# INPLASY PROTOCOL

To cite: Liu et al. Uric Acid Levels and Risk of Cognitive Impairment: Dose-Response Meta-Analysis of Prospective Cohort Studies. Inplasy protocol 2022100111. doi: 10.37766/inplasy2022.10.0111

Received: 27 October 2022

Published: 27 October 2022

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**Support:** **SDPNSF, China.**

**Review Stage at time of this submission:** **Completed but not published.**

**Conflicts of interest:**
**None declared.**

# Uric Acid Levels and Risk of Cognitive Impairment: Dose-Response Meta-Analysis of Prospective Cohort Studies

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**Review question / Objective:** **To investigate and quantify the potential dose-response relationship between uric acid level and cognitive impairment.**
**Condition being studied:** **Previous studies have confirmed that uric acid has dual characteristics of anti-oxidation and oxidation promotion based on the difference of physical and chemical environment and biological tissue level. It not only participates in oxidative stress as a bioactive proinflammatory factor, leading to the occurrence of neurodegenerative diseases, but also shows strong antioxidant activity under certain conditions, which has a protective effect on neurons. Uric acid may regulate cognitive function in different ways. Several prospective cohort studies investigated the relationship between serum uric acid levels and cognitive impairment. Since uric acid has dual characteristics of oxidation and reduction, it is particularly important to explore the relationship between different uric acid levels and cognitive impairment.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 October 2022 and was last updated on 31 January 2023 (registration number INPLASY2022100111).

## INTRODUCTION

**Review question / Objective:** **To investigate and quantify the potential dose-response relationship between uric acid level and cognitive impairment.**

**Condition being studied:** **Previous studies have confirmed that uric acid has dual characteristics of anti-oxidation and oxidation promotion based on the difference of physical and chemical environment and biological tissue level. It not only participates in oxidative stress as a bioactive proinflammatory factor, leading to the occurrence of neurodegenerative diseases, but also shows strong antioxidant activity under certain conditions, which has a protective effect on**

neurons. Uric acid may regulate cognitive function in different ways. Several prospective cohort studies investigated the relationship between serum uric acid levels and cognitive impairment. Since uric acid has dual characteristics of oxidation and reduction, it is particularly important to explore the relationship between different uric acid levels and cognitive impairment.

## METHODS

**Participant or population:** All subjects were free of cognitive impairment at baseline.

**Intervention:** No intervention.

**Comparator:** Not applicable.

**Study designs to be included:** Prospective cohort studies.

**Eligibility criteria:** 1) Prospective cohort studies, 2) cognitive impairment as a specific outcome, 3) The investigator reported the relative risks (RRs) with 95% confidence intervals (CIs) for at least three levels of UA.

**Information sources:** PubMed (Medline) and Embase.

**Main outcome(s):** cognitive impairment.

**Data management:** Data extraction was performed independently by two authors using standard extraction formats. We extracted the following information from each study: author, year of publication, study name, study location, participant characteristics (age and gender), year of follow-up, diagnostic criteria, uric acid levels, sample size (number of participants and cases of events), Endpoint (cognitive impairment or dementia), type of dementia,adjusted covariates in multivariate analysis, and hazard ratios (95% confidence intervals) for different uric acid levels.

**Quality assessment / Risk of bias analysis:** We assessed the quality of non-randomised studies according to Newcastle-Ottawa criteria. We defined a score of 0-3, 3.5-6, and 6.5-9 for low-quality, moderate-quality, and high-quality studies, respectively. When the study had multiple adjusted models, we extracted the model that reflected the most adjustment for potential confounders.If the data of interest is not directly shown in the publication, we will attempt to contact the author. To resolve differences by consensus, we used group consensus and consulted a third reviewer.

**Strategy of data synthesis:** This study used STATA software version 13.0 for meta-analysis. We compared the highest and lowest categories of uric acid levels using relative risk to obtain pooled estimates.

**Subgroup analysis:** We conducted stratified analyses by gender, age, study location, follow-up time, number of participants, type of dementia and diabetes status.

**Sensitivity analysis:** Each study was removed at a time and the analysis was conducted with the remaining studies to assess whether the result was affected by the excluded study.

**Language restriction:** English.

**Country(ies) involved:** China.

**Keywords:** uric acid, cognitive impairment, meta-analysis, dose-response, risk factor.

**Contributions of each author:**
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Author 4 - Min Peng.