Opioid drug utilization and comparative safety: a population-based cohort study

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Study Planned

Administrative details

EU PAS number

EUPAS36180

Study ID

43452

DARWIN EU® study

No

Study countries

Spain

Study description

This study aims to: 1.to describe the drug utilization (socio-demographic, clinical features, type, dosage, indication at the time of opioid therapy initiation) of the different opioids as well as to study the persistence of these drugs among

subjects aged ≥ 18 years old in Catalonia, Spain, 2. to assess and compare the risk of pre-specified adverse events first between incident users of opioids and then compared to non-opioids pain-killers, 3. to study the association between long-term use of opioids compared to paracetamol. Methods: population-based cohort study (www.SIDIAP.org). Inclusion criteria: all new users of study drugs (no use in previous year) between 2007-2016, ≥18 years old and with ≥1 year of valid data. Follow-up: (latest of) start of the study period, 1-year of valid data until (earliest of) end of enrolment, discontinuation, date of last capturing data or event of interest. Outcomes: 1. opioids and non-opioid (NSAIDs, Cox-2 inhibitors, paracetamol, metamizole, aspirin) exposure. Variables: Socio-demographic, BMI, Charlson comorbidity index (CCI), frailty, cognitive and quality of life indexes, opioid use (type/dosage), prescriber and indication, 2. cardiovascular events (myocardial ischemia, stroke, heart failure and arrhythmia), fractures, falls, sleep and gastro-intestinal disorders, opioid dependence/abuse, all-cause mortality. Confounders: socio-demographic and socioeconomic status (MEDEA), medical conditions, CCI, surgeries and drugs (hypnotics, benzodiazepines, SSRI, anticonvulsant), number of different ATCs prescribed, GP visits, hospital admissions, falls and traffic accidents. Statistics: Kaplan Meier plots for drug persistence. Propensity score analysis and Cox regression model to estimate the relative risk according to drug use.

Study status

Planned

Research institutions and networks

Institutions

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

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Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Carlen Reyes

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 28/06/2018

Study start date
Planned: 01/09/2020

Date of final study report
Planned: 31/03/2021

Sources of funding

- Other

More details on funding

IDIAP jordi Gol foundation

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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Main study objective:

To characterize the population that consume opioids and to compare the incidence of pre-defined adverse events between incident users of opioids and compared to non-opioid pain killers in subjects of at least 18 years old in Catalonia (Spain).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N02AA01) morphine

morphine

(N02AX02) tramadol

tramadol

(N01AH01) fentanyl

fentanyl

(R05DA04) codeine

codeine

(A01AD05) acetylsalicylic acid

acetylsalicylic acid

(N02BE01) paracetamol

paracetamol

(N02BB02) metamizole sodium

metamizole sodium

(M01AE01) ibuprofen

ibuprofen

(M01AC01) piroxicam

piroxicam

Medical condition to be studied

Cardiovascular event prophylaxis

Spinal fracture

Femoral neck fracture

Sleep apnoea syndrome

Constipation

Drug dependence

Drug abuse

Death

Additional medical condition(s)

Delirium, wrist and humerus fracture. co-morbid conditions and prescriptions that act as confounders

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)

Estimated number of subjects

1.186.887

Study design details

Data analysis plan

Drug Utilisation: Descriptive analysis for categorical and continuous variables. Kaplan-Meier for opioid treatment persistence.Drug Safety: Unadjusted IR (and 95%CIs) of the events of interest stratified by drug exposure cohort will be calculated. We will use a propensity score-matched survival analysis (PMS) to compare time to event between users of opioids, opioids vs anti-inflammatory drug users and between opioids vs non-anti-inflammatory drug users. PMS will be calculated by fitting multivariable logistic regression models (including confounders). On PMS, drug users will be matched to active comparison drug users, using a caliper width of 0.2 SD. Both “intention to treatment” and “on treatment” analyses will be adopted when estimate association between drugs. We will account for competing risk of death. Adjusted multivariable models will be done if there is remaining imbalance after PMS. Cox regression models will be used to estimate relative risk according to drug 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 sources (types)

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

No