INPLASY

INPLASY2025120090

doi: 10.37766/inplasy2025.12.0090

Received: 26 December 2025

Published: 26 December 2025

Acute kidney injury associated with nonsteroidal anti-inflammatory drug use in community-based populations: a protocol for a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None declared.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120090

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 December 2025 and was last updated on 26 December 2025.

INTRODUCTION

Review question / Objective The present meta-analysis synthesizes available evidence to evaluate the association between nonsteroidal anti-inflammatory drug (NSAID) exposure and acute kidney injury (AKI) in community-dwelling adults.

Rationale

Previous meta-analyses[1,2] have examined the association between NSAID exposure and AKI, but some included studies were hospital-based or focused on selected populations, limiting applicability to community-dwelling adults. In addition, previous meta-analyses lacked explicit definitions of NSAID exposure time windows or pooled estimates based on inconsistently defined measures of current use. Therefore, a meta-analysis focusing on community-based populations with specified exposure timing is warranted.

Condition being studied

AKI is a clinically important adverse event that has been observed among individuals using NSAIDs. NSAIDs can alter renal hemodynamics through inhibition of cyclooxygenase-dependent prostaglandin synthesis, leading to reduced renal blood flow and glomerular filtration rate, which potentially contribute to AKI.

METHODS

Search strategy

Both controlled vocabulary terms (Medical Subject Headings [MeSH] terms in PubMed, Emtree terms in Embase, and MeSH descriptors in the Cochrane Library) and free-text keywords related to NSAID exposure, AKI, and design of study are used in the search strategy. Search terms are combined using Boolean operators and truncation symbols. Filters are applied to restrict results to English-language publications, studies conducted in humans published as articles. In Embase, searches are

additionally limited to Embase-indexed records only.

Participant or population
This study includes community-dwelling adults aged 18 years and above.

Intervention
NSAID exposure is defined within the specified exposure window.

Comparator
Comparators include either within-person reference periods without NSAID use in crossover designs, or separate populations with no NSAID exposure during the same follow-up timeframe.

Study designs to be included
This study only includes observational studies.

Eligibility criteria
Eligibility criteria are based on the PECOS framework. Included studies must meet the criteria specified in the Participant or population, Intervention (Exposure), Comparator, and Study designs to be included sections described above. To be included, studies are also required to report adjusted effect estimates for the association between NSAID use and AKI, together with corresponding measures of precision such as 95% confidence intervals (95% CIs) or standard errors (SEs). All eligible studies are required to be published in English. Studies are excluded if they are conducted in non-community populations, assess NSAID exposure solely as part of combination drug regimens (such as concurrent use with diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or triple-drug therapy), do not represent original human observational research, or do not provide sufficient data.

Information sources
Five electronic databases—PubMed, Embase, the Cochrane Library, Scopus, and Web of Science — are searched to identify relevant studies.

Main outcome(s)
Effect estimates reflect the association between NSAID exposure and AKI.

Additional outcome(s)
None.

Data management
Search records are managed using EndNote X9. Study selection and data extraction are independently conducted by two reviewers, with disagreements resolved through discussion.

Quality assessment / Risk of bias analysis
The included studies are assessed using the Newcastle–Ottawa Scale (NOS), which evaluates study quality across three domains: Selection, Comparability, and Outcome/Exposure.

Strategy of data synthesis
Statistical analyses are carried out using Review Manager (RevMan), version 5.3 (The Cochrane Collaboration, Copenhagen, Denmark). Adjusted effect estimates are synthesized using the generic inverse-variance approach and pooled across predefined exposure windows, including current NSAID use; NSAID prescriptions ending within 1–30 days or 31–365 days; and NSAID prescriptions dispensed 0–30 or 1–90 days prior to the AKI event date. Current use refers to NSAID prescriptions that were active at the time of AKI events. AKI event dates were determined according to the date of diagnosis or the corresponding hospital admission date documented in medical records. SEs are derived from extracted 95% CIs using formulas recommended in the Cochrane Handbook for Systematic Reviews of Interventions[3]:

$$\mathrm{SE} = \frac{\ln(\text{Upper confidence limit}) - \ln(\text{Lower confidence limit})}{3.92}$$

If the data are not suitable for meta-analysis, a narrative summary is conducted.

Subgroup analysis
None.

Sensitivity analysis
For meta-analyses comprising three or more studies, robustness is assessed using a leave-one-out approach.

Language restriction
Only studies written in English are included.

Country(ies) involved
This systematic review involves authors from Vietnam and the Republic of Korea.

Keywords
NSAIDs; cyclooxygenase inhibitors; drug-induced nephrotoxicity; renal toxicity; acute kidney injury.

Dissemination plans
This study will be submitted for publication in a peer-reviewed journal.

Contributions of each author

Author 1 - Hoa Ngan Doan, participating in study selection and data extraction, synthesizing and analyzing the findings, preparing the table and figures, and writing the manuscript.
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