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GUIDELINE

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Guidelines of integrated Chinese and western medicine for diagnosis and treatment of chronic obstructive pulmonary disease (2022)

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Abstract

Chronic obstructive pulmonary disease (COPD), with high prevalence rate, mortality, disability rate, and heavy disease burden, has become a critical chronic disease seriously threatening public health worldwide. Traditional Chinese medicine and Western medicine both have shown advantages in diagnosing and treating COPD, which has been widely applied in the clinics. In order to improve the diagnostic and treatment level for COPD with integrated traditional Chinese and Western medicine, the Guidelines of Integrated Chinese and Western Medicine for Diagnosis and Treatment of COPD were developed by the Internal Medicine Committee of the World Federation of Chinese Medicine Societies. First, a multidisciplinary working group was established. Development methods and processes of international clinical practice guidelines were adopted in the whole research. In final, a total of 13 recommendations for the diagnosis and treatment of COPD were established based on available evidence with the best quality. Meanwhile, characteristics of integrated traditional Chinese and Western medicine in treating COPD were taken into account with pros and cons of each intervention. The guidelines could be used as a reference for physicians in respiratory medicine departments (traditional Chinese medicine, integrated traditional Chinese and Western medicine, and Western medicine) at various levels of medical institutions in their diagnosis and treatment.

KEYWORDS
chronic obstructive pulmonary disease, clinical practice guideline, integrative medicine

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1 | INTRODUCTION

Chronic obstructive pulmonary disease (COPD) was a common, preventable, and treatable chronic airway disease. It was characterized by persistent airflow restrictions and corresponding respiratory symptoms, associated with airway and/or alveolar damage caused by harmful gases or particles.[1] COPD had become a critical chronic disease that seriously endangered human health due to its high prevalence, high mortality, high disability rate, and heavy disease burden.[2] Traditional Chinese medicine (TCM) and Western medicine (WM) had their respective advantages in diagnosing and treating COPD and were widely applied in clinical practice. In order to promote the improvement of the level of integrated medicine (TCM and WM) in the diagnosis and treatment of COPD, a research and development team was formed by the Internal Medicine Professional Committee of the World Federation of Chinese Medicine Societies, in conjunction with Henan University of Chinese Medicine, the First Affiliated Hospital of Henan University of Chinese Medicine, the Evidence-based Medicine Center of Lanzhou University, and other institutions. The research and development methods and processes followed international clinical practice guidelines based on the best available evidence, combined with the characteristics of integrated medicine in the treatment of COPD, and weigh the advantages and disadvantages of intervention measures. The "Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease by Integrated Traditional Chinese and Western Medicine" (hereinafter referred to as the "Guidelines") were formulated to provide references for the clinical practice of integrated medicine in the prevention and treatment of COPD. To promote the dissemination and implementation of these guidelines, we adjusted the structure and content in accordance with the requirements of the journal and revised, improved, and released based on the opinions of journal editors and review experts.

2 | METHODS

The design and formulate of this document were based on the "World Health Organization Guidelines Development Manual"[3] and "Integrated Chinese and Western Medicine Diagnosis and Treatment Guidelines Development Manual."[4] The recommendations in this guideline were formulated based on evidence from existing guidelines, systematic reviews, clinical studies and developed using the Grading of Recommendations Assessment Development and Evaluation (GRADE) criteria.[5] The guideline was followed the Reporting Items for Practice Guidelines in Healthcare (RIGHT) statement[6] for reporting.

2.1 | Establishment and registration

The World Federation of Chinese Medicine Societies reviewed and approved this guideline as a group standard in April, 2020. Then, it was registered bilingually in Chinese and English (No. IPGRP-2019CN052) on the International Practice Guideline Registration Platform (http://www.guidelines-registry.cn/).

2.2 | Establishment of working groups

Four major working groups were established for this guideline, including the methodology expert group, clinical expert group, evidence evaluation group and secretary group. Members included experts from different disciplines such as TCM, combined Chinese and Western medicine respiratory disease, guideline methodology, clinical pharmacology, and epidemiology.

2.3 | Selection and identification of clinical questions

The clinical questions to be answered in this guideline were selected through the QuestionnaireStar platform. The first round of questionnaires was conducted through an open-ended questionnaire survey from 128 clinicians at different levels in 18 provinces, cities, and autonomous regions across China. After removing duplicated questions, 22 clinical questions were initially collected. The second round of questionnaire survey invited 26 clinicians (including members of the World Federation of Chinese Medicine Societies, Respiratory Disease Branch of China Medical Association of Minorities, and the National Regional (Central China) Traditional Chinese Medicine Pulmonary Disease Diagnosis and Treatment Center) across China to evaluate the importance of the above clinical questions and the technical framework of the guideline. The specialists scored the clinical questions with a point of 1–5. The higher scores indicated more importance for the questions. Then, the questions were selected according to the scores. Finally, we screened out 13 clinical questions (average score > 3.5), shown in Table 1.

2.4 | Retrieval, evaluation, and grading of evidence

Evidence searches for specific clinical questions were conducted according to the included clinical questions and outcomes following the PICO (Population, Intervention, Control, Outcome) principles. Databases, including Pubmed, Embase, The Cochrane Library, China Biomedical Literature Database (CBM), China Knowledge Network (CNKI), WanFang Data, and VIP database, were all systematically searched until June 16, 2020. Systematic reviews and meta-analyses were first searched and the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool[7] was used to evaluate their methodological quality. When a clinical question lacked a corresponding systematic review, the original studies were searched and a new systematic review was performed.[7] In the original studies, the risk of bias was assessed using the risk of bias tool[8] for randomized controlled studies, the ROBINS-I (risk of bias in nonrandomized studies of interventions) tool[9] for nonrandomized controlled studies, and the case series studies

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TABLE 1 Final included clinical question lists.

NO.	Clinical questions
1	Dose integrated Chinese and Western medicine shows good curative effect and safety in the treatment of stable chronic obstructive pulmonary disease (COPD)?
2	When should we apply the integrated Chinese and Western medicine program intervene in the treatment of stable COPD?
3	What is the scheme and curative effect of integrated Chinese and Western medicine for the treatment of stable COPD patients with lung function at levels 1 and 2?
4	What is the scheme and curative effect of integrated Chinese and Western medicine for the treatment of stable COPD patients with lung function at levels 3 and 4?
5	On the basis of the standardized treatment with Western medicine, is TCM rehabilitation therapy effective and safe for stable COPD patients?
6	Is integrated Chinese and Western medicine effective and safe in the treatment of COPD patients with acute exacerbation (AECOPD)?
7	When should the integrated Chinese and Western medicine program intervene be applied in the treatment of AECOPD with acute exacerbation?
8	On the basis of the standardized treatment of Western medicine, is the TCM rehabilitation effective and safe for AECOPD patients?
9	Can the integrated scheme of Chinese and Western medicine reduce the patient's dosage or shorten the course of treatment on systemic glucocorticoids use in the treatment of AECOPD patients?
10	Can integrated Chinese and Western medicine reduce the use of antibiotics in the treatment of AECOPD patients?
11	Is the integrated Chinese and Western medicine program effective and safe in the treatment of AECOPD risk-window period?
12	Is the integrated Chinese and Western medicine program effective and safe in the treatment of the complications of COPD (such as respiratory failure and pulmonary hypertension)?
13	Does the integrated Chinese and Western medicine program have any advantages in health economics in the treatment of COPD patients?

TABLE 2 Quality of evidence and strength of recommendations.

Grade	Implication
High (A)	We were very confident that the predicted effect value is close to the real effect value.
Moderate (B)	We have medium confidence in the effect prediction: the prediction may be close to the real value, but it may also be very different.
Low (C)	Our grasp of the predicted value is limited: the predicted value may be very different from the real value.
Very low (D)	We have little confidence in the forecast: the forecast is likely to be very different from the real one.
Grade	**Implication**
Strong	Evidences clearly show that the benefits of intervention outweigh the risks or the risks outweigh the benefits.
Weak	The pros and cons were uncertain or the pros and cons were equal regardless of the quality of the evidences.

using the Case Series Methodological Quality Appraisal Tool (a quality appraisal tool for case series studies).[10] The evidence evaluation group graded the quality of evidence and strength of recommendation according to the Grading of Recommendations Assessment Development and Evaluation (GRADE) criteria developed in 2004,[5] resulting in an evidence summary table. The strength of the recommendation was classified into strong and weak recommendations. The criteria for grading the quality of evidence and the meaning of recommendation strength were shown in Table 2.

2.5 | Survey of recommendation

A modified Delphi method was used to reach consensus on some recommendations based on the questionnaires. The research was conducted on 26 senior-level TCM (12 specialists), Western (7 specialists), or integrated medicine (7 specialists) respiratory specialists from 18 provinces in China. According to the advice given by the specialists, a total of 13 recommendations reached a consensus in the end.

2.6 | Final draft and external review

The working group prepared a first draft document of the guidelines based on the recommendations and then formed an exposure draft after internal review. External review was also an essential process in ensuring the quality and effectiveness of a guideline. A specialist discussion meeting was held in Zhengzhou in April 2022. We also invited eight specialists (including evidence-based medicine, pharmacists, and clinicians) for external review. The working group reported key issues

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that need to be discussed in the current situation. The specialists discussed the draft face to face and adopted some opinions. The draft was finally approved and revised.

2.7 | Publication of the guidelines

The secretary group refined the draft based on feedback. The final document was examined and appraised by World Federation of Chinese Medicine Societies and published on Nov 4 2022(NO: SCM-C 0054–2021).

2.8 | Version description

In order to promote and disseminate this guideline, the content was appropriately adjusted according to the standards of journal criteria. The Chinese version of this guideline was published in *the Chinese Journal of Evidence-based Medicine*, and the English version was published in the *Journal of Evidence-Based Medicine*.

3 | AREA OF APPLICATION

This guideline standardized the terminology of COPD, etiology, diagnostic criteria, and treatment goals and plans of TCM and Western Medicine, which applied to COPD patients. It could be applied by clinical respiratory physicians (TCM, Western medicine, integrated traditional Chinese, and Western medicine).

4 | PATHOGEN AND PATHOGENESIS

COPD belonged to the category of "Wheezing disease" or "lung distension" in TCM. Healthy *qi* deficiency was the internal factor of the disease, while invasion of exogenous pathogens was the external condition of the disease, accumulated damage due to healthy *qi* deficiency as the main pathogenesis. The healthy *qi* deficiency referred to that of the lung, spleen and kidney deficiency, which started with the deficiency of the lung *qi*, and based on the kidney deficiency. *Qi* deficiency was the root, and sometimes injured *yin* and *yang*; while the accumulated damage referred to that combined phlegm and blood stasis accumulation was difficult to remove and increasingly damages healthy *qi*, the deficiency of which led to the difficulty in recovering from the accumulated damage. The healthy *qi* deficiency and accumulated damage were mutually causal, resulting in the injury of both the lung body and lung *qi* that continuous progressed and was difficult to recover. The pathological nature of COPD was deficiency as the root cause while excess as the branch. In the stable phase, deficiency was the main feature, which could be shown as deficiency of *qi* (*yang*) deficiency, deficiency of both *qi* and *yin* accompanied with phlegm and blood stasis; in the acute exacerbation stage, excess was the main cause, and pathogenic phlegm (phlegm-heat, phlegm-dampness) obstructed in the lung or phlegm and blood stasis obstruct each other, often accompanied by *qi* deficiency or both *qi* and *yin* deficiency. In the AECOPD risk-window period, the deficiency and excess were mixed, and they both accounted half the cause. The excessive pathogen was gradually weakening, and the root cause of deficiency was gradually exposed, so phlegm-dampness, phlegm, and blood stasis with *qi* deficiency, and both *qi* and *yin* deficiency could all be seen.[11–15]

5 | DISEASE MECHANISMS

The mechanism of the onset of COPD was not fully elucidated, which was related to age, pulmonary dysplasia, family inheritance and other factors, and smoking was the most common risk factor for the disease. The use of biofuels was also an essential etiology for women in developing countries to develop COPD. The above risk factors contributed to the occurrence of the disease through causing airway inflammation, protease/antiprotease imbalance, oxidative stress and other pathways. Chronic inflammation of the airway, lung parenchyma, and pulmonary vessels was a characteristic change of COPD. Macrophages, neutrophils, lymphocytes, and other inflammatory cells were all involved in the onset of the disease. Activated inflammatory cells could release a variety of inflammatory mediators, leading to lung tissue damage and airway remodeling, and the inflammatory mediators could further increase the production of inflammatory cells, thereby aggravating the inflammatory process. Macrophage matrix metalloproteinase and neutrophil elastase could destroy elastin in lung connective tissues, and Tc1 lymphocytes could damage alveolar epithelium by releasing granzyme perforin, leading to irreversible lung injury and emphysema. Oxidative stress in the body of patients with COPD increased, and the oxides produced could cause cell dysfunction or apoptosis, promote inflammatory reaction, and cause protease-antiprotease imbalance and other pathological mechanisms, thus damaging the structure of lung tissues. Combining these mechanisms resulted in COPD.[1,16–18]

6 | DIAGNOSTIC CRITERIA

6.1 | Western medicine

Patients who had a history of dyspnea, chronic cough, expectoration and/or exposure to risk factors of COPD, with the exclusion of other diseases that could cause similar symptoms, could be diagnosed as COPD. The pulmonary function test of forced expiratory volume in the first second/forced vital capacity (FEV_1/FVC) < 0.7 after inhalation of bronchodilators, determined as persistent airflow restriction, was a necessary condition for diagnosing COPD.[1]

6.2 | Phases and grades

According to the current relevant diagnosis and treatment guidelines at home and abroad, as well as the severity of symptoms, COPD was managed with the stable phase and AE phase. In clinical practice, "the AECOPD risk window period" was a stage with obvious clinical

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TABLE 3 Pulmonary function grading based on the severity of airflow restriction among patients with COPD.

Grade	Severity	Pulmonary function (based on FEV_1 after using bronchodilators)
GOLD 1	Mild	FEV_1 accounts for ≥80% of the estimated value
GOLD 2	Moderate	50% ≤ FEV_1 < 80% of the estimated value
GOLD 3	Severe	30% ≤ FEV_1 < 50% of the estimated value
GOLD 4	Extremely severe	FEV_1 < 30% of the estimated value

characteristics, which had an important impact on the development of the disease. The formulation of this concept provided a new idea for the management and treatment of COPD. The current relevant evidence showed that the combination of traditional Chinese and Western medicines was effective in treating the AECOPD risk window period, which provided a good basis for improving the level of clinical prevention and treatment. Therefore, this document explained the definition, questions and treatment recommendations of the clinical phases as follows: (a) the stable phase was characterized with stability of symptoms including cough, expectoration, shortness of breath, etc., for a certain period; (b) the AE of COPD referred to when the respiratory symptoms aggravate and additional treatment was needed; and (c) the AECOPD risk-window period referred to the period after an AE of COPD until the stable phase, during which AEs were highly likely to occur again, leading to an increase in hospitalization and fatality rates, mostly within 8 weeks after an AE.[1,19–22]

6.3 | Grading and comprehensive evaluation of pulmonary function at the stable phase

6.3.1 | Pulmonary function grading

The severity of the disease was determined by the degree of airflow restriction according to the grading criteria issued by the Global Initiative For Chronic Obstructive Pulmonary Disease (GOLD), that was, the percentage of FEV1 in the estimated value, which was graded into 1 to 4 (Table 3).[1]

6.3.2 | Comprehensive evaluation

Patients were divided into A, B, C, and D groups based on the severity of clinical symptoms and the AEs in the latest one year (Table 4).

6.4 | Grading of AE phase

The severity of AE of COPD was affected by many factors such as underlying diseases and complications. Generally, it could be divided into ① mild: only short acting bronchodilators were needed; ② moderate: use short acting bronchodilators combined with antibacterial drugs, or/and oral glucocorticoids; ③ severe: it required hospitalization or emergency treatment or treatment in intensive care unit.[1,20]

TABLE 4 Grouping criteria based on comprehensive evaluation on COPD at stable phase.

≥2 times of moderate or severe acute aggravation or ≥1 AE resulting in hospitalization	C	D
zero or one time of AEs but not hospitalized	A	B
	CAT < 10 mMRC 0–1	CAT ≥10 mMRC ≥2

7 | TCM SYNDROME DIAGNOSIS STANDARD

The diagnostic criteria of the disease in TCM referred to the Diagnostic Criteria for TCM Syndromes of Chronic Obstructive Pulmonary Disease (2011 Edition),[21] SCM 44–2019,[12] and T/CACM1319-2019.[23] In clinic, it was mostly manifested as the combination of both deficiency and excess, therefore, when differentiating syndromes, paid attention to the diagnosis of the combined deficiency and excess, as well as different severity of both sides, and the mixed syndromes.

7.1 | Stable phase

7.1.1 | Syndrome of lung *qi* deficiency

① Cough or wheezing, shortness of breath, which aggravated while moving; ② mental fatigue, lack of strength, or spontaneous sweating; ③ aversion to wind, easy to catch cold; ④ light tongue with white coating, or deep and thready pulse, or thready and weak pulse. It could be diagnosed when meeting three items of the above ①–④. This syndrome was commonly seen in patients with mild and moderate pulmonary function (GOLD 1 and 2).

7.1.2 | Syndrome of lung and spleen *qi* deficiency

① Cough or wheezing, shortness of breath, which aggravated while moving; ② mental fatigue, lack of strength, or spontaneous sweating, which aggravated while moving; ③ aversion to wind, easy to catch cold; ④ poor appetite or less intake; ⑤ gastric distension and fullness, abdominal distension or loose stool; ⑥ enlarged tongue or with tooth marks, thin white or white greasy tongue coating, or deep and thready pulse, deep, and slow pulse, or thready and weak pulse. It could be diagnosed when meeting two items of the above ①–③, together with two items of ④–⑥. This syndrome could be seen in patients of all phases with pulmonary dysfunction, but it was commonly seen in mild and moderate (GOLD 1 and 2) patients.

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7.1.3 | Syndrome of lung and kidney *qi* deficiency

① Wheezing, shortness of breath, which aggravated while moving; ② lack of strength, or spontaneous sweating, which aggravated while moving; ③ aversion to wind, easy to catch cold; ④ sore and weak sensation of the lower back and knees; ⑤ tinnitus, dazed, or facial edema; ⑥ frequent urination, especially at night, or leakage of urine while coughing; ⑦ light tongue with white coating, or deep and thready, or thready and weak pulse. It could be diagnosed when meeting two items of the above ①–③, together with two items of ④–⑦. This syndrome could be seen in patients with moderate, severe and extremely severe pulmonary dysfunction (GOLD 2–4), but it was commonly seen in the latter two types of patients.

7.1.4 | Syndrome of both *qi* and *yin* deficiency in lung and kidney

① Wheezing, shortness of breath, which aggravated while moving; ② spontaneous sweating or lack of strength, which aggravated while moving; ③ easy to catch cold; ④ sore and weak sensation of the lower back and knees; ⑤ tinnitus, dazed, or dizziness; ⑥ dry cough or with less phlegm which was difficult to expectorate; ⑦ night sweating; ⑧ feverish feeling in palms and soles; ⑨ light or red tongue with thin and less coating, or partially peeling coating, or deep and thready pulse, thready and weak pulse, or thready and rapid pulse. It could be diagnosed when meeting two items of the above ①–③, together with one item of④ and ⑤, and two items of ⑥–⑨. This syndrome was commonly seen in patients with severe and extremely severe pulmonary dysfunction (GOLD 3 and 4).

7.2 | Acute exacerbation phase

7.2.1 | Syndrome of wind-cold attacking the lung

① Cough or wheezing, white and thin phlegm; ② fever, aversion to cold, without sweating, or soreness of limbs; ③ stuffy nose, thin nasal discharge; ④ white tongue coating, floating, or floating and tight pulse. It could be diagnosed when meeting the above ① and ②, together with one item of ③ and ④. This syndrome was commonly seen in the primary stage of the AE phase.

7.2.2 | Syndrome of exterior cold with interior fluid retention

① Cough or wheezing; ② aversion to cold, without sweating, or stuffy nose, thin nasal discharge, or soreness of limbs; ③ white and thin phlegm or with froth, and the phlegm was easy to expectorate; ④ wheezing due to phlegm retention in throat; ⑤ chest stuffiness that the patient even could not lie in supine position due to *qi* counterflow; ⑥ white and slippery tongue coating, or wiry and tight pulse, or floating and tight pulse. It could be diagnosed when meeting the above ① and ②, together with two items of ③–⑥. This syndrome was commonly seen in the primary stage of the AE phase.

7.2.3 | Syndrome of phlegm-heat obstructing the lung

① Cough or wheezing with shortness of breath; ② excessive yellow or white greasy phlegm, which was difficult to expectorate; ③ fever or thirsty, preferring cold drinks; ④ dry stool; ⑤ red tongue with yellow or yellow greasy coating, or rapid or slippery rapid pulse. It could be diagnosed when meeting the above ① and ②, together with two items of ③–⑤. This syndrome was commonly seen in the AECOPD patients combined with infection and large mucous secretion.

7.2.4 | Syndrome of phlegm turbidity obstructing the lung

① Cough or wheezing with shortness of breath; ② excessive white greasy phlegm, or with froth; ③ gastric stuffiness and fullness; ④ sticky or greasy feeling in the mouth, poor appetite or less intake; ⑤ white greasy coating, or slippery or wiry and slippery pulse. It could be diagnosed when meeting the above ① and ②, together with two items of ③–⑤. This syndrome was commonly seen in the AECOPD patients combined with infection and large mucous secretion.

7.2.5 | Syndrome of phlegm clouding orifices of spirit

① Mental abnormalities (dysphoria, wanderings, somnolence, delirium, and unconsciousness); ② limb spasm and even convulsion; ③ wheezing and shortness of breath; ④ wheezing due to phlegm retention in throat; ⑤ light or red tongue with white greasy or yellow greasy coating, or slippery or rapid pulse. It could be diagnosed when meeting one item of the above ① and ②, together with two items of ③–⑤. This syndrome was commonly seen in patients with severe conditions.

7.3 | AECOPD risk-window period

The criteria of differentiating main syndrome referred to those of AEs and stable phases.

8 | PREVENTION AND TREATMENT TARGETS

The combination of disease differentiation by phases and grades with syndrome differentiation was the main strategy of preventing and treating COPD with integrated TCM and WM. In the stable phase, the treatment goal was to alleviate symptoms, prevent disease progression

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and reduce the risk of AEs. On this basis, targeted and more specific prevention and treatment goals and measures should be adopted according to different degrees of lung dysfunction: for patients with GOLD 1 and 2, the treatment focuses on protecting the decline of lung function and delaying disease progression; for those with GOLD 3 and 4, the treatment aimed to reduce the risk of AEs and improved quality of life; for those at advanced phase (mostly with GOLD 4), we should pay attention to preventing and treating concurrent diseases, reducing the risk of death, and improving the quality of life, especially reducing the mortality due to chronic respiratory failure. The treatment goal of AECOPD was to minimize the impact of the AEs of this time, relieve clinical symptoms, and reduce the risk of death. The treatment goal of AECOPD risk-window period was to help patients to transfer to stable phase smoothly and prevent the recurrence to AEs.

9 | TREATMENT PRINCIPLES AND METHODS

In the stable phase, the treatment was based on the principle of "treating the root cause in a chronic case," that was, reinforcing healthy *qi* as the main target, and expelling pathogens as the second. The disease location of patients at this stage with mild and moderate conditions was relatively superficial, so the reinforcement targeted mainly the lung and spleen, as well as the kidney; while the disease location was relatively deep for those with severe and extremely severe conditions, thus the reinforcement targeted mainly the lung and kidney, as well as spleen. In terms of expelling pathogens, the treatment mainly included activating blood circulation and eliminating phlegm. In the AEs phase, the treatment followed the principle of "treating the branch cause in an acute case," specifically including clearing heat, clearing up phlegm, activating blood, ventilating and descending lung *qi*, and opening orifices, as well as considering regulation of *qi* and *yin*. In the AECOPD risk-window period, the treatment mainly included tonifying deficiency and reinforcing healthy *qi*, assisted by eliminating phlegm and activating blood.

The treatment plan for COPD with integrated traditional Chinese and Western medicine mainly included that of standardized Western medicine treatment combined with TCM treatment based on syndrome differentiation. Since the current diagnosis and treatment guidelines for COPD with TCM and Western medicine at home and abroad provided detailed treatment plans, the contents of relevant standardized Western medicine treatment plans recommended in this guideline would not be described here. For parts of prescriptions and Chinese herbs for TCM treatment based on syndrome differentiation, it could refer to relevant contents in T/CACM1319-2019(13) and SCM 44–2019,[23] and the Guidelines for the Diagnosis And Management Of Chronic Obstructive Pulmonary Disease (revised version 2021)[20] was referred to in terms of the standardized Western medicine treatment.

10 | CLINICAL QUESTIONS AND RECOMMENDATIONS

10.1 | Clinical question

Did integrated Chinese and Western medicine show good curative effect and safety in the treatment of stable chronic obstructive pulmonary disease (COPD)?

10.1.1 | Summary of the evidence

Commonly used drugs in Western medicine for the treatment of stable COPD included bronchodilators, hormones, expectorant, etc., which could effectively relieve clinical symptoms, prevent AEs, and improve the quality of patient's life, but the researches on the efficacy satisfaction and the long-term improvement goal still needed to be further strengthened. While the commonly used TCM treatment for stable COPD included TCM decoctions, proprietary Chinese medicines, TCM rehabilitation treatment, and other therapies. A systematic review involving 11 high-quality Randomized Controlled Trials (RCT) showed that TCM treatment based on syndrome differentiation combined with conventional Western medicine treatment could improve scores of CAT and those of The Saint George's Respiratory Questionnaire (SGRQ). It could also reduce the number of AEs, and improve the efficiency of clinical treatment.[24] Another systematic review within 19 RCTs showed that the integration of Chinese medicine ointment and conventional Western medicine treatment could reduce the number of AEs and improve scores of SGRQ and CAT.[25] One more systematic review covering 100 RCTs showed that, on the basis of the conventional Western medicine treatment, giving TCM treatment based on syndrome differentiation combined acupuncture and moxibustion treatment could improve patients' lung function, reduce the number of AEs, and improve scores of CAT, etc.[26] There were also two systematic reviews[25,26] both mentioned that the treatment of integrated Chinese and Western medicine showed good safety without obvious adverse events. Based on conventional Western medicine treatment, the combination of TCM treatment based on syndrome differentiation was more effective in improving patients' clinical symptoms and reducing the number of AEs with good safety for stable COPD.

10.1.2 | Recommendations

For stable COPD patient, it was recommended to apply TCM treatment based on syndrome differentiation, which could increase the curative effect and have a certain safety on the basis of conventional WM treatment (**moderate evidence quality, strong recommendation**).

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10.2 | Clinical question

When should we apply the integrated Chinese and Western medicine program intervene in the treatment of stable COPD?

Patients with early-stage COPD might be characterized by no obvious symptoms. When the condition progresses and obvious airflow limitation appears for COPD patients, the best time for treatment might be missed.[20] Therefore, early detection and treatment were crucial. When COPD patients were first diagnosed, TCM treatment was very important to delay the progress of the disease and improve the patient's prognosis.[2,27,28] For severe and very severe COPD patients, TCM treatment could reduce the number of AEs, improve the quality of life and exercise endurance, and so on based on conventional WM treatment.[2,28,29]

10.2.1 | Recommendations

In the whole course of COPD, TCM treatment based on syndrome differentiation would be recommend as needed on the basis of the application of conventional WM treatment (**moderate evidence quality, strong recommendation**).

10.3 | What was the scheme and curative effect of integrated Chinese and Western medicine for the treatment of stable COPD patients with lung function at levels 1 and 2?

10.3.1 | Summary of the evidence

The lung function of early COPD patients was classified as GOLD 1 and 2 with atypical clinical symptoms and attention was often insufficient. However, lung function had begun to decline with fast rate.[30] Therefore, the prevention and treatment goals of COPD patients with GOLD 1 and 2 focused on delaying lung function decline and disease progression. Common TCM syndromes (*zheng*) in COPD patients with GOLD 1 and 2 included lung *qi* deficiency, lung and spleen *qi* deficiency, lung and kidney *qi* deficiency. These TCM syndromes were often followed with phlegm or blood stasis. The treatment method should mainly focused on strengthening the body resistance, with dispelling phlegm and invigorate blood circulation. Moreover, strengthening the body resistance should focus on nourishing the lung and tonifying the spleen and kidney.[2] The results of a clinical trial with multicenters and large numbers of samples showed that TCM treatment based on syndrome differentiation (nourishing lung formula for lung *qi* deficiency, nourishing lung and tonifying spleen formula for lung and spleen *qi* deficiency, nourishing lung and tonifying kidney for lung and kidney *qi* deficiency) could reduce the number of AEs, improve clinical symptoms, exercise endurance and quality of life, delay lung function decline with a long-term and good prognosis effect.[27] A multicenter, double-blind, placebo parallel controlled trial including people at high risk of AEs with GOLD 2 and 3 had shown that oral administration of *Yupingfeng* Granule could reduce the annual occurrence of AEs and the recurrence risk and could also extend the stability time of the disease.[31]

10.3.2 | Recommendations

For stable COPD patient with GOLD 1 and 2, it was recommended to adopt a TCM treatment plan based on syndrome differentiation or integrating Chinese and Western medicine as soon as possible. and given bronchodilators or long-acting β2-receptor agonist combined inhalation of corticosteroids (ICS/LABA) as needed according to the patient's conditions (**moderate evidence quality, strong recommendation**).

The TCM treatment plan based on syndrome differentiation was shown as follows: For patients with lung *qi* deficiency syndrome, lung-nourishing formula should be adopted; or ginseng and walnut decoction combined with ginseng lung-nourishing pills (doses could be increased or reduced appropriately),[12,23] or the proprietary Chinese medicine *Yupingfeng* Granule[12,23,28,31] could also be given. For patients with lung and spleen *qi* deficiency syndrome, lung-nourishing and spleen-tonifying formula should be applied; or *Liujunzi* decoction combined with astragalus decoction (doses could be increased or reduced appropriately),[12,23] or the proprietary Chinese medicine *Yupingfeng* Granule,[12,23,31] *Liujunzi* Pills,[12,23,28] and *Renshen Jianpi* Pellets[28] could also be selected. For patients with lung and kidney *qi* deficiency syndrome, lung-nourishing and kidney-tonifying formula should be given; or ginseng lung-nourishing decoction (doses could be increased or reduced appropriately),[12,23] or the proprietary Chinese medicine *Jingui Shenqi* Pill[28] and *Bailing* capsules[28] could also be adopted as needed. Patients with the obvious blood stasis could be given *Bufei Huoxue* capsules.[12,23,28]

10.4 | Clinical question

What was the scheme and curative effect of integrated Chinese and Western medicine for the treatment of stable COPD patients with lung function at levels 3 and 4?

10.4.1 | Summary of the evidence

Relatively severe clinical symptoms, including obvious dyspnea, frequent AEs, increased hospitalizations, decreased quality of life, would be observed in COPD patients with GOLD 3 and 4. Then, increased case-fatality, disability rates and heavy economic burden emerge. Therefore, the prevention and treatment goals for patients at this stage focus on reducing AEs and improving quality of life. For late-stage patients (more common in patients with GOLD 4), attention should be paid to the prevention and treatment of comorbidities, reducing the risk of death and improving the quality of life, especially to reducing the case-fatality rate of chronic respiratory failure.[2,20] Common TCM syndromes in COPD patients with GOLD 3 and 4 included lung and spleen *qi* deficiency, lung and kidney *qi* deficiency, and lung and kidney

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qi and *yin* deficiency. These symptoms were also followed with phlegm obstruction and blood stasis. Treatment should be based on strengthening the body resistance, with dispelling phlegm and invigorating blood circulation. Moreover, strengthening the body resistance should focus on nourishing the lung and tonifying the spleen and kidney.[2] One high-quality RCT study involving 564 stable COPD patients with GOLD 3 and 4 showed that the integrated treatment plan of Chinese and Western medicine could reduce the numbers of AEs, improve quality of life and exercise capacity, and relieve the clinical symptoms and dyspnea.[32]

10.4.2 | Recommendations

For stable severe or very severe COPD patients, TCM treatment based on syndrome differentiation could be given on the basis of the conventional WM treatment (**moderate evidence quality, strong recommendation**).

The TCM treatment plan based on syndrome differentiation was as follows: nourishing the lung and tonifying the spleen formula for lung and spleen *qi* deficiency and giving *Liujunzi* decoction combined with astragalus decoction (doses could be increased or reduced appropriately),[12,23] or the proprietary Chinese medicine *Yupingfeng* Granule,[12,23,31] *Liujunzi* Pill,[12,23,28] and *Renshenjianpi* Pills[28] would also be selected. For lung and kidney *qi* deficiency, nourishing the lung and tonifying the kidney formula could be adopted, and ginseng lung-nourishing decoction (doses could be increased or reduced appropriately)[12,23] or the proprietary Chinese medicine *Jinguishenqi* Pill[28] and *Bailing* capsules[28] could also be applied. And for lung and kidney *qi* and *yin* deficiency, replenishing *qi* and tonifying kidney formula should be prescribed, and *Baoyuan* decoction combined with *Renshenbufei* decoction (doses could be increased or reduced appropriately)[12,23] or the proprietary Chinese medicine oral liquid of *Shengmai* Drink,[12,23] *Yangyinqingfei* Pills[12,23] *Gejiedingchuan* Pills,[12,23] and *Jinshuibao* capsule[33,34] could be given as needed. If the blood stasis was obvious, *Bufeihuoxue* capsules could be given.[12,23,28]

10.5 | Clinical question

On the basis of the standardized treatment with Western medicine, was TCM rehabilitation therapy effective and safe for stable COPD patients?

10.5.1 | Summary of the evidence

Pulmonary rehabilitation, as an important process of the treatment for COPD, could improve patients' lung function, reduce hospital readmission rate, mortality rate and disability rate significantly, and could also improve patients' quality of life.[35] TCM pulmonary rehabilitation was a comprehensive rehabilitation technology, which was formed through absorbing traditional rehabilitation techniques and modern rehabilitation technological concepts and methods under the guidance of the theory of TCM and integration of Chinese and Western medicine based on the characteristics of chronic respiratory diseases. TCM rehabilitation techniques, such as Taichi, acupuncture, pulmonary *daoyin*, acupoint application (such as lung-soothing application, anti-asthma ointment, etc.), and lung moxibustion, all had good curative effects in relieving clinical symptoms, improving exercise endurance, delaying the lung function decline, and improving the quality of life[36,37] for COPD patients.

10.5.2 | Recommendations

Stable COPD patients were recommended to give TCM rehabilitation treatment as appropriate with good safety (**low evidence quality, strong recommendation**).

The implementation of TCM rehabilitation treatments should be based on the patient's physical function, exercise convenience, and living habits. Simplified *Taichi*, medical exercise based on the Six-character Formula, acupoint application, lung-soothing application, acupuncture, traditional moxibustion, lung moxibustion, respiratory guidance and other therapies could be given as needed. For specific operation methods, please refer to the "Chinese Medicine Rehabilitation Guidelines for Chronic Obstructive Pulmonary Disease" in SCM-C 0015–2019.[36]

10.6 | Clinical question

Was integrated Chinese and Western medicine effective and safe in the treatment of AECOPD?

10.6.1 | Summary of the evidence

Patients in the AEs stage would be accompanied by worsening respiratory symptoms, which could easily lead to rapid disease progression and an increased risk of death. The treatment goal for AECOPD patients was to minimize its impact, alleviate clinical symptoms, and decrease the risk of death.[2] Common TCM syndromes included retention of heat-phlegm in the lung, phlegm-dampness accumulated in the lung, external cold with interior fluid retention, wind-cold attacking the lung, and other syndromes.[13] Treatments toward these should follow the principle of "treating the symptoms if in urgent." A multicenter, randomized, double-blind, placebo-controlled trial on moderate and severe COPD patients in the AEs stage (external cold with interior fluid retention/phlegm dampness accumulated in the lung/retention of heat-phlegm in the lung) has been performed. The results of the research showed that TCM treatment based on syndrome differentiation (that was, patients with syndromes of the external cold with interior fluid retention, retention of heat-phlegm in the lung, and phlegm-dampness accumulated in the lung would be given dispelling cold and resolving fluid retention formula, clearing heat and dispelling

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phlegm formula, and eliminating dampness and dispelling phlegm formula, respectively) could significantly improve the scores of patients' CAT and mMRC with good safety[38] based on conventional WM treatment. One systematic review incorporating 38 RCTs showed that the *Xiaoqinglong* decoction could improve clinical efficiency, delay lung function decline, and shorten the durations for symptoms such as coughing and expectoration to disappear for AECOPD patients on the basis of conventional WM treatment.[39] Another systematic review incorporating 24 clinical studies showed that the combination of three types of TCM infusion fluid could improve lung function for COPD patients in the AEs stage on the basis of based on conventional WM treatment.[40] Compared with the conventional WM treatment, the integrated treatment plan of Chinese and Western medicine did not increase the incidence of adverse events.[39,40]

10.6.2 | Recommendations

AECOPD patients were recommended to use TCM treatment based on syndrome differentiation on the basis of conventional WM treatment, which had certain advantages in improving clinical symptoms and reducing the number of AEs[12,41] with good safety (**moderate evidence quality; strong recommendation**).

The TCM treatment plan based on syndrome differentiation was as follows: for patients with TCM syndrome of wind-cold attacking the lung, *Sanao* decoction (decoction of three medicines including ephedra with root and nodes, almond with skin and tip, raw liquorice without grilling) combined with *Zhisou* casual treatment (Cough-Stopping Powder) (doses could be increased or reduced appropriately)[12,23] could be selected, or we could also choose the proprietary Chinese medicine *Tongxuanlifei* Pill,[12,23] *Suhuang Cough* capsules.[42–44] For TCM syndrome of the external cold with interior fluid retention, we could adopt the dispelling cold and resolving fluid formula[38] or *Xiaoqinglong* decoction (doses could be increased or reduced appropriately),[12,23] or *Xiaoqinglong* Granules, a proprietary Chinese medicine[12,23] might also be selected as needed. For retention of heat-phlegm in the lung, the clearing heat and dispelling phlegm formula[38] would be adopted, and we could also give *Qingrehuatan* Pills and *Beimugualou* Powder (doses could be increased or reduced appropriately),[12,23] or *Tanreqing* injection,[12,23] *Xuebijing* injection,[12,23] *Shufeng* detoxification capsule,[45–47] and *Tingbei* capsule[12,23] could be applied as needed. COPD patients with syndrome of pulmonary obstruction by phlegm should be given the prescription of dispelling phlegm and eliminating dampness,[38] or *Erchen* decoction or Banxia (Pinellia Tuber) Houpo (Cortex Magnoliae Officinalis) decoction combined with *Sanziyangqin* decoction (doses could be increased or reduced appropriately),[1,2,30] and we could also apply the proprietary Chinese medicines *Suzijiangqi* Pills[12,23] and *Lingguikechuanning* capsule.[12,23] For syndrome of mental confusion due to phlegm, *Ditan* decoction (doses could be increased or reduced appropriately)[12,23] might be the best choice, or proprietary Chinese medicine *Xingnaojing* injection,[12,23] *Qingkailing* injection,[12,23] *Suhexiang* Pills,[12,23] *Angongniuhuang* Pills,[12,23] and *Zhibao* Pills[12,23] would be the alternative treatment.

10.7 | Clinical question

When should the integrated Chinese and Western medicine program intervene be applied in the treatment of AECOPD with acute exacerbation?

10.7.1 | Summary of the evidence

AEs was the main cause of medical treatment, hospitalization, disease progression, disability, death, and heavy economic burden for COPD patients. Early identification and objective evaluation of the degree of AEs were of great significance for the prevention and improvement of COPD patients with AEs. Patients with mild symptoms might experience upper respiratory tract infection such as sore throat, nasal congestion, and runny nose in the early stage. When the symptoms of asthma and cough (with or without phlegm) worsen, Chinese medicine treatment on the basis of conventional WM treatment could reduce the frequency of readmission within 1 year and shorten the duration of readmission, etc.[48] The combination treatment of Chinese and Western medicine for moderate and severe patients had the effect in improving clinical efficiency, shortening the duration of hospitalization, reducing inflammation and other effects.[49]

10.7.2 | Recommendations

AECOPD patients could be given Chinese medicine dialectical treatment combined with Western medicine as soon as possible, whose prognosis would be effectively improved (**low evidence quality; strong recommendation**).

10.8 | Clinical question

On the basis of the standardized treatment of Western medicine, was the TCM rehabilitation effective and safe for AECOPD patients?

10.8.1 | Summary of the evidence

AECOPD patients would suffer from aggravated dyspnea and cough and increased phlegm, resulting in decreased physical function. Generally, it was not recommended to give rehabilitation exercises with large oxygen consumption. The preliminary results of an ongoing multicentered RCT showed that supine respiratory guidance (a technique that regulates viscera and invigorates meridian circulation through exhalation and inhalation combined with muscle training in the supine position) might improve the scores of SGRQ and Clinical COPD Questionnaire (CCQ)[50,51] of AECOPD patients. TCM rehabilitation therapies with low energy consumption, such as warm needling moxibustion and acupuncture, could improve the clinical symptoms and increase partial pressure of oxygen for AECOPD patients.[52,53]

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10.8.2 | Recommendations

For AECOPD patients, dialectical treatment of TCM rehabilitation therapy could relief patients' clinical symptoms and increase partial pressure of oxygen (**very low evidence quality; weak recommendation**).

COPD patients with phlegm-heat stasis in lung could be treated by use of Baical Skullcap root, Cortex Mori, and other heat-clearing and phlegm-reducing Chinese medicines. Mix and make them into a paste into a medicine cake by sesame oil and then applied it to acupoints of Da Zhui, Ding Chuan and, etc.[54–56] For patients with phlegm obstruction in lung, warm needling and moxibustion treatment could be given.[53] And AECOPD patients could be given corpse pose guiding treatment as appropriate according to the patient's condition.[50,51] It should also be noted that each rehabilitation technique had its own indications and contraindications, and the severity and physical condition of patients in the acute phase were different. Therefore, a certain TCM technique should be chosen from scientific evaluation and decision-making based on a full understanding of the characteristics of the technique combined with the patient's current condition.

10.9 | Clinical question

Could the integrated scheme of Chinese and Western medicine reduce the patient's dosage or shorten the course of treatment on systemic glucocorticoids use in the treatment of AECOPD patients?

10.9.1 | Summary of the evidence

Glucocorticoids, which is commonly used therapeutic drugs for AECOPD patients, would be effective in antispasmodic, anti-inflammatory, and other effects. So, they could quickly relieve patients' clinical symptoms. But corresponding complications would also emerge from long-term heavy use of the hormone, which was not conducive to the treatment of the disease. The TCM treatment based on syndrome differentiation could relieve clinical symptoms for AECOPD patients to a certain extent, thereby the use of glucocorticoids would also be generally reduced.[57] But the current evidence-based supports were insufficient. An ongoing RCT[58] glucocorticoids uses as the main outcome for the treatment of AECOPD patients by integrated Chinese and Western medicine. Maybe its results could provide high-level evidence-based supports.

10.9.2 | Recommendations

AECOPD patients were recommended to use integrated Chinese and Western medicine for treatment, which might reduce the use of hormones, and would help reduce complications and the risk of infection (**very low evidence quality; weak recommendation**).

10.10 | Clinical question

Could integrated Chinese and Western medicine reduce the use of antibiotics in the treatment of AECOPD patients?

10.10.1 | Summary of the evidence

Bacterial infection was one of the common factors of AEs for COPD patients. In addition to clinical symptoms such as fever and yellow phlegm, changes of C-reactive protein (CRP),[59] procalcitonin (PCT)[60] and other inflammatory indicators were of great significance to guide the use of antibiotics. However, the long-term heavy use of antibiotics not only causes gut flora disorder, but also induced antibiotic-resistance,[61,62] which would bring difficulties to later treatment for AECOPD patients. TCM syndrome of retention of heat-phlegm in the lung was the most common for AECOPD patients combined with bacterial infection. For patients with such syndrome, it was recommended, on the basis of the standardized treatment of Western medicine, to give heat-clearing and phlegm-reducing Chinese medicines as appropriate, which could reduce the use of antibiotics to a certain extent.[63,64] However, there was a lack of high quality of evidence, and further high-level evidence needs to be provided.

10.10.2 | Recommendations

AECOPD patients were recommended to use integrated Chinese and Western medicine treatment options, which might help to reduce the use of antibiotics (**very low evidence quality, weak recommendation**).

10.11 | Clinical question

Was the integrated Chinese and Western medicine program effective and safe in the treatment of AECOPD risk-window period?

10.11.1 | Summary of the evidence

Patients with AECOPD risk-window period were still unstable, and highly susceptible to recurrence of AEs or delay in entering the stable period. Therefore, it was an important prevention and treatment goal at this stage to reduce the recurrence risk of AE and promote recovery into a stable period. In this period, clinically common TCM syndromes included lung and kidney *qi* deficiency combined with phlegm-dampness accumulated in lung, lung and spleen *qi* deficiency combined with phlegm-dampness accumulated in the lung, dual lung and kidney *qi* and *yin* deficiency combined with phlegm-dampness accumulated in lung, lung and kidney *qi* deficiency combined with phlegm turbidity obstructing the lung, as well as dual lung and kidney *qi* and *yin* deficiency combined with phlegm turbidity obstructing

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the lung.[12] The treatment should focus on both dispelling evil spirits (dispelling phlegm and invigorating blood circulation) and strengthening the body resistance (nourishing lung *qi*, tonifying lungs and spleen, nourishing lungs and kidneys, etc.). The results of a multicenter, randomized, single-blind, placebo-controlled parallel trial showed that the application of integrated Chinese and Western medicine and sequential treatment plan (patients with syndrome differentiation of AEs should adopt prescriptions of dispelling cold and resolving fluid retention, clearing heat and dispelling phlegm, and eliminating dampness and dispelling phlegm for 1–3 weeks and should be given a 4-week-dialectical treatment if entering the window period of high risk) could prolong the stable duration time to next occurrence of AEs, ease dyspnea, and improve the quality of life[65] compared with the conventional WM treatment only. In addition, there was also an ongoing clinical trial on the evaluation of the efficacy of TCM treatment based on syndrome differentiation options for patients with AECOPD risk-window period (the main observation index was the incidence of AEs and CAT scores).[66] The results might also provide high-quality evidence for the evaluation of the curative effects of TCM.

10.11.2 | Recommendations

For patients with AECOPD risk-window period, it was recommended to adopt a sequential treatment of integrated Chinese and Western medicine to help improve clinical efficacy and reduce the risk of recurrence of WE (**moderate evidence quality, weak recommendation**).

10.12 | Clinical question

Was the integrated Chinese and Western medicine program effective and safe in the treatment of the complications of COPD (such as respiratory failure and pulmonary hypertension)?

10.12.1 | Summary of the evidence

Acute respiratory failure was one of the most common complications that cause death in COPD patients. Rapid correction of respiratory failure, reduction of endotracheal intubation rate, shortening of mechanical ventilation duration time, and reducing the case-fatality rates were the main prevention and treatment goals at this stage. The main TCM pathogenesis at this stage was deficiency in origin and excess in superficiality. Deficiency in origin means deficiency of lung, spleen, and kidney, which might involve the heart and liver. While excess in superficiality meant turbidity of phlegm, disturbance of water metabolism, blood stasis, and stasis of pathogenic factor.[67] They might obstruct the lung, involve the large intestine, or invade the brain, and lead to corresponding symptoms.[68] Common TCM syndromes included visceral deficiency, retention of heat-phlegm in lung, phlegm turbidity obstruction of the lung, phlegm stasis, and orifices confused by phlegm.[69] Treatments should give dispel phlegm,[70] clearing the lung,[71] tonifying the spleen,[72] purging the viscera,[73–75] invigorating blood circulation,[76] inducing resuscitation,[77] and so on according to the patient's condition. The treatment of acute respiratory failure with integrated Chinese and Western medicine might help to improve the overall efficiency and the success rate of machine removal, improve the partial pressure of blood oxygen and carbon dioxide, reduce the incidence of ventilator associated pneumonia and the case-fatality rate, but there was still a lack of high-quality evidence.

Chronic respiratory failure was a complication caused by the disease progress of COPD and the continuous decline of lung function. WM could give long-term oxygen therapy and correct acid-base imbalance. TCM focused on asthenia healthy *qi*, and most of the TCM syndromes included phlegm stasis. The TCM treatments were mostly based on nourishing the lung, nurturing the heart, and tonifying the kidney.[68] At present, there was a lack of high-quality clinical research on the intervention of TCM in COPD combined with chronic respiratory failure. A 14-center, randomized, double-blind, placebo-controlled study incorporating 372 cases was ongoing. It took all-cause mortality as the main outcome to evaluate the curative effect of Yiqi Huoxue Huatan formula in the treatment of COPD with chronic respiratory failure.[78] There was another ongoing exploratory clinical study on dialectical treatment options to reduce the AEs for COPD patients with chronic respiratory failure.[79] The results of these two studies might provide high-level evidence.

Pulmonary hypertension was the root cause of chronic heart disease for COPD patients. The TCM pathogenesis of this disease was deficiency in origin and evil excess, mainly *qi* deficiency with blood stasis. Over time, sputum obstruction would occur, and "stasis" runs through the whole course of the disease.[80] On the basis of the standardized treatment of Western medicine, adopting Chinese medicine therapies more to replenish deficiency, invigorate blood circulation, and dispel sputum[81–83] could improve the clinical symptoms of patients to a certain extent, reduce coagulation indexes, correct hypoxia of tissues and organs, etc., showing a good safety.[83]

10.12.2 | Recommendations

For COPD patients with respiratory failure and pulmonary hypertension, it was recommended to adopt an integrated treatment plan of Chinese and Western medicine, which might help to ease the symptoms, delay disease progression, and reduce the risk of death (**very low evidence quality, weak recommendation**).

10.13 | Clinical question

Did the integrated Chinese and Western medicine program have any advantages in health economics in the treatment of COPD patients?

10.13.1 | Summary of the evidence

Costs of AE-related hospitalization accounted for 45%–50%[84] of the total annual direct treatment costs for COPD. The use of integrated

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Chinese and Western medicine therapy could reduce the number of AEs, shorten the average duration time of AEs, and reduce the average direct medical expenses.[85] The cost of integrated Chinese and Western medicine treatment for a unit of effectiveness was lower than that of Chinese medicine or Western medicine alone. Therefore, the integrated treatment of Chinese and Western medicine might be the optimal treatment measure suitable for stable COPD patients.[82,86]

10.13.2 | Recommendations

In terms of health economics, the integrated Chinese and Western medicine program in the treatment of chronic obstructive pulmonary disease showed better cost-effectiveness advantages than other treatment options (**very low-quality evidence, weak recommendation**).

11 | DISCUSSION

This guideline was developed based on the standardized guideline development methods at home and abroad. First, a team with multidisciplinary experts was formed, and then clinical question research, evidence collection and evaluation, Delphi consultation, and expert consensus meetings were performed. In final, a total of 13 recommendations were formed based on the current best evidences as well as the pros and cons of the intervention and health economics. This document has practical guiding significance for standardizing the diagnosis and treatment of COPD, ensuring medical quality, improving clinical work level, improving quality of life, reducing mortality, and reducing the disease burden.

This guideline would be disseminated and promoted through the following ways: ① the group standard version was published on the official website of the World Federation of Chinese Medicine Societies for consultation and use by clinicians and scientific researchers; ② the World Federation of Chinese Medicine Societies uniformly conducted the promotion and implementation work within the industry; ③ the information related to this guide would also be published through the "World Federation of Chinese Medicine Societies" official account for promotion; ④ interpreting the guidelines at the academic annual meeting of the Lung Rehabilitation Professional Committee of the World Federation of Chinese Medicine Societies to promote the dissemination of the guidelines and facilitate the use of clinicians; ⑤ after the publication in the journal, the full text of this guide could be available on the official website of the journal and various database websites.

This guideline had the following limitations: ① the guideline working group did not involve patient representatives. The comprehensive survey on patient preferences and values did not conduct, which would be improved when this guideline was updated; ② for the included original studies, time span was large with different reference diagnostic criteria for diseases. The stages and TCM syndromes of COPD could not be unified; ③ patients involved in the studies in this guideline were from TCM hospitals or integrated traditional and western medicine hospitals mostly, while the number of patients from Western hospitals was relatively small. Therefore, the included evidence might induce some bias to a certain degree; ④ there was a lack of evidences for AECOPD patients and severe complications such as respiratory failure, and it was urgent to strengthen researches to clarify the efficacy of integrated traditional Chinese and Western medicine and provide high-quality evidence; ⑤ traditional Chinese patent medicines and simple preparations was widely applied in the clinical treatment for COPD, however, some questions such as nonstandard trial design and opaque implementation process had been observed in some of the studies included in the evidence body; ⑥ health economics related studies were mostly single-center researches, and there might be significant differences among different regions.

Based on current clinical practices and research needs, future research should focus on ① continuing to perform more high-quality clinical researches to reduce results bias caused by research factors; ② it was urgent to strengthen the study on COPD complications to clarify the efficacy of integrated traditional Chinese and Western medicine and provide high-quality evidences; ③ clinical trials should strictly follow international standards for RCT design, implementation process, and outcome reporting to ensure research quality; ④ we would also strengthen the researches and development of new Chinese medicine for COPD, perform more high-quality clinical studies on existing traditional Chinese patent medicines and simple preparations for COPD, so as to improve and enrich the diagnosis and treatment scheme of integrated traditional Chinese and western medicine for COPD, and provide references for the rational application of traditional Chinese patent medicines.

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CONFLICT OF INTEREST STATEMENT

All members completed a uniformly formatted conflict of interest declaration form, clearly indicating that there was no conflict of interest related to the subject matter of this guideline.

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