**Supplemental File**

# Health care resource use and costs of severe, uncontrolled eosinophilic asthma in the UK general population

Marjan Kerkhof,[1] Trung N. Tran,[2] Joan B. Soriano,[3] Sarowar Golam,[4] Danny Gibson,[5] Elizabeth V. Hillyer,[1] David B. Price[1,6]

[1]Observational and Pragmatic Research Institute Pte Ltd, Singapore; [2]Medical Evidence and Observational Research, AstraZeneca, Gaithersburg, MD, USA; [3]Instituto de Investigación Hospital Universitario de la Princesa (IISP), Universidad Autónoma de Madrid, Madrid, Spain; [4]Global Payer Evidence and Pricing, AstraZeneca, Gothenburg, Sweden; [5]AstraZeneca UK Ltd, Luton, UK; [6]Academic Primary Care, University of Aberdeen, Aberdeen, UK.

## SUPPLEMENTARY METHODS

The study was performed in compliance with all applicable local and national laws and regulations and in accordance with standards suggested for observational studies.[1] The use of the Clinical Practice Research Datalink (CPRD) dataset was approved by the CPRD Independent Scientific Advisory Committee (ISAC registration number, 15_141). The Optimum Patient Care Research Database (OPCRD) is approved by the Health Research Authority of the UK NHS for clinical research use (REC reference: 15/EM/0150), and the protocol for this study was approved by the Anonymised Data Ethics Protocols and Transparency (ADEPT) committee, the independent scientific advisory committee for the OPCRD (ADEPT registration number, PROTOCOL0515). The study protocol was registered in advance in the European Union electronic Register of Post-Authorisation Studies (EU PAS Register Number EUPAS10229).[2]

The two study data sets were constructed separately using CPRD and OPCRD data in a patient unidentifiable form with harmonised variables.[3] The data sets were checked for overlapping data for the purpose of exclusion of duplicate data by matching on the following variables: the year of birth, sex, and date of the last blood eosinophil count. During this process patients remained unidentifiable. In case of potentially duplicate data, the data from CPRD were kept in the data set.

### Study definitions

Blood eosinophil counts were recorded with one decimal place in about half of practices; therefore, all values recorded at two decimal places were rounded to one decimal.

Asthma attacks were defined, according to the consensus European Respiratory Society/American Thoracic Society task force definition of severe attacks, as the occurrence of any of the following events: respiratory-related hospital attendance or admission, emergency department (ED) attendance, or acute oral corticosteroid (OCS) course.[4] Any of these events occurring within a 14-day period of each other were considered as one attack.

High dosages of inhaled corticosteroids (ICS) were defined according to 2014 British Thoracic Society (BTS) asthma management guidelines, which state, "If asthma control remains suboptimal after the addition of an inhaled long-acting β2 agonist, then the dosage of inhaled corticosteroids should be increased to 800 micrograms/day in adults or 400 micrograms/day in children (5–12 years), if not already on these dosages".[5] The mean ICS daily dosage (cumulative exposure based on all prescriptions) was calculated separately for the baseline and outcome years as the [(number of inhalers prescribed per year x doses in pack) / 365) x µg strength]. The chlorofluorocarbon beclomethasone dipropionate (BDP)–equivalent dosage was calculated using non-extrafine BDP at the following ratios: 1:1 with budesonide and 2:1 with fluticasone, ciclesonide, and extrafine BDP.

We defined treatment steps based on the Global Initiative for Asthma (GINA) guidelines,[6] applying GINA definitions of low-, medium-, and high-beclomethasone–equivalent dosage to the last ICS prescription before the index date.

Prescribing of maintenance oral corticosteroids (OCS) was defined as any OCS prescription during the baseline year and included probable maintenance OCS as inferred from a daily dosage ≤10 mg, tablet strength ≤2.5 mg, and/or no features suggesting an acute OCS

prescription, such as descending dosage or a prescription coded in conjunction with an acute lower respiratory event.

Asthma-related general practice (GP) consultations were defined as those with an asthma Read code. Asthma review visits, generally performed by nurses in the UK,[7] were assigned the cost of a nurse consultation, while all other consultations were assigned a GP clinical consultation cost. The costs associated with primary care attendance were determined using published costs for 2015 by the Personal Social Services Research Unit (PSSRU)[8]:

1. GP clinical consultation of 11.7 minutes at £44.00 (cost including direct care staff costs and qualification costs)
2. Nurse consultations in GP practice of 15.5 minutes (face-to-face) at £14.47.

Costs for asthma-related hospital attendance and asthma- or respiratory-related services provided in secondary care were obtained from the UK National Health Service (NHS) Reference cost schedule for 2014–2015.[9] Hospital admissions with asthma as the primary diagnosis were identified in HES data using ICD-10 codes J45 and J46. The average costs below were assigned per hospital spell by calculating weighted averages of the unit costs reported for the five asthma-related HRG-codes DZ15M to DZ15R. Unit cost was calculated as the average of unit costs of the five asthma-related HRG-codes weighted by the observed number of hospital spells recorded for the HRG-codes. Outpatient department visits were priced as service code 340, Respiratory Medicine, Outpatient Attendances, and ED visits were priced as the weighted average of service codes T01A/VB06Z[1] (admitted patients) and T01NA/VB05Z[2] (non-admitted patients).[9]

[1] Emergency Medicine, Category 1 Investigation with Category 3-4 Treatment (based on the dominant treatment being a nebuliser and some patients requiring further investigation [e.g., biochemistry, xray]), national average unit cost £161

[2] Emergency Medicine, Category 2 Investigation with Category 3 Treatment, national average unit cost £187

1. Non-elective short stay in hospital: £614.87
2. Non-elective long stay in hospital: £1964.69
3. Hospital day case: £329.91
4. Outpatient department visit to specialist in respiratory medicine: £156.29
5. Emergency department attendance: £178.03

Drug costs were drawn from the Dictionary of Medicines and Devices browser,[10] which provides up-to-date costs for Systematized Nomenclature of Medicine Clinical Terms (SnoMed) codes. Read codes are mapped to SnoMed codes and costs were calculated for the following medications:

1. Inhaled corticosteroids (ICS)
2. Long-acting ß-agonists (LABA)
3. Short-acting ß-agonists (SABA)
4. Short-acting muscarinic antagonists (SAMA)
5. Long-acting muscarinic antagonists (LAMA)
6. Oral corticosteroids (OCS, maintenance and rescue courses)
7. Theophylline
8. Leukotriene receptor antagonists (LTRAs)
9. Omalizumab
10. Antibiotics prescribed for lower respiratory events

**Statistical analyses**

In the bootstrap analyses, data were repeatedly sampled with replacement from the study sample. For each bootstrap sample, parameters (cost ratios and frequencies of severe, uncontrolled eosinophilic asthma [SUEA]) were estimated. We repeated this process 1,000 times producing 1,000 parameter estimates. The distribution of these estimates approximates the sampling distribution. We estimated 95% confidence interval limits based on the $2.5^{th}$ and $97.5^{th}$ percentiles of the empirical bootstrap distribution. The bootstrapping technique was chosen because the assumption of independence of data, required for parametric tests, does not hold as patients with SUEA were part of the total population as well.[11]

**SUPPLEMENTARY RESULTS (Results for adult patients with active asthma and concomitant COPD)**

The overall prevalence of blood eosinophilia defined as a count of $\geq 0.3 \times 10^9$/L was 40% (14 932 of 37 703) for patients ≥40 years old with active asthma and concomitant chronic obstructive pulmonary disease (COPD), compared with 43% in the main analysis population of patients with active asthma and without COPD (see the main paper). Demographic and baseline clinical characteristics, together with asthma burden during the baseline year, of patients with concomitant COPD, including 17 490 (46%) men and 20 213 (54%) women, are summarised below in supplementary table S5.

Patients with concomitant COPD, versus those without COPD, were more frequently prescribed maintenance OCS (13% vs. 3%, respectively) and at least one antibiotics course (55% vs. 35%, respectively) in the baseline year.

Two or more attacks during the baseline year were more frequently observed for patients with concomitant COPD (22%) than those without (7%), although there was no difference in the rate of attacks between patients with and without high blood eosinophil count (table S5). The overall prevalence of severe, uncontrolled eosinophilic asthma was between 3 and 4 times higher amongst patients with concomitant COPD, compared with patients without COPD, ranging from 6.8% to 1.4% with increasing levels used to define a high eosinophil count (table S1).

## REFERENCES


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**Supplementary Table S1** Prevalence of severe, uncontrolled eosinophilic asthma (SUEA*) and Hospital Episode Statistics (HES†) data availability, using four definitions of high blood eosinophil count, by age group, for patients with asthma and without concomitant COPD (N=363 558) and for patients ≥40 years old with asthma and concomitant COPD diagnosis (n=37 703)

| | Blood eosinophil count (x$10^9$/L) | | | |
|---|---|---|---|---|
| Age group | **≥0.2** | **≥0.3** | **≥0.4** | **≥0.5** |
| SUEA* | | | | |
| 5–11 years (n=7740) | 20 (0.3) | 14 (0.2) | 13 (0.2) | 12 (0.2) |
| 12–17 years (n=17 915) | 48 (0.3) | 43 (0.2) | 34 (0.2) | 31 (0.2) |
| 18–64 years (n=242 714) | 2803 (1.2) | 1900 (0.8) | 1235 (0.5) | 797 (0.3) |
| ≥65 years (n=95 189) | 1560 (1.6) | 983 (1.0) | 595 (0.6) | 372 (0.4) |
| All ages (n=363 558) | 4431 (1.2) | 2940 (0.8) | 1877 (0.5) | 1212 (0.3) |
| SUEA + HES data† | | | | |
| All ages (n=146 458) | 1814 (1.2) | 1206 (0.8) | 764 (0.5) | 492 (0.3) |
| SUEA + COPD | | | | |
| 40–64 years (n=10 489) | 781 (7.4) | 480 (4.6) | 239 (2.3) | 122 (1.2) |
| ≥65 years (n=27 214) | 1796 (6.6) | 1116 (4.1) | 651 (2.4) | 391 (1.4) |
| All ages (n=37 703) | 2577 (6.8) | 1596 (4.2) | 890 (2.4) | 513 (1.4) |
| SUEA + COPD + HES | | | | |
| ≥40 years + COPD (n=14 954) | 1165 (7.8) | 720 (4.8) | 399 (2.7) | 229 (1.5) |

Data are reported as n (% of patients as noted for each age group).

*The definition of severe uncontrolled eosinophilic asthma (SUEA) was as follows: ≥2 attacks during the 1-year baseline period preceding an elevated blood eosinophil count (defined in this table by different levels, and defined for the main analyses as ≥0.3 x $10^9$/L) for patients who were prescribed combination maintenance therapy with LABA and high-dosage ICS during both the baseline and outcome years. High-dosage ICS was defined according to British guidelines as a cumulative beclomethasone dipropionate–equivalent dosage of ≥800 µg/day for adults and ≥400 µg/day for children 5–12 years old.[5]

†Linkage with Hospital Episode Statistics was available for 63% of patients with data in the Clinical Practice Research Datalink (CPRD) dataset.

COPD, chronic obstructive pulmonary disease; HES, Hospital Episode Statistics; ICS, inhaled corticosteroid; LABA, long-acting β2-agonist.

**Table S2** Baseline clinical characteristics of patients (ages ≥5 years) with severe, uncontrolled eosinophilic asthma (SUEA)* by applying different definitions of high blood eosinophil count

| Variable | SUEA ≥0.2x10$^9$/L (n=4431) | SUEA ≥0.3x10$^9$/L* (n=2940) | SUEA ≥0.4x10$^9$/L (n=1877) | SUEA ≥0.5x10$^9$/L (n=1212) |
|---|---|---|---|---|
| Male sex | 1399 (31.6) | 988 (33.6) | 658 (35.1) | 443 (36.6) |
| Age at index date, mean (SD) | 56.7 (17.2) | 55.8 (17.6) | 54.9 (18.1) | 54.3 (18.6) |
| 5-11 years | 20 (0.5) | 14 (0.5) | 13 (0.7) | 12 (1.0) |
| 12–17 years | 48 (1.1) | 43 (1.5) | 34 (1.8) | 31 (2.6) |
| 18–64 years | 2803 (63.3) | 1900 (64.6) | 1235 (65.8) | 797 (65.8) |
| ≥65 years | 1560 (35.2) | 983 (33.4) | 595 (31.7) | 372 (30.7) |
| Body mass index† | | | | |
| Underweight | 65 (1.6) | 47 (1.8) | 37 (2.1) | 27 (2.4) |
| Normal | 960 (23.7) | 674 (25.1) | 464 (26.9) | 322 (29.1) |
| Overweight | 1245 (30.7) | 828 (30.8) | 570 (33.1) | 361 (32.7) |
| Obese | 1788 (44.1) | 1135 (42.3) | 653 (37.9) | 395 (35.7) |
| Unknown, *n* | *373* | *256* | *153* | *107* |
| Smoking status | | | | |
| Current smoker | 837 (19.2) | 530 (18.3) | 285 (15.3) | 160 (13.3) |
| Ex-smoker | 1377 (31.5) | 899 (31.0) | 547 (29.4) | 335 (27.9) |
| Non-smoker | 2156 (49.3) | 1475 (50.8) | 1027 (55.2) | 707 (58.8) |
| Unknown, *n* | *61* | *36* | *18* | *10* |
| Ever-recorded comorbidity | | | | |
| Eczema | 1487 (33.6) | 999 (34.0) | 669 (35.6) | 434 (35.8) |
| Allergic rhinitis | 883 (19.9) | 608 (20.7) | 428 (22.8) | 290 (23.9) |
| Non-allergic rhinitis | 614 (13.9) | 422 (14.4) | 304 (16.2) | 218 (18) |
| Chronic sinusitis | 684 (15.4) | 456 (15.5) | 300 (16.0) | 200 (16.5) |
| Nasal polyps | 459 (10.4) | 376 (12.8) | 300 (16.0) | 236 (19.5) |
| Gastro-oesophageal reflux disease | 789 (17.8) | 515 (17.5) | 305 (16.2) | 198 (16.3) |
| %predicted PEF | | | | |
| Available | 3961 (89.4) | 2614 (88.9) | 1665 (88.7) | 1061 (87.5) |
| Mean (SD) | 67.1 (18.7) | 66.6 (18.6) | 66.6 (18.6) | 66.1 (18.8) |
| Blood eosinophil count, median (IQR) | 0.30 (0.20-0.50) | 0.40 (0.30-0.60) | 0.50 (0.40-0.70) | 0.60 (0.50-0.80) |
| ICS dosage (µg/day), baseline year, median (IQR) | 1447 (1066-1967) | 1425 (1069-1967) | 1421 (1066-1918) | 1443 (1069-1917) |
| Last ICS dosage prescribed‡ | | | | |
| No ICS prescribed | Not applicable | Not applicable | Not applicable | Not applicable |
| Low dosage | 173 (3.9) | 114 (3.9) | 66 (3.5) | 44 (3.6) |
| Medium dosage | 1434 (32.4) | 943 (32.1) | 587 (31.3) | 379 (31.3) |
| High dosage | 2824 (63.7) | 1883 (64.0) | 1224 (65.2) | 789 (65.1) |

| | | | | |
|---|---|---|---|---|
| ≥1 prescription during baseline | | | | |
| LTRA | 1501 (33.9) | 1001 (34.0) | 678 (36.1) | 465 (38.4) |
| Theophylline | 576 (13.0) | 397 (13.5) | 264 (14.1) | 182 (15.0) |

Data are reported as n (%) unless otherwise specified.

*Severe, uncontrolled eosinophilic asthma, defined as patients without concomitant COPD on high-dosage ICS/LABA during both baseline and outcome years, with ≥2 attacks in the baseline year and elevated blood eosinophil count, defined as noted in each column. A blood eosinophil count of $\geq 0.3 \times 10^9$/L was used for the primary health care resource use analyses.

†Body mass index (BMI) categories were determined closest to the index date and were defined as follows: underweight, <18.5 kg/m$^2$; normal weight, ≥18.5 kg/m$^2$ to <25 kg/m$^2$); overweight, ≥25 kg/m$^2$ to <30 kg/m$^2$; and obese, ≥30 kg/m$^2$ for patients ≥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. Patients with missing data for BMI represented 8–9% of patients and for smoking status, 1% of patients.

‡Definitions of low, medium, and high beclomethasone–equivalent dosage of the last prescription before the index date as per GINA guidelines.

§The medication possession ratio (i.e., the refill rate as a percentage) was calculated as (total ICS pack days/number of prescription days) x 100.

ICS, inhaled corticosteroid; IQR, interquartile range; LTRA, leukotriene receptor antagonist; PEF, peak expiratory flow; SUEA, severe, uncontrolled eosinophilic asthma.

**Table S3** Burden of SUEA in the outcome year, compared with the main study population of all patients with active asthma and no concomitant COPD (including patients with SUEA)

| | **Main study population (n=363 558)** | **SUEA (n=2940)** |
|---|---|---|
| Asthma attacks, mean (SD) | 0.28 (0.74) | 1.74 (1.78) |
| Median (range) | 0 (0−15) | 1 (0−13) |
| 0 attacks | 298081 (82.0) | 851 (28.9) |
| 1 attacks | 43769 (12.0) | 682 (23.2) |
| 2 attacks | 13556 (3.7) | 627 (21.3) |
| 3 attacks | 5165 (1.4) | 387 (13.2) |
| ≥4 attacks | 2987 (0.8) | 393 (13.4) |
| GP visits, mean (SD)* | 1.36 (1.57) | 2.67 (2.80) |
| Median (range) | 1 (0−68) | 2 (0−36) |
| 0 GP visits | 114561 (31.5) | 364 (12.4) |
| 1 GP visit | 126306 (34.7) | 794 (27.0) |
| 2 GP visits | 63048 (17.3) | 625 (21.3) |
| 3 GP visits | 29903 (8.2) | 438 (14.9) |
| ≥4 GP visits | 29740 (8.2) | 719 (24.5) |
| Hospital-based specialist visits, mean (SD)† | 0.04 (0.33) | 0.30 (0.96) |
| Median (range) | 0 (0−12) | 0 (0−12) |
| 0 OPD visits | 354474 (97.5) | 2541 (86.4) |
| 1 OPD visit | 5381 (1.5) | 179 (6.1) |
| 2 OPD visits | 1980 (0.5) | 91 (3.1) |
| 3 OPD visits | 914 (0.3) | 71 (2.4) |
| ≥4 OPD visits | 809 (0.2) | 58 (2.0) |
| Asthma-related ED visits, mean (SD) | 0.01 (0.11) | 0.04 (0.25) |
| Median (range) | 0 (0−6) | 0 (0−15) |
| 0 ED visits | 360541 (99.2) | 2856 (97.1) |
| 1 ED visit | 2805 (0.8) | 67 (2.3) |
| 2 ED visits | 167 (0.0) | 13 (0.4) |
| 3 ED visits | 35 (0.0) | 2 (0.1) |
| ≥4 ED visits | 10 (0.0) | 2 (0.1) |
| Hospitalisations, mean (SD) | 0.01 (0.12) | 0.05 (0.38) |
| Median (range) | 0 (0−12) | 0 (0−9) |
| 0 hospitalisations | 145 656 (99.5) | 1168 (96.8) |
| 1 hospitalisation | 680 (0.5) | 27 (2.2) |
| 2 hospitalisations | 70 (0.0) | 8 (0.7) |

| | | |
|---|---|---|
| 3 hospitalisations | 25 (0.0) | 1 (0.1) |
| ≥4 hospitalisations | 27 (0.0) | 2 (0.2) |

Data are reported as n (%) unless otherwise noted.

*GP visits included consultations with primary care physicians and asthma nurses.

†Outpatient departments are hospital-based specialist clinics.

ED, emergency department; GP, general practice; SUEA, severe uncontrolled eosinophilic asthma.

**Table S4** Asthma-related HCRU, associated direct costs (2015 pounds sterling, £), and HCRU and cost ratios during the outcome year for patients with SUEA, using three other definitions of high blood eosinophil count, compared with the main study population (including patients with SUEA)

| | | Severe uncontrolled eosinophilic asthma: blood eosinophil counts | | | | | |
|---|---|---|---|---|---|---|---|
| **Asthma-related HCRU outcome** | **All patients (n=363 558 / 146 485*)** | **≥0.2x10$^9$/L (n=4431/1814*)** | **HCRU and cost ratios (95% CI)†** | **≥0.4x10$^9$/L (n=1877/764*)** | **HCRU and cost ratios (95% CI)†** | **≥0.5x10$^9$/L (n=1212/492*)** | **HCRU and cost ratios (95% CI)†** |
| GP visit | | | | | | | |
| Number, mean (SD) | 1.36 (1.57) | 2.63 (2.73) | 2.4 (2.3−2.5) | 2.76 (2.98) | 2.6 (2.4−2.8) | 2.87 (3.25) | 2.8 (2.5−3.0) |
| Costs | £30.8 (49.8) | £74.9 (104.4) | | £80.7 (115.8) | | £85.2 (126.3) | |
| Costs, median (IQR) | £14.5 (0.0–43.4) | £44.0 (14.5–88.0) | -- | £44.0 (14.5–102.5) | -- | £44.0 (14.5–102.5) | -- |
| Outpatient department visit | | | | | | | |
| Number, mean (SD) | 0.04 (0.33) | 0.32 (0.99) | 6.8 (6.2−7.6) | 0.52 (1.51) | 7.2 (6.2−8.4) | 0.37 (1.08) | 8.3 (7.1−9.8) |
| Costs | £6.9 (52.2) | £47.0 (148.5) | | £49.8 (154.3) | | £57.4 (168.3) | |
| ED attendance | | | | | | | |
| Number, mean (SD) | 0.01 (0.11) | 0.04 (0.24) | 4.1 (3.3−5.0) | 0.03 (0.23) | 3.8 (2.7−5.1) | 0.03 (0.25) | 3.9 (2.4−5.7) |
| Costs | £1.6 (18.8) | £6.5 (43.0) | | £6.0 (41.7) | | £6.2 (45.3) | |
| Hospitalisation* | | | | | | | |
| Number, mean (SD) | 0.01 (0.12) | 0.05 (0.42) | 7.2 (4.7−10.6) | 0.06 (0.45) | 9.7 (4.9−16.1) | 0.08 (0.53) | 12.1 (5.3−22.0) |
| Costs | £10.4 | £74.8 | | £100.5 | | £125.6 | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | (194.7) | (628.1) | | (795.3) | | (935.0) | |
| Medication costs | £170.1 (218.2) | £648.9 (284.8) | 3.8 (3.8−3.9) | £641.3 (283.4) | 3.8 (3.7−3.9) | £641.0 (265.8) | 3.8 (3.7−3.9) |
| Costs, median (IQR) | £87.8 (18.0–244.9) | £596.8 (456.4–770.4) | -- | £593.6 (446.0–753.6) | -- | £598.1 (446.2–763.8) | -- |
| Total costs* | £222.0 (337.2) | £852.9 (783.3) | 3.8 (3.7−4.0) | £887.1 (940.6) | 4.0 (3.7−4.3) | £931.2 (1083.9) | 4.2 (3.8−4.7) |
| Costs, median (IQR) | £125.6 (43.1–297.9) | £706.8 (520.6–950.9) | -- | £709.5 (524.0–957.9) | -- | £715.9 (521.3–1017.6) | -- |

Data are reported as mean (SD) unless otherwise noted. The medians (IQRs) that are not included in the table were all 0 (0–0).

*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 hospitalisations and associated costs, as factored into total costs.

†95% confidence interval, based on 1000 bootstrap replicates.

ED, emergency department; GP, general practice; HCRU, health care resource use; IQR, interquartile range; SUEA, severe, uncontrolled eosinophilic asthma.

**Table S5** Demographic and clinical characteristics and asthma-related burden during the baseline year for patients ≥40 years old with active asthma and concomitant diagnosis of chronic obstructive pulmonary disease

| Characteristic | Total (n=37 703) |
|---|---|
| Age, mean (SD) | 71.2 (11.6) |
| 40–64 years | 10 489 (27.8) |
| ≥65 years | 27 214 (72.2) |
| Sex, female | 20 213 (53.6) |
| Sex, male | 17 490 (46.4) |
| Body mass index | |
| Underweight | 1461 (4.3) |
| Normal | 11469 (33.5) |
| Overweight | 10959 (32.0) |
| Obese | 10314 (30.2) |
| Missing, *n** | *3500* |
| Smoking status, all ages | |
| Current smoker | 9775 (26.5) |
| Ex-smoker | 19210 (52.0) |
| Never smoker | 7924 (21.5) |
| Missing, *n*† | *794* |
| Allergy- and respiratory-related comorbidities | |
| Eczema | 10016 (26.6) |
| Allergic rhinitis | 3900 (10.3) |
| Non-allergic rhinitis | 3421 (9.1) |
| Chronic sinusitis | 3840 (10.2) |
| Nasal polyps | 1507 (4.0) |
| Other comorbidities | |
| Gastro-oesophageal reflux disease | 6081 (16.1) |
| Diabetes mellitus | 8853 (23.5) |
| Osteopenia/osteoporosis | 5923 (15.7) |
| Hypertension | 6379 (16.9) |
| Cardiovascular disease | 20004 (53.1) |
| Chronic kidney disease | 5631 (14.9) |
| Cataract | 6717 (17.8) |
| Charlson comorbidity index | |
| 0 | 16018 (42.5) |
| 1–4 | 14991 (39.8) |
| ≥5 | 6694 (17.8) |
| %predicted PEF (within 5 years) | |
| Available data | 27 034 (71.7) |
| Mean (SD) | 59.25 (17.80) |
| Asthma therapy: GINA step† | |
| Step 1 | 2403 (6.4) |
| Step 2 | 3641 (9.7) |
| Step 3 | 6576 (17.4) |
| Step 4 | 20201 (53.6) |
| Step 5 | 4882 (12.9) |
| Prescribed ICS during the baseline year, n (%) | 33 244 (88.2) |
| Cumulative ICS exposure (µg/day), baseline year, median (IQR) | 822 (411–1479) |

| | |
|---|---|
| Cumulative high-dosage ICS+LABA, n (%)‡ | 15 063 (40.0) |
| Maintenance OCS, n (%)§ | 4882 (12.9) |
| Mean dosage OCS ≥5mg/day, n (%) | 2687 (7.1) |
| Antibiotics & lower respiratory consultation‖ | |
| 0 | 17601 (46.7) |
| 1 | 8800 (23.3) |
| 2–3 | 7590 (10.1) |
| ≥4 | 3712 (9.8) |
| Asthma attacks | |
| 0 | 21777 (57.8) |
| 1 | 7697 (20.4) |
| 2–3 | 6193 (16.4) |
| ≥4 | 2036 (5.4) |
| Risk-domain asthma control | 15555 (41.3) |
| Overall asthma control | 7039 (18.7) |
| Cumulative high-dosage ICS/LABA & ≥2 attacks | 4595 (12.2) |
| Cumulative high-dosage ICS/LABA & ≥4 attacks | 1294 (3.4) |

Data are n (% of known). Some percentages may not total 100 because of rounding.

*These numbers of patients with missing data represented 9% overall missing data for body mass index, and 2% missing data for smoking status.

†The study definitions used for the GINA treatment steps are in the supplementary methods.[6]

‡High-dosage ICS was defined according to British guidelines as a cumulative beclomethasone dipropionate–equivalent dosage exposure of ≥800 μg/day for adults.[5]

§Maintenance OCS at some time during the baseline year.

‖Antibiotics prescribed with evidence of a lower respiratory consultation.

GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; LABA, long-acting β2-agonist; OCS, oral corticosteroids.

**Table S6** Asthma-related HCRU, associated direct costs (2015 pounds sterling, £), and HCRU and cost ratios during the outcome year for patients ≥40 years old with SUEA with concomitant COPD, compared with patients ≥40 years old with active asthma and concomitant COPD (including patients with SUEA) in the UK general population

| **Asthma-related HCRU outcome** | **Asthma + COPD (n=37 703 / 14 954*)** | **SUEA + COPD (n=1596 / 720*)** | **HCRU and cost ratio (95% CI)†** |
|---|---|---|---|
| GP consultations | | | |
| Number, mean (SD) | 1.50 (1.58) | 1.97 (1.88) | 1.4 (1.3−1.4) |
| Costs | £46.2 (59.2) | £63.0 (72.4) | |
| Costs, median (IQR) | £44.0 (14.5–58.5) | £44.0 (14.5–88.0) | -- |
| Outpatient visits | | | |
| Number, mean (SD) | 0.16 (0.63) | 0.34 (0.93) | 2.2 (1.9−2.5) |
| Costs | £24.3 (98.6) | £53.1 (145.2) | |
| ED attendance | | | |
| Number, mean (SD) | 0.04 (0.24) | 0.07 (0.35) | 1.9 (1.5−2.5) |
| Costs | £6.7 (41.9) | £12.9 (63.0) | |
| Hospitalisations* | | | |
| Number, mean (SD) | 0.01 (0.11) | 0.01 (0.08) | 0.8 (0.2−1.6) |
| Costs | £15.6 (197.8) | £11.8 (147.9) | |
| Medication costs | £387.6 (324.6) | £702.2 (327.2) | 1.8 (1.8−1.9) |
| Costs, median (IQR) | £338.4 (135.0–553.0) | £631.8 (493.8–837.3) | -- |
| Total costs* | £529.7 (444.0) | £865.5 (445.1) | 1.6 (1.6−1.7) |
| Costs, median (IQR) | £459.2 (226.9–705.5) | £756.7 (585.3–1045.6) | -- |

Data are reported as mean (SD) unless otherwise noted. The medians (IQRs) that are not included in the table were all 0 (0–0).

*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 hospitalisations and associated costs, as factored into total costs.

†95% confidence interval, based on 1,000 bootstrap replicates.

COPD, chronic obstructive pulmonary disease; ED, emergency department; GP, general practice; HCRU, health care resource use; IQR, interquartile range; SUEA, severe uncontrolled eosinophilic asthma.