

# Health Care Resource Use and Costs of Severe, Uncontrolled Asthma With High Blood Eosinophil Counts in the UK General Population

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## Abstract

**Rationale:** Although the majority of patients with asthma can be treated effectively with currently available medications, asthma remains uncontrolled despite high-intensity treatment for some patients. Those with high blood eosinophil counts experience more severe exacerbations, a prominent feature of both poorly controlled and severe asthma [Price et al. *Lancet Respir Med*. 2015;3:49–58]. Our objectives were to determine the percentage of patients with severe, uncontrolled eosinophilic asthma (SUEA) and compare associated health care resource use (HRU) and costs with overall means estimated in the UK population of patients with active asthma.

**Methods:** We performed a historical cohort study analyzing de-identified medical record data for 363,558 patients with active asthma ( $\geq 1$  drug prescription), aged  $\geq 5$  years, without concurrent COPD, and with recorded eosinophil count, using a combined data set extracted from the Clinical Practice Research Datalink (CPRD) and the Optimum Patient Care Research Database (OPCRD). SUEA was defined as  $\geq 2$  exacerbations during 1 year (baseline) preceding a high blood eosinophil count ( $\geq 0.3 \times 10^9/L$ ) for patients receiving combined maintenance treatment with long-acting  $\beta_2$ -agonist (LABA) and high-dose inhaled corticosteroids (ICS; cumulative beclomethasone-equivalent dosage  $\geq 800 \mu g/day$ ;  $\geq 400 \mu g/day$  for children 5–12 years) during both the baseline and 1 year of follow up. We compared asthma-related HRU and costs during the follow-up year after the most recent eosinophil count for SUEA patients versus those for the total population with active asthma. Total costs, including hospitalizations, were evaluated for 1,206 patients from CPRD with available hospital episode statistics.

**Results:** In the total study population, mean (SD) age was 49 (21) years; 64% were women, 43% had high eosinophil counts, 7% had  $\geq 2$  exacerbations in the baseline year, and 13% were prescribed high-dose ICS/LABA. SUEA accounted for 0.81% (95% confidence interval: 0.78–0.84%; N=2,940) of the total population. Mean costs for each asthma-related HRU type were 3- to 8-times greater for patients with SUEA compared with those for all patients with active asthma. Total asthma-related costs were 4-times greater.

**Conclusions:** Less than 1% of patients with asthma in the UK population had severe uncontrolled asthma with high blood eosinophil counts while receiving treatment with high-dose ICS/LABA. These patients accounted for substantially greater asthma-related costs during follow up than average patients with asthma. The absolute difference in total costs may be greater in countries with relatively more expensive health care systems than that in the UK [Barnett et al. *J Allergy Clin Immunol*. 2011;145–52].

## Introduction

• Uncontrolled asthma accounts for a disproportionate share of asthma-related health care resource use (HRU) and costs<sup>1</sup>

• Eosinophilic asthma is a common phenotype of severe asthma<sup>2</sup>

• Patients with asthma and high blood eosinophil counts are at heightened risk of asthma attacks<sup>3</sup>

• The biologic agents mepolizumab and reslizumab, which target the interleukin-5 molecule directly to reduce eosinophils, have been demonstrated to reduce asthma attacks and improve symptoms for patients with severe, uncontrolled eosinophilic asthma (SUEA).<sup>4</sup> Benralizumab targets the interleukin-5 receptor  $\alpha$  and induces direct, rapid, and nearly complete depletion of eosinophils and significantly reduces asthma exacerbations and improves control for patients with SUEA.<sup>5,6</sup>

• Patients with recurrent exacerbations and high blood eosinophil counts have the best responses to the above-named agents<sup>4–6</sup>

## Aims

• We aimed to describe the distribution of SUEA in the UK general population and to determine the asthma-related HRU and associated costs for SUEA as compared with those of patients with asthma from the general population

## Methods

### Study design and population

• Anonymized patient data were assessed for 1 year preceding the index date (“baseline year”) and 1 year after the index date (“outcome year”) for the time period from December 6, 1990, to June 23, 2014

- The index date was defined as the date of the most recent blood eosinophil count measurement

• For the analyses, combined data from practices registered with the Optimum Patient Care Research Database (OPCRD; <http://optimumpatientcare.org/opcrd>) and Clinical Practice Research Datalink (CPRD; <http://www.cprd.com/>) were used

- OPCRD and CPRD house anonymized longitudinal medical record data for more than 650 and 500 UK primary care practices, respectively, for patients from throughout the United Kingdom

- The study population consisted of all patients with active asthma ( $\geq 1$  drug prescription), aged  $\geq 5$  years, without concurrent chronic obstructive pulmonary disease, and with recorded eosinophil counts

• **Figure 1** presents the flow chart of the patient selection process

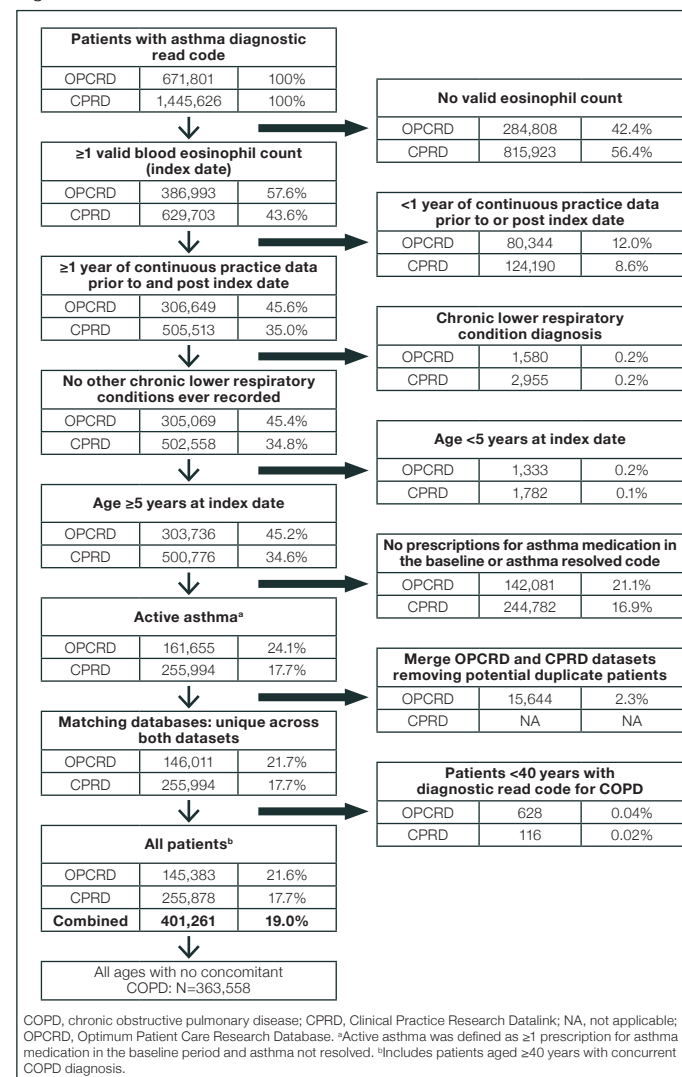
### Data analysis

• Definitions:

- SUEA was defined as having (1) combination maintenance therapy with high-dose inhaled corticosteroids (ICS) and long-acting  $\beta_2$ -agonist (LABA) in both the baseline year and the outcome year (severe asthma), and (2)  $\geq 2$  asthma attacks in the baseline year (uncontrolled asthma), and (3) an elevated blood eosinophil count of  $\geq 0.3 \times 10^9/L$  at the index date (eosinophilic asthma)

- High-dose ICS was defined as a cumulative average beclomethasone dipropionate–equivalent dosage over 1 year of follow up of  $\geq 800 \mu g/day$  for adults and  $\geq 400 \mu g/day$  for children aged 5–12 years. The definition was based on the 2014 British Guideline on the Management of Asthma,<sup>7</sup> and took adherence into account

Figure 1. Patient Flow Chart



• Asthma-related direct costs were determined by using standard unit costs for the United Kingdom National Health Service

• Summary statistics were used to describe the distribution of asthma severity and control, treatment status, high blood eosinophil counts, other asthma determinants, and their combinations in the baseline year before the index date

• Mean numbers of asthma-related HRU events per patient were multiplied by unit costs to provide annual health care costs for individuals

• Cost ratios were estimated by calculating the ratios of the mean costs for the subgroup of patients with SUEA to those for the reference group of all patients with asthma

## Results

• The mean (standard deviation [SD]) age of the total study population was 49 (21) years; the SUEA population was older, with a mean (SD) age of 56 (18) years (**Table 1**)

**Table 1. Demographics and Baseline Clinical Characteristics of the Total Study Population and Patients With SUEA**

Variable	Total study population (N=363,558)	SUEA <sup>a</sup> (N=2,940)
Female sex, n (%)	233,210 (64.1)	1,952 (66.4)
Age at index date, mean (SD)	49.4 (20.6)	55.8 (17.6)
BMI, n (%) <sup>b</sup>		
Normal	106,461 (34.3)	721 (26.9)
Overweight	100,937 (32.4)	828 (30.8)
Obese	103,738 (33.3)	1,135 (42.3)
Smoking status, n (%) <sup>b</sup>		
Current smoker	64,350 (18.0)	530 (18.3)
Ex-smoker	93,359 (26.2)	899 (31.0)
Never smoker	199,299 (55.8)	1,475 (50.8)
Charlson comorbidity index score, n (%)		
0	166,280 (45.7)	669 (22.8)
1–4	170,791 (47.0)	1,941 (66.0)
$\geq 5$	26,487 (7.3)	330 (11.2)
Ever-recorded comorbidity, n (%)		
Nonallergic rhinitis	32,285 (8.9)	422 (14.4)
Chronic rhinitis	35,708 (9.8)	456 (15.5)
Nasal polyps	12,949 (3.6)	376 (12.8)
Gastroesophageal reflux disease	42,154 (11.6)	515 (17.5)
Cardiovascular disease	93,443 (25.7)	1,080 (36.7)

BMI, body mass index; SD, standard deviation; SUEA, severe, uncontrolled eosinophilic asthma. <sup>a</sup>All patients with SUEA included 14 children who were 5–11 years old and 43 adolescents who were 12–17 years old. <sup>b</sup>The percentages for BMI and for smoking status were calculated for patients with available data. Overall, 14% of patients had missing data for BMI, and 2% had missing data for smoking status. The BMI categories, determined from data closest to the index date, were defined as follows: underweight,  $< 18.5 \text{ kg/m}^2$ ; normal weight,  $\geq 18.5 \text{ kg/m}^2$  to  $< 25 \text{ kg/m}^2$ ; overweight,  $\geq 25 \text{ kg/m}^2$  to  $< 30 \text{ kg/m}^2$ ; and obese,  $\geq 30 \text{ kg/m}^2$  for patients  $\geq 18$  years old. For children, BMI was not calculated because accurate information on age in months required to calculate BMI Z-scores was not provided for privacy reasons.

• 64% of the total study population were female, compared with 66% of the SUEA population

• In the total study population, 43% had high eosinophil counts, 7% had  $\geq 2$  exacerbations in the baseline year, 46,687 (13%) received high-dose ICS/LABA in the baseline year and 34,898 (10%) during both baseline and outcome years, and 6,326 (1.7%) received high-dose ICS/LABA during both baseline and outcome years and also experienced  $\geq 2$  attacks during the baseline year (**Table 2**)

• 0.81% (95% confidence interval [CI] 0.78–0.84%) of the total study population met the study definition of SUEA

**Table 2. Clinical Characteristics and Asthma Disease Burden of the Total Study Population and Patients With SUEA**

Variable	Total study population (N=363,558)	SUEA <sup>a</sup> (N=2,940)
BEC, median (IQR)	0.20 (0.11–0.35)	0.40 (0.30–0.60)
BEC $\geq 0.3 \times 10^9/L$ , n (%)	156,136 (42.9)	2,940 (100)
High BEC among females, n (%) <sup>b</sup>	91,865 (39.4)	1,952 (100)
High BEC among males, n (%) <sup>c</sup>	64,271 (49.3)	988 (100)
Prescribed ICS during the baseline year, n (%)	300,920 (82.8)	2,940 (100)
Cumulative ICS dosage [ $\mu g/day$ ], baseline year, median (IQR) <sup>d</sup>	329 (132–658)	1,425 (1,068–1,967)
Cumulative high-dose ICS/LABA, n (%) <sup>d</sup>	46,687 (12.8)	2,940 (100)
Cumulative high-dose ICS/LABA $\times 2$ years, n (%) <sup>d,e</sup>	34,898 (9.6)	2,940 (100)
Maintenance OCS, n (%) <sup>f</sup>	10,522 (2.9)	488 (16.6)
Asthma attacks, mean (SD)	0.31 (0.76)	2.89 (1.32)
0 attacks, n (%)	288,836 (79.4)	0
1 attack, n (%)	50,675 (13.9)	0
2–3 attacks, n (%) <sup>g</sup>	20,793 (5.7)	2,307 (78.5)
$\geq 4$ attacks, n (%) <sup>g</sup>	3,254 (0.9)	633 (21.5)
Cumulative high-dose ICS/LABA and $\geq 2$ attacks, n (%)	8,164 (2.2)	2,940 (100)

BEC, blood eosinophil count; ICS, inhaled corticosteroid; IQR, interquartile range; LABA, long-acting  $\beta_2$ -agonist; OCS, oral corticosteroid; SD, standard deviation; SUEA, severe, uncontrolled eosinophilic asthma. <sup>a</sup>All patients with SUEA included 14 children who were 5–11 years old and 43 adolescent patients 12–17 years old. <sup>b</sup>Percentage based on number of females in the total study population (n=233,210) and SUEA population (n=1,952). <sup>c</sup>Percentage based on total number of males in the total study population (n=130,348) and SUEA population (n=988). <sup>d</sup>Cumulative ICS dosage exposure during the baseline year was calculated as the mean of recorded prescriptions over 365 days. High-dose ICS was defined according to 2014 British Guideline on the Management of Asthma<sup>7</sup> as a cumulative beclomethasone dipropionate–equivalent dosage of  $\geq 800 \mu g/day$  for adults and  $\geq 400 \mu g/day$  for children aged 5–12 years. <sup>e</sup>Study definition of severe asthma, i.e., cumulative high-dose ICS/LABA during both baseline and outcome years. <sup>f</sup>Maintenance OCS at some time during the baseline year. <sup>g</sup>The study definition of uncontrolled asthma was  $\geq 2$  attacks during the baseline year.

• Mean HRU and direct, asthma-related costs for each HRU-related category were 2.5- to 7.6-times greater for the SUEA cohort compared with the total study population (**Table 3**)

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**Table 3. Mean Annual Asthma-related HRU and Costs (2015 Pounds Sterling, £) for Patients With SUEA Compared With Overall Mean Costs for Patients With Active Asthma in the UK General Population**

Asthma-related HRU outcome	Total study population (N=363,558/ 146,485 <sup>a</sup> ) Mean (SD)	SUEA (N=2,940/ 1,206 <sup>a</sup> ) Mean (SD)	HRU and cost ratio (95% CI) <sup>b</sup>
GP consultations <sup>c</sup>			
Number	1.36 (1.57)	2.67 (2.80)	
Costs	£30.8 (49.8)	£77.0 (107.5)	2.5 (2.4–2.6)
Outpatient visits			
Number	0.04 (0.33)	0.30 (0.96)	
Costs	£6.9 (52.2)	£46.7 (149.2)	6.8 (6.0–7.7)
ED attendances			
Number	0.01 (0.11)	0.04 (0.25)	
Costs	£1.6 (18.8)	£6.6 (44.7)	4.1 (3.2–5.3)
Hospitalizations with asthma as primary diagnosis			
Number	0.01 (0.12)	0.05 (0.38)	
Costs	£10.4 (194.7)	£78.7 (660.3)	7.6 (4.7–11.6)
Medication costs	£170.1 (218.2)	£645.4 (285.4)	3.8 (3.7–3.9)
Total costs	£222.0 (337.2)	£861.0 (811.9)	3.9 (3.7–4.1)

CI, confidence interval; GP, general practitioner; ED, emergency department; HRU, health care resource use; SD, standard deviation; SUEA, severe, uncontrolled eosinophilic asthma. <sup>a</sup>The second number of patients in the column headers represents those in the Clinical Practice Research Datalink who had linked Hospital Episode Statistics, used to determine hospitalizations and associated costs, as factored into total costs. The SUEA cohort with HES data included 26 (2.2%) patients  $< 18$  years old. <sup>b</sup>95% CI, based on 1000 bootstrap replicates. <sup>c</sup>GP visits included consultations with primary care physicians and asthma nurses.

## Conclusions

• Less than 1% of patients in a UK general asthma population sample have SUEA

• Individuals who have SUEA despite treatment with high dosages of ICS combined with LABA therapy account for substantially greater asthma-related HRU and associated direct costs than the general population with asthma

• The absolute difference in total costs may be greater in countries with relatively more expensive health care systems than that in the United Kingdom

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