Chinese Medicine for Coronavirus Disease 2019 (COVID-19): A GRADE-Assessed Systematic Review and Meta-Analysis

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Running Title: A systematic review for CM on COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) has caused enormous public health and socioeconomic burden globally. This study aims to evaluate the efficacy and safety of Chinese medicine (CM) against COVID-19. Eleven databases were searched on April 30, 2021, and 52 studies were included. The RoB 2.0, ROBINS-I, and GRADE tools were employed to assess the risks and evidence grades. The findings with the moderate certainty in GRADE showed that compared with routine treatment (RT), Lianhua Qingwen granules (LHQW) adjunctive to RT showed a significantly improved efficacy rate (Relative risk (RR) = 1.19, 95% confidence interval (CI) [1.09, 1.31]), febrile score (standard mean difference (SMD) = - 1.21, 95% CI [- 1.43, -0.99]), and computerized tomography (CT) lung images (RR= 1.23, 95% CI [1.10, 1.38]); Qingfei Paidu decoction (QFPD) plus RT significantly shortened the length of hospital stay (SMD = - 1.83, 95% CI [- 2.18, - 1.48]); Feiyan Yihao formula (FYYH) plus RT significantly improved the clinical efficacy rate (RR= 1.07, 95% CI [1.00, 1.15]), febrile time (SMD = - 0.02, 95% CI [- 0.23, 0.19]), and time to negative PCR test for COVID-19 (SMD = - 0.72, 95% CI [- 0.94, - 0.51]). Adjunctive effects of CM with lower certainty of evidence were found, including improvements of symptoms, laboratory findings, and mortality. No or mild adverse events were observed in most of the studies. In conclusion, current evidence indicates CM formulae, particularly LHQW, QFPD, and FYYH, have adjunctive effects on standard treatment of COVID-19.

Keywords: COVID-19; Chinese medicine; Lianhua Qingwen; Feiyan Yihao; Qingfei Paidu; controlled trials.

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), has considerably affected the world (Lu *et al.*, 2020; Wang *et al.*, 2020a), with over 149 million infected globally, resulting in more than 2.6 million deaths according to the data reported by WHO on 28 April 202. Chinese medicine (CM) has played a crucial role in treatments across several pandemics throughout history (Duan *et al.*, 2011; Wang *et al.*, 2011; Liu *et al.*, 2012; Liu *et al.*, 2014). During previous outbreaks, CM formulae, notably maxingshigan–yinqiaosan, could reduce febrile time in patients with influenza A (H1N1) virus infection (Wang *et al.*, 2011); several other CM also contributed to improving lung infiltration and quality of life of severe acute respiratory syndrome (SARS) patients (Liu *et al.*, 2012). Since March 2020, China's National Health Commission included CM in COVID-19 management guidelines (Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia, Trial Version 3). For patients with different CM syndromic diagnosis, the guidelines made the corresponding treatment recommendations.

Previous systematic reviews indicated that CM formulae combined with western medicine significantly improved clinical symptoms compared with western medicine alone (Wang *et al.*, 2021a; Yin *et al.*, 2021; Zhou *et al.*, 2021a). However, the definitive conclusion was not reached due to the heterogeneity of pooled studies and a small number of eligible studies. As more studies are published, the systematic reviews need to be updated. Particularly, these newly published studies followed China's guidelines for treatment and diagnosis of COVID-19, which might reduce the heterogeneity among studies. Our study aimed to systematically review the current clinical studies on each CM formula for COVID-19 treatment.

Methods

Search Strategy

This review was registered in PROSPERO on March 27, 2020 (registered no. CRD42020176347) and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati *et al.*, 2009). Eleven databases were searched by April 30, 2021, including PubMed, Excerpta Medica Database, Cochrane Library, Allied and Complementary Medicine Database, Cumulative Index to Nursing & Allied Health Literature Plus, Chinese National Knowledge Infrastructure Database, China Scientific Journal Database, Wanfang Database, ClinicalTrials.gov, Chinese Clinical Trial Registry, and MedRxiv. MeSH and free search words were combined to yield the following search criteria: "COVID-19 OR SARS-COV-2" AND "traditional Chinese medicine" AND "trials".

Eligible Criteria

The inclusion criteria for studies were as follows: (1) patients had a laboratory diagnosis of COVID-19; (2) either retrospective nonrandomized studies or RCTs; (3) the observation group was treated using CM plus routine treatment (RT) or CM alone; (4) inclusion of all forms of CM; and (5) treatment of the control group using RT (e.g., Western medicine, usual care). The exclusion criteria were as follows: (1) case control

and cohort studies; (2) case reports, protocols, reviews, comments, clinical experiences, guidelines, expert consensus, animal or cell experiments; (3) duplicate studies; (4) the control group receiving CM, acupuncture, or moxibustion; and (5) literature without specific essential data after contacting authors.

Literature Quality Assessment

Two researchers (JG and ZQ) independently assessed the quality of the included studies, with discrepancies being resolved by a third researcher (HC). Version 2 of the Cochrane risk-of-bias tool (RoB 2.0) and the risk of bias in nonrandomized studies of interventions (ROBINS-I) were used for bias assessment of RCTs (Sterne *et al.*, 2019) and retrospective nonrandomized studies (Sterne *et al.*, 2016), respectively. The RoB 2.0 assesses the following biases: randomization process, deviations from the intended interventions, missing outcome data, outcome measurements, selection of the reported results, and overall bias. The ROBINS-I assesses the following biases: confounding, classification of intervention, deviations from intended interventions, missing data, outcome measurements, selection of the reported result, and overall bias. The meta-analysis results were graded using grades of recommendation, assessment, development, and evaluation (GRADE).

Data Extraction and Analyses

The EndNote software (version X9.3.3) was employed to remove duplication and manage the literature. Two authors (NCL and TLF) extracted data independently, and a

third author (HC) supervised the process and solved the discrepancies. The following data were extracted from the included studies: (1) basic information, including the first author name, year of publication, sample size, age, routine treatment protocol, intervention group, control group, duration, and frequency of interventions; (2) primary outcome being the clinical efficacy according to the Criteria of Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine as represented by reduction of the main symptom scores of fever, cough, fatigue and dyspnea by $\geq$ 30%; (3) secondary outcomes including improvements in fever time, score and level; computerized tomography of lungs, length of hospital stay and death (4) minor outcomes include cough and fatigue recovery time, score and improvement rate; laboratory tests (COVID-19 PCR test, C-reactive protein, leukocytes, and lymphocytes) and adverse events. Additionally, the authors of the included studies were contacted for further clarification in case of incomplete published data.

Statistical analyses were performed using the Stata 17.0 software (Stata Corp., College Station, TX, USA). A random-effect model was used in case of significant heterogeneity of the pooled studies; otherwise, the fixed-effect model was employed. Cohen's d and relative risk (RR) were used for continuous and categorical variables, respectively, at 95% confidence interval (CI). Study heterogeneity was determined using Q statistics and I^2, with a *p*-value in Q statistics of < 0.1 or $I^2 \geq 50\%$, indicating significant among-study heterogeneity. The L'Abbe plot was used to test heterogeneity among categorical variables. Publication bias was evaluated using funnel plot and Egger test. Sensitivity analysis was conducted for studies with significant heterogeneity, and subgroup analysis was performed based on the outcome measures. The mean and standard deviation were estimated based on the reformative methods (Wan *et al.*, 2014; Luo *et al.*, 2018) for studies that reported the median and interquartile range.

Results

Literature Selection and Characteristics

The initial search yielded 3,858 studies, with 2,448 studies remaining after removing duplications. After screening titles, abstracts, and full texts, 52 studies were included. The flow chart of the screening and exclusion reasons were shown in Fig. 1. During the full-text assessments, specific reasons for exclusion were as follows: lack of matched control group (24 studies), lack of comparison of CM efficacy (20 studies), CM appears in the control group (3 studies), and the publication was retracted (1 study).

This study included 52 studies (12 (Guo *et al.*, 2020; Liu *et al.*, 2020b; Wang *et al.*, 2020c; Xiao *et al.*, 2020a; Xiong *et al.*, 2020; Zhang *et al.*, 2020b; Feng *et al.*, 2021; Hu *et al.*, 2021; Huang, 2021; Li *et al.*, 2021; Ni *et al.*, 2021; Xu *et al.*, 2021) and 40 published in English and Chinese, respectively, containing the details of 5,634 patients. 3,389 patients received CM or CM adjunctive to RT in the treatment group, while 2,245 patients received RT in the control group. Thirty-six studies reported that both groups received interventions for 3 to 28 days, while the remaining 16 studies did not report such details. The sample sizes of the included studies ranged from 22 to 563.

Individualized CM formulae were administered in 15 studies (Jin *et al.*, 2020; Lian *et al.*, 2020; Liao, 2020; Liu, 2020; Pan *et al.*, 2020; Shi *et al.*, 2020a; Song, 2020; Wang *et al.*, 2020d; Yang *et al.*, 2020c; Zhang *et al.*, 2020b; Zhang *et al.*, 2020c; Zheng *et al.*, 2020; Li *et al.*, 2021; Qin *et al.*, 2021; Zhou *et al.*, 2021b). Moreover, 37 studies

used the CM formulae described in China's guidelines for COVID-19 and CM classic formulae, including Lianhua Qingwen granules (LHQW), Jinhua Qinggan granules (JHQG), Feiyan Yihao formula (FYYH), Reyanning granules (RYN), Reduning injection (RDN), Shenmai injection (SM), Buzhong Yiqi decoction (BZYQ), Shuanghuanglian oral liquids (SHL), Huashi Baidu decoction (HSBD), Keguan-1 formula (KG-1), Huoxiang Zhengqi granules (HXZQ), Xuanfei Baidu decoction (XFBD), Xiyanping injection (XYP), Xuebijing injection (XBJ), Shufeng Jiedu formula (SFJD), Qingfei Paidu decoction (QFPD), and Jinye Baidu formula (JYBD). The characteristics of the included studies were shown in Supplementary Table 1.

Risk of Bias and Certainty of Evidence

The risk of bias of 21 RCTs (Ai *et al.*, 2020; Chen *et al.*, 2020a; Chen *et al.*, 2020c; Duan *et al.*, 2020; Jin *et al.*, 2020; Liao, 2020; Wang *et al.*, 2020c; Wang *et al.*, 2020d; Wen *et al.*, 2020; Xiao *et al.*, 2020a; Xiao *et al.*, 2020b; Xiong *et al.*, 2020; Yu *et al.*, 2020b; Zheng *et al.*, 2020; Chen *et al.*, 2021; He *et al.*, 2021; Hu *et al.*, 2021; Liu, 2021; Ni *et al.*, 2021; Wang *et al.*, 2021c; Xu *et al.*, 2021) was evaluated using the RoB 2.0 tool. Among them, four RCTs (Liao, 2020; Xiao *et al.*, 2020b; Zheng *et al.*, 2020; Liu, 2021) presented risk concerns regarding the randomization process because of unclear randomization methods. Almost all RCTs showed "low" risk regarding "deviations from intended intervention" except for one study that reported inconsistent intervention medicines (Xiao *et al.*, 2020b). Three RCTs (Chen *et al.*, 2020c; Liao, 2020; Zheng *et al.*, 2020) were ranked as having a "high" risk for failing to report essential items and were ranked as "high" risk in the overall bias.

The risk of bias of 31 retrospective nonrandomized studies (Chen *et al.*, 2020b; Cheng *et al.*, 2020; Guo *et al.*, 2020; Hu *et al.*, 2020; Huang *et al.*, 2020; Li *et al.*, 2020; Lian *et al.*, 2020; Liu, 2020; Liu *et al.*, 2020b; Pan *et al.*, 2020; Qu *et al.*, 2020; Shi *et al.*, 2020a; Song, 2020; Wang *et al.*, 2020e; Yang *et al.*, 2020a; Yang *et al.*, 2020b; Yang *et al.*, 2020c; Yao *et al.*, 2020; Yu *et al.*, 2020a; Yu *et al.*, 2020c; Zeng *et al.*, 2020; Zhang *et al.*, 2020a; Zhang *et al.*, 2020b; Zhang *et al.*, 2020c; Feng *et al.*, 2021; Huang, 2021; Li *et al.*, 2021; Qin *et al.*, 2021; Wang *et al.*, 2021b; Zhang and Pan, 2021; Zhou *et al.*, 2021b) was assessed using the ROBINS-I tool. All these nonrandomized studies were ranked as having "serious" risk in terms of "selection of participants into the study" and "classification of interventions" items. Moreover, 11 nonrandomized studies (Li *et al.*, 2020; Liu, 2020; Liu *et al.*, 2020b; Qu *et al.*, 2020; Yang *et al.*, 2020a; Yang *et al.*, 2020c; Yao *et al.*, 2020; Yu *et al.*, 2020a; Zhang *et al.*, 2020a; Zhang *et al.*, 2020b; Wang *et al.*, 2021b) missed essential data, and four nonrandomized studies (Yang *et al.*, 2020b; Zhang *et al.*, 2020c; Li *et al.*, 2021; Qin *et al.*, 2021) had confounding elements, which resulted in "serious" risks in terms of the overall bias. The certainty of the evidence for meta-analysis results was shown in Table 1.

Primary Outcomes

Clinical Efficacy

Ten studies (Ai *et al.*, 2020; Chen *et al.*, 2020a; Chen *et al.*, 2020b; Cheng *et al.*, 2020; Li *et al.*, 2020; Xiao *et al.*, 2020b; Yu *et al.*, 2020b; Hu *et al.*, 2021; Wang *et al.*, 2021b;

Wang *et al.*, 2021c) (Egger test: $p = 0,03$, revealed publication biases) reported the clinical efficacy rate involving four CM formulae. Subgroup analysis revealed that compared with the RT groups, the CM adjunctive to RT groups showed a significantly higher clinical efficacy rate (Fig. 2A): specifically, FYYH plus RT (RR = 1.07, 95% CI [1.00, 1.15], p < 0.05) with low heterogeneity (Q (1) = 0.15, p = 0.70, I^2 = 0.01%; GRADE, moderate); LHQW plus RT (RR = 1.19, 95% CI [1.09, 1.31], $p < 0.05$) with low heterogeneity (Q (3) = 3.35, $p = 0.34$, I^2 = 25.48%; GRADE, moderate); QFPD plus RT (RR = 1.09, 95% CI [1.01, 1.18], $p < 0.05$) without heterogeneity (Q (1) = 0.02, $p = 0.90$, I^2 = 0; GRADE, low); and SFJD plus RT (RR = 1.20, 95% CI [1.07, 1.35], p < 0.05) without heterogeneity (Q (1) = 0.47, $p = 0.49$, I^2 = 0; GRADE, low) (Fig. 2B-C).

Febrile Time, Score and Level

Ten studies (Chen *et al.*, 2020b; Cheng *et al.*, 2020; Li *et al.*, 2020; Qu *et al.*, 2020; Wang *et al.*, 2020e; Xiao *et al.*, 2020b; Yang *et al.*, 2020a; Chen *et al.*, 2021; Hu *et al.*, 2021; Wang *et al.*, 2021b) reported the febrile time with four CM formulae; namely, FYYH, LHQW, QFPD, and SFJD.

Subgroup analysis revealed that compared with RT alone, both the FYYH plus RT (SMD = -0.02, 95% CI [-0.23, 0.19], p > 0.05; Q (1) = 0.07, $p = 0.79$, I^2 = 0; GRADE, moderate) and LHQW plus RT (SMD = -0.66, 95% CI [-1.57, 0.25], p > 0.05; Q (2) = 31.11, p < 0.01, I^2 = 92.66%; GRADE, low) did not significantly shorten the febrile time. Compared with RT, QFPD (SMD = -1.27, 95% CI [-2.47, -0.07], p < 0.05; Q (1)

= 7.42, p = 0.01, I^2 = 86.54%; GRADE, low) and SFJD (SMD = -0.99, 95% CI [-1.65, -0.32], p < 0.05; Q (1) = 11.86, p < 0.01, I^2 = 81.99%; GRADE, low) adjunctive to RT significantly shortened the febrile time (Fig. 3A). Sensitivity analysis revealed that all pooled studies contributed to heterogeneity, and no study could be removed.

Two studies (Chen *et al.*, 2020a; Yu *et al.*, 2020b) indicated a significant improvement in the febrile score of LHQW plus RT compared with RT without significant heterogeneity (SMD = -1.21, 95% CI [-1.43, -0.99], p < 0.05; Q (1) = 0.47, p = 0.49, I^2 = 0; GRADE, moderate) (Fig. 3B).

Three studies (Cheng *et al.*, 2020; Xiao *et al.*, 2020a; Yao *et al.*, 2020) reported that LHQW plus RT lowered fever; however, there was high among-study heterogeneity (I^2 = 69.78%). Sensitivity analysis revealed the time point of one study (Xiao *et al.*, 2020a). After removing the study, LHQW plus RT (RR = 1.41, 95% CI [1.12, 1.78], p < 0.05) significantly lowered fever without heterogeneity between the remaining studies (Q (1) = 0.12, p = 0.73, I^2 = 0; GRADE, low) (Table 2).

Secondary Outcomes

CT Scan Image

Six studies (Chen *et al.*, 2020a; Cheng *et al.*, 2020; Yu *et al.*, 2020b; Zeng *et al.*, 2020; Hu *et al.*, 2021; Zhang and Pan, 2021) reported improvements in CT scans. Subgroup

analysis of the improvement rate in CT scans revealed that compared with RT, LHQW plus RT (RR = 1.23, 95% CI [1.10, 1.38], $p < 0.05$; GRADE, moderate) and QFPD plus RT (RR = 1.26, 95% CI [1.11, 1.43], $p < 0.05$; GRADE, low) significantly improved the lung images, with low (Q (3) = 2.74, $p = 0.43$, $I^2 = 17.43\%$) and no heterogeneity (Q (1) = 0.21, $p = 0.65$, $I^2 = 0$), respectively (Fig. 4).

Length of Hospital Stay

Three studies (Li *et al.*, 2020; Zeng *et al.*, 2020; Wang *et al.*, 2021c) reported the length of hospital stay, with high among-study heterogeneity (Q (2) = 62.98, $p < 0.01$, $I^2 = 99.50\%$). One study (Li, et al., 2020) lacking measurement criteria was removed through sensitivity analysis. Compared with RT, QFPD plus RT significantly shortened hospital stay (SMD = -1.83, 95% CI [-2.18, -1.48], $p < 0.01$; Q (1) = 1.98, $p = 0.16$, $I^2 = 49.43\%$; GRADE, moderate) with moderate heterogeneity (Fig. 5).

Mortality

Seven studies (Hu *et al.*, 2020; Huang *et al.*, 2020; Wang *et al.*, 2020c; Yang *et al.*, 2020c; Qin *et al.*, 2021; Wang *et al.*, 2021b; Zhang and Pan, 2021) reported lower mortality in patients treated with CM plus RT than in those treated with RT alone. Among them, three studies (Hu *et al.*, 2020; Wang *et al.*, 2020c; Zhang and Pan, 2021) indicated that KG-1 and QFPD led to zero deaths compared with four deaths in the RT group.

Minor Outcomes

Cough Recovery Time, Score and Improvement Rate

Five studies (Cheng *et al.*, 2020; Li *et al.*, 2020; Yang *et al.*, 2020a; Chen *et al.*, 2021; Hu *et al.*, 2021) reported that the time of cough recovery in LHQW plus RT was significantly shorter than that in RT (SMD = -1.75, 95% CI [-2.89, -0.62], $p < 0.05$; GRADE, low) with significant among-study heterogeneity (Q (2) = 17.15, $p < 0.01$, I^2 = 92.13%). Compared with RT, QFPD plus RT did not significantly shorten the recovery time (SMD = -1.85, 95% CI [-4.74, 1.04], $p > 0.05$; GRADE, low) with significant heterogeneity (Q (1) = 33.35, $p < 0.01$, I^2 = 97.00%) (Table 2). Inconsistent evaluation methods led to high heterogeneity in both groups.

Two studies (Chen *et al.*, 2020a; Yu *et al.*, 2020b) reported a significant improvement in the cough score of LHQW plus RT compared with RT (SMD = -2.35, 95% CI [-3.83, -0.86], $p < 0.01$; GRADE, low) with significant between-study heterogeneity (Q (1) = 22.09, p < 0.01, I^2 = 95.47%) (Table 2). This heterogeneity might be attributed to the different scoring criteria.

Three studies (Cheng *et al.*, 2020; Xiao *et al.*, 2020a; Yao *et al.*, 2020) reported the cough improvement rate. Pooled analysis revealed that LHQW plus RT were not superior to RT alone (RR = 1.60, 95% CI [0.63, 4.09], $p > 0.05$; GRADE, low); moreover, these studies showed significant heterogeneity (Q (2) = 11.28, p < 0.01, I^2 = 87.83%). Sensitivity analysis suggested different evaluation criteria in the three studies; therefore, the removal method could not be applied (Table 2).

Fatigue Recovery Time and Improvement Rate

Three studies (Cheng *et al.*, 2020; Xiao *et al.*, 2020a; Yao *et al.*, 2020) reported the fatigue improvement rates.   Three studies (Cheng *et al.*, 2020; Chen *et al.*, 2021; Hu *et al.*, 2021) reported the fatigue recovery time, which had moderate (Q (2) = 3.21, *p* = 0.20, I^2 = 44.54%) and high heterogeneity (Q (2) = 9.88, *p* = 0.01, I^2 = 81.62%). Sensitivity analysis revealed that the difference in criteria for evaluating the weakness improvement led to high heterogeneity.

Pooled analysis showed that compared with RT, LHQW plus RT did not significantly improve the rate of fatigue (SMD = 1.28, 95% CI [0.86, 1.90], *p* = 0.22; GRADE, low); however, it had a significantly shorter fatigue recovery time (SMD = -1.31, 95% CI [-2.03, -0.58], *p* = 0.01; GRADE, low) (Table 2**)**.

Other Clinical Symptoms

Two studies (Cheng *et al.*, 2020; Yao *et al.*, 2020) reported the effect of LHQW on other clinical symptoms. The meta-analysis showed that compared with RT, LHQW plus RT significantly improved dyspnea, appetite, chest tightness, expectoration, and muscle pain, but not nausea (overall RR = 3.10, 95% CI [2.03, 4.74], *p* < 0.05; Q (11) = 12.23, p = 0.35, I^2 = 15.37%; each GRADE, low) (Table 2).

Laboratory Findings

Covid-19 PCR Test

Two trials (Wen *et al.*, 2020; Zhang *et al.*, 2020a) reported the rate of Covid-19 Polymerase Chain Reaction (PCR) negative conversion for XBJ (50 ml per pax, bid) (Q (1) = 0.41, p = 0.52, I^2 = 0).   Four studies (Wang *et al.*, 2020e; Chen *et al.*, 2021; Hu *et al.*, 2021; Wang *et al.*, 2021b) reported the time to negative PCR tests for patients receiving the FYYH (Q (1) = 0.24, *p* = 0.63, I^2 = 0) and LHQW (Q (1) = 1.97, *p* = 0.16, I^2 = 49.17%). Pooled analysis revealed no significant difference between XBJ (50 ml/pax, bid) plus RT and RT (RR = 0.94, 95% CI [0.71, 1.24], *p* = 0.66; GRADE, low) (Table 2). Compared with RT alone, FYYH plus RT (RR = -0.72, 95% CI [-0.94, -0.51], *p* < 0.05; GRADE, moderate), but not LHQW plus RT (RR = -0.36, 95% CI [-0.74, 0.02], *p* > 0.05; GRADE, low), had a shorter time to negative nucleic acid (Table 2).

C-reactive Protein

Nine studies (Chen *et al.*, 2020c; Guo *et al.*, 2020; Wen *et al.*, 2020; Yu *et al.*, 2020b; Yu *et al.*, 2020c; Zhang *et al.*, 2020a; Chen *et al.*, 2021; Wang *et al.*, 2021c; Zhang and Pan, 2021) reported the C-reactive protein (CRP) levels. There was high among-study heterogeneity, including LHQW (I^2 = 96.81%), QFPD (I^2 = 80.29%), XBJ (100 ml/pax, bid) (I^2 = 85.08%), and XBJ (50 ml/pax, bid) (I^2 = 81.05%). Sensitivity analysis revealed that the heterogeneity of one study (Guo *et al.*, 2020) and another study (Wang *et al.*, 2021c) attributed to the disease severity and unreliable results, respectively.

After removing both studies, subgroup analysis showed the CRP levels in LHQW plus RT were not significantly higher than those in RT (SMD = -1.38, 95% CI [-3.40, 0.65], $p > 0.05$), QFPD plus RT (SMD = -0.08, 95% CI [-0.45, 0.29], $p > 0.05$; Q (1) = 0.58, $p = 0.45$, $I^2 = 0$), and XBJ 50 ml plus RT (SMD = -0.93, 95% CI [-1.99, 0.12], $p > 0.05$). However, pooled analysis revealed that XBJ 100 ml plus RT led to significantly lower CRP levels compared with RT (SMD = -2.17, 95% CI [-2.98, -1.36], $p < 0.05$; Q (1) = 1.86, $p = 0.17$, $I^2 = 46.23\%$) (Table 2). The GRADE evidence levels were low for the above CM formulae.

White Blood Cells

The white blood cell (WBC) levels were reported in seven studies (Chen *et al.*, 2020b; Guo *et al.*, 2020; Wen *et al.*, 2020; Xiao *et al.*, 2020b; Yang *et al.*, 2020a; Zhang *et al.*, 2020a; Zhang and Pan, 2021) which assessed four CM formulae; namely, QFPD, SFJD, XBJ injection. Subgroup analysis revealed that compared with RT, XBJ 50 ml plus RT significantly increased the WBC (SMD = 0.44, 95% CI [0.01, 0.88], $p < 0.05$; Q (1) = 0.04, p = 0.85, $I^2 = 0$). However, there was a certain degree of among-subgroup heterogeneity due to differences in treatment duration. Compared with RT (each GRADE, low), QFPD plus RT (SMD = 0.44, 95% CI [-0.19, 1.07], $p > 0.05$; Q (1) = 1.54, p = 0.21, $I^2 = 35.25\%$), SFJD plus RT (SMD = 0.30, 95% CI [-0.33, 0.94], $p > 0.05$; Q (1) = 5.28, p = 0.02, $I^2 = 81.05\%$), and XBJ 100ml plus RT (SMD = 1.48, 95% CI [-0.56, 3.52], $p > 0.05$; Q (1) = 14.07, $p < 0.01$, $I^2 = 92.89\%$) did not significantly increase WBC levels (Table 2).

Neutrophil and Lymphocytes

Two studies (Yu *et al.*, 2020c; Zhang and Pan, 2021) reported significantly increased neutrophil counts in QFPD plus RT than those in RT (SMD = -0.26, 95% CI [-1.13, 0.62], p = 0.56; GRADE, low). The different times assessed resulted in high heterogeneity (Q (1) = 3.76, p = 0.05, I^2 = 73.42%) (Table 2).

Four studies reported the absolute number and proportion of lymphocytes (Ai *et al.*, 2020; Yang *et al.*, 2020a; Yu *et al.*, 2020c; Wang *et al.*, 2021b) including those in the FYYH (Q (1) = 1.28, p = 0.26, I^2 = 21.81%) and QFPD (Q (1) = 1.16, p = 0.28, I^2 = 13.54%). Subgroup analysis revealed a significantly higher lymphocyte count in the FYYH plus RT than in RT alone (SMD = 0.34, 95% CI [0.09, 0.58], $p < 0.05$; GRADE, moderate). Moreover, the proportion of lymphocytes in QFPD plus RT was significantly higher than in RT (SMD = 0.41, 95% CI [0.02, 0.79], $p < 0.05$; GRADE, low) (Table 2).

Adverse Events

Adverse events were reported in 24 studies (Ai *et al.*, 2020; Chen *et al.*, 2020c; Duan *et al.*, 2020; Li *et al.*, 2020; Lian *et al.*, 2020; Liao, 2020; Liu, 2020; Liu *et al.*, 2020b; Song, 2020; Wang *et al.*, 2020c; Wang *et al.*, 2020d; Xiao *et al.*, 2020b; Xiong *et al.*, 2020; Yang *et al.*, 2020b; Yang *et al.*, 2020c; Yu *et al.*, 2020b; Zhang *et al.*, 2020a; Zhang *et al.*, 2020b; Chen *et al.*, 2021; Hu *et al.*, 2021; Huang, 2021; Qin *et al.*, 2021; Wang *et al.*, 2021b; Wang *et al.*, 2021c). Among them, two studies (Tan *et al.*, 2020;

Xiao *et al.*, 2020b) on LHQW (Q (1) = 0.58, *p* = 0.20, I^2 = 0) could be pooled for meta-analysis. Compared with RT alone, the LHQW plus RT had no significant adverse events (RR = 0.87, 95% CI [0.69, 1.08], *p* = 0.20; GRADE, low) (Table 2). Specifically, nine studies (Ai *et al.*, 2020; Liu, 2020; Liu *et al.*, 2020b; Song, 2020; Xiong *et al.*, 2020; Yang *et al.*, 2020b; Yu *et al.*, 2020b; Zhang *et al.*, 2020b; Wang *et al.*, 2021b) reported that none of the patients experienced treatment-induced discomfort.

Fifteen studies (Chen *et al.*, 2020c; Duan *et al.*, 2020; Li *et al.*, 2020; Lian *et al.*, 2020; Liao, 2020; Wang *et al.*, 2020c; Wang *et al.*, 2020d; Xiao *et al.*, 2020b; Yang *et al.*, 2020c; Zhang *et al.*, 2020a; Chen *et al.*, 2021; Hu *et al.*, 2021; Huang, 2021; Qin *et al.*, 2021; Wang *et al.*, 2021c) reported that patients experienced different degrees of adverse events. Among them, five studies (Wang *et al.*, 2020c; Xiao *et al.*, 2020b; Chen *et al.*, 2021; Hu *et al.*, 2021; Qin *et al.*, 2021) reported that patients suffered from diarrhea in both the treatment and control groups. One study (Duan *et al.*, 2020) reported that 27 patients experienced diarrhea in the JHQG plus RT group; among them, eight patients with moderate diarrhea resulted in cessation of treatment. Nausea was reported in both groups of five studies (Li *et al.*, 2020; Wang *et al.*, 2020c; Chen *et al.*, 2021; Hu *et al.*, 2021; Wang *et al.*, 2021c). Furthermore, two studies reported minor levels of dizziness and fatigue (Chen *et al.*, 2021; Wang *et al.*, 2021c). Laboratory findings revealed abnormal liver function in both groups of four studies (Lian *et al.*, 2020; Chen *et al.*, 2021; Hu *et al.*, 2021; Huang, 2021), without a significant between-group difference.

Recommendations

The national guidelines for COVID-19 diagnosis and treatment by China's National Health Commission, recommend the use of CM according to disease phases (mild, ordinary, severe, and critical) and symptom differentiation of patients. In line with the guidelines and symptom differentiation, recommendations of CM formulae were made for four phases of COVID-19 (Table 3).

Discussion

Previous systematic reviews (Liu *et al.*, 2020a; Sun *et al.*, 2020) have shown that CM has an advantage in COVID-19 treatment. Oral CM combined with RT improved overall efficacy and did not increase adverse events. As an adjunctive treatment, one review (Zhou *et al.*, 2021a) showed that CM can improve the main symptoms and reduce the progression of the disease. But pooled analysis of different formulae did not prove which was more effective. Our systematic review included several newly published RCTs (Duan *et al.*, 2020; Jin *et al.*, 2020; Xiao *et al.*, 2020a; Hu *et al.*, 2021; Ni *et al.*, 2021; Wang *et al.*, 2021c; Xu *et al.*, 2021) with better design quality. Moreover, we employed more appropriate tools, including ROB 2.0 and ROBINS-I, to assess RCTs and retrospective nonrandomized studies, respectively. As for the extraction of continuous variables, we took the method of extracting the difference value that increased the evaluability of the results. Additionally, we included CM injections and performed subgroup analysis according to different CM types. Based on the results of each meta-analysis, we graded the evidence based on the recommended levels, which also provided more reference information for clinical practice and further studies.

Among the candidate CMs, we found that the adjunctive effects of the FYYH, LHQW, QFPD, and SFJD were significantly higher than those of RT alone in overall clinical efficacy.

1. LHQW plus RT significantly improved febrile score, fever level and symptoms of dyspnea, appetite, chest tightness, expectoration, and muscle pain in addition to CT Scan outcome. Although it significantly improved the cough score and fatigue recovery time, high heterogeneity among the pooled studies decreased the evidence level.

2. Compared with RT alone, the FYYH adjunctive to RT shortens the febrile duration, the time to the negative PCR test (0.72 d), and increased lymphocytes with a moderate evidence level. Lymphopenia, common in patients with COVID-19, is negatively associated with disease severity (Tan *et al.*, 2020; Wang *et al.*, 2020b).

3. The QFPD plus RT was associated with lower CRP level, improved lymphocyte indices and CT images, significantly shortened the hospital stay, and may reduce mortality (zero vs. four deaths). In two previous large-scale studies, QFPD was observed to accelerate recovery, viral shedding and length of hospital stay during early treatment (Shi *et al.*, 2020b), and reduce mortality (Zhang *et al.*, 2021), which was consistent with our findings.

4. Regarding the pooled analysis of CM injection, the XBJ adjunctive to RT was significantly associated with lower CRP, but the increases in WBC were complicated by the heterogeneity of differences in treatment duration.

In China's national guidelines for the diagnosis and treatment for COVID-19, there are five disease phases, mild, ordinary, severe, critical, and convalescent. The moderate evidence supports the use of LHQW for patients at the mild and ordinary phases, FYYH for patients at mild to severe phrases, and QFPD for patients at mild to critical phases according to the syndrome differentiation. There is low evidence supporting the use of SFJD at mild to ordinary phase, and XBJ at severe and critical phases. Currently, few studies are conducted to evaluate the effects of CM for patients under COVID-19 rehabilitation (convalescent phase). A few study protocols have been published recently (Gao *et al.*, 2021; Zhong *et al.*, 2021). Evidence arising from these studies could be integrated with our findings to guide the treatment for COVID-19 patients.

This study has several limitations. First, we did not specify RT treatment in the meta-analysis. All included studies were conducted in China, where patients received RTs recommended by the China National Health Commission's guidelines for COVID-19; specifically, oxygen therapy, antiviral medications, and symptomatic therapies. We unified all RTs as the control group since it did not yield significant heterogeneity. Second, this systematic review included 31 retrospective nonrandomized studies. It was difficult to conduct prospective RCTs at the early pandemic stage. These retrospective studies introduced the bias into the results. Due to flaws in study design and reporting, there was a relatively high risk of bias in most studies. Third, according to the funnel plot (Fig. 2C), there are potential publication biases in the study. Imputing at least 3 studies reporting negative results could eliminate the publication bias. Finally, we did not analyze the outcomes of the CM formula alone compared with RT since the individualized CM formula could not be pooled. We only studied the adjunctive effect of the CM formula to RT; however, the effectiveness of each CM formula on its own

requires separate studies.

Conclusion

The moderate certainty level in GRADE shows that CM formulae have adjunctive effects on COVID-19, particularly clinical symptoms, clinical efficacy, severity, and duration of disease. Adjunctively to RT, the FYYH improves the clinical efficacy rate, shortens the febrile time, and time to negative PCR test; QFPD shortens the hospital stay, improves CT lung images and mortality; LHQW improves the clinical efficacy rate, febrile score, and severity of CT lung scan.

Acknowledgments

References

Ai, X.Y., C. Luo, L.P. Lin, M. Xie, H.M. Fan and X.H. Tan. Therapeutic effect of integrated traditional Chinese and western medicine on COVID-19 in Guangzhou. *China Trop. Med.* 20: 746-750, 2020.

Chen, C.W., X.L. Li, Y.F. Liu and S. Chen. Clinical study of Lianhua Qingwen capsule in the treatment of coronavirus disease 2019. *Res. Integr. Tradit. Chin. West. Med.* 13: 1-4, 2021.

Chen, J.J., Y.L. Zhou and F.G. Chen. Clinical study on treatment of COVID-19 in convalescent period treated with Lianhua Qingwen capsule combined with

Interferon α-2b. *Adv. Clin. Med.* 10: 1144-1149, 2020a.

Chen, L., F. Liu, J.H. Wu, H.Y. Song, J.S. Xia, B. Sheng and Y.G. Chen. Clinical efficacy of Shufeng Jiedu capsule combined with western medicine in treatment of common COVID-19 patients by retrospective analysis. *Chin. J. Exp. Tradit. Med. Formul.* 26: 14-20, 2020b.

Chen, L.Z., H. Liu and G.L. Xiao. Effect of Xuebijing injection on the treatment of COVID-19 and its effect on CRP. *J. China Prescr. Drug* 18: 110-111, 2020c.

Cheng, D.Z., W.J. Wang, Y. Li, X.D. Wu, B. Zhou and Q.Y. Song. Analysis of the efficacy of Lianhua Qingwen in 51 patients with COVID-19: a multi-center retrospective study. *Tianjin J. Tradit. Chin. Med.* 37: 509-516, 2020.

Duan, C., W.G. Xia, C.J. Zheng, G.B. Sun, Z.L. Li, Q.L. Li, P. Li and H.Y. Zhang. Clinical observation of Jinhua Qinggan granules in the treatment of novel coronavirus infection pneumonia. *J. Tradit. Chin. Med.* 1-5, 2020.

Duan, Z.P., Z.H. Jia, J. Zhang, S. Liu, Y. Chen, L.C. Liang, C.Q. Zhang, Z. Zhang, Y. Sun, S.Q. Zhang, Y.Y. Wang and Y.L. Wu. Natural herbal medicine Lianhuaqingwen capsule anti-influenza A (H1N1) trial: a randomized, double blind, positive controlled clinical trial. *Chin. Med. J. (Engl.)* 124: 2925-2933, 2011.

Feng, J., B. Fang, D. Zhou, J. Wang, D. Zou, G. Yu, Y. Fen, D. Peng, J. Hu and D. Zhan. Clinical effect of traditional Chinese medicine Shenhuang granule in critically Ill patients with COVID-19: a single-centered, retrospective, observational study. *J. Microbiol. Biotechnol.* 31: 380-386, 2021.

Gao, Y., L.L.D. Zhong, B. Quach, B. Davies, G.I. Ash, Z.X. Lin, Y. Feng, B.W.M. Lau, P.D. Wagner, X. Yang, Y. Guo, W. Jia, Z. Bian and J.S. Baker. COVID-19 rehabilitation with herbal medicine and cardiorespiratory exercise: protocol for a clinical study. *JMIR Res. Protoc.* 10: e25556, 2021.

Guo, H., J. Zheng, G. Huang, Y. Xiang, C. Lang, B. Li, D. Huang, Q. Sun, Y. Luo, Y. Zhang, L. Huang, W. Fang, Y. Zheng and S. Wan. Xuebijing injection in the treatment of COVID-19: a retrospective case-control study. *Ann. Palliat. Med.* 9: 3235-3248, 2020.

He, Q., Q.J. Zhang, X.W. Gan and X.G. Li. Clinical effect analysis of Buzhong Yiqi decoction in the treatment of mild COVID-19. *J. Emerg. Tradit. Chin. Med.* 30: 385-387, 2021.

Hu, K., W.J. Guan, Y. Bi, W. Zhang, L. Li, B. Zhang, Q. Liu, Y. Song, X. Li, Z. Duan, Q. Zheng, Z. Yang, J. Liang, M. Han, L. Ruan, C. Wu, Y. Zhang, Z.H. Jia and N.S. Zhong. Efficacy and safety of Lianhuaqingwen capsules, a repurposed Chinese herb, in patients with coronavirus disease 2019: a multicenter, prospective, randomized controlled trial. *Phytomedicine* 85: 153242, 2021.

Hu, Y.Q., J.Q. Lu, J. Huang, Q.H. Huang, H.T. Jin, Y.T. Ma, H.B. Yang, L.F. Mo and N. Tang. Clinical observation of 31 cases with COVID-19 treated with Guizhi Erchen decoction based on Sanjiao sequential therapy. *Chin. Arch. Tradit. Chin. Med.* 38: 1-5, 2020.

Huang, H., S.J. Tan, X.H. Zuo, J.S. Jin, Y. Zhao and Y. Ding. Analysis of TCM syndrome characteristics and clinical efficacy in 72 patients with COVID-19. *Mod. J. Integr. Tradit. Chin. West. Med.* 29: 2395-2399, 2020.

Huang, L. Efficacy and safety assessment of severe COVID-19 patients with Chinese medicine: a retrospective case series study at early stage of the COVID-19 epidemic in Wuhan, China. *J. Ethnopharmacol.* 113888, 2021.

Jin, W., Y. Lu, W. Zhao, S.Y. Tang, X.Y. Sang, L.S. Zhang, L.Y. Li, D.F. Liu, Y.L. Gu, K.M. Cheng, J.Y. Tang and C.G. Xie. The efficacy of recommended treatments with integrated Chinese and western medicine on coronavirus disease 2019 (COVID-19) in Sichuan: a clinical trial observation. *Pharmacol. Clin. Chin. Mater. Med.* 36: 6-10, 2020.

Li, K.Y., W. An, F. Xia, M. Chen, P. Yang, Y.L. Liao, X. Xu, Q. Zhou, S.S. Fang and M.W. Zhang. Observation on clinical effect of modified Qingfei Paidu decoction in treatment of COVID-19. *Chin. Tradit. Herb. Drugs* 51: 2046-2049, 2020.

Li, L., C.Y. Gou, X.M. Li, W.Y. Song, X.J. Wang, H.Y. Li, H.Y. Li and X.H. Li. Effects of Chinese medicine on symptoms, syndrome evolution, and lung inflammation absorption in COVID-19 convalescent patients during 84-day follow-up after

hospital discharge: a prospective cohort and nested case-control study. *Chin. J. Integr. Med.* 27: 245-251, 2021.

Lian, J., S.J. Zhang, G.L. Li, D. Shang, Q.Y. Wang, L.S. Xu, Y. Shi and X.X. Liu. Retrospective analysis of 38 cases with coronavirus disease 2019 treated by integrated traditional Chinese and western medicine. *J. Tradit. Chin. Med.* 61: 2126-2130, 2020.

Liao, G.R. Study on application effect and safety of self-prepared traditional Chinese medicine decoction in patients with COVID-19. *Int. Infect. Dis.* 9: 353, 2020.

Liberati, A., D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P. Ioannidis, M. Clarke, P.J. Devereaux, J. Kleijnen and D. Moher. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann. Intern. Med.* 151: W65-94, 2009.

Liu, F. Observation on the curative effect of integrated traditional Chinese and western medicine on COVID-19 42 cases. *Zhongguo Guanli Kexue Yanjiuyuan Shangxueyuan Guanli Chuangxin Chengguo Huibian* 202: 1-7, 2020.

Liu, M., Y. Gao, Y. Yuan, K. Yang, S. Shi, J. Zhang and J. Tian. Efficacy and safety of integrated traditional Chinese and western medicine for corona virus disease 2019 (COVID-19): a systematic review and meta-analysis. *Pharmacol. Res.* 158: 104896, 2020a.

Liu, P., Y. Guo, X. Qian, S. Tang, Z. Li and L. Chen. China's distinctive engagement in global health. *Lancet* 384: 793-804, 2014.

Liu, X., M. Zhang, L. He and Y. Li. Chinese herbs combined with western medicine for severe acute respiratory syndrome (SARS). *Cochrane Database Syst. Rev.* 10: Cd004882, 2012.

Liu, Y.J. Clinical efficacy analysis of Huashi Baidu decoction combined with western medicine in treatment of severe COVID-19. *Lab. Med. Clin.* 18: 1152-1153, 2021.

Liu, Z., X. Li, C. Gou, L. Li, X. Luo, C. Zhang, Y. Zhang, J. Zhang, A. Jin, H. Li, Y. Zeng, T. Li and X. Wang. Effect of Jinhua Qinggan granules on novel

coronavirus pneumonia in patients. *J. Tradit. Chin. Med.* 40: 467-472, 2020b.

Lu, R., X. Zhao, J. Li, P. Niu, B. Yang, H. Wu, W. Wang, H. Song, B. Huang, N. Zhu, Y. Bi, X. Ma, F. Zhan, L. Wang, T. Hu, H. Zhou, Z. Hu, W. Zhou, L. Zhao, J. Chen, Y. Meng, J. Wang, Y. Lin, J. Yuan, Z. Xie, J. Ma, W.J. Liu, D. Wang, W. Xu, E.C. Holmes, G.F. Gao, G. Wu, W. Chen, W. Shi and W. Tan. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 395: 565-574, 2020.

Luo, D., X. Wan, J. Liu and T. Tong. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat. Methods Med. Res.* 27: 1785-1805, 2018.

Ni, L., Z. Wen, X. Hu, W. Tang, H. Wang, L. Zhou, L. Wu, H. Wang, C. Xu, X. Xu, Z. Xiao, Z. Li, C. Li, Y. Liu, J. Duan, C. Chen, D. Li, R. Zhang, J. Li, Y. Yi, W. Huang, Y. Chen, J. Zhao, J. Zuo, J. Weng, H. Jiang and D.W. Wang. Effects of Shuanghuanglian oral liquids on patients with COVID-19: a randomized, open-label, parallel-controlled, multicenter clinical trial. *Front. Med.* 1-14, 2021.

Pan, G.T., C. Du, Y.H. Liu, Y. Liu, Y.F. Cheng, F. Han, Z.Y. Chen, Z.Q. He, Z.F. XIa and S.L. Yang. Integrated traditional Chinese and western medicine in the treatment of 40 cases of critical patients with COVID-19. *Acta Med. Univ. Sci. Technol. Huazhong* 49: 202-207, 2020.

Qin, L.X., W.L. Lv, M. Yang, Y. Xiao, H. Li, G.Q. Sun, L. Wei, D.C. He, X.G. Li, Y. Zeng, X.Y. Fei, C.Q. Huang, J.Q. Zeng, Y. Xiang, X.H. Xu, S.Y. Zhang and R.L. Wang. Clinical characteristics, drug treatments and prognoses in 605 patients with severe and critical corona virus disease 2019 in Hubei, China: a multi-center, retrospective, cohort study. *Chin. Arch. Tradit. Chin. Med.* 39: 89-95, 2021.

Qu, X.K., S.L. Hao, J.H. Ma, G.Y. Wei, K.Y. Song, C. Tang, Y.F. Gao, S.Q. Liang and W.J. Du. Observation on clinical effect of Shufeng Jiedu capsule combined with arbidol hydrochloride capsule in treatment of COVID-19. *Chin. Tradit. Herb. Drugs* 51: 1167-1170, 2020.

Shi, J., Z.G. Yang, C. Ye, S.S. Chen, Y.F. Lu, Y. Lv, Q.N. Xu, B.Z. Tang, K.S. Yin and

X.R. Chen. Clinical observation on 49 cases of non-critical COVID-19 in Shanghai treated by integrated traditional Chinese and western medicine. *Shanghai J. Tradit. Chin. Med.* 54: 30-35, 2020a.

Shi, N., B. Liu, N. Liang, Y. Ma, Y. Ge, H. Yi, H. Wo, H. Gu, Y. Kuang, S. Tang, Y. Zhao, L. Tong, S. Liu, C. Zhao, R. Chen, W. Bai, Y. Fan, Z. Shi, L. Li, J. Liu, H. Gu, Y. Zhi, Z. Wang, Y. Li, H. Li, J. Wang, L. Jiao, Y. Tian, Y. Xiong, R. Huo, X. Zhang, J. Bai, H. Chen, L. Chen, Q. Feng, T. Guo, Y. Hou, G. Hu, X. Hu, Y. Hu, J. Huang, Q. Huang, S. Huang, L. Ji, H. Jin, X. Lei, C. Li, G. Wu, J. Li, M. Li, Q. Li, X. Li, H. Liu, J. Liu, Z. Liu, Y. Ma, Y. Mao, L. Mo, H. Na, J. Wang, F. Song, S. Sun, D. Wang, M. Wang, X. Wang, Y. Wang, Y. Wang, W. Wu, L. Wu, Y. Xiao, H. Xie, H. Xu, S. Xu, R. Xue, C. Yang, K. Yang, P. Yang, S. Yuan, G. Zhang, J. Zhang, L. Zhang, S. Zhao, W. Zhao, K. Zheng, Y. Zhou, J. Zhu, T. Zhu, G. Li, W. Wang, H. Zhang, Y. Wang and Y. Wang. Association between early treatment with Qingfei Paidu decoction and favorable clinical outcomes in patients with COVID-19: a retrospective multicenter cohort study. *Pharmacol. Res.* 161: 105290, 2020b.

Song, X.Y. Clinical retrospective study on novel coronavirus pneumonia treated with Sanjiao treatment. *Hubei Univ. Chin. Med.* 1-65, 2020.

Sterne, J.A., M.A. Hernán, B.C. Reeves, J. Savović, N.D. Berkman, M. Viswanathan, D. Henry, D.G. Altman, M.T. Ansari, I. Boutron, J.R. Carpenter, A.W. Chan, R. Churchill, J.J. Deeks, A. Hróbjartsson, J. Kirkham, P. Jüni, Y.K. Loke, T.D. Pigott, C.R. Ramsay, D. Regidor, H.R. Rothstein, L. Sandhu, P.L. Santaguida, H.J. Schünemann, B. Shea, I. Shrier, P. Tugwell, L. Turner, J.C. Valentine, H. Waddington, E. Waters, G.A. Wells, P.F. Whiting and J.P. Higgins. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 355: i4919, 2016.

Sterne, J.A.C., J. Savović, M.J. Page, R.G. Elbers, N.S. Blencowe, I. Boutron, C.J. Cates, H.Y. Cheng, M.S. Corbett, S.M. Eldridge, J.R. Emberson, M.A. Hernán, S. Hopewell, A. Hróbjartsson, D.R. Junqueira, P. Jüni, J.J. Kirkham, T. Lasserson, T. Li, A. McAleenan, B.C. Reeves, S. Shepperd, I. Shrier, L.A.

Stewart, K. Tilling, I.R. White, P.F. Whiting and J.P.T. Higgins. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 366: l4898, 2019.

Sun, C.Y., Y.L. Sun and X.M. Li. The role of Chinese medicine in COVID-19 pneumonia: a systematic review and meta-analysis. *Am. J. Emerg. Med.* 38: 2153-2159, 2020.

Tan, L., Q. Wang, D. Zhang, J. Ding, Q. Huang, Y.Q. Tang, Q. Wang and H. Miao. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Tran. Target Ther.* 5: 33, 2020.

Wan, X., W. Wang, J. Liu and T. Tong. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med. Res. Methodol.* 14: 135, 2014.

Wang, C., B. Cao, Q.Q. Liu, Z.Q. Zou, Z.A. Liang, L. Gu, J.P. Dong, L.R. Liang, X.W. Li, K. Hu, X.S. He, Y.H. Sun, Y. An, T. Yang, Z.X. Cao, Y.M. Guo, X.M. Wen, Y.G. Wang, Y.L. Liu and L.D. Jiang. Oseltamivir compared with the Chinese traditional therapy maxingshigan-yinqiaosan in the treatment of H1N1 influenza: a randomized trial. *Ann. Intern. Med.* 155: 217-225, 2011.

Wang, C., P.W. Horby, F.G. Hayden and G.F. Gao. A novel coronavirus outbreak of global health concern. *Lancet* 395: 470-473, 2020a.

Wang, D., B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Y. Zhao, Y. Li, X. Wang and Z. Peng. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323: 1061-1069, 2020b.

Wang, H., B. Xu, Y. Zhang, Y. Duan, R. Gao, H. He, X. Li and J. Li. Efficacy and safety of traditional Chinese medicine in coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Front. Pharmacol.* 12: 609213, 2021a.

Wang, J.B., Z.X. Wang, J. Jing, P. Zhao, J.H. Dong, Y.F. Zhou, G. Yang, M. Niu, X. Zhao, T.J. Jiang, J.F. Bi, Z. Xu, P. Zhang, D. Wu, Z.F. Bai, Y.M. Guo, S.M. Yu, Y.Q. Sun, Z.T. Zhang, X.Y. Zhan, P.Y. Li, J.B. Ding, P.F. Zhao, X.A. Song, J.Y. Tang, D.C. He, Z. Chen, E.Q. Qin, R.L. Wang and X.H. Xiao. Exploring an integrative therapy for treating COVID-19: a randomized controlled trial. *Chin.*

J. Integr. Med. 26: 648-655, 2020c.

Wang, L., M. Xu, Y. Wang, H.B. Li, N. Liu and J.L. Zuo. Clinical study on Shengmai powder combined with Shenling Baizhu powder in the treatment of common corona virus disease 2019. *China J. Tradit. Chin. Med. Pharm.* 35: 4268-4271, 2020d.

Wang, L.Q., Y.M. Ba, C.X. He, W.N. Li, X.H. Zuo, R. Tao, X. Wu, X.Q. Wang, Q. Shi, D.B. Lu, Z.M. Zhou, Y.L. Hu, X.R. Zhang, Y. Feng, G.M. Hu, R. Wang and S.S. Yu. Study of Feiyan Yihao in the treatment of COVID-19. *Lishizhen Med. Mater. Med. Res.* 31: 1725-1728, 2020e.

Wang, L.Q., G.M. Hu, Y.M. Ba, C.X. He, W.N. Li and X. Zhang. A retrospective study on the treatment of coronavirus disease 2019 with Feiyan Yihao combined with conventional western medicine. *J. Emerg. Tradit. Chin. Med.* 30: 10-12, 2021b.

Wang, Y., L. Chen, L. Zheng, B.Q. Ku, R. Yu and X.F. Zhang. Clinical effects of Qingfei Paidu decoction combined with conventional treatment in patients with coronavirus disease 2019. *Chin. Tradit. Pat. Med.* 43: 656-659, 2021c.

Wen, L., Z.G. Zhou, D.L. Jiang and K. Huang. Effect of Xuebijing injection on inflammatory markers and disease outcome of coronavirus disease 2019. *Chin. Crit. Care Med.* 32: 426-429, 2020.

Xiao, M.Z., J.X. Tian, Y.N. Zhou, X. Xu, X. Min, Y. Lv, M. Peng, Y. Zhang, D. Yan, S. Lang, Q. Zhang, A. Fan, J. Ke, X. Li, B. Liu, M. Jiang, Q. Liu, J. Zhu, L. Yang, Z. Zhu, K. Zeng, C. Li, Y. Zheng, H. Wu, J. Lin, F. Lian, X. Li and X. Tong. Efficacy of Huoxiang Zhengqi dropping pills and Lianhua Qingwen granules in treatment of COVID-19: a randomized controlled trial. *Pharmacol. Res.* 161: 105126, 2020a.

Xiao, Q., Y.J. Jiang, S.S. Wu, Y. Wang, J. An, W.P. Xu and J.J. Wu. Clinical significance of Shufengjiedu capsule combined with abidol in the treatment of mild disease COVID-19. *J. Emerg. Tradit. Clin. Med.* 29: 756-758, 2020b.

Xiong, W.Z., G. Wang, J. Du and W. Ai. Efficacy of herbal medicine (Xuanfei Baidu decoction) combined with conventional drug in treating COVID-19: a pilot randomized clinical trial. *Integr. Med. Res.* 9: 100489, 2020.

Xu, X., J. Zhang, W. Zheng, Z. Yang, X. Zhao, C. Wang, H. Su, L. Zhao, L. Xue, F. Hu, X. Xu, M. Wen, J. Liao, Z. Zeng, L. Wang, J. Zeng, Y. Guo, B. Li and Q. Liu. Efficacy and safety of Reduning injection in the treatment of COVID-19: a randomized, multicenter clinical study. *Ann. Palliat. Med.* 2021.

Yang, M., Z. Sun, P. J. and S.Z. Liu. Efficacy analysis of Qingfei Paidu decoction combined with interferon α in the treatment of COVID-19. *Shenzhen J. Integr. Tradit. Chin. West. Med.* 30: 29-30, 2020a.

Yang, M.B., S.S. Dang, S. Huang, Y.J. Li and Y.L. Guo. Multi-center clinical observation of Reyanning mixture in treatment of COVID-19. *Chin. J. Exp. Tradit. Med. Formul.* 26: 7-12, 2020b.

Yang, Q., Q.G. Sun, B. Jiang, H.J. Xu, M. Luo, P. Xie, W. Huang and Z.W. Cong. Retrospective clinical study on treatment of COVID-19 patients with integrated traditional Chinese and western medicine. *Chin. Tradit. Herb. Drugs* 51: 2050-2054, 2020c.

Yao, K.T., M.Y. Liu, X. Li, J.H. Huang and H.B. Cai. Retrospective clinical analysis on treatment of coronavirus disease 2019 with traditional Chinese medicine Lianhua Qingwen. *Chin. J. Exp. Tradit. Med. Formul.* 26: 8-12, 2020.

Yin, B., Y.M. Bi, L. Sun, J.Z. Huang, J. Zhao, J. Yao, A.X. Li, X.Z. Wang and G.J. Fan. Efficacy of integrated traditional Chinese and western medicine for treating COVID-19: a systematic review and meta-analysis of RCTs. *Front. Public Health* 9: 622707, 2021.

Yu, H.Y., X.H. Ren, X.X. Qi, Q. Zuo and D. Liu. Retrospective study on the efficacy of abidol, Qingfei Paidu decoction, Lianhua Qingwen capsule, and Jinye Baidu granule on light/common COVID-19 patients in a cabin hospital. *Pharmacol. Clin. Chin. Mater. Med.* 36: 2-6, 2020a.

Yu, P., Y.Z. Li, S.B. Wan and Y. Wang. Effects of Lianhua Qingwen granules plus arbidol on treatment of mild corona virus disease-19. *Chin. Pharm. J.* 55: 1042-1045, 2020b.

Yu, X.Y., S. Zhang, F.F. Yan and D.Z. Su. Comparison of clinical efficacy of Qingfei Paidu decoction combined with western medicine in 43 cases and single western

medicine in 46 cases in the treatment of COVID-19. *J. Shandong Univ. (Health Sci.)* 58: 47-53, 2020c.

Zeng, X.H., W.H. Ma and J. Wang. Effects of Qingfei Paidu decoction on the clinical efficacy of COVID-19 pneumonia with phlegm heat blocking lung. *Med. J. West China* 32: 1799-1801, 1806, 2020.

Zhang, C.Y., Z.H. Li, S. Zhang, W. Wang and X.Q. Jiang. Clinical observation of Xuebijing in the treatment of COVID-19. *Chin. J. Hosp. Pharm.* 40: 964-967, 2020a.

Zhang, H.T., M.X. Huang, X. Liu, X.C. Zheng, X.H. Li, G.Q. Chen, J.Y. Xia and Z.S. Hong. Evaluation of the adjuvant efficacy of natural herbal medicine on COVID-19: a retrospective matched case-control study. *Am. J. Chin. Med.* 48: 779-792, 2020b.

Zhang, L., X. Zheng, X. Bai, Q. Wang, B. Chen, H. Wang, J. Lu, S. Hu, X. Zhang, H. Zhang, J. Liu, Y. Shi, Z. Zhou, L. Gan, X. Li and J. Li. Association between use of Qingfei Paidu Tang and mortality in hospitalized patients with COVID-19: a national retrospective registry study. *Phytomedicine* 85: 153531, 2021.

Zhang, N., Y.F. Qu, Y.Z. Jin, C. Qin, X.C. Niu, Y.J. Hu, W. Fang and J.R. Zhang. Retrospective study of traditional Chinese medicine Maxing Shigan decoction combined with western medicine in the treatment of ordinary COVID-19. *J. Front. Med.* 10: 31-34, 2020c.

Zhang, P. and G.T. Pan. Clinical study of Qingfei Paidu decoction on the improvement of inflammatory cytokines in critical patients with COVID-19. *Shijie Kexue Jishu Zhongyiyao Xiandaihua* 23: 391-395, 2021.

Zheng, Z.Z., Z.G. Bai, C.J. Li, S.P. Ge, Y. Luo and G.D. He. Effects of TCM syndrome differentiation on COVID-19. *Med. J. Commun.* 34: 117-118, 2020.

Zhong, L.L.D., Y.P. Wong, B. Peng, Z.X. Lin, V.C.W.W. Taam, Y. Luo, H.Y. Chen, C.D. Chao, C.F. Wong, F.S.C. Tam, K. Chan, K.Y. Lee, L.F. Ho, A.Y.L. Wong, C.F. Choy, B.F.L. Ng, R.H.W. Wong, Y.B. Feng, C. Liong, Z.X. Bian and C.-C.R.W. Group. The effect of Chinese medicine for rehabilitation of discharged COVID-19 patients: a protocol for multi-center observational study. *OBM Integr.*

Compliment. Med. 6: 9, 2021.

Zhou, L.P., J. Wang, R.H. Xie, S. Pakhale, D. Krewski, D.W. Cameron and S.W. Wen. The effects of traditional Chinese medicine as an auxiliary treatment for COVID-19: a systematic review and meta-analysis. *J. Altern. Complement. Med.* 27: 225-237, 2021a.

Zhou, Y.H., G. Sun, M.Y. Wu, X.H. Shen, W. Xu, D.W. Ran, Y. Ju and M.Z. Pu. Clinical observation on treating 66 cases of severe novel coronavirus pneumonia with simultaneous treatment of lung and spleen in Wuhan area. *World Latest Med. Inf.* 21: 286-288, 2021b.

Figure Legends

Figure 1. Flow chart for literature search (modified from PRISMA flow diagram).

Figure 2. Clinical efficacy rate. (A) Forest plot of subgroup analysis on the clinical efficacy rate. (B) L'Abbe and (C) funnel plots of the clinical effectiveness rate. RT, routine treatment.

Figure 3. Improvement in fever. (A) Febrile time. (B) Febrile score. RT, routine treatment

Figure 4. Chest improvement in CT scan image.

Figure 5. Length of hospital stay in patients receiving QFPD and RT or RT alone. QFPD, Qing Fei Pai Du decoction; RT, routine treatment.

Tables

Table 1. GRADE summary

Table 2. Other outcomes

Table 3. Recommendations of included CM formulae for different forms in COVID-19 patients

Supplementary Table 1. Characteristics of the included studies

Table 1. GRADE summary

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Assumed risk: routine treatment	Corresponding risk: Chinese medicine			
Clinical efficacy rate in Feiyan Yihao group	878 per 1000	940 per 1000 (878 to 1000)	RR 1.07 (1.00 to 1.15)	376 (2 studies)	⊕⊕⊕◯ MODERATE
Clinical efficacy rate in Lianhua Qingwen group	716 per 1000	852 per 1000 (780 to 938)	RR 1.19 (1.09 to 1.31)	745 (4 studies)	⊕⊕⊕◯ MODERATE
Clinical efficacy rate in Qingfei Paidu group	880 per 1000	959 per 1000 (739 to 922)	RR 1.09 (1.01 to 1.18)	200 (2 studies)	⊕⊕◯◯ LOW
Clinical efficacy rate in Shufeng Jiedu group	739 per 1000	887 per 1000 (791 to 997)	RR 1.20 (1.07 to 1.35)	268 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of fever in Lianhua Qingwen group	597 per 1000	841 per 1000 (668 to 1000)	RR 1.41 (1.12 to 1.78)	126 (2 studies)	⊕⊕◯◯ LOW
Febrile time in Feiyan Yihao group	The mean anti-febrile time in the control groups was 3.35	The mean -0.02-fold lower (-0.23- 0.19-fold higher)	-	365 (2 studies)	⊕⊕⊕◯ MODERATE
Febrile time in Lianhua Qingwen group	The mean anti-febrile time in the control groups was 3.30	The mean 2.67-fold lower (-1.57- 0.25-fold higher)	-	394 (3 studies)	⊕⊕◯◯ LOW
Febrile time in Qingfei Paidu group	The mean anti-febrile time in the control groups was 3.55	The mean 2.3-fold lower (-2.47- -0.07-fold higher)	-	100 (2 studies)	⊕⊕◯◯ LOW
Febrile time in Shufeng Jiedu group	The mean anti-febrile time in the control groups was 4.63	The mean 3.2-fold lower (-1.65- -0.32-fold higher)	-	307 (3 studies)	⊕⊕◯◯ LOW
Febrile score in Lianhua Qingwen group	The mean anti-febrile score in the control groups was -1.45	The mean -1.21-fold higher (-1.43- -0.99-fold higher)	-	365 (2 studies)	⊕⊕⊕◯ MODERATE

Improvement rate of cough in Lianhua Qingwen group	505 per 1000	809 per 1000 (318 to 1000)	RR 1.60 (0.63 to 4.09)	175 (3 studies)	⊕⊕◯◯ LOW
Cough recovery time in Lianhua Qingwen group	The mean cough recovery time in the control groups was 6.43	The mean 4.63-fold lower (-2.89- -0.62-fold higher)	-	372 (3 studies)	⊕⊕◯◯ LOW
Cough recovery time in Qingfei Paidu group	The mean cough recovery time in the control groups was 6.3	The mean 5-fold lower (-4.74- 1.04-fold higher)	-	100 (2 studies)	⊕⊕◯◯ LOW
Cough score in Lianhua Qingwen group	The mean cough score in the control groups was -1.6	The mean -2.85-fold lower (-3.83- -0.86-fold higher)	-	365 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of fatigue in Lianhua Qingwen group	513 per 1000	656 per 1000 (441 to 974)	RR 1.28 (0.86 to 1.90)	153 (3 studies)	⊕⊕◯◯ LOW
Fatigue recovery time in Lianhua Qingwen group	The mean cough score in the control groups was 5.4	The mean 3.6-fold lower (-2.03- -0.58-fold higher)	-	366 (3 studies)	⊕⊕◯◯ LOW
Improvement rate of dyspnea in Lianhua Qingwen group	105 per 1000	526 per 1000 (158 to 1000)	RR 5.00 (1.50 to 16.74)	41 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of appetite in Lianhua Qingwen group	105 per 1000	531 per 1000 (158 to 1000)	RR 5.04 (1.12 to 22.73)	57 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of chest tightness in Lianhua Qingwen group	179 per 1000	598 per 1000 (250 to 1000)	RR 3.35 (1.40 to 8.01)	46 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of expectoration in Lianhua Qingwen group	133 per 1000	556 per 1000 (212 to 1000)	RR 4.17 (1.59 to 10.89)	64 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of muscle pain in Lianhua Qingwen group	222 per 1000	647 per 1000 (212 to 1000)	RR 2.91 (1.14 to 7.38)	33 (2 studies)	⊕⊕◯◯ LOW
Improvement rate of nausea in Lianhua Qingwen group	500 per 1000	520 per 1000 (215 to 1000)	RR 1.04 (0.43 to 2.53)	19 (2 studies)	⊕⊕◯◯ LOW
Rate of negative nucleic acid test in Xuebijing 50ml group	690 per 1000	649 per 1000 (490 to 856)	RR 0.94 (0.71 to 1.24)	84 (2 studies)	⊕⊕◯◯ LOW

Time of negative nucleic acid test in Feiyan Yihao group	The mean time negative nucleic acid test in the control groups was 11.05	The mean 7.85-fold lower (-0.94- -0.51-fold higher)	-	365 (2 studies)	⊕⊕⊕◯ MODERATE
Time of negative nucleic acid test in Lianhua Qingwen group	The mean time of negative nucleic acid test in the control groups was 17.35	The mean 16.6-fold lower (-0.74- 0.02-fold higher)	-	335 (2 studies)	⊕⊕◯◯ LOW
CRP in Lianhua Qingwen group	The mean CRP in the control groups was -5.25	The mean -9-fold lower (-3.40- 0.65-fold higher)	-	352 (2 studies)	⊕⊕◯◯ LOW
CRP in Qingfei Paidu group	The mean CRP in the control groups was -36.1	The mean -31.95-fold lower (-0.45- 0.29-fold higher)	-	113 (2 studies)	⊕⊕◯◯ LOW
CRP in Xuebijing 100ml group	The mean CRP in the control groups was -13.15	The mean -36.3-fold lower (-2.98- -1.36-fold higher)	-	70 (2 studies)	⊕⊕◯◯ LOW
CRP in Xuebijing 50ml group	The mean CRP in the control groups was -3.4	The mean -10.3-fold lower (-1.99- 0.12-fold higher)	-	84 (2 studies)	⊕⊕◯◯ LOW
WBC in Qingfei Paidu group	The mean WBC in the control groups was 1	The mean 1.7-fold higher (-0.19- 1.07-fold higher)	-	64 (2 studies)	⊕⊕◯◯ LOW
WBC in Shufeng Jiedu group	The mean WBC in the control groups was 0.95	The mean 1.4-fold higher (-0.33- 0.94-fold higher)	-	268 (2 studies)	⊕⊕◯◯ LOW
WBC in Xuebijing 100ml group	The mean WBC in the control groups was 0.9	The mean 2.3-fold higher (-0.56- 3.52-fold higher)	-	72 (2 studies)	⊕⊕◯◯ LOW
WBC in Xuebijing 50ml group	The mean WBC in the control groups was 0.95	The mean 1.45-fold higher (0.01- 0.88-fold higher)	-	84 (2 studies)	⊕⊕◯◯ LOW
Neutrophil in Qingfei Paidu group	The mean NEUT in the control groups was 4	The mean 3.7-fold higher (-1.13- 0.62-fold higher)	-	113 (2 studies)	⊕⊕◯◯ LOW
Lymphocyte counts in Feiyan Yihao group	The mean LYMPH# in the control groups was 0.1	The mean 0.25-fold higher (0.09- 0.58-fold higher)	-	376 (2 studies)	⊕⊕⊕◯ MODERATE
Lymphocyte proportion in Qingfei Paidu group	The mean LYMPH% in the control groups was 3.6	The mean 5.3-fold higher (0.02- 0.79-fold higher)	-	129 (2 studies)	⊕⊕◯◯ LOW

CT scan in Lianhua Qingwen group	611 per 1000	752 per 1000 (672 to 844)	RR 1.23 (1.10 to 1.38)	745 (4 studies)	⊕⊕⊕◯ MODERATE
CT scan in Qingfei Paidu group	701 per 1000	883 per 1000 (778 to 1000)	RR 1.26 (1.11 to 1.43)	253 (2 studies)	⊕⊕◯◯ LOW
Length of hospital stay in Qingfei Paidu group	The mean length of hospital stay in the control groups was 19.75	The mean 15.8-fold lower (-2.18- -1.48-fold higher)	-	369 (2 studies)	⊕⊕⊕◯ MODERATE
Adverse events incidence in Lianhua Qingwen group	506 per 1000	440 per 1000 (349 to 546)	RR 0.87 (0.69 to 1.08)	335 (2 studies)	⊕⊕◯◯ LOW

Note: LOW (Low certainty): Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; MODERATE (Moderate certainty): We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Table 2. Other outcomes

Outcome indicator	CM formula	Pooled studies	Pooled sample size (T/C)	I²	RR with 95% CI
Improvement rate of fever	LHQW	Cheng D Z; Yao K T	126 (64/52)	0	1.41 [1.12, 1.78]
Cough recovery time	LHQW	Chen C W; Chen D Z; Hu K	372 (190/182)	92.13%	-1.75 [-2.89, -0.62]
	QFPD	Yang M; Li K Y	100 (50/50)	97.00%	-1.85 [-4.74, 1.04]
Cough score	LHQW	Chen J J; Yu P	365 (182/183)	95.47%	-2.35 [-3.83, -0.86]
Improvement rate of cough	LHQW	Xiao M Z; Cheng D Z; Yao K T	175 (84/91)	87.83%	1.60 [0.63, 4.09]
Improvement rate of fatigue	LHQW	Xiao M Z; Yao K T; Cheng D Z	153 (75/78)	44.54%	1.28 [0.86, 1.90]
Fatigue recovery time	LHQW	Cheng D Z; Chen C W; Hu K	366 (186/180)	81.62%	-1.31 [-2.03, -0.58]
Chest tightness	LHQW	Cheng D Z; Yao K T	46 (18/28)	0	3.35 [1.40, 8.01]
Dyspnea	LHQW	Cheng D Z; Yao K T	41 (22/19)	0	5.00 [1.50, 16.74]
Expectoration	LHQW	Cheng D Z; Yao K T	64 (34/30)	0	4.17 [1.59, 10.89]
Muscle pain	LHQW	Cheng D Z; Yao K T	33 (15/18)	0	2.91 [1.14, 7.38]
Appetite	LHQW	Cheng D Z; Yao K T	57 (19/38)	60.26%	5.04 [1.12, 22.73]
Nausea	LHQW	Cheng D Z; Yao K T	19 (11/8)	0	1.04 [0.43, 2.53]
Rate of negative PCR test	XBJ 50ml	Wen L; Zhang C Y	84 (42/42)	0	0.94 [0.71, 1.24]
Time to negative PCR test	FYYH	Wang L Q; Wang L Q*	365 (220/145)	0	-0.72 [-0.94, -0.51]
	LHQW	Chen C W; Hu K	335 (167/168)	49.17%	-0.36 [-0.74, 0.02]
C-reactive protein	LHQW	Chen C W; Yu P	352 (175/177)	96.81%	-1.38 [-3.40, 0.65]
	QFPD	Yu X Y; Zhang P	113 (55/58)	0	-0.08 [-0.45, 0.29]
	XBJ 100ml	Wen L; Chen L Z	70 (35/35)	46.23%	-2.17 [-2.98, -1.36]
	XBJ 50ml	Wen L; Zhang C Y	84 (42/42)	81.05%	-0.93 [-1.99, 0.12]
White blood cell count	QFPD	Yang M; Zhang P	64 (32/32)	35.25%	0.44 [-0.19, 1.07]
	SFJD	Chen L; Xiao Q	268 (134/134)	81.05%	0.30 [-0.33, 0.94]
	XBJ 100ml	Guo H; Wen L	72 (36/36)	92.89%	1.48 [-0.56, 3.52]

	XBJ 50ml	Wen L; Zhang C Y	84 (42/42)	0	0.44 [0.01, 0.88]
Neutrophils	QFPD	Yu X Y; Zhang P	113 (55/58)	73.42%	-0.26 [-1.13, 0.62]
Lymphocyte#	FYYH	Ai X Y; Wang L Q	376 (228/148)	21.81%	0.34 [0.09, 0.58]
Lymphocyte%	QFPD	Yang M; Yu X Y	129 (63/66)	13.54%	0.41 [0.02, 0.79]
Adverse events incidence	LHQW	Hu K; Chen C W	335 (167/168)	0	0.87 [0.69, 1.08]

Note: CM: Chinese medicine; LHQW: Lianhua Qingwen; QFPD: Qingfei Paidu decoction; XBJ: Xuebijing injection; T: Treatment group; C: Control group; RR: Relative risk; CI: confidence interval.

Table 3. Recommendations of included CM formulae for different forms in COVID-19 patients

Recommendation Grade	Mild	Ordinary	Severe	Critical
Moderate evidence	FYYH, LHQW, QFPD	FYYH, LHQW, QFPD	FYYH, QFPD	QFPD
Low evidence	SFJD	SFJD	XBJ	XBJ
No evidence	JHQG, BZYQ, SHL, HSBD, KG-1, HXZQ, XFBD, JYBD	JHQG, RYN, SHL, HSBD, KG-1, HXZQ, XFBD, JYBD	RDN, HSBD, XYP	RDN, SM

Note: LHQW: Lianhua Qingwen; JHQG: Jinhua Qinggan granules; FYYH: Feiyan Yihao formula; RYN: Reyanning granules; RDN: Reduning injection; BZYQ: Buzhong Yiqi decoction; SHL: Shuanghuanglian oral liquids; HSBD: Huashi Baidu decoction; KG-1: Keguan-1 formula; HXZQ: Huoxiang Zhengqi granules; XFBD: Xuanfei Baidu decoction; XYP: Xiyanping injection; XBJ: Xuebijing injection; SFJD: Shufeng Jiedu formula; QFPD: Qingfei Paidu decoction; JYBD: Jinye Baidu formula; SM: Shenmai injection

Identification

Databases sources: MEDLINE (n = 114), EMBASE (n = 149), AMED (n = 0), Cochrane (n = 118), CINAHL Plus (n = 70), ClinicalTrials. gov (n = 31), ChiCTR (n = 35), MedRxiv (n = 101), CNKI (n = 845), VIP (n = 579), Wanfang (n = 1816) , Supplementary sources: (n = 0)

(n = 3858)

Screening

Studies remaining after duplicate removal

(n = 2448)

Reasons for excluded:
Clinical experience (n = 634)
Review or comment (n = 236)
Protocol or case report (n = 145)
Not COVID-19 or TCM (n = 442)
Registered unfinished studies (n = 39)
Guidelines or expert consensus (n = 296)
Data mining or survey research (n = 391)
Animal or pharmacological studies (n = 165)

(n = 2348)

Studies remaining after tittle and abstract screening

(n = 100)

Reasons for excluded:
Not meet control group (n = 47)
Not available study (n = 1)

(n = 48)

Eligibility

Studies remaining after full text screening

(n = 52)

Included

Studies finally included

(n = 52)

Figure 1

41

A

Study	Treatment Yes	No	Control Yes	No	Risk Ratio with 95% CI	Weight (%)
Feiyan Yihao + RT vs. RT						
Wang L Q 2020	164	9	92	13	1.08 [1.00, 1.17]	23.87
Ai X Y 2020	51	4	38	5	1.05 [0.92, 1.20]	8.85
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.01\%$, $H^2 = 1.00$					1.07 [1.00, 1.15]	
Test of $\theta_i = \theta_j$: Q(1) = 0.15, p = 0.70						
Lianhua Qingwen + RT vs. RT						
Yu P 2020	119	28	96	52	1.25 [1.08, 1.44]	7.55
Cheng D Z 2020	44	7	35	16	1.26 [1.01, 1.56]	3.29
Chen J J 2020	30	5	22	13	1.36 [1.02, 1.82]	1.83
Hu K 2021	127	12	114	25	1.11 [1.01, 1.22]	17.58
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 25.48\%$, $H^2 = 1.34$					1.19 [1.09, 1.31]	
Test of $\theta_i = \theta_j$: Q(3) = 3.35, p = 0.34						
Qingfei Paidu + RT vs. RT						
Wang Y 2021	69	1	63	7	1.10 [1.01, 1.19]	22.12
Li K Y 2020	27	3	25	5	1.08 [0.88, 1.32]	3.83
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$					1.09 [1.01, 1.18]	
Test of $\theta_i = \theta_j$: Q(1) = 0.02, p = 0.90						
Shufeng Jiedu + RT vs. RT						
Chen L 2020	31	3	24	10	1.29 [1.02, 1.64]	2.63
Xiao Q 2020	88	12	75	25	1.17 [1.03, 1.34]	8.45
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$					1.20 [1.07, 1.35]	
Test of $\theta_i = \theta_j$: Q(1) = 0.47, p = 0.49						
Overall					1.12 [1.08, 1.17]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$						
Test of $\theta_i = \theta_j$: Q(9) = 9.00, p = 0.44						
Test of group differences: $Q_b(3) = 5.11$, p = 0.16						

0.88   1   1.82

Favours RT   Favours CM + RT

Random-effects REML model

B L'Abbé plot

C Funnel plot

Figure 2

A

Study	Treatment N	Mean	SD	Control N	Mean	SD	Cohen's d with 95% CI	Weight (%)
Feiyan Yihao + RT vs. RT								
Wang L Q 2020	47	3.6	1.9	40	3.7	.9	-0.07 [-0.49, 0.36]	10.31
Wang L Q 2020*	173	3	1.5	105	3	1.5	0.00 [-0.24, 0.24]	11.02
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$							-0.02 [-0.23, 0.19]	
Test of $\theta_i = \theta_j$: Q(1) = 0.07, p = 0.79								
Lianhua Qingwen + RT vs. RT								
Cheng D Z 2020	36	2.9	1.7	25	3.9	1.3	-0.65 [-1.17, -0.12]	9.81
Chen C W 2021	28	3.5	.5	29	3.4	.7	0.16 [-0.36, 0.68]	9.82
Hu K 2021	139	1.6	.7	139	2.6	.7	-1.43 [-1.69, -1.17]	10.95
Heterogeneity: $\tau^2 = 0.60$, $I^2 = 92.66\%$, $H^2 = 13.63$							-0.66 [-1.57, 0.25]	
Test of $\theta_i = \theta_j$: Q(2) = 31.11, p = 0.00								
Qingfei Paidu + RT vs. RT								
Yang M 2020	20	2.3	1.1	20	3.2	1.6	-0.66 [-1.29, -0.02]	9.19
Li K Y 2020	30	2.3	.9	30	3.9	.8	-1.88 [-2.49, -1.27]	9.35
Heterogeneity: $\tau^2 = 0.65$, $I^2 = 86.54\%$, $H^2 = 7.43$							-1.27 [-2.47, -0.07]	
Test of $\theta_i = \theta_j$: Q(1) = 7.43, p = 0.01								
Shufeng Jiedu + RT vs. RT								
Chen L 2020	18	4.1	1.9	19	5.7	2.2	-0.78 [-1.45, -0.11]	9.01
Xiao Q 2020	100	2.3	1.1	100	3.1	1.6	-0.58 [-0.87, -0.30]	10.88
Qu X K 2020	40	3.2	.9	30	5.1	1.4	-1.67 [-2.21, -1.12]	9.67
Heterogeneity: $\tau^2 = 0.28$, $I^2 = 81.99\%$, $H^2 = 5.55$							-0.99 [-1.65, -0.32]	
Test of $\theta_i = \theta_j$: Q(2) = 11.86, p = 0.00								
Overall							-0.74 [-1.18, -0.30]	
Test of group differences: $Q_b(3) = 12.22$, p = 0.01								

-3 -2 -1 0 1
Favours CM + RT   Favours RT

Random-effects REML model

B

Study	Treatment N	Mean	SD	Control N	Mean	SD	Cohen's d with 95% CI	Weight (%)
Chen J J 2020	35	-2.1	.3	35	-1.6	.6	-1.05 [-1.55, -0.55]	19.94
Yu P 2020	147	-1.8	.4	148	-1.3	.4	-1.25 [-1.50, -1.00]	80.06
Overall							-1.21 [-1.43, -0.99]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$								
Test of $\theta_i = \theta_j$: Q(1) = 0.47, p = 0.49								
Test of $\theta = 0$: z = -10.63, p = 0.00								

-2 -1 0 1
Favours Lianhua Qingwen + RT   Favours RT

Random-effects REML model

Figure 3

43

Study	Treatment Yes	No	Control Yes	No		Risk Ratio with 95% CI	Weight (%)
Lianhua Qingwen + RT vs. RT							
Yu P 2020	102	45	93	55		1.10 [0.94, 1.30]	22.13
Cheng D Z 2020	28	23	23	28		1.22 [0.82, 1.80]	3.87
Chen J J 2020	30	5	22	13		1.36 [1.02, 1.82]	7.16
Hu K 2021	117	22	90	49		1.30 [1.13, 1.50]	29.39
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 17.43\%$, $H^2 = 1.21$						1.23 [1.10, 1.38]	
Test of $\theta_i = \theta_j$: Q(3) = 2.74, p = 0.43							
Qingfei Paidu + RT vs. RT							
Zhang P 2021	10	2	7	5		1.43 [0.83, 2.45]	2.03
Zeng X H 2020	93	11	89	36		1.26 [1.10, 1.43]	35.41
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$						1.26 [1.11, 1.43]	
Test of $\theta_i = \theta_j$: Q(1) = 0.21, p = 0.65							
Overall						1.24 [1.15, 1.34]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$							
Test of $\theta_i = \theta_j$: Q(5) = 3.07, p = 0.69							
Test of group differences: $Q_b(1) = 0.11$, p = 0.74							

1   2

Favours RT   Favours CM + RT

Random-effects REML model
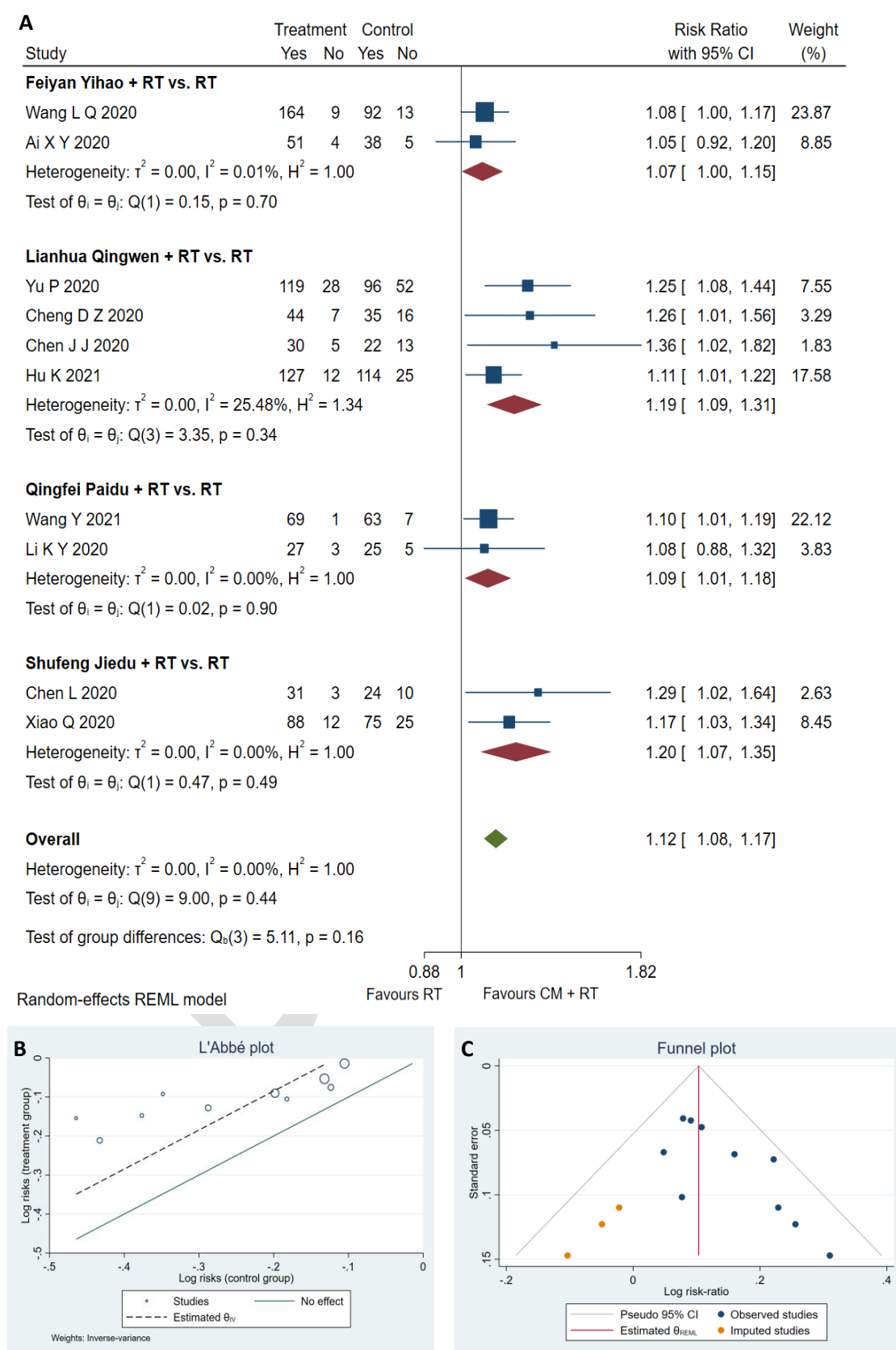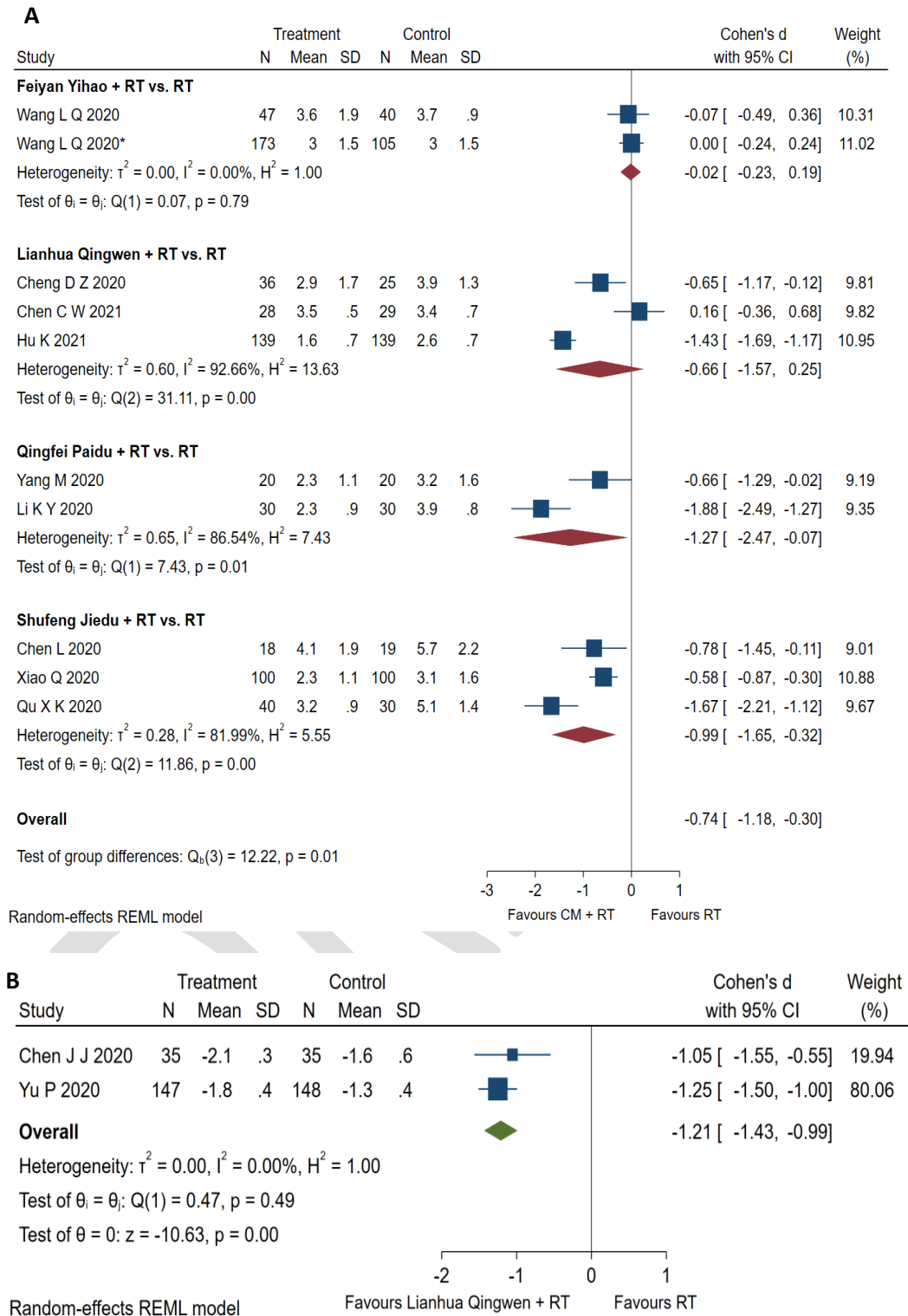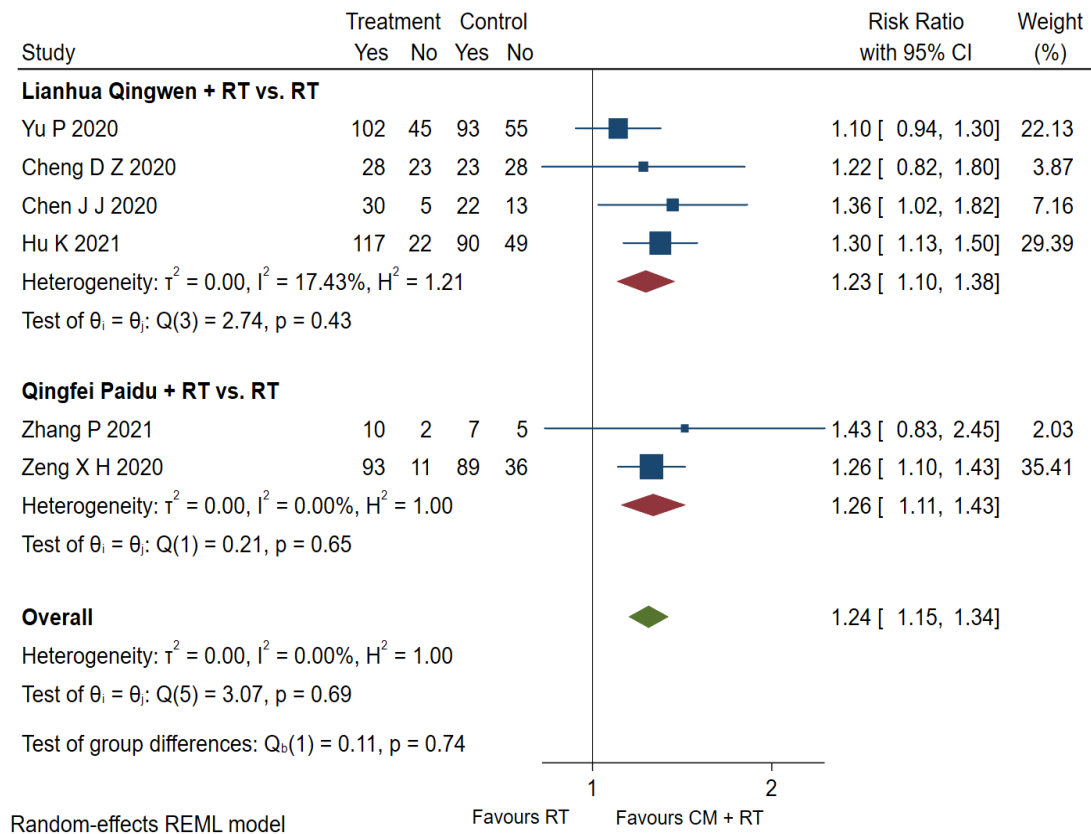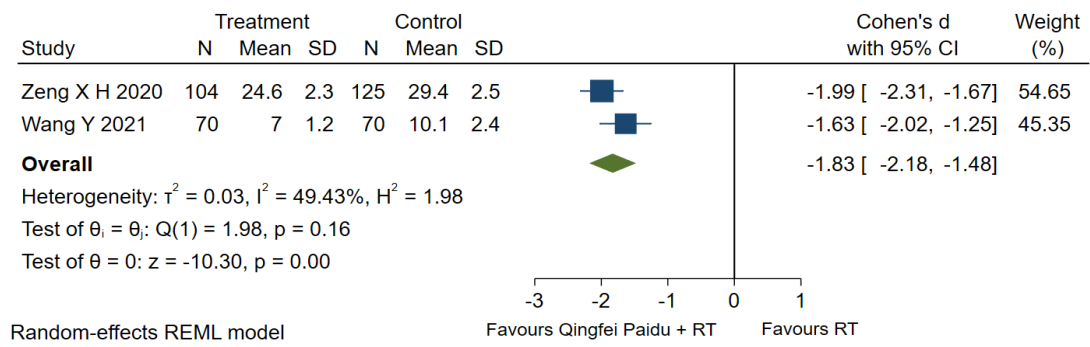
Figure 4

Figure 5

Supplementary table 1. Characteristics of the included studies

ID	Study type	Disease phase	Sample size (T/C)	Mean age (years)	CPGs for RTs	Intervention	Comparison	Duration of treatment	Outcomes
Duan C 2020	RCT	Mild	123 (82/41)	T:52.0±13.9 C:50.3±13.2	III	JHQG plus RT	RT	5 days	② ③ ④ ⑤ ⑧ ⑬ ⑮
Jin W 2020	RCT	Ordinary	38 (18/20)	T:43.6±14.5 C:41.3±9.9	II	CM plus RT	RT	NR	① ③ ④ ⑤ ⑥ ⑧ ⑪ ⑫ ⑭ ⑮
Liao G R 2020	RCT	NR	70 (35/35)	T:65.3±7.4 C:67.2±8.6	II	CM plus RT	RT	7 days	③ ④ ⑤ ⑬
Wang L 2020	RCT	Ordinary	80 (40/40)	T:41.1±14.5 C:40.8±13.7	III	CM plus RT	RT	NR	① ② ③ ④ ⑤ ⑥ ⑪ ⑫ ⑬ ⑮
Zheng Z Z 2020	RCT	Ordinary, Severe	130 (65/65)	NR	V	CM plus RT	RT	14 days	①
Wang J B 2020	RCT	NR	48 (24/24)	T:46.8±14.4 C:51.4±17.6	I	KG-1 plus RT	RT	14 days	① ③ ⑦ ⑧ ⑬ ⑭ ⑮
Xiao M Z 2020	RCT	NR	121 (58/63)	T:52.9±14.0 C:53.9±13.9	V	LHQW plus RT	RT	14 days	③ ④ ⑤ ⑧ ⑮
Xiao M Z 2020*	RCT	NR	124 (61/63)	T:56.1±12.1 C:53.9±13.9	V	LHQW plus HXZQ plus RT	RT	14 days	③ ④ ⑤ ⑧ ⑮
Xiong W Z 2020	RCT	Mild, Ordinary, Severe	42 (22/20)	T:57.1±14.0 C:62.4±12.3	II	XFBD plus RT	RT	7 days	③ ④ ⑤ ⑪ ⑫ ⑬
Yu P 2020	RCT	Mild, Ordinary	295 (147/148)	T: 47.3±8.7 C: 48.3±9.6	III	LHQW plus RT	RT	7 days	① ② ⑥ ⑧ ⑪ ⑫ ⑬
Wen L 2020	RCT	Ordinary, Severe, Critical	40 (20/20)	T: 49.1±4.8 C: 47.7±5.7	I	XBJ 50ml plus RT	RT	7 days	⑦ ⑧ ⑪ ⑫ ⑮
Wen L 2020*	RCT	Ordinary, Severe, Critical	40 (20/20)	T: 47.1±5.2 C: 47.7±5.7	I	XBJ 100ml plus RT	RT	7 days	⑦ ⑧ ⑪ ⑫ ⑮

Ai X Y 2020	RCT	Mild, Ordinary, Severe	98 (55/43)	T: 44.0±12.6 C: 46.0±18.3	IV	FYYH plus RT	RT	3 days	① ② ⑫ ⑬ ⑮
Chen C W 2021	RCT	Mild, Ordinary	60 (30/30)	T: 50.2±5.1 C: 49.5±5.1	I	LHQW plus RT	RT	NR	③ ④ ⑤ ⑦ ⑬ ⑮
Chen J J 2020	RCT	Convalescent	70 (35/35)	T: 44.8±4.9 C: 45.2±4.7	V	LHQW plus RT	RT	15 days	① ② ③ ④ ⑤ ⑥
Chen L Z 2020	RCT	NR	30 (15/15)	T: 42.6±3.5 C: 43.1±3.2	V	XBJ 100ml plus RT	RT	14 days	① ⑬ ⑮
Xu X L 2020	RCT	Mild, Ordinary, Severe	157 (77/80)	T: 49.1±15.7 C: 50.4±16.0	III	RDN plus RT	RT	14 days	① ③ ④ ⑤ ⑥ ⑦ ⑧ ⑨ ⑬ ⑮
Xiao Q 2020	RCT	Mild, Ordinary	200 (100/100)	T: 60.9±8.7 C: 62.2±7.5	II	SFJD plus RT	RT	14 days	⑥ ⑪ ⑫ ⑬ ⑮
Wang Y 2021	RCT	Ordinary	140 (70/70)	T: 48.0±13.2 C: 49.4±13.3	IV	QFPD plus RT	RT	10 days	① ② ⑨ ⑪ ⑫ ⑬ ⑮
Hu K 2020	RCT	NR	284 (142/142)	T: 50.4±15.2 C: 51.8±14.8	II	LHQW plus RT	RT	14 days	① ③ ④ ⑤ ⑥ ⑦ ⑧ ⑬ ⑮
He Q 2021	RCT	NR	71 (36/35)	NR	V	BZYQ plus RT	RT	10 days	① ② ⑮
Ni L 2021	RCT	Mild, Ordinary, Severe	235 (176/59)	NR	III	SHL plus RT	RT	14 days	⑥ ⑦ ⑬ ⑮
Liu Y J 2021	RCT	Severe	50 (25/25)	T: 48.0±1.6 C: 48.5±1.3	V	HSBD plus RT	RT	NR	① ⑪ ⑫ ⑬ ⑮
Cheng D Z 2020	NS-I	Ordinary	102 (51/51)	T:55.5±12.3 C:55.8±11.6	III	LHQW plus RT	RT	7 days	③ ④ ⑤ ⑥ ⑧
Lian J 2020	NS-I	Mild, Ordinary, Severe, Critical, Convalescent	64 (38/26)	T:61.3±14.1 C:58.1±12.0	IV	CM plus RT	RT	NR	② ③ ⑥ ⑧ ⑪ ⑫ ⑬ ⑮

Study		Severity	Sample (T/C)	Age		Treatment	Control	Duration	Outcomes
Liu F 2020	NS-I	Ordinary, Severe, Critical	84 (42/42)	T:52.7±16.8 C:49.5±13.8	III	CM plus RT	RT	NR	① ③ ⑨ ⑬
Pan G T 2020	NS-I	Critical	40 (26/14)	T:57.3±9.8 C:64.0±16.0	III IV	CM plus RT	RT	7 days	③ ⑥ ⑦ ⑪ ⑫
Qin L X 2021	NS-I	Severe, Critical	82 (42/40)	NR	V	CM plus RT	RT	NR	① ③ ⑥ ⑦ ⑧ ⑪ ⑫ ⑭ ⑮
Qin L X 2021*	NS-I	Severe, Critical	563 (523/40)	NR	V	CM	RT	NR	① ③ ⑥ ⑦ ⑧ ⑪ ⑫ ⑭ ⑮
Shi J 2020	NS-I	Mild, Ordinary, Severe	67 (49/18)	T: 47.9±14.5 C:46.7±17.4	III	CM plus RT	RT	6 days	① ② ③ ⑥ ⑧ ⑨
Song X Y 2020	NS-I	Mild, Ordinary	60 (30/30)	NR	III	CM plus RT	RT	3 days	① ③ ⑦ ⑨ ⑬ ⑮
Hu Y Q 2020	NS-I	Ordinary, Severe, Critical	52 (31/21)	T:48.3±16.6 C:49.8±17.2	II III IV	CM plus RT	RT	NR	① ② ③ ⑤ ⑥ ⑦ ⑧ ⑨ ⑪ ⑫
Yang M B 2020	NS-I	Ordinary	49 (26/23)	T:50.4±13.4 C:47.2±16.6	V	RYN plus RT	RT	7 days	② ⑥ ⑦ ⑫ ⑬ ⑮
Yang Q 2020	NS-I	Severe, Critical	103 (51/52)	T:61.6±1.8 C:66.4±1.8	III	CM plus RT	RT	NR	① ⑥ ⑫ ⑬ ⑭ ⑮
Yao K T 2020	NS-I	Ordinary	42 (21/21)	T:57.1±14.0 C:62.4±12.3	III	LHQW plus RT	RT	NR	③ ④ ⑤
Zhang N 2020	NS-I	Ordinary	120 (90/30)	T:51.7±12.5 C:49.2±13.6	II	CM plus RT	RT	5 days	③ ④ ⑤ ⑦ ⑧ ⑨ ⑮
Huang H 2020	NS-I	NR	45 (30/15)	T:58.4±15.5 C:66.3±14.1	V	CM Yihao plus RT	RT	3 days	③ ④ ⑤ ⑥ ⑧ ⑨ ⑪ ⑫ ⑭ ⑮
Huang H 2020*	NS-I	NR	43 (28/15)	T:61.9±12.2 C:66.3±14.1	V	CM Erhao plus RT	RT	3 days	③ ④ ⑤ ⑥ ⑧ ⑨ ⑪ ⑫ ⑭ ⑮
Zhang H T 2020	NS-I	Severe, Critical	22 (11/11)	T: 43.4±15.9 C: 40.7±13.3	II	CM plus RT	RT	NR	⑥ ⑦ ⑬ ⑮
Li L 2020	NS-I	Ordinary, Severe, Critical	96 (64/32)	T: 49.9±15.5 C: 47.5±14.1	V	CM	RT	28 days	① ③ ④ ⑤ ⑥ ⑮
Huang L Q 2020	NS-I	Severe	55 (23/32)	T: 56.0±5.3 C: 61.5±5.6	II	HSBD plus XYP plus XBJ plus SM	RT	16 days	⑥ ⑦ ⑪ ⑫ ⑬
Wang L Q 2021	NS-I	Ordinary, Severe	87 (47/40)	T: 44.7±11.4 C: 49.7±13.1	III	FYYH plus RT	RT	NR	② ③ ⑦ ⑧ ⑭
Wang L Q 2020*	NS-I	Mild, Ordinary, Severe, Critical	278 (173/105)	T:60.0±4.8 C:62.0±5.1	V	FYYH plus RT	RT	NR	① ② ③ ④ ⑤ ⑥ ⑧ ⑪ ⑫ ⑬ ⑭ ⑮
Guo H 2020	NS-I	Mild, Severe	32 (16/16)	T: 52.0±2.8 C: 54.0±6.8	V	XBJ 100ml plus RT	RT	7 days	③ ④ ⑤ ⑥ ⑦ ⑧ ⑨ ⑪ ⑫ ⑮

Zeng X H 2020	NS-I	Ordinary	229 (104/125)	T: 46.7±6.2 C: 46.2±5.6	V	QFPD plus RT	RT	NR	⑥ ⑦ ⑨ ⑮
Chen L 2020	NS-I	Ordinary	68 (34/34)	T: 65.1±10.6 C: 64.4±10.3	V	SFJD plus RT	RT	7 days	③ ④ ⑤ ⑥ ⑨ ⑪ ⑫ ⑮
Li K Y 2020	NS-I	NR	60 (30/30)	T: 53.6±0.3 C: 50.4±0.3	I	QFPD plus RT	RT	3 days	① ③ ④ ⑤ ⑥ ⑧ ⑨ ⑬ ⑮
Qu X K 2020	NS-I	Mild, Ordinary	70 (40/30)	T: 40.7±8.2 C: 39.8±6.4	II III	SFJD plus RT	RT	10 days	③ ④ ⑤ ⑦ ⑮
Yang M 2020	NS-I	Mild	40 (20/20)	T: 49.6±5.5 C: 50.2±5.8	III	QFPD plus RT	RT	7 days	③ ④ ⑤ ⑪ ⑫
Yu H Y 2020	NS-I	Mild, Ordinary	102 (64/38)	NR	V	QFPD	RT	NR	① ⑧ ⑨
Yu H Y 2020*	NS-I	Mild, Ordinary	123 (85/38)	NR	V	LHQW	RT	NR	① ⑧ ⑨
Yu H Y 2020**	NS-I	Mild, Ordinary	65 (27/38)	NR	V	JYBD	RT	NR	① ⑧ ⑨
Yu X Y 2020	NS-I	Ordinary, Severe, Critical	89 (43/46)	T: 64.2±2.5 C: 60.5±2.1	IV	QFPD plus RT	RT	14 days	⑦ ⑨ ⑫ ⑮
Zhang C Y 2020	NS-I	Ordinary	44 (22/22)	NR	IV	XBJ 50ml plus RT	RT	7 days	① ⑥ ⑪ ⑫ ⑬ ⑮
Zhang P 2021	NS-I	Severe, Critical	24 (12/12)	T: 61.4±13.2 C: 62.3±14.7	V	QFPD plus RT	RT	7 days	③ ⑥ ⑪ ⑫ ⑭ ⑮
Liu Z L 2020	NS-I	Ordinary, Severe	80 (44/36)	T: 50.7 C: 51.8	II	JHQG plus RT	RT	7 days	⑥ ⑦ ⑪ ⑫ ⑬ ⑮
Zhou Y H 2021	NS-I	Severe	104 (66/38)	T: 58.3±15.1 C: 58.8±14.1	V	CM plus RT	RT	NR	① ④ ⑤ ⑥ ⑧ ⑨ ⑮
Feng J 2021	NS-I	Severe	118 (33/85)	NR	V	CM plus RT	RT	9 days	⑨ ⑭ ⑮

Note: RCT: randomized controlled trial; NS-I: nonrandomized study of intervention; NR: not reported; T: treatment group; C: control group; CM: Chinese medicine; LHQW: Lianhua Qingwen; JHQG: Jinhua Qinggan granules; FYYH: Feiyan Yihao formula; RYN: Reyanning granules; RDN: Reduning injection; BZYQ: Buzhong Yiqi decoction; SHL: Shuanghuanglian oral liquids; HSBD: Huashi Baidu decoction; KG-1: Keguan-1 formula; HXZQ: Huoxiang Zhengqi granules; XFBD: Xuanfei Baidu decoction; XYP: Xiyanping injection; XBJ: Xuebijing injection; SFJD: Shufeng Jiedu formula; QFPD: Qingfei Paidu decoction; JYBD: Jinye Baidu formula; SM: Shenmai injection; RT: routine treatment (including oxygen therapy, antiviral medications and symptomatic therapies); CPGs: clinical practice guidelines; ①: effective clinical rate; ②: clinical symptom score; ③: improvement of fever; ④: improvement of fatigue; ⑤: improvement of cough; ⑥: improvement of CT; ⑦: negative nucleic acid conversion rate; ⑧: severe conversion rate; ⑨: length of hospital stay; ⑩: amount of virus; ⑪: white blood cell; ⑫: lymphocyte; ⑬: adverse events; ⑭: mortality; ⑮: other results; */**: different groups in the same study or different studies; I: diagnosis and treatment program for novel coronavirus pneumonia (the 3rd trial version from National Health Commission of the People's Republic of China); II: diagnosis and treatment program for novel coronavirus pneumonia (the 4th trial version from National Health Commission of the People's Republic of China); III: diagnosis and treatment program for novel coronavirus pneumonia (the 5th trial version from National Health Commission of the People's Republic of China); IV: diagnosis and treatment program for novel coronavirus pneumonia (the 6th trial version from National Health Commission of the People's Republic of China); V: adiagnosis and treatment program for novel coronavirus pneumonia (the 7th trial version from National Health Commission of the People's Republic of China)