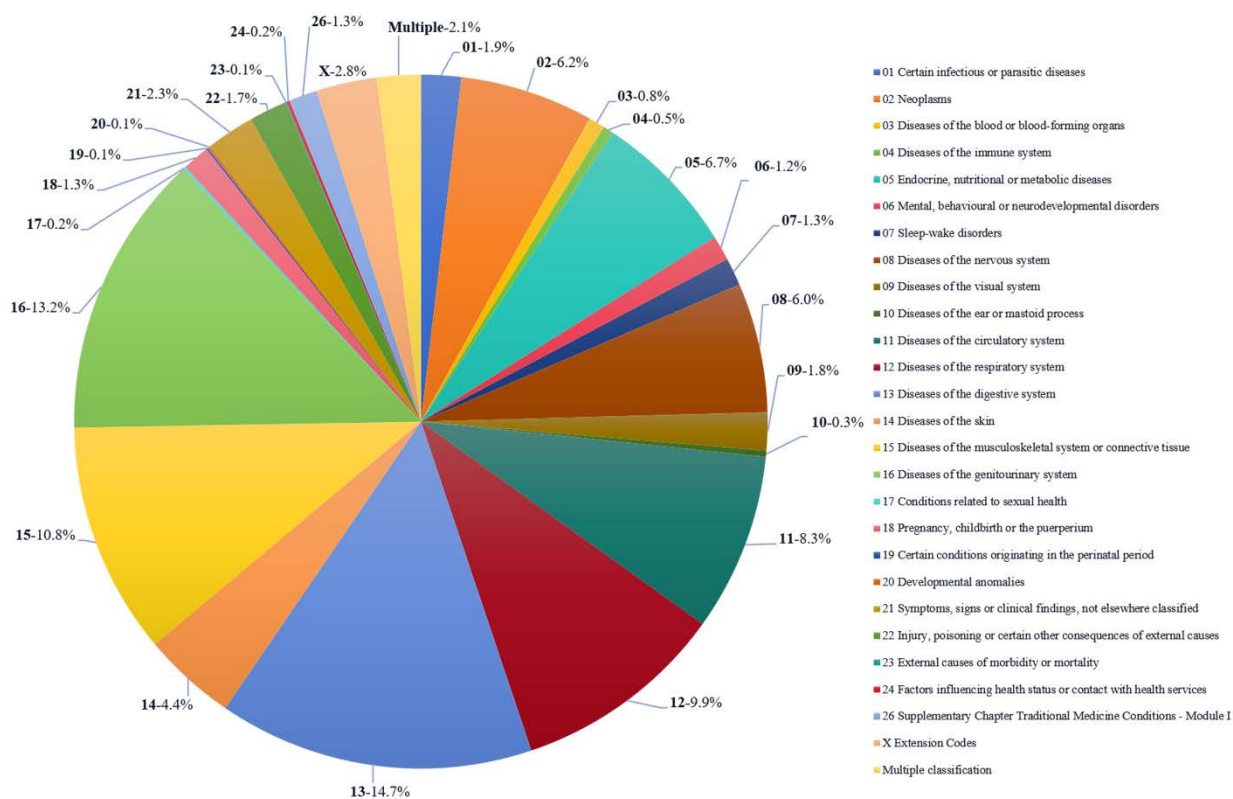
<b>Characteristics</b>	<b>N</b>	<b>%</b>
<b>Publication years</b>		
2018	902	27.6
2019	786	24.1
2020	724	22.2
2021	715	21.9
2022	138	4.2
<b>Languages of publications</b>		
Chinese	3,246	99.4
English	19	0.6
<b>Number of authors</b>		
≤10	3,214	98.4
>10	51	1.6
<b>Study objective</b>		
Clinical efficacy	1,781	54.5
Safety	1	0.1
Both	1,483	45.4
<b>Study centre</b>		
Single-Centre	3,092	94.7
Multi-Centre	138	4.2
Not reported	35	1.1
<b>Recruitment sites</b>		
China	3,265	100.0
<b>Number of arms</b>		
2	3,036	93.0
>2	229	7.0
<b>Type of randomization</b>		
Simple randomization	1,954	59.8
Stratified or block randomization	72	2.2
Not reported	1,239	37.9
<b>Including blinding</b>	144	4.4
<b>Including TCM pattern for the participants</b>	1,337	40.9
<b>Sample size</b>		
1-100	2,283	69.9
101-300	917	28.1
>300	55	1.7
<b>Gender of participants</b>		
Only Male	38	1.2
Only Female	398	12.2
Both	2,802	85.8
<b>Types of CHM formulas*</b>		
Fixed formulas	1,994	61.1
Individualized prescriptions	709	21.7
Chinese patent medicine	514	15.7
<b>Treatment Duration (week)</b>		
≤1	449	13.8
1.1-4	1,384	42.4
4.1-12	813	24.9

12.1-52	429	13.1
>52	12	0.4
Not reported	178	5.5
<b>Including Follow-up</b>	307	9.4
Follow-up period (week)		
≤12	112	3.4
12.1-52	178	5.5
>52	17	0.5
<b>Types of comparisons</b>		
Including placebo control	155	4.7
Including positive control	1,648	50.5
Add-on design	1,443	44.2
Including blank control	19	0.6
<b>Included TCM-related outcomes<sup>^</sup></b>	1,004	30.8
<b>Including the collection of biological samples</b>	1,659	50.8
<b>Have Funding supports</b>	1,328	40.7

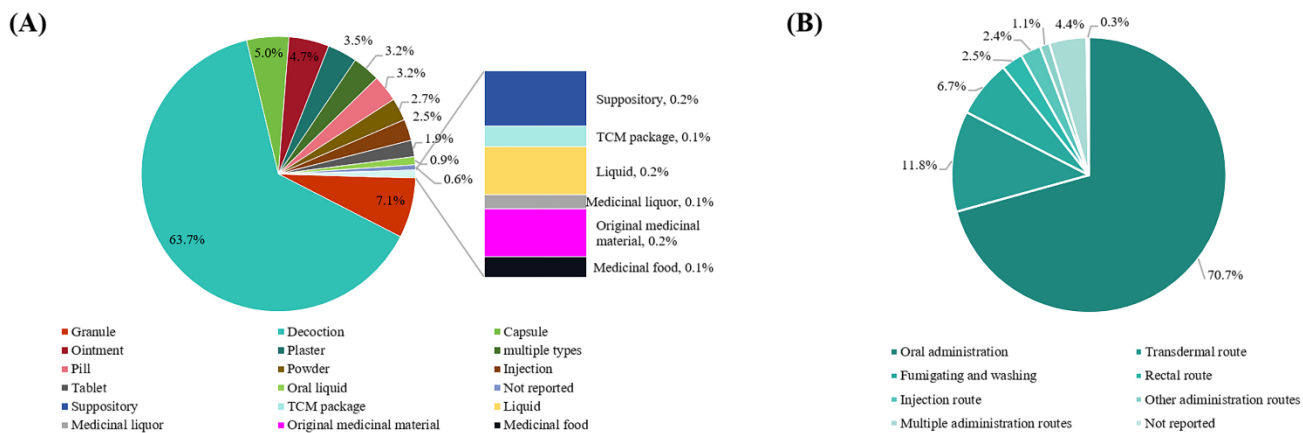
\* 48 studies applied more than one type of CHM formulas in the trial, including 36 with combination of fixed formulas and Chinese patent medicine, 12 with combination of individualized prescriptions and Chinese patent medicine.

<sup>^</sup> 1004 studies reported TCM related outcomes, 864 of them were TCM patterns and 140 were TCM symptoms.

**Additional file 5 The diseases classified with ICD-11 MMS involved in this review**



**Additional file 6 The information about dosage forms and administration routes of CHM formulas**



**(A) The dosage forms. (B) The administration routes.**

**Additional file 7 Safety assessment of the included studies (n=1,284)**

Safety assessment	N	%
<b>Including safety assessment<sup>†</sup></b>	1,284	39.3
Adverse effect reported <sup>†</sup>	820	25.1
No adverse effect identified <sup>†</sup>	444	13.6
<b>Measurement time of adverse effect<sup>‡</sup></b>		
During the Treatment period <sup>#</sup>	976	76.0
During the Follow-up period	31	2.4
Both treatment and follow-up periods	98	7.6
Not reported	291	22.7
<b>Measurements of adverse effect<sup>‡</sup></b>		
Physical examination	438	34.1
Physicochemical test	189	14.7
Both	355	27.6
Not specified	302	23.5
<b>Adverse effect occurrence<sup>†</sup></b>	820	25.1
Only in the intervention group <sup>λ</sup>	58	7.1
Only in the control group <sup>λ</sup>	71	8.7
Both <sup>λ</sup>	670	81.7
Not reported <sup>λ</sup>	21	2.6
<b>Relations to adverse effects<sup>λ</sup></b>		
Clearly related to CHM formulas	17	2.1
clearly not related to the CHM formula	20	2.4
Clearly related to the control	111	13.5
Not reported and/or not identified	672	83.0
<b>Adverse effects occurred in intervention group<sup>*λ</sup></b>		
Skin damage	201	24.5
Digestive system damage	525	64.0
Urinary system damage	71	8.7
Systemic damage	415	50.6

<sup>†</sup> The percentages were calculated based on 3265.

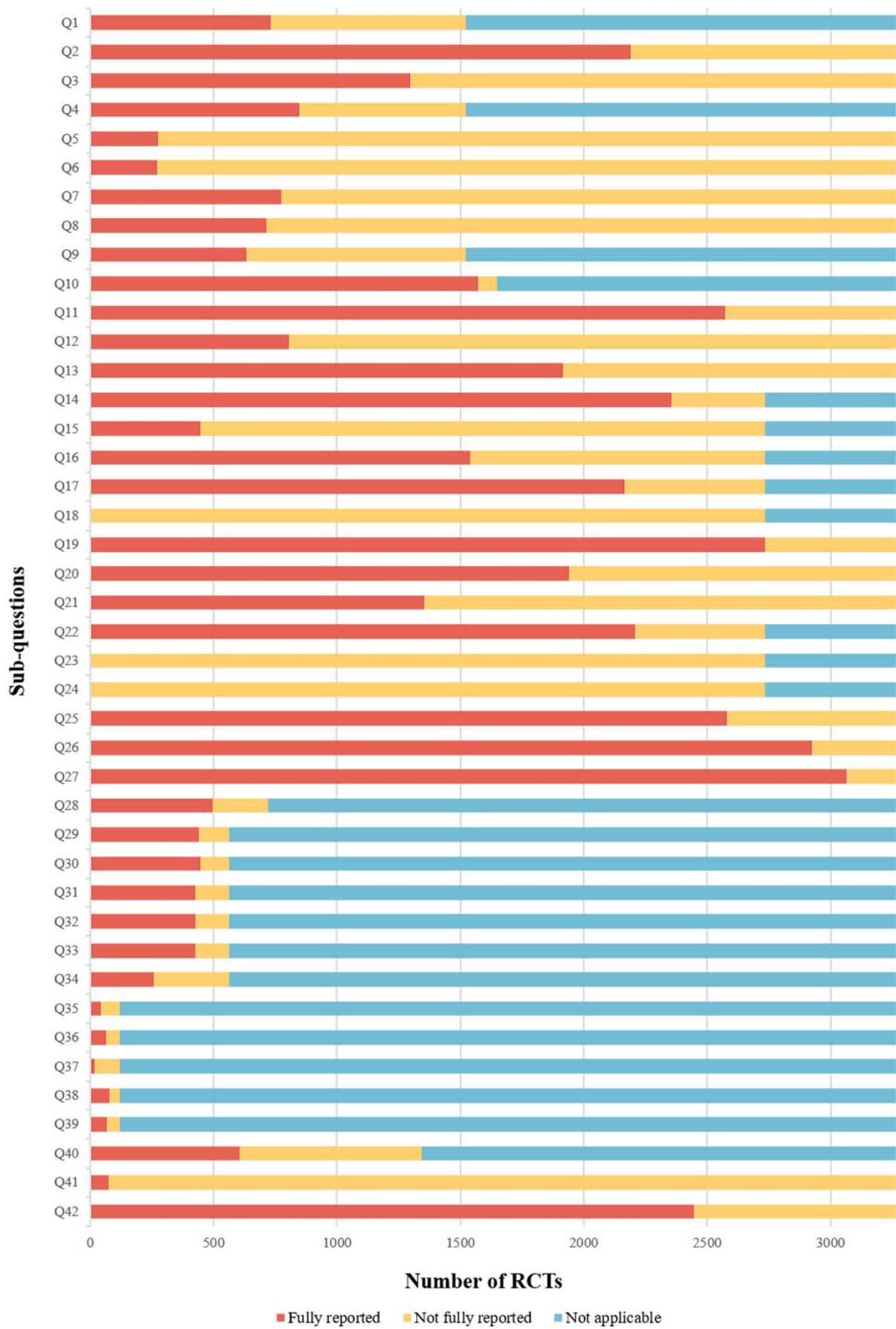
<sup>‡</sup> The percentages were calculated based on 1248.

<sup>#</sup> There were 864 studies that had reported the safety assessment during the treatment period, 27 studies reported the safety assessment at the end of treatment period, and 85 studies reported the safety assessment during and at the end of treatment.

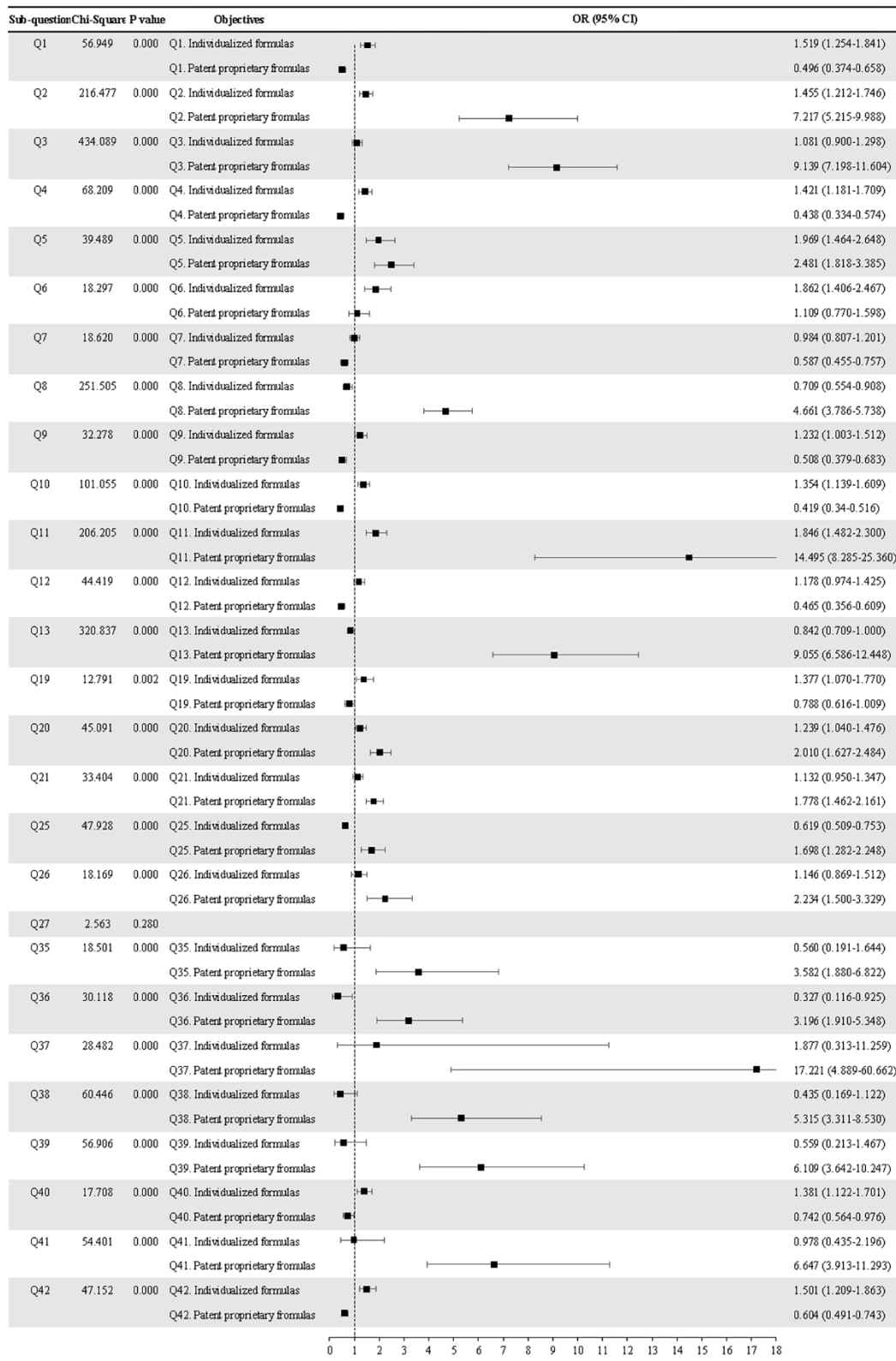
<sup>λ</sup> The percentages were calculated based on 820.

<sup>\*</sup> Several types of categories of adverse effects were recorded for one study so the sum of four categories is greater than the number of studies that reported adverse effects.

Additional file 8 Reporting details of 42 sub-questions among 3,265 studies



### Additional file 9 Reporting difference between three types of CHM formulas



Reporting difference between three types of CHM formulas. The Chi-square analyses were conducted to test the difference of reporting rate of 27 sub-questions in RCTs involving three types of CHM formulas, and the statistical significance was set at  $p < 0.05$ . The regression analyses utilized a reporting rate of fixed CHM formulas as the reference value, assigned a numerical value of 1. The results indicated that the reporting rate exceeded that of fixed formulas when the odds ratio (OR) value exceeded 1, accompanied by a statistically significant  $p$ -value of less than 0.05.

## **Additional file 10 Discussion about major results**

The CONSORT-CHM Formulas 2017 was developed in order to assist researchers in utilizing the checklist to report their findings more scientifically and completely [1]. It was therefore necessary to evaluate how compliantly the RCTs published after the CONSORT-CHM Formulas 2017 employing CHM formulas had included all the checklist items listed in the extension guideline. To our knowledge, this is the first comprehensive review to evaluate the reporting quality of RCTs that applied CHM formulas by the extended items of CONSORT-CHM Formulas 2017, with no limitation of diseases or specific formulas. Moreover, double check was applied to all 3,265 RCTs included in this review in the process of quality assessment to promote the accuracy of results.

In line with previous findings, the methodological quality was deficient in RCTs involving CHM formulas. Firstly, more than one-third of studies did not report the methods used to generate the random allocation sequence, which may generally yield biased results [2]. Secondly, there is a lack of big-sample, well-blinded RCTs which could be reviewed as the gold standards for clinical practices. Most of the trials recruited less than 100 participants and only 4.4% of trials used blinding. The difficulties in imitating the special texture, tastes, and smells of CHM formulas may be one of the primary reasons hindering the application of simulants and the conduction of blinding. The characteristics of the RCTs involving CHM formulas offered a glimpse into their practical application in clinical. As exemplified by the volume of literature we had to screen, the CHM formulas are applied in China extensively, without the conduction of relevant clinical trials legally international. Admittedly, the global acceptance and use of herbal medicines and related products continue to assume exponential increase [3-6]. However, it accounts for a significant portion of the Chinese retail market in treating common diseases [7-9], inversely only as biologically active supplements to foods for overall wellness and disease prevention instead of treatment for a specific health condition in European and American countries [10-11]. Moreover, the previous reviews also found that all RCTs employing CHM formulas were conducted in Chinese mainland, along with the Chinese participants [12-14]. Nevertheless, CHM formulas were widely used to treat various diseases according to the ICD-11 MMS categories in China, particularly in diseases of the digestive system (14.7%), genitourinary system (13.2%), and musculoskeletal system or connective tissue (10.8%). A number of examples exist in the literature of CHM formulas specifically being used as an effective therapy. The application of Chinese herbal medicine in the field of musculoskeletal tissue engineering involves the regulation of multiple signaling pathways in osteogenesis, angiogenesis, anti-inflammation, and chondrogenesis [15-19].

In line with previous findings, the paucity and limited knowledge of the potential adverse effects of CHM formulas leads to the identification of the safest and most effective therapies as well as the promotion of their rational use more difficult [20]. On the one hand, the reporting of CHM formulas is deficient. Numerous and irrefutable cases of poisoning have been reported in the literature [21-23]. However, only 39.3% of RCTs included in this review reported the safety outcomes and a mere few reported the reasons for harm occurrence on account of the CHM formula interventions. This makes it difficult to assign opposite roles to CHM formulas with undue respectability and credibility. On the other hand, conducting rigorous and sensible trials is crucial in determining the specific conditions where CHM formulas should be used. A prospective study, conducted by Tae-Young Jeong's team, found that herbal remedy alone is quite safe; but the risk of hepatotoxicity escalated when the combination of herbal medicines and conventional drugs was used in the treatment [24].

The overall reporting quality of RCTs with CHM formulas published in 2018-2022 was poor, which was assessed with the CONSORT-CHM Formulas 2017 [1]. The average reporting rate of 42 sub-questions was 52.1%, which means substantial information has remained unreported until the present. Notably, the results showed that the reporting rates of three extended items (Q18, Q23 and Q24) involved the safety administration and quality control of CHM formulas were extremely low, nearly at 0.0%. This indicates that, the mandatory safety or toxicological evaluation was missed in RCTs involving CHM formulas. The CHM formulas incorporated multiple medical substances, so detailed information about the authentication, modification, processing, and production of each substance is always considered of utmost importance [25]. Actually, due to the multiple component feature of raw medicinal materials, including the plant source, planting technology, harvest time, processing, manufacturing process, preservation complexity, drug regulation and application, etc, CHMs are often derived from complex systems, which may be one of the prime reasons to lead to difficulty in reporting detailed quality control and authentication methods of each medical substance of CHM formulas [26]. The detailed and standard quality control and authentication of each substance and the whole CHM formulas indeed contribute to the stability and safety of the clinical application. Research on quality standards of proprietary CHM formulas is

generally based on the application of thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC) for the content determination of specific components and the establishment of fingerprint profiles [27]. While there is no standard or method for the quality control of fixed formula which was the most commonly used type of CHM formulas (61.1%).

On the other hand, less than half of studies that targeted TCM Patterns reported the name of TCM Pattern in the title and abstract. TCM Pattern is a summary characteristic of pathologic changes at a certain stage of disease, which state the specific conditions where CHM formulas were applied [28]. The missing names of TCM Patterns could lead to confusion or misinterpretation of the indications of the CHM formulas, and the difficulty of evidence searching for readers and reviewers. At the same time, the names and forms of formulas in the abstract as well as two keywords “randomized controlled trial” alongside “Chinese herbal medicine formula” were deficient in most studies, which made it particularly challenging to identify the CHM formulas. The results are the same as another study that assessed the reporting quality of RCTs for the treatment of eczema with Chinese patent medicine [29]. When authors do not adhere to the checklist of CONSORT-CHM Formulas 2017, the reporting guideline does not achieve its full potential. As suggested by Cobo et al, when and how the reporting guideline is implemented within the editorial process and who takes responsibility for ensuring adherence to reporting guidelines could impact on RCT reporting [30]. And another review indicated that journal endorsement of the CONSORT Statement significantly influenced the completeness of reporting of trials published in medical journals [31]. Thus, strengthening the publicity and promotion of CONSORT-CHM Formulas 2017 via promoting journal endorsements may be the useful measure to promote the reporting quality of RCTs involving CHM formulas.

Previous studies have shown that the reporting quality of RCTs regarding the extended items has improved as a result of the CONSORT-CHM Formulas 2017 [32]. Although they were reported deficiently in “TCM background and explanation of the disease or the TCM Pattern”, “biomedical science explanation and/or TCM rationale about the CHM formulas”, “the source of CHM formulas”, and “the illustration of outcome measures with Pattern in detail”, the reporting quality rates of these items have increased obviously over the last five years. Moreover, the dosage of each medical substance and the composition and dosage of patent proprietary formulas were reported increasingly about from 75% to 90%. These findings demonstrated the efforts of authors in Chinese mainland to improve the reporting quality of RCTs employing CHM formulas.

Our study highlighted that the overall reporting completion rates of RCTs involving patent proprietary CHM formulas were higher than those with fixed or individualized formulas, but it is different in various sub-questions. Like the previous reviews [29, 33], the sections of “Title, abstract, and keywords” and “Methods- placebo control” were reported more completely in RCTs with patent proprietary CHM formulas than those with fixed CHM formulas, while the sections of “Methods-participants” and “Methods-outcomes” yielded the opposite results. Compared to fixed formulas and individualized formulas, the patent CHM formulas follow strict preparation procedure requirements and undergo rigorous quality testing processes, as well as subject to clear manufacturers, manual introduction, and quality control standards [34]. Indeed, these characteristics can impel researchers to provide clear criteria for the identification of specific targeted TCM patterns and TCM outcomes when they apply fixed or individualized CHM formulas in trials and clinical settings. Otherwise, researchers could prepare placebos that exhibit identical color, appearance, smell, and taste, to the patent proprietary CHM formulas with clear dosage forms and appearances, while it is difficult to imitate the fixed or individualized formulas that are always composed of raw materials [35]. Although more time is necessary to adopt recommendations from guidelines, we strongly suggest following the checklist of CONOSRT-CHM Formulas 2017 on RCTs, and the training courses and tools may be necessary to help authors comprehend and use the reporting guideline. Considering the different extended items for fixed CHM formulas, individualized CHM formulas, and patent proprietary CHM formulas, the subgroup analyses for specific sub-questions and overall reporting rate were both conducted to identify the influence of types of formulas on reporting quality. This was different from the data analysis in the protocol. Due to the characteristics of data and a more specific exploration of the influence of types of formulas on the reporting quality, we conducted a more detailed analysis, which was not predictable at the start of the project.

With respect to limitations, we acknowledge that every search strategy and choice of sources to search can still fail to capture every existing eligible record. First, we only limited the interventions as CHM formulas that were formulated and used based on traditional Chinese medicine principles, which means that we excluded the RCTs with only a single herbal medicine or drugs composed of chemical compositions extracted from herbal medicines. This may lead to risks of bias of included articles. Second,

we only included the articles published in English or Chinese, which may miss some RCTs involving CHM formulas that were published in other languages such as Japanese or Korean. Third, it cannot be determined whether RCTs not reported were actually not tested or tested but not published by the author(s) because the present study only relied on published data.

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