INPLASY PROTOCOL

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None declared.

The efficacy and safety of COVID-19 vaccine A protocol of systematic review and meta-analysis

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Review question / Objective: **The efficacy and safety of COVID-19 vaccine.P: Healthy male or non-pregnant female over 18 years of age; I: Get the COVID-19 vaccine; C: Placebo control; O: Local adverse reactions, systemic adverse reactions, geometric mean titer (GMT) of neutralizing antibodies measured by live virus neutralization test 14 or 28 days after the last vaccination, serum conversion, other laboratory indicators and mortality, etc.; S: Randomized controlled trials (RCTS).**
Condition being studied: **The coronavirus disease 2019 (COVID-19) has been prevalent worldwide since its discovery, becoming one of the most threatening infectious diseases in human history. Experts in the field of medicine and biology all over the world are working on finding, developing and preventing the treatment and prevention of COVID-19. However, at present, COVID-19 is still mainly treated with symptomatic therapy, and there is still a lack of effective antiviral therapy, so the prevention and control method of novel coronavirus is more focused on the research and development of vaccine. Currently, several vaccines have been developed, but their relative efficacy and safety have not been proven. Therefore, this study aims to investigate the efficacy and safety of COVID-19.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 March 2021 and was last updated on 15 March 2021 (registration number INPLASY202130048).

INTRODUCTION

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METHODS

Search strategy: The following electronic databases will be searched from inception to March 2021: PubMed, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), WanFang Data, Weipu Electronics. In addition, reference lists of the included studies were manually searched to identify additional relevant studies.

Participant or population: We will include healthy men 18 years of age and older or non-pregnant women who have been vaccinated against COVID-19, regardless of race, education or economic status. Excludes pregnant women, post-operative infections, patients with mental illness, patients with severe pneumonia or other reasons for inability to exercise, and patients with severe cardiovascular and/or liver and/or kidney disease.

Intervention: The experimental group received a prophylactic COVID-19 vaccine.

Comparator: The control group received a placebo.

Study designs to be included: We will review all studies on the efficacy and safety of the preventative COVID-19 vaccine in humans. Due to language limitations, we will search for articles in both Chinese and English. In order to obtain a more objective and authentic evaluation, all articles must meet the following two conditions: 1. Published documents with complete documents data; 2. The type of trial is randomized controlled trial (RCT).

Eligibility criteria: (1) languages other than English and Chinese; (2) lack of outcome indicator data; (3) studies that were not RCTs (4) duplicate studies, studies with incomplete data and abstracts without full texts.

Information sources: 1. Electronic data sources. The following electronic databases will be searched from inception to March 2021: PubMed, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), WanFang Data, Weipu Electronics. In addition, reference lists of the included studies were manually searched to identify additional relevant studies. 2. Other resources. Relevant references will be reviewed and screened. In addition, we will search the following registration website of the clinical trial: WHO ICTRP, http:// http://www.chictr.org.cn, http://www.ClinicalTrial.gov, and ISRCTN Register. Moreover, the relevant grey literature from the Health Management Information Database (HMIC), Open SIGLE Database, and the National Technical Information Service (NTIS) will be searched. Experts in the field will be consulted for relevant studies.

Main outcome(s): Clinical trial results indicators include at least one or more of the following: local reactions (pain, itching, redness, swelling and induration, etc.), systemic adverse reactions (fever, diarrhea, fatigue, nausea, vomiting, lethargy, etc.), 14 days or 28 days after the last vaccination with live virus neutralization test of neutralizing antibody geometric average drop degree (GMT), serum conversion rate

and other laboratory test index and mortality rate, etc.

Quality assessment / Risk of bias analysis: Two other researchers (LZ and FX) will independently extract the data and fill in a predesigned form. Information includes the first author, country, year, methods, quality and type of vaccine, vaccination dose, inoculation time interval, the number of participants, and baseline characteristics (race, sex ratio, age range, or average age), research, design, results, specific data, conclusions, follow-up, adverse events, local and systemic adverse reactions and laboratory examination indexes, and funds, sponsors and registration number, conflicts of interest, funding sources and ethical approval. The extracted data will be cross-checked by two researchers. If there is a disagreement, a third researcher (NL) will be involved. If necessary, we will contact the study authors for further information. All data will be transferred to the Review Manager software (RevMan v. 5.3) for analysis and synthesis.

Strategy of data synthesis: In this protocol, Efficacy data will be synthesized and statistically analyzed by 2 reviewers independently using RevMan 5.3. A risk ratio (RR) or odd ration with 95% CIs will be adopted for dichotomous data, whereas a mean difference (MD) or standard mean difference (SMD) with 95% CIs will be utilized for continuous data. SMD will be employed if different assessment tools are used.Statistical heterogeneity will be investigated using chi-square test and I2 statistic. Fixed-effect model will be applied when heterogeneity is low (I2< 50%) and random-effects model will be used for moderate heterogeneity (50% < I2< 75%). When heterogeneity is considerably high, meta-analysis will not be performed.In line with the Cochrane guideline, the fixed-effects model will be utilized for the pooled data if heterogeneity is deemed low and the random-effect model will be employed if heterogeneity is deemed moderate. Subgroup analysis or meta-regression will be performed to assess the potential sources with reasonable explanations if heterogeneity is considerably high. The statistical significance is defined as $P < 0.05$. If the meta-analysis is not feasible, a narrative description of the results will be provided.

Subgroup analysis: We will perform subgroup analysis according to the different details of interventions, study quality and outcome indicators.

Sensitivity analysis: We will perform sensitivity analysis based on sample size, research design, heterogeneity quality, methodological quality and statistical model, exclude trials with low quality, and ensure the stability of analysis results.

Country(ies) involved: China.

Keywords: COVID-19, vaccine, meta-analysis, systematic review, protocol.

Contributions of each author:

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