Systematic Review and Meta-Analysis

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# Xiaoqinglong decoction (a traditional Chinese medicine) combined conventional treatment for acute exacerbation of chronic obstructive pulmonary disease

## A systematic review and meta-analysis

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**Abstract**

**Background:** A traditional Chinese medicine classic herbal formula named Xiaoqinglong decoction (XQLD) is widely used in China for acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The efficacy and safety of XQLD for AECOPD was evaluated in this systematic review.

**Methods:** Five databases, including the Cochrane Library, PubMed, China National Knowledge Infrastructure, Wanfang database, and Chinese Science and Technology Periodical Database were searched up to October 5, 2018 for randomized control trials in treating AECOPD with XQLD.

**Result:** Thirty-eight trials were identified. Compared with conventional therapy (CT), XQLD plus CT significantly improve the total clinical efficacy rate (Risk Ratio [RR] = 1.22, 95% confidence interval [CI] = 1.18–1.26, $P < .00001$). Forced expiratory volume in the first second (FEV1) (mean difference [MD] = 0.37, 95% CI = 0.27–0.46; $P < .00001$), FEV1%pre (MD = 4.52, 95% CI = 2.42–6.62; $P < .00001$), FEV1/forced vital capacity (MD = 5.11, 95% CI = 4.21–6.00; $P < .00001$), $PaO_2$ (MD = 7.17, 95% CI = 4.80–9.54; $P < .00001$); lowered cough symptom score (MD = −0.65; 95% CI = −0.70 to −0.59; $P < .00001$), sputum symptom score (MD = −0.41; 95% CI = −0.45 to −0.37; $P < .00001$), wheezing symptom score (MD = −0.49; 95% CI = −0.60 to −0.38; $P < .00001$); reduce cough relief time (MD = −1.28; 95% CI = −1.53 to −1.02; $P < .00001$), sputum relief time (MD = −1.19; 95% CI = −1.42 to −0.96; $P < .00001$), wheezing relief time (MD = −1.65; 95% CI = −2.63 to −0.68; $P = .0009$), lassitude relief time (MD = −2.16; 95% CI = −3.44 to −0.89; $P = .0009$), and $PaCO_2$ (MD = −7.63, 95% CI = −9.62 to −5.63; $P < .00001$). Benefit for interleukin (IL)-4 (MD = −9.20, 95% CI = −13.59 to −4.81; $P < .00001$), IL-6 (MD = −5.07, 95% CI = −8.14 to −2.01; $P = .001$), IL-8 (MD = −5.59, 95% CI = −6.09 to −5.08; $P < .00001$), tumor necrosis factor (TNF)-α (MD = −5.93, 95% CI = −6.97 to −4.89; $P < .00001$), Interferon (INF)-γ (MD = 18.03, 95% CI = 13.22–22.84; $P < .00001$), and C-reactive protein (MD = −3.93, 95% CI = −5.97 to −1.89; $P = .0002$). For adverse events, there were no difference between XILD plus CT and CT.

**Conclusion:** XQLD plus CT was more effective than CT alone for treating chronic obstructive pulmonary disease. Further higher quality trials are needed. The safety of XQLD remained uncertain.

**Abbreviations:** AECOPD = acute exacerbation of chronic obstructive pulmonary disease, CI = confidence interval, CNKI = China National Knowledge Infrastructure, COPD = chronic obstructive pulmonary disease, CRP = C-reactive protein, CT = conventional treatment, FEV1 = forced expiratory volume in the first second, FEV1% = forced expiratory volume in one second to forced vital capacity ratio, FVC = forced vital capacity, IL = interleukin, MD = mean difference, NSD = no significant difference, PROSPERO = international prospective register of systematic review, RCTs = randomized controlled trials, TCER = total clinical efficacy rate, TCM =

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*Data supporting our findings are contained within the manuscript.*

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traditional Chinese medicine, TCMsrt = TCM symptom relief time, TCMss = TCM syndrome score, VIP = Chinese Science and Technology Periodical Database, XQLD = Xiaoqinglong decoction.

**Keywords:** chronic obstructive pulmonary disease, clinical efficacy, systematic review, traditional Chinese medicine, Xiaoqinglong decoction

## 1. Introduction

### 1.1. Description of the condition

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[1] COPD is generally associated with cough, sputum production, and dyspnea.[2] COPD has been a major public health problem in the 21st century,[3] which imposes a substantial economic burden on both patients and government in China. Patients who suffer from COPD may experience cough, dyspnea, chest tightness, and wheezing.[4,5] Symptoms such as chronic cough, sputum production, and decreased forced expiratory volume in the first second (FEV1) have proved to be independently associated with an increased risk of frequent exacerbations and hospitalizations.[6] Currently, treatment of COPD is suboptimal. Many clinical guidelines recommended pharmacological therapies for COPD, but acute exacerbation still occurs frequently and is significantly associated with morbidity and mortality.[7] Thus, many COPD patients resort to complementary and alternative medicine. And some complementary and alternative therapies may be available and beneficial for COPD.[8] In China and some other Asian counties, traditional Chinese medicine (TCM) has been used more than thousands of years for the treatment of respiratory disease. TCM is a prevalent treatment for COPD, is widely prescribed as an adjunct to western medicine to manage stable COPD in clinical guideline. Although TCM is not the mainstream for treating COPD in some western countries, it has becomes increasingly accepted as a form of complementary or complementary medicine in those countries.[9] Study showed that the efficacy of TCM combined with modern medicine in treating COPD is better than that of modern medicine alone, which is reflected in better improvement of patients' symptoms and quality of life.[10]

### 1.2. Description of intervention and the objective of this study

Xiaoqinglong decoction (XQLD) was from Zhang Ji's (150–219 CE) *Shanghanlun* (*Treatise on Cold Damage Disorders, just Treatise hereafter*), a famous formulary in TCM.[11] And it includes manchurian wildginger (*Xixin, Asari Radix et Rhizoma*), *Pinellia ternata* (*Banxia, Pinelliae Rhizoma*), liquorice root (*Gancao, Glycyrrhizae Radix et Rhizoma*), Chinese Magnoliavine Fruit (*Wuweizi, Schisandrae Chinensis Fructus*), dried ginger (*Ganjiang, Zingiberis Rhizoma*), Cassia Twig (*Guizhi, Ramulus Cinnamomi*), Chinese Ephedra herb *(mahuang, Ephedrae Herba*), and white peony root (*Baishao, Paeoniae Radix Alba*). XQLD has been used against acute airway diseases for thousands of year in ancient China.[12] XQLD was the most commonly used herbal preparation for chronic bronchitis in famous veteran TCM doctor.[13] The therapeutic effect of XQLD in COPD patients has received most traditional Chinese physicians' approval.[14] So it is necessary for us to assess the efficacy and safety of XQLD, which act as an adjuvant treatment with conventional treatment (CT). The aim of this study is to assess the available evidence of XQLD for COPD according to randomized controlled trials (RCTs).

## 2. Materials and methods

### 2.1. Registration

The study protocol has been registered on international prospective register of systematic review (PROSPERO). The study registration number of PROSPERO is CRD 42018115684. And the protocol for this systematic review was published in *Medicine*.[15] This systematic review and meta-analysis is reported according to the preferred reporting items for systematic reviews and meta-analysis: the PRISMA statement.[16]

### 2.2. Search strategy

PubMed, Cochrane Library, China National Knowledge Infrastructure, Chinese Science and Technology Periodical Database and Wanfang database were retrieved in English or in Chinese by using the following search terms:"(Chronic obstructive pulmonary disease) and (*xiaoqinglong decoction*)" or "(Chronic obstructive pulmonary disease) and (*Shoseiryuto*)" (*Shoseiryuto* is a Japanese Kampo medicine name of XQLD). The search time ranged from the inception of each database until October 5, 2018. Moreover, we also manually searched the additional relevant studies, using the references of the systematic reviews that published previously. Two reviewers independently screened the titles and abstracts for eligibility and examined the full text of the articles. Any discrepancies were resolved by consensus or after consulting a third party.

### 2.3. Study selection

All included trials met the following selection criteria: the study was a RCT; the study examined patients with diagnosed acute exacerbation of COPD, who received XQLD combined with conventional therapy as treatment compared with those receiving conventional therapy alone; the study included participants irrespective of gender, age, or ethnicity, who were diagnosed with COPD using clearly defined or internationally recognized criteria; and at acute exacerbation stage. The exclusion criteria were as follows: non-RCTs and quasi-RCTs. Studies were excluded if they did not meet the above eligibility criteria. Additionally, trials with any 1 of the following conditions were excluded: duplicated publications; case series, reviews, observation study, animal researches, and pharmacological experiments; TCM that were used in both treatment group and control group; combined with other TCM therapy.

An herbal formula that must include XQLD was used in the experiment group. There was no limitation on the form of the drug (e.g., liquid, direction, pill, and capsule), dosage, frequency, or duration of the treatment. The intervention of control groups included CT. The primary outcomes were total clinical efficacy rate (TCER), TCM symptom scores, TCM symptom relief time (TCMsrt). The secondary outcomes were lung function, blood gas analysis, inflammatory cytokines, and C-reactive protein (CRP).

### 2.4. Data extraction

Two reviewers independently extracted data using a predesigned collection form. The following data were extracted: general trial characteristics (title, authors, and year); baseline patient and disease data (sample size, age, and gender); interventions (dose, details of control interventions); and outcomes (outcome measures, adverse events). Discrepancies were settled by consensus or a third party.

### 2.5. Quality assessment

Methodological quality of included studies was assessed by using the risk of bias tools in accordance with Cochrane Handbook for Systematic Reviews of Interventions.[17] Seven components were as follows: adequate sequence generation; concealment of allocation; blinding (participants and personnel); blinding (outcome assessor); incomplete outcome data addressed (intention-to-treat analysis); selective reporting; and other potential threat to validity. Each of these indicators was categorized as low risk of bias, high risk of bias, and unclear. In the scale of 0 to 7, we included the studies to enter the final analysis only when they met at least 3 items. Disagreements between 2 reviewers about the assessment of quality of included literatures were solved through consultation with corresponding authors.

### 2.6. Description of possible mechanisms

Animal-based mechanism studies of XQLD and related autoimmune disease were searched.

### 2.7. Statistical analysis

Data were analyzed using Review Manager 5.3 software (Cochrane Collaboration, Oxford, UK). Given the characteristics of the extracted data in the review, continuous outcomes were expressed as mean difference (MD) with 95% confidence intervals (CIs). $I^2$ statistics were used to assess heterogeneity. A fixed-effects model was used if no significant heterogeneity was found in the data ($I^2 < 50\%$), and a random-effects model was used if significant heterogeneity was found ($I^2 \geq 50\%$). Sensitivity analysis was performed to assess the stability of conclusions. Where heterogeneity was detected, accepted methods were used to explore the statistical heterogeneity using clinical parameters such as treatment duration, sample size, publication year, diagnostic criteria, and publication language. Publication bias was analyzed by funnel plot analysis if sufficient studies ($n \geq 10$) were found.

## 3. Results

### 3.1. Study identification

According to our search strategy in 5 electronic databases, 170 potential relevant publications were searched, after duplication removed, 89 records remained. After screening the title/ abstracts, 32 records were excluded; among which 10 studies were basic studies, 7 studies were reviews, 8 studies' intervention included other TCM therapies, 4 studies were non-oral, 2 studies did not meet the inclusion criteria, and 1 study did not evaluate the effect of XQLD. After assessing 57 full-text for eligibility; 19 records were excluded for the following reasons: 1 study was basic research; 2 studies were without data in article; 10 studies did not meet the inclusion criteria, 2 studies had duplicate publication, 2 studies' intervention included other TCM therapies, 2 studies were without treatment duration. Finally, 38 eligible studies with Cochrane Risk of bias score ≥3 met the inclusion criteria and were included (Fig. 1).

### 3.2. Study characteristics

The characteristics of the 38 included studies were summarized in Table 1. All of the 38 studies included were single-centered, randomized, parallel, controlled clinical trials conducted in China and published in Chinese language. The sample size of the included studies ranged from 40 to 180, enrolling a total of 3306 participants, 1680 patients in treatment groups and 1626 patients in control groups. The treatment duration ranged from 7 to 28 days. All studies evaluated the efficacy of XQLD + CT compared with CT in COPD treatment. Patients in treatment groups were treated by XQLD + CT. Patients in the control groups were treated by CT alone.

### 3.3. Description of XQLD

The components of XQLD or modified XQLD were depicted in Table 2. Thirty-five herbs were used in the 38 different XQLDs. The frequency of use for a particular herb and their channel tropism were calculated, and those used at a high frequency are described in detail. The top 8 most frequently used were Chinese Ephedra herb (*mahuang, Ephedrae Herba*), *P ternata* (*Banxia, Pinelliae Rhizoma*), Cassia Twig (*Guizhi, Ramulus Cinnamomi*), manchurian wildginger (*Xixin, Asari Radix et Rhizoma*), Chinese Magnoliavine Fruit (*Wuweizi, Schisandrae Chinensis Fructus*), white peony root (*Baishao, Paeoniae Radix Alba*), dried ginger (*Ganjiang, Zingiberis Rhizoma*), and liquorice root (*Gancao, Glycyrrhizae Radix et Rhizoma*), which were used more than 35 times (Table 3). Channel tropism involved 11 regular channels, lung channel (*Fei jing*), heart channel (*Xin jing*), spleen channel (*Pi jing*), stomach channel (*Wei jing*), kidney channel (*Shen jing*), bladder channel (*pangguang jing*), liver channel (*Gan jing*), large intestine channel (*dachang jing*), gall bladder channel (*dan jing*), small intestine channel (*xiaochang jing*), and pericardium channel (*Xinbao jing*), with a total appearance frequency of 1085. The most frequent 5 channels were lung channel (*Fei jing*), heart channel, spleen channel, stomach channel, and kidney channel, with a total of 85.81% of the total frequency (Table 4). Drug dosage of XQLD (Table 5) and herbs' medicinal part and source of XQLD (Table 6) were showed as follow.

### 3.4. Decocting method of XQLD

According to *Shanghanlun*'s decocting method, "2000 mL water was used to boil those 8 herbs, *Mahuang* was boiled before other herbs until the liquid reduced to 400 mL. Then put other herbs together, boiling until the liquid reduced to 600 mL, reduce the

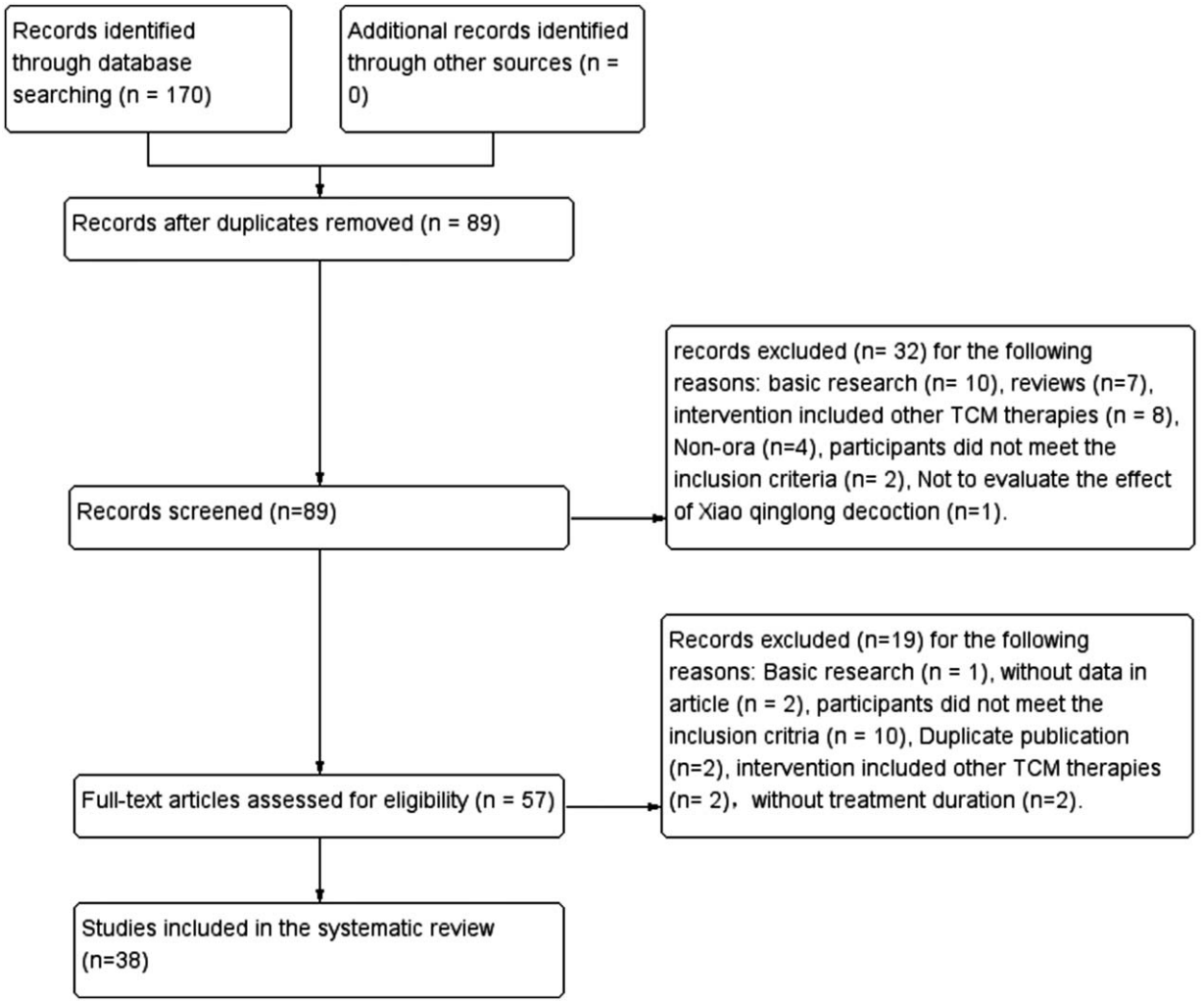


**Figure 1.** Flow diagram of study selection process. PubMed, Cochrane Library, CNKI, VIP, and Wanfang database. CNKI = China National Knowledge Infrastructure, VIP = Chinese Science and Technology Periodical Database.

liquid until the final volume of sauce liquid is at 4/5 the depth it was when you began." Nowadays, pottery pot or porcelain pot are used to boil the herbs, before the first boiling, let the herbs soak in the water for 20 minutes, then put them in pot, herbs covered with about 2 to 4 cm of water above the herbs. First boil *Mahuang* for about 20 minutes, then add other herbs and boil for about 10 to 15 minutes. Strain the liquid and keep it. Cover the herbs again with water, bring to a boil, simmer, and strain the liquid. Then mix all the liquid together.

### 3.5. Risk of bias

Risk of bias assessment is shown in Table 7. All included studies were described as "randomized" with appropriate methods of sequence generation. Thirteen studies used a random number table in the allocation of participants[18,21,24,30,32,40,42,43,45,47,51,52,54]; 2 studies used the method of lottery.[28,48] Those 15 studies were assessed to be low risk of bias in the domain of sequence generation. One study applied "sealed envelopes"[40] in the trial design. All studies had no dropouts.

### 3.6. Primary outcome measure

In this study, the TCER, TCM symptom scores, and TCMsrt were defined as primary outcome measure. TCER was reported in 32 trials with 2692 patients.[14,18,19,20,21,24–26,28–41,44–51,53,54] XQLD plus CT significantly improved TCER compared to CT (RR = 1.22, 95% CI 1.18–1.26, $P < .00001$, Fig. 2); TCM symptom scores (Fig. 3) including TCM syndrome score (TCMss), cough symptom score, sputum symptom score, wheezing symptom score. TCMss was reported in 5 trials[18,24,40,44,54] with 364 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −1.70; 95% CI = −2.08 to −1.31; $P < .00001$; Fig. 3A). Cough symptom score was reported in 6 trials[19,25,27,30,35,40] with 505 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −0.65; 95% CI = −0.70 to −0.59; $P < .00001$; Fig. 3B). Sputum symptom score was reported in 6 trials[19,25,27,30,35,40] with 505 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −0.41; 95% CI = −0.45 to −0.37; $P < .00001$; Fig. 3C). Wheezing symptom score was reported in 6

**Table 1**

**Basic characteristics of the included trials.**

| References | Sample size (intervention/control) | Age (years) Course of disease (years) | | Gender (male/female) | | | | Treatment duration | Outcome index | Baseline difference | Treatment determination based on TCM syndrome differentiation | Quality control |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Intervention | Control | Intervention | Control | Intervention | Control | | | | | |
| [18]* | 30/30 | 69.32±5.67 (18.51±3.16) | 67.56±6.18 (17.86±4.07) | 20/10 | 21/9 | Modified XQLD (200 mL, Bid)/d + CT | CT | 7 days | TCER, TCMss, TCMsrt | NSD | Y | NR |
| [19]* | 38/37 | 63.21±8.63 (14.57±7.69) | 64.01±8.13 (14.46±7.38) | 22/16 | 20/17 | Modified XQLD (1 dose/d) + CT | CT | 14 days | TCER, $PaO_2$, $PaCO_2$, TCMss | NSD | Y | NR |
| [14]* | 68/68 | 54.5 (15.3±5.4) | 86/58 | XQLD (1 dose/d) + CT | CT | 20 days | TCER | NSD | NR | NR | | |
| [20]* | 40/40 | 62.7±8.3 (11.8±3.7) | 63.4±8.6 (12.1±3.9) | 28/12 | 27/13 | XQLD (100 mL, Tid)/d + CT | CT | 5 days | TCER, FEV1, $PaO_2$, $PaCO_2$, FVC% | NSD | Y | NR |
| [21]* | 48/48 | 58.4±11.6 (18.2±12.2) | 60.2±10.1 (19.3±11.3) | 27/21 | 26/22 | XQLD (66 mL, Tid)/d + CT | CT | 28 days | TCER, FEV1, FVC, IL-4, IL-8, TNF-α | NSD | NR | NR |
| [22]* | 46/46 | 58.21±6.19 (13.24±2.17) | 56.39±4.51 (11.71±6.23) | 30/16 | 34/12 | XQLD (150 mL, Bid)/d + CT | CT | 14 days | FEV1, FVC, EV1/FVC, IL-6, IL-8, TNF-α, CRP | NSD | NR | NR |
| [23]* | 40/40 | 66±8 (18±7.4) | 69±5 (20±5.5) | 18/22 | 15/25 | XQLD (1 dose/d) + CT | CT | 7 days | $PaO_2$, $PaCO_2$ | NSD | NR | NR |
| [24]* | 33/30 | 68.69±5.83 (17.02±3.88) | 66.73±6.84 (17.32±4.28) | 26/7 | 24/6 | Modified XQLD (200 mL, Bid)/d + CT | CT | 7 days | TCER, FEV1%, TCMss, FEV1/FVC | NSD | Y | NR |
| [25]* | 60/60 | 62.5±8.5 (12.3±3.5) | 63.2±8.2 (12.5±4.1) | 46/14 | 44/16 | Modified XQLD (75 mL, Bid)/d + CT | CT | 10 days | TCER, $PaO_2$, $PaCO_2$, TCMss | NSD | Y | NR |
| [26] | 59/59 | 58.4±4.2 (5.2±1.3) | 62/56 | Modified XQLD (200 mL, Tid)/d + CT | CT | 10 days | TCER, FEV1, FEV1%, FVC, FEV1/FVC | NSD | NR | NR | | |
| [27]* | 50/50 | 65.4±3.5 (15.8±4.7) | 66.9±4.1 (14.9±4.4) | 27/23 | 29/21 | Modified XQLD (150 mL, Bid)/d + CT | CT | 7 days | FEV1, $PaO_2$, $PaCO_2$, TCMss, FVC, FEV1/FVC, CRP | NSD | NR | NR |
| [28] | 44/43 | 59.27±7.14 (10.25±3.11) | 58.33±6.89 (10.33±2.95) | 24/20 | 24/19 | XQLD (100 mL, Bid)/d + CT | CT | 28 days | TCER, FEV1, FVC, FEV1/FVC, IL-4, IL-8, TNF-α | NSD | NR | NR |
| [29] | 30/30 | 65.3±8.5 (25.1±6.8) | 60/30 | XQLD (1 dose/d) + CT | CT | 21 days | TCER, $PaO_2$, $PaCO_2$ | NSD | NR | NR | | |
| [30] | 40/40 | 48.4±11.6 (0.5–30) | 47.8±8.54 (0.6–30) | 23/17 | 24/16 | Modified XQLD (100 mL, Tid)/d + CT | CT | 14 days | TCER, FEV1%, TCMss, FEV1/FVC, FVC%, | NSD | Y | NR |
| [31]* | 80/80 | 65–87 (7–32) | 65–89 (5–32) | 52/28 | 56/24 | Modified XQLD (1 dose/d) + CT | CT | 15 days | TCER, FEV1%, $PaO_2$, $PaCO_2$ | NSD | NR | NR |
| [32] | 41/41 | 44.28±3.23 (2.18±0.28) | 43.97±2.38 (2.72±0.66) | 25/16 | 24/17 | XQLD (150 mL, Bid)/d + CT | CT | 10 days | TCER, FEV1%, FEV1/FVC | NSD | NR | NR |
| [33]* | 30/30 | 62.7±14.9 | 64.3±12.8 | 15/15 | 15/15 | XQLD (100 mL, Bid)/d + CT | CT | 14 days | TCER, TCMss | NSD | NR | NR |
| [34]* | 25/25 | – | – | 14/11 | 13/12 | XQLD (150 mL, Bid)/d + CT | CT | 10 days | TCER, FEV1, FVC% | NSD | NR | NR |
| [35]* | 35/35 | 61.91±4.48 (17.53±5.41) | 61.50±5.51 (17.62±4.36) | 17/17 | 18/16 | Modified XQLD (1 dose/d) + CT | CT | 10 days | TCER, $PaO_2$, $PaCO_2$, FVC, FEV1/FVC | NSD | Y | NR |
| [36]* | 25/25 | 66.73±8.16 (13.52±7.06) | 69.54±7.26 (12.96±6.80) | 18/7 | 20/5 | XQLD (100 mL, Bid)/d + CT | CT | 14 days | TCER, FEV1%, FEV1/FVC, IL-4, INF-γ, CRP | NSD | Y | NR |
| [37]† | 25/25 | 66.2±8.3 (25.6±6.6) | 65.3±8.5 (25.1±6.8) | 14/11 | 13/12 | XQLD (1 dose/d) + CT | CT | 21 days | TCER | NSD | NR | NR |
| [38]* | 56/30 | 60.1±13.2 (12.2±4.1) | 56/30 | XQLD (1 dose/d) + CT | CT | 21 days | TCER, $PaO_2$, $PaCO_2$ | NSD | NR | NR | | |
| [39]* | 20/20 | 65.5±13.1 (40.9±8.5) | 67.1±11.3 (40.7±8.9) | 15/5 | 14/6 | Modified XQLD (150 mL, Bid)/d + CT | CT | 14 days | TCER, FVC | NSD | Y | NR |
| [40]* | 30/30 | 75.03±6.22 | 75.20±6.45 | 22/8 | 24/6 | Modified XQLD (1 dose/d) + CT | CT | 14 days | TCER, FEV1, FEV1%, $PaO_2$, $PaCO_2$, TCMss, CRP | NSD | Y | NR |
| [41]* | 52/34 | 63.1±3.6 | 62.9±2.9 | 32/20 | 24/20 | Modified XQLD (100 mL, Bid)/d + CT | CT | 14 days | TCER, $PaO_2$, $PaCO_2$ | NSD | Y | NR |
| [42]* | 45/45 | 61.3±4.5 | 63.1±5.3 | 32/13 | 35/10 | XQLD (1 dose/d) + CT | CT | 14 days | $PaO_2$, $PaCO_2$ | NSD | Y | NR |
| [43]* | 50/50 | 63.81±8.56 | 63.27±8.41 | – | – | Modified XQLD (100 mL, Bid)/d + CT | CT | 14 days | FEV1, TCMss, FEV1/FVC, IL-4, IL-8, TNF-α | NSD | Y | NR |
| [44]* | 50/47 | 63.56±3.95 (12.3±3.65) | 63.13±4 (11.85±3.61) | 29/21 | 26/21 | Modified XQLD (100 mL, Bid)/d + CT | CT | 14 days | TCER, TCMss | NSD | Y | NR |
| [45]* | 30/30 | 60.8±11.22 (14.2±5) | 62.06±10.31 (15.6±5.6) | 18/12 | 17/13 | Modified XQLD (150 mL, Bid)/d + CT | CT | 10 days | TCER, FEV1/FVC, CRP | NSD | Y | NR |
| [46] | 40/40 | 56.49±5.32 (5.54±0.34) | 54.25±5.85 (5.64±0.99) | 21/19 | 26/14 | Modified XQLD (100 mL, Bid)/d + CT | CT | 10 days | TCER, FEV1, FVC, FEV1/FVC | NSD | NR | NR |
| [47]* | 49/49 | 69.0±6.5 | 68.5±6.3 | 24/25 | 26/23 | Modified XQLD (150 mL, Bid)/d + CT | CT | 14 days | TCER | NSD | NR | NR |
| [48] | 90/90 | 54.98±4.19 (8.39±4.67) | 55.09±5.19 (8.44±5.07) | 31/25 | 30/26 | Modified XQLD (1 dose/d) + CT | CT | 30 days | TCER, FEV1%, FEV1/FVC, IL-6, TNF-α | NSD | Y | NR |
| [49]* | 46/45 | 61.7±7.3 (14.5±6.7) | 62.3±7.5 (14.9±6.9) | 27/19 | 27/18 | XQLD (250 mL, Bid)/d + CT | CT | 14 days | TCER, FEV1, $PaO_2$, $PaCO_2$, FVC, FEV1/FVC | NSD | NR | NR |
| [50]* | 58/58 | 55.1±5.3 (7.6±2.3) | 54.7±5.2 (7.4±2.3) | 35/23 | 36/22 | Modified XQLD (250 mL, Bid)/d + CT | CT | 14 days | TCER, FEV1, $PaO_2$, $PaCO_2$ | NSD | NR | NR |
| [51]* | 30/30 | 62.9±2.7 | 62.1±3.5 | 21/9 | 20/10 | Modified XQLD (150 mL, Bid)/d + CT | CT | 14 days | TCER, FEV1, $PaO_2$, $PaCO_2$, FVC, EV1/FVC | NSD | NR | NR |
| [52]* | 76/76 | 66.9±7.5 (9.6±2.4) | 67.8±8.2 (9.3±2.7) | 47/29 | 46/30 | XQLD (1 dose/d) + CT | CT | 14 days | FEV1, $PaO_2$, $PaCO_2$, TCMsrt, FEV1/FVC, IL-4, IL-8, TNF-α, INF-γ | NSD | NR | NR |
| [53] | 30/29 | 54.6 | 33/26 | XQLD (1 dose/d) + CT | CT | 14 days | TCER, $PaO_2$, $PaCO_2$ | NSD | NR | NR | | |
| [54]* | 42/42 | 65.59±4.15 | 65.52±4.17 | 24/18 | 26/16 | XQLD (150 mL, Bid)/d + CT | CT | 14 days | TCER, FEV1, $PaO_2$, $PaCO_2$, TCMss, FVC, FEV1/FVC | NSD | Y | NR |

CRP = C-Reactive protein, CT = conventional treatment, FEV1 = forced expiratory volume in the first second, FEV1% = forced expiratory volume in one second to forced vital capacity ratio, FVC = forced vital capacity, N = no, NG = not give, NR = not been reported, NSD = no significant difference, TCER = total clinical efficacy rate, TCM = traditional Chinese medicine, TCMsrt = TCM symptom relief time, TCMss = TCM syndrome score, XQLD = Xiaoqinglong decoction, Y = yes.

* Guidelines for diagnosis and treatment of chronic obstructive pulmonary disease (Chinese Medical Association).

† Global Initiative for Chronic Obstructive Lung Disease (GOLD).

**Table 2**

**Components of Chinese herb formulas used in the included trials.**

| References | Formula | Components |
|---|---|---|
| [18] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, *Pinellia ternata* (Banxia, Pinelliae Rhizoma) 10 g, milkvetch root (Huangqi, Astragali Radix) 20 g, tangerine peel (Chenpi, Citri Reticulatae Pericarpium) 10 g, Largehead Atractylodes Rh (Baizhu, Atractylodis Macrocephalae Rhizoma) 15 g |
| [19] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, ginger (Shengjiang, Rhizoma Zingiberis Recens) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 6 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, pepperweed seed (Tinglizi, Descurainiae Semen, Lepidii Semen) 15 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 10 g |
| [14] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba), Cassia Twig (Guizhi, Ramulus Cinnamomi), manchurian wildginger (Xixin, Asari Radix et Rhizoma), white peony root (Baishao, Paeoniae Radix Alba), dried ginger (Ganjiang, Zingiberis Rhizoma), *P ternata* (Banxia, Pinelliae Rhizoma), Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus), liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) |
| [20] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba), Cassia Twig (Guizhi, Ramulus Cinnamomi), manchurian wildginger (Xixin, Asari Radix et Rhizoma), white peony root (Baishao, Paeoniae Radix Alba), dried ginger (Ganjiang, Zingiberis Rhizoma), *P ternata* (Banxia, Pinelliae Rhizoma), Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus), liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) |
| [21] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, white peony root (Baishao, Paeoniae Radix Alba) 9 g, *P ternata* (Banxia, Pinelliae Rhizoma) 9 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [22] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 15 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g |
| [23] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 15 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g |
| [24] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 12 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 5 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 8 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, tangerine peel (Chenpi, Citri Reticulatae Pericarpium) 8 g, Indian Buead Tuckahoe (Fuling, Poria) 15 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 12 g |
| [25] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 18 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 9 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, Biod Magnolia Bud (Xinyi, Magnoliae Biondii Immaturus Rlos) 9 g, earthworm (Dilong, Pheretima) 6 g, incised notopterygium rhizome and root (Qianghuo, Notopterygii Rhizoma et Radix) 10 g, Doubleteeth Pubescent Angelica Root (Duhuo, Angelicae Pubescentis Radix) 10 g |
| [26] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 8 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 8 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 8 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g |
| [27] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g |
| [28] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, white peony root (Baishao, Paeoniae Radix Alba) 9 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, *P ternata* (Banxia, Pinelliae Rhizoma) 9 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [29] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 8 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g |

(*continued*)

**Table 2**

**(continued).**

| References | Formula | Components |
|---|---|---|
| [30] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 15 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 15 g, Tatarian aster root (Ziwan, Asteris Radix et Rhizoma) 15 g, Malaytea Scurfpea Fruit (Buguzhi, Psoraleae Fructus) 15 g, Cultivated Purple Perilla seed (Suzi, Fructus Perillae) 15 g |
| [31] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 12 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g |
| [32] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba), Cassia Twig (Guizhi, Ramulus Cinnamomi), manchurian wildginger (Xixin, Asari Radix et Rhizoma), white peony root (Baishao, Paeoniae Radix Alba), dried ginger (Ganjiang, Zingiberis Rhizoma), *P ternata* (Banxia, Pinelliae Rhizoma), Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus), liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) |
| [33] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 6 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 15 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g |
| [34] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba), Cassia Twig (Guizhi, Ramulus Cinnamomi), manchurian wildginger (Xixin, Asari Radix et Rhizoma), white peony root (Baishao, Paeoniae Radix Alba), dried ginger (Ganjiang, Zingiberis Rhizoma), *P ternata* (Banxia, Pinelliae Rhizoma), Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus), liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) |
| [35] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 6 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 6 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 3 g, white peony root (Baishao, Paeoniae Radix Alba) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [36] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 6 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 5 g |
| [37]* | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 8 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g |
| [38] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba), Cassia Twig (Guizhi, Ramulus Cinnamomi), manchurian wildginger (Xixin, Asari Radix et Rhizoma), white peony root (Baishao, Paeoniae Radix Alba), dried ginger (Ganjiang, Zingiberis Rhizoma), *P ternata* (Banxia, Pinelliae Rhizoma), Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus), liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) |
| [39] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, desertliving cistanche herb (Roucongrong, Cistanches Herba) 10 g, short-horned epimedium herb (Yinyanghuo, Epimedii Folium) 10 g, Blackberrylily Rhizome (Shegan, Belamcandae Rhizoma) 10 g |
| [40] | Modified XQLD | Cassia Twig (Guizhi, Ramulus Cinnamomi) 12 g, Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 6 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 9 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 12 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 15 g, baical skullcap root (Huangqin, Scutellariae Radix) 6 g |
| [41] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [42] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 5 g, white peony root (Baishao, Paeoniae Radix Alba) 12 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 15 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 12 g, *P ternata* (Banxia, Pinelliae Rhizoma) 8 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 16 g |
| [43] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, stiff silkworm (Jiangcan, Bombyx Batryticatus) 10 g, earthworm (Dilong, Pheretima) 10 g, pepperweed seed (Tinglizi, Descurainiae Semen, Lepidii Semen) 10 g, Largehead Atractylodes Rh (Baizhu, Atractylodis Macrocephalae Rhizoma) 10 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 5 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 5 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 5 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 5 g |

(*continued*)

**Table 2**

**(continued).**

| References | Formula | Components |
|---|---|---|
| [44] | Modified XQLD | Tangshen (Dangshen, Codonopsis Radix) 15 g, Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, *P ternata* (Banxia, Pinelliae Rhizoma) 9 g, safflower (Honghua, Carthami Flos) 9 g, white peony root (Baishao, Paeoniae Radix Alba) 9 g, peach seed (Taoren, Persicae Semen) 9 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 6 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [45] | Modified XQLD | Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 9 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 9 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, white peony root (Baishao, Paeoniae Radix Alba) 12 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 5 g, Dan-Shen Root (Danshen, Salviae Miltiorrhizae Radix et Rhizoma) 30 g, Sichuan lovase rhizome (Chuanxiong, Chuanxiong Rhizoma) 12 g, Peach Seed (Taoren, Persicae Semen) 6 g, pepperweed seed (Tinglizi, Descurainiae Semen, Lepidii Semen) 15 g, white mustard seed (Baijiezi, Semen sinapis) 12 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 9 g, Szechuan-fritillary bulb (Chuanbeimu, Fritillariae Chrrhosae Bulbus) 9 g, Tomentose Pummelo Peel (Huajuhong, Citri Grandis Exocarpium) 12 g, Platycodon Grandiflorum (Jiegeng, Platycodonis Radix) 15 g |
| [46] | Modified XQLD | Manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, white mustard seed (Baijiezi, Semen sinapis) 15 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 15 g, tangshen (Dangshen, Codonopsis Radix) 15 g, Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g, Milkvetch Root (Huangqi, Astragali Radix) 30 g |
| [47] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 15 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 15 g, *P ternata* (Banxia, Pinelliae Rhizoma) 15 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 15 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 10 g |
| [48] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 6vg, Cassia Twig (Guizhi, Ramulus Cinnamomi) 6 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 3 g, white peony root (Baishao, Paeoniae Radix Alba) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [49] | XQLD | Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 12 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, Indian Buead Tuckahoe (Fuling, Poria) 9 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 9 g, Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 9 g, baical skullcap root (Huangqin, Scutellariae Radix) 9 g, white peony root (Baishao, Paeoniae Radix Alba) 9 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [50] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 9 g, white peony root (Baishao, Paeoniae Radix Alba) 9 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 9 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 12 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 9 g, baical skullcap root (Huangqin, Scutellariae Radix) 9 g, Indian Buead Tuckahoe (Fuling, Poria) 9 g, bitter apricot seed (Kuxingren, Armeniacae Semen Amarum) 9 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [51] | Modified XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 6 g, white peony root (Baishao, Paeoniae Radix Alba) 12 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 9 g |
| [52] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 5 g, cultivated Purple Perilla seed (Suzi, Fructus Perillae) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 9 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 12 g, tangerine peel (Chenpi, Citri Reticulatae Pericarpium) 6 g, Blackberrylily Rhizome (Shegan, Belamcandae Rhizoma) 10 g, Dan-Shen Root (Danshen, Salviae Miltiorrhizae Radix et Rhizoma) 9 g, white peony root (Baishao, Paeoniae Radix Alba) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 6 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, Tomentose Pummelo Peel (Huajuhong, Citri Grandis Exocarpium) 9 g, Indian Buead Tuckahoe (Fuling, Poria) 15 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 5 g, Platycodon Grandiflorum (Jiegeng, Platycodonis Radix) 5 g |
| [53] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 12 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 3 g, *P ternata* (Banxia, Pinelliae Rhizoma) 10 g, dried ginger (Ganjiang, Zingiberis Rhizoma) 10 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 10 g, earthworm (Dilong, Pheretima) 12 g, Dan-Shen Root (Danshen, Salviae Miltiorrhizae Radix et Rhizoma) 20 g, peach seed (Taoren, Persicae Semen) 15 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |
| [54] | XQLD | Chinese Ephedra herb (mahuang, Ephedrae Herba) 10 g, manchurian wildginger (Xixin, Asari Radix et Rhizoma) 5 g, *P ternata* (Banxia, Pinelliae Rhizoma) 12 g, Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) 9 g, Cassia Twig (Guizhi, Ramulus Cinnamomi) 10 g, white peony root (Baishao, Paeoniae Radix Alba) 15 g, ginger (Shengjiang, Rhizoma Zingiberis Recens) 10 g, liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) 6 g |

XQLD = Xiaoqinglong decoction.

**Table 3**

**Analysis of the top 8 frequency Chinese herb medicine in treatment of chronic obstructive pulmonary disease.**

| Herb name Latin (Chinese, English) | Frequency | Total frequency (%) | Cumulative percentiles (%) |
|---|---|---|---|
| Chinese Ephedra herb (mahuang, Ephedrae Herba) | 38 | 10.86 | 10.86 |
| *Pinellia ternata* (Banxia, Pinelliae Rhizoma) | 38 | 10.86 | 21.72 |
| Cassia Twig (Guizhi, Ramulus Cinnamomi) | 37 | 10.57 | 32.29 |
| Manchurian wildginger (Xixin, Asari Radix et Rhizoma) | 37 | 10.57 | 42.86 |
| Chinese Magnoliavine Fruit (Wuweizi, Schisandrae Chinensis Fructus) | 37 | 10.57 | 53.43 |
| White peony root (Baishao, Paeoniae Radix Alba) | 36 | 10.29 | 63.72 |
| Dried ginger (Ganjiang, Zingiberis Rhizoma) | 35 | 10.00 | 73.72 |
| Liquorice root (Gancao, Glycyrrhizae Radix et Rhizoma) | 35 | 10.00 | 83.72 |

**Table 4**

**Distribution of drugs by channel tropism used in the included studies for chronic obstructive pulmonary disease.**

| Channel | Frequency | Total frequency (%) | Cumulative percentiles (%) |
|---|---|---|---|
| Lung (Fei) | 331 | 30.51 | 30.51 |
| Heart (Xin) | 191 | 17.60 | 48.11 |
| Spleen (Pi) | 167 | 15.39 | 63.5 |
| Stomach (Wei) | 124 | 11.43 | 74.93 |
| Kidney (Shen) | 118 | 10.88 | 85.81 |
| Bladder (pangguang) | 83 | 7.65 | 93.46 |
| Liver (Gan) | 48 | 4.42 | 97.88 |
| Large intestine (dachang) | 15 | 1.38 | 99.26 |
| Gall bladder (dan) | 4 | 0.37 | 99.63 |
| Small intestine (xiaochang) | 3 | 0.28 | 99.91 |
| Pericardium (Xinbao) | 1 | 0.09 | 100 |

**Table 5**

**Drug dosage and quality control of Xiaoqinglong decoction.**

| | Mahuang (Ephedrae Herba, g) | Xixin (Asari Radix et Rhizoma, g) | Banxia (Pinelliae Rhizoma, g) | Gancao (Glycyrrhizae Radix et Rhizoma, g) | Wuweizi (Schisandrae Chinensis Fructus, g) | Ganjiang (Zingiberis Rhizoma, g) | Guizhi (Ramulus Cinnamomi, g) | Baishao (Paeoniae Radix Alba, g) | Volume of drug solution (mL) | XQLD (g/100 mL) | Processing methods of the compounds | Quality assessment of the compounds | Chemical assessment of the compounds |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [18] | 10 | 3 | 10 | 6 | 10 | 10 | 10 | 10 | 400 | 17.25 | NR | NR | NR |
| [19] | 10 | 6 | 15 | 10 | 10 | N | 10 | 15 | NG | / | NR | NR | NR |
| [14] | NR | NR | NR | NR | NR | NR | NR | NR | NR | / | NR | NR | NR |
| [20] | NR | NR | NR | NR | NR | NR | NR | NR | 200 | / | NR | NR | NR |
| [21] | 9 | 3 | 9 | 6 | 6 | 6 | 9 | 9 | 200 | 28.50 | NR | NR | NR |
| [22] | 15 | 3 | 15 | 10 | 10 | 10 | 15 | N | 300 | 26.00 | NR | NR | NR |
| [23] | 10 | 5 | 15 | 10 | 6 | 15 | 10 | 15 | NR | / | NR | NR | NR |
| [24] | 10 | 3 | 8 | 10 | 10 | 5 | 12 | 10 | 400 | 17.00 | NR | NR | NR |
| [25] | 9 | 3 | 9 | N | 10 | 10 | 15 | 18 | 150 | 49.33 | NR | NR | NR |
| [26] | 8 | 5 | 10 | 8 | 10 | 10 | 8 | 10 | 600 | 11.50 | NR | NR | NR |
| [27] | 15 | 3 | 15 | 10 | 10 | 10 | 15 | 15 | 300 | 31.00 | NR | NR | NR |
| [28] | 9 | 3 | 9 | 6 | 6 | 6 | 9 | 9 | 200 | 28.50 | NR | NR | NR |
| [29] | 10 | 5 | 10 | 8 | 10 | 10 | 10 | 10 | NR | / | NR | NR | NR |
| [30] | 10 | 3 | 10 | 15 | 15 | 10 | 15 | 15 | 300 | 31.00 | NR | NR | NR |
| [31] | 15 | 5 | 15 | 10 | 6 | 12 | 15 | 15 | NR | / | NR | NR | NR |
| [32] | NR | NR | NR | NR | NR | NR | NR | NR | NR | / | NR | NR | NR |
| [33] | 10 | 6 | 15 | 10 | 6 | 15 | 15 | 15 | 200 | 46.00 | NR | NR | NR |
| [34] | NR | NR | NR | NR | NR | NR | NR | NR | NR | / | NR | NR | NR |
| [35] | 6 | 3 | 12 | 6 | 6 | 3 | 6 | 6 | NR | / | NR | NR | NR |
| [36] | 6 | 6 | 10 | 5 | 10 | 10 | 15 | 15 | 200 | 38.50 | NR | NR | NR |
| [37]* | 10 | 5 | 10 | 8 | 10 | 10 | 10 | 10 | NR | / | NR | NR | NR |
| [38] | NR | NR | NR | NR | NR | NR | NR | NR | NR | / | NR | NR | NR |
| [39] | 10 | 5 | 10 | 10 | 10 | 10 | 10 | 10 | 300 | 25.00 | NR | NR | NR |
| [40] | 10 | 6 | 10 | 9 | 12 | 6 | 12 | 10 | NG | / | NR | NR | NR |
| [41] | 10 | 3 | 10 | 6 | 10 | 10 | 10 | 10 | 200 | 34.50 | NR | NR | NR |
| [42] | 5 | 3 | 8 | 10 | 16 | 15 | 12 | 12 | NG | / | NR | NR | NR |
| [43] | 10 | 5 | 10 | 5 | 5 | 5 | 5 | N | 100 | 45.00 | NR | NR | NR |
| [44] | 9 | 6 | 9 | 6 | 6 | 6 | 9 | 9 | 200 | 30.00 | NR | NR | NR |
| [45] | 9 | 9 | 12 | N | 5 | 9 | 9 | 12 | 300 | 21.67 | NR | NR | NR |
| [46] | 10 | 3 | 15 | 10 | N | N | N | N | 200 | 19.00 | NR | NR | NR |
| [47] | 15 | 10 | 15 | 10 | 10 | 15 | 15 | 15 | 150 | 70.00 | NR | NR | NR |
| [48] | 6 | 3 | 12 | 6 | 6 | 3 | 6 | 6 | NR | / | NR | NR | NR |
| [49] | 9 | NR | 12 | 6 | 12 | 9 | 9 | 9 | 500 | 13.20 | NR | NR | NR |
| [50] | 9 | 9 | 12 | 6 | 12 | 9 | 9 | 9 | 500 | 15.00 | NR | NR | NR |
| [51] | 10 | 3 | 10 | 9 | 6 | 6 | 10 | 12 | 300 | 22.00 | NR | NR | NR |
| [52] | 5 | 3 | 10 | NG | 5 | 6 | 9 | 12 | NR | / | NR | NR | NR |
| [53] | 10 | 3 | 10 | 6 | 10 | 10 | 10 | 12 | NR | / | NR | NR | NR |
| [54] | 10 | 5 | 12 | 6 | 9 | N | 10 | 15 | 300 | 25.67 | NR | NR | NR |
| $\bar{x} \pm s$ | 9.67 ± 2.46 | 4.56 ± 1.94 | 11.33 ± 2.32 | 8.10 ± 2.29 | 8.91 ± 2.82 | 9.03 ± 3.28 | 10.75 ± 2.86 | 11.67 ± 2.96 | 282.61 ± 123.01 | 29.35 ± 13.55 | / | / | / |

N = none, NR = not been reported, XQLD = Xiaoqinglong decoction.

**Table 6**

**Herbs' medicinal part and source of Xiaoqinglong decoction.**

| Chinese name (Latin name) | Family | Medicinal part | Source |
|---|---|---|---|
| Xixin (Asari Radix et Rhizoma) | Leguminosae | Dried roots and rhizomes | *Asarum heterotropoides* Fr. Schmidt var. mandshuricum (Maxim.) Kitag., *A sieboldii* Miq.var. seoulense Nakai, and *A sieboldii* Miq. |
| Banxia (Pinelliae Rhizoma) | Araceae | Dry tuber | *Pinellia ternata* (Thunb.) Breit. |
| Gancao (Glycyrrhizae Radix et Rhizoma) | Leguminosae | Dried roots and rhizomes | *Glycyrrhiza uralensis* Fisch., *G inflata* Bat., and *G glabra* L. |
| Wuweizi (Schisandrae Chinensis Fructus) | Magnoliaceae | Dry and ripe fruit | *Schisandra chinensis* (Turcz.) Baill. |
| Ganjiang (Zingiberis Rhizoma) | Zingiberaceae | Dried roots | *Zingiber officinale* Rosc. |
| Guizhi (Ramulus Cinnamomi) | Lauraceae | Dry twigs | *Cinnamomum cassia* Presl |
| Mahuang (Ephedrae Herba) | Ephedraceae | Dry straw | *Ephedra sinica* Stapf, *E intermedia* Schrenk et C. A. Mey., and *E equisetina* Bge. |
| Baishao (Paeoniae Radix Alba) | Ranunculaceae | Dried roots | *Paeonia lactiflora* Pall. |

**Table 7**

**Risk of bias assessments for included studies.**

| Included studies | A | B | C | D | E | F | G | Total |
|---|---|---|---|---|---|---|---|---|
| [18] | + | ? | ? | ? | + | + | + | 4 |
| [21] | + | ? | ? | ? | + | + | + | 4 |
| [24] | + | ? | ? | ? | + | + | + | 4 |
| [28] | + | ? | ? | ? | + | + | + | 4 |
| [30] | + | ? | ? | ? | + | + | + | 4 |
| [32] | + | ? | ? | ? | + | + | + | 4 |
| [42] | + | ? | ? | ? | + | + | + | 4 |
| [43] | + | ? | ? | ? | + | + | + | 4 |
| [45] | + | ? | ? | ? | + | + | + | 4 |
| [47] | + | ? | ? | ? | + | + | + | 4 |
| [48] | + | ? | ? | ? | + | + | + | 4 |
| [51] | + | ? | ? | ? | + | + | + | 4 |
| [52] | + | ? | ? | ? | + | + | + | 4 |
| [54] | + | ? | ? | ? | + | + | + | 4 |
| [40] | + | + | ? | ? | + | + | + | 5 |
| [19] | ? | ? | ? | ? | + | + | + | 3 |
| [14] | ? | ? | ? | ? | + | + | + | 3 |
| [20] | ? | ? | ? | ? | + | + | + | 3 |
| [22] | ? | ? | ? | ? | + | + | + | 3 |
| [23] | ? | ? | ? | ? | + | + | + | 3 |
| [25] | ? | ? | ? | ? | + | + | + | 3 |
| [26] | ? | ? | ? | ? | + | + | + | 3 |
| [27] | ? | ? | ? | ? | + | + | + | 3 |
| [29] | ? | ? | ? | ? | + | + | + | 3 |
| [31] | ? | ? | ? | ? | + | + | + | 3 |
| [33] | ? | ? | ? | ? | + | + | + | 3 |
| [34] | ? | ? | ? | ? | + | + | + | 3 |
| [35] | ? | ? | ? | ? | + | + | + | 3 |
| [36] | ? | ? | ? | ? | + | + | + | 3 |
| [37]* | ? | ? | ? | ? | + | + | + | 3 |
| [38] | ? | ? | ? | ? | + | + | + | 3 |
| [39] | ? | ? | ? | ? | + | + | + | 3 |
| [41] | ? | ? | ? | ? | + | + | + | 3 |
| [44] | ? | ? | ? | ? | + | + | + | 3 |
| [46] | ? | ? | ? | ? | + | + | + | 3 |
| [49] | ? | ? | ? | ? | + | + | + | 3 |
| [50] | ? | ? | ? | ? | + | + | + | 3 |
| [53] | ? | ? | ? | ? | + | + | + | 3 |

A = adequate sequence generation, B = concealment of allocation, C = blinding of participants and personnel, D = blinding of outcome assessment, E = incomplete outcome data, F = selective reporting, G = other bias, + = low risk of bias, − = high risk of bias, ? = unclear risk of bias.

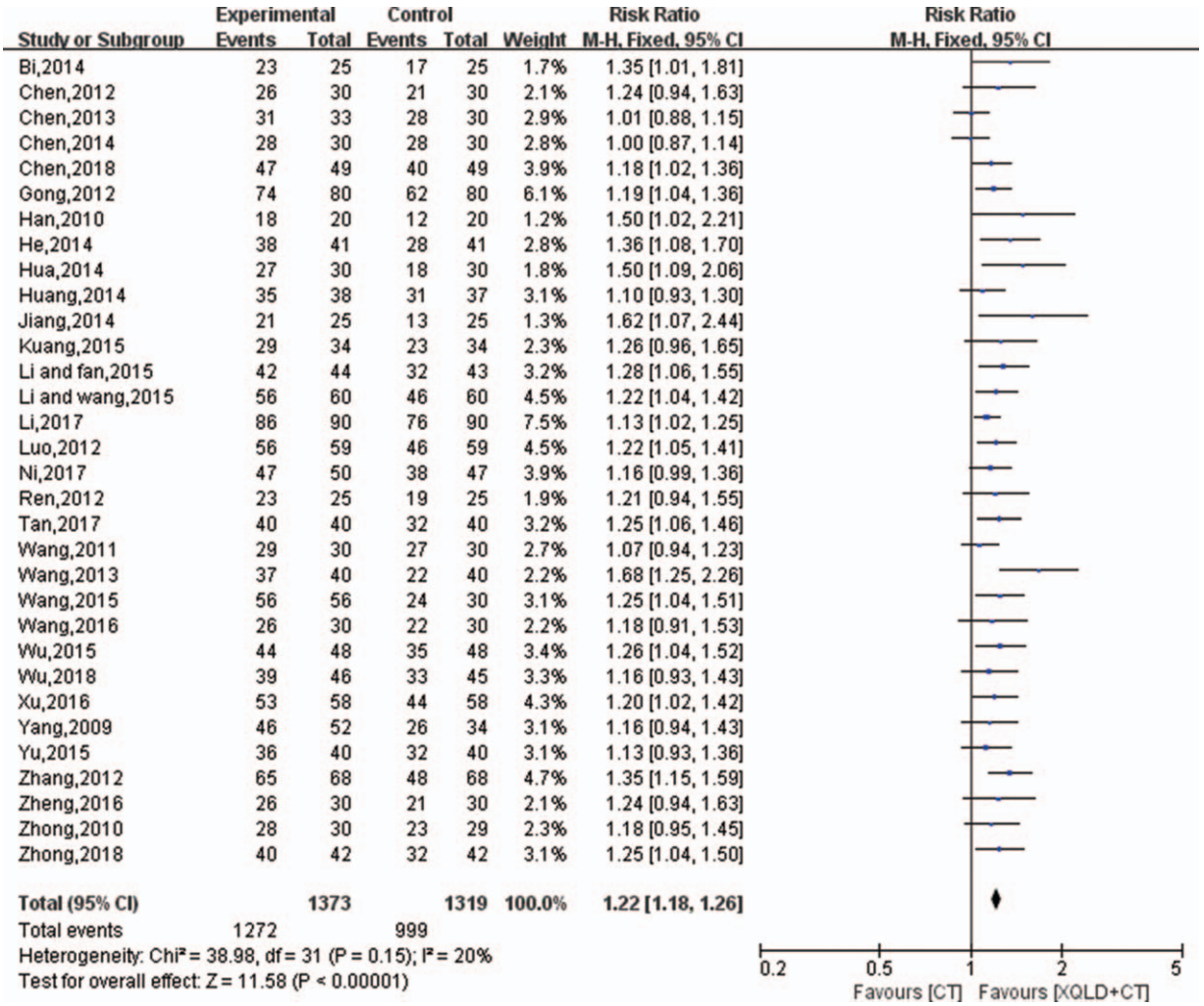


**Figure 2.** The forest plot of total clinical efficacy rate of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, XQLD = Xiaoqinglong decoction.

trials[19,25,27,30,35,40] with 505 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −0.49; 95% CI = −0.60 to −0.38; $P < .00001$; Fig. 3D).

TCMsrt (Fig. 4) includes cough relief time, sputum relief time, wheezing relief time, and lassitude relief time. Cough relief time was reported in 2 trials[18,52] with 212 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −1.28; 95% CI = −1.53 to −1.02; $P < .00001$; Fig. 4A). Sputum relief time was reported in 2 trials[18,52] with 212 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −1.19; 95% CI = −1.42 to −0.96; $P < .00001$; Fig. 4B). Wheezing relief time was reported in 2 trials[18,52] with 212 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −1.65; 95% CI = −2.63 to −0.68; $P = .0009$; Fig. 4C). Lassitude relief time was reported in 2 trials[18,52] with 212 patients. Compared with CT, data showed that XQLD plus CT was superior to CT (MD = −2.16; 95% CI = −3.44 to −0.89; $P = .0009$; Fig. 4D).

### 3.7. Secondary outcome measures

In this study, lung function, blood gas analysis, inflammatory cytokines, and CRP were defined as the secondary outcomes measure. Lung function (Fig. 5) includes FEV1, forced expiratory volume in 1 second to forced vital capacity (FVC) ratio (FEV1%)pre, and FEV1/FVC. Fifteen studies[20–22,26–28,34,40,43,46,49–52,54] with 1366 patients for FEV1 showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = 0.37, 95% CI = 0.27–0.46; $P < .00001$; Fig. 5A). Seven studies[24,26,30,31,36,48,40] with 711 patients for FEV1%pre showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = 4.52, 95% CI = 2.42–6.62; $P < .00001$; Fig. 5B). Fourteen studies[22,26–28,30,32,33,36,45,46,48,49,52,54] with 1319 patients for FEV1/FVC showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = 5.11, 95% CI = 4.21–6.00; $P < .00001$; Fig. 5C).

Blood gas analysis (Fig. 6) includes $PaO_2$ and $PaCO_2$. Seventeen trials with 1559 COPD patients that compared XQLD plus CT with CT were identified in this analysis.[19,20,23,25,27,29,31,38,40–42,49,54] Meta-analysis showed that

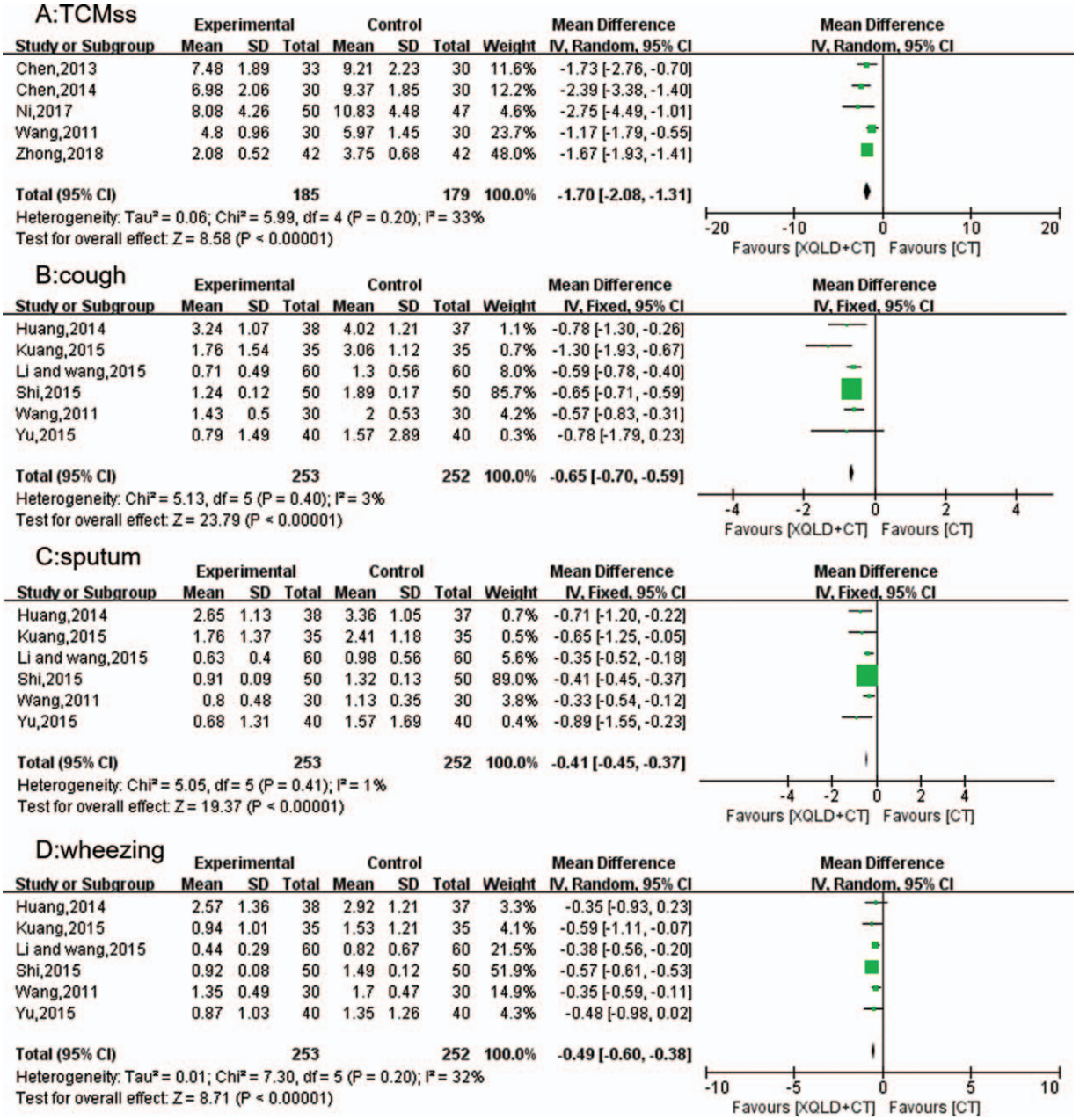


**Figure 3.** The forest plot of TCM symptom scores of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, TCM = traditional Chinese medicine, TCMss = TCM syndrome score, XQLD = Xiaoqinglong decoction.

$PaO_2$ was significantly improved by XQLD (MD = 7.17, 95% CI = 4.80–9.54; $P < .00001$; Fig. 6A); $PaCO_2$ was significantly reduced by XQLD (MD = −7.63, 95% CI = −9.62 to −5.63; $P < .00001$; Fig. 6B).

Inflammatory cytokines (Fig. 7) include interleukin (IL)-4, IL-6, IL-8, TNF-α, and INF-γ. Five studies[21,28,36,43,52] with 485 patients for IL-4 showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = −9.20, 95% CI = −13.59 to −4.81; $P < .00001$; Fig. 7A). Two studies[22,48] with 272 patients for IL-6 showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = −5.07, 95% CI = −8.14 to −2.01; $P = .001$; Fig. 7B). Five studies[21,22,28,43,52] with 366 patients for IL-8 showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = −5.59, 95% CI = −6.09 to −5.08; $P < .00001$; Fig. 7C). Six studies[21,22,28,48,43,52] with 615 patients for TNF-α showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = −5.93, 95% CI = −6.97 to −4.89; $P < .00001$; Fig. 7D). Two studies[36,52] with 202 patients for INF-γ showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = 18.03, 95% CI = 13.22–22.84; $P < .00001$; Fig. 7D).

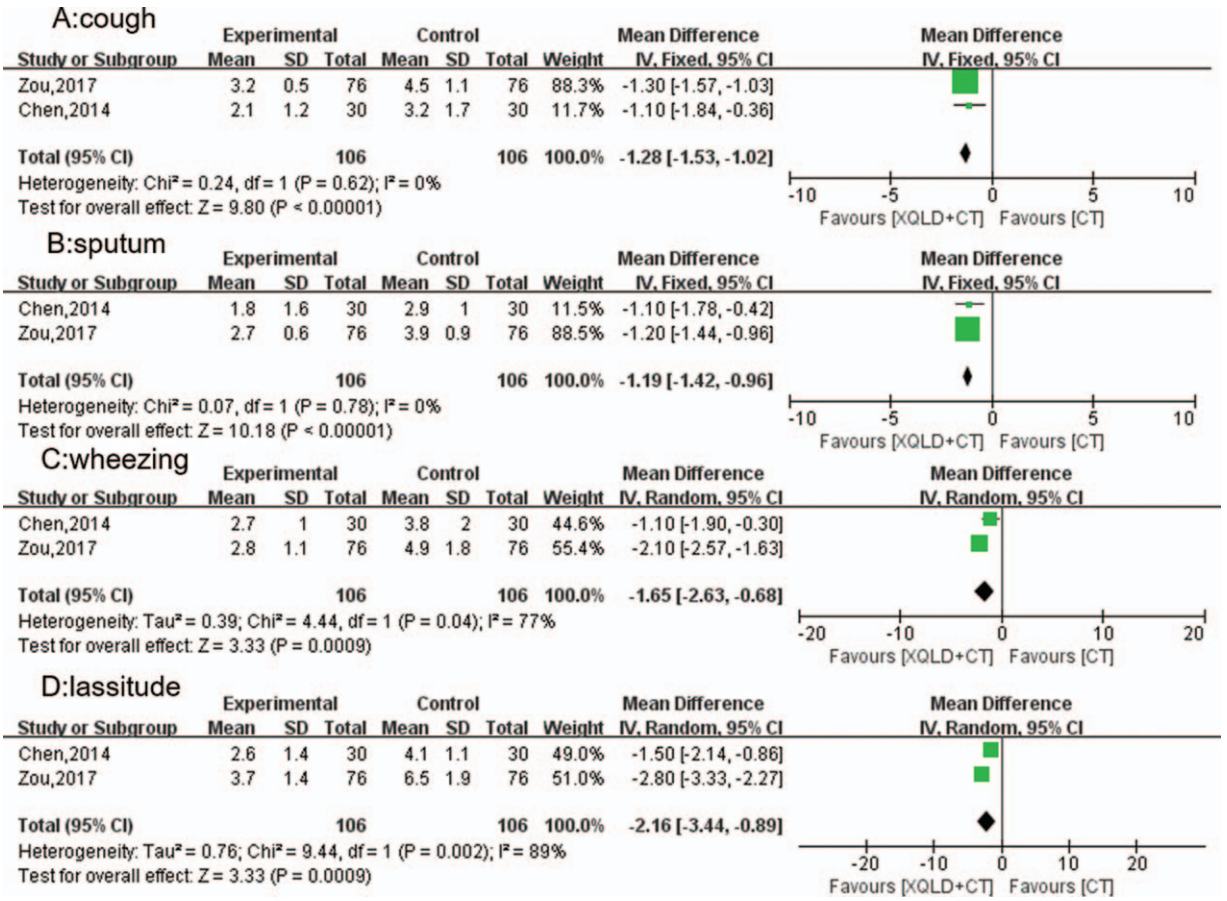


**Figure 4.** The forest plot of symptom relief time (d) of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, XQLD = Xiaoqinglong decoction.

Five studies[22,27,36,40,45] with 362 patients for CRP showed that there was a benefit for the XQLD plus CT group when compared with CT (MD = −3.93, 95% CI = −5.97 to −1.89; $P = .0002$; Fig. 8).

### 3.8. Adverse effects

Adverse effects were reported in 4 studies.[28,40,47,54] One study reported the adverse events occurring during the treatment, 5/49 (10.2%) patients suffered adverse events in the trial group and 4/49 (8.16%) patients did so in control group. Three studies[28,40,54] stated that no adverse events happened during the treatment.

### 3.9. Publication bias

Publication bias was assessed using a funnel plot based on the total efficacy rate reported in 32 studies. The funnel plot was asymmetrical, which indicated that the potential publication bias might influence the results of this review. The bias might result from these reasons: poor quality, and a high proportion of positive results (Fig. 9).

### 3.10. Possible mechanisms of XQLD

In XQLD, "jun" (emperor) herbs are Ephedra herb and Cassia Twig, "Chen" (minister) herbs are manchurian wildginger and dried ginger, "Zuo" (assistant) herbs are *P ternata*, Chinese Magnoliavine Fruit, and white peony root, while "shi" (delivering servant) is liquorice root; all of which exert effects of mutual reinforcement and detoxification. Studies have predicted that paeonol, glycyrrhizin, and geraniin are the 3 most effective ingredients in XQLD for cough and asthma.[55] XQLD could improve the airway hyperreactivity and airway reconstruction, and remiss the inflammation of COPD airway.[56] Oral administration of XQLD (Shoseiryuto) reduced the production of IL-4 and IL-5 in airway inflammatory model mice[57]; and increased FoxP3$^+$, CD4$^+$ (BALB/c mice).[58] Rectify imbalance of oxidation/antioxidation and alleviate inflammatory reactions,[11] exhibit higher levels of apoptosis, upregulate LC3II/LC3I ratio, and downregulate p62 level,[59] the transcription factor nuclear factor-κB (NF-κB),[60] and γ-glutamylcysteine synthetase[61] level in COPD rats. One experimental research[62] showed that, there are no side effects such as interstitial pneumonia, myopathy, or impaired liver function.

## 4. Discussion

### 4.1. Summary of evidence

TCM classic herb formulas XQLD have been recommended as complementary and alternative regimens for respiratory system including cough, asthma, COPD,[14] and allergic airway disease in Asian counties including China and Japan[63] for a long time. Studies showed that XQLD was an effective drug for COPD

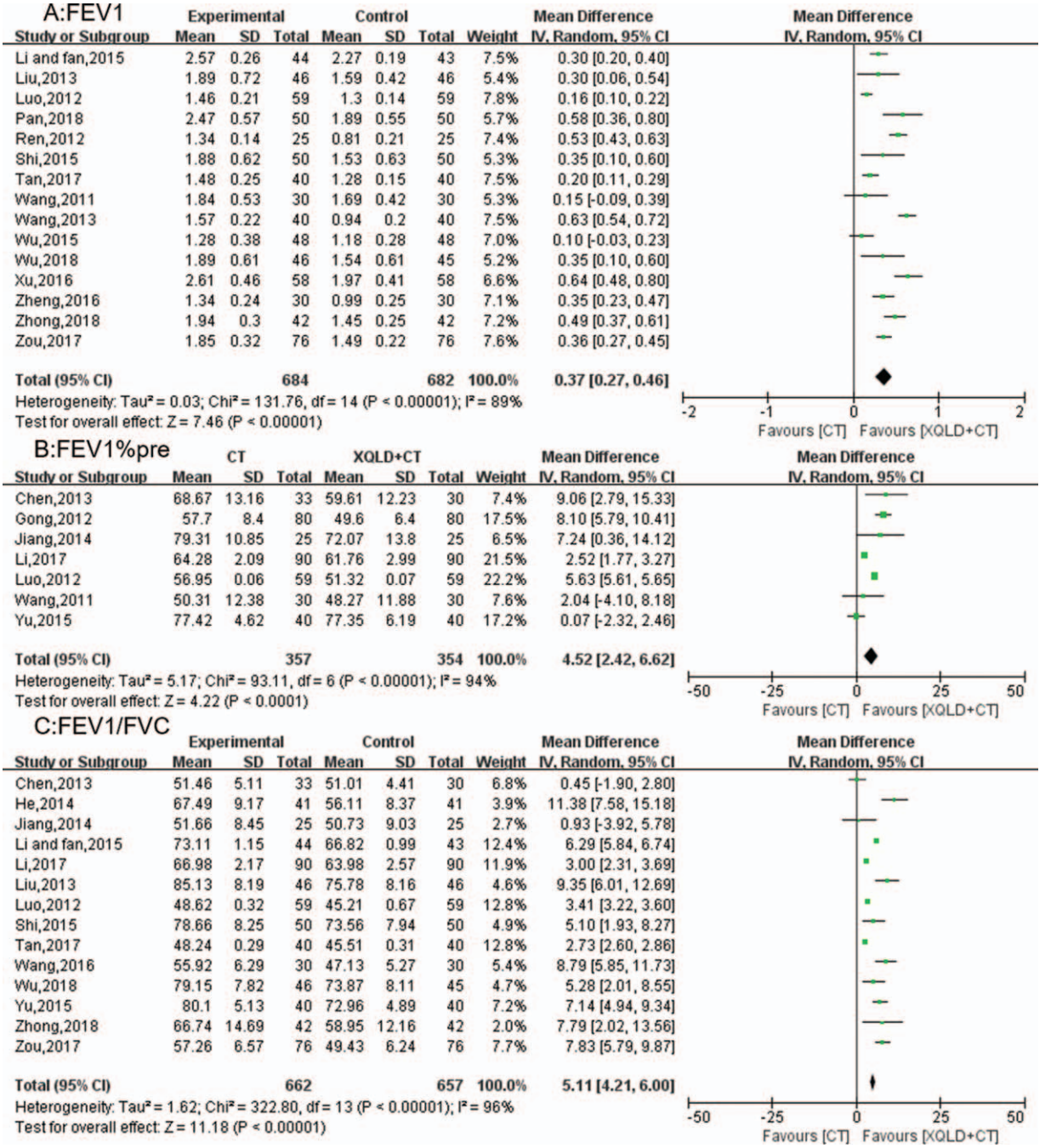


**Figure 5.** The forest plot of lung function of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, XQLD = Xiaoqinglong decoction.

treatment and its function was related to gene expression alteration,[64] it can inhibits the progress of COPD via attenuating the autophagy process.[59]

This study focuses on evaluating the efficacy and safety of XQLD in combination of CT for treating COPD compared with CT alone. Thirty-eight RCTs were included and most of them were assessed as having a high risk of bias. Our primary finding was that XQLD plus CT can improve TCER, alleviate the symptoms (cough symptom, sputum symptom, wheezing symptom), and reduce TCMsrt (cough, sputum, wheezing, lassitude). The second finding of this review was that XQLD plus CT can improve lung function (FEV1, FEV1%pre, and FEV1/FVC); raise $PaO_2$, reduce $PaCO_2$; regulate the body's inflammatory response. Because COPD is associated with chronic inflammation caused by cigarette smoking and leads to symptoms such as cough, shortness of breath, and increased sputum production The Global Initiative for Chronic Obstructive Lung Disease (2013 revised edition).[65] So XQLD may be suitable for COPD patients with uncontrolled symptoms, it can help alleviate symptoms and shorten the duration of symptoms.

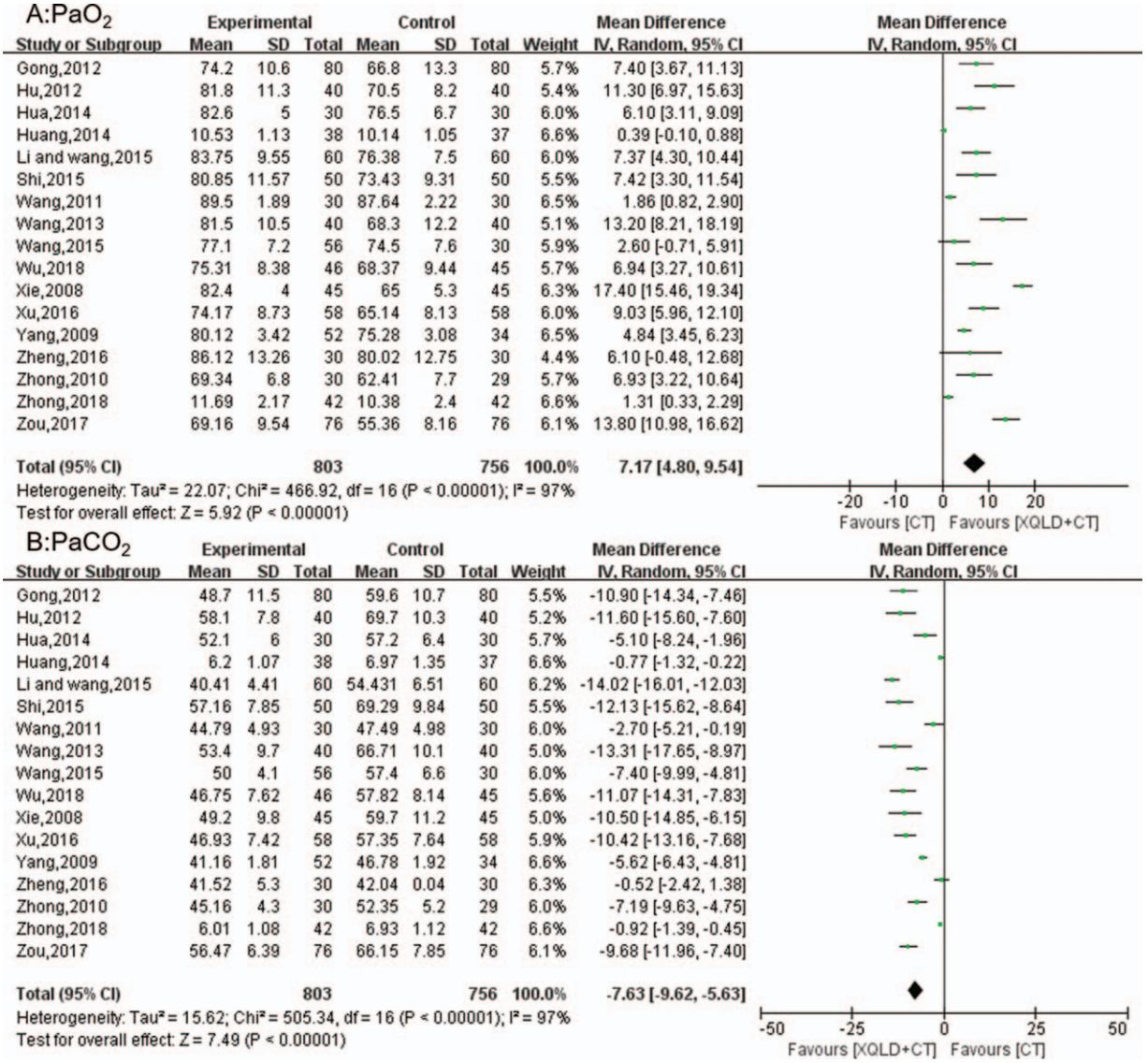


**Figure 6.** The forest plot of blood gas analysis of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, XQLD = Xiaoqinglong decoction.

Only 1 study reported adverse events, so it seems that XQLD in an effective and safe therapy option for COPD patients. Animal study[62] also showed that, there are no side effects such as interstitial pneumonia, myopathy, or impaired liver function.

XQLD (Shoseiryuto in Japanese) has been found to cause side effects in rare instances, such as interstitial pneumonia, myopathy, or impaired liver function.[66] However, these effects were not apparent in this review, animal study also approved this.[62]

### *4.2. Limitations for the review*

The study implemented strict inclusion and exclusion criteria. However, there were still statistical heterogeneity between some of the outcome indicators of the included trials, due to the main consideration and the limited sample size and the variation in the length of treatment. The quality of included studies was generally not high, no trials were identified as a multicenter, large sample, prospective, double-blinded, controlled randomized trial. Only 15 trials[18,21,24,28,30,32,40,42,43,45,47,48,51,52,54] described the method of randomization procedure. None of the included studies mentioned the allocation concealment and no studies mentioned the blinding of participants and personnel as well as blinding of outcome assessment.

## 5. Conclusion

This systematic review and meta-analysis suggested that XQLD plus CT is more efficacious than CT alone in the treatment of COPD patients. However, due to the high clinical heterogeneity and small sample size of the included trials, large-scale, randomized double-blind, multicenter trials are still required. Due to few data for safety analysis, we still cannot recommend XQLD as an effective and safe therapy.

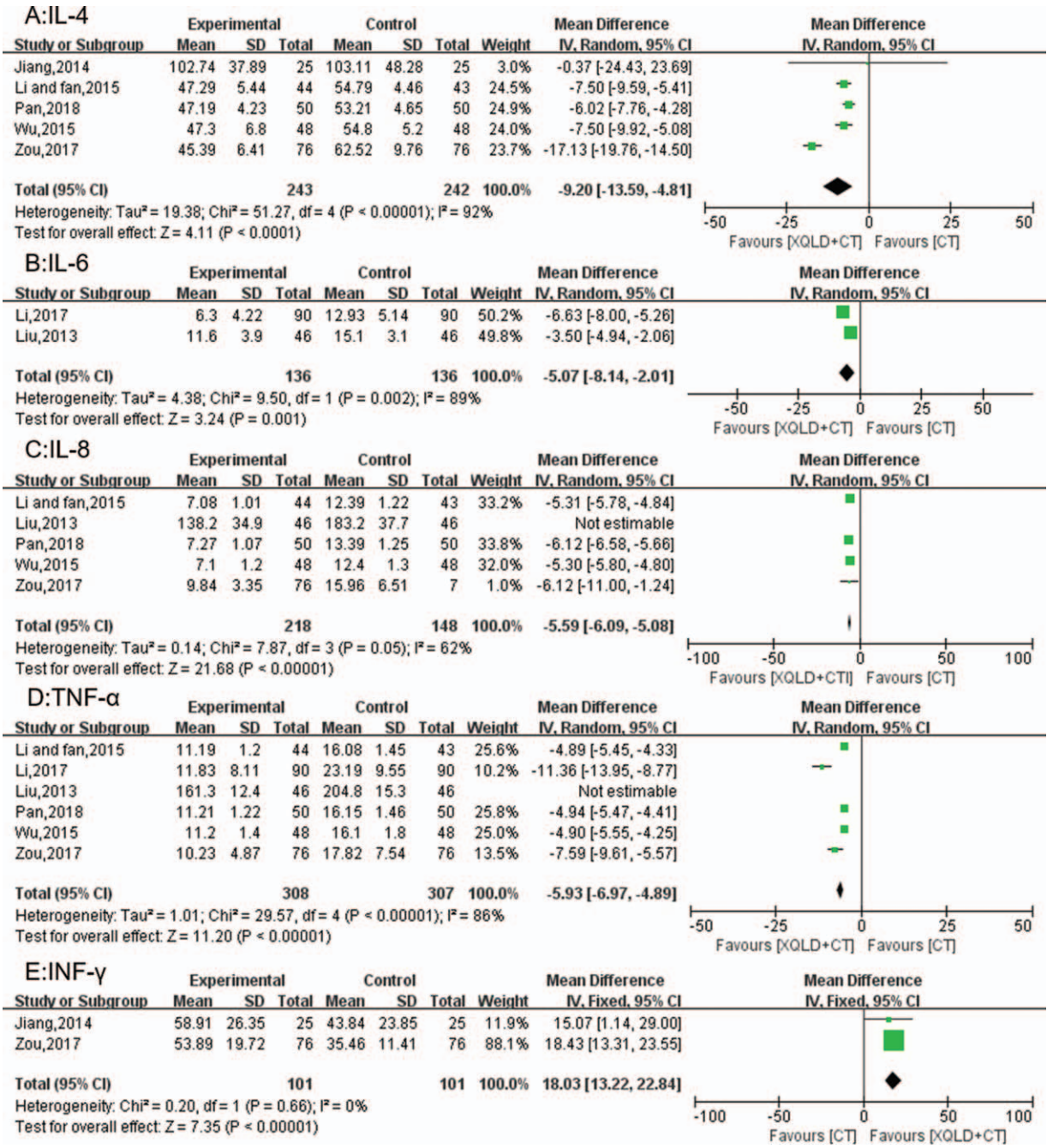


**Figure 7.** The forest plot of inflammatory cytokines of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, IL = interleukin, XQLD = Xiaoqinglong decoction.

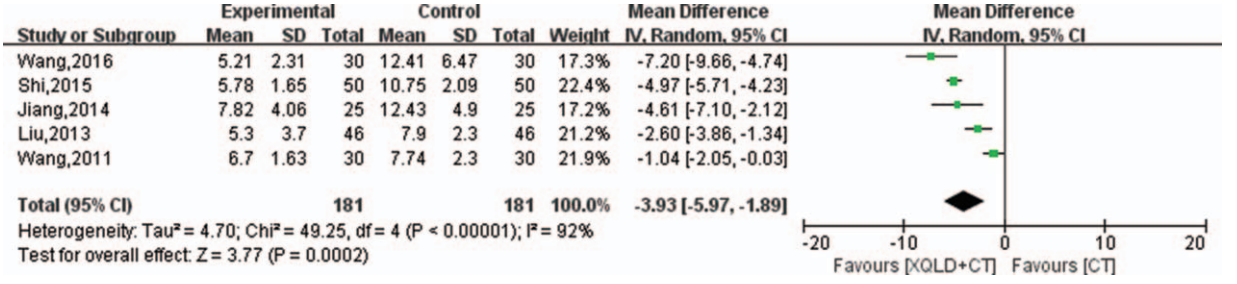


**Figure 8.** The forest plot of CRP of XQLD plus CT vs CT. CI = confidence interval, CT = conventional treatment, CRP = C-reactive protein, XQLD = Xiaoqinglong decoction.

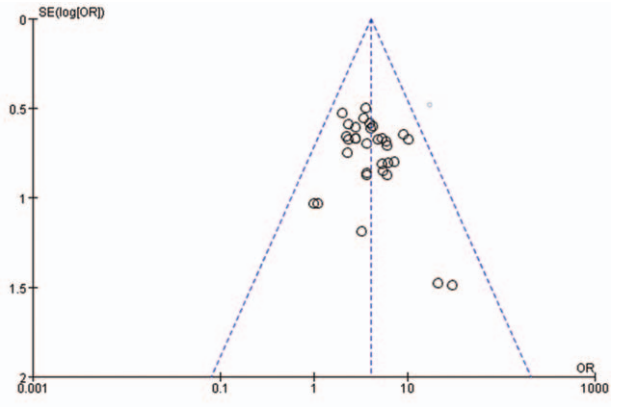


Figure 9. The funnel plots of the total clinical efficacy rate of Xiaoqinglong decoction on COPD. COPD = Chronic obstructive pulmonary disease.

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