Supplementary material

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Fractional exhaled nitric oxide measurement

Fractional exhaled nitric oxide (FeNO) was measured locally by site personnel according to the recommendation of the equipment manufacturer and the ATS/ERS recommendations [1]. Sites that did not have suitable FeNO equipment were provided with a Niox Vero device (Circassia, Oxford, UK) for the duration of the study. At baseline, 77% of patients were from sites using a Niox Vero device.

Covariates for multivariable ordinal regression models

Selection of covariates for the multivariable ordinal logistic regression models to identify factors associated with physician-assigned severity (mild, moderate and severe/very severe [pooled]) was guided by outputs from univariate ordinal regression models adjusted for age at baseline (p<0.2; figure S4), and by clinical relevance, with removal of variables that were known to be overlapping or considered to be highly correlated. Comorbidities were recorded in the electronic case report by selecting from a checklist rather than by yes/no responses; therefore, non-recording of a comorbidity may include both 'not present' and 'not known'. The resulting list of covariates included in the multivariable models was: age, body mass index, smoking status, modified Medical Research Council dyspnoea scale grade, time since diagnosis of asthma or chronic obstructive pulmonary disease, exacerbations in the past 12 months, post-bronchodilator forced expiratory volume in 1 second (FEV₁) % predicted, post-bronchodilator FEV₁/forced vital capacity, bronchodilator responsiveness, allergic rhinitis, non-allergic rhinitis, nasal or sinus polyps, and diagnosis of emphysema. The selected variables were entered into ordinal regression models fitted for asthma and COPD separately, and overall (excluding patients with asthma+COPD).
### TABLE S1 Patients included in the baseline analysis, by country

| Country         | Number (%) of patients (N=11,243) |
|-----------------|------------------------------------|
| Argentina*      | 521 (4.6)                          |
| Australia       | 818 (7.3)                          |
| Brazil          | 202 (1.8)                          |
| Canada*         | 1178 (10.5)                        |
| Colombia        | 252 (2.2)                          |
| Denmark         | 97 (0.9)                           |
| France*         | 747 (6.6)                          |
| Germany*        | 774 (6.9)                          |
| Italy*          | 590 (5.2)                          |
| Japan           | 820 (7.3)                          |
| Mexico*         | 143 (1.3)                          |
| The Netherlands | 318 (2.8)                          |
| Norway*         | 52 (0.5)                           |
| South Korea     | 606 (5.4)                          |
| Spain           | 975 (8.7)                          |
| Sweden          | 335 (3.0)                          |
| UK*             | 894 (8.0)                          |
| USA*            | 1921 (17.1)                        |

Patients enrolled between 25 July 2016 and 5 March 2018 were included in the baseline analysis. In China, after a later start to recruitment, a total of 47 patients were enrolled by 5 March 2018 but were excluded from the baseline analysis due to a change in regulations about data transfer in May 2019. All countries recruited patients ≥18 years of age. *Recruited patients ≥12–<18 years of age in addition to patients ≥18 years of age. See Table S7 for a list of study investigators in each country. N: total number of patients.
**TABLE S2 Medication categories**

| Label | Must have | Must not have | Allowed |
|-------|-----------|---------------|---------|
| No ICS | - | Any ICS-containing inhaler (maintenance or reliever) | All |
| Short-acting BD, no ICS | SABA and/or SAMA | Any ICS-containing inhaler (maintenance or reliever), LABA, LAMA, maintenance OCS, biologic therapy | Other respiratory medications |
| Any ICS | Any ICS-containing inhaler (maintenance and/or reliever) | - | All |
| LABA and/or LAMA, no ICS | LABA and/or LAMA | Any ICS-containing inhaler (maintenance or reliever), maintenance OCS, biologic therapy | Any non-ICS-containing reliever, other respiratory medications |
| Low-dose ICS | ICS low-dose* | LABA and/or LAMA, maintenance OCS, biologic therapy | Any reliever (including ICS-containing), other respiratory medications |
| Low-dose ICS+LABA | ICS low-dose* + LABA (separate or in combination) | LAMA, maintenance OCS, biologic therapy | Any reliever (including ICS-containing), other respiratory medications |
| Med/high-dose ICS+LABA | ICS medium or high-dose* | LABA and/or LAMA, maintenance OCS, biologic therapy | Any reliever (including ICS-containing), other respiratory medications |
| ICS+LABA+LAMA | ICS+LAMA+LABA (separate or combination) | Maintenance OCS, biologic therapy | Any reliever (including ICS-containing), other respiratory medications |
| Maintenance OCS | OCS (or injected corticosteroid) in the maintenance treatment section of the eCRF | - | All |
| Biologic therapy | Anti-IgE, anti-IL5/5R, anti-IL4 | - | All |
| Leukotriene modifier | LTRA and/or 5-LO inhibitor | - | All |
| Other respiratory medications | Leukotriene modifier, methylxanthine, long-term antibiotics and/or PDE4 inhibitor | - | All |

*ICS dose was classified according to the Global Initiative for Asthma 2019 definitions [2].

5-LO: 5-lipoxygenase; BD: bronchodilator; ICS: inhaled corticosteroid; IL: interleukin; IgE: immunoglobulin E; LABA: long-acting β2-agonist; LAMA: long-acting muscarinic.
antagonist; LTRA: leukotriene receptor antagonist; med: medium; n: number of patients in the specified category; N: total number of patients; OCS: oral corticosteroid; PDE4: phosphodiesterase 4; R: receptor.
|                          | Overall (N=11,243) | Primary care (N=5247) | All non-primary care (N=5996) | University hospital (N=3005) | Research facility (N=1331) | Non-university hospital (N=979) | Specialists (N=493) | Private practice (N=90) |
|--------------------------|--------------------|-----------------------|------------------------------|----------------------------|--------------------------|--------------------------------|---------------------|----------------------|
| **Physician-assigned diagnosis of asthma, n (%)‡** |                    |                      |                              |                            |                          |                                 |                     |                      |
| Mild                     | 5940 (52.8)        | 2813 (53.6)          | 3127 (52.2)                  | 1689 (56.2)                | 621 (46.7)               | 473 (48.3)                      | 235 (47.7)          | 40 (44.4)            |
| Moderate                 | 2175 (19.4)        | 1117 (21.3)          | 1058 (17.7)                  | 518 (17.2)                 | 280 (21.0)               | 153 (15.8)                      | 70 (14.2)           | 14 (15.6)            |
| Severe                   | 1475 (12.9)        | 706 (13.5)           | 769 (12.8)                   | 469 (15.6)                 | 241 (18.1)               | 134 (13.7)                      | 66 (13.4)           | 7 (7.8)              |
| **Physician-assigned diagnosis of asthma+COPD, n (%)‡** |                    |                      |                              |                            |                          |                                 |                     |                      |
| Mild                     | 1396 (12.4)        | 641 (12.2)           | 755 (12.6)                   | 316 (10.5)                 | 227 (17.1)               | 135 (13.8)                      | 54 (11.0)           | 13 (14.4)            |
| Moderate                 | 243 (2.2)          | 118 (2.3)            | 125 (2.1)                    | 40 (1.3)                   | 50 (3.8)                 | 27 (2.8)                        | 5 (1.0)             | 2 (2.2)              |
| Severe                   | 523 (4.7)          | 238 (4.5)            | 285 (4.8)                    | 129 (4.3)                  | 71 (5.3)                 | 54 (5.5)                        | 21 (4.3)            | 5 (5.6)              |
| **Physician-assigned diagnosis of COPD, n (%)‡** |                    |                      |                              |                            |                          |                                 |                     |                      |
| Mild                     | 3907 (34.7)        | 1793 (34.2)          | 2114 (35.3)                  | 1000 (33.3)                | 483 (36.3)               | 371 (37.9)                      | 204 (41.4)          | 37 (41.1)            |
| Moderate                 | 1125 (10.0)        | 459 (8.8)            | 666 (11.1)                   | 283 (9.4)                  | 208 (15.6)               | 90 (9.2)                        | 77 (15.6)           | 6 (6.7)              |
| Severe                   | 1206 (10.7)        | 580 (11.1)           | 626 (10.4)                   | 306 (10.2)                 | 132 (9.9)                | 77 (7.9)                        | 87 (17.6)           | 13 (14.4)            |
| **Sex, n (%) female**    |                    |                      |                              |                            |                          |                                 |                     |                      |
| 5875 (52.3)              | 2876 (54.8)        | 2999 (50.0)          | 1422 (47.3)                  | 760 (57.1)                 | 457 (46.7)               | 261 (52.9)                      | 47 (52.2)           |                     |
| Age (years), mean ± SD   | 58.7 ± 15.8        | 58.5 ± 16.1          | 58.8 ± 15.5                  | 58.2 ± 15.7                | 60.3 ± 14.8              | 60.8 ± 14.2                     | 57.1 ± 15.3         | 62.2 ± 12.8          |
| BMI (kg/m²), mean ± SD   | 28.0 ± 6.7         | 28.4 ± 6.9           | 27.7 ± 6.5                   | 26.9 ± 6.0                 | 29.6 ± 7.2               | 26.9 ± 5.8                      | 29.2 ± 7.9          | 26.2 ± 5.0           |
| N with data              | 10491              | 4741                 | 5750                         | 2829                      | 1313                    | 954                            | 479                 | 89                   |
| <18.5 kg/m², n (%)       | 347 (3.3)          | 161 (3.4)            | 186 (3.2)                    | 96 (3.4)                   | 27 (2.1)                 | 35 (3.7)                        | 18 (3.8)            | 1 (1.1)              |
| 18.5–<25.0 kg/m², n (%)  | 3377 (32.2)        | 1451 (30.6)          | 1926 (33.5)                  | 1066 (37.7)                | 314 (24.0)               | 339 (35.5)                      | 142 (29.7)          | 37 (41.6)            |
| 25.0–<30.0 kg/m², n (%)  | 3444 (32.8)        | 1524 (32.1)          | 1920 (33.4)                  | 963 (34.1)                 | 424 (32.4)               | 336 (35.2)                      | 133 (27.8)          | 35 (39.3)            |
| ≥30.0 kg/m², n (%)       | 3323 (31.7)        | 1605 (33.9)          | 1718 (29.9)                  | 699 (24.8)                 | 545 (41.6)               | 244 (25.6)                      | 185 (38.7)          | 16 (18.0)            |
TABLE S3 (Continued) Demographics, disease history and clinical characteristics of the NOVELTY population, overall and by recruitment setting

| Variable                                      | Overall (N=11,243) | Primary care (N=5247) | All non-primary care\(^*\) (N=5996) | University hospital (N=3005) | Research facility (N=1331) | Non-university hospital (N=979) | Specialists (N=493) | Private practice (N=90) |
|-----------------------------------------------|--------------------|-----------------------|-------------------------------------|-----------------------------|-----------------------------|--------------------------------|----------------------|------------------------|
| Smoking status, n (%)                         |                    |                       |                                     |                             |                             |                                |                      |                        |
| Never smoked                                  | 4065 (36.3)        | 1981 (38.0)           | 2084 (34.8)                         | 1091 (36.4)                 | 410 (31.0)                  | 332 (33.9)                     | 166 (33.7)          | 24 (26.7)              |
| Former smoker                                 | 5164 (46.1)        | 2312 (44.3)           | 2852 (47.7)                         | 1480 (49.3)                 | 628 (47.4)                  | 507 (51.8)                     | 169 (34.3)          | 44 (48.9)              |
| Current smoker                                | 1972 (17.6)        | 926 (17.7)            | 1046 (17.5)                         | 429 (14.3)                  | 286 (21.6)                  | 139 (14.2)                     | 157 (31.9)          | 22 (24.4)              |
| Age at diagnosis, mean ± SD                   |                    |                       |                                     |                             |                             |                                |                      |                        |
| Asthma                                        | 35.2 ± 22.0        | 34.0 ± 22.3           | 36.2 ± 21.7                         | 36.4 ± 21.3                 | 34.0 ± 22.0                 | 37.9 ± 21.6                     | 44.8 ± 20.7          | 38.3 ± 20.6            |
| COPD                                          | 58.4 ± 11.9        | 58.9 ± 11.6           | 57.9 ± 12.2                         | 59.1 ± 11.2                 | 57.2 ± 12.7                 | 57.2 ± 12.4                     | 55.9 ± 12.6          | 55.0 ± 16.8            |
| Asthma or COPD                                | 43.4 ± 22.1        | 42.8 ± 22.7           | 43.9 ± 21.6                         | 44.1 ± 21.4                 | 42.3 ± 22.2                 | 45.3 ± 20.9                     | 49.1 ± 18.5          | 45.5 ± 21.0            |
| Time since diagnosis (years), mean ± SD       |                    |                       |                                     |                             |                             |                                |                      |                        |
| Asthma                                        | 19.3 ± 18.2        | 20.0 ± 18.5           | 18.8 ± 17.9                         | 17.5 ± 17.3                 | 23.1 ± 19.2                 | 18.9 ± 17.8                     | 12.6 ± 15.6          | 19.6 ± 17.6            |
| COPD                                          | 7.8 ± 8.9          | 7.6 ± 8.6             | 8.1 ± 9.2                           | 7.6 ± 8.2                   | 8.6 ± 9.3                   | 9.2 ± 10.7                     | 5.5 ± 8.3            | 10.3 ± 13.6            |
| Asthma or COPD                                | 15.4 ± 16.5        | 15.9 ± 16.8           | 15.0 ± 16.2                         | 14.2 ± 15.6                 | 17.9 ± 17.8                 | 15.4 ± 16.2                     | 9.5 ± 13.7           | 16.5 ± 16.7            |
| Diagnosis of emphysema, n (%)                 | 2120 (18.9)        | 888 (16.9)            | 1232 (20.5)                         | 647 (21.5)                  | 238 (17.9)                  | 274 (28.0)                     | 39 (7.9)             | 28 (31.1)              |
| ≥1 allergy reported, n (%)                   | 5429 (48.3)        | 2536 (48.3)           | 2893 (48.2)                         | 1388 (46.2)                 | 687 (51.6)                  | 450 (46.0)                     | 270 (54.8)           | 40 (44.4)              |
| Allergy testing performed, n (%)             | 2819 (25.1)        | 1131 (21.6)           | 1688 (28.2)                         | 1022 (34.0)                 | 235 (17.7)                  | 243 (24.8)                     | 148 (30.0)           | 16 (20.0)              |
| Atopic, n (% of those with allergy testing)  | 2209 (78.4)        | 882 (78.0)            | 1327 (78.6)                         | 756 (74.0)                  | 207 (88.1)                  | 187 (77.0)                     | 143 (96.6)           | 17 (94.4)              |
| Nasal or sinus polyps, n (%)                 | 349 (3.1)          | 124 (2.4)             | 225 (3.8)                           | 154 (5.1)                   | 29 (2.2)                    | 20 (2.0)                       | 10 (2.0)             | 4 (4.4)                |
### TABLE S3 (Continued) Demographics, disease history and clinical characteristics of the NOVELTY population, overall and by recruitment setting

|                  | Overall (N=11,243) | Primary care (N=5247) | All non-primary care† (N=5996) | University hospital (N=3005) | Research facility (N=1331) | Non-university hospital (N=979) | Specialists (N=493) | Private practice (N=90) |
|------------------|--------------------|-----------------------|-------------------------------|-----------------------------|----------------------------|---------------------------------|---------------------|------------------------|
| Patients with PRO data, n (%) | 7791 (69.3) | 3634 (69.3) | 4157 (69.3) | 2189 (72.8) | 846 (63.6) | 754 (77.0) | 256 (51.9) | 56 (62.2) |
| Asthma§          | 4115 (69.3) | 1933 (68.7) | 2182 (69.7) | 1235 (73.1) | 386 (62.2) | 363 (76.7) | 138 (58.7) | 24 (60.0) |
| Asthma+COPD§     | 984 (70.5)  | 444 (69.3)  | 540 (71.5)  | 237 (75.0)  | 151 (66.5) | 103 (76.3) | 38 (70.4)  | 6 (46.2)  |
| COPD§            | 2692 (68.9) | 1257 (70.1) | 1435 (67.9) | 717 (71.7)  | 309 (64.0) | 288 (77.6) | 80 (39.2)  | 26 (70.3) |
| mMRC dyspnoea grade |                  |                      |                              |                            |                            |                                 |                     |                        |
| N with data      | 10 850        | 4970                 | 5880                         | 2984                       | 1318                       | 922                            | 469                 | 90                     |
| Grade ≥2, n (%)  | 3798 (35.0)  | 1655 (33.3) | 2143 (36.4) | 999 (33.5)  | 524 (39.8)  | 373 (40.5) | 182 (38.8) | 29 (32.2) |
| SGRQ total score, mean ± SD | 35.1 ± 22.1  | 35.4 ± 22.0 | 35.0 ± 22.2 | 34.2 ± 22.3 | 36.1 ± 21.5 | 36.6 ± 22.5 | 32.5 ± 23.4 | 35.0 ± 19.9 |
| CAAT total score, mean ± SD** | 15.4 ± 8.6  | 15.7 ± 8.5  | 15.2 ± 8.6  | 14.6 ± 8.6  | 15.9 ± 8.3  | 16.1 ± 8.9  | 14.7 ± 8.8  | 14.3 ± 7.6 |
| Patients with post-bronchodilator spirometry data, n (%) | 9389 (83.5) | 4217 (80.4) | 5172 (86.3) | 2656 (88.4) | 1129 (84.8) | 821 (83.9) | 396 (80.3) | 79 (87.8) |
| Asthma§          | 4917 (82.8) | 2194 (82.9) | 2723 (87.1) | 1482 (87.7) | 537 (86.5)  | 405 (85.6) | 197 (83.8) | 38 (95.0) |
| Asthma+COPD§     | 1188 (85.1) | 537 (83.8)  | 651 (86.2)  | 288 (91.1)  | 192 (84.6)  | 107 (79.3) | 47 (87.0)  | 8 (61.5)  |
| COPD§            | 3284 (84.1) | 1486 (82.9) | 1798 (85.1) | 886 (88.6)  | 400 (82.8)  | 309 (83.3) | 152 (74.5) | 33 (89.2) |
| Post-bronchodilator FEV₁ % predicted, mean ± SD†† | 75.4 ± 24.4 | 75.0 ± 24.4 | 75.7 ± 24.4 | 75.6 ± 24.4 | 76.8 ± 23.6 | 72.4 ± 26.3 | 78.9 ± 21.5 | 67.0 ± 21.6 |
| Post-bronchodilator FEV₁/FVC, mean ± SD | 0.66 ± 0.16  | 0.66 ± 0.16  | 0.66 ± 0.16  | 0.65 ± 0.16  | 0.68 ± 0.15  | 0.64 ± 0.18  | 0.74 ± 0.13  | 0.68 ± 0.14 |
| Bronchodilator responsiveness (%), mean ± SD | 6.7 ± 10.5  | 6.5 ± 10.3  | 6.8 ± 10.6  | 7.3 ± 9.9   | 5.7 ± 10.1   | 7.2 ± 11.3   | 5.8 ± 14.5   | 6.9 ± 8.1  |

Details of patients’ care settings other than their recruitment sites are not available. For percentages, the denominator is given when different from the total number of patients (N [excluding ‘unknown’]). BMI: body mass index; CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; eCRF: electronic case report form; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; n: number of patients in the specified category; N: total number of patients; PRO: patient-reported outcome; SD: standard deviation; SGRQ: St George’s Respiratory Questionnaire. *Approximately 80% of patients had post-
bronchodilator spirometry data, 70% had PRO data and >90% had complete data for other variables. †Includes patients recruited from unknown care settings (N=98).

‡Recruitment was stratified by diagnosis/severity with the aim of achieving similar numbers of patients in each group. For patients with asthma+COPD, the severity category is the worse of the two physician-assigned severity classifications. Patients with COPD classified as 'very severe' were included in the 'severe' group. §Percentage values have been calculated as a proportion of total patients in that physician-assigned diagnosis group, as opposed to the total patients from that respective care setting. **The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. ††Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3].
|                         | Diagnosis  | Suspected diagnosis |
|-------------------------|------------|---------------------|
|                         | (N=10,756) | (N=487)             |
| **Physician-assigned diagnosis of asthma, n (%)†** |            |                     |
| Mild                    | 2079 (19.3)| 96 (19.9)           |
| Moderate                | 2086 (19.4)| 22 (4.6)            |
| Severe                  | 1638 (15.2)| 14 (2.9)            |
| **Physician-assigned diagnosis of asthma+COPD, n (%)†** |            |                     |
| Mild                    | 200 (1.9)  | 43 (8.9)            |
| Moderate                | 536 (5.0)  | 90 (18.6)           |
| Severe                  | 452 (4.2)  | 71 (14.7)           |
| **Physician-assigned diagnosis of COPD, n (%)†**     |            |                     |
| Mild                    | 1017 (9.5) | 108 (22.4)          |
| Moderate                | 1175 (10.9)| 31 (6.4)            |
| Severe                  | 1566 (14.6)| 8 (1.7)             |
| **Care setting**        |            |                     |
| Primary care            | 4960 (46.1)| 287 (58.9)          |
| Non-primary care‡       | 5796 (53.9)| 200 (41.1)          |
| **Sex, n (%) female**   |            |                     |
|                         | 5638 (52.4)| 237 (48.7)          |
| **Age (years), mean ± SD** | 58.7 ± 15.8 | 58.7 ± 15.2        |
| **BMI (kg/m²), mean ± SD**  | 28.0 ± 6.7  | 29.5 ± 6.7          |
| N with data             | 10 043     | 448                 |
| <18.5 kg/m², n (%)      | 339 (3.4)  | 8 (1.8)             |
| 18.5–<25.0 kg/m², n (%) | 3274 (32.6)| 103 (23.0)          |
| 25.0–<30.0 kg/m², n (%) | 3299 (32.8)| 145 (32.4)          |
| ≥30.0 kg/m², n (%)      | 3131 (31.2)| 192 (42.9)          |
| **Smoking status, n (%)** |            |                     |
| N with data             | 10 716     | 485                 |
| Never smoked            | 3948 (36.8)| 117 (24.1)          |
| Former smoker           | 4929 (46.0)| 235 (48.5)          |
| Current smoker          | 1839 (17.2)| 133 (27.4)          |
| **Age at diagnosis, mean ± SD**  | 34.7 ± 21.9 | 45.0 ± 22.1        |
| Asthma                  | 34.7 ± 21.9| 45.0 ± 22.1         |
| COPD                    | 58.5 ± 11.7| 56.1 ± 14.3         |
| Asthma or COPD          | 43.2 ± 22.1| 47.6 ± 20.8         |
| **Diagnosis of emphysema, n (%)** | 2054 (19.1) | 66 (13.6)          |
| ≥1 allergy reported, n (%) | 5183 (48.2) | 246 (50.5)          |
| Allergy testing performed, n (%) | 2722 (25.3) | 97 (19.9)          |
| Atopic, n (% of those with allergy testing) | 2130 (78.3) | 79 (81.4)          |
| Nasal or sinus polyps, n (%) | 335 (3.1)  | 14 (2.9)            |
| **mMRC dyspnoea grade** |            |                     |
| N with data             | 10 375     | 475                 |
| Grade ≥2, n (%)         | 3652 (34.0)| 146 (30.0)          |
| **SGRQ total score, mean ± SD**  | 35.2 ± 22.2 | 34.9 ± 20.2        |
|                                  | Diagnosis (N=10,756) | Suspected diagnosis (N=487) |
|----------------------------------|----------------------|----------------------------|
| CAAT total score, mean ± SD§     | 15.5 ± 8.6           | 15.0 ± 8.0                 |
| Post-bronchodilator FEV₁ % predicted, mean ± SD** | 75.2 ± 24.5          | 79.5 ± 22.2                |
| Post-bronchodilator FEV₁/FVC, mean ± SD | 0.66 ± 0.16         | 0.69 ± 0.14                |
| Bronchodilator responsiveness (%), mean ± SD | 6.7 ± 10.5          | 5.9 ± 10.8                 |

For percentages, the denominator is given when different from the total number of patients (N with data [excluding ‘unknown’]). BMI: body mass index; CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; eCRF: electronic case report form; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; n: number of patients in the specified category; N: total number of patients; PRO: patient-reported outcome; SD: standard deviation; SGRQ: St George’s Respiratory Questionnaire. *Approximately 80% of patients had post-bronchodilator spirometry data, 70% had PRO data and >90% had complete data for other variables. †Recruitment was stratified by diagnosis/severity with the aim of achieving similar numbers of patients in each group. For patients with asthma+COPD, the severity category is the worse of the two physician-assigned severity classifications. Patients with COPD classified as ‘very severe’ were included in the ‘severe’ group. ‡Includes patients recruited from university hospitals (N=3005), specialist research facilities (N=1331), non-university hospitals (N=979), specialist clinics (N=493), private practice (N=90), and unknown care settings (N=98). § The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. **Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3].
| Table S5 Clinical characteristics of the NOVELTY population, by physician-assigned diagnosis |
|------------------------------------------------------------------------------------------|
| | Physician-assigned asthma (N=5940) | Physician-assigned asthma+COPD (N=1396) | Physician-assigned COPD (N=3907) | Total (N=11,243) |
| | | | | |
| Sex, n (%) female | 3714 (62.5) | 655 (46.9) | 1506 (38.5) | 5875 (52.3) |
| Age (years), mean ± SD | 52.0 ± 17.1 | 64.7 ± 10.3 | 66.6 ± 9.6 | 58.7 ± 15.8 |
| Ethnicity, n (%) | | | | |
| N with data | 5925 | 1396 | 3907 | 11,228 |
| Caucasian | 4193 (70.8) | 1065 (76.3) | 3144 (80.5) | 8402 (74.8) |
| African American | 271 (4.6) | 57 (4.1) | 268 (6.9) | 596 (5.3) |
| North East Asian† | 911 (15.4) | 200 (14.3) | 269 (6.9) | 1380 (12.3) |
| South East Asian | 109 (1.8) | 24 (1.7) | 36 (0.9) | 169 (1.5) |
| Other | 441 (7.4) | 50 (3.6) | 190 (4.9) | 681 (6.1) |
| Smoking status, n (%) | | | | |
| N with data | 5917 | 1390 | 3894 | 11,201 |
| Never smoked | 3652 (61.7) | 167 (12.0) | 246 (6.3) | 4065 (36.3) |
| Former smoker | 1787 (30.2) | 882 (63.5) | 2495 (64.1) | 5164 (46.1) |
| Current smoker | 478 (8.1) | 341 (24.5) | 1153 (29.6) | 1972 (17.6) |
| Age at diagnosis, mean ± SD | | | | |
| Asthma | 33.4 ± 21.4 | 42.6 ± 23.0 | NA | 35.2 ± 22.0 |
| COPD | NA | 57.2 ± 11.7 | 58.8 ± 11.9 | 58.4 ± 11.9 |
| Asthma or COPD | 33.4 ± 21.4 | 42.2 ± 22.4 | 58.8 ± 11.9 | 43.4 ± 22.1 |
| Onset of respiratory symptoms at age <12 years, n (%) | | | | |
| Family history, n (%) | | | | |
| Asthma | 2330 (39.2) | 541 (38.8) | 647 (16.6) | 3518 (31.3) |
| COPD | 722 (12.2) | 376 (26.9) | 937 (24.0) | 2035 (18.1) |
| Allergies | 2153 (36.2) | 370 (26.5) | 475 (12.2) | 2998 (26.7) |
| Physicin-assessed severity, n (%)‡ | | | | |
| N with data | 5935 | 1392 | 3905 | 11,232 |
| Mild | 2175 (36.6) | 243 (17.5) | 1125 (28.8) | 3543 (31.5) |
| Moderate | 2108 (35.6) | 626 (45.0) | 1206 (30.9) | 3940 (35.1) |
| Severe | 1652 (27.8) | 523 (37.6) | 1574 (40.3) | 3749 (33.4) |
| Overall health status, n (%) of patients with non-missing data§ | | | | |
| N with non-missing data | 4087 | 976 | 2688 | 7751 |
| Very good | 451 (11.0) | 43 (4.4) | 144 (5.4) | 638 (8.2) |
| Good | 1687 (41.3) | 303 (31.0) | 776 (28.9) | 2766 (35.7) |
| Fair | 1571 (38.4) | 451 (46.2) | 1297 (48.3) | 3319 (42.8) |
| Poor | 330 (8.1) | 148 (15.2) | 399 (14.8) | 877 (11.3) |
| Very poor | 48 (1.2) | 31 (3.2) | 72 (2.7) | 151 (1.9) |
| mMRC dyspnoea grade | | | | |
| N with data | 5704 | 1343 | 3803 | 10 850 |
| Grade ≥2, n (%) | 1189 (20.8) | 586 (43.6) | 2023 (53.1) | 3798 (35.0) |
TABLE S5 (continued) Clinical characteristics of the NOVELTY population, by physician-assigned diagnosis

|                        | Physician-assigned asthma (N=5940)* | Physician-assigned asthma+COPD (N=1396)* | Physician-assigned COPD (N=3907)* | Total (N=11,243)* |
|------------------------|---------------------------------------|--------------------------------------------|-----------------------------------|-------------------|
| **SGRQ total score, mean ± SD** | 29.9 ± 20.9                           | 39.9 ± 22.1                               | 41.5 ± 21.8                     | 35.2 ± 22.1       |
| **CAAT total score, mean ± SD**   | 14.0 ± 8.5                            | 17.2 ± 8.5                                | 17.0 ± 8.3                      | 15.4 ± 8.6        |
| Exacerbations in the past 12 months, mean ± SD†† | 0.7 ± 1.5                             | 1.0 ± 1.8                                 | 0.6 ± 1.3                       | 0.7 ± 1.5         |
| N with data            | 5892                                  | 1392                                      | 3870                             | 11,154            |
| ≥1, n (%)              | 2008 (34.1)                           | 654 (47.0)                                | 1350 (34.9)                     | 4012 (36.0)       |
| ≥2, n (%)              | 833 (14.1)                            | 313 (22.5)                                | 514 (13.3)                      | 1660 (14.9)       |
| **Post-bronchodilator FEV1 % predicted, mean ± SD‡‡** | 86.3 ± 20.3                           | 68.3 ± 21.5                               | 61.5 ± 23.0                     | 75.4 ± 24.4       |
| N with data (for LLN)  | 4799                                  | 1152                                      | 3198                             | 9149              |
| <LLN, n (%)            | 1363 (28.4)                           | 706 (61.3)                                | 2194 (68.6)                     | 4263 (46.6)       |
| **Post-bronchodilator FEV1/FVC, mean ± SD‡‡** | 0.74 ± 0.12                           | 0.60 ± 0.15                               | 0.57 ± 0.16                     | 0.66 ± 0.16       |
| N with data            | 4939                                  | 1187                                      | 3285                             | 9411              |
| <0.7, n (%)            | 1396 (28.3)                           | 873 (73.5)                                | 2463 (75.0)                     | 4732 (50.3)       |
| N with data (for LLN)  | 4819                                  | 1150                                      | 3202                             | 9171              |
| <LLN, n (%)            | 1118 (23.2)                           | 711 (61.8)                                | 2046 (63.9)                     | 3875 (42.2)       |
| **FVC % predicted, mean ± SD** | 90.8 ± 17.7                           | 85.1 ± 19.6                               | 80.7 ± 20.9                     | 86.5 ± 19.6       |
| N with data            | 4766                                  | 1148                                      | 3195                             | 9109              |
| <LLN, n (%)            | 834 (17.5)                            | 295 (25.7)                                | 1064 (33.3)                     | 2193 (24.1)       |
| **Bronchodilator responsiveness (%), mean ± SD** | 6.4 ± 9.5                             | 8.1 ± 11.2                                | 6.5 ± 11.5                      | 6.7 ± 10.5        |
| N with data            | 4777                                  | 1138                                      | 3119                             | 9034              |
| >12% and >200 mL, n (%) | 759 (15.9)                            | 217 (19.1)                                | 409 (13.1)                      | 1385 (15.3)       |
| **FEF25–75 % predicted, mean ± SD** | 73.0 ± 38.0                           | 48.6 ± 36.3                               | 50.3 ± 37.5                     | 62.7 ± 39.4       |
| **Inspiratory capacity (L), mean ± SD** | 80.9 ± 39.2                           | 52.7 ± 38.4                               | 50.4 ± 37.1                     | 67.3 ± 41.2       |
| N with data            | 2184                                  | 355 (25.4)                                | 280 (7.2)                       | 2819 (25.1)       |
| Atopic, n (% of those with allergy testing) | 1786 (81.8)                           | 262 (73.8)                                | 161 (57.5)                      | 2209 (78.4)       |
TABLE S5 (continued) Clinical characteristics of the NOVELTY population, by physician-assigned diagnosis

| Respiratory medications, n (%)§§ | Physician-assigned asthma (N=5940)* | Physician-assigned asthma+COPD (N=1396)* | Physician-assigned COPD (N=3907)* | Total (N=11,243)* |
|----------------------------------|-------------------------------------|----------------------------------------|----------------------------------|-------------------|
| N with medications data          | 5765                                | 1373                                    | 3631                             | 10 769            |
| N with ICS dose data             | 5202                                | 1373                                    | 3631                             | 9876              |
| No ICS***                        | 627 (10.9)                          | 218 (15.9)                              | 1599 (44.0)                       | 2444 (22.7)       |
| Short-acting BD, no ICS***       | 488 (8.5)                           | 148 (10.8)                              | 839 (23.1)                        | 1475 (13.7)       |
| LABA and/or LAMA, no ICS***      | 49 (0.8)                            | 137 (10.0)                              | 1276 (35.1)                       | 1462 (13.6)       |
| Low-dose ICS                     | 301 (5.8)                           | 13 (1.0)                                | 31 (0.9)                          | 345 (3.5)         |
| Low-dose ICS+LABA                | 960 (16.5)                          | 110 (8.7)                               | 174 (5.1)                         | 1244 (11.2)       |
| Med/high-dose ICS+LABA           | 1765 (33.9)                         | 218 (17.3)                              | 265 (7.8)                         | 2248 (20.2)       |
| ICS+LABA+LAMA†††                 | 489 (8.5)                           | 584 (42.5)                              | 1252 (34.5)                       | 2325 (21.6)       |
| Maintenance OCS                  | 340 (6.1)                           | 83 (6.0)                                | 97 (2.7)                          | 520 (4.8)         |
| Biologic therapy                 | 566 (9.8)                           | 58 (4.2)                                | 3 (0.1)                           | 627 (5.8)         |
| Leukotriene modifier            | 1671 (29.0)                          | 292 (21.3)                              | 112 (3.1)                         | 2075 (19.3)       |

Blood eosinophil count (10⁹/μL), geo mean ± geo SD

|                                             | Physician-assigned asthma (N=5940)* | Physician-assigned asthma+COPD (N=1396)* | Physician-assigned COPD (N=3907)* | Total (N=11,243)* |
|---------------------------------------------|-------------------------------------|----------------------------------------|----------------------------------|-------------------|
| N without OCS, anti-IL-4/4R or anti-IL-5/5R| 0.17 ± 0.20                         | 0.16 ± 0.20                            | 0.15 ± 1.89                      | 0.16 ± 2.01       |
| Excluding patients with OCS, anti-IL-4/4R or anti-IL-5/5R | 2356                                | 709                                    | 1716                             | 4781              |
|                                             | 0.17 ± 0.20                         | 0.16 ± 0.20                            | 0.15 ± 1.90                      | 0.16 ± 2.00       |

Blood eosinophil proportion (% of total leukocytes), geo mean ± geo SD

|                                             | Physician-assigned asthma (N=5940)* | Physician-assigned asthma+COPD (N=1396)* | Physician-assigned COPD (N=3907)* | Total (N=11,243)* |
|---------------------------------------------|-------------------------------------|----------------------------------------|----------------------------------|-------------------|
| Excluding patients with OCS, anti-IL-4/4R or anti-IL-5/5R | 2.30 ± 2.06                         | 2.10 ± 2.03                            | 1.76 ± 1.86                      | 2.06 ± 2.00       |

Blood neutrophil count (10⁹/μL), geo mean ± geo SD

|                                             | Physician-assigned asthma (N=5940)* | Physician-assigned asthma+COPD (N=1396)* | Physician-assigned COPD (N=3907)* | Total (N=11,243)* |
|---------------------------------------------|-------------------------------------|----------------------------------------|----------------------------------|-------------------|
| Excluding current smokers                   | 23 (14–40)                          | 19 (12–32)                             | 17 (11–27)                       | 21 (13–35)        |
| Current smokers                             | 14 (8–26)                           | 10 (6–18)                              | 10 (6–17)                        | 11 (7–19)         |

For percentages, the denominator is given when different from the total number of patients (N with data [excluding 'unknown']). BD: bronchodilator; CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; eCRF: electronic case report form; FEF25–75: forced expiratory flow at 25–75% of FVC; FeNO: fractional exhaled nitric oxide; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; geo: geometric; ICS: inhaled corticosteroid; IL-4/4R: interleukin-4 or interleukin-4 receptor; IL-5/5R: interleukin-5.
or interleukin-5 receptor; IQR: interquartile range; LABA: long-acting β2-agonist; LAMA: long-acting muscarinic antagonist; LLN: lower limit of normal; med: medium; mMRC: modified Medical Research Council; n: number of patients in the specified category; N: total number of patients; OCS: oral corticosteroid; PRO: patient-reported outcome; SD: standard deviation; SGRQ: St George’s Respiratory Questionnaire. Approximately 80% of patients had post-bronchodilator spirometry data, 70% had PRO data, 50% had biomarker data and >90% had complete data for other variables (see table 2 and table S2). Including Japanese patients. Recruitment was stratified by diagnosis/severity with the aim of achieving similar numbers of patients in each group. For patients with asthma+COPD, the severity category is the worse of the two physician-assigned severity classifications. Patients with COPD classified as ‘very severe’ were included in the ‘severe’ group. From the question that precedes the SGRQ: “please tick in one box to show how you describe your current health”. The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. Among all patients, including those with no exacerbations. Includes mild, moderate and severe exacerbations, from the following question in the eCRF: “During the past 12 months, on how many occasions has your patient experienced an exacerbation of their asthma or COPD beyond the patient’s usual day to day variance?” Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3]. Medication categories are defined in table S2. ICS dose was classified according to Global Initiative for Asthma 2019 definitions [2]. ‘No ICS’ was defined as neither maintenance nor reliever ICS; Without maintenance OCS or biologic therapy.
TABLE S6 Demographics, disease history and clinical characteristics of the total NOVELTY population, by physician-assigned severity

|                             | Total (N=3543)* | Mild (N=3940)* | Severe (N=3749)* |
|-----------------------------|-----------------|---------------|-----------------|
| **Physician-assigned diagnosis, n (%)**† |                 |               |                 |
| Asthma                      | 2175 (61.4)     | 2108 (53.5)   | 1652 (44.1)     |
| Asthma+COPD                 | 243 (6.9)       | 626 (15.9)    | 523 (14.0)      |
| COPD                        | 1125 (31.8)     | 1206 (30.6)   | 1574 (42.0)     |
| **Sex, % female**           |                 |               |                 |
|                             | 1943 (54.8)     | 2071 (52.6)   | 1854 (49.5)     |
| **Age (years), mean ± SD**  |                 |               |                 |
|                             | 55.8 ± 16.9     | 59.3 ± 15.5   | 60.8 ± 14.5     |
| BMI (kg/m²), mean ± SD      |                 |               |                 |
|                             | 27.9 ± 6.4      | 28.2 ± 6.9    | 27.9 ± 6.7      |
| **N with data**             | 3349            | 3640          | 3496            |
| <18.5 kg/m², n (%)          | 85 (2.5)        | 97 (2.7)      | 165 (4.7)       |
| 18.5—<25.0 kg/m², n (%)     | 1088 (32.5)     | 1188 (32.6)   | 1101 (31.5)     |
| 25.0—<30.0 kg/m², n (%)     | 1134 (33.9)     | 1177 (32.3)   | 1128 (32.3)     |
| ≥30.0 kg/m², n (%)          | 1042 (31.1)     | 1178 (32.4)   | 1102 (31.5)     |
| **Smoking status, n (%)**   |                 |               |                 |
| Never smoked                | 1469 (41.6)     | 1384 (35.2)   | 1211 (32.4)     |
| Former smoker               | 1395 (39.5)     | 1826 (46.5)   | 1940 (51.9)     |
| Current smoker              | 667 (18.9)      | 717 (18.3)    | 586 (15.7)      |
| ≥1 allergy reported, n (%)  | 1806 (51.0)     | 1932 (49.0)   | 1690 (45.1)     |
| Allergy testing performed, n (%) | 872 (24.6)   | 930 (23.6)    | 1015 (27.1)     |
| Atopic, n (% of those with allergy testing) | 693 (79.5) | 701 (75.4)    | 815 (80.3)      |
| Diagnosis of emphysema, n (%) | 363 (10.2)   | 656 (16.6)    | 1099 (29.3)     |
| **Comorbidities, n (%)**    |                 |               |                 |
| Chronic bronchitis           | 133 (3.8)       | 178 (4.5)     | 193 (5.1)       |
| Bronchiectasis‡              | 109 (3.1)       | 191 (4.8)     | 308 (8.2)       |
| Obstructive sleep apnoea     | 227 (6.4)       | 357 (9.1)     | 347 (9.3)       |
| Allergic rhinitis            | 685 (19.3)      | 782 (19.8)    | 630 (16.8)      |
| Recurrent/chronic non-allergic rhinitis/sinusitis | 204 (5.8) | 278 (7.1)    | 240 (6.4)       |
| Nasal/sinus polyps           | 76 (2.1)        | 114 (2.9)     | 159 (4.2)       |
| Hypertension                 | 1039 (29.3)     | 1419 (36.0)   | 1318 (35.2)     |
| Coronary artery disease or myocardial infarction | 208 (5.9) | 331 (8.4) | 342 (9.1) |
| Congestive heart failure     | 34 (1.0)        | 67 (1.7)      | 108 (2.9)       |
| Other cardiovascular disease§ | 253 (7.1)       | 339 (8.6)     | 362 (9.7)       |
| Gastro-oesophageal reflux    | 504 (14.2)      | 639 (16.2)    | 591 (15.8)      |
| Depression or anxiety        | 565 (15.9)      | 599 (15.2)    | 495 (13.2)      |
| Type 2 diabetes              | 398 (11.2)      | 504 (12.8)    | 507 (13.5)      |
| Osteoporosis                 | 138 (3.9)       | 201 (5.1)     | 236 (6.3)       |
| Chronic kidney disease       | 40 (1.1)        | 75 (1.9)      | 70 (1.9)        |
| Inflammatory bowel disease   | 50 (1.4)        | 50 (1.3)      | 42 (1.1)        |
| Demographics, disease history and clinical characteristics of the total NOVELTY population, by physician-assigned severity* | Total | Mild (N=3543)* | Moderate (N=3940)* | Severe (N=3749)* |
|---|---|---|---|---|
| mMRC dyspnoea grade |  |  |  |  |
| N with data |  | 2370 | 2696 | 2679 |
| Grade ≥2, n (%) |  | 591 (16.7) | 1102 (28.0) | 2103 (56.1) |
| SGRQ total score, mean ± SD |  | 26.3 ± 18.8 | 32.1 ± 20.8 | 46.1 ± 21.6 |
| Overall health status, n (% of patients with non-missing data)** |  | 2370 | 2696 | 2679 |
| Very good |  | 306 (12.9) | 226 (8.4) | 106 (4.0) |
| Good |  | 1010 (42.6) | 1033 (38.3) | 723 (27.0) |
| Fair |  | 886 (37.4) | 1121 (41.6) | 1308 (48.8) |
| Poor |  | 148 (6.2) | 283 (10.5) | 445 (16.6) |
| Very poor |  | 20 (0.8) | 33 (1.2) | 97 (3.6) |
| CAAT total score, mean ± SD†† |  | 12.5 ± 7.7 | 14.4 ± 8.1 | 19.0 ± 8.5 |
| Post-bronchodilator FEV1 % predicted, mean ± SD‡‡ |  | 88.5 ± 17.9 | 78.4 ± 20.8 | 60.1 ± 24.9 |
| Post-bronchodilator FEV1/FVC, mean ± SD |  | 0.74 ± 0.11 | 0.68 ± 0.14 | 0.57 ± 0.18 |
| Bronchodilator responsiveness (%), mean ± SD |  | 5.3 ± 9.0 | 6.1 ± 9.8 | 8.6 ± 12.0 |
| N with data |  | 2841 | 3116 | 3072 |
| >12% and >200 mL, n (%) |  | 352 (12.4) | 457 (14.7) | 576 (18.8) |
| Exacerbations in the past 12 months, mean ± SD§§ |  | 0.4 ± 1.0 | 0.6 ± 1.2 | 1.2 ± 1.9 |
| N with data |  | 3520 | 3906 | 3722 |
| ≥1, n (%) |  | 838 (23.8) | 1254 (32.1) | 1916 (51.5) |
| ≥2, n (%) |  | 249 (7.1) | 474 (12.1) | 934 (25.1) |
| Healthcare utilisation, n (%)*** |  | 3520 | 3906 | 3722 |
| ≥1 hospital admission related to an exacerbation in the past 12 months |  | 68 (1.9) | 179 (4.6) | 501 (13.5) |
| Respiratory medications, n (%)**** |  | 3230 | 3845 | 3688 |
| N with medications data |  | 2919 | 3527 | 3426 |
| N with ICS dose data |  | 998 (30.9) | 819 (21.3) | 627 (17.0) |
| No ICS††† |  | 654 (20.2) | 477 (12.4) | 344 (9.3) |
| Short-acting BD, no ICS††† |  | 441 (13.7) | 576 (15.0) | 445 (12.1) |
| LABA and/or LAMA, no ICS††† |  | 255 (8.7) | 72 (2.0) | 18 (0.5) |
| Low-dose ICS |  | 517 (17.7) | 563 (16.0) | 164 (4.8) |
| Low-dose ICS+LABA |  | 586 (20.1) | 1039 (29.5) | 621 (18.1) |
| Med/high-dose ICS+LABA |  | 257 (8.0) | 770 (20.0) | 1296 (35.1) |
| ICS+LABA+LAMA†‡‡ |  | 56 (1.7) | 119 (3.1) | 345 (9.4) |
| Maintenance OCS |  | 16 (0.5) | 69 (1.8) | 542 (14.7) |
| Biologic therapy |  | 464 (14.4) | 762 (19.8) | 848 (23.0) |
TABLE S6 (continued) Demographics, disease history and clinical characteristics of the total NOVELTY population, by physician-assigned severity

|                                | Mild (N=3543)* | Moderate (N=3940)* | Severe (N=3749)* |
|--------------------------------|----------------|--------------------|------------------|
| Blood eosinophil count (10^9/μL), geo mean ± geo SD | 0.15 ± 1.95 | 0.16 ± 2.02 | 0.16 ± 2.06 |
| N without OCS/anti-IL-5/5R       | 1514           | 1679               | 1587             |
| Excluding patients with OCS/anti-IL-5/5R | 0.15 ± 1.96 | 0.16 ± 2.01 | 0.17 ± 2.02 |
| Blood eosinophil proportion (% of total leukocytes), geo mean ± geo SD | 2.12 ± 1.92 | 2.19 ± 1.99 | 1.89 ± 2.08 |
| Excluding patients with OCS, anti-IL-4/4R or anti-IL-5/5R | 2.17 ± 1.92 | 2.21 ± 1.98 | 1.97 ± 2.02 |
| Blood neutrophil count (10^9/μL), geo mean ± geo SD | 4.01 ± 1.42 | 4.23 ± 1.44 | 4.69 ± 1.47 |
| Blood neutrophil proportion (% of total leukocytes), geo mean ± geo SD | 54.24 ± 1.18 | 55.68 ± 1.17 | 52.61 ± 1.17 |
| FeNO (ppb), median (IQR)         | Excluding current smokers | 21 (13–35) | 21 (13–36) | 20 (12–34) |
| Current smokers                  | 12 (7–21)      | 10 (6–17.75)      | 10 (6–18)       |

For percentages, the denominator is given when different from the total number of patients (N with data [excluding ‘unknown’]). BD: bronchodilator; BMI: body mass index; CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; eCRF: electronic case report form; FeNO: fractional exhaled nitric oxide; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; geo: geometric; ICS: inhaled corticosteroid; IL-5/5R: interleukin-5 or interleukin-5 receptor; IQR: interquartile range; LABA: long-acting β₂-agonist; LAMA: long-acting muscarinic antagonist; Med: medium; mMRC: modified Medical Research Council; n: number of patients in the specified category; N: total number of patients; OCS: oral corticosteroid; PRO: patient-reported outcome; SD: standard deviation; SGRQ: St George’s Respiratory Questionnaire. Approximately 80% of patients had post-bronchodilator spirometry data, 70% had PRO data, 50% had biomarker data and >90% had complete data for other variables. *Recruitment was stratified by diagnosis/severity with the aim of achieving similar numbers of patients in each group. For patients with asthma+COPD, the severity category is the worse of the two physician-assigned severity classifications. Patients with COPD classified as ‘very severe’ were included in the ‘severe’ group. †From an eCRF entry under ‘Respiratory Comorbidities’ and/or from a record of abnormal CT findings. §Any cardiovascular disease other than hypertension, coronary artery disease, myocardial infarction, or congestive heart failure. §§The question that precedes the SGRQ: “please tick in one box to show how you describe your current health”. ††The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. †‡Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3]. §§Among all patients, including those with no exacerbations. Exacerbations include mild, moderate and severe exacerbations, from the following question in the eCRF: “During the past 12 months, on how many occasions has your patient experienced an exacerbation of their asthma or COPD beyond the patient’s usual day to day variance?” †††Medication categories are defined in table S2. ICS dose was classified according to Global Initiative for Asthma 2019 definitions [2]. †‡‡No ICS was defined as neither maintenance nor reliever ICS; ††††Without maintenance OCS or biologic therapy.
FIGURE S1 Criteria that physicians reported having used in making a diagnosis of asthma and/or COPD among patients diagnosed in the last 5 years.

Criteria were selected from a checklist including all of the listed items; multiple criteria could be selected. COPD=chronic obstructive pulmonary disease. CT: computed tomography. *Any lung function test includes spirometry, bronchodilator reversibility, peak expiratory flow or other lung function test. †Consistent with the recommendations of the Global Initiative for Asthma for initial diagnosis of asthma (before treatment) [4]. ‡Consistent with the criteria required by the Global Initiative for Chronic Obstructive Lung Disease for diagnosis of COPD [5].
FIGURE S2 Distribution of patient-reported symptoms and health status (A, B, C), and spirometry data (D, E, F) by physician-assigned diagnosis group and among all NOVELTY patients.
For continuous data, density is calculated as frequency divided by category width. The solid black lines show median values. Grey shading shows spirometric thresholds used in asthma/COPD diagnostic criteria [4, 5]. See table 2 and table S2 for the number of patients with spirometry and PRO data. CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; PRO: patient-reported outcome; SGRQ: St George's Respiratory Questionnaire. *The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. †Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3].
FIGURE S3 Heterogeneity in patient-reported symptoms and health status (A, B, C) and spirometry data (D, E, F) by physician-assigned diagnosis and/or severity.

A

![Bar charts for patient-reported symptoms and health status by diagnosis and severity level.](image)
For continuous data, density is calculated as frequency divided by category width. The solid black lines show median values. Grey shading shows spirometric thresholds used in asthma/COPD diagnostic criteria [4, 5]. See table 2 and table S2 for the number of patients with spirometry and PRO data. CAAT: Chronic Airways Assessment Test; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; SGRQ: St George’s Respiratory Questionnaire. *The CAAT is a trademark of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved. It has been modified from the COPD Assessment Test, with permission, by replacement of the term ‘COPD’ with ‘chronic airways’ and ‘pulmonary disease’ in the questionnaire title and instruction, respectively. †Global Lung Function Initiative multi-ethnic reference equations were used to calculate % predicted values [3].
FIGURE S4 Proportional odds ratios from multivariable ordinal regression models for factors associated with physician-assigned severity in patients with asthma or COPD overall (A) and for asthma and COPD separately (B)

A

| Variable                                      | Overall | Proportional OR | 95% CI  |
|-----------------------------------------------|---------|-----------------|---------|
| Age (per +10 years)                          | 0.85    | [0.82–0.88]     |         |
| Underweight (vs normal)*                     | 1.37    | [1.04–1.80]     |         |
| Overweight (vs normal)*                      | 0.99    | [0.88–1.11]     |         |
| Obese (vs normal)*                           | 0.85    | [0.75–0.96]     |         |
| Current smoker (vs never/former)             | 0.55    | [0.48–0.62]     |         |
| Time since diagnosis (per +10 years)         | 1.15    | [1.11–1.19]     |         |
| ≥1 exacerbation past year†                   | 1.77    | [1.60–1.95]     |         |
| Post-BD FEV1 (% predicted (per –10%)         | 1.32    | [1.28–1.37]     |         |
| Post-BD FEV1/FVC (per –10%)                  | 1.29    | [1.22–1.36]     |         |
| BD resp ≥12% and ≥200 mL, yes vs no          | 1.24    | [1.08–1.41]     |         |
| mMRC dyspnoea (per higher grade)             | 1.67    | [1.58–1.76]     |         |
| Allergic rhinitis, yes vs no†                | 1.41    | [1.25–1.59]     |         |
| Non-allergic rhinitis, yes vs no‡            | 1.59    | [1.31–1.91]     |         |
| Nasal/sinus polyps, yes vs no‡               | 2.19    | [1.67–2.86]     |         |
| Diagnosis of emphysema, yes vs no            | 1.16    | [1.01–1.35]     |         |

Odds ratio (95% CI) | N=7292

B

| Variable                                      | Asthma | COPD |
|-----------------------------------------------|--------|------|
| Age (per +10 years)                          | 0.91   | 1.07 | [0.97–1.17]     |
| Underweight (vs normal)*                     | 1.41   | 1.37 | [0.88–2.14]     |
| Overweight (vs normal)*                      | 1.03   | 1.05 | [0.86–1.29]     |
| Obese (vs normal)*                           | 0.92   | 0.90 | [0.79–1.07]     |
| Current smoker (vs never/former)             | 0.73   | 0.76 | [0.59–0.90]     |
| Time since diagnosis (per +10 years)         | 1.06   | 1.14 | [1.02–1.11]     |
| ≥1 exacerbation past year†                   | 1.85   | 1.62 | [1.63–2.09]     |
| Post-BD FEV1 (% predicted (per –10%)         | 1.21   | 1.80 | [1.17–1.26]     |
| Post-BD FEV1/FVC (per –10%)                  | 1.35   | 1.26 | [1.25–1.45]     |
| BD resp ≥12% and ≥200 mL, yes vs no          | 1.21   | 1.35 | [1.03–1.42]     |
| mMRC dyspnoea (per higher grade)             | 1.69   | 1.75 | [1.57–1.82]     |
| Allergic rhinitis, yes vs no†                | 1.30   | 0.86 | [1.14–1.48]     |
| Non-allergic rhinitis, yes vs no‡            | 1.50   | 0.97 | [1.23–1.84]     |
| Nasal/sinus polyps, yes vs no‡               | 1.81   | 2.18 | [1.37–2.38]     |
| Diagnosis of emphysema, yes vs no            | 0.88   | 1.65 | [0.56–1.37]     |

Odds ratio (95% CI) | N=4361 | N=2931

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Proportional odds ratios represent the odds of having higher physician-assigned severity (severe vs mild or moderate, moderate vs mild) per the increment stated for continuous variables, or for different levels of categorical variables (vs their reference). See supplementary material page 2 for details of the methodology.

Patients with asthma+COPD were excluded because, for them, the severity category was assigned as the higher of the physician’s two severity classifications for asthma and for COPD. Only patients without missing data for the selected variables were included. Univariate associations are shown in figure S5. *Body mass index categories (kg/m²): underweight: <18.5, normal: 18.5 to <25, overweight: 25 to <30, obese: ≥30. †Exacerbations include mild, moderate and severe exacerbations, from the following question in the eCRF: “During the past 12 months, on how many occasions has your patient experienced an exacerbation of their asthma or COPD beyond the patient’s usual day to day variance?” ‡Comorbidities were recorded by the physician via a checklist; therefore, the ‘no’ group includes both ‘not present’ and ‘unknown’. BD: bronchodilator; CI: confidence interval; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; N: total number of patients; OR: odds ratio; Resp: responsiveness.

Summary of findings for panel A: Multivariable ordinal regression analysis among all patients with asthma or COPD showed that several clinical and spirometric factors were associated with greater physician-assessed severity. Notably, current smoking was associated with lower severity classification than never/former smoking; obesity was also independently associated with lower severity.

Summary of findings for panel B: Multivariable ordinal regression analyses for asthma and COPD separately showed that higher mMRC dyspnoea grade, longer time since diagnosis, ≥1 exacerbation in the previous year, bronchodilator responsiveness and lower post-bronchodilator FEV₁/FVC were associated with greater severity in both asthma and COPD. Younger age, allergic and non-allergic rhinitis and nasal or sinus polyps were associated with greater severity of asthma, together with allergic and non-allergic rhinitis and nasal or sinus polyps, whereas a diagnosis of emphysema was associated with greater severity of COPD, independent of lung function. The post-bronchodilator FEV₁ % predicted was more strongly associated with severity in COPD than in asthma.
FIGURE S5 Proportional odds ratios from univariate ordinal regression models for factors associated with physician-assigned severity in patients with physician-assigned diagnoses of asthma or COPD

| Variable                                      | Asthma | Proportional OR | 95% CI      | COPD | Proportional OR | 95% CI      |
|-----------------------------------------------|--------|-----------------|-------------|------|-----------------|-------------|
| Female (vs male)                              | 0.95   | [0.85–1.06]     | 0.90        | [0.79–1.04]     |
| Underweight (vs normal)*                      | 1.61   | [1.13–2.28]     | 2.15        | [1.49–3.09]     |
| Overweight (vs normal)*                       | 1.08   | [0.94–1.24]     | 0.72        | [0.61–0.85]     |
| Obese (vs normal)*                            | 1.26   | [1.09–1.44]     | 0.68        | [0.58–0.81]     |
| Former smoker (vs never)                      | 1.02   | [0.90–1.15]     | 1.36        | [1.03–1.81]     |
| Current smoker (vs never)                     | 0.89   | [0.73–1.09]     | 0.78        | [0.56–0.89]     |
| Time since diagnosis (per +10 years)          | 1.15   | [1.11–1.18]     | 1.47        | [1.34–1.62]     |
| Exacerbations past year (per 1)†             | 2.42   | [2.16–2.72]     | 2.75        | [2.38–3.18]     |
| Post-BD FEV (per –10%)                        | 1.41   | [1.37–1.46]     | 2.25        | [2.14–2.36]     |
| Post-BD FVC (per –10%)                        | 1.75   | [1.66–1.85]     | 2.32        | [2.19–2.45]     |
| BD resp ≥12 and ≥200 mL, yes vs no           | 1.77   | [1.53–2.06]     | 1.16        | [0.95–1.41]     |
| mMRC dyspnea (per higher grade)               | 1.94   | [1.82–2.08]     | 2.49        | [2.32–2.69]     |
| Diagnosis of emphysema, yes vs no             | 0.99   | [0.65–1.52]     | 2.77        | [2.40–3.20]     |
| Atopy confirmed by test, yes vs no            | 1.53   | [1.36–1.73]     | 1.02        | [0.74–1.41]     |
| Allergic rhinitis, yes vs no†                 | 1.09   | [0.97–1.23]     | 0.84        | [0.63–1.14]     |
| Non-allergic rhinitis, yes vs no              | 1.52   | [1.26–1.84]     | 0.73        | [0.48–1.11]     |
| Nasal/sinus polyps, yes vs no†                | 2.23   | [1.72–2.87]     | 1.65        | [0.56–4.74]     |
| Obstructive sleep apnoea, yes vs no          | 1.36   | [1.09–1.69]     | 1.04        | [0.83–1.31]     |
| Gastro-oesophageal reflux, yes vs no          | 1.34   | [1.15–1.57]     | 0.72        | [0.60–0.87]     |
| Depression or anxiety, yes vs no              | 0.90   | [0.78–1.04]     | 0.88        | [0.75–1.04]     |
| Cardiovascular disease, yes vs no             | 1.07   | [0.86–1.33]     | 1.27        | [1.08–1.48]     |
| Type 2 diabetes, yes vs no                   | 1.24   | [1.02–1.51]     | 0.93        | [0.77–1.11]     |
| Osteoporosis, yes vs no                       | 1.37   | [1.04–1.80]     | 1.19        | [0.88–1.60]     |
| Chronic kidney disease, yes vs no             | 1.07   | [0.60–1.91]     | 1.35        | [0.86–2.14]     |
| Inflammatory bowel disease, yes vs no         | 0.32   | [0.58–1.45]     | 0.78        | [0.39–1.56]     |
Proportional odds ratios represent the odds of having higher physician-assigned severity (severe vs mild or moderate, moderate vs mild) per the increment stated for continuous variables, or for different levels of categorical variables (vs their reference). See supplementary material page 2 for details of methodology. Patients with asthma+COPD were excluded because for them, the severity category was assigned as the higher of the physician’s two severity classifications for asthma and for COPD. Only patients without missing data for the selected variables were included. Body mass index categories (kg/m²): underweight: <18.5, normal: 18.5 to <25, overweight: 25 to <30, obese: ≥30. Exacerbations include mild, moderate and severe exacerbations, from the following question in the eCRF: “During the past 12 months, on how many occasions has your patient experienced an exacerbation of their asthma or COPD beyond the patient’s usual day to day variance?” Comorbidities were recorded by the physician via a checklist; therefore, the ‘no’ group includes both ‘not present’ and ‘unknown’. BD: bronchodilator; CI: confidence interval; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; mMRC: modified Medical Research Council; N: total number of patients; OR: odds ratio; Resp: responsiveness.
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