

# INPLASY PROTOCOL

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None declared.

## Serum 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 serum uric acid level and cognitive impairment.

**Condition being studied:** Previous studies have confirmed that uric acid has dual characteristics of antioxidation 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. Serum 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 27 October 2022 (registration number INPLASY2022100111).

### INTRODUCTION

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**Condition being studied:** Previous studies have confirmed that uric acid has dual characteristics of antioxidation 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. Serum 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) have diagnostic criteria for cognitive impairment, 4) Baseline estimates of serum uric acid levels, 5) The investigator reported the relative risk of at least three levels of uric acid, 6) Relative risk (HR) data with 95% confidence intervals (CI) were included to assess the association of cognitive impairment with SUA levels. 7) For each identified study, all subjects were free of cognitive impairment at baseline and participated in the entire follow-up survey according to diagnostic criteria.

**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 a series of subgroup analysis based on age, gender, geographical location, follow-up duration, number of participants, whether to control diabetes in the model, whether to adjust serum cholesterol level, and whether to adjust sports activities.

**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:** Serum uric acid, Cognitive Impairment, Dose-Response, Meta-analysis.

**Contributions of each author:**

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Author 2 - Guomin Si.

Author 3 - Tiantian Yang.

Author 4 - Min Peng.