Investigating biases in observational studies of inhaled corticosteroids and the risk of COVID-19-related outcomes

First published: 12/09/2022

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Study Ongoing

Administrative details

PURI

https://redirect.ema.europa.eu/resource/47886

EU PAS number

EUPAS47885

Study ID

47886

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

Inhaled corticosteroids (ICS) are anti-inflammatory drugs widely used as maintenance medications in asthma and chronic obstructive pulmonary disease (COPD). At the beginning of the COVID-19 pandemic, there was interest in ICS as potential disease-modifying drugs in COVID-19. Several observational studies investigated the effects of ICS on COVID-19 outcomes but found inconsistent results that may be affected by biases. The aim of this study is to investigate the effects of ICS at different stages of the COVID-19 disease pathway among patients with asthma or COPD, and apply methods of quantitative bias analysis (QBA) to these effect estimates to account for potential biases arising in these estimates of association. This study will use cohorts of patients with asthma and COPD, respectively, to investigate the association between ICS use compared to use of a non-ICS active comparator and SARS-CoV-2 infection, COVID-19 hospitalisation, and COVID-19 death. All analyses will be conducted separately for an asthma and COPD cohort and for the first and second wave of COVID-19. CPRD data will be linked to HES data to determine COVID-19 related hospitalisations, and to the ONS death registry to determine COVID-19 related deaths. The association between ICS prescription and each outcome will be estimated using a Cox regression model to calculate hazard ratios and 95% confidence intervals, with confounding adjustment using multivariable regression and propensity scores. QBA will be used to account for potential sources of bias in these estimates of association, including exposure and outcome misclassification, residual confounding and selection bias. This project will allow an evaluation of whether and how more widespread use of QBA may have allowed researchers to make better inferences using observational data about the role of ICS in COVID-19. Outputs from this project will provide recommendations and tools to help researchers implement QBA in pharmacoepidemiologic studies.

Study status

Ongoing

Research institutions and networks

Institutions

Electronic Health Records (EHR) Research Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010

Last updated: 30/10/2024

Institution | Educational Institution | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 19/04/2021

Study start date
Actual: 01/03/2017

Data analysis start date
Planned: 02/01/2023

Date of final study report
Planned: 31/10/2024

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GlaxoSmithKline

Study protocol

ICS_COVID Encepp.pdf(210.15 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:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Effectiveness study (incl. comparative)

Main study objective:

1. To describe prescription patterns of ICS among patients with respiratory diseases before and during the COVID-19 pandemic. 2. To investigate the association between prevalent ICS use and COVID-19 related outcomes among patients with respiratory diseases. 3. To develop approaches and apply methods of QBA to account for potential biases arising in these estimates of association.

Study Design

Non-interventional study design

Cohort

Cross-sectional

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(R03AK) Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics

Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics

(R03BA) Glucocorticoids

Glucocorticoids

(R03BA01) beclometasone

beclometasone

(R03BA02) budesonide

budesonide

(R03BA05) fluticasone

fluticasone

(R03BA07) mometasone

mometasone

(R03BA08) ciclesonide

ciclesonide

(R03BA09) fluticasone furoate

fluticasone furoate

Medical condition to be studied

Asthma

Chronic obstructive pulmonary disease

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

1000000

Study design details

Outcomes

1. SARS-CoV-2 infection (positive test for SARS-CoV-2 in the primary care record sourced from the Second Generation Surveillance System). 2. hospitalisation with COVID-19 (admission to hospital with an ICD-10 code for COVID-19, ascertained using HES data). 3. death with COVID-19 (ICD-10 code for COVID-19 listed as an underlying or contributing cause of death in the ONS death registry).

Data analysis plan

We will conduct descriptive analyses to assess characteristics of the patients in each cohort, stratified by exposure group at baseline. Time to each outcome will be presented using Kaplan-Meier plots using time in study as the time scale. Propensity scores will be generated using logistic regression to estimate likelihood of ICS prescription based on baseline characteristics. All pre-specified covariates will be included in the logistic regression. The association between ICS prescription and each outcome will be estimated using a Cox regression model to calculate hazard ratios and 95% CIs, using time in study as the time scale. Univariable models, models adjusted for age and sex, and propensity score weighted models will be presented. If a time-updated exposure definition is used, we will account for potentially informative censoring using inverse-probability of censoring weights. Propensity scores will also be time-updated confounding.

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

Hospital Episode Statistics

Data source(s), other

ONS death registry United Kingdom, Index of multiple deprivation United Kingdom

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Data sources (types)

Electronic healthcare records (EHR)

Other

Data sources (types), other

ONS: Population registry IMD: official measure of relative deprivation for small areas in England

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