

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

**First published:** 09/08/2024

**Last updated:** 09/08/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS1000000292

---

### Study ID

1000000292

---

### DARWIN EU® study

No

---

### Study countries

 United Kingdom

---

### Study description

Asthma affects 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

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

Educational Institution

## Contact details

### Study institution contact

Matthew Eastwood [m.eastwood@qub.ac.uk](mailto:m.eastwood@qub.ac.uk)

Study contact

[m.eastwood@qub.ac.uk](mailto:m.eastwood@qub.ac.uk)

### 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 ( $\geq 18$  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 OPCR. D.

Study 1: In the first study, adult ( $\geq 18$  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 ( $\pm 5$  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 one 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

## 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 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