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Methodological and evidence quality of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing in China: a critical appraisal

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Complete List of Authors:	Jin, Ying-Hui; School of Nursing, Tianjin University of Traditional Chinese Medicine, 1. Department of Surgical and Gynecological Nursing, Evidence- Based Nursing Center Wang, Guo-Hao; School of Nursing, Tianjin University of Traditional Chinese Medicine Zhao, Chen; Graduate College, Tianjin University of Traditional Chinese Medicine Zhang, Yan; School of Nursing, Tianjin University of Traditional Chinese Medicine Li, Ge; Public Health Department of Tianjin University of Traditional Chinese Medicine Li, Yan; School of Nursing, Tianjin University of Traditional Chinese Medicine Li, Yan; School of Nursing, Tianjin University of Traditional Chinese Medicine Lu, Cui Shang, Hong-Cai; Dongzhimen Hospital, Beijing University of Chinese Medicine, Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing
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Methodological and evidence qualities of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing in China: a critical appraisal Ying-Hui Jin¹, Guo-Hao Wang¹, Chen Zhao², Yan Zhang¹, Ge Li³, Yan Li¹, Cui Lu¹, Hongcai Shang⁴

1. Department of Surgical and Gynecological Nursing, Evidence-Based Nursing Center,

School of Nursing, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China

2. Graduate College, Tianjin University of Traditional Chinese Medicine, Tianjin 300193,

China

Public Health Department of Tianjin University of Traditional Chinese Medicine, Tianjin
 300193, China

4. Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing, Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing 100700, China

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Correspondence to: Prof. Hongcai Shang, Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing, Dongzhimen Hospital, Beijing University of Chinese Medicine, No. 5 Haiyuncang, Dongcheng District, Beijing 100700, China. E-mail: shanghongcai0301@163.com. Tel: +86-22-15822772648.

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ABSTRACT

Objective: To assess the methodology and quality of evidence of systematic reviews and meta-analyses regarding Traditional Chinese Medical Nursing (TCMN) in Chinese journals. **Design:** A systematic literature search for systematic reviews and meta-analyses of TCMN was performed. The review characteristics were extracted. The methodological and evidence qualities were evaluated using the Assessment of Multiple Systematic Reviews (AMSTAR) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

Result: Nineteen systematic reviews and meta-analyses were included, and 10 TCMN interventions were assessed in the 19 reviews. The compliance with the AMSTAR checklist items ranged from 4.5 to 8, and the systematic reviews / meta-analyses had, on average, a medium methodological quality. The quality of the evidence assessed ranged from very low to moderate, and no high quality evidence was identified. The top-two causes for rating down confidence in the effect estimates among the 29 bodies of evidence assessed included the risk of bias and inconsistency.

Conclusion: A critical appraisal of systematic reviews / meta-analyses of TCMN prior to evidence use and decision-making is particularly important.

Strengths and limitations of this study

This study is the first attempt to assess the methodology and quality of evidence of systematic reviews and meta-analyses regarding Traditional Chinese Medical Nursing (TCMN) in Chinese journals using the Assessment of Multiple Systematic Reviews (AMSTAR) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

The results highlight that the critical appraisal of systematic reviews/ meta-analyses of TCMN prior to evidence use and decision-making is particularly important, and suggestions are provided regarding how improvements may be incorporated in the future.

The main limitation of this study is that the methodology and quality of the evidence assessments were based on information regarding the assessment items in the individual systematic reviews and meta-analyses reported, which may not reflect the construction process. Moreover, there is no appropriable tool in the nursing field.

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Introduction

Despite considerable developments in medicine, a substantial number of individuals in both developed and developing countries utilize complementary and alternative medicine (CAM), including Traditional Chinese Medicine (TCM)¹. In general, TCM, which is a science nourished by the Chinese culture, is delivered by qualified practitioners, and it has been practiced for thousands of years in China². Traditional Chinese Medical Nursing (TCMN) is a significant branch of Nursing in China; it primarily consists of TCM mental nursing, diet nursing, TCM exercise, and TCM nursing techniques (medication of TCM nursing, acupoint massage and cupping).

To date, the concept of a health and medical model, as well as the scope of nursing, have been extended from disease nursing to disease prevention and health promotion with changes in disease patterns. The holistic philosophy and the personalized nature of TCMN concur with the patient-centred approach used in modern nursing. In the Chinese Nursing Development Program (2010-2015), it is explicitly noted that TCMN should be developed to contribute to the prevention and control of geriatric diseases and chronic diseases, and it should also be combined with Western and Chinese medicine nursing techniques ³. In China, with the development of specialized TCM clinical nursing, the increasing popularity of TCMN techniques and the gradual establishment of a standardization of nursing specialties, the service ability and scientific research level of TCMN has significantly improved. A survey of 137 TCM institutions in China indicated that there were 85 TCMN techniques provided for patients, and the top-ten techniques included moxibustion, cupping therapy, auricular application pressure, TCM fumigation, acupuncture point massage, acupoint sticking, TCM enema, ironing with Chinese medicine, inunction with Chinese medicine, and scrapping therapy ⁴.

The effectiveness of TCMN techniques in clinical trials should be reported. In the previous decade, the number of papers that report trials of TCMN has steadily increased in addition to the number of systematic reviews and meta-analyses based on these findings. Systematic

reviews and meta-analyses serve a vital role in clinical practice guideline (CPG) development ⁵. The assessment and synthesis of primary studies of TCMN in systematic reviews and meta-analyses, followed by the development of CPGs regarding integrated TCM and Western Medicine care may promote the sustainable development of TCMN.

Systematic reviews and meta-analyses are considered the highest level of evidence in the hierarchy of evidence-based medicine (EBM) for preventive and therapeutic interventions. Although systematic reviews and meta-analyses strive to provide scientifically rigorous, independent, and accurate summaries of the scientific evidence with respect to a specific question of interest ⁶, methodological deficiencies of systematic reviews and meta-analyses may result in misleading results and over- or under-estimation of the investigated effects ⁷. Moreover, even methodologically sound systematic reviews and meta-analyses may not guarantee the output of high quality evidence unless the included primary studies consistently exhibit an adequate quality. Moreover, systematic reviews and meta-analyses may only provide indirect or imprecise evidence for the question of interest. For CPG developers, the quality ratings reflect the extent of our confidence that estimates of an effect are adequate to support a specific decision or recommendation ⁸.

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In this EBM era, nurses must also learn how to apply evidence (including systematic reviews, meta-analyses, and CPGs) for TCM to their daily practice. A critical appraisal of the systematic reviews and meta-analyses of TCMN may increase nurse confidence and facilitate the efficient application of the evidence ⁹. In this study, we used widely accepted and utilized instruments, including the Assessment of Multiple Systematic Reviews (AMSTAR) tool ^{10 11} and the Grades of Recommendations Assessment, Development and Evaluation (GRADE) approach ¹², to critically assess the methodology and quality of evidence of TCMN in Chinese journals and determine their contribution to the development of evidence-based decision-making.

Methods

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The technology road mapping of this study is presented in Figure 1.

Eligibility criteria

We included a study if it met the following criteria: (1) the study design is a systematic review, meta-analysis, or systematic review and meta-analysis; (2) the topic is TCMN care in China; and (3) the paper was published as a full-text article. Articles were excluded if the interventions focused on a broad concept of TCM (e.g., TCM care vs. Western Medicine care) without a subgroup analysis; this approach indicates that the review defined a relatively broad scope of the review question, which reflected substantial clinical heterogeneity.

Data sources

A comprehensive literature search was conducted to identify systematic reviews and meta-analyses by searching the China academic Journals Full-text Databases, Chinese Biomedical Literature Database, Chinese Scientific Journal Databases, and Chinese Medical Association Journals from inception through March 2015. We also searched the 29 professional nursing journals and four professional EBM journals in China. The reference lists of the retrieved review articles were also screened to identify potential studies. If several updates of a study were available, only the most recent version was included.

Study selection and data extraction

Two reviewers independently screened the abstracts and titles of the studies and subsequently reviewed the full text articles for inclusion; data extraction was subsequently performed. We categorized the outcomes of the systematic reviews and meta-analyses into the following types: endpoint, quality of life (QOL), the target event occurred, symptoms, laboratory outcomes, composite outcome (synthesis of multi-type outcomes), adverse events and economic evaluations. The odds ratio (OR), risk ratio (RR), or hazard ratio (HR) and the 95% confidence interval (CI) of each outcome were extracted when possible. In addition, the surname of the first author, year of publication, methodological quality of the original studies,

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Quality assessment

The quality assessment of every systematic review and meta-analysis was independently assessed by two assessors using the AMSTAR tool ^{10 11} and GRADE approach ¹². To improve standardization, a special training and pre-test were performed. Disagreements between the reviewers were solved by discussion or consulting a third assessor. The agreement between the two reviewers was determined by the Kappa statistic with the corresponding 95%CI. Different individuals comprised the assessors for the AMSTAR evaluation and the GRADE evaluation, respectively, to ensure that their judgement was not affected by previous impressions. Appraisers were not allowed to communicate or confer with each other during the appraisal process.

According to the AMSTAR criteria ¹⁰¹¹, a score of 0 or 1 was assigned to each criterion, with equal weight given to each domain. Each item was judged as "yes (1 score)" when the criterion was explicitly met, "no (0 score)" when the criterion was not explicitly met, "cannot answer" when the item was relevant but was not adequately described or not reported at all, and "not applicable" when the item was not relevant. When specific domains were not reported in sufficient detail, a score of 0.5 was assigned for the domain. The overall score was categorized into three levels: 8 to 11 indicated a high quality; 4 to 7 indicated a medium quality, and 0 to 3 indicated a low quality. All assessors set a more complete and unanimous standard for the AMSTAR criteria following a careful and complete discussion among all authors.

For grading the evidence quality, the authors identified outcomes that are of key importance to patients. The reviewers subsequently applied the GRADE to determine the quality of the evidence and considered the five possible reasons to downgrade the evidence or

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the three possible reasons to upgrade the evidence ^{8 9 12}. The assessors were conservative in the judgement of downgrading or upgrading. When the systematic review did not provide sufficient information to judge the quality of the evidence, the assessor attempted to contact the authors of the individual studies. Finally, the definitions of "high", "moderate", "low" and "very low" were used in grading the quality of the evidence.

Data analysis

We established a database using Microsoft Excel 2007 software to extract the data. Information regarding each included paper was imported into the database for analysis. We conducted descriptive statistics on the distribution of the scores per AMSTAR item and summary statistics for the observed AMSTAR scores for each included systematic review and meta-analysis. The GRADE evidence profiles, which included an explicit judgement of each factor that determines the quality of the evidence for the outcome of each included systematic review and meta-analysis, were provided using GRADEprofiler 3.6 software.

The AMSTAR instrument and the GRADE approach were applied to assess the methodological and evidence quality based on different criteria and systems; however, several similarities exist between them. For example, item 3 regarding a thorough and comprehensive search (for example, searching international, national, regional and subject-specific databases, the Cochrane Central Register of Controlled Trials (CENTRAL), conference abstracts, and other grey literature and ongoing trials) to identify as many relevant studies as possible helps to reduce a high probability of publication bias (GRADE rating down item). The correlation between the AMSTAR and GRADE instruments was investigated via scatter plot using SPSS version 17.0.

Results

Characteristics of included studies

The literature search yielded 726 potentially relevant references, which included 21 references that were selected for full text review. Nineteen studies ¹³⁻³¹ were included in this

study (Technology road mapping, Fig. 1). The year of publication ¹³⁻³¹ ranged from 2010 to 2014, and the number of reviews published in 2014 accounted for approximately half of these reviews (9/19, 47.4%). Ten TCMN interventions were assessed, which included acupressure, acupoint massage, acupoint stimulation, auricular point therapy, Tai Chi, electro-acupuncture combined with auricular point plaster therapy, Chinese herbal retention enema, inunction with Chinese medicine, foot bath therapy or foot massage with TCM, and compression of the umbilicus with Chinese herbs. None of the studies included observational research. Two studies involved both RCT and quasi-RCT. No systematic review or meta-analysis applied an indirect comparison. None of the 19 studies used the GRADE approach to summarize the evidence.

AMSTAR methodological quality

The two reviewers had a satisfactory agreement (k=0.87). The methodological quality of all included reviews is presented in Table 1. In summary, the compliance with the AMSTAR checklist items ranged from 4.5 to 8, and the majority of the systematic reviews and meta-analyses were of medium (18/19, 94.7%) methodological quality.

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None of the 19 studies provided a registered protocol. For all 19 studies, the study selection and data extraction were conducted by two independent reviewers. Most studies (14/19, 73.7%) adequately described the characteristics of the included trials; however, no studies provided a list of included and excluded studies. The search strategy design was not sufficiently comprehensive in 9 studies (47.4%). The mean number of electronic databases searched in the reviews was 3.7 (SD 2.8, range 2-9). The most frequently searched databases were PubMed (17/19, 89.5%) and CNKI (16/19, 84.2%). Two studies only searched Chinese databases. Only one study considered the status of publication (e.g., grey literature). The literature search in 10 studies was supplemented by consulting textbooks, experts in the particular field of study or retracing references. No review searched ongoing trials. All reviews assessed the scientific quality of the included studies. The risk of bias tool from the Cochrane handbook criteria (10/19, 52.6%) and the Jadad scale (6/19, 31.6%) were the most

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common criteria for the quality assessment of the included studies.

The majority of the systematic reviews and meta-analyses used appropriate methods to combine the findings of the studies included. They all stated that a random effects model was used to combine the study data when there was heterogeneity. When substantial heterogeneity was identified, potential explanations were explored in subgroup analyses in 5 studies. No reviews applied a meta-regression. Two reviews conducted a sensitivity analysis by exchanging the statistical approach for data synthesis (random-effects vs. fixed effects) to determine the robustness of the conclusion. Most studies appropriately used the methodological quality of the included trials in formulating conclusions. None of the studies conducted an evaluation of the quality of the evidence. All included studies drew definitely positive conclusions in favour of TCMN, whereas all reviewers suggested that there may be benefits in the interventions; however, the findings should be interpreted with caution because of the poor quality of trials or limited trial sample. Five systematic reviews and meta-analyses (26.3%) assessed the publication bias using funnel plots, and one review used the Egger's test. Only one study stated the conflict of interest.

GRADE evidence quality

The two reviewers had a satisfactory agreement (k=0.82). None of the 19 studies cited observational research; thus, upgrading items were excluded from the assessment of evidence quality. The evidence qualities of all included reviews are presented in Table 2.

The outcomes included the occurrence of adverse events (1/19, 5.3%) and symptoms (5/19, 27.8%), laboratory outcomes (5/19, 44.5%), and composite outcomes, such as the total effectiveness rate (16/19, 84.2%), in the 19 reviews; no review considered endpoint, economic evaluations or QOL. We initially determined the critical outcomes for each review. Judgements regarding what constitutes a critical outcome may change for different research goals and results. For example, in a review entitled "acupressure wristbands prevents postoperative nausea and vomiting: a meta-analysis", the research goal was to evaluate the

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therapeutic effects on nausea and vomiting; thus, the raters defined nausea and vomiting as the critical outcome. Furthermore, the outcomes of a systematic review of electro-acupuncture combined with auricular point plaster therapy for patients with simple obesity included the measures of the rate of effectiveness, BMI and waist circumference. The rate of effectiveness was equal to the number of patients in recovery, in which the treatments were considered to be almost equally split between markedly effective and effective, according to author's description.

The criteria for recovery, markedly effective, effective and ineffective are stated as follows: Recovery: body weight was in the normal weight range or BMI was less than 23 kg/m²; Markedly effective: body weight decreased by no less than 5 kg or BMI decreased by no less than 2 kg/m²;

Effective: body weight decreased by no less than 2 kg and less than 5 kg or BMI decreased by no less than 0.5 kg/m² and less than 2 kg/m²;

Ineffective: body weight decreased by less than 2 kg or BMI decreased by less than 0.5 kg/m^2 .

The rate of effectiveness was considered to contain substantially more therapeutic information compared with the BMI and waist circumference; thus, the rate of effectiveness was defined as the critical outcome by the raters. Twenty-nine bodies of evidence in the 19 reviews were assessed for quality.

Rationale for rating down

The quality of the evidence assessed ranged from very low to moderate, and no high quality evidence was identified.

The causes for rating down confidence in the effect estimates among the 29 bodies of evidence assessed included the risk of bias (24 times, 82.8%), inconsistency (14 times, 48.3%), indirectness (8 times, 27.6%), imprecision (3 times, 10.3%), and publication bias (9 times, 30.0%) (Fig. 2). The detailed reasons for downgrading in terms of the risk of bias (41

times total) included the failure to conceal allocation (15 times, 36.6%), failure to blind (12 times, 29.3%), incomplete reporting of random sequence generation in most included studies (9 times, 22.0%), use of an invalidated outcome measure (1 time, 2.4%), loss to follow-up and failure to adhere to the intention-to-treat principle (1 time, 2.4%), non-RCT included (2 times, 4.9%), and large sample size trial with serious limitations (1 time, 2.4%).

In general, the downgrading for inconsistency was a result of specific CIs that indicated little overlap from the individual studies and significant heterogeneity. The quality of the evidence was downgraded for indirectness (8 times total) in which substantial differences exist between the interventions (3 of 8 times, 37.5%) or the controls (4 of 8 times, 50.0%) or patient-important endpoints were replaced by surrogate endpoints (1 of 8 times, 12.5%). In a review that evaluated the effectiveness of Tai Chi in the prevention of falls in elderly individuals, the authors stated that the Berg balance scale scores in the Tai Chi group were increased compared with the control group, and they argued that Tai Chi may effectively reduce the risk of falls for elderly individuals. However, the Berg balance scale is a surrogate outcome for the occurrence of falls.

The detailed reasons for downgrading the evidence for imprecision (3 times total) included the failure to meet the optimal information size criterion (2 of 3 times, 66.7%) and wide confidence intervals (1 of 3 times, 33.3%).

The quality of evidence decreased for publication bias (12 times total) because of flaws in the literature search (7 of 12 times, 58.3%) and funnel plot asymmetry (5 of 12 times, 41.7%). There was no correlation between the AMSTAR and GRADE instruments assessed via observation of the scatter plot (Fig. 3).

Discussion

It is important to assess the methodological and evidence qualities of a systematic review/ meta-analysis before the conclusions may be used for clinical decision making. To the best of our knowledge, this is the first study that assessed the methodological quality and evidence

quality of systematic reviews and meta-analyses of TCMN in Chinese Journals using the AMSTAR and GRADE tools.

All systematic reviews, meta-analyses and primary studies lack important outcomes that depressed the quality rating of the evidence

The GRADE specifies that both the conductance of systematic reviews and the development of practice guidelines should be initiated by specifying every important outcome of interest ³². Unfortunately, the systematic reviews and meta-analyses in our study typically did not address all important outcomes. For example, one review aimed to verify the effect of foot bath therapy or foot massage with traditional Chinese medicine for diabetic foot ulcers because foot ulcers are a high risk factor for infection, gangrene, amputation and death in diabetic patients. Thus, we thought the amputation rate may represent the preferable long-term outcome to verify the effect of the intervention; however, this outcome was not considered by the reviewers ¹⁷. In general, systematic reviews and meta-analyses should include all outcomes that are likely to be meaningful to clinicians, patients, the general public, administrators and policy makers. For example, the outcomes may include survival, clinical events, patient-reported outcomes (e.g., symptoms and quality of life), adverse events, burdens (e.g., demands on caregivers, frequency of tests, and restrictions on lifestyle) and economic outcomes (e.g., cost and resource use) ⁵⁶⁸⁹¹²³²³³. However, the primary studies typically focused on the short-term benefits without considering the long-term harm or economic outcomes. None of the reviews listed adverse effects as outcomes of TCMN interventions. These findings confirmed that the systematic reviews, meta-analyses and primary studies had shortcomings in the research design, which also rendered the results of the systematic reviews and meta-analyses difficult to use to make appropriate recommendations because they were based on incomplete outcomes.

Risk of bias resulted in downgrading in most reviews

RCTs are critical for assessing and providing valuable evidence regarding the effectiveness of TCMN practices. However, the reliability and acceptability of intervention study results

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depends on the extent to which the studies employ scientific principles and use a valid research design. In this study, we used the Cochrane Collaboration tool to assess the risk of bias ¹¹. Most of the reviews were downgraded because of the lack of allocation concealment and blinding, as well as the lack of details regarding randomization in the primary studies. Two hundred sixteen RCTs were included in the 19 systematic reviews and meta-analyses, and the authors noted that 181 RCTs (83.8%) were published in Chinese journals. The number of RCTs in nursing research in China has increased over time; however, the quality of most RCTs remains unsatisfactory.

This finding is consistent with the results of previous research regarding the quality of nursing intervention studies in Mainland China. Xing et al ³⁴ published a comprehensive evaluation of 7391 nursing intervention studies published in simplified Chinese from 1979 to 2012. The results demonstrated that among the 10 characteristics considered in the quality evaluations, the lowest ratings were identified for the "utilization of blind method", "description of loss of follow-up", "appropriate calculation of sample size" and "randomized assignment of patients to treatments".

Current systematic reviews and meta-analyses are often limited in their usefulness as guidelines because they rate the risk of bias by studies across outcomes rather than by outcomes across studies ³³. The authors of systematic reviews and meta-analyses should consider that the sources of bias may vary in importance across outcomes; thus, the summary of study limitations must be outcome specific ³⁵. For example, the assessors downgraded the evidence many times for not using blinding based on subjective outcomes, which are substantially more vulnerable to biased judgements. The previously described review that evaluated the effect of foot bath therapy or foot massage for diabetic foot ulcers used the rate of effectiveness as the only outcome, which was based on a subjectively observable judgement of the condition (e.g., ulcer area, local swelling and skin colour). The raters categorized this evidence as having serious study limitations because of the lack of blinding during the study ¹⁷. Problems with the design and execution of individual studies of TCMN

interventions raise questions regarding the validity of the intervention effect of TCMN and resulted in the downgrading of the quality of evidence.

Lack of adequate investigation of heterogeneity or inappropriate combination of study findings typically leads to decreasing the quality of evidence because of inconsistency The raters decreased the quality of evidence when significant heterogeneity was identified for which the authors failed to identify a reasonable source or explanation. Studies analysed together in a systematic review will inevitably have differences; however, reviewers should look for robust explanations for significant heterogeneity ³³.

Clinical variation will lead to heterogeneity if the intervention effect is affected by the factors that vary across individual studies, such as the patient characteristics or specific interventions. In our study, the variability in the interventions is the most common reason for heterogeneity, e.g., different points for acupoint massage, different medicines for Chinese herbal retention enema, or different Chinese herbal prescriptions for umbilical compression. The raters considered that the true intervention effect may be different in different studies and decreased the evidence quality for inconsistencies in the results, as well as the methodological quality for the inappropriate combination of study findings.

When there is heterogeneity that cannot be readily explained, incorporating it into a random-effects model is often the only option for reviewers. Reviewers should understand that a random-effects model does not "take account" of the heterogeneity (12). When the meta-analysis results indicate that the heterogeneity is statistically significant, the most important treatment method is to analyse the potential reasons for the heterogeneity rather than simply using the random effects model.

Methodological quality assessment using the AMSTAR should be a precondition for further evaluation with the GRADE approach

Systematic reviews/ meta-analyses may considerably differ in their methodological quality ³⁶.

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Using a rigorous methodology with a clearly formulated research question and a comprehensive search strategy, systematic reviews should provide reproducible results and include all potentially relevant studies, which thereby limits bias and random errors ³². Systematic reviewers should clearly specify the interventions of interest in their eligibility criteria to ensure that only directly relevant studies are eligible. However, in our study, there were several systematic reviews/ meta-analyses that included studies inconsistent with the eligibility criteria. For example, a review that aimed to evaluate foot massage for diabetic peripheral neuropathy included studies with different interventions: foot massage or massage in the foot reflection area or acupoint massage for lower limbs.

In addition, systematic reviews require a thorough, objective and reproducible search of a range of sources to identify as many relevant studies as possible to minimize bias ³³. However, in this respect, some systematic reviews/ meta-analyses in this study are far from satisfactory. Some systematic reviews/ meta-analyses utilized a flawed search strategy, for example, they only used free-text searching without performing Mesh (index terms) searching, only searched the Chinese database, and failed to identify "negative" studies. Moreover, in our study, the assessors determined that high-quality clinical trials do not always exist especially in TCMN, and in some cases, non-RCTs were included in the systematic reviews/ meta-analyses resulted in dropping of the AMSTAR scores, as well as downgrading the quality of evidence. The GRADE guideline suggests that it should not be used for systematic reviews/ meta-analyses with serious flaws; however, we did not exclude any study because no review was rated with a low methodological quality score. Nevertheless, some imperfect methodologies in conducting systematic reviews/ meta-analyses do exist.

In our study, we were unable to identify a correlation between the methodological quality and the evidence quality via a scatter plot. This finding is easy to understand. Because the GRADE is substantially more than a simple rating system, it offers a transparent and structured process for developing and presenting evidence summaries for systematic reviews⁸,

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which not only surveys the methodological characteristics of the production of the systematic review/meta-analysis that influenced the evidence quality but also explores factors that resulted in the inconsistency or imprecision.

Methodological flaws in the quality of a systematic review/meta-analysis may severely affect decision-making and the application of evidence. We suggest assessing the methodological quality prior to the evidence quality assessment. Moreover, there is no need to evaluate the evidence quality for a systematic review/ meta-analysis in which a low methodological quality score is assigned because of major flaws.

Sub-optimal reporting may contribute to an underestimation of methodological quality

A component of the research items regarding the GRADE and AMSTAR rely on transparency in reporting the systematic review/ meta-analysis document. Even the most methodologically rigorous process, if not clearly described in the systematic review/meta-analysis document, will leave assessors or users uncertain regarding the reliability of the systematic reviews/ meta-analyses. BMJ Open: first published as 10.1136/bmjopen-2016-011514 on 14 November 2016. Downloaded from http://bmjopen.bmj.com/ on April 20, 2024 by guest. Protected by copyright

Most Chinese journals impose strict limits on word count. The Chinese journal editors typically encourage authors to focus on the research results and discussion sections of their manuscripts and shorten the research methods section of their papers. Even the Chinese Journal of Nursing, which represents a leading domestic journal in China, typically limits the length of articles regarding nursing intervention studies to no more than 4 pages ³⁴. Although we attempted to contact the developers of the included reviews, it was difficult because most of the authors' contact information was not presented in the published papers. Thus, the results in this study may have been underestimated because of the lack of important information reporting.

Implications for research and practice

A high methodological quality is the basic precondition of systematic reviews for identifying

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the best available evidence for specific research questions and conducting the GRADE evaluation. Systematic review/ meta-analysis authors and editors should make every effort to adhere to well-established methodological standards to enhance the impact of their research efforts. However, a high methodological quality does not fully reflect the quality of a review, and the quality of a body of evidence is critical in decision-making. The GRADE approach provides clinicians and patients with a guide to use the results from systematic reviews/ meta-analyses in clinical practice, as well as policy makers with a guide to use in health policy.

The overall quality of systematic reviews/ meta-analyses of TCMN published in Chinese Journals remains suboptimal, especially in terms of the risk of bias, which reduces the evidence quality for nearly all indications. These findings raise concerns regarding their roles in influencing clinical practice; thus, the conclusions must be treated with caution. A critical appraisal of systematic reviews/ meta-analyses of TCMN is particularly important.

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Author contributions

signed u. s. G.L. and Y.L. u. ritical appraisal; Y.H.J. an. r. of interest Mathematical data are available. Y.H.J. and H.C.S designed this study; G.H.W. and Y.Z. searched the databases and collected

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Figure legends

Fig. 1 Technology road mapping of this study. EBM, Evidence-Based Medicine; EBN, Evidence-Based Nursing; TCM, Traditional Chinese Medicine; AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

Fig. 2 Proportional distribution of factors for downgrading the evidence quality.

Fig. 3 Scatter plot of the correlation between the AMSTAR and GRADE instruments.

AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of

Recommendations Assessment, Development and Evaluation.

Study	Priori	Data	Comprehensive	Status of	List of	Characteristics of	Quality	Forming	Method for	Р
	design	extraction	literature search	publication	studies	the included studies	assessment	conclusion	combining	
Wangqin Shen 2010	1	1	0	0	0	1	1	0	0.5	
Hongying Pu 2011	1	1	0	0	0	0	1	1	1	
Na Li 2011	1	1	0	0	0	1	1	0	1	
Xuan Zhou 2011	1	1	0	0	0	1	1	1	0.5	
Xiaoli Wu 2012	1	1	0	0	0	1	1	1	0.5	
Xilan Zheng 2012	1	1	0	0	0	0	1	0	0.5	

Study	Priori	Data	Comprehensive	Status of	List of	Characteristics of	Quality	Forming	Method for	Publication	Conflict of	Score/Rank
	design	extraction	literature search	publication	studies	the included studies	assessment	conclusion	combining	bias	interest	
Wangqin Shen 2010	1	1	0	0	0	1	1	0	0.5	0	0	4.5/medium
Hongying Pu 2011	1	1	0	0	0	0	1	1	1	1	0	6/medium
Na Li 2011	1	1	0	0	0	1	1	0	1	1	0	6/medium
Xuan Zhou 2011	1	1	0	0	0	1	1	1	0.5	0	0	5.5/medium
Xiaoli Wu 2012	1	1	0	0	0	1	1	1	0.5	1	0	6.5/medium
Xilan Zheng 2012	1	1	0	0	0	0	1	0	0.5	0	1	4.5/medium
Jiaqi Xu 2013	1	1	1	0	0	1	1	1	1	1	0	8/high
Yuan Zhao 2013	1	1	1	0	0	1	1	1	0.5	0	0	6.5/medium
Xiaoyan Wen 2013	1	1	1	1	0	1	1	1	1	0	0	8/high
Pingping Zheng 2013	1	1	1	0	0	1	1	1	0	0	0	6/medium
Guohao Wang 2014	1	1	0	0	0	1	1	1	1	1	0	7/medium
Jihuan Feng 2014	1	1	1	0	0	1	1	1	1	0	0	7/medium
Shaoxia Meng 2014	1	1	1	0	0	1	1	1	0.5	0	0	6.5/medium
Xijuan Cui 2014	1	1	1	0	0	1	1	1	1	1	0	8/high
Zhong Sun 2014	1	1	0	0	0	0	1	1	1	0	0	5/medium
Ye Li 2014	1	1	0	0	0	1	1		1	1	0	7/medium
Yuanyuan Yang 2014	1	1	1	0	0	1	1	1	1	0	0	7/medium
Baoxia Chang 2014	1	1	1	1	0	1	1	1	0.5	0	0	7.5/medium
Yue Ma 2014	1	1	0	0	0	1	1	1	1	1	0	7/medium
Total	1.00 ± 0	1.00±0.00	0.47+0.51	0.11±0.32	0.00 ± 0	0.84+0.27	1.00±0.00	0 84+0 27	0.76+0.21	0 42+0 51	0.05+0.22	6 50+1 09
Mean±SD	.00	1.00±0.00	0.47±0.51	0.11±0.32	.00	0.84±0.37	1.00±0.00	0.84±0.37	0.76±0.31	0.42±0.51	0.05±0.23	6.50±1.08

Table 1 AMSTAR scores on the methodology of reviews included in this study

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Table 2 GRADE evaluation of the evidence quality of the reviews included in this study

Study	Patients	Intervention	Comparison	Outcome	No. of P/S	Effect RR/MD (95% CI)	Quality	AMSTA score
Baoxia Chang 2014	Simple obesity	Electro-acupuncture combined with auricular point plaster	Electro-acupuncture	Rate of effectiveness	397(5)	RR1.18 (1.07 to 1.25)	LOW (1a, 4a)	7.5
Wangqin Shen 2010	Phlebitis	Ruyijinhuangsan	Magnesium sulphate by wet compression	Rate of effectiveness	327(6)	RR1.32 (1.26 to 1.34)	LOW (1a, 1b, 5a)	4.5
Hongying Pu 2011	Pressure ulcers	Moist exposed burn ointment	Skin disinfection solution or antibiotic ointment	Cure rate	432(11)	RR2.22 (2.07 to 2.33)	VERY LOW($1a_{1}$ 1b, $1c_{2}$ 1d, $3a_{2}$ 5a, 5b)	6
				Time of cure	261(5)	MD6.93 (7.7 to 6.15)	VERY LOW($1a$, $1b$, $1c$, $1d$, $3a$, $5a$, $5b$)	6
Xuan Zhou 2011	Postoperative patients	Acupressure wristbands	Placebo wristband	Incidence of nausea	1117(9)	RR0.85 (0.72 to 1)	LOW $(4a, 5a)$	5.5
				Incidence of vomiting	1117(9)	RR0.44 (0.31 to 0.62)	MODERATE (4a、5a)	5.5
Xiaoli Wu 2012	Diabetic foot ulcers	Foot bath therapy or foot massage with traditional Chinese medicine	Hot foot bath	Effective rate	845(8)	RR1.44 (1.4 to 1.46)	VERY LOW (1a、1b、2、5a、5b)	6.5
Xilan Zheng 2012	Postoperative patients	Traditional Chinese medicine for elimination of necrotic tissues	Skin disinfection solution or antibiotic ointment	Cure rate	551(9)	RR1.89 (1.65 to 2.17)	LOW (1a、1b、1c、2)	5.5
				Cure time	355(6)	MD9.33 (9.9 to 8.76)	LOW (1a、1b、1c、2)	5.5
Na Li 2011	Phlebitis	External application with aloe vera	Magnesium sulphate by wet compression	Effective rate	712(7)	RR1.25 (1.2 to 1.27)	LOW (1a、1b、1c、5a)	6
Jiaqi Xu 2013	Pressure ulcer	Resina draconis	Skin disinfection solution or antibiotic ointment	Effective rate	573(13)	RR1.2 (1.13 to 1.28)	MODERATE (1a、1b、1c)	8
Yuan Zhao 2013	Elderly individuals	Tai Chi	Regular sport or physical therapy	Rate of falls	1443(4)	RR0.82 (0.73 to 0.92)	$\begin{array}{c} \text{MODERATE} \\ (3a, 4b) \end{array}$	6.5
			· · · · · · · · · · · · · · · · · · ·	Berg balance scale, BBS	345(2)	MD2.45 (1.47 to .43)	MODERATE (3a、3b)	6.5
Xiaoyan Wen 2013	Virus hepatitis	Chinese herbal retention enema and comprehensive treatment	Comprehensive treatment	Effective rate: after 2 weeks from cure time	260(4)	RR 1.51 (1.3 to 1.67)	MODERATE (1a, 1b, 1c)	8
				Effective rate: after 4 weeks from cure time	333(5)	OR 4.17 (2.37 to 7.32)	MODERATÉ (1a、1b、1c)	8
Pingping Heng 2013	Elders living in home	Tai Chi	Regular sport or physical therapy or blank control	Rate of fall	2624(9)	RR 0.85 (0.79 to 0.92)	MODERATE (2)	6
Guohao Wang 2014	Constipation	Acupoint massage and ventral massage	routine nursing	Rate of effectiveness	2170(19)	RR 1.93 (1.86 to 2)	LOW (1a, 1c, 2, 3a)	7
Jihuan Feng 2014	Cancer patients receiving adjuvant	Acupoint massage	Routine nursing	Duration of chemotherapy-induced nausea	942(7)	MD 1.52 (1.77 to 1.26)	$\begin{array}{c} \text{LOW} \\ \text{(1a, 1b, 1c, 1e, 2)} \end{array}$	7

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	chemotherapy			Frequency of chemotherapy-induced	942(7)	MD 1.08 (1.32 to 0.83)	$\begin{array}{c} \text{LOW} \\ (1a, 1b, 1c, 1e, 2) \end{array}$	7
				nausea Severity of chemotherapy-induced	942(7)	MD 1.17(1.37 to 0.96)	LOW (1a, 1b, 1c, 1e, 2)	7
Shaoxia Meng 2014	diabetics with peripheral	Foot massage or massage in foot reflection area or acupoint massage	Routine nursing	nausea Rate of effectiveness	323(5)	RR 1.47 (1.29 to 1.68)	LOW (1a、1b、1c、3a)	6.5
Xijuan Cui 2014	neuropathy postoperative patients with abdominal operation ^Δ	for lower limbs Acupoint massage for Zusanli, Zusanli point acupuncture, Chinese medicine application at the Zusanli point	Routine nursing	First aerofluxus time: subgroup for Zusanli point acupuncture∆	317(3)	MD 14.52 (15.49 to 13.54)	LOW (1a、1f、2)	8
	operation			subgroup for acupoint massage for Zusanli Δ	326(4)	MD 22.7 (25.67 to 19.73)	LOW (1a、1f、2)	8
				subgroup for Chinese medicine application at the Zusanli point∆	1048(6)	MD 18.25 (18.6 to 17.9)	LOW (1a、1f、2)	8
Zhong Sun 2014	primary dysmenorrhea patients	umbilical compression with Chinese herbs	Analgesic drug	Rate of effectiveness	496(5)	RR 1.93 (1.45 to 2.57)	VERY LOW (1a、1b、2、3a)	5
Ye Li 2014	women in labour	acupoint massage for Sanyinjiao, Hegu, Zhiyin, Taichong, Ashi,	Blank control	Rate of effectiveness	766(6)	RR 1.64 (1.56 to 1.7)	LOW (1a、1b、2、5a、5b)	7
Yuanyuan Yang 2014		Shenshu et al. auricular point therapy	Acupuncture or drug therapy	Effective rate after 2 weeks from cure time	606(3)	RR 1.28 (1.2 to 1.37)	LOW (1a、1b、1c、2)	7
	insomnia ^{\triangle}	auricular point therapy	Acupuncture or drug therapy	Effective rate after 4 weeks from cure time	333(4)	RR 1.25 (1.13 to 1.37)	MODERATE (1a、1b、1c)	7
Baoxia Chang 2014	ileus	enema and gastrointestinal intubation with traditional Chinese medicine	Blank control	Rate of effectiveness	2821(27)	RR 1.24 (1.2 to 1.29	LOW (1a、1b、1c、1f、5b)	8
nconsistency: (2)Unexpl ndirectness: (3a)differen mprecision: (4a)optimal	lained heterogeneity of ices in therapeutic me information size crite	the intention-to-treat principle; (1 f)non-F or inconsistency of results thods between control groups; (3b)Surre erion is not met; (4b)Wide confidence in ; (5b)funnel plot asymmetry	ogate outcome					
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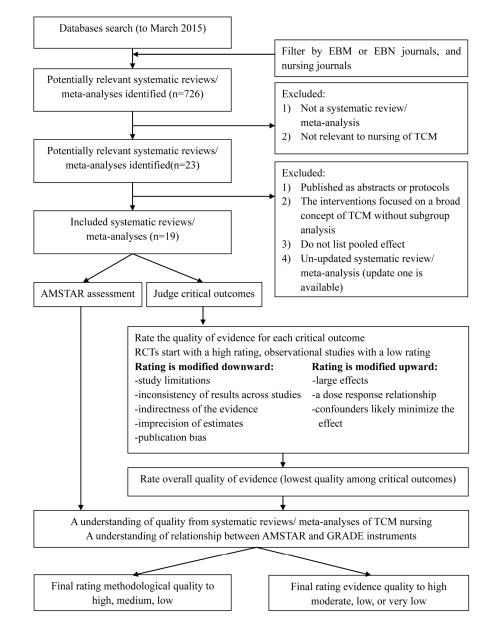


Fig. 1 Technology road mapping of this study. EBM, Evidence-Based Medicine; EBN, Evidence-Based Nursing; TCM, Traditional Chinese Medicine; AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

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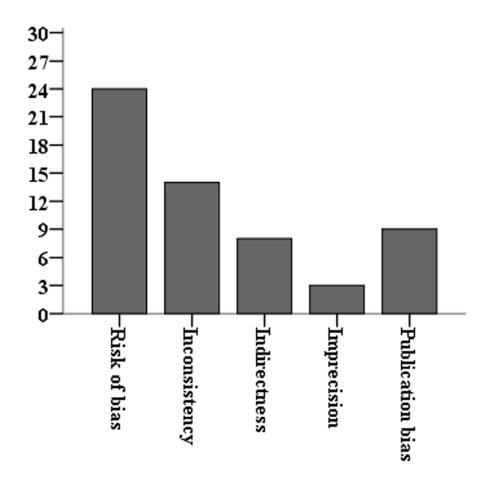
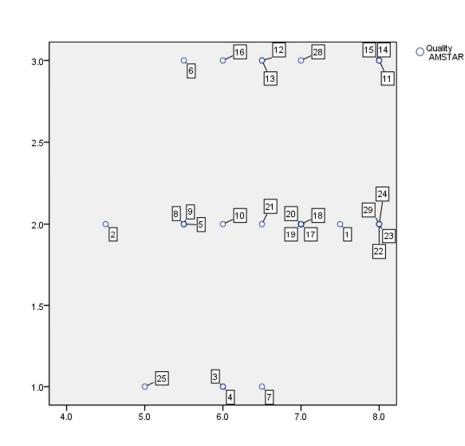
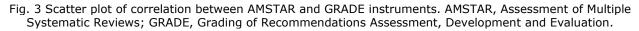


Fig. 2 Proportional distribution of factors for downgrade of quality of bodies of evidence.

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Top-level heading
TITLE Bleeding Risk	and M	ortality of Edoxaban: A pooled Meta-analysis of Randomized Controlled Trials	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7-8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml Page 1 of 2	8



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Top-level heading
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	1
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	1
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8-9, Fig.1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-9, Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9-10, Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-11, Table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-12, Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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A critical appraisal of the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing: a systematic review of reviews

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Secondary Subject Heading:	Evidence based practice, Epidemiology, Nursing
Keywords:	Traditional Chinese Medical Nursing, Systematic review, Meta-analysis, AMSTAR tool, GRADE approach

SCHOLARONE[™] Manuscripts

A critical appraisal of the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing: a systematic review of reviews

Ying-Hui Jin¹, Guo-Hao Wang², Yirong Sun¹, Qi Li³, Chen Zhao³, Ge Li⁴, Yan Li¹, Cui Lu⁵, Hongcai Shang⁶

1. Evidence-Based Nursing Center, School of Nursing, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China;

Nursing department, North China University of Science and Technology Affiliated Hospital;
 063000, China;

3. Graduate College, Tianjin University of Traditional Chinese Medicine, Tianjin 300193,

China;

 Public Health Department of Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China;

5. Department of emergency, Tianjin TEDA hospital, Tianjin 300457, China;

6. Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing,

Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing 100700, China

Running title: Quality of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing

Correspondence to: Prof. Hongcai Shang, Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing, Dongzhimen Hospital, Beijing University of Chinese Medicine, No. 5 Haiyuncang, Dongcheng District, Beijing 100700, China. E-mail: shanghongcai@foxmail.com. Tel: +86-22-15822772648.

Key words: Traditional Chinese Medical Nursing; Systematic review; Meta-analysis; AMSTAR tool; GRADE approach

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ABSTRACT

Objective: To assess the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing (TCMN) in Chinese journals. **Design:** A systematic literature search for systematic reviews and meta-analyses of TCMN was preformed. Review characteristics were extracted. The methodological quality and the quality of the evidence were evaluated using the Assessment of Multiple Systematic Reviews (AMSTAR) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

Result: We included 20 systematic reviews and meta-analyses, and a total of 11 TCMN interventions were assessed in the 20 reviews. The compliance with AMSTAR checklist items ranged from 4.5 to 8, and systematic reviews/ meta-analyses were on average medium methodological quality. The quality of the bodies of evidence we assessed ranged from very low to moderate, and no high quality bodies of evidence were found. The top-two causes for rating down confidence in effect estimates among the 31 bodies of evidence assessed were the risk of bias and inconsistency.

Conclusion: There is room for improvement in the methodological quality of systematic reviews/ meta-analyses of TCMN published in Chinese Journals. Greater efforts should to be devoted to ensure a more comprehensive search strategy, more clear specification the interventions of interest in eligibility criteria and meaningful outcomes for clinicians and patients (consumers). The overall quality of evidence among reviews remains sub-optimal which raise concerns regarding their roles in influencing clinical practice. Thus, the conclusions in reviews we assessed must be treated with caution and their roles in influencing clinical practice should be limited. A critical appraisal of systematic reviews/meta-analyses of TCMN is particularly important to provide sound guidance for TCM nursing.

Strengths and limitations of this study

• This study is the first attempt to assess the methodology and quality of evidence of systematic reviews and meta-analyses undertaken within Traditional Chinese Medical Nursing (TCMN) published in Chinese journals using the Assessment of Multiple Systematic Reviews (AMSTAR) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

• The results highlight that the critical appraisal of systematic reviews/ meta-analyses of TCMN published prior to this review showed weaknesses especially in the areas of evidence use and decision-making, and suggestions are provided regarding how improvements may be incorporated into future work.

• The main limitation of this study is that the methodology and quality of the evidence assessments presented were based on information regarding the assessment items in the individual systematic reviews and meta-analyses reported, which may not actually reflect the construction process.

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Introduction

Despite considerable developments in medicine, a large amount of people both in the developed and developing countries turn to complementary and alternative medicine (CAM), including Traditional Chinese Medicine (TCM).¹ TCM, which is a science nourished by the Chinese culture, is generally delivered by qualified practitioners and has been practiced over thousands of years in China.² Traditional Chinese Medical Nursing (TCMN) is a significant branch of Nursing in China, and mainly consists of the TCM mental nursing, diet nursing, exercise of TCM, nursing techniques of TCM (medication of TCM nursing, acupoint massage and cupping).

The holistic philosophy and the personalized nature of TCMN concur with the patient-centered approach found in modern nursing. In the Chinese Nursing Development Program (2010-2015) it is explicitly pointed out that TCMN should be developed to contribute to the prevention and control of geriatric diseases and chronic diseases, also should be combined with Western and Chinese medicine nursing techniques.³ In China, with the development of specialized TCM clinical nursing, increasing popularity of TCMN techniques and gradually established standardization of nursing specialities, the service ability and scientific research level of TCMN has been improved significantly. A survey of 137 TCM institutions in China showed that there were 85 TCMN techniques provided for patients, and the top-ten techniques were moxibustion, cupping therapy, auricular application pressure, TCM fumigation, acupuncture point massage, acupoint sticking, TCM enema , ironing with Chinese medicine, inunction with Chinese medicine, and scrapping therapy.⁴

Reporting the effectiveness of TCMN techniques in clinical trials is needed. Over the last decade, the number of papers that reporting trials of TCMN have steadily increased, as well as systematic reviews and meta-analyses based on them. Systematic reviews and meta-analyses serve a vital role in the clinical practice guidelines (CPGs) development.⁵ Assessing and synthesizing primary studies of TCMN in systematic review and meta-analysis, and then forming CPG of integrated TCM and Western Medicine care can promote sustainable development of TCMN. Although systematic reviews and meta-analyses strive to provide scientifically rigorous, independent, and accurate summaries of the scientific

evidence with respect to a specific question of interest,⁶ methodological deficiencies of systematic review and meta-analysis may result in misleading results and over- or under-estimation of the investigated effects.⁷ Even methodologically sound systematic reviews and meta-analyses may provide indirect or imprecise evidence for the question of interest. For the CPG developers, the quality ratings reflect the extent of our confidence that estimates of an effect are adequate to support a particular decision or recommendation.⁸

A critical appraisal of systematic review and meta-analysis of TCMN can increase the nurses' confidence and facilitate efficient application of evidences.⁹ In this study, we used the widely accepted and utilized instruments, i.e. the Assessment of Multiple Systematic Reviews (AMSTAR) tool ^{10 11} and Grades of Recommendations Assessment, Development and Evaluation (GRADE) approach ¹² to critically assess the methodology and quality of evidence of TCMN in Chinese journals and obtain their contribution to the development of the evidence-based decision-making.

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Methods

The technology road mapping of this study was presented in Figure 1.

Eligibility criteria

We included the study if it met the following criteria: (1) the study design is a systematic review, meta-analysis, or systematic review and meta-analysis; (2) the topic is TCMN care in China; (3) the papers are published as full-text article in professional nursing journals and the four professional EBM journals in China. Articles were excluded (1) if the interventions focused on a broad concept of TCMN (e.g. for TCM care vs. Western Medicine care) without subgroup analysis which means that the review set a particularly broad scope of a review question reflecting great clinical heterogeneity; (2) the intervention group include non-TCMN (e.g. TCMN combined with western medicine or combined with acupuncture). The flow diagram of systematic reviews and meta-analyses selection was presented in Figure 2.

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Data sources

A comprehensive literature search was conducted to identify systematic reviews and meta-analyses written in Chinese by searching CNKI, VIP, Wanfang, CBM from inception through April 2016. The following search terms "systematic review", "meta-analysis" was used by means of electronic journal navigation to locate systematic reviews/ meta-analyses of TCMN published in nursing journals and EBM journals. The reference lists of the retrieved review articles were also screened to identify potential studies. If several updates of a study were available, only the most recent version was included. The reference lists of the retrieved review articles were also screened to identify potential studies. If several updates of a study were available, only the most recent version was included.

Study selection and data extraction

Two reviewers independently screened the abstracts and titles of studies and subsequently reviewed the full text articles for inclusion, and afterwards data extraction was performed. We categorized the outcomes of systematic reviews and meta-analyses into the following types: endpoint, quality of life (QOL), the target event occurred, symptom, laboratory outcome, composite outcome (synthesis of multi-type outcomes), adverse event and economic evaluations. The risk ratio (RR) and the 95% confidence interval (CI) of dichotomous data and weighted mean difference (WMD) or standardized mean difference (SMD) with the 95% confidence interval (CI) of continuous data of the outcome were extracted when possible. In addition, basic characteristics of every review, such as the surname of the first author, year of publication, journal names, intervention and comparison, were extracted. In addition, information related to AMSTAR and GRADE evaluation also were extracted, such as methodological quality of the original studies(allocation concealment, blinding, follow-up and whether or not the research adhered to the intention-to-treat principle), details of interventions and controls used in all included original studies in systematic reviews/ meta-analyses, reporting of outcomes and outcome measures, the pooled estimate and 95% confidence interval (CI) around the difference in effect between intervention and control for outcome, total sample of outcome, the extent to which each trial contributes toward the

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Quality assessment

The quality assessment of every systematic review and meta-analysis was assessed by two assessors using the AMSTAR tool ^{10 11} and GRADE approach ¹² independently. In order to improve standardization, a special training and pre-test were performed. The disagreement of the reviewers was solved by discussion or asking a third assessor. Agreement between the two reviewers was determined by the Kappa statistic with corresponding 95%CI. Different people were used as assessors for AMSTAR evaluation and GRADE evaluation respectively to ensure that their judgment is not affected by previous impressions. Appraisers were not allowed to communicate or confer with each other during the appraisal process.

According to the AMSTAR criteria, a score of 0 or 1 was given for each criterion, with equal weight given to each domain. We judged each item as "yes (1 score)" when the criterion was explicitly met, "no (0 score)" when the criterion was explicitly not met, "cannot answer" when the item was relevant but not described adequately or not reported at all, and "not applicable" when the item was not relevant. When specific domains were not reported in sufficient detail, we gave a score of 0.5 for that domain. The overall score was categorized into three levels: 8 to 11 was high quality; 4 to 7 was medium quality, and 0 to 3 was low quality. All assessors set a more complete and unanimous standard for AMSTAR criteria after carefully and full discussion between all authors.

For grading the quality of evidence, the authors identify outcomes that are of key importance to patients, and then reviewers applied the GRADE to determine the quality of the evidence and considered the five possible reasons to downgrade the evidence or the three possible reasons to upgrade the evidence.^{8 9 12} The assessors should be conservative in the judgment of downgrading or upgrading. When the systematic review did not provide

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sufficient information to judge the quality of evidence, the assessor made an attempt to contact author of individual studies. Finally, the definitions of "high," "moderate," "low," and "very low" were used in grading the quality of evidence.

Data analysis

We established a database using the Microsoft Excel 2007 software to extract data. Information on each included paper was imported into the database for analysis. We performed descriptive statistics on the distribution of scores per AMSTAR item and summary statistics for the observed AMSTAR scores for each included systematic review and meta-analysis. GRADE evidence profile which included an explicit judgment of each factor that determines the quality of evidence for the outcome of each included systematic review and meta-analysis were provided using the GRADEprofiler 3.6 software.

The AMSTAR instrument and GRADE approach were applied respectively to assess the methodological and evidence quality based on different criteria and systems, but some similarities do exist between them. For example, the item 3 about a thorough and comprehensive searching (for example, searching in international, national, regional and subject-specific databases, the Cochrane Central Register of Controlled Trials (CENTRAL), conference abstracts, and other gray literature and ongoing trials) to identify as many relevant studies as possible help reduce a high probability of publication bias (GRADE rating down item). The correlation between AMSTAR and GRADE instruments was studied by scatter plot using SPSS version 17.0.

Results

Characteristics of included studies

The literature search yielded 809 potentially relevant references; of which, 28 were selected to be reviewed in full text. Finally, 20 studies ¹³⁻³² were included in this study. The year of publication ¹³⁻³² ranged from 2010 to 2016, and the number of reviews published in 2014 accounted for near a half of these reviews (9/20, 45%). A total of 11 TCMN interventions

were assessed, which included acupressure, acupoint massage, acupoint stimulation, auricular point therpy, Tai Chi, Qi Gong, electro-acupuncture combined with auricular point plaster therapy, Chinese herbal retention enema, inunction with Chinese medicine, foot bath therapy or foot massage with TCM, compressing the umbilicus with Chinese herbs. None of the studies included observational research. Two included RCT and quasi-RCT both. No systematic review or meta-analysis applied indirect comparison. None of the 20 studies used the GRADE approach to summarize evidence. The general characteristics of the assessed systematic reviews and meta-analyses were shown in Table 1.

AMSTAR methodological quality

The two reviewers had a satisfactory agreement (k=0.87). The methodological quality of all the included reviews is presented in Table 2. In summary, the compliance with AMSTAR checklist items ranged from 4.5 to 8, and the majority of the systematic reviews and meta-analyses were of medium (18/20, 90.0%) methodological quality.

None of the 20 studies provided a registered protocol. For all the 20 studies, study selection and data extraction was conducted respectively by two independent reviewers. Most of them (13/20, 65%) adequately described the characteristics of the included trials, but no one provided a list of included and excluded studies. The search strategy design was not sufficiently comprehensive in 10 studies (50.0%). The mean number of electronic databases searched in the reviews was 6 (SD 2.2, range 2-11). The most frequently searched databases were Pubmed (14/20, 70%) and CNKI (19/20, 95%). Two ones^{14 24} only searched the Chinese databases. Only two studies considered the status of publication (e.g. grey literature^{19 23}). The literature search in 10 of them was supplemented by consulting textbooks, experts in the particular field of study or by retracing references. No review searched ongoing trials. All of the reviews assessed scientific quality of the included studies. The risk of bias tool from the Cochrane handbook criteria (11/20, 55%) and the Jadad scale (6/20, 30%) were the most common criteria for quality assessment of included studies.

The majority of the systematic reviews and meta-analyses used appropriate methods to combine the findings of the studies included. They all stated that a random effects model was used to combine study data when there was heterogeneity. When substantial heterogeneity

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was detected, possible explanations has been explored in subgroup analyses in 6 ones. There were no reviews in which meta-regression was applied. Two reviews conducted sensitivity analysis by exchanging the statistical approach for data synthesis (random-effects vs. fixed effects) to determine the robustness of conclusion. Most of them appropriately used the methodological quality of the included trials in formulating conclusions. None of them conducted evaluation of the quality of the body of evidence. All the included studies drew definitely positive conclusions in favor of TCMN, while all reviewers suggested that there might be some benefits in the interventions, the findings should be interpreted with caution due to the poor quality of trials or limited trial sample. Ten systematic reviews and meta-analyses (50%) assessed publication bias using funnel plots and one review³⁰ used the Egger's test. Only one¹⁸ stated the conflict of interest.

GRADE evidence quality

The two reviewers had a satisfactory agreement (k=0.82). None of the 20 studies cited any observational research, so upgrading items were excluded from the assessment of evidence quality. The evidence quality of all the included reviews is presented in Table 3. For outcomes, there were occurrence of adverse events (1/20, 5.0%), and symptoms (6/20, 5.0%)30.0%), laboratory outcomes (5/20, 25.0%), and composite outcomes such as total effectiveness rate (17/20, 85.0%) in the 20 reviews, and no review considered endpoint, economic evaluations or QOL. At the beginning, we determined the critical outcomes for each review. Judgments about what constitutes a critical outcome may change for different research goals and results. For instance, in a review titled "acupressure wristbands prevents postoperative nausea and vomiting: a meta-analysis", the research goal was to evaluate the therapeutic effects on nausea and vomiting, so raters set nausea and vomiting as the critical outcome. Meanwhile, the outcomes of a systematic review of electro-acupuncture combined with auricular point plaster therapy for patients with simple obesity were the rate of effectiveness, BMI and waist circumference. The rate of effectiveness is equal to the patients numbers of recovery, markedly effective and effective divide the total according to author's description.

The criteria for recovery, markedly effective, effective and ineffective were stated as follows:

Recovery: body Weight was in the normal weight range or BMI less than 23 kg/m²; Markedly effective: body weight decreased by no less than 5 kg, or BMI decreased by no less than 2 kg/m²;

Effective: body weight decreased by no less than 2 kg and less than 5 kg, or BMI decreased by no less than 0.5 kg/m² and less than 2 kg/m²;

*Ineffective: body weight decreased by less than 2 kg, or BMI decreased by less than 0.5 kg/m*². Because it was considered that the rate of effectiveness contained far more therapeutic information than BMI and waist circumference, the rate of effectiveness was set as the critical outcome by raters. Totally 31 bodies of evidence in the 20 reviews were assessed for quality.

Rationale for rating down

The quality of the bodies of evidence we assessed ranged from very low to moderate, and no high quality bodies of evidence were found.

The causes for rating down confidence in effect estimates among the 31 bodies of evidence assessed were the risk of bias (26 times, 83.9%), inconsistency (16 times, 51.6%),

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indirectness (8 times 25.8%), imprecision (13 times, 42.0%), and publication bias (15 times , 48.4%). The detailed reasons for downgrading in terms of risk of bias (80 times in total) included failure to conceal allocation(26 times, 32.5%), failure to blind (23times, 28.8%), incomplete reporting of random sequence generation in most of studies included (24 times, 30.0%), use of invalidated outcome measure (0 time, 0.0%), loss to follow-up and failure to adhere to the intention-to-treat principle (3 time, 3.8%), non-RCT included (4 times, 5.0%). Downgrading for inconsistency was generally due to certain CIs showing little overlap from individual studies and significant heterogeneity. The quality of evidence was downgraded for indirectness (9 times in total) where substantial differences exist between the interventions (3times in 9 times, 33.3%) or the controls (5 times in 9 times, 55.6%), or patient-important endpoints replaced by surrogate endpoints (1 time in 9 times, 11.1%). In a review evaluating the effectiveness of Tai Chi in preventing fall in the elderlies, the authors stated that the scores of Berg balance scale in the Tai Chi group were higher than in the control group, and argued that Tai Chi can effectively reduce the risk of fall for the elderly people. However the Berg balance scale is a surrogate outcome for occurrence of fall.

The detailed reasons for downgrading of evidence for imprecision (13 times in total) included failure to meet optimal information size criterion (12 times in 13 times, 92.3%) and wide confidence intervals (1 times in 13 times, 7.7%).

The quality of evidence decreased for publication bias (19 times in all) because of flaws in literature searching (12 times in 19 times, 63.2%) and funnel plot asymmetry (7 times in 19 times, 36.8%). There were no correlation between AMSTAR and GRADE instruments through observation from scatter plot (see Fig. 3).

Discussion

It is important to assess the methodological and evidence quality of a systematic review/ meta-analysis before any conclusions being used for clinical decision making. To the best of our knowledge, this is the first study which assessed methodological quality and evidence quality of systematic reviews and meta-analyses of TCMN in Chinese Journals using AMSTAR and GRADE tool.

All systematic reviews and meta-analyses and primary studies lack of important outcomes that depressed the quality rating of evidence

GRADE specifies that both those conducting systematic reviews and those developing practice guidelines should begin by specifying every important outcome of interest.³³ Unfortunately, systematic reviews and meta-analyses in our study usually did not address all important outcomes. For instance, a review aiming to verify the effect of foot bath therapy or foot massage with traditional Chinese medicine for diabetic foot ulcers, since foot ulcers are a high risk factor for infection, gangrene, amputation and even death among diabetes patient, we thought amputation rate maybe the preferable long-term outcome to verify the effect of the intervention, but this outcome was not considered by that reviewers.¹⁷ In general, systematic reviews and meta-analyses should include all outcomes that are likely to be meaningful to clinicians, patients, the general public, administrators and policy makers. For example, outcomes may include survival, clinical events, patient-reported outcomes (e.g. symptoms or quality of life), adverse events, burdens (e.g. cost and resource use). But

primary studies typically focused on short-term benefit without considering long-term, harm or economic outcomes. None of the reviews listed any adverse effects as outcomes of TCMN interventions. These all confirmed that systematic reviews and meta-analyses and primary studies all had shortcomings in research design which also rendered the results of systematic reviews and meta-analyses difficult to be used to make appropriate recommendations as these were based on incomplete outcomes.

Risk of bias resulted in downgrading in most reviews

RCT is critical for assessing and providing valuable evidence about the effectiveness of TCMN practices. However, the reliability and acceptability of any intervention study results depends on the extent to which the studies employ scientific principles and use a valid research design. In this study, we used the Cochrane Collaboration's tool for assessing risk of bias.¹¹ Most of the reviews were downgraded because of lack of allocation concealment and blinding, and lack of details of randomization in primary studies. 228 RCTs were included in 20 systematic reviews and meta-analyses, of these the authors noted that 184 (80.7%) were published in Chinese journal.

This finding is consistent with the results of similar research. Yao conducted a systematic review using GRADE system to assess the quality of evidence of Chinese meta-analyses. Authors indicated risk of bias was the most common factor for downgrading evidence in Chinese meta analyses and stressed that the poorer quality of evidence in meta analyses related to TCMs might be caused by the poor quality reporting in RCTs.³⁴ Wu found that more than 90% of RCTs published in core Chinese journals lacked an adequate description of randomization in 2009, and most trials despite being claimed to be RCTs did not fulfill the criteria of a real RCT.³⁵ Although the number of RCTs in nursing research in China is increasing over time, the quality of most of them remains unsatisfactory. Xing et al ³⁶ published a comprehensive evaluation of 7391 nursing intervention studies published in simplified Chinese from 1979 to 2012, and the result showed that among the 10 characteristics considered in quality evaluations, the lowest ratings were observed for "utilization of blind method", "description of loss of follow-up", "appropriate calculation of sample size" and "randomized assignment of patients to treatments".

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Current systematic reviews and meta-analyses are often limited in their usefulness as guidelines because they rate risk of bias by studies across outcomes rather than by outcome across studies.³⁷ Authors of systematic reviews and meta-analyses should keep it in mind that sources of bias may vary in importance across outcomes; it means that summarizing study limitations must be outcome specific.³⁷ For example, the assessors downgraded the evidence many times for not using blinding based on subjective outcomes which are much more vulnerable to biased judgments. The above mentioned review evaluating the effect of foot bath therapy or foot massage for diabetic foot ulcers used rate of effectiveness as the only outcome, which was based on subjectively observable judgment of the condition (e.g. ulcer area, local swelling and skin color). Raters categorized this evidence as having serious study limitations on account of lack of blinding during the study.¹⁷ Problems with the design and execution of individual studies of TCMN interventions raise questions about the validity of intervention effect of TCMN and resulted in downgrading to quality of evidence.

Heterogeneity has not been adequately explored or inappropriate combination of study's findings usually leading to decreasing the quality of evidence because of inconsistency The raters decreased the quality of evidence when was detected significant heterogeneity for which the authors failed to identify a reasonable source or explanation. Although studies brought together in a systematic review will inevitably have some differences, reviewers should look for robust explanations for any significant heterogeneity.³⁷

Clinical variation will lead to heterogeneity if the intervention effect is affected by the factors that vary across individual studies; most obviously, the patient characteristics or specific interventions. In our study, variability in interventions is the most common reason for heterogeneity, e.g. different points for acupoint massage, different medicine for Chinese herbal retention enema, or different Chinese herbal prescriptions for umbilical compression. Raters considered the true intervention effect might be different in different studies and decreased the evidence quality for inconsistency of results and methodological quality for inappropriate combination of the study's findings.

When there is heterogeneity that cannot readily be explained, incorporating it into a random-effects model is often the only option for reviewers. Reviewers should know

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random-effects model does not "take account" of the heterogeneity. When the meta-analysis results show that heterogeneity is statistically significant, the most important treatment method is to analyze possible reasons for heterogeneity rather than simply using the random effects model.

Information about study limitations, imprecision, inconsistency, indirectness, and publication bias is necessary for TCMN to understand and have confidence in the assessment of quality and estimate of effect size. GRADE provides a framework for assessing outcome quality that encourages transparency and explicit accounting of the judgments made. In this study, the quality of evidence was low in 20, and very low in 4 among the 31 bodies of evidence. High quality evidence is more likely to be associated with strong recommendation, but it is important to note that sometimes low or very low quality evidence can lead to a strong recommendation. When use the evidence of TCMN, nurses should consider patient values and preferences, resource implications besides confidence in estimates of effect of primary outcome used in the GRADE system. In addition, in view of the unsatisfactory methodological and evidence quality of systematic review and meta-analysis of TCMN which we included, we were inclined to present to readers the built-in problems existing within systematic reviews and meta-analyses of TCMN rather than to only present to readers the available evidence.

Methodological quality assessment using AMSTAR should be a precondition for further evaluation with the GRADE approach

Systematic reviews/ meta-analyses may differ considerably in their methodological quality.³⁸ Using a rigorous methodology with a clearly formulated research question and a comprehensive search strategy, systematic reviews should provide reproducible results and include all potentially relevant studies, thereby limiting bias and random errors.³³ Systematic reviewers will clearly specify the interventions of interest in their eligibility criteria, ensuring that only directly relevant studies will be eligible. But in our study, there were several systematic reviews/ meta-analyses that included studies inconsistent with their eligibility criteria. For instance, a review aiming to evaluating foot massage for diabetic peripheral neuropathy, included studies with different interventions: foot massage or massage in foot

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reflection area or acupoint massage for lower limbs.

In addition, systematic reviews require a thorough, objective and reproducible search of a range of sources to identify as many relevant studies as possible for minimizing bias. But in this respect, some systematic reviews/ meta-analyses in this study are far from satisfactory. Some systematic reviews/ meta-analyses set a flawed search strategy, for example, only using free-text searching without performing Mesh (index terms) searching, only searching the Chinese database, and failing to identify "negative" studies. Moreover, in our study, assessors found high-quality clinical trials do not always exist especially in TCMN, and non-RCTs were sometimes included in systematic reviews/ meta-analyses resulted in dropping of AMSTAR scores, as well as downgrading to the quality of bodies of evidence. Although GRADE guideline suggests not using GRADE for systematic reviews/ meta-analyses with serious flaws, we did not exclude any study since no review was rated with a low methodological quality score, although some imperfect methodology in conducting systematic reviews/ meta-analyses do exist.

In our study, we were unable to identify correlation between methodological quality and quality of body of evidence through scatter plot. It is easy to understand. Because GRADE is much more than a simple rating system, it offers a transparent and structured process for developing and presenting evidence summaries for systematic reviews,⁸ not only surveying some methodology characteristic of production of systematic review/meta-analysis which influenced quality of evidence but also explore factors resulted in inconsistency or imprecision.

Methodological flaws in quality of systematic review/meta-analysis could severely affect decision-making and the application of evidence. We suggest assessing methodological quality before evidence quality assessment, and there is no need to evaluate the evidence quality for systematic review/ meta-analysis for which a low methodological quality score is assigned due to major flaws.

Sub-optimal reporting may contribute to an underestimation of methodological quality

A part of the research items regarding GRADE and AMSTAR rely on transparency in reporting the systematic reviews/ meta-analyses document. Even the most methodologically rigorous process, if not clearly described in the systematic reviews/meta-analyses document, will leave assessors or users uncertain about the reliability of the systematic reviews/ meta-analyses.

Most Chinese journals impose strict limits on word numbers. The Chinese journal editors usually encourage authors to focus on the research results and discussion sections of their manuscripts and shorten the research methods section of their papers. Even the Chinese Journal of Nursing, a leading domestic journal in China, typically limits the length of articles regarding nursing intervention studies to no more than 4 pages.³⁸ Although we made an attempt to contact developers of reviews we included, we found it was difficult since most of author's contact information were not presented in published papers. So results in this study were possibly underestimated due to the lack of some important information reporting. PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-analyses), which consists of 27-item checklist and a four-phase flow diagram, inform authors the preferred way to present every part of a report of a systematic reviews/meta-analyses. We hope that editors of medical journals in China recognize and promote the use of reporting guidelines in their publications, and hope authors adhere to reporting guidelines.

Implications for research and practice

A high methodological quality is the basic precondition of systematic reviews for identifying the best available evidence for specific research questions and conducting GRADE evaluation. Systematic review/ meta-analysis authors and editors should make every effort to adhere to well-established methodological standards to enhance the impact of their research efforts. But a high methodological quality does not fully reflect the quality of a review, the quality of a body of evidence is critical in decision-making. The GRADE approach can provide clinicians and patients with a guide to use results from systematic review/meta-analysis in clinical practice and policy makers with a guide to their use in health policy.

Journals remains suboptimal, especially in terms of the risk of bias which reduces the quality of evidence for almost all indications, raising concerns about their role in influencing clinical practice, so their conclusions needs to be treated with caution. Critical appraisal of systematic reviews/meta-analyses of TCMN is particularly important.

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Author contributions

signed ta. papers; G.L. and ritical appraisal; Y.H.J. an. of interest Machine data are available. Y.H.J. and H.C.S designed this study; G.H.W., Q.L. and Y.R.S searched databases and

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Figure legends

Figure 1 Technology road mapping of this study. EBM, Evidence-Based Medicine; EBN, Evidence-Based Nursing; TCM, Traditional Chinese Medicine; AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

Figure 2 Flowchart of identified, included and excluded of systematic reviews or meta analyses of TCMN.

Figure 3 Scatter plot for exploring correlation between AMSTAR and GRADE instruments. AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of

Recommendations Assessment, Development and Evaluation.

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Study	Journal	Design	No. of patients	Population	Intervention	Comparison	Outcomes	The rage of literature search
Baoxia Chang	Chinese Nursing	RCT	467	Simple obesity	Electro-acupuncture	Electro-acupuncture	Rate of effectiveness, BMI,	Cochrane Library, PubMed, VIP, CNKI, CBM,
2014	Research				combined with auricular		Percentage of body fat, Waist	references of the included literatures, the grey
					point plaster		circumference	literature
Wangqin Shen	Chinese Nursing	RCT	327	Phlebitis	Ruyijinhuangsan	Magnesium sulphate	Rate of effectiveness	Medline, CBM, CNKI, the references of the included
2010	Research					by wet compression		literatures
Hongying Pu	Journal of	RCT	703	Pressure ulcers	Moist exposed burn	Skin disinfection	Cure rate, Rate of effectiveness,	PubMed, EMBASE, Cochrane database, CBM, VIP,
2011	Nursing Science				ointment	solution or antibiotic	Time of cure	the references of the included literatures
						ointment		
Xuan Zhou	Journal of	RCT	1117	Postoperative	Acupressure wristbands	Placebo wristband	Incidence of nausea, Incidence	Medline, CNKI, CBM, VIP, WanFang
2011	Nursing Science			patients			of vomiting	
Xiaoli Wu 2012	Nursing Journal	RCT	860	Diabetic foot	Foot bath therapy or foot	Hot foot bath	Effective rate	Medline, CNKI, CBM, VIP
	of Chinese			ulcers	massage with traditional			
	People's				Chinese medicine			
	Liberation Army							
Xilan Zheng 2012	Chinese Journal	RCT	551	Postoperative	Traditional Chinese	Skin disinfection	Cure rate, Cure time, Frequency	Medline, EMBASE, PubMed, Cochrane Library,
	of Practical			patients	medicine for elimination	solution or antibiotic	of dressing change	CBM, VIP, CNKI, WanFang
	Nursing				of necrotic tissues	ointment		
Na Li 2011	Journal of Qilu	RCT	712	Phlebitis	External application with	Magnesium sulphate	Effective rate	CNKI, VIP, WanFang
	Nursing	CCT			aloe vera	by wet compression		
Jiaqi Xu 2013	Chinese Journal	RCT	610	Pressure ulcer	Resina draconis	Skin disinfection	Effective rate, Cure time	Cochrane Library, PubMed, Elsevier SDOL, Web of
	of					solution or antibiotic		Knowledge, CBM, CNKI, VIP , WanFang, the
	Evidence-Based					ointment		references of the included literatures
	Medicine							

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	Chinese Journal	RCT	2796	Elderly	Tai Chi	Regular sport or	Rate of falls, Time up and go	PubMed, Web of Science, Cochrane Library,
2013	of			individuals		physical therapy	test, Functional reach test,	EMBASE, CBM, CNKI, VIP, WanFang Database, th
	Evidence-Based						Berg balance scale	references of the included literatures
	Medicine							
Xiaoyan Wen	Chinese Journal	RCT	1735	Virus hepatitis	Chinese herbal retention	Comprehensive	Overall effective rate, liver	Cochrane library, PubMed, EMBASE, VIP, CNKI,
2013	of				enema and	treatment	function index	CBM, WanFang, the references of the included
	Evidence-Based				comprehensive treatment			literatures, SIGLE
	Medicine							http//www.opengrey.eu/search/request)
Pingping	Chinese Journal	RCT	3194	Elders living in	Tai Chi	Regular sport or	Rate of fall, Falls efficacy, Time	Cochrane Library, Medline, EBSCO, CNKI, Wanfang
Zheng 2013	of Modern			home		physical therapy or	of standing on one leg with	the references of the included literatures
	Nursing					blank control	eyes close or open, Body	
							flexibility	
Guohao Wang	Chinese Journal	RCT	3084	Constipation	Acupoint massage and	Routine nursing	Rate of effectiveness,	CNKI, VIP, CBM, Wanfang, EBSCO, PubMed,
2014	of Practical	Quasi-			ventral massage		Defecation frequency in the	Cochrane Library
	Nursing	RCT					first day, Defecation frequency	
							in the first two days, Defecation	
							difficulty rate, Defecation time	
							Dry stool rate, Defecating	
							unfinished feeling rate,	
							Laxative provided	
Jihuan Feng	Chinese Journal	RCT	959	Cancer patients	Acupoint massage	Routine nursing	Duration of	PubMed, Medline, Embase, AMED, Cochrane Librar
2014	of Practical			receiving			Chemotherapy-induced nausea,	CBM, CNKI, VIP, Wanfang
	Nursing			adjuvant			vomiting and retching,	
				chemotherapy			Frequency of	

							vomiting and retching, Severity	
							of Chemotherapy-induced	
							nausea, vomiting and retching	
							Anti-emetic medication dosage	
							Quality of life	
Shaoxia Meng	Chinese Nursing	RCT	383	Diabetics with	Foot massage or massage	Routine nursing	Rate of effectiveness, Nerve	PubMed, CBM, CNKI, VIP, Wanfang database, th
2014	Research			peripheral	in foot reflection area or		conduction velocity	references of the included literatures
				neuropathy	acupoint massage for			
					lower limbs			
Xijuan Cui 2014	Today Nurse	RCT,	860	Postoperative	Acupoint massage for	Routine nursing	First bowel sound time, First	CNKI, Wanfang
		Quasi-		patients with	Zusanli, Zusanli point		aerofluxus time, First	
		RCT		abdominal	acupuncture, Chinese		defecation time	
				operation	medicine application at			
					the Zusanli point			
Zhong Sun 2014	Chinese Nursing	RCT	524	Primary	Umbilical compression	Analgesic drug	Rate of effectiveness	Cochrane Library, PubMed, Proquest, CNKI, VIP,
	Research			dysmenorrhea	with Chinese herbs		Cure rate	WanFang
				patients			Comparison of the score and	
							scale of symptoms	
							Hemorheology and estradiol,	
							pregnendione	
Ye Li 2014	Journal of	RCT	888	Women in	Acupoint massage for	Blank control	Rate of effectiveness	CNKI, VIP, CBM, WanFang, PubMed
	Nursing			labour	Sanyinjiao, Hegu,			
					Zhiyin, Taichong, Ashi,			
					Shenshu et al.			
Yuanyuan	Journal of	RCT	939	Insomnia	Auricular point therapy	Acupuncture or drug	Rate of effectiveness	PubMed, Cochrane library, CBM, CNKI, VIP,

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Yang 2015	Nursing Science					therapy		WanFang, the references of the included 1 iteratures
Yue Ma 2014	Chinese Journal	RCT,	3074	Ileus	Enema and	Blank control	Rate of effectiveness,	PubMed, Web of Science, EMBASE, The Cochrane
	of	Quasi-			gastrointestinal		Hospitalization time, Time of	Library, CBM, CNKI, VIP, WanFang
	Evidence-Based	RCT			intubation with		anus exhaust, Time of	
	Medicine				traditional Chinese		defecation, Time using	
					medicine		indwelling gastric tube,	
							Symptoms complete resolution	
Weiwei Wu	Chinese Journal	RCT	711	Elderly	Traditional Chinese	Other intervention or	Sleep quality, Anxiety status	PubMed, EMBASE, Cochrane Library, CINAHL, VIP
2016	of Nursing			individual	exercise	regular nursing		CNKI, the references of the included literatures
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Study	Priori	Data	Comprehensive	Status of	List of	Characteristics of the	Quality	Forming	Method for	Publication	Conflict of	Score/Ran
	design	extraction	literature search	publication	studies	included studies	assessment	conclusion	combining	bias	interest	
Wangqin Shen	1	1	0	0	0	0	1	0	0.5	0	0	4.5/mediu
Hongying Pu	1	1	0	0	0	0	1	1	1	1	0	6/mediun
Na Li	1	1	0	0	0	1	1	0	1	1	0	6/medium
Kuan Zhou	1	1	0	0	0	0	1	1	0.5	0	0	5.5/mediu
Kiaoli Wu	1	1	0	0	0	0	1	1	0.5	1	0	6.5/mediu
Kilan Zheng	1	1	0	0	0	0	1	0	0.5	0	1	4.5mediu
iaqi Xu	1	1	1	0	0	1	1	1	1	1	0	8/high
Yuan Zhao	1	1	1	0	0	1	1	1	0.5	0	0	6.5/mediu
Kiaoyan Wen	1	1	1	1	0	1	1	1	1	0	0	8/high
Pingping Zheng	1	1	1	0	0	1	1	1	0	0	0	6/mediur
Guohao Wang	1	1	0	0	0	1	1	1	1	1	0	7/mediur
ihuan Feng	1	1	1	0	0	1	1	1	1	0	0	7/mediur
Shaoxia Meng	1	1	1	0	0	1	1	1	0.5	0	0	6.5/mediu
Kijuan Cui	1	1	1	0	0	1	1	1	1	1	0	8/high
Zhong Sun	1	1	0	0	0	1	1	1	1	0	0	5/mediur
Ye Li	1	1	0	0	0	1	1	1	1	1	0	7/mediur
Yuanyuan Yang	1	1	1	0	0	0	1	1	1	0	0	7/mediur
Baoxia Chang	1	1	1	1	0	0	1	1	0.5	0	0	7.5/mediu
Yue Ma	1	1	0	0	0	1	1	1	1	1	0	7/mediur
Weiwei Wu	1	1	1	0	0	1	1	1	1	1	0	8/high
Total	1.00±0.0	1.00+0.00	0.50+0.51	0.10+0.21	0.00±0.	0.65+0.40	1.00+0.00	0.95+0.25	0.70+0.20	0.45+0.51	0.05+0.22	(50) 1 1
Mean±SD	0	1.00±0.00	0.50±0.51	0.10±0.31	00	0.65±0.49	1.00±0.00	0.85±0.37	0.78±0.30	0.45±0.51	0.05±0.22	6.58±1.1

Table 2 AMSTAR scores wiews included in this study +h athadal **. .**

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Study	Patients	Intervention	Comparison	Outcome	No.of patients/studies	Effect RR/MD (95% CI)	Absolute effect (95%)	Quality	AMSTA score
Baoxia Chang 2014	Simple obesity	Electro-acupuncture combined with auricular point plaster	Electro-acupuncture	Rate of effectiveness	397(5)	RR1.18 (1.07 to 1.25)	132 more per 1000 (from 51 more to 183 more)	MODERATE (1a、1c)	7.5
Wangqin Shen 2010	Phlebitis	Ruyijinhuangsan	Magnesium sulphate by wet compression	Rate of effectiveness	327(6)	RR1.32 (1.26 to 1.34)	236 more per 1000 (from 191 more to 250)	VERY LOW (1a、1b、1c、3a、4a、 5a)	4.5
Hongying Pu 2011	Pressure ulcers	Moist exposed burn ointment	Skin disinfection solution or antibiotic ointment	Cure rate	432(11)	RR2.22 (2.07 to 2.33)	468 more per 1000 (from 410 more to 510 more)	VERY LOW (1a, 1b, 1c, 2, 3a, 5a, 5b)	6
			Time of cure	261(5)	MD6.93 (7.7 to 6.15)	MD 6.93 lower (7.7 to 6.15 lower)	VERY LOW (1a, 1b, 1c, 3a, 4a, 5a, 5b)	6	
Xuan Zhou 2011	Postoperative patients	Acupressure wristbands	Placebo wristband	Incidence of nausea	1117(9)	RR0.85 (0.72 to 1)	46 fewer per 1000 (from 86 fewer to 0 more)	MODERATE (4b、5a)	5.5
				Incidence of vomiting	1117(9)	RR0.44 (0.31 to 0.62)	107 fewer per 1000 (from 72 fewer to 131 fewer)	MODERATE (4a、5a)	5.5
Xiaoli Wu 2012	Diabetic foot ulcers	Foot bath therapy or foot massage with traditional Chinese medicine	Hot foot bath	Effectiverate	845(8)	RR1.44 (1.4 to 1.46)	293 more per 1000 (from 267 more to 307 more)	LOW (1a, 1b, 2, 5a, 5b)	6.5
Xilan Zheng 2012	Xilan Zheng 2012 Postoperativepati ents	Traditional Chinese medicine for elimination of necrotic tissues	Skin disinfection solution or antibiotic ointment	Cure rate	551(9)	RR1.89 (1.65 to 2.17)	401 more per 1000 (from 293 more to 527 more)	LOW (1a, 1b, 1c, 2)	5.5
				Cure time	355(6)	MD9.33 (9.9 to 8.76)	MD 9.33 lower (9.9 to 8.76 lower)	LOW (1a, 1b, 1c, 2)	5.5
Na Li 2011	Phlebitis	External application with aloe vera	Magnesium sulphate by wet compression	Effectiverate	712(7)	RR1.25 (1.2 to 1.27)	192 more per 1000 (from 153 to 206)	LOW (1a、1b、1c、5a)	6
Jiaqi Xu 2013	Pressure ulcer	Resina draconis	Skin disinfection solution or antibiotic ointment	Effective rate	573(13)	RR1.2 (1.13 to 1.28)	162 more per 1000 (from 105 more to 227 more)	MODERATE (1a、1b、1c)	8
Yuan Zhao 2013	Elderly individuals	Tai Chi	Regular sport or physical therapy	Rate of falls	1443(4)	RR0.82 (0.73 to 0.92)	83 fewer per 1000 (from 37 fewer to 124 fewer)	MODERATE (3a)	6.5
				Berg balance scale, BBS	345(2)	MD2.45 (1.47 to .43)	MD 2.45 higher (1.47 to 3.43 higher)	LOW (3a、3b、4a)	6.5
Xiaoyan Wen 2013	Virus hepatitis	Chinese herbal retention enema and comprehensivetreatment	Comprehensivetreatment	Effective rate: after 2 weeks from cure time	260(4)	RR 1.51 (1.3 to 1.67)	259 more per 1000 (from 152 more to 340 more)	LOW (1a, 1b, 1c, 4a)	8
				Effective rate: after 4 weeks from cure time	333(5)	OR 4.17 (2.37 to 7.32)	250 more per 1000 (from 173 more to 300 more)	LOW (1a, 1b, 1c, 4a)	8
Pingping Zheng 2013	Elders living in home	Tai Chi	Regular sport or physical therapy or blankcontrol	Rate of fall	2624(9)	RR 0.85 (0.79 to 0.92)	73 fewer per 1000 (from 39 fewer to 102 fewer)	MODERATE (2)	6
Guohao Wang 2014	Constipation	Acupoint massage and ventral massage	Routine nursing	Rate of effectiveness	2170(19)	(0.17) (0.05)2) RR 1.93 (1.86 to 2)	396 more per 1000 (from 366 more to 426 more)	$\begin{array}{c} \text{LOW} \\ \text{(1a, 1c, 2, 3a)} \end{array}$	7

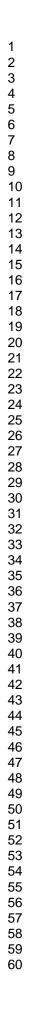
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	Cancer patients receiving	Acupoint massage	Routine nursing	Duration of chemotherapy-induced	942(7)	MD 1.52 (1.77 to 1.26)	MD 1.52 lower (1.77 to 1.26 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
	adjuvant chemotherapy			nausea Frequency of chemotherapy-induced	942(7)	MD 1.08 (1.32 to 0.83)	MD 1.08 lower (1.32 to 0.83 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
				nausea Severity of chemotherapy-induced	942(7)	MD 1.17(1.37 to 0.96)	MD 1.17 lower (1.37 to 0.96 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
				nausea		0.90)	0.50 lower)		
Shaoxia Meng 2014	Diabetics with peripheral neuropathy	Foot massage or massage in foot reflection area or acupoint massage for lowerlimbs	Routine nursing	Rate of effectiveness	323(5)	RR 1.47 (1.29 to 1.68)	297 more per 1000 (from 183 more to 430 more)	LOW (1a, 1c, 3a, 4a, 5a)	6.5
Xijuan Cui 2014	Postoperative	Acupoint massage for Zusanli,		First aerofluxus time:	317(3)	MD 14.52	MD 14.52 lower (15.49	LOW	8
-	patients with abdominal operation ⁴	Zusanli point acupuncture, Chinese medicine application at the Zusanli point	Routine nursing	subgroup for Zusanli point acupuncture∆		(15.49 to 13.54)	to 13.54 lower)	(1a, 1b, 1c, 1f, 2, 4a, 5a)	
	operation			Subgroup for acupoint massage for Zusanli∆	326(4)	MD 22.7 (25.67 to 19.73)	MD 22.7 lower (25.67 to 19.73 lower)	LOW (1a、1b、1c、1f、2、 4a、5a)	8
			Subgroup for Chinese medicine application at	1048(6)	MD 18.25 (18.6 to 17.9)	MD 18.25 lower (18.6 to 17.9 lower)	MODERATE (1a, 1b, 1c, 1f, 2, $5a$)	8	
Zhong Sun 2014	Primary	Umbilical compression with Chinese	Analgesic drug	the Zusanli point∆ Rate of effectiveness	496(5)	RR 1.93 (1.45 to	214 more per 1000	5a) VERY LOW	5
	dysmenorrhea patients	herbs			()	2.57)	(from 104 more to 362 more)	(1a, 1b, 2, 3a, 4a)	
Ye Li 2014	Women in labour	Acupoint massage for Sanyinjiao, Hegu, Zhiyin, Taichong, Ashi, Shenshu et al.	Blank control	Rate of effectiveness	766(6)	RR 1.64 (1.56 to 1.7)	347 more per 1000 (from 304 more to 380	LOW (1a、1b、1c、2、5a、 5b)	7
Yuanyuan Yang 2015	Insomnia [△]	Auricular point therapy	Acupuncture or drug therapy	Effective rate after 2 weeks from cure time	606(3)	RR 1.28 (1.2 to 1.37)	more) 212 more per 1000 (from 152 more to 281	50) LOW (1a, 1b, 1c, 2)	7
		Auricular point therapy	Acupuncture or drug therapy	Effective rate after 4 weeks from cure time	333(4)	RR 1.25 (1.13 to 1.37)	more) 186 more per 1000 (from 97 more to 276	LOW (1a, 1b, 1c, 4a)	7
Yue Ma 2014	Ileus	Enema and gastrointestinal intubation with traditional Chinese	Blank control	Rate of effectiveness	2821(27)	RR 1.24 (1.2 to 1.29	more) 179 more per 1000 (from 149 more to 216	LOW (1a, 1b, 1c, 1f, 5b)	8
Weiwei Wu 2016	Elderly individual	medicine Traditional Chinese exercise	Other intervention or regular	Subgroup for PSQI for	554(8)	MD -2.15(-4.61	more) MD 2.15 lower (4.61	LOW	8
			nursing	Tai Chi	× /	to 0.30)	lower to 0.3 higer)	(1a, 1b, 1c, 2, 5b)	
				Subgroup for PSOI for Qigong	55(2)	to -3.29)	MD 4.29 lower (5.29 lower to 3.29 lower)	LOW (1a、1b、1c、4a、5b)	8
Risk of bias: (1a) (1e) loss to follow	failed to conceal all up and failure to ad unexplained hetero	ocation; (1b) no blinding used; here to the intention-to-treat princip geneity or inconsistency of results peutic methods between intervention	(1c) incomplete reporting of le; (1f) non-RCT was incl	Tai Chi Subgroup for PSOI for <u>Qigong</u> of random sequence gener luded	55(2)	to 0.30) MD -4.29(-5.29 to -3.29)	lower to 0.3 higer) MD 4.29 lower (5.29 lower to 3.29 lower)	(1a、1b、1c、2、5b) LOW (1a、1b、1c、4a、5b)	

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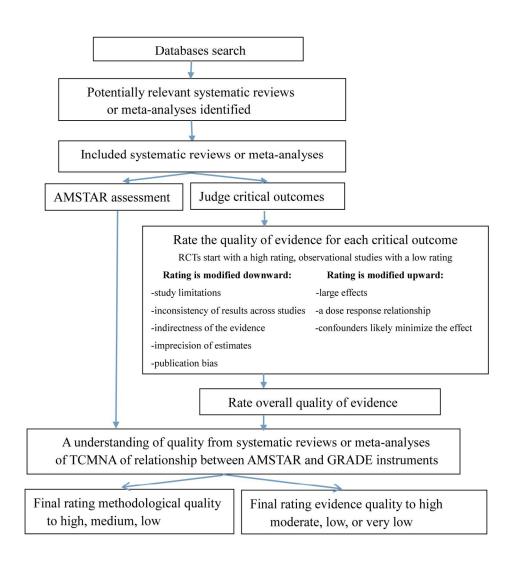


Figure 1 Technology road mapping of this study

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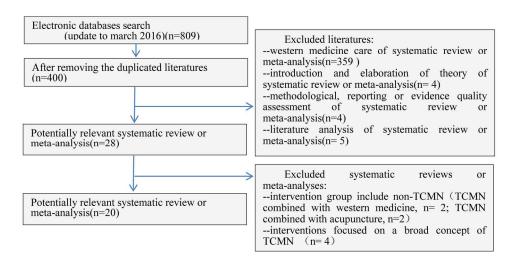
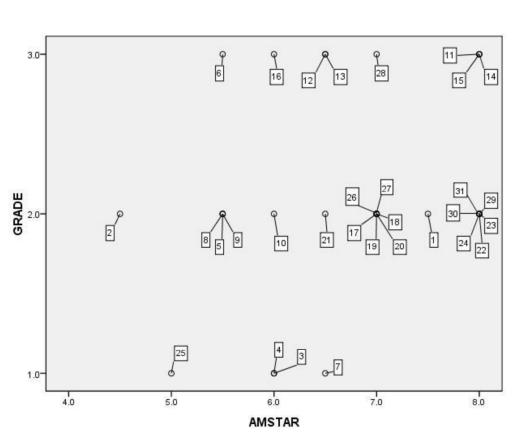


Figure 2 Flowchart of identified, included and excluded of systematic reviews or meta-analyses of TCMN

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The rating was based on the following five downgrading criteria:

Risk of bias

Risk of bias was assessed on the basis of the methodological quality of included RCTs, which considered allocation concealment, blinding, incomplete outcome data, selective reporting, and other factors. When we rate risk of bias, there are also other considerations, such as, the outcome we evaluated may be from a subset of studies, so we should evaluate the extent to which each trial contributes toward the estimate of magnitude of effect, and we also consider that sources of bias will vary in importance across outcomes(for example, blinding of outcome assessors is irrelevant for some outcomes but crucial for other outcome).

Inconsistency Inconsistency(i.e., heterogeneity) was assessed according to the outcomes of X2 test and I2 statistic reported in the MAs. If I2 > 50% and P < 0.05, and the heterogeneity could not be explained by conducting subgroup analysis or meta regression, the quality of evidence was downgraded

Indirectness Indirectness was defined as having an indirect comparison in one of the following four aspects: population, intervention, comparator, and outcome (PICO). These four aspects were judged depending on the target PICO of interest. Indirectness related to measurement of outcomes is the use of substitute or surrogate endpoints in place of the patient-important outcome of interest. In general, the use of a surrogate outcome requires rating down the quality of evidence.

Imprecision Imprecision was assessed in different ways for different types of data. For dichotomous outcomes, the quality of evidence was downgraded if either of the following two conditions were true : (1) total number of events was less than 300; (2) the 95% confidence interval

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(CI) of pooled risk ratio/odds ratio included both 1 and either 0.75 or 1.25(rough clinical decision threshold). For continuous outcomes, the reasons for downgrading were as follows: (1) total population size was less than 400 or (2) the 95% CI of pooled mean difference/weighted mean difference included both 0 and either clinical decision threshold. If the CI around the estimate of treatment effect is not sufficiently narrow, we rate down the evidence quality by one level. If the CI is very wide, we might rate down by two levels.

Publication bias Publication bias was assessed through funnel plots and Egger's test. When there are only few studies included in the MA,

the publication bias is challenging to interpret by funnel plots or statistical tests. Under these circumstances, we assessed publication bias based on the search methodology, in terms of databases searched, whether filters had been used, and if unpublished studies and gray literature (conference abstracts, protocols, books) were searched. êvie

Jiaqi Xu 2013

Xu JQ, He YN, Li J, et al. Effectiveness and Safety of Resina Draconis for Pressure Ulcer: A Systematic Review. Chinese Journal of Evidence-Based Medicine 2013;13:1236-43.

			Quality as	sessment	No of patie	ents		Quality			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute	

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13	randomised	serious ¹	no	serious	no serious	no serious	none	286/294	226/279	RR 1.2 (1.13	162 more per 1000 (from	⊕⊕⊕O
	trials		inconsi	stency	indirectness	imprecision		(97.3%)	(81%)	to 1.28)	105 more to 227 more)	MODERATE

1 Risk of bias:(1a)failed to conceal allocation;(1b) uesd no blinding;(1c)incomplete reporting of random sequence generation in most of studies De la included(1level).

Yuan Zhao 2013

Zhao Y, Wang Y, Xu XD, et al. Effectiveness of Tai Chi in Fall Prevention and Balance Function in the Elderly: A Meta-Analysis. Chinese Journal of Evidence-Based Medicine 2013;13:339-45.

	Quality assessment							its		Quality	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute	
4	randomised	no serious	no serious	no serious	serious	none	265/718	334/725	RR 0.82	83 fewer per 1000	⊕⊕⊕O
	trials	risk of bias	inconsistency	indirectness ¹			(36.9%)	(46.1%)	(0.73 to	(from 37 fewer to 124	MODERATE
									0.92)	fewer)	

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2	randomised	no serious	no serious	serious ³	serious	none	168	177	-	MD 2.45 higher (1.47	⊕⊕OO
	trials	risk of bias	inconsistency		imprecision ⁴					to 3.43 higher)	low

1 Indirectness:(3a)differences in therapeutic method between control groups; the difference are considered sufficient to make a difference in outcome, since the reviewer did not specify the control group in their eligibility criteria, and the control groups are regular exercise or physical therapy. Reviewer author did not address it using subgroup analysis leading to rating down for indirectness of control(1level).

3 Indirectness:(3a)differences in therapeutic method between control groups;(3b)surrogate outcome. This result showed that patients in Taiji group have a higher scores of Berger Balance Scale than that of control group, and the review author concluded that Taiji can decreased the occurrence of fall. It is the use of substitute endpoints in place of the patient-important outcome of interest(1 level).

4 Imprecision: (4a) for continuous outcomes, the reasons for downgrading were as follows: (1) total population size was less than400(1level).

Xiaoyan Wen 2013 Wen XY, Meng FJ, Jin YH, et al. Effectiveness of Chinese Herbal Retention Enema in Viral Hepatitis Patients: A Meta-Analysis. Chinese Journal of Evidence-Based Medicine 2013;13:339-45.

			Quality asse	essment			No of patie	ents		Effect	Quality
No of	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intervention		Relative	Absolute	

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studies						considerations			(95% CI)		
4	randomised	serious ¹	no serious	no serious	serious ²	none	106/141	65/128	RR 1.51 (1.3	259 more per 1000	⊕⊕OO
	trials		inconsistency	indirectness			(75.2%)	(50.8%)	to 1.67)	(from 152 more to 340	LOW
			Č,							more)	
5	randomised	serious ¹	no serious	no serious	serious ²	none	154/179	96/154	OR 4.17	250 more per 1000	$\oplus \oplus OO$
	trials		inconsistency	indirectness			(86%)	(62.3%)	(2.37 to 7.32)	(from 173 more to 300	LOW
										more)	

1 Risk of bias:(1a)failed to conceal allocation;(1b) uesd no blinding;(1c)incomplete reporting of random sequence generation in most of studies included. Assessments of risk of bias resulting from lack of blinding may need to be made separately for different outcomes. In this article, the intervention group gave Chinese acupressure and ventral massage, and it is difficult or not applicable to apply blinding of implementer and participants, but blinding of outcome assessors is relevant for this outcome(1 level).

2 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded if either of the following two conditions were true : (1) total number of events was less than 300(1 level).

Yue Ma 2014

Ma Y, Meng F, Jin Y, et al. Chinese herbal enema plus gastrointestinal intubation for ileus: A systematic review. Chinese Journal of Evidence-Based Medicine 2014;14:1254-62.

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			Quality asse	essment			ations Intervention (95% CI) Absolute								
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention			Absolute					
	randomised trials		no serious inconsistency		no serious imprecision	reporting bias ²	1416/1488 (95.2%)	994/1333 (74.6%)	RR 1.24 (1.2 to 1.29)	179 more per 1000 (from 149 more to 216	⊕⊕OO LOW				
					0					more)					

1 Risk of bias:(1a)failed to conceal allocation;(1b) uesd no blinding;(1c)incomplete reporting of random sequence generation in most of studies included;(1f)non-RCT was included(1 level).

2 Publication bias: (5b)funnel plot asymmetry(1 level).

Pingping Zheng 2013

Zheng P, Zhang J, Tong L. Meta analysis of the effect of Tai chi on reducing falls among elders living at home. Chinese Journal of Modern Nursing 2013;19:1123-27.

Quality assessment	No of patients	Effect	Quality

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No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute	
					serious	none		633/1307		73 fewer per 1000	⊕⊕⊕O
	trials	risk of bias		indirectness			(41.1%)	(48.4%)	(0.79 to 0.92)	(from 39 fewer to 102 fewer)	MODERATE

1 Inconsistency:(2)unexplained heterogeneity or inconsistency of results. $I^2 > 50\%$ and P < 0.05, and the heterogeneity could not be explained by conducting subgroup analysis or meta regression, the quality of evidence was downgraded. (1 level).

Xilan Zheng 2012

Zheng X, Jiang Z, Hu R. Effect of traditional Chinese medicine which eliminating necrotic tissues and promoting granulation on pressure ulcer of III to IV stage: a Meta-analysis. Chinese Journal of Practical Nursing2012;28.

			Quality ass	sessment			No of patient	ts		Effect	Quality
No of	Design	Risk of	Inconsistency	Indirectness	Imprecision	Other	Intervention		Relative	Absolute	

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studies		bias			considerations			(95% CI)		
9	randomised trials	serious ¹	no serious indirectness	no serious imprecision	none		123/273 (45.1%)		401 more per 1000 (from 293 more to 527 more)	
6	randomised trials	serious ¹	no serious indirectness	no serious imprecision	none	200	155	-	MD 9.33 lower (9.9 to 8.76 lower)	⊕⊕OO LOW

1 Risk of bias:(1a)failed to conceal allocation;(1b) uesd no blinding;(1c)incomplete reporting of random sequence generation in most of studies included (1.5 level).

2 Inconsistency:(2)unexplained heterogeneity or inconsistency of results : Unexplained heterogeneity or inconsistency of results. $I^2 > 50\%$ and P < 0.05,and the heterogeneity could not be explained by conducting subgroup analysis or meta regression, the quality of evidence was downgraded(0.5 level).

Guohao Wang 2014

Wang G, Jin Y, Wang X, et al. Prevention and treatment effect of acupressure and ventral massage in constipation: A systematic review. Chinese Journal of Practical Nursing2014;30.

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No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		
19	randomised	serious ¹	serious ²	no serious	no serious	none	872/1087	461/1083	RR 1.93	396 more per 1000 (from	⊕⊕00	CRITICAL
	trials			indirectness ³	imprecision		(80.2%)	(42.6%)	(1.86 to 2)	366 more to 426 more)	LOW	

1 Risk of bias:(1a)failed to conceal allocation;(1c)incomplete reporting of random sequence generation in most of studies included : assessments of risk of bias resulting from lack of blinding may need to be made separately for different outcomes. In this article, the intervention group gave Chinese acupressure and ventral massage, and it is difficult or not applicable to apply blinding of implementer and participants, and blinding of outcome assessors is irrelevant for this objective outcome(1level).

2 Inconsistency:(2)unexplained heterogeneity or inconsistency of results(0.5level).

3Indirectness:(3a)differences in therapeutic method between control groups(0.5level). There are large difference between some control groups to those in the studies, especially some other difference pharmacological and non-pharmacological method to promote bowel movements were used. We rated down 0.5 level because of considering that this discrepancy make a difference in outcome likely.

Jihuan Feng2014

Feng J, Yang G, Jiao L. Effect of acupressure on chemotherapy-induced digestive tract reaction for malignant tumor patients. Chinese Journal of Practical Nursing2014;30:51-55.

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			Quality	assessment			No of patients		Effect	Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention		Relative (95% Cl)	Absolute	Guanty	importance
								•				
7	randomised	serious ¹	serious ²	no serious	no serious	none	505	498	-	MD 1.52 lower (1.77 to	⊕⊕OO	CRITICAL
	trials			indirectness	imprecision	6.				1.26 lower)	LOW	
									1			
7	randomised	Serious ¹	serious ²	no serious	no serious	none	472	470	-	MD 1.08 lower (1.32 to	⊕⊕OO	CRITICAL
	trials			indirectness	imprecision					0.83 lower)	LOW	
	1	1		<u> </u>			·					
7	randomised	Serious ¹	serious ²	no serious	no serious	none	472	470	-	MD 1.17 lower (1.37 to	⊕⊕OO	CRITICAL
	trials			indirectness	imprecision					0.96 lower)	LOW	

1 Risk of bias: (1a)failed to conceal allocation;(1b)used no blinding;(1c)incomplete reporting of random sequence generation in most of studies included; (1e) loss to follow-up and failure to adhere to the intention-to-treat principle (4/7,4/7 and 2/2 included studies among those three

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outcomes exist "loss to follow-up")(1.5 level).

2Inconsistency:(2)unexplained heterogeneity or inconsistency of results (0.5level).

Baoxia Chang2014

Chang B, Meng F. Meta-analysis on effect of electro-acupuncture combined with auricular point plaster therapy for patients with simple obesity. Chinese Nursing Research 2014;28:884-87.

			Quality asse	ssment		No of patients Effect			Quality	Importance		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% CI)			
	randomised trials		no serious inconsistency	indirectness	no serious imprecision	none		136/186 (73.1%)		132 more per 1000 (from 51 more to 183 more)		⊕⊕⊕O MODERATE

1 Risk of bias:(1a)failed to conceal allocation;(1c)incomplete reporting of random sequence generation in most of studies included : assessments of risk of bias resulting from lack of blinding may need to be made separately for different outcomes. In this article, the intervention group gave auricular acupuncture, and it is difficult or not applicable to apply blinding of implementer and participants, and blinding of outcome assessors is

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irrelevant for this objective outcome(1level).

Wangqin Shen2010

Shen W, Qian H, Yu H. Meta-analysis of efficacy on satisfactory golden powder to treat patients with phlebitis. Chinese Nursing Research2010;24:85-86.

			Quality assess	ment			No of patients Effect			Quality	Importance	
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		
6	randomised	serious ¹	no serious	serious ²	Serious ³	reporting bias ⁴	160/164	120/163	RR 1.32 (1.26	236 more per 1000 (from	⊕000	CRITICAL
	trials		inconsistency				(97.6%)	(73.6%)	to 1.34)	191 more to 250 more)	very	
									5		LOW	

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding (intervention for external application of Ruyijinhuangsanis difficult or not applicable to apply blinding to implementer and participants, but blinding of outcome assessors is relevant for this subjective outcome); (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

2 Indirectness:(3a)difference in intervention (Ruyijinhuangsan was compatible with different components in four studies(honey, vinegar, strong

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⊿0 tea, sesame oil) (0.5 level).

3 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded based on the total number of events was less than 300(1 level).

4 Publication bias: (5a) flaws in literature searching (0.5 level).

Zhong Sun2014

Sun Z, Wang Q, Li J, et al. Systematic review on intervention effect of compressing umbilical with Chinese herbal for primary dysmenorrheal patients. Chinese Nursing Research 2014;28:506-10.

				Quality asses	ssment			No of patie	ents		Effect	Quality	Importance
	No of tudies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		
5		randomised trials	serious ¹	serious ²	serious ³	serious⁴	none	118/264 (44.7%)	53/230 (23%)	RR 1.93 (1.45 to 2.57)	214 more per 1000 (from 104 more to 362 more)	⊕000 VERY	CRITICAL
								LOW					

1 Risk of bias: (1a)failed to conceal allocation;(1b)used no blinding (intervention in this research difficult or not applicable to apply blinding to

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implementer and participants, but blinding of outcome assessors is relevant for this subjective outcome)(1 level).

2Unexplained: (2) heterogeneity or inconsistency of results(0.5 level).

3 Indirectness:(3a)differences in therapeutic method between intervention (different components of Chinese Traditional Medicine) (1 level).

4 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded based on the total number of events was less than 300(0.5 level).

Shaoxia Meng2014

Meng Z, Zhi C, Li Y. System evaluation of foot massage using for treatment of patients with diabetic peripheral neuropathy. Chinese Nursing Research 2014;28:3187-89.

			Quality assess	ment			No of patien	ts		Effect	Quality	Importance
No of studies	Design	Risk of Inconsistency Indirectness Imprecision bias		Other considerations	Intervention Control		Relative (95% Cl)	Absolute				
5	randomised	serious ¹	no serious	serious ²	serious ³	None ⁴	164/176	93/147	RR 1.47 (1.29	297 more per 1000 (from	⊕⊕OO	CRITICAL

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 trials	inconsistency		(93.2%)	(63.3%)	to 1.68)	183 more to 430 more)	LOW	

1 Risk of bias: (1a) failed to conceal allocation;(1c) incomplete reporting of random sequence generation in most of studies included (0.5 level).

2 Indirectness:(3a)differences in therapeutic method between intervention (different massage part of foot and lower limb) (0.5 level).

3 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded based on the total number of events was less than 300(0.5 level).

4 Publication bias: (5a) limited electronic literature databases searching (0.5 level).

Ye Li2014

Li Y, Tang L. Effect of acupoint massage on labor pain relief of puerperae: A meta-analysis of randomized controlled trials. Journal of Nursing 2014;21:12-15.

			Quality as	sessment			No of patie	ents		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		

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6 randomised	serious ¹ no seri	ousno seriou:	sno serious	reporting bias ³	336/388	205/378	RR 1.64 (1.56	347 more per 1000 (from	⊕⊕00	CRITICAL
trials	inconsistency ²	indirectness	imprecision		(86.6%)	(54.2%)	to 1.7)	304 more to 380 more)	LOW	

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding; (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

2 Inconsistency:(2)unexplained heterogeneity or inconsistency of results: although variability of interval estimations is substantial, but the differences are between small and large treatment effects (0.5 level).

3 Publication bias:(5a)flaws in literature searching (only using free-text searching, and lack of Mesh(index terms);(5b)funnel plot

asymmetry(0.5 level).

Yuanyuan Yang 2015

Yang Y, Wang Y, Li W, et al. Effectiveness of auricular point insomnia: a meta-analysis. Journal of Nursing Science 2015;30:4-8.

			Quality asse	essment			No of pa	tients		Effect	Quality	Importanc
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Interventio n	Control	Relative (95% Cl)	Absolute		ç

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3	randomised trials	serious ¹	serious ²	no serious	no serious	none	303/312	223/294	RR 1.28 (1.2	212 more per 1000	⊕⊕OO	CRITICAL
			6	indirectness	imprecision		(97.1%)	(75.9%)	to 1.37)	(from 152 more to 281 more)	LOW	
			•									
4	randomised trials		no serious inconsistency	no serious indirectness	Serious ³	none	160/172 (93%)	120/161 (74.5%)	RR 1.25 (1.13 to 1.37)	186 more per 1000 (from 97 more to 276	⊕⊕OO LOW	CRITICAL

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding; (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

2Inconsistency:(2)Unexplained heterogeneity or inconsistency of results (1 level).

3 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded based on the total number of events was less than 300(1 level).

Hongying Pu2011

Pu H, Cheng W, He J. The effect of Moist Exposed Burn Ointment (MEBO) on pressure ulcers: a Meta-analysis. Journal of Nursing Science 2011;26:79-81.

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Absolute (Absolute)	
.22 (2.07 468 more per 1000 (from \oplus OO	OO CRITICAL
2.33) 410 more to 510 more) VER	۲Y
LOV	N
- MD 6.93 lower (7.7 to 6.15 \oplus OO	OO CRITICAL
lower) VER	₹Y
LOV	N
2	2.33) 410 more to 510 more) VER LOV - MD 6.93 lower (7.7 to 6.15 \oplus OC lower) VER

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding; (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

2Inconsistency:(2)unexplained heterogeneity or inconsistency of results: although variability of interval estimations is substantial, but the differences are between small and large treatment effects (0.5 level).

3 Indirectness:(3a)differences in therapeutic method between control groups (0.5 level).

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4 Publication bias: (5a)limited electronic literature databases searching; (5b)funnel plot asymmetry (1 level).

5 Imprecision: (4a) For continuous outcomes, the reasons for downgrading were total population size was less than400 (0.5 level).

Xuan Zhou2011

Zhou X, Wang Q. Acupressure wristbands prevent postoperative nausea and vomiting: a Meta-analysis. Journal of Nursing Science 2011;26:81-84.

			Quality ass	essment			No of patie	ents		Effect	Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		
	-											
9	randomised	no serious	no serious	no serious	no serious	reporting bias ²	145/555	173/562	RR 0.85	46 fewer per 1000	⊕⊕⊕O	CRITICAL
	trials	risk of bias	inconsistency	indirectness	imprecision ¹		(26.1%)	(30.8%)	(0.72 to 1)	(from 86 fewer to 0	MODERATE	
										more)		
9	randomised	no serious	no serious	no serious	Serious ³	reporting bias ²	52/555	107/562	RR 0.44	107 fewer per 1000	⊕⊕⊕O	CRITICAL

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trials	risk of bias	inconsistency	indirectness		(9.4%)	(19%) (0.31 to 0.62)	(from 72 fewer to 131	MODERATE	
							fewer)		

1 Imprecision: (4b) for dichotomous outcomes, the quality of evidence was downgraded because that the 95% confidence interval (CI) of pooled risk ratio/odds ratio included both 1 and either 0.75 or 1.25 (0.5level).

2Publication bias:(5a)flaws in literature searching (only using free-text searching, and lack of Mesh(index terms)(0.5 level).

3 Imprecision:(4a)optimal information size criterion is not met the quality of evidence was downgraded based on the total number of events was less than 300(0.5 level).

Na Li2011

Li N. Meta analysis of the comparison of the effects between external application with Aloe vera and wet dressings with Magnesium sulfate in the treatment of phlebitis. Journal of Qilu Nursing 2011;17:3-5.

	Quality assessment						No of patien	nts		Effect	Quality	Importance
No of Design Risk of Inconsistency Indirectness Imprecision Other						Intervention		Relative	Absolute			

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	studies		bias					considerations			(95% CI)			
7	7	randomised	serious ¹	no s	serious	no serious	no serious	reporting bias ²	351/369	262/343	RR 1.25 (1.2	191 more per 1000 (from	⊕⊕00	CRITICAL
		trials		inconsistend	cy	indirectness	imprecision		(95.1%)	(76.4%)	to 1.27)	153 more to 206 more)	LOW	

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding; (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

2 Publication bias: (5a)limited electronic literature databases searching(1 level).

Xiaoli Wu 2012

Wu X, Yin L, Ji H. Meta-analysis on effects of clinical nursing of integrated traditional Chinese medicine. Nursing Journal of Chinese People's Liberation Army 2012;29:24-26.

	Quality assessment								No of patients Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute		

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8	randomised	serious ¹	serious ²	no serious	No serious	None ³	427/445	270/405	RR 1.44 (1.4 to	293 more per 1000 (from 267	⊕⊕00	CRITICAL
	trials			indirectness	Imprecision		(96%)	(66.7%)	1.46)	more to 307 more)	LOW	

1 Risk of bias: (1a)failed to conceal allocation; (1b)used no blinding(0.5level).

2Inconsistency:(2)unexplained heterogeneity or inconsistency of results(0.5level).

3 Publication bias: (5a)limited electronic literature databases searching; (5b)funnel plot asymmetry (1 level).

Xijuan Cui2014

Cui X, Qiao L, Shan T. Effect of acupuncture of zusanli on postoperative function of gastrointestinal tract: A systematic review. Today Nurse 2014:50-54.

			Quality as	sessment	No of patien	ts		Effect	Quality	Importance		
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% CI)	Absolute	Quanty	importance

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3	randomised	serious ¹	no serious	no serious	no serious	None ⁴	160	157	-	MD 14.52 lower	⊕⊕OO	CRITICAL
	trials		inconsistency ²	indirectness	imprecision ³					(15.49 to 13.54 lower)	low	
4	randomised	serious ¹	no serious	no serious	no serious	None⁴	162	164	-	MD 22.7 lower (25.67	⊕⊕OO	CRITICAL
	trials		inconsistency ^{,2}	indirectness	imprecision ³					to 19.73 lower)	low	
6	randomised	serious ¹	no serious	no serious	no serious	None⁴	530	518	-	MD 18.25 lower (18.6	$\oplus \oplus \oplus \Theta$	CRITICAL
	trials		inconsistency ²	indirectness	imprecision		<u>م.</u> (to 17.9 lower)	MODERATE	

1 Risk of bias: (1a) failed to conceal allocation; (1b) used no blinding; (1c) incomplete reporting of random sequence generation in most of studies

included;(1f)non-RCT was included(1 level).

2Inconsistency:(2)unexplained heterogeneity or inconsistency of results (1level).

3 Imprecision: (4a)For continuous outcomes, the reasons for downgrading were total population size was less than400 (0.5 level).

4 Publication bias: (5a)limited electronic literature databases searching(0.5level).

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Weiwei Wu 2016

 Wu W, Lan X, Kwong W, Jing X, et al. The effects of traditional exercises on sleep quality in older adults: a Meta-analysis. Chinese Journal of Nursing 2016:51.

			Quality ass	sessment	No of patient	s		Effect				
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% Cl)	Absolute	-Quality	Importance
			, 									
	randomised trials		no serious inconsistency ²		no serious imprecision	None	290	264	-	MD 2.15 lower (4.61 lower to 0.3 higher)	⊕⊕OO LOW	Critical outcome
		I						1		I	J	
	randomised trials		no serious inconsistency	no serious indirectness	Serious4	None ³	47	48	J	MD 4.29 lower (5.29 to 3.29 lower)	⊕⊕OO LOW	

1 Risk of bias: (1a)failed to conceal allocation in most of studies;(1b)used no blinding in most of studies (intervention in this research difficult or not applicable to apply blinding to implementer and participants, but blinding of outcome assessors is relevant for this subjective outcome); (1c)incomplete reporting of random sequence generation in most of studies included (1 level).

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2 Inconsistency:(2)unexplained heterogeneity or inconsistency of results (0.5level).

3 Publication bias:(5b)funnel plot asymmetry (0.5 level).

4 Imprecision: (4a)for continuous outcomes, the reasons for downgrading were total population size was less than400 (0.5 level).

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Top-level heading
TITLE A critical appr	aisal o	f the methodology and quality of evidence of systematic reviews and meta-analyses of	
Traditional Chinese Me	dical N	Nursing: a systematic review of reviews	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7-8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	8

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Synthesis of results		Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	8
		Page 1 of 2	
Section/topic	#	Checklist item	Top-level heading
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	1
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	1
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8-9, Fig.1, Fig.2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-9, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9-10, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-11, Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-12, Table 3, Fig.3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19



PRISMA 2009 Checklist

Joup (2009). Preferred Reportu. Page 2 of 2 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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A critical appraisal of the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing interventions: a systematic review of reviews

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Primary Subject Heading :	Nursing
Secondary Subject Heading:	Evidence based practice, Epidemiology, Nursing
Keywords:	Traditional Chinese Medical Nursing, Systematic review, Meta-analysis, AMSTAR tool, GRADE approach

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A critical appraisal of the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing interventions: a systematic review of reviews

Ying-Hui Jin¹, Guo-Hao Wang², Yi-rong Sun¹, Qi Li³, Chen Zhao³, Ge Li⁴, Jin-hua Si⁵, Yan Li¹, Cui Lu⁶, Hong-cai Shang^{7*}

 Evidence-Based Nursing Center, School of Nursing, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China;

Nursing department, North China University of Science and Technology Affiliated Hospital;
 063000, China;

3. Graduate College, Tianjin University of Traditional Chinese Medicine, Tianjin 300193,

China;

 Public Health Department of Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China;

5. Library of Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China;

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6. Emergency Department, Tianjin TEDA hospital, Tianjin 300457, China;

7. Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing,

Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing 100700, China

Running title: Quality of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing interventions

Correspondence to: Prof. Hongcai Shang, Key Laboratory of Chinese Internal Medicine of Ministry of Education and Beijing, Dongzhimen Hospital, Beijing University of Chinese Medicine, No. 5 Haiyuncang, Dongcheng District, Beijing 100700, China. E-mail: shanghongcai@foxmail.com. Tel: +86-22-15822772648.

Key words: Traditional Chinese Medical Nursing; Systematic review; Meta-analysis; AMSTAR tool; GRADE approach

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ABSTRACT

Objective: To assess the methodology and quality of evidence of systematic reviews and meta-analyses of Traditional Chinese Medical Nursing (TCMN) interventions in Chinese journals. These interventions include: acupressure, massage, Tai Chi, Qi Gong, electro-acupuncture, and use of Chinese herbal medicines for example in enemas, foot massage and compressing the umbilicus.

Design: A systematic literature search for systematic reviews and meta-analyses of TCMN interventions was preformed. Review characteristics were extracted. The methodological quality and the quality of the evidence were evaluated using the Assessment of Multiple Systematic Reviews (AMSTAR) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

Result: We included 20 systematic reviews and meta-analyses, and a total of 11 TCMN interventions were assessed in the 20 reviews. The compliance with AMSTAR checklist items ranged from 4.5 to 8, and systematic reviews/meta-analyses were on average of medium methodological quality. The quality of the bodies of evidence we assessed ranged from very low to moderate, and no high quality bodies of evidence were found. The top-two causes for down rating confidence in effect estimates among the 31 bodies of evidence assessed were the risk of bias and inconsistency.

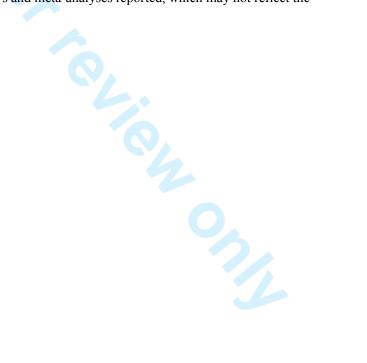
Conclusion: There is room for improvement in the methodological quality of systematic reviews/meta-analyses of TCMN interventions published in Chinese Journals. Greater efforts should to be devoted to ensuring a more comprehensive search strategy, clearer specification of the interventions of interest in the eligibility criteria and identification of meaningful outcomes for clinicians and patients (consumers). The overall quality of evidence among reviews remains sub-optimal, which raise concerns regarding their roles in influencing clinical practice. Thus, the conclusions in reviews we assessed must be treated with caution and their roles in influencing clinical practice should be limited. A critical appraisal of systematic reviews/meta-analyses of TCMN interventions is particularly important to provide sound guidance for TCM nursing.

Strengths and limitations of this study

• This study is the first attempt to assess the methodology and quality of evidence of systematic reviews and meta-analyses undertaken within Traditional Chinese Medical Nursing (TCMN) published in Chinese journals using the Assessment of Multiple Systematic Reviews (AMSTAR) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) approaches.

• The results highlight that the critical appraisal of systematic reviews/meta-analyses of TCMN interventions published prior to this review showed weaknesses, especially in the areas of use of evidence and decision-making, and suggestions are provided regarding how improvements may be incorporated into future work.

• The main limitation of this study is that the methodology and quality of the evidence assessments presented were based on published information regarding the assessment items in the individual systematic reviews and meta-analyses reported, which may not reflect the actual methodology used.



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Introduction

Despite considerable developments in medicine, a large number of people both in developed and developing countries turn to complementary and alternative medicine (CAM). This includes Traditional Chinese Medicine (TCM),¹ which is a science nourished by Chinese culture. It is generally delivered by qualified practitioners and has been practiced over thousands of years in China.² Traditional Chinese Medical Nursing (TCMN) is a significant branch of Nursing in China, and this involves TCM nurses using various interventions such as psychological interventions, diet therapy, TCM exercises and medications, acupoint, massage and cupping.

The holistic philosophy and the personalized nature of TCMN concur with the patient-centered approach found in modern nursing elsewhere. In the Chinese Nursing Development Program (2010-2015) it is explicitly pointed out that TCMN should be developed to contribute to the prevention and control of degenerative and chronic diseases, and should also be combined with Western medicine nursing techniques.³ In China, as specialized TCM clinical nursing has developed, TCMN techniques have become more popular this has allowed standardization of nursing specialties to gradually become established. As a result the level of both TCMN service delivery and scientific research has been significantly improved. A survey of 137 TCM institutions in China showed that there were 85 TCMN techniques provided for patients, and the top-ten techniques were moxibustion, cupping therapy, auricular application pressure, TCM fumigation, acupuncture point massage, acupoint sticking, TCM enema, poultices with Chinese medicine, inunction with Chinese medicine, and scraping therapy.⁴

There is a great need for reporting of clinical trials assessing the effectiveness of TCMN techniques. .Over the last decade, the number of papers that reported trials of TCMN have steadily increased, as well as systematic reviews and meta-analyses based on them. Systematic reviews and meta-analyses serve a vital role in the development of clinical practice guidelines (CPGs) .⁵ Assessing and synthesizing primary studies of TCMN interventions in systematic reviews and meta-analyses, and then forming CPG for integrated TCM and Western Medicine care can promote the sustainable development of TCMN.

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Although systematic reviews and meta-analyses strive to provide scientifically rigorous, independent, and accurate summaries of the scientific evidence with respect to a specific question of interest,⁶ methodological deficiencies in systematic reviews and meta-analysis may result in misleading results and over- or under-estimation of the investigated effects.⁷ Even methodologically sound systematic reviews and meta-analyses may provide only indirect or imprecise evidence for the question of interest. For the CPG developers, the quality ratings reflect the extent of our confidence that estimates of an effect are adequate to support a particular decision or recommendation.⁸

A critical appraisal of systematic review and meta-analysis of TCMN can increase nurses' confidence and facilitate efficient application of evidence.⁹ In this study, we used the widely accepted and utilized instruments, i.e. the Assessment of Multiple Systematic Reviews (AMSTAR) tool ^{10 11} and Grades of Recommendations Assessment, Development and Evaluation (GRADE) approach ¹² to critically assess the methodology and quality of evidence of TCMN interventions in Chinese journals and obtain their contribution to the development of evidence-based decision-making.

Methods

The technology road mapping of this study is presented in Figure 1.

Eligibility criteria

We included a study if it met the following criteria: (1) the study design is a systematic review, meta-analysis, or systematic review and meta-analysis; (2) the topic is TCMN care in China; (3) the papers are published as full-text articles in professional nursing journals or the four professional EBM journals in China. Articles were excluded (1) if the interventions focused on a broad concept of TCMN (e.g. for TCM care vs. Western Medicine care) without subgroup analysis which means that the review set a particularly broad scope of a review question reflecting great clinical heterogeneity; (2) the intervention group included non-TCMN interventions (e.g. TCMN combined with Western Medicine or combined with

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acupuncture). The flow diagram of systematic reviews and meta-analyses selection is presented in Figure 2.

Data sources

A comprehensive literature search was conducted to identify systematic reviews and meta-analyses written in Chinese by searching CNKI, VIP, Wanfang, CBM from inception through to April 2016. The following search terms "systematic review" or, "meta-analysis" were used as a means to navigate electronic journals to locate systematic reviews/meta-analyses of TCMN interventions published in nursing journals and EBM journals. The reference lists of the retrieved review articles were also screened to identify potential studies. If several updates of a study were available, only the most recent version was included (detail search strategy see Supplementary file).

Study selection and data extraction

Two reviewers independently screened the abstracts and titles of studies and subsequently reviewed the full text articles for inclusion, and following this data extraction was performed. We categorized the outcomes of systematic reviews and meta-analyses into the following types: endpoint, quality of life (QOL), the target event occurred, symptom, laboratory outcome, composite outcome (synthesis of multi-type outcomes), adverse event and economic evaluations. The risk ratio (RR) and the 95% confidence interval (CI) of dichotomous data and weighted mean difference (WMD) or standardized mean difference (SMD) with the 95% confidence interval (CI) of continuous data of the outcome were extracted when possible. In addition, basic characteristics of every review, such as the surname of the first author, year of publication, journal names, intervention and comparison, were extracted. In addition, information related to AMSTAR and GRADE evaluation was also extracted, such as methodological quality of the original studies (allocation concealment, blinding, follow-up and whether or not the research adhered to the intention-to-treat principle), details of interventions and controls used in all included original studies in systematic reviews/meta-analyses, reporting of outcomes and outcome measures, the pooled estimate and 95% confidence interval (CI) around the difference in effect between intervention and control

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for outcome, total sample of outcome, the extent to which each trial contributes toward the estimate of magnitude of effect based on study sample size and number of outcome events, tests of heterogeneity and I^2 , subgroup effects, and the method and the result of assessment of publication bias.

Quality assessment

The quality assessment of every systematic review and meta-analysis was assessed by two assessors independently using the AMSTAR tool ^{10 11} and GRADE approach ¹². In order to improve standardization, special training and a pre-test were performed. The disagreement of the reviewers was solved by discussion or asking a third assessor. Agreement between the two reviewers was determined by the Kappa statistic with corresponding 95%CI. Different people were used as assessors for AMSTAR evaluation and GRADE evaluation respectively to ensure that their judgment is not affected by previous impressions. Appraisers were not allowed to communicate or confer with each other during the appraisal process.

According to the AMSTAR criteria, a score of 0 or 1 was given for each criterion, with equal weight given to each domain. We judged each item as "yes (1 score)" when the criterion was explicitly met, "no (0 score)" when the criterion was explicitly not met, "cannot answer" when the item was relevant but not described adequately or not reported at all, and "not applicable" when the item was not relevant. When specific domains were not reported in sufficient detail, we gave a score of 0.5 for that domain. The overall score was categorized into three levels: 8 to 11 was high quality; 4 to 7 was medium quality, and 0 to 3 was low quality. All assessors set a more complete and unanimous standard for AMSTAR criteria after carefully and full discussion between all authors.

For grading the quality of evidence, the authors identify outcomes that are of key importance to patients, and then reviewers applied GRADE to determine the quality of the evidence and considered the five possible reasons to downgrade the evidence or the three possible reasons to upgrade the evidence.^{8 9 12} The assessors should be conservative in the

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judgment of downgrading or upgrading. When the systematic review did not provide sufficient information to judge the quality of evidence, the assessor made an attempt to contact authors of individual studies. Finally, the definitions of "high," "moderate," "low," and "very low" were used in grading the quality of evidence.

Data analysis

We established a database using Microsoft Excel 2007 software to extract data. Information on each included paper was imported into the database for analysis. We performed descriptive statistics on the distribution of scores as per AMSTAR items and summary statistics for the observed AMSTAR scores for each included systematic review and meta-analysis. A GRADE evidence profile which included an explicit judgment of each factor that determines the quality of evidence for the outcome of each included systematic review and meta-analysis was provided using the GRADE profiler 3.6 software.

The AMSTAR instrument and GRADE approach were applied respectively to assess the methodological and evidence quality based on different criteria and systems, but some similarities do exist between them. For example, item 3 about a thorough and comprehensive search (for example, searching in international, national, regional and subject-specific databases, the Cochrane Central Register of Controlled Trials (CENTRAL), conference abstracts, and other gray literature and ongoing trials) to identify as many relevant studies as possible helps to reduce a high probability of publication bias (GRADE downrating item). The correlation between AMSTAR and GRADE instruments was studied by scatter plot using SPSS version 17.0.

Results

Characteristics of included studies

The literature search yielded 809 potentially relevant references; of which, 28 were selected to be reviewed in full text. Finally, 20 studies ¹³⁻³² were included in this study. The year of publication ¹³⁻³² ranged from 2010 to 2016, and the number of reviews published in 2014

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accounted for near a half of these reviews (9/20, 45%). A total of 11 TCMN interventions were assessed, these were acupressure, acupoint massage, acupoint stimulation, auricular point therpy, Tai Chi, Qi Gong, electro-acupuncture combined with auricular point plaster therapy, Chinese herbal retention enema, inunction with Chinese medicine, foot bath therapy or foot massage with TCM medicine, compressing the umbilicus with Chinese herbs. None of the studies included observational research. Two included both RCTs and quasi-RCTs. No systematic review or meta-analysis used indirect comparison. None of the 20 studies used the GRADE approach to summarize evidence. The general characteristics of the assessed systematic reviews and meta-analyses are shown in Table 1.

AMSTAR methodological quality

The two reviewers had a satisfactory agreement (k=0.87). The methodological quality of all the included reviews is presented in Table 2. In summary, the compliance with AMSTAR checklist items ranged from 4.5 to 8, and the majority of the systematic reviews and meta-analyses were of medium (18/20, 90.0%) methodological quality. None of the 20 studies provided a registered protocol. For all the 20 studies, study selection and data extraction was conducted respectively by two independent reviewers. Most of them (13/20, 65%) adequately described the characteristics of the included trials, but no one provided a list of included and excluded studies. The search strategy design was not sufficiently comprehensive in 10 studies (50.0%). The mean number of electronic databases searched in the reviews was 6 (SD 2.2, range 2-11). The most frequently searched databases were Pubmed (14/20, 70%) and CNKI (19/20, 95%). Two reviews^{14 24} only searched the Chinese databases. Only two studies^{19 23} considered the status of publication (e.g. grey literature). The literature search in 10 of them was supplemented by consulting textbooks, experts in the particular field of study or by retracing references. No review searched ongoing trials. All of the reviews assessed scientific quality of the included studies. The risk of bias tool from the Cochrane handbook criteria (11/20, 55%) and the Jadad scale (6/20, 30%) were the most common criteria for quality assessment of included studies.

The majority of the systematic reviews and meta-analyses used appropriate methods to combine the findings of the studies included. They all stated that a random effects model was

used to combine study data when there was heterogeneity. When substantial heterogeneity was detected, possible explanations has been explored in subgroup analyses in 6 cases. There were no reviews in which meta-regression was applied. Two reviews conducted sensitivity analysis by exchanging the statistical approach for data synthesis (random-effects vs. fixed effects) to determine the robustness of conclusion. Most of them appropriately used the methodological quality of the included trials in formulating conclusions. None of them conducted evaluation of the quality of the body of evidence. All the included studies drew definitely positive conclusions in favor of TCMN interventions, while all reviewers suggested that there might be some benefits in the interventions, the findings should be interpreted with caution due to the poor quality of trials or limited trial sample. Ten systematic reviews and meta-analyses (50%) assessed publication bias using funnel plots and one review³⁰ used the Egger's test. Only one¹⁸ stated any conflict of interest.

GRADE evidence quality

The two reviewers had a satisfactory agreement (k=0.82). None of the 20 studies cited any observational research, so upgraded items were excluded from the assessment of evidence quality. The evidence quality of all the included reviews is presented in Table 3. For outcomes, there were occurrence of adverse events (1/20, 5.0%), and symptoms (6/20, 5.0%)30.0%), laboratory outcomes (5/20, 25.0%), and composite outcomes such as total effectiveness rate (17/20, 85.0%) in the 20 reviews, and no review considered endpoint, economic evaluations or QOL. At the beginning, we determined the critical outcomes for each review. Judgments about what constitutes a critical outcome may change for different research goals and results. For instance, in a review titled "acupressure wristbands prevent postoperative nausea and vomiting: a meta-analysis", the research goal was to evaluate the therapeutic effects on nausea and vomiting, so raters set nausea and vomiting as the critical outcome. Meanwhile, the outcomes of a systematic review of electro-acupuncture combined with auricular point plaster therapy for patients with simple obesity were the rate of effectiveness, BMI and waist circumference. The rate of effectiveness is equal to the numbers of patients recovering, markedly effective and effective divide the total according to the author's description.

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The criteria for recovery, markedly effective, effective and ineffective were stated as follows: *Recovery: body weight was in the normal weight range or BMI less than 23 kg/m²; Markedly effective: body weight decreased by no less than 5 kg, or BMI decreased by no less than 2 kg/m²;*

Effective: body weight decreased by no less than 2 kg and less than 5 kg, or BMI decreased by no less than 0.5 kg/m2 and less than 2 kg/m²;

Ineffective: body weight decreased by less than 2 kg, or BMI decreased by less than 0.5 \text{ kg/m}^2. Because it was considered that the rate of effectiveness contained far more therapeutic information than BMI and waist circumference, the rate of effectiveness was set as the critical outcome by raters. Totally 31 bodies of evidence in the 20 reviews were assessed for quality.

Rationale for downgrading

The quality of the bodies of evidence we assessed ranged from very low to moderate, and no high quality bodies of evidence were found.

The causes for down rating confidence in effect estimates among the 31 bodies of evidence assessed were the risk of bias (26 times, 83.9%), inconsistency (16 times, 51.6%), indirectness (8 times 25.8%), imprecision (13 times, 42.0%), and publication bias (15 times, 48.4%). The detailed reasons for downgrading in terms of risk of bias (80 times in total) included failure to conceal allocation(26 times, 32.5%), failure to blind (23 times, 28.8%), incomplete reporting of random sequence generation in most of studies included (24 times, 30.0%), use of invalidated outcome measure (0 times, 0.0%), loss to follow-up and failure to adhere to the intention-to-treat principle (3 times, 3.8%), non-RCT included (4 times, 5.0%). Downgrading for inconsistency was generally due to certain CIs showing little overlap from individual studies and significant heterogeneity. The quality of evidence was downgraded for indirectness (9 times in total) where substantial differences exist between the interventions (3 times in 9 times, 33.3%) or the controls (5 times in 9 times, 55.6%), or patient-important endpoints replaced by surrogate endpoints (1 time in 9 times, 11.1%). In a review evaluating the effectiveness of Tai Chi in preventing falls in the elderly, the authors stated that the scores of The Berg Balance Scale in the Tai Chi group were higher than in the control group, and argued that Tai Chi can effectively reduce the risk of falls for elderly people. However the

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Berg balance scale is a surrogate outcome for occurrence of fall.

The detailed reasons for downgrading of evidence for imprecision (13 times in total) included failure to meet optimal information size criterion (12 times in 13 times, 92.3%) and wide confidence intervals (1 times in 13 times, 7.7%).

The quality of evidence decreased for publication bias (19 times in all) because of flaws in literature searching (12 times in 19 times, 63.2%) and funnel plot asymmetry (7 times in 19 times, 36.8%). There were no correlation between AMSTAR and GRADE instruments through observation from scatter plot (see Fig. 3).

Discussion

It is important to assess the methodological and evidence quality of a systematic review/ meta-analysis before any conclusions can be used for clinical decision making. To the best of our knowledge, this is the first study which assessed methodological quality and evidence quality of systematic reviews and meta-analyses of TCMN interventions in Chinese Journals using AMSTAR and GRADE tools.

All systematic reviews and meta-analyses and primary studies lacked important outcomes that depressed the quality rating of evidence

GRADE specifies that both those conducting systematic reviews and those developing practice guidelines should begin by specifying every important outcome of interest.³³ Unfortunately, systematic reviews and meta-analyses in our study usually did not address all important outcomes. For instance, a review aiming to verify the effect of foot bath therapy or foot massage with traditional Chinese medicine for diabetic foot ulcers did not consider amputation as an outcome although foot ulcers are a high risk factor for infection, gangrene, amputation and even death among diabetes patient. We thought amputation rate maybe the preferable long-term outcome to verify the effect of the intervention but this was not considered by the reviewers.¹⁷ In general, systematic reviews and meta-analyses should include all outcomes that are likely to be meaningful to clinicians, patients, the general public, administrators and policy makers. For example, outcomes may include survival, clinical events, patient-reported outcomes (e.g. symptoms or quality of life), adverse events, burdens (e.g. demands on caregivers, frequency of tests, restrictions on lifestyle) and economic

outcomes (e.g. cost and resource use). But primary studies typically focused on short-term benefit without considering long-term outcomes, harm or economic outcomes. None of the reviews listed any adverse effects as outcomes of TCMN interventions. These all confirmed that systematic reviews and meta-analyses and primary studies all had shortcomings in research design which also rendered it difficult to use the results of systematic reviews and meta-analyses to make appropriate recommendations as these were based on incomplete outcomes.

Risk of bias resulted in downgrading in most reviews

RCTs are critical for assessing and providing valuable evidence about the effectiveness of TCMN interventions. However, the reliability and acceptability of any intervention study results depends on the extent to which the studies employ scientific principles and use a valid research design. In this study, we used the Cochrane Collaboration's tool for assessing risk of bias ¹¹. Most of the reviews were downgraded because of lack of allocation concealment and blinding, and lack of details of randomization in primary studies. 228 RCTs were included in 20 systematic reviews and meta-analyses, of these the authors noted that 184 (80.7%) were published in Chinese journal.

This finding is consistent with the results of similar research. Yao conducted a systematic review using GRADE to assess the quality of evidence of Chinese meta-analyses. The authors indicated risk of bias was the most common factor for downgrading evidence in Chinese meta analyses and stressed that the inferior quality of evidence in meta analyses related to TCMs might be caused by the poor quality reporting in RCTs.³⁴ Wu found that more than 90% of RCTs published in core Chinese journals lacked an adequate description of randomization in 2009, and most trials despite claiming to be RCTs did not fulfill the criteria for a true RCT.³⁵ Although the number of RCTs in nursing research in China is increasing over time, the quality of most of them remains unsatisfactory. Xing et al ³⁶ published a comprehensive evaluation of 7391 nursing intervention studies published in simplified Chinese from 1979 to 2012, and the result showed that among the 10 characteristics considered in quality evaluations, the lowest ratings were observed for "utilization of blind method", "description of loss of follow-up", "appropriate calculation of sample size" and "randomized assignment

of patients to treatments".

Current systematic reviews and meta-analyses are often limited in their usefulness as guidelines because they rate risk of bias by studies across outcomes rather than by outcome across studies.³⁷ Authors of systematic reviews and meta-analyses should keep it in mind that sources of bias may vary in importance across outcomes; it means that summarizing study limitations must be outcome specific.³⁷ For example, the assessors downgraded the evidence many times for not using blinding in studies with subjective outcomes which are much more vulnerable to biased judgments. The above mentioned review evaluating the effect of foot bath therapy or foot massage for diabetic foot ulcers used rate of effectiveness as the only outcome, which was based on subjective observable judgment of the condition (e.g. ulcer area, local swelling and skin color). Raters categorized this evidence as having serious study limitations on account of lack of blinding during the study.¹⁷ Problems with the design and execution of individual studies of TCMN interventions raise questions about the validity of TCMN intervention effects and resulted in downgrading of the quality of evidence.

Heterogeneity has not been adequately explored or there is inappropriate combination of studies' findings which usually decreases the quality of evidence on the grounds of inconsistency

The raters decreased the quality of evidence when significant heterogeneity was detected for which the authors failed to identify a reasonable source or explanation. Although studies brought together in a systematic review will inevitably have some differences, reviewers should look for robust explanations for any significant heterogeneity.³⁷ Clinical variation will lead to heterogeneity if the intervention effect is affected by the factors

that vary across individual studies; most obviously, the patient characteristics or specific interventions. In our study, variability in interventions is the most common reason for heterogeneity, e.g. different points for acupoint massage, different medicine for Chinese herbal retention enema, or different Chinese herbal prescriptions for umbilical compression. Raters considered the true intervention effect might be different in different studies and decreased the evidence quality for inconsistency of results and methodological quality for inappropriate combination of the study's findings.

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When there is heterogeneity that cannot readily be explained, incorporating it into a random-effects model is often the only option for reviewers. Reviewers should know a random-effects model does not "take account" of the heterogeneity. When the meta-analysis results show that heterogeneity is statistically significant, the most important treatment method is to analyze possible reasons for heterogeneity rather than simply using the random effects model.

Information about study limitations, imprecision, inconsistency, indirectness, and publication bias is necessary for TCMN to understand and have confidence in the assessment of quality and estimate of effect size. GRADE provides a framework for assessing outcome quality that encourages transparency and explicit accounting of the judgments made. In this study, the quality of evidence was low in 20, and very low in 4 among the 31 bodies of evidence. High quality evidence is more likely to be associated with strong recommendation, but it is important to note that sometimes low or very low quality evidence can lead to a strong recommendation. When using the evidence for TCMN interventions, nurses should consider patient values and preferences and resource implications alongside confidence in estimates of effect of primary outcome used in the GRADE system. In addition, in view of the unsatisfactory methodological and evidence quality of systematic reviews and meta-analyses of TCMN which we included, we considered it important to present to readers the built-in problems existing within systematic reviews and meta-analyses of TCMN interventions rather than to only present to readers with the available evidence.

Methodological quality assessment using AMSTAR should be a precondition for further evaluation with the GRADE approach

Systematic reviews/meta-analyses may differ considerably in their methodological quality.³⁸ Using a rigorous methodology with a clearly formulated research question and a comprehensive search strategy, systematic reviews should provide reproducible results and include all potentially relevant studies, thereby limiting bias and random errors.³³ Systematic reviewers will clearly specify the interventions of interest in their eligibility criteria, ensuring that only directly relevant studies will be eligible. But in our study, there were several systematic reviews/meta-analyses that included studies inconsistent with their eligibility

criteria. For instance, a review aiming to evaluating foot massage for diabetic peripheral neuropathy, included studies with different interventions: foot massage or massage in foot reflection area or acupoint massage for lower limbs.

In addition, to minimize bias, systematic reviews require a thorough, objective and reproducible search of a range of sources to identify as many relevant studies as possible . But in this respect, some systematic reviews/meta-analyses in this study are far from satisfactory. Some systematic reviews/meta-analyses set a flawed search strategy, for example, only using free-text searching without performing Mesh (index terms) searching, only searching the Chinese database, and failing to identify "negative" studies. Moreover, in our study, assessors found high-quality clinical trials do not always exist especially in TCMN, and non-RCTs were sometimes included in systematic reviews/meta-analyses. The problem in methodology in some systematic reviews/meta-analyses discussed above resulted in dropping of AMSTAR scores, as well as downgrading to the quality of bodies of evidence. Although GRADE guideline suggests not using GRADE for systematic reviews/meta-analyses with serious flaws, we did not exclude any study since no review was rated with a low methodological quality score, although some imperfect methodology in conducting systematic reviews/meta-analyses does exist in the studies reviewed.

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In our study, we were unable to identify any correlation between methodological quality and quality of body of evidence using a scatter plot. It is easy to understand. Because GRADE is much more than a simple rating system, it offers a transparent and structured process for developing and presenting evidence summaries for systematic reviews,⁸ not only surveying some methodological characteristics of the production of systematic reviews/meta-analyses which influence quality of evidence but also explores factors resulting in inconsistency or imprecision.

Methodological flaws in quality of systematic reviews/meta-analyses could severely affect decision-making and the application of evidence. We suggest assessing methodological quality before evidence quality assessment, and there is no need to evaluate the evidence quality for a systematic review/meta-analysis for which a low methodological quality score is assigned due to major flaws.

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Sub-optimal reporting may contribute to an underestimation of methodological quality

Some of the research items regarding GRADE and AMSTAR rely on transparency in reporting in the systematic reviews/meta-analyses document. Even the most methodologically rigorous process, if not clearly described in the systematic reviews/meta-analyses document, will leave assessors or users uncertain about the reliability of the systematic reviews/meta-analyses in question.

Most Chinese journals impose strict limits on word numbers. The Chinese journal editors usually encourage authors to focus on the research results and discussion sections of their manuscripts and shorten the research methods section of their papers. Even the Chinese Journal of Nursing, a leading domestic journal in China, typically limits the length of articles regarding nursing intervention studies to no more than 4 pages.³⁸ Although we made an attempt to contact developers of reviews we included, we found it was difficult since most of author's contact information were not presented in published papers. So results in this study were possibly underestimated due to the lack of some important information reporting. PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-analyses), which consists of 27-item checklist and a four-phase flow diagram, informs authors of the preferred way to present every part of a report of a systematic reviews/meta-analyses. We hope that editors of medical journals in China recognize and promote the use of reporting guidelines in their publications, and hope authors adhere to reporting guidelines.

Implications for research and practice

A high methodological quality is the basic precondition of systematic reviews for identifying the best available evidence for specific research questions and conducting GRADE evaluation. Systematic review/meta-analysis authors and editors should make every effort to adhere to well-established methodological standards to enhance the impact of their research efforts. But high methodological quality does not fully reflect the quality of a review, the quality of a body of evidence is critical in decision-making. The GRADE approach can provide clinicians and patients with guidance as to how to use results from systematic review/meta-analysis in clinical practice and give policy makers a guide to their use in developing health policy. The overall quality of systematic reviews/meta-analyses of TCMN interventions published in

Chinese Journals remains suboptimal, especially in terms of the risk of bias which reduces the quality of evidence for almost all indications, raising concerns about their role in influencing clinical practice, so their conclusions needs to be treated with caution. Critical appraisal of systematic reviews/meta-analyses of TCMN interventions are particularly important.

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Author contributions

signed ta. papers; G.L., J.H. d the critical appraisal; Y. nanuscript. d interest Machine additional data are available. Y.H.J. and H.C.S designed this study; G.H.W., Q.L. and Y.R.S searched databases and

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Fig. 1 Technology road mapping of this study. EBM, Evidence-Based Medicine; EBN, Evidence-Based Nursing; TCM, Traditional Chinese Medicine; AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

Fig. 2 Flowchart of identified, included and excluded of systematic reviews or meta analyses of TCMN interventions.

Fig. 3 Scatter plot for exploring correlation between AMSTAR and GRADE instruments.

AMSTAR, Assessment of Multiple Systematic Reviews; GRADE, Grading of

Recommendations Assessment, Development and Evaluation.

Supplementary file File 1 Search strategy

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Table 1 The characteristics of included systematic reviews/ meta-analyses Study Journal Design No. of patients Population Intervention Comparison Outcomes The rage of literature search Baoxia Chang Chinese Nursing RCT 467 Simple obesity Electro-acupuncture Electro-acupuncture Rate of effectiveness, BMI, Cochrane Library, PubMed, VIP, CNKI, CBM, 2014 Research combined with auricular Percentage of body fat, Waist references of the included literatures, the grey point plaster circumference literature Wangqin Shen Chinese Nursing RCT 327 Phlebitis Ruyijinhuangsan Magnesium sulphate Rate of effectiveness Medline, CBM, CNKI, the references of the included 2010 Research by wet compression literatures Hongying Pu Journal of RCT 703 Pressure ulcers Moist exposed burn Skin disinfection Cure rate PubMed, EMBASE, Cochrane database, CBM, VIP, 2011 Nursing Science ointment solution or antibiotic Time of cure the references of the included literatures ointment Xuan Zhou Journal of RCT 1117 Postoperative Acupressure wristbands Placebo wristband Incidence of nausea, Incidence Medline, CNKI, CBM, VIP, WanFang 2011 Nursing Science patients of vomiting Xiaoli Wu Hot foot bath RCT Nursing Journal 860 Diabetic foot Foot bath therapy or foot Effectiveness rate Medline, CNKI, CBM, VIP 2012 of Chinese ulcers massage with traditional People's Chinese medicine Liberation Army Xilan Zheng Chinese Journal RCT 551 Pressure ulcers Traditional Chinese Skin disinfection Cure rate, Cure time, Frequency Medline, EMBASE, PubMed, Cochrane Library, 2012 of Practical medicine for elimination solution or antibiotic of dressing change CBM, VIP, CNKI, WanFang Nursing of necrotic tissues ointment Na Li 2011 Journal of Qilu RCT 712 Phlebitis CNKI, VIP, WanFang External application with Magnesium sulphate Effectiveness rate Nursing CCT aloe vera by wet compression Jiaqi Xu 2013 Chinese Journal RCT 610 Pressure ulcer Resina draconis Skin disinfection Effectiveness rate. Cure time Cochrane Library, PubMed, Elsevier SDOL, Web of of solution or antibiotic Knowledge, CBM, CNKI, VIP, WanFang, the Evidence-Based ointment references of the included literatures Medicine

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Yuan Zhao	Chinese Journal	RCT	2796	Elderly	Tai Chi	Regular sport or	Rate of falls, Time up and go	PubMed, Web of Science, Cochrane Library,
2013	of			individuals		physical therapy	test, Functional reach test,	EMBASE, CBM, CNKI, VIP, WanFang Database, t
	Evidence-Based						Berg balance scale	references of the included literatures
	Medicine							
Xiaoyan Wen	Chinese Journal	RCT	1735	Virus hepatitis	Chinese herbal retention	Comprehensive	Effectiveness rate, liver	Cochrane library, PubMed, EMBASE, VIP, CNKI,
2013	of				enema and	treatment	function index	CBM, WanFang, the references of the included
	Evidence-Based				comprehensive treatment			literatures, SIGLE
	Medicine							http//www.opengrey.eu/search/request)
Pingping	Chinese Journal	RCT	3194	Elders living in	Tai Chi	Regular sport or	Rate of fall, Falls efficacy, Time	Cochrane Library, Medline, EBSCO, CNKI, Wanfa
Zheng 2013	of Modern			home		physical therapy or	of standing on one leg with	the references of the included literatures
	Nursing					blank control	eyes close or open, Body	
							flexibility	
Guohao Wang	Chinese Journal	RCT	3084	Constipation	Acupoint massage and	Routine nursing	Rate of effectiveness,	CNKI, VIP, CBM, Wanfang, EBSCO, PubMed,
2014	of Practical	Quasi-			ventral massage		Defecation frequency in the	Cochrane Library
	Nursing	RCT					first day, Defecation frequency	
							in the first two days, Defecation	
							difficulty rate, Defecation time	
							Dry stool rate, Incomplete	
							defecation feeling rate,	
							Laxative provided	
Jihuan Feng	Chinese Journal	RCT	959	Cancer patients	Acupoint massage	Routine nursing	Duration of	PubMed, Medline, Embase, AMED, Cochrane Libr
2014	of Practical			receiving			Chemotherapy-induced nausea,	CBM, CNKI, VIP, Wanfang
	Nursing			adjuvant			vomiting and retching,	
				chemotherapy			Frequency of	
							Chemotherapy-induced nausea,	

							vomiting and retching, Severity of Chemotherapy-induced	
							nausea, vomiting and retching	
							Anti-emetic medication dosage	
<i>a</i>		D (77)					Quality of life	
Shaoxia Meng	Chinese Nursing	RCT	383	Diabetics with	Foot massage or massage	Routine nursing	Rate of effectiveness, Nerve	PubMed, CBM, CNKI, VIP, Wanfang databas
2014	Research			peripheral	in foot reflection area or		conduction velocity	references of the included literatures
				neuropathy	acupoint massage for			
Xijuan Cui	T 1 N	DOT	0.00		lower limbs	D		
2014	Today Nurse	RCT,	860	Postoperative	Acupoint massage for Zusanli point, Zusanli	Routine nursing	First bowel sound time, First	CNKI, Wanfang
		Quasi- RCT		patients having abdominal			aerofluxus time, First defecation time	
		KC I		operation	point acupuncture, Chinese medicine		delecation time	
				operation	application at the Zusanli			
					point			
Zhong Sun	Chinese Nursing	RCT	524	Primary	Umbilical compression	Analgesic drug	Rate of effectiveness	Cochrane Library, PubMed, Proquest, CNKI,
2014	Research			dysmenorrhea	with Chinese herbs		Cure rate	WanFang
				patients			Comparison of the score and	
							scale of symptoms	
							Rate of prostaglandin excretion	
							Level of hemorheology and	
							estradiol,	
							A/B, RI, and PI	
Ye Li 2014	Journal of	RCT	888	Women in	Acupoint massage for	Blank control	Rate of effectiveness of	CNKI, VIP, CBM, WanFang, PubMed
	Nursing			labour	Sanyinjiao, Hegu,		relieving labor pain	

					Zhiyin, Taichong, Ashi,			
¥	Lauran 1 af	DCT	939	Insomnia	Shenshu et al.	A	Dete of effections	DebMed Costante library CDM CNIZI VID
Yuanyuan	Journal of	RCT	939		Auricular point therapy	Acupuncture or drug	Rate of effectiveness	PubMed, Cochrane library, CBM, CNKI, VIP,
Yang 2015	Nursing Science					ulerapy		WanFang, the references of the included 1 iteratures
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Characteristics of the

included studies

0.65±0.49

Quality

assessment

 1.00 ± 0.00

Forming

conclusion

0.85±0.37

Method for

combining

0.5

0.5

0.5

0.5

0.5

0.5

0.5

0.78±0.30

Publication

bias

0.45±0.51

Conflict of

interest

 0.05 ± 0.22

Score/Rank

4.5/medium

6/medium

6/medium

5.5/medium

6.5/medium

4.5medium 8/high

6.5/medium

8/high

6/medium

7/medium

7/medium

6.5/medium

8/high

5/medium

7/medium

7/medium

7.5/medium

7/medium

8/high

6.58±1.10

Study	Priori	Data	Comprehensive	Status of
	design	extraction	literature search	publication
Wangqin Shen	1	1	0	0
Hongying Pu	1	1	0	0
Na Li	1	1	0	0
Xuan Zhou	1	1	0	0
Xiaoli Wu	1	1	0	0
Xilan Zheng	1	1	0	0
Jiaqi Xu	1	1	1	0
Yuan Zhao	1	1	1	0
Xiaoyan Wen	1	1	1	1
Pingping Zheng	1	1	1	0
Guohao Wang	1	1	0	0
Jihuan Feng	1	1	1	0
Shaoxia Meng	1	1	1	0
Xijuan Cui	1	1	1	0
Zhong Sun	1	1	0	0
Ye Li	1	1	0	0
Yuanyuan Yang	1	1	1	0
Baoxia Chang	1	1	1	1
Yue Ma	1	1	0	0
Weiwei Wu	1	1	1	0
Total	1.00±0.0	1.00+0.00	0.50 0.51	0.10.0.2
Mean±SD	0	1.00±0.00	0.50±0.51	0.10±0.3

Table 2 AMSTAR scores for the methodology of reviews included in this study

List of

studies

0.00±0.

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Study	Patients	Intervention	Comparison	Outcome	No. of patients/studies	Effect RR/OR/MD/SMD (95% CI)	Absolute effect (95%)	Quality	AMST/ score
Baoxia Chang 2014	Simple obesity	Electro-acupuncture combined with auricular point plaster	Electro-acupuncture	Rate of effectiveness	397(5)	RR1.18 (1.07 to 1.25)	132 more per 1000 (from 51 more to 183 more)	MODERATE (1a, 1c)	7.5
Wangqin Shen 2010	Phlebitis	Ruyijinhuangsan	Magnesium sulphate by wet compression	Rate of effectiveness	327(6)	RR1.32 (1.26 to 1.34)	236 more per 1000 (from 191 more to 250)	VERY LOW (1a, 1b, 1c, 3a, 4a, 5a)	4.5
Hongying Pu 2011	Pressure ulcers	Moist exposed burn ointment	Skin disinfection solution or antibiotic ointment	Cure rate	432(11)	RR2.22 (2.07 to 2.33)	468 more per 1000 (from 410 more to 510 more)	VERY LOW (1a、1b、 1c、2、3a、5a、5b)	6
				Time of cure	261(5)	MD6.93 (7.7 to 6.15)	MD 6.93 lower (7.7 to 6.15 lower)	VERY LOW (1a, 1b, 1c, 3a, 4a, 5a, 5b)	6
Xuan Zhou 2011	Postoperative patients	Acupressure wristbands	Placebo wristband	Incidence of nausea	1117(9)	RR0.85 (0.72 to 1)	46 fewer per 1000 (from 86 fewer to 0 more)	MODERATE (4b, 5a)	5.5
				Incidence of vomiting	1117(9)	RR0.44 (0.31 to 0.62)	107 fewer per 1000 (from 72 fewer to 131 fewer)	MODERATE (4a、5a)	5.5
Xiaoli Wu 2012	Diabetic foot ulcers	Foot bath therapy or foot massage with traditional Chinese medicine	Hot foot bath	Effectiverate	845(8)	RR1.44 (1.4 to 1.46)	293 more per 1000 (from 267 more to 307 more)	LOW (1a, 1b, 2, 5a, 5b)	6.5
Xilan Zheng 2012	Postoperativepati ents	Traditional Chinese medicine for elimination of necrotic tissues	Skin disinfection solution or antibiotic ointment	Cure rate	551(9)	RR1.89 (1.65 to 2.17)	401 more per 1000 (from 293 more to 527 more)	LOW (1a, 1b, 1c, 2)	5.5
				Cure time	355(6)	MD9.33 (9.9 to 8.76)	MD 9.33 lower (9.9 to 8.76 lower)	LOW (1a, 1b, 1c, 2)	5.5
Na Li 2011	Phlebitis	External application with aloe vera	Magnesium sulphate by wet compression	Effectiverate	712(7)	RR1.25 (1.2 to 1.27)	192 more per 1000 (from 153 to 206)	LOW (1a, 1b, 1c, 5a)	6
Jiaqi Xu 2013	Pressure ulcer	Resina draconis	Skin disinfection solution or antibiotic ointment	Effective rate	573(13)	RR1.2 (1.13 to 1.28)	162 more per 1000 (from 105 more to 227 more)	MODERATE (1a, 1b, 1c)	8
Yuan Zhao 2013	Elderly individuals	Tai Chi	Regular sport or physical therapy	Rate of falls	1443(4)	RR0.82 (0.73 to 0.92)	83 fewer per 1000 (from 37 fewer to 124 fewer)	MODERATE (3a)	6.5
				Berg balance scale, BBS	345(2)	MD2.45 (1.47 to .43)	MD 2.45 higher (1.47 to 3.43 higher)	LOW (3a, 3b, 4a)	6.5
Xiaoyan Wen 2013	Virus hepatitis	Chinese herbal retention enema and comprehensivetreatment	Comprehensivetreatment	Effective rate: after 2 weeks from cure time	260(4)	RR 1.51 (1.3 to 1.67)	259 more per 1000 (from 152 more to 340 more)	LOW (1a, 1b, 1c, 4a)	8
				Effective rate: after 4 weeks from cure time	333(5)	OR 4.17 (2.37 to 7.32)	250 more per 1000 (from 173 more to 300 more)	LOW (1a, 1b, 1c, 4a)	8
Pingping Zheng 2013	Elders living in home	Tai Chi	Regular sport or physical therapy or blankcontrol	Rate of fall	2624(9)	RR 0.85 (0.79 to 0.92)	73 fewer per 1000 (from 39 fewer to 102 fewer)	MODERATE (2)	6
Guohao Wang 2014	Constipation	Acupoint massage and ventral massage	Routine nursing	Rate of effectiveness	2170(19)	RR 1.93 (1.86 to 2)	396 more per 1000 (from 366 more to 426 more)	LOW (1a, 1c, 2, 3a)	7

Table 3 GARDE evaluation of the quality of evidence of reviews included in this study

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Jihuan Feng 2014	Cancer patients receiving adjuvant	Acupoint massage	Routine nursing	Duration of chemotherapy-induced nausea	942(7)	MD 1.52 (1.77 to 1.26)	MD 1.52 lower (1.77 to 1.26 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
	chemotherapy			Frequency of chemotherapy-induced nausea	942(7)	MD 1.08 (1.32 to 0.83)	MD 1.08 lower (1.32 to 0.83 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
				Severity of chemotherapy-induced nausea	942(7)	MD 1.17(1.37 to 0.96)	MD 1.17 lower (1.37 to 0.96 lower)	LOW (1a, 1b, 1c, 1e, 2)	7
Shaoxia Meng 2014	Diabetics with peripheral neuropathy	Foot massage or massage in foot reflection area or acupoint massage for lowerlimbs	Routine nursing	Rate of effectiveness	323(5)	RR 1.47 (1.29 to 1.68)	297 more per 1000 (from 183 more to 430 more)	LOW (1a, 1c, 3a, 4a, 5a)	6.:
Xijuan Cui 2014	Postoperative patients with abdominal operation ⁴	Acupoint massage for Zusanli, Zusanli point acupuncture, Chinese medicine application at the Zusanli point	Routine nursing	First aerofluxus time: subgroup for Zusanli point acupuncture∆	317(3)	MD 14.52 (15.49 to 13.54)	MD 14.52 lower (15.49 to 13.54 lower)	LOW (1a, 1b, 1c, 1f, 2, 4a, 5a)	8
				Subgroup for acupoint massage for Zusanli△	326(4)	MD 22.7 (25.67 to 19.73)	MD 22.7 lower (25.67 to 19.73 lower)	LOW (1a、1b、1c、1f、2、 4a、5a)	8
				Subgroup for Chinese medicine application at the Zusanli point∆	1048(6)	MD 18.25 (18.6 to 17.9)	MD 18.25 lower (18.6 to 17.9 lower)	MODERATE (1a, 1b, 1c, 1f, 2, $5a$)	8
Zhong Sun 2014	Primary dysmenorrhea patients	Umbilical compression with Chinese herbs	Analgesic drug	Rate of effectiveness	496(5)	RR 1.93 (1.45 to 2.57)	214 more per 1000 (from 104 more to 362 more)	VERY LOW (1a, 1b, 2, 3a, 4a)	5
Ye Li 2014	Women in labour	Acupoint massage for Sanyinjiao, Hegu, Zhiyin, Taichong, Ashi, Shenshu et al.	Blank control	Rate of effectiveness	766(6)	RR 1.64 (1.56 to 1.7)	347 more per 1000 (from 304 more to 380 more)	LOW (1a、1b、1c、2、5a、 5b)	7
Yuanyuan Yang 2015	Insomnia [△]	Auricular point therapy	Acupuncture or drug therapy	Effective rate after 2 weeks from cure time	606(3)	RR 1.28 (1.2 to 1.37)	212 more per 1000 (from 152 more to 281 more)	LOW (1a, 1b, 1c, 2)	7
		Auricular point therapy	Acupuncture or drug therapy	Effective rate after 4 weeks from cure time	333(4)	RR 1.25 (1.13 to 1.37)	186 more per 1000 (from 97 more to 276 more)	LOW (1a, 1b, 1c, 4a)	7
Yue Ma 2014	Ileus	Enema and gastrointestinal intubation with traditional Chinese medicine	Blank control	Rate of effectiveness	2821(27)	RR 1.24 (1.2 to 1.29	179 more per 1000 (from 149 more to 216 more)	LOW (1a, 1b, 1c, 1f, 5b)	8
Weiwei Wu 2016	Elderly individual	Traditional Chinese exercise	Other intervention or regular nursing	Subgroup for PSQI for Tai Chi	554(8)	MD -2.15(-4.61 to 0.30) MD -4.29(-5.29	MD 2.15 lower (4.61 lower to 0.3 higer)	LOW (1a、1b、1c、2、5b)	8
				Subgroup for PSOI for Qigong	55(2)	to -3.29)	MD 4.29 lower (5.29 lower to 3.29 lower)	LOW (1a, 1b, 1c, 4a, 5b)	8
(1e) loss to follow Inconsistency: (2) Indirectness: (3a)	-up and failure to ad unexplained hetero differences in therap	ocation; (1b) no blinding used; here to the intention-to-treat princip geneity or inconsistency of results peutic methods between intervention size criterion is not met; (4b) w	le; (1f) non-RCT was incl or control groups; (3b) s	luded	eration in most stu	idies included; (1d)	use of unvalidated outc	ome measure;	

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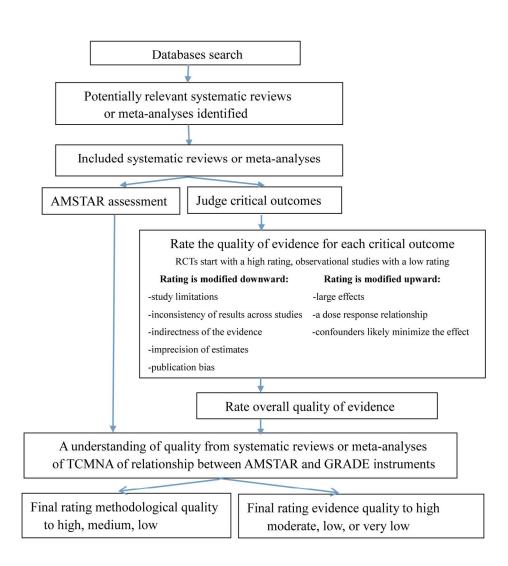
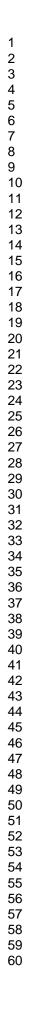


Figure 1 Technology road mapping of this study

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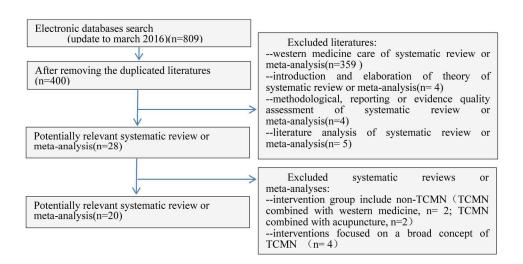
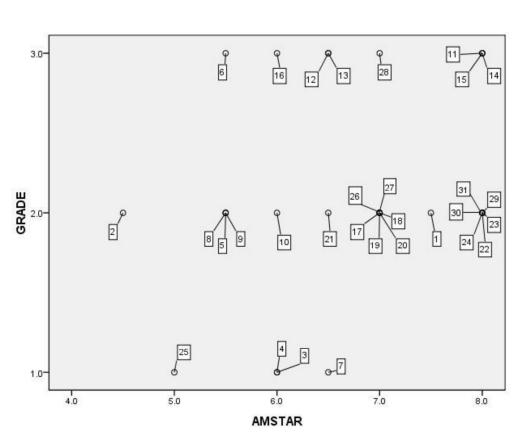


Figure 2 Flowchart of identified, included and excluded of systematic reviews or meta-analyses of TCMN

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Search strategy

(SU:("systematic review") OR SU:("meta analysis") OR SU:("huicui analysis") OR SU:("huizong analysis")) AND (JN:("nurs*") OR JN:("care*") OR

JN:("evidence-based"))

SU means subject search, and it include title, abstract and key words

JN means journal name

"huicui analysis" means systematic review and "huizong analysis" means meta analysis (Articles without English names are named in Hanyu Pinyin)



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Top-level heading
TITLE A critical appr	aisal o	f the methodology and quality of evidence of systematic reviews and meta-analyses of	
Traditional Chinese Me	dical N	Nursing: a systematic review of reviews	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS	•	·	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7-8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8

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PRISMA 2009 Checklist

		Page 1 of 2	
Section/topic	_#	Checklist item	Top-level heading
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	1
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	1
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8-9, Fig.1, Fig.2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8-9, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9-10, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-11, Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-12, Table 3, Fig.3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12-17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19



PRISMA 2009 Checklist

Joup (2009). Preferred Reportu. Page 2 of 2 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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