## INPLASY PROTOCOL

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#### **Conflicts of interest:**

None declared.

#### INTRODUCTION

Review question / Objective: To provide a route map to guide the global research agenda to conduct studies in areas where more or better evidence is required, or to implement available acupuncture

# Evidence mapping and overview of systematic reviews on the effects of acupuncture and related-techniques

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Review question / Objective: To provide a route map to guide the global research agenda to conduct studies in areas where more or better evidence is required, or to implement available acupuncture applications that, although proved effective, are still unknown and underutilized in practice.

Condition being studied: For this overview, only systematic reviews that include meta-analysis (MA) of randomized controlled trials (RCTs) will be included. An eligible review will need to fulfil the following criteria: • To report a search in at least one electronic database. • To report at least one criterion for the inclusion of studies. • To report an effect estimate for at least one patient important outcome. • To evaluate the risk of bias of included studies. Overviews of SR, narrative reviews and protocols for SR will be excluded. No restrictions are set on study language.

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#### **METHODS**

Search strategy: We will search for relevant systematic reviews in the Epistemonikos database (www.epistemonikos.org/). Epistemonikos database is a comprehensive source of systematic reviews that screens 10 electronic databases (PubMed, EMBASE, Cochrane Database of Systematic Reviews (CDSR), **Cumulative Index to Nursing and Allied** Health Literature (CINAHL), PsycINFO, Latin American and Caribbean Health Sciences (LILACS), Database of Abstracts of Reviews of Effectiveness (DARE), Campbell library, Joanna Briggs Institute (JBI) Database, EPPI-Centre Library) to identify reviews relevant for health decision-making. In addition, 4 Chinese electronic databases (Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), WangFang Database, and Chinese Scientific Journal Database (VIP)) will be searched for potential SRs. In order to obtain recent research evidence, we will only search the meta-analysis of acupuncture published in the last 5 years. The date range of search will start from January 2015 to the search date. We will search the Chinese and English databases for updated acupuncture RCTs. The systematic reviews and included primary studies retrieved from the Chinese databases will be uploaded to the Epistemonikos database, and the evidence matrix will be formed together with the existing evidence in the database. A matrix of evidence is a tabular approach for displaying the cluster of systematic reviews that share included studies. It includes all systematic reviews addressing a similar

question (ie, sharing at least one included study) and all studies addressing the question in those reviews.

Participant or population: There are no restrictions on type of participants. We will use ICD-10 to classify the diseases and conditions.

Intervention: We use the World Health Organization's definition: Acupuncture literally means to puncture with a needle. However, there may also involve the application of other kinds of stimulation to certain points. We included any type of commonly used acupunctures that simulate certain points with needle, laser, electricity, or pressure. The specific types of acupuncture therapies included in this manuscript are traditional body needling, manual acupuncture, electroacupuncture(electro-acupuncture), ear(auricular), scalp acupuncture, laser acupuncture, and transcutaneous electrical nerve stimulation (TENS), and acupressure. In this collection, we define acupuncture as any type of interventions involving the penetration of the skin with needles or stimulation of certain points with other methods regardless of its theoretical basis excluding the forms combined with moxibustion or medication such as warm needling, acupoint injection or hydroacupuncture.

Comparator: No intervention or waiting list, sham/placebo, standard of care / usual care, western medicine, other interventions (such as psychotherapy, rehabilitation.) We will exclude SRs in which the control group received TCM related therapies, such as acupuncture, moxibustion, scraping, cupping, bloodletting, acupoint catgut embedding, massage, Chinese herbal medicine, tai chi.

Study designs to be included: Randomized controlled trial

Eligibility criteria: We will use the matrix of evidence in Epistemonikos database to select the reviews. As collaborators of the Epistemonikos database, we will link the

RCTs included to the systematic reviews to create an evidence matrix for each clinical condition. To select one from multiple systematic reviews for the same condition, we will apply below selection criteria in the order listed: (1) For each clinical question, we will select the systematic review that contains the most RCTs. (2) if the primary studies are completely overlapping, that is to say the primary studies are consistent in quantity and content, we will select the highest-quality review using AMSTAR-2. If the primary studies partially overlapped or do not overlap, we will update the metaanalysis with all eligible primary studies. (3) when there are both Network Meta-Analysis(NMA) and pairwise comparison meta-analyses addressing the same patients and the same outcomes with overlap in the interventions, we will prioritize NMA. If there is no NMA, we would choose pairwise comparison SRs. Then two reviewers (### and ###) will independently screen titles and abstracts to identify relevant meta analysis and updated RCTs. The full text of potentially eligible reviews and RCTs will be retrieved and independently evaluated by two authors for final inclusion. Disagreements will be addressed through discussion; if a consensus cannot be reached, a third author (###) will resolve the disagreements.

Information sources: Epistemonikos database and 4 Chinese electronic databases (Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), WANFANG Database, and Chinese Scientific Journal Database (VIP)).

Main outcome(s): At least include one patient important outcome. Some patient-important outcomes are shown below: I Mortality. 1. all cause mortality 2. disease specific mortality II Morbidity. 1. cardiovascular major morbid events 2. other major morbid events (e.g. loss of vision, seizures, fracture) 3. onset/recurrence/relapse of cancer and other chronic diseases (e.g. COPD exacerbation, symptomatic diabetes) 4. renal failure requiring dialysis 5. hospitalization, medical and surgical procedures (e.g. placement of

a pacemaker, cardioversion and revascularization) 6.symptomatic infections 7. dermatological/rheumatologic disorders III Quality of life/Functional status (e.g. failure to become pregnant, failure to nurse/breastfeed, depression).

Data management: Two reviewers will independently extract data from selected review for each condition using standardized forms, including study ID, first author, study published year, country, sample size of included trials, number of participants, number of included primary studies, type of diseases and conditions classified by ICD-10, interventions and comparisons, outcome, certainty of evidence assessed by GRADE (Grading of recommendations assessment, development and evaluation) methodology, effect sizes and related 95% CI (confidence interval), AMASTAR2, adverse events, cost effective. To ensure consistency, we will conduct calibration exercises before the review. Discrepancies in the extracted data will be resolved by discussion and, if needed, a third author will arbitrate. For individual updated RCT, the information we will extract includes: study ID, first author, year of publication, number of participants, study population, interventions and comparisons, result data, patient important outcomes that matches with the selected reviews. If new patient important outcomes that match with the selected reviews are in three or more updated RCTs, we will conduct quantitative synthesis of the data and add the result to the systematic reviews. If the outcomes cannot be combined or the number of RCTs containing the new patient important outcomes are less than three, we will describe the results qualitatively.

#### Quality assessment / Risk of bias analysis:

We will assesse the methodological quality of all SRs using AMSTAR (A Measurement Tool to Assess SRs) 2 tool. The overall quality of the SRs can be divided into High, Moderate, Low and Critically Low. Two independent investigators will do each quality assessment, with discrepancies adjudicated by a third investigator.

Strategy of data synthesis: We will reanalysis the selected meta-analysis if new primary studies are added. According to the Cochrane handbook 10, if the intervention effect of each study is the same in direction, the overall effect is calculated using a fixed-effect model. A random-effects model is used when the studies are likely to vary such that they are estimating related but not identical effects. If results of smaller studies are systematically different from results of larger ones, we will perform a sensitivity analysis in which small studies are excluded to avoid possible misleading. The heterogeneity between different studies is assessed using the Chi<sup>2</sup> test and the I2 statistic.

Subgroup analysis: Subgroup analysis will not be done.

Sensitivity analysis: If results of smaller studies are systematically different from results of larger ones, we will perform a sensitivity analysis in which small studies are excluded to avoid possible misleading.

Language: No restrictions are set on study language.

Country(ies) involved: China, Canada, Chile.

Keywords: Evidence mapping, acupuncture, systematic reviews.

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