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Regional variations in the prevalence and misdiagnosis of air flow obstruction in China: baseline results from a prospective cohort of the China Kadoorie Biobank (CKB)

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ABSTRACT

Background: Despite the great burden of chronic respiratory diseases in China, few large multicentre, spirometry-based studies have examined its prevalence, rate of underdiagnosis regionally or the relevance of socioeconomic and lifestyle factors.

Methods: We analysed data from 512 891 adults in the China Kadoorie Biobank, recruited from 10 diverse regions of China during 2004–2008. Air flow obstruction (AFO) was defined by the lower limit of normal criteria based on spirometry-measured lung function. The prevalence of AFO was analysed by region, age, socioeconomic status, body mass index (BMI) and smoking history and compared with the prevalence of self-reported physician-diagnosed chronic bronchitis or emphysema (CB/E) and its symptoms.

Findings: The prevalence of AFO was 7.3% in men (range 2.5–18.2%) and 6.4% in women (1.5–18.5%). Higher prevalence of AFO was associated with older age ($p<0.0001$), lower income ($p<0.0001$), poor education ($p<0.001$), living in rural regions ($p<0.001$), those who started smoking before the age of 20 years ($p<0.001$) and low BMI ($p<0.001$). Compared with self-reported diagnosis of CB/E, 88.8% of AFO was underdiagnosed; underdiagnosis proportion was highest in 30–39-year olds (96.7%) compared with the 70+ age group (81.1%), in women (90.7%), in urban areas (89.4%), in people earning 5K–10 K ¥ monthly (90.3%) and in those with middle or high school education (92.6%).

Interpretation: In China, the burden of AFO based on spirometry was high and significantly greater than that estimated based on self-reported physician-diagnosed CB/E, especially in rural areas, reflecting major issues with diagnosis of AFO that will impact disease treatment and management.

KEY MESSAGES

- This is the largest population-based multi-centre study of prevalence and socioeconomic and life-styles correlates of air flow obstruction (AFO) representative of adult Chinese population selected from ten diverse regions of China.
- The data suggests up to 10-fold difference in prevalence of AFO between different regions in China for both men and women.
- The result highlights that mis-diagnosis of AFO (>80%) in Chinese population is a major issue requiring immediate attention to improve both appropriate management and prevention programs.

INTRODUCTION

Globally, chronic obstructive pulmonary disease (COPD) is responsible for about three million annual deaths, and for an even greater burden from disability,[1] with particularly high-disease prevalence in low-income and middle-income countries such as China where smoking prevalence is very high among men.[2] In China, over 90% of 1.4 million respiratory-related deaths[3] and 10.4 million disability-adjusted life years[4] are attributed to COPD in adults, with most of the COPD-related deaths occurring at the age of 60 years or older.[4] Among published epidemiological studies conducted in China, there are large unexplained variations in the age-specific rates of COPD between men and women and between different regions, with reported prevalence ranging from 3% to 12% in ages above 40 years.[5–7]

Smoking is a major risk factor for COPD but few women in China smoke (<5%), so this exposure cannot explain the relatively high prevalence of COPD seen in many parts of China.[8] There is also evidence that

exposure to environmental air pollutants particularly coal and wood smoke for cooking and heating, low socioeconomic status and lung infections such as tuberculosis earlier in life may contribute to increased risk of COPD, but the evidence is still extremely limited in China.[5] As well as risk exposures, difference in survey methods and COPD diagnosis methods between different studies could also affect the burden of the disease estimated for different populations. There is good evidence that defining COPD based only on self-reported physician-diagnosis tends to significantly underestimate the true burden, particularly in resource-poor areas where access to healthcare is limited and also possibly due to lack of awareness of their condition.[9] Despite this, most of the previous studies in China tended to use self-reported information rather than spirometry-defined COPD. Consequently, substantial uncertainty remains about the true burden of COPD in the population.

To help fill the gap in knowledge, we analysed the cross-sectional data of the China Kadoorie Biobank (CKB) of over 0.5 million adults from 10 diverse regions of China.[10] The aims of the study were (1) to estimate the prevalence of air flow obstruction (AFO) based on the measured lung function and its variation with socioeconomic and lifestyle factors, (2) to examine the prevalence of self-reported physician-diagnosed chronic bronchitis/emphysema (CB/E), rates of treatment and (3) to assess the proportion of underdiagnosis by comparing the prevalence of AFO based on spirometry with self-reported physician-diagnosed CB/E and any variation with socioeconomic and lifestyle factors.

METHODS

Study design and participants

A detailed description of the study design, survey methods and characteristics of participants for the CKB prospective study is published elsewhere.[8 10] In brief, the baseline survey took place between 2004 and 2008 involving five rural and five urban regions, chosen according to local disease patterns, exposure to certain risk factors, population stability, quality of death and diseases registries, local commitment and capacity. Overall, a total of 512 891 adults (210 222 men and 302 669 women) aged 30–79 were enrolled. All participants gave informed written consent.

Data collection

Laptop-based questionnaire was administered to each participant by trained health workers, who collected detailed information on demographic and socioeconomic status, dietary and other lifestyle factors (eg, smoking, alcohol use), exposure to passive smoking and household air pollution, respiratory symptoms (eg, chronic cough, production of chronic phlegm, breathlessness and severity of breathlessness), medical history of physician-diagnosed respiratory (chronic bronchitis, emphysema, asthma, tuberculosis) and other conditions (eg, stroke, ischaemic heart disease, cancer and diabetes), physical activity, sleeping and mental status and reproductive history (for women) at baseline. A range of physical measurements was taken, including standing and sitting height, weight, bioimpedance, exhaled carbon-monoxide and blood pressure.

Spirometry and diagnostic criteria for AFO

Spirometry was carried out by trained health technicians, using portable handheld 'Micro spirometer' (Micro Medical Limited, Rochester, Kent, England) in accordance with modified American Thoracic Society (ATS)[11] procedures developed by our respiratory team. The spirometer we used during the baseline survey did not display flow volume loops, and hence the acceptability criterion of blows was modified. Participants made some practice blows, after which the results of two successful manoeuvres (as judged by the technician) were recorded for each participant. The larger of the two forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were used for calculating FEV_1/FVC ratio and for further analysis. No bronchodilators were used at the baseline survey. Overall, 202 men and 194 women with an FEV_1/FVC >1 were excluded, leaving 210 020 (99.9%) men and 302 475 (99.9%) women for the present analysis.

For the present analysis, AFO is defined according to the lower limit of normal (LLN) definition as FEV_1/FVC <LLN. Values for the LLN were obtained from the Global Lung Initiative (GLI) reference equations for southeast Asian and northeast Asian population.[12] The prevalence of modified restrictive abnormality, defined as an FEV_1/FVC ≥LLN and FVC<LLN, was also calculated, with LLN estimates also estimated by the GLI reference equations.[12] For comparability with previous published studies, we also report AFO based on the Global Initiative for Obstructive Lung Disease (GOLD) criterion (FEV_1/FVC <0.7), but without postbronchodilator lung function indices.

We defined chronic bronchitis as the presence of cough and phlegm for more than 3 months in the past 12 months. Underdiagnosis was defined as participants with AFO defined by spirometry but not physician-diagnosed CB/E and overdiagnosis was defined as those participants with physician-diagnosed CB/E but not AFO defined by spirometry.

Statistical methods

All analyses were conducted separately for men and women. Baseline demographic characteristics were calculated by rural/urban area, and crude prevalence of AFO was calculated by region and urban/rural area. The prevalence of AFO (directly standardised to the study population male or female 5-year age group structure) was calculated for each region. Further, AFO prevalence for strata of various potential risk factors or correlates within urban and rural areas was calculated (directly standardised to the study population 10-year age group and region structure, as necessary). Similarly,

we also calculated age and region-standardised prevalence of a number of chronic health conditions among those with AFO. Association between participants' characteristics and AFO diagnosis type was carried out using multivariate logistic regression. All statistical analyses were performed using SAS V.9.3.

RESULTS

At baseline, the overall mean age of participants was 52.0 ±10.7 years, 59% were women and 56% were from rural areas (table 1). The proportion of participants having at least 6 years of formal education was higher in urban compared with rural areas and higher in men than in women. The prevalence of ever regular smoking was significantly higher among men than women (74.3% vs 3.2%) and somewhat higher in rural than in urban men (77.7% vs 70.1%). The proportion reporting current use of clean fuel (ie, gas or electricity for cooking) was much higher in urban than in rural areas for men (56.5% vs 7.1%) and women (83.6% vs 12.4%). The mean body mass index (BMI) was lower in rural than in urban areas for men (24.3 vs 22.7 kg/m^2) and women (24.3 vs 23.5 kg/m^2), with approximately 5–6% of rural participants classified as underweight (BMI <18.5 kg/m^2) compared with around 3% of urban participants (table 1).

The lung function indices (FEV_1, FVC and FEV_1/FVC) decreased steeply with increasing age (see online supplementary figures S1–S3) and were lower in rural than urban areas for men and women at all age groups (data not shown). Among women and men, ever smokers had higher FEV_1 until the mid-40s; whereas FVC continued to be higher until the 50s, but then FEV_1 and FVC decreased steeply with increasing age and were lower in ever smokers compared with never smokers.

Overall at baseline, 4.1% reported having chronic cough and phlegm, which was higher in rural than in urban areas for men (7.3% vs 6.2%, p<0.001) and women (2.6% vs 1.8%, p<0.001). Similar rural and urban differences were seen for breathlessness while walking on level ground for men (5.8% vs 3.4%, p<0.001) and women (8.5% vs 4.7%, p<0.001), but the reported prevalence was higher in women (table 2).

The prevalence of AFO (based on LLN) was higher in rural than urban areas for men (9.2% vs 4.8%, p<0.001) and women (7.7% vs 4.8%, p<0.001). Similar patterns were observed when AFO was based on fixed ratio criterion (GOLD grade 1+), and the overall prevalence was slightly lower compared with LLN (FEV_1/FVC) except for those aged >60 years (figure 1, table 3 and see online supplementary table S2). Regardless of the different definitions used, there was a nearly 10-fold variation in the prevalence of AFO across the 10 study regions, with the highest prevalence observed in Sichuan (18.2% vs 18.5%) and lowest in Harbin province (2.5% vs 1.5%) for men and women (figure 1, see online supplementary table S1). Age-adjusted prevalence based on GOLD grade 2+ was lower than LLN (FEV_1/FVC) estimates in rural and urban men and women (figure 1, see online supplementary table S3). Similarly, the prevalence of AFO (adjusted for region) increased sharply among smokers particularly after the age of 50 (figure 2 and see online supplementary table S4). The prevalence of AFO among rural men and women increased significantly with age, exposure to wood or coal smoke while cooking, initiation of smoking at a younger age (under 20 years), ex-smokers who stopped smoking due to ill health and BMI <18.5 kg/m^2, while AFO decreased with higher annual income and education (table 3, see online supplementary tables S2 and S3).

The prevalence of chronic bronchitis was somewhat greater in rural than in urban areas for men (7.3% vs 6.2%) and women (2.6% vs 1.8%). The prevalence of self-reported physician-diagnosed CB/E was lower and approximately the same in the rural and urban areas for men (3.2% vs 2.9%) and women (2.1% vs 2.4%), among whom less than one-third reported currently taking medication for the condition. Around 80% of rural and 71% of urban men who reported a prior diagnosis of CB/E were regular smokers and also reported chronic cough or breathlessness.

In most regions, the prevalence of CB/E was lower than that of AFO diagnosed by spirometry. Of participants with prior physician diagnosis of CB/E, 29.2% and 28.0% had AFO based on LLN and GOLD criteria, respectively (figure 3 and supplementary figure S4). The overall underdiagnosis proportion of AFO was 88.8%, higher in urban than in rural areas (89.4% vs 88.4%) and higher in women compared with men (90.7% vs 86.2%). Similarly, the AFO overdiagnosis proportion was slightly higher in urban than in rural areas (81% vs 62.2%) and higher in women compared with men (73.7% vs 67.7%) (table 4). Of those classified as AFO by spirometry, only 11.2% were correctly diagnosed previously by the physician. The underdiagnosis proportion of AFO was higher in those with lower household income, younger age, having less chronic respiratory symptoms, women, in current regular smokers, but lower in ex-smokers (see online supplementary table S4). There was wide regional variation in the underdiagnosis and overdiagnosis proportion, as well as variation in the treatment for physician-diagnosed CB/E cases (see online supplementary table S1 and figure S5). Sichuan, with the highest prevalence of AFO, had the lowest percentages of overdiagnosed (<40%) AFO. Patterns similar to underdiagnosis were observed for overdiagnosis as well, except it was lower in women. There was also a lack of concordance between self-reported symptom-based chronic bronchitis and spirometry-based AFO (table 3, see online supplementary table S1 and figure 4, see online supplementary figure S6).

The prevalence of self-reported doctor-diagnosed asthma was <1% among men and women, whereas tuberculosis was marginally greater in urban than in rural areas for men (2.6% vs 1.6%) and women (1.5% vs 0.8%). The prevalence of restrictive abnormality was highest among the ex-regular smokers (men vs women:

Table 1 Baseline characteristics of participants by sex and region types (figures in the column are % of total)

Characteristics	Men		Women	
	Rural (%) N=118 837	Urban (%) N=91 220	Rural (%) N=167 727	Urban (%) N=134 711
Height (mean±SD in cm)	164.1±6.3	166.8±6.5	153.2±5.9	155.3±5.9
Age (years)				
30–39	14.5	13.5	18.2	13.1
40–49	27.7	28.8	31.4	30.2
50–59	31.2	29.1	31.2	30.7
60–69	19.8	19.5	15.0	18.8
70–79	6.8	9.1	4.2	7.2
Mean (SE)	52.6 (0.03)	53.1 (0.04)	50.5 (0.02)	52.6 (0.03)
BMI (kg/m^2)				
<18.5	5.7	2.8	5.2	3.2
18.5 to <25	71.5	55.3	64.3	57.9
≥25	22.7	41.8	30.5	38.9
Mean (SE)	22.7 (0.01)	24.3 (0.01)	23.5 (0.01)	24.3 (0.01)
Smoking status				
Never smoker	11.3	18.4	94.4	95.5
Occasional smoker	11.0	11.5	2.0	1.6
Ex-regular smoker	11.8	15.3	0.9	0.8
Current regular smoker	65.9	54.8	2.6	2.1
Pack years*				
<10	19.7	19.3	47.7	51.7
10–20	23.1	26.3	26.5	25.1
>20	57.1	54.5	25.8	23.2
Mean (SE)	26.7 (0.07)	24.8 (0.07)	15.2 (0.2)	13.7 (0.22)
Age started smoking (years)				
<20	34.7	33.1	35.1	21.9
20–24	38.0	36.6	21.4	16.6
25–29	12.5	15.8	12.2	12.4
≥30	14.8	14.6	31.4	49.1
Number of cigarettes smoked daily (or equivalent)				
1–4	7.2	4.7	29.1	24.9
5–14	27.5	30.8	47.2	51.3
15–24	45.1	47.8	20.4	20.7
≥25	20.2	16.7	3.3	3.1
Reason for stopping among ex-smokers				
Physical illness	53.2	45.9	64.1	40.8
Other reason	46.8	54.1	35.9	59.2
Exposure to passive smoking†	73.7	63.0	87.5	83.2
Highest education completed				
No formal education	12.7	4.0	31.7	17.3
Primary school	43.8	19.7	40.4	20.3
Middle or high school	41.8	60.5	27.2	53.3
College or university	1.7	15.9	0.6	9.2
Household income (yuan/year)				
2500–4999	14.3	2.6	15.1	4.1
5000–9999	23.5	8.0	26.1	11.5
10 000–19 999	28.9	27.6	28.9	30.4
≥20 000	33.3	61.7	29.9	54.1
Exposure to cooking fuels‡				
Currently cooks with coal/wood	27.7	5.3	81.0	8.7
Ever cooked with coal/wood	32.7	33.6	92.6	61.0
Currently cooks with gas/electricity	7.1	56.5	12.4	83.6
Respiratory symptoms				
Chronic cough and phlegm	7.3	6.2	2.6	1.8
Breathlessness	5.8	3.4	8.5	4.7

*Restricted to ever regular smokers.
†Defined as never smokers who lived with a smoker or were exposed at work for 1–5 days/week or daily.
‡Restricted to participants who reported cooking daily or weekly.
BMI, body mass index.

Table 2 Participant characteristics relating to AFO, by region and sex (figures are in percentage of total unless stated)

	Men			Women		
	Rural	Urban	Overall	Rural	Urban	Overall
Total	118 837	91 220	210 057	167 727	134 711	302 438
Mean age (years)	52.6	53.1	52.9	50.5	52.6	51.5
AFO GOLD stage I–IV	8.4	4.5	6.7	5.5	3.3	4.4
AFO GOLD stage II–IV	7.0	3.6	5.5	4.6	2.4	3.5
AFO LLN	9.2	4.8	7.3	7.7	4.8	6.3
Classification of severity of AFO (values are % predicted)*						
Mild (FEV_1 ≥80%)	1.4	0.9	1.2	0.9	0.9	1.4
Moderate (50% ≤ FEV_1 ≥80%)	4.2	2.4	3.4	2.9	1.7	4.2
Severe (50% ≤ FEV_1 ≥80%)	2.2	1.0	1.6	1.4	0.6	2.2
Very severe (FEV_1 <80%)	0.7	0.3	0.5	0.3	0.1	0.7
Doctor diagnosed CB/E	3.2	2.9	3.1	2.1	2.4	2.2
Doctor diagnosed CB/E and still on treatment	34.8	28.4	32.1	37.8	27.4	32.7
Doctor diagnosed CB/E and						
AFO GOLD stage I–IV†	40.5	22.8	33.1	31.5	14.3	23.0
AFO GOLD stage II–IV†	39.6	21.7	32.2	30.4	12.9	21.7
AFO LLN†	39.5	22.0	32.3	35.6	16.7	26.3
Under diagnosis	86.1	86.6	86.2	90.3	91.5	90.7
Over diagnosis	60.5	78.0	67.7	64.4	83.3	73.7
Doctor diagnosed asthma	0.4	0.8	0.6	0.3	0.8	0.5
Breathlessness‡	5.8	3.4	4.7	8.5	4.7	6.8
Chronic cough§	6.8	4.5	5.8	3.0	1.8	2.4
Chronic cough and sputum¶	7.3	6.2	6.8	2.6	1.8	2.2
Chronic cough with sputum and						
AFO GOLD stage I–IV**	17.3	9.8	14.4	17.5	8.4	14.1
AFO GOLD stage II–IV**	15.8	8.6	13.1	15.8	7.2	12.7
AFO LLN**	18.9	10.1	15.5	20.8	10.0	16.9

p Value for difference between urban and rural <0.0001 except men: doctor-diagnosed CB/E (p=0.0002); underdiagnosis (p=0.3775) women: underdiagnosis (p=0.0032).
*Based on prebronchodilator FEV_1 in participants with FEV_1/FVC <0.70 according to modified GOLD definition.
†Figures are percentage of different GOLD stages of AFO or LLN based AFO in those with doctor diagnosed CB/E.
‡Becomes short of breath while walking on level ground with healthy people of same age.
§Had cough for at least 3 months in the past 12 months.
¶Cough up sputum in the morning for at least 3 months in the past 12 months.
**Figures are percentage of different GOLD stages of AFO or LLN based AFO in those with chronic cough and sputum.
AFO, air flow obstruction; CB/E, chronic bronchitis/emphysema; FEV_1, forced expiratory volume in 1 s; GOLD, Global Initiative for Obstructive Lung Disease; LLN, lower limit of normal.

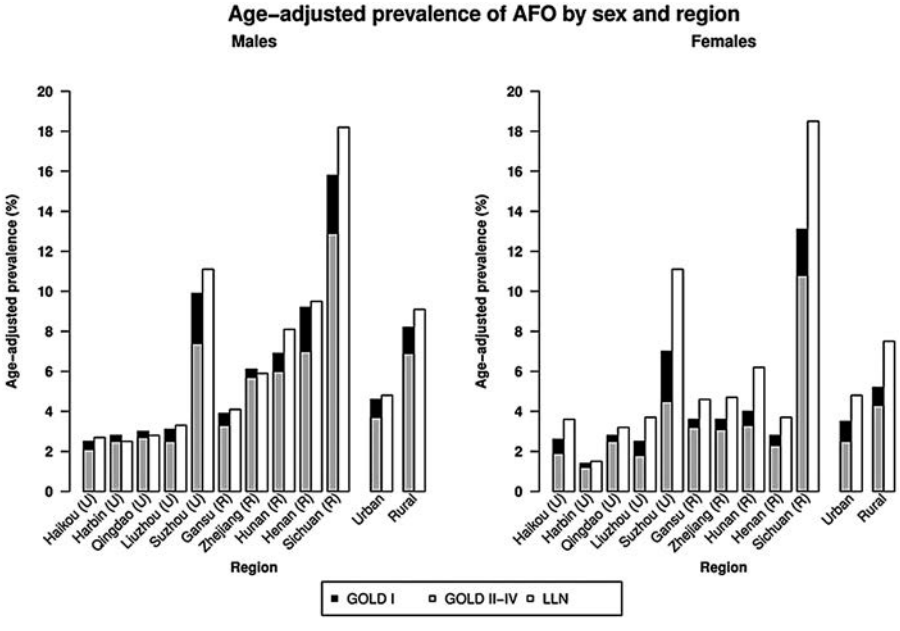

Figure 1 Prevalence of air flow obstruction (age-adjusted) by sex and region.

Table 3 Age and region standardised prevalence of AFO based on LLN definition, by patient characteristics

	Men				Women			
	Rural		Urban		Rural		Urban	
Characteristics	N	Per cent	N	Per cent	N	Per cent	N	Per cent
Overall	118 837	9.2	91 220	4.8	167 727	7.7	134 711	4.8
Age group (%)								
30–39	17 204	6.2	12 361	2.8	30 478	6.9	17 695	4.7
40–49	32 932	6.3	26 230	3.3	52 743	5.6	40 707	4.1
50–59	37 100	8.7	26 571	4.6	52 371	7.1	41 400	4.3
60–69	23 544	12.9	17 766	6.9	25 137	10.4	25 269	5.9
70–79	8057	16.8	8292	9.6	6998	15.3	9640	7.8
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
BMI group (%)								
<18.5	6821	18.0	2599	10.8	8680	12.7	4259	7.7
18.5–24	85 013	9.5	50 482	5.5	107 832	7.8	78 023	5.3
≥25	27 002	5.9	38 139	3.4	51 214	6.0	52 429	3.9
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
Smoking category (%)								
Never	13 486	7.8	16 796	3.5	158 401	7.3	128 716	4.8
Occasional	13 123	7.6	10 487	3.3	3389	7.8	2133	4.2
Ex-regular	13 980	9.7	13 913	5.4	1561	7.8	1083	6.2
Current regular	78 248	9.5	50 024	5.3	4376	9.8	2779	5.8
Ever regular	92 228	9.6	63 937	5.4	5937	9.7	3862	5.7
p for heterogeneity	<0.0001		<0.0001		<0.0001		<0.0001	
Pack years*								
<10	18 211	8.4	12 322	4.2	2831	10.0	1998	5.7
10–19	21 324	8.8	16 786	4.9	1574	11.0	968	5.1
>20	52 693	10.4	34 829	6.0	1532	13.8	896	9.0
p for trend	<0.0001		<0.0001		0.2402		0.1224	
Age started smoking (years)								
<20	32 031	10.5	21 159	6.6	2083	13.6	846	10.1
20–24	35 021	9.7	23 375	5.3	1268	14.0	643	5.4
25–29	11 572	9.1	10 097	5.0	724	8.9	477	5.2
≥30	13 604	8.3	9306	4.5	1862	9.9	1896	5.2
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
Number of cigarettes smoked daily (or equivalent)								
1–4	6605	9.3	2992	4.6	1726	9.6	961	5.5
5–14	25 376	9.2	19 681	5.2	2805	11.3	1982	5.2
15–24	41 631	9.8	30 558	5.5	1212	12.1	801	6.8
≥25	18 616	10.1	10 706	5.8	194	8.9	118	5.5
p for trend	0.0019		0.0227		0.3553		0.1128	
Reason for stopping among ex-smokers								
Physical illness	7442	13.2	6386	8.7	1001	31.8	442	6.7
Other reason	6538	8.8	7527	4.4	560	21.9	641	4.5
p for heterogeneity	<0.0001		<0.0001		<0.0001		0.0918	
Passive smoking†								
No	3546	9.4	6211	4.1	19 783	9.0	21 643	4.8
Yes	9940	7.4	10 585	3.3	138 618	7.1	107 073	4.7
p for heterogeneity	0.0001		0.1538		<0.0001		0.3864	
Highest education completed								
No formal education	15 043	12.0	3606	8.3	53 238	9.9	23 254	5.5
Primary school	52 103	10.0	17 983	5.8	67 726	7.4	27 309	4.8
Middle/high school	49 621	7.6	55 167	4.2	45 690	6.3	71 772	4.4
College/university	2070	7.1	14 464	4.3	1073	5.7	12 376	3.9
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	
Household income (¥)								
2500–4999	17 022	12.9	2413	8.4	25 256	10.5	5461	5.7
5000–9999	27 939	10.9	7319	6.2	43 775	8.5	15 521	5.4
10 000–19 999	34 326	9.2	25 184	5.4	48 506	7.2	40 887	5.2
≥20 000	39 550	6.7	56 304	4.3	50 190	6.1	72 842	4.4
p for trend	<0.0001		<0.0001		<0.0001		<0.0001	

Continued

Table 3 Continued

	Men				Women			
	Rural		Urban		Rural		Urban	
Characteristics	N	Per cent	N	Per cent	N	Per cent	N	Per cent
Currently cooks with coal/wood								
No	85 965	8.7	86 428	4.7	31 872	7.5	122 950	4.8
Yes	32 872	10.1	4792	6.5	135 855	7.6	11 761	5.5
p for heterogeneity	<0.0001		<0.0001		<0.0001		0.7517	
Ever cooked with coal/wood								
No	80 005	8.6	60 591	4.6	12 381	7.8	52 523	4.6
Yes	38 832	10.0	30 629	5.2	155 346	7.6	82 188	5.0
p for heterogeneity	<0.0001		0.0014		<0.0001		0.0160	

*Restricted to ever regular smokers.
†Among never smokers, exposed to others' tobacco smoke regularly at home or work.
BMI, body mass index.

29.5% vs 25.1%), men aged 70–79 years (37.5%) and women aged 30–39 years (28.7%; see online supplementary table S5).

DISCUSSION

This is by far the largest population-based study in China of the prevalence and socioeconomic and lifestyle correlates of AFO in adult Chinese men and women. It involved 10 geographically and socioeconomically diverse regions and showed that there is a wide heterogeneity in the prevalence of AFO by region, age, socioeconomic and lifestyle factors such as smoking and BMI. Overall, self-reported prior diagnosis of CB/E was found to be poorly correlated with AFO based on the measured lung function and less than one-third of those

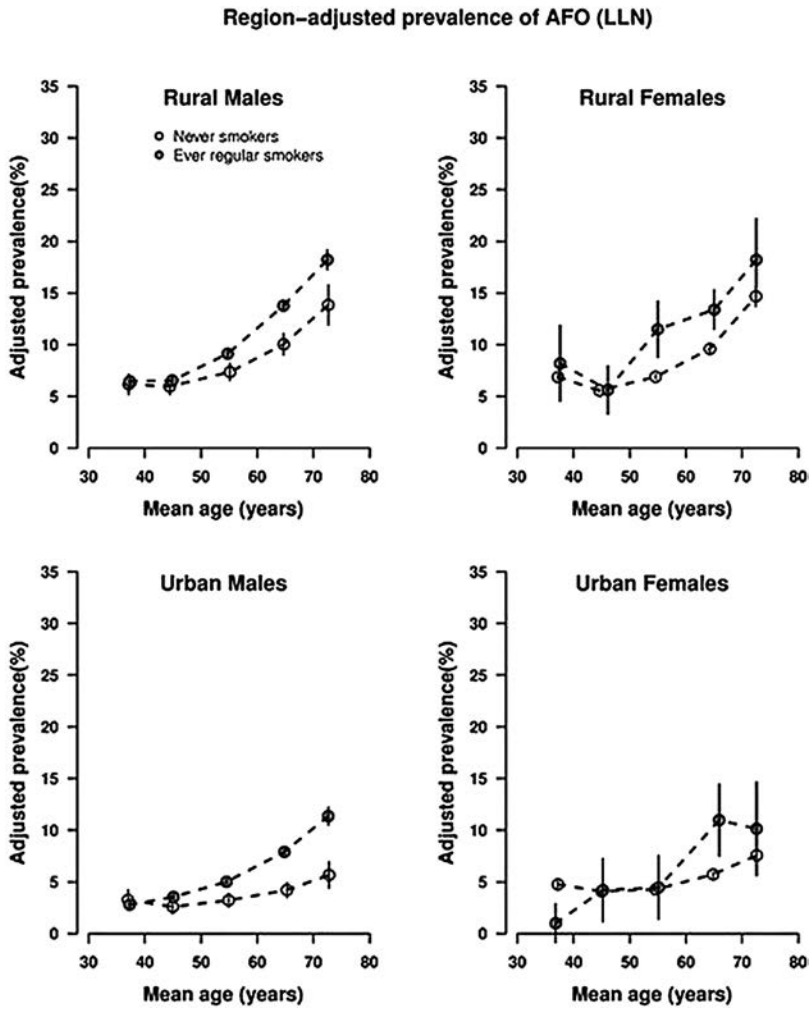

Figure 2 Prevalence of air flow obstruction (region-adjusted) by age group.

Table 4 Age and region-adjusted prevalence, stratified by various baseline variables

	Men (prevalence (%), unless otherwise stated)						Women (prevalence (%) unless otherwise stated)					
Characteristics	**N**	**CB/E**	**AFO**	**UD**	**OD**	**CB/E$_T$**	**N**	**CB/E**	**AFO**	**UD**	**OD**	**CB/E$_T$**
All	210 057	3.1	7.3	86.2	67.7	32.1	302 438	2.2	6.3	90.7	73.7	32.7
Sampling regions												
Rural	118 837	3.2	9.2	86.1	60.5	34.8	167 727	2.1	7.7	90.3	64.4	37.8
Urban	91 220	2.9	4.8	86.6	78.0	28.4	134 711	2.4	4.8	91.5	83.3	27.4
Monthly household income (¥)												
2500–4999	19 435	4.1	10.9	81.2	48.0	36.1	30 717	2.8	8.4	85.3	62.9	35.8
5000–9999	35 258	3.5	8.9	85.9	61.8	33.3	59 296	2.3	7.1	90.7	73.5	36.1
10 000–19 999	59 510	3.0	7.5	86.7	67.4	31.9	89 393	2.2	6.3	90.9	73.9	33.2
≥20 000	95 854	3.0	5.6	84.5	71.3	29.4	123 032	2.3	5.3	89.3	78.1	29.0
Highest education completed												
No formal education	18 649	3.1	10.4	85.5	54.4	32.1	76 492	2.4	7.9	87.5	62.9	35.1
Primary school	70 086	3.2	8.1	84.4	62.6	34.5	95 035	2.2	6.2	89.7	72.3	31.2
Middle/high school	104 788	2.8	6.1	86.9	70.9	28.7	117 462	2.3	5.4	91.8	78.2	29.1
College/university	16 534	3.7	5.9	79.8	69.5	21.3	13 449	2.9	4.9	71.2	60.3	7.5
Smoking status												
Never	30 282	3.3	5.9	83.8	70.3	32.2	287 117	2.1	5.9	91.2	76.2	31.6
Occasional	23 610	3.1	5.7	88.1	75.4	27.6	5522	2.7	10.2	90.1	59.6	39.5
Ex-regular	27 893	5.6	7.8	73.9	61.7	38.6	2644	6.1	14.7	77.7	40.1	43.4
Current regular	128 272	2.5	7.7	89.6	67.7	27.7	7155	2.3	12.9	92.9	59.5	30.7
Body mass index (kg/m^2)												
<18.5	9420	6.0	14.9	77.5	45.8	39.2	12 939	4.4	10.5	83.4	59.9	36.4
18.5 to <25	135 495	2.9	7.8	87.1	66.4	31.7	185 855	2.1	6.7	91.2	72.1	32.7
≥25	65 141	3.0	4.8	86.4	78.3	28.6	103 643	2.2	5.1	92.0	80.8	31.7
Age group (years)												
30–39	29 565	1.1	4.7	96.0	81.8	19.7	48 173	1.0	5.9	96.8	80.5	22.7
40–49	59 162	1.4	5.0	93.9	78.9	21.0	93 450	1.4	4.9	94.8	81.0	25.0
50–59	63 671	2.7	6.9	88.6	71.9	28.9	93 771	2.4	5.9	90.0	75.8	32.2
60–69	41 310	5.6	10.3	79.8	63.5	35.2	50 406	3.8	8.4	85.5	68.8	37.4
70–79	16 349	7.5	13.7	78.3	59.1	41.1	16 638	4.7	12.0	86.0	65.4	40.7
Respiratory symptoms												
None	188 303	2.1	6.3	92.1	74.6	24.6	277 510	1.5	5.8	94.6	77.4	27.1
Cough or breathlessness	19 287	10.1	13.1	72.5	59.6	38.2	22 717	8.5	11.0	77.4	69.2	38.5
Cough and breathlessness	2467	26.1	27.6	54.6	50.7	54.4	2211	26.1	20.5	53.7	59.5	52.6

AFO, air flow obstruction; CB/E, chronic bronchitis and/or emphysema; CB/E$_T$, participants currently under treatment for CB/E; OD, overdiagnosis; UD, underdiagnosis.

with physician diagnosis were receiving treatment at the time of the survey. The estimated underdiagnosis and overdiagnosis proportions were high in rural and urban areas.

Several studies from China have estimated COPD prevalence in adult populations, but the results have not been consistent, with the reported prevalence between 3% and 12%.[5–7] In our study, the overall weighted prevalence of AFO based on GOLD 1+ definition for ages 40–79 was 6% (ranging from 2% in Harbin to 14% in Sichuan), much lower than that reported by Buist *et al*[7] for China (11.4%) and many other countries such as the USA (19.6%), Australia (19.2%), Turkey (10.1%), Austria (26.1%), Iceland (17.8%) and Poland (22.1%). Although the study by Buist *et al*[7] measured postbronchodilator lung function, the sample sizes were much smaller (473–893 in each country) than ours (>0.5 million) and the majority of them were from one region or city in each of the countries and thus, could not be nationally representative, particularly in a country with large heterogeneity such as China. Despite this, the large difference in the prevalence of AFO between CKB population and previous studies of Western and Chinese populations is likely to be largely real, for the CKB participants were much younger, with only 6.4% aged ≥70 years compared with 10–25% participants in other studies.[5] The huge variation in the reported prevalence from different countries and even in different or same regions of a country could be accounted for by several factors, including data acquisition methods, quality control of spirometry measurements, types of sampling population (such as exposure to environmental pollutants, age, previous history of diseases, smoking history and family history, dietary patterns and physical activity) as well as the diagnostic criteria used (eg, GOLD, ERS/ATS criteria used to define COPD).[13 14]

Our study confirms the previous observations[5] of large heterogeneity in the prevalence of AFO across different

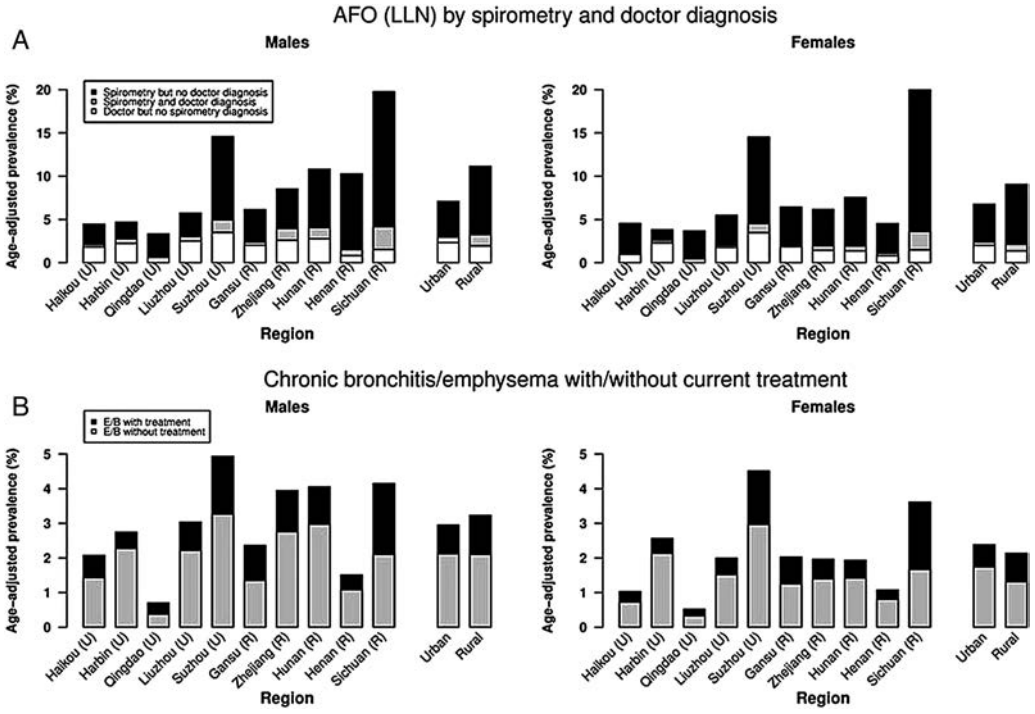

Figure 3 Prevalence of air flow obstruction (age-adjusted) by (A) lower limit of normal of forced expiratory ratio versus self-reported doctor diagnosis and (B) self-reported doctor diagnosis with/without current treatment.

regions of China, with very high prevalence in the Sichuan region for men and women. We did not compare the nutrient intake and physical activities across different regions in this paper, but hypothesise that it is highly unlikely that lifestyle factors could completely explain the substantial heterogeneity observed across different regions. Most of the rural participants were farmers and there were no major differences in the dietary patterns or smoking habit across different regions. Sichuan, 1 of the 10 regions with the

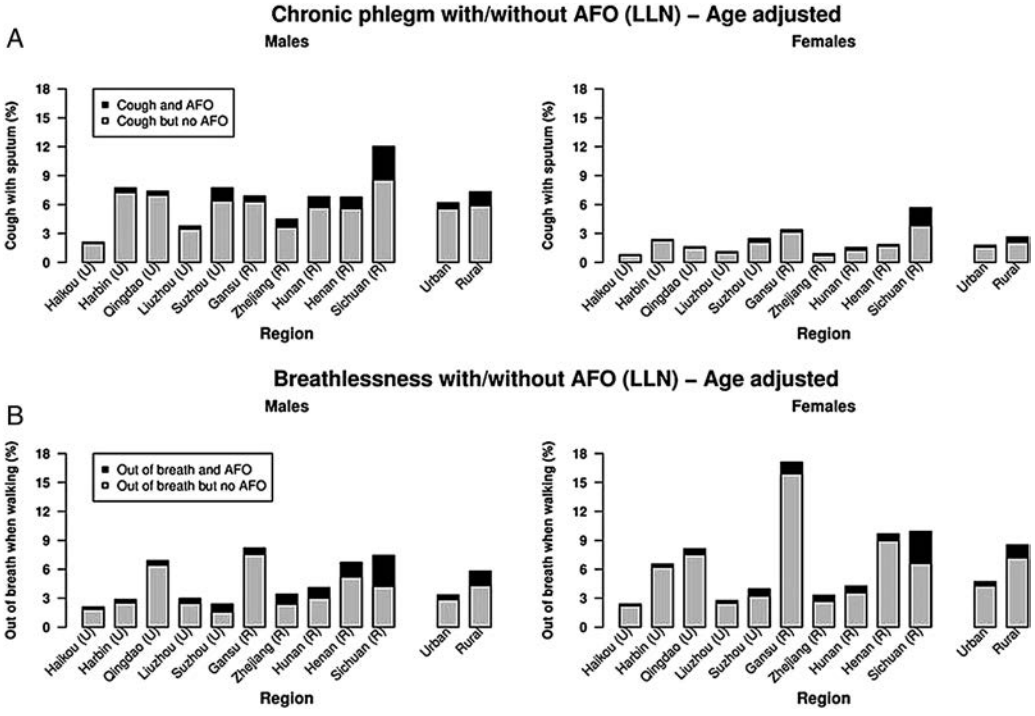

Figure 4 Prevalence of age-adjusted (A) chronic cough and phlegm with air flow obstruction (lower limit of normal, LLN), and (B) breathlessness with airflow obstruction (LLN).

highest prevalence of AFO, was included because of higher mortality rate from COPD reported in our previous studies.[15] The study area in Sichuan is situated in a valley and environmental conditions such as temperature inversion could play a role in the prevalence of AFO as it is related to pollution levels. Currently, data on genetic biomarkers for a number of health outcomes, including respiratory health, is being studied in this population that could possibly explain some of the variations in the prevalence of AFO in different regions. The prevalence of asthma in our sampling population was low and similar to previous findings[16]; lower diagnosed asthma prevalence in China could be due to poor diagnostic facilities making it difficult to differentiate between obstructive lung diseases.

As in previous studies,[5] we found that men had higher prevalence of AFO than women, probably due to high smoking prevalence in Chinese men. The higher prevalence observed among rural women could be due to greater exposure to environmental pollutants including household air pollution while cooking food using solid fuel, low socioeconomic status or lung infections early in life.

In the present study we reported AFO results based on fixed forced expiratory ratio and LLN of forced expiratory ratio so that comparison with previous studies with different diagnostic criteria could be made. The AFO prevalence based on LLN criteria using GLI reference equations was higher than the forced expiratory ratio criteria. This could be due to higher cut-off values for forced expiratory ratio in the Chinese population with age under 60. Previous papers have reported higher false-positive in the elderly population when using the fixed ratio criteria as it lacks specificity, but using the GLI reference equations to some extent overcomes the problem, although it needs to be validated independently.[17 18]

The extent of underdiagnosis and overdiagnosis of AFO in the present study population is much greater than that reported previously in western countries.[19–24] The spirometry-based prevalence of AFO is much greater than self-reported prior physician-diagnosed CB/E. In China, the majority of COPD diagnoses are based on clinical examination and measurement of lung function is not common, particularly, in rural health clinics.[25] Our study showed that younger participants, particularly those who are asymptomatic and current smokers and have middle-household income, are relatively more likely to be underdiagnosed. When subgrouped for severity of AFO based on the percent predicted FEV_1, the majority of participants had either moderate or severe AFO suggesting that underdiagnosis might be more likely. Validation of this finding would be important as these participants are at a higher risk of developing COPD and early preventive action such as smoking cessation in these groups would be expected to gain the most long-term benefit.

Those with a smoking history and presence of respiratory symptoms were more likely to be overdiagnosed for AFO. Similar findings have also been reported in other studies. A recent study in the USA[26] found that 42.5% of those diagnosed with COPD were false positive with no airway obstruction, with most of the false-positive diagnosis seen among smokers with presence of respiratory symptoms. New GOLD guidelines recommend that spirometry should be one of the essential criteria for the clinical diagnosis and management of COPD[27 28] among those reporting chronic productive cough or sputum production, dyspnoea and exposure to risk factors. Although spirometry is more reproducible and has greater sensitivity and specificity compared with peak expiratory flow, its use is not that frequent in many low-income and middle-income countries, particularly in rural areas.[29] The relatively low prevalence of self-reported CB/E in our study could be due to lack of awareness of the problem in the participants and also lack of adequate health facilities in proximity where the participants dwell. Further, recall bias could also not be excluded as a cause of the observed low proportion of diagnosed participants with AFO.

In spite of a large sample size and wide geographical locations covered, our study has some limitations. First, we did not administer a bronchodilator as part of the spirometry procedure, and hence no postbronchodilator lung function measurement was carried out. Postbronchodilator forced expiratory ratio lower than LLN or 0.70 is suggested to confirm persistent air flow limitation and thus the presence of COPD in the latest ERS/ATS and GOLD guidelines.[28 30] This means the AFO observed in our study could be either COPD or asthma related, therefore the prevalence may be somewhat overestimated. Although postbronchodilator is often used to identify patients with COPD and the course of treatment, its use to differentiate from asthma could be influenced by the day of testing, the baseline lung function before the delivery of testing and also the number of drugs given to test.[31] Second, the instrument we used at baseline did not give us the spirogram and thus incomplete exhalation could not be ruled out completely although every effort was made to explain to the participants to blow out as long as possible. A reduction in FVC due to incomplete exhalation could lead to underestimation of AFO and also could be the reason for higher prevalence of restrictive lung disease observed in our population where we used a modified definition, considering that we did not collect total lung capacity data that is usually required to define the restrictive lung disease. Third, we did not collect exacerbation history data at baseline and used GLI predictive equations[12] based on the latest predictive equations for north China and southeast Asia where bias due to internal migration from south to the north cannot be completely excluded. Although most of the participants in our study were Han Chinese, some degree of misclassification of grade of AFO as classified by GOLD criteria may have occurred.

In summary, this extremely large study provides good evidence about the burden of AFO in adult Chinese

men and women. Owing to the lack of use of spirometry for diagnosing AFO in routine clinical practice, a high proportion of such patients were not identified previously. Even among those with prior diagnosis of COPD, two-thirds lacked long-term treatment. Although a number of socioeconomic and lifestyle factors were associated with poor detection and treatment, a large proportion of regional variation remained unexplained. These findings highlight major respiratory health problems in China that need immediate attention to carry out appropriate interventions for optimal disease management as well as to develop the prevention strategies to be implemented in order to improve the current and future respiratory health in the Chinese population.

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Contributors ZC, LL, RP and RC were involved in the concept, design of the study and reviewing the manuscript. OK was involved in the analysis plan, preparing the first draft and editing of the manuscript. MS and MA were involved in the analysis plan, analysis of the data and reviewing the manuscript. JC, YG, YH, JQ, GX, JW, ZB and GZ were involved in the supervision of the data collection, data monitoring and reviewing the manuscript. KD was involved in the analysis plan and reviewing the manuscript. ZC is the PI and also was responsible for overall supervision of the project.

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Competing interests KD is employed by GlaxoSmithKline.

Ethics approval Central ethics approvals were obtained from Oxford University, the China National Centres for Disease Control and Prevention (CDC) and local ethics approvals from institutional research boards at the local CDCs in the 10 regions

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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