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Keywords:	postpartum, constipation, Chinese herbal medicine, systematic review, meta-analysis

Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis

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ABSTRACT

Introduction:

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. This systematic review aims to evaluate the efficacy and safety of Chinese herbal medicine for postpartum constipation.

Methods and analysis:

We will search PubMed (1946 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) to identify any eligible study. No language, publication date or status will be restricted.

The primary outcome is the spontaneous bowel movement. Secondary outcomes include stool consistency, quality of life, transit time, relief of constipation symptoms, and adverse events.

We will perform the meta-analysis when the comparisons and outcomes are similar across eligible studies. If the heterogeneity is not significant statistically ($P > 0.10$ or $I^2 < 50\%$), the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results.

Ethics and dissemination:

No ethical issues are foreseen because no primary data will be collected. The results will be published in a peer-reviewed scientific journal.

This protocol has been registered on PROSPERO (CRD42018093741).

Strengths and limitations of this study

- This is the first systematic review to evaluate the efficacy and safety of Chinese herbal medicine for postpartum constipation.
- This study will only consider parallel-group randomized controlled trials (RCTs) to provide unbiased estimates of treatment effects.
- The Prefered Reporting Items for Systematic reviews and Meta-Aanlyses guidelines for protocols (PRISMA-P) 2015 is followed.
- A large degree of heterogeneity in terms of methodological quality and outcome measures will likely pose challenges for study comparisons.

Introduction

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers[1]. A prospective study showed that the prevalence of constipation was 24% with 95% confidence interval 13-36% at three months postpartum in the united states[2]. A survey found that 25% and 11.6% of women suffered from constipation at three and twelve months postpartum in China, respectively[3].

The aetiology of postpartum constipation is multifactorial. The mode of delivery and pelvic floor injury may largely contribute to defecation disorders during the postpartum period[4]. Local trauma could be responsible for the anal sphincter spasm[5]. Furthermore, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, irregular meals due to baby-care and many other situations could also lead to constipation[6].

Postpartum constipation can lead to abdominal distension, abdominal pain, insomnia, inappetence, and so forth[7]. These symptoms have negative impacts on postpartum recovery, breastfeeding, newborn health, and so forth[8].

Conventional therapies for constipation include stool softener, prokinetic agent, osmotic and stimulant laxative, dietary manipulation, and so forth[9]. They may be associated with unwanted side effects, such as bloating, dehydration, a high recurrence rate after ceasing drugs, and abdominal pain[10]. According to clinical guidelines, no clinical recommendations have be provided for the management of postpartum constipation[8,11,12]. The choice of treatments for postpartum constipation remains a challenging clinical problem.

Chinese herbal medicine (CHM) is defined as a preparation derived from plants or parts of plants[13,14]. CHM includes a single herb or complex formula consisting of herbal ingredients[15]. The forms of CHM include tablet, pill, decoction, oral liquid, powder, injection liquid, and so forth[16].

CHM has become increasingly popular as an alternative therapy for constipation. A randomized double-blind trial showed that a hemp seed pill significantly increased the responder rate in complete spontaneous bowel movement when compared with placebo[17]. A multi-center randomized controlled trial found that a CHM decoction had a beneficial effect on reducing the cleveland constipation score and improving quality of life[18].

A 2009 systematic review examined the effectiveness of CHM interventions for functional constipation[19]. It showed that CHM was effective for functional constipation. However, no studies associated with postpartum constipation were included. Whether the evidence is transferrable to women diagnosed with postpartum constipation remains unclear.

Quite a few clinical trials found CHM could have a role to play in the management of postpartum constipation. For example, a clinical trial found that Xiaoyao powder significantly increased the effective rate when compared with polyethylene glycol[20]. Another trial suggests that a CHM enema treatment is more effective for relieving constipation symptoms of postpartum mothers than glycerine enema[21].

A 2014 Cochrane systematic review assessed the efficacy and safety of interventions for treating postpartum constipation[22]. Because of strict criteria, no eligible RCTs were included. Unfortunately, the potentially eligible studies from China could be missing as no Chinese medical databases were searched. And it has not been updated so far.

To sum up, the evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.

This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.

Methods

This protocol is developed following the Prefered Reporting Items for Systematic reviews and Meta-Aanlyses guidelines for protocols (PRISMA-P) 2015[23].

Inclusion criteria

Types of studies

Parallel-group randomized controlled trials (RCTs) will be included. Quasi-randomized controlled trials, cross-over trials and non-randomized controlled trials will be excluded. No language, publication date or status will be restricted.

Types of participants

Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery or caesarean section), gastrointestinal diseases and so forth.

The postpartum period ranges from an hour after the delivery of placenta to six weeks[8].

Participants should be clinically diagnosed with constipation according to the Rome Ⅱ/Ⅲ diagnostic criteria, clinical guidelines or defined by trialists.

Types of interventions

Experimental interventions

The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered.

Comparator interventions

The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted.

The following comparisons will be considered if available:

(1) CHM alone versus no treatment;

(2) CHM alone versus placebo;

(3) CHM alone versus another active treatment;

(4) CHM plus another active treatment versus another active treatment alone;

(5) CHM plus another active treatment versus placebo plus another active treatment.

Types of outcome measures

Primary outcomes

The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequecy of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,24-26].

Secondary outcomes

Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first

perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[24,27,28]. We will also consider other outcomes reported by the investigators when possible.

Data on adverse events (AEs) will be extracted and the incidence of AEs will be estimated if possible.

Search methods for identification of studies

Electronic searches

We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) to identify any eligible study.

The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews[19,22]. The detailed search strategy for the PubMed database is attached (appendix 1). The terms will be modified for other databases if necessary. No language, publication date or status will be restricted.

Searching other resources

Reference lists of primary studies and relevant reviews will be manually searched to identify additional references.

We will also conduct a search of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.

Data collection and analysis

Selection of studies

Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The results of the literature searches will be imported to the EndNote X7 software. Duplicates will be omitted using the EndNote.

The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection process[29]. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).

Data extraction and management

A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (JYL and SD) will independently extract the following information:

(1) General information (title, first author, year of publication, funding);

(2) Study characteristics (design, randomization, allocation. blinding, inclusion and exclusion criteria, sample size);

(3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery);

(4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration);

(5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).

If necessary, we will contact authors of included studies for providing further details or clarification.

Assessment of risk of bias in included studies

Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool[30]. The following seven domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias[30]. The risk of bias for each domain will be graded as low, high or unclear for each included study[30]. The overall risk of bias of a study will be estimated low only if all seven domains are rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).

Measures of treatment effect

For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs) [30]. If the same outcome is measured using different scales, the standardized mean difference (SMD) with 95% CI will be used to express intervention effects[30]. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes[30].

Dealing with missing data

We will contact original authors for requesting the missing data if possible. Only available data will be included in the primary analysis. However, extreme worst-case and best-case analysis will be used to assess the potential impact of the missing data in sensitivity analysis[31].

Assessment of heterogeneity

Statistical heterogeneity across included studies will be tested using Chi-square test and I^2 statistic. The heterogeneity is significant statistically when the P value based on Chi^2 test less than 0.10 or I^2 more than 50%[32,33]. If so, exploratory sensitivity or subgroup analyses will be performed to identify possible reasons[34].

Assessment of reporting biases

The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in a meta-analysis[30]. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis[30].

Data synthesis

We will perform the meta-analysis when the comparisons and outcomes were similar across eligible studies. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects[30]. Otherwise, the random-effect model will be used to provide more conservative results[30]. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible[30]. All statistical analyses will be performed by the RevMan 5.3 software. The statistical significance is defined as $P < 0.05$. If the meta-analysis is not feasible, we will provide a narrative description of the results.

Subgroup analysis and investigation of heterogeneity

If possible, subgroup analyses will be conducted based on the following variables:

(1) History of prenatal constipation;

(2) Frequency of delivery;

(3) Mode of delivery (vaginal delivery or caesarean section);

(3) History of gastrointestinal diseases;

(4) Type of comparisons;

(5) Type of preparations (such as decoction, granula, ointment and capsule);

(6) Different diagnostic criteria of constipation (Rome Ⅱ/Ⅲ diagnostic criteria,

clinical guidelines or defined by trialists);

The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance.

Sensitivity analysis

We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible:

(1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis[35];

(2) Impact of high risk of bias: removing studies in which overall risk of bias is high;

(3) Impact of selected models: fixed-effect models versus random-effect models;

(4) Impact of missing data: extreme worst-case analysis and best-case analysis[35].

Summary of findings' tables

Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system[30]. It will be categorized as high, moderate, low, or very low[30]. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome[30]. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).

Amendments

If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.

Ethics and dissemination

No ethical issues are foreseen because no primary data will be collected. This systematic review will provide a comprehensive review of the efficacy and safety of Chinese herbal medicine for postpartum constipation. It will contribute to the development of revelant clinical guidelines.

The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

Protocol registration:

This protocol has been registered on PROSPERO (CRD42018093741).

Contributors:

JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

Funding:

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Competing interests: None declared.

Ethics approval: Not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

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Appendix 1.

PubMed Search strategy:

1. EXP ‘Medicine, Chinese Traditional’/
2. (‘Traditional Chinese Medicine’ OR ‘Chung I Hsueh’ OR ‘Zhong Yi Xue’ OR ‘Chinese Traditional Medicine’ OR TCM).tw
3. EXP "Drugs, Chinese Herbal"/
4. (‘Chinese Herbal Drugs’ OR ‘Chinese Plant Extracts’ OR ‘Chinese herbal medicine’ OR CHM).tw
5. OR /1-4
6. EXP Postpartum Period/
7. Premature Birth/
8. Postnatal Care/
9. Pregnancy Complications/
10. (postpartum OR Puerperium OR post-partum OR ‘post partum’ OR postnatal OR post-natal OR ‘post delivery’ OR ‘after delivery’ OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR ‘breast feeding’ OR breast-feed OR breast-fed OR Lactation sucking OR ‘after birth’ OR childbirth OR child-birth OR Childbed OR childbad).tw
11. OR /6-10
12. Constipation/
13. (constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR ‘bowel movement’ OR ‘hard stool’ OR ‘lumpy stool’ OR constipat* OR ‘impacted stool’ OR ‘rock-like stool’ OR Impaction OR obstipation OR evacuation).tw
14. delayed bowel movement.tw
15. (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)).tw
16. colon transit.tw
17. intestinal motility.tw
18. OR /12-17
19. randomized controlled trial.pt
20. controlled clinical trial.pt
21. randomized.tw
22. placebo.tw
23. clinical trials as topic/
24. randomly .tw
25. trial.tw
26. OR/19-25
27. Animals/ NOT humans/
28. 26 NOT 27
29. 5 AND 11 AND 18 AND 28

PRISMA-P 2015 checklist

Section and topic	Item No	Page	Checklist item
Administrative information			
Title			
Identification	1a	1	Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis
Update	1b		No
Registration	2	2	This protocol has been registered on PROSPERO (CRD42018093741).
Authors:			
Contact	3a	1	Jingbo Zhai[1†], Yan Li[2†], Jingyi Lin[1], Shuo Dong[1], Jinhua Si[3*], Junhua Zhang[1*] [1]Research institute of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [2]School of Nursing, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [3]Library, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [†]Jingbo Zhai and Yan Li contributed equally. [*]Correspondence to Junhua Zhang, zjhtcm@foxmail.com; Jinhua Si, sjh665@163.com
Contributions	3b	9	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

Amendments	4	8	If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.
Support:			
Sources	5a	9	This study is supported by the Tianjin Education Commission ‘‘Innovative Team Training Program” [No. TD13-5047] and the National Natural Science Foundation of China [grant number 81703936].
Sponsor	5b	9	JBZ, JHS and JHZ are sponsors.
Role of sponsor or funder	5c	9	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JHS designed the search strategy. JBZ, JHS and JHZ drafted the manuscript. JBZ, JHS and JHZ reviewed and revised the manuscript.
Introduction			
Rationale	6	2-3	Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. The evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.
Objectives	7	3	This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.
Methods			
Eligibility criteria	8	3-5	Types of studies: Parallel-group randomized controlled trials (RCTs) will be included. Quasi-randomized controlled trials, cross-over trials and non-randomized controlled trials will be excluded. No language, publication date or status will be restricted. Types of participants: Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery

			or caesarean section), gastrointestinal diseases and so forth. The postpartum period ranges from an hour after the delivery of placenta to six weeks. Participants should be clinically diagnosed with constipation according to the Rome Ⅱ/Ⅲ diagnostic criteria, clinical guidelines or defined by trialists. Types of interventions: Experimental interventions The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered. Comparator interventions: The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted. The following comparisons will be considered if available: (1) CHM alone versus no treatment; (2) CHM alone versus placebo; (3) CHM alone versus another active treatment; (4) CHM plus another active treatment versus another active treatment alone; (5) CHM plus another active treatment versus placebo plus another active treatment. Types of outcome measures: Primary outcomes The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequecy of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline.

			Secondary outcomes Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[24,27,28]. We will also consider other outcomes reported by the investigators when possible. Data on adverse events (AEs) will be extracted and the incidence of AEs will be estimated if possible.
Information sources	9	5	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) to identify any eligible study. Reference lists of primary studies and relevant reviews will be manually searched to identify additional references. We will also conduct a search of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.
Search strategy	10	5	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) to identify any eligible study. The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews. The detailed search strategy for the PubMed database is attached (appendix 1). The terms

			will be modified for other databases if necessary. No language, publication date or status will be restricted. Reference lists of primary studies and relevant reviews will be manually searched to identify additional references. We will also conduct a search of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.
Study records			
Data management	11a	5	The results of the literature searches will be imported to the EndNote X7 software. Duplicates will be omitted using the EndNote.
Selection process	11b	5	Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection process. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).
Data collection process	11c	6	A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (JYL and SD) will independently extract the information. If necessary, we will contact authors of included studies for providing further details or clarification.
Data items	12	6	(1) General information (title, first author, year of publication, funding); (2) Study characteristics (design, randomization, allocation. blinding, inclusion and exclusion criteria, sample size);

			(3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery); (4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration); (5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).
Outcomes and prioritization	13	4-5	The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequecy of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline. Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [Maternal postpartum quality of life (MAPP-QOL) questionnaire], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain). We will also consider other outcomes reported by clincial trialists if possible. Data on adverse events (AEs) will be extracted and the incidence of AEs will be estimated if possible.
Risk of bias in individual studies	14	6	Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool. The following seven domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias. The risk of bias for each domain will be graded as low, high or unclear for each included study. The overall risk of bias of a study will be estimated low only if all seven domains are

			rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).
Data synthesis	15a	7	We will perform the meta-analysis when the comparisons and outcomes were similar across eligible studies.
	15b	6-7	For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs). If the same outcome is measured using different scales, the standardized mean difference (SMD) with 95% CI will be used to express intervention effects. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible. All statistical analyses will be performed by RevMan 5.3 software. The statistical significance is defined as $P < 0.05$.
	15c	7-8	If possible, subgroup analyses will be conducted based on the following variables: (1) History of prenatal constipation; (2) Frequency of delivery; (3) Mode of delivery (vaginal delivery or caesarean section); (3) History of gastrointestinal diseases; (4) Type of comparisons; (5) Type of preparations (such as decoction, granula, ointment and capsule); (6) Different diagnostic criteria of constipation (Rome Ⅱ/Ⅲ diagnostic criteria, clinical guidelines

			or defined by trialists); The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance. We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible: (1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis; (2) Impact of high risk of bias: removing studies in which overall risk of bias is high; (3) Impact of selected models: fixed-effect models versus random-effect models; (4) Impact of missing data: extreme worst-case analysis and best-case analysis.
	15d	7	If the meta-analysis is not feasible, we will provide a narrative description of the results.
Meta-bias(es)	16	7	The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in the same meta-analysis. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis.
Confidence in cumulative evidence	17	8	Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. It will be categorized as high, moderate, low, or very low. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).

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Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis

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Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis

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ABSTRACT

Introduction:

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. This systematic review aims to evaluate the efficacy and safety of Chinese herbal medicine for postpartum constipation.

Methods and analysis:

We will search PubMed (1946 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study. No restriction will be put on the language, publication date or status of the study.

The primary outcome will be the spontaneous bowel movement. Secondary outcomes will be stool consistency, quality of life, transit time, relief of constipation symptoms, and adverse events.

We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations. If the heterogeneity is not significant statistically ($P > 0.10$ or $I^2 < 50\%$), the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results.

Ethics and dissemination:

No ethical issues are foreseen because no primary data will be collected. The

results will be published in a peer-reviewed scientific journal.

This protocol has been registered on PROSPERO (CRD42018093741).

Strengths and limitations of this study

- This is the first systematic review to evaluate the efficacy and safety of Chinese herbal medicine for postpartum constipation.
- This study will only consider parallel-group randomized controlled trials (RCTs) to provide unbiased estimates of treatment effects.
- The Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines for protocols (PRISMA-P) 2015 is followed.
- A large degree of heterogeneity in terms of methodological quality and outcome measures will likely pose challenges for study comparisons.

Introduction

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers[1]. A prospective study showed that the prevalence of constipation was 24% with 95% confidence interval 13-36% at three months postpartum in the United States [2]. A survey found that 25% and 11.6% of women suffered from constipation at three and twelve months postpartum in China, respectively[3].

The aetiology of postpartum constipation is multifactorial. The mode of delivery and pelvic floor injury may largely contribute to defecation disorders during the postpartum period[4]. Local trauma could be responsible for the anal sphincter spasm[5]. Furthermore, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, and irregular meals due to baby-care as well as many other situations could also lead to constipation[6]. Obviously, some factors account for both functional constipation in adults and postpartum constipation. Others are only associated with postpartum constipation.

Postpartum constipation can lead to abdominal distension, abdominal pain, insomnia, inappetence, and so forth[7]. These symptoms have negative impacts on postpartum recovery, breastfeeding, newborn health, and so forth[8].

Conventional therapies for constipation include stool softener, prokinetic agent, osmotic and stimulant laxative, dietary manipulation, and so forth[9]. They may be associated with unexpected side effects, such as bloating, dehydration, a high recurrence rate after ceasing drugs, and abdominal pain[10]. According to clinical guidelines, no clinical recommendations have be provided for the management of postpartum constipation[8,11,12]. The choice of treatments for postpartum constipation remains a challenging clinical problem.

Chinese herbal medicine (CHM) is defined as a preparation derived from plants

or parts of plants[13,14]. CHM includes a single herb or complex formula consisting of herbal ingredients[15]. The forms of CHM include tablet, pill, decoction, oral liquid, powder, injection liquid, and so forth[16].

CHM has become increasingly popular as an alternative therapy for constipation. A randomized double-blind trial showed that a hemp seed pill significantly increased the responder rate in complete spontaneous bowel movement when compared with placebo[17]. A multi-center randomized controlled trial (RCT) found that a CHM decoction had a beneficial effect on reducing the Cleveland constipation score and improving quality of life[18].

A 2009 systematic review examined the effectiveness of CHM interventions for functional constipation[19]. It showed that CHM was effective for functional constipation. However, no studies associated with postpartum constipation were included. Whether the evidence is transferrable to women diagnosed with postpartum constipation remains unclear.

Many clinical trials found that CHM was beneficial for the management of postpartum constipation. For example, a clinical trial found that Xiaoyao powder significantly increased the effective rate when compared with polyethylene glycol[20]. Another trial suggested that a CHM enema treatment was more effective for relieving constipation symptoms of postpartum mothers than glycerine enema[21].

A 2014 Cochrane systematic review assessed the efficacy and safety of interventions for treating postpartum constipation[22]. Because of strict criteria, no eligible RCTs were included. Unfortunately, the potentially eligible studies from China could be missed as no Chinese medical databases were searched. And it has not been updated so far.

To sum up, the evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.

This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.

Methods

This protocol is developed following the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines for protocols (PRISMA-P) 2015[23].

Inclusion criteria

Types of studies

Parallel-group RCTs will be included. No restriction will be put on the language,

publication date or status of the study.

Types of participants

Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery or caesarean section), gastrointestinal diseases and so forth.

The postpartum period ranges from an hour after the delivery of placenta to six weeks[8].

Participants should be clinically diagnosed with constipation according to the Rome Ⅱ or Ⅲ diagnostic criteria, Bristol stool form scale, clinical guidelines or defined by trialists. The Rome II Criteria for constipation should include at least two of the following symptoms lasting for 12 weeks or more over the period of a year: (1) Straining with more than 25% of defecations, (2) Hard stool with more than 25% of defecations, (3) Feeling of incomplete evacuation with more than 25% of defecations, (4) Sensation of anorectal obstruction with more than 25% of defecations, (5) Manual maneuvers to facilitate more than 25% of defecations, (6) Fewer than three bowel movements per week, (7) Insufficient criteria for irritable bowel syndrome[24]. The Rome III Criteria for functional constipation should include two or more of the following: (1) Straining during defecation for at least 25% of bowel movements, (2) Lumpy or hard stools in at least 25% of defecations, (3) Sensation of incomplete evacuation for at least 25% of defecations, (4) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (5) Manual maneuvers to facilitate at least 25% of defecations, (6) Fewer than 3 defecations per week, (7) Loose stools are rarely present without the use of laxatives, (8) There are insufficient criteria for irritable bowel syndrome[25]. These symptoms should start for at least 6 months prior to diagnosis and be present for the past three months[25].

Types of interventions

Experimental interventions

The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered.

Comparator interventions

The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted.

The following comparisons will be considered if available:

(1) CHM alone versus no treatment;

(2) CHM alone versus placebo;
(3) CHM alone versus another active treatment;
(4) CHM plus another active treatment versus another active treatment alone;
(5) CHM plus another active treatment versus placebo plus another active treatment.

Types of outcome measures

Primary outcomes

The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28].

Secondary outcomes

Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible.

Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.

Search methods for identification of studies

Electronic searches

We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study.

The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews[19,22]. The detailed search strategy is available at appendix 1. The terms will be modified for other databases if necessary. No language, publication date or status will be restricted.

Searching other resources

Reference lists of primary studies and relevant reviews will be manually searched to identify additional references.

We will also conduct a search on the website of ClinicalTrials.gov, the World

Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.

Data collection and analysis

Selection of studies

Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The results of the literature searches will be input to the EndNote X7 software. Duplicates will be omitted by using the EndNote.

The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection process[31]. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).

Data extraction and management

A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (JYL and SD) will independently extract the following information:

(1) General information (title, first author, year of publication, funding);

(2) Study characteristics (design, randomization, allocation. blinding, inclusion and exclusion criteria, sample size);

(3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery);

(4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration);

(5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).

If necessary, we will contact authors of the studies included for providing further details or clarification.

Assessment of risk of bias in included studies

Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool[32]. The following seven domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of

bias[32]. The risk of bias for each domain will be graded as low, high or unclear for each included study[32]. If a study described that it was a randomized controlled trial without reporting randomization method, we will contact authors for providing further details or clarification whenever possible. If the information about the sequence generation process is insufficient to permit judgment of 'Low risk' or 'High risk', this study will still be included in this systematic review and the risk of selection bias will be graded as 'unclear'.

The overall risk of bias of a study will be estimated low only if all seven domains are rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).

Measures of treatment effect

For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs) [32]. If the same outcome is measured using different scales, the standardized mean difference (SMD) with 95% CI will be used to express intervention effects[32]. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes[32].

Dealing with missing data

We will contact original authors for requesting the missing data if possible. Only available data will be included in the primary analysis. However, extreme worst-case and best-case analysis will be used to assess the potential impact of the missing data in sensitivity analysis[33].

Assessment of heterogeneity

Statistical heterogeneity across the studies included will be tested using Chi-square test and I^2 statistic. The heterogeneity is significant statistically when the P value based on Chi^2 test less than 0.10 or I^2 more than 50%[34,35]. If so, exploratory sensitivity or subgroup analyses will be performed to identify possible reasons[36].

Assessment of reporting biases

The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in a meta-analysis[32]. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis[32].

Data synthesis

We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects[32]. Otherwise, the random-effect model will be used to provide more conservative results[32]. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible[32]. All statistical analyses will be performed by the RevMan 5.3 software. The statistical significance is defined as $P < 0.05$. If the meta-analysis is not feasible, we will provide a narrative description of the results.

Subgroup analysis and investigation of heterogeneity

If possible, subgroup analyses will be conducted based on the following variables:

(1) History of prenatal constipation;

(2) Frequency of delivery;

(3) Mode of delivery (vaginal delivery or caesarean section);

(3) History of gastrointestinal diseases;

(4) Type of comparisons;

(5) Type of preparations (such as decoction, granula, ointment and capsule);

(6) Different diagnostic criteria of constipation (Rome Ⅱ / Ⅲ diagnostic criteria, clinical guidelines or defined by trialists);

(7) Language or publication date;

(8) The aetiology of postpartum constipation (pelvic floor injury, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, irregular meals, et al.);

The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance.

Sensitivity analysis

We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible:

(1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis[37];

(2) Impact of high risk of bias: removing studies in which overall risk of bias is high;

(3) Impact of selected models: fixed-effect models versus random-effect models;

(4) Impact of missing data: extreme worst-case analysis and best-case analysis[37].

Summary of findings' tables

Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system[30]. It will be categorized as high, moderate, low, or very low[30]. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome[30]. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).

Patient and Public Involvement

Patients and public were not involved in development of the research question and outcome measures, the design of this study, or the recruitment to and conduct of the study. There are no plans to disseminate the results to study participants. The burden of the intervention was not assessed by patients themselves for randomised controlled trials.

Amendments

If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.

Ethics and dissemination

No ethical issues are foreseen because no primary data will be collected.

The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

Discussion

This systematic review will provide a comprehensive review of the efficacy and safety of Chinese herbal medicine for postpartum constipation. The evidence from this review may benefit patients with postpartum constipation and clinicians. It will also contribute to the development of relevant clinical guidelines. However, a large degree of heterogeneity in terms of methodological quality and outcome measures will likely pose challenges for study comparisons.

Protocol registration:

This protocol has been registered on PROSPERO (CRD42018093741).

Contributors:

JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

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Competing interests: None declared.

Ethics approval: Not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

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Appendix 1.

PubMed Search strategy:

1. EXP ‘Medicine, Chinese Traditional’/
2. (‘Traditional Chinese Medicine’ OR ‘Chung I Hsueh’ OR ‘Zhong Yi Xue’ OR ‘Chinese Traditional Medicine’ OR TCM).tw
3. EXP "Drugs, Chinese Herbal"/
4. (‘Chinese Herbal Drugs’ OR ‘Chinese Plant Extracts’ OR ‘Chinese herbal medicine’ OR CHM).tw
5. OR /1-4
6. EXP Postpartum Period/
7. Premature Birth/
8. Postnatal Care/
9. Pregnancy Complications/
10. (postpartum OR Puerperium OR post-partum OR ‘post partum’ OR postnatal OR post-natal OR ‘post delivery’ OR ‘after delivery’ OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR ‘breast feeding’ OR breast-feed OR breast-fed OR Lactation sucking OR ‘after birth’ OR childbirth OR child-birth OR Childbed OR childbad).tw
11. OR /6-10
12. Constipation/
13. (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR ‘bowel movement’ OR ‘hard stool’ OR ‘lumpy stool’ OR constipat* OR ‘impacted stool’ OR ‘rock-like stool’ OR Impaction OR obstipation OR evacuation).tw
14. delayed bowel movement.tw
15. (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)).tw
16. colon transit.tw
17. (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)).tw
18. OR /12-17
19. randomized controlled trial.pt
20. controlled clinical trial.pt
21. randomized.tw
22. placebo.tw
23. clinical trials as topic/
24. randomly .tw
25. trial.tw
26. OR/19-25
27. Animals/ NOT humans/
28. 26 NOT 27
29. 5 AND 11 AND 18 AND 28

EMBASE Search strategy:

#1 Chinese medicine/exp

#2 ('Traditional Chinese Medicine' OR 'Chung I Hsueh' OR 'Zhong Yi Xue' OR 'Chinese Traditional Medicine' OR TCM): ti,ab,kw

#3 herbaceous agent/exp

#4 ('herbaceous drug' OR 'herbaceous plant' OR 'herbal agent' OR 'herbal material product' OR 'herbal preparation') .ti,ab,kw

#5 1-4/OR

#6 Puerperium/exp

#7 postnatal care/

#8 pregnancy/

#9 (postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR 'post delivery' OR 'after delivery' OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad) .ti,ab,kw

#10 6-9/OR

#11 Constipation/

#12 (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR 'bowel movement' OR 'hard stool' OR 'lumpy stool' OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation) .ti,ab,kw

#13 delayed bowel movement. ti,ab,kw

#14 (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)). ti,ab,kw

#15 colon transit. ti,ab,kw

#16 intestine motility/

#17 (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)). ti,ab,kw

#18 11-17/OR

#19 randomized controlled trial/epx

#20 'randomized controlled trial (topic)'/exp

#21 randomized. ti,ab,kw

#22 placebo. ti,ab,kw

#23 randomly . ti,ab,kw

#24 trial. ti,ab,kw

#25 19-24/ OR

#26 (exp animal/ or exp animal experiment/ or nonhuman/) not exp human/

#27 25 NOT 26

#28 #5 AND #10 AND #18 AND #27 AND [embase]/lim

Cochrane Central Register of Controlled Trials (CENTRAL) Search strategy:

#1 'MeSH descriptor: [Medicine, Chinese Traditional] explode all trees'

#2 MeSH descriptor: [Drugs, Chinese Herbal] explode all trees

#3 (Traditional Chinese Medicine):ti,ab,kw OR (Chung I Hsueh):ti,ab,kw OR (Zhong Yi Xue):ti,ab,kw OR (Chinese Traditional Medicine):ti,ab,kw OR ("TCM"):ti,ab,kw

#4 (Chinese Herbal Drugs) :ti,ab,kw OR (Chinese Plant Extracts) :ti,ab,kw OR (Chinese herbal medicine OR CHM) :ti,ab,kw

#5 OR /1-4

#6 MeSH descriptor: [Postpartum Period] explode all trees

#7 MeSH descriptor: [Premature Birth] explode all trees

#8 MeSH descriptor: [Postnatal Care] explode all trees

#9 MeSH descriptor: [Pregnancy Complications] explode all trees

#10 (postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR 'post delivery' OR 'after delivery' OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad) :ti,ab,kw

#11 OR /6-10

#12 MeSH descriptor: [Constipation] explode all trees

#13 (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR 'bowel movement' OR 'hard stool' OR 'lumpy stool' OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation) :ti,ab,kw

#14 delayed bowel movement:ti,ab,kw

#15 (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)):ti,ab,kw

#16 colon transit:ti,ab,kw

#17 (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)) :ti,ab,kw

#18 OR /12-17

#19 MeSH descriptor: [Randomized Controlled Trial] explode all trees

#20 MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees

#21 randomized. ti,ab,kw

#22 placebo. ti,ab,kw

#23 MeSH descriptor: [Controlled Clinical Trials as Topic] explode all trees

#24 randomly ti,ab,kw

#25 trial. ti,ab,kw

#26 OR/19-25

#27 #5 AND #11 AND #18 AND #26

Web of science Search strategy:

#1 TS=(Chinese Medicine OR Chung I Hsueh OR Zhong Yi Xue OR TCM OR Chinese Herbal Drugs OR Chinese Plant Extracts OR Chinese herbal medicine OR CHM)

#2 TS=(Postpartum OR Premature Birth OR Postnatal Care OR Pregnancy Complications OR postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR "post delivery" OR "after delivery" OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad)

#3 TS=(Constipation OR dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR "bowel movement" OR "hard stool" OR "lumpy stool" OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation)

#4 TS=(delayed bowel movement)

#5 TS=(bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*))

#6 TS= (colon transit)

#7 TS=(intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying))

#8 3-7/OR

#9 TS=Random*

#10 #1 AND #2 AND #8 AND #9

Chinese Biomedical Literatures database (CBM) Search strategy:
#1 产后 OR 分娩后 OR 产褥
#2 主题词=产后期/全部副主题词[不加权:扩展]
#3 主题词=产褥期/全部副主题词[不加权:扩展]
#4 #1~#3/OR
#5 便秘 OR 排便 OR 大便 OR 秘结腹胀 OR 腹痛
#6 主题词=便秘/全部副主题词[不加权:扩展]
#7 #5~#6/OR
#8 主题词=中草药/全部副主题词[不加权:扩展]
#9 主题词=中成药/全部副主题词[不加权:扩展]
#10 主题词=方剂/全部副主题词[不加权:扩展]
#11 中医 OR 中药 OR 中草药 OR 中医药 OR 中西医结合 OR 综合疗法 OR 传统疗法 OR 治疗 OR 疗效
12 #8~#11/OR
#13 随机 OR 盲法 OR 安慰剂
#14 主题词=随机对照试验(主题) /全部副主题词[不加权:扩展]
#15 主题词=随机分配[不加权:扩展]
#16 主题词=随机对照试验[不加权:扩展]
#17 #13~#16/OR
#18 #4 AND #7 AND #12 AND #17

China National Knowledge Infrastructure (CNKI) Search strategy:
(SU=产后 OR SU=分娩后 OR SU=产褥) AND (SU=便秘 OR SU=排便 OR SU=大便 OR SU=秘结 SU=腹胀 OR SU=腹痛) AND (SU=随机 OR FT=随机)

WANFANG data Search strategy:
主题:(产后+分娩后+产褥)*主题:(便秘+排便+大便+秘结+腹胀+腹痛)*随机

PRISMA-P 2015 checklist

Section and topic	Item No	Page	Checklist item
Administrative information			
Title			
Identification	1a	1	Chinese herbal medicine for postpartum constipation: protocol of systematic review and meta-analysis
Update	1b		No
Registration	2	2	This protocol has been registered on PROSPERO (CRD42018093741).
Authors:			
Contact	3a	1	Jingbo Zhai[1†], Yan Li[2†], Jingyi Lin[1], Shuo Dong[1], Jinhua Si[3*], Junhua Zhang[1*] [1]Institute of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [2]School of Nursing, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [3]Library, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [†]Jingbo Zhai and Yan Li contributed equally. [*]Correspondence to Junhua Zhang, zjhtcm@foxmail.com; Jinhua Si, sjh665@163.com
Contributions	3b	10	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

Amendments	4	9	If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.
Support:			
Sources	5a	10	This study is supported by the Tianjin youth top talent project 2015 (lead by Junhua Zhang) and the National Natural Science Foundation of China (grant number 81703936).
Sponsor	5b	10	JBZ, JHS and JHZ are sponsors.
Role of sponsor or funder	5c	10	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JHS designed the search strategy. JBZ, JHS and JHZ drafted the manuscript. JBZ, JHS and JHZ reviewed and revised the manuscript.
Introduction			
Rationale	6	2-3	Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. The evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.
Objectives	7	3	This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.
Methods			
Eligibility criteria	8	3-5	**Types of studies** Parallel-group RCTs will be included. No restriction will be put on the language, publication date or status of the study. **Types of participants** Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery

			or caesarean section), gastrointestinal diseases and so forth. The postpartum period ranges from an hour after the delivery of placenta to six weeks[8]. Participants should be clinically diagnosed with constipation according to the Rome Ⅱ or Ⅲ diagnostic criteria, Bristol stool form scale, clinical guidelines or defined by trialists. The Rome II Criteria for constipation should include at least two of the following symptoms lasting for 12 weeks or more over the period of a year: (1) Straining with more than 25% of defecations, (2) Hard stool with more than 25% of defecations, (3) Feeling of incomplete evacuation with more than 25% of defecations, (4) Sensation of anorectal obstruction with more than 25% of defecations, (5) Manual maneuvers to facilitate more than 25% of defecations, (6) Fewer than three bowel movements per week, (7) Insufficient criteria for irritable bowel syndrome[24]. The Rome III Criteria for functional constipation should include two or more of the following: (1) Straining during defecation for at least 25% of bowel movements, (2) Lumpy or hard stools in at least 25% of defecations, (3) Sensation of incomplete evacuation for at least 25% of defecations, (4) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (5) Manual maneuvers to facilitate at least 25% of defecations, (6) Fewer than 3 defecations per week, (7) Loose stools are rarely present without the use of laxatives, (8) There are insufficient criteria for irritable bowel syndrome[25]. These symptoms should start for at least 6 months prior to diagnosis and be present for the past three months[25]. **Types of interventions** **Experimental interventions** The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered. **Comparator interventions**

			The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted. The following comparisons will be considered if available: (1) CHM alone versus no treatment; (2) CHM alone versus placebo; (3) CHM alone versus another active treatment; (4) CHM plus another active treatment versus another active treatment alone; (5) CHM plus another active treatment versus placebo plus another active treatment. **Types of outcome measures** **Primary outcomes** The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28]. **Secondary outcomes** Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible. Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.

Information sources	9	5	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study.
Search strategy	10	5-6	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study. The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews[19,22]. The detailed search strategy is available at appendix 1. The terms will be modified for other databases if necessary. No language, publication date or status will be restricted. Reference lists of primary studies and relevant reviews will be manually searched to identify additional references. We will also conduct a search on the website of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.
Study records			
Data management	11a	6	The results of the literature searches will be imported to the EndNote X7 software. Duplicates will be omitted using the EndNote.
Selection process	11b	6	Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection

			process. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).
Data collection process	11c	6	A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (YYL and SD) will independently extract the information. If necessary, we will contact authors of included studies for providing further details or clarification.
Data items	12	6	(1) General information (title, first author, year of publication, funding); (2) Study characteristics (design, randomization, allocation, blinding, inclusion and exclusion criteria, sample size); (3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery); (4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration); (5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).
Outcomes and prioritization	13	5	**Primary outcomes** The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28]. **Secondary outcomes** Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools],

			transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible. Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.
Risk of bias in individual studies	14	6-7	Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool[32]. The following seven domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias[32]. The risk of bias for each domain will be graded as low, high or unclear for each included study[32]. If a study described that it was a randomized controlled trial without reporting randomization method, we will contact authors for providing further details or clarification whenever possible. If the information about the sequence generation process is insufficient to permit judgment of 'Low risk' or 'High risk', this study will still be included in this systematic review and the risk of selection bias will be graded as 'unclear'. The overall risk of bias of a study will be estimated low only if all seven domains are rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).
Data synthesis	15a	8	We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations.
	15b	8	For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs). If the same outcome is measured using different scales, the standardized

			mean difference (SMD) with 95% CI will be used to express intervention effects. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible. All statistical analyses will be performed by RevMan 5.3 software. The statistical significance is defined as $P < 0.05$.
	15c	8	If possible, subgroup analyses will be conducted based on the following variables: (1) History of prenatal constipation; (2) Frequency of delivery; (3) Mode of delivery (vaginal delivery or caesarean section); (3) History of gastrointestinal diseases; (4) Type of comparisons; (5) Type of preparations (such as decoction, granula, ointment and capsule); (6) Different diagnostic criteria of constipation (Rome I / II / III diagnostic criteria, clinical guidelines or defined by trialists); (7) Language or publication date; (8) The aetiology of postpartum constipation (pelvic floor injury, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, irregular meals, et al.); The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance. We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible:

			(1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis; (2) Impact of high risk of bias: removing studies in which overall risk of bias is high; (3) Impact of selected models: fixed-effect models versus random-effect models; (4) Impact of missing data: extreme worst-case analysis and best-case analysis.
	15d	8	If the meta-analysis is not feasible, we will provide a narrative description of the results.
Meta-bias(es)	16	7	The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in the same meta-analysis. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis.
Confidence in cumulative evidence	17	8-9	Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. It will be categorized as high, moderate, low, or very low. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).

BMJ Open

Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis

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Secondary Subject Heading:	Reproductive medicine, Gastroenterology and hepatology
Keywords:	postpartum, constipation, Chinese herbal medicine, systematic review, meta-analysis

Chinese herbal medicine for postpartum constipation: a protocol of systematic review and meta-analysis

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ABSTRACT

Introduction:

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. This systematic review aims to evaluate the efficacy and safety of Chinese herbal medicine for postpartum constipation.

Methods and analysis:

We will search PubMed (1946 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study. No restriction will be put on the language, publication date or status of the study.

The primary outcome will be the spontaneous bowel movement. Secondary outcomes will be stool consistency, quality of life, transit time, relief of constipation symptoms, and adverse events.

We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations. If the heterogeneity is not significant statistically ($P > 0.10$ or $I^2 < 50\%$), the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results.

Ethics and dissemination:

No ethical issues are foreseen because no primary data will be collected. The

results will be published in a peer-reviewed scientific journal.

This protocol has been registered on PROSPERO (CRD42018093741).

Strengths and limitations of this study

- This study will only consider parallel-group randomized controlled trials (RCTs) to provide unbiased estimates of treatment effects.
- No language or publication date will be restricted.
- The robustness of the pooled effects will be investigated by the sensitivity analysis.
- The extreme worst-case and best-case analysis will be used to assess the potential impact of the missing data.
- A large degree of heterogeneity in terms of methodological quality and outcome measures will likely pose challenges for study comparisons.

Introduction

Constipation is one of the most common gastrointestinal symptoms in postpartum mothers[1]. A prospective study showed that the prevalence of constipation was 24% with 95% confidence interval 13-36% at three months postpartum in the United States [2]. A survey found that 25% and 11.6% of women suffered from constipation at three and twelve months postpartum in China, respectively[3].

The aetiology of postpartum constipation is multifactorial. The mode of delivery and pelvic floor injury may largely contribute to defecation disorders during the postpartum period[4]. Local trauma could be responsible for the anal sphincter spasm[5]. Furthermore, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, and irregular meals due to baby-care as well as many other situations could also lead to constipation[6]. Obviously, some factors account for both functional constipation in adults and postpartum constipation. Others are only associated with postpartum constipation.

Postpartum constipation can lead to abdominal distension, abdominal pain, insomnia, inappetence, and so forth[7]. These symptoms have negative impacts on postpartum recovery, breastfeeding, newborn health, and so forth[8].

Conventional therapies for constipation include stool softener, prokinetic agent, osmotic and stimulant laxative, dietary manipulation, and so forth[9]. They may be associated with unexpected side effects, such as bloating, dehydration, a high recurrence rate after ceasing drugs, and abdominal pain[10]. According to clinical guidelines, no clinical recommendations have be provided for the management of

postpartum constipation[8,11,12]. The choice of treatments for postpartum constipation remains a challenging clinical problem.

Chinese herbal medicine (CHM) is defined as a preparation derived from plants or parts of plants[13,14]. CHM includes a single herb or complex formula consisting of herbal ingredients[15]. The forms of CHM include tablet, pill, decoction, oral liquid, powder, injection liquid, and so forth[16].

CHM has become increasingly popular as an alternative therapy for constipation. A randomized double-blind trial showed that a hemp seed pill significantly increased the responder rate in complete spontaneous bowel movement when compared with placebo[17]. A multi-center randomized controlled trial (RCT) found that a CHM decoction had a beneficial effect on reducing the Cleveland constipation score and improving quality of life[18].

A 2009 systematic review examined the effectiveness of CHM interventions for functional constipation[19]. It showed that CHM was effective for functional constipation. However, no studies associated with postpartum constipation were included. Whether the evidence is transferrable to women diagnosed with postpartum constipation remains unclear.

Many clinical trials found that CHM was beneficial for the management of postpartum constipation. For example, a clinical trial found that Xiaoyao powder significantly increased the effective rate when compared with polyethylene glycol[20]. Another trial suggested that a CHM enema treatment was more effective for relieving constipation symptoms of postpartum mothers than glycerine enema[21].

A 2014 Cochrane systematic review assessed the efficacy and safety of interventions for treating postpartum constipation[22]. Because of strict criteria, no eligible RCTs were included. Unfortunately, the potentially eligible studies from China could be missed as no Chinese medical databases were searched. And it has not been updated so far.

To sum up, the evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.

This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.

Methods

This protocol adheres to the Preferred Reporting Items for Systematic reviews and Meta-Analysis protocols (PRISMA-P) 2015[23].

Inclusion criteria

Types of studies

Parallel-group RCTs will be included. No restriction will be put on the language, publication date or status of the study.

Types of participants

Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery or caesarean section), gastrointestinal diseases and so forth.

The postpartum period ranges from an hour after the delivery of placenta to six weeks[8].

Participants should be clinically diagnosed with constipation according to the Rome Ⅱ or Ⅲ diagnostic criteria, Bristol stool form scale, clinical guidelines or defined by trialists. The Rome II Criteria for constipation should include at least two of the following symptoms lasting for 12 weeks or more over the period of a year: (1) Straining with more than 25% of defecations, (2) Hard stool with more than 25% of defecations, (3) Feeling of incomplete evacuation with more than 25% of defecations, (4) Sensation of anorectal obstruction with more than 25% of defecations, (5) Manual maneuvers to facilitate more than 25% of defecations, (6) Fewer than three bowel movements per week, (7) Insufficient criteria for irritable bowel syndrome[24]. The Rome III Criteria for functional constipation should include two or more of the following: (1) Straining during defecation for at least 25% of bowel movements, (2) Lumpy or hard stools in at least 25% of defecations, (3) Sensation of incomplete evacuation for at least 25% of defecations, (4) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (5) Manual maneuvers to facilitate at least 25% of defecations, (6) Fewer than 3 defecations per week, (7) Loose stools are rarely present without the use of laxatives, (8) There are insufficient criteria for irritable bowel syndrome[25]. These symptoms should start for at least 6 months prior to diagnosis and be present for the past three months[25].

Types of interventions

Experimental interventions

The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered.

Comparator interventions

The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted.

The following comparisons will be considered if available:

(1) CHM alone versus no treatment;

(2) CHM alone versus placebo;

(3) CHM alone versus another active treatment;

(4) CHM plus another active treatment versus another active treatment alone;

(5) CHM plus another active treatment versus placebo plus another active treatment.

Types of outcome measures

Primary outcomes

The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28].

Secondary outcomes

Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible.

Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.

Search methods for identification of studies

Electronic searches

We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study.

The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews[19,22]. The detailed search strategy is available at appendix 1. The terms will be modified for other databases if necessary. No language, publication date or status will be restricted.

Searching other resources

Reference lists of primary studies and relevant reviews will be manually searched

to identify additional references.

We will also conduct a search on the website of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.

Data collection and analysis

Selection of studies

Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The results of the literature searches will be input to the EndNote X7 software. Duplicates will be omitted by using the EndNote.

The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection process[31]. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).

Data extraction and management

A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (JYL and SD) will independently extract the following information:

(1) General information (title, first author, year of publication, funding);

(2) Study characteristics (design, randomization, allocation. blinding, inclusion and exclusion criteria, sample size);

(3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery);

(4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration);

(5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).

If necessary, we will contact authors of the studies included for providing further details or clarification.

Assessment of risk of bias in included studies

Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool[32]. The following seven domains will be assessed: random sequence generation, allocation

concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias[32]. The risk of bias for each domain will be graded as low, high or unclear for each included study[32]. If a study described that it was a randomized controlled trial without reporting randomization method, we will contact authors for providing further details or clarification whenever possible. If the information about the sequence generation process is insufficient to permit judgment of 'Low risk' or 'High risk', this study will still be included in this systematic review and the risk of selection bias will be graded as 'unclear'.

The overall risk of bias of a study will be estimated low only if all seven domains are rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).

Measures of treatment effect

For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs) [32]. If the same outcome is measured using different scales, the standardized mean difference (SMD) with 95% CI will be used to express intervention effects[32]. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes[32].

Dealing with missing data

We will contact original authors for requesting the missing data if possible. Only available data will be included in the primary analysis. However, extreme worst-case and best-case analysis will be used to assess the potential impact of the missing data in sensitivity analysis[33].

Assessment of heterogeneity

Statistical heterogeneity across the studies included will be tested using Chi-square test and I^2 statistic. The heterogeneity is significant statistically when the P value based on Chi^2 test less than 0.10 or I^2 more than 50%[34,35]. If so, exploratory sensitivity or subgroup analyses will be performed to identify possible reasons[36].

Assessment of reporting biases

The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in a meta-analysis[32]. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis[32].

Data synthesis

We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects[32]. Otherwise, the random-effect model will be used to provide more conservative results[32]. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible[32]. All statistical analyses will be performed by the RevMan 5.3 software. The statistical significance is defined as $P < 0.05$. If the meta-analysis is not feasible, we will provide a narrative description of the results.

Subgroup analysis and investigation of heterogeneity

If possible, subgroup analyses will be conducted based on the following variables:

(1) History of prenatal constipation;

(2) Frequency of delivery;

(3) Mode of delivery (vaginal delivery or caesarean section);

(3) History of gastrointestinal diseases;

(4) Type of comparisons;

(5) Type of preparations (such as decoction, granula, ointment and capsule);

(6) Different diagnostic criteria of constipation (Rome Ⅱ / Ⅲ diagnostic criteria, clinical guidelines or defined by trialists);

(7) Language or publication date;

(8) The aetiology of postpartum constipation (pelvic floor injury, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, irregular meals, et al.);

The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance.

Sensitivity analysis

We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible:

(1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis[37];

(2) Impact of high risk of bias: removing studies in which overall risk of bias is high;

(3) Impact of selected models: fixed-effect models versus random-effect models;

(4) Impact of missing data: extreme worst-case analysis and best-case analysis[37].

Summary of findings' tables

Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system[30]. It will be categorized as high, moderate, low, or very low[30]. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome[30]. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).

Patient and Public Involvement

Patients and public were not involved in development of the research question and outcome measures, the design of this study, or the recruitment to and conduct of the study. There are no plans to disseminate the results to study participants. The burden of the intervention was not assessed by patients themselves for randomised controlled trials.

Amendments

If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.

Ethics and dissemination

No ethical issues are foreseen because no primary data will be collected.

The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

Discussion

This systematic review will provide a comprehensive review of the efficacy and safety of Chinese herbal medicine for postpartum constipation. The evidence from this review may benefit patients with postpartum constipation and clinicians. It will also contribute to the development of relevant clinical guidelines. However, a large degree of heterogeneity in terms of methodological quality and outcome measures will likely pose challenges for study comparisons.

Protocol registration:

This protocol has been registered on PROSPERO (CRD42018093741).

Contributors:

JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

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Competing interests: None declared.

Ethics approval: Not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: The final report of this systematic review will be published in a peer-reviewed scientific journal, and data set will be made freely available.

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Appendix 1.

PubMed Search strategy:

1. EXP ‘Medicine, Chinese Traditional’/
2. (‘Traditional Chinese Medicine’ OR ‘Chung I Hsueh’ OR ‘Zhong Yi Xue’ OR ‘Chinese Traditional Medicine’ OR TCM).tw
3. EXP "Drugs, Chinese Herbal"/
4. (‘Chinese Herbal Drugs’ OR ‘Chinese Plant Extracts’ OR ‘Chinese herbal medicine’ OR CHM).tw
5. OR /1-4
6. EXP Postpartum Period/
7. Premature Birth/
8. Postnatal Care/
9. Pregnancy Complications/
10. (postpartum OR Puerperium OR post-partum OR ‘post partum’ OR postnatal OR post-natal OR ‘post delivery’ OR ‘after delivery’ OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR ‘breast feeding’ OR breast-feed OR breast-fed OR Lactation sucking OR ‘after birth’ OR childbirth OR child-birth OR Childbed OR childbad).tw
11. OR /6-10
12. Constipation/
13. (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR ‘bowel movement’ OR ‘hard stool’ OR ‘lumpy stool’ OR constipat* OR ‘impacted stool’ OR ‘rock-like stool’ OR Impaction OR obstipation OR evacuation).tw
14. delayed bowel movement.tw
15. (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)).tw
16. colon transit.tw
17. (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)).tw
18. OR /12-17
19. randomized controlled trial.pt
20. controlled clinical trial.pt
21. randomized.tw
22. placebo.tw
23. clinical trials as topic/
24. randomly .tw
25. trial.tw
26. OR/19-25
27. Animals/ NOT humans/
28. 26 NOT 27
29. 5 AND 11 AND 18 AND 28

EMBASE Search strategy:

#1 Chinese medicine/exp

#2 ('Traditional Chinese Medicine' OR 'Chung I Hsueh' OR 'Zhong Yi Xue' OR 'Chinese Traditional Medicine' OR TCM): ti,ab,kw

#3 herbaceous agent/exp

#4 ('herbaceous drug' OR 'herbaceous plant' OR 'herbal agent' OR 'herbal material product' OR 'herbal preparation') .ti,ab,kw

#5 1-4/OR

#6 Puerperium/exp

#7 postnatal care/

#8 pregnancy/

#9 (postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR 'post delivery' OR 'after delivery' OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad) .ti,ab,kw

#10 6-9/OR

#11 Constipation/

#12 (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR 'bowel movement' OR 'hard stool' OR 'lumpy stool' OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation) .ti,ab,kw

#13 delayed bowel movement. ti,ab,kw

#14 (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)). ti,ab,kw

#15 colon transit. ti,ab,kw

#16 intestine motility/

#17 (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)). ti,ab,kw

#18 11-17/OR

#19 randomized controlled trial/epx

#20 'randomized controlled trial (topic)'/exp

#21 randomized. ti,ab,kw

#22 placebo. ti,ab,kw

#23 randomly . ti,ab,kw

#24 trial. ti,ab,kw

#25 19-24/ OR

#26 (exp animal/ or exp animal experiment/ or nonhuman/) not exp human/

#27 25 NOT 26

#28 #5 AND #10 AND #18 AND #27 AND [embase]/lim

Cochrane Central Register of Controlled Trials (CENTRAL) Search strategy:

#1 'MeSH descriptor: [Medicine, Chinese Traditional] explode all trees'

#2 MeSH descriptor: [Drugs, Chinese Herbal] explode all trees

#3 (Traditional Chinese Medicine):ti,ab,kw OR (Chung I Hsueh):ti,ab,kw OR (Zhong Yi Xue):ti,ab,kw OR (Chinese Traditional Medicine):ti,ab,kw OR ("TCM"):ti,ab,kw

#4 (Chinese Herbal Drugs) :ti,ab,kw OR (Chinese Plant Extracts) :ti,ab,kw OR (Chinese herbal medicine OR CHM) :ti,ab,kw

#5 OR /1-4

#6 MeSH descriptor: [Postpartum Period] explode all trees

#7 MeSH descriptor: [Premature Birth] explode all trees

#8 MeSH descriptor: [Postnatal Care] explode all trees

#9 MeSH descriptor: [Pregnancy Complications] explode all trees

#10 (postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR 'post delivery' OR 'after delivery' OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad) :ti,ab,kw

#11 OR /6-10

#12 MeSH descriptor: [Constipation] explode all trees

#13 (dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR 'bowel movement' OR 'hard stool' OR 'lumpy stool' OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation) :ti,ab,kw

#14 delayed bowel movement:ti,ab,kw

#15 (bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*)):ti,ab,kw

#16 colon transit:ti,ab,kw

#17 (intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying)) :ti,ab,kw

#18 OR /12-17

#19 MeSH descriptor: [Randomized Controlled Trial] explode all trees

#20 MeSH descriptor: [Randomized Controlled Trials as Topic] explode all trees

#21 randomized. ti,ab,kw

#22 placebo. ti,ab,kw

#23 MeSH descriptor: [Controlled Clinical Trials as Topic] explode all trees

#24 randomly ti,ab,kw

#25 trial. ti,ab,kw

#26 OR/19-25

#27 #5 AND #11 AND #18 AND #26

Web of science Search strategy:

#1 TS=(Chinese Medicine OR Chung I Hsueh OR Zhong Yi Xue OR TCM OR Chinese Herbal Drugs OR Chinese Plant Extracts OR Chinese herbal medicine OR CHM)

#2 TS=(Postpartum OR Premature Birth OR Postnatal Care OR Pregnancy Complications OR postpartum OR Puerperium OR post-partum OR 'post partum' OR postnatal OR post-natal OR "post delivery" OR "after delivery" OR puerperal OR puerperium OR post-labour OR pregnancy OR pregnant OR gestation OR fetation OR conception OR maternity OR conceive OR breastfeeding OR 'breast feeding' OR breast-feed OR breast-fed OR Lactation sucking OR 'after birth' OR childbirth OR child-birth OR Childbed OR childbad)

#3 TS=(Constipation OR dyschezia OR obstipation OR constipation OR constipated OR astriction OR costive OR costiveness OR defecation OR defecatory OR defecate OR belly-bound OR oppilated OR oppilate OR oppilation OR Cacation OR "bowel movement" OR "hard stool" OR "lumpy stool" OR constipat* OR 'impacted stool' OR 'rock-like stool' OR Impaction OR obstipation OR evacuation)

#4 TS=(delayed bowel movement)

#5 TS=(bowel AND (function* OR habit* OR movement* OR symptom* OR motility OR stool*))

#6 TS= (colon transit)

#7 TS=(intestin* AND (motility OR mobility OR peristalsis OR propulsion OR movement OR emptying))

#8 3-7/OR

#9 TS=Random*

#10 #1 AND #2 AND #8 AND #9

Chinese Biomedical Literatures database (CBM) Search strategy:
#1 产后 OR 分娩后 OR 产褥
#2 主题词=产后期/全部副主题词[不加权:扩展]
#3 主题词=产褥期/全部副主题词[不加权:扩展]
#4 #1~#3/OR
#5 便秘 OR 排便 OR 大便 OR 秘结腹胀 OR 腹痛
#6 主题词=便秘/全部副主题词[不加权:扩展]
#7 #5~#6/OR
#8 主题词=中草药/全部副主题词[不加权:扩展]
#9 主题词=中成药/全部副主题词[不加权:扩展]
#10 主题词=方剂/全部副主题词[不加权:扩展]
#11 中医 OR 中药 OR 中草药 OR 中医药 OR 中西医结合 OR 综合疗法 OR 传统疗法 OR 治疗 OR 疗效
12 #8~#11/OR
#13 随机 OR 盲法 OR 安慰剂
#14 主题词=随机对照试验(主题) /全部副主题词[不加权:扩展]
#15 主题词=随机分配[不加权:扩展]
#16 主题词=随机对照试验[不加权:扩展]
#17 #13~#16/OR
#18 #4 AND #7 AND #12 AND #17

China National Knowledge Infrastructure (CNKI) Search strategy:
(SU=产后 OR SU=分娩后 OR SU=产褥) AND (SU=便秘 OR SU=排便 OR SU=大便 OR SU=秘结 SU=腹胀 OR SU=腹痛) AND (SU=随机 OR FT=随机)

WANFANG data Search strategy:
主题:(产后+分娩后+产褥)*主题:(便秘+排便+大便+秘结+腹胀+腹痛)*随机

PRISMA-P 2015 checklist

Section and topic	Item No	Page	Checklist item
Administrative information			
Title			
Identification	1a	1	Chinese herbal medicine for postpartum constipation: protocol of systematic review and meta-analysis
Update	1b		No
Registration	2	2	This protocol has been registered on PROSPERO (CRD42018093741).
Authors:			
Contact	3a	1	Jingbo Zhai[1†], Yan Li[2†], Jingyi Lin[1], Shuo Dong[1], Jinhua Si[3*], Junhua Zhang[1*] [1]Institute of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [2]School of Nursing, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [3]Library, Tianjin University of Traditional Chinese Medicine, 312 Anshanxi Road, Nankai District, Tianjin 300193, China; [†]Jingbo Zhai and Yan Li contributed equally. [*]Correspondence to Junhua Zhang, zjhtcm@foxmail.com; Jinhua Si, sjh665@163.com
Contributions	3b	10	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JBZ and YL drafted the protocol. JHS designed the search strategy. JBZ, YL, JYL, SD, JHS and JHZ drafted the manuscript. JBZ, YL, JYL, SD, JHS and JHZ reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript.

Amendments	4	9	If the protocol is modified, the change, the rationale and the date of any amendment will be described in the final report.
Support:			
Sources	5a	10	This study is supported by the Tianjin youth top talent project 2015 (lead by Junhua Zhang) and the National Natural Science Foundation of China (grant number 81703936).
Sponsor	5b	10	JBZ, JHS and JHZ are sponsors.
Role of sponsor or funder	5c	10	JBZ, JHS and JHZ conceived the study. JBZ, JHS and JHZ provided general guidance to the drafting of the protocol. JHS designed the search strategy. JBZ, JHS and JHZ drafted the manuscript. JBZ, JHS and JHZ reviewed and revised the manuscript.
Introduction			
Rationale	6	2-3	Constipation is one of the most common gastrointestinal symptoms in postpartum mothers. The choice of treatments for postpartum constipation remains a challenging clinical problem. Chinese herbal medicine has become increasingly popular as an alternative therapy for constipation. The evidence of the efficacy and safety of Chinese herbal medicine for postpartum constipation still remains inconclusive due to the lack of well-performed systematic reviews on this topic.
Objectives	7	3	This systematic review aims to evaluate the efficacy and safety of CHM for postpartum constipation.
Methods			
Eligibility criteria	8	3-5	**Types of studies** Parallel-group RCTs will be included. No restriction will be put on the language, publication date or status of the study. **Types of participants** Women with constipation during the postpartum period will be included regardless of age, race, nationality, history of prenatal constipation, frequency of delivery, mode of delivery (vaginal delivery

			or caesarean section), gastrointestinal diseases and so forth. The postpartum period ranges from an hour after the delivery of placenta to six weeks[8]. Participants should be clinically diagnosed with constipation according to the Rome Ⅱ or Ⅲ diagnostic criteria, Bristol stool form scale, clinical guidelines or defined by trialists. The Rome II Criteria for constipation should include at least two of the following symptoms lasting for 12 weeks or more over the period of a year: (1) Straining with more than 25% of defecations, (2) Hard stool with more than 25% of defecations, (3) Feeling of incomplete evacuation with more than 25% of defecations, (4) Sensation of anorectal obstruction with more than 25% of defecations, (5) Manual maneuvers to facilitate more than 25% of defecations, (6) Fewer than three bowel movements per week, (7) Insufficient criteria for irritable bowel syndrome[24]. The Rome III Criteria for functional constipation should include two or more of the following: (1) Straining during defecation for at least 25% of bowel movements, (2) Lumpy or hard stools in at least 25% of defecations, (3) Sensation of incomplete evacuation for at least 25% of defecations, (4) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (5) Manual maneuvers to facilitate at least 25% of defecations, (6) Fewer than 3 defecations per week, (7) Loose stools are rarely present without the use of laxatives, (8) There are insufficient criteria for irritable bowel syndrome[25]. These symptoms should start for at least 6 months prior to diagnosis and be present for the past three months[25]. **Types of interventions** **Experimental interventions** The experimental interventions include a CHM alone and a combination of CHM and another active treatment (pharmacological or non-pharmacological intervention). Any CHM preparation (such as decoction, granula, ointment and capsule) will be considered. **Comparator interventions**

			The control interventions include no treatment, placebo and another active treatment. The route of delivery (such as oral and enema), dosage, frequency and duration will not be restricted. The following comparisons will be considered if available: (1) CHM alone versus no treatment; (2) CHM alone versus placebo; (3) CHM alone versus another active treatment; (4) CHM plus another active treatment versus another active treatment alone; (5) CHM plus another active treatment versus placebo plus another active treatment. **Types of outcome measures** **Primary outcomes** The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28]. **Secondary outcomes** Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools], transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible. Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.

Information sources	9	5	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study.
Search strategy	10	5-6	We will search PubMed (1966 to present), EMBASE (1974 to present), Cochrane Central Register of Controlled Trials (CENTRAL, all years), Web of science (1900 to present), Chinese Biomedical Literatures database (CBM, 1978 to present), China National Knowledge Infrastructure (CNKI, 1979 to present) and WANFANG data (1998 to present) to identify any eligible study. The search strategy is developed by a senior librarian (JHS) based on previous systematic reviews[19,22]. The detailed search strategy is available at appendix 1. The terms will be modified for other databases if necessary. No language, publication date or status will be restricted. Reference lists of primary studies and relevant reviews will be manually searched to identify additional references. We will also conduct a search on the website of ClinicalTrials.gov, the World Health Organization International Clinical trials Registry platform (ICTRP) and Chinese Clinical Trial Registry (ChiCTR) to identify additional ongoing or unpublished studies.
Study records			
Data management	11a	6	The results of the literature searches will be imported to the EndNote X7 software. Duplicates will be omitted using the EndNote.
Selection process	11b	6	Two review authors (JBZ and YL) will independently run search strategy to identify potentially eligible studies. The irrelevant studies will be removed by scanning titles and abstracts of references identified by the literature searches according to the inclusion criteria. Then full-text articles will be screened to identify eligible studies. A PRISMA diagram will be used to illustrate the selection

			process. Any disagreement will be resolved through consensus or discussion with a third reviewer (JHZ).
Data collection process	11c	6	A predetermined form will be used to extract data. The pilot test will be conducted to ensure consistency before performing the review. Two reviewers (YYL and SD) will independently extract the information. If necessary, we will contact authors of included studies for providing further details or clarification.
Data items	12	6	(1) General information (title, first author, year of publication, funding); (2) Study characteristics (design, randomization, allocation, blinding, inclusion and exclusion criteria, sample size); (3) Participant characteristics (age, ethnicity, diagnosis criteria, number in each group, history of prenatal constipation, frequency of delivery, mode of delivery); (4) Intervention characteristics (experimental intervention, comparator intervention, route of delivery, dosage, frequency and duration); (5) Outcomes (primary and secondary outcomes, time points, methods of outcome assessments, blinding of outcome assessment, adverse events).
Outcomes and prioritization	13	5	**Primary outcomes** The primary outcome is spontaneous bowel movement (SBM). We will consider the incidence and frequency of SBM in 24 hour or per week, the mean number or the change of SBM per week from baseline[10,26-28]. **Secondary outcomes** Secondary outcomes include stool consistency (measured by Bristol Stool Form Scale or other tools), proportion of patients using rescue medication (such as laxatives, rectal evacuants), quality of life [measured by Maternal postpartum quality of life (MAPP-QOL) questionnaire or other tools],

			transit time (the time from the first perception of wanting to defaecate to the finish of defaecation), relief of constipation symptoms (such as sensation of straining, bloating, abdominal pain)[26,29,30]. We will also consider other outcomes reported by the investigators when possible. Any adverse event of the intervention on both the mother and baby (such as influence of milk production, milk rejection, et al.) will be extracted and the incidence will be estimated if possible.
Risk of bias in individual studies	14	6-7	Two reviewers (JBZ and YL) will independently conduct the risk of bias assessment of included references using the Cochrane 'risk of bias' tool[32]. The following seven domains will be assessed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential sources of bias[32]. The risk of bias for each domain will be graded as low, high or unclear for each included study[32]. If a study described that it was a randomized controlled trial without reporting randomization method, we will contact authors for providing further details or clarification whenever possible. If the information about the sequence generation process is insufficient to permit judgment of 'Low risk' or 'High risk', this study will still be included in this systematic review and the risk of selection bias will be graded as 'unclear'. The overall risk of bias of a study will be estimated low only if all seven domains are rated to be at low risk of bias. Otherwise, the overall risk of bias for the study is high. We will summarize the results of the risk of bias assessments with a 'risk of bias graph' and 'risk of bias summary' figure. Any disagreement will be resolved by discussion or involving a third reviewer (JHZ).
Data synthesis	15a	8	We will perform the meta-analysis when more than one trial examines the same intervention and outcomes with comparable methods in similar populations.
	15b	8	For the continuous outcomes, we will calculate the mean differences (MDs) with 95% confidence intervals (CIs). If the same outcome is measured using different scales, the standardized

			mean difference (SMD) with 95% CI will be used to express intervention effects. Risk ratio (RR) with 95% CI will be used to present results for dichotomous outcomes. If the statistical heterogeneity is not identified, the fixed-effect model will be built to estimate the overall intervention effects. Otherwise, the random-effect model will be used to provide more conservative results. When multiple intervention groups are used in a study, we will make pair-wise comparisons by combining groups if possible. All statistical analyses will be performed by RevMan 5.3 software. The statistical significance is defined as $P < 0.05$.
	15c	8	If possible, subgroup analyses will be conducted based on the following variables: (1) History of prenatal constipation; (2) Frequency of delivery; (3) Mode of delivery (vaginal delivery or caesarean section); (3) History of gastrointestinal diseases; (4) Type of comparisons; (5) Type of preparations (such as decoction, granula, ointment and capsule); (6) Different diagnostic criteria of constipation (Rome I / II / III diagnostic criteria, clinical guidelines or defined by trialists); (7) Language or publication date; (8) The aetiology of postpartum constipation (pelvic floor injury, taking painkillers, a lack of adequate dietary fibre, vegetable, fruit and water, irregular meals, et al.); The difference of intervention effects across subgroups will be compared by Chi-square test with $P < 0.05$ indicating statistical significance. We will investigate the robustness of the pooled effects using sensitivity analyses according to the following variables if possible:

			(1) Impact of sample size: removing one or two studies in which sample size is more than 80% of participants in a meta-analysis; (2) Impact of high risk of bias: removing studies in which overall risk of bias is high; (3) Impact of selected models: fixed-effect models versus random-effect models; (4) Impact of missing data: extreme worst-case analysis and best-case analysis.
	15d	8	If the meta-analysis is not feasible, we will provide a narrative description of the results.
Meta-bias(es)	16	7	The reporting bias will be investigated using visual funnel plots if more than ten RCTs are included in the same meta-analysis. If the reporting bias is identified, we will explore possible reasons using the subgroup analysis or meta-regression analysis.
Confidence in cumulative evidence	17	8-9	Two review authors (JBZ and YL) will evaluate the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. It will be categorized as high, moderate, low, or very low. We will present the findings with a 'summary of finding' table. It will include all important outcomes, absolute and relative magnitude of effects, number of participants, and a grade of the overall quality of the body of evidence for each outcome. Any discrepancy will be resolved by discussion or a consultation of a third review author (JHZ).