## INPLASY PROTOCOL

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# Hydroxychloroquine use reduces mortality risk in systemic lupus erythematosus: a meta-analysis of cohort studies

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Review question / Objective: The aim of this meta-analysis of cohort studies is to evaluate the effect of hydroxychloroquine use on the mortality risk in SLE patients.

Condition being studied: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that is associated with considerable morbidity and mortality. Hydroxychloroquine (HCQ) is near-universally recommended for patients with SLE. However, the effect of HCQ on SLE mortality has not been systematically reviewed and summarized in large population groups.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 March 2022 and was last updated on 28 March 2022 (registration number INPLASY202230157).

#### INTRODUCTION

Review question / Objective: The aim of this meta-analysis of cohort studies is to evaluate the effect of hydroxychloroquine use on the mortality risk in SLE patients. Condition being studied: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that is associated with considerable morbidity and mortality. Hydroxychloroquine (HCQ) is near-universally recommended for patients with SLE. However, the effect of HCQ on SLE

mortality has not been systematically reviewed and summarized in large population groups.

#### **METHODS**

Participant or population: Inclusion: SLE patients (as diagnosed using any recognised diagnostic criteria; with no definite of age limit). Exclusion: Patients with other autoimmune diseases without SLF.

Intervention: Long-term treatment with HCQ (Follow-up period should be no less than 12 months).

Comparator: Never used HCQ (either with other drugs or untreated).

Study designs to be included: Cohort studies including prospective studies, retrospective cohort studies, or longitudinal observational cohort studies.

Eligibility criteria: The inclusion criteria for this meta-analysis are listed below: (1) Assessed the impact of HCQ on the mortality of patients with SLE; (2) The outcome of concern is the risk of death or mortality of the patients; (3)cohort studies including prospective studies, retrospective cohort studies, or longitudinal observational cohort studies; (4) Follow-up period should be no less than 12 months; (5) Articles provided sufficient data of risk estimates of SLE patients mortality, such as hazard ratio(HR) with 95% confidence interval (95%CI).

Information sources: We searched articles in electronic database including PubMed, Embase, Web of Science and Cochrane Library. All the English publications until 21 January 2021 were searched with restriction of cohort studies. Reference list of all selected articles will independently screened to identify additional studies left out in the initial search.

Main outcome(s): The outcome of concern is the risk of death or mortality of SLE patients.

#### Quality assessment / Risk of bias analysis:

The Newcastle Ottawa Scale (NOS) will be used to assess the quality of cohort studies. According to NOS criteria, the quality of the study is starred according to three aspects: representativeness of participants (4 stars), comparability between groups(2 stars), and credibility of results(3 stars). Studies with a total of 5-9 stars are designated as a medium to high quality, while studies with 0-4 stars are of low quality.

Strategy of data synthesis: HRs with 95%CIs are pooled to assess the association between HCQ exposure and SLE mortality. Fixed-effect model are used for meta-analysis when heterogeneity is less significant, and random-effect model are used to pool data when heterogeneity is greater.

Subgroup analysis: Subgroup analyses are conducted out by SLE comorbidity, age, sex, follow-up time, study design, HCQ dosage, etc.

Sensitivity analysis: Sensitivity analyses omit each study in sequence in order to explore studies that have a greater confounding effect on the pooled outcomes.

Country(ies) involved: China.

**Keywords:** Hydroxychloroquine ;systemic lupus erythematosus; ; overall survival.

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