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Acupuncture for urinary incontinence after stroke: a protocol for systematic review

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Primary Subject Heading:	Evidence based practice
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Keywords:	acupuncture, stroke, urinary incontinence, systematic review

Acupuncture for urinary incontinence after stroke: a protocol for systematic review

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ABSTRACT

Introduction: The aim of this study is to assess the efficacy and safety of acupuncture for stroke patients with urinary incontinence.

Methods and analysis: Randomised controlled trials (RCTs) will be searched electronically in the MEDLINE, EMBASE, CENTRAL, CINAHL, and four Chinese medical databases from their inception to 1 January 2015. Manual retrieval will also be conducted. RCTs will be included if acupuncture was evaluated as the sole or adjunct treatment for stroke patients with urinary incontinence. The primary outcome will be measured by using the pad-weighing test. The secondary outcomes will include a urination diary, bladder capacity, clinical symptom scores, clinical efficacy assessment (curative rate and total efficacy ratio), and adverse events. The study selection, data extraction, and evaluation of study quality will be performed independently by two researchers. The methodological quality of the included trials will be assessed by using the Cochrane risk-of-bias criteria.

Dissemination: This systematic review will assess the current evidence of acupuncture treatment for stroke patients with urinary incontinence. The findings of this study will be published through a peer-reviewed journal or presented at a relevant conference.

Trial registration number: PROSPERO CRD42014015611.

Keywords: acupuncture; stroke; urinary incontinence; systematic review

INTRODUCTION

Urinary incontinence (UI) is defined by the International Continence Society (ICS) as involuntary leakage of urine, which causes hygienic or social problems [1]. UI affects 32–79% of patients hospitalised for stroke [2-4], 25% of patients at hospital discharge, and 15% of patients after 1 year [4]. A report indicated that the more severe the stroke, the greater the likelihood of UI [5]. In addition, the risk factors of UI include older age, female sex, speech difficulties, motor weakness, visual field defects, and cognitive impairment [6].

Acupuncture is defined as the stimulation of specific acupuncture points, or acupoints, on the skin of the body by using thin disposable needles [7]. When performed by qualified acupuncturists, it often has an excellent safety profile, with rare serious adverse events [8, 9]. Acupuncture is often used for treating various diseases such as pressure ulcers [10], neck pain [11, 12], knee pain [13], stroke rehabilitation [14, 15], and UI [16].

Currently, acupuncture as a popular intervention for stroke patients with UI [16-18]. Its efficacy and safety have been assessed in several randomised controlled trials (RCTs) [17, 18], but not systematically. In addition, no systematic review or meta-analysis is available on this topic. Therefore, the objective of this systematic review is to critically assess the efficacy and safety of acupuncture in the treatment of UI after stroke.

Objectives

This study aims to evaluate the efficacy and safety of acupuncture intervention for UI after stroke.

METHODS

Study registration

Our systematic review protocol is registered in PROSPERO 2014 (CRD42014015611;

http://www.crd.york.ac.uk/PROSPERO/) [19]. This study will be conducted and reported according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [20].

Criteria for considering studies for this review

Type of studies

All RCTs that compared acupuncture with non-acupuncture intervention in stroke patients with UI will be included in the review. Studies will be excluded if they are non-RCTs, uncontrolled clinical trials (e.g. case studies), and qualitative studies.

Type of participants

Patients diagnosed with UI after stroke will be the focus of the review, without restrictions on age, sex, or race.

Types of interventions

Any type of acupuncture therapy (as the sole treatment or a significant adjunct to other treatments) used in an experimental group will be included. Control interventions with no acupuncture treatment will also be included.

Studies with the following comparisons will be included:

Acupuncture compared with a non-acupuncture intervention

Acupuncture plus other interventions (non-acupuncture) compared with other treatments (the same as the acupuncture group)

Types of outcome measures

Primary outcomes

The primary outcome will be measured by using the pad-weighing test.

Secondary outcomes

The secondary outcomes include a urination diary, bladder capacity, clinical symptom scores, clinical efficacy assessment (curative rate and total efficacy ratio), and adverse

events.

Search methods for identification of studies

Electronic searches

The following 8 databases will be searched from their inception to January 2015: MEDLINE, EMBASE, CENTRAL, CINAHL, the Chinese Biomedical Literature Database, the China National Knowledge Infrastructure, VIP Information, and Wanfang Data. The search terms will consist of three parts: stroke (e.g. 'stroke', 'apoplexy', or 'cerebral vascular'), urinary incontinence (e.g. 'urinary incontinence', 'urinary tract', or 'urination disorders'), and acupuncture (e.g. 'acupuncture', 'electroacupuncture', or 'scalp acupuncture'). The words to be used in the search in the Chinese databases have the same meaning as those used in the English databases.

Searching other resources

The reference lists of previously published reviews related to urinary incontinence after stroke and acupuncture will be manually searched to avoid missing eligible trials.

Data collection and analysis

Selection of studies

Two review authors (J.H.Y. and Q.H.Z.) will independently screen the titles and abstracts of existing literature for potentially relevant studies according to the inclusion and exclusion criteria. The remaining studies will be read in full text after the exclusion of the duplicated and apparently irrelevant studies. Any disagreement will be discussed by consensus with a third review author (Z.R.S.). The primary selection process will be presented in the PRISMA flow diagram (Figure 1).

Data extraction

The following data will be independently extracted by the two review authors (J.H.Y. and Q.H.Z.) into a predefined data extraction sheet: first author, publication year,

country of origin, characteristics of the participants, study size, randomisation, allocation concealment, and blinding; acupuncture intervention, control intervention, main outcomes and adverse effects, follow-up, withdrawals, and conflicts of interest.

Quality assessment

Quality assessment of each RCT will be independently conducted by the two reviewers (Y.J.H. and Z.Q.H.) by using the Cochrane Risk of Bias Tool [21-22]. All discrepancies will be resolved by discussion and consensus with a third author (S.Z.R.).

Measures of treatment effect

For continuous data, the mean difference (MD) with the corresponding 95% confidence intervals (CIs) will be used. Other forms of data will be changed into MD values. For dichotomous data (e.g. adverse events), we will use risk ratio (RR) with the corresponding 95% CIs. Other dichotomous data will be converted into RR values.

Unit of analysis issues

Cluster-randomised trials and crossover studies will not be included because of the lack of an appropriate design for this research question.

Missing data

Whenever possible, we will request data from the corresponding author for missing data. If the missing data cannot be obtained, we will exclude such studies and only analyse the available data and address the potential impact of missing data in the discussion.

Assessment of heterogeneity

If it is possible, the random- or fixed-effect model will be used in the meta-analysis. The statistical heterogeneity in each meta-analysis will be investigated by using the I^2

and χ^2 tests [23]. If trials are homogenous (i.e. $I^2 \leq 50\%$, the cut off point for our I^2 statistics) [24], the fixed-effects model will be used to pool the data. Otherwise, the random-effects model will be used. If the heterogeneity remains significant, the findings will be discussed as a narrative summary.

Assessment of reporting biases

Funnel plots will be constructed to evaluate the publication bias, if the studies included are sufficient (at least 10 trials) [25].

Data synthesis

We will use Review Manager V.5.3 [26] (http://tech.cochrane.org/revman) in our meta-analysis. We will calculate the RR with the 95% CIs for the dichotomous data and MD with the 95% CIs for the continuous data. Where outcome data are measured by using different scales, standardised mean differences (SMD) will be used [27]. Otherwise, for the data measured on the same scale and for which the same units are used, the weighted mean differences (WMD) will be used. If heterogeneity is not high ($I^2 \leq 50\%$), the RR, WMD, or SMD will be calculated by using the fixed-effects model. Otherwise, the random-effects model will be used.

Subgroup analysis

A subgroup analysis will be performed based on the type of acupuncture, type of control, and different outcomes.

Sensitivity analysis

A sensitivity analysis will be performed to evaluate the robustness of our results by removing the impact of high risk of bias if heterogeneity remains after subgroup analysis. The meta-analysis will be repeated after the trials with high risk of bias are excluded. In addition, we will also assess whether the statistical model (random- vs fixed-effects model) will affect the results.

DISCUSSION

To our best knowledge, our study will be the first systematic review and meta-analysis to evaluate the efficacy and safety of acupuncture in the treatment of UI after stroke. The results of this study will provide a summary of the current evidence related to the efficacy and safety of acupuncture in patients with UI after stroke. The evidence will provide important information and will also benefit practitioners, patients, and health-policy makers, as well as the future research regarding the use of acupuncture.

Conflict of interest

The authors declare that they have no conflict of interests.

Authors' contributions

JHY and ZRS contributed equally to this work. QHZ, JHY, and ZRS conceived the study and designed the study protocol, drafted the manuscript. All authors contributed to the further writing of the manuscript as well as read and approved the final manuscript.

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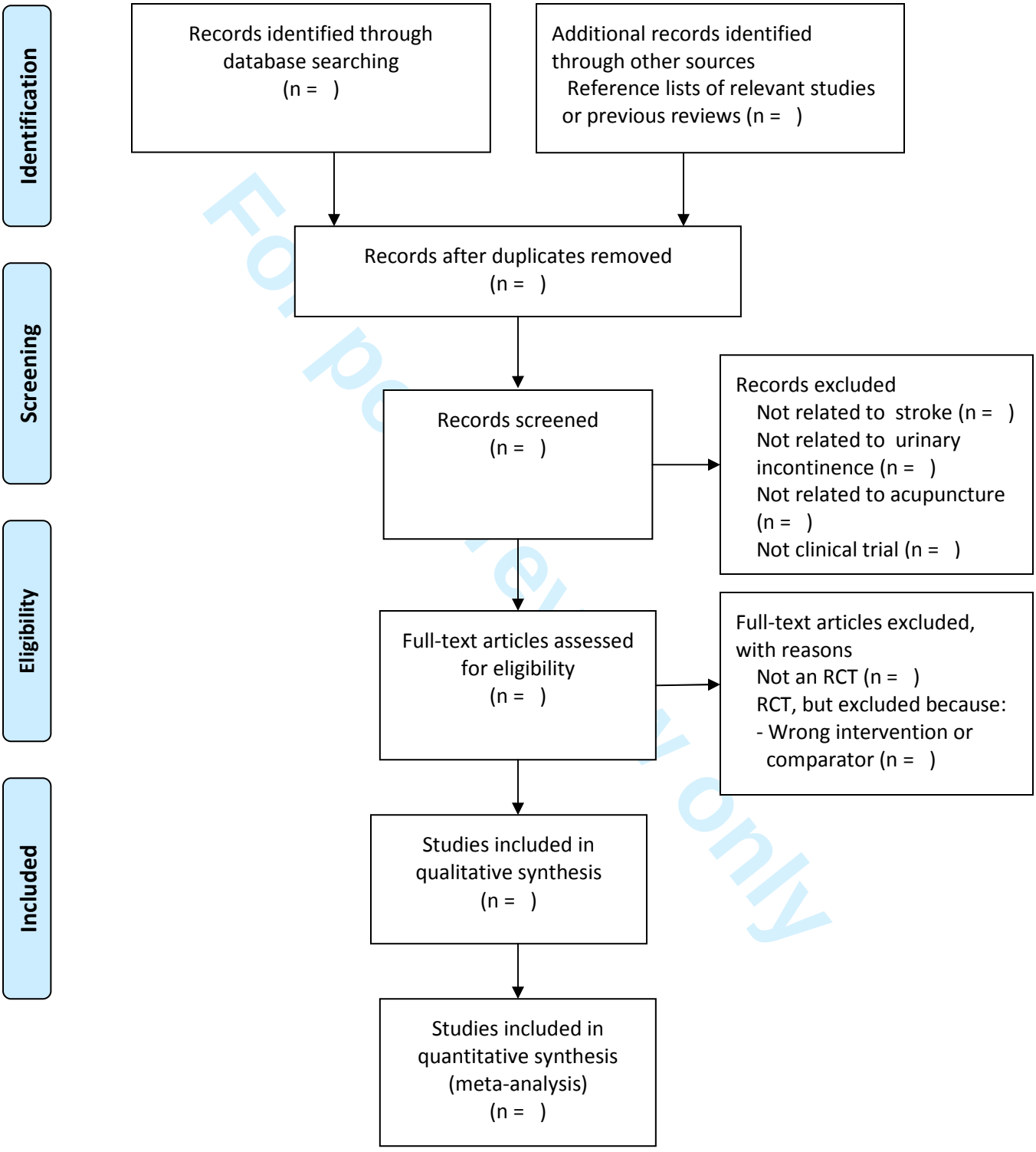

Figure 1 Flow diagram of the trial selection process

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Primary Subject Heading:	Evidence based practice
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Keywords:	acupuncture, stroke, urinary incontinence, systematic review, randomized controlled trial

Acupuncture for urinary incontinence after stroke: a protocol for systematic review

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ABSTRACT

Introduction: The aim of this study, which will include randomised controlled trials (RCTs), is to assess the efficacy and safety of acupuncture for stroke patients with urinary incontinence.

Methods and analysis: RCTs will be searched electronically in the MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL, and four Chinese medical databases from their inception to present. Manual retrieval will also be conducted. RCTs will be included if acupuncture was evaluated as the sole or adjunct treatment for stroke patients with urinary incontinence. The primary outcome will be measured by using the pad-weighing test. The secondary outcomes will include a urination diary, bladder capacity, clinical symptom scores, number of wounds healed completely in trial follow-up period, and adverse events. The study selection, data extraction, and evaluation of study quality will be performed independently by two researchers. The methodological quality of the included trials will be assessed by using the Cochrane risk-of-bias criteria.

Dissemination: This systematic review will assess the current evidence of acupuncture treatment for stroke patients with urinary incontinence. The findings of this study will be published through a peer-reviewed journal and presented at a relevant conference.

Trial registration number: PROSPERO CRD42014015611.

Keywords: acupuncture; stroke; urinary incontinence; randomized controlled trial; systematic review

INTRODUCTION

Urinary incontinence (UI) is defined by the International Continence Society (ICS) as involuntary leakage of urine, which causes hygienic or social problems [1]. It is often classified as stress urinary incontinence (SUI), urgency urinary incontinence (UUI) and mixed urinary incontinence (MUI) [2]. SUI differs from UUI. It is defined as an involuntary leakage from the urethra when the abdominal pressure raised. However, UUI occurs with a sudden sensation of the need to urinate, and then followed by immediate leakage of a large volume of urine [3]. MUI is a combination of the both.

UI affects 32–79% of patients hospitalised for stroke [4-6], 25% of patients at hospital discharge, and 15% of patients after 1 year [7]. A report indicated that the more severe the stroke, the greater the likelihood of UI [8]. In addition, the risk factors of UI include older age, female sex, speech difficulties, motor weakness, visual field defects, and cognitive impairment [9].

Acupuncture is defined as the stimulation of specific acupuncture points, or acupoints, on the skin of the body by using thin disposable needles [10]. When performed by qualified acupuncturists, it often has an excellent safety profile, with rare serious adverse events [11, 12]. Acupuncture is often used for treating various diseases such as neck pain [13], knee pain [14], stroke rehabilitation [15], and UI [16].

Acupuncture has thousands of years history to treat diseases. According to the theory of traditional Chinese medicine, UI is mainly resulted from kidneys' *qi* deficiency, which often causes bladder dysfunction to control urine. Thus, the objective of acupuncture is to reinforce *qi* of kidneys and promote the bladder function recover. Currently, acupuncture as a popular intervention for stroke patients with UI [17-18]. Its efficacy and safety have been assessed in several randomised controlled trials (RCTs) [17, 18]. One study found that electroacupuncture (EA) could significantly alleviate UI and increase bladder capacity of stroke patients, which had better efficacy than indwelling catheter therapy[17]. The other study concluded that EA could lower

the severity of UI and improve clinical symptoms of micturition in stroke patients[18].

A previous systematic review found limited results supporting acupuncture as an effective treatment method for urinary incontinence [19]. However, this study failed to search and include Chinese databases; and only three included RCTs focused on acupuncture for urinary incontinence with different control interventions, including sham acupuncture, placebo acupuncture and drug. This systematic review aims to update the previous systematic review and to further critically assess the efficacy and safety of acupuncture in the treatment of UI after stroke.

Objectives

This study included RCTs aims to evaluate the efficacy and safety of acupuncture intervention for UI after stroke.

METHODS

Study registration

Our systematic review protocol is registered in PROSPERO 2014 (CRD42014015611; http://www.crd.york.ac.uk/PROSPERO/). This study will be reported according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement guidelines [20].

Criteria for considering studies for this review

Type of studies

All RCTs except cluster randomised trials and crossover studies that compared acupuncture with non-acupuncture intervention in stroke patients with UI will be included in the review.

Type of participants

Patients diagnosed with UI [21] after stroke will be the focus of the review, without restrictions on age, sex, or race.

Types of interventions

Any type of acupuncture therapy (as the sole treatment or a significant adjunct (reflects the efficacy and safety of acupuncture) to other treatments), such as electroacupuncture, manual acupucntrue used in an experimental group will be included. Control interventions with no acupuncture treatment will also be included. Studies with the following comparisons will be included:

Acupuncture compared with a non-acupuncture intervention

Acupuncture plus other interventions (non-acupuncture) compared with other treatments (the same as the acupuncture group)

In this study, significant adjunct will be defined as the acupuncture plus other non-acupuncture interventions VS. other non-acupuncture interventions (the same as the previous treatments), which can reflect the efficacy and safety of acupuncture. But not reflect the efficacy of acupuncture combine other interventions.

Types of outcome measures

Primary outcomes

The primary outcome will be measured by using the pad-weighing test [22-23]. This test is a non-invasive method of detecting and quantifying severity of urine leakage. The 4th International Consultation on Incontinence defined pad testing as "an optional test for evaluation of urinary incontinence"[23-24].

Secondary outcomes

The secondary outcomes will be measured through urination diary, bladder capacity, clinical symptom scores, the number of patients healed completely in trial follow-up period, and adverse events.

Search methods for identification of studies

Electronic searches

The following 8 databases will be searched from their inception to present:

MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL, the Chinese Biomedical Literature Database, the China National Knowledge Infrastructure, VIP Information, and Wanfang Data. The search terms will consist of three parts: stroke (e.g. 'stroke', 'apoplexy', or 'cerebral vascular'), urinary incontinence (e.g. 'urinary incontinence', 'urinary tract', or 'urination disorders' or 'urinary bladder'), and acupuncture (e.g. 'acupuncture', or 'manual acupuncture', or 'electroacupuncture', or 'scalp acupuncture'). The words to be used in the search in the Chinese databases have the same meaning as those used in the English databases. The search strategy for CENTRAL is shown in table 1.

Searching other resources

The reference lists of previously published reviews related to UI after stroke and acupuncture will be manually searched to avoid missing eligible trials, such as previous review published at journal Exp Ther Med by Paik SH [19].

Data collection and analysis

Selection of studies

Two review authors (J.H.Y. and Q.H.Z.) will independently screen the titles and abstracts of existing literature for potentially relevant studies according to the inclusion and exclusion criteria. The remaining studies will be read in full text after the exclusion of the duplicated and apparently irrelevant studies. Any disagreement will be discussed by consensus with a third review author (Z.R.S.). The primary selection process will be presented in the PRISMA flow diagram (Figure 1).

Data extraction

The following data will be independently extracted by the two review authors (J.H.Y. and Q.H.Z.) into a predefined data extraction sheet: first author, publication year, country of origin, characteristics of the participants, study size, randomisation, allocation concealment, and blinding; acupuncture intervention, control intervention, main outcomes and adverse effects, follow-up, withdrawals, and conflicts of interest.

Quality assessment

Quality assessment of each RCT will be independently conducted by the two reviewers (Y.J.H. and Z.Q.H.) by using the Cochrane Risk of Bias Tool [25]. This tool addresses seven specific domains, including sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other issues (e.g. extreme baseline imbalance) [25]. All discrepancies will be resolved by discussion and consensus with a third author (S.Z.R.).

Measures of treatment effect

For continuous data (e.g. pad-weighing test, urination diary, bladder capacity, and clinical symptom scores), the mean difference (MD) with the corresponding 95% confidence intervals (CIs) will be used. Other forms of data will be changed into MD values. In addition, if it is necessary, we will use standardised mean differences (SMD). For dichotomous data (e.g. the number of patients healed completely in trial follow-up period, and adverse events), we will use risk ratio (RR) with the corresponding 95% CIs. Other dichotomous data will be converted into RR values.

Unit of analysis issues

Cluster-randomised trials and crossover studies will not be included because of the lack of an appropriate design for this research objectives. If more than one acupuncture arms are reported, we will carry out multiple meta analyses using one treatment arm respectively. If multiple non-acupuncture control groups are used, we will combine all control group results and carry out a pooled analyses of all control groups against the intervention group. If there are multiple assessment time points in a study, we will only pool data from one time point that is closest to the other included studies.

Missing data

Whenever possible, we will request data from the corresponding author for missing data mainly regarding the primary outcomes. If the those missing data cannot be obtained, we will exclude such studies and only analyse the available data and address the potential impact of missing data in the discussion.

Assessment of heterogeneity

If it is possible, the random- or fixed-effect model will be used in the meta-analysis. The statistical heterogeneity in each meta-analysis will be investigated by using the I^2 and χ^2 tests [26]. If trials are homogenous (i.e. $I^2 \leq 50\%$, the cut off point for our I^2 statistics) [27], the fixed-effects model will be used to pool the data. Otherwise, the random-effects model will be used. If the heterogeneity remains significant, we will consider a subgroup analysis and a meta regression to locate the heterogeneity sources. If it still not work out, then the findings will be discussed as a narrative summary.

Assessment of reporting biases

Funnel plots will be constructed to evaluate the publication bias, if the studies included are sufficient (at least 10 trials) [28].

Data synthesis

We will use Review Manager V.5.3 [29] (http://tech.cochrane.org/revman) in our meta-analysis. We will calculate the RR with the 95% CIs for the dichotomous data and SMD with the 95% CIs for the continuous data. Where outcome data are measured by using different scales, SMD will be used [30]. Otherwise, for the data measured on the same scale and for which the same units are used, the weighted mean differences (WMD) will be used. If heterogeneity is not high ($I^2 \leq 50\%$), the RR, WMD, or SMD will be calculated by using the fixed-effects model. Otherwise, the random-effects model will be used.

Subgroup analysis

A subgroup analysis will be performed based on the type of acupuncture, type of

control, and different outcomes.

Sensitivity analysis

A sensitivity analysis will be performed to evaluate the robustness of our results by removing the impact of high risk of bias if heterogeneity remains after subgroup analysis. The meta-analysis will be repeated after the trials with high risk of bias are excluded. In addition, we will also assess whether the statistical model (random- vs fixed-effects model) will affect the results.

DISCUSSION

To our best knowledge, our study will be the first systematic review and meta-analysis to evaluate the efficacy and safety of acupuncture in the treatment of UI after stroke. The results of this study will provide a summary of the current evidence related to the efficacy and safety of acupuncture in patients with UI after stroke. The evidence will provide important information and will also benefit practitioners, patients, and health-policy makers, as well as the future research regarding the use of acupuncture.

Conflict of interest

The authors declare that they have no conflict of interests.

Authors' contributions

JHY and ZRS contributed equally to this work. QHZ, JHY, and ZRS conceived the study and designed the study protocol, drafted the manuscript. All authors contributed to the further writing of the manuscript as well as read and approved the final manuscript.

Acknowledgments

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Table 1 Search strategy used in CENTRAL database

Number	Search terms
1	MeSH descriptor: [stroke] explode all trees
2	((apoplexy *) or (cerebro next vascular*) or (cerebral *)):ti, ab, kw
3	or 1-2
4	MeSH descriptor: [urinary incontinence] explode all trees
5	((urinary tract) or (urination disorders) or (urinary bladder *)):ti, ab, kw
6	or 4-5
7	MeSH descriptor: [acupuncture] explode all trees
8	MeSH descriptor: [acupuncture therapy] explode all trees
9	((manual acupuncture) or (manual next acupuncture*) or (electroacupuncture) or (electro next acupuncture *) or (scalp acupuncture*) or (scalp next acupuncture*)):ti, ab, kw
10	or 7-9
11	3 and 6 and 10

This search strategy will be modified as required for other electronic databases.

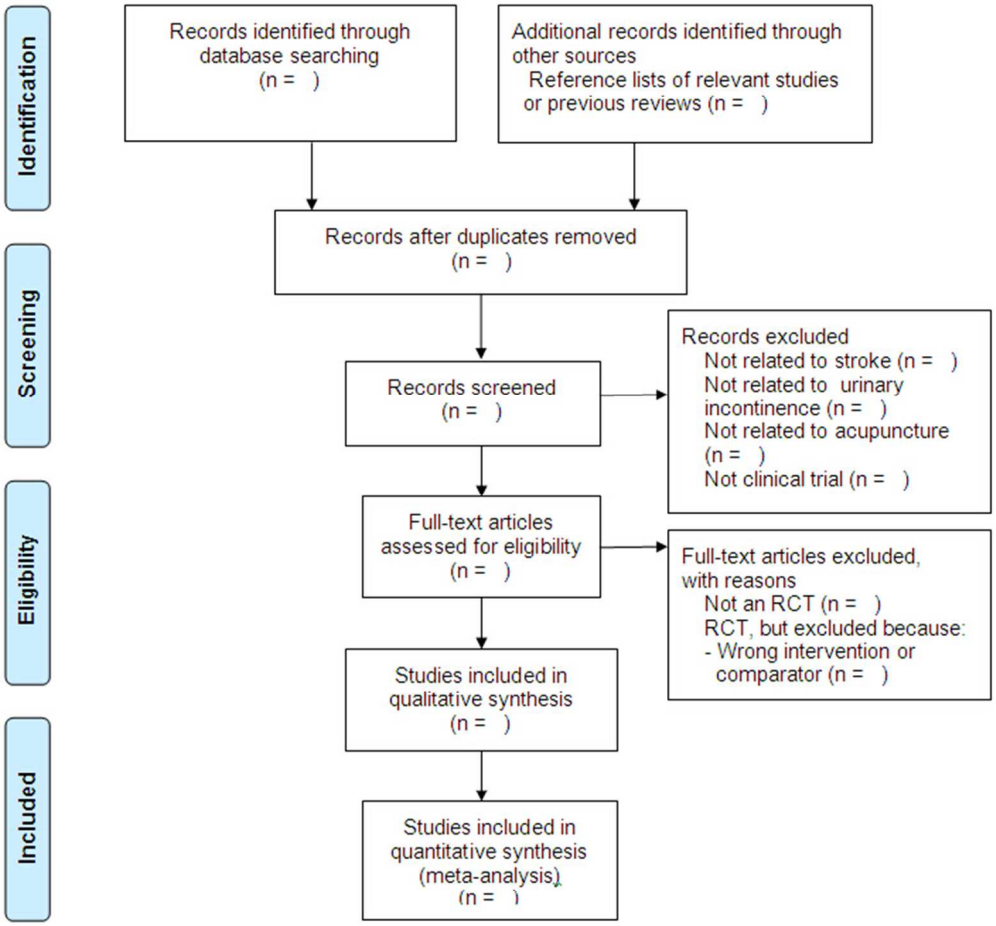

Figure 1 Flow diagram of the trial selection process

Flow diagram of the trial selection process
187x185mm (96 x 96 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Pages
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	1
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	No
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	9
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	9
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4-5
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5-6

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5-6
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-8
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6-7

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Acupuncture for urinary incontinence after stroke: a protocol for systematic review

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Keywords:	acupuncture, stroke, urinary incontinence, systematic review, randomized controlled trial

Acupuncture for urinary incontinence after stroke: a protocol for systematic review

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ABSTRACT

Introduction: The aim of this study, which will include randomised controlled trials (RCTs), is to assess the efficacy and safety of acupuncture for stroke patients with urinary incontinence.

Methods and analysis: RCTs will be searched electronically in the MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL, and four Chinese medical databases from their inception to present. Manual retrieval will also be conducted. RCTs will be included if acupuncture was evaluated as the sole or adjunct treatment for stroke patients with urinary incontinence. The primary outcome will be measured by using the pad-weighing test. The secondary outcomes will include a urination diary, bladder capacity, clinical symptom scores, the number of patients healed completely in trial follow-up period, and adverse events. The study selection, data extraction, and evaluation of study quality will be performed independently by two researchers. The methodological quality of the included trials will be assessed by using the Cochrane risk-of-bias criteria and the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) checklist.

Dissemination: This systematic review will assess the current evidence of acupuncture treatment for stroke patients with urinary incontinence. The findings of this study will be published through a peer-reviewed journal and presented at a relevant conference.

Trial registration number: PROSPERO CRD42014015611.

Keywords: acupuncture; stroke; urinary incontinence; randomized controlled trial; systematic review

INTRODUCTION

Urinary incontinence (UI) is defined by the International Continence Society (ICS) as involuntary leakage of urine, which causes hygienic or social problems [1]. It is often classified as stress urinary incontinence (SUI), urgency urinary incontinence (UUI) and mixed urinary incontinence (MUI) [2]. SUI differs from UUI. It is defined as an involuntary leakage from the urethra when the abdominal pressure raised. However, UUI occurs with a sudden sensation of the need to urinate, and then followed by immediate leakage of a large volume of urine [3]. MUI is a combination of the both.

UI affects 32–79% of patients hospitalised for stroke [4-6], 25% of patients at hospital discharge, and 15% of patients after 1 year [7]. A report indicated that the more severe the stroke, the greater the likelihood of UI [8]. In addition, the risk factors of UI include older age, female sex, speech difficulties, motor weakness, visual field defects, and cognitive impairment [9].

Acupuncture is defined as the stimulation of specific acupuncture points, or acupoints, on the skin of the body by using thin disposable needles [10]. When performed by qualified acupuncturists, it often has an excellent safety profile, with rare serious adverse events [11, 12]. Acupuncture is often used for treating various conditions such as neck pain [13], knee pain [14], stroke rehabilitation [15], and UI [16].

Acupuncture has thousands of years history to treat diseases. According to the theory of traditional Chinese medicine, UI is mainly resulted from kidneys' *qi* deficiency, which often causes bladder dysfunction to control urine. Thus, the objective of acupuncture is to reinforce *qi* of kidneys and promote the bladder function recover. Currently, acupuncture as a popular intervention for stroke patients with UI [17-18]. Its efficacy and safety have been assessed in several randomised controlled trials (RCTs) [17, 18]. One study found that electroacupuncture (EA) could significantly alleviate UI and increase bladder capacity of stroke patients, which had better efficacy than indwelling catheter therapy [17]. The other study concluded that EA could lower

the severity of UI and improve clinical symptoms of micturition in stroke patients [18].

Previous systematic reviews found limited results supporting acupuncture as an effective treatment method for UI [19-21]. However, only two studies specifically focused on the acupuncture for UI after stroke [19-20]. Moreover, both studies failed to search and include Chinese databases; and most included RCTs suffered from poor quality. This systematic review aims to update the previous systematic review and to further critically assess the efficacy and safety of acupuncture in the treatment of UI after stroke.

Objectives

This study included RCTs aims to evaluate the efficacy and safety of acupuncture intervention for UI after stroke.

METHODS

Study registration

Our systematic review protocol is registered in PROSPERO 2014 (CRD42014015611; http://www.crd.york.ac.uk/PROSPERO/). This manuscript is reported according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement guidelines [22].

Criteria for considering studies for this review

Type of studies

All RCTs except cluster randomised trials and crossover studies that compared acupuncture with either sham acupuncture or non-acupuncture intervention in stroke patients with UI will be included in the review.

Type of participants

Patients diagnosed with UI [23] after stroke will be the focus of the review, without

restrictions on age, sex, or race.

Types of interventions

Any type of acupuncture therapy (as the sole treatment or a significant adjunct (reflects the efficacy and safety of acupuncture) to other treatments), such as electroacupuncture, manual acupucntrue used in an experimental group will be included. Control interventions with either sham acupuncture or no acupuncture treatment will also be included. Studies with the following comparisons will be included:

Acupuncture compared with either a sham acupuncture or a non-acupuncture intervention

Acupuncture plus other interventions (non-acupuncture) compared with other treatments (the same as the acupuncture group)

In this study, significant adjunct will be defined as the acupuncture plus other non-acupuncture interventions VS. other non-acupuncture interventions (the same as the previous treatments), which can reflect the efficacy and safety of acupuncture. But not reflect the efficacy of acupuncture combine other interventions.

Types of outcome measures

Primary outcomes

The primary outcome will be measured by using the pad-weighing test [24-25]. This test is a non-invasive method of detecting and quantifying severity of urine leakage. The 4th International Consultation on Incontinence defined pad testing as "an optional test for evaluation of urinary incontinence" [25-26].

Secondary outcomes

The secondary outcomes will be measured through urination diary, bladder capacity, clinical symptom scores, the number of patients healed completely in trial follow-up period, and adverse events.

Search methods for identification of studies

Electronic searches

The following 8 databases will be searched from their inception to present: MEDLINE, EMBASE, Cochrane CENTRAL, CINAHL, the Chinese Biomedical Literature Database, the China National Knowledge Infrastructure, VIP Information, and Wanfang Data. The search terms will consist of three parts: stroke (e.g. 'stroke', 'apoplexy', or 'cerebral vascular'), urinary incontinence (e.g. 'urinary incontinence', 'urinary tract', or 'urination disorders' or 'urinary bladder'), and acupuncture (e.g. 'acupuncture', or 'manual acupuncture', or 'electroacupuncture', or 'scalp acupuncture'). The words to be used in the search in the Chinese databases have the same meaning as those used in the English databases. The search strategy for CENTRAL is shown in table 1.

Searching other resources

The reference lists of previously published reviews related to UI after stroke and acupuncture will be manually searched to avoid missing eligible trials, such as previous review published at journal Exp Ther Med by Paik SH [19].

Data collection and analysis

Selection of studies

Two review authors (J.H.Y. and N.N.Y.) will independently screen the titles and abstracts of existing literature for potentially relevant studies according to the inclusion and exclusion criteria. The remaining studies will be read in full text after the exclusion of the duplicated and apparently irrelevant studies. Any disagreement will be discussed by consensus with a third review author (Z.R.S.). The primary selection process will be presented in the PRISMA flow diagram (Figure 1).

Data extraction

The following data will be independently extracted by the two review authors (J.H.Y. and Q.H.Z.) into a predefined data extraction sheet: first author, publication year,

country of origin, characteristics of the participants, study size, randomisation, allocation concealment, and blinding; acupuncture intervention, control intervention, main outcomes and adverse effects, follow-up, withdrawals, conflicts of interest, and the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) checklist.

Quality assessment

Quality assessment of each RCT will be independently conducted by the two reviewers (Y.J.H. and N.N.Y.) by using the Cochrane Risk of Bias Tool [27] and completeness of STRICTA checklist. This tool addresses seven specific domains, including sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other issues (e.g. extreme baseline imbalance) [27]. All discrepancies will be resolved by discussion and consensus with a third author (S.Z.R.).

Measures of treatment effect

For continuous data (e.g. pad-weighing test, urination diary, bladder capacity, and clinical symptom scores), the mean difference (MD) with the corresponding 95% confidence intervals (CIs) will be used. Other forms of data will be changed into MD values. In addition, if it is necessary, we will use standardised mean differences (SMD). For dichotomous data (e.g. the number of patients healed completely in trial follow-up period, and adverse events), we will use risk ratio (RR) with the corresponding 95% CIs. Other dichotomous data will be converted into RR values.

Unit of analysis issues

Cluster-randomised trials and crossover studies will not be included because of the lack of an appropriate design for this research objectives. If more than one acupuncture arms are reported, we will carry out multiple meta analyses using one treatment arm respectively. If multiple non-acupuncture control groups are used, we

will combine all control group results and carry out a pooled analyses of all control groups against the intervention group. If there are multiple assessment time points in a study, we will only pool data from one time point that is closest to the other included studies.

Missing data

Whenever possible, we will request data from the corresponding author for missing data mainly regarding the primary outcomes. If the those missing data cannot be obtained, we will exclude such studies and only analyse the available data and address the potential impact of missing data in the discussion.

Assessment of heterogeneity

If it is possible, the random- or fixed-effect model will be used in the meta-analysis. The statistical heterogeneity in each meta-analysis will be investigated by using the I^2 and χ^2 tests [28]. If trials are homogenous (i.e. $I^2 \leq 50\%$, the cut off point for our I^2 statistics) [29], the fixed-effects model will be used to pool the data. Otherwise, the random-effects model will be used. If the heterogeneity remains significant, we will consider a subgroup analysis and a meta regression to locate the heterogeneity sources. If it still not work out, then the findings will be discussed as a narrative summary.

Assessment of reporting biases

Funnel plots will be constructed to evaluate the publication bias, if the studies included are sufficient (at least 10 trials) [30].

Data synthesis

We will use Review Manager V.5.3 [31] (http://tech.cochrane.org/revman) in our meta-analysis. We will calculate the RR with the 95% CIs for the dichotomous data and SMD with the 95% CIs for the continuous data. Where outcome data are measured by using different scales, SMD will be used [32]. Otherwise, for the data measured on the same scale and for which the same units are used, the weighted mean

differences (WMD) will be used. If heterogeneity is not high ($I^2 \leq 50\%$), the RR, WMD, or SMD will be calculated by using the fixed-effects model. Otherwise, the random-effects model will be used. If any meta-analysis will not be able to be conducted, the results will be reported as the narrative description.

Subgroup analysis

A subgroup analysis will be performed based on the type of acupuncture, type of control, and different outcomes.

Sensitivity analysis

A sensitivity analysis will be performed to evaluate the robustness of our results by removing the impact of high risk of bias if heterogeneity remains after subgroup analysis. The meta-analysis will be repeated after the trials with high risk of bias are excluded. In addition, we will also assess whether the statistical model (random- vs fixed-effects model) will affect the results.

DISCUSSION

To our best knowledge, our study will be the first systematic review and meta-analysis to evaluate the efficacy and safety of acupuncture in the treatment of UI after stroke. The results of this study will provide a summary of the current evidence related to the efficacy and safety of acupuncture in patients with UI after stroke. The evidence will provide important information and will also benefit practitioners, patients, and health-policy makers, as well as the future research regarding the use of acupuncture.

Conflict of interest

The authors declare that they have no conflict of interests.

Authors' contributions

NNY and ZRS contributed equally to this work. ZRS, NNY, JHY and QHZ conceived the study and designed the study protocol, drafted the manuscript. All authors

contributed to the further writing of the manuscript as well as read and approved the final manuscript.

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Figure legend

Figure 1 Flow diagram of the trial selection process

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Table 1 Search strategy used in CENTRAL database

Number	Search terms
1	MeSH descriptor: [stroke] explode all trees
2	((apoplexy *) or (cerebro next vascular*) or (cerebral *)):ti, ab, kw
3	or 1-2
4	MeSH descriptor: [urinary incontinence] explode all trees
5	((urinary tract) or (urination disorders) or (urinary bladder *)):ti, ab, kw
6	or 4-5
7	MeSH descriptor: [acupuncture] explode all trees
8	MeSH descriptor: [acupuncture therapy] explode all trees
9	((manual acupuncture) or (manual next acupuncture*) or (electroacupuncture) or (electro next acupuncture *) or (scalp acupuncture*) or (scalp next acupuncture*)):ti, ab, kw
10	or 7-9
11	3 and 6 and 10

This search strategy will be modified as required for other electronic databases.

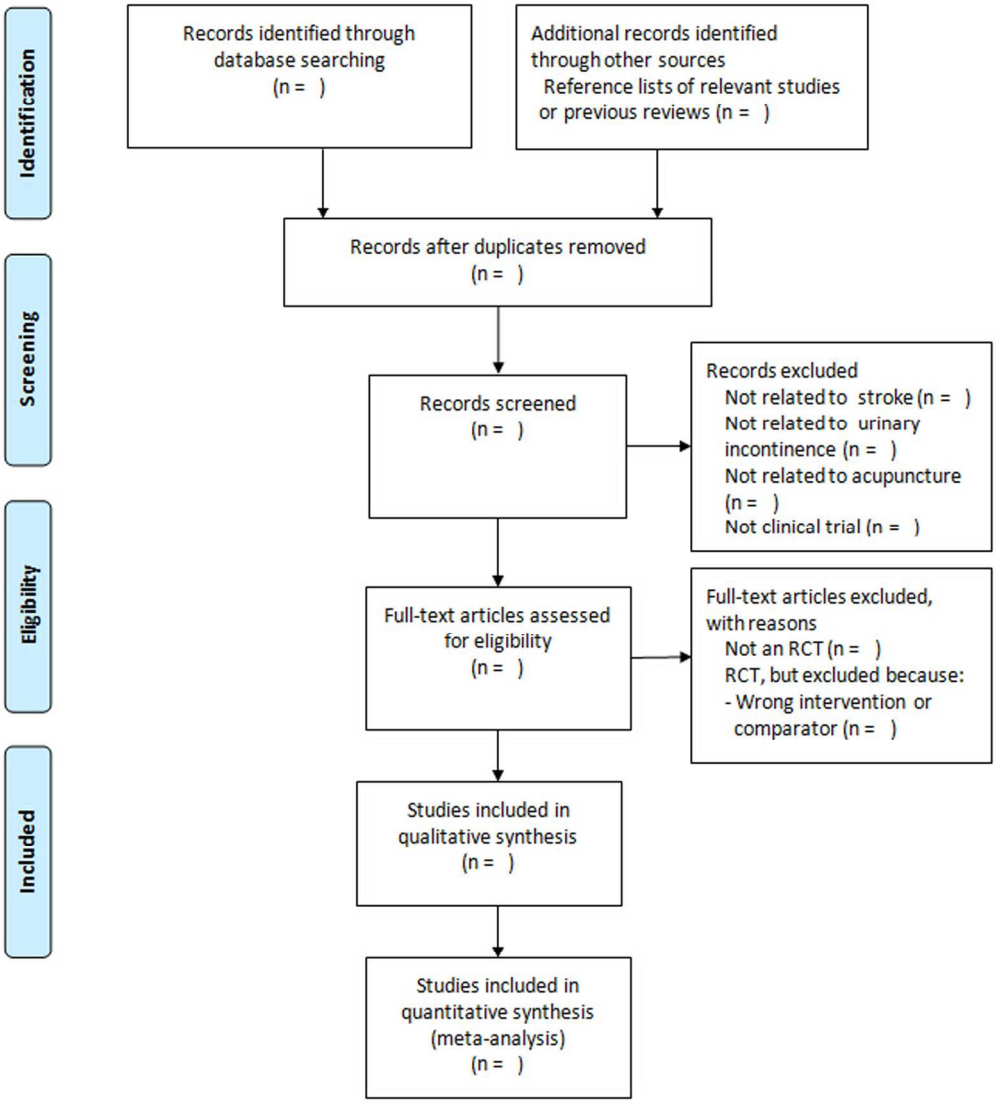

Figure 1 Flow diagram of the trial selection process

Flow diagram of the trial selection process
855x994mm (96 x 96 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Pages
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	1
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	No
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	9
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	9
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4-5
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5-6

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5-6
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6-8
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6-7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	6-7

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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