Clinical characteristics of adults with self-reported diagnosed asthma and/or COPD: data from the BOLD Australia Study

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Australian adults aged ⩾40 years with self-reported asthma and COPD had more severe disease, with more frequent respiratory symptoms and greater airflow limitation, than those with self-reported asthma or COPD alone https://bit.ly/3oywWF7

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Abstract

Background Diagnosis of asthma and chronic obstructive pulmonary disease (COPD) in the community is variable, often without spirometry. Some studies report that adults with both diagnostic labels (asthma +COPD) have worse health outcomes than those with asthma or COPD only, but data for Australian adults are limited. We investigated the relationship between clinical characteristics and self-reported diagnoses of asthma, COPD and both.

Method We used data from the BOLD Australia study, which included randomly selected adults aged ⩾40 years from six study sites. The BOLD questionnaires and spirometry test were used in all sites. Participants were grouped by self-reported diagnosis. Demographic and clinical characteristics and lung function were compared between groups.

Results Of the study sample (n=3522), 336 reported asthma only, 172 reported COPD only, 77 reported asthma+COPD and 2937 reported neither. Fewer than half of participants with a COPD diagnosis (with or without asthma) had airflow limitation. Participants with asthma+COPD had more respiratory symptoms and greater airflow limitation than those with either diagnosis alone. Having asthma+COPD was independently associated with a higher probability of having clinically important breathlessness (modified Medical Research Council score ⩾2) than asthma only (adjusted OR 3.44, 95% CI 1.86–6.33) or COPD only (adjusted OR 3.28, 95% CI 1.69–6.39). Airflow limitation (Global Initiative for Chronic Obstructive Lung Disease 2 or higher, using post-bronchodilator forced expiratory volume in 1 s/forced vital capacity ratio <0.7) was similar between asthma only and COPD only, but twice as prevalent in asthma+COPD (adjusted OR 2.18 and 2.58, respectively).

Conclusions Adults with diagnoses of asthma+COPD have a higher symptom and disease burden than those with diagnoses of asthma only or COPD only. These patients should receive regular comprehensive reviews because of the substantially increased burden of having both diagnoses.

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are common chronic respiratory diseases that lead to a significant burden for patients and healthcare systems [1, 2]. These two diseases share some similar clinical features and overlap in their diagnostic criteria [3, 4]. This can make it difficult to distinguish asthma from COPD, particularly among smokers and older adults. Hence, some patients have been diagnosed with both asthma and COPD. In 2009, the term “overlap syndrome of asthma and COPD”

was introduced [5]. Subsequent literature, including the Global Initiative for Asthma (GINA) and Global Initiative for Obstructive Lung Disease (GOLD), referred to asthma–COPD overlap syndrome (ACOS) [6]. More recent literature has referred to "asthma–COPD overlap" or "asthma+COPD" [3, 7]; we have used "asthma+COPD" in this report.

Epidemiological studies have reported prevalence for asthma+COPD ranging from 0.6% to 3.2%, depending on age, data source and criteria used to define asthma+COPD [8–10]. Current evidence suggests that adults diagnosed with asthma+COPD may have more respiratory symptoms and exacerbations and a greater disease burden than those with asthma or COPD only [5, 7, 11]. To our knowledge, there have not been any general Australian population studies comparing clinical characteristics between patients with diagnosed asthma+COPD, asthma only or COPD only.

Most mechanistic studies and regulatory clinical trials are limited to asthma, defined by reversibility, or COPD, defined by airflow limitation, based on conventional diagnostic criteria [7]. Several studies have shown that such studies exclude up to 90% of patients in real-world community studies [12, 13]. Therefore, self-reported diagnostic data that reflect real-world diagnoses of asthma and COPD in Australia were used in this study, as is also the approach in Australian National Health Surveys [14].

The international Burden of Obstructive Lung Disease (BOLD) study aimed to measure the prevalence of COPD and its risk factors and estimate the burden of COPD [15]. In collaboration with the international BOLD study, the BOLD Australia study collected self-report and clinical test information from a large number of Australian adults. Using BOLD Australia data, we investigated the relationship between clinical characteristics and self-reported doctor diagnoses of asthma and/or COPD in adults aged ⩾40 years.

Methods

Study population

BOLD Australia was a cross-sectional study of adults aged ⩾40 years living in six sites [16] covering urban, rural, remote, inland and coastal areas, selected to reflect the sociodemographic and geographic diversity of Australia. Participants in Sydney, rural New South Wales, Melbourne and Hobart and Launceston in Tasmania were randomly selected from the electoral rolls using a sex-stratified simple random sample [16]. In Western Australia, participants were recruited from household census data in Broome (a centre with a significant Aboriginal and Torres Strait Islander (hereafter termed Indigenous Australian) population) or were randomly recruited from the Busselton Health Study [16, 17]. Data collection was completed between 2006 and 2012. Participants who were not contactable, institutionalised or aged <40 years were excluded. More detailed information for the sample selection has been published previously [16, 17].

Study questionnaire

The BOLD study questionnaires were used in all sites [15, 16]. The core questionnaire included information such as demographics, weight and height, body mass index (BMI), smoking status, self-reported clinical diagnosis of asthma and/or COPD, respiratory symptoms, comorbidities, medication use, time lost from work or daily activities, and healthcare utilisation [15]. Demographic characteristics examined included age, sex, ethnicity and education level. Respiratory symptoms included cough, phlegm, wheeze and breathlessness, which were measured by the modified Medical Research Council (mMRC) dyspnoea scale [18]. We defined "clinically important breathlessness" as mMRC dyspnoea grade ⩾2.

Specific comorbidities and respiratory medication use were also collected. Healthcare utilisation included visits to a general practitioner (GP) and hospitalisations in the last 12 months due to breathing problems.

The questions used to define self-reported diagnosed asthma+COPD, asthma only and COPD only in BOLD were:

Q1. Has a doctor or other healthcare provider ever told you that you have asthma, asthmatic bronchitis or allergic bronchitis?
Q2. Do you still have asthma, asthmatic bronchitis or allergic bronchitis?
Q3. Has a doctor or other healthcare provider ever told you that you have a) emphysema, b) chronic bronchitis or c) COPD? (Each condition was included in a separate question.)

Asthma only was defined as a "yes" to Q1 and Q2 and "no" to Q3. COPD only was defined as "no", "no" and "yes" to these questions, respectively, and asthma+COPD was defined as "yes" to all three questions.

Spirometry and atopy

Spirometry was performed using the EasyOne spirometer (ndd Medizintechnik, Zürich, Switzerland), before and 15 min after the administration of salbutamol 200 µg *via* metered dose inhaler and spacer. The quality of all spirograms was reviewed and assessed for acceptability by a senior respiratory scientist [15, 16]. Patients were required to have withheld any bronchodilator inhaler during the 6–12 h before testing [16]. The highest recorded forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) from acceptable trials [19] were collected.

Two criteria for airflow limitation, based on post-bronchodilator FEV_1/FVC ratio, were included: one was based on then-current GOLD classification (FEV_1/FVC <0.70) [20] while the other was an FEV_1/FVC ratio below the lower limit of normal, defined as the fifth percentile of the distribution using the Global Lung Initiative 2012 reference values [4, 21]. A positive bronchodilator response was defined as having an increase in FEV_1 (or FVC) of ⩾200 mL and ⩾12% from baseline [22].

Skin prick tests were used to assess sensitisation to nine common aeroallergens, including *Dermatophagoides farinae*, *D. pteronyssinus*, cat, dog, cockroach, *Alternaria*, *Aspergillus*, ryegrass and mixed-grass pollen. Participants with any allergen skin prick test ⩾4 mm were classified as atopic [23].

Statistical analysis

The study population was grouped according to self-reported doctor diagnosis. Descriptive statistics were used to describe baseline characteristics, with numbers (proportions) reported for categorical variables and mean±SD for continuous variables. The differences between groups were assessed using Chi-squared tests for categorical variables and ANOVA for continuous variables, with p-values <0.05 considered statistically significant. Multivariate logistic regression models were used to estimate adjusted odds ratios with 95% confidence intervals. To look for the difference in respiratory symptoms between participants with and without airflow limitations in the asthma+COPD and COPD-only group, we added a second multivariate logistic regression model. The approach used to select potential confounders for adjustment in the analyses was informed by the causal inference approach. The directed acyclic graphs (examples included in supplementary figures S1–S3) identified age, sex, BMI status and smoking status as potential confounders because they could open a back-door pathway association between "exposure" (diagnostic label) and "outcome" (clinical feature) and therefore should be adjusted for in the analyses [24]. All data were analysed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

From among 10 760 eligible participants in the BOLD Australia study [16], 3522 (32.7%) completed the BOLD questionnaire and performed acceptable pre- and post-bronchodilator spirometry and thus were included in the present analysis. Compared with minimal data from those who chose not to participate, participants included in this analysis were younger and more likely to have a diagnosed respiratory illness [16]. Of the 3522 participants, 336 (9.5%) self-reported a doctor diagnosis of asthma only, 172 (4.9%) COPD only, 77 (2.2%) asthma+COPD and 2937 (83.4%) no diagnosis of asthma or COPD.

Table 1 shows the demographic characteristics of the participants. The characteristics of age, being female, smoking status, BMI status and highest education were significantly different between the four diagnostic groups. There were no significant differences in ethnicity.

All respiratory symptoms and respiratory medication use were reported most frequently in the asthma+COPD group compared with the other groups (table 2). For almost all respiratory symptoms, the odds of having symptoms were higher in the asthma+COPD group compared with the asthma-only or COPD-only groups. Only cough without a cold and any wheeze in the last 12 months were not significantly different between the asthma+COPD and asthma-only groups. Almost all (96.1%) of the asthma+COPD group reported using respiratory medications, compared with 83.3% of those with an asthma-only diagnosis but only 30.8% of those reporting COPD only (table 2). The asthma+COPD group reported the highest proportion of comorbidities, but there were no significant differences between the asthma+COPD and asthma-only or COPD-only groups (table 2). The asthma+COPD group also had higher proportions of participants reporting absences from work or daily activities and healthcare utilisation compared with the asthma-only and COPD-only groups (table 2).

The spirometry results showed that, of the four groups, the asthma+COPD group had the lowest mean pre- and post-bronchodilator FEV_1 and FVC (table 3). Of patients with self-reported COPD (with or without asthma), <40% had post-bronchodilator airflow limitation, assessed either as an FEV_1/FVC ratio below the lower limit of normal or <0.7. Compared with the asthma-only and COPD-only groups, the asthma+COPD

TABLE 1 Demographic characteristics of the BOLD Australia sample, by self-reported diagnosed disease

Characteristic	Neither asthma nor COPD	Asthma only	Asthma+COPD	COPD only	Total	p-value
Subjects, n	2937	336	77	172	3522	
Age, years	58.3±11.6	57.5±11.4	62.5±12.4	61.9±11.9	58.5±11.7	<0.0001
Female	1472 (50.1)	210 (62.5)	47 (61.0)	92 (53.5)	1821 (51.7)	<0.0001
Ethnicity						0.09
Total with data, n	2936	336	77	172	3521	
Caucasian	2602 (88.6)	281 (83.6)	71 (92.2)	154 (89.5)	3108 (88.3)	
Indigenous Australian	207 (7.1)	37 (11.0)	4 (5.2)	14 (8.1)	262 (7.4)	
Other	127 (4.3)	18 (5.4)	2 (2.6)	4 (2.3)	151 (4.3)	
Smoking status						<0.0001
Never-smoker	1422 (48.4)	169 (50.3)	25 (32.5)	43 (25.0)	1659 (47.1)	
Former smoker	1173 (39.9)	128 (38.1)	45 (58.4)	93 (54.1)	1439 (40.9)	
Current smoker	342 (11.6)	39 (11.6)	7 (9.1)	36 (20.9)	424 (12.0)	
Pack-years						<0.0001
Total with data, n	2934	336	77	171	3518	
0	1422 (48.5)	169 (50.3)	25 (32.5)	43 (25.2)	1659 (47.2)	
⩽10	652 (22.2)	67 (19.9)	18 (23.4)	19 (11.1)	756 (21.5)	
10–<20	329 (11.2)	41 (12.2)	5 (6.5)	20 (11.7)	395 (11.2)	
⩾20	531 (18.1)	59 (17.6)	29 (37.7)	89 (52.1)	708 (20.1)	
BMI, kg·m^{-2}	27.9±4.9	28.4±5.7	28.7±6.3	27.9±6.1	28.0±5.1	0.15
BMI status						0.0009
Total with data, n	2886	324	75	166	3451	
<18.5 kg·m^{-2}	18 (0.6)	2 (0.6)	1 (1.3)	7 (4.2)	28 (0.8)	
18.5–<25.0 kg·m^{-2}	826 (28.6)	92 (28.4)	20 (26.7)	50 (30.1)	988 (28.6)	
25.0–<30.0 kg·m^{-2}	1167 (40.4)	127 (39.2)	30 (40.0)	55 (33.1)	1379 (40.0)	
⩾30.0 kg·m^{-2}	875 (30.3)	103 (31.8)	24 (32.0)	54 (32.5)	1056 (30.6)	
Highest education						0.0004
Total with data, n	2374	251	58	134	2817	
Primary education or less	45 (2.0)	4 (1.6)	3 (5.2)	8 (6.0)	63 (2.2)	
High school	857 (36.1)	83 (33.1)	28 (48.3)	64 (47.8)	1032 (36.6)	
Technical or further education	829 (34.9)	90 (35.9)	19 (32.8)	40 (29.9)	978 (34.7)	
University	640 (27.0)	74 (29.5)	8 (13.8)	22 (16.4)	744 (26.4)	

Data are presented as mean±SD or n (%), unless otherwise stated. For percentages, the denominator is given when different from the total number of patients (total with data, excluding "unknown"). COPD: chronic obstructive pulmonary disease; BMI: body mass index.

group had higher odds of airflow limitation. In addition, a higher proportion of participants in the asthma+COPD group had significant bronchodilator responsiveness than in the COPD-only group, and proportionately fewer had atopy compared with the asthma-only group (table 3 and table 4).

In the asthma+COPD group, a significantly lower proportion of participants with airflow limitation reported cough but a significantly higher proportion reported clinically important breathlessness than did participants without airflow limitation. In the COPD-only group, only any wheeze in the last 12 months was reported significantly more often by participants with airflow limitation (table 5).

Figure 1 shows four key characteristics across groups by self-reported diagnostic label.

Discussion

To our knowledge, this is the first Australian population-based study that has compared clinical and spirometric characteristics in adults based on their self-reported diagnosis of obstructive lung diseases. This is also the basis for official Australian government data about asthma and about COPD. We found, in adults aged ⩾40 years, that <40% of participants self-reporting a diagnosis of COPD, with or without asthma, had airflow limitation on spirometry. However, participants with asthma+COPD had more respiratory symptoms, greater airflow limitation, were more likely to use respiratory medications, and more often reported absences from work or daily activities, GP visits and hospitalisation owing to breathing problems than those with asthma or COPD only. Additionally, there was important heterogeneity (meaning variation in clinical characteristics) within the asthma-only, COPD-only and asthma+COPD groups, and overlap between these groups. These findings have important implications for clinical practice and for research.

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TABLE 2 Respiratory symptoms, comorbidities and health burden of the BOLD Australia sample, by self-reported diagnosed disease

Characteristics	Neither asthma nor COPD	Asthma only	Asthma+COPD	COPD only	Total	Asthma+COPD *versus* Asthma only		Asthma+COPD *versus* COPD only	
						OR (95% CI)	p-value	OR (95% CI)	p-value
Subjects, n	2937	336	77	172	3522				
Respiratory symptoms									
Cough without a cold	790 (26.9)	159 (47.3)	45 (58.4)	76 (44.2)	1070 (30.9)	1.49 (0.89–2.51)	0.13	2.08 (1.19–3.68)	0.01
Cough on most days for ⩾3 months[#]	224 (7.6)	68 (20.2)	27 (35.1)	36 (20.9)	355 (10.1)	2.32 (1.33–4.03)	0.003	2.72 (1.46–5.07)	0.002
Phlegm without a cold	479 (16.3)	103 (30.7)	43 (55.8)	60 (34.9)	685 (19.5)	2.76 (1.63–4.72)	0.0002	3.20 (1.80–5.74)	<0.0001
Phlegm on most days for ⩾3 months[#]	164 (5.6)	47 (14.0)	22 (28.6)	28 (16.4)	261 (7.4)	2.38 (1.28–4.34)	0.005	2.99 (1.51–5.90)	0.002
Any wheeze in the last 12 months	639 (21.8)	246 (73.2)	64 (83.1)	81 (47.1)	1030 (29.3)	1.58 (0.84–3.17)	0.17	6.64 (3.44–13.6)	<0.0001
Wheeze with SOB in the last 12 months[#]	219 (7.5)	186 (55.5)	52 (67.5)	41 (23.8)	498 (14.2)	1.74 (1.02–3.03)	0.048	7.92 (4.33–14.9)	<0.0001
mMRC ⩾2[#]	138 (4.9)	54 (17.5)	29 (42.0)	31 (20.5)	252 (7.6)	3.44 (1.86–6.33)	<0.0001	3.28 (1.69–6.39)	0.0005
Medication use									
Any respiratory medication use	181 (6.2)	280 (83.3)	74 (96.1)	53 (30.8)	588 (16.7)	6.56 (1.96–40.7)	0.01	84.6 (25.1–529)	<0.0001
Comorbidities									
Heart disease	251 (8.6)	39 (11.6)	17 (22.1)	25 (14.5)	332 (9.4)	1.63 (0.80–3.24)	0.17	1.90 (0.88–4.02)	0.10
Hypertension	974 (33.2)	138 (41.1)	37 (48.1)	68 (39.5)	1217 (34.6)	1.04 (0.60–1.80)	0.90	1.46 (0.80–2.66)	0.22
Diabetes	292 (9.9)	41 (12.2)	11 (14.3)	24 (14.0)	368 (10.5)	1.07 (0.48–2.22)	0.86	1.12 (0.48–2.47)	0.79
Lung cancer	10 (0.3)	1 (0.3)	1 (1.3)	7 (4.1)	19 (0.5)	2.43 (0.09–63.1)	0.54	0.43 (0.02–2.84)	0.45
Stroke	52 (1.8)	13 (3.9)	8 (10.4)	9 (5.2)	82 (2.3)	1.99 (0.73–5.11)	0.16	2.41 (0.82–7.10)	0.11
Number of comorbidities ⩾2	331 (11.3)	56 (16.7)	21 (27.3)	31 (18.0)	439 (12.5)	1.51 (0.79–2.84)	0.20	1.96 (0.97–3.93)	0.06
Time lost from work/social activities[¶]									
⩾1 episode in the past 12 months[#]	95 (3.2)	43 (12.8)	24 (31.2)	14 (8.1)	176 (5.0)	3.68 (2.00–6.73)	<0.0001	5.45 (2.60–11.9)	<0.0001
Healthcare use in the past 12 months[#,¶]									
⩾1 GP visit[#]	70 (2.6)	34 (10.1)	18 (23.4)	10 (5.8)	132 (3.8)	3.27 (1.66–6.33)	0.0005	4.67 (2.04–11.2)	0.0003
⩾1 hospitalisation	15 (0.5)	9 (2.7)	4 (5.2)	1 (0.6)	29 (0.8)	1.98 (0.51–6.66)	0.29	9.95 (1.41–198)	0.04

Data are presented as n (%) unless otherwise stated; adjusted for age, sex, body mass index status and smoking status. COPD: chronic obstructive pulmonary disease; SOB: shortness of breath; mMRC: modified Medical Research Council; GP: general practitioner. [#]: does not include all observations due to missing data; [¶]: described as "When breathing problems got so bad that they interfered with usual daily activities or caused participants to miss work".

TABLE 3 Lung function results of the BOLD Australia sample, by self-reported diagnosed disease

Characteristics	Neither asthma nor COPD	Asthma only	Asthma +COPD	COPD only	Total	Asthma+COPD *versus* Asthma only p-value	Asthma+COPD *versus* COPD only p-value
Subjects, n	2937	336	77	172	3522		
Pre-BD spirometry[#]							
FEV_1, % pred	94.8±16.2	82.1±19.6	70.3±24.1	83.6±19.9	92.5±17.8	<0.0001	<0.0001
FEV_1, % pred (GLI)	94.8±16.1	82.3±19.6	70.2±24.3	83.3±19.7	92.5±17.7	<0.0001	<0.0001
FVC, % pred (GLI)	98.5±15.7	92.2±17.3	86.1±20.0	93.0±16.9	97.4±16.2	0.001	<0.0001
Post-BD spirometry[#]							
FEV_1, % pred	97.2±15.9	87.0±18.9	74.5±23.9	86.5±19.7	95.2±17.3	<0.0001	<0.0001
FEV_1, % pred (GLI)	97.2±15.7	87.1±18.9	74.4±24.1	86.2±19.6	95.2±17.1	<0.0001	<0.0001
FVC, % pred (GLI)	98.0±15.2	93.7±17.0	88.6±18.5	94.0±17.3	97.2±15.7	0.006	0.002
Post-BD FEV_1/FVC[#]	0.8±0.1	0.7±0.1	0.7±0.2	0.7±0.1	0.8±0.1	<0.0001	<0.0001

Data are presented as mean±SD, unless otherwise stated; adjusted for age, sex, body mass index status and smoking status. p-values determined by ANOVA. COPD: chronic obstructive pulmonary disease; BD: bronchodilator; FEV_1: forced expiratory volume in 1 s; GLI: Global Lung Initiative; FVC: forced vital capacity. [#]: does not include all observations due to missing data.

We found that 31% of the adults aged ⩾40 years reporting a COPD diagnosis had also been told by a doctor that they had asthma. This is similar to the 29% reported from a large nationally representative study of Australian adults aged ⩾18 years [25], but less than the 43% reported by another survey by the Australian Bureau of Statistics of adults aged ⩾45 years [14]. As in our analysis, diagnoses in these studies were based on patient self-report.

A clinical trial in Australian primary care found that 23% of COPD patients also had an asthma diagnosis recorded by the GP [26]. However, these estimates cannot directly be compared with ours owing to the age distribution of the samples, and the different definitions of COPD and asthma+COPD used. Previous studies reported that asthma+COPD was more common in women and less educated people, consistent with our findings [9]. The prevalence of smoking among participants with asthma+COPD was higher than among those with asthma only and neither asthma nor COPD, but lower than among those with COPD only, similar to previous studies [7, 9].

Reports comparing lung function between asthma+COPD and asthma only or COPD only have been inconsistent [7, 27]. We observed those with asthma+COPD had worse lung function than those with either diagnosis alone. The NOVELTY study [7], a large observational study that recruited patients from primary and specialist care, found that the proportion of patients with persistent airflow limitation was similar between patients with asthma+COPD and patients with COPD but higher than in patients with asthma [7]. The average post-bronchodilator FEV_1 % predicted was much lower in the NOVELTY COPD and asthma+COPD populations than in BOLD, likely because recruitment to NOVELTY was stratified by severity [7]. The characteristics of the groups vary in ways that may explain these differences in lung function, with the asthma group being younger and having a larger proportion of never-smokers. Looking at the >20 pack-year history shows this exposure was greatest in the asthma+COPD and COPD-only groups. Phlegm on most days for at least 3 months was more common in the asthma+COPD group, indicating increased mucus hypersecretion, which is associated with worse lung function and is another potential pathobiological mechanism for the differences in lung function observed between groups.

Bronchodilator responsiveness for the asthma+COPD and asthma-only group was similar to the results reported by previous studies, but the proportion in the COPD-only group was much lower than in previous studies [7, 28]. We found the asthma+COPD group had significantly lower odds of atopy than the asthma-only group, as observed previously [29].

Turning to burden for patients, we found more respiratory symptoms in the asthma+COPD group, similar to previous studies [27, 30]. Most strikingly, the occurrence of clinically important breathlessness (mMRC ⩾2) was similar in participants with asthma only and COPD only, but the odds were three times higher for those with asthma+COPD. The significantly higher proportions of participants without airflow limitation in the asthma+COPD group who reported cough without a cold and cough on most days for at least 3 months may be due to overdiagnosis of COPD. Because chronic cough is often the first symptom

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TABLE 4 Airflow limitation, responsiveness and atopy results of the BOLD Australia sample, by self-reported diagnosed disease

Characteristics	Neither asthma nor COPD	Asthma only	Asthma +COPD	COPD only	Total	Asthma+COPD *versus* Asthma only		Asthma+COPD *versus* COPD only	
						OR (95% CI)	p-value	OR (95% CI)	p-value
Subjects, n	2937	336	77	172	3522				
Severity of airflow limitation by GOLD category, if post-BD FEV_1/FVC <0.7[#]									
Any FEV_1 pred (GOLD 1 or higher)	356 (12.1)	95 (28.3)	37 (48.0)	61 (35.5)	549 (15.6)	1.61 (0.90–2.88)	0.11	2.28 (1.21–4.28)	0.01
FEV_1 <80% pred (GOLD 2 or higher)	126 (4.3)	58 (17.3)	30 (39.0)	41 (23.8)	255 (7.3)	2.18 (1.20–3.94)	0.01	2.58 (1.36–4.90)	0.004
FEV_1 <50% pred (GOLD 3 or higher)	10 (0.3)	11 (3.3)	14 (18.2)	8 (4.7)	43 (1.2)	4.76 (1.95–11.9)	0.0006	7.90 (2.81–24.5)	0.0001
Severity of airflow limitation by GOLD category, if post-BD FEV_1/FVC <LLN)[#]									
Any FEV_1 pred (GOLD 1 or higher)	152 (5.2)	75 (22.3)	35 (45.5)	40 (23.3)	302 (8.6)	2.38 (1.36–4.17)	0.003	4.03 (2.16–7.58)	<0.0001
FEV_1 <80% pred (GOLD 2 or higher)	80 (2.7)	52 (15.5)	30 (39.0)	29 (16.9)	191 (5.4)	2.64 (1.46–4.75)	0.001	4.53 (2.33–8.91)	<0.0001
FEV_1 <50% pred (GOLD 3 or higher)	9 (0.3)	11 (3.3)	15 (19.5)	8 (4.7)	43 (1.2)	5.13 (2.11–12.8)	0.0003	9.52 (3.39–29.8)	<0.0001
BD responsiveness									
⩾12% and ⩾200 mL	97 (3.3)	58 (17.3)	11 (14.3)	11 (6.4)	177 (5.0)	0.70 (0.33–1.40)	0.34	3.06 (1.21–7.81)	0.02
Skin prick tests[#]									
Any atopy	942 (44.2)	159 (72.3)	23 (46.9)	52 (48.2)	1176 (46.9)	0.40 (0.21–0.75)	0.005	1.00 (0.50–2.00)	0.99

Data are presented as n (%) unless otherwise stated; adjusted for age, sex, body mass index status and smoking status. COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Pulmonary Disease 2022; BD: bronchodilator; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal. [#]: does not include all observations due to missing data.

TABLE 5 Self-reported respiratory symptoms of the asthma+COPD and COPD only group, by airflow limitation (FEV_1/FVC <0.7)

Respiratory symptoms	Asthma+COPD[#]				COPD only[¶]			
	Airflow limitation	No airflow limitation	OR (95% CI)	p-value	Airflow limitation	No airflow limitation	OR (95% CI)	p-value
Subjects, n	37	40			61	111		
Cough without a cold	16 (43.2)	29 (72.5)	0.30 (0.10–0.83)	0.02	34 (55.7)	42 (37.8)	1.61 (0.77–3.35)	0.20
Cough on most days for ⩾3 months	8 (21.6)	19 (47.5)	0.27 (0.08–0.83)	0.03	18 (29.5)	18 (16.2)	1.55 (0.62–3.81)	0.34
Phlegm without a cold	20 (54.1)	23 (57.5)	0.73 (0.25–2.05)	0.56	28 (45.9)	32 (28.8)	1.27 (0.59–2.73)	0.54
Phlegm on most days for ⩾3 months	9 (24.3)	13 (32.5)	0.41 (0.11–1.35)	0.16	16 (26.2)	12 (10.9)	1.55 (0.56–4.30)	0.40
Any wheeze in the last 12 months	31 (83.8)	33 (82.5)	2.08 (0.54–9.01)	0.30	38 (62.3)	43 (38.7)	2.32 (1.11–4.97)	0.03
Wheeze with SOB in the last 12 months	23 (62.2)	29 (72.5)	1.04 (0.34–3.25)	0.08	19 (31.2)	22 (19.8)	1.79 (0.76–4.21)	0.18
mMRC ⩾2	19 (55.9)	10 (28.6)	4.33 (1.34–16.1)	0.02	15 (30.0)	16 (18.4)	1.63 (0.64–4.12)	0.30

Data are presented as n (%) unless otherwise stated; adjusted for age, sex, body mass index status and smoking status. COPD: chronic obstructive pulmonary disease; SOB: shortness of breath; mMRC: modified Medical Research Council. [#]: n=77; [¶]: n=172.

of COPD [4], patients reporting a chronic cough may be more likely to be diagnosed with COPD in primary care settings, given the poor utilisation of spirometry [31].

Respiratory medication use was more often reported by participants with asthma+COPD than by those with COPD only or asthma only, consistent with previous studies [32]. Guidelines for the treatment of asthma and COPD are different, with long-acting bronchodilators alone (without inhaled corticosteroids (ICS)) recommended for initial treatment of COPD [4] but contraindicated in asthma due to increased risk of hospitalisation and death [3, 33], including in patients with asthma+COPD. Owing to more frequent

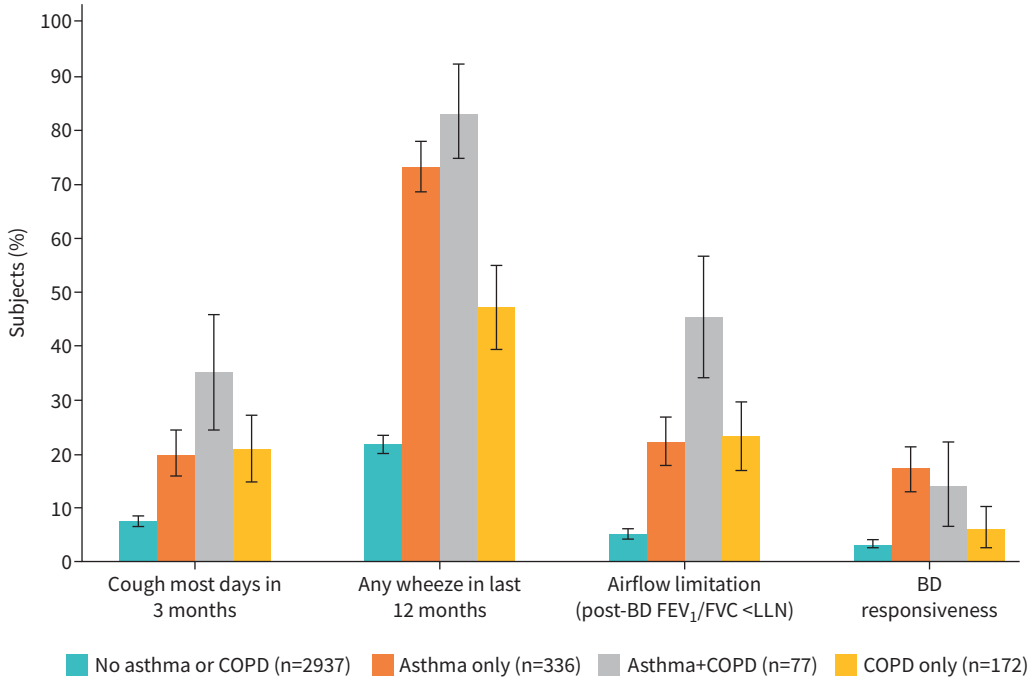

FIGURE 1 Four key characteristics of obstructive lung disease, by self-reported diagnosis of asthma and/or chronic obstructive pulmonary disease (COPD). Data presented with 95% confidence intervals. BD: bronchodilator; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal.

symptoms and exacerbations, patients with asthma+COPD may visit medical practices more frequently, which potentially increases the likelihood of receiving a prescription.

Although there are few randomised controlled trials in patients with asthma+COPD, GINA recommends that these patients should receive at least low-dose ICS (as well as bronchodilators). This is based on strong evidence in asthma alone [3] and from population studies showing that, in patients with both asthma and COPD, treatment with ICS and a long-acting β_2-agonist (LABA) significantly reduced the risk of hospitalisation and death compared with the use of a LABA alone [34–36]. Of concern, only 83% of participants with asthma+COPD received treatment with any ICS in the present analysis (supplementary table S1). These results may indicate that at the time the study was conducted, many patients with asthma+COPD might not have been receiving appropriate treatment.

Previous studies found that asthma+COPD was associated with a greater burden of multimorbidity [9]. We also showed this trend for a range of comorbidities and also for time lost from work or daily activities and healthcare utilisation, which reflected an increased disease burden in participants with asthma+COPD than in those with asthma only or COPD only [8, 9]. Combined with the clinical features shown in this analysis, this increased burden might be attributable to frequent or severe exacerbations caused by more respiratory symptoms and greater airflow limitation. Previous studies reported a greater burden of exacerbations among asthma+COPD patients than among those with either diagnosis alone [7, 11].

The main strengths of our study were that the data were from a large nationwide population sample [16], the use of self-reported diagnoses of asthma and/or COPD (allowing comparison with Australian government data) and the use of standardised measurements from the BOLD international protocol, allowing comparisons between countries [37]. We were able to compare different diagnostic groups, including participants not diagnosed with asthma and COPD, and used both fixed cut-off and lower limit of normal methods to assess airflow limitation, allowing comparison with studies using either criterion.

Limitations were the cross-sectional design that did not allow for the assessment of causality or long-term outcomes. Use of self-reported doctor diagnoses without any ability to assess the appropriateness of the diagnosis could also be regarded as a limitation, because it may introduce recall bias and misclassification given that undiagnosed and misdiagnosed asthma and COPD are undoubtedly common [38, 39]. The low overall response rate may introduce the possibility of selection bias, with those included in the analysis being slightly younger and more likely to self-report a diagnosis of COPD compared with those who provided only minimal data [16]. Finally, the study participants were not a simple random sample of the Australian population because the six study sites were not chosen completely at random. Although *post hoc* weights were used in previous work to adjust prevalence estimates to better reflect the Australian population [16], in this analysis sample prevalence estimates were used.

Our findings have significant implications for health service development in Australia. In real-life clinical practice, the diagnostic classifications used by health professionals, as reported by patients, distinguish poorly between clinical phenotypes [7]. Because of differences in the optimal treatment of asthma and COPD, a more accurate diagnostic classification can help to avoid inappropriate or unsafe treatment decisions. These findings could also increase health professionals' attention to asthma+COPD in real-life clinical practice. Identification of asthma+COPD should be made at an early stage and distinguished from purely COPD in order to initiate appropriate treatment and optimise patient prognosis.

Conclusion

This study provided a comprehensive characterisation of Australian adults aged ⩾40 years with self-reported doctor diagnoses of asthma only, COPD only, asthma+COPD and neither asthma nor COPD. Adults with asthma+COPD had the most severe disease, as demonstrated by the most frequent respiratory symptoms and greater airflow limitation, compared with those with asthma only or COPD only. Additionally, there was important heterogeneity, indicating variation in clinical characteristics within groups, and overlap between the asthma-only, COPD-only and asthma+COPD groups. These findings indicate that the diagnostic classifications used by health professionals in real-life clinical practice, as reported by patients, distinguish poorly between clinical phenotypes, which may lead to inappropriate or unsafe treatment decisions [7].

Future research is needed to improve diagnostic tools for asthma and/or COPD in real-world clinical practice, further understanding of their pathophysiological mechanisms and molecular endotypes, and trials of better-targeted treatments, which may help to make more precise clinical classifications and treatment

decisions. Based on increasing evidence, this is a group of patients that may benefit from targeted pharmacological interventions in the future.

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Data availability statement: The data that support the findings of this study are available at reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Human/animal ethics approval declaration: The BOLD Australia Study was approved by the Human Research Ethics Committee (HREC) of the University of Sydney (ref. 12-2006/9724). Each study site also obtained local HREC approval, including approval from the Western Australian Aboriginal Health Information and Ethics Committee. Informed participant consent was obtained as per site-specific ethics approvals.

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