Risk of suicide attempt and suicide associated with benzodiazepine: a nationwide case crossover study (R.SUB)

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Study Finalised

Administrative details

EU PAS number

EUPAS48070

Study ID

48101

DARWIN EU® study

No

Study countries

☐ France

Study description

While benzodiazepines are commonly prescribed in patients with suicidal ideation, their impact on the risk of suicidal behaviours is unknown. Previous studies that found a positive association between benzodiazepine exposure and suicidal behaviours were confounded by indication bias. The association between benzodiazepines and suicidal behaviours has to be clarified to inform evidence-based practice guidelines for suicidal risk management. The main objective of the present study is to estimate the risk of suicide attempt and suicide associated with benzodiazepines. This is a case crossover study (CCO) in a national healthcare claims and hospitalisations databases including patients ≥16y, with hospitalised suicide attempt or suicide between 2013 and 2016, and at least one benzodiazepine dispensing within the 120 days before their act (i.e., the observation period). Individuals are separated according to the identification of psychiatric history over the year preceding the observation period. For each patient, frequency of benzodiazepine dispensing is compared between a risk period (days -30 to -1 before the event) and two matched reference periods (days -120 to -91, and -90 to -61). Self-controlled CCO analyses are adjusted for psychotropic drugs use within the observation period. A CCO considering a negative control explores residual indication bias, and a case-case-time-control analysis addresses time-trend bias.

Study status

Finalised

Research institutions and networks

Institutions

Academic Center for Pharmacoepidemiology (DRUGS-SAFEr)

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Institution

Contact details

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Study contact

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Primary lead investigator

Antoine Pariente

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 07/11/2019

Study start date

Actual: 05/05/2021

Date of final study report

Actual: 10/06/2022

Sources of funding

- Other

More details on funding

ANSM

Study protocol

R.SUB_Protocole_V1.8_20220225.pdf(792.3 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

This study aimed at estimating the risk of suicide attempt and suicide death associated with recent exposure to benzodiazepines in patients with or without recent psychiatric history using methods minimizing confounding factors.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case-crossover

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N05BA) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CD) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CF) Benzodiazepine related drugs

Benzodiazepine related drugs

Medical condition to be studied

Suicide attempt

Completed suicide

Population studied

Short description of the study population

Patients ≥16 years , with hospitalised suicide attempt or suicide between 2013 and 2016, and at least one benzodiazepine dispensing within the 120 days before their act.

Age groups

Adults (18 to < 46 years)

Estimated number of subjects

70000

Study design details

Outcomes

Suicide attempts as hospitalisation with hospital discharge codes for intentional self-harm. Suicide deaths identified through the causes-of-death registry as those with intentional self-harm codes as well.

Data analysis plan

The suicidal outcomes were hospitalised suicide attempts and suicide, identified through the hospital discharge and causes-of-death registry, using ICD-10 codes X60-X84. Patients were considered exposed to benzodiazepines within one of the studied periods of interest (risk/reference) if they have been reimbursed for at least one dispensing of a benzodiazepine during this period. Conditional logistic regression models were used to estimate the crude and adjusted odds ratios (OR) of suicidal behaviours associated with benzodiazepine over the risk period compared with the reference periods. Models were adjusted for time-varying confounders (other psychotropics). Sensitivity analyses concerned: varying lengths of risk and reference periods, performing another CCO analysis using cyamemazine as a negative control with similar risk of indication bias, performing a case-case-time-control model to examine whether the main CCO analysis was confounded by a time trend in benzodiazepine use.

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

SNDS France

Data sources (types)

Administrative healthcare records (e.g., claims)

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