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Past dust and GAS/FUME exposure and COPD in Chinese: The Guangzhou Biobank Cohort Study

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Summary
The impact of occupational dust and gas/fume exposure on chronic obstructive pulmonary disease (COPD) in developing countries has not been quantified. We examined the relationship between past dust and fume exposure and prevalence of COPD and respiratory symptoms in a cross-sectional analysis of a large Chinese population sample.

Participants in the Guangzhou Biobank Cohort Study ($n = 8216$; 27.3% men, mean age 61.9 ± 6.8 years) had spirometry and a structured interview including exposures, symptoms, and lifestyle. Self-reported intensity and duration of dust and gas/fume exposure was used to derive cumulative exposure. COPD was diagnosed from spirometry using lower limit of normal based on prediction equations.

COPD was associated with high exposure to dust or gas/fume (exposed: 87/1206 v non-exposed: 191/3853; adjusted odds ratio: 1.41; 95% confidence interval (CI) 1.06, 1.87) with no evidence of effect modification by smoking. Respiratory symptoms were associated with exposures to dust and gas/fume, with adjusted odds ratios for chronic cough/phlegm of 1.57 (1.13, 2.17) and 1.39 (1.20, 1.60) for dyspnoea. The overall population attributable fraction for COPD due to occupational exposure was 10.4% (95% CI -0.9%, 19.5%).

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Occupational dust and gas/fume exposure is associated with an increased prevalence of COPD in this Chinese sample, independent of smoking. The population attributable fraction in Chinese is similar to that in Western populations.

Introduction

A growing body of evidence has suggested that risk factors other than smoking have contributed substantially to the global burden of chronic obstructive pulmonary disease (COPD).[1] Approximately 15% of all COPD cases could be attributed to workplace exposure to dust and gas/fume.[2,3] Nevertheless, this estimation of the true population attributable fraction due to occupational exposure is limited by the inconsistent definition of COPD. Most previous studies reported chronic respiratory symptoms as the outcome; and among those that measured lung function, the definition of airflow obstruction differed.[2,3] While developing countries, e.g. China, host the majority of the world's labour force, most of the available information has been derived from Western populations. Existing data in China have been largely collected in specific occupational groups.[4–12] Among the few studies based on community samples,[13–18] most used respiratory symptoms[13–15] or asthma[13] as the outcome. We have used a large population-based study with a high proportion of non-smoking women from Guangzhou, south China, to examine the relationships between self-reported past dust and gas/fume exposure in the workplace and prevalence of spirometry-defined COPD and respiratory symptoms. We also looked for evidence of interaction between smoking and occupational exposure.

Methods

Design and study sample

The Guangzhou Biobank Cohort Study was conducted jointly by the Guangzhou Number 12 People's Hospital and the Universities of Birmingham and Hong Kong. Details of sampling and recruitment have been reported.[19,20] About 10000 Guangzhou residents aged $\geq$50 years were randomly selected from the Guangzhou Health and Happiness Association for the Respectable Elders, a community social and welfare association whose membership is open to all older persons for a nominal fee (US$0.50 per month), to take part in each of the two phases (2003-2004 and 2005–2006), and were included if they were capable of consenting, ambulatory, and not receiving treatment for life threatening conditions. Of those eligible, 90% of the men and 99% of the women participated ($n = 20431$). The Medical Ethics Committee of the Guangzhou Medical Association approved the study. All participants gave written informed consent.

Assessment of occupational exposures

Participants were asked if their longest-held job exposed them to dust, and to specify the intensity (mild, moderate, severe) and duration (number of years) of exposure. A similar set of questions was used to identify their exposure to gas, vapour or fume (hereafter as *gas/fume*). Participants could be exposed to either dust or gas/fume, both or neither. We derived a three-level cumulative exposure index (low, medium, and high) for dust and gas/fume separately according to both exposure intensity and duration.[13] Participants were classified as having low exposure if they reported mild intensity exposure below the median duration (26 years for dust and 25 years for gas/fume). High cumulative exposure indicated moderate or severe intensity exposure at or above the median duration. Others were included as medium. In addition, a three-level cumulative composite dust and gas/fume index was derived from the two individual dust and gas/fume cumulative exposure indices. High cumulative composite exposure was defined as having either high level of dust or gas/fume exposure index or both. Those who had any medium level cumulative exposure (but no high exposure) were grouped into medium cumulative composite exposure. The rest fell under the low cumulative composite exposure category. Participants who were not exposed to dust or gas/fume were the reference group. A job exposure matrix was not developed for this study as it would not be feasible in a study with over 20000 participants engaged in a wide range of occupations.

This classification system depends entirely on individual's perception on exposure intensity without consideration on the relative levels of exposure across occupations. For example, a miner and a teacher could have both reported high level of dust exposure, but the former would have been exposed at a much higher intensity. Therefore, based on the nature of the jobs (likelihood of being exposed to higher level of dust or gas/fume) and the reported prevalence of dust or gas/fume exposure (Table 1), we categorised the occupations into high risk (farming/forestry/fishing and elementary process plant/construction) and low risk (managerial/administrative/secretarial, professional/technical, sales/customer service, protective service and other) groups.

Assessment of respiratory outcomes

Respiratory symptoms were based on the British Medical Research Council respiratory questionnaire and included chronic cough/phlegm and dyspnoea.[21] Spirometry was done in a standing position without nose clips with at least three manoeuvres performed.[20] The results were screened by a numerical quality-check algorithm, developed according to European Respiratory Society recommendations following the criteria used in the BRONCUS trial,[22] and the flow-volume and volume-time loops were visually inspected independently by two trained assessors (KBHL, PY). Only data that satisfied all the criteria in both numerical check and visual inspection were included. To minimise over-diagnosis of COPD in the elderly,[23] we defined COPD as $FEV_1/FVC <$ lower limit of normal (LLN), using prediction equations for Chinese populations.[24] To

Table 1 Characteristics of 8216 Chinese adults aged ≥50 years, according to self-reported dust and gas/fume exposure.

	No exposure	Any dust or gas/fume	*p*
n (row %)	3853 (46.9)	4363 (53.1)	
Sex; *n* (%)			
Men	1021 (26.5)	1216 (27.9)	
Women	2832 (73.5)	3147 (72.1)	0.163
Age (years); mean (SD)	61.9 (7.0)	61.9 (6.6)	0.686
Educational level; *n* (%)			
Primary or below	1318 (34.2)	2286 (52.4)	
Junior middle	1077 (28.0)	1087 (24.9)	
Senior middle or above	1458 (37.8)	990 (22.7)	<0.001
Longest held occupation; *n* (%)			
Farming/forestry/fishing	196 (5.1)	801 (18.4)	
Elementary process plant/construction	1074 (27.9)	2376 (54.5)	
Managerial/administrative/secretarial	889 (23.1)	279 (6.4)	
Professional/technical	684 (17.8)	531 (12.2)	
Sales/customer service	564 (14.6)	177 (4.1)	
Protective service	68 (1.8)	15 (0.3)	
Other	378 (9.8)	184 (4.2)	<0.001
Years employed in the longest-held occupation; mean (SD)	26.1 (9.9)	27.8 (9.9)	0.856
Smoking history and exposure; *n* (%)			
Never	3191 (82.8)	3457 (79.2)	
Ever, <10 pack years	93 (2.4)	148 (3.4)	
Ever, 10–29 pack years	277 (7.2)	311 (7.1)	
Ever, ≥30 pack years	292 (7.6)	447 (10.3)	<0.001
Passive smoking exposure; *n* (%)			
<2 years of 40 h per week	1780 (46.2)	1878 (43.0)	
2–5 years of 40 h per week	892 (23.2)	1061 (24.3)	
>5 years of 40 h per week	1181 (30.7)	1424 (32.6)	0.016
Exposure to indoor air pollution; *n* (%)			
No	2288 (59.4)	2622 (60.1)	
Yes	1565 (40.6)	1741 (39.9)	0.510
Prior TB; *n* (%)			
No	2877 (74.7)	3355 (76.9)	
Yes	976 (25.3)	1008 (23.1)	0.019

assess the robustness of our findings, and for comparability with some previous studies, analyses were repeated by redefining COPD as $FEV_1/FVC < 0.70$. Because dust exposure has been shown to be associated with restrictive lung function impairment,[25] participants with restrictive abnormality, defined as $FEV_1/FVC \geq$ LLN and FVC < LLN[26] were removed in a sensitivity analysis.

Covariates

Participants were classified as never and ever smokers, and exposure was quantified by pack years as described previously.[27] The total hours of passive smoking exposure at home and at work since age 18 years were calculated, then categorised into three levels (<2, 2–5, and>5 years of 40 h/week).[20] As indoor air pollution has been shown to be a risk factor of COPD,[28] we included a binary variable (no, yes) to evaluate the exposure. The participants were considered as being exposed if they had ever used solid fuel (coal, charcoal or wood) for heating or cooking without ventilation or their residence (current or previous) had been smoky during winter. We also assessed the presence of prior tuberculosis (TB) (self-report and/or evidence suggestive of inactive TB on chest X-ray) (no, yes).[27] We used educational attainment (primary or below, junior middle, and senior middle or above) as a proxy for socioeconomic status as it is a good indicator of childhood and working conditions in China.

Statistical analysis

Logistic regression models were built, from which odds ratios (OR) with 95% CIs were computed. Potential confounders considered were age (continuous), sex, educational level, occupational groups (low risk/high risk), pack years (never, <10, 10–29, ≥30 pack years), passive smoking, exposure to indoor air pollution, and prior TB. Potential joint effects between occupational exposure and smoking were assessed by the presence of departure from multiplicativity and additivity. In the former, model fit (adjusted for the confounders above except pack years which was entered as a continuous variable) was compared with and without the interaction term (high composite index × smoking [never, ever]) using likelihood ratio test, whereas in the latter, three measures of additive interaction (relative excess risk due to interaction [RERI], attributable proportion due to interaction [AP], and synergy index [S]) were calculated according to Andersson *et al.*,[29] where in the absence of interaction, both RERI and AP = 0 and $S = 1$. Population attributable fraction for different exposures and outcomes was calculated using two methods: firstly by the formula[2]: *[proportion of cases exposed × (OR −1)]/OR*; and secondly by the command *aflogit* in Stata (version 10.1; StataCorp, College Station, TX), which adjusts for confounders.

Results

Of the 20431 participants enrolled, 18787 had complete information on relevant variables. Application of the quality assurance in spirometry data resulted in the inclusion of 8216 participants (5979 [72.8%] women; mean age 61.1 ± 6.7 years; 2237 men; mean age 64.1 ± 6.3 years) for analyses in this report. Participants included were similar to those excluded in terms of smoking history, occupational exposure, prevalence of chronic respiratory symptoms and prior TB (Table S1 in additional material). Exposure to any dust or gas/fume was reported by 4363 (53.1%; 95% CI 52.0%, 54.2%), similar in men (54.4%) and women (52.6%). Table 1 shows the demographic characteristics of the participants according to their exposure. Participants who were exposed were less highly educated and had higher exposure to smoking and passive smoking, but were less likely to have prior TB than the non-exposed participants. Not surprisingly, a higher prevalence of exposure was observed among participants engaged in agriculture and elementary process plant/construction work.

The prevalence of dust exposure was 46.6% (95% CI 45.4%, 47.7%; $n = 3362$) and that of gas/fume was 37.0% (95% CI 35.8%, 38.2%; $n = 2266$). About half of the exposed participants reported mild exposure to dust (52.4%) or gas/fume (49.7%). Overall, men were more likely to be exposed with greater intensity and duration than women. As a result, a higher proportion of men had high cumulative exposure of dust and gas/fume than women (dust: 29.0% *vs.* 22.8% and gas/fume: 33.0% *vs.* 25.4%, respectively), as well as high cumulative composite exposure index (33.0% *vs.* 25.6%) (Table 2).

Despite the sex difference in exposure, there was no evidence that the relationship between exposure and respiratory outcomes varied with sex (p for interaction for chronic cough/phlegm, dyspnoea and COPD = 0.508, 0.572 and 0.491, respectively). Results are therefore presented for both sexes together. There was a dose-dependent relationship between dust and gas/fume exposure and chronic respiratory symptoms (Table 3). The adjusted ORs for high exposure to any dust or gas/fume (cumulative composite index) were 1.57 (95% CI 1.13, 2.17) and 1.39 (1.20, 1.60) respectively for chronic cough/phlegm and dyspnoea after adjusting for age, sex, educational level, occupational group, pack years, passive smoking, exposure to indoor air pollution, and prior TB.

Dust and gas/fume exposure was associated with higher risk of COPD (Table 3). The adjusted ORs at the highest exposure category were 1.36 (95% CI 0.99, 1.88) for dust, 1.48 (1.03, 2.12) for gas/fume, and 1.41 (1.06, 1.87) for any of the two. There was an excess risk for COPD among never smokers who had a high occupational exposure index compared to their non-exposed counterpart (adjusted OR = 1.29; 95% CI 0.92, 1.81), although this was not statistically significant. The likelihood ratio test showed no evidence of multiplicative interaction by smoking on the association between occupational exposure and COPD ($p = 0.433$) and all three measures of interaction (RERI [0.74; 95% CI -0.51, 1.98], AP [0.26; −0.08, 0.59], and S [1.65; 0.78, 3.50]) suggested there was no evidence of additive interaction.

Table 4 shows that except dyspnoea, the magnitude of population attributable fraction calculated by both methods was similar, although the value derived by *aflogit* (adjusted for confounders) was always slightly attenuated. The population attributable fraction for COPD with any dust or gas/fume exposure was 10.4% (95% CI -0.9%, 19.5%), while that with high composite exposure was 5.5% (1.2%, 8.8%), which were slightly greater than the two individual component indices (4.0% [0.2%, 7.1%] and 4.3% [0.4%, 7.1%], respectively for high dust and gas/fume exposure indices).

As a sensitivity analysis, we re-estimated the models by replacing the LLN-based definition of COPD with $FEV_1/FVC < 0.70$. The adjusted OR for COPD associated with any dust or gas/fume exposure was 1.17 (95% CI 0.99, 1.39), and the

Table 2 Intensity, duration and type of dust and gas/fume exposure, according to sex.

	Total	Men	Women	*p*
No exposure; *n*	3853	1021	2832	
Any dust; *n*	3362	929	2433	
Dust exposure intensity; *n* (%)				
Mild	1763	476 (51.2)	1287 (52.9)	
Moderate	1222	334 (36.0)	888 (36.5)	
Severe	377	119 (12.8)	258 (10.6)	0.190
Dust exposure duration; *n* (%)				
<26 years (median)	1641	408 (43.9)	1233 (50.7)	
≥26 years	1721	521 (56.1)	1200 (49.3)	<0.001
Dust exposure index; *n* (%)				
Low	866	224 (24.1)	642 (26.4)	
Medium	1672	436 (46.9)	1236 (50.8)	
High	824	269 (29.0)	555 (22.8)	0.001
Any gas/fume; *n*	2266	682	1584	
Gas/fume exposure intensity; *n* (%)				
Mild	1126	338 (49.6)	788 (49.8)	
Moderate	839	227 (33.3)	612 (38.6)	
Severe	301	117 (17.2)	184 (11.6)	0.001
Gas/fume exposure duration; *n* (%)				
<25 years (median)	1036	276 (40.5)	760 (48.0)	
≥25 years	1230	406 (59.5)	824 (52.0)	0.001
Gas/fume exposure index; *n* (%)				
Low	523	157 (23.0)	366 (23.1)	
Medium	1116	300 (44.0)	816 (51.5)	
High	627	225 (33.0)	402 (25.4)	<0.001
Any dust or gas/fume; *n*	4363	1216	3147	
Composite exposure index; *n* (%)				
Low	1029	269 (22.1)	760 (24.1)	
Medium	2128	546 (44.9)	1582 (50.3)	
High	1206	401 (33.0)	805 (25.6)	<0.001

Table 3 Adjusted[a] odds ratios for self-reported respiratory symptoms and spirometry-defined COPD[b] according to dust and gas/fume exposure indices.

	n	Chronic cough/phlegm		Dyspnoea		COPD	
		n (%)	Adjusted or (95% CI)	*n* (%)	Adjusted or (95% CI)	*n* (%)	Adjusted or (95% CI)
No exposure	3853	128 (3.3)	1.00 (Reference)	1272 (33.0)	1.00 (Reference)	191 (5.0)	1.00 (Reference)
Dust exposure index							
Low	866	22 (2.5)	0.77 (0.48, 1.23)	310 (35.8)	1.13 (0.96, 1.33)	40 (4.6)	0.92 (0.64, 1.32)
Medium	1672	61 (3.7)	1.09 (0.78, 1.52)	640 (38.3)	1.25 (1.10, 1.42)	105 (6.3)	1.20 (0.92, 1.57)
High	824	50 (6.1)	1.76 (1.23, 2.53)	338 (41.0)	1.40 (1.19, 1.64)	60 (7.3)	1.36 (0.99, 1.88)
p for trend			0.003		<0.001		0.035
Gas/fume exposure index							
Low	523	15 (2.9)	0.86 (0.49, 1.51)	188 (36.0)	1.15 (0.95, 1.41)	33 (6.3)	1.41 (0.95, 2.10)
Medium	1116	47 (4.2)	1.29 (0.89, 1.87)	414 (37.1)	1.19 (1.02, 1.38)	62 (5.6)	1.13 (0.82, 1.56)
High	627	33 (5.3)	1.56 (1.02, 2.37)	248 (39.6)	1.31 (1.09, 1.58)	44 (7.0)	1.48 (1.03, 2.12)
P for trend			0.022		0.002		0.052
Composite exposure index							
Low	1029	25 (2.4)	0.72 (0.46, 1.12)	361 (35.1)	1.09 (0.94, 1.27)	58 (5.6)	1.15 (0.84, 1.57)
Medium	2128	80 (3.8)	1.11 (0.82, 1.51)	804 (37.8)	1.22 (1.09, 1.38)	125 (5.9)	1.14 (0.89, 1.47)
High	1206	66 (5.5)	1.57 (1.13, 2.17)	492 (40.8)	1.39 (1.20, 1.60)	87 (7.2)	1.41 (1.06, 1.87)
P for trend			0.003		<0.001		0.019

[a] Adjustments for age, sex, educational level, occupational group, pack years of smoking, passive smoking, exposure to indoor air pollution, and prior TB.
[b] COPD defined as $FEV_1/FVC < LLN$.

population attributable fraction was 8.4% (−0.8%, 16.1%), both being diminished in magnitude and of borderline significance. The corresponding values for high composite exposure index were 1.40 (1.11, 1.76) and 5.6% (2.0%, 8.5%), respectively. The removal of those who had restrictive lung function impairment from the sample did not alter the association between occupational exposure and COPD (adjusted OR for high composite exposure index = 1.41; 95% CI 1.07, 1.87).

Discussion

These findings confirm an association between occupational dust and gas/fume exposures and increased risk of chronic respiratory symptoms and COPD in China, with the population attributable fraction being similar to that derived from the Western populations.[2,3] We did not find evidence of additive or multiplicative interaction between occupational exposure and smoking.

Table 4 Population attributable fraction for respiratory outcomes due to dust and gas/fume exposure.

Exposure	Outcome	OR	Population attributable fraction; % (95% CI)	
			Calculated by formula from Ref. 3,[a]	Calculated by *aflogit*[b]
Any dust	Chronic cough/phlegm	1.16	7.2 (−6.5, 17.6)	6.9 (−6.2, 18.4)
	Dyspnoea	1.25	10.0 (5.5, 14.1)	6.7 (3.4, 9.8)
	COPD	1.17	7.4 (−3.8, 16.3)	6.9 (−3.6, 16.3)
High dust exposure index	Chronic cough/phlegm	1.76	8.3 (3.6, 11.6)	8.0 (2.2, 13.4)
	Dyspnoea	1.40	3.8 (2.1, 5.2)	2.5 (1.3, 3.7)
	COPD	1.36	4.0 (0.2, 7.1)	3.8 (−0.5, 7.8)
Any gas/fume	Chronic cough/phlegm	1.26	8.8 (−3.2, 17.6)	8.5 (−3.3, 18.9)
	Dyspnoea	1.21	7.0 (2.7, 10.8)	4.7 (1.7, 7.6)
	COPD	1.29	9.5 (0.1, 16.8)	8.9 (−0.4, 17.3)
High gas/fume exposure index	Chronic cough/phlegm	1.56	5.3 (0.3, 8.5)	5.1 (−0.4, 10.3)
	Dyspnoea	1.31	2.8 (1.0, 4.3)	1.9 (0.6, 3.1)
	COPD	1.48	4.3 (0.4, 7.1)	4.0 (−0.1, 8.0)
Any dust or gas/fume	Chronic cough/phlegm	1.14	6.9 (−7.7, 18.2)	6.7 (−7.2, 18.8)
	Dyspnoea	1.23	10.6 (5.8, 15.0)	7.0 (3.6, 10.3)
	COPD	1.22	10.4 (−0.9, 19.5)	9.7 (−1.1, 19.4)
High composite exposure index	Chronic cough/phlegm	1.57	8.0 (2.6, 11.9)	7.7 (1.6, 13.4)
	Dyspnoea	1.39	4.7 (2.9, 6.3)	3.1 (1.8, 4.5)
	COPD	1.41	5.5 (1.2, 8.8)	5.1 (0.7, 9.4)

[a] Calculated by the formula: *proportion of cases exposed* $\times$ *(OR − 1)]/OR* (Reference 3).
[b] Calculated by the Stata command *aflogit*, adjusting for age, sex, educational level, occupational group, pack years of smoking, passive smoking, exposure to indoor air pollution, and prior TB.

Our results are consistent with previous Chinese studies, which suggested occupational exposure is related to poor respiratory outcomes. A case–control study reported an increased risk of COPD (OR = 5.80; 95% CI 3.13, 10.76) among workers exposed to high level of coke oven emissions.[5] Another case–control study nested in the population-based Shanghai Women's Health Study[15] identified a higher risk of chronic bronchitis in a number of occupational groups, most notably raw fibre material processing (OR = 2.55; 95% CI 1.27, 5.10), tea production (OR = 2.52; 1.20, 5.30), and production of movie, camera and office equipment (OR = 2.12; 1.39, 3.25). The Burden of Obstructive Lung Disease study[16] collected information on occupational exposure to dust in its study sites, including Guangzhou, and found high levels of occupational exposure in sites where the prevalence of COPD in men was high but no further analysis was performed. The Chinese Epidemiological Survey of COPD,[17] a national COPD prevalence survey in seven provinces/cities in China, reported an adjusted OR for COPD of 1.20 (95% CI 1.04, 1.39) among those who had exposure to dust or gas/fume compared to the non-exposed, which is in keeping with the present study (1.18 [0.99, 1.39]) when the same definition of COPD (FEV_1/FVC <0.70) was used. The smaller magnitude in risk in the Chinese Epidemiological Survey of COPD and the present study using same definition is likely to be due to the lower overall exposure level in the general population, and also the different definition of COPD.

Our estimation of population attributable fraction for COPD, 10.4%, is close to the median of estimates from previous studies (15%).[2,3] The figures for dyspnoea (10.0% for dust and 7.0% for gas/fume) were not dissimilar from that calculated[2] based on the data from a community sample in Beijing[13] (11% and 6%, respectively). Given that the effect size for dust exposure in our study is similar to that reported in the literature, the slightly lower population attributable fraction is likely to be due to the lower prevalence of cumulative high level exposure in our general population sample of older individuals, who were survivors.

We detected a non-significant association between occupational exposure and COPD among never smokers. Conflicting results have been reported by others. Zhou and colleagues found that while there was no overall excess risk in Chinese non-smokers (OR = 1.03; 95% CI 0.79, 1.35), occupational exposure did increase risk of mild COPD (1.40; 0.90, 2.18).[20] Whilst the European Community Respiratory Health Survey (ECRHS) found no association between chronic bronchitis and dust and fume exposure in never smokers,[30] a significant association between dust exposure and spirometry-defined COPD (OR = 1.8; 95% CI 1.1, 2.9) was reported in a sample of never-smoking patients in the United States referred to a pulmonary function laboratory. Pre-existing chronic lung conditions could have explained the reported high risk in this patient sample.[31]

We found no evidence of interaction between smoking and exposure to dust or gas/fume in relation to COPD, which is in keeping with the ECRHS study.[30] However, a synergistic effect of coke oven emissions and smoking on COPD was suggested, with a 58-fold increase in COPD risk in the joint exposure group compared with non-exposed non-smokers in China.[5] Similar but smaller additive interaction was found in two studies based on population samples in the United States (6-fold[32] and 14-fold,[33] respectively). A study in male Italian workers identified a multiplicative interaction,[34] where both incidence and prevalence of COPD were higher in workers exposed to both smoking and dust/fume/vapour. The lack of evidence suggesting effect modification by smoking in our study could be a result of the relatively smaller proportions of heavy smokers (especially in women) and high level of cumulative exposure compared with other study samples, leading to insufficient power in detecting interaction. This could also have explained the borderline non-significance observed in the RERI, AP, and S indices.

There are several strengths in the present study. It is one of the largest population-based studies in China addressing the relationship between occupational exposure and COPD showing no sex modification, using both objective spirometry and self-reported respiratory symptoms. The comprehensive baseline measures allowed us to adjust for a number of important potential confounding factors, including smoking, passive smoking, exposure to indoor air pollution, and prior TB.

Our study has some limitations. Misclassification of exposure and outcome (respiratory symptoms) might arise due to the use of self-reports. We argue, however, that objective assessment of occupational exposure and the development of job exposure matrix are neither practical nor feasible in a large scale study like ours. One might question the validity of the use of longest-held job in the estimation of exposure level. However, under the planned economy several decades ago, urban Chinese were allocated to state-owned enterprises and had lifetime secured employment, while rural dwellers were tied to their native villages (state-controlled people's communes). As a result of this rigidity in the labour market, most Chinese remained in the same occupation for a long time, and workplace environment in China remained largely unaltered until the late 1980s[35] when the effects of market economy, labour market reform and the privatisation or demise of most state-owned enterprises became apparent. Furthermore, the mean number of years in the longest-held job was 30.6 ± 10.2 years for men and 25.7 ± 9.5 years for women, accounting for about three-quarters of the working life of these participants by the time they retired at 55 (men) and 50 (women) (assuming they started work at 16). Therefore, the use of longest-held job can reflect the cumulative occupational exposure in this population. It is possible that bias arose from differential reporting of occupational exposure due to the presence of COPD or respiratory symptoms (*recall* bias). In this regard, the participants and the interviewers were unaware of the research question and spirometry findings were blinded at the time of interview. In addition, information on occupational exposure was obtained early in the interview, followed by a large number of questions concerning personal lifestyle before the subset on respiratory symptoms. Therefore it is unlikely for the participants with COPD to have exaggerated their exposure intensity and duration. On the other hand, misclassification would be more likely to be caused by under-reporting of symptoms, which would lead to an under-estimation of the association. Ambient air pollution, which we did not adjust for, might have confounded the association, but air pollution has only become a major issue in China in more recent years, whereas our participants would have already been exposed to high levels of dust and gas/fume for many years, which would be the major contributor of the association.

The overall quality of spirometry was fairly poor, leading to the exclusion of a large proportion of participants from analysis. This is due to the difficulty in obtaining satisfactory data from these older participants, the majority of whom had never performed spirometry and many had difficulty in comprehending and complying with the instructions by the technicians. However, the stringent quality-check ensured only valid and reliable data were included. Also, the baseline characteristics (including occupational exposure and respiratory symptoms) of those whose spirometry data were or were not included were similar. Likewise, reported occupational exposure and respiratory symptoms were very similar in both the included and excluded groups, and a sensitivity analysis using all participants with complete information ($n = 18787$) showed consistency in the association between respiratory symptoms and occupational exposure (see Table S2 in additional material). Thus it is unlikely that the exclusion of unsatisfactory tests has resulted in a systematic bias that has otherwise altered the conclusion. Although post-bronchodilator spirometry is mandated by current clinical guidelines for the diagnosis of COPD,[36] it was not performed in the current study due to practicality issues ($n = 20431$). As such, there is a risk of overdiagnosing COPD, partly due to the misclassification of individuals with asthma. However, the prevalence of self-reported physician-diagnosed asthma in our sample (1.7%) was the same as that reported in a population survey (1.8% in those $>$45 years),[37] suggesting it is unlikely that asthmatic individuals have been misclassified.

Our participants are unlikely to be entirely representative of the older population in China. Over-representation of women in our sample could have limited the generalisability of results, but we have found no sex difference in the associations. Nevertheless, our findings are relevant to many developing countries, where the burden of COPD in the non-smoking population, predominantly women, is growing.[1] While the cross-sectional setting does not allow the inference of temporal sequence, given the long duration of occupational history and the progressive nature of COPD,[38] we asked for past history of exposure, which was likely to have preceded disease. Hence, our study could be interpreted as a case—control study nested in a cross-sectional survey.

Conclusions

Our results show a significant association between past dust and gas/fume exposure in the workplace and COPD with dose response relationship in a large sample of older Chinese adults. We have found that, separate from smoking, a significant burden of COPD in this population may be attributable to occupational exposure. It is therefore necessary for governments of developing countries to take immediate actions to limit such exposure as far as possible. Awareness of occupational exposure as a contributor to COPD is important for clinicians. Although no interaction was observed between smoking and occupational exposure, the high risk among the exposed smokers warrants the provision of smoking cessation services in occupational settings.

Conflict of interest statement

The Guangzhou Biobank Cohort Study was funded by The University of Hong Kong Foundation for Educational Development and Research, Hong Kong; the Guangzhou Public Health Bureau and the Guangzhou Science and Technology Bureau, Guangzhou, China; and the University of Birmingham, UK. The sponsors had no involvement in the study design, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. The authors have no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.rmed.2012.05.009.

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