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Original Article

Reporting quality of economic evaluations of the negotiated Traditional Chinese Medicines in national reimbursement drug list of China: A systematic review



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ABSTRACT

Background: Traditional Medicine (TM) has a wide uptake in most countries. In China, Traditional Chinese Medicine (TCM) is a common kind of primary health because of its beneficial effects. This review aimed to appraise the publication reporting quality of economic evaluations for selective TCM in the National Reimbursement Drug List (NRDL), Version 2020, based on the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement.

Methods: Electronic databases were searched for economic evaluation that supported the TCM negotiations in NRDL (2020 version) published from 2001 to 2021, including PubMed, Web of Science, Embase, CNKI, WanFang, and SinoMed. The CHEERS statement was used to appraise the reporting quality of included TCM economic evaluations.

Results: A total of 360 articles were retrieved, but only 38 economic evaluations met the inclusion criteria. None of the articles reported all items in the CHEERS checklist. The mean score of included articles is low at 10.93 ± 2.62 , with an average scoring rate of 51.31 ± 10.53 %. The least reported items included: "Characterizing heterogeneity," "Conflicts of interest", "Discount rate," and "Study perspective," with a reporting rate of 0.00%, 5.26%, 7.89%, and 15.79%, respectively.

Conclusion: An upward trend occurred in the quantity and quality of the economic evaluation publications of TCM in China. TCM economic evaluations are still at an early stage, with an urgent need for improving reporting quality. It may result from research experiences or different ideas between TCM and Western Medicine. Adhering to reporting guidelines like CHEERS and educating economic evaluation investigators can improve TCM economic evaluations' reporting quality.

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1. Introduction

Traditional medicine (TM) is an essential and usually underestimated part of health services, with a long history of use in health

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maintenance and in disease prevention and treatment, particularly for chronic disease.¹ In China, Traditional Chinese Medicine (TCM) has been a common kind of primary health intervention because of its many beneficial effects.² The theoretical foundation of TCM stems from the ideas and theories of Holism of Human Beings and the Universe, Yin-Yang, Five Elements, Mutual Generation and Restriction, Concept of Holism and Syndrome Differentiation and Treatment, which aims to cure the cause of a disease rather than to alleviate its symptoms.^{3,4} With a prevalent belief that TCM is

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natural and low in price, demands for this form of therapy are increasing in developing and developed countries worldwide. ^{5,6} In China, where TCM originated, the number of TCM visits in 2009 was 907 million. The number of TCM inpatients was 13.6 million (16%) among all surveyed institutions based on a national survey, indicating TCM practice has been integrated into the Chinese national health care system adequately.⁷

Economic evaluations are intended to guide choices by estimating the cost-effectiveness trade-off of two or more interventions.⁸ Cost-utility analysis (CUA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA), and cost-minimization analysis (CMA) are the four common types of economic analyses.⁹ Globally, economic evaluations are increasingly regarded as an essential component in the decision-making process for allocating healthcare resources, such as health policy and medical insurance reimbursements, widely used in evaluating diagnostics, treatment interventions, care and rehabilitation.¹⁰ When it comes to TCM, the precise and valid economic evaluation evidence will also improve priority settings and reimbursement decision-making.

However, TCM has evolved based on empirical knowledge and a belief to use a holistic approach in treating individuals with a customized treatment, following the concept of "Syndrome Differentiation", which is quite different from the standard disease-targeted approach adopted by Western Medicine.¹¹ Because of the unique characteristics of TCM, like individualization and holism, it is more challenging to evaluate the safety, efficacy, and cost-effectiveness of TCM treatments than Western Medicine protocol.¹² And there is still no consensus achieved on the health economic evaluation of TCM among academics.¹³ In addition, pharmacists and clinicians performed most TCM pharmacoeconomic studies and the disconnection between real clinical practice and the pharmacoeconomic study hinders its quality and usability.¹⁴

The reimbursement decision-making process has evolved, increasingly incorporating economic evaluation in the past decades. In several countries worldwide, it has gradually become one of the most critical factors determining whether a drug or a health technology can enter the reimbursement list.¹⁵ In China, the HTA or pharmacoeconomic evaluation evidence and procedures have been included in the National Reimbursement Drug List (NRDL) updating since 2017.^{16,17} In 2020, National Healthcare Security Administration enrolled 59 cataloged TCM for renewal in NRDL (2020 version), through economic evaluation and budget impact analysis negotiation.¹⁸ Given that poor reporting quality may limit the usefulness of economic evidence in informing and guiding reimbursement decisions,¹⁹ it is worth appraising the TCM economic evidence to improve health decision-making.

The Consolidated Health Economic Reporting Standards (CHEERS) statement is a guideline published in 2013, in order to optimize and improve the reporting of health economic evaluations, which many journals have recommended adherence to CHEERS.¹⁰ The CHEERS checklist concludes 24 items, recommending the minimum amount of information that should be included for each aspect of the publication.²⁰ Although some limitations exist in this reporting guideline, the CHEERS statement has still been widely utilized to review the reporting quality of economic evaluations focusing on various treatment aspects, involving drugs, surgery, medical instruments, and so on.^{20–25}

Up to now, insufficient research has been conducted to review the reporting quality of economic evaluations on TCM in China. This review selected the negotiated TCM in NRDL (2020 version) as a pilot sample, therefore, aims to evaluate the published studies that examined the cost-effectiveness of the selected TCM, based on the CHEERS statement, in order to inform the HTA analysts and policymakers, provide suggestions on how to improve the reporting quality of the economic evaluations on TCM, and support evidence-based decision-making.

2. Methods

In July 2021, a systematic review was conducted to identify the economic evaluation of the TCMs enrolled in the NRDL negotiation (2020). Those publications were not reflecting their corresponding NRDL dossiers. We performed this study through the methods recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.²⁶

2.1. Literature Search Strategy

The PICO (Patients, Interventions, Comparators, and Outcomes) statement was followed to identify and define the search criteria for the economic evaluation research involved in this systematic review. Several electronic databases were searched for global economic evaluations of the negotiated TCM in NRDL (2020 version), including PubMed, Web of Science, Embase, CNKI, WanFang, and SinoMed. We used the following Medical Subject Heading (MeSH) terms to develop the literature search: cost, cost analysis, cost-benefit, cost-effectiveness, cost-minimization, cost-utility, economic assessment, economic evaluation, health economics, pharmacoeconomic. Besides, all NRDL (2020 version) enrolled negotiated TCM interventions were included in the search strategy of this review. The search time of this study was set from January 2001 to July 2021. The details of the search strategy was showed in the Appendix 1.

2.2. Eligibility criteria

The eligible articles must be peer-reviewed publications focusing on the negotiated TCM in NRDL (2020 version). This review includes all forms of economic evaluations: CEA, CBA, CUA, and CMA. While, the articles written in a language other than Chinese or English, and other studies like reviews, letters, editorial comments, notes, conference communications, non-economic studies, and grey literature were excluded. In addition, duplicate literature was also not included.

2.3. Data screening and extraction

In this study, two reviewers (YJT and BSY) independently screened the titles and abstracts of the searched literature and collected the eligible publications data based on a standardized data extraction form, according to the PICO statement. And two reviewers also independently extracted data from full articles for study designs, methodological details, and interpretation of results into standardized summary tables. The following data was extracted and collected: the general characteristics of the eligible literature (author, published year, Journal), population, interventions, comparisons, outcome indicators, type of economic analysis, funding, and conclusion. Discrepancies in the data collection process were resolved by discussion and consensus. If discrepancies occurred between the two reviewers which could not be solved by discussion, another reviewer (LL) would clarify and resolve them independently.

2.4. Quality of reporting assessment

The quality of reporting of the selected economic evaluation publications was assessed by two independent reviewers (YJT and BSY), based on the CHEERS checklist,¹⁰ and discrepancies were resolved by a third reviewer (LL) in the vent of disagreement. According to the CHEERS statement, a total of 24 items were used to assess the quality of reporting the cost-effectiveness of the TCM in NRDL (2020 version) in the included studies. The CHEERS checklist includes six categories: the title and abstract, introduction, methods, results, and discussion sections, and meanwhile, a maximum score of 24 is regarded as full reporting compliance.^{10,20} For each item, we assumed that studies containing all and partial contents in the recommendation of the checklist would be assessed as "Yes" and "Part", or, conversely, the result was "No". In this review, we assigned a value of 1 if the study fulfilled the requirement of reporting item completely ("Yes"), 0.5 for partially completing the requirement ("Part"), and otherwise 0 ("No"), to estimate the CHEERS score of the included TCM economic evaluations.

2.5. Statistical analysis

In this study, we estimated the descriptive summary statistics for basic information and economic evaluation characteristics of the included studies. Besides, the means and standard deviation (SD) of the reporting quality scores according to the CHEERS statement were also calculated. And all data were summarized and analyzed with Microsoft Excel 2019 and STATA version 16.

3. Results

3.1. Selected studies

Initially, a total of 360 studies were retrieved from the electronic database search without any additional records. After the removal of duplicates, 266 studies were obtained for screening. We identified 148 studies for potential inclusion through screening the titles and abstracts, excluding 118 studies as they did not meet the selection criteria. Besides, we read the full text of the remaining studies and resulted in 38 articles that fulfilled the selection criteria.^{27–63} Fig. 1 summarized the details of the articles identified and selected in this systematic review.

3.2. General characteristics of the included studies

All 38 studies were conducted in China. The selected articles were published between 2010 and 2021, while 20 articles (52.63%) were performed in the last 5 years. The trend of change in the number of economic evaluation publications of TCM in the past 10 years is displayed in Fig. 2., and the most annual economic evaluation articles were published in 2020 (n=8).

Table 1 describes the general characteristics and details of the 38 included studies. The majority of included articles were CEA (n=31, 81.58%), and five (13.16%) were CUA with the other two (5.26%) CMA analyses. For the treatment fields, most studies focused on cerebrovascular diseases (n=15, 39.47%), $^{32,33,36-41,49-55}$ then following the cardiovascular diseases (n=13, 34.21%), $^{29-31,34,35,42-48}$ and the rest ten studies were respectively about cancer (n=7, 18.42%)⁵⁶⁻⁶² and other disease (n=3, 7.90%).^{27,28,63} In addition, 13 articles (34.21%) reported whether received any source of funding (Yes: n=11, 28.95%; No: n=2, 5.26%), while 25 articles (65.79%) did not state it.

3.3. Quality of reporting

Appendix 2. shows the details of the quality of reporting of the articles included in the review according to the CHEERS checklist. None of the 38 articles met all the 24 items of the CHEERS statement. Most economic evaluations appraised (n=33, 86.84%) reported 21 items out of the whole CHEERS statement. We found the CHEERS checklist reporting compliance score of the included articles was between 7 and 21.5, with an average score of 10.93 \pm 2.62, and the average scoring rate was 51.31 \pm 10.53%.

Fig. 3. displays the specific results of the reporting compliance with the CHEERS checklist items of each appraised article. We found that most articles got "Yes" in the items of "Setting and location" (n=36, 94.74%), "Target population and subgroups" (n=31, 81.58%), "Background and objectives" (n=23, 60.53%), and "Choice of health outcomes" (n=23, 60.53%), while the least reported CHEERS checklist items were "Characterizing heterogeneity" (n=0, 0.00%). Besides, very few articles (n=2, 5.26%) stated the information about "Conflicts of interest" and the discount rate was reported in 3 out of the 38 appraised articles (7.89%). In addition, only two articles (5.26%) utilized a model to conduct the economic evaluation, and then the items of "Synthesis-based estimates", "Measurement and valuation of preference-based outcomes", "Model-based economic evaluation", "Choice of model", and "Assumptions" were not applicable for majority of the included articles. None of the included articles reported the potential differences in economic evaluation results like costs, outcomes, and cost-effectiveness through subgroups analysis or other methods.

The average scoring rate and the composition of the results of 38 appraised articles in each CHEERS checklist item were illustrated in Fig. 4. Based on Fig. 4. (A), the only two articles using the model both reported the "Assumption" and "Choice of model". And then, the included articles showed the highest average scoring rate in the item "Setting and location" (96.05%) and "Target population" (90.79%), followed by "Background and objectives", "Choice of health outcomes", and "Measurement and valuation of preferencebased outcomes". Except for the item "Characterizing heterogeneity" (0.00%), the included articles got the least average scoring rate in the items "Conflicts of interest" (5.26%), "Discount rate" (7.89%), "Study perspective" (15.79%), "Source of funding" (25.00%), and "Characterizing uncertainty" (31.58%), respectively. Besides, the majority of appraised articles stated the information partly in the items of "Study parameters" (n=35, 92.11%), "Abstract" (n=35, 92.11%), "Study findings, limitations, generalizability, and current knowledge" (n=34, 89.47%), "Incremental costs and outcomes" (n=33, 86.84%), and "Analytical methods" (n=33, 86.84%), compared with the recommendations of the CHEERS statement (Fig. 4. B).

We also calculated the average score and average scoring rate of the included articles in different sections according to the CHEERS statement. The average score in the sections of "Methods", "Results", and "Title and Abstract" was 6.62, 1.42, and 1.24, respectively, followed by "Introduction" (0.80), "Discussion" (0.55), and "Other" (0.33). As shown in Fig. 5., the "Introduction" section of the included articles presents the highest average scoring rate (80.26%), while the sections "Results" (35.53%) and "Other" (15.13%) are relatively low in this rate.

In addition, there were some differences in the average scoring rate of the various subgroup articles in this review. The average scoring rates of different subgroups of the 38 included articles were summarized in Table 2 in detail. It showed that the economic evaluation studies without funding presented a higher average scoring rate of the CHEERS statement than those with any source of funding, statistically. Besides, the average scoring rate differed from the subgroup articles classified by the type of economic evaluation and published year.

4. Discussion

In this study, a systematic review of the economic evaluation publications about the negotiated TCM in NRDL (2020 version) was conducted for the first time, to our knowledge. The main objective of this study was to assess the quality of current evidence likely used to inform economic evaluations about TCM enrolled in NRDL, according to the CHEERS statement. With the present work, we aimed to evaluate the quality of potential evidence, reveal the current status of the TCM economic evaluation, and inform the HTA 4

Reference	Country	Year	Population	Intervention	Comparisons	Outcome indicators	Economic evaluation	Funding source
Ziyi et al. ²⁷	China	2019	Patients with acute upper respiratory tract infection	Chaiqin Qingning Capsule	Qingkailing Capsule	The disappearance rate of fever and pharvngalgia	CEA	N/A
Zheng et al. ²⁸	China	2017	Patients suffering from acute URTIs	Yuxingcao Qinlan mixture	LanQin oral liquid	response and cure rates at three and five days	CEA	No
Yu et al. ²⁹	China	2020	Patients with coronary heart disease and angina pectoris	ShuXueNing Injection	Salvianolate, YiQi FuMAi	Total effective rate	CEA	Yes
Wei et al. ³⁰	China	2018	Patients suffering from heart failure with a reduced left ventricular ejection fraction	Basic treatment+ Xinmailong injection	Basic treatment	Total response rates of cardiac functional, The improved data of LVEF	CEA	No
Clinical research collaborative group ³¹	China	2020	HFrEF patients	conventional therapy+ Xinmailong injection	conventional therapy	decrease in MLHFQ score, increase in LVEF, the cumulative mortality	CUA	Yes
Rongwei et al. ³²	China	2020	Patients diagnosed with acute cerebral infarction	Basic treatment+ Xueshuantong	Basic treatment+ Dengzhanxixin/ Danhong/ Shuxuetong/ Ginkolide	The total effective rate	CEA	Yes
Jinwei et al. ³³	China	2012	Patients of infarction of the brain	Basic treatment+ Sanqi Panax Notoginseng Injection	Basic treatment+ Danhong Injection/ Xingnaojing Injection/	The total effective rate	CEA	N/A
Suirong et al. ³⁴	China	2010	Patients with coronary heart disease angina pectoris	Danhong Injection	Dengzhanhuasu Injection, Danshen Ligustrazine Injection	The total effective rate	CEA	N/A
Fuwen et al. ³⁵	China	2012	Patients with coronary heart disease angina pectoris	Danhong Injection	Salvia miltiorrhiza polyphenolate Injection, Safflower Yellow Pigment for Injection	The total effective rate	CEA	N/A
Zhiqin ³⁶	China	2019	Patients with ischemic stroke	Danhong Injection	Salvia miltiorrhiza polyphenolic Injection, Xiangdan Injection, Danshen Ligustrazine Injection	Decrease in NIHSS	CEA	N/A
Huijian ³⁷	China	2012	Patients with acute cerebral infarction	Danhong	Shuxuetong, Xueshuantong, Xuesaitong, Danshen Ligustrazine Injection	Decrease in NDS	CEA	N/A
Jialan ³⁸	China	2015	Patients with ischemic stroke	Danhong	Shuxuetong, Xueshuantong, Xuesaitong, Danshen Ligustrazine Injection	The total effective rate	CEA	N/A
Bin ³⁹	China	2018	Patients with acute ischemic stroke	Danhong Injection	Shuxuetong Injection	The total effective rate	CEA	Yes
Menglan et al. ⁴⁰	China	2020	Patients with ischemic stroke	Xueshuantong Injection, Danhong Injection	Ginkgo biloba extract injection	The total effective rate	CEA	N/A
Lina et al. ⁴¹ Wenbo ⁴²	China China	2019 2012	Patients with cerebral ischemic stroke Patients with coronary heart disease and angina pectoris	Salvianolic Acids Injection Danshen ligustrazine injection	Butylphthalide & Sodium Chloride Injection Salvianolate for injection, Shenqiong glucose injection	The total effective rate The total effective rates of AP improvement	CEA CMA	N/A N/A
Yanquan ⁴³	China	2019	Patients with coronary heart disease and angina pectoris	Danshen Injection	Salvia miltiorrhiza, Tanshinone IIA Sodium Sulfonate	The total effective rate	CEA	N/A
Jun et al. ⁴⁴	China	2016	Patients with coronary heart disease and angina pectoris	Basic Treatment+ Shenxiong Glucose Injection	Basic Treatment+ Salvia miltiorrhiza polyphenolate for injection, Ligustrazine Hydrochloride for Injection	The total effective rate	CEA	N/A
Yufang et al. ⁴⁵	China	2016	Patients with coronary heart disease and angina pectoris	Basic Treatment+ Danshen Injection, Salvia miltiorrhiza polyphenolate for injection, Tanshinone IIA Sodium Sulfonate Injection, Danshen Ligustrazine Injection	Basic Treatment	The total effective rate	CEA	Yes
Tianchi et al. ⁴⁶	China	2014	Patients with coronary heart disease and angina pectoris	Basic Treatment+ Tanshinone	Basic Treatment+ Danhong Injection, Salvia miltiorrhiza polyphenolate for injection	The total effective rate	CEA	N/A
Xiaoyan et al. ⁴⁷	China	2019	Patients with coronary heart disease and angina pectoris	Danshen Ligustrazine Injection + Isosorbide mononitrate	Salvia Miltiorrhiza Polyphenolate Injection/ Tanshinone IIA Sodium Sulfonate Injection+ Isosorbide mononitrate	The total effective rate	CEA	N/A

(continued on next page)

Table 1 (continued)

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Reference	Country	Year	Population	Intervention	Comparisons	Outcome indicators	Economic evaluation	Funding source
. 10								
Ke et al. ⁴⁸ Chundong et al. ⁴⁸	China China	2020 2011	Patients with coronary heart disease Patients with coronary heart disease	Basic Treatment + Shengmai Injection Salvia miltiorrhiza polyphenolate for injection	Basic Treatment + Salvia miltiorrhiza Injection Danshen Injection, Tanshinone IIA Injection, Danshen Chuanxiong Injection	The total effective rate The total effective rate	CEA CEA	Yes N/A
Yi et al. ⁴⁹	China	2017	Patients with ischemic stroke	Ginkgolide Injection+ Basic Treatment	Basic Treatment+ other blood stasis drugs	ADL score, cure rate, self-care rate, the work	CEA	N/A
Chuanping et al. ⁵⁰	China	2018	Patients with severe ischemic stroke	Ginkgolide Injection+ Basic treatment	Basic treatment+ other blood stasis drugs	recovery rate of ADL score, recovery rate_self-care rate	CEA	N/A
Zhaoting et al. ⁵¹	China	2021	Patients with ischemic stroke	Ginkgolide injection	Shuxuening injection	The decline of NIHSS score	CUA	Yes
Li et al. ⁵²	China	2020	Patients with Ischaemic Stroke of Large-artery Atherosclerosis	Ginkgolide injection+Asprin	Butylphthalide injection+ Asprin	recurrence rate, mortality, NIHSS score	СМА	Yes
Xuecheng et al. ⁵³	China	2019	Patients with Ischaemic Stroke	Ginkgo diterpene lactone meglumine injection	Ginkgo biloba extract injection	NIHSS score	CUA	N/A
Jing et al. ⁵⁴	China	2017	Patients with Ischaemic Stroke	Ginkgolides Meglumine Injection	The extract of Ginkgo biloba injection	NIHSS score, QALY, Rankin score	CUA	N/A
Yun et al. ⁵⁵	China	2020	Patients with Ischaemic Stroke	Ginkgo diterpene lactone meglumine injection	Ginkgo biloba extract injection	QALY	CUA	N/A
Ping et al. ⁵⁶	China	2013	Patients with Non-small Cell Lung Cancer	Chemotherapy + Aidi injection	chemotherapy +Xiaoaiping injection/ Kangai injection/ Kanglaite injection	effective rate, stability rate	CEA	N/A
Yanying et al. ⁵⁷	China	2013	The elderly patients with advanced non-small-cell lung cancer	Chemotherapy + Aidi injection	Chemotherapy + Kangai injection/ Cinobufotalin injection/ Shenmai injection	The total effective rate	CEA	Yes
Guiling et al. ⁵⁸	China	2013	Patients with Non-small Cell Lung Cancer	Chemotherapy + Aidi injection	Chemotherapy + Kanglaite injection	The total effective rate	CEA	N/A
Bing et al. ⁵⁹	China	2013	Patients with Liver Cancer	Mitomycin, pirarubicin and cisplatin + Aidi Injection, Kanglaite Injection, Elemene Injection, Xiaoaiping Injection	Mitomycin, pirarubicin and cisplatin	The rates of disease control	CEA	N/A
Jianging et al. ⁶⁰	China	2013	Patients with breast cancer	Chemotherapy + Kushen injection	Chemotherapy + Kangai injection	The total effective rate	CEA	Yes
Jianwu et al. ⁶¹	China	2013	Patients with advanced ovarian cancer	Chemotherapy + Kangai injection, Aidi injection	Chemotherapy	The clinic effective rate	CEA	N/A
Huihuang et al. ⁶²	China	2014	Patients with Non-small Cell Lung Cancer	Chemotherapy + Compound Cantharidum Capsules, Shenyi Capsules, Zilongiin tablets	Chemotherapy	The effective rate	CEA	N/A
Haiping ⁶³	China	2016	Children with upper respiratory tract infection	Anerning Granules	Jinlian Qingre Effervescent Tablets	The clinic effective rate	CEA	Yes



Fig. 1. Flowchart for studies selection.

Та	bl	e	2

Туре	Subgroups	Number of articles (%)	Average scoring rate (%)
Type of economic evaluation	CEA	31 (81.58)	49.14
	CUA	5 (13.16)	60.54
	CMA	2 (5.26)	61.91
Type of disease	Cardiovascular diseases	13 (34.21)	51.78
	Cerebrovascular diseases	15 (39.47)	57.28
	Cancer	7 (18.42)	44.56
	Others	3 (7.90)	55.35
Published year	Before 2017	18 (47.37)	47.21
	2017 and beyond	20 (52.63)	54.54
Funding	Yes	11 (28.95)	56.95
	No	2 (5.26)	63.10
	N/A	25 (65.79)	47.88



YEAR





Fig. 3. The specific reporting results of each appraised article based on the CHEERS checklist items.

analysts and policymakers, contributing to improving the reporting quality of the economic evaluations about TCM.

According to the results of reporting quality, we found that the included economic evaluation publications presented the least average scoring rate in the section of "Results" (35.53%) and "Other" (15.13%). In the "Results" section, it could be attributed to the items of "Characterizing heterogeneity" and "Characterizing uncertainty". Besides, the fact that few articles stated the information about the source of funding and conflicts of interest might be subjective to whether the journals had pointed out these requirements before. As opposed to a relatively high average scoring rate in the sections of "Title and Abstract" and "Introduction", we found that only six (15.79%) articles defined clearly the chosen study perspective in

the "Methods" section, which could accordingly decide the evaluation process, such as the study design, the analytical method, and calculation of costs and effectiveness, playing a critically essential role in the economic evaluations.⁶⁴

In this review, the majority of included articles were CEA studies (84.58%), which was far more than the number of CUAs. This finding could be attributed to the fact that CEAs are easier and quicker to conduct than CUAs, relatively. However, the CUA is a commonly used and highly useful technique in economic evaluations, because it reports cost per quality-adjusted life-year (QALY) which is a standardized health outcome allowing for comparisons of "value-for-money" between different interventions.⁶⁵ As a more comprehensive health outcome indicator, the QALY takes the effect



(A) The average score rate

(B) The composition of the results

Fig. 4. The average scoring rate (A) and the composition of the results (B) of 38 included articles in each CHEERS item.





of the treatment regimen on the patient's survival time and quality of life into account,⁶⁶ fitting the concept and ideal of TCM to some extent. Given that TCM aims to use a holistic approach in treating individuals with a customized therapy, rather than to alleviate the symptoms,⁴ it may be not suitable to evaluate the effectiveness of TCM just based on several observable health outcomes or short-term benefits, without considering whether it improves the patient's quality of life and long-term benefits. Therefore, it pays to encourage more CUAs or more value-based analyses conducted for the economic evaluation of TCM, which can reflect its humanistic outcomes.

To put the growth of TCM economic evaluation literature into perspective, more than half of all articles ever published through 2021 were published after 2017, showing a tendency to grow constantly. Besides, the included articles published in 2017 and beyond presented a higher scoring rate in compliance with the CHEERS statement than those published before 2017. These both suggest that there exists an increasing interest and effort in TCM economic evaluations on the part of researchers, journal editors, funders, and users. Presumably, it can be attributed to the fact that in 2017, China's national drug reimbursement policy, the NRDL, began to include the evidence of HTA or economic evaluation as one of the criteria to decide whether a drug could be covered by the national health insurance.⁶⁷ Correspondingly, increasing economic evaluations were conducted after that, and the quality of implementing and reporting improved gradually with the guidance and recommendation of the Chinese government as well.

Limited economic evaluation publications were found in this review, and only 38 related articles were identified for 59 kinds of negotiated TCM enrolled in NRDL (2020 version). Based on the CHEERS statement, compared to Western Medicine economic evaluations,^{24,25,68} TCM ones only scored approximately half on the average score (10.93 vs 20-24), which was consistent with the results of Zhang J. et al's research.⁶⁹ There are potential reasons: First, despite the growing prevalence of TCM usage and the worldwide interest in its benefits, TCM is still not accepted by the Western medicine community and integrated into mainstream healthcare following evidence-based medicine (EBM).¹¹ At present, the high-level evidence of the effectiveness of TCM, like randomized controlled trials (RCT), is lacking, especially in the field of herbal medicine and proprietary Chinese medicine, as it is a long subject of debate on whether the EBM model can be applied to TCM.⁶⁹ According to a much more prevalent usage of herbal medicine and TCM drug in China than that in other countries or regions, the

related research and economic evaluations of TCM were mainly conducted in China. Second, because of its delayed introduction, the quality of economic evaluation studies in China varies substantially, remaining room for the improvement of the overall quality.⁶⁴ Third, the majority of the first author of the included articles in this study were pharmacists and clinicians, and they may be not familiar with the implementing and reporting paradigm of economic evaluations, which could be revealed by the extremely low average scoring rate at the items of "Discount rate" and "Currency, price date, and conversion" based on the results of this study.

These findings provide the basis for the following recommendations for the future economic evaluations of TCM and the further development of TCM: Given the low-level reporting quality of the current TCM economic evaluations, standardized reporting guidelines like CHEERS should be promoted and used. Besides, the government needs to constantly formulate the measures and policies to support and regulate the TCM industry, and provide guidance for the standardized clinical trials and economic evaluation of TCM in time, integrating the existing policies and guidelines.^{64,70} In addition, training health economists and promoting collaborations between clinicians and health economists will improve the overall quality of TCM economic evaluations.

This study has several limitations in assessing economic evaluations. It was hard to avoid some significant differences caused by subjective conflicts when assessing the articles, and in this study, the corresponding measures had been taken, like reaching a consensus with the discussion between two reviewers and resolving discrepancies by a third reviewer. Besides, as a guide for reporting, not conducting economic evaluations, the CHEERS statement used in this study could not guide how to improve the health economic evaluation studies themselves, where further research needs to be conducted in the future.²⁰ And meanwhile, we also noticed that an updated version of CHEERS has been released in 2022.⁷¹ Given that the economic evaluations included in this study were published before 2022, when only the CHEERS 2013 statement was available, the old version was more likely to be applicable for the researchers at that time. In the future study, we will definitely consider to utilize the CHEERS 2022 as the criteria for evaluating reporting quality.

In conclusion, the overall reporting quality of the economic evaluations supporting the negotiated TCM in NRDL (2020 Version) is low, with an average CHEERS score of 10.93±2.62 and an average scoring rate of 51.31±10.53%. This may be due to the unfamiliar investigators of pharmacoeconomic studies, most of whom were pharmacists and clinicians, and the perceived difference between TCM and Western Medicine. And it has an urgent need for improving the reporting quality of economic evaluations on the negotiated TCM, especially for the items "Characterizing heterogeneity", "Discount rate", and "Study perspective". However, this systematic review also shows an upward trend in the quantity and quality of TCM economic evaluations in the past ten years. To improve TCM economic evaluation study and reporting quality, researchers should report following the CHEERS statement. Chinese economic evaluation investigators, including pharmacists, clinicians, and health economists also require more training in reporting.

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Ethical statement

No ethical approval was required as this study did not involve human participants or laboratory animals.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that they have no conflicts of interest.

CRediT authorship contribution statement

Juntao Yan: Conceptualization, Methodology, Software, Formal analysis, Investigation, Resources, Visualization, Data curation, Writing – original draft, Writing – review & editing. Shiyi Bao: Investigation, Software. Liu Liu: Software, Investigation. Yu-Qing Zhang: Writing – review & editing. Jian Ming: Writing – review & editing. Yan Wei: Funding acquisition, Writing – review & editing. Yingyao Chen: Supervision, Project administration, Funding acquisition, Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2022.100915.

Appendix 1. Details of the search strategies for the identification of studies.

Appendix 2. Details of the quality of reporting of articles evaluated in the review based on the CHEERS statement.

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