Quality Evaluation and Problem Analysis of China's Pharmacoeconomics on Hypertension Management

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Abstract

Objective To systematically evaluate the quality of pharmacoeconomics on hypertension management, and provide reference for promoting the development of pharmacoeconomics in China. **Methods** Some Chinese databases including CNKI, VIP, Wanfang, as well as international databases such as PubMed and Web of Science were searched to collect studies of economic evaluation on hypertension management in China. The quality of health economic studies (QHES) scale was used to assess the quality of the literature and to analyze the current situation and shortcomings of pharmacoeconomics in the field of hypertension in China. **Results and Conclusion** A total of 363 articles were included in this study. The quality assessment results showed that the average score of pharmacoeconomics on hypertension management was 42.54 points. The quality of literature published by medical institutions was significantly lower than that published by universities/research institutes (41.25 *vs.* 54.68, $P < 0.05$). Among the 363 articles, 3.31% (12 articles) were of high quality (75−100 points), 29.20% (106 articles) were of moderate quality (50−74 points), 66.12% (240 articles) were of low quality (25−49 points), and 1.38% (5 articles) were of extremely low quality (0−24 points). These papers have such problems as unclear research perspectives, single research methods, ambiguous data sources, inappropriate study duration for disease characteristics, and insufficient sensitivity analysis factors. Overall, the quality evaluation of pharmacoeconomics on hypertension management in China is generally low with poor standardization, which should be improved in the future.

Keywords: hypertension; pharmacoeconomics; QHES scale; quality assessment

In recent years, with the deepening of China's medical and health system reform, pharmacoeconomics has played an important role in improving the overall efficiency of medical and health resource allocation and addressing some problems in China's healthcare sector [1]. The number of literature on economic evaluations has also been increasing [2]. High-quality results from pharmacoeconomics analyses can help the health department to choose more cost-effective solutions toreduce the burden on patients. However, the quality of current research on pharmacoeconomics varies greatly, and poor-quality studies not only hinder scientific decision-making, but also can lead to misguided decisions.

Therefore, this article uses the QHES scale as an evaluation tool to assess the quality of literature on pharmacoeconomics of hypertension management in China, which can qualitatively and quantitatively analyze the current status and deficiencies of

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pharmacoeconomics of hypertension management to provide reference for improving the quality of such research.

1 Data and methods

1.1 Sources of data

CNKI, VIP, Wanfang, PubMed, and Web of Science were searched to collect economic evaluations of hypertension management published by Chinese scholars. The keywords such as "cost-effectiveness" "cost-benefit" "cost-utility" "minimum cost" "economy" "economics" and "hypertension" were used for advanced search. In English, "pharmacoeconomics" "pharmaceutical economics" "cost effectiveness" "cost utility" "cost benefit" "cost minimization" "hypertension" and "blood pressure" were used as the keywords. Besides, Chinese or China was used to limit the population for advanced retrieval and the retrieval time was set from the establishment of the database to February 2023.

1.2 Inclusion and exclusion criteria

Inclusion criteria: (1) Essential hypertension; (2) Published by Chinese scholars; (3) Drug therapy; (4) Published in an open-access journal.

Exclusion criteria: (1) Non-economic evaluation literature; (2) Non-pharmacological treatment options; (3) Inconsistent disease types; (4) Duplicate or inaccessible literature.

1.3 Data extraction and statistics

The Endnote software was used to de-duplicate and screen literature, and Excel 2016 software was used for data extraction and statistical analysis. The extracted information includes: (1) Basic information, such as title, publication date, first author and occupation, and research institution; (2) Study content, including treatment plans, study design, and evaluation methods; (3) Quality assessment-related content, including research objectives, research perspectives, data source types, target population characteristics, research time limits, discount rates, health outcome indicators and sources, cost accounting items, incremental analysis, sensitivity analysis, funding support, etc.

1.4 Quality evaluation tool

In this study, the QHES scale was applied to assess the quality of included studies. The scale consisted of 16 items (Table 1) [3], with each item carrying a different weight represented by scores ranging from 1 to 9. Studies were assessed as "yes" or "no" for each item, with a score of 0 given for a "no" response. For example, if a study met the criteria for item 1, which pertained to research objectives, then it would receive a score of 7, otherwise, it would receive a score of 0. For items containing two questions, such as item 5, this study would be judged based on the first half of the item. If the literature analyzed uncertain factors, it was considered yes, otherwise it would be no. For item 8, considering that hypertension was a chronic disease, long-term studies (> 1 year) that applied discounting were judged as yes, while others were judged as no. The QHES scale had a maximum score of 100, and final quality ratings were determined based on the scores: high quality (75−100 points), fair quality (50−74 points), low quality (25−49 points), and very low quality (0−24 points) [4, 5].

Table 1 Specific contents of QHES scale

Item	Question	Score
1	Was the study objective presented in a clear, specific, and measurable manner?	7
2	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4
3	Were variable estimates used in the analysis from the best available source (i.e., randomized control trial − best, expert opinion − worst)?	8

(to be continued)

Continued Table 1

Item	Question	Score
4	If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1
5	Was uncertainty handled by (1) Statistical analysis to address random events; (2) Sensitivity analysis to cover a range of assumptions?	9
6	Was incremental analysis performed between alternatives for resources and costs?	6
7	Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5
8	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7
9	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8
10	Were the primary outcome measure (s) for the economic evaluation clearly stated and did they include the major short-term was justification given for the measures/scales used?	6
11	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7
12	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8
13	Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7
14	Did the author (s) explicitly discuss direction and magnitude of potential biases?	6
15	Were the conclusions/recommendations of the study justified and based on the study results?	8
16	Was there a statement disclosing the source of funding for the study?	3

2 Results

2.1 Literature search results

According to the target database, a preliminary search yielded 3 611 relevant papers, of which 2 482 were identified as valid after duplicate removal. 363 papers were finally included in the study after screening by the exclusion criteria. The literature screening process is shown in Fig. 1.

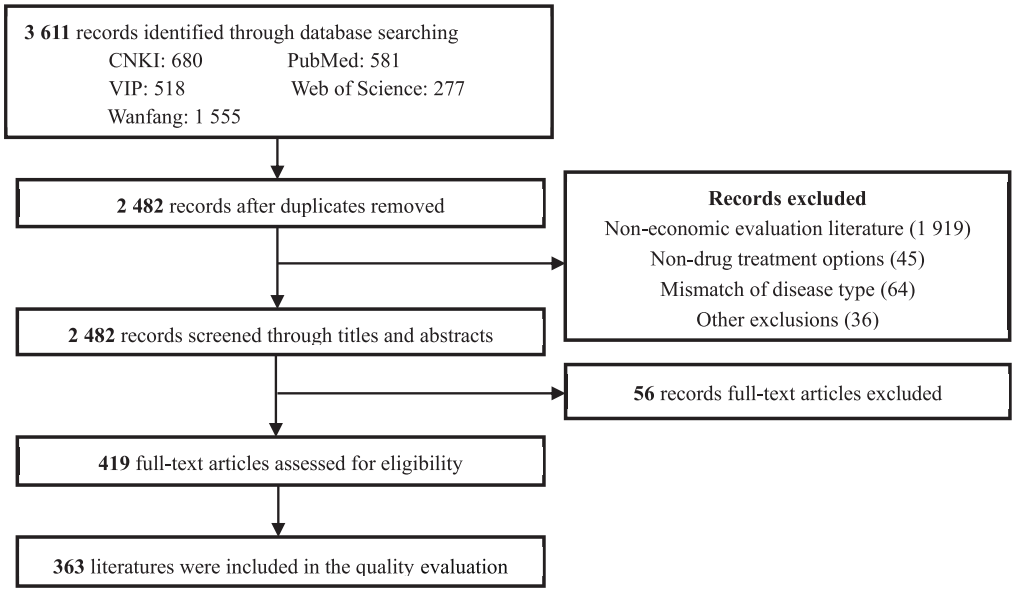

Fig. 1 Literature screening flow chart

2.2 Basic information of literature

2.2.1 Publication time

The annual publication of economic evaluations of antihypertensive drugs in China is shown in Fig. 2. The peak period for the publication of these economic evaluation studies was from 2010 to 2014, with 28 papers published in 2012. The number of publications has since fluctuated and declined.

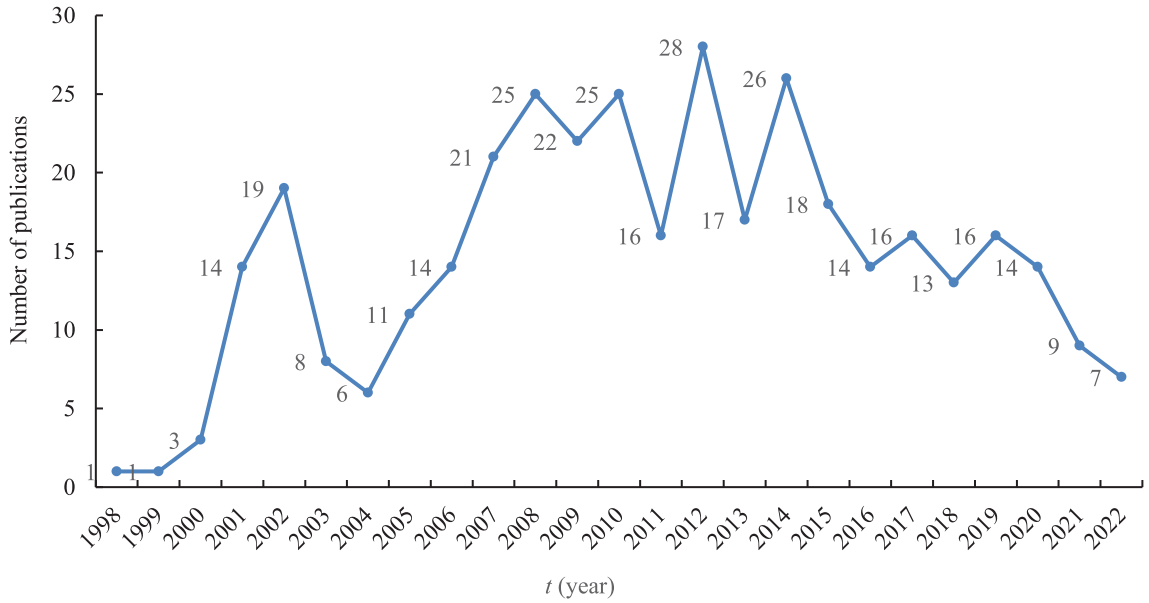

Fig 2 Annual publication of Chinese pharmacoeconomics of hypertension management

2.2.2 Publishing institutions and authors

The affiliation of the first authors in the statistical literature showed that 91.18% (331 articles) were published by medical institutions, 8.54% (31 articles) were from universities or research institutions, and only one article was from a company. The authors' professions from different publishing institutions are shown in Table 2. Clinical pharmacists (36.56%) are the main source of authors from medical institutions, followed by clinical physicians (7.55%). Graduates or Ph. D students (25.81%) are the main source of authors from universities/research institutes, followed by professors/associate professors (12.90%).

Table 2 Professions of authors from different publishing institutions

Publishing institution	Author occupation	Number (Proportion)
Medical institutions	Pharmacists	121 (36.56%)
	Physicians	25 (7.55%)
	Others	8 (2.42%)
	Unspecified	177 (53.47%)
Universities/Research institutes	Professors/Associate professors	4 (12.90%)
	Master's or Ph.D students	8 (25.81%)
	Researchers	1 (3.23%)
	Undergraduates	1 (3.23%)
	Unspecified	17 (54.84%)

2.3 Results of quality evaluation

2.3.1 Overall score

The QHES scale score results showed that the average score of 363 articles was 42.54 points. Among them, 3.31% (12 articles) were of high quality, 29.20% (106 articles) were of moderate quality, 66.12% (240 articles) were of low quality, and 1.38% (5 articles) were of very low quality.

2.3.2 Score by year

After calculating the average score of economic evaluations of papers on antihypertensive drugs by year (Fig. 3), we found that from 2000 to 2016, the quality scores of papers fluctuated around 40 points. After 2016, the quality scores slightly increased, decreased in 2019, and rapidly rose in 2022. Further analysis revealed that among the 7 articles published in 2022, 4 articles were from universities/research institutes and 3 articles were from medical institutions. The quality scores of universities/research institutes were all 75 points or higher, leading to a rise in the overall average score in 2022.

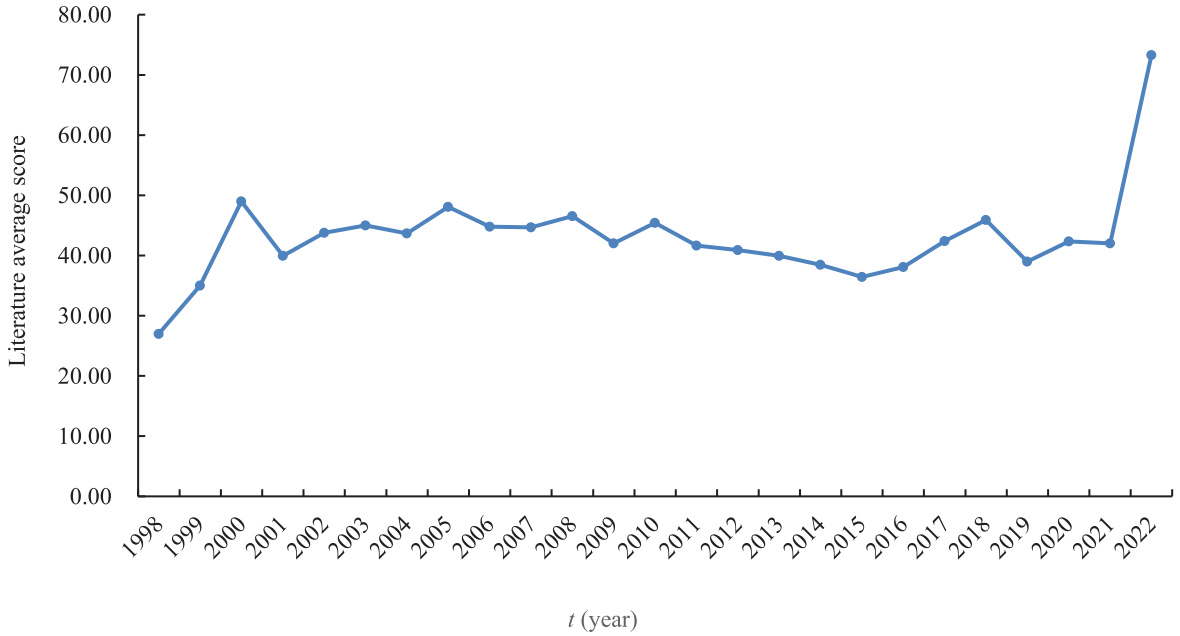

Fig. 3 Annual average score distribution of China's pharmacoeconomics of hypertension management

2.3.3 Scores in each item

The scores and qualification status of each item on the QHES scale are shown in Table 3. According to the statistics, items 1, 4, 7, 10, and 15 have a qualification rate of over 90%, which are more inclined towards the normative evaluation of the article, and most articles meet the requirements. The qualification rates of items 5, 6, and 9 are between 50% and 80%. The qualification rates of 8 items are poor, less than 20%, including items 2, 3, 8, 11, 12, 13, 14, and 16.

Table 3 Scores and eligibility of each item of the QHES rating scale

Item	Item score	Average item score	Quantity of eligible literature	Qualified rate (%)
1 Purpose of study	7	6.83	354	97.52
2 Research angle	4	0.22	20	5.45
3 Data source	8	0.64	29	7.90
4 Target population	1	0.95	344	93.73
5 Uncertainty analysis	9	4.86	196	53.41
6 Incremental analysis	6	3.27	198	53.95
7 Method of data acquisition	5	4.97	361	98.37
8 Study duration and discount	7	0.19	10	2.72
9 Cost measurement	8	5.69	258	70.30
10 Health output	6	5.59	338	92.10
11 Measure method verification	7	0.02	1	0.27
12 Model analysis	8	0.29	13	3.54
13 Model assumptions and limitations	7	0.23	12	3.27
14 Research bias	6	0.99	60	16.35
15 Study conclusions	8	7.54	342	93.19
16 Source of funding	3	0.27	33	8.99

2.3.4 Scores from different publishing institutions

The statistical results showed that the average quality score of papers published by medical institutions was significantly lower than that of universities/research institutes (41.25 *vs.* 54.68, $P < 0.05$). There was only one study on pharmacoeconomics evaluation from enterprises, with a quality score of 93 points. The qualification rates of QHES items for papers published by medical institutions and universities/research institutes are shown in Table 4.

As can be seen from the table, the qualification rates of papers on pharmacoeconomics evaluation of hypertension management published by universities/research institutes in terms of research perspective, data sources, and data collection methods were significantly higher than those of medical institutions ($P < 0.05$). Analysis revealed that authors from medical institutions were mostly clinical pharmacists or physicians, who had a focus on medicine, but lacked professional theoretical knowledge of pharmacoeconomics. However, universities/research institutes have a solid foundation in pharmacoeconomics theory as academic institutions, with more in-depth research on the design and methodology of pharmacoeconomic evaluation, resulting in higher research quality.

Table 4 Scores and eligibility of each item of the QHES scale

Item	Medical institutions (%)	Universities/Research institutes (%)	*P*
1 Purpose of study	97.58	96.77	0.78
2 Research angle	3.32	25.81	0.00*
3 Data source	4.83	38.71	0.00*
4 Target population	94.86	93.55	0.75
5 Uncertainty analysis	53.17	61.29	0.38
6 Incremental analysis	53.17	67.74	0.11
7 Method of data acquisition	99.70	96.77	0.03*
8 Study duration and discount	0.91	19.35	0.00*
9 Cost measurement	71.30	67.74	0.67
10 Health output	93.35	90.32	0.52
11 Measure method verification	0.00	3.23	0.00*
12 Model analysis	1.21	25.81	0.00*
13 Model assumptions and limitations	1.21	22.58	0.00*
14 Research bias	12.39	58.06	0.00*
15 Study conclusions	93.66	100.00	0.14
16 Source of funding	6.95	29.03	0.00*

Note: *$P < 0.05$.

3 Problem analysis

Specific analysis was conducted on items with low scores and qualification rates in the QHES evaluation scale, revealing problems in the pharmacoeconomics evaluation of hypertension drugs in China, and finding out the reasons behind them.

3.1 Unclear research perspective and its ineffectiveness

The research perspective is an important prerequisite in the process of drug economic evaluation. Only by clarifying the research perspective can the evaluation process, such as research design and cost accounting items, be determined. According to statistics, the average score for the research perspective item in the QHES scale was 0.22, and the qualification rate of the item was only 5.45%. 94.77% of the literature (344 articles) did not specify the research perspective, of which 93.02% (320 articles) were published by medical institutions. The reason for this phenomenon was related to researchers' lack of familiarity with relevant theories of pharmacoeconomics and their failure to understand the role of research perspectives. Additionally, different research perspectives lead to different cost accounting. When the cost calculation process of literature that specified the research perspective was analyzed, we found that no matter what perspective was adopted for the study, the costs only included direct medical costs, such as drug costs, hospitalization expenses, and

adverse reaction costs. It did not reflect the differences in cost accounting brought about by different research perspectives, rendering the ineffectiveness of the research perspective.

3.2 Single research method and careless research process

According to statistics, 88.15% (320 articles) of the literature adopted short-term cost-effectiveness analysis, fewer used cost-utility analysis (11 articles, 3.03%) and model analysis (14 articles, 3.86%), resulting in low scores for quality evaluation items related to the model in the QHES scale. Further analysis found that 93.75% (300 articles) of the 320 studies using cost-effectiveness analysis came from medical institutions, which may be related to the large number of research objects and more convenient research conditions in medical institutions. However, clinical professionals may not have a deep understanding of drug cost-effectiveness evaluation and the research methods are relatively single. In addition, biases in the study and whether health outcomes have been validated can also affect the accuracy of the evaluation results, and only 16.53% (60 articles) of the literature included in this study elaborated on the study biases. Few articles validated the measurement methods of health outcome variables, indicating that the research process was not rigorous.

3.3 Ambiguity in data sources

The qualification rate of item 3 (data source) in China's cost-effectiveness evaluation of hypertension drug is only 7.90%. According to statistics, 67.49% (245 articles) of the literature have unclear descriptions of their data sources. Although random grouping is mentioned in the text, it is difficult to judge the type of data source and the quality of evidence due to the vague descriptions in the article. For example, some literature described the selection of hypertensive patients from a hospital for random grouping, but it was difficult to determine whether the study was prospective in collecting data or randomly selecting from an existing case library, leading to poor standardization of the literature.

3.4 Failure to consider characteristics of chronic diseases and short study time

For chronic disease such as hypertension, short-term studies cannot guarantee that all costs and health outcomes of treatment will occur within this period, making it difficult to accurately estimate the actual costs and health outcomes of patients, such as preventing the occurrence of cardiovascular and cerebrovascular complications. Therefore, long-term studies are more reasonable for chronic diseases. The statistical results showed that 89.81% (326 articles) of hypertension drug cost-effectiveness evaluations were short-term studies with a research time limit of no more than one year, resulting in QHES scale qualification rates of only 2.72% for research time limits and discounting items. 3.03% (11 articles) simulated a longer time frame exceeding 10 years. 4.41% (16 articles) only vaguely described the duration of the study, such as choosing different average medication times for the study and control groups, and 5.51% (20 articles) did not report the research time limit.

3.5 Health outcomes indicators having difficulty in capturing the full benefit of patients

6.89% (25 articles) of the literature did not clearly define health outcome indicators, and most of the defined output indicators were effective blood pressure reduction rates. 5.51% (20 articles) had short-term and single output indicators such as blood pressure reduction values or blood pressure control rates (systolic or diastolic), which could not evaluate the role of anti-hypertensive drugs in preventing cardiovascular events. Therefore, there are certain limitations in evaluating the actual quality of life of patients from the impact of drugs. Long-term indicators such as quality-adjusted life years (QALYs) can reflect

patient benefits through quality of life that are more comprehensive in comparison, but only 3.58% (13 articles) of the studies used this indicator.

3.6 Overly simple sensitivity analysis factors

Statistical results showed that only 53.99% (196 articles) of the literature conducted sensitivity analysis. In addition, all parameters and assumptions in drug cost-effectiveness evaluation should be included in the list of candidate variables for sensitivity analysis [6]. However, most of China's literature on economic evaluation of hypertension drugs used single-factor sensitivity analysis, and evaluated the impact only after the cost of the drug decreased, which was simplistic. There was almost no sensitivity analysis of the selected effect indicators. In fact, due to factors such as sample size and clinical observation, the uncertainty or sensitivity of the effect indicators may be greater, so considering only changes in drug prices is difficult to comprehensively evaluate the stability of the results.

4 Summary and discussion

This study evaluated China's literature on hypertension drug cost-effectiveness evaluation using the QHES scale. The results showed that the overall research quality was low and the standardization was poor. Literature published by medical institutions had lower quality compared to universities/research institutes. There are such problems as unclear research perspectives, single research method, ambiguous data sources, and short research time limits in China's hypertension drug cost-effectiveness evaluation. It is recommended that relevant researchers further improve their research method, standardize report writing, and improve their research results. On the other hand, it is also suggested to strengthen cooperation between medical institutions and universities/research institutes to combine the convenient research conditions of medical institutions with the solid foundation of pharmacoeconomics research in universities, which will improve the quality of research. This study also has certain limitations, as the QHES scale is a "yes/no" type scale, and the evaluation criteria are too broad. In addition, some items contain multiple questions (such as question 8), and the scale does not provide weights for multiple question scores. Therefore, subjective judgments by evaluators may lead to biases in the evaluation results.

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