INPLASY PROTOCOL

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The authors declare that they have no competing interests.

Efficacy and safety of Lianhua Qingwen combined with conventional antiviral Western Medicine in the treatment of coronavirus disease (covid-19) in 2019: Protocol for a systematic review and meta-analysis

Zhang, X[1]; Liu, M[2]; Cao, D[3]; Zhang, Q[4]; Liu, J[5].

Review question / Objective: **Is effective and safe of Lianhua Qingwen combined with conventional antiviral western medicine in the treatment of coronavirus disease (COVID-19) in 2019?**
Condition being studied: **The novel coronavirus pneumonia (Corona Virus Disease 2019, COVID-19) epidemic is spreading continuously and classified as class B infectious diseases (class a management) . Over 200 countries and regions in the world have reported the confirmed cases successively, and become the global fast spreading epidemic disease 2. At present, there is no effective antiviral drug confirmed by covid-19. The intervention of Chinese traditional medicine compound Lianhua Qingwen and other traditional Chinese medicine has played an important role. Data shows that the total effective rate of traditional Chinese medicine has reached more than 90%. However, there are "individual differences" in the efficacy of traditional Chinese medicine compound Lianhuaqingwen, which makes the quality of evidence of clinical efficacy of traditional Chinese medicine low. Therefore, it is necessary to carry out rigorous and objective quality evaluation for different types of clinical research, and the effectiveness analysis results obtained on this basis are more convincing.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 June 2020 and was last updated on 18 June 2020 (registration number INPLASY202060067).

INTRODUCTION

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Condition being studied: **The novel coronavirus pneumonia (Corona Virus Disease 2019, COVID-19) epidemic is spreading continuously and classified as class B infectious diseases (class a management) . Over 200 countries and regions in the world have reported the confirmed cases successively, and become**

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METHODS

Participant or population: 2.1.2.Patients diagnosed with COVID-19 of all ages and racial groups will be included,All patients must be diagnosed with prediabetes by clearly defined or internationally recognized criteria.

Intervention: Taditional Chinese medicine compound Lianhuaqingwen combined with conventional antiviral western medicine intervention, including all the treatment of any dosage form of traditional Chinese medicine compound Lianhuaqingwen dry, such as Lianhuaqingwen granules, Lianhuaqingwen capsules, lianhuaqingke granules, decoction, etc.Nexclude:Multiple traditional Chinese medicine compounds will be used as interventions will be excluded.

Comparator: Conventional antiviral western medicine.

Study designs to be included: All randomized controlled trials(RCTs), Retrospective cohort study (RCSs) , Comparison before and after the study (BAs).

Eligibility criteria: All randomized controlled trials(RCTs), Retrospective cohort study (RCSs) , Comparison before and after the study (BAs)of Lianhua Qingwen combined with Conventional antiviral Western Medicine for COVID-19 will be included.Excluded from the meta-analysis are duplicated publications,the control group also used traditional Chinese medicine intervention, studies with unavailable or incorrect data, articles not reporting outcomes of interest. Also excluded are studies enrolling fewer than 30 participants .

Information sources: System searches CNKI, CBM, VIP and Wanfang databases, PubMed, EMBASE, MEDLINE, Cochrane central, and clinical trial registration centers, such as ChiCTR, NTR and clinicalTrials.gov. In addition, Manual retrieval of papers, conference papers, ongoing experiments, internal reports, etc. to supplement electronic retrieval.Select all eligible studies published by May 8, 2020.

Main outcome(s): Primary outcomes: Clinical effective rate, CT improvement rate and severe conversion rate. Secondary outcomes: Fever time, disappearance rate of fever symptoms, disappearance rate of cough symptoms, improvement and disappearance rate of asthenia symptoms.

Quality assessment / Risk of bias analysis: Two reviewers/authors (ZXL and ZQ) will independently evaluate the quality of the included trials through assessing the risk of bias using the following tools, when appropriate: a. For RCTs, the Cochrane Collaboration's tool for assessing risk of bias will be used[29]; b. For NRIs,Tevaluation of methodological quality with Newcastle Ottawa scale (NOS). The following aspects of included trials will be assessed: sequence generation, allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, and selective outcome reporting. We will judge the each domains as 'low risk of bias', 'high risk of bias', or 'uncertain risk of bias' according to Higgins (2011), and pay particular

attention to the risk of bias of cluster-randomised trials. Also illustrates the potential biases within each of the included studies by presenting a 'risk of bias' table, graph and summary.

Strategy of data synthesis: Dichotomous outcomes will be presented as risk ratio and 95% confidence intervals (CIs),and continuous outcomes will be presented as mean difference/standard mean difference and 95% CIs. Statistical analysis was conducted by Revman 5.3 software. Risk ratio (RR) was used to express the severe conversion rate and CT improvement rate absorption rate; mean difference (MD) was used to express the time of fever reduction in secondary indexes; ratio Ratio (OR) was used to express clinical efficiency and symptom disappearance rate. Data synthesis reports the intervention effect of the original study by integrating the cohort study. At the same time, the single arm study was included in the analysis, not involved in data synthesis, only used to assist in displaying the clinical characteristics of the subjects, not for efficacy evaluation. After determining how to combine different types of studies, NRIs uses the method of inverse variance of random effect model to evaluate and calculate the 95% confidence interval (CI) of the effect value.

Subgroup analysis: We plan to carry out the followingsubgroup analyses if possible: The study area is different, the average course of disease is different, and the length of treatment is different. We will use the formal test for subgroup interactions in Review Manager 5.3.

Sensibility analysis: We will per-forme the Sensitivity analysis to explore the effects of trial risk of bias on primary outcomes if possible. In the analysis, we will exclude lowerquality trials and repeat the meta-analyses to examine whether the quality of included studies influences the pooled results.

Country(ies) involved: China.

Keywords: Corona Virus Disease 2019, Lianhua Qingwen, meta-analysis, protocol, systematic review.

Contributions of each author:
Author 1 - Xiaolin Zhang - conceived of the study, perform this review, and drafted the manuscript.
Author 2 - Mingjun Liu - arbitrate any disagreement and ensure that no errors occur during the review.
Author 3 - Di Cao - Data curation and drafted the manuscript.
Author 4 - Qi Zhang - developed the search strategy.
Author 5 - Junnan Liu - assess the risk of bias and perform data synthesis.