# Effect of the “Triple whammy” in hospitalization due to acute kidney injury: a case-control study nested in a cohort

**First published:** 03/03/2021

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Study Planned

## Administrative details

**EU PAS number**

EUPAS35832

**Study ID**

42755

**DARWIN EU® study**

No

**Study countries**

Spain

**Study description**

Background: the term “triple whammy” refers to the simultaneous use of diuretics, renin-angiotensin-aldosterone system inhibitors (angiotensin-converting enzime inhibitors (ACEI) and angiotensin II receptor blockers (ARBs)) and nonsteroidal anti-inflammatory drugs (NSAIDs). The use of this combination has been associated with an increased risk of kidney injury (AKI). Main objective: to analyze the incidence of hospitalization due to AKI associated to the exposure to the “triple whammy” combination versus non-exposure to that combination. Secondary objectives: 1) To assess the risk of hospitalization due to AKI with the combination "triple whammy" that includes metamizole versus the combination that includes an NSAID different to metamizole, 2) To evaluate the risk of hospitalization due to AKI based on the time window from the index date and according to its duration, 3) To determine the risk of requiring renal replacement therapy and mortality associated to the "triple whammy" combination.

**Study status**

Planned

# Research institutions and networks

## Institutions

### Navarre Health Service

**First published:** 01/02/2024

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**Institution**

# Contact details

**Study institution contact**

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**Study contact**

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**Primary lead investigator**

Leire Leache

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**

Planned: 18/11/2019

**Study start date**

Planned: 03/05/2021

**Data analysis start date**

Planned: 01/10/2021

**Date of interim report, if expected**

Planned: 31/12/2021

**Date of final study report**

Planned: 31/03/2021

## Sources of funding

- Other

## More details on funding

Government of Navarre

## Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Main study objective:**

To analyze the incidence of hospitalization due to acute kidney injury (AKI) associated to the exposure to the “triple whammy” combination versus non-

exposure to that combination.

## Study Design

**Non-interventional study design**

Case-control

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(C03) DIURETICS

DIURETICS

(C09) AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

(M01AE53) ketoprofen, combinations

ketoprofen, combinations

(N02BB02) metamizole sodium

metamizole sodium

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**Medical condition to be studied**

Acute kidney injury

## Population studied

**Age groups**

- Adults (18 to < 46 years)
- Adults (46 to < 65 years)

- Adults (65 to < 75 years)
- Adults (75 to < 85 years)
- Adults (85 years and over)

**Special population of interest**

Renal impaired

**Estimated number of subjects**

1.000

## Study design details

**Outcomes**

Incidence of hospitalization due to acute kidney injury (AKI) associated to the exposure to the “triple whammy” combination versus non-exposure to that combination. 1) Hospitalization due to AKI with the combination "triple whammy" that includes metamizole versus the combination that includes an NSAID different to metamizole 2) Hospitalization due to AKI based on the time window from the index date and according to its duration 3) Incidence of requiring renal replacement therapy and mortality associated to the "triple whammy" combination.

**Data analysis plan**

The comparison of categorical variables between cases and controls will be analyzed through the Chi-square test or Fisher's test, and in the case of quantitative variables through the t-Student or Mann-Whitney test. The association between the exposure and the risk of hospitalization due to AKI will be analyzed using conditional logistic regression models, adjusting for possible confounding factors. The adjusted Odds Ratio and 95% confidence interval will be estimated. The risk of hospitalization due to AKI will be determined

according to the time of exposure to the "triple whammy" combination ("current users" vs "recent users" vs "past users"), the "continuous duration" and the "cumulative duration" of this association (≤3 months, >3 and ≤6 months, >6 and ≤9 months and >9 months and ≤12 months), compared with no exposure to this association. Additionally, the main variable will be analyzed in the subgroup of patients over 75 years of age.

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s), other**

BIFAP Spain

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**Data sources (types)**

Disease registry

Electronic healthcare records (EHR)

Other

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**Data sources (types), other**

Exposure registry, Case-control surveillance database

## Use of a Common Data Model (CDM)

**CDM mapping**

No

# Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

# Data characterisation

**Data characterisation conducted**

No