Efficacy and Safety of Traditional Chinese Medicine (Lianhua Qingwen) for Coronavirus Disease 2019: a Systematic Review and Meta-analysis

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Research

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Abstract

Background: The coronavirus disease 2019(COVID-19) had become an epidemic and spread across the world, lead to severe respiratory failure and death. Traditional Chinese Medicine(TCM), Such as Lianhua Qingwen has been widely used in the prevention and treatment of COVID-19, This systematic review and meta-analysis will assess the effects of traditional Chinese herbal medicine(Lianhua Qingwen) in COVID-19 pneumonia from the randomized controlled trials(RCTs) and case control studies(CCSs).

Method: we search the literatures in databases inculding PubMed, Embase, *Web of science,* Cochrane Library, Wanfang, Chinese Science and Technology Periodical Database (VIP), Chinese Biomedical Literature Database (CBM) and China National Knowledge Infrastructure(CNKI)*, setting the date* from December 1, 2019, to June 1, 2021, Cochrane Risk of Bias tool and the Newcastle-Ottawa Scale were used to assess the quality of randomized controlled trials. All analyses were conducted by Stata 14.0.

Results: nine studies with 1163 patients(616males) were included, six were RCTs, three are CCSs. Compared with patients treated by western medicine alone, patients treated by Lianhua Qingwen combined with western medicine have a higher overall effective rate[RR=1.20, 95%CI1.20(1.11, 1.31), *P*=0.000], cardinal symptom disappearance rate[disappearance rate of fever: OR:3.64, 95%CI(1.57, 8.47), P=0.001;disappearance rate of cough: OR:1.97, 95%CI(1.45, 2.68), P=0.001; disappearance rate of fatigue: OR:2.55, 95%CI(1.09, 5.99), P=0.032] and CT recovery rate[RR:1.25, 95%*CI*(1.13,1.38), *P*=0.000], reduce the rate of the progress into severe diseases of COVID-19 patients[RR:0.43, 95%CI(0.30, 0.62), *P*=0.000], with more shorter duration of fever[WMD=-1.07，95%CI(-1.77, -0.37), *P*=0.003], The including studies described that Lianhua Qingwen did not increase the adverse drug reactions.

Conclusion: Lianhua Qingwen may have advantages in improving the clinical effective rate and cardinal symptom disappearance rate. Besides, it also had an excellent effect on the improvement of the chest CT and the proportion reducing of progress into severe clinical disease, which could be used as an effective therapy for COVID-19.

Introduction

Since December 2019, A new type of coronavirus named Coronavirus disease 2019(COVID-19, formerly named as SARS-CoV-2) broke out in Wuhan city, Hubei province, China, with amounts of patients complained of unexplained fever, cough fatigue, and accompanied by obvious effusion with grinding glass nodular shadows in the chest CT. The virus traveled in the respiratory tract and droplet transmission was the main route of transmission, with a typical phenomenon of human-to-human transmission, and led to respiratory failure, acute respiratory distress syndrome, septic shock, even death[1]. Quickly, it spread to more than a dozen of countries around the world[2], and World Health Organization (WHO) had defined it as a global pandemic. up to now, According to the report from Coronavirus Resource Center of the Johns Hopkins University & Medicine, the cumulative number of diagnoses worldwide had reached more than one hundred and seventy million, inculding three million deaths[3]. However, the number of confirmed cases continued to rise, which had imposed a heavy burden on the global, and urgent threat to global health, led a severe socio-economic damage, become a major global public health problem. Countries had also carried out clinical trials research and development, with a view to finding therapeutic drugs as soon as possible. Unfortunately, the western medicine including antiviral and antibacterial drugs, antitussive, expectorant and antiasthmatic drugs, no specific anti-viral drugs had been discovered for this virus. Although novel coronavirus vaccination had been carried out in some countries, there are still no specific antiviral treatment for COVID-19. At present, symptomatic controls and prevention of complications are remaining the most critical and cornerstone therapeutic regimens[4, 5].

In China, with the government strong measure, public surveillance, and the treatment of both western medicine and traditional chinese medicine, the pandemic had been under control.As a necessary part of the health care system in the china, the traditional chinese medicine had been developed over thousands of years, used in many countries and regions around the world. especially the chinese herbal medicine, had played an important role in the treatment of infectious diseases including severe acute respiratory syndrome (SARS), influenza A H1N1, avian influenza, malaria, etc[6, 7]. thus, in view of the previous experience of herbal medicine use in the treatment of several acute epidemic diseases[8, 9], Lianhua Qingwen and other three Chinese herb medicine were recommended for the COVID-19 patients in the clinical treatment[10]. Lianhua Qingwen is made from the ancient prescription Yin Qiao San and Ma Xing Shi Gan Decoction, cinsists of thirteen herbs such as Guanzhong, Houttuynia cordata, patchouli, rhubarb, Rhodiola rosea, menthol, and licorice, Common formulations of this formula are capsules, granules, and decoctions. Since the launch of the Lianhua Qingwen, it had been widely used as a broad spectrum of antiviral agent in the clinical practice, especially for the various respiratory virus infections[11]. Meanwhile, a lot of reports showed that the usage of Lianhua Qingwen had a favorable performance in the treatment of COVID-19, including some systematic reviews, case reports, observational studies and clinical trials [12]. These studies showed that Lianhua Qingwen could improve clinical symptom and and lung CT image, shorten fever reduction time and average length of hospital stay, and reduce the conversion rate from mild to severe, bringing new hope for clinical treatment and new drug discovery in treating COVID-19. Although some systematic reviews[13, 14] regarding Lianhua Qingwen for COVID-19 have been published in advance respectively, serious methodological shortcomings were also identified, more databases, randomized controlled trials(RCTs), and case-control studies(CCSs) should be updated in order to reduce potential bias.

Therefore, this meta-analysis aimed to evaluate the efficacy of Lianhua Qingwen in the treatment of COVID-19 based on currently available studies, to provide a more convincing proof for rational clinical application.

Method

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [15]. The protocol for this study has been registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD42021248211).

2.1 Data resources and search strategies

The systematic literature search was conducted by two authors(He YH and Qiang L)from the China National Knowledge Infrastructure (CNKI), the Wanfang database, the Chinese Science and Technology Periodical Database (VIP), Chinese Biomedical Literature Database (CBM), PubMed, Embase, Cochrane Library, Web of science. The retrieval date was set from the available date from December 1, 2019, to June 1, 2021. All the publications from the databases was searched by following search strategies: ("Coronavirus disease 2019" OR "COVID-19" OR "2019 novel coronavirus" OR "2019-nCov" OR "Novel Coronavirus Pneumonia" OR "NCP" OR "Severe aute respiratory syndrome coronavirus 2" OR "SARS-Cov-2" OR "new coronavirus" OR "novel coronavirus") AND ("Lianhuaqingwen" OR " lianhuaqingwen capsule" OR " Lianhua Qingwen" OR " lianhuaqingwen capsules" OR "lianhuaqingwen granules" OR "Lianhua Qingwen granules").

2.2 The inclusion and exclusion criteria

The inclusion criteria were: 1.Types of studies: all the enrolled articles were randomized trials, and case-control studies which were about the clinical efficacy;2. Patients diagnosed with COVID-19 of all ages and racial groups will be included, without life-threatening comorbidities; 3. the intervention group got a therapy of Lianhua Qingwen capsule or granules combining with western medicine. And the control groups were given western medications alone, Both of the two groups had the same conventional treatment, such as nutritional support, healthcare, etc; 4. included a sample size of larger than ten; 5. in Chinese or English language.

2.3 exclusion criteria

The exclusion criteria were as follows: 1. suspected cases ; 2. duplicate report, incomplete and unclear outcome effect, data that cannot be extracted after contacting original authors. 4. animal experiment 5. the language of the studies was not Chinese or English.

2.4 Study selection

We exported the identified records into EndnoteX8 (Thomson Reuters (Scientifific) LLC Philadelphia, PA, US) software and use this to remove and manage the duplicates. two researchers (He YH and Qiang L) screened the studies that should be further evaluated by reviewing the the titles and abstracts independently, Then, the full text of the eligible studies would be checked by two researchers (Deng J and Huang L), and the disagreements were discussed and resolved by another third researcher(Wang SP).

2.4 Quality assessment

We used the risk of bias assessment tool of the cochrane handbook[16] to assess the quality of the RCTs, and each RCT was assessed at low risk, high risk, or unclear risk relating to the following items: sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias, the Newcastle-Ottawa Scale (NOS) standard to evaluate the quality of case-control studies[17]. Three aspects were assessed: subject selection, inter-group comparability, and exposure factor measurement. The full NOS score is 9 points, with a score $\geq$ 6 indicating high quality. Two reviewers independently completed the data extraction and quality assessment (Deng J and Huang L). Any disagreements were resolved by discussion.

2.5 Data extraction

According to the inclusion and exclusion criteria, two researchers conducted data extraction independently(Deng J and Huang L), and the disagreements were solved by another third researcher(WSP). The information was extracted from research as follow: 1. general information: including the first name of author, size of sample, age of patient and sex, etc; 2. types of the research; 3. intervention time and measure;4. outcomes, study results, and adverse events. In the treatment and control group. all the data was extracted from each study as follow: 1. the clinical effective rate; 2. Improvement of abnormalities in chest CT; 3. cardinal symptom disappearance rate (fever, cough, fatigue); 4. duration of fever; 5. the progress into severe clinical disease; 6. adverse events.

2.6 Statistical methods

Stata version 14.0 statistical software (Stata Corp, College Station, TX, USA) was used in our article for all data processing and analysis. the measurement data adopts weight mean difference (WMD) for effect combination, and the count data uses relative risk (RR) or odds ratio (OR) to combine effect amounts. All of which were demonstrated with effect size and 95% confidence intervals (CI). We used the Q test and I_2 statistics to analyze the heterogeneity of the included studies. The fifixed-effect model was employed for data combination if $P \geq 0.05$ and $I_2 \leq 50\%$ which indicated that there was no statistical difference in heterogeneity between the studies. The random-effect model was adopted if the converse was true. We planned to explore the publication bias using funnel plots if the number of included studies exceeded ten. $P < 0.05$ indicated a statistically signifificant difference.

Results

3.1 literature search

As shown in Fig. 1, 608 articles were initially collected in total. The duplicates, reviews, comments, animal experiments were removed (n = 559). After reading the abstract and full-text of the remain articles, forty articles that did not meet the inclusion criteria were excluded. Finally, nine literatures were included [18–26].

3.2 Characteristics of the included studies

Six studies were RCTs, and three studies were case-control studies, and all the studies were published in 2020, seven written in Chinese and two written in English, The total sample size was 1163 (616 males), and sample size per study ranged from 42 to 295,The oldest age of the participants was 75 and the youngest was 21the disease stages of the patients with COVID-19 were mild or ordinary, and the shortest duration of the Lianhua Qingwen treatment was 7 days and the longest was 21 days, All the characteristics of the included studies were shown in Table 1.

3.3 Risk of bias assessment and quality assessment

The quality of the included RCTs were shown in the Table 2, all the six studies described the low risk of the random sequence generation, allocation concealment, incomplete outcome data, Selective reporting. but only one study reported the blinding of participants, personnel, and outcome assessment. The other bias is not clear in four RCTs, Overall, the quality of the included RCTs was high.

As was shown in the Table 3, three CCSs were assessed for quality by the NOS, all the studies did not decscribed representativeness of the cases, selection of controls, no study reported non-response rate.

Table 1
Summary of included studies.

Study (year,country)	Sample Size(I/C) gender (M/F) Age (Years)(I/C)	Study type	Type of disease	Intervention group	control group	study outcomes
Hu (2020, China)	284(142/142); 150/134; 37.1 ± 0.7/37.09 ± 0.668	RCT	Common	Plan I:Qingwen capsule, 4 capsules for 3 times daily for two weeks,and with the plan II	paln II: antiviral and antimicrobial therapy	the clinical symptom effective rate; Improvement of abnormalities in chest CT; the progress into severe clinical disease.
Wang (2020, China)	60(30/30); 23/37; 28～69/29～68	RCT	Common	plan I: Lianhua Qingwen capsule, 4 capsules for 3 times daily for 7–10 days,and with the plan II	paln II: antiviral and antimicrobial therapy	The clinical effective rate.
Yu (2020, China)	295(147/148); 171/124; 48.3 ± 9.6/47.3 ± 8.3	RCT	Light /Common	Plan I:Lianhua Qingwen granules, 1 packet per time for 2 times daily for 7 days,and with the plan II	PlanII:Arbidol Hydrochloride Tablets, 200 mg + Ambroxol Hydrochloride Tablets, 30 mg for 3 times daily + Moxifloxacin tablets, 400 mg for 1 time daily, 30 mg for 3 times daily	The clinical effective rate; Improvement of abnormalities in chest CT; Rate of conversion of severe cases.
Chen JJ(2020, China)	70(35/35); 38/32; 45.21 ± 4.68/44.75 ± 4.92	RCT	Light	plan I: Lianhua Qingwen capsule, 4 capsules for 2 times daily for 15 days, and nutriton support antiviral and antimicrobial therapy	paln II: Arbidol Hydrochloride Tablets, 200 mg for 2 times daily for 15 days, and nutriton support antiviral and antimicrobial therapy	clinical effective rate Improvement of abnormalities in chest CT
CW Chen(2020, China)	60(30/30); 35/25; 49.52 ± 5.06/50.16 ± 5.11	RCT	Light /Common	plan I: Lianhua Qingwen capsule, 4 capsules for 3 times daily for 7–10 days,and with the plan II	paln II:nutriton support antiviral and antimicrobial therapy	Rate of conversion of severe cases

Study (year,country)	Sample Size(I/C) gender (M/F) Age (Years)(I/C)	Study type	Type of disease	Intervention group	control group	study outcomes
Liu(2020, China)	108(68/40); 47/61; 54.8 ± 19.1/59.5 ± 15.6	RCT	Common	plan I:Lianhua Qingwen 1400mg for 3 times daily for 5–21 days,and with the plan II.	paln II: Arbidol Hydrochloride Tablets, 200 mg for 2 times daily for 5–21 days, and nutriton support antiviral and antimicrobial therapy	□ Improvement of abnormalities in chest CT
Cheng (2020, China)	102(51/51); 53/49; 55.5 ± 12.3/55.8 ± 11.6	CCs	Common	plan I: Lianhua Qingwen granules, 1 packet for 3 times daily for 7 days.and with the plan II	paln II:nutriton support antiviral and antimicrobial therapy	□The clinical effective rate;□ Improvement of abnormalities in chest CT; □ Rate of conversion of severe cases;□ duration of fever;□disappearance rate of fever;□disappearance rate of cough;□disappearance rate of fatigue
HY Yu (2020,China)	123(85/38); 62/61; 21～69/ 21～68	CCs	Light	plan I: Lianhua Qingwen capsule, 4 capsules for 3 times daily for 8 days, and nutriton support antiviral and antimicrobial therapy	paln II: Arbidol Hydrochloride Tablets, 200 mg for 3 times daily for 5 days, and nutriton support antiviral and antimicrobial therapy	□ Rate of conversion of severe cases
Yao (2020, China)	42(21/21);28/14;57. 1 ± 14. 0/62. 4 ± 12. 3	CCs	Common	plan I:Lianhua Qingwen granules, 1 packet for 3 times daily for 7 days.and with the plan II.	plan II:antiviral and antimicrobial therapy	□clinical effective rate □ duration of fever; □cardinal symptom disappearance rate (fever, cough, fatigue).

Table 2
The risk of bias of included Randomized Controlled Trials

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Hu	L	L	U	H	L	L	L
Liu	L	L	H	H	L	L	U
Wang	L	L	U	U	L	L	U
Yu	L	L	H	H	L	L	U
CW Chen	L	L	L	L	L	L	U
JJ Chen	L	L	H	U	L	L	L

H: High risk, L: Low risk, U: Unclear risk

Table 3
The quality of included Case-Control Studies

Author(year)	case definition	Representativeness of the Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Control	Ascertainment of Exposure	Same method of ascertainment for cases and controls	Non-Response Rate	NOS
Cheng(2020)	□	-	-	□	□□	□	□	-	6
Yao(2020)	□	-	-	□	□□	□	□	-	6
HY Hu(2020)	□	-	-	□	□□	□	□	-	6

Table 4
Comparison of the adverse drug reaction between two group

Outcome measure	Total	Events/Intervention	Events/Control	Statistical method	Effect estimate	*P*-value
Liver damage	341	36/170	35/171	RR (Random) 95%CI	1.03(0.68,1.56)	0.880
nausea vomiting	341	10/170	10/171	RR (Random) 95%CI	1.01(0.43, 2.36)	0.987
headache	341	2/170	3/171	RR (Random) 95%CI	0.68(0.117,3.972)	0.699

3.4 Meta-analysis

(1) The clinical effective rate: six researches[18–21, 24, 25], reported the clinical effective rate in the two groups. The intervention group that combined Lianhua Qingwen with the western medicine showed a significantly better effective rate.(Fig. 3)[RR = 1.20, 95%CI 1.20(1.11, 1.31), *P* = 0.000].

(2) Cardinal symptom disappearance rate:two studies[24, 26] reported the symptom disappearance rate, including symptom of fever, cough and fatigue. Compared with the control group, the intervention group performed a higher disappearance rate.[disappearance rate of fever: OR:3.64, 95%CI(1.57, 8.47), *P* = 0.001;disappearance rate of cough: OR:3.96, 95%CI(1.72, 9.14), *P* = 0.001; disappearance rate of fatigue: OR:2.55, 95%CI(1.09, 5.99), *P* = 0.032] (Fig. 4–6).

(3) Improvement of abnormalities in chest CT: the improvement of abnormalities in chest CT cases were investigated by five[18, 20, 21, 23, 24] studies, finding that the patients, CT manifestations had been improved in the group of Lianhua Qingwen [RR:1.25, 95%CI(1.13,1.38), *P* = 0.000].(Fig. 7)

(4) The progress into severe diseases: Five [18, 20, 25, 22, 24] studies compared the progress into severe diseases between the two groups. Compared with the western medicine alone, the combination of Lianhua Qingwen can significantly reduce the rate of the progress into severe diseases of COVID-19 patients.[RR:0.43, 95%CI(0.30, 0.62), *P* = 0.000](Fig. 8).

(5) Duration of fever: Two studies[24, 26] evaluated the duration of fever between the two groups. The results indicated that the patients with the therapy of combining Lianhua Qingwen with western medicine had a shorter duration of fever than those patients given western medicine alone, with a significant *P* value[WMD=-1.07,95%CI(-1.77, -0.37), *P* = 0.003].

(6) Adverse events: two studies[22, 25] reported the adverse events in two gourps, and the common adverse events were nausea and vomiting, liver damage, and headache. These studies described that there was no significant difference adverse drug reactions caused by the two different interventions(Table 4)

3.5 Publication bias

Since the number of studies in any comparative analysis did not exceed ten, we did not assess the publication bias.

Discussion

As a new betacoronavirus which had not previously affected humans, the coronavirus disease 2019(COVID-19) had been a huge public health problem in the world. the high through sequencing found that the novel virus was similar to bat coronavirus, and shared about 80% genetic sequence with the coronavirus which caused the sever acute respiratory syndrome(SARS)[27]. the COVID-19 spread though air and aerosols rapidly, with obvious human to human tansmission, developed cough, dyspnea, fever, abnormalities in chest computed tomography(CT), and the ground-glass opacity on the chest CT was one of the typical characteristics of COVID-19. A series of complications occurred in the severe patients, like the respiratory failure, acute respiratory distress syndrome, the severe patients multiple organ dysfunction syndrome, etc, even death[28]. Currently, COVID-19 had been detected in more than 215 countries, caused serious damage to public health and huge losses to economic development around the world, the world health organization(WHO)

announced that the COVID-19 had become a pandemic break on the global scale. Great efforts had been made to identify some medical products about COVID-19, like drugs, vaccines, which helped us to diagnose and treat COVID-19 patients. but to our konwledge, there are still no specifific therapeutic drugs for COVID-19.

Traditonal chinese medicine(TCM), had been developed over thousands of years, Not only become an important part in the treatment of infectious disease since ancient times in china, but also used in the other countries around the world, such as Japan, South Korea, USA, United Kingdom. Some studies had reported that Traditonal chinese medicine, especially herbal formula, such as San Wu Huangqin Decoction, Lianhua Qingwen Capsule, had antiviral effects which associated with blocking of the proliferation, and could improve the lung damage caused by influenza viruses[29, 30]. In the 2003, as a supplementary treatment for SARS, the TCM played an important role in combating SARS-COV virus, demonstrating an obvious therapeutic effect on the clinical effective rate and reducing the rate of progression into severe diseases [31]. With a similarity of genetic sequence with the SARS-COV, COVID-19 caused the same clinical symptoms researchers find that SARS-COV-2 and SARS-CoV have the same spike protein which could enter human alveolar epithelial cells through binding the receptor of angiotensin converting enzyme 2 (ACE2) [32]. Blocking the ACE2 may play a role in preventing the infection of 2019-nCoV. And many TCM like the baicalin, scutellarin, hesperidin, glycyrrhizin which were also important parts of the chinese herbal medicine Lianhua Qingwen were reported could interact with ACE2 [33]. this mean that Traditonal chinese medicine would have advantage in the treatment of COVID-19 with different severity from light to critical. So as a common herbal medicine in the treatment of viral influenza in china [34], Lianhua Qingwen plays a part in broad-spectrum antiviral, antibacterial, anti-inflammatory, enhancing immunity, antifebrile, cough, expectorant and analgesic [35]. In the treatment of COVID-19, Lianhua Qingwen's main components might had a good ability in binding with ACE2, and which may do some effects on coronavirus through multi-component, multi-target and multi-pathway. and the specific mechanism of the effectiveness of Lianhua Qingwen in the treatment of COVID-19 still needs more studies to reveal.

In this study, it was the first strictly designed systematic review and meta-analysis of the published RCTs and CCs to assess the efficacy and safety of the Traditonal chinese medicine Lianhua Qingwen for COVID-19 in English. with systematic search, some including studies investigated the efficacy of Lianhua Qingwen in COVID-19 treatment. Compared with the western medicine alone, the combined therapy of Lianhua Qingwen with western medicine showed more advantages in improving the clinical effective rate, cardinal symptom disappearance rate (fever, cough, fatigue) and decreasing the duration of fever. Besides, it also had an excellent effect on the improvement of the chest CT and the proportion reducing of progress into severe clinical disease. These therapeutic effects were related to the herbal medicine Lianhua Qingwen can affect immune cells and cytokine production associated with immune responses[36]. compared with werstern medicine, Lianhua Qingwen might have better effect on improving the symptoms and quality of life of patients. And all the studies did not report the serious adverse events in the treatment.

The results in this meta-analysis got some positive findings, but there still exist some limitations. First, the number of the included studies in this review was limited, and the included studies' content about Lianhua Qingwen was also restricted. With the more studies being reported in the future time, the function of Lianhua Qingwen in the COVID-19 will be furtherly revealed. Second, the included studies may have some unclear bias, with some included studies did not report on the generation of sequences, blinding of participants, study investigators, concealment of allocation or the alternative methods used to reduce potential performance bias. Thus, all the documents from the analysis might have a certain degree of bias. Finally, there were few RCTs related to Lianhua Qingwen, and the publications were almost from mainland China, which may lead to the bias from language. And these researches may be considered less informative, thus being difficult to generalize.

Conclusion

The meta-analysis results showed great effects of the combined therapy of Lianhua QingWen with Western medicine on the clinical effective rate and improvement of symptoms. And reveals the potential role of Lianhua QingWen in treating COVID-19. More high-quality and quantity RCTs are needed to further corroborate the effectiveness and adverse events of Lianhua Qingwen in the treatment of COVID-19.

Declarations

Ethical Approval and Consent to participate

It is not necessary for ethical approval because this article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

Consent for publication

Not applicable

Availability of supporting data

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

All the authors declare that they have no competing interests.

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Author Contributions

He YH designed the study, analyzed the data and writed the manuscript. Qiang L the search strategy, collected data. Huan L and Deng J were responsible for the quality assessment, re-checked. Wang Sp funded and control the project. All listed authors reviewed and revised the manuscript.

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References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
2. Kam Wa Chan, Vivian Taam Wong, Sydney Chi Wai Tang. COVID-19: An Update on the Epidemiological, Clinical,Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease. American Journal of Chinese Medicine. 2020;48(3):737-62.
3. Johns Hopkins University & Medicine, Coronavirus Resource Center Total confifirmed cases and deaths. (2021-06-01). [2021-06-01]. https://coronavirus.jhu.edu/map.html.
4. Zumla A, Chan JFW, Azhar EI, et al. Coronaviruse-drug discovery and therapeutic options. Nature Reviews Drug Discovery. 2016;15;327-47.
5. Xie X, Zhong Z, Zhao W, et al. Chest CT for Typical Coronavirus Disease 2019 (COVID-19) Pneumonia: Relationship to Negative RT-PCR Testing. Radiology. 2020;296(2):E41-E45.
6. Wang C, Cao B, Liu QQ, et al. Oseltamivir compared with the Chinese traditional therapy maxingshigan-yinqiaosan in the treatment of H1N1 influenza: a randomized trial. Ann Intern Med. 2011;155(4):217-25.
7. Wang J, Xiong X. Current situation and perspectives of clinical study in integrative medicine in china. Evid Based Complement Alternat Med. 2012;2012:268542.
8. Liu D, Liang B, Huang L, et al. Clinical observation on the preventive effect of kangdu bufei decoction on acute severe respiratory syndrome. Chinese Journal of Integrated Traditional and Western Medicine. 2004;24(685-688)
9. Tong X, Li A, Zhang Z, et al. TCM treatment of infectious atypical pneumonia–a report of 16 cases. Journal of Traditional Chinese Medicine. 2004;24(4):266–9
10. Runfeng L, Yunlong H, Jicheng H, et al. Lianhuaqingwen exerts anti-viral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2). Pharmacol Res. 2020;156:104761.
11. Yang Y, Islam MS, Wang J, et al. Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective. Int J Biol Sci. 2020;16(10):1708-1717.
12. Ang L, Lee HW, Choi JY, et al. Herbal medicine and pattern identification for treating COVID-19: A rapid review of guidelines. Integr Med Res. 2020;9(2):100407.
13. Wang SX, Li MY, Chen XL, et al. Meta-analysis of clinical efficacy of Lianhua Qingwen combined with Western medicine in the treatment of COVID-19. Chinese traditional and herbal drugs. 2020;14:3763-3769.
14. Wang SH, Liu JF, Zhang YL, et al. Systematic review of efficacy and safety of Lianhua Qingwen Capsules in treatment of viral influenza. Zhongguo Zhong Yao Za Zhi. 2019;44(7):1503-1508.
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
16. Higgins JP, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
17. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010 Sep;25(9):603-5.
18. Hu K, Guan WJ, Bi Y, et al. Efficacy and safety of Lianhuaqingwen capsules, a repurposed Chinese herb, in patients with coronavirus disease 2019: A multicenter, prospective, randomized controlled trial. Phytomedicine. 2020 16:153242.
19. Wang SZ, WANG HJ, Chen HM, et al.Lianhua Qingwen capsule and interferon-α combined with lopinavir/ritonavir for the treatment of 30 COVID-19 patients. Journal of Bengbu Medical College. 2020;02:154-155.
20. Yu P, Li Y, Wan SB, et al. Efficacy observation of Lianhua Qingwen Granule combined with Abidor in the treatment of mild COVID-19. Chinese Pharmaceutical Journal. 2020;1-9.
21. Chen JJ, Zhou YL, Chen FG, et al. Clinical Study on Treatment of COVID-19 in Convalescent Period Treated with Lianhua Qingwen Capsule Combined with Interferon α-2b. Advances in Clinical Medicine. 2020, 10(6), 1144-1149

22. Chen CW, Li XL, Liu YF, et al. Clinical study of Lianhua Qingwen Capsule in the treatment of Corona Virus Disease 2019. Research of Intergrated traditional Chinese and western medicine. 2021,13(01):1-4.
23. Liu L, Shi F, Tu P, et al. Arbidol combined with the Chinese medicine Lianhuaqingwen capsule versus arbidol alone in the treatment of COVID-19. Medicine (Baltimore). 2021;100(4):e24475.
24. Cheng D, Wang WJ, Li Y, et al, Analysis of curative effect of 51 patients with novel coronavirus pneumonia treated with Chinese medicine Lianhua Qingwen：a multicentre retrospective study.Tianjin Journal of Traditional Chinese Medicine. 2020,05:509-516.
25. Yu HY, Reng XH, Qi XX, et al. Efficacy Study of Arbidol, Qingfei Paidu Decoction, Lianhua Qingwen Capsule, and Jinye Baidu Granules in the Treatment of Mild / Moderate COVID-19 in a Fangcang Shelter Hospital. Pharmacology and Clinics of Chinese Materia Medica. 2020,26(11):8-12.
26. Yao KT, Liu MY, Li X, et al. Retrospective Clinical Analysis on Treatment of Coronavirus Disease 2019 with Traditional Chinese Medicine Lianhua Qingwen. Chinese Journal of Experimental Traditional Medical Formulae. 2020,26(11):8-12.
27. Fu L, Wang B, Yuan T, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. J Infect. 2020;80(6):656-665.
28. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.
29. Ma Q, Yu Q, Xing X, et al, a Chinese Herbal Formula, Inhibits Influenza a/PR/8/34 (H1N1) Virus Infection In Vitro and In Vivo. Viruses. 2018 ;10(3):117.
30. Ding Y, Zeng L, Li R, et al. The Chinese prescription lianhuaqingwen capsule exerts anti[1]influenza activity through the inhibition of viral propagation and impacts immune function. Bmc Complementary & Alternative Medicine. 2017;17(1):130.
31. Chung-Hua Hsu, Kung-Chang Hwang, Chung-Liang Chao, et al. The lesson of supplementary treatment with Chinese medicine on severe laboratory-confirmed SARS patients. Am J Chin Med. 2006;34(6):927-935.
32. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270-273.
33. Ren X, Shao XX, Li XX, et al. Identifying potential treatments of COVID-19 from Traditional Chinese Medicine (TCM) by using a data-driven approach. J Ethnopharmacol. 2020;258:112932.
34. Hiroaki Kiyohara, Chikara Ichino, Yuka Kawamura, et al. Patchouli alcohol: in vitro direct anti-influenza virus sesquiterpene in Pogostemon cablin Benth. J Nat Med. 2012;66(1):55-61.
35. Dong L, Xia J W, Gong Y, et al. Effect of Lianhuaqingwencapsules on airway inlammation in patients with acuteexacerbation of chronic obstructive pulmonary disease. Evid-Based Compl Alter Med. 2014;2014:637969.
36. Huang CF, Lin SS, Liao PH, et al. The immunopharmaceutical effects and mechanisms of herb medicine. Cell Mol Immunol. 2008 ;5(1):23-31.

Figure

Figure 2 not available with this version.

Figures

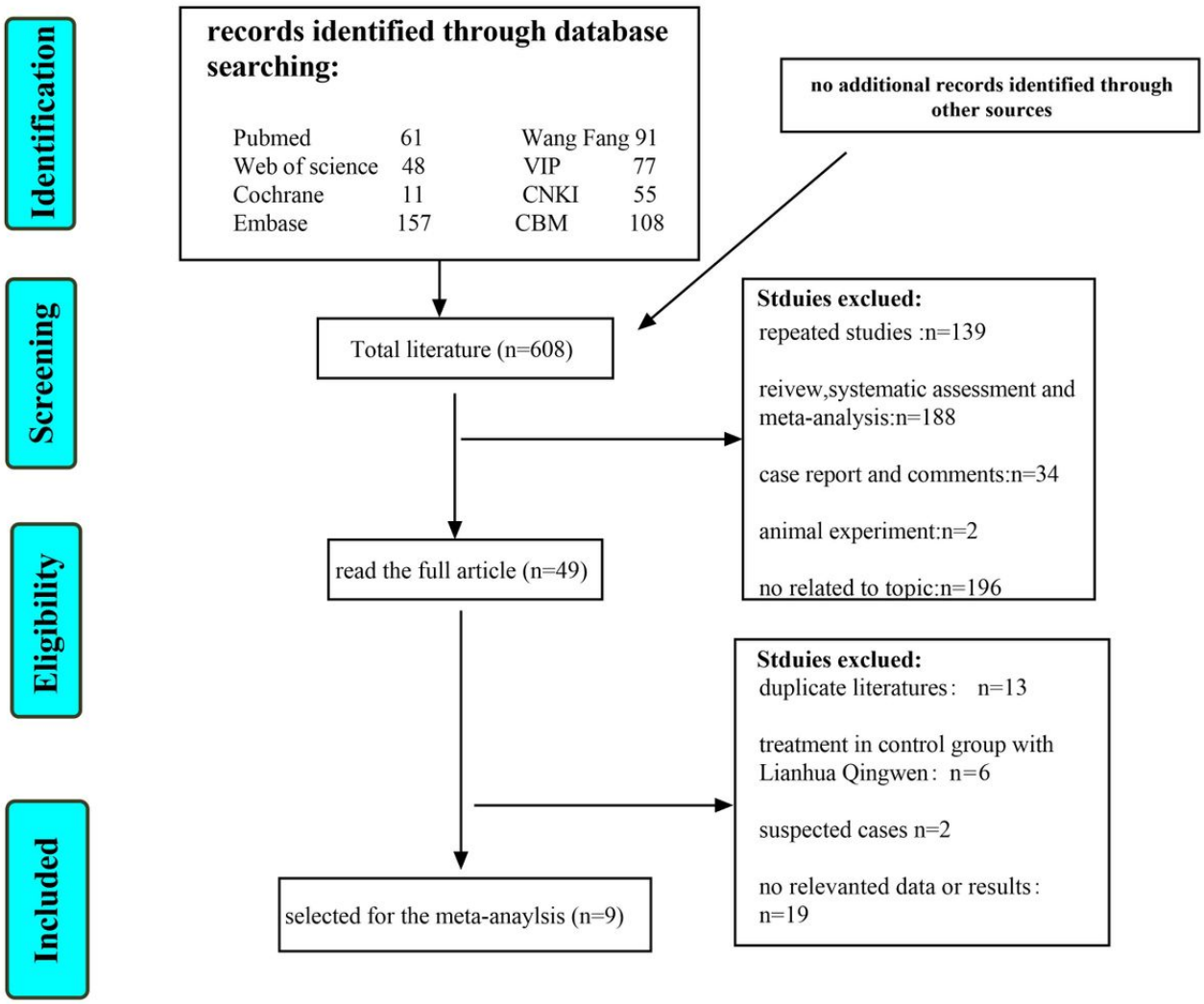

Figure 1

Flow Chart

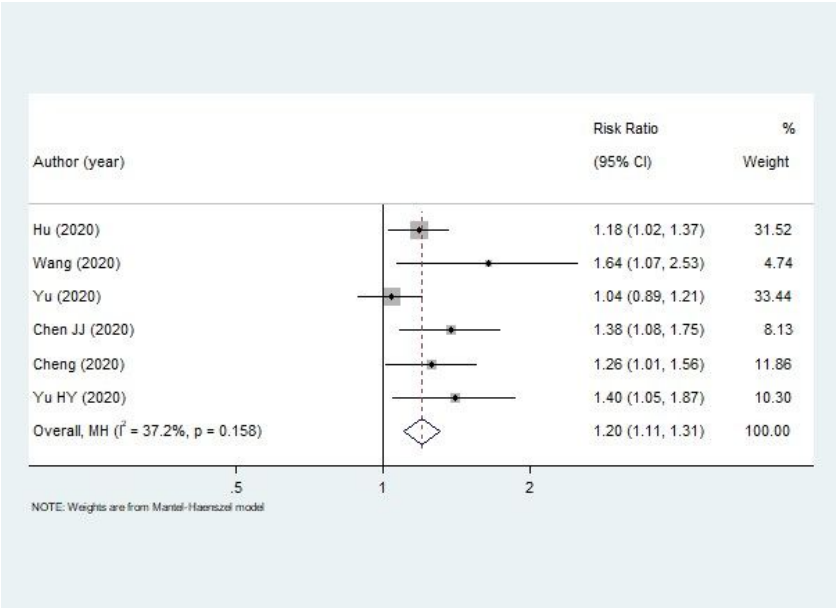

Figure 2

The clinical effective rate

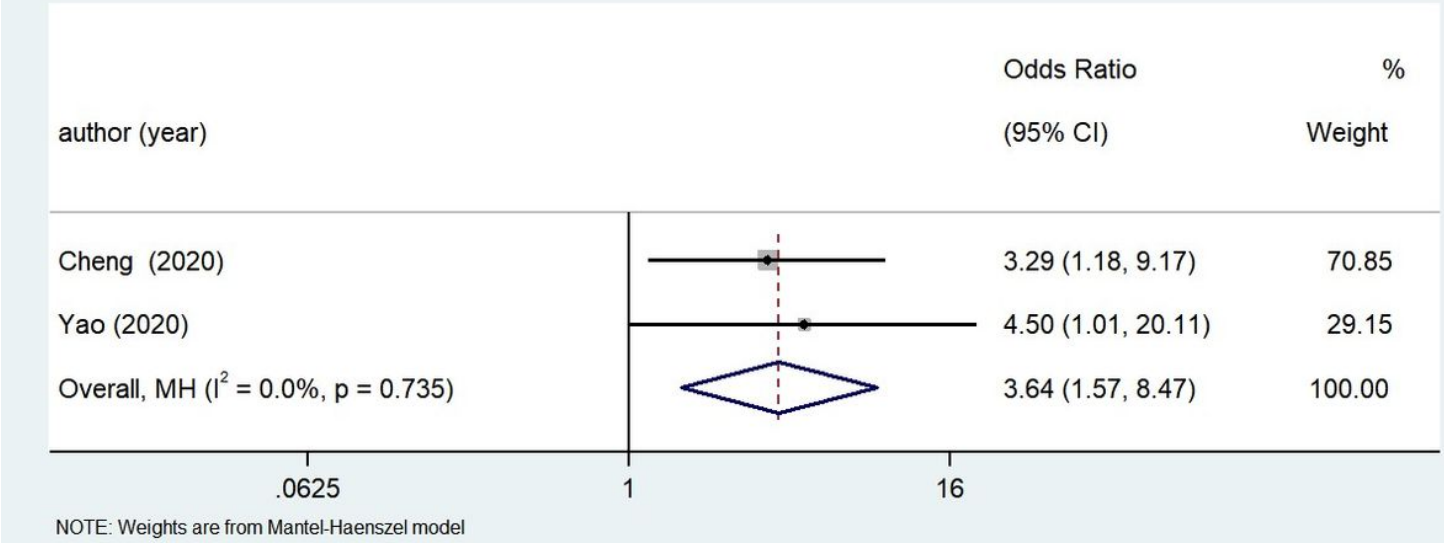

Figure 3

disappearance rate of fever

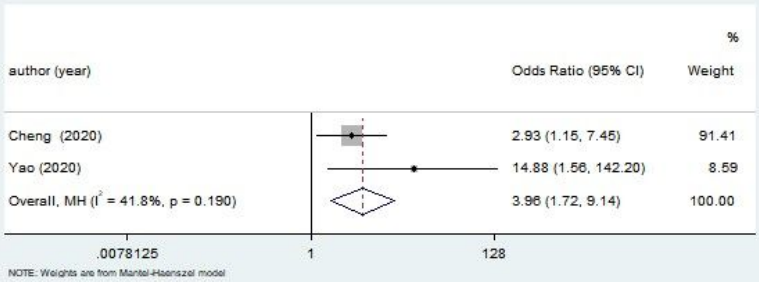

Figure 4

disappearance rate of cough

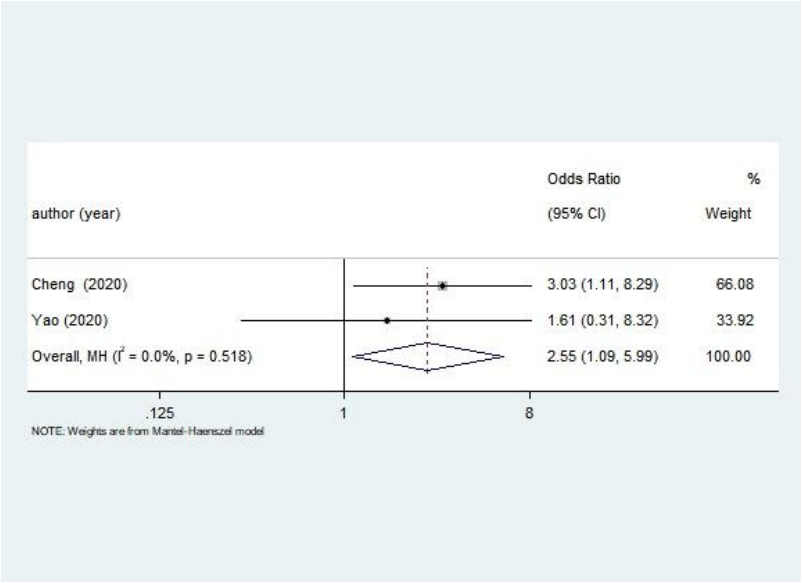

Figure 5

disappearance rate of fatigue

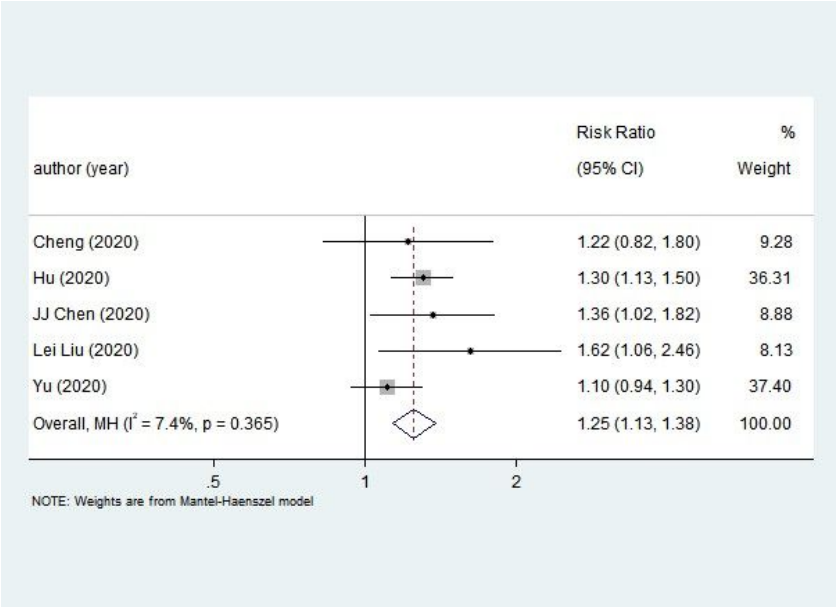

Figure 6

Improvement of abnormalities in chest CT

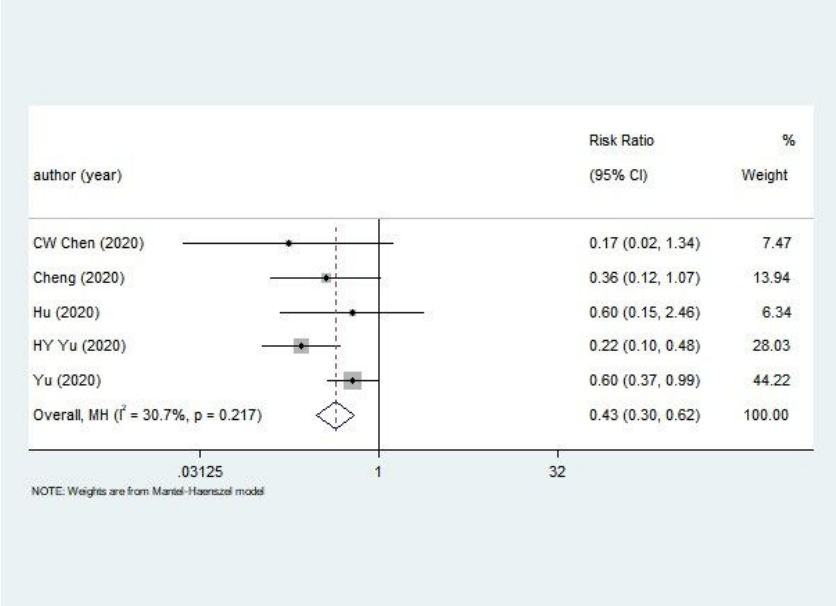

Figure 7

The progress into severe diseases

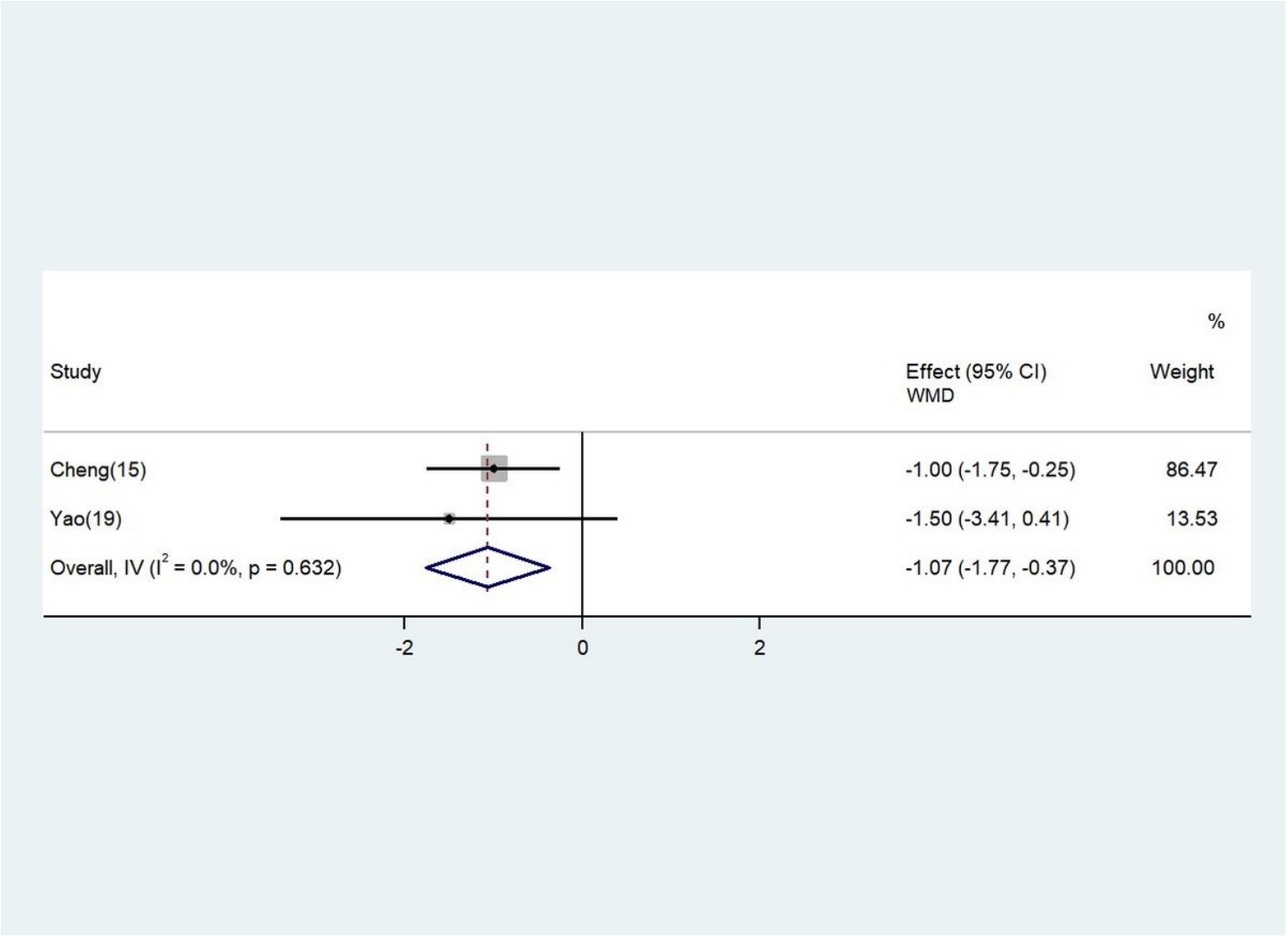

Figure 8

Duration of fever