

ORIGINAL RESEARCH

Respiratory Symptoms, Disease Burden, and Quality of Life in Australian Adults According to GOLD Spirometry Grades: Data from the BOLD Australia Study

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Purpose: Population data on the burden of chronic obstructive pulmonary disease (COPD) are often based on patient-reported diagnoses of COPD, emphysema or chronic bronchitis, without spirometry. We aimed to investigate the relationship between health burden, quality of life and severity of airway obstruction in Australian adults aged ≥40 years.

Methods: We used data from the BOLD Australia study, which included randomly selected adults aged ≥40 years from six study sites to reflect the sociodemographic and geographic diversity of the Australian population (n = 3522). Participants with post-bronchodilator airflow limitation (ratio of forced expiratory volume in 1 second FEV₁ to forced vital capacity <0.7) were grouped by GOLD spirometry grades 1-4. Quality of life was assessed with Short Form 12 (SF-12) Health Survey Questionnaire. Health burden was assessed as lost time off work or social activities, and healthcare utilization.

Results: Of the study sample, 2969 participants did not have airflow limitation, 294 (8.4%) were classified as GOLD Grade 1, 212 (6.0%) as GOLD 2 and 43 (1.2%) as GOLD 3-4. Participants with higher GOLD grades had more respiratory symptoms, more comorbidities and greater burden than those with lower GOLD grades. The scores of mental and physical subscales of SF-12 were lower, indicating worse quality of life, from the no airflow limitation group to the GOLD 3-4 group (P = 0.03 and P < 0.001, respectively).

Conclusion: Greater airflow limitation is associated with greater burden and poor quality of life. Interventions to prevent, or reduce the level of, airflow limitation will reduce the symptom burden and improve quality of life for patients.

Keywords: chronic obstructive pulmonary disease, airflow limitation, comorbidities, The Burden of Obstructive Lung Disease, quality of life

Introduction

Chronic obstructive pulmonary disease (COPD) is the most prevalent chronic respiratory disease that leads to a significant burden on health. In 2017, COPD was the seventh leading cause of global disability. In 2019, COPD caused 3.23 million deaths globally, making it the third leading cause of death. In Australia, COPD was one of the top 5 leading causes of death; there were 7113 deaths due to COPD in 2018, and COPD was the third leading cause of overall disease burden in Australia in 2015. 4,5 Moreover, COPD is associated with multimorbidity including osteoporosis, diabetes, hypertension, cardiovascular disease, depression, and lung cancer. 1,6–8

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Because of the significant worldwide burden of COPD, the Global initiative for chronic Obstructive Lung Disease (GOLD) has created evidence-based guidelines that are updated annually. According to the self-reported data from the 2017–18 Australian Bureau of Statistics (ABS) National Health Survey (NHS), approximately 4.8% of Australians aged 45 years and over have COPD. The weighted prevalence of COPD in Australians, based on the ratio of post-bronchodilator forced expiratory volume in 1 second to forced vital capacity (FEV₁/FVC) <0.7, was estimated to be 8.3% in adults aged 40+ years, and 19.8% in adults aged 75+ years. Although COPD is relevant in Australia and associated with a significant health burden, previous Australian studies have not reported indirect burdens such as lost time off work or social activities and healthcare utilization in community-living patients with a diagnosis of COPD based on GOLD spirometric criteria. Indeed, core Australian data on COPD from the Australian Institute of Health and Welfare (AIHW) come from surveys in which people with COPD are identified only by self-reporting a diagnosis of COPD, emphysema or chronic bronchitis, without lung function testing.

COPD is a highly symptomatic disease that requires symptom-based treatments.¹ The physical and emotional symptoms of COPD are known to have a negative impact on the quality of life in patients.¹¹ Because COPD is irreversible and progressive, quality of life is a useful tool for assessing COPD severity and treatment outcomes.

The Burden of Obstructive Lung Disease (BOLD) Australia study collected measures of lung function by spirometry and self-reported outcomes by questionnaires including indirect burdens (defined as lost time off work or social activities and healthcare utilization), respiratory symptoms, comorbidities, and quality of life. Although the GOLD 2023 report¹ has proposed an assessment tool based on symptoms and exacerbation history, the BOLD Australia database did not have complete information on the ABE assessment tool, especially the exacerbation history and the Australian and New Zealand guidelines for the management of COPD (COPD-X)¹³ has not yet adopted the ABE classification. BOLD Australia could still provide an opportunity to more thoroughly understand the impacts of different GOLD grades of airflow limitation in Australians aged ≥40 years.

Our study aimed to investigate the relationship between health burden and different GOLD grades of severity of airflow limitation in Australian adults aged \geq 40 years.

Methods

Sample

We used data from the BOLD Australia study, which is the largest geographically diverse population-based study of spirometrically confirmed COPD in Australia. It was a cross-sectional study conducted between 2006 and 2012 of individuals aged ≥40 years from six study sites across Australia, including Sydney, rural New South Wales, Melbourne, Tasmania (Hobart and Launceston) and Busselton and Broome in Western Australia. ¹² In Western Australia, participants were recruited from a household census data in Broome and local aboriginal communities within the Kimberley region or were randomly recruited from the Busselton Health Study. The study design and detailed information for the sample selection were published previously. ^{12,14} Participants who were not contactable, institutionalized, or aged younger than 40 years were excluded. Participants in the BOLD Australia study who were missing spirometry test results were excluded from these analyses. Data for all six Australian sites are included in this analysis; some results from the Sydney site have been published previously in an analysis of data from 17 BOLD countries. ¹⁵

Description of Variables

All participants completed the BOLD core questionnaire that included details of demographics, smoking status, occupational exposures, respiratory medication use, and respiratory symptoms (<u>Supplementary Information S1</u>). ^{12,16} Socioeconomic status was reported by using quintiles of Socio-Economic Indexes for Areas (SEIFA), with SEIFA 1 being the "most disadvantaged" and SEIFA 5 being the "least disadvantaged" area. ¹⁷ Occupational exposures were reported as having worked in a dusty job for at least 1 year.

Respiratory symptoms included cough, phlegm, wheeze, and breathlessness. Activity limitation due to breathlessness was measured by the modified Medical Research Council (mMRC) dyspnoea scale. 18 We defined "linically important breathlessness" as mMRC dyspnoea grade ≥ 2 . Specific comorbidities reported were asthma, heart disease, hypertension,

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diabetes, lung cancer, and stroke. The disease-related indirect burdens reported were lost time off work or social activities, and healthcare utilization. Healthcare utilization included visits to a general practitioner (GP) and hospitalizations in the last 12 months, due to breathing problems.

Quality of life was reported as domain scores of the Short-Form (SF)-12 questionnaire. The BOLD Australia survey did not collect the answer to all SF-12 questions for Indigenous participants, those participants only answered the first question in the SF-12 questionnaire ("In general, would you say your health is"). Thus, we use the result of the first question (SF-1) in the SF-12 to define self-reported general health status. We defined participants who reported excellent, very good, and good as good or above general health. Since there were no Australian norms available, the physical and mental component summary scores (PCS, MCS) of SF-12 were computed using US norms. ¹⁹

Spirometry was measured according to the American Thoracic Society/European Respiratory Society standards, using the EasyOne spirometer (ndd Medizintechnik, Zürich, Switzerland). All spirograms were reviewed and quality graded by a senior respiratory scientist. The highest recorded post-bronchodilator forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) from acceptable trials were collected. Spirometry predicted values were calculated using the Global Lung Function Initiative (GLI) reference equations. Caucasian predicted values were used. The severity of airflow limitation was graded using the GOLD criterion for COPD (post-bronchodilator FEV₁/FVC ratio <0.70): mild, GOLD 1, FEV₁ \geq 80% predicted; moderate, GOLD 2, 50% \leq FEV₁ < 80% predicted; severe or very severe, GOLD 3 or 4, FEV₁ < 50% predicted.

Statistical Analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). The study population was grouped according to GOLD spirometry grades (No airflow limitation, GOLD 1, GOLD 2, and GOLD 3–4). Data are presented as numbers with proportions for categorical variables and means \pm standard deviations (SD) or median with interquartile range [IQR] for continuous variables. The differences between groups were assessed using χ^2 tests for categorical variables, analysis of variance for continuous variables that followed normal distributions, and Wilcoxon rank-sum tests for continuous variables that did not follow normal distributions. A p-value <0.05 was considered statistically significant.

A multivariate logistic regression model was used to analyze general health by the severity of airflow limitation, and multiple linear regression was used in the multiple variable analyses with PCS and MCS. In this analysis, the selection of potential confounders for adjustment was based on a causal inference approach, using Directed Acyclic Graphs (DAGs). As shown in <u>Figures S1–S3</u>, these identified age, sex, body mass index (BMI) status, smoking status, socioeconomic status, heart disease, hypertension, and diabetes as potential confounders, because they may open a back-door pathway association between exposure and outcome, therefore, should be adjusted for in the analyses.²²

Results

From among 10760 eligible participants in the BOLD Australia study, ¹² 3518 (32.7%) participants with acceptable pre- and post-bronchodilator spirometry results were included in the present analysis. Using minimal information data collected from those who chose not to participate, we found that the sample included in this analysis was younger and more likely to have self-reported diagnosed respiratory disease. Among all participants, 2969 (84.4%) did not have airflow limitation, 294 (8.4%) were classified as GOLD stage 1, 212 (6.0%) GOLD 2 and 43 (1.2%) GOLD 3 or 4.

Table 1 describes the demographic characteristics of all participants. The characteristics of age, gender, ethnicity, smoking status, BMI status, highest education, and experience of working in a dusty job were significantly different among the four groups. However, there were no significant differences in socioeconomic status among the four groups.

From the no airflow limitation group to the GOLD 3 or 4 group, the proportions having any of the self-reported respiratory symptoms were increased, and there were significant differences across the four groups (Table 2). Almost three quarters (72.1%) of the GOLD 3 or 4 group reported using respiratory medications, compared with 41.5% of those with GOLD 2 and 20.4% of GOLD 1. The proportions of having current asthma, hypertension, diabetes, lung cancer, stroke, and having 2 or more comorbidities were reported most frequently in the GOLD 3 or 4 group, followed by GOLD 2, GOLD 1, and no airflow

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Table I Demographic Characteristics of the BOLD Australia Sample, by GOLD Spirometric Grades

| Characteristic | No Airflow Limitation ^a (n=2969) | GOLD I FEV ₁ ≥ 80% Predicted (n=294) | GOLD 2 50% ≤ FEV ₁ < 80% predicted (n=212) | GOLD 3 or 4 FEV ₁ < 50% predicted (n=43) | Total (n=3518) | P-values |
|--|---|--|---|---|-------------------|-----------|
| Mean age, years (SD) | 57.1 (11.1) | 66.2 (11.7) | 66.1 (11.7) | 67.9 (11.6) | 58.5 (11.7) | P<0.0001 |
| Sex, female | 1581 (53.3) | 114 (38.8) | 106 (50.0) | 18 (41.9) | 1819 (51.7) | P<0.0001 |
| Ethnicity | | | | | | P=0.0005 |
| N with data | 2968 | 294 | 212 | 43 | 3517 | |
| Caucasian | 2596 (87.5) | 283 (96.3) | 192 (90.6) | 35 (81.4) | 3106 (88.3) | |
| Indigenous | 236 (8.0) | 5 (1.7) | 13 (6.1) | 6 (14.0) | 260 (7.4) | |
| Other | 136 (4.6) | 6 (2.0) | 7 (3.3) | 2 (4.7) | 151 (4.3) | |
| Smoking status | | | | | | P<0.0001 |
| Never smoked | 1482 (49.9) | 103 (35.0) | 60 (28.3) | 11 (25.6) | 1656 (47.1) | |
| Former smoker | 1165 (39.2) | 145 (49.3) | 108 (50.9) | 21 (48.8) | 1439 (40.9) | |
| Current smoker | 322 (10.9) | 46 (15.7) | 44 (20.8) | 11 (25.6) | 423 (12.0) | |
| Mean BMI, kg/m² (SD) | 28.1 (5.0) | 26.6 (4.6) | 28.1 (5.5) | 28.4 (7.1) | 28 (5.1) | P =0.0001 |
| N with data | 2916 | 287 | 204 | 40 | 3447 | |
| BMI status | | | | | | |
| BMI $<$ 18.5 kg/m ² | 21 (0.7) | 2 (0.7) | 3 (1.5) | 2 (5.0) | 28 (0.8) | P<0.0001 |
| 18.5≤ BMI <25.0 | 800 (27.4) | 116 (40.4) | 62 (30.4) | 10 (25.0) | 988 (28.7) | |
| 25.0≤ BMI <30.0 | 1186 (40.7) | 104 (36.2) | 72 (35.3) | 15 (37.5) | 1377 (39.9) | |
| BMI ≥30.0 kg/m ² | 909 (31.2) | 65 (22.7) | 67 (32.8) | 13 (32.5) | 1054 (30.6) | |
| Highest Level of Schooling | | | | | | P<0.0001 |
| N with data | 2359 | 256 | 168 | 32 | 2815 | |
| Primary Education or less | 39 (1.7) | 13 (5.1) | 6 (3.6) | 4 (12.5) | 62 (2.2) | |
| High School | 817 (34.6) | 122 (47.7) | 79 (47.0) | 14 (43.8) | 1032 (36.7) | |
| Technical or Further Education | 844 (35.8) | 74 (28.9) | 51 (30.4) | 9 (28.1) | 978 (34.7) | |
| University | 659 (27.9) | 47 (18.4) | 32 (19.1) | 5 (15.6) | 743 (26.4) | |
| Socioeconomic status (SEIFA) | | | | | | P=0.18 |
| N with data | 2815 | 293 | 207 | 38 | 3353 | |
| Quintile I (most disadvantaged) | 700 (25.9) | 67 (22.9) | 57 (27.5) | 15 (39.5) | 839 (25.0) | |
| Quintile 2 | 368 (13.1) | 47 (16.0) | 25 (12.1) | 7 (18.4) | 447 (13.3) | |
| Quintile 3 | 913 (32.4) | 105 (35.8) | 76 (36.7) | 9 (23.7) | 1103 (32.9) | |
| Quintile 4 | 281 (10.0) | 22 (7.5) | 19 (9.2) | 3 (7.9) | 325 (9.7) | |
| Quintile 5 (least disadvantaged) | 553 (19.6) | 52 (17.8) | 30 (14.5) | 4 (10.5) | 639 (19.1) | |
| Occupational exposures | | | | | | |
| Experience of working in a dusty job (≥1 year) | 991 (33.4) | 126 (42.9) | 83 (39.2) | 21 (48.8) | 1221 (34.7) | P=0.0009 |

Notes: For percentages, the denominator is given when different from the total number of patients (N with data [excluding "unknown"]); data are presented as n (%), unless stated otherwise. ^aAirflow limitation was defined by post-bronchodilator FEV₁/FVC ratio < 0.70.

Abbreviations: BOLD, Burden of Obstructive Lung Diseases; GOLD, Global Initiative for Obstructive Lung Disease; SD, standard deviation; BMI, body mass index; SEIFA, Socio-Economic Indexes for Areas.

limitation groups (Table 2). Only the GOLD 2 group reported a higher proportion of having heart disease compared to the GOLD 3 or 4 group.

Participants with GOLD 3 or 4 reported the highest proportions of lost time off work or lost time for social activities (25.6%), and healthcare utilization (25.8% for GP visits and 5.9% for hospitalizations), followed by GOLD 2, GOLD 1, and no airflow limitation groups (Table 3). However, although the proportion of healthcare utilization varied across Dovepress Zhou et al

Table 2 Respiratory Symptoms Respiratory Medication Use and Comorbidities of the BOLD Australia Sample, by GOLD Spirometric Grades

| Characteristic | No Airflow Limitation ^a (n=2969) | GOLD I FEV₁ ≥ 80% Predicted (n=294) | GOLD 2 50% ≤ FEV ₁ < 80% Predicted (n=212) | GOLD 3 or 4 FEV ₁ < 50% Predicted (n=43) | Total (n=3518) | P-values |
|---|---|--|---|---|-------------------|----------|
| Respiratory symptoms | | | | | | |
| Cough without a cold | 846 (28.5) | 108 (36.7) | 94 (44.3) | 22 (51.2) | 1070 (30.4) | P<0.0001 |
| Cough most days for 3 months a year ^b | 265 (8.9) | 42 (14.3) | 36 (17.0) | 12 (27.9) | 355 (10.1) | P<0.0001 |
| Phlegm without a cold | 514 (17.3) | 71 (24.2) | 74 (34.9) | 24 (55.8) | 683 (19.4) | P<0.0001 |
| Phlegm most days for 3 months a year ^b | 189 (6.4) | 30 (10.2) | 30 (14.2) | 12 (27.9) | 261 (7.4) | P<0.0001 |
| Wheeze in last 12 months ^b | 756 (25.5) | 108 (36.7) | 130 (61.3) | 33 (76.7) | 1027 (29.2) | P<0.0001 |
| Wheeze that created the feeling of SOB ^b | 350 (11.8) | 46 (15.7) | 78 (36.8) | 21 (48.8) | 495 (14.1) | P<0.0001 |
| Clinically important breathlessness ^b | 172 (6.1) | 13 (4.7) | 42 (23.0) | 25 (75.8) | 252 (7.6) | P<0.0001 |
| Any respiratory medication used | 409 (13.8) | 60 (20.4) | 88 (41.5) | 31 (72.1) | 588 (16.7) | P<0.0001 |
| Comorbidities | | | | | | |
| Current asthma | 281 (9.5) | 44 (15.0) | 63 (29.7) | 25 (58.1) | 413 (11.7) | P<0.0001 |
| Heart disease | 232 (7.8) | 33 (11.2) | 57 (26.9) | 10 (23.3) | 332 (9.4) | P<0.0001 |
| Hypertension | 981 (33.0) | 115 (39.1) | 96 (45.3) | 21 (48.8) | 1213 (34.5) | P=0.0001 |
| Diabetes | 302 (10.2) | 27 (9.2) | 30 (14.2) | 8 (18.6) | 367 (10.4) | P=0.07 |
| Lung cancer | 10 (0.3) | 2 (0.7) | 4 (1.9) | 3 (7.0) | 19 (0.5) | P<0.0001 |
| Stroke | 55 (1.9) | 10 (3.4) | 10 (4.7) | 7 (16.3) | 82 (2.3) | P<0.0001 |
| Number of comorbidities, Median [IQR] | 0 (1.0) | 1.0 (1.0) | 1.0 (2.0) | 2.0 (1.0) | 0 (1.0) | P<0.0001 |
| Number of comorbidities ≥2 | 422 (14.2) | 51 (17.4) | 75 (35.4) | 23 (53.5) | 571 (16.2) | P<0.0001 |

Notes: Data are presented as n (%), unless stated otherwise; ^aAirflow limitation was defined by post-bronchodilator FEV₁/FVC ratio < 0.70; ^bDo not include all observations due to missing.

Abbreviations: BOLD, Burden of Obstructive Lung Diseases; GOLD, Global Initiative for Obstructive Lung Disease; IQR, interquartile range; SOB, shortness of breath.

groups, among those who had reported any healthcare utilization, there were no significant differences in the median number of GP visits or median number of hospitalizations across the four groups.

Quality of life among the four groups is compared in Table 4. Regarding general health, the no airflow limitation group reported the highest proportion of excellent general health and the lowest proportion of poor general health, while the GOLD 3 or 4 group reported the lowest proportion of excellent and highest proportion of poor health. The proportion

Table 3 Lost Time from Work/Social Activities and Hospital/GP Visits of the BOLD Australia Sample, by GOLD Spirometric Grades

| Characteristic | No Airflow Limitation ^a (n=2969) | GOLD I FEV₁ ≥ 80% Predicted (n=294) | GOLD 2 50% ≤ FEV₁ < 80% Predicted (n=212) | GOLD 3 or 4 FEV ₁ < 50% Predicted (n=43) | Total (n=3518) | P-values |
|--|---|--|--|---|-------------------|----------|
| Lost time off work or social activities b,c | | | | | | |
| ≥I in the past I2 months | 132 (4.5) | 16 (5.4) | 17 (8.0) | 11 (25.6) | 176 (5.0) | P<0.0001 |
| Healthcare utilisation ^{b,c} | | | | | | |
| ≥I GP visit in the past 12 months | 102 (3.8) | 10 (3.8) | 12 (7.3) | 8 (25.8) | 132 (4.2) | P<0.0001 |
| Number of GP visits in the past | | | | | | |
| 12 months, Median [IQR] | 1.0 (1.0) | 1.0 (1.0) | 1.5 (2.0) | 2 (3.5) | 1.0 (1.0) | P=0.19 |
| ≥1 Hospitalisations in the past 12 months | 21 (0.8) | 3 (1.2) | 3 (1.8) | 2 (5.9) | 29 (0.9) | P=0.01 |
| Number of hospitalisations in the past 12 months, Median (IQR) | 1.0 (0) | 1.0 (0) | 1.0 (0) | 1.5 (1.0) | 1.0 (0) | P=0.49 |

Notes: Data are presented as n (%), unless stated otherwise; ^aAirflow limitation was defined by post-bronchodilator FEV₁/FVC ratio < 0.70; ^bDo not include all observations due to missing; ^cDescribed as "When breathing problems got so bad that they interfered with usual daily activities or caused participants to miss work".

Abbreviations: BOLD, Burden of Obstructive Lung Diseases; GOLD, Global Initiative for Obstructive Lung Disease; IQR, interquartile range; GP, general practitioner.

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Table 4 Quality of Life (SF-12) of the BOLD Australia Sample, by GOLD Spirometric Grades

| | No Airflow Limitation ^a (n=2969) | GOLD I FEV ₁ ≥ 80% Predicted (n=294) | GOLD 2 50% ≤ FEV₁ < 80% Predicted (n=212) | GOLD 3 or 4 FEV ₁ < 50% Predicted (n=43) | Total (n=3518) | P-values, Adjusted Estimates (95% CI) |
|---|---|---|--|---|-------------------|--|
| General health (SF-I) | | | | | | P<0.0001 |
| Good and above | 2668 (89.9) | 258 (87.8) | 153 (72.2) | 21 (48.8) | 3100 (88.1) | |
| Adjusted OR (95% CI) | Reference | 0.77 (0.51-1.18) | 0.40 (0.27-0.59) | 0.11 (0.05-0.23) | | |
| SF-12 Mental and physical scores ^b | | | | | | |
| MCS, | 54.8 (9.2) | 57.2 (9.5) | 54.3 (11.4) | 55.3 (16.3) | 54.8 (9.3) | P =0.03, -0.61 |
| Median (IQR) | | | | | | (-1.17 to -0.05) |
| PCS, | 53.5 (8.9) | 51.9 (10.9) | 47.6 (16.8) | 31.8 (16.4) | 53.0 (9.9) | P<0.0001 -2.15 |
| Median (IQR) | | | | | | (-2.70 to -1.61) |

Notes: Data are presented as n (%), unless stated otherwise; Data of general health are presented as adjusted odds ratios (95% confidence intervals) compared to No airflow limitation group; PCS and MCS are presented as adjusted estimates (95% confidence interval); adjusted for age, sex, BMI status, smoking status, socioeconomic status, heart disease, hypertension, and diabetes; ^aAirflow limitation was defined by post-bronchodilator FEV₁/FVC ratio < 0.70; ^bDo not include all observations due to missing.

Abbreviations: BOLD, Burden of Obstructive Lung Diseases; GOLD, Global Initiative for Obstructive Lung Disease; SF-12, Short-Form-12; PCS, physical component summary scores; MCS, mental component summary scores; OR, odds ratio; CI, confidence intervals; IQR, interquartile range.

of self-reported good or above general health decreased as airflow limitation became worse across the groups. The PCS and MCS also decreased from the no airflow limitation group to the GOLD 3 or 4 group.

Discussion

To our knowledge, this is the first Australian study to evaluate the relationship between respiratory symptoms, comorbidities, indirect health burdens, quality of life, and GOLD spirometry grades in a general population sample including healthy subjects and subjects with COPD. We found, in adults aged ≥40 years, that presence of respiratory symptoms and respiratory medication use was associated with worse airflow limitation. The likelihood of multimorbidity and disease-related indirect burden (lost time off work or social activities and healthcare utilization) also increased with worsening/increasing airflow limitation. Additionally, the quality of life evaluated by SF-12, including general health SF-1, MCS, and PCS, deteriorated as the GOLD spirometry grade severity worsened. However, the mental component scale (MCS) did not deteriorate as much as the GOLD spirometry grade severity worsened.

We found that the proportions of people having any respiratory symptoms and using respiratory medications were progressively higher from the no airflow limitation group to the GOLD 3 or 4 group. However, we found that large proportions of participants in the GOLD 2 and GOLD 3 or 4 group (post-bronchodilator $FEV_1 < 80\%$ predicted) did not receive any respiratory medication treatment in the past 12 months. The reason for these COPD patients not receiving respiratory medication may be misdiagnosis or underdiagnosis, as reported in the BOLD Australia study, ²³ and as also observed internationally. ^{24,25} These findings help confirm the importance of spirometry in the diagnosis of COPD in real-life clinical practice, especially in primary care.

A previous global BOLD paper reported that participants with airflow limitation (GOLD 1 to 4) were more likely to suffer from heart disease, hypertension, and stroke than those without COPD, and only having diabetes had a weak association between participants with and without COPD, consistent with our findings.¹⁵ Previous studies found that patients with both asthma and COPD had worse lung function,²⁶ we also found that the proportion having current asthma was increased from participants without airflow limitation to GOLD 3 or 4.

Previous studies found that adults with COPD had more work absences than the general population.²⁷ We also showed a trend toward increased time lost from work or daily activities with higher GOLD spirometry grades. We observed that the proportion of healthcare utilization increased across grades of airflow limitation, as observed previously.²⁸ However, for participants who visited GPs or hospitalizations in 12 months, the number of GP visits and hospitalizations was not significantly different across the four groups. These results may be attributed to the small number of participants in the GOLD 2 and GOLD 3 or 4 group.

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We found that general health was independently associated with the severity of GOLD spirometry grades. The proportion of participants reporting good or above general health status significantly decreased from participants without airflow limitation to participants with GOLD 3 or 4. Previous studies also reported that COPD is related to poorer health status.¹⁵ We also observed that the negative impact on quality of life increased with increasing severity of GOLD spirometry grades, which has also been reported previously.^{15,28} The impact of COPD was greater on the physical than the mental aspects of quality of life, which was similar to previous studies.^{15,29}

The main strengths of this study included the data from a large nationwide population sample, the use of standardized methods of data collection, together with a high level of quality control, increasing the internal validity of the analyses. ^{12,16} The study protocol and core questionnaire were harmonized with the BOLD international protocol, allowing for comparisons between countries. ³⁰

However, our study also had several limitations. The cross-sectional design did not allow for the assessment of causality or long-term outcomes. The low overall response rate may introduce the possibility of selection bias, with participants included in this analysis being slightly younger and more likely to self-report a diagnosis of respiratory disease compared with those who provided only minimal data. The GOLD 2023 report introduced an ABE assessment tool to assess the severity of COPD, but the BOLD Australia dataset did not include complete information about exacerbations required by the GOLD ABE assessment tool. Thus, we used the GOLD spirometry grades to assess the severity of COPD in our analysis. BOLD Australia also did not collect data on depression, which has been confirmed to be associated with worse health status in patients with COPD.

Another limitation was that the information on comorbidities in BOLD Australia was collected from the self-reported questionnaire, which could introduce recall bias. The BOLD Australia data did not include the answer to all SF-12 questions for Indigenous participants, so we could not calculate the MCS and PCS of those participants. Participants were not a completely random sample of the Australian population as the six study sites themselves were not randomly selected. Another limitation is that the BOLD Australia study was conducted between 2006 and 2012, the study data is old and could not provide recent information. However, post-hoc weights were used in previous work to adjust prevalence estimates to reflect the Australian population better; in this analysis sample prevalence estimates were used. Finally, the single spirometry measurement was also a limitation as spirometry results can vary between days, resulting in differences in diagnostic criteria.

Nonetheless, our findings have significant implications for the development of COPD management strategies. These findings confirm the value of the GOLD grades of airflow limitation for providing insight into the impact and burden of COPD. Therefore, the GOLD grades of airflow limitation remain important to health professionals in clinical practice. Further research should include information on the exacerbation history, which may provide a more comprehensive indication of the impact of different severities of COPD. Further research is also needed to improve prevention and treatment strategies for airflow limitation, which may help to reduce future long-term risks. Patients with COPD may benefit from improved interventions in the future.

Conclusion

This study comprehensively characterized respiratory symptoms, disease-related indirect burdens, and quality of life in Australian adults aged 40 years and over, according to GOLD spirometry grade. Adults with greater severity of airflow limitation, as indicated by higher GOLD grades, had more frequent respiratory symptoms and comorbidities compared with those with lower grades or without airflow limitation. The severity of airflow limitation was also associated with indirect burdens in terms of lost time off work or social activities, and healthcare utilization. Additionally, higher severity of airflow limitation was related to a lower quality of life. The effects of different airflow limitation grades on the physical aspects of quality of life were stronger than on the mental aspects. These findings confirm the utility of the GOLD spirometry grades for providing insight into the impact and burden of COPD. Most importantly, there was significant variation across the GOLD grades, especially with regard to the use of respiratory medicines.

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Data Sharing 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 of the University of Sydney (ref. no. 12-2006/9724) and complies with the Declaration of Helsinki. 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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