Outcome Measures in Randomized Controlled Trials of Traditional Chinese Medicine for Refractory Mycoplasma Pneumoniae Pneumonia in Children

SU Die, ZHANG Yan, CHEN Xiaosong, HAN Yuxia, YAN Yongbin, DUAN Junya, CHEN Xinying, ZHAO Chenghao

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Abstract

Background: Mycoplasma pneumoniae pneumonia is a common type of community-acquired pneumonia in children, and 2.3%–6.8% of affected children continue to experience disease progression after more than 7 d of macrolide antibiotic treatment, developing refractory pneumonia. In recent years, given the increasing number of children with this disease, randomized controlled clinical studies on traditional Chinese medicine for its treatment have made some progress, but the corresponding outcome indicator system remains to be improved. Objective: To systematically analyze the current status of outcome indicators in randomized controlled trials (RCTs) of traditional Chinese medicine for the treatment of refractory Mycoplasma pneumoniae pneumonia in children, with the aim of providing a reference for improving treatment indicators for this disease and designing clinical trials of traditional Chinese medicine. Methods: Studies related to traditional Chinese medicine treatment of refractory Mycoplasma pneumoniae pneumonia in children, published in five Chinese and English databases over the past 10 years, were systematically retrieved. Literature screening, data extraction, and risk-of-bias assessment were conducted according to predefined criteria, and outcome indicator data were processed and analyzed. Results: A total of 38 relevant studies were included, involving 50 types of outcome indicators, with a total count of 282 occurrences. The top five outcome indicators were clinical efficacy (32 occurrences, 84.21%), incidence of adverse reactions (25 occurrences, 65.79%), time to fever resolution (24 occurrences, 63.16%), time to cough disappearance (23 occurrences, 60.53%), and interleukins (19 occurrences, 50.00%). Western medical diagnostic criteria were reported in 30 studies, traditional Chinese medicine syndrome differentiation reference criteria in 23 studies, no study clearly distinguished primary from secondary outcome indicators, and 8 studies reported evaluation criteria for the efficacy of traditional Chinese medicine syndromes. Conclusion: At present, clinical outcome indicators for refractory Mycoplasma pneumoniae pneumonia in children are mainly clinical symptoms and signs as well as physicochemical indicators. In addition to long-standing common problems such as unclear prioritization of outcomes and inconsistent standards, issues such as a gradual decrease in health economic evaluation reports and a lack of long-term prognostic indicators have also emerged. Further exploration by clinicians is needed in the future to establish a core outcome set and to reintroduce health economic evaluations and long-term prognostic indicators when appropriate, thereby providing an objective basis for conducting more rigorous clinical research in the future.

Full Text

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【Abstract】**Background** Mycoplasma pneumoniae pneumonia is a common type of community-acquired pneumonia in children. Among these patients, 2.3% to 6.8% continue to show clinical deterioration despite treatment with macrolide antibiotics for 7 days or longer, progressing to refractory pneumonia. In recent years, given the increasing number of pediatric cases, randomized controlled clinical trials on the treatment of this condition using traditional Chinese medicine have made some progress; however, the corresponding set of outcome measures still needs to be refined. **Objective** To provide references for the improvement of treatment indicators for this disease and the design of clinical trials in TCM, this study systematically analyzes the current status of outcome measures in randomized controlled trials (RCTs) of traditional Chinese medicine (TCM) for treating refractory Mycoplasma pneumoniae pneumonia in children. **Methods** Publicly published relevant studies on TCM treatment of pediatric refractory Mycoplasma pneumoniae pneumonia in five Chinese and English databases over the past 10 years were systematically searched. Literature was screened according to standards, data were extracted, risk of bias was assessed, and outcome-measure data were processed and analyzed. **Results** A total of 38 relevant studies were included, involving 50 outcome measures, with a total frequency of 282 occurrences. The top five outcome measures were clinical efficacy (32 times, 84.21%), incidence of adverse reactions (25 times, 65.79%), fever abatement time (24 times, 63.16%), time to disappearance of cough (23 times, 60.53%), and interleukin (19 times, 50.00%). Thirty reports described Western-medicine diagnostic criteria, 23 studies reported TCM syndrome-differentiation reference criteria, no study clearly distinguished primary and secondary outcome measures, and 8 studies reported TCM syndrome efficacy evaluation criteria. **Conclusion** At present, clinical outcome measures for pediatric refractory Mycoplasma pneu-

moniae pneumonia mainly consist of clinical symptoms and signs as well as physicochemical indicators. There remain unresolved common problems such as unclear primary and secondary outcomes and inconsistent standards; issues have also emerged such as gradually decreasing reports of economic evaluations and a lack of long-term prognostic indicators. In the future, clinical workers need to further explore, establish a core indicator set, and, when appropriate, reincorporate health economic evaluations and long-term prognostic indicators, so as to provide objective evidence for the conduct of more rigorous clinical research in the future.

【Keywords】 pneumonia; mycoplasma; refractory Mycoplasma pneumoniae pneumonia; children; traditional Chinese medicine; outcome measures; randomized controlled trial

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【Abstract】**Background** Mycoplasma pneumoniae pneumonia is a common type of community-acquired pneumonia in children. Among these patients, 2.3% to 6.8% continue to show clinical deterioration despite treatment with macrolide antibiotics for 7 days or longer, progressing to refractory pneumonia. In recent years, given the increasing number of pediatric cases, randomized controlled clinical trials on the treatment of this condition using traditional Chinese medicine have made some progress; however, the corresponding set of outcome measures still needs to be refined. **Objective** To provide references for the improvement of treatment indicators for this disease and the design of clinical trials in TCM, this study systematically analyzing the current status of outcome indicators in randomized controlled trials (RCTs) of traditional Chinese medicine (TCM) for

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refractory Mycoplasma pneumoniae pneumonia in children. **Methods** This study systematically searched five Chinese and English databases for published research on the treatment of refractory Mycoplasma pneumoniae pneumonia in children using traditional Chinese medicine over the past 10 years. Literature was screened, data were extracted, and the risk of bias was assessed according to established criteria, and the outcome data were processed and analyzed. **Results** The results included a total of 38 relevant studies, covering 50 outcome measures, with a total of 282 observations. The top 5 outcome indicators were clinical efficacy (32 times, 84.21%), incidence of adverse reactions (25 times, 65.79%), time to defervescence (24 times, 63.16%), time to disappearance of cough (23 times, 60.53%), and interleukin (19 times, 50.00%). 30 studies reported Western medical diagnostic criteria, 23 studies reported reference criteria for TCM syndrome differentiation, and no study clearly distinguished primary and secondary outcome indicators. 8 studies reported the evaluation criteria for TCM syndrome efficacy. **Conclusion** Our findings indicate that current outcome indicators for refractory Mycoplasma pneumoniae pneumonia (RMPP) in children are predominantly based on clinical symptoms, signs, and laboratory parameters. This field is burdened by longstanding unresolved issues, including the unclear delineation between primary and secondary outcomes and the lack of standardized evaluation criteria. In addition, emerging challenges have been identified, such as a progressive decline in health economic evaluation reports and a notable absence of long-term prognostic indicators. In the future, clinicians need to further explore these issues, establish a core indicator system, and, at the appropriate time, reintroduce health economic evaluations and long-term prognostic indicators. This study contributes to providing an objective basis for conducting more rigorous clinical research in the future.

【Key words】 Pneumonia, Mycoplasma; Refractory Mycoplasma pneumoniae pneumonia; Child; Traditional Chinese medicine; Outcome indicators; Randomized controlled trial

Mycoplasma pneumoniae pneumonia (MPP) is a common respiratory disease in children caused by Mycoplasma pneumoniae (MP). The incubation period of MP infection is 1–3 weeks. It is transmitted by droplets and direct contact, and the population is generally susceptible; therefore, it is the main pathogen of community-acquired pneumonia in preschool- and school-age children[^1], accounting for approximately 10%–40% of pediatric community-acquired pneumonia[^2]. Macrolide drugs are the first-line drugs for its treatment, but 2.3%–6.8% of children still experience continued disease progression after more than 7 days of macrolide antibiotic treatment, with persistent fever, aggravation of clinical manifestations, extrapulmonary complications, prolonged disease course, and progression of pulmonary imaging findings; this is known as refractory Mycoplasma pneumoniae pneumonia (RMPP)[^3]. In recent years, RMPP cases have shown a gradually increasing trend[^4]. At present, clinical treatment of RMPP mainly includes combined therapy with tetracyclines and quinolones, glucocorticoids, gamma globulin, and bronchoscopic lavage. Traditional Chinese medicine classifies this disease under the categories of "cough," "pneumonia with wheezing," and "externally contracted febrile disease." The advantages of traditional Chinese medicine in the prevention and treatment of RMPP have become increasingly prominent, and its mechanisms are mainly related to inhibiting MP, reducing the expression of inflammatory factors[^5], improving cough and wheezing symptoms, alleviating pulmonary inflammation, and reducing complications[^6]. Randomized controlled trials (RCTs) are the gold standard for verifying the clinical efficacy of interventions[^7]. The reliability of clinical efficacy judgments is closely related to the selection of outcome indicators. In recent years, clinical research on traditional Chinese medicine treatment of pediatric RMPP has made some progress, but the current outcome indicator system for relevant RCTs remains imperfect. By systematically analyzing the current status of outcome indicators in RCTs of traditional Chinese medicine treatment for pediatric RMPP over the past 10 years, this study aims to provide a reference basis for improving therapeutic indicators for this disease and for the design of traditional Chinese medicine clinical trials.

1 Materials and Methods

1.1 Inclusion and Exclusion Criteria

1.1.1 Inclusion Criteria

(1) Study subjects: children with RMPP; (2) study type: randomized controlled trials; (3) interventions: the observation group received integrated Chinese and Western medicine treatment or traditional Chinese medicine treatment, including Chinese herbal medicine, Chinese patent medicine, acupuncture, tuina, acupoint application, etc.; the control group was not

restricted.

1.1.2 Exclusion Criteria

(1) Combined with other serious underlying diseases or complications; (2) reviews, conference papers, patents, traditional Chinese medicine-related medical records, dissertations; (3) information on outcome indicators could not be obtained.

1.2 Literature Search

CNKI, Wanfang Data Knowledge Service Platform, VIP, PubMed, and Web of Science were searched to collect studies related to RMPP published from January 2015 to October 2025. Literature was screened according to the inclusion and exclusion criteria; relevant information from included studies was extracted, and outcome indicator data were processed and analyzed. The Chinese database search strategy combined subject terms with free-text terms, for example: ("traditional Chinese medicine" OR "Chinese medicine" OR "integrated Chinese and Western medicine" OR "acupuncture" OR "tuina") AND ("refractory Mycoplasma pneumoniae pneumonia" OR "refractory Mycoplasma pneumoniae pneumonia") AND ("children" OR "pediatric" OR "child") AND ("randomized controlled"). An example English database search strategy was: ("traditional Chinese medicine" OR "Chinese herbal medicine" OR "TCM") AND ("refractory mycoplasma pneumoniae pneumonia" OR "refractory MPP") AND ("children" OR "pediatric") AND ("randomized controlled trial" OR "RCT"). Relevant references cited in the included literature were also searched manually to avoid omissions.

1.3 Literature Screening

First, the retrieved literature was imported into EndNote for duplicate checking, and duplicate records were deleted. After deduplication, titles and abstracts were read to further remove literature that did not meet the requirements. Finally, the full texts of potentially eligible literature were read to determine the final included studies.

1.4 Data extraction

Data were extracted from the included studies, mainly including the following aspects: (1) basic information: title, authors, year of publication, etc.; (2) basic content: sample size, intervention measures, course of treatment, intervention type (oral Chinese medicine / external treatment with Chinese medicine / oral Chinese medicine combined with external treatment with Chinese medicine), TCM syndrome type, etc.; (3) outcome indicators: type, name, frequency of occurrence, evaluation criteria, and whether primary and secondary indicators were distinguished, etc. The extracted data were organized and classified and presented in tabular form.

1.5 Risk-of-bias assessment

The Cochrane risk-of-bias assessment tool was used to assess the risk of bias in the included studies. The evaluation items included random sequence generation, allocation concealment, blinding of participants and researchers, blinding of outcome assessors, completeness of outcome data, selective reporting of study results, and other sources of bias. A total of 7 items were used to evaluate the risk of bias; each item was rated as low risk of bias, high risk of bias, or unclear[^8].

1.6 Data analysis

(1) Basic information such as the category of included studies, intervention measures, sample size, and course of treatment, as well as Western-medicine diagnostic criteria, TCM syndrome differentiation reference criteria, and TCM syndrome types, were statistically analyzed; (2) outcome indicators were divided into 7 categories: TCM symptoms/syndromes, clinical symptoms and signs, laboratory tests, safety events, long-term prognosis, economic evaluation, and other indicators. The classification and frequency of outcome indicators, the use of primary and secondary outcome indicators, the use of outcome indicators for different intervention measures, the characteristics of changes in outcome indicators over time, the reporting of clinical efficacy, and the reporting of efficacy according to TCM syndromes were statistically analyzed, as were ethics approval and informed consent in the included literature.

2 Results

2.1 Literature screening

A total of 2,469 relevant articles were retrieved from the databases. Using EndNote X9 software, 998 duplicate articles were removed. After reading titles and abstracts, 1,401 articles that did not meet the criteria were excluded. After full-text reading, 32 articles were excluded, and finally 38 articles[^9-^46] were included. The literature screening flow chart is shown in Figure 1, and the categories, intervention measures, and basic information of the included studies are shown in Tables 1 and 2.

Figure 1 Literature screening flow chart

- Relevant literature obtained through database searches ($n = 2\,469$): CNKI ($n = 410$), Wanfang Data Knowledge Service Platform ($n = 1\,266$), VIP ($n = 463$), PubMed ($n = 110$), Web of Science ($n = 220$)
  - Duplicate articles removed by EndNote software ($n = 998$)
- Initial screening by reading titles and abstracts ($n = 1\,471$)
  - Excluded literature ($n = 1\,401$)
    1. Did not meet the inclusion criteria

2. Unable to obtain information on outcome indicators

3. Had other serious underlying diseases or complications

- Re-screening by reading full texts ($n = 70$)
  - Excluded literature ($n = 32$)
    1. Intervention measures did not conform

    2. Study type did not conform

    3. Dissertation
- Included literature ($n = 38$)

Table 1 Category and Intervention Measures of the included studies

Category	Content	Quantity (articles)
Study type	Randomized controlled trial	38[^9-^46]
Category	Integrated Chinese and Western medicine	38[^9-^46]
Intervention measures	Oral Chinese medicine	32[[9-]10, [12-]23, [26-]30, [33-]42, [44-]46]
Intervention measures	External treatment with Chinese medicine	3[[24-]25, ^43]
Intervention measures	Oral Chinese medicine combined with external treatment with Chinese medicine	3[^11, [31-]32]
Whether primary and secondary outcome indicators were distinguished	Yes	0

2.2 Distribution characteristics of sample size and course of treatment

The sample sizes of the studies included in this review were mainly small to medium-sized, and no large-sample clinical studies were found overall. Among them, there were 14 small-sample studies with a total sample size ( )80 cases[^11, ^13, [16-]17, ^21, ^24, ^26, ^30, [32-]33, ^39, [41-]43], and 24 medium-sample studies with 81-300 cases[[9-]10, ^12, [14-]15, [18-]20, [22-]23, ^25, [27-]29, ^31, [34-]38, ^40, [44-]46], constituting the main body of the included literature. The intervention course of treatment in each study ranged from 5 to 30 d, showing an obvious concentrated distribution. The largest number of studies used 14 d as the course of treatment, totaling 20 studies[[10-]11, ^14, ^16, [19-]23, [27-]32, ^35, [37-]38, ^41,

^44]; there were relatively few studies with a short course (5–10 d), totaling 13 studies[^9, ^12, [17-]18, ^26, [33-]34, ^36, [39-]40, [42-]43, ^46], and studies with a long course (( )21 d) were fewer, only 5 studies[^13, ^15, [24-]25, ^45], as shown in Table 2.

2.3 Western-medicine diagnostic criteria and TCM syndrome differentiation criteria

Among the 38 included studies, 30 studies[[11-]12, [14-]16, [19-]28, [30-]34, [36-]39, [41-]46] reported Western-medicine diagnostic criteria. The most frequently used was the *Expert Consensus on the Diagnosis and Treatment of Mycoplasma pneumoniae Pneumonia in Children (2015 Edition)*[^47] (13 times, 34.21%). A total of 23 studies[^15, [19-]21, [23-]34, ^36, ^38, ^41, [43-]46] reported TCM syndrome differentiation reference criteria. The most frequently used was the *Diagnostic and Therapeutic Criteria for TCM Diseases and Syndromes*[^48] (10 times, 26.31%), as shown in Tables 3–4.

Twenty-five studies[^9, ^17, [19-]24, [26-]36, ^38, ^41, [43-]46] reported TCM syndrome types, involving 6 syndrome types: phlegm-heat obstructing the lung (12 times, 31.58%), toxic heat obstructing the lung (7 times, 18.42%), wind-heat invading the lung (3 times, 7.89%), lung-spleen qi deficiency (1 time, 2.63%), lung abscess stage of pus formation (1 time, 2.63%), and phlegm-heat syndrome (1 time, 2.63%). The most frequently reported was phlegm-heat obstructing the lung.

2.4 Outcome indicators

2.4.1 Indicator classification and frequency of use A total of 50 types of outcome indicators were reported, with an overall count of 282 times. The summarized categories were as follows: each individual study used 1–5 outcome indicators, namely TCM symptoms/syndromes (3 types), clinical symptoms and signs (15 types), laboratory tests (26 types), safety events (1 type), long-term prognosis (2

Table 2 Basic information of the included studies

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Meng Xianhong [9]	2015	100	50/50	Reduning injection + azithromycin + routine treatment	Azithromycin + routine treatment	7	
Qiu Zainian [10]	2015	84	42/42	Tongluo Huoxue decoction + methylprednisolone + routine treatment	Azithromycin + routine treatment	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Li Yanling [11]	2016	72	36/36	Oral Chinese medicine treatment + external Chinese medicine application + cupping therapy + methylprednisolone	Methylprednisolone + routine treatment	14	
Li Wenjin [12]	2016	82	41/41	Xiao'er Feire Kechuan oral liquid + lung-vesicle lavage + routine treatment	Lung-vesicle lavage + routine treatment	10	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Wang Honglian [13]	2016	62	30/32	Yupingfeng granules + routine treatment	Routine treatment	30	
Yuan Pingbo [14]	2016	84	42/42	Qingfei Zhike decoction + azithromycin + routine treatment	Azithromycin + routine treatment	14	
Zhu Haiyan [15]	2017	90	45/45	Qingre Jiedu prescription + azithromycin	Azithromycin	28	
Wang Zhengkuan [16]	2018	66	33/33	Oral Chinese medicine treatment + methylprednisolone + routine treatment	Methylprednisolone + routine treatment	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Yang Huirong [17]	2018	79	41/38	Qingre Jiedu prescription + lung-vesicle lavage	Lung-vesicle lavage + routine treatment	5–7	
Zhang Baozhen [18]	2018	134	67/67	Qingre Xiaotan Yangyin prescription + glucocorticoid	Glucocorticoid	7	
He Weichao [19]	2020	116	59/57	Qingre Jiedu prescription + erythromycin	Erythromycin	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Zhang Weijie [20]	2020	92	50/42	Huanglian Jiedu decoction combined with Maxing Shigan decoction + erythromycin + ambroxol + low-dose methylprednisolone + budesonide nebulization	Erythromycin + ambroxol + low-dose methylprednisolone + budesonide nebulization	14	
Liu Xiaomin [21]	2020	60	30/30	Futan Tongluo decoction + routine treatment	Azithromycin + routine treatment	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Ma Yingxiang [22]	2020	120	60/60	Xiao'er Chiqiao Qingre granules + methylprednisolone	Methylprednisolone	14	
Wang Shuling [23]	2020	120	60/60	Jingjing decoction combined with Maxing Shigan decoction plus/minus modification + methylprednisolone	Lianhua Qingwen granules + methylprednisolone	14	
Li Wenhui [24]	2021	61	31/30	Moxibustion + azithromycin + methylprednisolone	Azithromycin + methylprednisolone	21	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Liu Lili [25]	2021	102	51/51	Qingre Runfei patch + gamma globulin + routine treatment	Gamma globulin + routine treatment	30	
Yang Huirong [26]	2021	60	30/30	Qingre Jiedu prescription + azithromycin + methylprednisolone + lung-vesicle lavage	Azithromycin + methylprednisolone + lung-vesicle lavage	5	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Gao Lina [27]	2022	84	42/42	Jingjing decoction combined with Maxing Shigan decoction plus/minus modification + azithromycin + routine treatment	Azithromycin + routine treatment	14	
Yang Huirong [28]	2022	87	45/42	Qingre Jiedu Qutan prescription + azithromycin + lung-vesicle lavage	Azithromycin + lung-vesicle lavage	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Liu Xuelian [29]	2022	96	48/48	Jinzhen oral liquid + methylprednisolone + routine treatment	Methylprednisolone + routine treatment	14	
Zhang Xiao [30]	2022	65	33/32	Qingfei Huatan prescription + azithromycin + routine treatment	Azithromycin + routine treatment	14	
Yu Suping [31]	2022	95	47/48	Qingbei Jingjing decoction + azithromycin + routine treatment	Azithromycin + routine treatment	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Shi Li [32]	2022	72	36/36	Futan Tongluo decoction + acupoint application + routine treatment	Azithromycin + glucocorticoid + routine treatment	14	
Yang Huirong [33]	2022	60	30/30	Qingre Jiedu prescription + azithromycin + methylprednisolone + flexible bronchoscopy intervention	Azithromycin + methylprednisolone + flexible bronchoscopy	7	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Li Qianqian [34]	2023	96	48/48	Feining Paidu decoction + azithromycin + methylprednisolone + routine treatment	Azithromycin + methylprednisolone + routine treatment	7	
Tu Yana [35]	2023	98	49/49	Jiedu Quxie Fuzheng prescription + azithromycin + routine treatment	Azithromycin + routine treatment	14	
Gan Xiquan [36]	2023	100	50/50	Jinzhen oral liquid + interferon nebulization + routine treatment	Interferon nebulization + routine treatment	7	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Zeng Wanju [37]	2024	88	44/44	Xuanfei Qutan Touya prescription + routine treatment	Azithromycin + routine treatment	14	
Chen Hongrui [38]	2024	150	75/75	Maxing Shigan decoction combined with Qingjin Huatan decoction plus/minus modification + azithromycin + methylprednisolone + lung-vesicle lavage	Azithromycin + methylprednisolone + lung-vesicle lavage	14	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Shan Ruijing [39]	2024	60	30/30	Maganmixture plus/minus modification + lung-vesicle lavage + routine treatment	Lung-vesicle lavage + routine treatment	10	
Li Shanshan [40]	2024	92	46/46	Qingxuan Zhike granules + methylprednisolone	Methylprednisolone	7	
Liu Min [41]	2024	65	33/32	Futan pills + azithromycin + routine treatment	Azithromycin + routine treatment	14	
Su Dan [42]	2024	80	40/40	Maxing Shigan decoction + erythromycin	Erythromycin	7–10	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Xiao Yuyao [43]	2024	73	36/37	Pediatric massage + azithromycin + routine treatment	Azithromycin + routine treatment	8	
Zhao Shuyi [44]	2024	81	41/40	Xuanfei Qutan Touya prescription + azithromycin	Azithromycin	14	
Jin Fei [45]	2025	105	53/52	Qingre Huatan prescription + azithromycin + montelukast + routine treatment	Azithromycin + montelukast + routine treatment	21	

First author	Publication year	Sample size (cases)	Observation group / control group	Intervention measures—observation group	Intervention measures—control group	Course (d)	Outcome indicators
Zhang He [46]	2025	296	148/148	Jinzhen oral liquid + josamycin hydrochloride + routine treatment	Josamycin hydrochloride + routine treatment	10	

Note: Outcome indicators are traditional Chinese medicine symptoms/signs, clinical symptoms and physical signs, physicochemical testing, safety events, long-term prognosis, economic evaluation, and others.

species), economic evaluation (1 type), and others (2 types). The top five outcome indicators by frequency were clinical efficacy (32 times, 84.21%), incidence of adverse reactions (25 times, 65.79%), defervescence time (24 times, 63.16%), time to disappearance of cough (23 times, 60.53%), and procalcitonin (19 times, 50.00%); see Table 5.

2.4.2 Primary and secondary outcome indicators

Among the literature included in this study, no study was found that clearly distinguished primary from secondary outcome indicators.

2.4.3 Reporting of outcome indicators by different intervention types

Among the 38 included studies, the top five outcome indicators with the highest frequencies were, in order, clinical efficacy, incidence of adverse reactions, defervescence time, time to disappearance of cough, and procalcitonin. In studies in which the intervention measures were oral Chinese medicine, external TCM treatment, and oral Chinese medicine combined with external TCM treatment, the top five reported items all included clinical efficacy and incidence of adverse reactions. In addition, studies of external TCM treatment also reported TCM syndrome scores, and studies of oral Chinese medicine combined with external

TCM treatment reported TCM symptom scores, time to disappearance of pulmonary rales, and C-reactive protein. The specific numbers of reports are shown in Table 6.

2.4.4 Reporting of clinical efficacy

Thirty-two studies

9–12, 14, 16, 18–25, 27–37, 39–43, 45–46

reported clinical efficacy, involving different expressions such as "clinical efficacy," "clinical effect," and "overall effective rate." Criteria for judging various types of efficacy appeared a total of 18 times; the most frequently used was the *Criteria for Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine*

48

(8 times, 21.05%); see Table 7.

2.4.5 Reporting of TCM syndrome efficacy

Seventeen studies reported TCM symptoms/syndromes; 8 studies

19, 30, 35–36, 41, 43, 45–46

reported criteria for evaluating TCM syndrome efficacy. The most commonly applied was the *Guiding Principles for Clinical Research of New Chinese Medicines*

49

(6 times, 15.79%); see Table 8.

2.5 Risk-of-bias assessment

(1) Generation of the random sequence: 24 studies

10–12, 14–15, 18, 21–25, 27, 30–33, 37, 39–45

were assessed as having low risk of bias; 14 studies

9, 13, 16–17, 19–20, 26, 28–29, 34–36, 38, 46

were assessed as having high risk of bias. (2) Allocation concealment: none mentioned it, and all were assessed as unclear. (3) Blinding of participants and researchers: none mentioned it, and all were assessed as unclear. (4) Blinding of outcome assessors: none mentioned it, and all were assessed as unclear. (5) Completeness of outcome data: 32 studies

9–16, 18–22, 25–29, 31, 33, 35–46

had complete outcome-data collection and were assessed as having low risk of bias; 6 studies

17, 23–24, 30, 32, 34

had incomplete data collection and were assessed as having high risk of bias. (6) Selective reporting of study results: all were judged to have low risk of bias. (7) Other sources of bias: none mentioned them, and all were assessed as unclear; see Table 9.

2.6 Ethical approval and informed consent

Among the 38 studies included this time, most studies conducted ethical review and informed-consent procedures in a standardized manner. Among them, 26 studies

12, 15, 17–21, 23, 25–30, 32–43

explicitly mentioned that approval had been obtained from the hospital ethics committee and that the study participants had signed informed-consent forms, accounting for 68.42%; 10 studies

9–11, 14, 16, 22, 24, 31, 45–46

only stated that the participants and their family members had signed informed-consent forms, without mentioning content related to ethical approval, accounting for 26.32%; only 2 studies

13, 44

did not describe matters related to ethical approval or informed consent, accounting for 5.26%. Overall, the vast majority of the included studies followed the ethical principles of clinical research and performed relevant informed-consent procedures; only a very small number of studies had incomplete reporting of ethical information.

Table 3 Western medical diagnostic criteria

Western medical diagnostic criteria	Frequency (times)	Percentage (%)
Expert Consensus on the Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia in Children (2015 Edition)	13	34.21

Western medical diagnostic criteria	Frequency (times)	Percentage (%)
Zhu Fu-tang Practice of Pediatrics	5	13.16
Practical Pediatrics	3	7.89
Expert Consensus on the Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia in Children (2023)	2	5.26
Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia	2	5.26
Chinese Expert Consensus on the Laboratory Diagnosis of Respiratory Tract Infection with Mycoplasma Pneumoniae in Children	2	5.26
Guidelines for the Management of Community-Acquired Pneumonia in Children	1	2.63
Pediatrics	1	2.63
Criteria for Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine	1	2.63

Table 4 TCM syndrome differentiation reference standard

TCM syndrome differentiation reference standard	Frequency (times)	Percentage (%)
Criteria for Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine	10	26.32
Expert Consensus on the Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Mycoplasma Pneumoniae Pneumonia in Children (2017)	4	10.52
Chinese Pediatrics	2	5.26
Interpretation of Guidelines for TCM Clinical Diagnosis and Treatment—Pediatric Diseases Volume	2	5.26
Modern TCM Pediatric Diagnostics and Therapeutics	1	2.63
Zhu Fu-tang Practice of Pediatrics	1	2.63
Guidelines for TCM Diagnosis and Treatment of Pediatric Pneumonia and Wheezing	1	2.63

TCM syndrome differentiation reference standard	Frequency (times)	Percentage (%)
Guidelines for the Diagnosis and Treatment of Common Diseases in TCM Pediatrics	1	2.63
Guiding Principles for Clinical Research of New Chinese Medicines (Trial)	1	2.63

3 Discussion

A total of 38 studies were included in this study. The outcome indicators involved multiple aspects, including TCM symptoms/syndromes, clinical symptoms and signs, physicochemical tests, safety events, long-term prognosis, and economic evaluation. The study showed that the system of clinical outcome indicators for RCTs of traditional Chinese medicine treatment of refractory mycoplasma pneumoniae pneumonia in children is still imperfect, with problems mainly in the following five aspects: (1) the primary and secondary status of outcome indicators is unclear; (2) the selection of outcome indicators is markedly heterogeneous; (3) TCM syndrome differentiation reference standards and efficacy-evaluation criteria are inconsistent; (4) reporting of economic-evaluation indicators shows a decreasing trend; (5) long-term prognostic indicators are scarce. In addition, the risk-of-bias assessment of the included literature showed that allocation concealment, blinding of participants and researchers, and blinding of outcome assessors were all not mentioned and were assessed as unclear. This means that the clinical efficacy data of the included studies may have a high degree of credibility, and interpretation of the analytical results for the reporting frequency of the above outcome indicators should be approached with caution.

Table 5 Reporting of outcome indicators

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
TCM symptoms / syndromes (17 times)	TCM syndrome score	12	31.58

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
TCM symptoms / syndromes (17 times)	TCM symptom score	4	10.53
TCM symptoms / syndromes (17 times)	TCM syndrome efficacy	1	2.63
Clinical symptoms and signs (113 times)	Clinical efficacy	32	84.21
Clinical symptoms and signs (113 times)	Time to fever resolution	24	63.16
Clinical symptoms and signs (113 times)	Time to disappearance of cough and wheezing	23	60.53
Clinical symptoms and signs (113 times)	Time to disappearance of pulmonary rales	15	39.47
Clinical symptoms and signs (113 times)	Reduction in cough and sputum	3	7.89
Clinical symptoms and signs (113 times)	Time to chest X-ray absorption	3	7.89
Clinical symptoms and signs (113 times)	Time to pulmonary imaging absorption	2	5.26
Clinical symptoms and signs (113 times)	Time to marked absorption on chest CT	2	5.26

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
Clinical symptoms and signs (113 times)	Clinical symptom score	2	5.26
Clinical symptoms and signs (113 times)	Pulmonary imaging score	2	5.26
Clinical symptoms and signs (113 times)	Time to disappearance of pleural effusion	1	2.63
Clinical symptoms and signs (113 times)	Time to disappearance of wheezing sounds	1	2.63
Clinical symptoms and signs (113 times)	Time to disappearance of dyspnea	1	2.63
Clinical symptoms and signs (113 times)	Time to disappearance of pulmonary signs	1	2.63
Clinical symptoms and signs (113 times)	Time to disappearance of pulmonary shadows	1	2.63
Physicochemical tests (113 times)	Procalcitonin	19	50.00
Physicochemical tests (113 times)	C-reactive protein	16	42.10
Physicochemical tests (113 times)	Tumor necrosis factor-α	12	31.58
Physicochemical tests (113 times)	Lung function	10	26.31
Physicochemical tests (113 times)	Erythrocyte sedimentation rate	8	21.05

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
Physicochemical tests (113 times)	Total white blood cell count	7	18.42
Physicochemical tests (113 times)	T lymphocytes	6	15.79
Physicochemical tests (113 times)	γ-interferon	6	15.79
Physicochemical tests (113 times)	Lactate dehydrogenase	5	13.16
Physicochemical tests (113 times)	Coagulation indicators	4	10.53
Physicochemical tests (113 times)	降钙素原	2	5.26
Physicochemical tests (113 times)	Neutrophils	2	5.26
Physicochemical tests (113 times)	Immunoglobulin	2	5.26
Physicochemical tests (113 times)	Serum ferritin	2	5.26
Physicochemical tests (113 times)	High-sensitivity C-reactive protein	1	2.63
Physicochemical tests (113 times)	Platelets	1	2.63
Physicochemical tests (113 times)	Myocardial enzyme profile	1	2.63
Physicochemical tests (113 times)	Soluble B7-H3	1	2.63

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
Physicochemical tests (113 times)	T-cell immunoglobulin mucin molecule 3	1	2.63
Physicochemical tests (113 times)	High-mobility group box protein B1 (HMGB1)	1	2.63
Physicochemical tests (113 times)	Soluble triggering receptor expressed on myeloid cells 1 (sTREM-1)	1	2.63
Physicochemical tests (113 times)	Cysteinyl leukotrienes (CysLTs)	1	2.63
Physicochemical tests (113 times)	Monocyte chemoattractant protein-4 (MCP-4)	1	2.63
Physicochemical tests (113 times)	Neutrophil elastase (NE)	1	2.63
Physicochemical tests (113 times)	Cathepsin G	1	2.63
Physicochemical tests (113 times)	CXC chemokine ligand	1	2.63
Safety events (25 times)	Incidence of adverse reactions	25	65.79
Long-term prognosis (2 times)	Readmission rate	1	2.63
Long-term prognosis (2 times)	Rate of recurrent respiratory tract infection	1	2.63
Economic evaluation (8 times)	Length of hospital stay	8	21.05

Indicator domain	Indicator name	Frequency (times)	Percentage (%)
Other (4 times)	Bacterial load of *Mycoplasma pneumoniae*	3	7.89
Other (4 times)	Main quality-of-life score	1	2.63

Table 6 Top five reported outcome indicators by intervention type

Intervention type	Outcome indicator name	Number of reports
Oral Chinese medicine	Clinical efficacy	26
Oral Chinese medicine	Incidence of adverse reactions	21
Oral Chinese medicine	Time to fever resolution	20
Oral Chinese medicine	Time to disappearance of cough and wheezing	19
Oral Chinese medicine	Procalcitonin	19
External treatment with Chinese medicine	Clinical efficacy	3
External treatment with Chinese medicine	Time to fever resolution	3
External treatment with Chinese medicine	Time to disappearance of cough and wheezing	3
External treatment with Chinese medicine	Incidence of adverse reactions	2
External treatment with Chinese medicine	TCM syndrome evaluation	2
Oral Chinese medicine combined with external treatment with Chinese medicine	Clinical efficacy	3

Intervention type	Outcome indicator name	Number of reports
Oral Chinese medicine combined with external treatment with Chinese medicine	Incidence of adverse reactions	2
Oral Chinese medicine combined with external treatment with Chinese medicine	TCM symptom score	2
Oral Chinese medicine combined with external treatment with Chinese medicine	Time to disappearance of pulmonary rales	2
Oral Chinese medicine combined with external treatment with Chinese medicine	C-reactive protein	2

Table 7 Criteria for clinical efficacy

Criteria for judging clinical efficacy	Frequency (times)	Percentage (%)
Criteria for Diagnosis and Efficacy of Diseases and Syndromes in Traditional Chinese Medicine	8	21.05
Guiding Principles for Clinical Research of New Chinese Medicines	4	10.53
Criteria for Diagnosis and Efficacy of Clinical Diseases and Syndromes in Traditional Chinese Medicine	3	7.89

Criteria for judging clinical efficacy	Frequency (times)	Percentage (%)
Guidelines for Diagnosis and Treatment of Pediatric Pneumonia and Asthma with Chinese Medicine	1	2.63
Zhu Futang Practice of Pediatrics	1	2.63
Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Mycoplasma Pneumoniae Bronchitis in Children (formulated in 2017)	1	2.63

Table 8 Chinese medicine syndrome efficacy criteria

Criteria for Chinese medicine syndrome efficacy	Frequency (times)	Percentage (%)
Guiding Principles for Clinical Research of New Chinese Medicines	6	15.79
Criteria for Diagnosis and Efficacy of Diseases and Syndromes in Traditional Chinese Medicine	1	2.63

Criteria for Chinese medicine syndrome efficacy	Frequency (times)	Percentage (%)
Essentials for Clinical Diagnosis and Treatment in Internal Medicine of Traditional Chinese Medicine	1	2.63

Table 9 Risk of literature bias assessment [items (%)]

Evaluation item	Low risk of bias	High risk of bias	Unclear
Random sequence generation	24 (63.16)	14 (36.84)	0
Allocation concealment	0	0	38 (100.00)
Blinding of participants and researchers	0	0	38 (100.00)
Blinding of outcome assessors	0	0	38 (100.00)
Completeness of outcome data	32 (84.21)	6 (15.79)	0
Selective reporting	38 (100.00)	0	0
Other sources of bias	0	0	38 (100.00)

···methods and allocation concealment are absent on a large scale, which is an important reason for the insufficient commonality of RCTs in this field and directly affects the reliability of the statistical results for existing outcome indicators. This study covers the literature of the past 10 years. With the deepening of modern medicine' s understanding of the pathogenesis of RMPP and the iteration of treatment regimens—such as the widespread use of tetracyclines after macrolide resistance and glucocorticoids—the selection of indicators shows obvious temporal evolution. Below, data from the two periods of 2015–2019 and 2020–2025 are combined to conduct an in-depth analysis of the core issues and evolutionary trends.

3.1 Limitations of outcome indicators

3.1.1 Unclear primary and secondary outcome indicators Outcome indicators directly reflect the study purpose and affect the estimation of sample size, study duration, and cost in clinical research[^50]. Reasonable and correct outcome indicators help improve the scientific nature of research protocols and make the selection of clinical treatment regimens and the evaluation of therapeutic effects more precise and rational. Inflammatory response and immune dysfunction are the core pathogenic mechanisms of RMPP. Interleukins and C-reactive protein are common indicators for evaluating inflammatory responses; among them, interleukins play important regulatory roles in inflammatory responses, participate in immune-cell activation, and rise abnormally

when inflammatory reactions occur in human tissues. Clinical efficacy, fever, and cough duration, as the main symptoms in children, are highly sensitive in reflecting the effect of clinical treatment. Because of the problem of macrolide resistance, after 2019 most studies used tetracyclines (minocycline), glucocorticoids (methylprednisolone), and bronchoalveolar lavage in the control group. Since the above drugs have relatively significant adverse reactions, while paying attention to efficacy, researchers also included the incidence of adverse reactions as an important outcome indicator. For the above reasons, most researchers used interleukins, C-reactive protein, clinical efficacy, fever, cough duration, and incidence of adverse reactions as outcome indicators. Although the above indicators were selected by most studies, all 38 articles did not clearly distinguish between primary and secondary outcome indicators, and there were many cases in which multiple outcome indicators were listed. This suggests that although clinical studies of traditional Chinese medicine treatment for RMPP emphasize the selection of outcome indicators, a clear and unified core outcome set has not yet been formed. Such a disordered situation will undoubtedly cause difficulties for subsequent studies, making it difficult to accurately guide the selection of clinical treatment regimens and the evaluation of therapeutic effects. Therefore, it is necessary to improve the establishment of a core outcome set for RCTs of traditional Chinese medicine treatment for this disease, so that subsequent researchers can accurately guide the selection of clinical treatment regimens and the evaluation of treatment effects, thereby improving the quality of clinical trials of traditional Chinese medicine treatment for RMPP.

3.1.2 Marked heterogeneity in the application of outcome indicators
Among the 50 indicators compiled in this study, the number of secondary indicators reported cumulatively ( )3 times was 32 (64.00%), and the number of outcome indicators reported only once was 21 (42.00%). These data fully indicate that no consensus has yet been reached in the selection of outcome indicators for similar studies. The reasons for this phenomenon are multidimensional, mainly including the following aspects. (1) Differences in types of intervention measures: intervention methods such as oral Chinese medicine, external treatment with traditional Chinese medicine (acupoint application, massage), and oral Chinese medicine combined with external traditional Chinese medicine correspond to markedly different efficacy indicators. External therapies such as acupoint application and massage mainly improve local pulmonary signs and traditional Chinese medicine syndromes, and related studies tend to focus more on TCM syndrome scores and the disappearance time of clinical symptoms; whereas combined internal and external treatment takes into account both systemic and local efficacy, and the outcome indicators include multiple dimensions such as physicochemical indicators, TCM syndromes, and pulmonary rales. The differences in interventions further widen the differences in the selection of different research indicators. (2) Differences in research objectives and treatment course: short-course (( )7 d) studies mostly focus on acute-phase indicators such as fever reduction and cough, whereas long-course (( )21 d) studies pay more attention

to pulmonary function and long-term prognosis. (3) Differences in age stratification and TCM syndrome types among children: children in different age groups and with different TCM syndrome types have different symptom characteristics, and the selected indicators therefore also differ. (4) Obvious temporal evolution characteristics: early studies from 2015 to 2019 mostly selected common clinical indicators, such as erythrocyte sedimentation rate and neutrophils[^11,^16]. However, after entering 2020–2025, related studies no longer used these as observation indicators; instead, new outcome indicators appeared, such as neutrophil elastase (NE), tissue proteinase G[^44], cysteinyl leukotrienes (CysLTs), and monocyte chemoattractant protein-4 (MCP-4)[^45]. This reflects that, with the development of detection methods, clinical research is gradually exploring new outcome indicators and shows a developmental trend toward precise molecular inflammatory indicators. In addition, after 2020, with the increase in clinical trials of traditional Chinese medicine treatment for RMPP, researchers have paid greater attention to indicators related to TCM syndrome scores, and the number of reports has increased significantly compared with the previous stage. (5) Uneven medical resources: constrained by objective conditions such as hospitals' basic equipment and medical level, for example, studies in primary hospitals may find it difficult to carry out "pulmonary function assessment" because of the lack of pulmonary function testing instruments; molecular indicators such as CysLTs and MCP-4[^45] have high requirements for laboratory hardware and personnel, so laboratory departments in primary hospitals often do not carry them out routinely. This also reflects from the side that, in medical research, the uneven distribution of resources affects the standardization of outcome indicators. Therefore, when setting outcome indicators, it is necessary to further explore more universal physicochemical indicators, improve the feasibility of indicators, set the number of indicators reasonably, and reduce the waste of scientific research and medical resources, thereby promoting the unification and improvement of outcome indicators.

3.1.3 Non-uniform reference standards for TCM syndrome differentiation and efficacy evaluation standards Twenty-three studies[^15,^19–^21,^23–^34,^36,^38,^41,^43–^46] reported reference standards for TCM syndrome differentiation. The most commonly used was the *Criteria for Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine*[^48] (10 times, 26.31%). Eight studies[^19,^30,^35–^36,^41,^43,^45–^46] included TCM syndrome therapeutic-effect standards; the most commonly used was the *Guiding Principles for Clinical Research of New Chinese Medicines*[^49] (6 times, 15.79%). However, when each study evaluated this indicator, the symptom manifestations on which it was based were not entirely the same. Therefore, differences in TCM syndrome differentiation and therapeutic-effect evaluation standards occurred. This is very likely because TCM syndrome differentiation and treatment advocates individualized treatment, causing large differences in intervention measures and increasing the difficulty of TCM clinical efficacy evaluation[^51]. From the perspective of the

inheritance and development of TCM, while maintaining the characteristics of individualized TCM treatment, attention should be paid to outcome indicators that can reflect the TCM holistic view and the characteristics of syndrome differentiation and treatment. In view of the current problems of fragmented TCM syndrome indicators and inconsistent names, the specific plan is as follows. (1) Standardize the nomenclature of syndrome indicators: uniformly name "TCM syndrome score, TCM symptom score, and TCM syndrome evaluation score" as "TCM syndrome score," and unify the scoring items on the basis of the *Guiding Principles for Clinical Research of New Chinese Medicines*[ˆ49] (primary symptoms: cough, fever, wheezing, asthma; secondary symptoms: tongue coating and pulse manifestation, thirst, stool); (2) formulate quantitative rules according to syndrome type: for the two most common syndrome types in this study, phlegm-heat obstructing the lung and toxic heat obstructing the lung, develop dedicated rating scales; (3) establish syndrome···

Indicator candidate pool: In the future, the Delphi method can be tried to integrate the opinions of Chinese and Western medicine experts and formulate a candidate pool of effective Chinese medicine indicators that takes both individualization and standardization into account. Subsequent researchers can select indicators from it, reducing the fragmentation caused by self-designed indicators; (4) increase indicators reflecting the characteristics of Chinese medicine, quality of life, and overall condition.

3.1.4 Economic evaluation indicators show a decreasing trend in reporting

This study showed that economic evaluation indicators (mainly length of hospital stay) were reported a total of 8 times (21.05%). According to segmented statistics by time axis: 3 times in 2015–2019, and the remaining 5 times were concentrated in 2020–2022 (belonging to 2020–2025). In studies published after 2022, they were no longer discussed separately as outcome indicators, suggesting that economic indicators showed a marked decreasing trend over time. This change may be because the clinical treatment protocols for RMPP have gradually matured and the average length of hospital stay has become more stable, so its sensitivity for distinguishing the effects of different treatment regimens has decreased. In addition, researchers' attention may have shifted more toward indicators that more clearly reflect therapeutic effects, such as improvement of clinical symptoms, objective physicochemical indicators, and safety events, while relatively insufficient importance has been attached to health economic indicators. However, the authors believe that the application of health economic indicators is of great significance to both doctors and patients and to related research. From the physician' s perspective, they can comprehensively consider the choice of treatment regimen, making the regimen more economical and effective; from the patient' s perspective, they can make it easier for patients to accept and cooperate with treatment, thereby improving the effectiveness of clinical treatment. Therefore, it is recommended that future studies appropriately

include economic indicators such as length of hospital stay and direct medical costs in the outcome indicator system, so as to comprehensively evaluate the overall benefits of Chinese medicine treatment for RMPP.

3.1.5 Long-term prognosis indicators are scarce

Among the 38 studies included in this study, none mentioned follow-up status, and only 1 study

[13]

reported long-term prognostic indicators (rehospitalization rate and recurrent respiratory tract infection rate), accounting for an extremely low proportion. On the one hand, this may be related to the short treatment courses selected in the relevant RCTs. The duration of intervention treatment included in this study ranged from 5 to 30 d, and there were only 5 studies with longer-term duration of ( )21 d

[13, 15, 24–25, 45]

. Researchers were unable to complete collection of prognostic indicators within the short course of treatment. On the other hand, this reflects the general lack of standardized post-discharge follow-up design in current clinical trials and the lack of follow-up visits and tracking of patients. Until now, most studies have focused on short-term prognostic indicators such as the clinical symptoms of the disease and laboratory indicators, with relatively little attention paid to the long-term prognosis of the disease. Children with RMPP are at risk of long-term complications such as lung function impairment and recurrent respiratory tract infections. Focusing solely on short-term efficacy is insufficient to comprehensively reflect the therapeutic value of Chinese medicine. From the perspective of patients' long-term health and quality-of-life protection, paying attention only to short-term indicators may ignore potential risks and is not conducive to implementing complete rehabilitation plans or comprehensively evaluating treatment effects. It is recommended that future study designs include follow-up of at least 3 months to assess long-term prognostic indicators such as recovery of pulmonary function, incidence of recurrent infections, and quality of life.

3.2 Limitations of this study

3.2.1 Study bias caused by blinding and lack of allocation concealment

All 38 studies included in this study were rated as unclear because they did not mention allocation concealment, blinding of participants and researchers, or blinding of outcome assessors. This is a core methodological limitation of this study. First, no allocation concealment can easily lead to selective enrollment. Researchers may artificially screen mildly ill children into the observation group, shortening the time to fever resolution and cough disappearance and causing an inflated clinical effective rate. Second, Chinese medicine dosage forms (decoctions, plasters, tuina) differ significantly from Western medicines in appearance and administration method, making it difficult to implement double blinding

clinically. After researchers and family members of the children know the grouping, they are likely to subjectively and preferentially evaluate subjective outcome indicators such as cough and sputum, causing distortion in Chinese medicine syndrome scores and clinical effective-rate results. Finally, if outcome assessors are not blinded, they may tend to observe improvements in theoretical indicators in the observation group, causing intergroup differences in theoretical indicators to be exaggerated. The above methodological defects cause systematic bias in the utilization rates and effectiveness data of the indicators counted in this study based on existing literature, and they cannot completely and objectively reflect the true efficacy of Chinese medicine and the rules for indicator selection. Subsequent RMPP clinical trials can explore the implementation of protocols such as comfort-agent Chinese medicines and simulated plasters to improve randomized allocation concealment schemes, reduce outcome-assessment bias, and ensure that outcome-indicator data are true and reliable.

3.2.2 Lack of ethics approval and informed consent reporting

Among the 38 studies, 2

$$13, 44$$

did not report ethics or informed-consent content, and 10

$$9–11, 14, 16, 22, 24, 31, 45–46$$

only reported informed consent and lacked ethics approval. First, the lack of reporting on ethics approval and informed consent does not conform to the requirements for clinical research and violates the *Declaration of Helsinki* and China' s *Quality Management Standard for Drug Clinical Trials*. Study trial protocols not subject to ethics supervision lack institutional constraints to protect participants' rights and interests, privacy, and protection against accidental injury. Second, studies lacking ethics approval are at risk of non-standard enrollment screening of participants. Selective enrollment may occur, causing case-selection bias and indirectly causing bias in outcome-indicator results such as effective rate and time to symptom improvement, thereby reducing the reliability of research findings. The above limitations suggest that when subsequently summarizing the core outcome indicator set for RMPP, it is necessary to combine RCT data with complete high-quality ethical documentation.

3.2.3 Single study type and small sample size

The types of studies analyzed were relatively single; only RCTs were included, and no comparative analysis was conducted on literature of other different study types. Moreover, only studies related to the past 10 years were included. The sample sizes of the literature included in this study were mainly small and medium-sized, with a lack of multicenter, large-sample clinical controlled studies, and the universality and representativeness of the conclusions were relatively poor. Because of the large time span, modern medicine' s understanding of

RMPP and treatment regimens have changed, resulting in large differences in the indicators used across different studies; it is difficult to conduct horizontal comparisons or combined analyses of similar study results. The analytical results obtained in this study are limited to some extent in terms of the number, years, types, and quality of included literature, and there is a lack of more in-depth exploratory research; they still cannot cover all clinical outcome indicator types for RMPP. Therefore, it is necessary to further improve related studies to enhance the clinical guiding value of the above outcome indicators and thereby promote consensus.

4 Summary

In clinical work and research, the selection of outcome indicators has important guiding significance for evaluating the effects of treatment regimens and judging disease prognosis, and is an important issue that clinical researchers need to consider

52

. Based on the analysis results of this study, the top five reported indicators—clinical efficacy, incidence of adverse reactions, time to fever resolution, time to cough disappearance, and interleukins—can be used as core

outcome indicator set. However, owing to the limitations of this study, the importance of the outcome indicators was not reported. In the future, further research is still needed on the construction of a core indicator set for TCM treatment of RMPP. Meanwhile, clinical workers need to further explore, closely integrate the latest advances in modern medical understanding of diseases and innovations in clinical testing technologies, explore new indicators, and, at appropriate times, attach importance to and strengthen reporting of health-economics evaluation indicators and long-term prognosis indicators, so as to promote the standardized development of clinical research on traditional Chinese medicine.

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The authors declare no conflicts of interest.

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