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ORIGINAL RESEARCH

Prevalence and Characteristics of Asthma–Chronic Obstructive Pulmonary Disease Overlap in Routine Primary Care Practices

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Abstract

Rationale: Adults may exhibit characteristics of both asthma and chronic obstructive pulmonary disease (COPD), a situation recently described as asthma–COPD overlap (ACO). There is a paucity of information about ACO in primary care.

Objectives: To estimate the prevalence and describe characteristics of individuals with ACO in primary care practices among patients currently diagnosed with asthma, COPD, or both; and to compare the prevalence and characteristics of ACO among the three source populations.

Methods: The Respiratory Effectiveness Group conducted a cross-sectional study of individuals ≥40 years old and with ≥2 outpatient primary care visits over a 2-year period in the UK Optimum Patient Care Research Database. Patients were classified into one of three source populations based on diagnostic codes: *1)* COPD only, *2)* both asthma and COPD, or *3)* asthma only. ACO was defined as the presence of all of the following *1)* age ≥40 years, *2)* current or former smoking, 3) post-bronchodilator airflow limitation (forced expiratory volume in 1 second/forced vital capacity <0.7), and 4) ≥12% and ≥200 ml reversibility in post-bronchodilator forced expiratory volume in 1 second.

Results: Among 2,165 individuals (1,015 COPD only, 395 with both asthma and COPD, and 755 asthma only), the overall prevalence of ACO was 20% (95% confidence interval, 18–23%). Patients with ACO had a mean age of 70 years (standard deviation, 11 yr), 60% were men, 73% were former smokers (the rest were current smokers), and 66% were overweight or obese. Comorbid conditions were common in patients with ACO, including diabetes (53%), cardiovascular disease (36%), hypertension (30%), eczema (23%), and rhinitis (21%). The prevalence of ACO was higher in patients with a diagnosis of both asthma and COPD (32%) compared with a diagnosis of COPD only (20%; $P < 0.001$) or asthma only (14%; $P < 0.001$). Demographic and clinical characteristics of ACO varied across these three source populations.

Conclusions: One in five individuals with a diagnosis of COPD, asthma, or both asthma and COPD in primary care settings have ACO based on the Respiratory Effectiveness Group ACO Working group criteria. The prevalence and characteristics of patients with ACO varies across the three source populations.

Keywords: asthma–COPD overlap; asthma; comorbidities; COPD; primary care

Asthma and chronic obstructive pulmonary disease (COPD) are respiratory conditions defined by the presence of airflow limitation that is typically variable in asthma and persistent in COPD. In clinical practice, it has long been recognized that some patients present with characteristics consistent with both asthma and COPD (1). Yet, there is limited evidence on the optimal approach to evaluate and manage this population, because they are typically excluded from clinical trials (2, 3).

In 2014, the Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) published a joint statement proposing the term "asthma–COPD overlap syndrome" (ACOS) to refer to individuals with features of both conditions (4). GINA and GOLD subsequently revised the term ACOS to "asthma–COPD overlap" (ACO) to reduce the likelihood that clinicians would regard ACOS as a single entity or disease rather that an umbrella term comprising many phenotypes (5). Guidelines (e.g., from Spain, Czech Republic, and Finland) have similarly identified the need to acknowledge individuals with features of both asthma and COPD and the paucity of evidence to guide their care (6–8).

The GINA and GOLD joint statements describe 11 clinical characteristics that may be used to distinguish asthma from COPD and identify patients with ACO (exhibiting a similar number of asthma and COPD features), including age, lung function, and comorbid conditions (3–5). The joint statement also acknowledges the paucity of evidence to support these recommendations and that further research is essential. Various groups have subsequently used different criteria for the diagnosis of ACO, so not surprisingly have reported a wide range of prevalences (~10–50%) (9–16).

Although most patients with asthma or COPD receive health care in primary care settings, there is limited information about the prevalence and characteristics of individuals with ACO in these settings. Also, to our knowledge, no studies have compared the prevalence and characteristic of individuals with features suggestive of ACO according to the source population (e.g., those currently diagnosed with asthma only vs. COPD only vs. both diagnoses). The Respiratory Effectiveness Group (REG) ACO Working Group therefore conducted a study that included two objectives: to estimate the prevalence and describe characteristics of individuals with ACO in primary care practices among patients currently diagnosed with asthma, COPD, or both asthma and COPD; and to compare the prevalence and characteristics of ACO within the three source populations. To increase the generalizability of our findings to "real-world" patients in primary care settings, the REG ACO Working group used clinical information documented in primary care practices to define ACO. Results of the current study are intended to support the design of subsequent longitudinal observational studies that will estimate the clinical and economic burden of ACO in primary care, and practice-based clinical trials of different management strategies for individuals with ACO in primary care.

Methods

REG ACO Working Group
This working group is a group of primary care and specialist clinicians and researchers from 14 countries with expertise in comparative effectiveness research in respiratory medicine (17–19).

Data Source and Ethics
The Optimum Patient Care Research Database (OPCRD) contains anonymized demographic, clinical, and physiological data from primary care practices in the United Kingdom. At the time of the study, the OPCRD contained longitudinal medical records from 576 practices. Clinical diagnoses (including asthma, COPD, and both) are recorded in the OPCRD as "Read codes," a dictionary of clinical codes routinely used by general practitioners in the UK National Health Service. Read code lists are created for the OPCRD through consensus by a panel of UK clinical academics with expertise working in (and coding) primary care respiratory medicine. The Read code lists for the OPCRD are routinely reviewed to ensure they remain up to date and follow the model previously validated for the Clinical Practice Research Datalink, another large UK primary care database (20). The OPCRD has been approved for clinical research use by the Health Research Authority of the UK National Health System (REC reference #15/EM/0150) (21).

The study was conducted in line with the Strengthening the Reporting of Observational Studies in Epidemiology Statement for observational research and included an *a priori* research plan, study registration with commitment to publish, and an independent steering committee not remunerated for their participation (22). The study protocol was developed by a REG ACO Working Group, approved by the OPCRD's independent Anonymized Ethics and Protocol Transparency Review Committee (ADEPT1316), and registered with the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP; reference: EUPAS13959). Written informed consent was not necessary because of the deidentified nature of the data and because patients are given the option to prohibit use of their data for research.

Study Design
This was a cross-sectional study using data from clinical encounters (visits) documented in the OPCRD from January 1, 2014, through December 31, 2015.

Study Population
Patients were eligible if they had at least two outpatient visits in primary care during the 2-year study period; no missing data for

information used to identify individuals with ACO (see DEFINITION OF ACO); were at least 40 years old; and had a diagnosis (i.e., had a Read code) of asthma, COPD, or both asthma and COPD (see Figure E1 in the online supplement). Patients were classified into one of three source populations according to the documentation in the OPCRD: 1) COPD only: two visits with a COPD diagnosis and no visits with a diagnosis of asthma; 2) both asthma and COPD: one visit with an asthma diagnosis and one visit with a COPD diagnosis, or two visits with diagnoses of both asthma and COPD; or 3) asthma only: two visits with an asthma diagnosis and no visits with a diagnosis of COPD. In individuals with more than two primary care outpatient visits over a 2-year period, we used the information documented at the two most recent visits.

Definition of ACO

Various publications have used a range of criteria for ACO, indicating the lack of consensus on a definition for ACO (6–16). Previous studies have defined ACO as self-reported asthma in individuals with post-bronchodilator (post-BD) airflow limitation (10), *International Classification of Diseases* codes for both asthma and COPD (14), and a combination of criteria (e.g., post-BD airflow limitation, a history of smoking at least 10 pack-years or equivalent indoor or outdoor air pollution, asthma diagnosis before the age of 40 yr, and peripheral blood eosinophilia) (16). To estimate the prevalence of ACO that would be applicable to a real-world primary care setting, rather than in subspecialty care settings or using data collected as part of cohort studies or clinical trials, the REG ACO Working

Group elected to define ACO on the basis of information documented by clinicians in primary care. We did not rely on a clinician diagnosis of both asthma and COPD to define ACO. In this report, ACO is defined as the presence of all four of the following: 1) age $\geq$40 years, 2) current or former smoking, 3) post-BD airflow limitation (forced expiratory volume in 1 second [FEV_1]/forced vital capacity <0.7), and 4) a post-BD response ($\geq$12% and $\geq$200 ml reversibility in post-BD FEV_1). Smoking history was based on the question: "What best describes you? A) Never smoked, B) Used to smoke, but don't now, C) Still smoking." Individuals who reported they were B or C were considered as current or former smokers. Documentation of pack-years smoked was inconsistent, so we did not require a specific threshold of pack-years smoked. Because we intended to assess and compare the prevalence and characteristics of ACO in three source populations (diagnosis of asthma, COPD, or both), we did not include these diagnoses as criteria for ACO.

Demographic and Clinical Characteristics

We queried the OPCRD to collect information on age, sex, smoking history (current, former, never), physician-recorded comorbid diagnoses, height, and weight. We calculated the body mass index (BMI) and categorized individuals as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese ($\geq$30 kg/m^2) (23).

Analyses

Descriptive statistics used means, standard deviations, and proportions with 95%

confidence intervalss. Student's *t* tests and chi-square tests, where appropriate, were used to compare the prevalence of ACO and their clinical characteristics across the three source populations. A two-tailed *P* value <0.05 defined a significant difference. We did not adjust for multiple comparisons across the different source populations, because these were exploratory (rather than confirmatory) hypothesis tests.

Results

Prevalence and Characteristics of ACO in the Combined Study Population

Of 233,054 healthcare encounters with two or more primary care visits over a 2-year period, information needed to apply the REG ACO Working Group definition of ACO was not available in 229,285 (98%) visits (see online supplement). Of 3,433 individuals at least 40 years of age in whom there was sufficient information to apply the ACO criteria, 1,015 (30%) had a diagnosis of COPD only, 395 (11%) had diagnoses of both asthma and COPD, 755 (22%) had a diagnosis of asthma only, and 1,268 (37%) did not have diagnosis of asthma or COPD.

Table 1. ACO prevalence in the source populations

	Diagnosis of COPD Only (n = 1,015)	Diagnosis of Both Asthma and COPD (n = 395)	Diagnosis of Asthma Only (n = 755)	All (n = 2,165)
ACO prevalence	20.5% (208/1,015) 95% CI, 18.0–23.1%	32.1% (127/395) 95% CI, 27.6–37.0%	14.4% (109/755) 95% CI, 12.0–17.1%	20.5% (444/2,165) 95% CI, 18.8–22.2%
P value (vs. both asthma and COPD)	*P* < 0.001	Reference	*P* < 0.001	Not applicable

Definition of abbreviations: ACO = asthma–COPD overlap; CI = confidence interval; COPD = chronic obstructive pulmonary disease.
P values denote comparisons with ACO within individuals currently diagnosed as both asthma and COPD (Reference population).
Prevalence is defined as the proportion of individuals in each source population (diagnosis of COPD only, both asthma and COPD, and asthma only among those who were at least 40 yr old) with documentation of all of the following: history of current or past smoking, post-bronchodilator airflow limitation, and post-bronchodilator reversibility (see METHODS for details).

In the 2,165 individuals with a diagnosis of COPD, asthma, or both (three "source populations"), 444 (20%; 95% confidence interval, 19–22%) met the REG ACO Working Group criteria for ACO (Table 1). Individuals with ACO had a mean age of 70 years, 60% were men, 73% were former smokers, and 66% were overweight or obese. Comorbid conditions were common in patients with ACO; the five most common comorbid conditions were diabetes (53%), cardiovascular disease (36%), hypertension (30%), eczema (23%), and rhinitis (21%) (Table 2).

Prevalence and Characteristics of ACO within Each Source Population

The prevalence of ACO in individuals with a diagnosis of both asthma and COPD (32%) was significantly higher than in those with a diagnosis of COPD only (20%) (Figures 1 and 2) or asthma only (14%) (Figure 3) ($P < 0.001$ for each pair-wise comparison) (Table 1). The lack of post-BD reversibility was the most common reason that patients with COPD only (53%; 542/1,015) (Figure 1) or both asthma and COPD (30%; 117/395) (Figure 2) did not meet ACO criteria. By contrast, the absence of a smoking history was the most common reason that patients with asthma only did not meet criteria for ACO (43%; 326/755) (Figure 3).

Sex and the prevalence of several common (e.g., diabetes, cardiovascular disease, hypertension, and eczema) and less common (e.g., bronchiectasis, heart failure, and cerebrovascular disease) comorbid

conditions were not significantly different in the individuals with ACO across the three source populations (Table 2). Conversely, individuals with ACO within the COPD-only population were older (mean age, 72 vs. 68 yr; $P = 0.04$), more likely to be current smoker (29 vs. 17%; $P = 0.03$), had a lower BMI (e.g., 58 vs. 76% were overweight or obese), were less likely to have rhinitis (17 vs. 33%; $P < 0.01$), and more likely to have chronic kidney disease (14 vs. 6%; $P = 0.04$) compared with those with ACO within the asthma-only population.

There were fewer differences in clinical characteristics when comparing individuals with ACO within the group diagnosed as both asthma and COPD compared with those within the asthma-only or within the COPD-only populations. Compared with

Table 2. Clinical characteristics of patients with ACO identified within each source population

Characteristics		All ACO (n = 444)	COPD Only (n = 208)	Both Asthma and COPD (n = 127)	Asthma Only (n = 109)	COPD Only versus Asthma Only, P Value	COPD Only versus Both Asthma and COPD, P Value	Asthma Only versus Both Asthma and COPD, P Value
Age*	yr, mean (SD)	70.0 (10.6)	72.0 (10.1)	68.4 (10.5)	68.1 (11.1)	0.04	0.04	0.73
Sex	Male	264 (59.5)	131 (63.0)	71 (55.9)	62 (56.9)	0.30	0.20	0.80
Smoking history*	Current smoker	118 (26.6)	60 (28.9)	39 (30.7)	19 (17.4)	0.03	0.72	0.02
	Former smoker	326 (73.4)	148 (71.1)	88 (69.3)	90 (82.6)			
BMI*	Underweight	15 (3.4)	11 (5.3)	2 (1.6)	2 (1.8)	0.01	0.03	0.72
	Normal weight	136 (30.6)	76 (36.5)	36 (28.4)	24 (22.0)			
	Overweight	160 (36.0)	73 (35.1)	44 (34.7)	43 (39.5)			
	Obese	133 (30.0)	48 (23.1)	45 (35.4)	40 (36.7)			
Comorbidities	Diabetes	236 (53.2)	112 (53.9)	64 (50.4)	50 (55.1)	0.84	0.54	0.47
	Cardiovascular disease	161 (36.3)	81 (38.9)	38 (29.9)	42 (38.5)	0.94	0.10	0.16
	Hypertension	134 (30.2)	66 (31.7)	34 (26.8)	34 (31.2)	0.92	0.34	0.46
	Eczema	101 (22.8)	50 (24.0)	24 (18.9)	27 (24.8)	0.90	0.27	0.27
	Rhinitis*	95 (21.4)	36 (17.3)	23 (18.1)	36 (33.0)	<0.01	0.85	0.01
	Ischemic heart disease	91 (20.5)	48 (23.1)	23 (18.1)	20 (18.4)	0.33	0.28	0.96
	Gastroesophageal reflux	81 (18.2)	38 (18.3)	21 (16.5)	22 (20.2)	0.68	0.69	0.88
	Chronic kidney disease*	51 (11.5)	30 (14.4)	14 (11.0)	7 (6.4)	0.04	0.37	0.21
	Osteoporosis	41 (9.2)	20 (9.6)	14 (11.0)	7 (6.4)	0.33	0.68	0.22
	Anxiety or depression	37 (8.3)	16 (7.7)	10 (7.9)	11 (10.1)	0.47	0.95	0.51
	Myocardial infarction	34 (7.7)	17 (8.2)	10 (7.9)	7 (6.4)	0.58	0.92	0.67
	Cerebrovascular disease	27 (6.1)	15 (7.2)	4 (3.2)	8 (7.3)	0.97	0.12	0.14
	Heart failure	21 (4.7)	12 (5.6)	6 (4.7)	3 (2.8)	0.23	0.68	0.43
	Bronchiectasis	18 (4.1)	10 (4.8)	6 (4.7)	2 (1.8)	0.20	0.97	0.22

Definition of abbreviations: ACO = asthma–COPD overlap; BMI = body mass index; COPD = chronic obstructive pulmonary disease; SD = standard deviation.
Comorbidities as recorded in clinical documentation.
Values represent n (%), unless otherwise indicated.
BMI categorized as underweight (<18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), or obese (≥30 kg/m²).
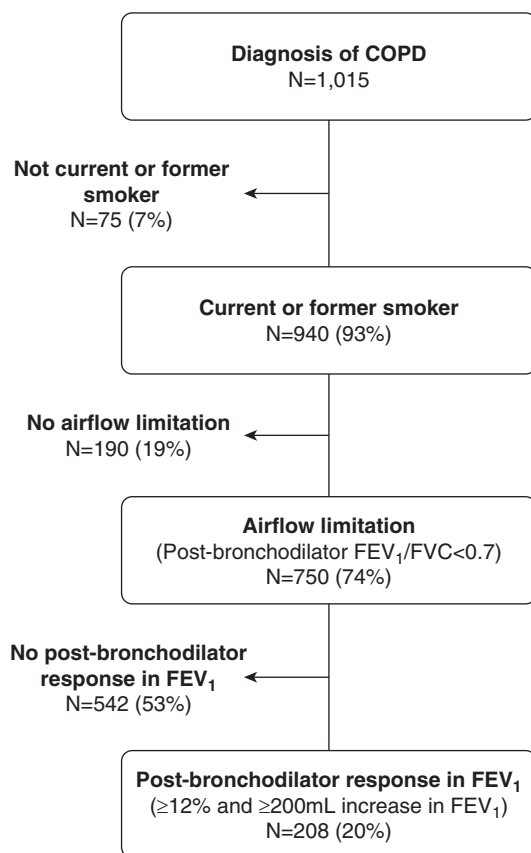*$P < 0.05$ for each pairwise comparison.

Figure 1. Asthma–chronic obstructive pulmonary disease (COPD) overlap (ACO) in patients with a current diagnosis of COPD only. Among individuals with a current diagnosis of COPD only, 208/1,015 (20.5%) met Respiratory Effectiveness Group ACO Working Group criteria for ACO. The most common reason for not meeting criteria for ACO is the lack of a post-bronchodilator response in forced expiratory volume in 1 second (542/1,015; 53.3%). FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

asthma and COPD to define ACO and reported a prevalence of ACO of 6 per 1,000 population, compared with 30 per 1,000 population for COPD only (14). Our study contributes to the literature on ACO in primary care by using an expanded combination of patient-reported and lung function criteria to define ACO (age ≥40 yr, current or former smoking, post-BD airflow limitation, and a post-BD response in FEV_1) and by comparing the prevalence of ACO within three different source populations (current diagnosis of COPD only, asthma only, or both asthma and COPD). The results indicate that about one in five individuals diagnosed with COPD only and about one in seven individuals diagnosed with asthma only in primary care meet the REG ACO Working Group criteria for ACO. In a review of studies conducted in 19 different countries, the prevalence of ACO varied from 11% to 61% of patients with a diagnosis of asthma and 4% to 66% of patients with a diagnosis of COPD (24). A range of ACO definitions were used in these various studies and likely contributed to 5- to 10-fold range in the estimates of ACO prevalence.

The estimates of the prevalence of ACO presented in our study are consistent with these previous reports, but our report is unique in presenting the prevalence ACO using the same criteria in three different source populations (patients with a diagnosis of COPD only, patients with a diagnosis of both asthma and COPD, patients with a diagnosis of asthma only). We are now planning to test the ACO definition used in this report in other populations, which will help us more directly assess the generalizability of findings. In addition, we found that only one in three individuals currently diagnosed with both asthma and COPD meet the REG ACO Working Group criteria for ACO, calling into question the basis on which this combination of diagnoses is made in primary care. More than 20% (86/395) of patients with a current diagnosis of both asthma and COPD in our report failed to demonstrate post-BD airflow limitation, suggesting a possible overdiagnosis of COPD in patients with asthma, although even in populations with asthma reversibility is known to be variable between and within individuals.

We also noted differences in some demographic and clinical characteristics (e.g., age, smoking history, BMI, and some

individuals with ACO within the COPD-only source population, those with ACO within the group with a diagnosis of both asthma and COPD were younger (68 vs. 72 yr; $P = 0.04$) and had higher BMI (e.g., 70 vs. 58% were overweight or obese). By contrast, compared with individuals with ACO within the asthma-only source population, those with ACO within the both asthma and COPD population were more likely a current smoker (31 vs. 17%; $P = 0.02$) and less likely to have rhinitis (18 vs. 33%; $P = 0.01$).

Discussion

In this cross-sectional study in primary care practices, approximately one in five patients with a current diagnosis of COPD, asthma, or both conditions fulfilled the REG

Working Group definition for ACO. Individuals with ACO were in the sixth decade, were predominantly men, former smokers, overweight or obese, and had various comorbid conditions. The prevalence of ACO varied according to the source population. ACO prevalence was highest among individuals with a current diagnosis of both asthma and COPD, and lowest in individuals with a diagnosis of asthma only, chiefly because of absence of smoking history. Demographic and comorbid diagnoses among individuals with ACO varied across the three source populations.

There are limited data about ACO in primary care. In an analysis of the MAJORICA (Majorca Real-Life Investigation in COPD and Asthma) cohort, investigators used *International Classification of Diseases*-9 codes for both
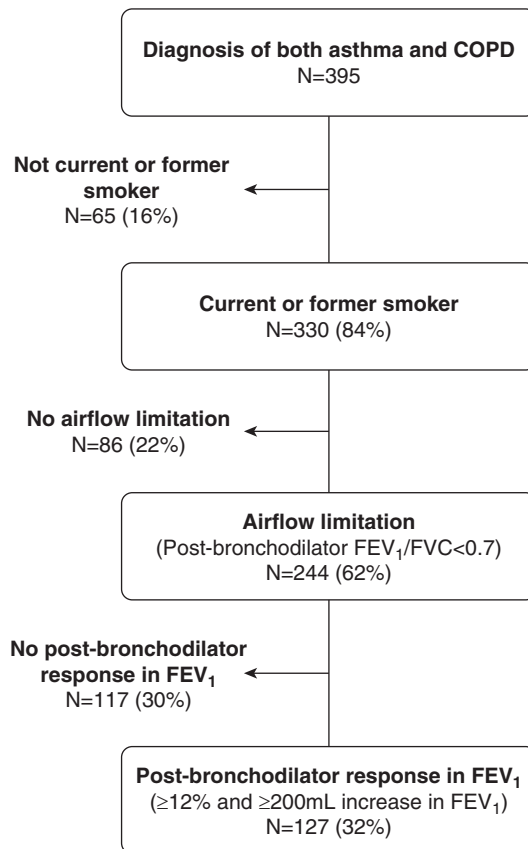
Figure 2. Asthma–chronic obstructive pulmonary disease (COPD) overlap (ACO) in patients with a current diagnosis of both asthma and COPD. Among individuals with a current diagnosis of both asthma and COPD, 127/395 (32.1%) met Respiratory Effectiveness Group ACO Working Group criteria for ACO. The most common reason for not meeting criteria for ACO is the lack of a post-bronchodilator response in forced expiratory volume in 1 second (117/395; 29.6%). FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

comorbid conditions) of individuals with ACO across the three source populations. Several phenotypic features found in patients with ACO have been suggested to influence prognosis. These include smoking history, peripheral blood eosinophil counts, patterns of airway inflammation, and age of onset of asthma (25–27). Our observations suggest that the source population from which individuals with ACO are identified may contribute to heterogeneity, in estimates of prevalence, demographics, clinical characteristics, and health outcomes. Additional studies are needed to confirm this speculation.

Strengths of our study are the size of the cohort (more than 2,000 patients), the use of both clinical and lung function criteria to define ACO, and the use of clinical data from primary care practices. Use of routine clinical data increased the likelihood of our

results being representative of primary care populations.

The current study also has several limitations. It included patients from a single country (the United Kingdom). Also, information needed to apply the REG ACO Working Group definition of ACO (smoking history, airflow limitation, and post-BD response) was not available in 229,285 of 233,054 (98%) healthcare encounters in individuals with two or more primary care visits over a 2-year period. These findings raise concerns about relying on information recorded for clinical purposes (as we did in our study), because it could have led to selection bias. Defining ACO without spirometry results would have reduced the number of people with missing data, but would have raised concerns about the validity of defining ACO without objective evidence of airflow limitation and

improvement in airflow limitation after use of BDs. Also, we did not have information about pack-years smoked, so may have misclassified individuals with minimal (e.g., <1 pack-year) smoking history as having ACO. Although these missing data prevent us from considering the study population as representative of all patients with asthma, COPD, both diagnoses in primary care, the low proportion of patients with sufficient data to apply REG Working Group ACO criteria corresponds to what is unfortunately observed in many real-life primary care settings. Moreover, we used evidence of a post-BD response in FEV_1 as one of the criteria for ACO. Studies have shown that the post-BD response may vary within an individual over a period of 1 week to 2 months (28–30), and this variability could have contributed to misclassification of individuals with ACO. We considered including peripheral blood eosinophilia as a criterion for ACO, but were concerned that this information may not be collected at the time of the other criteria or may be affected by concurrent treatment with systemic corticosteroids.

Our ACO criteria were based on convenience (information recorded in health records during primary care practice) and consensus of primary care and specialist clinicians and researchers from 14 countries with expertise in comparative effectiveness research in respiratory medicine, rather than data related to the pathogenesis of airways disease. As in previous studies of ACO, the absence of a widely accepted consensus definition of ACO is a limitation in the field (9–16). Until then, we are left with different opinions when defining ACO, similar to the approaches currently used to define acute respiratory distress syndrome or sepsis (31, 32). Additional studies are needed to compare the prevalence and clinical characteristics (e.g., clinical response to pharmacotherapy) of individuals with ACO as defined by the REG Working Group criteria and alternate ACO definitions. Such studies will help us to identify definitions for ACO that have a functional consequence. A further limitation of our study is that we did not have information about potential contributory factors for airway disease, such as indoor or outdoor air pollution, which might have an effect similar to smoking. We used spirometry results
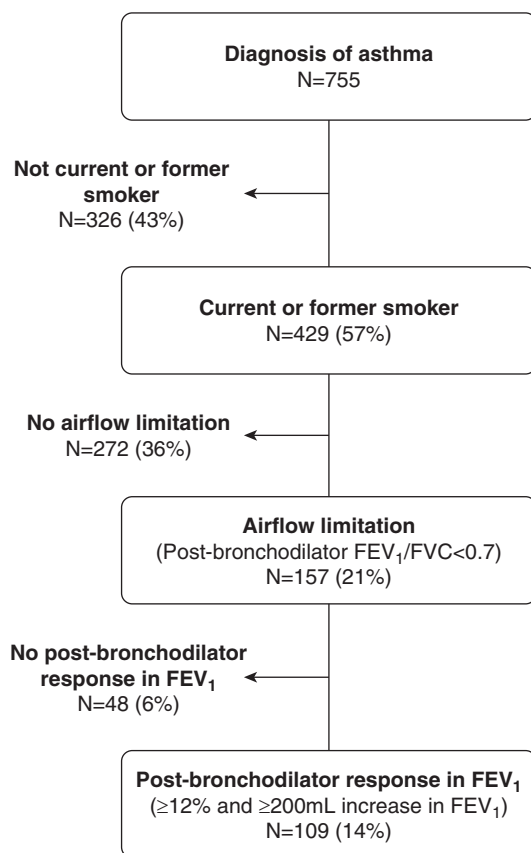
Figure 3. Asthma–chronic obstructive pulmonary disease (COPD) overlap (ACO) in patients with a current diagnosis of asthma only. Among individuals with a current diagnosis of asthma only, 109/395 (14.4%) met Respiratory Effectiveness Group ACO Working Group criteria for ACO. The most common reason for not meeting criteria for ACO is the lack of a history of smoking (326/755; 43.2%). FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

eosinophil counts), and the consequence of ACO among individuals identified within different source populations.

In conclusion, we found that about one in five patients with a clinical diagnosis of asthma, COPD, or both conditions in routine primary care practices met REG ACO Working Group criteria for ACO. The prevalence of ACO in primary care was highest among patients with a diagnosis of both asthma and COPD (one in three), followed by individuals with a diagnosis of COPD only (one in five) and individuals with a diagnosis of asthma only (one in seven). The characteristics of patients with ACO, including age, sex, smoking status, BMI, and pattern of some comorbid conditions, varied significantly across the different source populations, suggesting ACO as defined in our report likely comprises a heterogeneous set of subpopulations. Although use of information recorded by clinicians in primary care offered the opportunity for our results to be more generalizable, our study also highlights the disadvantage of relying on clinical documentation (i.e., potential for missing data or variable quality of information). Nevertheless, we recommend use of the REG ACO Working Group definition in other patient populations to estimate the prevalence of ACO, and longitudinal studies using observational and clinical trial designs to understand the functional consequence in ACO patients in primary care settings. ■

obtained as part of clinical practice, which may have varied in quality and led to misclassification. Lastly, we used a cross-sectional design. Cohort studies are needed to assess the consequence of clinical and physiologic characteristics (e.g., age at diagnosis of asthma, change in BD response in COPD, smoking patterns, and blood

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