Association of respiratory symptoms and lung function with occupation in the multinational Burden of Obstructive Lung Disease (BOLD) study

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Shareable abstract (@ERSpublications)
Occupational exposures associate with more respiratory symptoms but do not appear to be major determinants of differences in lung function. https://bit.ly/3zFjalu

Cite this article as: Ratanachina J, Amaral AFS, De Matteis S, *et al*. Association of respiratory symptoms and lung function with occupation in the multinational Burden of Obstructive Lung Disease (BOLD) study. *Eur Respir J* 2023; 61: 2200469 [DOI: 10.1183/13993003.00469-2022].

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Received: 13 March 2022
Accepted: 2 Aug 2022

Abstract

Background Chronic obstructive pulmonary disease has been associated with exposures in the workplace. We aimed to assess the association of respiratory symptoms and lung function with occupation in the Burden of Obstructive Lung Disease study.

Methods We analysed cross-sectional data from 28 823 adults (⩾40 years) in 34 countries. We considered 11 occupations and grouped them by likelihood of exposure to organic dusts, inorganic dusts and fumes. The association of chronic cough, chronic phlegm, wheeze, dyspnoea, forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1)/FVC with occupation was assessed, per study site, using multivariable regression. These estimates were then meta-analysed. Sensitivity analyses explored differences between sexes and gross national income.

Results Overall, working in settings with potentially high exposure to dusts or fumes was associated with respiratory symptoms but not lung function differences. The most common occupation was farming. Compared to people not working in any of the 11 considered occupations, those who were farmers for ⩾20 years were more likely to have chronic cough (OR 1.52, 95% CI 1.19–1.94), wheeze (OR 1.37, 95% CI 1.16–1.63) and dyspnoea (OR 1.83, 95% CI 1.53–2.20), but not lower FVC (β=0.02 L, 95% CI −0.02–0.06 L) or lower FEV_1/FVC (β=0.04%, 95% CI −0.49–0.58%). Some findings differed by sex and gross national income.

Conclusion At a population level, the occupational exposures considered in this study do not appear to be major determinants of differences in lung function, although they are associated with more respiratory symptoms. Because not all work settings were included in this study, respiratory surveillance should still be encouraged among high-risk dusty and fume job workers, especially in low- and middle-income countries.

Introduction

Irreversible airflow obstruction often accompanied by dyspnoea, persistent cough and phlegm production are characteristic of chronic obstructive pulmonary disease (COPD). It has been estimated that workplace exposure may account for 10–18% of COPD cases in the population [1]. However, these estimates are based on studies whose designs, definitions of disease and exposure assessments are not easily comparable. In addition, most of the studies were undertaken in high-income countries (HICs) [2], and there is a relative lack of knowledge concerning low- and middle-income countries (LMICs), where farming and manufacturing under weak health and safety regulations remain common.

In this analysis, we assessed the association of respiratory symptoms (*i.e.* chronic cough, chronic phlegm, dyspnoea and wheeze) and lung function parameters (*i.e.* forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1)/FVC) with occupational exposures in the large multinational population-based Burden of Obstructive Lung Disease (BOLD) study, which collected data across several regions of the world in a standardised manner.

Materials and methods

Study participants

The BOLD study design and rationale have been described elsewhere [3]. Representative samples of at least 600 non-institutionalised adults, aged ⩾40 years, were recruited from 41 sites in 34 countries (table 1) [4]. As classified by their gross national income per capita [5], 14 sites were in HICs and 27 sites in LMICs. Information on respiratory symptoms and exposure to potential risk factors, including occupation, was collected through face-to-face interviews conducted by trained and certified staff in the participant's native language. This report is based on data from 28 823 participants who completed the core and occupational questionnaires and provided acceptable and repeatable post-bronchodilator spirometry measurements. All sites received approval from their local ethics committee, and participants provided informed consent.

Occupational exposure

Participants were asked if they had ever worked, for at least 3 months, in at least one of 11 work settings likely to be associated with significant exposures to particulates or fumes and loss of lung function. These were 1) farming; 2) flour, feed or grain milling; 3) cotton or jute processing; 4) hard-rock mining; 5) coal mining; 6) sandblasting; 7) working with asbestos; 8) chemical or plastics manufacturing; 9) foundry or steel milling; 10) welding; and 11) firefighting. In addition, they were asked about their longest-held job, which was coded using the International Standard Classification of Occupations (ISCO-88) (supplementary table S1) [6]. Based on expert opinion, these self-reported occupational data were used to group occupations into three categories according to likely exposure to organic dusts, inorganic dusts and fumes. For each occupation and category of exposure, we calculated the total number of cumulative years of exposure based on the self-reported number of years worked in each setting.

Respiratory symptoms and lung function

Chronic cough was defined as a frequent cough, without having a cold, on most days for at least 3 months each year. Chronic phlegm was defined as a frequent production of phlegm, without a cold, on most days for at least 3 months each year. Wheeze was defined as having had any whistling in the chest at any time in the last 12 months. Dyspnoea was assessed using the modified Medical Research Council dyspnoea scale as breathlessness at least when walking more slowly than people of the same age or sufficient to have to stop walking [7].

https://doi.org/10.1183/13993003.00469-2022

TABLE 1 Characteristics of participants from 41 sites of the BOLD Study with acceptable and repeatable post-bronchodilator spirometry and occupational exposure data

BOLD site	Albania (Tirana)	Algeria (Annaba)	Australia (Sydney)	Austria (Salzburg)	Benin (Sèmè-Kpodji)	Cameroon (Limbe)	China (Guangzhou)	Canada (Vancouver)	England (London)	Estonia (Tartu)	Germany (Hannover)	Iceland (Reykjavik)	India (Kashmir)	India (Mumbai)
Subjects, n	939	890	541	1253	698	331	461	827	675	613	680	757	760	439
Age (year)	54.6±10.8	52.5±9.9	58.9±12.4	57.7±11.4	51.5±9.8	51.3±9.9	54.0±10.6	56.0±11.8	58.2±11.5	60.9±12.0	58.1±11.0	56.4±11.7	51.4±10.4	51.1±8.9
Height (cm)	164.2±8.8	164.6±9.7	165.3±9.6	170.1±8.9	164.9±8.0	165.8±8.0	160.0±8.4	167.2±10.1	168.1±9.7	169.2±9.8	169.1±9.6	173.1±9.4	160.5±8.8	160.8±8.4
BMI (kg·m^{-2})	28.0±4.7	28.3±5.7	28.0±5.2	26.4±4.2	26.4±5.6	26.6±5.4	23.3±3.3	26.7±5.2	27.1±5.0	28.5±5.3	27.3±4.6	27.9±4.9	22.4±3.6	23.8±4.0
Sex (male)	49.7	49.7	49	54.5	43.3	59.5	49.7	41.6	47.6	50.2	51	53.2	54.7	62.6
Never-smokers	62.9	61.7	46	44.8	98	77.6	56.4	43.2	35.9	52.4	38.1	33.7	45.1	90.2
<20 pack-years	10.2	15.7	31.1	28.6	1.9	16.6	18.7	33.9	32.9	30.2	30.2	41	7.4	7.7
⩾20 pack-years	26.8	22.6	22.9	26.7	0.1	5.7	25	23	31.3	31.8	31.8	25.4	47.5	2.1
Chronic cough	8.8	3.2	7	5.3	2.4	0.9	5.6	11.3	12.2	7	8.4	11.5	5.7	2.1
Chronic phlegm	1.8	2.6	5.7	7.9	2.2	1.2	6.9	10.6	11.7	9.4	8.2	9.3	5.7	2.3
Wheeze	3.7	14.5	25.4	13.2	2.8	4.5	1.5	26	34.2	22.8	18.7	24.2	3	3.2
Dyspnoea	8	11.8	7	6.6	1.4	5.8	3.8	6.9	12.1	14	4	8.4	4.9	9.9
FEV_1/FVC (%)	78.4±9.0	78.6±7.3	76.4±8.9	74.3±8.6	79.3±7.1	80.4±6.9	78.1±7.3	76.0±8.8	75.0±9.2	77.2±7.8	76.2±7.9	76.1±8.5	76.4±10.6	79.1±7.5
FVC (L)	3.6±0.9	3.4±0.9	3.6±1.0	4.0±1.0	2.8±0.7	3.0±0.8	3.1±0.8	3.9±1.1	3.7±1.0	3.8±1.1	3.9±1.0	4.0±1.0	3.3±0.9	2.8±0.7
FEV_1 (L)	2.8±0.8	2.7±0.8	2.8±0.9	3.0±0.8	2.2±0.6	2.4±0.7	2.4±0.7	3.0±0.9	2.7±0.8	3.0±0.9	3.0±0.9	3.1±0.9	2.5±0.8	2.3±0.6

https://doi.org/10.1183/13993003.00469-2022

TABLE 1 Characteristics of participants from 41 sites of the BOLD Study with acceptable and repeatable post-bronchodilator spirometry and occupational exposure data (continued)

BOLD site	India (Mysore)	India (Pune)	Jamaica	Kyrgyzstan (Chui)	Kyrgyzstan (Naryn)	Malawi (Blantyre)	Malawi (Chikwawa)	Malaysia (Penang)	Morocco (Fes)	Netherlands (Maastricht)	Nigeria (Ife)	Norway (Bergen)	Pakistan (Karachi)	Philippines (Manila)
Subjects, n	604	845	578	891	859	403	448	663	768	590	884	658	610	892
Age (year)	46.7±7.3	52.4±9.9	55.9±11.6	52.4±9.1	52.7±10.2	52.2±10.0	53.7±10.5	54.5±9.5	55.1±10.3	57.5±10.7	55.3±12.0	59.8±12.6	51.6±9.6	52.4±10.2
Height (cm)	158.6±6.6	158.8±8.9	165.7±8.8	161.1±8.8	160.1±8.7	161.2±8.2	161.6±9.1	158.8±8.2	161.7±9.1	169.9±9.6	162.7±7.7	170.9±9.5	159.5±9.6	156.4±8.6
BMI ($kg \cdot m^{-2}$)	24.7±3.8	22.1±3.8	27.5±6.6	28.4±5.7	27.0±5.0	25.0±5.4	21.8±3.9	26.1±4.5	27.9±5.3	27.4±4.5	25.3±5.4	26.5±4.3	26.5±5.5	24.9±4.7
Sex (male)	42.7	59.4	42	31.4	38.2	40	51.3	51.3	46.1	50.9	39.1	49.2	44.1	42.4
Never-smokers	89.7	87.5	62.3	70.4	75.4	86.3	69.7	74.5	72.1	32.9	88.6	35.7	74.1	46.6
<20 pack-years	8.4	11.7	19.4	14.5	14.9	12.7	27.8	12.4	13.4	34.8	10.4	38.6	13.3	35.4
⩾20 pack-years	1.8	0.8	18.3	15.2	9.7	1	2.6	13.1	14.5	32.4	1	25.7	12.5	17.9
Chronic cough	1.7	1.9	4.2	10.2	10.7	2.2	1.4	4.5	9.8	5.3	0.5	7.9	11.4	4.5
Chronic phlegm	1.7	1.4	4.3	7	7.8	0.3	0.5	4.2	7.9	3.2	0.3	10	10.1	11.4
Wheeze	0.8	4.7	16.4	14.5	13.4	8	3	6.6	12.1	16.7	2.2	23.7	11.5	15.5
Dyspnoea	0	6.6	12.9	14.2	21.1	2	1.3	9.2	14.5	9.5	3.5	5.4	30.7	21.8
FEV_1/FVC (%)	79.5±7.4	79.7±8.1	78.4±9.2	77.4±8.1	78.0±7.2	78.2±7.8	76.3±9.2	81.0±6.8	78.1±8.3	74.6±10.0	78.5±8.4	74.9±8.8	80.1±9.7	79.0±8.9
FVC (L)	2.6±0.7	2.7±0.7	2.9±0.8	3.4±0.9	3.5±0.9	3.0±0.7	3.1±0.7	2.7±0.7	3.3±0.9	4.0±1.1	2.7±0.7	3.9±1.1	2.5±0.8	2.6±0.7
FEV_1 (L)	2.1±0.6	2.2±0.6	2.3±0.7	2.6±0.7	2.7±0.7	2.3±0.6	2.4±0.6	2.2±0.6	2.6±0.7	2.9±0.9	2.1±0.6	2.9±0.9	2.0±0.6	2.1±0.6

https://doi.org/10.1183/13993003.00469-2022

TABLE 1 Characteristics of participants from 41 sites of the BOLD Study with acceptable and repeatable post-bronchodilator spirometry and occupational exposure data (continued)

BOLD site	Philippines (Nampicuan & Talugtug)	Poland (Krakow)	Portugal (Lisbon)	Saudi Arabia (Riyadh)	South Africa (Uitsig & Ravensmead)	Sri Lanka	Sudan (Gezira)	Sudan (Khartoum)	Sweden (Uppsala)	Trinidad & Tobago	Tunisia (Sousse)	Turkey (Adana)	USA (Lexington, KY)
Subjects, n	722	526	711	700	846	1035	590	517	547	1097	661	806	508
Age (year)	54.1±10.5	55.7±11.5	63.3±11.3	50.3±7.7	54.2±10.5	53.7±9.5	53.7±10.2	54.0±10.4	58.4±10.9	54.1±10.8	53.0±9.1	53.6±10.4	56.6±9.9
Height (cm)	158.7±8.6	167.0±8.5	160.7±9.4	162.5±8.9	161.6±8.9	156.4±8.8	163.0±10.8	165.5±9.5	171.0±9.7	165.1±11.3	163.2±9.4	160.7±9.3	167.1±9.9
BMI (kg·m^{-2})	21.5±3.9	27.7±4.7	28.2±4.6	31.2±6.0	27.9±7.5	24.2±4.6	27.3±17.1	26.5±6.4	27.0±4.4	29.1±10.0	29.2±5.6	29.6±5.3	30.8±6.8
Sex (male)	49.3	50.6	46.6	53.6	37.2	44.9	51.5	59.4	51.7	39.8	46.8	48.3	40.6
Never-smokers	46.8	38.2	59.5	73.1	32.3	78.1	74.3	76	39.1	72.4	57.8	45.2	35.8
<20 pack-years	26.2	28.5	16.6	11.7	48.1	17.5	19.9	17	38.8	14.2	12.3	23.3	21.3
⩾20 pack-years	27	33.3	23.9	15.1	19.6	4.4	5.8	7	22.1	13.4	30	31.5	42.9
Chronic cough	7.1	8.2	10.6	12.1	11.5	6.6	2.6	4.1	7.9	7.5	11.4	7.8	19.5
Chronic phlegm	9.6	7.8	13.1	12.9	13.7	10.9	3.8	4.6	11.5	3.7	15.4	8.7	16.3
Wheeze	28	26.3	27.9	40.7	27.7	30.2	19.9	8.5	25.4	11.8	25	35	44.1
Dyspnoea	25.5	23.7	14.6	22	29.2	26.8	8	6.7	5.1	8.7	16.4	23.3	20
FEV_1/FVC (%)	77.0±10.6	75.1±9.2	75.8±9.0	82.6±6.0	75.6±11.1	79.7±8.7	80.1±7.2	77.9±8.4	76.3±8.0	79.6±7.6	80.0±7.5	75.8±8.7	76.2±9.4
FVC (L)	2.7±0.8	3.8±1.0	3.2±0.9	3.0±0.8	2.9±0.8	2.3±0.6	3.0±0.8	2.9±0.8	4.0±1.1	2.7±0.8	3.4±0.9	3.4±0.9	3.4±1.0
FEV_1 (L)	2.1±0.7	2.9±0.9	2.4±0.8	2.5±0.7	2.2±0.7	1.9±0.5	2.4±0.7	2.3±0.6	3.0±0.9	2.2±0.7	2.7±0.8	2.6±0.7	2.6±0.9

Data are presented as mean±SD or the percentage, unless otherwise indicated. BOLD: Burden of Obstructive Lung Disease; BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

Lung function testing was undertaken using an EasyOne spirometer (NDD Medizintechnik AG, Zurich, Switzerland) and each participant performed between three and eight manoeuvres. FEV_1 and FVC were measured before and after the delivery of 200 µg of salbutamol through a metered-dose inhaler, *via* a spacer. All lung function measurements were individually evaluated at the coordinating centre. To be considered usable for analysis, the measurements had to fulfil the following criteria, based on the American Thoracic Society (ATS) criteria at the time the study began [8]: 1) no hesitation, *i.e.* back-extrapolated volume <150 mL and peak expiratory flow time <120 ms; 2) complete blow, *i.e.* lasting ⩾6 s or evidence of clear plateau (end-of-time volume <40 mL; 3) no artefact affecting the FEV_1 or FVC (*e.g.* cough, zero flow error); and 4) the two best blows within 200 mL of each other. We used FEV_1/FVC as a marker of airflow obstruction, and FVC as a proxy for lung volumes.

Statistical analysis

Participants with no exposure to any of the considered work settings were used as the reference group for all analyses. We used regression analysis to assess the association of respiratory symptoms (logistic) and lung function (linear) with occupation and occupational exposure category. All regression models were adjusted for sex, age (years) and smoking status (never-smoker, <20 pack-years and ⩾20 pack-years). Models with FVC as the outcome were further adjusted for height (cm), and those with wheeze or dyspnoea as outcomes were also adjusted for body mass index [9]. Exposure-response trends were evaluated using both continuous and categorical exposure variables, with the median of years of exposure used as the cut-off value for examining cumulative exposures. The effect size for each association was estimated for each site, and the estimates from all sites were combined through random effects meta-analysis. The level of between-site heterogeneity was summarised by the I^2 statistic [10].

In sensitivity analyses, we examined the associations of lung function with each of the three occupational categories among never-smokers only. In addition, we re-ran analyses by sex and by gross national income groups (HICs and LMICs). Stata 15 (Stata Corp., College Station, TX, USA) was used to perform all data analyses. Weights were used to account for sampling strategy. All results were considered statistically significant at $p<0.05$.

Results

Table 1 summarises the characteristics of the study participants from the 41 BOLD sites included in this report. The mean age across sites ranged from 46.7 to 63.3 years; 47.4% of participants were male. The mean FEV_1/FVC varied from 74.3% in Austria (Salzburg) to 82.6% in Saudi Arabia (Riyadh) and the mean FVC from 2.3 L in Sri Lanka to 4.0 L in Austria (Salzburg), Iceland (Reykjavik), the Netherlands (Maastricht) and Sweden (Uppsala). The highest proportion of people likely exposed to organic dusts in the workplace was in a rural site in India (Pune, 87.9%), while workers likely exposed to inorganic dust were more common in Poland (Krakow, 26.4%) and those likely exposed to fumes were in the USA (Lexington, KY; 27.6%). The proportion of participants who did not work in any occupation with exposure to dusts or fumes varied across sites from 8.8% in India (Pune) to 98.2% in India (Mumbai). Further details on the distributions among the 11 occupations in each site can be seen in table 2.

Respiratory symptoms and occupational factors

Figures 1 and 2 show the relationships between respiratory symptoms and occupational exposures. Overall, chronic cough, chronic phlegm, wheeze and dyspnoea were associated with most high-risk occupations. Farming, the most common occupation among participants, was associated with chronic cough (⩾20 years: OR 1.52, 95% CI 1.19–1.94), chronic phlegm (<20 years: OR 1.36, 95% CI 1.15–1.61), wheeze (<20 years: OR 1.53, 95% CI 1.29–1.83; ⩾20 years: OR 1.37, 95% CI 1.16–1.63) and dyspnoea (⩾20 years: OR 1.83, 95% CI 1.53–2.20). Flour, feed or grain milling regardless of duration of exposure was associated with all respiratory symptoms studied. Working with asbestos for ⩾7 years was clearly associated with chronic cough (OR 4.15, 95% CI 2.29–7.53). Hard-rock mining for ⩾3 years was associated with chronic phlegm (OR 3.91, 95% CI 1.79–8.58). Coal mining was associated with wheeze (<13 years: OR 4.15, 95% CI 2.40–7.19). Sandblasting was highly associated with dyspnoea (<3 years: OR 4.87, 95% CI 2.02–11.76; ⩾3 years: OR 6.87, 95% CI 2.63–17.95).

Lung function and occupational factors

We found no significant associations between post-bronchodilator FEV_1/FVC ratio or FVC and work in any of the high-risk occupations. FEV_1/FVC was low in coal miners, sandblasters, chemical or plastic processors and steel millers with long durations of exposure, but these associations were not statistically significant. Moreover, there was no evidence of exposure-response associations of either post-bronchodilator lung function measures with any of the specific occupations (supplementary table S2).

https://doi.org/10.1183/13993003.00469-2022

TABLE 2 Participants from 41 sites of the BOLD study across 11 work settings likely linked to significant exposure to particulates or fumes and loss of lung function

BOLD site	Albania (Tirana)	Algeria (Annaba)	Australia (Sydney)	Austria (Salzburg)	Benin (Sèmè-Kpodji)	Cameroon (Limbe)	Canada (Vancouver)	China (Guangzhou)	England (London)	Estonia (Tartu)	Germany (Hannover)	Iceland (Reykjavik)	India (Kashmir)	India (Mumbai)
Subjects, n	939	890	541	1253	698	331	827	461	675	613	680	757	760	439
Unexposed to any high-risk occupation	486 (51.8)	356 (40.0)	442 (81.7)	831 (66.3)	650 (93.1)	108 (32.6)	678 (82.0)	396 (85.9)	596 (88.3)	439 (71.6)	491 (72.2)	306 (40.4)	495 (65.1)	431 (98.2)
Occupational exposure to organic dusts	352 (37.5)	33 (3.7)	40 (7.4)	307 (24.5)	9 (1.3)	194 (58.6)	80 (9.7)	20 (4.3)	36 (5.3)	99 (16.2)	71 (10.4)	369 (48.8)	259 (34.1)	7 (1.6)
Farming	334 (35.6)	24 (2.7)	31 (5.7)	288 (23.0)	8 (1.2)	194 (58.6)	66 (8.0)	1 (0.2)	27 (4.0)	91 (14.9)	51 (7.5)	350 (46.2)	259 (34.1)	0 (0.0)
Flour, feed or grain milling	7 (0.8)	9 (1.0)	7 (1.3)	37 (3.0)	1 (0.1)	0 (0.0)	21 (2.5)	3 (0.7)	5 (0.7)	13 (2.1)	16 (2.4)	43 (5.7)	0 (0.0)	0 (0.0)
Cotton or jute processing	15 (1.6)	0 (0.0)	6 (1.1)	19 (1.5)	0 (0.0)	0 (0.0)	4 (0.5)	16 (3.5)	7 (1.0)	4 (0.7)	13 (1.9)	18 (2.4)	0 (0.0)	7 (1.6)
Occupational exposure to inorganic dusts	68 (7.2)	24 (2.7)	30 (5.6)	59 (4.7)	17 (2.4)	8 (2.4)	44 (5.3)	8 (1.7)	18 (2.7)	24 (3.9)	58 (8.5)	62 (8.2)	4 (0.5)	0 (0.0)
Hard-rock mining	20 (2.1)	3 (0.3)	4 (0.7)	16 (1.3)	3 (0.4)	2 (0.6)	14 (1.7)	3 (0.7)	3 (0.4)	5 (0.8)	6 (0.9)	27 (3.6)	0 (0.0)	0 (0.0)
Coal mining	16 (1.7)	1 (0.1)	3 (0.6)	6 (0.5)	3 (0.4)	0 (0.0)	2 (0.2)	2 (0.4)	1 (0.2)	1 (0.2)	11 (1.6)	1 (0.1)	0 (0.0)	0 (0.0)
Sandblasting	10 (1.1)	7 (0.8)	1 (0.2)	15 (1.2)	0 (0.0)	1 (0.3)	8 (1.0)	0 (0.0)	5 (0.7)	4 (0.7)	14 (2.1)	13 (1.7)	4 (0.5)	0 (0.0)
Working with asbestos	34 (3.6)	15 (1.7)	26 (4.8)	30 (2.4)	14 (2.0)	5 (1.5)	26 (3.1)	3 (0.7)	12 (1.8)	19 (3.1)	36 (5.3)	29 (3.8)	0 (0.0)	0 (0.0)
Occupational exposure to fumes	57 (6.1)	194 (21.8)	64 (11.8)	162 (12.9)	10 (1.4)	4 (1.2)	59 (7.3)	42 (9.1)	41 (6.1)	88 (14.4)	115 (16.9)	177 (23.4)	3 (0.4)	1 (0.2)
Chemical/ plastics manufacturing	22 (2.3)	14 (1.6)	28 (5.2)	44 (3.5)	0 (0.0)	0 (0.0)	25 (3.0)	11 (2.4)	24 (3.6)	45 (7.3)	50 (7.4)	78 (10.3)	1 (0.1)	0 (0.0)
Foundry or steel milling	11 (1.2)	156 (17.5)	11 (2.1)	22 (4.1)	0 (0.0)	0 (0.0)	20 (2.4)	18 (3.9)	8 (1.2)	17 (1.4)	16 (2.6)	30 (4.4)	1 (0.1)	0 (0.0)
Welding	24 (2.6)	50 (5.6)	28 (5.2)	77 (6.2)	10 (1.4)	4 (1.2)	19 (2.3)	16 (3.5)	14 (2.1)	34 (5.6)	62 (9.1)	95 (12.6)	0 (0.0)	1 (0.2)
Firefighting	3 (0.3)	7 (0.8)	6 (1.2)	52 (4.2)	0 (0.0)	0 (0.0)	6 (0.7)	1 (0.2)	2 (0.3)	10 (1.6)	8 (1.2)	11 (1.5)	1 (0.1)	0 (0.0)

https://doi.org/10.1183/13993003.00469-2022

TABLE 2 Participants from 41 sites of the BOLD Study across 11 work settings likely linked to significant exposure to particulates or fumes and loss of lung function (continued)

BOLD site	India (Mysore)	India (Pune)	Jamaica	Kyrgyzstan (Chui)	Kyrgyzstan (Naryn)	Malawi (Blantyre)	Malawi (Chikwawa)	Malaysia (Penang)	Morocco (Fes)	Netherlands (Maastricht)	Nigeria (Ife)	Norway (Bergen)	Pakistan (Karachi)	Philippines (Manila)
Subjects, n	604	845	578	891	859	403	448	663	768	590	884	658	610	892
Unexposed to any high-risk occupation	506 (83.8)	74 (8.8)	353 (61.1)	535 (60.0)	240 (27.9)	204 (50.6)	396 (88.4)	557 (84.0)	514 (66.9)	444 (75.3)	417 (47.2)	419 (63.7)	556 (91.2)	674 (75.6)
Occupational exposure to organic dusts	91 (15.1)	743 (87.9)	172 (29.8)	317 (35.6)	617 (71.8)	189 (46.9)	28 (6.3)	69 (10.4)	209 (27.2)	55 (9.3)	424 (49.1)	95 (14.4)	24 (3.9)	159 (17.8)
Farming	91 (15.1)	739 (87.5)	163 (28.2)	307 (34.5)	617 (71.8)	182 (45.2)	21 (4.7)	52 (7.8)	184 (24.0)	38 (6.4)	416 (47.1)	64 (9.7)	21 (3.44)	128 (14.4)
Flour, feed or grain milling	0 (0.0)	12 (1.4)	1 (0.2)	8 (0.9)	1 (0.1)	4 (1.0)	0 (0.0)	3 (0.5)	17 (2.2)	14 (2.4)	24 (2.7)	21 (3.2)	0 (0.0)	11 (1.2)
Cotton or jute processing	98 (16.2)	5 (0.6)	8 (1.4)	17 (1.9)	0 (0.0)	9 (2.2)	8 (1.8)	16 (2.4)	18 (2.3)	7 (1.2)	16 (1.8)	24 (3.7)	3 (0.5)	29 (3.3)
Occupational exposure to inorganic dusts	1 (0.2)	60 (7.1)	26 (4.5)	24 (2.7)	0 (0.0)	13 (3.2)	14 (3.1)	9 (1.4)	19 (2.5)	49 (8.3)	46 (5.2)	87 (13.2)	10 (1.6)	13 (1.5)
Hard-rock mining	0 (0.0)	48 (5.7)	0 (0.0)	6 (0.7)	0 (0.0)	7 (1.7)	7 (1.6)	4 (0.6)	8 (1.0)	4 (0.7)	15 (1.7)	9 (1.4)	0 (0.0)	4 (0.5)
Coal mining	0 (0.0)	2 (0.2)	0 (0.0)	14 (1.6)	0 (0.0)	2 (0.5)	1 (0.2)	3 (0.5)	2 (0.3)	7 (1.2)	3 (0.3)	4 (0.6)	0 (0.0)	0 (0.0)
Sandblasting	0 (0.0)	7 (0.8)	1 (0.2)	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.6)	3 (0.4)	2 (0.3)	12 (1.4)	20 (3.0)	0 (0.0)	5 (0.6)
Working with asbestos	1 (0.2)	5 (0.6)	25 (4.3)	2 (0.2)	0 (0.0)	6 (1.5)	6 (1.3)	1 (0.2)	10 (1.3)	39 (6.6)	24 (2.7)	73 (11.1)	10 (1.6)	6 (0.7)
Occupational exposure to fumes	3 (0.5)	61 (7.2)	44 (7.6)	42 (4.7)	3 (0.4)	10 (2.5)	5 (1.1)	33 (5.0)	48 (6.3)	84 (14.2)	36 (4.1)	156 (23.7)	13 (2.1)	59 (6.6)
Chemical/ plastics manufacturing	0 (0.0)	18 (2.1)	13 (2.3)	18 (2.0)	0 (0.0)	2 (0.5)	1 (0.2)	20 (3.0)	15 (2.0)	43 (7.3)	8 (0.9)	102 (15.5)	4 (0.7)	19 (2.1)
Foundry or steel milling	2 (0.3)	43 (5.1)	0 (0.0)	13 (1.5)	0 (0.0)	1 (0.3)	1 (0.2)	8 (1.2)	12 (1.6)	92 (12.2)	13 (1.5)	26 (4.4)	2 (0.3)	6 (0.7)
Welding	1 (0.2)	4 (0.5)	29 (5.0)	12 (1.4)	3 (0.4)	3 (0.7)	3 (0.7)	7 (1.1)	25 (3.3)	35 (5.9)	22 (2.5)	64 (9.7)	8 (1.3)	33 (3.7)
Firefighting	0 (0.0)	0 (0.0)	3 (0.5)	0 (0.0)	0 (0.0)	4 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.7)	2 (0.2)	6 (0.9)	0 (0.0)	6 (0.7)

https://doi.org/10.1183/13993003.00469-2022

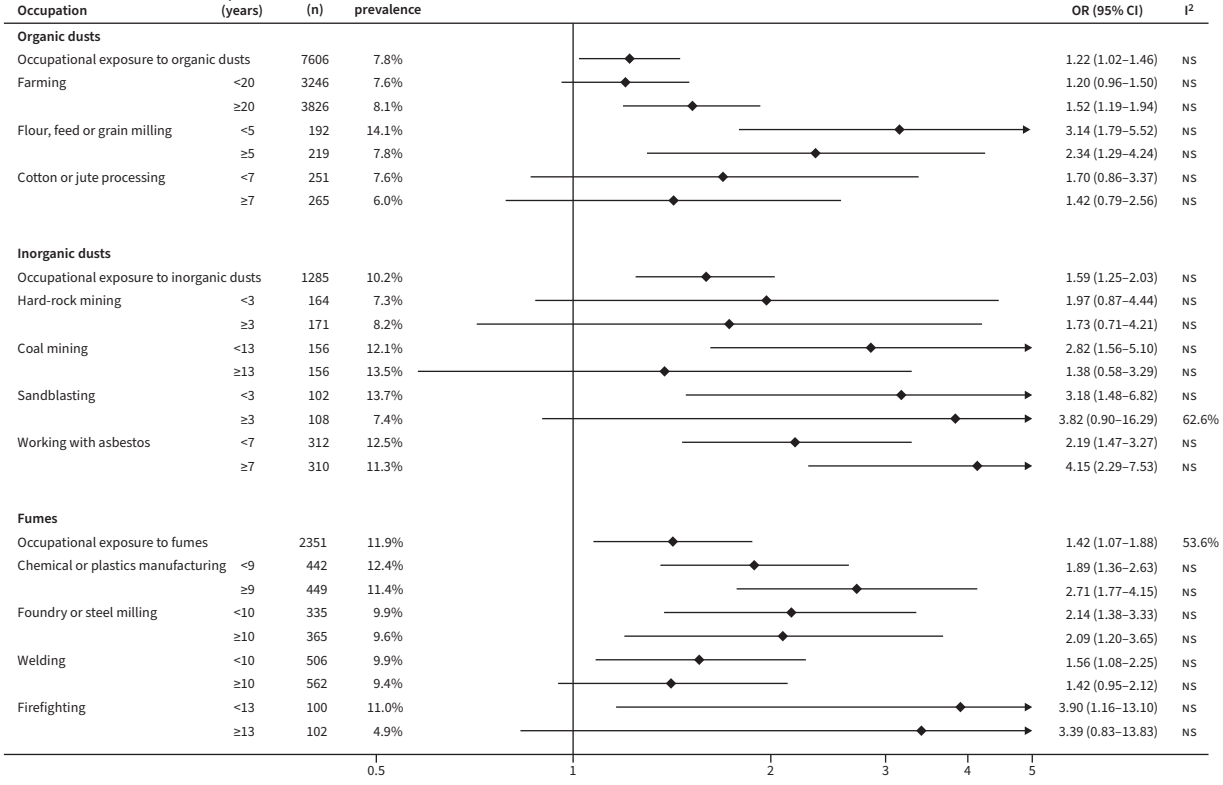
TABLE 2 Participants from 41 sites of the BOLD Study across 11 work settings likely linked to significant exposure to particulates or fumes and loss of lung function (continued)

BOLD site	Philippines (Nampicuan & Talugtug)	Poland (Krakow)	Portugal (Lisbon)	Saudi Arabia (Riyadh)	South Africa (Uitsig & Ravensmead)	Sri Lanka	Sudan (Gezira)	Sudan (Khartoum)	Sweden (Uppsala)	Trinidad & Tobago	Tunisia (Sousse)	Turkey (Adana)	USA (Lexington, KY)
Subjects, n	722	526	711	700	846	1035	590	517	547	1097	661	806	508
Unexposed to any high-risk occupation	145 (20.1)	193 (36.7)	544 (76.5)	617 (88.1)	641 (75.8)	715 (69.1)	265 (44.9)	322 (62.3)	381 (69.7)	909 (82.9)	613 (92.7)	339 (42.1)	206 (40.6)
Occupational exposure to organic dusts	574 (79.5)	176 (33.5)	132 (18.6)	60 (8.6)	92 (10.9)	228 (22.0)	291 (49.3)	124 (24.0)	91 (16.6)	96 (8.8)	23 (3.5)	436 (54.1)	211 (41.5)
Farming	559 (77.4)	164 (31.2)	120 (16.9)	60 (8.6)	21 (2.5)	218 (21.1)	284 (48.1)	116 (22.4)	86 (15.7)	92 (8.4)	13 (2.0)	394 (48.9)	204 (40.2)
Flour, feed or grain milling	8 (1.1)	18 (3.4)	2 (0.3)	0 (0.0)	16 (1.9)	3 (0.3)	13 (2.2)	8 (1.2)	25 (4.6)	4 (0.4)	2 (0.3)	15 (1.9)	19 (3.7)
Cotton or jute processing	34 (4.7)	3 (0.6)	12 (1.7)	0 (0.0)	62 (7.3)	10 (1.0)	14 (2.4)	14 (2.7)	5 (1.0)	1 (0.1)	8 (1.2)	73 (9.1)	11 (2.2)
Occupational exposure to inorganic dusts	17 (2.4)	139 (26.4)	10 (1.4)	3 (0.4)	44 (5.2)	21 (2.0)	31 (5.3)	11 (2.1)	49 (9.0)	27 (2.5)	6 (0.9)	18 (2.2)	116 (22.8)
Hard-rock mining	4 (0.6)	27 (5.1)	2 (0.3)	0 (0.0)	8 (1.0)	9 (0.9)	26 (4.4)	4 (0.8)	8 (1.5)	2 (0.2)	5 (0.8)	7 (0.9)	15 (3.0)
Coal mining	14 (1.9)	117 (22.2)	2 (0.3)	0 (0.0)	3 (0.4)	3 (0.3)	5 (0.9)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	4 (0.5)	78 (15.4)
Sandblasting	0 (0.0)	6 (1.1)	1 (0.1)	3 (0.4)	14 (1.7)	1 (0.1)	0 (0.0)	0 (0.0)	11 (2.0)	6 (0.6)	1 (0.2)	9 (1.1)	19 (3.7)
Working with asbestos	1 (0.1)	13 (2.5)	5 (0.7)	0 (0.0)	30 (3.6)	10 (1.0)	2 (0.3)	7 (1.4)	36 (6.6)	21 (1.9)	0 (0.0)	0 (0.0)	41 (8.1)
Occupational exposure to fumes	23 (3.2)	103 (19.6)	38 (5.3)	24 (3.4)	102 (12.0)	17 (1.6)	35 (5.9)	26 (5.0)	87 (15.9)	74 (6.8)	19 (2.9)	50 (6.2)	140 (27.6)
Chemical/plastics manufacturing	7 (1.0)	29 (5.5)	35 (3.5)	8 (1.1)	54 (6.4)	5 (0.5)	12 (2.0)	11 (2.1)	37 (6.8)	20 (1.8)	4 (0.6)	15 (1.9)	60 (11.8)
Foundry or steel milling	4 (0.6)	19 (3.6)	59 (9.0)	0 (0.0)	16 (1.9)	0 (0.0)	2 (0.3)	2 (0.4)	21 (3.8)	5 (0.5)	2 (0.3)	16 (2.0)	33 (6.5)
Welding	13 (1.8)	46 (8.8)	9 (1.3)	14 (2.0)	47 (5.6)	12 (1.2)	23 (3.9)	14 (2.7)	42 (7.7)	52 (4.7)	14 (2.1)	28 (3.5)	71 (14.0)
Firefighting	0 (0.0)	20 (3.8)	2 0.3)	2 (0.3)	1 (0.1)	0 (0.0)	2 (0.3)	3 (0.6)	9 (1.7)	2 (0.2)	1 (0.2)	4 (0.5)	24 (4.7)

Data presented as n (%), unless otherwise indicated. BOLD: Burden of Obstructive Lung Disease.

a)

Occupation	Cumulative exposure (years)	Subjects (n)	Symptom prevalence	OR (95% CI)	I^2
Organic dusts					
Occupational exposure to organic dusts		7606	7.8%	1.22 (1.02–1.46)	NS
Farming	<20	3246	7.6%	1.20 (0.96–1.50)	NS
	≥20	3826	8.1%	1.52 (1.19–1.94)	NS
Flour, feed or grain milling	<5	192	14.1%	3.14 (1.79–5.52)	NS
	≥5	219	7.8%	2.34 (1.29–4.24)	NS
Cotton or jute processing	<7	251	7.6%	1.70 (0.86–3.37)	NS
	≥7	265	6.0%	1.42 (0.79–2.56)	NS
Inorganic dusts					
Occupational exposure to inorganic dusts		1285	10.2%	1.59 (1.25–2.03)	NS
Hard-rock mining	<3	164	7.3%	1.97 (0.87–4.44)	NS
	≥3	171	8.2%	1.73 (0.71–4.21)	NS
Coal mining	<13	156	12.1%	2.82 (1.56–5.10)	NS
	≥13	156	13.5%	1.38 (0.58–3.29)	NS
Sandblasting	<3	102	13.7%	3.18 (1.48–6.82)	NS
	≥3	108	7.4%	3.82 (0.90–16.29)	62.6%
Working with asbestos	<7	312	12.5%	2.19 (1.47–3.27)	NS
	≥7	310	11.3%	4.15 (2.29–7.53)	NS
Fumes					
Occupational exposure to fumes		2351	11.9%	1.42 (1.07–1.88)	53.6%
Chemical or plastics manufacturing	<9	442	12.4%	1.89 (1.36–2.63)	NS
	≥9	449	11.4%	2.71 (1.77–4.15)	NS
Foundry or steel milling	<10	335	9.9%	2.14 (1.38–3.33)	NS
	≥10	365	9.6%	2.09 (1.20–3.65)	NS
Welding	<10	506	9.9%	1.56 (1.08–2.25)	NS
	≥10	562	9.4%	1.42 (0.95–2.12)	NS
Firefighting	<13	100	11.0%	3.90 (1.16–13.10)	NS
	≥13	102	4.9%	3.39 (0.83–13.83)	NS



b)

Occupation	Cumulative exposure (years)	Subjects (n)	Symptom prevalence	OR (95% CI)	I^2
Organic dusts					
Occupational exposure to organic dusts		7606	7.4%	1.16 (0.98–1.37)	NS
Farming	<20	3246	8.1%	1.36 (1.15–1.61)	NS
	≥20	3826	6.8%	1.22 (0.93–1.60)	NS
Flour, feed or grain milling	<5	192	12.5%	2.28 (1.36–3.82)	NS
	≥5	219	11.0%	2.72 (1.52–4.88)	NS
Cotton or jute processing	<7	251	8.8%	1.75 (1.07–2.85)	NS
	≥7	265	5.3%	1.34 (0.70–2.55)	NS
Inorganic dusts					
Occupational exposure to inorganic dusts		1285	10.1%	1.40 (1.09–1.79)	NS
Hard-rock mining	<3	164	12.2%	2.05 (1.16–3.62)	NS
	≥3	171	9.4%	3.91 (1.78–8.58)	NS
Coal mining	<13	156	13.4%	1.59 (0.83–3.04)	NS
	≥13	156	12.2%	1.56 (0.63–3.86)	NS
Sandblasting	<3	102	12.8%	3.49 (1.56–7.82)	NS
	≥3	108	5.6%	2.26 (0.73–6.98)	NS
Working with asbestos	<7	312	10.9%	2.26 (1.19–4.30)	67.2%
	≥7	310	10.0%	2.80 (1.79–4.39)	NS
Fumes					
Occupational exposure to fumes		2351	11.3%	1.31 (0.98–1.75)	56.5%
Chemical or plastics manufacturing	<9	442	11.3%	1.73 (1.23–2.44)	NS
	≥9	449	11.4%	2.31 (1.62–3.29)	NS
Foundry or steel milling	<10	335	10.2%	1.77 (1.16–2.69)	NS
	≥10	365	10.1%	2.62 (1.46–4.69)	NS
Welding	<10	506	11.1%	1.41 (0.98–2.02)	NS
	≥10	562	9.8%	1.60 (1.14–2.25)	NS
Firefighting	<13	100	15.0%	2.03 (0.98–4.22)	NS
	≥13	102	8.8%	3.46 (1.19–10.06)	NS

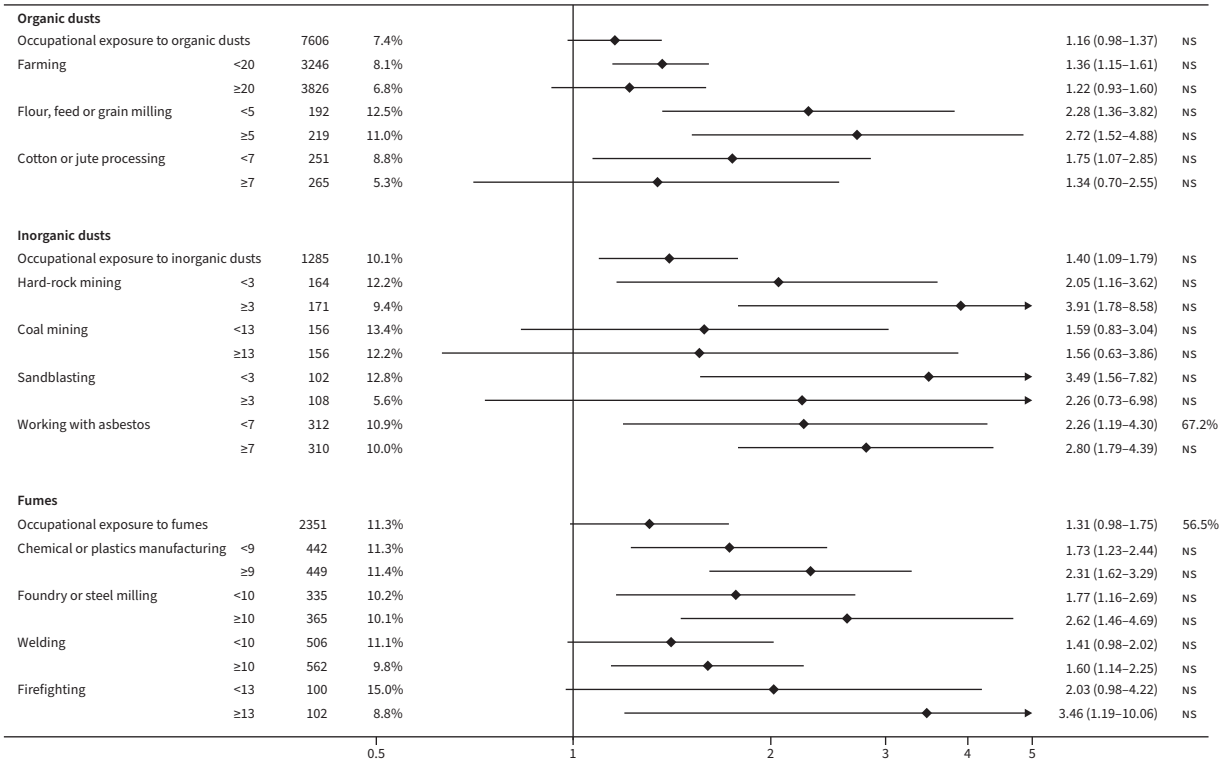


FIGURE 1 Association of a) chronic cough and b) chronic phlegm with high-risk occupations. NS: nonsignificant.

a)

Occupation	Cumulative exposure (years)	Subjects (n)	Symptom prevalence	OR (95% CI)	I^2
Organic dusts					
Occupational exposure to organic dusts		7606	18.3%	1.37 (1.21–1.55)	NS
Farming	<20	3246	20.0%	1.53 (1.28–1.83)	NS
	≥20	3826	16.2%	1.37 (1.15–1.63)	NS
Flour, feed or grain milling	<5	192	38.0%	2.64 (1.78–3.92)	NS
	≥5	219	25.1%	2.52 (1.72–3.70)	NS
Cotton or jute processing	<7	251	28.7%	2.58 (1.42–4.69)	65.5%
	≥7	265	18.5%	1.44 (1.02–2.03)	NS
Inorganic dusts					
Occupational exposure to inorganic dusts		1285	26.9%	1.92 (1.46–2.52)	54.5%
Hard-rock mining	<3	164	23.8%	2.71 (1.83–4.01)	NS
	≥3	171	22.8%	2.28 (1.60–3.24)	NS
Coal mining	<13	156	30.8%	4.15 (2.40–7.19)	NS
	≥13	156	35.3%	2.52 (1.48–4.30)	NS
Sandblasting	<3	102	41.2%	2.55 (1.51–4.31)	NS
	≥3	108	17.6%	2.00 (0.84–4.76)	NS
Working with asbestos	<7	312	32.4%	1.99 (1.44–2.75)	NS
	≥7	310	22.6%	2.14 (1.46–3.14)	NS
Fumes					
Occupational exposure to fumes		2351	27.6%	1.42 (1.21–1.66)	NS
Chemical or plastics manufacturing	<9	442	30.5%	1.74 (1.31–2.31)	NS
	≥9	449	24.7%	1.78 (1.31–2.41)	NS
Foundry or steel milling	<10	335	31.9%	2.07 (1.54–2.78)	NS
	≥10	365	21.6%	2.34 (1.49–3.67)	50.4%
Welding	<10	506	28.9%	1.65 (1.27–2.15)	NS
	≥10	562	22.6%	1.39 (1.07–1.80)	NS
Firefighting	<13	100	34.0%	2.18 (1.16–4.10)	NS
	≥13	102	24.5%	2.73 (1.58–4.73)	NS

b)

Occupation	Cumulative exposure (years)	Subjects (n)	Symptom prevalence	OR (95% CI)	I^2
Organic dusts					
Occupational exposure to organic dusts		7606	14.4%	1.40 (1.21–1.62)	NS
Farming	<20	3246	11.2%	1.22 (1.00–1.49)	NS
	≥20	3826	16.9%	1.83 (1.52–2.20)	NS
Flour, feed or grain milling	<5	192	12.2%	2.78 (1.19–6.49)	NS
	≥5	219	12.9%	2.94 (1.75–4.94)	NS
Cotton or jute processing	<7	251	17.4%	2.43 (1.27–4.64)	NS
	≥7	265	17.5%	2.02 (1.07–3.82)	NS
Inorganic dusts					
Occupational exposure to inorganic dusts		1285	12.2%	1.67 (1.28–2.18)	NS
Hard-rock mining	<3	164	7.8%	2.02 (0.81–5.05)	NS
	≥3	171	12.3%	2.64 (1.34–5.20)	NS
Coal mining	<13	156	20.2%	4.01 (2.30–6.99)	NS
	≥13	156	19.7%	1.77 (0.85–3.69)	NS
Sandblasting	<3	102	12.6%	4.87 (2.02–11.76)	NS
	≥3	108	9.9%	6.87 (2.63–17.95)	NS
Working with asbestos	<7	312	10.9%	2.33 (1.22–4.44)	NS
	≥7	310	10.7%	2.90 (1.72–4.88)	NS
Fumes					
Occupational exposure to fumes		2351	13.0%	1.42 (1.16–1.74)	NS
Chemical or plastics manufacturing	<9	442	14.9%	2.22 (1.18–4.18)	56.5%
	≥9	449	11.1%	1.76 (1.03–3.00)	NS
Foundry or steel milling	<10	335	11.0%	3.07 (1.82–5.18)	NS
	≥10	365	11.8%	3.24 (1.69–6.21)	NS
Welding	<10	506	12.2%	2.89 (1.69–4.95)	NS
	≥10	562	10.7%	1.75 (1.26–2.43)	NS
Firefighting	<13	100	9.4%	2.50 (0.71–8.83)	NS
	≥13	102	8.5%	1.97 (0.71–5.43)	NS

FIGURE 2 Association of a) wheeze and b) dyspnoea with high-risk occupations. NS: nonsignificant.

Sensitivity analyses of lung function among men in HICs indicated that working in a job with organic dust exposure for ⩾20 years was associated with a significantly decreased FEV_1/FVC (β= −0.34%, 95% CI −0.42– −0.27%; supplementary table S3) and FVC (β= −0.18 L, 95% CI −0.32– −0.04 L; supplementary table S4). In LMICs, we found that men working in an organic dust job for a longer duration had a lower FEV_1/FVC than in HICs; however, this finding was not statistically significant (β= −1.01%, 95% CI −2.77–0.75%) and there was high heterogeneity across the LMIC sites (I^2=92.2%, p<0.001). There were no significant associations, in sensitivity analyses, between work with inorganic dusts and FEV_1/FVC (supplementary table S5). Among never-smoking women in HICs, workplace exposure to inorganic dusts for ⩾6 years was associated with greater FVC (β=0.60 L, 95% CI 0.53–0.66 L; supplementary table S6). Among men exposed to fumes at work for ⩾11 years in LMICs, a sensitivity analysis showed a significant association with a lower FEV_1/FVC (β= −0.29%, 95% CI −0.39– −0.17%; supplementary table S7). In contrast, there was no such association in HICs. There was no significant association between workplace exposure to fumes with FVC (supplementary table S8).

Discussion

In this large international population-based study we found that respiratory symptoms were associated with working in settings where exposure to dusts and fumes is likely to be high. Overall, these findings agree with two recent reviews reporting significant relationships of chronic bronchitis and breathlessness with occupational exposures to organic dusts, inorganic (mineral) dusts or fumes [1, 2]. In contrast, we found no consistent associations between occupational exposures and measures of lung function. Lung function was lower in miners and chemical or plastic processors with long durations of exposure, but these differences were not statistically significant. One explanation for the association of chronic respiratory symptoms without significant lung function differences may be irritation of the airways leading to chronic bronchitis without obstruction. These findings are similar to those we found previously in the BOLD study, where chronic phlegm but not chronic airflow obstruction was more likely to occur among users than among never-users of solid fuels [11]. The “English Hypothesis” of a strong link between bronchitis and obstruction was largely discredited by the study of Fletcher and Peto [12], and the lack of a strong association in this study should not be entirely unexpected. Another explanation could be the occurrence of occupational asthma, presenting with wheeze and breathlessness without affecting post-bronchodilator lung function. This can be induced by substances in workplaces such as animal dusts, flour, chemicals and metals [13]. In addition, non-differential misclassification of exposure might have hampered the ability to detect a statistically significant association.

Stratifying analyses by sex, gross national income and smoking status among male participants in HICs showed that working in an organic dust job for ⩾20 years was associated with slightly lower FEV_1/FVC and FVC. In a combined analysis of the European Community Respiratory Health Survey (ECRHS) and the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), a decline in FEV_1/FVC was associated with exposure to organic dust [14]. However, this association was not evident among never-smokers, suggesting that this relationship may have been due to residual confounding by smoking. A population-based study in Denmark reported an increased prevalence of COPD, defined by the lower limit normal (LLN) of FEV_1/FVC, among workers exposed to high levels (⩾15 years) of organic dust [15]. In LMICs, we found that men working in an organic dust job for ⩾20 years had a greater, but insignificant, decrement in FEV_1/FVC. However, this finding was highly heterogeneous across the LMIC sites. A potential explanation for these results is that farming was the most prevalent industry sector involving exposures to organic dusts in both HICs and LMICs. While HICs have similar commercial agriculture systems, LMICs are characterised by diverse and less intense agricultural practices, which might cause the significant heterogeneity in our LMIC analyses [16].

No significant association was observed in overall or sensitivity analyses between each lung function measure and inorganic dust exposure among men. Adjustment for passive smoking and education made no material difference to our findings. In the recent ECRHS and SAPALDIA report, FEV_1/FVC decline was associated with mineral dust but again only if ever-smokers were included in the analysis [14]. The ECRHS had already reported no significant association of incident COPD, defined as FEV_1/FVC<LLN, with inorganic (mineral) dust exposures [17]. For FVC, the only significant association we found was among never-smoking women exposed to inorganic dust for ⩾6 years in HICs, whose FVC was on average 0.6 L greater than their unexposed counterparts. However, the women exposed in HICs were few (n=5) and diverse: two from the USA had worked with asbestos for 19 years and in hard-rock mining for 8 years, respectively; one from Estonia had worked with asbestos for 24 years; one from Germany had worked in sandblasting for 11 years; and one from Norway had worked with asbestos for 10 years. Therefore, the greater FVC in this group might have occurred by chance or might reflect a healthy worker effect [18].

The ECRHS study, which was conducted in 12 high-income European countries, reported an increased risk of COPD based on the LLN of FEV_1/FVC among workers with occupational gas and fume exposures [17]. However, the association between FEV_1/FVC decline and gases and fumes was not significant in the combined analysis of ECRHS and SAPALDIA [14]. In the current analysis of the BOLD study, we found no association between fumes and FEV_1/FVC among men exposed to fumes for ⩾11 years in HICs. This result is consistent with the recent findings of the UK Biobank, a large population-based study on lifetime job histories and spirometry-defined COPD that found no increased risk for fume-related jobs including chemical processing, metal processing and firefighting [19]. In contrast, there was a significant small effect on FEV_1/FVC (decreased by 0.29%) among men in LMICs. An explanation for our study's contradictory findings might be related to different standards of industrial control between HICs and LMICs, where working conditions remain poor [20].

This study has several strengths. To the best of our knowledge, it is the first large population-based study covering both HICs and LMICs. We used a rigorous standardised protocol for data collection and lung function testing across all 41 sites. This is an advantage over published meta-analyses, which pooled findings from a mixture of study designs (cross-sectional surveys, case–control, longitudinal) with varying outcome definitions (either measured or based on self-report), because it reduces the heterogeneity across sites [1, 2]. Data collection was undertaken by certified technicians and trained interviewers. We tried to control for a potential recall bias by asking participants about their jobs (coded using the standard ISCO-88 classification) instead of their exposures at work. Furthermore, we undertook post-bronchodilator spirometry with centralised quality control for precision of spirometric measurements. In BOLD, about 96% of the manoeuvres met the ATS/European Respiratory Society 2005 goals for acceptability and 90% for repeatability [21].

We also recognise limitations. This study is cross-sectional, which makes it difficult to infer temporality and to distinguish causal relationships. Self-reported respiratory symptoms may be influenced by recall bias. Measurement error might have occurred due to misclassification of occupational histories and poor precision on durations of exposure, particularly in LMIC sites. For example, participants who worked on subsistence farms might not consider and report themselves as farmers. The inclusion of participants with an exposure ⩾3 months but <1 year in the least exposed category may partly explain the lack of association among this category. However, this group of participants was relatively small (2% of those exposed to organic dust, 15% of those exposed to inorganic dust and 6% of those exposed to fumes) and the contrast between the highest exposure category and the non-exposed category should have been enough to detect a true association, if one existed. In addition, the questionnaire did not collect information on the intensity of each occupational exposure, which might limit analyses of the exposure-response relationship. Although the overall prevalence of occupational exposure to organic dust, inorganic dust and fumes was like that of other studies (37% *versus* 36–42%) [14], we are aware that the prevalence of exposure to inorganic dust is much lower than reported in those same studies. Regarding sensitivity analyses of lung function, we restricted these to just three main groups of dust and fume exposures rather than the 11 specified occupations because for some of these there were too few participants, particularly among women. Moreover, it is also noted that workers in industrial workplaces are generally exposed to combinations of respiratory hazards, which affects grouping of dusty and fume jobs so that we were not able to adjust our models for co-exposure to multiple occupational exposures. We are also conscious that our analysis is based on lung function measured using spirometry, not lung diffusion capacity or blood gases, which have been previously linked to occupational exposure to pesticides [22]. Finally, although the study is large, it does not necessarily imply representativeness of the population in each country.

We suggest a further longitudinal study on the association of occupational exposure with respiratory outcomes, which would more easily distinguish causal from non-causal relationships. In addition, to evaluate high-quality occupational exposure assessment, comprehensive data collection on exposure magnitude (*e.g.* dose, frequency and intensity) is suggested. Therefore, personal monitoring for a larger global prospective cohort and application of a job-exposure matrix are recommended [23, 24]. We also found clear evidence that occupational dusty jobs were related to chronic respiratory symptoms with, in some cases, effects on lung function. Further laboratory studies to understand the mechanism of how workplace exposures to dusts and fumes affect lung function are also suggested.

In conclusion, we found that exposure to selected work settings, which are thought to be associated with substantial exposures to particulates or fumes and loss of lung function, may increase the risk of chronic respiratory symptoms, without significant changes in spirometric measures of lung function. This does not mean that unlimited occupational exposure is acceptable or cannot have an effect on the lungs. It just suggests that, in this study, occupational exposures do not appear to be major determinants of low

spirometric values, compared with other exposures. Because we are aware that many work settings were not included in the BOLD study and individual risk might be higher in certain settings, interventions to avoid or reduce occupational exposures are advised. Industrial hygiene is still important and respiratory surveillance should be encouraged among high-risk dusty and fume job workers, especially those living in LMICs.

Acknowledgements: The authors thank all study participants and field workers for their time and cooperation.

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Grant School of Public Health, BRAC (Building Resources Across Communities) University, Institute of Global Health, Dhaka, Bangladesh); Benin: Herve Lawin (PI), Arsene Kpangon, Karl Kpossou, Gildas Agodokpessi, Paul Ayelo and Benjamin Fayomi (Unit of Teaching and Research in Occupational and Environmental Health, University of Abomey Calavi, Cotonou, Benin); Cameroon: Bertrand Mbatchou (PI) and Atongno Humphrey Ashu (Douala General Hospital, Douala, Cameroon); Canada: Wan C. Tan (PI) and Wen Wang (iCapture Center for Cardiovascular and Pulmonary Research, University of British Columbia, Vancouver, BC, Canada); China: NanShan Zhong (PI), Shengming Liu, Jiachun Lu, Pixin Ran, Dali Wang, Jingping Zheng and Yumin Zhou (Guangzhou Institute of Respiratory Diseases, Guangzhou Medical College, Guangzhou, China); Estonia: Rain Jõgi (PI), Hendrik Laja, Katrin Ulst, Vappu Zobel and Toomas-Julius Lill (Lung Clinic, Tartu University Hospital, Tartu, Estonia); Gabon: Ayola Akim Adegnika (PI) (Centre de Recherches Medicale de Lambarene, Lambarene, Gabon); Germany: Tobias Welte (PI), Isabelle Bodemann, Henning Geldmacher and Alexandra Schweda-Linow (Hannover Medical School, Hannover, Germany); Iceland: Thorarinn Gislason (PI), Bryndis Benedikdtsdottir, Kristin Jörundsdottir, Lovisa Gudmundsdottir, Sigrun Gudmundsdottir and Gunnar Gundmundsson (Dept of Allergy, Respiratory Medicine, and Sleep, Landspitali University Hospital, Reykjavik, Iceland); India: Mahesh Padukudru Anand (PI) (JSS Medical College, JSSAHER, Mysuru, India); Parvaiz A Koul (PI), Sajjad Malik, Nissar A. Hakim and Umar Hafiz Khan (Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J&K, India); Rohini Chowgule (PI), Vasant Shetye, Jonelle Raphael, Rosel Almeda, Mahesh Tawde, Rafiq Tadvi, Sunil Katkar, Milind Kadam, Rupesh Dhanawade and Umesh Ghurup (Indian Institute of Environmental Medicine, Mumbai, India); Sanjay Juvekar (PI), Siddhi Hirve, Somnath Sambhudas, Bharat Chaidhary, Meera Tambe, Savita Pingale, Arati Umap, Archana Umap, Nitin Shelar, Sampada Devchakke, Sharda Chaudhary, Suvarna Bondre, Savita Walke, Ashleshsa Gawhane, Anil Sapkal, Rupali Argade and Vijay Gaikwad (Vadu Health and Demographic Surveillance System, King Edward Memorial Hospital Research Centre Pune, Pune, India); Sundeep Salvi (PI), Bill Brashier, Jyoti Londhe and Sapna Madas (Chest Research Foundation, Pune, India); Jamaica: Althea Aquart-Stewart (PI), Akosua Francia Aikman (University of the West Indies, Kingston, Jamaica); Kyrgyzstan: Talant M. Sooronbaev (PI), Bermet M. Estebesova, Meerim Akmatalieva, Saadat Usenbaeva, Jypara Kydyrova, Eliza Bostonova, Ulan Sheraliev, Nuridin Marajapov, Nurgul Toktogulova, Berik Emilov, Toktogul Azilova, Gulnara Beishekeeva, Nasyikat Dononbaeva and AijamalTabyshova (Pulmunology and Allergology Dept, National Centre of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan); Malawi: Kevin Mortimer (PI), Wezzie Nyapigoti, Ernest Mwangoka, Mayamiko Kambwili, Martha Chipeta, Gloria Banda, Suzgo Mkandawire and Justice Banda (the Malawi Liverpool Wellcome Trust, Blantyre, Malawi); Malaysia: Li Cher Loh (PI), Abdul Rashid and Siti Sholehah (Penang Medical College, and Royal College of Surgeons in Ireland and University College Dublin Malaysia Campus, Penang, Malaysia); Morocco: Mohamed C Benjelloun (PI), Chakib Nejjari, Mohamed Elbiaze and Karima El Rhazi (Laboratoire d'épidémiologie, Recherche Clinique et Santé Communautaire, Fès, Morroco); Netherlands: E.F.M. Wouters (PI), F.F. E. Franssen (PI) and G.J. Wesseling (Maastricht University Medical Center, Maastricht, the Netherlands); Nigeria: Daniel Obaseki (PI), Gregory Erhabor, Olayemi Awopeju and Olufemi Adewole (Obafemi Awolowo University, Ile-Ife, Nigeria); Norway: Amund Gulsvik (PI), Tina Endresen and Lene Svendsen (Dept of Thoracic Medicine, Institute of Medicine, University of Bergen, Bergen, Norway); Pakistan: Asaad A. Nafees (PI), Muhammad Irfan, Zafar Fatmi, Aysha Zahidie, Natasha Shaukat and Meesha Iqbal (Aga Khan Univeristy, Karachi, Pakistan); Philippines: Luisito F. Idolor (PI), Teresita S. de Guia, Norberto A. Francisco, Camilo C. Roa, Fernando G. Ayuyao, Cecil Z. Tady, Daniel T. Tan, Sylvia Banal-Yang, Vincent M. Balanag, Jr., Maria Teresita N. Reyes and Renato B. Dantes (Lung Centre of the Philippines, Philippine General Hospital, Nampicuan and Talugtug, the Philippines); Renato B. Dantes (PI), Lourdes Amarillo, Lakan U. Berratio, Lenora C. Fernandez, Norberto A. Francisco, Gerard S. Garcia, Teresita S. de Guia,

Luisito F. Idolor, Sullian S. Naval, Thessa Reyes, Camilo C. Roa, Jr., Ma. Flordeliza Sanchez and Leander P. Simpao (Philippine College of Chest Physicians, Manila, the Philippines); Poland: Ewa Nizankowska-Mogilnicka (PI), Jakub Frey, Rafal Harat, Filip Mejza, Pawel Nastalek, Andrzej Pajak, Wojciech Skucha, Andrzej Szczeklik and Magda Twardowska, (Division of Pulmonary Diseases, Dept of Medicine, Jagiellonian University School of Medicine, Krakow, Poland); Portugal: Cristina Bárbara (PI), Fátima Rodrigues, Hermínia Dias, João Cardoso, João Almeida, Maria João Matos, Paula Simão, Moutinho Santos and Reis Ferreira (the Portuguese Society of Pneumology, Lisbon, Portugal); Saudi Arabia: M. Al Ghobain (PI), H. Alorainy (PI), E. El-Hamad, M. Al Hajjaj, A. Hashi, R. Dela, R. Fanuncio, E. Doloriel, I. Marciano and L. Safia (Saudi Thoracic Society, Riyadh, Saudi Arabia); South Africa: Eric Bateman (PI), Anamika Jithoo (PI), Desiree Adams, Edward Barnes, Jasper Freeman, Anton Hayes, Sipho Hlengwa, Christine Johannisen, Mariana Koopman, Innocentia Louw, Ina Ludick, Alta Olckers, Johanna Ryck and Janita Storbeck, (University of Cape Town Lung Institute, Cape Town, South Africa); Sri Lanka: Kirthi Gunasekera (PI) and Rajitha Wickremasinghe (Medical Research Institute, Central Chest Clinic, Colombo, Sri Lanka); Sudan: Asma Elsony (PI), Hana A. Elsadig, Nada Bakery Osman, Bandar Salah Noory, Monjda Awad Mohamed, Hasab Alrasoul Akasha Ahmed Osman, Namarig Moham ed Elhassan, Abdel Mu'is El Zain, Marwa Mohamed Mohamaden, Suhaiba Khalifa, Mahmoud Elhadi, Mohand Hassan, Dalia Abdelmonam, Rana Ahmed, Rashid Kamal, Hind Eltigani, Stephen's Umar, Aya Abdeen, Mihad Osman, Malaz Mohamed, Roa Eltayeb, Mohamed Abelazeez, Hoyam Altaher, Lina Mohamed, Rabee Abdarahman, Rayan Mohamed, Haram and Rimaz Ismaeel (the Epidemiological Laboratory, Khartoum, Sudan); Sweden: Christer Janson (PI), Inga Sif Olafsdottir, Katarina Nisser, Ulrike Spetz-Nyström, Gunilla Hägg and Gun-Marie Lund (Dept of Medical Sciences: Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden); Trinidad and Tobago: Terence Seemungal (PI), Fallon Lutchmansingh and Liane Conyette (University of the West Indies, St. Augustine, Trinidad and Tobago); Tunisia: Imed Harrabi (PI), Myriam Denguezli, Zouhair Tabka, Hager Daldoul, Zaki Boukheroufa, Firas Chouikha and Wahbi Belhaj Khalifa (Faculté de Médecine, University Hospital Farhat Hached, Sousse, Tunisia); Turkey: Ali Kocabaş (PI), Attila Hancioglu, Ismail Hanta, Sedat Kuleci, Ahmet Sinan Turkyilmaz, Sema Umut and Turgay Unalan (Dept of Chest Diseases, Cukurova University School of Medicine, Adana, Turkey); UK: Peter G.J. Burney (PI), Anamika Jithoo, Louisa Gnatiuc, Hadia Azar, Jaymini Patel, Caron Amor, James Potts, Michael Tumilty, Fiona McLean and Risha Dudhaiya (National Heart and Lung Institute, Imperial College London, London, UK); USA: A. Sonia Buist (PI) (Oregon University of Health Sciences, Portland, OR, USA); Mary Ann McBurnie, William M. Vollmer and Suzanne Gillespie (Kaiser Permanente Center for Health Research, Portland, OR, USA); Sean Sullivan (University of Washington, Seattle, WA, USA); Todd A. Lee and Kevin B. Weiss, (Northwestern University, Chicago, IL, USA); Robert L. Jensen and Robert Crapo (Latter Day Saints Hospital, Salt Lake City, UT, USA); Paul Enright (University of Arizona, Tucson, AZ, USA); David M. Mannino (PI), John Cain, Rebecca Copeland, Dana Hazen and Jennifer Methvin, (University of Kentucky, Lexington, KY, USA).

Additional local support for BOLD clinical sites was provided by: Boehringer Ingelheim China (GuangZhou, China); Turkish Thoracic Society, Boehringer Ingelheim and Pfizer (Adana, Turkey); Altana, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck Sharpe & Dohme, Novartis, Salzburger Gebietskrankenkasse and Salzburg Local Government (Salzburg, Austria); Research for International Tobacco Control, the International Development Research Centre, the South African Medical Research Council, the South African Thoracic Society GlaxoSmithKline Pulmonary Research Fellowship, and the University of Cape Town Lung Institute (Cape Town, South Africa); Landspítali-University Hospital-Scientific Fund, GlaxoSmithKline Iceland and AstraZeneca Iceland (Reykjavik, Iceland); GlaxoSmithKline Pharmaceuticals, Polpharma, Ivax Pharma Poland, AstraZeneca Pharma Poland, ZF Altana Pharma, Pliva Kraków, Adamed, Novartis Poland, Linde Gaz Polska, Lek Polska, Tarchomińskie Zakłady Farmaceutyczne Polfa, Starostwo Proszowice, Skanska, Zasada, Agencja Mienia Wojskowego w Krakowie, Telekomunikacja Polska, Biernacki, Biogran, Amplus Bucki, Skrzydlewski, Sotwin and Agroplon (Krakow, Poland); Boehringer Ingelheim and Pfizer Germany (Hannover, Germany); the Norwegian Ministry of Health's Foundation for Clinical Research and Haukeland University Hospital's Medical Research Foundation for Thoracic Medicine (Bergen, Norway); AstraZeneca, Boehringer Ingelheim, Pfizer and GlaxoSmithKline (Vancouver, Canada); Marty Driesler Cancer Project (Lexington, KY, USA); Altana, Boehringer Ingelheim (Phil), GlaxoSmithKline, Pfizer, Philippine College of Chest Physicians, Philippine College of Physicians and United Laboratories (Phil) (Manila, Philippines); Air Liquide Healthcare P/L, AstraZeneca P/L, Boehringer Ingelheim P/L, GlaxoSmithKline Australia P/L, Pfizer Australia P/L (Sydney, Australia), Dept of Health Policy Research Programme, Clement Clarke International (London, UK); *Boehringer Ingelheim and Pfizer* (Lisbon, Portugal), Swedish Heart and Lung Foundation, The Swedish Association against Heart and Lung Diseases, GlaxoSmithKline (Uppsala, Sweden); Seed Money Grant (PF20/0512), Aga Khan University, Karachi, and Chiesi Pakistan (Pvt.) Limited (Karachi, Pakistan).

Conflict of interest: J. Ratanachina, A.F.S. Amaral, S. De Matteis, H. Lawin, K. Mortimer, D.O. Obaseki, I. Harrabi, M. Denguezli, E.F.M. Wouters, C. Janson, A. Gulsvik, H.H. Cherkaski, F. Mejza, P.A. Mahesh, A. Elsony, R. Ahmed, W. Tan, L.C. Loh, A. Rashid, M. Studnicka, A.A. Nafees, T. Seemungal, A. Aquart-Stewart, M. Al Ghobain, J. Zheng, S. Juvekar, S. Salvi, R. Jogi, T. Gislason, A.S. Buist, P. Cullinan and P. Burney have no conflict of interest to disclose. R. Nielsen reports grants from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline and Novartis, and receipt of equipment/material/services from ResMed Norway; and is President of the Norwegian Respiratory

Society. D. Mannino reports royalties from Up to Date; personal fees from GlaxoSmithKline, AstraZeneca and Schlesinger Law Firm; honoraria from American Association of Respiratory Care; and stock in GlaxoSmithKline; and is the Medical Director of the COPD Foundation.

Support statement: Supported by Wellcome Trust grant 085790/Z/08/Z for the BOLD (Burden of Obstructive Lung Disease) Study. The initial BOLD programme was funded in part by unrestricted educational grants to the Operations Center in Portland, Oregon from Altana, Aventis, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck, Novartis, Pfizer, Schering-Plough, Sepracor and the University of Kentucky (Lexington, KY). A full list of local funders can be found at https://www.boldstudy.org/ Funding information for this article has been deposited with the Crossref Funder Registry.

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