

# Comparing the Estimated Risk of Hip Fracture Among Subjects Exposed to Tramadol as Compared to Subjects Exposed to Codeine (Tramadol vs Codeine)

**First published:** 27/06/2020

**Last updated:** 30/01/2025

Study

Finalised

## Administrative details

### EU PAS number

EUPAS36038

### Study ID

48348

### DARWIN EU® study

No

### Study countries

☐ United States

## Study description

Hip fractures greatly impact an individual's quality of life and carry a high risk of death within 1 year. Tramadol is a commonly used weak opioid for treatment of pain. A recent study by Wei et al. found that risk for hip fractures was higher for new users of tramadol than for new users of codeine or NSAIDs. We were concerned of that study's design choices because of several limitations such as: A less-than-optimal propensity score adjustment strategy, the absence of negative controls, the failure to address possible differences in the initial doses of tramadol versus codeine, and the fact that the study was done in only one data source limited to one countries data. We propose to do a study to assess hip fracture incidence among users of tramadol versus codeine that will reassess the relationship and address the Wei et al. study limitations. Wei, J., et al., Association of Tramadol Use With Risk of Hip Fracture. J Bone Miner Res, 2020.

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## Study status

Finalised

## Research institutions and networks

### Institutions

**Johnson & Johnson**

**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**

Erica Voss

Primary lead investigator

## Study timelines

**Date when funding contract was signed**

Planned: 19/02/2020

Actual: 19/02/2020

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**Study start date**

Planned: 19/02/2020

Actual: 19/02/2020

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**Data analysis start date**

Planned: 19/02/2020

Actual: 19/02/2020

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**Date of final study report**

Planned: 24/09/2021

Actual: 09/07/2022

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Janssen Research & Development, LLC.

## Study protocol

[Protocol - Tramadol vs Codeine and Risk of Hip Fracture.pdf](#)(1.45 MB)

[Protocol - Tramadol vs Codeine and Risk of Hip Fracture - Admendment.pdf](#)  
(633.46 KB)

## 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 topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**Main study objective:**

Does exposure to tramadol have a different risk of experiencing hip fracture within 1 year, relative to codeine?

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Retrospective, observational, comparative

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**

CODEINE

TRAMADOL

## Population studied

## Short description of the study population

The study used two variants of the target (tramadol) and comparator (codeine) cohorts among 50-89-year-olds with 365 days of continuous observable time prior to the index date. The first cohort variants (T1, C1) excluded subjects who had been exposed to tramadol, codeine, or other opioids within 365 days prior to the index date, hip fracture, cancer, or opioid abuse diagnoses. The second cohort variants (T2, C2) aimed to make the target and comparator cohorts more comparable by excluding subjects diagnosed with cough or cold within 30 days of initial exposure to the opioids of interest and those prescribed cold or cough medications, antibiotics, or antihistamines within 30 days.

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## Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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## Special population of interest

Frail population

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## Estimated number of subjects

1000000

# Study design details

## Outcomes

Hip fracture

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## Data analysis plan

This study will follow a retrospective, observational, comparative cohort design . The target cohort is new users of tramadol, the comparator cohort are new users of codeine, and the outcome hip fracture. A Cox proportional hazards regression model will be used to model the time to the first outcome occurrence for the target group relative to the comparator group while accounting for the propensity score (PS) matching. Estimates of risk will be generated as the empirically calibrated hazard ratios (HR), 95% confidence intervals (CI), and p-values. This will be done across four observational datasets.

## Documents

### Study publications

[Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, Van Staa T, Smeeth L...](#)

[Voss EA, Makadia R, Matcho A, Ma Q, Knoll C, Schuemie M, DeFalco FJ, Londhe A, ...](#)

[Voss EA, Ma Q, Ryan PB. The impact of standardizing the definition of visits on...](#)

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## Data management

## Data sources

### Data source(s)

Clinical Practice Research Datalink

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### Data sources (types)

[Electronic healthcare records \(EHR\)](#)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

### Check conformance

Unknown

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### Check completeness

Unknown

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### Check stability

Unknown

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### Check logical consistency

Unknown

## Data characterisation

### Data characterisation conducted

No