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Diagnosis and management of asthma, COPD and asthma-COPD overlap among primary care physicians and respiratory/allergy specialists: a global survey

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AUTHORSHIP STATEMENT

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Thys van der Molen: contributed to the design of the work, provided patient cases from the asthma COPD service Groningen and contributed to draft reviews and the finalization of the paper.

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Peter Calverley: contributed to the study planning, execution and interpretation of the study data, and to the draft reviews and finalization of the paper.

DISCLOSURES

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DSP: The University of Groningen has received money from AstraZeneca, Boehringer Ingelheim, Chiesi, Novartis and TEVA for advisorships and lectures by DSP.

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ABSTRACT

Introduction: Asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO) is a heterogenous condition with clinical features shared by both asthma and COPD.

Objectives: This online global survey of respiratory/allergy specialists and primary care practitioners (PCPs) was performed to understand current clinical approaches to the differential diagnosis and management of asthma, COPD and ACO.

Methods: Respondents were recruited through: (1) a global online physician respondent community (49,980 PCPs and 7205 specialists); (2) market research agents; (3) experts; (4) professional societies; (5) colleague invitation. Respondents were presented with a survey including hypothetical clinical scenarios of diagnostic uncertainty to identify management approaches.

Results: 891 responses (447 PCPs and 444 specialists) were collected across 13 countries. Reported features used for diagnosis of asthma and COPD were consistent with practice guidelines, but there was variability in those selected for ACO diagnosis. Features typically selected by specialists focused on spirometry/history, while PCPs focused on previous treatment/symptoms. Most respondents

could correctly diagnose patients with features of ACO; however, features selected for theoretical diagnosis were often different to those selected in the case scenarios. Additionally, treatment selection was often inconsistent with guidelines, with over half of respondents not recommending inhaled corticosteroids in a patient with ACO and dominant features of asthma.

Conclusion: While most PCPs and respiratory/allergy specialists can reach a working diagnosis of ACO, there remains uncertainty around which diagnostic features are most important and what constitutes optimal management. It is imperative that clinical studies including patients with ACO are initiated, allowing the generation of evidence-based management strategies.

Key words: Allergists; Clinical decision-making; General practitioners; Lung diseases, obstructive; Pulmonologists; Quality of health care; Surveys and questionnaires

INTRODUCTION

Between 15 and 45% of individuals with obstructive airways disease (OAD) exhibit clinical features of both asthma and chronic obstructive pulmonary disease (COPD) (1). This estimation varies widely depending on the population studied and the metrics used to assign the overlap label. The asthma-COPD mixed phenotype has been referred to as asthma-COPD overlap (ACO), and is described as a heterogenous condition characterized by persistent airflow limitation with several features shared by both asthma and COPD (2). Overall health outcomes in individuals with ACO may be poorer than those with classical COPD or asthma (3-7).

Despite inclusion of ACO in clinical practice guidelines (2), there remains uncertainty about the phenotypic and diagnostic stability of the condition (8), with ongoing controversy around the relevance of ACO as a discrete clinical entity (1, 2, 9). Furthermore, patients with ACO features are typically excluded from asthma or COPD randomized controlled trials (10), thereby limiting the evidence on which therapeutic decisions can be based.

The International Steering Committee (ISC) for the Advancement of Consensus on OAD (e-Appendix 1; Supplementary file) performed an online global survey of respiratory/allergy specialists and primary care practitioners (PCPs) to gain understanding of current clinical approaches to the differential diagnosis and management of asthma, COPD and ACO. Respondents were asked general questions about OAD management and were presented with clinical scenarios of varying diagnostic certainty to identify common approaches to the management of these difficult cases.

MATERIALS AND METHODS

This was a closed survey designed to map self-reported behavior and practices of a convenience sample of PCPs and respiratory/allergy specialists with respect to the diagnosis and management of patients with asthma, COPD and possible ACO. The survey was developed by the ACO consensus ISC

and was completed by physicians in 13 countries between November 3, 2015 and June 13, 2016. Prior to participating, respondents were informed of the purpose of the survey, the approximate time that the survey would take to complete, and the identities of the survey investigators and sponsor. All responses were confidential and anonymous. Data were managed in accordance with the Data Protection Act (UK, 1998). In view of the study design, specifically a voluntary online questionnaire completed by healthcare practitioners who were informed of its existence through available networks, no ethical approval was necessary.

The survey was developed in English and originally contained 31 questions, including three hypothetical patient case-based scenarios, unanimously determined by the ISC to represent asthma, COPD or ACO (Box 1). Five additional questions were added following the interim data analysis to gather additional general information (data cut: November 30, 2015). The full survey is shown in the e-Appendix 2; Supplementary file.

The survey was organized in six sections. Participants were not able to move to the next section until all questions in the current section had been completed. Once a section had been submitted, participants were not able to revisit their responses or information provided in the case scenarios. To encourage respondents to make a decision for each question, opt-out choices (e.g. 'Don't know' or 'Undecided') were not provided for most questions.

The questionnaire was translated into German, French, Spanish, Dutch, Italian, and Japanese; native speakers employed by the study sponsor ensured that the translations were correct. The ISC members tested the survey content before it was fielded and uploaded onto SurveyMonkey (SurveyMonkey, Palo Alto, CA, USA). Usability and technical functionality were tested before distribution. The survey web link was emailed to potential respondents, with a due date specified. No reminders were sent. Upon completion, respondents received remuneration (gift card or pre-paid credit card) in line with fair market value. Respondents in Japan were remunerated through a points-based system. Data collection was automated.

Participants

Participants were recruited by: (1) requesting participation from 49,980 PCPs and 7205 respiratory/allergy specialists who were members of a global online physician respondent community (Medefield, London, UK); (2) identification of PCPs or respiratory/allergy specialists by market research field agents in the Netherlands and Japan; (3) recommendations for PCPs or respiratory/allergy specialists by the ISC and national faculties of recognized experts in OAD; and (4) requesting relevant professional societies to forward the survey link to their members. Participants were also invited to send the survey link to interested colleagues.

Statistical analysis

All questionnaires were included in the analysis. Numerical data were analyzed using descriptive statistics, according to a pre-specified statistical analysis plan. Categorical data were analyzed using the chi-square test (with a Holm-Bonferroni adjustment for unrestricted multiple-choice questions),

with comparisons between professional disciplines (i.e. PCPs versus respiratory/allergy specialists). Mean and median scores were calculated for Likert scale questions, and Kruskal-Wallis tests were carried out to determine whether there was a statistically significant difference between professional disciplines.

RESULTS

Eight hundred and ninety-one responses were collected: 447 PCPs and 444 respiratory/allergy specialists practicing in Australia (n=71), Canada (109), France (79), Germany (90), Italy (82), Japan (81), New Zealand (4), Spain (98), South Africa (1), Sweden (1), the Netherlands (88), UK (85), USA (91), and other (11). A total of 106 respondents completed the survey before the five further questions were added, while 785 respondents completed the survey after the additional questions were included. Demographic characteristics of respondents are shown in Table 1.

Current practice regarding OAD

The top five tests performed in practice or via referral to support a diagnosis of OAD were clinical history (98.9%), clinical examination (98.0%), spirometry – baseline (94.7%), spirometry – before and after bronchodilator (93.7%), and oximetry (87.8%) [Q6]. The most notable differences between specialty groups were use of the diffusing capacity of the lungs for carbon monoxide (DLCO) test (used/referred by 89.0% of respiratory/allergy specialists vs 47.0% of PCPs; $p<0.001$) and body plethysmography (79.3% vs 34.9%, respectively; $p<0.001$).

Respiratory/allergy specialists felt extremely comfortable in knowing when spirometry can aid diagnosis and interpreting spirometry results [Q7] (median scores of 5 for both questions on a scale of 1–5), while PCPs were slightly less comfortable (median scores of 4 for both questions; $p<0.001$ vs specialists for both sub-questions). Further details about spirometry use are given in e-Appendix 3 in the Supplementary File.

The features most commonly used for making an asthma or COPD diagnosis are shown in e-Appendix 3 of the Supplementary File (Supplementary figures 1A and 1B, respectively), while the most common features of an ACO diagnosis are shown in Figure 1 [Q11]. There was a wide variation in the features selected to support an ACO diagnosis by both respiratory/allergy specialists and PCPs.

The most frequent reasons that PCPs cited for referring a patient with OAD for specialist care were persistent symptoms despite treatment (35.0%), exacerbations despite treatment (23.2%) and diagnostic uncertainty (21.8%) [Q12]. The reasons for respiratory/allergy specialists receiving referrals mirrored these findings: persistent symptoms despite treatment (31.3%), exacerbations despite treatment (27.0%) and diagnostic uncertainty (22.5%).

More respiratory/allergy specialists than PCPs used an agreed algorithm to diagnose and/or manage patients with OAD in their practice (55.5% and 42.8%, respectively) [Q43]. When respondents were asked if they or their practice would use, or find it helpful to use an agreed algorithm to diagnose

and/or manage patients with airways disease, 73.6% of specialists and 82.4% of PCPs responded with 'yes' [Q44].

Case scenarios

The tests that respondents most frequently indicated as preferred to confirm a diagnosis and assess the impact and severity of disease in each case are shown in Table 2 [Q13, 19, 25], with key features used to confirm the diagnosis shown in Figure 2A, 2B, and 2C for each respective case. [Q15, 21, 27]. Table 3 shows the level of consistency and inconsistency between features that physicians indicated they would use in clinical practice to diagnose the patient and the features that they selected to confirm their diagnosis in each case.

Case #1 – consensus diagnosis asthma

The patient in Case #1 was diagnosed as having asthma by 91.0% and 79.5% of respiratory/allergy specialists and PCPs, respectively [Q14]. A relatively high level of consistency between theory and practice was reported for this case scenario (Table 3).

In terms of management, 50.3% of specialists and 52.1% of PCPs indicated that no maintenance medication was required in this patient and they would refer for further investigation, while 29.4% of specialists and 27.9% of PCPs recommended inhaled corticosteroids (ICS) monotherapy [Q16]. Most respondents indicated that they would review the patient again within 3 months (80%) [Q17]; 64% expected to review the patient two or three times within the next year [Q18].

Case #2 – consensus diagnosis ACO

The patient in Case #2 was diagnosed as having ACO by 80.0% of respiratory/allergy specialists and 64.2% of PCPs [Q20]. Of the respondents who did not select the most useful diagnostic features in the theoretical question (i.e. presence of OAD; smoking status), a high proportion did select these features in the case scenario (Table 3).

In terms of use of maintenance medications, 3.7%, 50.5% and 19.1% of specialists recommended ICS monotherapy, ICS + long-acting beta agonists (LABA), or LABA + long-acting anti-muscarinic agent (LAMA), respectively; corresponding recommendations from PCPs were 4.3%, 25.3% and 32.0%, respectively [Q22]. Of those respondents who favored an ACO diagnosis, only 48.7% indicated that they would prescribe ICS for this patient. Most respondents (98%) indicated that they would see the patient again within the next 6 months [Q23] with 64% expecting to review the patient two or three times and 30% four times or more within the next year [Q24].

Case #3 – consensus diagnosis ACO

The patient in Case #3 was accurately diagnosed as having ACO by 70.3% and 70.6% of respiratory/allergy specialists and PCPs, respectively [Q26]. Similar to Case #2, most of the respondents who did not select the most useful ACO diagnostic features in the theoretical question, did select these features when faced with Case #3 (Table 3).

In terms of use of maintenance medications, 7.4%, 61.3% and 13.7% of specialists recommended ICS monotherapy, ICS + LABA, or LABA + LAMA, respectively; corresponding recommendations from PCPs were 10.3%, 31.8% and 29.5%, respectively [Q28]. Of those respondents who favored a diagnosis of ACO, 58.1% indicated that they would prescribe maintenance ICS. Twenty-eight percent of respondents indicated they would review this patient again within one month, while 55% indicated a review would be scheduled for within one to three months [Q29]. Nearly all respondents expected to review the patient two or three times (72%) or at least four times within the next year (25%) [Q30].

DISCUSSION

This survey of respiratory/allergy specialists and PCPs showed that, while reported features used for diagnosis of asthma and COPD were consistent with current management strategies (2, 11), there was considerable variability in the features selected for an ACO diagnosis. Furthermore, the features typically selected by respiratory/allergy specialists focused on spirometry or history, while PCPs focused on previous treatment and symptoms. We noted an apparent mismatch between physicians' self-reported behavior in the theoretical diagnosis of ACO and their responses to a case with an unknown diagnosis. While most respondents could correctly diagnose patients with features of ACO, the features selected for theoretical diagnosis were often different to those selected in the case scenario – in other words, although physicians may not select the most important diagnostic features related to ACO in theory, they are able to diagnose ACO when faced with a patient expressing this condition. Of course, it should be noted that there was no single correct answer to the diagnostic strategy chosen. Other studies have also found that PCPs' self-confidence in terms of diagnosing COPD has not been reflected in their responses when presented with case scenarios (12).

Responses from a large number of PCPs and respiratory/allergy specialists were included in this analysis, with representation from 13 countries. Nevertheless, it should be noted that the response rate was low (around 1.4% of invited participants), introducing a strong probability of self-selection bias. Our findings must also be interpreted with the understanding that clinical scenarios are incomplete reflections of a complex diagnostic and treatment decision-making process. For example, self-reported behaviors and answers may have been aspirational and factors such as patient preferences or formulary influences were not considered. Furthermore, there may have been potential bias in physician selection, as most respondents came from the Medefield physician panel and were thus self-selected with an interest in completing surveys. Despite these limitations, however, there is a striking difference in the congruence seen between the theoretical and case-based diagnosis/management of asthma and COPD and the mismatch seen between the theoretical and case-based diagnosis/management of ACO. In a sense, this provides an internal control for any potential response bias, allowing a greater degree of confidence in the reliability of our findings.

The variability in features selected for an ACO diagnosis in our study was not surprising, given the heterogeneity of ACO and the ongoing debate around its definition, diagnosis and management (1, 13-16). Indeed, a survey of Spanish pulmonologists found that the most frequently mentioned characteristics of ACO were a history of asthma, significant smoking exposure and not fully reversible airflow limitation (17). Interestingly, this group considered the most accepted diagnostic criterion for

ACO to be eosinophilia in sputum, which did not rank highly in the current survey, perhaps because it is available only in specialist units. In clinical practice, diagnosis may be aided by an OAD management algorithm; our survey indicated that these were lacking in almost 50% of clinics/hospitals, although this may be much greater in community practice. Use and comfort with spirometry for OAD diagnosis was relatively high for both respiratory/allergy specialists and PCPs in our study, which was surprising given that other studies have indicated that spirometry is underutilized in newly diagnosed patients with asthma or COPD (18-21). Nevertheless, it should be remembered that spirometry access does not necessarily equate with use, respondents were self-selected and probably had an airway-interest bias, and that the PCPs' answers to spirometry use may have been aspirational.

The most recent update of the Global Initiative for Asthma (GINA) management strategy indicates that ACO includes a spectrum of phenotypes with a range of etiologies, and recommends referral for confirmatory investigations in patients for whom ACO is suspected (2). In our survey, secondary care referrals were typically for persistent symptoms, exacerbations despite treatment and diagnostic uncertainty. Interestingly, referral reasons cited by PCPs were highly concordant with the reasons that specialists received referrals, indicating internal validity in the survey and validity with current approaches between specialists and PCPs in the participating countries.

Treatment selection for each case scenario showed a level of inconsistency with GINA guidelines at the time of the survey (22). In terms of ACO, GINA 2018 recommends ICS monotherapy (but not LABA or LAMA monotherapy) for patients primarily with features of asthma; bronchodilators alone or in combination with ICS (but not ICS monotherapy) for patients primarily with features of COPD; and low/moderate-dose ICS with add-on LABA and/or LAMA as necessary for patients with a differential diagnosis balanced equally between asthma and COPD (2). Case #1 had asthma, which was spontaneously symptomatic several times a week and associated with moderately severe pre-bronchodilator airflow obstruction and a marked acute bronchodilator response (790 mL and 22% FEV₁ change from baseline). It is of concern that approximately 50% respondents did not think there should be any maintenance therapy, given current guidelines suggest patients with these characteristics should be given maintenance ICS monotherapy or low dose ICS/LABA (2). Case #2 had ACO (with dominant features of asthma). Despite this, over half of respondents who diagnosed the patient with ACO did not recommend use of an ICS. In contrast, 96.2% of respondents in a survey of Spanish pulmonologists indicated that first-line treatment for ACO was the combination of an ICS + LABA, with a LAMA added as second-line therapy (17).

The survey highlights that there is uncertainty for physicians around the diagnosis and management of ACO. Further evidence on the diagnostic assessment and treatment of ACO patients is urgently needed from a combination of database and observational analyses, clinical studies and real-world comparative effectiveness studies.

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BOXES

Box 1. Patient case-based scenario descriptions

Case #1 – Male, 43 years of age (consensus diagnosis: asthma)

Reason for visit: Does this patient have asthma?

Presenting problem: Intermittent, spontaneous episodes of chest tightness, occurring at rest (evening), especially since a recent viral URTI, as well as occasionally on exposure to cold air, cigarette smoke (passive) and while jogging. Since recent URTI, episodes of chest tightness occur 3–5 times a week. Relieved by SABA.

Occupation: Construction worker

Smoking pattern: Never smoked

Family history: Grandmother had asthma, one sibling had childhood asthma but not as an adult

Clinical history: Hay fever; skin prick tests positive to dust mites

Exacerbations: No episodes requiring corticosteroids (last year)

Symptom onset: First symptoms occurred at age 39, none previously

Medical treatment: Has previously been prescribed LABA + ICS, and SABA when needed. Taken only for short periods (4–6 weeks) until symptoms settled

Total MRC score: 1

Spirometry: FEV₁/FVC 0.723 post-bronchodilator; FEV₁ 105% predicted post-bronchodilator; bronchodilator response of 790 mL and 22% change in FEV₁ from baseline. *Refer to e-Appendix 2 of the Supplementary file for complete results*

Case #2 – Female, 56 years of age (consensus diagnosis: ACO)

Reason for visit: Diagnostic uncertainty: is this asthma or COPD or both?

Presenting problem: Intermittent cough, sputum and dyspnea dating back >20 years

Occupation: Housewife

Smoking pattern: Started age 17, total 30–35 pack-years, current smoker

Family history: Father and sibling have allergic rhinitis. No family history of asthma. Grandfather was a heavy smoker and developed COPD

Clinical history: Respiratory symptoms began at the age of 25 – experienced increased cough, wheeze and breathlessness after colds. Symptoms lasted 10–14 days and she took SABA for relief; often also prescribed antibiotics. Last 1–2 years, dyspnea is limiting day-to-day activities. She has to stop for a rest on most hills and stairs

Atopy: Positive skin prick tests. Sneezing/rhinitis on exposure to cats and house dust

Other triggers: Fog, paint fumes, perfume and exertion

Exacerbations: Two episodes of worsening dyspnea, cough and purulent sputum in the last year: one treated with antibiotics only, one treated with prednisone and antibiotics

Medical treatment: LABA + SAMA

Other relevant medical history: Osteopenia (on vitamin D and calcium)

Total MRC score: 3–4

Spirometry: FEV₁/FVC 0.532 post-bronchodilator; FEV₁ 58% predicted post-bronchodilator; bronchodilator response of 330 mL and 28% change in FEV₁ from baseline. *Refer to e-Appendix 2 of the Supplementary file for complete results*

Case #3 – Male, 65 years of age (consensus diagnosis: ACO)

Reason for visit: Previous diagnosis of asthma for review

Presenting problem: Increasing exertional dyspnea last 6–12 months. Finds he is breathless doing things that were previously easy – mowing the lawn without a break, walking up hills or more than two flights of stairs

Occupation: Teacher

Smoking pattern: Former smoker (15 pack-years; stopped smoking at 50 years of age)

Family history: No family history of lung disease or allergy

Clinical history: Previous hay fever in adolescence, tendency to develop bronchitis after colds

Other triggers: Seasonal hay fever to grasses; dyspnea only on exertion, no spontaneous shortness

of breath to a range of inhaled triggers (allergic or irritant)

Exacerbations: One – last year required antibiotics and prednisone for bronchitis, wheeze and dyspnea after a cold

Disease course: Exertional dyspnea since age of 64

Medical treatment: Daily LABA and SABA as needed (usually 1–2 times a day)

Other relevant medical history: Osteopenia (on vitamin D and calcium)

Total MRC score: 2

Spirometry: FEV₁/FVC 0.406 post-bronchodilator; FEV₁ 69% predicted post-bronchodilator; bronchodilator response of 610 mL and 51% change in FEV₁ from baseline. *Refer to e-Appendix 2 of the Supplementary file for complete results*

ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting beta antagonist; MRC, Medical Research Council breathlessness scale; SABA, short-acting beta agonist; SAMA, short-acting anti-muscarinic agent; URTI, upper respiratory chest infection.

TABLES

Table 1. Demographic characteristics of respondents

	Respiratory/allergy specialist	Primary care physician
Q3. Duration of time as a practicing physician (%)	(n=444)	(n=447)
<5 years	1.1	0.7
5–10 years	13.7	11.4
>10 years	85.1	87.9
Q4. Best description of expertise (%)	(n=444)	(n=447)
Family physician, GP or PCP	0	70
GP or PCP with special interest in respiratory medicine	2.3	25.7
Hospital physician – general medical practice	3.2	3.8
Hospital physician – respiratory specialist or allergist	76.8	0.2
Non-hospital physician – general medical practice	0.9	0
Non-hospital physician – respiratory specialist or allergist	14.9	0.2
Other	2.0	0
Q5. Patients with OAD seen each week	(n=443)	(n=447)
<10 patients	3.6	16.6
10–50 patients	60.5	70.2
>50 patients	35.9	13.2
A1.^a Practice location	(n=348)	(n=437)
Regional city or major town	38.8	33.4
Rural or remote	3.4	19.2
Urban: major/capital city and suburbs	57.8	47.4
A2.^a Type of practice^b	(n=185)	(n=421)
Group practice	75.7	70.3
Solo practice	24.3	29.7

a. Additional questions added to the survey following the interim data analysis to gather additional general information; b. Question restricted to those identified as a GP/PCP or non-hospital physician. GP, general practitioner, OAD, obstructive airways disease; PCP, primary care physician.

Table 2. Case scenario responses for diagnosis and assessment of OAD

	Respiratory/allergy specialist	Primary care physician
Case #1 (asthma)	Top five tests used to confirm diagnosis [Q13]	
	(n=433)	(n=438)
	Spirometry – before and after bronchodilator (85.0%)	Spirometry – before and after bronchodilator (70.3%)
	Atopy – specific IgE (57.3%)	Spirometry – baseline (58.4%)
	Blood eosinophilia (56.6%)	None of the specified tests (37.0%)
	Spirometry – baseline (50.8%)	Asthma Control Questionnaire (34.0%)
	Airway hyper-responsiveness test (46.7%)	Airway hyper-responsiveness test (32.9%)
	Top five tests used to assess impact/severity [Q13]	
	(n=433)	(n=438)
	Asthma Control Questionnaire (57.0%)	Asthma Control Questionnaire (34.2%)
	Spirometry – before and after bronchodilator (37.2%)	Spirometry – before and after bronchodilator (32.2%)
	Spirometry – baseline (33.9%)	Spirometry – baseline (30.4%)
	FeNO (15.9%)	Clinical COPD Questionnaire (14.4%)
	Blood eosinophilia (15.0%)	Arterial blood gases (13.2%)
Case #2 (ACO)	Top five tests used to confirm diagnosis [Q19]	
	(n=434)	(n=438)
	Spirometry – before and after bronchodilator (85.3%)	Spirometry – before and after bronchodilator (76.5%)
	DLCO (57.1%)	Spirometry – baseline (66.4%)
	Spirometry – baseline (51.8%)	COPD Assessment Test (39.7%)
	Blood eosinophilia (48.6%)	Clinical COPD Questionnaire (36.8%)
	Test for atopy – specific IgE and/or skin prick (47.0%)	Test for atopy – specific IgE and/or skin prick (23.3%)
	Top five tests used to assess impact/severity [Q19]	
	(n=434)	(n=438)
	COPD Assessment Test (45.9%)	Spirometry – before and after bronchodilator (41.8%)
	Spirometry – before and after bronchodilator (40.1%)	Spirometry – baseline (31.5%)
	Clinical COPD Questionnaire (29.5%)	Clinical COPD Questionnaire (29.7%)
	Spirometry – baseline (29.5%)	COPD Assessment Test (23.5%)
	Asthma Control Questionnaire (24.2%)	Arterial blood gasses (20.3%)
Case #3 (ACO)	Top five tests used to confirm diagnosis [Q25]	
	(n=428)	(n=439)
	Spirometry – before and after bronchodilator (87.1%)	Spirometry – baseline (63.4%)
	DLCO (54.4%)	Spirometry – before and after bronchodilator (56.4%)
	Spirometry – baseline (51.4%)	COPD Assessment Test (35.5%)
	Blood eosinophilia (47.0%)	Asthma Control Questionnaire (30.4%)
	Test for atopy – specific IgE or skin prick (44.2%)	Clinical COPD Questionnaire (29.5%)
	Top five tests used to assess impact/severity [Q25]	
	(n=428)	(n=439)

Spirometry – before and after bronchodilator (39.5%)	Spirometry – before and after bronchodilator (33.3%)
COPD Assessment Test (36.7%)	Spirometry – baseline (33.2%)
Spirometry – baseline (33.2%)	Asthma Control Questionnaire (24.3%)
Asthma Control Questionnaire (27.1%)	Clinical COPD Questionnaire (23.8%)
Clinical COPD Questionnaire (23.6%)	COPD Assessment Test (17.4%)

ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; DLCO, diffusing capacity of the lungs for carbon monoxide; FeNO, fractional exhaled nitric oxide; IgE, immunoglobulin E; OAD, obstructive airways disease.

Table 3. Diagnostic features selected consistently and inconsistently between theoretical question and case scenarios. For consistent features, this reflects the percentage of respondents who selected the feature in the theoretical question (denominator) who also selected it in the case scenario (numerator). For inconsistent features, this reflects the percentage of respondents who did not select the feature in the theoretical question (denominator) but did select it in the case scenario (numerator).

Case #1 – consensus diagnosis: asthma	Asthma (%) (n=744)	ACO (%) (n=70)	COPD (%) (n=30)
Diagnostic features selected in both theoretical question about diagnostic features and in case scenario			
Reversibility (bronchodilator test)	90.3	57.1	0.0
Symptom pattern (allergy, irritants)	75.1	76.9	50.0
Smoking status: never smoked	73.2	27.3	50.0
Personal history of allergy/atopy	68.6	55.6	25.0
Response to inhaled medications	61.7	47.1	0.0
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	40.0	74.1	57.1
Previous diagnosis of asthma	28.9	23.1	33.3
Length of history (since age 39)	14.0	28.6	42.9
Age ≥40 years	13.0	40.7	55.6
Diagnostic features selected in case scenario but not in theoretical question about diagnostic features			
Reversibility (bronchodilator test)	75.9	54.3	34.5
Symptom pattern (allergy, irritants)	70.9	48.8	25.0
Smoking status: never smoked	50.4	27.4	19.2
Personal history of allergy/atopy	49.8	39.5	26.9
Response to inhaled medications	47.6	34.6	21.4
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	28.8	63.2	56.2
Previous diagnosis of asthma	15.0	25.6	7.4
Length of history (since age 39)	9.9	35.1	21.7
Age ≥40 years	3.3	42.6	47.6

Case #2 – consensus diagnosis: ACO	Asthma (%) (n=31)	ACO (%) (n=628)	COPD (%) (n=208)
Diagnostic features selected in both theoretical question about diagnostic features and in case scenario			
Reversibility (bronchodilator test)	77.8	70.4	15.4
Personal history of allergy/atopy	52.9	46.6	33.3
Co-morbidities	50.0	5.3	12.5
Length of history (since age 25)	50.0	72.7	58.8
Age ≥40 years	50.0	44.3	60.3
Symptom pattern (allergy, irritants)	25.0	64.6	50.0
Previous diagnosis of asthma	21.4	14.1	33.3
Response to inhaled medications	14.3	31.8	40.0
Family history of COPD	0.0	25.0	37.8
Smoking status: current smoker, 30 pack-years	0.0	88.4	87.5
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	0.0	79.4	81.2
Diagnostic features selected in case scenario but not in theoretical question about diagnostic features			
Reversibility (bronchodilator test)	35.3	54.7	20.0
Personal history of allergy/atopy	22.2	38.7	7.0
Co-morbidities	0.0	2.4	11.3
Length of history (since age 25)	27.3	58.3	48.1
Age ≥40 years	8.3	26.7	51.6
Symptom pattern (allergy, irritants)	45.5	41.2	19.9
Previous diagnosis of asthma	16.7	8.5	1.9
Response to inhaled medications	42.1	24.0	25.3
Family history of COPD	4.0	7.9	19.8
Smoking status: current smoker, 30 pack-years	8.0	88.6	71.2
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	29.2	71.2	69.1
Case #3 – consensus diagnosis: ACO	Asthma (%) (n=125)	ACO (%) (n=611)	COPD (%) (n=110)

Diagnostic features selected in both theoretical question about diagnostic features and in case scenario

Reversibility (bronchodilator test)	85.9	81.4	14.3
Smoking status: previous smoker, 15 pack-years	80.0	83.6	88.3
Personal history of allergy/atopy	65.0	58.9	50.0
Symptom pattern (allergy, irritants)	60.9	48.3	0.0
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	44.4	81.8	73.2
Age ≥40 years	33.3	57.3	73.6
Previous diagnosis of asthma	32.1	24.1	-
Length of history (since age 64)	26.7	35.1	54.5

Diagnostic features selected in case scenario but not in theoretical question about diagnostic features

Reversibility (bronchodilator test)	62.3	60.9	19.4
Smoking status: previous smoker, 15 pack-years	20.0	73.9	66.7
Personal history of allergy/atopy	51.1	34.6	11.1
Symptom pattern (allergy, irritants)	65.8	42.0	25.0
Obstructive airways disease (spirometry results: FEV ₁ /FVC ≤0.7)	40.5	70.3	71.0
Age ≥40 years	6.7	38.5	50.9
Previous diagnosis of asthma	34.8	19.8	6.4
Length of history (since age 64)	28.2	31.7	61.4

ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

FIGURE LEGENDS

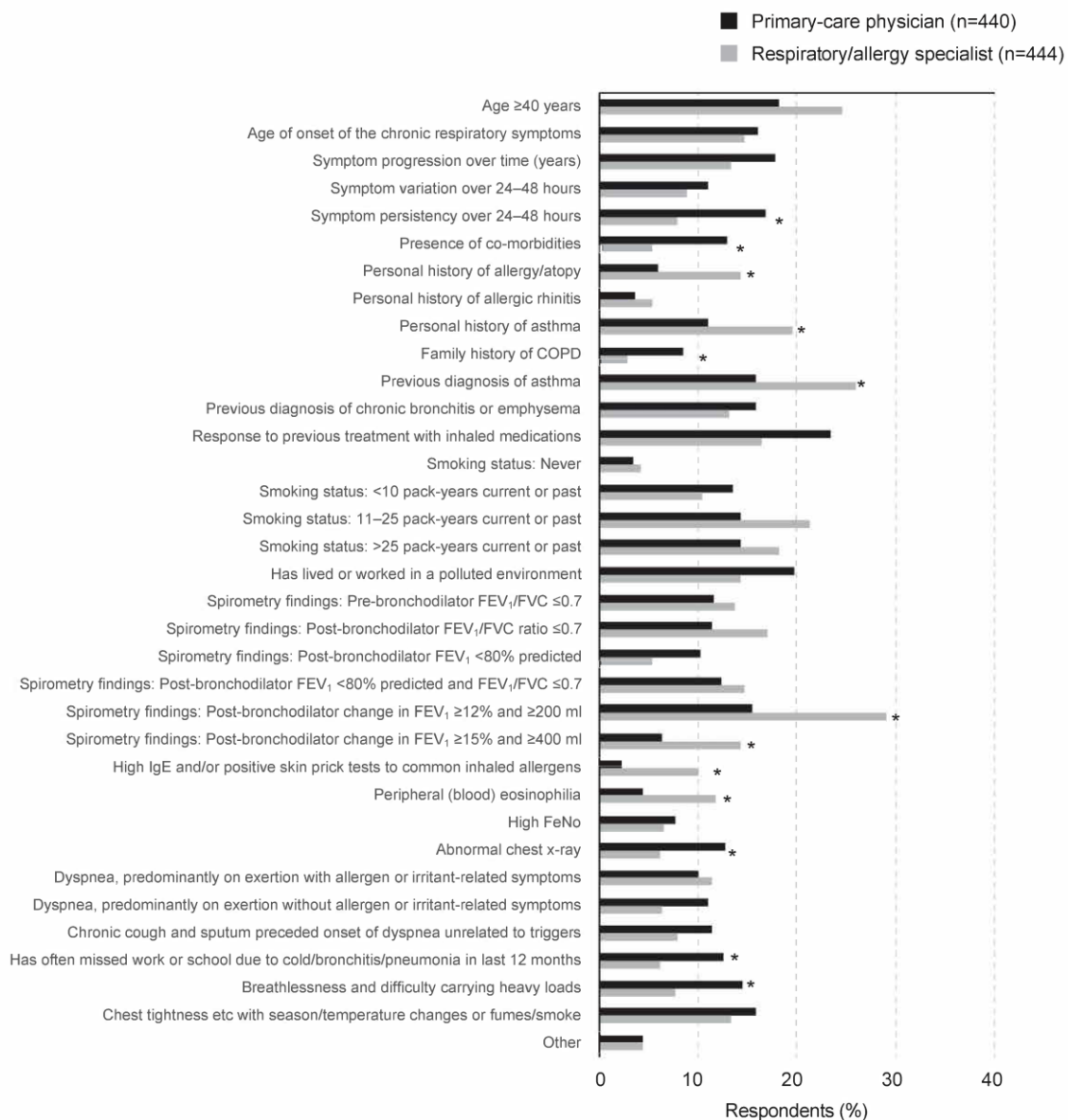
Figure 1. Features most strongly favoring a diagnosis of ACO. Respondents were asked to select up to five diagnostic features that strongly favored a diagnosis of ACO [Q11]. * $p < 0.05$ for primary care physician vs respiratory/allergy specialist.

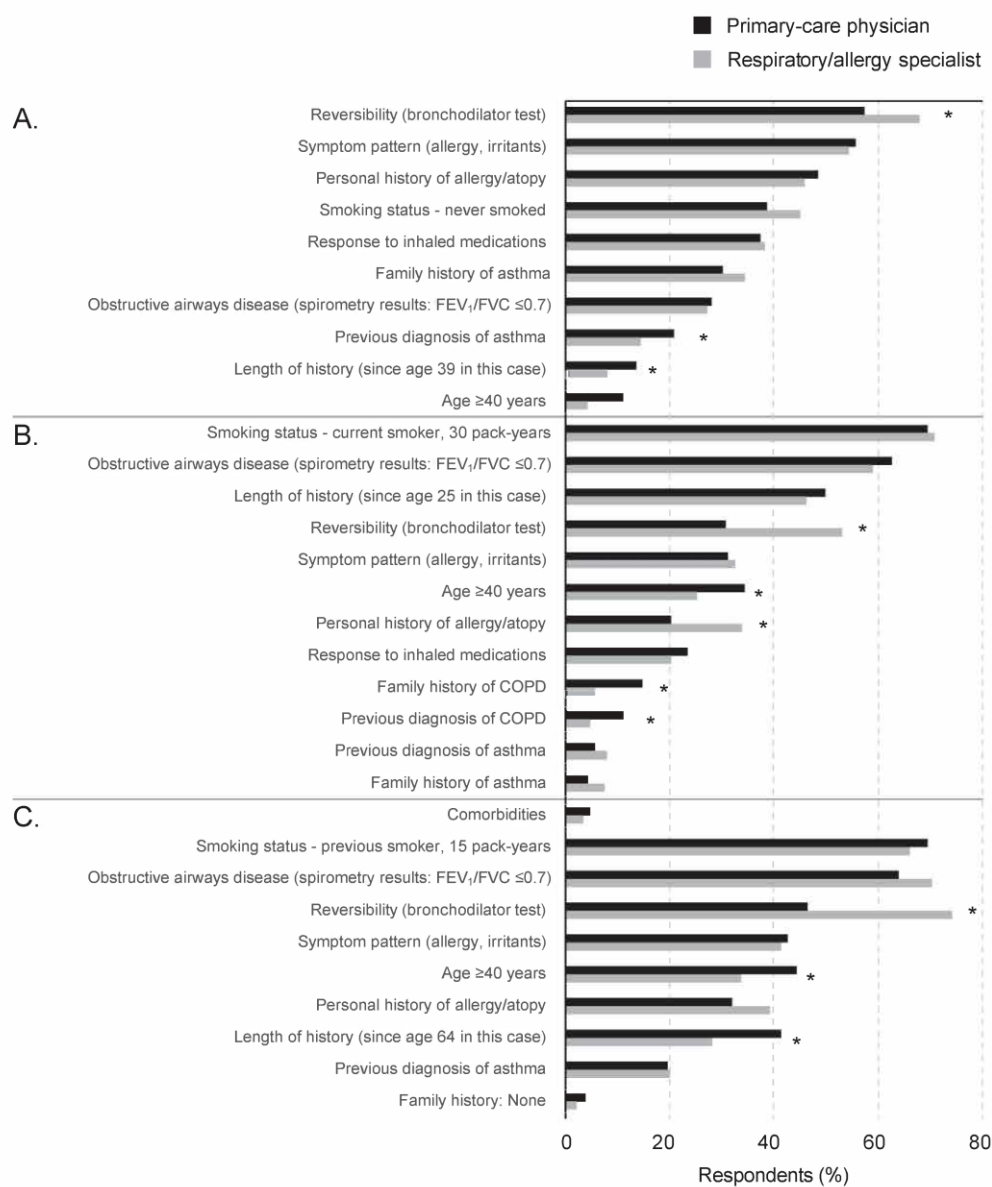
Footnote: ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E.

Figure 2. Diagnostic features selected for supporting diagnosis for (A) Case #1 (asthma) [Q15]; (B) Case #2 (ACO) [Q21]; and (C) Case #3 (ACO) [Q27]. Respondents were asked to select up to five diagnostic features that they would use to support their diagnosis. Note that the agreed diagnosis was not shown to survey respondents. * $p < 0.05$ for primary care physician vs respiratory/allergy specialist.

Footnote: Number of respondents: A: 438 PCPs and 435 specialists; B: 371 PCPs and 382 specialists; C: 447 PCPs and 444 specialists.

ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PCPs, primary care physicians.





Diagnosis and management of asthma, COPD and asthma-COPD overlap among primary care physicians and respiratory/allergy specialists: results of a global survey

e-Appendix 1

The Advancement of Consensus on Obstructive Airways Disease (OAD) is a group of international experts in asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO), brought together to develop expert guidance for improving ACO management through enhanced awareness and accurate diagnosis. The group consisted of an International Steering Committee [CJ, JMF, FM, DP, SR, TV, PC] and representatives from participating countries. SR was a member of the International Steering Committee from the beginning of the project, first as an employee of the University of Nebraska Medical School, then as an employee of AstraZeneca. AG and EG are employees of AstraZeneca, who contributed to the planning, design and implementation of the survey and writing of the manuscript. AstraZeneca provided funding to the Lucid Group, Loudwater, UK, to manage the Advancement of Consensus on OAD program.

e-Appendix 2

SURVEY ON THE DIAGNOSIS AND MANAGEMENT OF OBSTRUCTIVE AIRWAYS DISEASE

SECTION 1: General information about you

1. Please click here if you are already an invited member of the National Faculty for the Asthma COPD Overlap program [*Check box*]
2. In which country do you practice? [*Drop down box*]
3. How many years have you been a practicing physician? [*Drop down box*]
4. Please select one of the following terms which best describes your expertise:
 - ☐ Family physician, general practitioner (GP) or primary care physician (PCP)
 - ☐ GP or PCP with special interest in respiratory medicine
 - ☐ Hospital physician – respiratory specialist or allergist
 - ☐ Hospital physician – general medical practice
 - ☐ Non-hospital physician – respiratory specialist or allergist
 - ☐ Non-hospital physician – general medical practice
 - ☐ Other
5. How many patients with obstructive airways disease do you see per week?
 - ☐ <10 patients
 - ☐ 10–50 patients
 - ☐ >50 patients

SECTION 2: Diagnosis and management of obstructive airways disease

6. Which of the following assessments/tests do you normally use to support the diagnosis of obstructive airways disease?

	Yes, in my own practice (perform yourself)	Yes, via referral (refer to someone else to perform)	Rarely or never
Clinical history	☐	☐	☐
Assessment of cluster symptoms (e.g. via questionnaires or other)	☐	☐	☐
Clinical examination	☐	☐	☐
Spirometry – baseline	☐	☐	☐
Spirometry – before and after baseline	☐	☐	☐
Airway hyper-responsiveness test	☐	☐	☐
Small airway measurements	☐	☐	☐
Plethysmograph or ‘body box’	☐	☐	☐
Diffusing capacity of the lungs for carbon monoxide (DLCO)	☐	☐	☐
Arterial blood gases	☐	☐	☐
Oximetry	☐	☐	☐
Computerized tomography (CT) scan	☐	☐	☐
Test for atopy – specific IgE	☐	☐	☐
Test for atopy – skin prick tests	☐	☐	☐
Fractional exhaled nitric oxide (FeNO)	☐	☐	☐
Blood eosinophilia	☐	☐	☐
Sputum inflammatory cell analysis	☐	☐	☐

7. Please rate how comfortable you are in the following areas of spirometry:
(1 = not at all comfortable and 5 = extremely comfortable)

	1	2	3	4	5
Knowing when spirometry can aid diagnosis	☐	☐	☐	☐	☐
Interpreting spirometry results	☐	☐	☐	☐	☐

8. Do you have access to spirometry?

- ☐ Yes, in my practice location
- ☐ Yes, readily on hand via referral
- ☐ Yes, only if the patient is referred to a specialist
- ☐ No access (please move to question 10)

9. For what purpose do you use spirometry? (Select all that are relevant)

- ☐ Diagnosing chronic airways disease
- ☐ Diagnosing COPD
- ☐ Diagnosing asthma
- ☐ Distinguishing between asthma and COPD
- ☐ Follow-up of patients with asthma
- ☐ Follow-up of patients with COPD

10. Consider you see 10 patients with suspected asthma or COPD. In how many (out of 10) would you perform or refer for spirometry?

	1	2	3	4	5	6	7	8	9	10
Before starting treatment	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
At any time in the next 12 months to confirm the diagnosis	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

11. Please select which diagnostic features most strongly favor a diagnosis of asthma, COPD or asthma-COPD overlap. (Please select up to 5 for asthma, up to 5 for COPD and up to 5 for asthma-COPD overlap).

	Asthma	COPD	Overlap of asthma & COPD
Age ≥40 years	☐	☐	☐
Age of onset of the chronic respiratory symptoms	☐	☐	☐
Symptom progression over time (years)	☐	☐	☐
Symptom variation over 24–48 hours	☐	☐	☐
Symptom persistency over 24–48 hours	☐	☐	☐
Presence of co-morbidities e.g. hypertension, ischemic heart disease, diabetes, etc.	☐	☐	☐
Personal history of allergy/atopy	☐	☐	☐
Personal history of allergic rhinitis	☐	☐	☐
Personal history of asthma	☐	☐	☐
Family history of COPD	☐	☐	☐
Previous diagnosis of asthma	☐	☐	☐
Previous diagnosis of chronic bronchitis or emphysema	☐	☐	☐
Response to previous treatment with inhaled medications	☐	☐	☐
Smoking status: never	☐	☐	☐
Smoking status: <10 pack-years current or past	☐	☐	☐
Smoking status: 11–25 pack-years current or past	☐	☐	☐
Smoking status: >25 pack-years current or past	☐	☐	☐
Has lived or worked in an environment with dirty or polluted air (tobacco smoke, second-hand smoke, biomass fuels)	☐	☐	☐
Spirometry findings: Pre-bronchodilator FEV ₁ /FVC ratio ≤0.7	☐	☐	☐
Spirometry findings: Post-bronchodilator FEV ₁ /FVC ratio ≤0.7	☐	☐	☐
Spirometry findings: Post-bronchodilator FEV ₁ <80% predicted	☐	☐	☐
Spirometry findings: Post-bronchodilator FEV ₁ <80% predicted and post bronchodilator FEV ₁ /FVC ratio ≤0.7	☐	☐	☐
Spirometry findings: Post-bronchodilator change in FEV ₁ ≥12% and ≥200 ml (standard reversibility criterion)	☐	☐	☐
Spirometry findings: Post-bronchodilator change in FEV ₁ ≥15% and ≥400ml (strict reversibility criterion)	☐	☐	☐
High IgE and/or positive skin prick tests to common inhaled	☐	☐	☐

allergens			
Peripheral (blood) eosinophilia	☐	☐	☐
High FeNO	☐	☐	☐
Abnormal chest X-ray	☐	☐	☐
Dyspnea, predominantly on exertion with allergen or irritant-related symptoms	☐	☐	☐
Dyspnea, predominantly on exertion without allergen or irritant-related symptoms	☐	☐	☐
Chronic cough and sputum preceded onset of dyspnea unrelated to triggers	☐	☐	☐
Has often missed work or school due to cold/bronchitis/pneumonia in last 12 months	☐	☐	☐
Experiences breathlessness and difficulty carrying heavy loads	☐	☐	☐
Experiences chest tightness, wheeze or dyspnea with season or temperature changes, or fumes/smoke exposure	☐	☐	☐
Other	☐	☐	☐

12. Please rank the following features in order of importance as triggers for referral (primary care)/receipt of referral (specialist care) for further investigation: (1 = most important and 6 = least important)

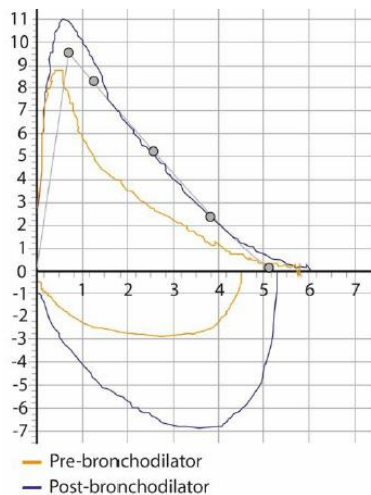
- ☐ Persistent symptoms despite treatment
- ☐ Exacerbations despite treatment
- ☐ Diagnostic uncertainty (alternative cause of respiratory symptoms suspected e.g. cardiovascular (CV) disease)
- ☐ Multiple features of either asthma or COPD
- ☐ Atypical symptoms of asthma or COPD
- ☐ Comorbidities present

SECTION 3: Case-based patient scenarios – patient 1

Patient: Male, 43 years of age Reason for visit: Does this patient have asthma?	
Presenting problem	Intermittent, spontaneous episodes of chest tightness, occurring at rest (evening), especially since a recent viral upper respiratory tract infection (URTI), as well as occasionally on exposure to cold air, cigarette smoke (passive) and while jogging. Since recent URTI, episodes of chest tightness occur 3–5 times a week. Relieved by short-acting beta agonist (SABA)
Occupation	Construction worker
Smoking pattern	Never smoked
Family history	Grandmother had asthma, one sibling had childhood asthma but not as an adult
Clinical history	Hay fever; skin prick tests positive to dust mites
Exacerbations	No episodes requiring corticosteroids (last year)
Symptom onset	First symptoms occurred at age 39, none previously
Medical treatment	Has previously been prescribed long-acting beta agonist (LABA) + inhaled corticosteroid (ICS), and SABA when needed. Taken only for short periods (4–6 weeks) until symptoms settled
Total Medical Research Council breathlessness scale (MRC) score	1

13. Would you conduct any of the following tests for this patient to (A) confirm the diagnosis (B) assess impact/severity? (Select all that apply)

	To confirm diagnosis	To assess impact/severity
COPD Assessment Test (CAT)	☐	☐
Clinical COPD Questionnaire (CCQ)	☐	☐
Asthma Control Questionnaire (ACQ)	☐	☐
Spirometry (baseline)	☐	☐
Spirometry (before and after bronchodilator)	☐	☐
Airway hyper-responsiveness test	☐	☐
DLCO	☐	☐
Arterial blood gases	☐	☐
High resolution CT scan	☐	☐
Test for atopy (specific IgE)	☐	☐
FeNO	☐	☐
Blood eosinophilia	☐	☐
Sputum inflammatory cell analysis	☐	☐
Other	☐	☐
None	☐	☐



Best Effort							
Parameter	Units	Ref.	Pre	%Pred	Post	%Pred	%Change
FVC	(L)	5.08	5.75	113.2	6.00	118.0	4.3%(0.25)
FEV1	(L)	4.13	3.55	85.9	4.34	105.0	22.2%(0.79)
FEV1/FVC	(%)	79.5	61.7	77.7	72.3	91.0	17.2%(10.6)
PEF	(L/s)	9.54	8.82	92.5	11.03	115.6	25.0%(2.21)

Post Medication: Salbutamol 400µg

14. What is your diagnosis in this patient (please select one option)

- ☐ Asthma
- ☐ COPD
- ☐ Asthma-COPD overlap
- ☐ Other

15. Please select up to 5 key features on which you based your diagnosis:

- ☐ Age ≥ 40 years
- ☐ Length of history (since age 39 in this case)
- ☐ Obstructive airways disease (spirometry results: $FEV_1/FVC \leq 0.7$)
- ☐ Symptom pattern (allergy, irritants)
- ☐ Personal history of allergy/atopy
- ☐ Smoking status – never smoked
- ☐ Reversibility (bronchodilator test)
- ☐ Family history of asthma
- ☐ Previous diagnosis of asthma
- ☐ Response to inhaled medications

16. Which maintenance medications would you prescribe to this patient to maintain daily control until next review (assuming SABA as needed)?

- ☐ No medication change: LABA + low-dose ICS
- ☐ ICS monotherapy
- ☐ Short-acting anti-muscarinic agent (SAMA)
- ☐ Long-acting anti-muscarinic agent (LAMA)
- ☐ Leukotriene receptor antagonist
- ☐ Other combination therapy
- ☐ None: refer to a specialist for further investigation
- ☐ Don't know

17. How soon would you see this patient again for the next review?

- ☐ <1 month
- ☐ 1–3 months
- ☐ 3–6 months
- ☐ >6 months

18. How often would you expect to review this patient in the next year?

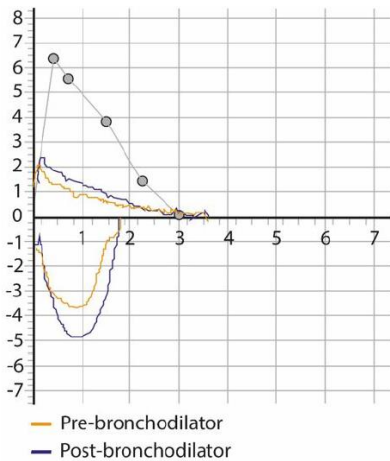
- ☐ Not at all
- ☐ Once more only
- ☐ 2–3 times
- ☐ ≥4 times

SECTION 4: Case-based patient scenarios – patient 2

Patient: Female, 56 years of age Reason for visit: Diagnostic uncertainty: is this asthma or COPD or both?	
Presenting problem	Intermittent cough, sputum and dyspnea dating back >20 years
Occupation	Housewife
Smoking pattern	Started age 17, total 30–35 pack-years, current smoker
Family history	Father and sibling have allergic rhinitis. No family history of asthma. Grandfather was a heavy smoker and developed COPD
Clinical history	Respiratory symptoms began at the age of 25 – experienced increased cough, wheeze and breathlessness after colds. Symptoms lasted 10–14 days and she took SABA for relief; often also prescribed antibiotics. Last 1–2 years, dyspnea is limiting day-to-day activities. She has to stop for a rest on most hills and stairs
Atopy	Positive skin prick tests. Sneezing/rhinitis on exposure to cats and house dust
Other triggers	Fog, paint fumes, perfume and exertion
Exacerbations	Two episodes of worsening dyspnea, cough and purulent sputum in the last year: one treated with antibiotics only, one treated with prednisone and antibiotics
Medical treatment	LABA + SAMA
Other relevant medical history	Osteopenia (on vitamin D and calcium)
Total MRC score	3–4

19. Would you conduct any of the following tests for this patient to (A) confirm the diagnosis (B) assess impact/severity? (Select all that apply)

	To confirm diagnosis	To assess impact/severity
COPD Assessment Test (CAT)	☐	☐
Clinical COPD Questionnaire (CCQ)	☐	☐
Asthma Control Questionnaire (ACQ)	☐	☐
Spirometry (baseline)	☐	☐
Spirometry (before and after bronchodilator)	☐	☐
Airway hyper-responsiveness test	☐	☐
DLCO	☐	☐
Arterial blood gases	☐	☐
High resolution CT scan	☐	☐
Test for atopy (specific IgE and/or skin prick tests)	☐	☐
FeNO	☐	☐
Blood eosinophilia	☐	☐
Sputum inflammatory cell analysis	☐	☐
Other	☐	☐
None	☐	☐



Best Effort							
Parameter	Units	Ref.	Pre	%Pred	Post	%Pred	%Change
FVC	(L)	3.01	3.61	120.2	3.58	119.0	-1.0%(-0.04)
FEV1	(L)	2.56	1.17*	45.6	1.49*	58.4	28.2%(0.33)
FEV1/FVC	(%)	78.5	32.2	41.1	41.7	53.2	29.4%(9.5)
PEF	(L/s)	6.34	2.10*	33.1	2.39*	37.7	13.9%(0.29)

Post Medication: Salbutamol 400ug

Post Medication: Salbutamol 400µg
*Under lower limit of normal

20. What is your diagnosis in this patient (please select one option)

- ☐ Asthma
- ☐ COPD
- ☐ Asthma-COPD overlap
- ☐ Other

21. Please select up to 5 key features on which you based your diagnosis:

- ☐ Age ≥ 40 years
- ☐ Length of history (since age 25 in this case)
- ☐ Obstructive airways disease (spirometry results: $FEV_1/FVC \leq 0.7$)
- ☐ Symptom pattern (allergy, irritants)
- ☐ Personal history of allergy/atopy
- ☐ Smoking status – current smoker, 30 pack-years
- ☐ Reversibility (bronchodilator test)
- ☐ Family history of asthma
- ☐ Previous diagnosis of asthma
- ☐ Previous diagnosis of COPD
- ☐ Response to inhaled medications
- ☐ Comorbidities

22. Which maintenance medications would you prescribe to this patient (assuming SABA as needed)?

- ☐ No medication change: Daily maintenance LABA + SAMA
- ☐ ICS monotherapy
- ☐ LAMA
- ☐ LABA + LAMA
- ☐ ICS + LABA
- ☐ Leukotriene receptor antagonist
- ☐ Other combination therapy
- ☐ None: refer to a specialist for further investigation
- ☐ Don't know

23. How soon would you see this patient again for the next review?

- ☐ <1 month
- ☐ 1–3 months
- ☐ 3–6 months
- ☐ >6 months

24. How often would you expect to review this patient in the next year?

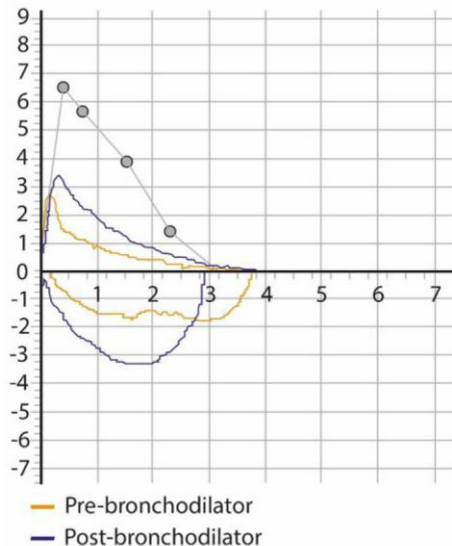
- ☐ Not at all
- ☐ Once more only
- ☐ 2–3 times
- ☐ ≥4 times

SECTION 5: Case-based patient scenarios – patient 3

Patient: Male, 65 years of age Reason for visit: Previous diagnosis of asthma for review	
Presenting problem	Increasing exertional dyspnea last 6–12 months. Finds he is breathless doing things that were previously easy – mowing the lawn without a break, walking up hills or more than two flights of stairs.
Occupation	Teacher
Smoking pattern	Former smoker (15 pack-years; stopped smoking at 50 years of age)
Family history	No family history of lung disease or allergy
Clinical history	Previous hay fever in adolescence, tendency to develop bronchitis after colds
Other triggers	Seasonal hay fever to grasses; dyspnea only on exertion, no spontaneous shortness of breath to a range of inhaled triggers (allergic or irritant)
Exacerbations	One – last year required antibiotics and prednisone for bronchitis, wheeze and dyspnea after a cold
Disease course	Exertional dyspnea since age of 64
Medical treatment	Daily LABA and SABA as needed (usually 1–2 times a day)
Total MRC score	2

25. Would you conduct any of the following tests for this patient to (A) confirm the diagnosis (B) assess impact/severity? (Select all that apply)

	To confirm diagnosis	To assess impact/severity
COPD Assessment Test (CAT)	☐	☐
Clinical COPD Questionnaire (CCQ)	☐	☐
Asthma Control Questionnaire (ACQ)	☐	☐
Spirometry (baseline)	☐	☐
Spirometry (before and after bronchodilator)	☐	☐
Airway hyper-responsiveness test	☐	☐
DLCO	☐	☐
Arterial blood gases	☐	☐
High resolution CT scan	☐	☐
Test for atopy (specific IgE and/or skin prick tests)	☐	☐
FeNO	☐	☐
Blood eosinophilia	☐	☐
Sputum inflammatory cell analysis	☐	☐
Other	☐	☐
None	☐	☐



Best Effort							
Parameter	Units	Ref.	Pre	%Pred	Post	%Pred	%Change
FVC	(L)	3.11	3.75	120.7	4.49	144.4	19.6%(0.74)
FEV1	(L)	2.63	1.21*	45.8	1.82*	69.2	50.9%(0.61)
FEV1/FVC	(%)	76.9	32.2	41.8	40.6	52.7	26.2%(8.4)
PEF	(L/s)	6.49	2.61*	40.3	3.38*	52.2	29.5%(0.77)

Post Medication: Salbutamol 400µg

*Under lower limit of normal

26. What is your diagnosis in this patient (please select one option)

- ☐ Asthma
- ☐ COPD
- ☐ Asthma-COPD overlap
- ☐ Other

27. Please select up to 5 key features on which you based your diagnosis:

- ☐ Age ≥ 40 years
- ☐ Length of history (since age 64 in this case)
- ☐ Obstructive airways disease (spirometry results: $FEV_1/FVC \leq 0.7$)
- ☐ Symptom pattern (allergy, irritants)
- ☐ Personal history of allergy/atopy
- ☐ Smoking status – previous smoker, 15 pack-years
- ☐ Reversibility (bronchodilator test)
- ☐ Family history: none
- ☐ Previous diagnosis of asthma

28. How would you treat this patient in the first instance (assuming SABA as needed)?

- ☐ No medication change: maintain LABA
- ☐ ICS
- ☐ Regular SAMA
- ☐ LAMA
- ☐ LABA and LAMA
- ☐ ICS and LABA
- ☐ Leukotriene receptor antagonist
- ☐ Other combination therapy
- ☐ None: refer to a specialist for further investigation
- ☐ Don't know

29. How soon would you see this patient again for the next review?

- ☐ <1 month
- ☐ 1–3 months
- ☐ 3–6 months
- ☐ >6 months

30. How often would you expect to review this patient in the next year?

- ☐ Not at all
- ☐ Once more only
- ☐ 2–3 times
- ☐ ≥4 times

SECTION 6: Educational resources

31. Would you find any of the educational materials about asthma-COPD overlap listed below of interest for your future development? (Select all that apply)

- ☐ Summary of the data from this study
- ☐ Certificate of completion for your continued professional development (CPD) portfolio
- ☐ Literature summary on asthma-COPD overlap
- ☐ Annotated case studies
- ☐ Summary of GINA/GOLD recommendations
- ☐ Summary of spirometry findings associated with asthma, COPD and asthma-COPD overlap

Additional questions added to the survey following the interim data analysis:

A1. Please select which term best describes the location of your practice:

- ☐ Urban: major/capital city and suburbs
- ☐ Regional city or major town
- ☐ Rural or remote

A2. If you are a GP/PCP or non-hospital physician, please select which term best describes the structure of your practice

- ☐ Group practice
- ☐ Solo practice

A3. Do you or your practice use an agreed algorithm to diagnose and/or manage patients with airways disease?

- ☐ Yes
- ☐ No

A4. Would you or your practice use/find it helpful to use an agreed algorithm to diagnose and/or manage patients with airways disease?

- ☐ Yes
- ☐ No

A5. Are there financial or other incentives to perform spirometry in your clinical practice?

- ☐ Yes
- ☐ No

e-Appendix 3

Use of spirometry

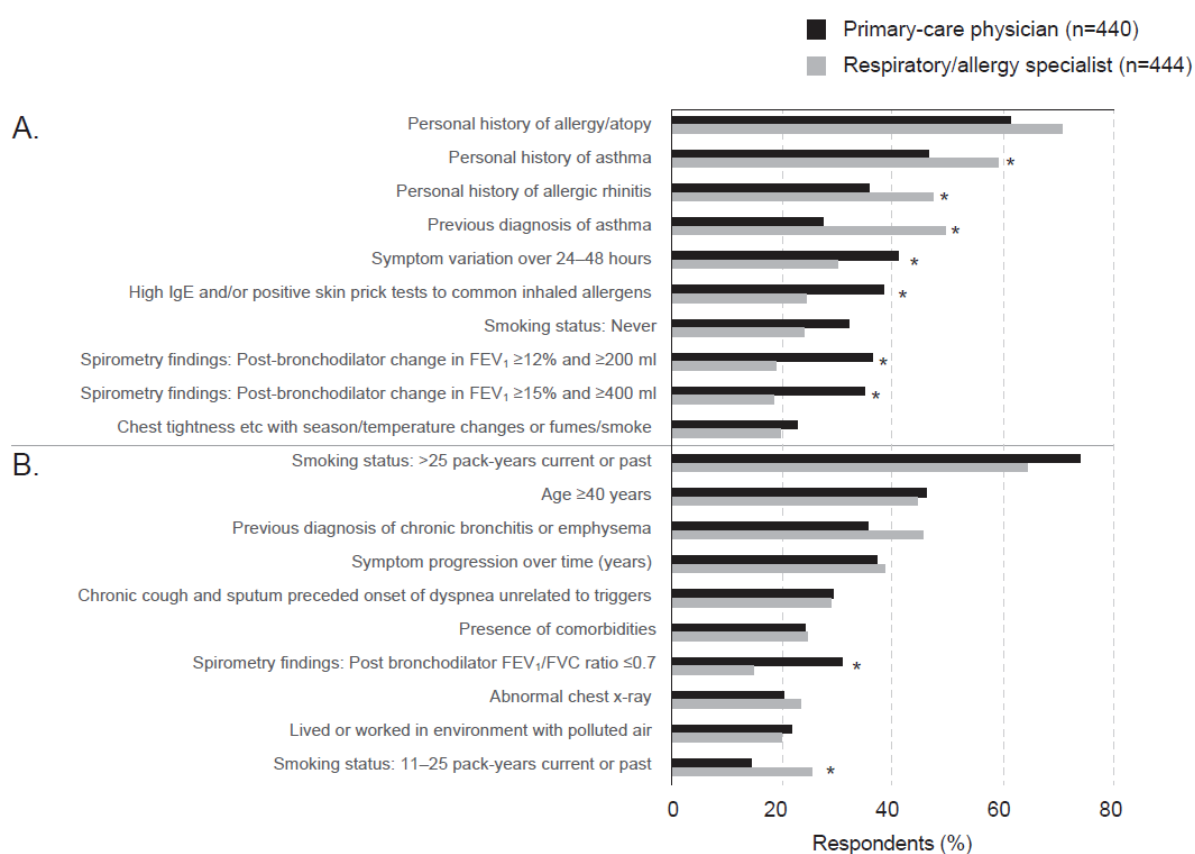
Overall access to spirometry was significantly better for respiratory/allergy specialists than PCPs ($p<0.001$) [Q8]. Nearly all respiratory/allergy specialists had access to spirometry at their practice (92.8%) compared with 62.9% of PCPs. However, only 3.6% of PCPs reported having no access to spirometry. The respective reasons that respiratory/allergy specialists and PCPs used spirometry were for: diagnosing COPD (95.7% vs 88.8%), diagnosing chronic airways diseases (93.7% vs 83.4%), diagnosing asthma (92.8% vs 80.3%), follow-up of patients with COPD (92.3% vs 78.5%), follow-up of patients with asthma (89.2% vs 65.1%) and distinguishing asthma from COPD (81.5% vs 69.4%; $p<0.001$ for all comparisons) [Q9].

Respiratory/allergy specialists indicated that they would refer a mean of 9.2/10 (SD 2.0) patients for spirometry before treatment and 8.6/10 (SD 2.5) patients for spirometry to confirm diagnosis, while PCPs reported referring fewer patients for spirometry (mean of 7.1/10 [SD 2.9] before treatment and 7.1/10 [SD 2.8] to confirm diagnosis; $p<0.001$ for both comparisons) [Q10]. Approximately one-quarter of respondents indicated that they receive reimbursement to perform spirometry (25.0% of respiratory/allergy specialists and 23.8% of PCPs) [AQ3].

e-Figures

e-Figure 1. Features most strongly favoring a diagnosis of (A) asthma and (B) COPD [Q11].

Respondents were asked to select up to five diagnostic features that strongly favored a diagnosis of asthma and COPD. Only the top 10 features for each diagnosis are shown. * $p < 0.05$ for primary-care physicians vs respiratory/allergy specialists.



ACO, asthma-COPD overlap; COPD, chronic obstructive pulmonary disease; FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E.