

# Association between anxiolytic or hypnotic drugs and total mortality

**First published:** 05/04/2013

**Last updated:** 23/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS3772

---

### Study ID

20236

---

### DARWIN EU® study

No

---

### Study countries

 France

 United Kingdom

---

### Study description

Benzodiazepines and related drugs are indicated either for the short-term treatment of moderate or severe anxiety or insomnia. They could be involved in

a wide range of fatal and non-fatal outcomes. However, the ways by which these drugs can lead to an increased mortality are not entirely elucidated. This study intends to investigate the impact of benzodiazepine and related exposure on all cause and specific mortality among cohorts obtained from a representative sample of French beneficiaries of the national health insurance scheme (EGB) and through a large healthcare database (CPRD) in the United Kingdom. Patients > 18 and exposed to at least one benzodiazepine derivative or related substance will be matched to one to 10 unexposed controls, and followed up from their inclusion to either death or 90 days following the last benzodiazepine exposure. All cause and cause specific mortality will be investigated, together with patients' sociodemographics, medicines use, medical history, and life-style (alcohol, smoking, for CPRD exclusively). Time to death will be analysed using an extended Cox regression model with time-dependent covariates

---

## Study status

Finalised

## Research institutions and networks

### Institutions

Pharmacologie En Population cohorteS biobanques (PEPSS), Hopitaux de Toulouse

 France

**First published:** 31/03/2022

**Last updated:** 01/07/2024

Institution

Educational Institution

Hospital/Clinic/Other health care facility

ENCePP partner

## Contact details

### Study institution contact

Maryse Lapeyre-Mestre maryse.lapeyre-mestre@univ-tlse3.fr

Study contact

[maryse.lapeyre-mestre@univ-tlse3.fr](mailto:maryse.lapeyre-mestre@univ-tlse3.fr)

### Primary lead investigator

Maryse Lapeyre-Mestre

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 17/09/2012

Actual: 17/09/2012

---

### Study start date

Planned: 17/04/2013

Actual: 29/04/2013

---

### Date of interim report, if expected

Planned: 17/07/2013

Actual: 23/08/2013

---

### **Date of final study report**

Planned: 17/09/2013

Actual: 07/10/2013

## Sources of funding

- EMA

## Study protocol

[STUDY\\_PROTOCOL\\_2013\\_0404.pdf](#) (1.14 MB)

## Regulatory

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

Yes

---

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

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

---

**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:**

The aim of this project will be to investigate mortality associated with benzodiazepine derivatives or related substances exposure in France and in the UK.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(M03BX07) tetrazepam

tetrazepam

(N03AE01) clonazepam

clonazepam

(N05BA) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CD) Benzodiazepine derivatives

Benzodiazepine derivatives

(N05CF) Benzodiazepine related drugs

Benzodiazepine related drugs

## Population studied

### Short description of the study population

The French and the UK adult population, including both genders.

Patients aged 18 and more, patients with First Registration Date or Current Registration Date > 12 months, acceptable Patient Flag (patients records meeting sufficient quality standard for research) (for CPRD), patients whose practice consented for linkage scheme (ONS mortality data available) (for CPRD) were included.

---

### 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)
- 

### Estimated number of subjects

120000

## Study design details

## Outcomes

All-cause mortality, Cause-specific mortality

---

## Data analysis plan

The role of potential confounding or explanatory variables will be taken into account by the extended Cox regression model. A univariate analysis will be first performed to select the variables with a p value < 0.2, followed by a multivariate approach using the Cox proportional hazard regression model with time dependent covariates, with stratification on the matched pairs. Continuous variables will be tested for linearity. Relevant interactions between covariates will be checked. Proportional hazards assumption will be tested for all covariates. The estimation of the crude and adjusted Hazard Ratio and their 95% confidence interval will be provided.

## Documents

### Study results

[BZD mortality France UK.pdf](#) (1.18 MB)

[Summary Deliverable 3a\\_2013\\_0822.pdf](#) (139.06 KB)

---

### Study publications

[Palmaro A, Dupouy J, Lapeyre-Mestre M. Benzodiazepines and risk of death: Resul...](#)

---

## 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.

This study has been awarded the ENCePP seal

### **Conflicts of interest of investigators**

[Declaration of Interests\\_completed\\_2013\\_0226.pdf](#) (81.08 KB)

---

### **Composition of steering group and observers**

[EUPAS3772-3777.pdf](#) (300.02 KB)

---

### **Signed code of conduct**

[2013-0015\\_DoC ENCePP CoC\\_SDPP\\_3772.pdf](#) (31.06 KB)

---

### **Signed code of conduct checklist**

[2013-0015\\_ENCePP Checklist CoC\\_SDPP\\_3772.pdf](#) (376.56 KB)

---

### **Signed checklist for study protocols**

[2013-0015\\_ENCePP Checklist Study Protocol\\_SDPP\\_3772.pdf](#) (165.38 KB)

---

## Data sources

### **Data source(s)**

Clinical Practice Research Datalink

---

### **Data source(s), other**

CPRD

---

### **Data sources (types)**

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

## 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**

Unknown