Prevalence and burden of chronic cough in China: a national cross-sectional study

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Shareable abstract (@ERSpublications)
In the general adult population in China, chronic cough is prevalent and associated with poorer health status, especially in individuals aged ⩾50 years and those with COPD or small airway dysfunction https://bit.ly/3785LYZ

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Abstract

Background Chronic cough is a common complaint, but there are no population-based data on its burden in China. We determined the prevalence of chronic cough and its impact on health status in adults stratified by sex, age and the diagnosis of COPD or the presence of small airway dysfunction (SAD).

Methods A representative sample of 57 779 Chinese adults aged 20 years or older was recruited and pulmonary function test was measured. Chronic cough was defined as cough lasting for >3 months in each year. Quality of life was assessed by the 12-item Short Form Health Survey (SF-12), and self-reported history of hospital visits was recorded.

Results Chronic cough was found in 3.6% (95% CI 3.1–4.1) of Chinese adults, 2.4% (95% CI 1.9–3.1) of those aged 20–49 years and 6.0% (95% CI 5.3–6.8) of those aged 50 years or older. Individuals with chronic cough had an impaired physical component summary (PCS) score of the SF-12 ($p<0.0001$) and

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more emergency visits (p=0.0042) and hospital admissions (p=0.0002). Furthermore, the impact of chronic cough on PCS score was more significant in those aged 50 years or older, or with COPD (p=0.0018 or 0.0002, respectively), with the impact on hospital admission being more significant in those with COPD or with SAD (p=0.0026 or 0.0065, respectively).

Conclusions Chronic cough is prevalent in China and is associated with a poorer health status, especially in individuals aged 50 years or older and those with the diagnosis of COPD or SAD.

Introduction

Chronic cough is a common complaint in the clinic and can be a major manifestation of many lung diseases including asthma and COPD [1–3]. Although cough for >8 weeks is recommended as the cut-off duration of chronic cough by clinical guidelines [4], many studies have utilised the 3-month cut-off duration based on the Medical Research Council definition of chronic bronchitis [5]. Using the definition of chronic cough as present for at least 3 months each year, the prevalence of chronic cough has been reported to vary quite widely both in studies conducted among the general population (2.6–11.7%) [6–8] and among COPD patients (14.4–74.1%) [9, 10]. The reported risk factors for chronic cough have included tobacco smoke, air pollution and occupational exposures [11, 12]. Despite having a population of >1.3 billion, which is the largest in the world [13], China does not have any data on the prevalence and risk factors of chronic cough in a representative population of adults.

Previous studies have reported that chronic cough was associated with impaired lung function, poor quality of life, more disease severity in the general population [11, 14] and subjects with COPD [3, 15]. However, there has been no direct comparison of the impact of chronic cough on health status in different populations, such as males *versus* females, younger *versus* older, with or without COPD, and the presence or absence of small airway dysfunction (SAD).

To address these issues, we used data from the national cross-sectional China Pulmonary Health (CPH) study to estimate the prevalence of chronic cough, where chronic cough was defined as cough for ⩾3 months each year. Additionally, we identified the risk factors and assessed the impact of chronic cough on health status stratified by sex, age and the diagnosis of COPD or SAD.

Methods

Study design and population

The CPH study was conducted between June 2012 and May 2015, which enrolled a nationally representative sample of 57 779 Chinese adults aged 20 years or older. The study design and the questionnaires used have been previously described [16]. Briefly, we used a multistage stratified cluster sampling procedure, which considered geographical region, degree of urbanisation, economic development status, and sex and age distribution. In stage one, we selected ten provinces, autonomous regions and municipalities (only regions below 1500 m of altitude were included), which represented the socioeconomic statuses and lifestyles of six major geographical regions in China. We randomly selected a large city, a midsize city, an economically developed county and an underdeveloped county from each province or autonomous region in stage two. We randomly selected two urban districts from every city and two rural townships from every county in stage three. We further randomly selected two urban residential communities or rural village communities (about 1000–2000 households) from the urban districts or rural townships, respectively, in stage four. Finally, we randomly selected individuals aged 20 years or older from the selected communities stratified by sex and age distribution based on the 2010 China census data [17]. We selected only one participant from every household, without replacement. Temporary residents (living in their current residence <1 year); those who were physically incapable of taking a spirometry test; those admitted to hospital for any cardiac condition in the past 3 months, or with treated tuberculosis; or women who were pregnant or breastfeeding were excluded.

Trained interviewers administered the questionnaire in Chinese to obtain information regarding demographic characteristics, medical history, parental history of respiratory disease and risk factors. The study protocol was approved by the ethics committees of the Capital Medical University (Beijing, China) and all other participating institutes. Written informed consent was obtained from all participants.

Procedures

Chronic cough was defined as an affirmative response to both questions: Do you often cough when you don't have a cold? Does your cough last >3 months each year? The use of 3 months' cut-off duration in cough was derived from the definition of chronic bronchitis [5], and this definition has been commonly used in epidemiological investigations of chronic cough [1]. COPD was defined as a post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) ratio of <0.70 [18]. SAD was

diagnosed on the basis of at least two of the following three indicators of lung function being <65% of predicted: maximal mid-expiratory flow (MMEF), forced expiratory flow (FEF) at 50% of the FVC (FEF 50%) and FEF 75% after bronchodilator inhalation [19, 20]. We obtained information on cigarette smoking, history of childhood pneumonia or bronchitis, and history of chronic bronchitis, as previously described [16]. We defined allergic rhinitis as having two or more of the following symptoms for >1 h on most days according to the Allergic Rhinitis and Its impact on Asthma questionnaire [21]: 1) watery rhinorrhea; 2) sneezing, especially paroxysmal; 3) nasal obstruction; and 4) nasal pruritis. Additionally, we defined biomass use as using woody fuels or animal waste for cooking or heating during the past 6 months or longer. We defined occupational exposure as exposure to dust, allergens, noxious gases (*e.g.* mining, forging, chemical industry, cement, greenhouse planting) for >3 months. We derived exposure to ambient particulate matter with a diameter <2.5 µm ($PM_{2.5}$) from the regional satellite-retrieved aerosol optical depth model [22]. We measured the health status of all participants using the physical component summary (PCS) score and the mental component summary (MCS) score of the 12-item Short Form Health Survey (SF-12) [23].

Trained and certified technicians carried out pulmonary function tests on all participants using a MasterScreen Pneumo PC spirometer (CareFusion, Yorba Linda, CA, USA). We carried out daily calibration with a 3-L syringe. Participants were required to do up to eight forced expiratory manoeuvres until FVC and FEV_1 were reproducible within 150 mL. We administered a bronchodilator (salbutamol 400 µg) by inhalation through a 500-mL spacer and repeated spirometry 20 min later, using the same criteria. Test results were stored in the spirometer and downloaded daily to a central computer system. All the spirometric data were reviewed centrally by an expert panel on the basis of the criteria of the American Thoracic Society and European Respiratory Society [24], and reference values for spirometry [25]. Poor-quality data were excluded.

Statistical analysis

All calculations were weighted to represent the general adult population aged 20 years or older in China [17]. A technique appropriate for this complex survey design, the Taylor series linearisation method, was used to calculate standard errors [26]. We used all participants for whom the variables of interest were available, and we did not imput missing data.

We assessed the significance of differences using t-test for continuous variables and χ^2 test for categorical variables. The comparisons were performed according to chronic cough status, sex and other characteristics including age (20–49 years and ⩾50 years), COPD and SAD. The comparisons were weighted taking into account the multistage cluster sampling design. We examined the association between risk factors and chronic cough by multivariable adjusted logistic regression analyses. The associations of chronic cough with continuous outcomes (including FEV_1/FVC, FEV_1 % pred, MMEF % pred, FEF 50% pred, FEF 75% pred, PCS and MCS) and categorical outcomes (including FEV_1/FVC <70%, SAD, positive bronchodilator reversibility, emergency and hospital admission) were estimated with multivariable adjusted linear regression and logistic regression models, respectively. The adjusted variables included age, sex, urbanisation, body mass index, cigarette smoking, biomass, annual mean $PM_{2.5}$, education, occupational exposure, visible mould spots in the current residence, history of pneumonia or bronchitis during childhood, parental history of respiratory diseases and allergic rhinitis. The above logistic or linear regression analyses were weighted, taking into account the multistage cluster sampling design.

Subgroup analyses were also performed for the association of chronic cough with PCS, MCS, and emergency or hospital admission due to acute exacerbation of respiratory symptoms in the preceding 12 months according to sex, age (20–49 years and ⩾50 years), diagnosis of COPD and the presence of SAD. Furthermore, the interaction terms between chronic cough and the subgroup variables were added into the above regression model in order to explore any potential interactions.

All statistical analyses were performed with SUDAAN (Version 11.0; Research Triangle Institute, Research Triangle Park, NC, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The final analysis included 50 991 subjects (21 446 men and 29 545 women) who completed the questionnaire survey and provided reliable pulmonary function tests before and after a bronchodilator. A total of 1985 people with chronic cough were identified from the 50 991 participants. The demographics and risk factors by diagnosis of chronic cough are summarised in table 1.

The prevalence of chronic cough was 3.6% (95% CI 3.1–4.1) among the general Chinese population aged 20 years or older (table 2). The prevalence of chronic cough in the different regions is shown in figure 1. Men had a higher prevalence (4.6%, 95% CI 3.9–5.4) than women (2.6%, 95% CI 2.1–3.3) (p=0.0005) across the whole age group. The prevalence of chronic cough increased with age, being 2.4% (95% CI 1.9–3.1) among individuals aged 20–49 years and 6.0% (95% CI 5.3–6.8) among those aged 50 years or older (p <0.0001). We also observed that the prevalence of chronic cough was higher in the individuals with SAD than in those without SAD (4.4% *versus* 2.8%, p=0.0039). However, the prevalence of chronic cough was not significantly different between those with COPD and those without COPD (6.0% *versus* 3.2%, p=0.0845) (table 2). Not surprisingly, smokers had a higher prevalence (5.9%, 95% CI 4.9–7.0) than never-smokers (2.5%, 95% CI 2.0–3.0) (p<0.0001) (supplementary table E1). With respect to the concomitant symptoms accompanying chronic cough, phlegm was the most common, present in 67.5% of those with chronic cough, and only 404 (22.6%) subjects with chronic cough had neither phlegm nor dyspnoea and wheeze (supplementary table E2).

Multivariable adjusted analyses in the entire population showed that age, cigarette smoking, occupational exposure, history of pneumonia or bronchitis during childhood, and allergic rhinitis were consistently associated with the prevalence of chronic cough (p<0.01 for all). However, biomass use and exposure to high concentrations of $PM_{2.5}$ ($\geqslant$75 μg·m^{-3}) were not associated with the prevalence of chronic cough (table 3). When considering only never-smokers, similar results were observed (supplementary table E3).

People with chronic cough had lower lung function after bronchodilator inhalation, including FEV_1/FVC, FEV_1%pred (p<0.0001, p=0.0155, respectively) than those without chronic cough (table 4). Compared with people without chronic cough, those with chronic cough had an impaired physical health state (mean PCS scores of 48.7 *versus* 52.6 points, p<0.0001) as measured by PCS scores based on the SF-12 questionnaire. Furthermore, among people with chronic cough, 3.5% and 5.5% reported at least one emergency room visit or hospital admission in the past 12 months due to an exacerbation of respiratory symptoms, respectively, which were significantly higher than those without chronic cough of 0.5% for emergency room visit and 0.4% for hospital admission (p =0.0042 and 0.0002, respectively). The impact

TABLE 1 Demographics and risk factors by diagnosis of chronic cough in the general Chinese adult population

Variables	No chronic cough	Chronic cough	p-value
Subjects n	49 006	1985	
Men	20 255 (50.0)	1191 (64.0)	0.0031
Age years	43.5±0.8	52.0±1.5	<0.0001
Urban residents	31 637 (51.6)	1242 (52.1)	0.9135
Education level			0.0359
Primary school or less	12 090 (22.2)	665 (33.0)	
Middle and high school	28 113 (52.5)	1057 (46.8)	
College and higher	8803 (25.3)	263 (20.2)	
Cigarette smoking			0.0001
Never-smoker	35 466 (69.4)	963 (45.9)	
Ever-smoker[#]	13 540 (30.6)	1022 (54.1)	
Passive smoking at home[¶]	17 130 (47.8)	470 (52.9)	0.2546
Biomass use	12 967 (25.8)	661 (32.4)	0.0747
Annual mean $PM_{2.5}$ exposure μg·m^{-3}	70.7±2.9	72.3±3.6	0.3203
Occupational exposure	11 608 (24.5)	719 (37.3)	0.0017
Visible mould spots in the current residence			0.2377
Rarely	36 152 (69.1)	1319 (62.3)	
Sometimes	10 098 (24.2)	487 (28.7)	
Often	2265 (6.7)	170 (9.0)	
History of pneumonia or bronchitis during childhood	2227 (4.9)	217 (11.3)	0.0033
Parental history of respiratory diseases	8070 (16.5)	539 (24.4)	0.0006
Body mass index kg·m^{-2}	23.6±0.1	23.9±0.2	0.1855
Allergic rhinitis	4676 (10.6)	407 (25.0)	0.0006

Values are weighted and shown as n (%) or mean±SE unless otherwise indicated. p-values are weighted, taking into account the multistage cluster sampling design and based on χ^2 test for categorical variables or *t*-test for continuous variables. $PM_{2.5}$: particulate matter with a diameter <2.5 μm. [#]: ever-smoker was defined as having smoked equal to or >100 cigarettes in the lifetime; [¶]: demographics of passive smoking at home were shown for never-smokers.

TABLE 2 Age-specific and age-standardised prevalence of chronic cough in the general adult population

Variables	Total	Men	Women	p-value
Total	3.6 (3.1–4.1)	4.6 (3.9–5.4)	2.6 (2.1–3.3)	0.0005
Age years				
20–49	2.4 (1.9–3.1)	3.0 (2.2–4.2)	1.7 (1.1–2.7)	0.0433
⩾50	6.0 (5.3–6.8)	7.7 (6.7–8.8)	4.3 (3.6–5.0)	<0.0001
p-value for difference	<0.0001	<0.0001	<0.0001	
COPD[#]				
No	3.2 (2.7–3.7)	4.1 (3.4–5.0)	2.3 (1.8–3.0)	0.0006
Yes	6.0 (3.5–10.0)	5.2 (4.0–6.7)	6.9 (2.5–18.1)	0.5777
p-value for difference	0.0845	0.1155	0.1846	
SAD[¶]				
No	2.8 (2.3–3.5)	3.7 (3.0–4.5)	2.0 (1.5–2.8)	0.0010
Yes	4.4 (3.7–5.2)	5.4 (4.2–6.9)	3.2 (2.4–4.2)	0.0101
p-value for difference	0.0039	0.0229	0.0233	

Values are represented as percentage (95% confidence interval). p-value for difference is for the comparison of binary variables. All the calculations of p-values are weighted, taking into account the multistage cluster sampling design and based on χ^2 test. SAD: small airway dysfunction. [#]: COPD was defined as those individuals with post-bronchodilator FEV_1/FVC <70%. [¶]: SAD was diagnosed on the basis of at least two of the following three indicators of lung function being <65% of predicted: maximal mid-expiratory flow, forced expiratory flow (FEF) 50% and FEF 75% after bronchodilator inhalation.

of chronic cough on lung function before bronchodilator inhalation and medication use is shown in supplementary table E4. To test the impact of chronic cough solely on lung function, health status and medication use, we have also performed a sensitivity analysis in 404 patients solely presenting with

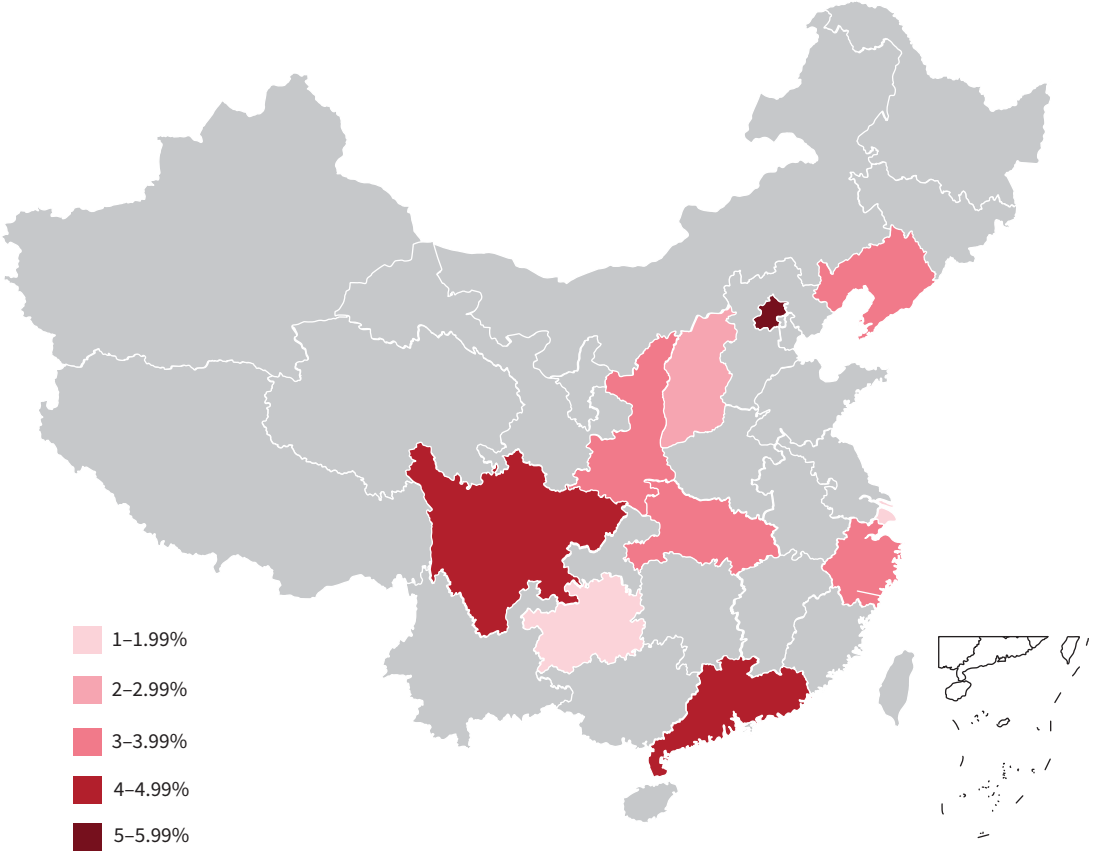

FIGURE 1 The prevalence of chronic cough in different regions of China.

TABLE 3 Multiple adjusted odds ratios of chronic cough in the general Chinese adult population

Variables	OR (95% CI)	p-value
Male	0.93 (0.63–1.37)	0.7045
Age (10 years)	1.43 (1.26–1.61)	<0.0001
Rural resident	0.84 (0.59–1.19)	0.3094
Smoking status		
Never-smoker	1.00 (Reference)	
Ever-smoker[#]	2.61 (2.10–3.25)	<0.0001
Biomass use	1.04 (0.86–1.26)	0.6621
Annual mean $PM_{2.5}$ $\mu g \cdot m^{-3}$		
<50	1.00 (Reference)	-
50–75	0.96 (0.59–1.57)	0.8784
⩾75	1.05 (0.62–1.79)	0.8471
Education level		
Primary school and lower	1.00 (Reference)	-
Middle and high school	0.80 (0.61–1.05)	0.1083
College and higher	0.97 (0.68–1.39)	0.8770
Occupational exposure	1.41 (1.10–1.80)	0.0086
Visible mould spots in the current residence		
Rarely	1.00 (Reference)	-
Sometimes	1.31 (0.91–1.90)	0.1414
Often	1.19 (0.73–1.93)	0.4652
History of pneumonia or bronchitis during childhood	2.23 (1.49–3.34)	0.0006
Parental history of respiratory diseases	1.23 (0.95–1.59)	0.1165
Body mass index $kg \cdot m^{-2}$		
<18.5	1.45 (0.97–2.16)	0.0662
18.5–24.9	1.00 (Reference)	-
⩾25	1.23 (0.94–1.61)	0.1197
Allergic rhinitis	2.84 (1.98–4.09)	<0.0001

The variables listed in the table are all included in the model. The logistic regression analyses are weighted, taking into account the multistage cluster sampling design. OR: odds ratio; 95% CI: 95% confidence interval; $PM_{2.5}$: particulate matter with a diameter <2.5 µm. [#]: ever-smoker was defined as having smoked equal to or >100 cigarettes in the lifetime.

chronic cough and observed the similar adverse impact of chronic cough solely on FEV_1/FVC (supplementary table E5).

After adjusting for confounding factors, such as age, sex, smoking status, biomass or $PM_{2.5}$ exposure, chronic cough was associated with reduced spirometry parameters after bronchodilator inhalation, including FEV_1/FVC, MMEF % pred, FEF 50% pred and FEF 75% pred ($p<0.05$ for all) (table 5). The similar impact on spirometry parameters before bronchodilator inhalation is shown in supplementary table E6.

Finally, subgroup analysis showed that the association of chronic cough with PCS scores or hospital admission was independent of sex, age, the diagnosis of COPD and the presence of SAD. Furthermore, interaction analysis showed that the impact of chronic cough on PCS score was significantly greater in people aged 50 years or those with COPD than those aged 20–49 years without COPD ($p=0.0018$ and $p=0.0002$, respectively). Similarly, the impact of chronic cough on hospital admission was significantly greater in those with COPD or SAD than those without COPD or SAD ($p=0.0026$ and $p=0.0065$, respectively) (figure 2).

Discussion

The main findings of the present analysis from the CPH database are: 1) chronic cough was prevalent in the general adult population in China; 2) age, cigarette smoking, occupational exposure, history of pneumonia or bronchitis during childhood and allergic rhinitis were the main risk factors associated with the prevalence of chronic cough; and 3) the impact of chronic cough on quality of life or medication utilisation was more significant in those aged ⩾50 years and in those with COPD or SAD.

The present study involving a large comprehensive survey in a nationally representative sample of Chinese adults indicated that the prevalence of chronic cough was 3.6% in Chinese adults aged 20 years or older;

TABLE 4 Clinical characteristics and use of healthcare resources by diagnosis of chronic cough

Variables	No chronic cough	Chronic cough	p-value
Subjects n	49 006	1985	
Lung function[#]			
FEV_1/FVC %	82.0±0.4	75.2±1.2	<0.0001
FEV_1 % pred	99.8±0.9	94.5±2.5	0.0155
FEV_1/FVC <70%	4420 (8.1)	488 (22.8)	0.0010
MMEF % pred	76.0±1.0	62.6±2.8	<0.0001
FEF 50% pred	88.4±1.0	74.4±3.4	<0.0001
FEF 75% pred	77.2±1.3	62.7±2.6	<0.0001
SAD[¶]	15 991 (28.3)	988 (48.0)	0.0017
Positive bronchodilator reversibility[+]	3059 (6.1)	222 (13.0)	0.0315
Short form (SF)-12 scores			
PCS scores	52.6±0.2	48.7±0.6	<0.0001
MCS scores	54.1±0.3	53.1±0.6	0.0656
Comorbidities			
Hypertension	3846 (6.4)	309 (13.1)	0.0116
Coronary heart disease	698 (1.9)	87 (3.2)	0.3501
Diabetes	1203 (2.6)	96 (3.9)	0.2589
Acute exacerbation of respiratory symptoms in the last 12 months			
Emergency	174 (0.5)	89 (3.5)	0.0042
Hospital admission	167 (0.4)	119 (5.5)	0.0002

Values are weighted and shown as n (%) or mean±SE. All the calculations of p-value are weighted, taking into account the multistage cluster sampling design and based on χ^2 test for categorical variables or t-test for continuous variables. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MMEF: maximal mid-expiratory flow; FEF50%: forced expiratory flow at 50% of the FVC; FEF 75%: forced expiratory flow at 75% of the FVC; SAD: small airway dysfunction; PCS: physical component summary; MCS: mental component summary. [#]: the parameters were measured at 20 min after inhalation of 400 µg of salbutamol; [¶]: SAD was diagnosed on the basis of at least two of the following three indicators of lung function being <65% of predicted – maximal mid-expiratory flow, forced expiratory flow (FEF) 50% and FEF 75% after bronchodilator inhalation. [+]: a positive bronchodilator reversibility test was defined as an increase in post-bronchodilator forced expiratory volume in 1 s of >12% and >200 mL from baseline, 20 min after inhalation of 400 µg of salbutamol.

TABLE 5 Associations of chronic cough with lung function after bronchodilator inhalation

Variables	OR or β (95% CI)	p-value
FEV_1/FVC	−3.30 (−4.93– −1.66)	0.0005
FEV_1 %pred	−4.42 (−8.89–0.05)	0.0522
FEV_1/FVC <70%	1.59 (1.13–2.23)	0.0106
MMEF % pred	−5.73 (−9.06– −2.40)	0.0020
FEF 50% pred	−7.64 (−12.16– −3.11)	0.0023
FEF 75% pred	−6.51 (−10.29– −2.74)	0.0019
SAD[#]	1.47 (1.14–1.89)	0.0049
Positive bronchodilator reversibility[¶]	1.87 (1.01–3.47)	0.0472

Adjusted for age, sex, urbanisation, body mass index, cigarette smoking, biomass, annual mean $PM_{2.5}$, education, occupational exposure, visible mould spots in the current residence, history of pneumonia or bronchitis during childhood, parental history of respiratory diseases and allergic rhinitis. The logistic or linear regression analyses are weighted, taking into account the multistage cluster sampling design. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MMEF: maximal mid-expiratory flow; FEF 50%: forced expiratory flow at 50% of the FVC; FEF 75%: forced expiratory flow at 50% of the FVC; SAD: small airway dysfunction. [#]: SAD was diagnosed on the basis of at least two of the following three indicators of lung function being <65% of predicted – MMEF, FEF 50% and FEF 75% after bronchodilator inhalation; [¶]: a positive bronchodilator reversibility test was defined as an increase in post-bronchodilator forced expiratory volume in 1 s of >12% and >200 mL from baseline, 20 min after inhalation of 400 µg of salbutamol.

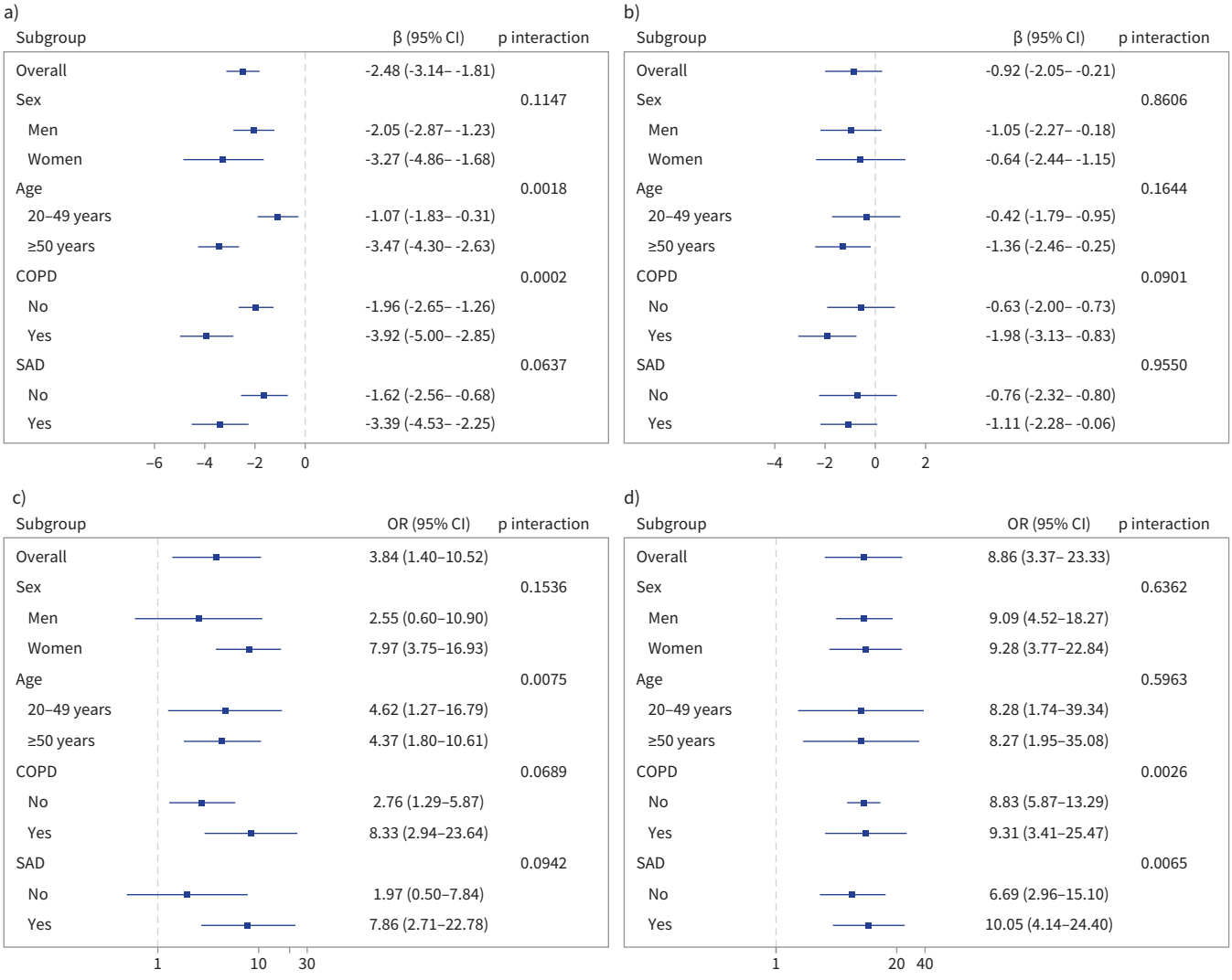

FIGURE 2 Association of chronic cough with quality of life and respiratory exacerbations: a) physical component summary (PCS) score; b) mental component summary (MCS) score; c) emergency; and d) hospital admission. Adjusted for age, sex, urbanisation, body mass index, cigarette smoking, biomass, annual mean particulate matter with a diameter <2.5 μm ($PM_{2.5}$), education, occupational exposure, visible mould spots in the current residence, history of pneumonia or bronchitis during childhood, parental history of respiratory diseases and allergic rhinitis. The subgroup variables were not adjusted in the corresponding subgroup analysis for themselves, except that age was still adjusted as continuous variable for the subgroup analysis conducted among those aged 20–49 and ⩾50 years. SAD: small airway dysfunction.

prevalence increased with age from 2.4% in individuals aged 20–49 years to 6.0% in those aged 50 years or older. Consistent with previous epidemiological studies, we used 3 months as the cut-off duration for chronic cough, which has been widely used in epidemiological surveys of chronic cough in the general population [27–29].

The prevalence of 3.6% in the present study is very similar to the value of 3.48% found among adults aged 40 years or older based on the same criterion reported by Won *et al.* [29] from the Korean National Health and Nutrition Examination survey of 2010–2016 and was also similar to the 4% prevalence reported in Denmark in adults aged 20 years and older using an ⩾8-week duration of chronic cough [30]. The prevalence of 3.6% in the present study was higher than the value of 1.7% among the general population aged 40 years or older reported by Omori *et al.* [31] in Japan, in which chronic cough was defined as having both cough and phlegm for at least 3 months of the year and for at least 2 consecutive years, or as receiving any treatment for chronic bronchitis at the time of recruitment. However, the prevalence of 3.6% in the present study was far lower than the estimation of 7.9% in the global general adult population using the 3 months cut-off definition reported from a systematic review and meta-analysis

by Song *et al.* [1] and the 16% prevalence in Northern Europe from the Respiratory Health in Northern Europe (RHINE) III cohort using a definition of chronic cough lacking a specified timeframe but described as protracted and troublesome [32]. Existing chronic cough prevalence data vary widely, which might be due to differences in survey method, sample populations, definition and ethnicity.

By contrast, a recent meta-analysis of several Chinese studies showed that the prevalence of chronic cough was 6.22% (95% CI 5.03–7.41%) in Chinese adults [33]. However, the studies included in this pooled analysis were of small sample sizes often conducted in specific regions of China and using different diagnostic criteria and sampling methods. Therefore, this reported prevalence may not be representative of the real prevalence of chronic cough in China.

Most previous reports from clinics showed that prevalence of chronic cough was greater in women [34, 35]. However, we observed that men had a higher prevalence than women in the representative general adult population. The higher prevalence of chronic cough in men might be partly due to higher smoking rates in men (47.2%) than in women (2.7%) [36]. Another possible explanation is that women have a heightened cough reflex sensitivity, resulting in more hospital visits for their cough [37].

For the prevalence of chronic cough, we did not find a statistically significant difference between participants with and without COPD (6.0% *versus* 3.2%, p=0.0845), although the multivariable adjusted analysis (table 5) showed that the risk of COPD was 59% higher among participants with chronic cough compared with those without chronic cough (OR 1.59; 95% CI 1.13–2.23). The present results also support our previous findings that asymptomatic patients with COPD are common in China, especially in those with a mild degree of airflow limitation, such as patients at Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage I or II [16]. A similar result was also reported from the general population in Denmark where only 10% of people with COPD diagnosed by spirometry had chronic cough, defined as cough lasting for >8 weeks [3]. These results demonstrate that chronic cough may not be a common symptom of early COPD and imply that screening for early COPD in the community based on self-reported chronic cough may not be appropriate, at least in the Chinese general population.

The identified risk factors associated with chronic cough in this study have been reported previously, including age, smoking, occupational exposure, history of pneumonia or bronchitis during childhood, and allergic rhinitis [30, 38–40]. We found that ever-smokers had double to triple the risk of chronic cough compared with never-smokers. Likewise, occupational exposure also increased the risk of chronic cough by 40%. Therefore, smoking cessation and avoiding occupational exposure should be mandatory in the management of patients with chronic cough. In accordance with previous studies reporting an inconsistent association of ambient air pollution with chronic cough [12, 41], we did not observe an impact of air pollution on the prevalence of chronic cough. This lack of association may be due to the use of only one measure of $PM_{2.5}$ level averaged over a year within the geographical region of the participant, when the degree of personal exposure to $PM_{2.5}$ and other constituents of air pollution may also be more important in the underlying cough response.

In the present study, people with allergic rhinitis had nearly three times the risk for chronic cough compared with people who did not have allergic rhinitis, which is supported by the report that upper airway inflammation is one of the most commonly identified causes of chronic cough [42]. In addition, a multicentre survey to identify causes of chronic cough in Chinese adults showed that cough variant asthma (32.6%) and upper airway cough syndrome (18.6%) were the two top-ranking causes of chronic cough [43]. We also showed that 21.0% of people with chronic cough reported concomitant recurrent wheezing (supplementary table E2). Therefore, in some cases, chronic cough in individuals with allergic rhinitis or concomitant recurrent wheezing may represent undiagnosed asthma, and these individuals will most likely benefit from treatment with inhaled corticosteroids.

Although a previous study from a small hospital-based asthma cohort reported that cough frequency was not associated with lung function [44], our present study from a large general population showed that chronic cough was associated with an adverse impact on the lung function, consistent with previous findings in COPD patients [3] and from the general population [11]. These inconsistent results might be due to a different scale of cough measurement (*e.g.* cough frequency *versus* cough duration) and size of population recruited.

Our study showed that chronic cough was associated with an adverse impact on PCS score using the SF-12 questionnaire and healthcare resource use. Furthermore, the impact of chronic cough on PCS score was independent of age, sex, the diagnosis of COPD and the presence of SAD. Our results are similar to those

conducted in an elderly population from a small community in Korea showing that chronic cough was associated with an adverse impact on the PCS and also on the MCS of the SF-36 questionnaire [45].

A previous study has reported that women have a heightened cough reflex sensitivity and experience a greater impact on health-related quality of life, resulting in more women seeking medical attention for their cough [37]. However, we did not observe that chronic cough had a greater impact on PCS score in women than in men, even though women with chronic cough had more night-time sleep disturbance compared with men with chronic cough (supplementary table E2). This is similar to a previous report of no significant difference in overall quality of life between men and women, although embarrassment, frustration and sleep disturbance were more common in women [46].

We observed that the prevalence of chronic cough increased with age and that chronic cough was more prevalent in subjects aged 50 years and above, similar to results from the Copenhagen General Population Study in Denmark or the Rotterdam Study in the Netherlands [30, 38]. The impact of chronic cough on quality of life in the elderly is complex. On the one hand, the elderly have more concomitant symptoms accompanying chronic cough, such as sputum production, wheezing, dyspnoea and urinary incontinence as we and others have reported [47], which contribute to chronic cough having a notably large impact on quality of life in the elderly [29]. On the other hand, a reduced cough reflex may also be a significant problem in the elderly, which may be associated with a greater risk of aspiration pneumonia [48]. In the present study, the interaction analysis showed that the impact of chronic chough on PCS scores was significantly stronger among people aged 50 years and above. This “duality” of cough in the elderly indicates the need for a more comprehensive but balanced clinical approach in this age group.

Consistent with previous findings [3], our present study further showed that comorbid chronic cough in individuals with COPD was associated with a more severe disease in terms of poorer quality of life and more healthcare utilisations than those without COPD. These findings accord well with the fact that individuals with COPD and chronic cough have more accompanying respiratory symptoms, such as phlegm and wheezing.

SAD is considered as a precursor of COPD and asthma and is common in the general population [20, 49, 50]. In our previous analysis of the same population, the presence of COPD or asthma was associated with about a two-fold higher odds ratio for SAD [20]. In the present study, we also observed that chronic cough was associated with SAD. Furthermore, we found that those with SAD had more hospital admissions than those without SAD as we have observed in those with COPD. These findings imply that individuals with SAD and chronic cough represent a more vulnerable group compared with those without SAD, and they should be paid more attention in the clinic.

We assessed the impact of overall chronic cough on health status stratified by sex, age and diagnosis of COPD or SAD, but not stratified by the diagnosis of asthma, because sex, age and diagnosis of COPD or SAD defined by spirometry are objective indicators, while asthma determined by epidemiological definition is not.

To our knowledge, our study is the first nationally representative survey reporting the prevalence and risk factors for chronic cough in China, and investigating its impact on health status and healthcare resource use in adults according to age, sex and the diagnosis of COPD or the presence of SAD. However, there are some limitations. First, chronic cough was defined by period prevalence, not by point prevalence, which is prone to recall bias. The definition was also dependent on the duration of cough, which has limited value in disease burden and risk factors. Second, similar to other large-scale population-based surveys, we did not exclude lung parenchymal diseases by chest radiograph or computed tomography and nor did we pursue the clinical cause(s) of chronic cough. Third, we assessed the impact of chronic cough overall on health status in the present study, without considering the synergistic effects of other concomitant symptoms accompanying chronic cough, such as phlegm, dyspnoea and wheeze. We recognise that besides the cough symptom, other respiratory symptoms such as dyspnoea, wheezing and sputum would also affect a worse clinical outcome in subjects with COPD or SAD. Thus, whether the impact of chronic cough on health status is independent of cough itself needs to be further investigated in the future.

Conclusion

Our finding in this representative general population is that chronic cough is common, increases with age and is associated with poorer health status. Furthermore, the impact of chronic cough on health status is more significant in individuals aged 50 years or older and those with COPD or with SAD. It is important to determine the long-term outcomes of the various subgroups of chronic cough in future studies.

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