Prevalence and burden of chronic bronchitis symptoms: results from the BOLD study

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Chronic bronchitis symptoms are associated with significant burden regardless of the presence of airflow obstruction http://ow.ly/kP9P30eFELK

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ABSTRACT  We studied the prevalence, burden and potential risk factors for chronic bronchitis symptoms in the Burden of Obstructive Lung Disease study.

Representative population-based samples of adults aged ≥40 years were selected in participating sites. Participants completed questionnaires and spirometry. Chronic bronchitis symptoms were defined as chronic cough and phlegm on most days for ≥3 months each year for ≥2 years.

Data from 24,855 subjects from 33 sites in 29 countries were analysed. There were significant differences in the prevalence of self-reported symptoms meeting our definition of chronic bronchitis across sites, from 10.8% in Lexington (KY, USA), to 0% in Ile-Ife (Nigeria) and Blantyre (Malawi). Older age, less education, current smoking, occupational exposure to fumes, self-reported diagnosis of asthma or lung cancer and family history of chronic lung disease were all associated with increased risk of chronic bronchitis. Chronic bronchitis symptoms were associated with worse lung function, more dyspnoea, increased risk of respiratory exacerbations and reduced quality of life, independent of the presence of other lung diseases.

The prevalence of chronic bronchitis symptoms varied widely across the studied sites. Chronic bronchitis symptoms were associated with significant burden both in individuals with chronic airflow obstruction and those with normal lung function.

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Introduction
Chronic bronchitis is defined epidemiologically as cough and sputum production for $\geq 3$ months in each of least two consecutive years [1]. It affects about a third of patients with chronic obstructive pulmonary disease (COPD), but also occurs in individuals with normal lung function, with prevalence estimates varying widely both in population-based studies (2.6–16%) [2–7] and among COPD patients (7.4–53%) [8–10]. Presence of chronic bronchitis symptoms correlates with faster forced expiratory volume in 1 s (FEV1) decline and increased risk of death in most [11–15], but not all [16, 17] published studies. In addition, it is associated with worse health status in affected subjects [4, 9, 10]. Reported risk factors for chronic bronchitis include tobacco smoke, indoor and outdoor air pollution and occupational exposures [18–21].

Although chronic bronchitis symptoms are commonly reported, data on their prevalence across countries and burden in affected individuals, especially in those with normal lung function, are limited [2–4]. The Burden of Obstructive Lung Disease (BOLD) study is an international, cross-sectional study assessing the prevalence and burden of COPD across different parts of the world [22]. In this article we report data from the BOLD study on the prevalence, burden and potential risk factors of chronic bronchitis symptoms.

Material and methods
The methods used in the BOLD study are described in detail elsewhere [22]. In brief, representative population-based samples of adults aged $\geq 40$ years were selected randomly in participating centres. Participants who had provided written informed consent completed a detailed questionnaire and pre- and post-bronchodilator spirometry, administered by trained and certified staff. The questionnaires were translated into languages used in local sites, back-translated and verified. Spirometry was performed using the Easy-One spirometer (ndd Medical Technologies, Zurich, Switzerland) before and 15 min after administration of bronchodilator (200 $\mu$g salbutamol). All spiromgrams were centrally assessed for quality, and only measurements of appropriate quality (based on the American Thoracic Society/European Respiratory Society criteria) were used for analyses [23]. Forced vital capacity (FVC) and FEV1 were calculated as % predicted values based on the Third National Health and Nutrition Examination Survey (NHANES III) equations for Caucasians [24]. Data from the 33 BOLD sites that had completed datasets at the time of writing were used for analyses.

Definitions
Chronic bronchitis symptoms were defined as both cough and phlegm on most days for $\geq 3$ months each year for $\geq 2$ years using affirmative answers to all the following questions: “Do you usually cough when you don’t have a cold?”, “Are there months in which you cough on most days?”, “Do you cough on most days for as much as 3 months each year?” and confirmation that cough lasts $\geq 2$ years in a question “For how many years have you had this cough?” plus affirmative answers to a series of similar questions on phlegm. Chronic airflow obstruction (CAO) was defined by a post-bronchodilator FEV1/FVC ratio less than the lower limit of normal for age and sex, based on NHANES III equations for Caucasians. Among those meeting this criteria, we classified severity of disease based on post-bronchodilator FEV1, according to the Global Initiative for Chronic Obstructive Lung Disease spirometric classification (FEV1 $\geq 80\%$ pred, 50–<80$\%$ pred, 30–<50$\%$ pred and <30$\%$ pred) [25]. The presence of other medical conditions was determined based on questionnaire data. Biomass fuel use was defined as self-reported ever use of coal, coke, wood, crop residues or dung for cooking or heating for $>6$ months. Dyspnoea was measured using the modified Medical Research Council (mMRC) dyspnoea scale [26], mMRC grade 2 (“dyspnoea when walking at own pace on the level”) or higher was used to define clinically significant dyspnoea. Respiratory exacerbations were assessed based on the response to the question about “breathing problems that interfered with usual daily activities or caused the participant to miss work” and use of healthcare resources on the basis of self-reported breathing problems causing subjects to see a healthcare provider or be hospitalised. Quality of life was measured using the 12-item Short Form Health Survey (SF-12) questionnaire. Composite physical and mental health SF-12 scores were calculated and used for analyses. The summary scores range from 0 to 100, with 100 representing the best quality of life [27].

Data analysis
Apart from site-specific prevalence estimates, which were weighted to reflect the sampling design at each site, all other analyses used unweighted data. Factors associated with the presence of chronic bronchitis symptoms were examined by multiple logistic regression, with the following covariates as potential risk factors: age, sex, education, smoking status and exposure to passive smoke, occupational exposures to dust and fumes, biomass fuels use (use of coal, coke, wood, crop residues or dung for cooking or heating), comorbid conditions including other lung diseases (asthma, tuberculosis or lung cancer) and heart disease,
family history of chronic lung diseases and hospitalisation for breathing problems prior to the age of 10 years. A similar model was applied, restricted to: 1) subjects with CAO, 2) subjects without CAO and 3) current smokers.

Linear regression models were applied to predict FEV1 and change in FEV1 after bronchodilator administration (ΔFEV1) as a function of chronic bronchitis symptoms and the covariates listed earlier. In addition, we applied separate logistic regression models to predict clinically significant dyspnoea, respiratory exacerbations, the use of healthcare resources and quality of life (lowest quartile) as a function of the same set of covariates as well as lung function data (CAO and FVC). These covariates were complemented with self-reported data on medical diagnoses of hypertension, diabetes and stroke in the analysis of the quality of life. These analyses were all performed in the cohort overall and separately in those with and without CAO. All regression models were adjusted for study site as a fixed effect, class variable.

Using the Wald Chi-squared statistic for site as a measure of the variability in prevalence of chronic bronchitis symptoms across sites, we used the reduction in this statistic after adjusting for covariates as a proxy for the proportion of overall site-to-site variability in chronic bronchitis prevalence that was attributable to the covariates.

Analyses were performed with R statistical software (version 3.3.1; www.R-project.org). Statistical significance refers to a p-value <0.05.

**Results**

**Prevalence of and potential risk factors for chronic bronchitis symptoms**

Data from 23 855 males and females from 33 BOLD study sites in 29 countries were analysed. The proportion of self-reported chronic bronchitis symptoms overall was 3.1%: 3.6% for males and 2.6% for females. Chronic bronchitis symptoms were present in 10.2% of individuals with CAO and 2.2% of those without CAO (1.06% and 1.97% of the total sample, respectively). Overall, proportion of subjects reporting chronic bronchitis symptoms increased with age, worse lung function and exposure to potential risk factors (table 1).

Figure 1 shows the weighted prevalence of chronic bronchitis symptoms by sex, site, smoking status and history of asthma. The prevalence of chronic bronchitis symptoms varied significantly across sites, with Lexington (KY, USA), Chui (Kyrgyzstan) and London (UK) having the highest rates (10.8%, 8.3% and 7.7%, respectively) and Pune (India), Cotonou (Benin), Ile-Ife (Nigeria) and Blantyre (Malawi) each having a prevalence <0.5%. In all sites where prevalence of chronic bronchitis symptoms was >1%, they were reported by both individuals with and without CAO. ~18% of the variance in the prevalence of chronic bronchitis symptoms between sites could be explained by the differences in the measured covariates.

In the multivariable analysis, factors significantly associated with an increased risk of reporting chronic bronchitis symptoms were older age, less education, current smoking, occupational exposure to fumes, a self-reported diagnosis of asthma or lung cancer and a family history of chronic lung disease (table 2). The potential risk factors profile was similar in subjects with and without CAO, although there were no significant associations with either a family history of chronic lung disease or education in those without CAO. In an analysis restricted to current smokers, number of cigarettes smoked daily was an independent predictor of chronic bronchitis symptoms (for increase of 10 cigarettes per day OR 1.63, 95% CI 1.37–2.00; p<0.001).

**Burden associated with chronic bronchitis symptoms**

The presence of chronic bronchitis symptoms was related to worse lung function both in CAO and asthma groups as well as more pronounced response to bronchodilator administration (table 3). The proportion of subjects with improvement in FEV1 ≥12% and ≥200 mL after bronchodilator administration was similar in subjects with self-reported asthma and CAO (21.5% versus 21.8%, p=0.820), while the proportion of those with FEV1 improvement of >15% and >400 mL was larger in the former group (6.9% versus 5.3%, p=0.039). The association of chronic bronchitis symptoms with worse lung function (FEV1 % pred) was present after adjustment for potential confounders, both in the whole sample (~2.74%, p<0.001) and in subgroups of those with CAO (~4.04%, p<0.001) and without CAO (~1.92%, p<0.001). Similarly, the association of chronic bronchitis symptoms with increased FEV1 improvement after bronchodilator administration was independent from lung function (FEV1) and other potential confounders (ΔFEV1 17 mL, p=0.011). In logistic regression analysis the presence of chronic bronchitis symptoms was associated with increased risk of other respiratory symptoms, respiratory exacerbations and reduced quality of life (table 4). After adjustment for possible confounders, the influence of chronic bronchitis symptoms on quality of life was significantly larger than that of asthma or CAO (SF-12 physical score −5.9 versus −4.9 versus −1.7, respectively, p<0.001; SF-12 mental score −3.5 versus −1.4 versus −1.0, respectively, p<0.001).
| TABLE 1 Basic characteristics of the study population |
|-----------------------------------------------|
| Proportion of population | CBS | OR (95% CI) | p-value |
| Total# | 100 | 3.1 |  |
| Sex | | | |
| Female | 52.5 | 2.6 | | 1 | 0.001 |
| Male | 47.5 | 3.6 | | 1.35 (1.17–1.57) | |
| Age years | | | |
| 40–49 | 36.5 | 2.2 | | 1 | <0.001 |
| 50–59 | 31.1 | 3.2 | | 1.49 (1.23–1.80) | |
| 60–69 | 20.4 | 3.6 | | 1.64 (1.33–2.02) | |
| ≥70 | 12.0 | 4.3 | | 2.01 (1.60–2.53) | |
| Education years | | | |
| >12 | 22.7 | 2.5 | | 1 | 0.083 |
| 6–12 | 55.9 | 3.2 | | 1.26 (1.04–1.53) | |
| <6 | 10.2 | 3.3 | | 1.30 (0.98–1.71) | |
| None | 11.2 | 3.3 | | 1.30 (0.99–1.71) | |
| Smoking status | | | |
| Never-smoker | 59.8 | 1.8 | | 1 | <0.001 |
| Ex-smoker | 21.2 | 3.3 | | 1.81 (1.48–2.20) | |
| Current smoker | 19.0 | 6.7 | | 3.81 (3.22–4.51) | |
| Exposure to passive smoke | | | |
| No | 78.5 | 2.8 | | 1 | <0.001 |
| Yes | 21.5 | 4.2 | | 1.51 (1.28–1.78) | |
| Dusty job | | | |
| No (<1 year) | 66.2 | 2.4 | | 1 | <0.001 |
| Yes | 33.8 | 4.4 | | 1.89 (1.63–2.19) | |
| Occupational exposure to fumes | | | |
| No | 90.7 | 3.0 | | 1 | 0.035 |
| Yes | 9.3 | 3.8 | | 1.28 (1.02–1.62) | |
| Biomass fuel use¶ | | | |
| No | 34.9 | 2.9 | | 1 | 0.539 |
| Yes | 65.1 | 3.0 | | 1.05 (0.89–1.25) | |
| Chronic airway obstruction§ | | | |
| FEV1/FVC ≥ LLN | 89.6 | 2.2 | | 1 | <0.001 |
| FEV1/FVC < LLN and FEV1 ≥ 80% pred | 3.0 | 4.8 | | 2.20 (1.54–3.14) | |
| FEV1/FVC < LLN and FEV1 50–80% pred | 5.3 | 10.1 | | 4.93 (4.03–6.05) | |
| FEV1/FVC < LLN and FEV1 30–50% pred | 1.8 | 16.9 | | 8.92 (6.81–11.67) | |
| FEV1/FVC < LLN and FEV1 < 30% pred | 0.3 | 23.7 | | 13.57 (7.93–23.12) | |
| FVC | | | |
| ≥ 80% pred | 68.4 | 2.9 | | 1 | 0.065 |
| < 80% pred | 31.6 | 3.4 | | 1.16 (0.99–1.35) | |
| Asthma | | | |
| No | 94.5 | 2.3 | | 1 | <0.001 |
| Yes | 5.5 | 15.7 | | 7.89 (6.65–9.38) | |
| Diagnosed heart disease | | | |
| No | 92.1 | 2.3 | | 1 | 0.035 |
| Yes | 7.9 | 3.4 | | 1.46 (1.03–2.08) | |
| History of tuberculosis | | | |
| No | 97.3 | 3.0 | | 1 | 0.001 |
| Yes | 2.7 | 5.3 | | 1.81 (1.27–2.58) | |

Data are presented as %, unless otherwise stated. CBS: chronic bronchitis symptoms; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal; % pred: % predicted. #: n=23855; ¶: self-reported use of coal, coke, wood, crop residues or dung for cooking or heating; §: post-bronchodilator FEV1/FVC < LLN.
FIGURE 1 Estimated prevalence of chronic bronchitis symptoms across study sites.

TABLE 2 Predictors of chronic bronchitis symptoms in multivariable analysis

| Predictor                                      | OR (95% CI)       | p-value |
|------------------------------------------------|-------------------|---------|
| Male sex                                       | 1.25 (0.91–1.71)  | 0.163   |
| Age per 10-year increase                       | 1.39 (1.22–1.58)  | 0.001   |
| Education per 1-year increase                  | 0.97 (0.94–0.99)  | 0.031   |
| Smoking status                                 |                   |         |
| Past smoking                                   | 1.12 (0.76–1.68)  | 0.557   |
| Current smoking                                | 2.74 (1.94–3.87)  | 0.001   |
| Exposure to passive smoke                      |                   |         |
| Current smoking                                | 1.00 (0.71–1.40)  | 0.995   |
| Dusty job                                      | 1.08 (0.83–1.46)  | 0.606   |
| Occupational exposure to fumes                 | 1.90 (1.24–2.92)  | 0.003   |
| Biomass fuel use                               | 0.52 (0.16–1.71)  | 0.282   |
| Current asthma (self-reported)                 | 7.9 (5.73–10.91)   | 0.001   |
| Diagnosed heart disease                        | 1.05 (0.70–1.57)  | 0.818   |
| Ever-diagnosed tuberculosis                   | 0.82 (0.36–1.86)  | 0.641   |
| Diagnosed lung cancer                          | 6.42 (1.34–30.70) | 0.020   |
| Family history of chronic lung disease         | 1.78 (1.19–2.66)  | 0.005   |
| Hospitalisation for breathing problems prior to the age of 10 years | 1.26 (0.59–2.70) | 0.556   |

Results based on logistic regression analysis with all of these variables and indicators for study site.
| Subjects n | 18551 | 345 | 1192 | 129 | 746 | 121 | 257 | 77 |
|------------|-------|-----|------|-----|-----|-----|-----|----|
| FEV1 % pred | 89.7±17.1 | 89.8±17.9 | 66.6±19.8 | 56.4±18 | 86.6±16.4 | 82.9±17.5 | 59.8±18.3 | 55.8±21 |
| FVC % pred | 88.1±16.8 | 90.3±18 | 86.5±21.8 | 81.4±18.8 | 86.8±16 | 84.3±17.9 | 82.6±20.1 | 79.2±20.5 |
| FEV1/FVC | 79.4±6.0 | 77.0±6.4 | 58.4±8.8 | 52.3±11 | 78.1±6.2 | 76.8±6.5 | 55.5±10.6 | 53.2±11.4 |
| ΔFEV1 mL | 67.9±14.2 | 93.7±184.5 | 110.2±171.0 | 131.0±141.1 | 113.9±176.7 | 127.8±192.8 | 177.3±184.7 | 154.9±169.4 |
| ΔFEV1 % of initial value | 3.1±7.0 | 4.0±7.5 | 7.9±12.4 | 10.8±12.3 | 5.6±9.0 | 6.7±10.3 | 14±15.3 | 13.1±13.2 |
| Proportion of subjects with ΔFEV1 ≥12% and >200 mL | 5.3 | 9.3 | 18.6 | 30.2 | 13.5 | 19.0 | 38.9 | 32.5 |
| Proportion of subjects with ΔFEV1 >15% and >400 mL | 1.4 | 2.0 | 4.1 | 3.9 | 4.6 | 5.0 | 11.7 | 6.5 |

Data are presented as mean±SD or %, unless otherwise stated. n=21418. CBS: chronic bronchitis symptoms; FEV1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; ΔFEV1: change in FEV1; #: comparison across mutually exclusive groups; ¶: post-bronchodilator; +: thresholds for significant bronchodilator response suggested in the Global Initiative for Asthma guidelines [28].
Discussion

We observed that prevalence of chronic bronchitis symptoms varied widely across the studied sites. More importantly, we have demonstrated that presence of chronic bronchitis symptoms is associated with a significant burden in affected individuals whether or not they have concurrent airflow obstruction, as evidenced by the associations with worse lung function and increased likelihood of dyspnoea, respiratory exacerbations and decreased quality of life.

Chronic bronchitis symptoms prevalence data from most, but not all studied sites are in the range of the previously published results based on questionnaires assessing symptoms [2–7]. Surprisingly, we have identified a few centres where only single subjects (0–0.5%) reported chronic bronchitis symptoms. In addition, in these centres (Pune, India; Cotonou, Benin; Ile-Ife, Nigeria; and Blantyre, Malawi) the proportions of subjects who reported cough and who reported sputum production were lower in comparison to other sites. This observation is supported by some [4, 29, 30], but not all studies from these countries [31]. More local data are needed to verify whether this is a reporting issue or if chronic productive cough is indeed rare in these populations, but the observations are consistent with the low prevalence of smoking and asthma in these populations. The magnitude of differences in prevalence of chronic bronchitis symptoms across sites reported here is large, but similar to that described in a younger population by the only other published study using standardised methods in different regions of the world [2]. Only 18% of the variance in the prevalence of chronic bronchitis symptoms between sites could be explained by variations across sites in the measured covariates. Part of this discrepancy may be due to limitations of the BOLD questionnaire, which does not ask questions about some potential risk factors, such as chronic rhinosinusitis and gastro-oesophageal reflux. Differences in the stigma associated with respiratory symptoms and the likelihood of reporting them are also probably important considerations.

The association between smoking and chronic bronchitis is well known [2, 18, 20] and, in our data, holds for current but not ex-smokers (consistent with reports demonstrating that chronic bronchitis symptoms disappear after smoking cessation [32, 33]). The association with a family history of chronic lung disease may be partially mediated by an increased risk of chronic bronchitis symptoms in asthma, but the effect shown in table 2 is at least partially independent of a personal history of asthma, and a genetic trait related with chronic bronchitis has also been reported [34].

We have described the wide spectrum of the negative outcomes (worse lung function, worse quality of life, more symptoms and more exacerbations) related to chronic bronchitis symptoms. Previous studies are concordant in reporting worse health status of chronic bronchitis subjects both in those with CAO and in those with normal lung function [4, 9, 10, 35, 36]. Similarly, in patients with asthma the presence of chronic cough and phlegm production has been associated with increased risk of uncontrolled asthma [37]. Of note, the adverse influence of chronic bronchitis on quality of life is probably larger than that of asthma or COPD, which confirms previously published results [38]. Despite associations of chronic bronchitis with airflow

### Table 4

|                     | Total study sample | CAO+ | CAO− |
|---------------------|--------------------|------|------|
| mMRC dyspnoea scale |                    |      |      |
| ≥ 2                 | 1.54 (1.08–2.22)   | 2.06 (1.01–4.22) | 1.63 (1.06–2.74) |
| Respiratory exacerbations |                |      |      |
| Breathing problems interfering with daily activities or causing subject to miss work in the previous year | 4.28 (3.07–5.95) | 5.66 (3.08–10.41) | 3.66 (2.41–5.55) |
| Breathing problems causing subject to see a healthcare provider in the previous year | 4.93 (3.28–7.41) | 3.93 (2.00–7.72) | 5.21 (3.06–8.88) |
| Hospitalisation for breathing problems in the previous year | 4.86 (2.67–8.82) | 4.54 (1.98–10.44) | 4.18 (1.65–10.59) |
| Quality of life     |                    |      |      |
| SF-12 mental score (lowest quartile) | 2.06 (1.52–2.77) | 4.04 (2.30–7.08) | 1.59 (1.10–2.30) |
| SF-12 physical score (lowest quartile) | 4.00 (2.89–5.53) | 5.43 (2.88–10.26) | 3.34 (2.26–4.95) |

Data are presented as OR (95% CI). Results adjusted for study site, age, sex, education, smoking status and exposure to passive smoke, occupational exposures to dust and fumes, biomass fuels use, asthma, tuberculosis, lung cancer, heart disease, chronic airway obstruction (CAO) [in the total study sample] and forced vital capacity, plus data on hypertension, diabetes and stroke in the analysis of the quality of life. mMRC: modified Medical Research Council; SF-12: 12-item Short Form Health Survey.
obstruction, negative outcomes from chronic bronchitis symptoms are also evident in individuals without airway obstruction. In our sample the number of these subjects was almost double that of chronic bronchitis subjects with CAO. For this group, chronic bronchitis has received surprisingly little attention outside epidemiological studies. There is a high prevalence of chronic airflow obstruction in those with the symptoms of chronic bronchitis and this is true in both smokers and never-smokers, and chronic bronchitis is a better predictor of future obstruction than the presence of dyspnoea [38]. The main limitation in using this information for COPD case finding is that this association is greatest for those with persistent symptoms, and symptoms are highly variable [39, 40]. However, evidence for significant chronic bronchitis burden together with data demonstrating that chronic bronchitis symptoms may disappear after smoking cessation suggest that identification of these subjects and interventions aiming at smoking cessation may be of potential benefit.

In addition, we observed the association of chronic bronchitis symptoms with increased response to bronchodilator. The bronchodilator test is commonly used in differential diagnosis of asthma and COPD; however, is not an ideal tool because significant improvement is present in a substantial proportion of patients with both of these diseases [41]. When applying Global Initiative for Asthma (GINA) criteria for significant bronchodilator response to our population, the lower threshold in particular (FEV1 improvement of ≥12% and 200 mL) was of little value. Interestingly, in our sample the presence of chronic bronchitis symptoms was related to a more pronounced response to bronchodilator both in CAO and asthma groups and after the exclusion of chronic bronchitis subjects absolute improvement after bronchodilator was similar in asthma and CAO. Differential diagnosis of asthma and COPD is often troublesome, with 15–45% of subjects having the features of both of these diseases [42]. Chronic bronchitis symptoms have a significant impact on lung function/bronchodilator response, quality of life and probably prognosis, and the inclusion of these symptoms in classification of obstructive airway diseases could lead to more precise categorisation.

This study has some limitations. The cross-sectional survey design precludes assessment of causality. Data on chronic bronchitis and other respiratory symptoms are self-reported and thus prone to recall bias or to a culturally defined understanding of the symptoms being assessed. Similarly, data on asthma diagnoses are self-reported; observed lack of significant differences in response to bronchodilator between asthma and CAO groups could be due to this issue, at least partially, and underlines the low precision of self-reported asthma diagnoses. Questionnaire-based prevalence rates of chronic bronchitis symptoms are overestimated, because chronic cough and sputum production in some subjects are caused by asthma, bronchiectasis, gastro-oesophageal reflux, heart failure or chronic rhinosinusitis (post-nasal drip) [43]. In our study, asthma was reported by approximately one-third of those with chronic bronchitis symptoms. However, a large proportion of subjects who are troubled by chronic productive cough may not answer positively to all questions defining chronic bronchitis. In our sample, ~11% of subjects reported that they “usually” cough and produce phlegm “when [they] don’t have a cold” (compared with ~3% reporting chronic bronchitis).

How the questionnaire is understood in different settings will be influenced by language and local cultural differences [44, 45], and even small changes in phrasing of a question can influence the estimates of respiratory symptoms [46]. The use of standardised questionnaires with strict quality control (including verifying the back-translations into each local language) and using trained staff to administer the questionnaires minimised, but could not eliminate the bias caused by such issues. However, there is a clear association between the prevalence of chronic bronchitis symptoms and the prevalence of smoking, suggesting that these responses to the questionnaire are relatively consistent. Finally, a dose of 200 μg of salbutamol will not produce maximum bronchodilation in all participants, and in clinics a dose of 400 μg is commonly recommended. The BOLD programme has used 200 μg for both ethical and pragmatic reasons. Participants in the study, unlike clinic patients, have not asked for help with a specific problem, are less likely to have taken a β-agonist before and will not be used to the temporary side-effects. Standardising the dose to 200 μg provides valuable and standardised information, but interpretation of the results needs to consider that the bronchodilation may not always be maximal. Published studies have used different doses of salbutamol, and GINA guidelines mention doses in the 200–400 μg range as appropriate.

In conclusion, the prevalence of chronic bronchitis symptoms varied widely across the studied sites and their presence was associated with significant negative outcomes, not only in obstructed subjects, but also in those without airflow obstruction.

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