Use of antidepressants and risk of hip/femur fracture. A methodological comparison across data sources and epidemiological design

First published: 06/09/2012
Last updated: 02/07/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/28309

EU PAS number
EUPAS2382

Study ID
28309

DARWIN EU® study
No

Study countries
Denmark
Germany
Netherlands
Spain
United Kingdom

Study description
The studies described in this protocol are all performed within the framework of PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium) Work Package 2 and Working Group 1. The primary aim of these studies is to develop, test and disseminate methodological standards for the design, conduct and

analysis of Pharmacoepidemiological (PE) studies applicable to different safety issues and using different data sources. To achieve this, results from PE studies on 5 key Drug / adverse events (D-AEs) pairs performed in different databases will be evaluated. The use of antidepressants associated with the risk of hip/femur fracture is one of the key D-Ae pair of interest. Therefore, emphasis will be on the methodological aspects of the studies in this protocol and not on the clinical consequences of studying the association under investigation.

Study status
Finalised

Research institution and networks

Institutions

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands
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23/05/2024

Institution
Educational Institution
ENCePP partner

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) Spain, European Medicines Agency (EMA) United Kingdom, Lægemiddelstyrelsen (Danish Medicines Agency) (DKMA) Denmark, Ludwig-Maximilians-Universität-München (LMU Muenchen) Germany, MerckSerono Switzerland

Networks

PROTECT

Belgium
Denmark
France
Germany
Italy
Netherlands
Poland
Spain
Sweden
Switzerland
United Kingdom
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Network
ENCePP partner

Contact details

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Primary lead investigator
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Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
19/08/2009
Actual:
19/08/2009

Study start date
Planned:
03/10/2011
Actual:
03/10/2011

Date of final study report

Planned:
01/09/2014
Actual:
01/03/2016

Sources of funding

- EU institutional research programme
- Pharmaceutical company and other private sector

More details on funding

Amgen, AstraZeneca, Genzyme, GlaxoSmithKline, MerckSerono, Novartis, Roche, Pfizer, Innovative Medicines Initiative (IMI)

Study protocol

PROTECT WP2_ Final Protocol_Antidep_HIP_14Nov2011_Amend1 30May2012.pdf(1.15 MB)

PROTECTWP2_FinalProtocol_Antidep_HIP_14nov2011_Amend5_220114.pdf(1.12 MB)

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:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness
Disease epidemiology
Other

If 'other', further details on the scope of the study
Analysis of discrepancies in results between different databases

Data collection methods:
Secondary data collection

Main study objective:
To assess the association between the use of antidepressants and the risk of hip/femur fracture with different study designs across different primary care databases and to compare the results between databases, across designs to evaluate the impact of design/database/population differences on the outcome of the studied association.

Study Design

Non-interventional study design
Case-control
Cohort
Other

Non-interventional study design, other
Case-crossover, Descriptive study= description of exposure and/or outcome in the whole database during a defined period of time

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(N06AA) Non-selective monoamine reuptake inhibitors
(N06AB) Selective serotonin reuptake inhibitors

Medical condition to be studied
Hip fracture
Femur fracture

Population studied

Short description of the study population
All patients included in the period of valid data collection. The study period will be defined from January 1, 2001 to December 31, 2009.

Age groups
Preterm newborn infants (0 – 27 days)
Term newborn infants (0 – 27 days)
Infants and toddlers (28 days – 23 months)
Children (2 to < 12 years)
Adolescents (12 to < 18 years)
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
55700000

Study design details

Data analysis plan
Retrospective cohort: incidence rates (IR) of hip/femur fractures (outcome) will be calculated in current, recent & past users. Past use will be the reference category. Poisson regression (regr) will be used to estimate age & gender adjusted IRR. Time-dependent Cox proportional hazards models will also be used to calculate HR and 95% CIs. Nested case control:Conditional logistic regr analysis will be used to estimate the risk of the outcome associated with the current use of AD as compared to past use. The risks will be calculated in terms of odds ratios (OR) with corresponding 95% CI. case-crossover For each case, the cumulative exposure will be assessed in the 6 months before the index date (at-risk period). For each case up to 4 control moments will be defined at 6 months intervals starting immediately prior to the at-risk period. Cumulative exposure will also be assessed in these 'control' person moments.Conditional logistic regression analysis will be done

Documents

Study publications
The results of this project have been published in Pharmacoepidemiology & Drug …

Data management

Signed checklist for study protocols
ENCePPChecklistforStudyProtocols_H Gardarsdottir signed.pdf(264.77 KB)

Data sources

Data source(s)
THIN® (The Health Improvement Network®)

Data sources (types)
Administrative data (e.g. claims)
Drug dispensing/prescription data
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