

# INPLASY PROTOCOL

To cite: Cai et al.  
Hydroxychloroquine use  
reduces mortality risk in  
systemic lupus erythematosus:  
a meta-analysis of cohort  
studies. Inplasy protocol  
202230157. doi:  
10.37766/inplasy2022.3.0157

Received: 28 March 2022

Published: 28 March 2022

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**Support:** NSFC.

**Review Stage at time of this  
submission:** Formal screening  
of search results against  
eligibility criteria.

**Conflicts of interest:**  
None declared.

## **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.

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

Cai, TT<sup>1</sup>; Zhao, J<sup>2</sup>; Yang, YP<sup>3</sup>; Jiang, YF<sup>4</sup>; Zhang, JA<sup>5</sup>.

**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.

**Information sources:** We conducted a systematic literature search through PubMed, Embase, Web of science, and the Cochrane Central Register of Controlled Trials (CENTRAL). The four databases were systematically searched from inception to 21 January 2022, without any language, geographic, or type of article restrictions. The search was updated on 17 April 2022. The references and citations of the articles identified were also screened.

**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 15 May 2022 (registration number INPLASY202230157).

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

## METHODS

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

**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).

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**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) was used to evaluate the quality of each included cohort study. The NOS score ranges from 0 to 9 points, and a score  $\geq 6$  indicates low risk of bias or high quality study.

**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 were performed by complications (renal or cardiopulmonary involvement), drug type (HCQ/CQ or HCQ), region (Asia, Europe or America), study quality (high risk of bias, or low risk of bias), study design (perspective or retrospective), variable type (adjusted HR or crude HR) and sample size (N1,000).

**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; mortality; cohort studies; meta-analysis.

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