There is growing interest in asthma–chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) [1, 2]. Yet, there is no consensus on the best definition of ACOS [1, 2] and, therefore, it is difficult to appropriately characterise these patients. Here, we compare the main clinical characteristics and outcomes of COPD patients with and without ACOS in the ECLIPSE cohort [3] according to six different definitions of ACOS.

The design and methodology used in the ECLIPSE study (ClinicalTrials.gov identifier: NCT00292552; GSK study code SCO104960) have been published elsewhere [3]. ECLIPSE was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committees of participating centres. All participants signed their written consent [3].

The current analysis is restricted to COPD patients (n=1976, 91.3% of the total population studied in ECLIPSE) with a recorded response to the question in the ATS-DLD-78A questionnaire “Have you ever had asthma?” [4]. For the primary study definition, COPD patients answering “yes” were considered to have ACOS. Besides, we considered five additional features of airways disease in conjunction to ACOS: 1) presence of bronchodilator reversibility at recruitment (change in forced expiratory volume in 1 s (FEV1) ≥12% and ≥200 mL); 2) presence of current asthma (affirmative answer to two questions: “Have you ever had asthma?” and “Do you still have it?”); 3) presence of wheeze (affirmative answer to the question “Does your chest ever sounds wheezy or whistling?”); 4) presence of atopy (affirmative answer to the question “Have you ever had hay fever?”); and 5) presence of both wheeze and atopy.

Results are presented as n (%), mean±SD or median (IQR), as appropriate. Groups were compared using the Wilcoxon and Chi-squared tests for continuous and categorical variables, respectively. Negative binomial regression (risk ratios) and multiple regression (least squared mean differences) were used to compare clinically relevant outcomes (exacerbations during follow-up and St. George Respiratory Questionnaire (SGRQ) scores) in patients with and without ACOS, after adjustment for age, sex, baseline FEV1 % and previous exacerbation history. Patients with missing post-bronchodilator FEV1 (or any other missing covariate) were not included in the adjusted analyses.

The main results (table 1) showed that 493 (25%) patients had ACOS according to the primary definition used, and 462 (94%) of them reported that their diagnosis of asthma had been confirmed by a doctor. Patients with ACOS were slightly younger, more often female, had a longer duration of COPD and used respiratory medications and statins more often. They had slightly less cumulative smoking exposure but the proportion of former smokers was similar between groups. The prevalence of chronic bronchitis and emphysema was also similar, as was the average FEV1 before and after bronchodilation. The proportions of co-morbidities were higher in ACOS patients (66% had at least one of osteoporosis, osteoarthritis, reflux/heartburn, depression requiring treatment or anxiety/panic attacks, compared with 43% in COPD patients without ACOS). They also had a higher proportion of autoimmune disease (11% had rheumatoid arthritis and inflammatory bowel diseases, compared with 5% in those without ACOS). The reported prevalence of cardiovascular diseases was similar in both groups. The circulating levels of eosinophils and several inflammatory biomarkers (determined as detailed elsewhere [5]) were also similar between groups except for plasma fibrinogen, which was higher in patients with ACOS (table 1).

After adjusting for age, sex, baseline FEV1, and prior exacerbation history, the SGRQ total score was higher in patients with ACOS (LS mean difference 3.1, 95% confidence interval 1.2–5.0). Adjusted exacerbation rates during follow-up were also more frequent in patients with ACOS (RR 1.32, 95% CI 1.19–1.46). Mortality rates during follow-up were similar in COPD patients with (10%) and without (9%) ACOS.

Among the 493 patients that reported ever having had asthma, 432 (88%) also reported wheeze, 353 (72%) reported current asthma, 135 (27%) reported atopy and 127 (26%) reported both wheeze and atopy. Demographics and clinical characteristics of patients stratified according to these additional features were similar to those of patients with ACOS as defined by the primary definition alone (data not shown). On the other hand, 111 patients with ACOS (23%) had significant bronchodilator reversibility (as defined above). Although the number of patients in this group is small, it seemed to include fewer females, patients with COPD duration greater than 10 years, and patients with lower SGRQ total scores (data not shown).
These findings confirm prior research demonstrating that patients with ACOS are younger, and more likely to be female, report more symptoms, experience more exacerbations and have worse health-status than COPD patients [6–10]. We found that BMI was similar between groups (table 1) also in keeping with prior literature [7, 9] with the exception of a National Health and Nutrition Examination Survey study that noted a higher proportion of obese patients with ACOS [11]. The fact that patients with ACOS had a lower smoking exposure is also consistent with published studies [7, 12]. Previous reports found significantly higher concentrations of blood and sputum eosinophils in ACOS patients [12], but we could not reproduce these observations. By contrast, we found that plasma fibrinogen and serum TNF-α concentration were slightly higher in ACOS, an observation that is consistent with its association with worse outcomes in COPD [5].

Our study provides two novel observations of potential relevance, depicted in figure 1. Firstly, symptoms and exacerbations were higher among ACOS patients than COPD patients, irrespective of their severity of airflow limitation, age, sex, lung function and exacerbation history. Secondly, we found that patient demographics and clinical characteristics did not differ substantially when the diagnosis of ACOS was established using several different definitions. Yet, it has some limitations that deserve comment. First, because ECLIPSE patients were mostly recruited in secondary and tertiary hospitals, results may not be generalisable to milder COPD or patients in primary care. Second, many of the study characteristics are based on patient self-report. Third, our airflow limitation reversibility categorisation considered reversibility status at recruitment only, whereas it may vary with time [13]. Fourth, almost all patients included in ECLIPSE were of Caucasian origin (98%), so our ability to examine a potential ethnic effect was limited. Finally, the molecular basis of the observed differences between ACOS and COPD is unclear and deserves specific focus in future research.
In summary, these results help to better characterise ACOS and suggest that its primary definition is not sensitive to the addition of specific clinical criteria related to asthma. These findings may assist in the development of optimal strategies for the definition and management of ACOS, as ACOS patients may need closer medical supervision.

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ECLIPSE offers an opportunity to examine ACOS in a large well-characterised COPD cohort followed over 3 years http://ow.ly/Zcycr

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