The Effects of Traditional Chinese Exercise on Cardiac Rehabilitation After Percutaneous Coronary Intervention : Study Protocol for Network Meta-analysis of Randomized Controlled Trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023096
Article Type:	Protocol
Date Submitted by the Author:	25-Mar-2018
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Keywords:	Traditional Chinese Exercise, Cardiac Rehabilitation, Coronary heart disease < CARDIOLOGY

The Effects of Traditional Chinese Exercise on Cardiac Rehabilitation After Percutaneous Coronary Intervention：Study Protocol for Network Meta-analysis of Randomized Controlled Trials

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ABSTRACT

Introduction: Coronary heart disease (CHD) is the most common cause of death worldwide. Percutaneous coronary intervention (PCI) has been shown to reduce mortality in patients with CHD. However, there are still recurrences of cardiovascular events after PCI. Cardiac rehabilitation (CR) in patients with established CHD is associated with reductions in cardiovascular mortality and hospital admissions, as well as improved quality of life. More and more clinical trials suggest that traditional Chinese exercise (TCE) plays a positive role in patients post-PCI.

Objective: The primary purposes of the current study are to conduct a network meta-analysis of randomized trials to determine the effects of TCE in patients after PCI, and to separately compare the effects of tai chi, baduanjin and yijinjing on cardiac rehabilitation after PCI.

Methods and analysis: Studies will be retrieved from the following databases: PubMed, Embase, Cochrane Library, Chinese National Knowledge Infrastructure, Wanfang Data, Chinese BioMedical Database and Chinese Science and Technology Periodicals Database, from inception to February 2018. We will include RCTs that are related to the effects of TCE therapies in patients after PCI. The primary outcomes will be all-cause mortality, revascularisations, health-related quality of life (HRQL), and hospitalisations. Two reviewers will independently select eligible articles. For each included article, two reviewers will independently extract the data and assess the risk of bias by using the Cochrane risk of bias tool. Bayesian network meta-analyses will be conducted to pool all treatment effects. The ranking probabilities for the optimal intervention of various treatments (tai chi, baduanjin or yijinjing) will be estimated by the mean ranks and surface under the cumulative ranking curve (SUCRA). The Grading of Recommendations Assessment, Development and Evaluation System will be utilized to assess the quality of evidence.

Ethics and dissemination: The results will be disseminated through peer-reviewed publications. They will provide consolidated evidence to inform clinicians on the potential functions of TCE in CR, and to provide reliable evidence for the application of TCE.

Trial registration number: CRD42018088415

Strengths and limitations of this study

- This is the first systematic review to use network meta-analysis to compare various forms of traditional Chinese exercise.
- This is the first systematic review to compare the effects of baduanjin, yijinjing and tai chi on cardiac rehabilitation post-PCI.
- This study will assess the effects of TCEs and their safety regarding cardiac rehabilitation after PCI.
- The study will use the Grading of Recommendations Assessment, Development and Evaluation System to further assess the quality of the evidence.
- Due to the changes in the frequency and duration of treatment, there may be clinical heterogeneity.

INTRODUCTION

Description of the condition

Coronary heart disease (CHD), also known as coronary artery disease (CAD), is the most common cause of death worldwide, causing 7.4 million deaths in 2013, accounting for one-third of all deaths globally (WHO 2014)[1]. In addition to the requisite medical therapy, mechanical revascularization with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is needed for patients with CHD. PCI has been shown to reduce mortality in patients with CHD[2]. During follow-up, however, the benefits of PCI surgery still carry significant risks of coronary spasm, endothelial cell injury, recurrent ischemia, and even restenosis or thrombus[3-5]. Numerous guidelines endorse the necessities of cardiac rehabilitation (CR), which is recommended for patients with chronic stable angina, acute coronary syndromes or for patients post-PCI surgery[6-11]. Combined with routine therapy, exercise-based CR, which has been recommended by American Heart Association (AHA) guidelines[12], is a safe option, and is preferred by both clinicians and patients after PCI. It has been reported that light to moderate intensity physical activity can reduce coronary heart disease mortality[13].

Description of the intervention

For centuries, traditional Chinese exercise (TCE) (Figure 1), including tai chi, baduanjin and yijinjing, has been widely practiced in China for both preventive and therapeutic purposes. Considered to be a low-risk, promising intervention that is used widely in the prevention of cardiovascular disease nowadays, TCEs are easy to master in a short time and have few physical demands[14]. Regardless of previous exercise experience or aerobic capacity, the exercise intensity of TCE is suited for persons of all ages. Moreover, TCE requires no expensive equipment and can be performed either individually or in groups. Most existing systematic reviews have focused on specific forms of TCE, such as tai chi or baduanjin[15-17]. Whether TCE has positive clinical effects on patients with CHD after PCI, however, remains unclear.

Therefore, we will conduct the present network meta-analysis to explore the following points (Figure 2): to explore whether TCE affects the primary endpoint events of cardiac death, recurrence of MI, repeated PCI, and restenosis after PCI; to determine whether TCE could be an effective method for improving secondary endpoint measures such as quality of life (QoL), physical functions and symptoms, after PCI; to separately compare the effects of Tai chi, Baduanjin and Yijinjing on patients post-PCI.

METHODS AND ANALYSIS

Registration

This protocol has been developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. It has also been registered with the International Prospective Register of Systematic Reviews (registration number CRD42018088415).[18]

Eligibility criteria

Study type

We will include randomised controlled trials that investigate the effects of three different traditional Chinese exercise therapies (Tai chi, Baduanjin and Yijinjing） on CR following PCI. The following study designs or publication types will be excluded: (1) non-clinical research literature, such as animal experiments, reviews or case

reports; (2) duplicate publications; (3) literature with incomplete data, the study of chaos; (4) studies which lack primary outcome measures.

Participants

This network-analysis will include patients with coronary heart disease who have received TCE intervention after PCI.

Patient and Public Involvement

patients and public will not be involved.

Interventions

We plan to include the following TCE therapies: tai chi, baduanjin and yijinjing, and patients who have received TCE interventions either alone or in combination with appropriate training.

Outcomes

The primary outcomes will include: (1) all-cause mortality; (2) revascularisations (CABG or PTCA); (3) generic instrument of HRQL, such as SF-36 health survey scores; (4) hospitalisations: hospital readmission dates.

The secondary outcomes will include: (1) BNP; (2) blood lipid indexes, such as TC, TG, LDL-C and HDL-C; (3) Echocardiography; (4) Adverse events.

Search strategy

We will retrieve articles from the following databases: PubMed, Embase, Cochrane Library, Chinese National Knowledge Infrastructure, Wanfang Data, Chinese BioMedical Database and Chinese Science and Technology Periodicals Database. We anticipate that the databases will be searched from their inception to February 2018. The search strategy in PubMed database is as follows, ((((((((((Tai Ji Quan) OR Tai chi) OR Tai ji) OR Taijiquan) OR Baduanjin) OR Baduanjin exercise) OR eight section brocades) OR Yi Jinjing) OR Yijinjing) OR Yijinjing exercise)) AND ((((((((((Coronary Heart Disease) OR Coronary artery atherosclerosis heart disease) OR CHD) OR Acute coronary syndrome) OR ACS) OR Acute myocardial infarction) OR AMI) OR Heart failure) OR HF) OR percutaneous coronary intervention) OR PCI). The search strategy for PubMed is shown in Table 1.

The search strategy will be developed by two reviewers (Weipeng Sun and Ting Li) who will independently review the full texts of potentially eligible studies. Discrepancies in the meta-analysis will be discussed and settled by a third reviewer. We will use a preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart to discern, filter, and eliminate selected articles. We will express the study selection process with a PRISMA flow chart (http: //www.prisma-statement.org) (Figure 3).

Data collection process

All titles and abstracts of potential trials will be retrieved and organised by two authors (Weipeng Sun and Ting Li) in Endnote X7. Duplicate records will be excluded. The database will then be copied and provided to the first author for duplicate screening. Any disagreements between the two authors will be resolved by discussion with the whole team at a regular meeting. We will allocate the trials to the following five groups: inclusion group, non-patient group, intervention group, outcome group and awaiting group. For this project, Microsoft Excel will be used for preliminary data collection. Four spreadsheets including general information (author list, publication year, and journal), characteristics of the included trials (diagnostic criteria, age range, study drugs, and dose range), risk of bias assessed using the Cochrane risk of bias tool[19] and outcome data extraction (number of participants who responded to treatment and the number who dropped out during the treatment), will be represented in the table. Relevant original data will be submitted as attachments.

Quality assessment

The methodological quality of the eligible studies, concealment allocation, covering randomisation, blinding and other biases will be evaluated by two authors (Tian Zhang, Xiaoqi Zhou) according to the Cochrane revised tool for Risk of Bias[20]. Particular attention will be paid to the adequacy of random allocation concealment and blinding due to the potential failure of inadequate concealment in the randomisation test. Considering the diagnostic criteria, the sample size calculation method, reporting of withdrawals and follow-up, any other sources of bias will be cautiously assessed. Another two authors (Xiaojiang Yu, Wei Wu) will assess the

quality of evidence using the GRADE framework, covering study limitations, inconsistency, indirectness, imprecision and publication bias. The complete assessment procedures are as follows[21]: (1) offer direct and indirect effect estimates; (2) assess the quality of direct and indirect estimates; (3) present the results of the network meta-analysis; (4) assess the quality of the network meta-analysis effect estimates.

Dealing with missing data

We will initially contact both senior and/or corresponding author to obtain any missing data. If no one responds, the following approaches will be used to estimate the missing data. Instead of providing the mean and SD, the number of responding patients employing a validated imputation method will be calculated for studies failing to report the patients' numbers after treatment. We will also try to estimate from graphs if possible. The reason for exclusion of the available data will be excluded, but the reason for exclusion will be reported.

Network meta-analysis

We will use the Markov Chain Monte Carlo algorithm (MCMC) by applying WinBUGS 1.4.3 to conduct the network meta-analysis (NMA) in a Bayesian hierarchical framework. The magnitude of heterogeneity variance will be used to investigate the statistical heterogeneity of all of the NMAs. If direct evidence is feasible, NMAs will be evaluated comprehensively. In treatment effect assessed by indirect and direct comparisons, the potential difference can be evaluated by several methods, and 95% CIs and z-α values will be calculated for each outcome from each study. The antilogy of the model will be explored by using the node-splitting method, which generates a p-value for the difference between direct and indirect estimates in each closed loop in the network (p-values of <0.05 indicate the presence of inconsistency between direct and indirect estimates in a particular closed loop). We will use the deviance information criterion (DIC) to compare the random and fixed effects models to evaluate model fitness by taking references from the guidelines commonly used in the analogous Akaike Information Criteria: values which decrease by at least 10 points indicate significantly better model fit and parsimony. The mean

ranks and surface under the cumulative ranking curve (SUCRA) will be used to sequence the probabilities of the optimal intervention of various treatments. We will describe SUCRA with percentages. For the treatment, better ranks are indicated by higher values. Stata v. 12 will be used to generate result figures and NMA graphs. If the data cannot be used for quantitative analysis, the evidence will be described and summarised.

Sensitivity analysis and subgroup analysis

The strategies can be used to address the problem of heterogeneity of pairwise meta-analysis, as well as be employed to tackle incongruity of network analysis. Inconsistent sources will be explored by performing a network meta-regression. We will conduct a sensitivity analysis to explore the strong conclusions of the main results wherever practical. The overall results will be influenced because the methodological quality levels of the studies vary. To conduct sensitivity analysis, we will remove trails that report the generation of non-random sequences.

Publication bias

If feasible, we will also convey any small study effects that exist within a network of interventions. Publication bias will be assessed by performing Egger's regression test. If feasible, a statistical model will be used to convey the network of interventions, including small study effects.

Quality of evidence

For the main outcomes, the quality of evidence will be assessed based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE). Five projects, including the limitations of research design, indirectness, incongruity, imprecision and publication bias, will be investigated.

DISCUSSION

TCE, a series of mind-body exercises including baduanjin, yijinjing, and tai chi (TC, also known as 'taiji chuan') originated in ancient Chinese philosophy. TCE has been practised for over 1,000 years. Based on the theoretical principles of traditional Chinese medicine (TCM), in clinical rehabilitation focuses on posture, meditation,

and coordination of breath. The common characteristics of these movements is that they are slow, relaxing and systematic, and therefore suitable for physically weak patients. By correcting body posture and movements, adjusting breathing patterns, and maintaining stillness of mind, a wide array of natural self-regulatory/self-healing mechanisms can be activated to stimulate the balanced release of endogenous neurohormones[22-23].

Previous reviews have indicated that left ventricular (LV) remodeling after myocardial infarction (MI) can be reduced by baduanjin; Another study demonstrated that baduanjin provides clinically meaningful improvement for SBP, DBP, BMI, blood glucose, TG, HDL-C, LDL-C and QoL [24]. Research on TC has discovered that it can improve VO_2 max in patients with coronary disease. This suggests that TC could be applied in cardiac rehabilitation (CR) as an adjuvant therapy[25]; Another study has indicated that TC might improve 6-MWD, QoL, and LVEF in patients, and could be associated with significant reductions in BNP and HR[26]. This would signify the clinical importance of CR post-PCI. Research has also shown that the effects of TCE on blood pressure and blood lipids commonly acknowledged as the primary targets for cardiovascular risk reduction (e.g. LDL-C) are clinically significant[27].

TCE could therefore be used in CR therapy post-PCI, but its efficacy and mechanisms remain unclear. More larger-scale well-designed studies using standardized training protocols are needed in order for specific and accurate conclusions to be made. Thus, the aim of the present study is to systematically assess the effects of TCE on patients in CR post-PCI by using enough studies to ensure adequate power for the meta-analysis. To the best of our knowledge, this review will be the first network meta-analysis to evaluate the impact of TCE for patients in CR post-PCI. We hope the results of this review will help establish a better approach for exploring the potential functions of TCE in CR and will also provide reliable evidence supporting the use of TCE.

Contributors

CL and RL conceived of the study and drafted the protocol. JW, WS and XZ revised it. TL, WW and XY developed the search strategies and conducted data collection. TZ analysed the data independently. All authors have approved the final manuscript.

Funding

This study is supported by the 2017 Diagnosis and Treatment Innovation Project at The First Affiliated Hospital of Guangzhou University of Chinese Medicine.

Competing interests

None declared.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No additional data are available.

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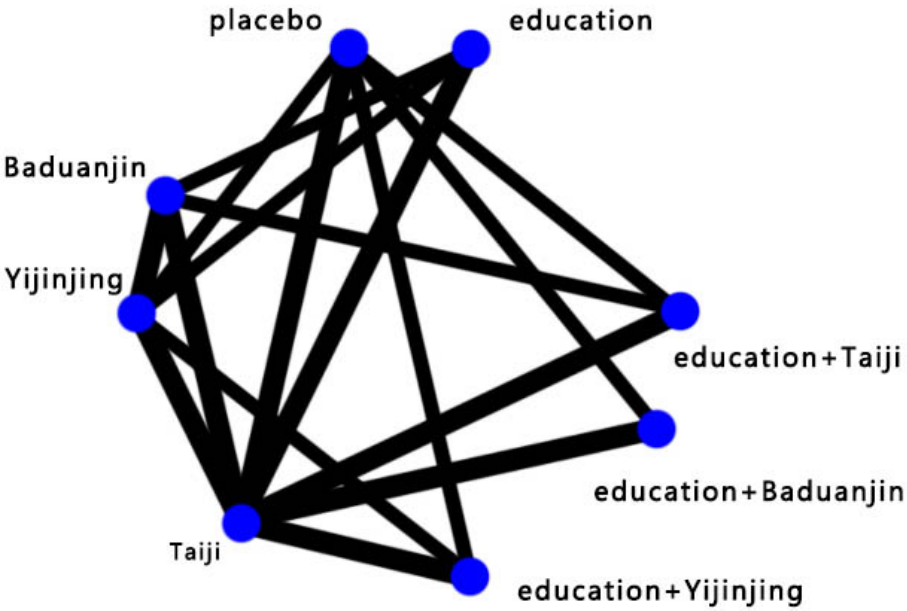
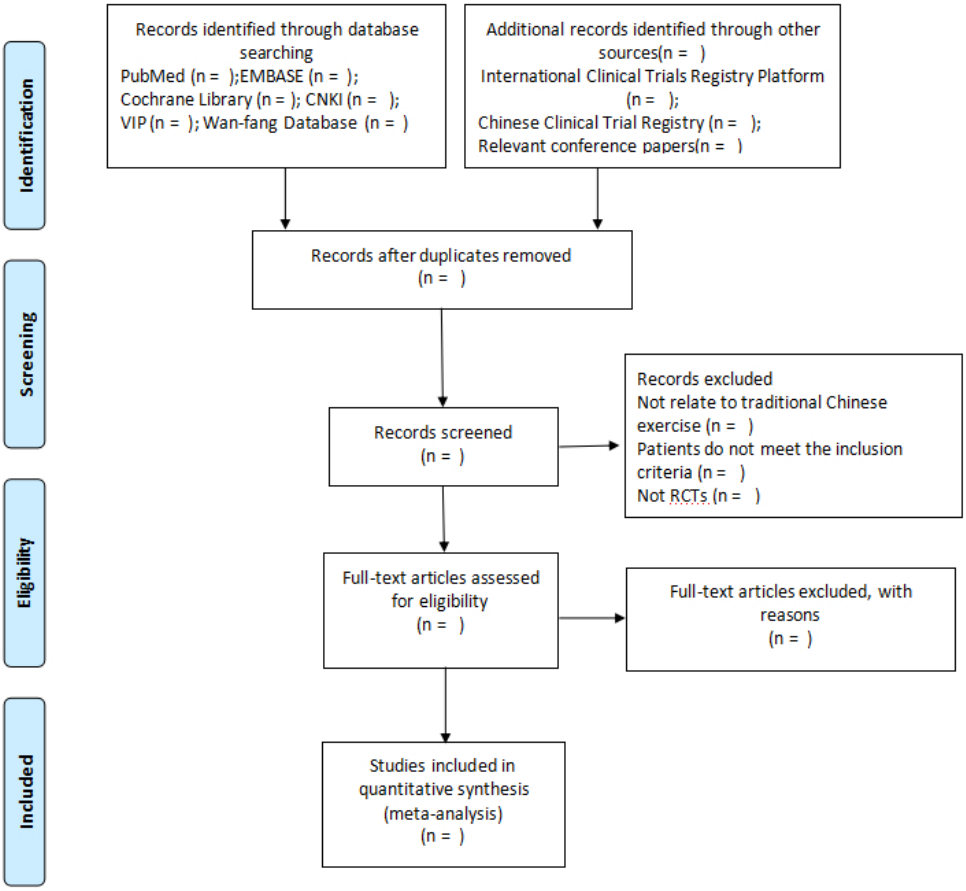
Table 1. Search strategy utilized for the PubMed database

No.	Search terms
1	Tai Ji Quan
2	Tai chi
3	Tai ji
4	Taijiquan
5	Baduanjin
6	Baduanjin exercise
7	eight section brocades
8	Yi Jinjing
9	Yijinjing
10	Yijinjing exercise
11	or1-10
12	Coronary Heart Diseases
13	CHD
14	Coronary artery atherosclerosis heart disease
15	Acute coronary syndrome
16	ACS
17	Acute myocardial infarction
18	AMI
19	Heart failure
20	HF
21	Cardiovascular events
22	percutaneous coronary intervention
23	PCI
24	or12-23
25	11 and 24

Figure 1. Traditional Chinese exercise (A is Tai chi, B is Baduanjin, C is Yi Jinjing).
Figure 2. Network plot of all possible direct comparisons between the eligible interventions.
Figure 3. Flow diagram of the study selection process.



177x140mm (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	Reported on page #
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	no
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
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	14
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	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	2-3
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	6-7
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	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	7-8

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
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)	8
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	8,9
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	8-10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
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	11,12
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	10,11
	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)	10-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11,12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11,12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

*** 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.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023096.R1
Article Type:	Protocol
Date Submitted by the Author:	22-Oct-2018
Complete List of Authors:	Luo, Chuanjin; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Cardiovascular Disease Wen, Junmao; Guangzhou University of Chinese Medicine Sun, Weipeng; Guangzhou University of Chinese Medicine Li, Ting; Guangzhou University of Chinese Medicine Yu, Xiaojiang; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Rehabilitation Center Zhang, Tian; Guangzhou University of Chinese Medicine Zhou, Xiaoqi; Guangzhou University of Chinese Medicine Wu, Wei; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Cardiovascular Disease Li, Rong;
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine
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ABSTRACT

Introduction: Coronary heart disease (CHD) is the most common cause of death worldwide. Percutaneous coronary intervention (PCI) has been shown to reduce mortality in patients with CHD. However, there are still recurrences of cardiovascular events after PCI. Cardiac rehabilitation (CR) in patients with established CHD is associated with reductions in cardiovascular mortality and hospital admissions, as well as improved quality of life. More and more clinical trials suggest that traditional Chinese exercise (TCE) plays a positive role in patients post-PCI.

Objective: The primary purposes of the current study are to conduct a network meta-analysis of randomized trials to determine the effects of TCE in patients after PCI, and to separately compare the effects of tai chi, baduanjin and yijinjing on cardiac rehabilitation after PCI.

Methods and analysis: Studies will be retrieved from the following databases: PubMed, Embase, Cochrane Library, Chinese National Knowledge Infrastructure, Wanfang Data, Chinese BioMedical Database and Chinese Science and Technology Periodicals Database, from inception to February 2018. We will include RCTs that are related to the effects of TCE therapies in patients after PCI. The primary outcomes will be all-cause mortality, revascularisations, health-related quality of life (HRQL), and hospitalisations. Two reviewers will independently select eligible articles. For each included article, two reviewers will independently extract the data and assess the risk of bias by using the Cochrane risk of bias tool. Bayesian network meta-analyses will be conducted to pool all treatment effects. The ranking probabilities for the optimal intervention of various treatments (tai chi, baduanjin or yijinjing) will be estimated by the mean ranks and surface under the cumulative ranking curve (SUCRA). The Grading of Recommendations

Assessment, Development and Evaluation System will be utilized to assess the quality of evidence.

Ethics and dissemination: The results will be disseminated through peer-reviewed publications. They will provide consolidated evidence to inform clinicians on the potential functions of TCE in CR, and to provide reliable evidence for the application of TCE.

Trial registration number: CRD42018088415

Strengths and limitations of this study

- This is the first systematic review to use network meta-analysis to compare various forms of traditional Chinese exercise.
- This is the first systematic review to compare the effects of baduanjin, yijinjing and tai chi on cardiac rehabilitation post-PCI.
- This study will assess the effects of TCEs and their safety regarding cardiac rehabilitation after PCI.
- The study will use the Grading of Recommendations Assessment, Development and Evaluation System to further assess the quality of the evidence.
- Due to the changes in the frequency and duration of treatment, there may be methodological heterogeneity.

INTRODUCTION

Description of the condition

Coronary heart disease (CHD), also known as coronary artery disease (CAD), is the most common cause of death worldwide, causing 7.4 million deaths in 2013, accounting for one-third of all deaths globally (WHO 2014)[1]. In addition to the requisite medical therapy, mechanical revascularization with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is needed for patients with CHD. PCI has been shown to reduce mortality in patients with CHD[2]. During follow-up, however, the benefits of PCI surgery still carry significant risks of coronary spasm, endothelial cell

injury, recurrent ischemia, and even restenosis or thrombus[3-5]. Numerous guidelines endorse the benefits of cardiac rehabilitation (CR), which is recommended for patients with chronic stable angina, acute coronary syndromes or for patients post-PCI surgery[2,6-10]. Combined with routine therapy, exercise-based CR, which has been recommended by American Heart Association (AHA) guidelines[11], is a safe option. It has been reported that light to moderate intensity physical activity can reduce coronary heart disease mortality[12].

Description of the intervention

For centuries, traditional Chinese exercise (TCE) (Figure 1), a series of mind-body exercises including baduanjin, yijinjing, and tai chi (TC, also known as 'taiji chuan'), has been widely practiced in China for both preventive and therapeutic purposes. Based on the theoretical principles of traditional Chinese medicine (TCM), in clinical rehabilitation focuses on posture, meditation, and coordination of breath. The common characteristics of these movements is that they are slow, relaxing and systematic, and therefore suitable for physically weak patients. By correcting body posture and movements, adjusting breathing patterns, and maintaining stillness of mind, a wide array of natural self-regulatory/self-healing mechanisms can be activated to stimulate the balanced release of endogenous neurohormones[13-14]. Considered to be a low-risk, promising intervention that is used widely in the prevention of cardiovascular disease, TCEs are easy to master in a short time and have few physical demands[15]. Regardless of previous exercise experience or aerobic capacity, the exercise intensity of TCE is suited for persons of all ages. Moreover, TCE requires no expensive equipment and can be performed either individually or in groups. Most existing systematic reviews have focused on specific forms of TCE, such as tai chi or baduanjin[16-18]. Whether TCE has positive clinical effects on patients with CHD after PCI, however, remains unclear.

Therefore, we will conduct the present network meta-analysis to explore whether TCE affects the primary endpoint events of cardiac death, recurrence of MI, repeated PCI, and restenosis after PCI; to determine whether TCE could be an effective method for

improving secondary endpoint measures such as quality of life (QoL), physical functions and symptoms, after PCI; to separately compare the effects of Tai chi, Baduanjin and Yijinjing on patients post-PCI. (Figure 2)

METHODS AND ANALYSIS

Registration

This protocol has been developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. It has also been registered with the International Prospective Register of Systematic Reviews (registration number CRD42018088415).[19]

Supplementary Appendix (Patient_Consent)

The pictured individual had signed a consent form confirming that he understood the situation (Appendix of “Patient_Consent ”).

Eligibility criteria

Study type

We will include randomised controlled trials that compare the effects of three different traditional Chinese exercise therapies (Tai chi, Baduanjin and Yijinjing） with a no exercise control on patients with CHD following PCI. The following study designs or publication types will be excluded: (1) non-clinical research literature, such as animal experiments, reviews or case reports; (2) duplicate publications; (3) literature with incomplete data, the study of chaos; (4) studies which lack primary outcome measures. If multiple intervention data can be obtained, the trails can be adopted. If data for comparison of multiple interventions cannot be directly obtained, we will try E-mailing the corresponding author to obtain the original data. If the data cannot be obtained, the trails will also be excluded.

Participants

This network-analysis will include patients with coronary heart disease who have received TCE intervention after PCI.

Patient and Public Involvement

patients and public will not be involved.

Interventions

We plan to include the following TCE therapies: tai chi, baduanjin and yijinjing, and patients who have received TCE interventions either alone or in combination with appropriate training. For comparisons, both active (e.g. walking) or non-active (e.g. usual care) controls compared with TCEs will be included. For the reason that some RCTs set a placebo controlled arm as the comparator, information about interventions from placebo controlled trails will also be extracted.

Outcomes

The primary outcomes will include: (1) all-cause mortality; (2) revascularisations (CABG or PTCA); (3)results of Medical Outcome Study (MOS) 36-Item Short-Form Health Survey (SF-36); (4) hospitalisations: hospital readmission dates.

The secondary outcomes will include: (1) b-type natriuretic peptide ; (2) blood lipid indexes (i.e. serum total cholesterol, triglyceride , low density lipoprotein cholesterol and high-density lipoprotein cholesterol); (3) echocardiography; (4) adverse events.

Search strategy

We will search the following databases: PubMed, Embase, Cochrane Library, Chinese National Knowledge Infrastructure, Wanfang Data, Chinese BioMedical Database and Chinese Science and Technology Periodicals Database. We anticipate that the databases will be searched from their inception to February 2018. The search strategy in PubMed database is as follows, ((((((((((Tai Ji Quan) OR Tai chi) OR Tai ji) OR Taijiquan) OR Baduanjin) OR Baduanjin exercise) OR eight section brocades) OR Yi Jinjing) OR Yijinjing) OR Yijinjing exercise)) AND ((((((((((Coronary Heart Disease) OR Coronary artery atherosclerosis heart disease) OR CHD) OR Acute coronary syndrome) OR ACS) OR Acute myocardial infarction) OR AMI) OR Heart failure) OR HF) OR percutaneous coronary intervention) OR PCI). The search strategy for PubMed is shown in Table 1. The search strategy will be developed by two reviewers (Weipeng

Sun and Ting Li) who will independently review the full texts of potentially eligible studies. Discrepancies regarding included studies will be discussed and settled by a third reviewer.

Data collection process

All titles and abstracts of potential trials will be retrieved and organised by two authors (Weipeng Sun and Ting Li) in Endnote X7. Duplicate records will be excluded. The database will then be copied and provided to the first author for duplicate screening. Any disagreements between the two authors will be resolved by discussion with the whole team at a regular meeting. We will allocate the trials to the following five groups: inclusion group, non-patient group, intervention group, outcome group and awaiting group. For this project, Microsoft Excel will be used for preliminary data collection. Four spreadsheets including general information (i.e. author list, publication year, and journal, etc), characteristics of the included trials (i.e. diagnostic criteria, age range, study drugs, and dose range, etc), risk of bias assessed using the Cochrane risk of bias assessment tool[19] and outcome data extraction (i.e. numbers of response events and non-response events, time points, mean or mean difference, reported outcome definitions, summary data related to treatment effects, etc.), will be represented in the table. Relevant original data will be submitted as attachments.

We will express the study selection and data colletion process with a PRISMA flow chart (http: //www.prisma-statement.org) (Figure 3).

Quality assessment

The methodological quality of the eligible studies, concealment allocation, covering randomisation, blinding and other biases will be evaluated by two authors (Tian Zhang, Xiaoqi Zhou) according to the Cochrane risk of bias assessment tool [20]. Particular attention will be paid to the adequacy of random allocation concealment and blinding due to the potential failure of inadequate concealment in the randomisation test. Considering the diagnostic criteria, the sample size calculation method, reporting of withdrawals and

follow-up, any other sources of bias will be cautiously assessed. The complete assessment procedures are as follows[21]: (1) offer direct and indirect effect estimates; (2) assess the quality of direct and indirect estimates; (3) present the results of the network meta-analysis; (4) assess the quality of the network meta-analysis effect estimates.

Dealing with missing data

We will initially contact both senior and/or corresponding author to obtain any missing data. If no one responds, the following approaches will be used to estimate the missing data. Instead of providing the mean and SD, the number of responding patients employing a validated imputation method will be calculated for studies failing to report the patients' numbers after treatment. We will also try to estimate from graphs if possible. The reason for exclusion of the available data will be reported.

Network meta-analysis

We will use the Markov Chain Monte Carlo algorithm (MCMC) by applying WinBUGS 1.4.3 to conduct the network meta-analysis (NMA) in a Bayesian hierarchical framework. The inverse variance heterogeneity method will be used in order to overcome the limitations of the fixed and random effects models. Minimally informative prior distributions will be used for the main outcome.The magnitude of heterogeneity variance will be used to investigate the statistical heterogeneity of all of the NMAs.If direct evidence is feasible, NMAs will be evaluated comprehensively. In treatment effect assessed by indirect and direct comparisons, the potential difference can be evaluated by several methods, and 95% CIs and z-α values will be calculated for each outcome from each study. The antilogy of the model will be explored by using the node-splitting method, which generates a p-value for the difference between direct and indirect estimates in each closed loop in the network (p-values of <0.05 indicate the presence of inconsistency between direct and indirect estimates in a particular closed loop). We will use the deviance information criterion (DIC) to compare the random and fixed effects models to evaluate model fitness by taking references from the guidelines commonly used in the analogous Akaike Information Criteria: values which decrease by at least 10

points indicate significantly better model fit and parsimony. The mean ranks and surface under the cumulative ranking curve (SUCRA) will be used to sequence the probabilities of the optimal intervention of various treatments. We will describe SUCRA with percentages. For the treatment, better ranks are indicated by higher values. Stata 12 will be used to generate result figures and NMA graphs. If the data cannot be used for quantitative analysis, the evidence will be described and summarised.

Sensitivity analysis and subgroup analysis

The strategies can be used to address the problem of heterogeneity of pairwise meta-analysis, as well as be employed to tackle incongruity of network analysis. Inconsistent sources will be explored by performing a network meta-regression. We will conduct a sensitivity analysis to explore the strong conclusions of the main results wherever practical. The overall results will be influenced because the methodological quality levels of the studies vary. Sensitivity analysis will be conducted to exclude trials with small sample sizes (i.e. arms of less than 10 patients) and remove trails that report the generation of non-random sequences. It is planned (if the number of trials is high enough) to perform sensitivity analysis with respect to age difference and geographical region.

Publication bias

If feasible, we will also convey any small study effects that exist within a network of interventions. Publication bias will be assessed by performing Egger's regression test. If feasible, a statistical model will be used to convey the network of interventions, including small study effects.

Quality of evidence

For the main outcomes, two authors (Xiaojiang Yu, Wei Wu) will assess the quality of evidence based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE), covering study limitations, inconsistency, indirectness,

imprecision and publication bias. Five factors, including the limitations of research design, indirectness, incongruity, imprecision and publication bias, will be investigated.

DISCUSSION

Previous reviews have indicated that left ventricular (LV) remodeling after myocardial infarction (MI) can be reduced by baduanjin; Another study demonstrated that baduanjin provides clinically meaningful improvement for SBP, DBP, BMI, blood glucose, TG, HDL-C, LDL-C and QoL[22]. Research on TC has discovered that it can improve VO_2 max in patients with coronary disease. This suggests that TC could be applied in cardiac rehabilitation (CR) as an adjuvant therapy[23]; Another study has indicated that TC might improve 6-MWD, QoL, and LVEF in patients, and could be associated with significant reductions in BNP and HR[24]. This would signify the clinical importance of CR post-PCI. Research has also shown that the effects of TCE on blood pressure and blood lipids commonly acknowledged as the primary targets for cardiovascular risk reduction (e.g. LDL-C) are clinically significant[25].

TCE could therefore be used in CR therapy post-PCI, but its efficacy and mechanisms remain unclear. More larger-scale well-designed studies using standardized training protocols are needed in order for specific and accurate conclusions to be made. Thus, the aim of the present study is to systematically assess the effects of TCE on patients in CR post-PCI by using enough studies to ensure adequate power for the meta-analysis. To the best of our knowledge, this review will be the first network meta-analysis to evaluate the impact of TCE for patients in CR post-PCI. We hope the results of this review will help establish a better approach for exploring the potential functions of TCE in CR and will also provide reliable evidence supporting the use of TCE.

Contributors

CL and RL conceived of the study and drafted the protocol. JW, WS and XZ revised it. TL, WW and XY developed the search strategies and conducted data collection. TZ analysed the data independently. All authors have approved the final manuscript.

Funding

This study is supported by the 2017 Diagnosis and Treatment Innovation Project at The First Affiliated Hospital of Guangzhou University of Chinese Medicine.

Competing interests

None declared.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No additional data are available.

Consent for the pictured individual

The pictured individual had signed a consent form confirming that he understood the situation (Appendix of "Patient Consent ").

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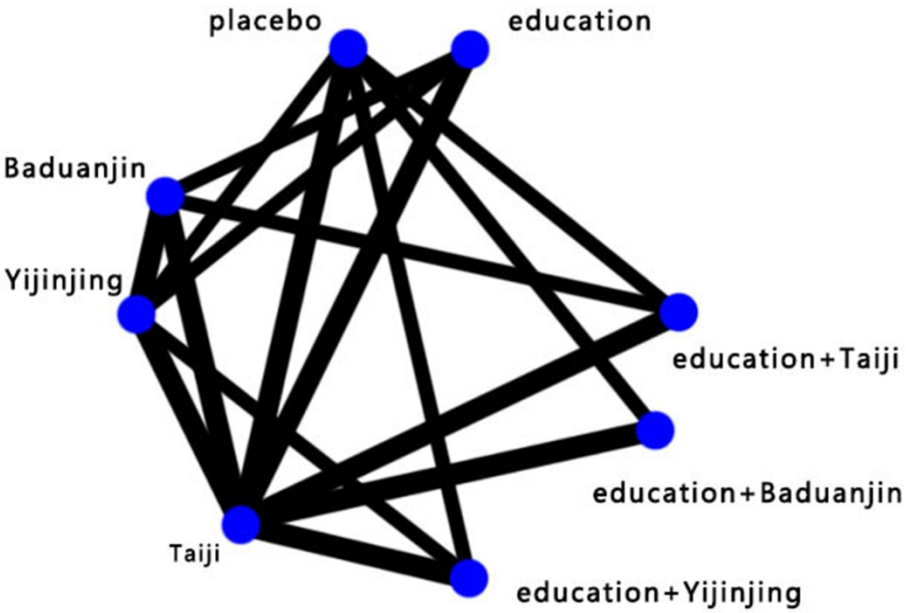
Table 1. Search strategy utilized for the PubMed database

No.	Search terms
1	Tai Ji Quan
2	Tai chi
3	Tai ji
4	Taijiquan
5	Baduanjin
6	Baduanjin exercise
7	eight section brocades

8	Yi Jinjing
9	Yijinjing
10	Yijinjing exercise
11	or1-10
12	Coronary Heart Diseases
13	CHD
14	Coronary artery atherosclerosis heart disease
15	Acute coronary syndrome
16	ACS
17	Acute myocardial infarction
18	AMI
19	Heart failure
20	HF
21	Cardiovascular events
22	percutaneous coronary intervention
23	PCI
24	or12-23
25	11 and 24

Figure 1. Traditional Chinese exercise (A is Tai chi, B is Baduanjin, C is Yi Jinjing).
Figure 2. Network plot of all possible direct comparisons between the eligible interventions.
Figure 3. Flow diagram of the study selection process.

175x175mm (300 x 300 DPI)



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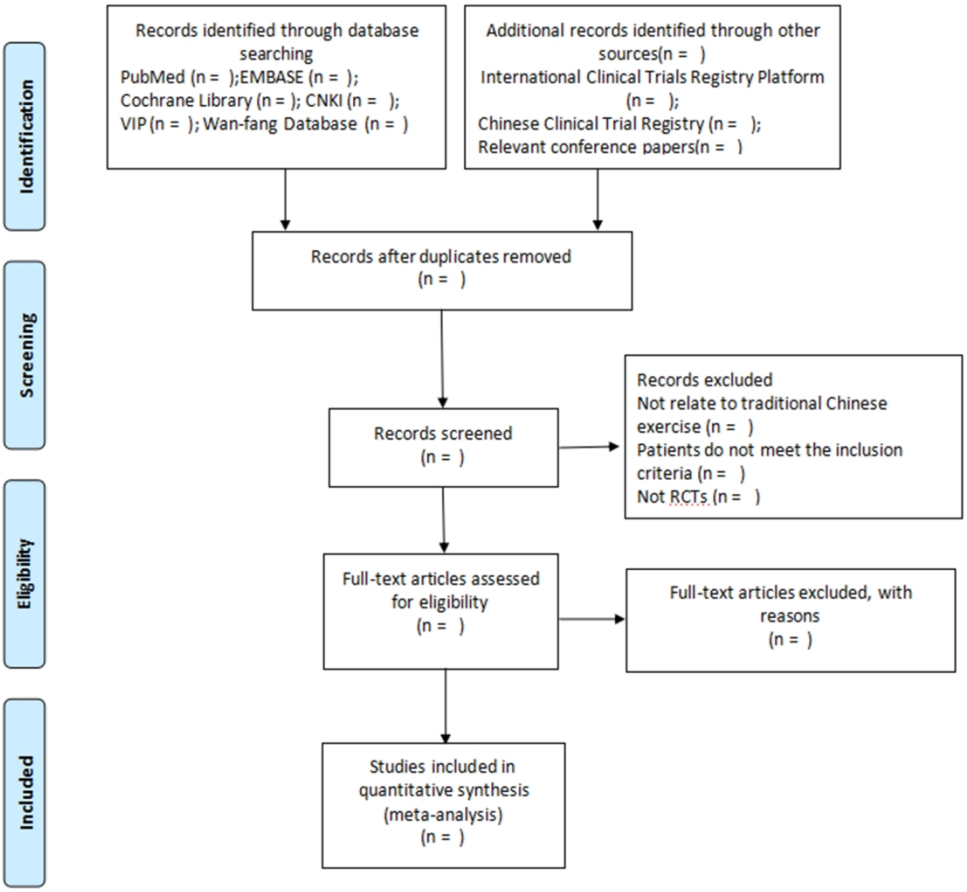

193x175mm (300 x 300 DPI)

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	Reported on page #
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	no
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
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	14
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	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	2-3
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	6-7
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	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	7-8

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
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)	8
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	8,9
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	8-10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
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	11,12
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	10,11
	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)	10-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11,12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11,12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

*** 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.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

The Effects of Traditional Chinese Exercise on Cardiac Rehabilitation After Percutaneous Coronary Intervention : Study Protocol for Network Meta-analysis of Randomized Controlled Trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023096.R2
Article Type:	Protocol
Date Submitted by the Author:	27-Nov-2018
Complete List of Authors:	Luo, Chuanjin; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Cardiovascular Disease Wen, Junmao; Guangzhou University of Chinese Medicine Sun, Weipeng; Guangzhou University of Chinese Medicine Li, Ting; Guangzhou University of Chinese Medicine Yu, Xiaojiang; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Rehabilitation Center Zhang, Tian; Guangzhou University of Chinese Medicine Zhou, Xiaoqi; Guangzhou University of Chinese Medicine Wu, Wei; First Affiliated Hospital of Guangzhou University of Chinese Medicine, Department of Cardiovascular Disease Li, Rong;
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine
Keywords:	Traditional Chinese Exercise, Cardiac Rehabilitation, Coronary heart disease < CARDIOLOGY

The Effects of Traditional Chinese Exercise on Cardiac Rehabilitation After Percutaneous Coronary Intervention：Study Protocol for Network Meta-analysis of Randomized Controlled Trials

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ABSTRACT

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Ethics and dissemination: The results will be disseminated through peer-reviewed publications. They will provide consolidated evidence to inform clinicians on the potential functions of TCE in CR, and to provide reliable evidence for the application of TCE.

Trial registration number: CRD42018088415

Strengths and limitations of this study

- This is the first systematic review to use network meta-analysis to compare various forms of traditional Chinese exercise.
- This is the first systematic review to compare the effects of baduanjin, yijinjing and tai chi on cardiac rehabilitation post-PCI.
- This study will assess the effects of TCEs and their safety regarding cardiac rehabilitation after PCI.
- The study will use the Grading of Recommendations Assessment, Development and Evaluation System to further assess the quality of the evidence.
- Due to the changes in the frequency and duration of treatment, there may be methodological heterogeneity.

INTRODUCTION

Description of the condition

Coronary heart disease (CHD), also known as coronary artery disease (CAD), is the most common cause of death worldwide, causing 7.4 million deaths in 2013, accounting for one-third of all deaths globally (WHO 2014)[1]. In addition to the requisite medical therapy, mechanical revascularization with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is needed for patients with CHD. PCI has been shown to reduce mortality in patients with CHD[2]. During follow-up, however, the benefits of PCI surgery still carry significant risks of coronary spasm, endothelial cell injury, recurrent ischemia, and even restenosis or thrombus[3-5]. Numerous guidelines endorse the benefits of cardiac rehabilitation (CR), which is recommended for patients with chronic stable angina, acute coronary syndromes or for patients post-PCI surgery[2,6-10]. Combined with routine therapy, exercise-based CR, which has been recommended by American Heart Association (AHA) guidelines[11], is a safe option. It has been reported that light to moderate intensity physical activity can reduce coronary heart disease mortality[12].

Description of the intervention

For centuries, traditional Chinese exercise (TCE) (Figure 1), a series of mind-body exercises including baduanjin, yijinjing, and tai chi (TC, also known as

'taiji chuan'), has been widely practiced in China for both preventive and therapeutic purposes. Based on the theoretical principles of traditional Chinese medicine (TCM), in clinical rehabilitation focuses on posture, meditation, and coordination of breath. The common characteristics of these movements is that they are slow, relaxing and systematic, and therefore suitable for physically weak patients. By correcting body posture and movements, adjusting breathing patterns, and maintaining stillness of mind, a wide array of natural self-regulatory/self-healing mechanisms can be activated to stimulate the balanced release of endogenous neurohormones[13-14]. Considered to be a low-risk, promising intervention that is used widely in the prevention of cardiovascular disease, TCEs are easy to master in a short time and have few physical demands[15]. Regardless of previous exercise experience or aerobic capacity, the exercise intensity of TCE is suited for persons of all ages. Moreover, TCE requires no expensive equipment and can be performed either individually or in groups. Most existing systematic reviews have focused on specific forms of TCE, such as tai chi or baduanjin[16-18]. Whether TCE has positive clinical effects on patients with CHD after PCI, however, remains unclear.

Therefore, we will conduct the present network meta-analysis to explore whether TCE affects the primary endpoint events of cardiac death, recurrence of MI, repeated PCI, and restenosis after PCI; to determine whether TCE could be an effective method for improving secondary endpoint measures such as quality of life (QoL), physical functions and symptoms, after PCI; to separately compare the effects of Tai chi, Baduanjin and Yijinjing on patients post-PCI. (Figure 2)

METHODS AND ANALYSIS

Registration

This protocol has been developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. It has also been registered with the International Prospective Register of Systematic Reviews (registration number CRD42018088415).[19]

Eligibility criteria

Study type

We will include randomised controlled trials that compare the effects of three different traditional Chinese exercise therapies (Tai chi, Baduanjin and Yijinjing）with a no exercise control on patients with CHD following PCI. The following study designs or publication types will be excluded: (1) non-clinical research literature, such as animal experiments, reviews or case reports; (2) duplicate publications; (3) literature with incomplete data, the study of chaos; (4) studies which lack primary outcome measures. If multiple intervention data can be obtained, the trails can be adopted. If data for comparison of multiple interventions cannot be directly obtained, we will try E-mailing the corresponding author to obtain the original data. If the data cannot be obtained, the trails will also be excluded.

Participants

This network-analysis will include patients with coronary heart disease who have received TCE intervention after PCI.

Interventions

We plan to include the following TCE therapies: tai chi, baduanjin and yijinjing, and patients who have received TCE interventions either alone or in combination with appropriate training. For comparisons, both active (e.g. walking) or non-active (e.g. usual care) controls compared with TCEs will be included. For the reason that some RCTs set a placebo controlled arm as the comparator, information about interventions from placebo controlled trails will also be extracted.

Outcomes

The primary outcomes will include: (1) all-cause mortality; (2) revascularisations (CABG or PTCA); (3)results of Medical Outcome Study (MOS) 36-Item Short-Form Health Survey (SF-36); (4) hospitalisations: hospital readmission dates.

The secondary outcomes will include: (1) b-type natriuretic peptide ; (2) blood lipid indexes (i.e. serum total cholesterol, triglyceride , low density lipoprotein cholesterol and high-density lipoprotein cholesterol); (3) echocardiography; (4) adverse events.

Search strategy

We will search the following databases: PubMed, Embase, Cochrane Library, Chinese National Knowledge Infrastructure, Wanfang Data, Chinese BioMedical Database and Chinese Science and Technology Periodicals Database. We anticipate that the databases will be searched from their inception to December 2018. The search strategy in PubMed database is as follows, ((((((((((Tai Ji Quan) OR Tai chi) OR Tai ji) OR Taijiquan) OR Baduanjin) OR Baduanjin exercise) OR eight section brocades) OR Yi Jinjing) OR Yijinjing) OR Yijinjing exercise)) AND ((((((((((Coronary Heart Disease) OR Coronary artery atherosclerosis heart disease) OR CHD) OR Acute coronary syndrome) OR ACS) OR Acute myocardial infarction) OR AMI) OR Heart failure) OR HF) OR percutaneous coronary intervention) OR PCI). The search strategy for PubMed is shown in Table 1. The search strategy will be developed by two reviewers (Weipeng Sun and Ting Li) who will independently review the full texts of potentially eligible studies. Discrepancies regarding included studies will be discussed and settled by a third reviewer.

Data collection process

All titles and abstracts of potential trials will be retrieved and organised by two authors (Weipeng Sun and Ting Li) in Endnote X7. Duplicate records will be excluded. The database will then be copied and provided to the first author for duplicate screening. Any disagreements between the two authors will be resolved by discussion with the whole team at a regular meeting. We will allocate the trials to the following five groups: inclusion group, non-patient group, intervention group, outcome group and awaiting group. For this project, Microsoft Excel will be used for preliminary data collection. Four spreadsheets including general information (i.e. author list, publication year, and journal, etc), characteristics of the included trials (i.e. diagnostic criteria, age range, study drugs, and dose range, etc), risk of bias assessed using the Cochrane risk of bias assessment tool[19] and outcome data extraction (i.e. numbers of response events and non-response events, time points, mean or mean difference, reported outcome definitions, summary data related to treatment effects, etc.), will be represented in the table. Relevant original data will be submitted as attachments.

We will express the study selection and data colletion process with a PRISMA flow chart (http: //www.prisma-statement.org) (Figure 3).

Quality assessment

The methodological quality of the eligible studies, concealment allocation, covering randomisation, blinding and other biases will be evaluated by two authors (Tian Zhang, Xiaoqi Zhou) according to the Cochrane risk of bias assessment tool [20]. Particular attention will be paid to the adequacy of random allocation concealment and blinding due to the potential failure of inadequate concealment in the randomisation test. Considering the diagnostic criteria, the sample size calculation method, reporting of withdrawals and follow-up, any other sources of bias will be cautiously assessed. The complete assessment procedures are as follows[21]: (1) offer direct and indirect effect estimates; (2) assess the quality of direct and indirect estimates; (3) present the results of the network meta-analysis; (4) assess the quality of the network meta-analysis effect estimates.

Dealing with missing data

We will initially contact both senior and/or corresponding author to obtain any missing data. If no one responds, the following approaches will be used to estimate the missing data. Instead of providing the mean and SD, the number of responding patients employing a validated imputation method will be calculated for studies failing to report the patients' numbers after treatment. We will also try to estimate from graphs if possible. The reason for exclusion of the available data will be reported.

Network meta-analysis

We will use the Markov Chain Monte Carlo algorithm (MCMC) by applying WinBUGS 1.4.3 to conduct the network meta-analysis (NMA) in a Bayesian hierarchical framework. The inverse variance heterogeneity method will be used in order to overcome the limitations of the fixed and random effects models. Minimally informative prior distributions will be used for the main outcome.The magnitude of heterogeneity variance will be used to investigate the statistical heterogeneity of all of the NMAs.If direct evidence is feasible, NMAs will be evaluated comprehensively. In

treatment effect assessed by indirect and direct comparisons, the potential difference can be evaluated by several methods, and 95% CIs and z-α values will be calculated for each outcome from each study. The antilogy of the model will be explored by using the node-splitting method, which generates a p-value for the difference between direct and indirect estimates in each closed loop in the network (p-values of <0.05 indicate the presence of inconsistency between direct and indirect estimates in a particular closed loop). We will use the deviance information criterion (DIC) to compare the random and fixed effects models to evaluate model fitness by taking references from the guidelines commonly used in the analogous Akaike Information Criteria: values which decrease by at least 10 points indicate significantly better model fit and parsimony. The mean ranks and surface under the cumulative ranking curve (SUCRA) will be used to sequence the probabilities of the optimal intervention of various treatments. We will describe SUCRA with percentages. For the treatment, better ranks are indicated by higher values. Stata 12 will be used to generate result figures and NMA graphs. If the data cannot be used for quantitative analysis, the evidence will be described and summarised.

Sensitivity analysis and subgroup analysis

The strategies can be used to address the problem of heterogeneity of pairwise meta-analysis, as well as be employed to tackle incongruity of network analysis. Inconsistent sources will be explored by performing a network meta-regression. We will conduct a sensitivity analysis to explore the strong conclusions of the main results wherever practical. The overall results will be influenced because the methodological quality levels of the studies vary. Sensitivity analysis will be conducted to exclude trials with small sample sizes (i.e. arms of less than 10 patients) and remove trails that report the generation of non-random sequences. It is planned (if the number of trials is high enough) to perform sensitivity analysis with respect to age difference and geographical region.

Publication bias

If feasible, we will also convey any small study effects that exist within a network of interventions. Publication bias will be assessed by performing Egger's

regression test. If feasible, a statistical model will be used to convey the network of interventions, including small study effects.

Quality of evidence

For the main outcomes, two authors (Xiaojiang Yu, Wei Wu) will assess the quality of evidence based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE), covering study limitations, inconsistency, indirectness, imprecision and publication bias. Five factors, including the limitations of research design, indirectness, incongruity, imprecision and publication bias, will be investigated.

Patient and Public Involvement

Patients and public will not be involved.

DISCUSSION

Previous reviews have indicated that left ventricular (LV) remodeling after myocardial infarction (MI) can be reduced by baduanjin; Another study demonstrated that baduanjin provides clinically meaningful improvement for SBP, DBP, BMI, blood glucose, TG, HDL-C, LDL-C and QoL[22]. Research on TC has discovered that it can improve VO_2 max in patients with coronary disease. This suggests that TC could be applied in cardiac rehabilitation (CR) as an adjuvant therapy[23]; Another study has indicated that TC might improve 6-MWD, QoL, and LVEF in patients, and could be associated with significant reductions in BNP and HR[24]. This would signify the clinical importance of CR post-PCI. Research has also shown that the effects of TCE on blood pressure and blood lipids commonly acknowledged as the primary targets for cardiovascular risk reduction (e.g. LDL-C) are clinically significant[25].

TCE could therefore be used in CR therapy post-PCI, but its efficacy and mechanisms remain unclear. More larger-scale well-designed studies using standardized training protocols are needed in order for specific and accurate conclusions to be made. Thus, the aim of the present study is to systematically assess the effects of TCE on patients in CR post-PCI by using enough studies to ensure adequate power for the meta-analysis. To the best of our knowledge, this review will

be the first network meta-analysis to evaluate the impact of TCE for patients in CR post-PCI. We hope the results of this review will help establish a better approach for exploring the potential functions of TCE in CR and will also provide reliable evidence supporting the use of TCE.

Ethics and dissemination: The results will be disseminated through peer-reviewed publications. They will provide consolidated evidence to inform clinicians on the potential functions of TCE in CR, and to provide reliable evidence for the application of TCE.

Contributors

CL and RL conceived of the study and drafted the protocol. JW, WS and XZ revised it. TL, WW and XY developed the search strategies and conducted data collection. TZ analysed the data independently. All authors have approved the final manuscript.

Funding

This study is supported by the 2017 Diagnosis and Treatment Innovation Project at The First Affiliated Hospital of Guangzhou University of Chinese Medicine.

Competing interests

None declared.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

No additional data are available.

Consent for the pictured individual

The individual in Figure 1 has provided informed written consent for the publication of their image.

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Table 1. Search strategy utilized for the PubMed database

No.	Search terms
1	Tai Ji Quan
2	Tai chi
3	Tai ji
4	Taijiquan
5	Baduanjin
6	Baduanjin exercise
7	eight section brocades
8	Yi Jinjing
9	Yijinjing
10	Yijinjing exercise
11	or1-10
12	Coronary Heart Diseases
13	CHD
14	Coronary artery atherosclerosis heart disease
15	Acute coronary syndrome

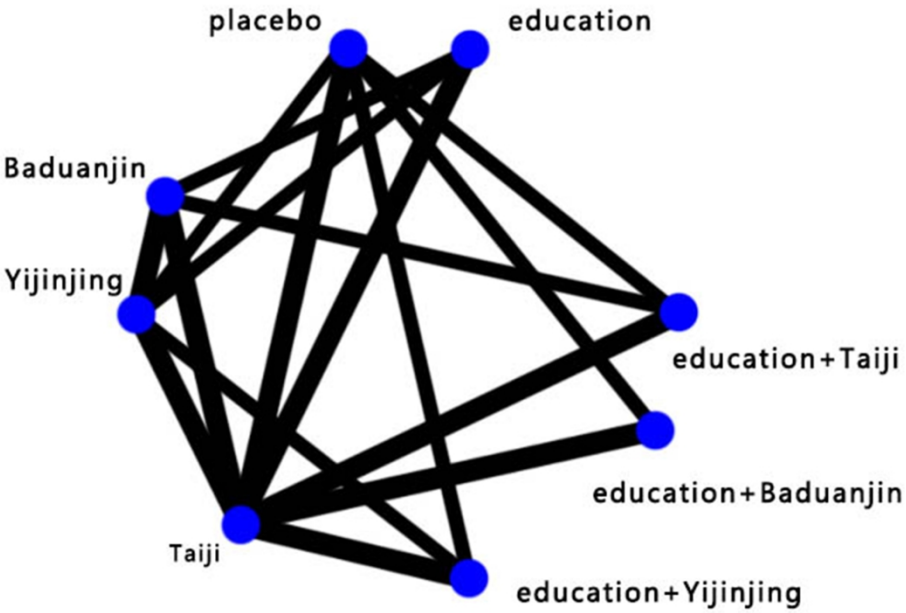
16	ACS
17	Acute myocardial infarction
18	AMI
19	Heart failure
20	HF
21	Cardiovascular events
22	percutaneous coronary intervention
23	PCI
24	or12-23
25	11 and 24

Figure 1. Traditional Chinese exercise (A is Tai chi, B is Baduanjin, C is Yi Jinjing), and the pictured individual has provided consent for publication of their image.

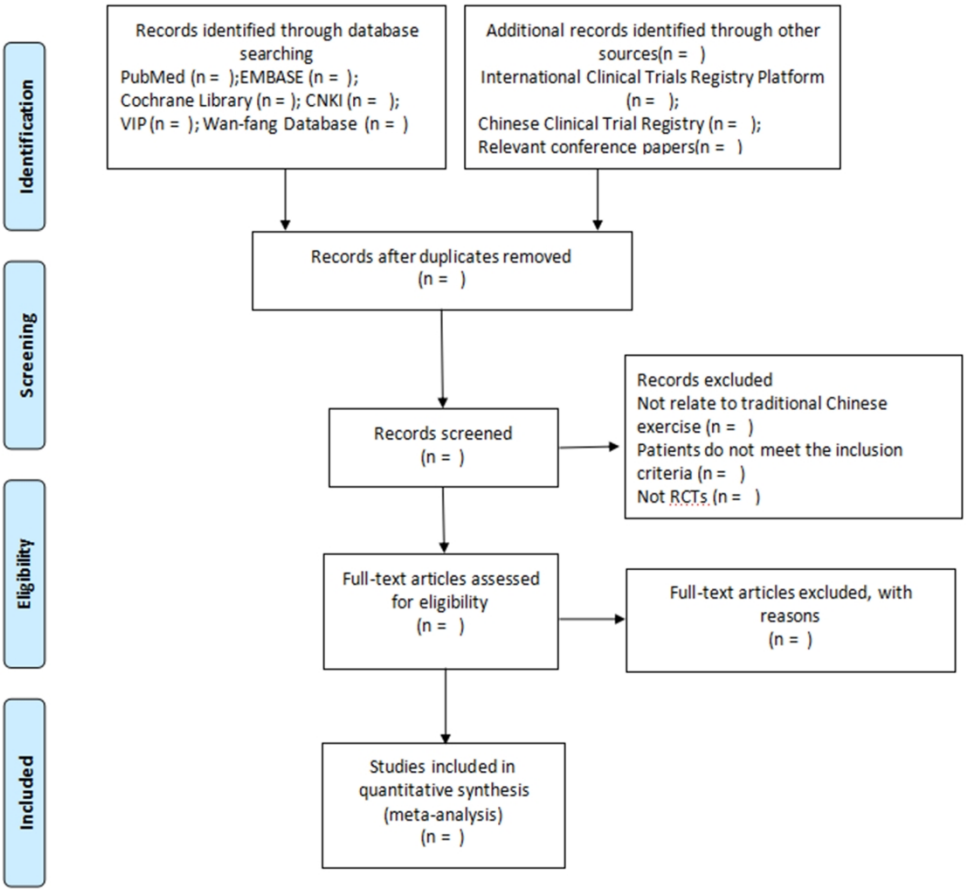
Figure 2. Network plot of all possible direct comparisons between the eligible interventions.

Figure 3. Flow diagram of the study selection process.

175x175mm (300 x 300 DPI)



177x140mm (300 x 300 DPI)



193x175mm (300 x 300 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	Reported on page #
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	no
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
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	14
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	14
Sponsor	5b	Provide name for the review funder and/or sponsor	14
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	14
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	2-3
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	6-7
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	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	7-8

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	7
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)	8
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	8,9
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	8-10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
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	11,12
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	10,11
	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)	10-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	11,12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	11,12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

*** 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.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.