Title Page

Title:

CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation and Elaboration

Short title: CONSORT–CHM Formulas 2017

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Abstract

Chinese herbal medicine (CHM) formulas are the major components of traditional Chinese medicine (TCM) interventions. The general reporting quality of randomized clinical trials (RCTs) of CHM formulas is disappointing although there are CONSORT (Consolidated Standards of Reporting Trials) Statement extensions for herbal medicinal interventions and acupuncture interventions. A group of TCM clinical experts, methodologists, epidemiologists and editors has developed CONSORT–CHM Formulas through a comprehensive process including publication of the CONSORT–CHM Formulas (Draft), solicitation of comments, revision and finalization.

The CONSORT 2010 Statement was extended by introducing the idea of TCM *Pattern* and the features of CHM formulas. One new checklist sub-item, Keywords was added to facilitate the indexation and data searching. Seven of the 25 CONSORT checklist items, namely Title and Abstract, Background and Objectives, Participants, Interventions, Outcomes, Generalizability and Interpretation, are now elaborated upon and the explanation of Harms of CHM formulas is revised. Illustrative examples and explanations are also provided. We hope that CONSORT–CHM Formulas 2017 can improve the reporting quality of RCTs of CHM formulas.

Introduction

Traditional Chinese medicine (TCM), one of the oldest medical systems in the world, is based on its own unique principles and comprehensive theory. Today, it plays an indispensable role in the Chinese health care system while its impact worldwide is increasing (1). Since the first randomized controlled trial (RCT) of Chinese herbal medicine (CHM) formula was published in 1982 (2), tens of thousands clinical reports have been published (3). However, the quality of reporting is not optimal (4-6). Inadequate reporting not only compromises the values of the CHM but also may affect reviewers' and readers' judgments about the efficacy and safety of TCM in general, inviting skepticism and criticism (6). As a result, clinical practice and patient care suffer.

The Consolidated Standards of Reporting Trials (CONSORT) Statement and its extensions have substantially improved the reporting quality of RCTs (7). CONSORT extensions for herbal medicinal interventions (8) and acupuncture interventions (9) have been developed. However, neither of them can be used for reporting clinical trials of CHM formulas, which is the most common intervention in TCM practice. These CONSORT extensions do not adequately take into account the unique characteristics of TCM – theory, principles, formulas and Chinese medicinal substances (Boxes 1-4). Therefore, a new extension has been developed, to guide the reporting of trials using CHM formulas.

Methods for the development of CONSORT–CHM Formulas 2017

The development of CONSORT–CHM Formulas (formerly known as CONSORT for TCM) has been a comprehensive process. The first draft of CONSORT–CHM Formulas, including a 22-item checklist and a flow diagram, was published in Chinese (16) and English (17) in 2007 for open solicitation of comments. After that, the Draft was disseminated in workshops and academic conferences by executive members of the working group to attract further discussion. A series of papers on the significance of the CHM formula extension (18), study design rationale (19), CHM

formula composition (20), outcome measures (21), adverse effects (22), and further development (23) were published in Chinese and/or English.

Based on the comments and suggestions received, and on the 2010 version of CONSORT Statement (24), executive members of the working group discussed and revised this extension in Chengdu in late 2012. A consensus meeting, including executive members of working groups, 12 TCM clinical trial experts from China and two herbal medicine experts from Korea, was held in Beijing, China in June 2013. After the meeting, a further revision was made by executive members and circulated to the working group members. The executive working group finalized the recommendation at the end of 2016.

Highlights of CONSORT–CHM Formulas 2017

CONSORT–CHM Formulas 2017 includes the key concepts of *Pattern* and the features of CHM formulas. With regard to the Checklist, compared to CONSORT 2010, CONSORT–CHM Formulas includes one new sub-item, Keywords (Item 1c). It elaborates on seven of 25 CONSORT checklist items, namely Title and Abstract (Item 1a and 1b), Background and Objectives (Item 2a and 2b), Participants (Item 4a), Interventions (Item 5), Outcomes (Item 6a), Generalizability (Item 21) and Interpretation (Item 22), and revises the explanation of Harms specific to CHM formulas (Item 19). The items of Template for Intervention Description and Replication (TIDieR) are also combined in this extension (25).

The Checklist is presented in **Table 1,** for which elaborations of CHM formulas are in italicized. Explanations of corresponding items are given below while available published examples of good reporting are illustrated in Appendix 1. There is no modification for the CONSORT flow diagram.

Extension of CONSORT 2010 to CONSORT–CHM Formulas

Title, abstract and keywords

Item 1a

- Standard CONSORT item: Identification as a randomized trial in the title
- *CHM Formulas extension: Statement of whether the trial targets on a TCM Pattern, a Western medicine-defined disease or a Western medicine-defined disease with a specific TCM Pattern, if applicable*

Item 1b

- Standard CONSORT item: Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts [26,27])
- *CHM Formulas extension: Illustration of the name and form of the formula used, and the TCM Pattern applied, if applicable*

Item 1c

- *New CONSORT item for CHM Formulas extension: Determination of appropriate keywords, including "Chinese herbal medicine formula" and "randomized control trial"*

Explanation – Every scientific paper should have a self-explanatory title, comprehensive abstract and appropriate keywords. These are the tags by which readers retrieve relevant literatures from bibliographic databases. However, identifying RCTs of CHM formulas is particularly challenging (3). In general, authors give only the name of the CHM formula and the targeting disease in the keywords. Different from conventional medicine, the name of a CHM formula can be an English translation, a Chinese *PinYin* or just an acronym. It may be difficult for readers to determine whether it is a Chinese herbal intervention or not. When authors use the general term "Chinese herbal medicine", they can be referring to a Chinese medicinal component, single herb or compound formula. This vagueness, inconsistency and incompleteness impede access to and

dissemination of information from clinical trials of CHM formulas, and discourage secondary studies. To ensure that a CHM study is appropriately indexed and easily identified, a new CONSORT sub-item "Keywords (Item 1c)" is recommended. Apart from the name of intervention, "Chinese herbal medicine formula" and "randomized controlled trial" are recommended.

Background and Objectives

Item 2a

- Standard CONSORT item: Scientific background and explanation of rationale
- *CHM Formulas extension: Statement with biomedical science approaches and/or TCM approaches*

Item 2b

- Standard CONSORT item: Specific objectives or hypotheses
- *CHM Formulas extension: 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*

Explanation – In the introduction of a scientific paper, it is important to provide the background and underlying rationale of study design. For any study of CHM formulas, whether the rationale is on the basis of biomedical science findings, TCM theory or both should be well elucidated. It should preferably include a reference to a pilot study or literature review. Moreover, any evidence of the benefits and harms of the CHM formula to be studied and its active ingredients should also be reported.

The objectives or hypotheses are the questions that the trial is designed to answer. Whether the CHM formula targets on a Western medicine-defined disease, a *Pattern* or a Western medicine-defined disease with a specific *Pattern* should be clarified. In this way, readers can easily

understand which conditions are targeted in the trial, and the results will be more easily applied in clinical practice.

Participants

Item 4a

- Standard CONSORT item: Eligibility criteria for participants
- *CHM Formulas extension: Statement of whether participants with a specific TCM Pattern were recruited, in terms of i) diagnostic criteria, and ii) inclusion and exclusion criteria. All criteria used should be universally recognized, or reference given to where detailed explanation can be found*

Explanation - *Pattern* plays an important role in determining therapeutic principles. How the *Pattern* is diagnosed and what criteria are used for including and excluding participants should be comprehensively described if *Pattern* concept is involved in the participant selection. It is crucial to cite the nationally or internationally recognized *Pattern* diagnosis criteria in the study. Starting from the 1980's, various diagnostic criteria for *Pattern* of specific diseases have been published, such as the Reference Criteria of Deficiency Syndrome Diagnosis (30), the Diagnosis Criteria of Blood Stasis (31), and the Criteria of Diagnosis and Therapeutic Effect of Diseases and Syndromes in TCM (32). If standardized diagnostic criteria of *Pattern* are not available, authors should clearly explain how the criteria for their studies were developed, and how these criteria were applied in the trial. Such information is necessary for readers to interpret and repeat the study.

Interventions

Item 5

- Standard CONSORT item: The interventions for each group with sufficient details to allow replication, including how and when they were actually administered

- *CHM Formulas extension: Description[s] for different types of formulas should include the following:*

5A. For fixed CHM formulas

1. *Name, source and dosage form (e.g. decoction, granules, power)*
2. *Name, source, processing method and dosage of each medical substance. Names of substances should be presented in at least two languages: Chinese (PinYin), Latin or English. Names of the parts of the substances used should be specified*
3. *Authentication method of each ingredient, and how, when, where, by whom it was conducted; statement of whether any voucher specimen were retained, and if yes, where they were kept and whether they are accessible*
4. *Principles, rationale and interpretation of forming the formula*
5. *Reference(s) as to the efficacy of the formula, if any*
6. *Pharmacological study results of the formula, if any*
7. *Production method of the formula, if any*
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*
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*
10. *Dosage of the formula, and how the dosage was determined*
11. *Administration route (e.g. oral, external)*

5B. For individualized CHM formulas

1. *See recommendations 5A 1-11*
2. *Additional information: how, when and by whom the formula was modified.*

5C. For patent proprietary CHM formulas

1. *Reference to publicly available materials, such as Pharmacopeia, for the details about the composition, dosage, efficacy, safety, and quality control of the formula*
2. *Illustration the details of the formula, namely i) the proprietary product name (i.e. brand name), ii) name of manufacturer, iii) lot number, iv) production date and expiry date, v) name and percentage of added materials; vi) any additional quality control measures were conducted*
3. *Statement of whether the patent proprietary formula is used in the trial for the condition which is identical to the publicly available reference*

5D. Control groups

-Placebo control

1. *Name and amount of each ingredient*
2. *Description of the similarity of placebo with the intervention (e.g. color, smell, taste, appearance, packaging)*
3. *Quality control and safety assessment, if any*
4. *Administration route, regimen and dosage*
5. *Production information: where, when, how by whom the placebo was produced*

-Active control

1. *If a CHM formula was used, see the recommendations 5A to 5C*

2. *If a chemical drug was used, see Item 5 of CONSORT statement (24)*

Explanation – Chinese herbal interventions are always in the form of formulas with multiple medical substances. The reproducibility of a CHM formula is highly dependent on whether the substances and related authentication, modification, processing and production are reported in enough detail. Otherwise, the whole study cannot be replicated by other researchers (33). Therefore, item 5 (Interventions) is revised to include the reporting recommendations for common types of CHM formulas (fixed, individualized and patent proprietary) and their controls (placebo and active). Also, the ideas of TIDieR Checklist items were embedded (25). Readers can follow the reporting items for each type of CHM formulas one by one.

In addition, quality control methods used for the substances and preparation of the formula are recommended to be reported and should detail any references used, such as pharmacopoeias from different countries and regions. The Chinese Pharmacopoeia is an official monograph citing the preparation details and quality control of 2165 crude Chinese medicinal substances, patent proprietary drugs and extracts, etc. (34). The Japanese Pharmacopeia records the methods of preparations and quality control of 148 formulations (mainly herbal extracts) (35). All these are important references that authors can cite in reporting the details of CHM formulas used in RCTs.

The choice of control group affects the conclusions that can be drawn from the study, such as whether the outcomes are caused by the treatment effects, natural progression of the disease, observer or patient expectations, or any other potential influences (36). Among these, placebo design of CHM formulas has been the topic of lively discussion for years. It is not only a science but also an art for investigators to design a placebo similar to the formula product with identical color, smell, taste and texture yet without active properties (36). Transparently reporting the name and amount of each ingredient, processing method, quality control and safety assessment,

administration route, regimen and dosage, and success of masking (if applicable) are essential for readers to assess the validity of study results and to be able to duplicate the study protocol.

We emphasize that the information about quality, safety and efficacy of CHM formulas should be reported in detail. A complete description helps readers to easily understand the results of a trial. Any novel application of a fixed or patent proprietary CHM formula for conditions different from those traditionally treated, should be well illustrated by providing underlying rationale and supporting evidence. Further, we understand that some items in the checklist, especially quality control methods, are not easily achieved at the current stage. By making the reporting recommendation more practicable, we allow a compromise proposal with "if any", but it does not mean that these items are not crucial. From the beginning of trial preparation, efforts should be made to produce the highest quality study in every aspect, including the preparation of CHM interventions. Following these guidelines will make the trial transparent, secure the safety of participants, and thereby increase the scientific value of the trial results.

Outcomes

Item 6a

- Standard CONSORT item: Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
- *CHM Formulas extension: Illustration of outcome measures with Pattern in detail*

Explanation - Valid and reliable outcome measures are prerequisites to justify any conclusion regarding the efficacy and safety of an intervention. Commonly used indexes for outcome measures in an RCT of a CHM formula can be categorized into Western medicine-specific outcomes and TCM-specific outcomes (21). The former is often measured using objective biomedical indexes, such as blood tests, blood pressures, X-rays, etc. The latter is more likely to include symptoms and

signs assessed by TCM diagnostic methods. As being outcome measures, symptoms and signs, as well as *Pattern,* can be measured in terms of occurrence (e.g. presence or absence of individual symptom or sign), a rating scale (e.g. 7-point ordinal scale) (37), or by validated *Pattern* assessment questionnaire (38). In addition, how and by whom the outcomes with *Pattern* are assessed should be reported. All methods used to enhance the quality of measurement should be reported. Supporting references, underlying rationales and details of assessment procedures must be clearly described.

Harms

Item 19

- Standard CONSORT item: All important harms or unintended effects in each group (for specific guidance see CONSORT for harms [28]).
- *CHM Formulas extension: (There is no extension for this item)*

Explanation – It is widely and mistakenly assumed that Chinese medicinal substances originating from natural sources are harmless. Therefore, harms are less emphasized in RCTs of CHM formulas (16). In general, adverse effects derive from 1) unpredictable adverse events, 2) improper use, 3) contamination,4) misidentification, and 5) drug-herb interactions (23). For CONSORT–CHM Formulas, any harms or suspected harms of a formula should be reported and explained in terms of TCM theory and/or biomedical science. Secondly, outcome measures specific to safety assessment should be addressed. Thirdly, the rationale for selection and the specific assessment methods should be defined with supporting references. Fourthly, the details of all adverse events (e.g. time of occurrence, frequency, degree of severity, number of cases who withdraw or reduce their doses) should be reported. If no adverse events reported, the author should make a statement, e.g., "no adverse events were reported". Lastly, in the event of any adverse effects, interpretation about the potential underlying causality is recommended.

Generalizability

Item 21

- Standard CONSORT item: Generalizability (external validity, applicability) of the trial findings
- *CHM Formulas extension: Discussion of how the formula works on different TCM Patterns or diseases*

Explanation – Each CHM formula is determined on the basis of *Pattern* differentiation. The same method of treatment can be applied to patients with different diseases, but with the same *Pattern*. On the other hand, different CHM formulas can be applied to patients with same disease but with different *Patterns*. Therefore, the applicability of trial findings to different *Patterns* of the same disease or same *Pattern* as manifest in different diseases can further be discussed.

Interpretation

Item 22

- Standard CONSORT item: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
- *CHM Formulas extension: Interpretation with TCM theory*

Explanation - *Pattern* is the core of TCM theory and the effectiveness of a formula depends on the accuracy of *Pattern* differentiation. Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence in terms of *Pattern* is crucial. Most importantly, because the formula is designed based on the *Pattern,* its application should follow the *Pattern* differentiation.

Discussion

Several CONSORT Extensions have been developed covering aspects of design, data and intervention (http://www.consort-statement.org/extensions). CONSORT–CHM Formulas is developed to expand CONSORT, applying the principles of transparency, consistency, and full disclosure in the use of CHM formulas in RCTs.

The Checklist of CONSORT–CHM Formulas was completed through extensive consultations with and solicitation of comments from epidemiologists, journal editors, clinical methodologists, clinical research experts and TCM clinicians for over a decade. It had been getting concerns from the peers. In December 2016 searches of the China Academic Journals Full-text Database (CKNI) and PubMed with “CONSORT for TCM” or “Consolidated Standards of Reporting Trials for Traditional Chinese Medicine” yielded 141 articles related to the CONSORT–CHM Formulas (Draft). Of these, 24 systematic reviews had used the Checklist to appraise the quality of included studies, and 70 articles had cited or supported adherence to the Draft when reporting RCTs of CHM formulas.

We understand that all requirements set in the Extension may not be easy to meet at this stage. We want to emphasize that all items are critically related to the quality of trial with CHM formulas. Trial quality relies on design, implementation and reporting. Therefore, researchers are expected to do their best starting from the study design, preparation and implementation, not only the final reporting stage.

The value of a recommendation ultimately depends on its usage. The CONSORT Statement has achieved great success in encouraging implementation of research-based recommendations, ensuring changes in practice and improving the general quality of RCTs. For better disseminating the CONSORT- CHM Formulas, specific strategies are indispensable. We hope to introduce the Extension to all TCM practitioners, researchers, peer reviewers and journal editors through medical programs, workshops and conferences. At same time, the working group continues to welcome and

collect comments and feedbacks from those in research or clinical practice, thus to revise CONSORT-CHM Formulas and keep it relevant. Further, journals can play an important role if they endorse the use of CONSORT–CHM Formulas. Journals wanting to endorse CONSORT-CHM Formulas can do so using the following language in their 'instructions to authors' section "[journal name] requires a completed CONSORT–CHM Formulas checklist as a condition of submission when reporting the results of clinical trial of CHM formula(s). Templates can be found at the CONSORT website (http://www.consort-statement.org/consort-statement/). You should ensure that your article, at minimum, reports content addressed by each item of the Checklist". Funding agencies can require the final report of a clinical trial following the recommendations of CONOSRT - CHM Formulas. Finally, special grants or awards can be set up for high quality RCTs of CHM formula adhering to the Extension as well.

Conclusion

The CONSORT–CHM Formulas 2017 expands the original CONSORT by applying its principles to the design, execution and reporting of RCTs of CHM formulas. We hope that the recommendations will promote better reporting and influence design methodology of RCTs testing CHM formulas. CONSORT-CHM Formulas 2017 will be periodically reappraised and further modified in order to ensure that it always well serves those doing clinical research of CHM formulas.

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Box 1. Fundamental of traditional Chinese medicine theory

Traditional Chinese medicine (TCM) is a unique and systematic medical system deeply influenced by the ancient Chinese philosophy. TCM believes that the human body is an organic whole, which is closely tied with the universe. Therefore, the activities of the nature can affect the human body directly or indirectly. Distinctive theories of *Qi*, Yin-Yang and Five Elements commonly used to understand and explain natural phenomena are fundamental of TCM theory (10).

Qi, also translated as "vital energy", is the basic substance that constitutes the universe. This basic understanding gives rise to the key medical concept in TCM. Yin and Yang are two relative opposite manifestations of *Qi*, namely Yang-*Qi* and Yin-*Qi*, and they are opposite and restraint, mutual dependent and supportive, equilibrium and waning, and mutual transformable. The theory of Yin and Yang forms the TCM theoretical structure. The theory of Five Elements holds that the universal is comprised with Wood, Fire, Earth, Metal and Water, and the phenomena of universal come from the movements and changes of the Elements. The interpromoting and interrestraining of the Elements are complementary. Promotion and restraint among the Elements bear each other, and only in this way can a relative harmony and coordination of the internal organs be maintained. All these fundamental ideas are especially important for understanding the structure of body, physiology, pathology, and for guiding clinical diagnosis and treatment in TCM (10).

Box 2. Therapeutic principle of traditional Chinese medicine

Therapeutic principles are the strategies, on the basis of differentiation of *Pattern*, to determinate appropriate treatment and select appropriate medicinal substances in order to form a formula. The identification of therapeutic principles is highly dependent on the accuracy of *Pattern* differentiation.

Determination of *Pattern* is the basis for developing the therapeutic principles, namely *bianzhenglunzhi*. *Pattern*, also called syndrome or *Zheng*, is a summary of the cause, nature and location of pathological changes at a certain stage of disease (11). Traditional Chinese medicine (TCM) practitioners comprehensively analyze all the clinical information collected by the four methods of diagnosis, i.e. inspection, auscultation and olfaction, interrogation and palpation with TCM theory, identify the etiology and pathogenesis, and differentiate the diagnosis of *Pattern*. In general, *Pattern* is formed by the elements of "location of disease" and "feature of disease" (12).

Differentiation of *Pattern* is the foundation for the identification of therapeutic principles, which is the crucial part in clinical practice. In a clinical trial, the concept of differentiation of Pattern should be carried out throughout the entire process with regard to the rationale of study design, selection of inclusion and exclusion criteria, formulation of Chinese medicine prescription, selection of outcome measures and data interpretation, etc..

Box 3. Chinese herbal medicine formula

Chinese herbal medicine (CHM) formulas are specific grouping or configurations of Chinese medicinal substances, that serve as tools for instituting treatment. The treatment is guided with traditional Chinese medicine (TCM) principles, which is determined by the *Pattern* differentiation (13). If the pattern of a condition is misdiagnosed, the treatment principles will be incorrect, and its derivative formula will be ineffective. Normally, the CHM Formula is a formed with more than two Chinese medicinal substances, although, there is a formula with one single herb. CHM formula is the most common intervention in TCM practice.

Preparation forms of CHM formulas include decoctions, granules, pills, tablets, capsules, powders, medicated tea and medicated wine, etc. Currently, common types of CHM formulas in randomized controlled trials (RCTs) are self-designed formulas and patent proprietary formulas. The former is formulated by the investigators and prepared under the supervision of investigators, for which the composition can be fixed or modified for individual subjects. The latter has been manufactured into fixed dosage form.

Box 4. Chinese medicinal substances

Chinese medicinal substances, also refer to Chinese materia medica, mainly originate from natural sources, including plants, animals, minerals and some chemical or biological products, which can be raw (fresh or dried) or processed (14). Because majority of Chinese medicinal substances comes from herbal plants, they are commonly called "Chinese herbal medicine".

The properties of Chinese medicinal substances include five aspects: four *qi*, five *Tastes*, lifting, lowering, floating and sinking capability, meridian affinity, and toxicity. Four *qi* refers to "cold", "hot", "warm" and "cool" of nature. The five *Tastes* are "acrid", "sweet", "sour", "bitter" and "salty". Meridian affinity indicates which meridian the medical substance acts upon selectively. Toxicity, in the broader sense, means that substances can eliminate the pathogenic factors and preserve heath; but in its narrower sense, refers to undesirable efforts (10).

The quality of medicinal substances varies with locations of cultivation, parts of collection, seasons of collections, processing methods, and potential contamination with heavy metals, pesticides or micotoxins. All these factors can affect the quality of Chinese herbal medicine formulas, as well as the assessment results about the efficacy and safety of formulas in a clinical trial (15).

Table 1 Checklist of Items for Reporting Trials of Chinese Herbal Medicine Formulas

Section / Tropic	Item No.	Standard CONSORT Checklist Item	Extension for CHM Formulas	Reported on page number
Title, abstract and keywords	1a	Identification as a randomized trial in the title	*Statement of whether the trial targets on a TCM Pattern, a Western medicine-defined disease or a Western medicine-defined disease with a specific TCM Pattern, if applicable*	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance, see CONSORT for abstracts[26, 27])	*Illustration of the name and form of the formula used, and the TCM Pattern applied, if applicable*	
	1c		*Determination of appropriate keywords, including "Chinese herbal medicine formula" and "randomized control trial"*	
Introduction				
Background and objectives	2a	Scientific background and explanation of rationale	*Statement with biomedical science approaches and/or TCM approaches*	
	2b	Specific objectives or hypotheses	*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*	
Methods				
Trial design	3a	Description of trial design (such as parallel, factorial), including allocation ratio		
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		
Participants	4a	Eligibility criteria for participants	*Statement of whether participants with a specific TCM Pattern were*	

			recruited, in terms of i) diagnostic criteria, and ii) inclusion and exclusion criteria. All criteria used should be universally recognized, or reference given to where detailed explanation can be found
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	*Description[s] for different types of formulas should include the following:* ***5A. For fixed CHM formulas*** *1. Name, source and dosage form (e.g. decoction, granules, power)* *2. Name, source, processing method and dosage of each medical substance. Names of substances should be presented in at least two languages: Chinese (PinYin), Latin or English. Names of the parts of the substances used should be specified* *3. Authentication method of each ingredient, and how, when, where, by whom it was conducted; statement of whether any voucher specimen were retained, and if yes, where they were kept and whether they are accessible* *4. Principle, rationale and interpretation of forming the formula* *5. Reference(s) as to the efficacy of the formula, if any* *6. Pharmacological study results of the formula, if any* *7. Production method of the formula, if any* *8. Quality control of each substance 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* *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

10.Dosage of the formula, and how the dosage was determined

11.Administration route (e.g. oral, external)

5B. For individualized CHM formulas

1. See recommendations 5A 1-11

2. Additional information: how, when and by whom the formula was modified.

5C. For patent proprietary CHM formulas

1. Reference to publicly available materials, such as Pharmacopeia, for the details about the composition, dosage, efficacy, safety, and quality control of the formula

2. Illustration the details of the formula, namely i) the proprietary product name (i.e. brand name), ii) name of manufacturer, iii) lot number, iv) production date and expiry date, v) name and percentage of added materials; and vi) any additional quality control measures were conducted

3. Statement of whether the patent proprietary formula is used in the trial for the condition which is identical to the publicly available reference

5D. Control groups

-Placebo control

1.Name and amount of each ingredient

2.Description of the similarity of placebo with the intervention (e.g. color, smell, taste, appearance, packaging)

3 Quality control and safety assessment, if any

4. Administration route, regimen and dosage

5. Production information: where, when, how by whom the placebo was

			produced *-Active control* *1.If CHM formula was used, see the recommendations 5A to 5C* *2.If chemical drug was used, see Item 5 of CONSORT statement (24)*
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	*Illustration of outcome measures with Pattern in detail*
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomization	8a	Method used to generate the random allocation sequence	
Sequence generation	8b	Type of randomization; details of any restriction (such as blocking and block size)	
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	

Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	
	13b	For each group, losses and exclusions after randomization, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific	*(There is no extension for this item)*

		guidance see CONSORT for harms[28])	
Discussion			
Limitations	20	Trial limitations; addressing sources of potential bias; imprecision; and, if relevant, multiplicity of analyses	
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	*Discussion on how the formula works on different TCM Patterns or diseases*
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	*Interpretation with TCM theory*
Other information			
Registration	23	Registration number and name of trial registry	
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

Note: CONSORT: Consolidated Standards of Reporting Trials; TCM: Traditional Chinese medicine; CHM Formulas: Chinese Herbal Medicine Formulas.

*The original CONSORT items are in normal text while elaborations for CHM formulas are in italicized text.

**We strongly recommend reading this checklist in conjunction with the CONSORT 2010 Explanation and Elaboration (29) for important clarifications on all original items of CONSORT Statement.