

## Systematic Evaluation and Reevaluation of Oral Chinese Herbal Decoction in the Treatment of Primary Nephrotic Syndrome

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Abstract: His methodological quality and the evidence quality of the outcome indicators of the systematic evaluation of oral Chinese herbal decoction in the treatment of primary nephrotic syndrome (PNS) were evaluated, so as to provide evidence for the treatment of primary nephrotic syndrome with oral Chinese herbal decoction. The databases of CNKI, WanFang Data, VIP, CBM, PubMed, The Cochrane Library and EMbase were searched for systematic evaluation or meta-analysis on the treatment of PNS with oral Chinese herbal decoction from the establishment of the database to November 30, 2022. Two researchers independently used AMSTAR2 scale to evaluate the methodological quality of the included study and GRADE system to evaluate the outcome indicators of the included study. A total of 11 items related to the systematic evaluation or meta-analysis of the treatment of PNS with oral Chinese herbal decoction were screened. The evaluation results of AMSTAR2 scale revealed that the 11 meta-analyses included were of extremely low quality. The GRADE system evaluation revealed that the evaluation results of five outcome indicators were intermediate (6.3%), 35 outcome indicators were low (44.3%), and 39 outcome indicators were extremely low (49.4%). Oral Chinese herbal decoction has certain clinical effect on the treatment of PNS, but there are many defects in the included systematic evaluation or meta-analysis in methodology. At the same time, the evidence quality of outcome indicators is low and more high-quality research results are urgently needed to provide evidence-based evidence support for clinical practice and provide guidance for clinical treatment of this disease.

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#### **1. Introduction**

PNS refers to the clinical syndromes caused by primary glomerular diseases with large amounts of proteinuria (>3.5g/24h), hyperlipidemia, hypoproteinemia, edema and other symptoms or signs as the main manifestations. At the same time, hereditary and secondary nephropathy should be excluded [1]. Glucocorticoids, immunosuppressants and other drugs are widely used in modern clinical medicine, but the treatment of PNS is characterized by large individual differences in clinical effects and high recurrence rate after treatment, as well as deficiencies such as hormone dependence, resistance, ineffectiveness and many significant adverse reactions [2-3], so clinical treatment is difficult.

Oral traditional Chinese medicine decoction with its significant clinical efficacy and fewer side effects has shown more and more significant clinical status in the treatment of PNS. In recent years, the systematic evaluation on the treatment of PNS with oral TCM decoction has gradually increased, but the quality of the evidence is inconsistent, and there are many differences in the outcome indicators selected by different studies, and the results of different studies are inconsistent, leading to the failure to present convincing evidence-based medical evidence for the effectiveness and safety of oral TCM decoction in the treatment of PNS. With the entry of evidence-based medicine into traditional Chinese medicine and its significant impact on the development of traditional Chinese medicine, the re-evaluation of system evaluation at a higher level can more comprehensively synthesize related studies, make the evidence more intensive, and facilitate the users of evidence to make favorable decisions by applying relevant evidence, and enhance the practicability of evidence-based medicine evidence [4-6]. This study aims to further evaluate the systematic evaluation of oral Chinese medicine decoction in the treatment of PNS, evaluate the methodological quality of the systematic evaluation of oral Chinese medicine decoction in the treatment of PNS and the evidence level of all outcome indicators included in the study, hoping to provide a higher level of evidence support for further clinical research of oral Chinese medicine decoction in the treatment of PNS and the concentrated and effective application of evidence.

## 2. Data and Methods

#### 2.1. Inclusion Criteria

(1) Type of studies: systematic reviews (SR) or meta-analyses, randomized controlled trials (RCTS); (2) Subjects: patients meeting the diagnostic criteria of "Diagnosis and Therapy of Renal Diseases", and secondary nephrotic syndromes caused by diabetic nephropathy and lupus nephritis were excluded. Age, gender, onset time and race of the included patients were not restricted; (3) Treatment measures: experimental group was treated with oral TCM decoction (including granules) alone or together with Western medicine; control group was treated with Western medicine alone or placebo intervention or no treatment; (4) Outcome indicators: All outcome indicators included in the included literature: 24-hour urinary protein quantification (24h UTP), total clinical response rate, serum creatinine (Scr), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), Serum albumin (ALB), total cholesterol (TC), triglyceride (TG), prothrombin time (PT), Interleukin-6 (IL-6), Interleukin-8 (IL-8), Interleukin-10 (IL-10) , urea nitrogen (BUN), platelet count (PLT), incidence of adverse reactions and other outcome indicators included in the study.

#### 2.2. Exclusion Criteria

(1) republished studies; (2) Studies where complete data cannot be obtained; (3) Acute

progression of nephropathy; (4) The intervention measures were acupuncture, massage and other traditional Chinese Therapy; (5) Reviews, traditional reviews and basic experimental studies on animals, organoids and cells.

## 2.3. Literature Search Strategy

We searched CNKI, WanFang Data, VIP, CBM, PubMed, EMbase and The Cochrane Library. To search for systematic reviews or meta-analyses of oral Chinese herbal decoction in the treatment of primary nephrotic syndrome, the time limit was from the establishment of the database to November 30, 2022. The retrieval method adopted is a combination of the title and the free word. Chinese search terms are as follows: meta-analysis, meta-analysis, systematic review, systematic review, primary nephrotic syndrome, TCM, TCM, etc. The English search terms are as follows: systematic review, meta-analysis, Primary nephrotic syndrome, traditional Chinese medicine, Chinese traditional, drugs, Chinese herbal, etc.

## 2.4. Literature Screening and Content Extraction

Literature screening, content extraction, and further cross-checking were performed independently by two researchers based on the above inclusion and exclusion criteria. At the initial screening, read the title and abstract, keep relevant literature, and further screen the full text. At this time, if there is any disagreement, you can discuss and solve, or ask a third party to help solve, to determine whether to include. The contents extracted are as follows: (1) Authors of each included study, publication (or update) year, number of included studies and total sample size, intervention programs of trial and control groups, bias risk assessment tools, main conclusions and other basic information; (2) The methodological content of SR, such as literature retrieval, included studies, research samples and methodological quality evaluation of included studies; (3) Quantitative statistical results of all outcome indicators included in the study.

## 2.5. Evaluation Method

The methodological quality evaluation and evidence level evaluation involved in the included research were independently evaluated by two researchers, and then cross-checked after completion. If there was any disagreement, discussion and negotiation were conducted or a third party was invited to help solve the problem.

## 2.5.1. Methodology Quality Evaluation

The AMSTAR2 scale was used by two researchers to evaluate the included studies. It contained 16 entries, among which the key entries were 2, 4, 7, 9, 11, 13 and 15, all of which could be "yes", "partly yes" or "no" according to the evaluation criteria. The credibility of each study can be divided into four levels, namely "high", "medium", "low" and "very low" [7].

## **2.5.2. Evidence Quality Evaluation**

The evidence quality of outcome indicators was evaluated according to the GRADE system, and each outcome indicator was evaluated by two researchers respectively, mainly from the five aspects of limitation, inconsistency, indirection, inaccuracy and publication bias. The decrease of one level was intermediate evidence, the decrease of two levels was low evidence, and the decrease of three levels was extremely low evidence [8-10]. List the final results.

## 3.1. Literature Screening Process and Results

A total of 177 SR or meta-analyses were obtained in the initial examination. After further screening, 11 studies were finally included. The screening process and results are shown in Figure 1.

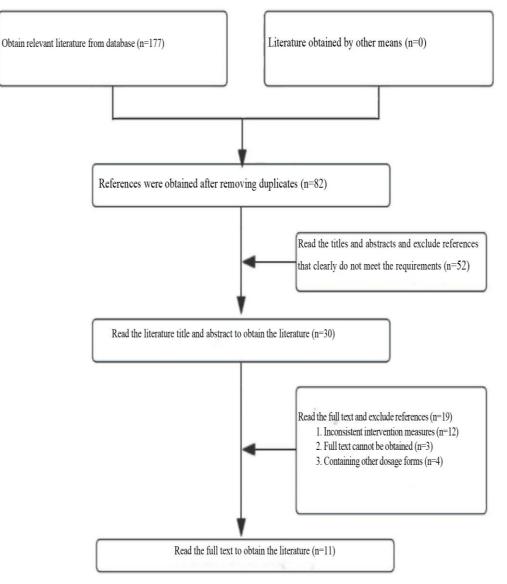


Figure 1. Flowcharts of the screening and results

Figure Note: The number of databases searched and literature checked are as follows: CNKI (n=37), WanFang Data (n=46), VIP (n=35), CBM (n=38), PubMed (n=10), The Cochrane Library (n=5), and EMbase (n=6)

## 3.2. Basic Features Included in the Study

The 11 included studies were all meta-analyses, including 1 English study (9.1%) and10 Chinese studies (90.9%), published from 2013 to 2022. A total of 166 original studies were included, with a total sample size of 12048 people. The basic characteristics of statistical inclusion are shown in Table 1.

Number of Bias risk assessment tool									
Included literature	number of participants/ number of participants Intervention measure	Experimental group	Control group	Main conclusion					
Hongyun Wang 2021 [11]	12/981	Astragalus decoction + hormone	hormone	Cochrane Bias risk assessment tool	Fangji Huangqi Decoction can improve the efficacy and safety in the intervention of PNS, but high-quality studies are needed to prove it				
Dongdong Ruan 2021 [12]	26/1827	Zhenwu Decoction + conventional treatment	Conventional treatment	Cochrane Bias risk assessment tool	Zhenwu decoction plus or minus combined with Western medicine in the treatment of PNS has certain clinical efficacy in the total effective rate and high safety				
Jingwei Liu 2020 [13]	18/1231	Tonifying kidney and Huoxue prescriptions + control group	Conventional treatment with or without symptomatic treatment	Cochrane Bias risk assessment tool	The treatment of adult PNS has good effect and can improve the diseaseSymptoms, and had a significant effect on certain laboratory indicators				
Mengdi Li 2020 [14]	25/2060	TCM decoction + control group treatment	Conventional reatment with or without symptomatic treatment	Cochrane Bias risk assessment tool	The efficacy of TCM decoction combined with hormones in adult PNS is positive, requiring more reliable RCT with more higher quality and more sample size				
JiaojiaoLi u , 2019 [15]	22/1672	Warming Yang activating blood and benefiting water - based treatment + control group	Conventional treatment with or without symptomatic treatment	Modified version of the Jadad scale	The treatment of PNS by warming Yang and promoting blood circulation and rehydrating water has a significant effect, which needs to be confirmed by RCT				

 Table 1. Basic characteristics of meta-analysis of 11 included oral Chinese herbal decoction interventions in PNS

Lijie Li 2018[16]	18/1210	Tonifying kidney and activating blood mainly + control group treatment	Hormone with or without cyclophospha mide	Cochrane Bias risk assessment tool	Tonifying kidney and promoting blood circulation in the treatment of PNS can increase efficacy and reduce toxicity, but large samples and RCT are needed to prove it	
Xing Xiao 2017[17]	10/634	TCM decoction + conventional treatment	Conventional treatment with or without symptomatic treatment	Modified version of the Jadad scale	TCM warm Yang method can reduce the 24 h UTP of adult PANS, reduce TC and TG, improve ALB and effective rate, and reduce the incidence of adverse reactions	
Shisheng Han 2015 [18]	12/936	Supplementin g qi and reinforcing prescription + control group	Conventional treatment plus symptomatic treatment	Modified version of the Jadad scale	Yiqigu decoction was superior to conventional treatment group in reducing albuminuria in PNS	
Shunjin Hu 2014[19]	12/738	TCM syndrome differentiatio n Decoction + Prednisone	prednisone	Cochrane Bias risk assessment tool	The treatment of PNS by Chinese medicine is better in increasing effect and decreasing toxicity	
Yu Wang 2013[20]	4/272	Glucocorticoi d + traditional Chinese medicine warming Yang method medicine mainly	glucocorticoid	Cochrane Bias risk assessment tool	The combination of corticosteroids with warm Yang method can improve clinical efficacy and improve laboratory indicators such as plasma albumin	
Li Zhang 2022[21]	7/487	Huai Qi Huang granules + hormone	hormone	Cochrane Bias risk assessment tool	Huai Qi Huang granulesReducing the recurrence rate of PNS, the incidence of infection and the dosage of prednisone can improve immunity with high safety	

## 3.3. Methodological quality evaluation of included studies

AMSTAR2 scale was used to evaluate the quality of jurisprudence, and statistical analysis showed that the methodological quality of the 11 included studies was very low. The proportion of complete reports on 7 key items including 2, 4, 7, 9, 11, 13 and 15 was 9.1%, 0%, 0%, 81.8%, 100%, 72.7% and 45.5%, respectively. The main methodological quality deficiencies of the 11 studies included were the lack of a preliminary design plan, the lack of a comprehensive literature search strategy, the lack of a list of excluded literatures, and the lack of clarification of funding and conflicts of interest. The specific results are shown in Table 2.

PRISMA entry		satisfy		Partial satisfaction		isfied
	article	%	article	%	article	%
1. Do the research questions and inclusion criteria include PICO?	11	100	0	0	0	0
2. Is it stated that research methods for systematic evaluation are determined before systematic evaluation? Are any inconsistencies with the study protocol stated?	1	9.1	0	0	10	90.9
3. Were the types of studies included indicated when the literature was included?	0	0	0	0	11	100
4. Did the authors adopt a comprehensive search strategy?	0	0	8	72.8	3	27.2
5. Is the two-person repetitive literature selection adopted?	10	90.9	0	0	1	9.1
6. Is two-person repetitive data extraction?	10	90.9	0	0	1	9.1
7. Did the authors of the systematic evaluation provide a list of excluded documents and explain the reasons?	0	0	0	0	11	100
8. Did the authors describe the included studies in great detail?	0	0	9	81.8	2	18.2
9. Do the authors use appropriate instruments to assess the risk of bias for each included study?	9	81.8	1	9.1	1	9.1
10. Do the authors report funding sources for each study?	0	0	0	0	11	100
11. Whether the authors used appropriate statistical methods for results consolidation analysis	11	100	0	0	0	0
12. Did the authors assess the impact of each bias risk on the results of the meta-analysis?	1	9.1	0	0	10	90.9
13. Does the investigator consider the risk of bias for inclusion when interpreting or discussing each study result?	8	72.7	0	0	3	27.3
14. Do the authors have a reasonable explanation and discussion of any heterogeneity of the findings?	7	63.6	0	0	4	36.4
15. Is publication bias investigated and its implications discussed for quantitative consolidation?	5	45.5	0	0	6	54.5
16. Did the author report all sources of conflicts of interest?	6	54.5	0	0	5	45.5

 Table 2. AMSTAR2 evaluation results of 11 systematic evaluation of oral TCM decoction intervention PNS

## 3.4. Quality Evaluation of Outcome Indicators Included in the Study

The study included a total of 79 outcome measures. Statistical analysis showed that there were 5 outcome indicators (accounting for 6.3%) with intermediate evidence quality, 35 outcome indicators (accounting for 44.3%) with low evidence quality, and 39 outcome indicators (accounting for 49.4%) with very low evidence quality. This indicated that most of the results of meta-analysis confirmed the efficacy of oral TCM decotion in the intervention of PNS to some extent, but the evidence level of the included outcome indicators needed to be further improved, but the reference level for clinicians, guideline makers, patients and other personnel would be reduced to some extent. The main reasons for the downgrading were random assignment methods, blindness, and assignment of hidden or selective reporting. Other factors such as publication bias, imprecision and inconsistencies also had an impact on the quality of the evidence included in the study. The specific evaluation results are shown in Table 3.

Included in the literature	Outcome measures (Number of studies)	limitation s	inconsiste ncy	Indire ct	inaccur acy	Publica tion bias	Quality of evidence
Hongyu	total effective rate (11)	-1(1)	0	0	0	0	middle
n Wang 2021[11]	24hUT(11)	-1(1)	-1(2)	0	0	0	low
2021[11]	Scr(5)	-1(1)	-1(2)	0	-1(3)	-1(4)	low
	total effective rate (26)	-1(1)	0	0	0	-1(5)	low
Densla	24hUT(19)	-1(1)	-1(2)	0	0	-1(5)	low
Dongdo	Scr(6)	-1(1)	-1(2)	0	-1(3)	-1(5)	low
ng Ruan 2021[12]	BUN(5)	-1(1)	-1(2)	0	-1(3)	-1(4)	low
2021[12]	syndrome points(4)	0	0	0	-1(3)	-1(4)	low
	Prevalence of adverse reaction(4)	0	0	0	-1(3)	-1(4)	low
Jingwei	total effective rate (18)	-1(1)	0	0	0	0	middle
Liu	24hUT(15)	-1(1)	-1(2)	0	0	-1(5)	low
2020[13]	Scr(8)	-1(1)	-1(2)	0	0	0	low
	BUN(7)	-1(1)	-1(2)	0	0	0	low
Mengdi Li 2020[14]	total effective rate(24)	-1(1)	0	0	0	-1(5)	low
	24hUT(25)	-1(1)	0	0	0	-1(5)	low
	Prevalence of adverse reaction(6)	-1(1)	0	0	0	-1(4)	low
Jiao jiaoLiu 2019[15]	CRR(21)	-1(1)	0	0	0	-1(5)	low
	Show efficiency(14)	-1(1)	0	0	-1(3)	-1(5)	low
	total effective rate (13)	-1(1) 0	0	0	-1(5)	low	
	24hUT(21)	-1(1)	-1(2)	0	0	-1(5)	low
	Scr(10)	-1(1)	-1(2)	0	-1(3)	-1(5)	low

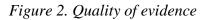
 Table 3. GRADE evaluation results of 11 systematic evaluation of oral TCM decoction intervention

 PNS

	BUN(9)	-1(1)	-1(2)	0	0	-1(4)	low
	recurernce rate (3)	-1(1)	0	0	-1(3)	-1(4)	low
	Prevalence of adverse reactions(8)	-1(1)	0	0	-1(3)	-1(4)	low
Lijie Li	-1(1)	0	0	0	-1(5)	low	
2018[16]	24h UTP(14)	-1(1)	-1(2)	0	0	-1(5)	low
]total	BUN(6)	0	-1(2)	0	0	-1(4)	low
effective rate (16)	Scr(7)	0	-1(2)	0	0	-1(4)	low
Xing	24hUT(8)	-1(1)	-1(2)	0	0	-1(5)	low
Xiao 2017[17]	Total effective rate (9)	-1(1)	0	0	-1(3)	-1(5)	low
Han	24hUT(9)	-1(1)	-1(2)	0	0	-1(5)	low
Shisheng	ALB(8)	-1(1)	-1(2)	0	-1(3)	0	low
2015[18]	CRR (11)	-1(1)	0	0	0	0	middle
	CRR (11)	-1(1)	0	0	-1(3)	0	low
Hu Shunjin	And a 12-month recurrence rate(5)	-1(1)	0	0	-1(3)	-1(4)	low
2014[19]	Prevalence of adverse reactions(8)	-1(1)	0	0	0	-1(5)	low
	CRR (4)	-1(1)	0	0	0	-1(4)	low
Wang	ALB(4)	-1(1)	0	0	0	-1(4)	low
Yu	24hUT(4)	-1(1)	0	0	0	-1(4)	low
2013[20]	]plasma viscosity (2)	-1(1)	0	0	0	-1(4)	low
	contractinogen (2)	-1(1)	0	0	0	-1(4)	low
	infection rate (4)	-1(1)	0	0	0	0	middle
	recurernce rate (4)	-1(1)	0	0	0	-1(5)	low
	Prevalence of adverse reactions(4)	-1(1)	0	0	-1(3)	0	low
	ALB(4)	-1(1)	-1(2)	0	0	0	low
	TC(3)	-1(1)	0	0	0	-1(4)	low
Li Zhang 2022[21]	Negative urinary protein time(4)	-1(1)	-1(2)	0	0	0	low
	Edema regression time(3)	-1(1)	-1(2)	0		-1(4)	low
	Glucocorticoid dose(3)	-1(1)	0	0	0	-1(4)	low
	Tlymphocytesthym usdependent lymphocytes (5)	-1(1)	-1(2)	0	-1(3)	0	low
	immunoglobulin (5)	-1(1)	-1(2)	0	0	0	low

Note: 0: not degraded; -1: one level lower. (1) There are certain defects in randomization, blind method, allocation of hidden or selective reports; (2) The overlap of confidence interval is poor, and the I2 value of the combined result is large; (3) Wide confidence interval or small sample size; (4) The number of included studies was small and positive, suggesting the existence of publication bias;

(5) The poor symmetry of funnel plot suggests that there is a certain bias. The proportion of evidence levels is shown in Figure 2.



middle 5 % (6)

#### 4. Discussion

A total of 11 meta-analyses on the intervention of oral middle decoction in PNS were included in this study, and there were 1 in middle English and 10 in middle Chinese literature, with a relatively low proportion of English literature. The period of publication was from 2013 to 2022, and the number of studies has increased in recent years. An in-depth analysis of all included meta-analyses suggested that oral middle drug decoction had significant advantages in the treatment of PNS in terms of clinical efficacy such as total effective rate, symptom improvement, reduction of side effects of western drugs and improvement of related laboratory indicators, with high safety. However, all the included studies need to be further improved in terms of methodological quality, and there are still defects in the evidence quality of the outcome indicators included in the included studies.

## **4.1.** The Quality of SR Methodology for the Treatment of PNS with oral Middle Decoction needs to be Further Improved

In this study, the AMSTAR2 scale was used to evaluate the methodological quality of the included meta-analyses. The results showed that the methodological quality of the included 11 meta-analyses was low. It is manifested in the lack of preliminary research design scheme, the lack of registration of the scheme, the lack of comprehensive literature search strategy, the lack of excluded literature list and the lack of financial support and conflict of interest. The main problems are as follows: (1) The failure to identify and register the study protocol before the implementation of the design types of included studies; (2) Lack of search of grey literature, and no mention of inclusion or consultation of appropriate experts in the corresponding field; (3) When the literature was screened, the list of excluded literatures and the reasons for excluding each literature were not listed; (4) Failure to explain the source of funding for the implementation of the research and failure to declare conflicts of interest, which may lead to the research results. Based on the above problems, this study suggests that the research scheme should be designed before the implementation of this series of studies, and the scheme should be registered on relevant websites at the same time, so as to

reduce the possible risk of bias. Explain the selection of research types to be included; Carry out a more comprehensive search of grey literature and other resources, and include/consult appropriate experts in the corresponding field; Make a detailed list of excluded documents and the reasons for excluding each document; provide a comprehensive explanation and annotation of funding sources and conflicts of interest.

# **4.2.** The Evidence Level of Outcome Indicators in the Meta-analysis of Oral TCM Decoction in the Treatment of PNS Was Low

In this study, GRADE system was applied to evaluate the evidence quality of all outcome indicators included in the literature. There were 5 outcome indicators in the middle level of evidence quality (6.3%), 35 outcome indicators in the low level of evidence quality (44.3%), and 39 outcome indicators in the low level of evidence quality (49.4%). The main factors contributing to this result are the implementation of randomized methods, the implementation of blind methods, the assignment of hidden schemes or selective reports. Other factors, such as publication bias, imprecision and inconsistencies, also affect the quality of the evidence included in the study.

The existing problems are mainly manifested in the following aspects. Affected by the quality of the original RCTS included in the meta-analysis, some RCTS did not systematically clarify the specific method of randomization, the assignment of hidden implementation plan, the implementation of blind method and selective reporting, which resulted in the increased risk of bias. Some studies have small sample sizes, resulting in poor accuracy; The number of studies related to some outcome indicators is small and all show positive results. Some negative results may not be disclosed, and then form publication bias, resulting in the deterioration of evidence quality. It is suggested that follow-up clinical researchers actively seek cooperation with methodological or evidence-based medicine experts to further improve the quality of the original RCTS, standardize the research methods, and provide higher-level and reliable evidence for clinicians, guideline makers and patients.

## 4.3. Clinical Guiding Significance of this Study

In this study, meta-analysis related studies on oral middle drug decoction in the treatment of PNS were re-evaluated, and the results showed that compared with the control group, the experimental group showed significant clinical effects in the total effective rate, complete response rate, recurrence rate and other clinical efficacy indicators. The 24-hour urinary protein quantification, serum albumin, Scr and other key laboratory indicators also showed significant advantages, while reducing the side effects of hormones and reducing the clinical dose of low glucocorticoid, suggesting that oral middle decoction combined with Western medicine in the treatment of PNS showed significant advantages compared with Western medicine intervention alone. In terms of safety, the incidence of adverse reactions in the intervention of PNS with oral middle decoction is indeed low, indicating good safety, but the quality of evidence needs to be further improved. In conclusion, the intervention of PNS with oral middle decoction has significant clinical effects and certain advantages, with good safety. However, due to the low quality of evidence in the included meta-analysis, the reliability of the study results is reduced. Therefore, it is necessary to collaborate with methodological or evidence-based medicine experts to improve the level of the overall study and further prove the clinical effect and safety of oral middle drug decoction intervention in PNS.

## 4.4. Limitations of this Study

Through a comprehensive search of relevant databases, this study is the first to use the method of systematic review and re-evaluation to comprehensively and systematically evaluate the SR of oral middle decoction intervention in PNS. However, in view of the deficiencies of the original study and its own study, this study still has some limitations: (1) At present, there are few SR interventions for PNS with oral middle decoction, and most reports are not standardized. Meanwhile, the completeness needs to be further improved to reduce the credibility of the study to a certain extent. (2) At present, oral middle decoction is used to treat SRmiddle of PNS. Some literatures only include adult patients, some literatures only include children patients, and some literatures include both. In view of the difference in therapeutic effect between children and adults. And that affects the results. (3) Although this study conducted a comprehensive search of relevant databases and searched grey literature, it may not be able to guarantee the inclusion of all eligible studies.

## 4.5. Outlook

Through a comprehensive and systematic analysis of SR in the intervention of oral middle decoction in PNS, this study presents evidence-based evidence support for clinical intervention of oral middle decoction in PNS. Meta-analysis studies on the included oral middle drug decoction intervention in PNS revealed that the methodological quality and evidence quality of outcome indicators of current meta-analyses in this field needed to be further improved, and the reliability of clinical applications needed to be further verified. Therefore, the following recommendations were made in this study: (1) To collaborate with experts in methodology or evidence-based medicine, while clinical researchers attach importance to training and strict implementation of methodological quality of published literature by referring to AMSTAR2 scale and other relevant documents when making SR or meta-analysis; (3) Before the implementation of the system evaluation, strengthen the writing and registration of the research proposal. To improve the methodological quality and reporting standards of SR in this field, and further provide clinicians, patients, and guideline makers with a higher level of evidence-based evidence.

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No funds.

#### **Data Availability**

The datasets used during the current study are available from the corresponding author on reasonable request.

## **Conflict of Interest**

The author states that this article has no conflict of interest.

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