Disease trajectory and treatment escalation in severe asthma: A retrospective analysis of data from the Optimum Patient Care Research Database (OPCRD)

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Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000292

EU PAS number

EUPAS1000000292

Study ID

1000000292

DARWIN EU® study

No

Study countries

☐ United Kingdom

Study description

Asthma effects over 300 million globally with 5-10% estimated to have severe disease. Many patients achieve disease control on inhaled medications and are managed within primary care, however, a small number prove challenging to treat and are often exposed to high dose oral corticosteroid (OCS) therapies which can lead to significant co-morbidities developing. Current asthma guidelines advocate a stepwise approach to increasing treatment based on symptoms and exacerbations; however, treatment is often escalated despite symptoms not being related to asthma.

At present, it is unclear if extra-pulmonary factors directly influence treatment escalation in severe asthma or are simply a consequence of treatment i.e., reverse causation. Further work is needed to examine the temporal relationship between extra-pulmonary comorbidities and treatment escalation in patients with severe disease.

This is an observational, retrospective, UK-wide analysis comprising of two nested case-control studies set within with the OPCRD.

The specific aims of this study are to:
1) To explore factors associated with treatment escalation from mild to moderate treatment to high dose treatments (Global initiative for asthma [GINA]: step 2/3 to step 4/5).
2) To investigate factors associated with treatment escalation in patients with severe asthma (GINA step 4 to GINA step 5).
3) To assess the temporal relationship between key extra-pulmonary factors and treatment escalation.

4) To explore the relationship between blood eosinophil count and treatment escalation.

Study status

Planned

Research institutions and networks

Institutions

Queen's University Belfast

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Institution | Educational Institution

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Liam Heaney

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 31/05/2023

Actual: 31/05/2023

Study start date
Planned: 01/08/2024

Data analysis start date
Planned: 07/08/2024

Date of final study report
Planned: 30/09/2024

Sources of funding

- Other

More details on funding

Health data research UK (HDR UK)

Study protocol

OPCRD protocol submission encepp.pdf(331.89 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

Study type:

Not applicable

Scope of the study:

Other

Validation of study variables (exposure outcome covariate)

If ‘other’, further details on the scope of the study

To assess the relationship between treatment escalation in asthma and different co-variates

Data collection methods:

Primary data collection

Study design:

This is an observational, retrospective, UK-wide analysis comprising of two nested case-control studies set within with the OPCRD.

Main study objective:

1) To explore factors associated with treatment escalation from mild to moderate treatment to high dose treatments (Global initiative for asthma [GINA]: step 2/3 to step 4/5).
2) To investigate factors associated with treatment escalation in patients with severe asthma (GINA step 4 to GINA step 5).
3) To assess the temporal relationship between key extra-pulmonary factors and treatment escalation.
4) To explore the relationship between blood eosinophil count and treatment escalation.

Study drug and medical condition

Medical condition to be studied

Asthma

Obesity

Depression

Anxiety

Additional medical condition(s)

Asthma exacerbations

Population studied

Age groups

Adult and elderly population (≥18 years)

Special population of interest

Other

Special population of interest, other

Patients with severe asthma

Estimated number of subjects

3000000

Study design details

Setting

This is an observational, retrospective, UK-wide analysis comprising of two nested case-control studies set within with the OPCRD.

Study 1: In the first study, adult (≥18 years) patients who transition from their first diagnosis of mild-persistent/moderate asthma (GINA: step 2/3) to difficult-to-treat asthma (GINA: step 4/5) will be compared with a matched patient cohort remaining on step 2/3 (1).

Study 2: In the second study, adult patients with severe asthma who transition from their first diagnosis of step 4 asthma to their first diagnosis of step 5 asthma will be compared with a matched patient cohort remaining on step 4.

Interventions

This is an observational case-control study. No intervention is being assessed.

Comparators

This nested case-control control compares matches cases controls by age (+/- 5 years), time of study entry, GINA step at study entry, general practice, and length of follow-up (minimum 5 years).

Outcomes

For all analyses, the primary outcome will be treatment escalation, either from Step 2/3 to step 4/5, or from step 4 to Step 5. A wide variety of covariates, including sociodemographic factors, comorbidities and asthma variables will be considered in relation to treatment escalation.

Data analysis plan

Demographics, comorbidities and asthma covariates will be analysed descriptively with comparisons made between cases and controls for each analysis. Univariate analyses will be conducted using t-tests, chi-square tests, Fisher’s exact test and Mann-Whitney U tests as appropriate. Conditional logistic regression will be used to estimate the association between covariates and treatment escalation on the odds ratio scale. The matched design will implicitly adjust for age-group, GP, time of entry into study (+/- 1 year) and GINA step at study entry, with additional adjustments made for age (years)and exacerbations by including these covariates in the model. If data is missing, associations between covariates and treatment escalation will be re-estimated using multiple imputation for chained equations, a simulation-based method appropriate for handling missing data when it is assumed that such values are missing at random or missing completely at random.

Subgroup analyses: Subgroup analyses will be undertaken to explore potential changes in commonly occurring conditions and asthma co-variates (obesity/depression/anxiety and exacerbations). We will explore the prevalence

of these in the lead up towards the index date. This will be explored by re-running each analysis, restricted to patients whose point of study entry (either Step 2/3 or Step 4) occurred at least twelve-months after the earliest date they could have entered the study. For each year, described as “t”, (t=-4,-3,-2,-1,0) the incidence of certain co-morbidities will be calculated between study entry and t. The probability of each condition, as well as oone or more exacerbation, will be plotted for the year prior to study entry and each year in the five-year period prior to the index date.

Statistical software: Descriptive statistics will be calculated using Stata-16 SE and on the basis of a two-sided estimation, statistical significance was set at 5%.

Summary results

The results are not available for this study yet

Data management

Data sources

Data source(s)

Optimum Patient Care Research Database

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