A RETROSPECTIVE, REAL-LIFE EVALUATION OF THE CARDIOVASCULAR DISEASE RISK ASSOCIATED WITH EXPOSURE TO PHARMACOLOGICAL SMOKING CESSATION INTERVENTIONS IN A REPRESENTATIVE UK PRIMARY CARE PATIENT POPULATION

First published: 02/07/2013
Last updated: 02/07/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/28219

EU PAS number
EUPAS4238

Study ID
28219

DARWIN EU® study
No

Study countries
United Kingdom

Study description
Preliminary study data have indicated a possible increased cardiovascular disease (CVD) risk in patients exposed to nicotine replacement therapy (NRT) compared with controls (i.e. non-NRT exposed patients) of a magnitude that could not reasonably be accounted for by

differences in the cardiovascular (CV) risk profile of the two patient groups. Further in-depth studies in this area are warranted.This retrospective study will compare the CVD event risk in a group of smokers undertaking unaided smoking cessation attempts with the event rate in a group of smokers attempting smoking cessation assisted by pharmacological interventions (any of NRT, bupropion or varenicline) in a representative UK primary care population. There will be a baseline and outcome period designed to assess CVD risk. The baseline period will be a minimum of one year prior to an index date (IPD) – the date of first recorded smoking cessation intervention, either pharmacological or non-pharmacological – for confounder definition. Of primary interest will be the CV event rate over a 4-week outcome period (secondary outcomes periods of 12, 26 and 56 weeks may also be investigated). Also of interest will be all-cause mortality and survival analysis.

Study status
Finalised

Research institution and networks

Institutions

Research in Real Life
First published: 01/02/2024
Last updated 01/02/2024
Institution

Networks

Respiratory Effectiveness Group (REG)
Belgium
Denmark
France
Germany
Greece
Hungary
Italy
Netherlands
Spain
Sweden
United Kingdom
First published: 07/07/2021
Last updated 04/06/2024

Network ENCePP partner

Contact details

Study institution contact
David Price
Study contact

dprice@opri.sg
Primary lead investigator
David Price
Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
30/11/2009
Actual:
18/12/2009

Study start date
Planned:
01/01/2000
Actual:
31/12/2009

Date of final study report
Planned:
01/08/2013
Actual:
06/02/2015

Sources of funding

- Other

More details on funding

MEDICAL RESEARCH COUNCIL, Research in Real Life Ltd, Respiratory Effectiveness Group

Study protocol

ISAC application_study protocol _final_update_26_07_11_clean.pdf(241.52 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:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

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

Data collection methods:
Secondary data collection

Main study objective:
To compare the CVD event rate in smokers undertaking unaided smoking cessation attempts (controls) with the event rate in those attempting cessation supported by nicotine replacement therapy (NRT) (any of: nasal spray, transdermal patches, inhaler or gum and tablets) or other pharmacological smoking cessation aids (buproion or varenecline) in a

representative primary care population

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name
NICOTINE
BUPROPION
VARENICLINE

Medical condition to be studied
Cardiovascular disorder

Population studied

Short description of the study population
Exposure group: Smokers with no past history of cardiovascular disease (CVD) and no recorded smoking cessation attempts using pharmacological aids in the prior year, whose first recorded smoking cessation intervention was a cessation attempt assisted by either NRT (using any of, or a combination of products) or another pharmacological smoking cessation intervention (e.g. bupropion, varenicline) at the index date. Patients must meet the following criteria:
• Aged: 18–75 years
• Have at least one year of up-to-standard (UTS) baseline data as defined by GPRD (prior to the IPD) and at least 4 weeks' of UTS outcome data (following the IPD) or UTS data up to the time of death if death occurred within the outcome period

Non-exposure group: smokers with no past history of CVD and no recorded smoking cessation attempts using pharmacological aids in the prior year, whose first recorded smoking cessation intervention involved receipt of smoking cessation advice that resulted in a quit attempt unaided by pharmacological therapies at the IPD and during the outcome periods. Patients must meet the following criteria:
tients must also meet the following inclusion criteria:
• Aged: 18–75 years.
• Current smoker throughout the prior year (any quantity of cigarettes)
• Received smoking cessation advice at IPD
• Have at least one year of UTS baseline data as defined by GPRD (prior to the IPD) and at least 4 weeks' of UTS outcome data (following the IPD), or UTS data up to the time of

death if death occurred within the follow-up period(s)

Age groups
Adults (18 to < 46 years)
Adults (46 to < 65 years)
Adults (65 to < 75 years)

Estimated number of subjects
61050

Study design details

Outcomes
The incident of the following CV events over a 4-week outcome period: CHD diagnosis and No of days from IPD, CHD-related death and No Of days from IPD, CerebroVD diagnosis and No Of Days from IPD, CerebroVD death and No of Days from IPD, Recorded GP consultations or hospital attendances for CHD or CebebroVD, including admission, A&E attendance, out-of-hours or Out-Patient Department attendance. The incident of the following CV events over a 52-week outcome period: CHD diagnosis and No of days from IPD, CHD-related death and No Of days from IPD, CerebroVD diagnosis and No Of Days from IPD, CerebroVD death and No of Days from IPD, Recorded GP consultations or hospital attendances for CHD or CebebroVD, including admission, A&E attendance, out-of-hours or Out-Patient Department attendance.

Data analysis plan
All times until diagnosis (CHD or CerebroVD) and survival times (until death due to CHD or CerebroVD) will be analysed using Cox's Proportional Hazards Models, adjusting for baseline confounders. Censored times will be 4/52 weeks (primary/secondary outcomes). Total number of GP consultations and hospital attendances for CHD or CerebroDisease during the outcome periods will be compared between treatment groups using a Poisson regression model (conditional Poisson regression model for matched analyses) to obtain estimates of consultation / hospitalisation rates relative to the control group. The model will be adjusted for over-dispersion using robust standard errors and adjustments will be made for potential baseline confounders. For all models, variables that are strongly predictive of the outcome or that are significantly different (or show trend to significance, ie. $p<0.01$) between the treatment groups over baseline will be treated as potential confounders.

Documents

Study publications
Dollerup, J., Vestbo, J., Murray-Thomas, T., Kaplan, A., Martin, R.J., Pizzichi…

Data management

Data sources

Data source(s)
Clinical Practice Research Datalink

Data source(s), other
General Practice Research Database (GPRD)

Data sources (types)
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