

INPLASY PROTOCOL

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**Review Stage at time of this
submission:** Preliminary
searches.

Conflicts of interest:
None declared.

INTRODUCTION

Review question / Objective: How is the efficacy of corticosteroid use on COVID-19, and whether corticosteroid could be used for COVID-19 patients in clinical practice.

Rationale: Effective treatments for coronavirus disease 2019 (COVID-19) are

Systemic Corticosteroids Administration in Coronavirus Disease 2019 Outcomes: an Umbrella Meta-analysis

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Condition being studied: Considering great impact from the pandemic and the inconsistency, this study aimed to comprehensively summarize the emerging secondary evidence (systematic review and/or meta-analysis) being reported worldwide. We sought to (i) determine the association between outcomes of interest and corticosteroid use; (ii) better understand the strength of the data and the extent potential bias in the claimed results via umbrella method; (iii) show reliable evidence by summarizing abundant sample size, totally analyze heterogeneity and subgroup analyses; (iv) provide potential effective treatment for COVID-19 in clinical use.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 January 2021 and was last updated on 30 January 2021 (registration number INPLASY202110116).

urgently needed. Real role of corticosteroid use on COVID-19 has long been interested and disputable.

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and/or meta-analysis) being reported worldwide. We sought to (i) determine the association between outcomes of interest and corticosteroid use; (ii) better understand the strength of the data and the extent potential bias in the claimed results via umbrella method; (iii) show reliable evidence by summarizing abundant sample size, totally analyze heterogeneity and subgroup analyses; (iv) provide potential effective treatment for COVID-19 in clinical use.

METHODS

Search strategy: We searched Pubmed, EMBASE, Cochrane Library, preprint platforms for related systematic review and/or meta-analysis from the database inception to Dec-01-2020 with no language restrictions. Search keywords used are below: COVID-19, corticosteroid, systematic review and meta-analysis. A manual search of reference lists from the retrieved studies was also p.

Participant or population: Hospitalized patients with confirmed COVID-19.

Intervention: Reasonable corticosteroid use during the hospital stay.

Comparator: No corticosteroid use including SOC and placebo.

Study designs to be included: Meta-analysis with/without systematic review with available data. Eligible secondary studies should have at least two primary studies except network meta-analysis.

Eligibility criteria: The eligible criteria were: Population: Hospitalized patients with confirmed COVID-19. Intervention: Reasonable corticosteroid use during the hospital stay. Comparison: No corticosteroid use including SOC and placebo. Outcomes: Mortality, MV, hospital stay, virus clearance time (VCT), intensive care unit (ICU) stay, adverse events (AEs). Eligible studies should have at least one of the intended outcomes. Study design: Meta-analysis with/without systematic review with available data. Eligible

secondary studies should have at least two primary studies except network meta-analysis.

Information sources: We searched Pubmed, EMBASE, Cochrane Library, preprint platforms for related systematic review and/or meta-analysis from the database inception to Dec-01-2020 with no language restrictions. Search keywords used are below: COVID-19, corticosteroid, systematic review and meta-analysis. Reference lists were also manually searched.

Main outcome(s): Mortality, MV, hospital stay, virus clearance time (VCT), intensive care unit (ICU) stay, adverse events (AEs). Eligible studies should have at least one of the intended outcomes.

Data management: Data extraction was performed independently by two authors, any disagreements were resolved by a discussion with a third author. For each eligible article, we recorded the first author, publication year, number of included studies, number of participants, comparisons, study design, quality assessment methods, subgroup data, searching and registration information and the pooled risk estimates (RR, OR, hazard ratio (HR), incident RR, mean difference (MD), weighted MD (WMD)) and 95% CI. For each primary study from the eligible meta-analyses, the first author, number of cases and subjects, maximally adjusted risk estimate and 95% CI was extracted for further analysis if available.

Quality assessment / Risk of bias analysis: We took the I² statistic and derived P values of Cochran Q statistic to assess heterogeneity among studies. Where I² was beyond 50% or 75%, the heterogeneity was considered to be substantial or considerable, respectively. We also calculated the 95% CI of I² to assess the uncertainty around heterogeneity estimates.

Strategy of data synthesis: For the largest data set of each meta-analysis, we calculated the SE of the effect size and

determined whether the SE was less than 0.10. For binary variables, HRs and 95% CI were used to pool results from each meta-analysis together based on extracted RR, OR, HR and incident RR, because influence from time on mortality and MV could be properly considered, and there was still heterogeneity and missing information about sample size across the involved populations of each study. For continuous variables, MDs and WMDs were used. 95% prediction interval (PI) was also calculated to predict the expected effect size range in the new original studies.

Subgroup analysis: Subgroup analysis was reasonably conducted if there were available data.

Sensitivity analysis: Sensitivity analysis was reasonably conducted if there were available data.

Language: English.

Country(ies) involved: China.

Other relevant information: None.

Keywords: Corticosteroids; COVID-19, Umbrella Meta-analysis.

Dissemination plans: The intended study is aimed to be published on high impact journals.

Contributions of each author:

Author 1 - Binghao Zhao.