

# *A Meta-analysis of the Efficacy and Safety of TCM Intestinal Cleansing Method on Sputum Fever AECOPD*

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**Abstract:** Objective: This article systematically reviews the efficacy and safety of TCM Intestinal Cleansing Method in the treatment of acute exacerbation of chronic pulmonary obstructive pulmonary disease, and provides clinical reference for the treatment of acute exacerbation of chronic obstructive pulmonary disease. Methods: A computer search of the major databases such as China Knowledge Network (CNKI), VIP, WanFang, CBM, PubMed, Embase, and Cochrane (January 1995-July 2022) was conducted to collect the results of a randomized controlled trial on the use of TCM Intestinal cleansing method combined with western medicine treatment compared with western medicine treatment alone in the acute exacerbation of the chronic obstructive pulmonary disease. Conclusion: The TCM Intestinal cleansing method combined with western medicine treatment can improve the lung function of patients with acute exacerbation of chronic obstructive pulmonary disease and provide new ideas for the treatment of patients with acute exacerbation of the chronic obstructive pulmonary disease.

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) refers to the sudden and rapid deterioration of symptoms in patients with COPD in a short period of time, which makes cough, asthma, fever and other symptoms significantly worse than before <sup>[1]</sup>. The number of deaths due to COPD in China accounts for 31.1% of the world's deaths of the same cause, and COPD patients have about 0.5~3.5 acute exacerbations every year, and the acute onset of chronic obstructive pulmonary disease is the most important cause of death <sup>[2]</sup>. Western medicine often uses antibiotics, phlegm-reducing drugs and other treatments for the acute exacerbation of COPD, which can cause intestinal flora disorders and phlegm-reducing drugs can not eliminate the production of sputum. According to clinical case statistics, among several common types of AECOPD, phlegm fever lung evidence is the most common symptom type of AECOPD<sup>[3]</sup>. COPD lung lung deficiency for a long time, external evil attack lung injury, refining into phlegm, depression and fever, phlegm fever, or the patient's body phlegm dampness, daily fever, phlegm fever lung obstruction of the airway, lungs and large intestine as each other, phlegm heat stagnant, qi machine blockage, heat evil downward shift, colon intestines, intestinal qi blockage, intestinal conduction loss, qi machine up, aggravate cough, phlegm, asthma and other symptoms. If in the treatment of AECOPD, blindly clear the lungs and heat and dissolve phlegm fever, the effect will not be ideal. The use of the

method of tong, clearing up and down, so that the internal qi is smooth, the lungs are hot and diarrhea, the phlegm is hot, and the lungs are declared, which can reduce the symptoms of AECOPD and improve the condition. At present, many RCTs and animal experiments have proved that TCM can effectively improve the symptoms and lung function of AECOPD during acute attacks <sup>[4]</sup>. In order to further provide evidence-based evidence for clinical treatment, a clinical randomized controlled trial on the treatment of AECOPD by TCM is collected for systematic review, and the results are reported as follows.

## 1. Information and Methods

### 1.1. Inclusion Criteria

(1) Research type: A randomized controlled trial publicly published domestically and internationally on the use of traditional Chinese medicine for the treatment of AECOPD with phlegm heat stagnation in the lung syndrome. (2) Research object: The diagnostic criteria of Western medicine refer to the "Chinese Expert Consensus on the Diagnosis and Treatment of Acute exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) (2017 updated version)", or the "Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2013 revised version)", and in the short term, symptoms such as dyspnea, cough, expectoration, and chest tightness worsen. The presence of mucopurulent sputum in large quantities indicates bacterial infection, and dry and/or wet rales can be heard during lung auscultation; May be accompanied by fever. The diagnostic criteria for traditional Chinese medicine refer to the "Diagnosis Criteria for Traditional Chinese Medicine Syndromes of Chronic Obstructive Pulmonary Disease (2011 Edition)". Phlegm heat obstructing the lung syndrome is characterized by cough, fever, thirst, yellow phlegm or blood in the phlegm, wheezing, chest tightness, abdominal distension and pain, dry mouth, dry tongue, stool nodules, short and red urine, red tongue, yellow and greasy fur, and smooth pulse. Adult (age $\geq$ 18 years old) patients who meet the above diagnostic criteria, regardless of gender. (3) Intervention measures: Both groups of patients were given routine symptomatic treatment with Western medicine. The observation group is based on Western medicine treatment and combined with a prescription or classic formula (such as Chengqi Tang) that specifies the application of traditional Chinese medicine to clear the internal organs <sup>[12]</sup> as the main Chinese medicine formula. The treatment method (such as oral administration, acupoint application, enema, etc.) is also indicated. The control group is mainly treated with Western medicine, with or without placebo. (4) Outcome indicators: ① The main outcome indicator is the total clinical effective rate; ② Secondary outcome indicators were pulmonary function indicators, including the percentage of forced expiratory volume in the first second to forced vital capacity [FEV1/FVC (%)]; ③ Serum inflammatory factor (IL-6)

### 1.2. Exclusion Criteria

(1) Repeatedly published Chinese and English literature; (2) Non clinical trial studies such as reviews, animal trials, personal clinical experience summaries, theoretical explanations, and evaluative articles; (3) No randomized or semi randomized controlled controlled trials; (4) Research with unclear diagnostic and therapeutic criteria.

### 1.3. Literature Search Strategy

Computer search of seven major databases, including China National Knowledge Infrastructure (CNKI), VIP database, WanFang database, CBM, PubMed, Embase, and Cochrance, was conducted

from the establishment of the database until July 30, 2022, and references included in the literature were tracked. The Chinese database is searched using theme words, while the English database is searched using theme words and free words. The search period is from January 1, 1995 to July 1, 2022.

### 1.4. Data Extraction and Quality Assessment

Firstly, relevant literature searches were conducted on major databases based on pre-established search strategies to screen out duplicate studies.

Seven indicators in the Cochrane collaborative network evaluation tool: ① random allocation scheme; ② Hidden allocation scheme; ③ Blind method; ④ Result evaluation is blinded; ⑤ The completeness of the result data; ⑦ Other sources of bias: Apart from the above 6 points, are there any other factors that can cause bias. Each item is divided into three bias risk levels: "high risk", "low risk", and "uncertain".

### 1.5. Statistical Methods

Use the Review Manager 5.4 statistical software provided by the Cochrane collaborative network for data statistical analysis.

## 2. Results

### 2.1. Literature Search Results

The initial screening yielded a total of 354 articles related to the topic of the article, as follows: Zhiwang: n=93; Wanfang database: n=133; Wipu: n=37; Sinomed: n=88; PubMed: n=2; Medline: n=1. The information obtained was continuously screened to remove duplicates of a total of 150 articles, while excluding those that did not meet the criteria A total of 175 papers were removed, resulting in 29 papers. The full text of these papers was then analyzed in detail, resulting in the inclusion of 11 RCTs.<sup>[5-15]</sup> The literature was then analysed in detail, resulting in the inclusion of 11 RCTs. The basic information of the included studies is shown in Table 1, and the literature screening process and results are shown in Figure 1.

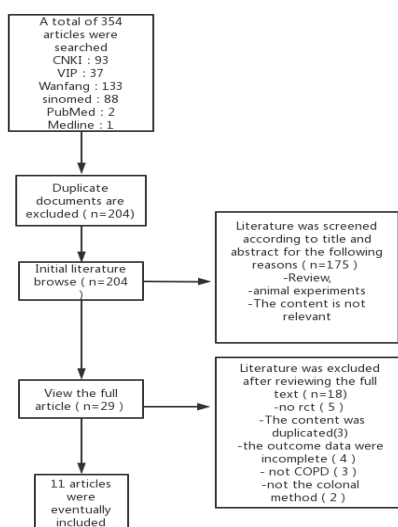


Figure 1: Flow chart of literature screening

Table 1: Inclusion of basic information about the literature

Note: 1: Total effective rate; 2:FEV1/FVC%; 3:IL-6;

Author/Y ear	Average age		Sample size (cases, m/f)		Interventions		Treatment time (d)	Closing indicators
	Test group	Control group	Test group	Control group	Test group	Control group		
Zhang Shan	73.930 ± 8.519	75.030±8.357	31 (18/13)	29 (13/16)	Enema with the formula of benefitting the qi and clearing the internal organs + western medical treatment	Western medical treatment	10	1,2
Liao Yu Sui	65.38±11.48	65.03±10.04	34 (26/8)	33 (24/9)	Mulberry Bark Soup with Xiao Cheng Qi Tang + Western Treatment	Western medical treatment	14	1,2
Lui Ming Sheng	78.03±10.07	75.39±9.35	28 (18/10)	28 (16/12)	Clearing heat, resolving phlegm and clearing internal organs with acupressure + Western medicine treatment	Western medical treatment	7	1
Li Li	54.37±9.23	53.35±7.35	30 (16/14)	30 (17/13)	Xuan Bai Cheng Qi Tang with Addition + Western Medicine Treatment	Western medical treatment	7	1,2
Cai Qiling	68.63±5.78	67.67±5.42	27 (16/11)	26 (14/12)	Xuan Bai Cheng Qi Tang with Addition + Western Treatment	Western medical treatment	10	1,2
Li Shufang	76.42±12.26	77.34 ±11.14	50 (29/21)	50 (32/18)	Tongxiao lung formula + Western medicine treatment	Western medical treatment + placebo	10	1
Cao Qingqing	70.86±7.18	70.23±4.38	48 (26/22)	48 (28/20)	Self-formulated formula for clearing the lungs and toning the internal organs + Western medical treatment	Western medical treatment	10	1,2,3
Feng Yuan	72.01±7.04	71.85±6.78	40 (26/14)	40 (24/16)	Clearing the lungs, resolving phlegm and clearing the internal organs + Western medicine treatment	Western medical treatment + placebo	10	1
Li Jing	54.60±3.30	57.50±4.10	46 (23/18)	46 (25/21)	Rhubarb powder 5g + Western medicine treatment	Western medical treatment	6	1
Xu Changqing	60.14±5.15	58.24±4.25	30 (23/7)	30 (25/5)	Adding Xingguo Chengqi Tang + Western Medicine Treatment	Western medical treatment	10	1
Zhao Hui	56.72±6.38	56.13±6.14	50 (29/21)	50 (28/22)	Enema with Phlegm Removal, Stasis Removal, and Internal Organ Removal Soup + Western Medical Treatment	Western medical treatment	14	1,2,3

## 2.2. Results of the quality evaluation of the included literature

The 11 RCTs<sup>[5-15]</sup> incorporated in this article are random methods, so there may be a selective bias evaluation as "low risk" due to random sequences; The allocation of allocation was adopted; 1<sup>[7]</sup> studied the blind method for subjects, experiments and data analysts; all studies did not describe the disclosure of research cases, and the data data was complete; all studies were not obviously selective descriptions The situation, so selectively describes the possibility of the report. In summary, the possibility of bias cannot be ruled out. See Figure 2 incorporated on the bias of the research.

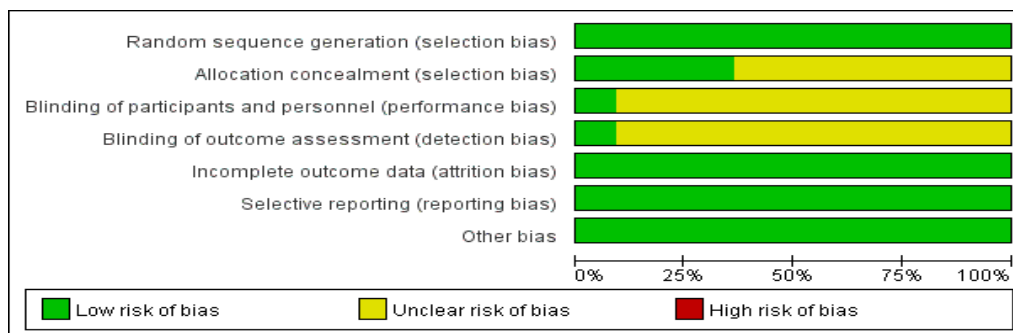


Figure 2: Risk of bias assessment

## 2.3 Clinical efficacy

### 2.3.1. Efficient

A total of 11<sup>[5-15]</sup> research reported the clinical effectiveness of the acute aggravation of chronic obstructive pulmonary disease in the treatment of chronic obstructive pulmonary disease. Each study has no statistical heterogeneity ( $P = 0.93$ ,  $I^2 = 0\%$ ), and uses a fixed effect model for META analysis. The results are shown in Figure 3,  $OR = 3.21$ ,  $95\%CI (2.17, 4.74)$ ,  $P < 0.00001$ , and in terms of treating chronic obstructive pulmonary disease in the period of acute aggravation of the acute aggravation of chronic obstructive pulmonary diseases, the traditional Chinese medicine method and conventional western medicine group are better than simple applications than simple applications The conventional western medicine group has statistically significant differences.

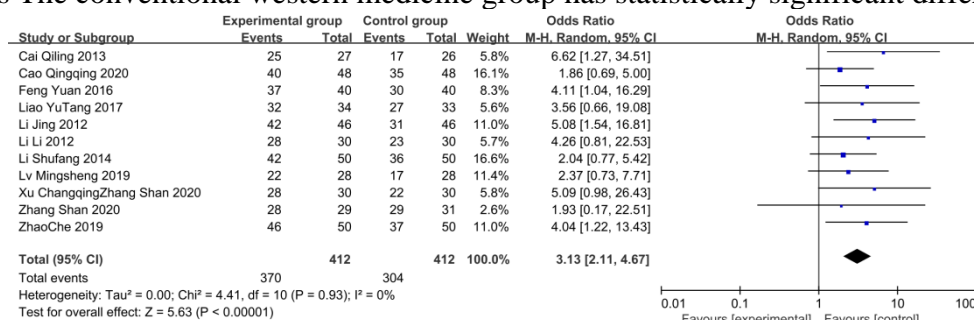


Figure 3: Efficient forest diagram

### 2.3.2 Lung function

FEV1/FVC%: 6 documents<sup>[5-8, 10, 14, 15]</sup> reported the situation of FEV1/FVC%, heterogeneity test results ( $i^2 = 68\%$ ,  $P = 0.007$ ) show that there are statistical sciences in each study. Heterogeneous, using a random effect model for METE analysis. Results were  $MD = 3.02$ ,  $95\%CI (0.57, 5.30)$ ,  $P = 0.009$ , and the difference was statistically significant. It is prompted that the improvement of

FEV1/FVC % of FEV1/FVC % is better than Western Medicine Treatment Group (Figure 4). Essence.

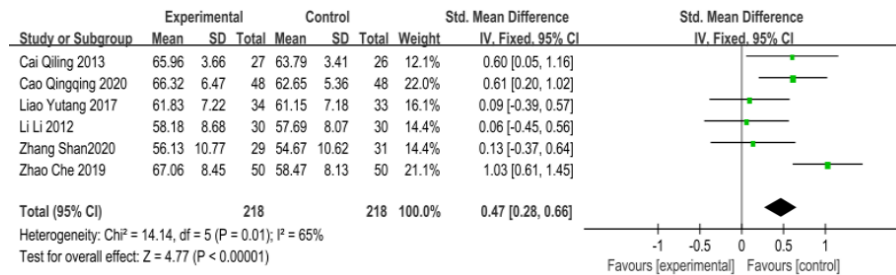


Figure 4: FEV1/FVC% forest plot

### 2.3.3 IL-6

A total of 2 literatures [10, 15] reported the situation of IL-6 in the observation group and the control group, and analyzed the difference before and after treatment. Heterogeneity test results ( $i^2 = 0\%$ ,  $P = 0.87$ ) display each. The research room has heterogeneity, so when performing META analysis, select a random effect model. The result was MD = 2.36, 95% CI (1.94, 2.79),  $P < 0.00001$ , the difference is statistically significant. It is prompted that the removal rate of the IL-6 is stronger than the Western Medicine Treatment Group (Figure 5) Essence.

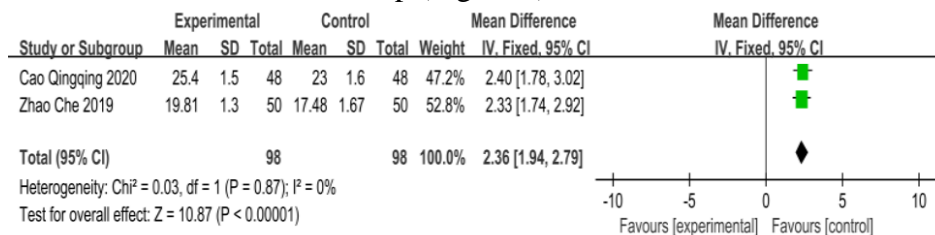


Figure 5: IL-6 forest diagram

### 2.3.4 Incidence of Adverse Reactions

None of the articles included reported adverse reactions such as blood routine, urine routine, routine faces, abnormal liver and kidney skills, and gastrointestinal dysfunction.

## 3. Discussion

The acute exacerbation of chronic obstructive pulmonary disease (COPD) belongs to the category of "lung distension" in Chinese medicine. The main clinical symptoms include shortness of breath and urgency, fever and constipation, congestion of phlegm and heat, yellow dryness of the moss or yellow slippage, and a large solid right-inch pulse. The pathogenesis of AECOPD is that the evil spirits offend the lung health, refining liquid into phlegm over time, or there is phlegm and saliva, which turns into heat over time, resulting in phlegm-heat congestion in the lung and obstruction of the lung qi, which depends on the lung qi. In modern medical research, the inflammatory response is an important mechanism for the development of AECOPD. During the acute exacerbation of the chronic obstructive pulmonary disease, the airway inflammatory response increases dramatically. IL-6 is a common pro-inflammatory factor released by the inflammatory response of AECOPD, which can promote the breakdown of the extracellular matrix and play an important role in airway remodeling, and is the main cause of lung injury. It has been demonstrated that levels of high mobility group protein (high mobility group protein B1, HMGB1) are elevated in

AECOPD and that HMGB1 induces an immune response that is a major cause of IL-6 production, and that the expression of HMGB1 can be inhibited by the drug topic, which regulates gut microbes. In contrast, the TCM method has been shown to promote the restoration of normal composition and function of the intestinal flora, regulate intestinal metabolites and improve the environment and function.

### 3.1 Summary of Results

The TCM method with conventional western medicine was significantly better than western medicine alone for symptomatic treatment in the aspects of overall efficiency, lung function (FEV1/FVC%) and IL-6. In terms of safety, no definite adverse reactions were reported in the included RCTs and further studies are still needed to prove this. The results of this study illustrate that in the development of AECOPD, the combination of Western medicine treatment with the TCM Intestinal cleansing method can increase the overall efficiency of treatment and enhance the lung function of patients and improve their clinical symptoms. It can be speculated that the TCM Intestinal cleansing method is used to increase the oxygen content in the body by enhancing intestinal dynamics, accelerating the excretion of toxic substances from the intestine, reducing the inflammatory response in the airways, and decreasing inflammatory factors such as IL-6. Reducing lung tissue damage and improving the symptoms of chronic obstructive pulmonary disease.

### 3.2 Sensitivity Analysis

Eleven studies reported the effectiveness of the TCM Intestinal cleansing method in combination with conventional Western medicine in the treatment of chronic obstructive pulmonary disease. 6 publications reported FEV1/FVC%, while other outcome indicators were more heterogeneous, which was considered to be due to the differences in treatment duration and measurement time between trials and the severity of patients' disease.

### 3.3 Limitations of the Study

The deficiencies of this meta-analysis are twofold: (1) The search included a small amount of literature, the sample size included was low and the quality was limited, no safety analysis was seen in the data, and no detailed documentation of missing and dislodged cases was available. (2) The variety of treatments included in the clinical trials in this paper and the lack of clarity in the specific selection and treatment methods prevented a uniform comparison to assess outcome indicators, which was considered one of the reasons for the high study heterogeneity.

In conclusion, the TCM method can effectively improve the symptoms of AECOPD phlegm-heat congestion, improve lung function, improve oxygen levels and other related indicators, and also open up a new way of treating other lung diseases with "lung and intestine".

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