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China Kadoorie Biobank (CKB) Collaborative Group

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Prevalence and correlates of airflow obstruction in ~317 000 never-smokers in China

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ABSTRACT In China, the burden of chronic obstructive disease (COPD) is high in never-smokers but little is known about its causes in this group.

We analysed data on 287 000 female and 30 000 male never-smokers aged 30–79 years from 10 regions in China, who participated in the China Kadoorie Biobank baseline survey (2004–2008). Prevalence of airflow obstruction (AFO) (pre-bronchodilator forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) <0.7 and below the lower limit of normal (LLN)) was estimated, by age and region. Cross-sectional associations of AFO (FEV₁/FVC <0.7), adjusted for confounding, were examined.

AFO prevalence defined as FEV₁/FVC <0.7 was 4.0% in females and 5.1% in males (mean ages 51 and 54 years, respectively). AFO prevalence defined as FEV₁/FVC <LLN was 5.9% and 5.2%, respectively. In females, odds ratios of AFO were positively associated with lower household income (1.63, 95% CI 1.55–1.72 for lowest *versus* highest income groups), prior tuberculosis (2.36, 95% CI 2.06–2.71), less education (1.17, 95% CI 1.12–1.23 for no schooling *versus* college education), rural region and lower body mass index. AFO was positively associated with cooking with coal but not with other sources of household air pollution. Associations were similar for males.

AFO is prevalent in Chinese never-smokers, particularly among those with low socioeconomic status or prior tuberculosis, and in rural males.



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Airflow obstruction is prevalent in Chinese never-smokers and particularly associated with low socioeconomic status <http://ow.ly/sG481>

For editorial comments see page 8.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide with a particularly high burden of disease in some low- and middle-income countries, including China [1]. This high burden of disease may be partly due to greater exposure to risk factors but also to disparities in diagnosis and treatment, particularly between urban and rural regions [2]. ~70% of Chinese males smoke regularly [3] and cigarette smoking has long been established as the primary cause of COPD [4]. However, more recently, it has become apparent that the burden of disease due to COPD in never-smokers is much higher than previously recognised [5]. Household air pollution (HAP) has been proposed as an important risk factor for COPD in never-smokers, along with ambient air pollution, passive smoking, occupational exposure to air pollutants and factors associated with low socioeconomic status [2, 5]. A few observational studies in the Chinese population have attempted to investigate the association of non-smoking-related risk factors with COPD [6–14], but the results have been inconsistent, particularly for HAP. This might be due to small studies confined to a single area, the use of spirometrically defined and doctor-diagnosed COPD in different studies, or incomplete control for confounding by smoking. We report here the results of a detailed cross-sectional analysis, within ~317 000 male and female never-smokers who took part in the baseline survey of the China Kadoorie Biobank (CKB) study. We estimate the prevalence of air flow obstruction (AFO) defined by pre-bronchodilator spirometry (*i.e.* consistent with COPD and/or asthma) and examine the associations of AFO with socioeconomic and lifestyle variables and with exposures to HAP.

Methods

Baseline survey

The study design and procedures and the detailed baseline questionnaire have been described previously [15, 16]. The CKB baseline survey took place in five urban and five rural regions, selected to cover a diverse range of exposures and disease profiles (online supplementary fig. S1). One of these, Sichuan, was chosen because of the known high prevalence of COPD [17]. In each region, temporary assessment clinics were set up within local residential centres during 2004–2008. All residents aged 35–74 years were invited to participate and ~30% responded to this invitation [3]. A few volunteers outside the defined age range also enrolled, hence the age range of the studied population was 30–79 years. At the baseline survey, an interviewer-administered laptop-based questionnaire was used to collect detailed sociodemographic and lifestyle data including level of education, annual household income, smoking history, history of exposure to HAP, passive smoking exposure and medical history (including self-reports of previous physician diagnoses of asthma, emphysema/bronchitis and tuberculosis) [16]. A range of physical measurements were also made by trained staff using standard procedures, including lung function, height and body weight. Body mass index (BMI) was calculated as weight divided by height squared.

The CKB study was approved by the ethics committees of the University of Oxford (Oxford, UK) and the Chinese Center for Disease Control and Prevention (CDC), and by each of the ten regional CDCs. Written, informed consent was obtained from all participants.

Exposures to HAP and passive smoking

Possible exposure to HAP in each participant's current house and in up to two previous houses was assessed in the baseline questionnaire including: time period lived in the house; cooking frequency and kitchen ventilation, and winter heating; and the types of fuel used for cooking (gas, electricity, wood, coal or unspecified other) and for winter heating (gas, electricity, central heating, wood, coal or unspecified other). Variables were derived to describe the different combinations of fuel types used for heating or cooking in different houses (these did not take into account the temporal order of using different fuels). For example, those cooking with wood in all houses were classified as cooking only with wood; those cooking with electricity in the present house but wood in their previous two houses were included in the mixed wood and gas/electricity category. Cooking with gas or electricity, or heating with electricity or central heating or gas in the current or all homes were included in the baseline category of the relevant variable and considered as low exposure to HAP. Further variables were developed to describe length of exposure to HAP from burning coal or wood (table S1).

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TABLE 1 Sociodemographic characteristics and body mass index (BMI) in never smokers

Variable	Females	Males
Subjects n	287 153	30 246
Living in a rural area	158 421 (55.2)	13 466 (44.5)
Age at baseline years mean \pm SD	51.1 \pm 10.4	54.4 \pm 11.9
30–39	47 094 (16.4)	4600 (15.2)
40–49	90 588 (31.5)	7011 (23.2)
50–59	89 483 (31.2)	7798 (25.8)
60–69	45 462 (15.8)	7185 (23.8)
70–79	14 526 (5.1)	3652 (12.1)
Highest education completed		
No formal school	71 909 (25.0)	2213 (7.3)
Primary school	89 066 (31.0)	8032 (26.6)
Middle/high school	113 128 (39.4)	15 121 (50.0)
College/university	13 050 (4.5)	4880 (16.1)
Household income yuan per year		
<4999	27 099 (9.4)	2538 (8.4)
5000–9999	55 563 (19.3)	4511 (14.9)
10 000–19 999	84 947 (29.6)	8595 (28.4)
20 000–34 999	71 037 (24.7)	8075 (26.7)
\geq 35 000	48 507 (16.9)	6527 (21.6)
BMI kg·m⁻²	23.8 \pm 3.4	23.9 \pm 3.2
<18.5	11 872 (4.1)	1089 (3.6)
18.5–<22.5	94 185 (32.8)	9296 (30.7)
22.5–<25	82 687 (28.8)	8942 (29.6)
25–<30	84 546 (29.4)	9853 (32.6)
\geq 30	13 862 (4.8)	1066 (3.5)

Data are presented as n (%) or mean \pm SD, unless otherwise stated.

The baseline questionnaire assessed passive smoking through questions on residing with a smoker, and current frequency and number of hours per week of exposure at home, work or in public places. Participants were classified as never being exposed to passive smoking if they had never lived with a smoker and were currently never or only occasionally exposed. Passive smokers were categorised by duration of residing with a smoker (\geq 20 or <20 years) and weekly exposure time for (\geq 20 or <20 h per week). These cut-points were chosen to include reasonable proportions of participants in each category.

Spirometry and definition of AFO

Measurements of forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were made using a handheld Micro Spirometer (MS01; CareFusion UK Ltd, Basingstoke, UK) by trained technicians following recommended procedures [18]. Participants performed some practice exhalations, after which the results of two successful manoeuvres (as judged by the technician) were recorded. The highest FEV₁ and FVC values, not necessarily from the same manoeuvre, were used in the analyses. As no bronchodilator was administered, participants were categorised by AFO status using modified Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (GOLD grade \geq 1: FEV₁/FVC <0.7; GOLD \geq 2: FEV₁/FVC <0.7 and FEV₁/predicted FEV₁ for age, sex and height <0.8) [19] or the lower limit of normal (LLN) definition. Predicted values for lung function were obtained using the Global Lung Function Initiative (GLI) 2012 equations, assigning participants from Harbin, Qingdao, Gansu and Henan (fig. S1) to the North East Asian ethnic group, and the others to the South East Asian group [20].

Statistical analysis

Of the 210 222 males and 302 669 females who attended the baseline survey, 202 males and 194 females had a recorded FEV₁/FVC >1 and so were excluded from further analyses. The present study was conducted on 30 246 (14.4%) of the males and 287 153 (94.9%) of the females (total 317 399 participants) who had never smoked, *i.e.* reported never smoking at baseline or in the past and had smoked <100 cigarettes or equivalent in their lifetime.

All analyses were conducted separately for males and females. Age-standardised prevalences of AFO (directly standardised to the male or female population age structure in the study) were calculated for each region. Crude prevalence of AFO in strata of years of education, annual household income, BMI, tuberculosis prior to baseline, and exposure to HAP and passive smoking was calculated. Associations of these variables with AFO were further investigated by calculating crude and adjusted odds ratios (for AFO *versus* no AFO according to the same AFO definition) using logistic regression. Age group (30–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69 and 70–79 years), region, annual household income and level of

education were all included as categorical variables in the multivariable adjusted logistic regression models together with the region by age group interaction. For variables with more than two groups, odds ratios and their 95% confidence intervals were floated so that comparisons could be made between all categories [21]. All analyses were conducted in SAS 9.3 (SAS Institute, Cary, NC, USA).

Results

Female never-smokers were slightly younger than male never-smokers (51.1 *versus* 54.4 years) (table 1). Relatively more females than males (55.2% *versus* 44.5%) lived in a rural region, had received no formal schooling (25.0% *versus* 7.3%) or lived in households with annual household incomes <10 000 yuan (28.8% *versus* 23.3%).

Cooking and heating practices differed between the sexes and also changed over time, with trends differing between urban and rural regions. Only 29.5% of rural males cooked regularly in their present home, compared with 52.4% of urban males and 91.9% of females overall. (figs 1 and 2, and table 2). There was also a trend towards increased use of relatively clean fuels for cooking and heating in urban regions, but in rural regions, the use of coal for cooking by females increased at the expense of wood in more recent homes. Among households using clean fuel for cooking, most used gas rather than electricity (figs 1 and 2) but there was almost no use of gas for winter heating. Because males who cooked regularly were mostly from urban regions, 30.3% of males who had cooked regularly in all homes had always used gas/electricity, compared with only 14.8% of females. Of those who had heated all homes in winter, 7.2% and 11.2% of females and males, respectively, had always used gas/electricity/central heating (table 2). Different fuel types were also associated with different levels of ventilation: 23.8%, 24.6% and 19.4% of females who cooked with wood had chimneys or extractors on all of their stoves in their current and former two houses respectively, compared with only 13.8%, 9.5% and 9.6% who cooked with coal.

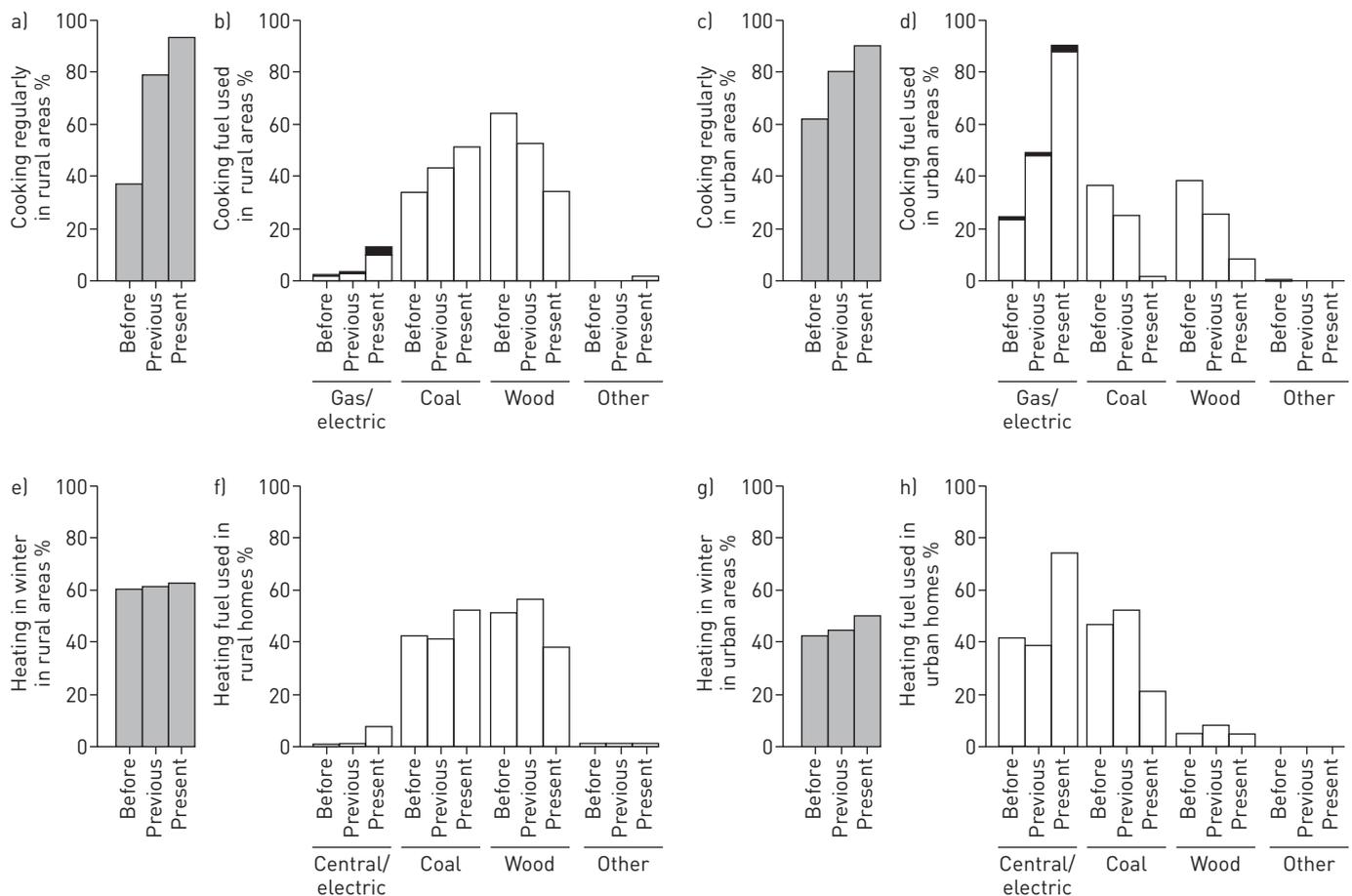


FIGURE 1 Percentages of female never-smokers who a, c) cooked regularly or e, g) used winter heating in their present, previous and before-previous houses, and type of fuel used by those b, d) cooking regularly or f, h) heating their houses, in a, b, e, f) rural and c, d, g, h) urban areas. b, d) For cooking with gas/ electricity, the bar was divided into those cooking with electricity (black) and those cooking with gas (white). f, h) Very few participants used gas for heating any house (0.16% of females heated their current home with gas and considerably fewer used gas for heating previous homes) so the bar was not divided.

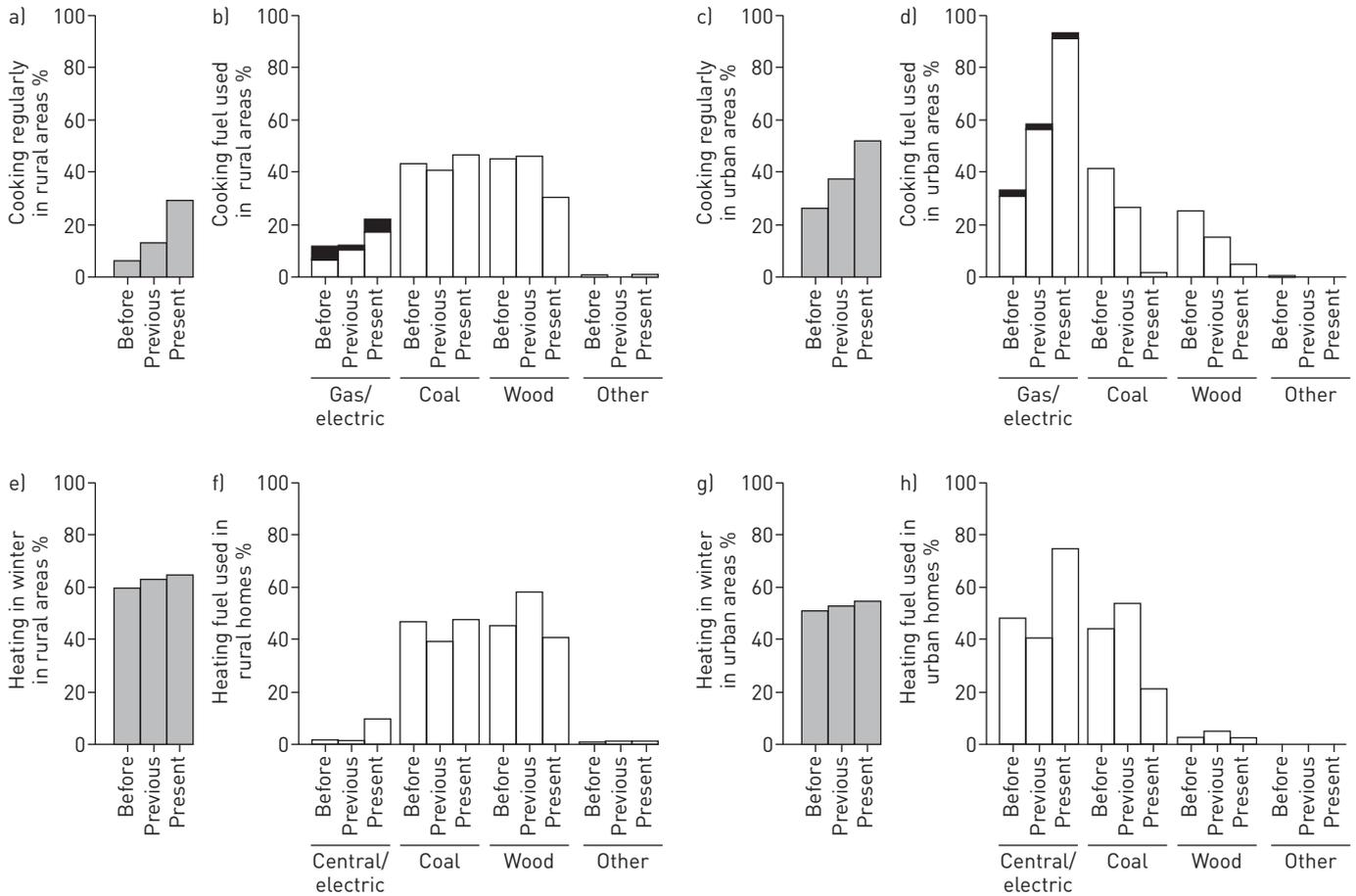


FIGURE 2 Percentages of male never-smokers who a, c) cooked regularly or e, g) used winter heating in their present, previous and before-previous houses, and type of fuel used by those b, d) cooking regularly or f, h) heating their homes, in a, b, e, f) rural and c, d, g, h) urban areas. b, d) For cooking with gas/ electricity, the bar was divided into those cooking with electricity (black) and those cooking with gas (white). f, h) Very few participants used gas for heating any house (0.26% of males heated their current home with gas and considerably fewer used gas for heating previous homes) so the bar was not divided.

Overall, 4.0% of females and 5.1% of males had AFO (GOLD ≥ 1), among whom 78.7% and 83.9%, respectively, were classified as GOLD ≥ 2 (table 3). Prevalence according to the GOLD ≥ 1 definition was lower than that according to the LLN definition up to ages 55–59 years in males and to 65–69 years in females (fig. 3). Overall prevalence according to the LLN definition was slightly higher: 5.9% in females and 5.2% in males. Age-adjusted prevalence of AFO varied greatly across the 10 regions (fig. 4), with Sichuan having particularly high prevalence (GOLD ≥ 1 : 11.9% of females and 16.9% of males). AFO prevalence was higher in rural regions for all age groups. 7.6% and 3.1% of rural and urban males, respectively, had AFO (GOLD ≥ 1), compared with 4.5% and 3.4% of rural and urban females.

With the exception of associations with age, odds ratios for associations of AFO with baseline variables were similar across AFO definitions (data not shown). Therefore, only the associations of AFO defined as GOLD ≥ 1 are reported in detail here (tables 4 and 5). Higher crude prevalence and odds ratio of AFO were associated with living in a rural area, older age, less education, lower household income, lower BMI and a doctor diagnosis of tuberculosis prior to the baseline. Higher crude prevalence of AFO was also associated with cooking or heating with coal or wood (table 5) and with duration of exposure to HAP (table S1). However AFO prevalence was inversely associated with exposure to passive smoking. Crude associations tended to be stronger in males than females (tables 4 and 5).

In the adjusted model, the associations in males were no longer consistently stronger than in females (tables 4 and 5). AFO remained positively associated with rural region, less education, lower household income, lower BMI and a doctor diagnosis of tuberculosis prior to baseline. After adjustment for age and region (and their interaction) alone, there were strong inverse associations of AFO prevalence with both income and education (table S2), but after mutual adjustment, the association with education was much weaker. Only females with no formal schooling had a higher odds ratio than the reference category (1.17,

TABLE 2 History of exposure to household air pollution in never smokers

Variable	Females	Males
Subjects n	287 153	30 246
Passive smoker		
No exposure	41 437 (14.4)	9746 (32.2)
Lived with smoker ≥ 20 years and current exposure ≥ 20 h per week	52 249 (18.2)	11 048 (36.5)
Lived with smoker ≥ 20 years and current exposure < 20 h per week	161 361 (56.2)	8169 (27.0)
Lived with smoker < 20 years	32 106 (11.2)	1283 (4.2)
Cook regularly in current home	263 943 (91.9)	12 761 (42.2)
Current exposure to smoke from cooking [#]		
Gas or electricity	124 113 (47.0)	9096 (71.3)
Coal	77 860 (29.5)	1985 (15.6)
Wood	59 836 (22.7)	1628 (12.8)
Other fuel	2134 (0.8)	52 (0.4)
Cook regularly in all homes	127 773 (44.5)	4407 (14.6)
History of exposure to smoke from cooking [†]		
Gas/electricity only	18 869 (14.8)	1336 (30.3)
Coal only	16 303 (12.8)	286 (6.5)
Coal and gas/electricity	26 461 (20.7)	1295 (29.4)
Wood only	24 616 (19.3)	560 (12.7)
Wood and gas/electricity	23 502 (18.4)	647 (14.7)
Coal and wood	13 551 (10.6)	169 (3.8)
Coal, wood and gas/electricity	3415 (2.7)	99 (2.2)
Combinations involving other fuel types	1056 (0.8)	15 (0.3)
Heat current house in winter	163 540 (57.0)	17 978 (59.4)
Current exposure to smoke from heating [‡]		
Gas/electricity/central heating	56 005 (34.2)	7768 (43.2)
Coal	65 321 (39.9)	6234 (34.7)
Wood	41 025 (25.1)	3897 (21.7)
Other fuel	1189 (0.7)	79 (0.4)
Heated all homes in winter	141 678 (49.3)	16 078 (53.2)
History of exposure to smoke from heating [§]		
Gas/electricity/central heating only	10 185 (7.2)	1807 (11.2)
Coal only	39 689 (28.0)	4386 (27.3)
Coal and gas/electricity/central heating	26 349 (18.6)	4242 (26.4)
Wood only	36 815 (26.0)	3509 (21.8)
Wood and gas/electricity/central heating	3519 (2.5)	404 (2.5)
Coal and wood	22 910 (16.2)	1530 (9.5)
Coal, wood and gas/electricity/central heating	975 (0.7)	111 (0.7)
Combinations involving other fuel types	1236 (0.9)	89 (0.6)

Data are presented as n (%), unless otherwise stated. [#]: among those who cook regularly in their current home; [†]: among those who cooked regularly in all homes; [‡]: among those who heat their current house in winter; [§]: among those who have heated all homes in winter.

95% CI 1.12–1.23; $p=0.038$) (table 4). Adjusting for education and household income had little effect on the large between-region variation in AFO (data not shown).

Associations of AFO with HAP exposures were considerably attenuated by adjusting for confounding (and, in particular, by adjusting for region; data not shown). After adjustment, AFO was also still positively

TABLE 3 Spirometry and prevalence of airflow obstruction and other respiratory disease in never-smokers

Variable	Females	Males
Subjects n	287 153	30 246
FEV₁ L	2.00 \pm 0.48	2.62 \pm 0.68
FEV₁ % of predicted[#]	88.4 \pm 16.9	86.8 \pm 17.6
FVC L	2.36 \pm 0.54	3.06 \pm 0.75
FVC % of predicted[#]	86.2 \pm 16.6	82.4 \pm 16.7
FEV₁/FVC	85.0 \pm 7.8	85.5 \pm 8.9
FEV₁/FVC < 0.7[†]	11 473 (4.0)	1540 (5.1)
FEV₁/FVC < 0.7 and FEV₁ $< 80\%$ predicted[‡]	9033 (3.1)	1292 (4.3)
FEV₁/FVC $< LLN$[#]	16 906 (5.9)	1585 (5.2)
Ever diagnosed with chronic bronchitis/emphysema	6064 (2.1)	962 (3.2)
Ever diagnosed with asthma	1477 (0.5)	242 (0.8)
Ever diagnosed with tuberculosis	3134 (1.1)	780 (2.6)

Data are presented as mean \pm SD or n (%), unless otherwise stated. FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; LLN: lower limit of normal. [#]: predicted values of FEV₁, FVC and the LLN of FEV₁/FVC were calculated with Global Lung Function Initiative reference equations; [†]: Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) grade ≥ 1 ; [‡]: GOLD ≥ 2 .

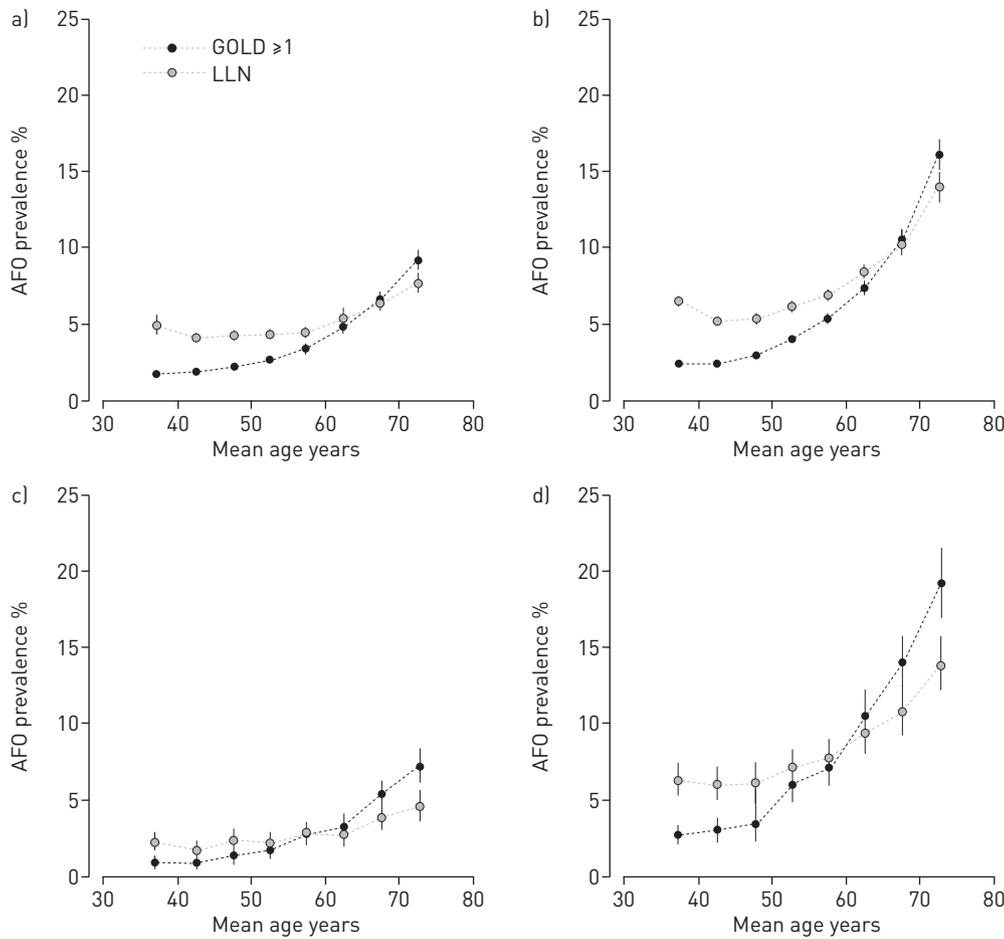


FIGURE 3 Prevalence of airflow obstruction (AFO) in a, c) urban and b, d) rural a, b) females and c, d) males plotted against mean baseline age (age groups: 30–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69 and 70–79 years). AFO was defined according to modified Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade ≥ 1 (forced expiratory volume in 1s/forced vital capacity < 0.7) and according to the lower limit of normal (LLN). Vertical lines represent 95% confidence intervals. Prevalences are directly adjusted to the region structure of the male or female baseline population.

associated with some HAP exposures, but only in females (table 5): cooking with coal in the current house (OR 1.10, 95% CI 1.04–1.17; $p=0.014$ for contrast with baseline category), always cooking with coal (OR 1.29, 95% CI 1.14–1.47; $p=0.0048$) and heating the current house in winter with unspecified other fuels (OR 2.65, 95% CI 2.15–3.27; $p<0.0001$). There were no clear trends of adjusted odds ratio with years of exposure to coal or wood smoke (table S1). AFO was still inversely associated with exposure to passive smoking (table 5).

Discussion

In this extremely large cross-sectional study of nonsmoking correlates of AFO, confounding by smoking was completely controlled for by confining the analysis to never-smokers. Since this was a cross-sectional study, we cannot be certain of the direction of causality of any of the observed associations. AFO prevalence (GOLD ≥ 1) in this nonsmoking population was 4.0% in females and 5.1% in males. Because of the relatively young age of this study population (mean females 51 years and males 54 years), the overall prevalence according to the LLN definition was slightly higher (5.9% in females and 5.2% in males). AFO prevalence varied considerably across regions, in part due to study design. However, the between-region variation in AFO was not accounted for by differences in age, education or household income. This suggests that there are other important risk factors for AFO in never-smokers than have been considered in the present study. In particular, the high AFO prevalence in rural males suggests that some of these exposures must differ between males and females (e.g. occupational exposures). AFO was also positively associated with older age, lower household income and education level, lower BMI and a history of tuberculosis. AFO was only associated with certain exposures related to HAP.

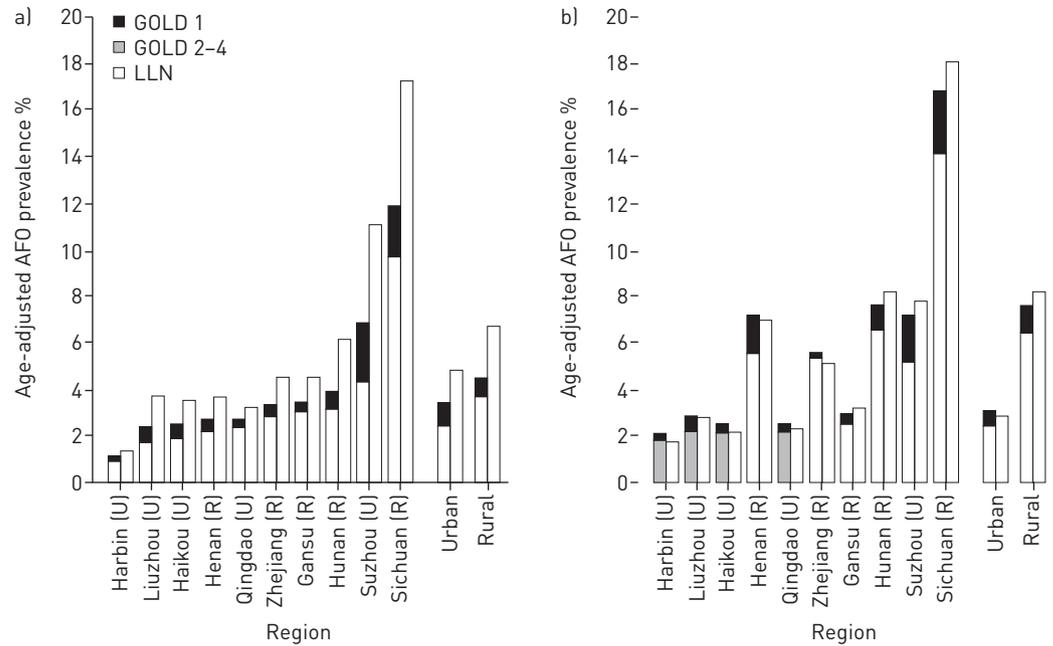


FIGURE 4 Prevalence of airflow obstruction (AFO) in a) female and b) male never-smokers by region. AFO was defined according to modified Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (GOLD grade ≥ 1 : forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) < 0.7 ; GOLD ≥ 2 : FEV₁/FVC < 0.7 and FEV₁/predicted FEV₁ for age, sex and height < 0.8) and according to the lower limit of normal (LLN). Prevalences are directly adjusted to the 5-year age structure of the female or male never-smoker population at baseline. U: urban; R: rural.

COPD has been associated with lower socioeconomic status in several studies in China and elsewhere [5, 6, 12], which may be due to various factors (*e.g.* low birth weight, exposure to respiratory infections, previous tuberculosis, poor nutrition, occupational exposures, and exposures to HAP and ambient air pollution) [22]. The stronger association with household income in our study, compared with education, suggests that exposures related to low socioeconomic status that occur in adulthood may be as important as early-life exposures for COPD development. We also found independent associations of AFO with previous tuberculosis and with low BMI. Tuberculous infection would generally have preceded AFO as the mean age of tuberculosis diagnosis in the CKB was 29 years. Studies in China and developing countries have found pulmonary tuberculosis to be amongst the strongest determinants of COPD [5, 8] and tuberculosis is still prevalent in some rural areas of China [23]. The combined burden of COPD and TB in these areas could therefore be a serious public health concern. The cross-sectional nature of the present study means that we cannot distinguish poor nutrition as a cause of COPD from weight loss resulting from COPD. Other cross-sectional studies in China found a positive association of AFO with passive smoking [6, 11] but we found a statistically significant inverse association. As only 14% of males participating in the CKB were never-smokers the females who reported that they had always lived with never-smokers may have been atypical in some way, so we hypothesise that this association might have been affected by some residual confounding.

HAP caused by burning of solid fuel in poorly ventilated conditions is an established risk factor for respiratory disease, including COPD [24]. In China, burning solid fuels inside has been associated with increased levels of HAP [25]. HAP was ranked fifth as a cause of morbidity and mortality in China in 2010 (smoking third and particulate matter ambient air pollution fourth), and was the largest contributor to morbidity and mortality from chronic respiratory diseases [1]. However, apart from studies in Xuanwei province, known for its very high lung cancer and respiratory disease mortality rates due to burning coal in open fires [14, 17], results from only a few relatively small observational studies of associations of COPD and solid-fuel burning in Chinese never-smokers have been reported in the English-language literature [6, 9, 13]. Two of these examined associations of COPD and HAP in specific regions, one finding weak evidence of a positive association with winter heating using coal (but not with cooking with coal or kitchen ventilation) [13] and one finding a strong positive association with use of biomass fuels for cooking, substantiated by measured levels of HAP [9]. However, in that study using biomass fuel was collinear with urban/rural location and so the relatively large odds ratio may have been inflated by residual confounding. The third study ($\sim 12\,000$ never-smokers in urban and rural communities of seven regions, surveyed 2002–2004) [6] found that using biomass for cooking, coal for heating (together with a trend with years of exposure) and poor ventilation in the kitchen

TABLE 4 Odds ratio for airflow obstruction by certain baseline characteristics in never-smokers

Variable	Females [#]			Males [†]		
	Subjects n (%)	Crude OR (95% CI) [*]	Adjusted OR (95% CI) ^{*‡}	Subjects n (%)	Crude OR (95% CI) [*]	Adjusted OR (95% CI) ^{*‡}
Region type						
Urban	4377 (3.4)	1.00	1.00	516 (3.1)	1.00	1.00
Rural	7096 (4.5)	1.33 (1.28–1.38)	1.17 (1.12–1.22)	1024 (7.6)	2.59 (2.33–2.89)	2.15 (1.89–2.45)
Age at baseline years						
30–39	1113 (2.4)	1.00 (0.94–1.06)	1.00 (0.94–1.07)	94 (2.0)	1.00 (0.82–1.23)	1.00 (0.81–1.24)
40–49	2143 (2.4)	1.00 (0.96–1.04)	1.08 (1.03–1.13)	143 (2.0)	1.00 (0.85–1.18)	1.09 (0.92–1.30)
50–59	3480 (3.9)	1.67 (1.62–1.73)	1.65 (1.59–1.71)	339 (4.3)	2.18 (1.95–2.43)	2.05 (1.83–2.30)
60–69	3110 (6.8)	3.03 (2.93–3.15)	3.00 (2.88–3.11)	560 (7.8)	4.05 (3.72–4.42)	3.81 (3.49–4.16)
70–79	1627 (11.2)	5.21 (4.95–5.49)	5.15 (4.86–5.46)	404 (11.1)	5.96 (5.38–6.61)	6.28 (5.59–7.06)
Education						
No formal school	4624 (6.4)	3.86 (3.75–3.98)	1.17 (1.12–1.23)	251 (11.3)	4.50 (3.94–5.13)	1.16 (0.99–1.36)
Primary school	3888 (4.4)	2.57 (2.48–2.65)	0.94 (0.91–0.97)	696 (8.7)	3.33 (3.09–3.60)	1.01 (0.93–1.11)
Middle/high school	2733 (2.4)	1.39 (1.34–1.45)	0.88 (0.84–0.92)	458 (3.0)	1.10 (1.00–1.20)	0.78 (0.70–0.87)
College/university	228 (1.7)	1.00 (0.88–1.14)	1.00 (0.87–1.15)	135 (2.8)	1.00 (0.84–1.19)	1.00 (0.82–1.23)
Household income yuan per year						
<4999	2351 (8.7)	3.01 (2.88–3.14)	1.63 (1.55–1.72)	323 (12.7)	5.06 (4.50–5.68)	2.10 (1.82–2.42)
5000–9999	2621 (4.7)	1.57 (1.51–1.63)	1.38 (1.33–1.45)	307 (6.8)	2.53 (2.25–2.84)	1.88 (1.65–2.14)
10 000–19 999	2993 (3.5)	1.16 (1.11–1.20)	1.21 (1.17–1.26)	459 (5.3)	1.96 (1.78–2.15)	1.71 (1.55–1.88)
20 000–34 999	2023 (2.8)	0.93 (0.89–0.97)	1.01 (0.96–1.06)	268 (3.3)	1.19 (1.05–1.34)	1.20 (1.05–1.37)
≥35 000	1485 (3.1)	1.00 (0.95–1.05)	1.00 (0.94–1.06)	183 (2.8)	1.00 (0.86–1.16)	1.00 (0.84–1.19)
BMI kg·m⁻²						
<18.5	1034 (8.7)	2.51 (2.36–2.68)	2.04 (1.91–2.19)	157 (14.4)	3.57 (3.01–4.23)	2.53 (2.10–3.04)
18.5–<22.5	4338 (4.6)	1.27 (1.23–1.31)	1.25 (1.21–1.29)	643 (6.9)	1.57 (1.45–1.71)	1.29 (1.18–1.40)
22.5–<25	3026 (3.7)	1.00 (0.96–1.04)	1.00 (0.96–1.04)	403 (4.5)	1.00 (0.90–1.11)	1.00 (0.90–1.11)
25–<30	2647 (3.1)	0.85 (0.82–0.88)	0.82 (0.79–0.86)	304 (3.1)	0.67 (0.60–0.76)	0.76 (0.67–0.85)
≥30	428 (3.1)	0.84 (0.76–0.92)	0.81 (0.74–0.90)	33 (3.1)	0.68 (0.48–0.96)	0.89 (0.63–1.28)
Ever diagnosed with TB						
No	11 226 (4.0)	1.00	1.00	1465 (5.0)	1.00	1.00
Yes	247 (7.9)	2.08 (1.82–2.37)	2.36 (2.06–2.71)	75 (9.6)	2.03 (1.59–2.60)	1.81 (1.40–2.34)

All p-values for trend or heterogeneity <0.0001 except for adjusted odds ratios for years of education in males (p=0.0016). BMI: body mass index; TB: tuberculosis. [#]: n=287 153; [†]: n=30 246; ^{*}: for variables with more than two categories, odds ratios and confidence intervals are floated; [‡]: odds ratios for airflow obstruction (Global Initiative for Chronic Obstructive Lung Disease [GOLD] grade ≥1) were adjusted for age, education, household income, region and age by region.

were associated with spirometrically defined COPD. One further study [26] of 14 populations from different countries including China also failed to find any association between COPD and burning wood or coal, either in the study as a whole or within the Chinese population; however, that study included smokers.

Our study is the first that we know of to try to document a detailed exposure history to different fuels over several homes. Although we found strong crude associations of HAP with AFO and evidence of a dose response, these associations were attenuated greatly and were inconsistent after adjustment for region. Some factors associated with burning coal or wood and AFO that acted at the region level might explain the attenuations in these associations. In addition, even after adjustment, the 1268 participants who used another unknown fuel for winter heating, 84% of whom lived in Gansu, had very high odds ratios for AFO (in females OR 2.65, 95% CI 2.15–3.27 (p<0.0001) for contrast with baseline category) (table 5). The result from such a *post hoc* comparison should be interpreted with caution but it suggests that some high-risk heating methods might still occur locally in China, which should be verified in future studies.

Our study illustrates some of the difficulties involved in identifying risks associated with HAP through the use of exposure histories in observational studies. Exposures to coal and wood smoke have changed rapidly over time in China, and therefore there were considerable proportions of participants with mixed exposure histories which were difficult to interpret. In addition, use of coal or wood for cooking or heating fuel may not in themselves be correlated with COPD. Risks associated with specific fuel types are likely to have been modified by kitchen ventilation and probably by further unidentified stove characteristics. In our study, relatively more females who cooked with wood had ventilation associated with all stoves than those cooking with coal. The cooking and heating fuels commonly used were also clearly different between urban and rural regions, and cooking and heating practices may also have differed in further unknown ways. We did not have any measurements of HAP to validate the current exposures obtained from questionnaire responses.

There are several further limitations to our study. First, our prevalence estimates may be inflated compared with those from other studies that have used post-bronchodilator spirometry to estimate COPD prevalence.

TABLE 5 Odds ratio for airflow obstruction by exposures to household air pollution in never smokers

Variable	Females [#]			Males [†]		
	Subjects n (%)	Crude OR [95% CI] [*]	Adjusted OR [95% CI] ^{*,§}	Subjects n (%)	Crude OR [95% CI] [*]	Adjusted OR [95% CI] ^{*,§}
Passive smoking						
No exposure	1714 (4.1)	1.00 (0.95–1.05)	1.00 (0.95–1.05)	554 (5.7)	1.00 (0.92–1.09)	1.00 (0.91–1.10)
Lived with smoker ≥20 years and current exposure ≥20 h per week	1588 (3.0)	0.73 (0.69–0.76)	0.92 (0.88–0.97)	467 (4.2)	0.73 (0.67–0.80)	0.80 (0.72–0.87)
Lived with smoker ≥20 years and current exposure <20 h per week	6809 (4.2)	1.02 (1.00–1.05)	0.83 (0.81–0.85)	459 (5.6)	0.99 (0.90–1.09)	0.83 (0.75–0.92)
Lived with smoker <20 years	1362 (4.2)	1.03 (0.97–1.08)	0.93 (0.88–0.98)	60 (4.7)	0.81 (0.63–1.05)	0.77 (0.58–1.01)
Current exposure to smoking from cooking^f						
Gas/electricity only	4086 (3.3)	1.00 (0.97–1.03)	1 (0.95–1.06)	290 (3.2)	1.00 (0.89–1.12)	1.00 (0.80–1.25)
Coal	3214 (4.1)	1.26 (1.22–1.31)	1.10 (1.04–1.17)	168 (8.5)	2.81 (2.40–3.29)	1.01 (0.80–1.28)
Wood	3203 (5.4)	1.66 (1.60–1.72)	0.91 (0.88–0.95)	191 (11.7)	4.04 (3.47–4.69)	1.04 (0.88–1.22)
Other	35 (1.6)	0.49 (0.35–0.68)	0.68 (0.48–0.96)	5 (9.6)	3.23 (1.28–8.12)	1.85 (0.72–4.72)
History of exposure to smoke from cooking^{##}						
Gas/electricity only	450 (2.4)	1.00 (0.91–1.10)	1.00 (0.89–1.12)	30 (2.2)	1.00 (0.70–1.44)	1.00 (0.66–1.53)
Coal only	718 (4.4)	1.89 (1.75–2.03)	1.29 (1.14–1.47)	28 (9.8)	4.72 (3.20–6.98)	0.91 (0.53–1.55)
Coal and gas/electricity	807 (3.0)	1.29 (1.20–1.38)	1.05 (0.95–1.16)	39 (3.0)	1.35 (0.98–1.86)	1.00 (0.66–1.50)
Wood only	1598 (6.5)	2.84 (2.70–2.99)	0.92 (0.86–0.98)	64 (11.4)	5.62 (4.33–7.29)	1.13 (0.81–1.57)
Wood and gas/electricity	1278 (5.4)	2.35 (2.22–2.49)	0.89 (0.83–0.96)	40 (6.2)	2.87 (2.08–3.95)	1.20 (0.83–1.74)
Coal and wood	842 (6.2)	2.71 (2.53–2.91)	0.97 (0.88–1.07)	28 (16.6)	8.65 (5.76–12.97)	1.18 (0.72–1.92)
Coal, wood and gas/electricity	137 (4.0)	1.71 (1.44–2.03)	0.83 (0.70–0.99)	3 (3.0)	1.36 (0.43–4.29)	0.72 (0.24–2.13)
Other fuel combinations	29 (2.7)	1.16 (0.80–1.67)	0.92 (0.63–1.35)	2 (13.3)	6.70 (1.51–29.68)	2.58 (0.58–11.53)
Current exposure to smoke from heating^{††}						
Gas/electricity/central heating only	1604 (2.9)	1.00 (0.95–1.05)	1.00 (0.91–1.10)	251 (3.2)	1.00 (0.88–1.13)	1.00 (0.78–1.28)
Coal	1858 (2.8)	0.99 (0.95–1.04)	0.93 (0.88–0.99)	300 (4.8)	1.51 (1.35–1.70)	1.07 (0.90–1.27)
Wood	1624 (4.0)	1.40 (1.33–1.47)	1.06 (0.99–1.13)	249 (6.4)	2.04 (1.80–2.32)	1.04 (0.87–1.26)
Other	105 (8.8)	3.29 (2.69–4.01)	2.65 (2.15–3.27)	6 (7.6)	2.46 (1.07–5.66)	2.03 (0.83–4.98)
History of exposure to smoke from heating^{†††}						
Gas/electricity/central heating only	128 (1.3)	1.00 (0.84–1.19)	1.00 (0.79–1.27)	36 (2.0)	1.00 (0.72–1.39)	^{§§}
Coal only	1120 (2.8)	2.28 (2.15–2.42)	0.99 (0.86–1.14)	212 (4.8)	2.50 (2.18–2.87)	^{§§}
Coal and gas/electricity/central heating	437 (1.7)	1.33 (1.21–1.46)	1.02 (0.85–1.22)	117 (2.8)	1.40 (1.16–1.68)	^{§§}
Wood only	1387 (3.8)	3.08 (2.92–3.25)	0.92 (0.85–1.00)	217 (6.2)	3.24 (2.83–3.72)	^{§§}
Wood and gas/electricity/central heating	128 (3.6)	2.97 (2.49–3.54)	1.23 (1.01–1.49)	18 (4.5)	2.29 (1.43–3.68)	^{§§}
Coal and wood	643 (2.8)	2.27 (2.10–2.45)	0.77 (0.71–0.84)	67 (4.4)	2.25 (1.76–2.88)	^{§§}
Coal, wood and gas/electricity/central heating	36 (3.7)	3.01 (2.16–4.20)	1.44 (1.01–2.04)	4 (3.6)	1.84 (0.68–4.99)	^{§§}
Combinations involving other fuel types	114 (9.2)	7.99 (6.59–9.68)	2.95 (2.41–3.60)	6 (6.7)	3.56 (1.55–8.14)	^{§§}

All p-values for heterogeneity of crude odds ratios <0.0001; p<0.0001 for all adjusted odds ratios in females; p>0.05 for all adjusted odds ratios in males except passive smoking (p=0.0046). [#]: n=287 153; [†]: n=30 246; ^{*}: for variables with more than two categories, odds ratios and confidence intervals are floated; [§]: odds ratios for airflow obstruction (Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade ≥ 1) were adjusted for age, education, household income, region and age by region; ^f: amongst those who cook regularly in their current home; ^{##}: among those who have cooked regularly in all homes; ^{††}: among those who heat current their house in winter; ^{†††}: amongst those who have heated all homes in winter; ^{§§}: adjusted model did not converge for history of exposure to smoke from heating in males.

2.3% of never-smokers in the CKB reported a previous doctor diagnosis of chronic bronchitis/emphysema compared, with 0.5% who reported one of asthma. Recent work also suggests that that bronchodilator reversibility does not discriminate reliably between COPD and asthma, and that the proportion of COPD patients exhibiting reversibility may vary (e.g. according to disease severity or the drug used) [27]. Asthma in nonsmokers has some risk factors in common with COPD (e.g. exposure to HAP and to passive smoking) but our study did not confirm these findings for AFO. In contrast to COPD, some other risk factors for asthma have been linked with higher socioeconomic status and living in high income countries [28]. Second, the spirometer used did not produce a spirogram so we could not assess acceptability or reproducibility of blows. Participants were carefully instructed and encouraged to make practice blows and technicians would have rejected expirations with coughs. Incomplete inhalation or early termination of a manoeuvre would have resulted in a reduced FVC and, hence, underestimation of the AFO prevalence. Nondifferential misclassification of AFO would be expected to bias odds ratios for associations towards the null.

Third, we could not explain the very large between-region variation in AFO prevalence, which suggests that some unmeasured variables are important, probably including ambient air pollution, occupational exposures, details of diet and details of childhood infections/exposures. High AFO prevalence in Sichuan may be partially explained by high levels of various types of ambient air pollution that are exacerbated by stable climatic conditions and frequent temperature inversions [29]. Categories of occupation and some dietary frequency variables were included in the baseline questionnaire [3, 16] but these were not detailed enough for inclusion in the present analysis.

In conclusion, there is very large between-region variability in AFO prevalence among never-smokers in the CKB, which highlights the importance of nonsmoking risk factors in the aetiology of AFO. We found low socioeconomic status and prior TB, which are often associated with living in a rural area, to be the strongest correlates of AFO after region, adding to the high burden of COPD in rural areas. In addition, rural males were at increased risk of AFO. Further detailed studies to identify the exact nature of the modifiable and non-modifiable risk factors associated with low socioeconomic status are needed, including the role of low BMI and poor nutrition, and the nature of exposures in rural males (e.g. occupational exposures). The inconsistent associations of AFO with exposures related to burning coal and wood in our study are contrary to the ranking of HAP in China in the 2010 Global Burden of Disease study [1]. This needs to be further investigated in the CKB by further assessment of cooking and heating practices linked to specific fuel types, complemented by measurement of short-term exposures and association with COPD-related morbidity and mortality in longitudinal analyses.

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