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Prevalence, risk factors, and mortality of COPD in young people in the USA: results from a population-based retrospective cohort

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ABSTRACT

Background Chronic obstructive pulmonary disease (COPD) has been considered a disease of the elderly, but it could also occur in young people aged 20–50 years. However, the characteristics and prognosis of COPD in such young people remain unclear.

Methods Our retrospective cohort study was based on the National Health and Nutrition Examination Survey (NHANES). Participants who 20–50 years old at baseline and completed the pulmonary function test were enrolled in our study cohort. These participants were followed up to 31 December 2019. The sample weight and Taylor Linearization Procedures were adapted to make representative estimations of prevalence and baseline characteristics. The weighted logistic regression model was used to assess the risk factors. The propensity score method and Cox proportional hazard models were applied to calculate the risk of mortality.

Results The weighted prevalence of COPD in young people in the USA was 1.64% and it increased with age, with a higher prevalence in males than females (2.59% vs 0.72%, p<0.001). The proportion of Global Initiative for COPD 1–2 was 96.7%. Males (OR=4.56, 95% CI: 2.74 to 7.61), non-Hispanic black (OR=2.77; 95% CI: 1.14 to 6.75), non-Hispanic white (OR=4.93; 95% CI: 2.16 to 11.28) and smoking (current smoking, OR=2.36; 95% CI: 1.40 to 3.98; ever smoking, OR=1.92; 95% CI: 1.05 to 3.51; passive smoking, OR=2.12; 95% CI: 1.41 to 3.20) were shown to be independent risk factors for COPD in young people. Compared with those matched by sex, age and race, the young people with COPD had a higher risk of all-cause death (HR=3.314, p<0.001).

Conclusion COPD in young people has a low prevalence in the USA and its independent risk factors included male, race (non-Hispanic black and non-Hispanic white) and smoking. Young COPD has a higher risk of all-cause mortality than the matched non-COPD.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Chronic obstructive pulmonary disease could also occur in young people and present different clinical characteristics. However, there is a paucity of data with respect to COPD in young people based on large-scale and longitudinal observations.

WHAT THIS STUDY ADDS

⇒ The weighted prevalence of COPD in young people in the USA was 1.64% and it increased with age. Male, race (non-Hispanic black and non-Hispanic white) and smoking were independent risk factors for COPD in young people. Young COPD had a higher risk of all-cause mortality.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests that it is necessary to detect COPD in young people and take some measures to improve their long-term outcomes.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable chronic respiratory disease with significant morbidity and mortality burden. A recent report showed that COPD led to 3.3 million deaths and 74.4 million disability-adjusted life years (DALYs) losses worldwide in 2019.[1] For a long time, COPD has been considered a disease of the elderly. However, previous research revealed that COPD could also occur in young people, and the concept of 'young COPD' has gained increasing interest. In the 2022 report of the Global Initiative for COPD (GOLD), 'COPD in young people' was proposed to be those patients in the 20–50 years range.[2–4]

Previous studies showed that COPD in young people who were often undiagnosed had significant structural and functional abnormalities.[5] Compared with healthy controls without airflow limitation, young COPD showed an increased risk of exacerbations[6] and has a higher comorbidity prevalence and mortality risk.[7 8] Therefore, COPD

in young people is worthy of extensive attention and research.

Although COPD in young people has gained some attention, there is a paucity of data with respect to these individuals, especially large-scale population-based studies and longitudinal observations. Previous studies that focused on relevant topics still had some limitations. For example, a study focused on the Korean population aged 40–50 years old.[6] However, people younger than 40 years were not observed. Another study described the characteristics of 'early COPD' in the Copenhagen population,[7] but its diagnosis of 'COPD' was according to pre-bronchodilator spirometry. Additionally, a previous study merely enrolled smokers under the age of 50 years old and the results could not be generalised to the whole population.[8] Therefore, the prevalence and clinical characteristics of COPD in young people cannot be accurately assessed. Therefore, it is necessary to accurately assess the characteristics and prognosis of COPD in young people, which may contribute to the early detection and intervention of COPD and thus reduce the health and socioeconomic burden of COPD.

In this study, we established a retrospective cohort based on the National Health and Nutrition Examination Survey (NHANES) to investigate the demographic characteristics, prevalence, risk factors, and risk of all-cause mortality of COPD in young people.

METHODS

Study population

NHANES adopted a complex, multi-stage, probability sampling method to collect participants representative of the USA population. Data were obtained by personal interview and mobile physical examination (www.cdc.gov/nchs/nhanes). Since 1999, NHANES has been conducted on an ongoing basis with public-use data being released in 2-year cycles. The sample for each 2-year cycle is representative of the US population. Pulmonary function test (PFT) was carried out in NHANES 2007–2008, 2009–2010 and 2011–2012.

Participants aged 20–50 years old with results of PFT were enrolled in our cohort for analysis at baseline and followed up to 31 December 2019.

Assessments of COPD, covariates, and deaths

Given that lung function always peaks at around 20 years, the definition of COPD in young people is COPD patients (post-bronchodilator forced expiratory volume in the first second/forced vital capacity (FEV_1/FVC) <0.7) included in the 20-year to 50-year age range.

Information on covariates was available through baseline interviews, including sex, age, race, body mass index, family income poverty ratio, smoking status, passive smoking, occupational exposure, self-report chronic diseases and self-reported respiratory symptoms.

Follow-up time and mortality status were ascertained with the linked mortality files from National Death Index using a unique participant identifier.

Additional detail on the method for making measurements on the predicted value of personal FEV_1, personal lower limit of normal (LLN) value of FEV_1/FVC, the classification of GOLD stage, bronchodilator response (BDR) and asthma–COPD overlap syndrome (ACOS) was provided in an online supplemental data.

Statistical analysis

Weights and Taylor Linearization Procedures accounted for the complex survey design, survey non-response and planned oversampling of the elderly and races were adapted to make estimates that are representative of the US population (www.cdc.gov/nchs/nhanes/tutorials).

Demographic characteristics of the young people who completed the spirometry were presented as mean (SD) for continuous measures and number (percentage) for categorical measures. Comparisons among groups were performed using t-test for continuous variables and χ^2 test for categoric variables. Both weighted (representative of the US population) and unweighted (representative of the enrolled population) demographic characteristics were estimated.

The prevalence of young COPD was estimated with study weights (representative of the US population) and was stratified by age and gender. Time trends of prevalence were assessed by linear regression models using age groups as continuous variables.

A sensitivity analysis using the LLN in addition to the fixed ratio of FEV_1/FVC<0.70 was conducted.

The association between each potential risk factor and the presence of COPD was determined using logistic regression with study weights.[9] The relationship between risk factors and young COPD was presented by OR.

The propensity score method was used to account for the baseline imbalance.[10] A logistic regression model was adapted to generate a propensity score for each participant based on confounding factors. Demographic characteristics (sex, age and race) and exposure history (smoking status, passive smoking, and occupational exposure) were introduced in this logistic regression model.

Cox proportional hazard models were applied to calculate the hazard ratios and corresponding 95% CIs for all-cause mortality between COPD and non-COPD groups.[11] The baseline of survival analysis was defined as the time when participants had their physical examinations. Months from baseline to the date of mortality, loss to follow-up or 31 December 2019 was counted. For the primary analyses, we assessed the HRs of mortality for the COPD group compared with sex, age and race-matched population.

Statistical significance was defined at a two-sided p<0.05. All analyses were performed using the R software (V.4.1) with 'tableone', 'survey', 'MatchIt' and 'survival' packages.

Table 1 Demographic and clinical characteristics of COPD and non-COPD in young people in the NHANES

	Unweighted			Weighted		
Level	**Non-COPD**	**COPD**	**P values**	**Non-COPD**	**COPD**	**P values**
Sex (%)						
Female	3896 (50.9)	28 (21.5)	<0.001	64 888 155 (51.1)	471 368 (22.2)	<0.001
Male	3758 (49.1)	102 (78.5)		62 186 874 (48.9)	1 652 709 (77.8)	
Age (mean (SD))	34.86 (9.02)	40.72 (7.79)	<0.001	35.17 (9.11)	41.36 (7.40)	<0.001
Race (%)						
Mexican American	1365 (17.8)	6 (4.6)	<0.001	13 937 594 (11.0)	45 274 (2.1)	0.001
Non-Hispanic black	1558 (20.4)	22 (16.9)		15 734 511 (12.4)	192 977 (9.1)	
Non-Hispanic white	3115 (40.7)	94 (72.3)		78 672 445 (61.9)	1 762 937 (83.0)	
Other Hispanic	825 (10.8)	3 (2.3)		8 666 670 (6.8)	22 101 (1.0)	
Other race	791 (10.3)	5 (3.8)		10 063 810 (7.9)	100 787 (4.7)	
BMI (mean (SD))	28.72 (7.07)	26.73 (5.67)	0.002	28.42 (6.85)	27.04 (5.40)	0.005
Family income to poverty (mean (SD))	2.40 (1.64)	2.45 (1.74)	0.722	2.81 (1.68)	3.08 (1.75)	0.142
Smoking status (%)						
Current	1988 (26.0)	77 (59.2)	<0.001	31 227 546 (24.6)	1 125 638 (53.0)	<0.001
Ever	1097 (14.3)	19 (14.6)		20 619 373 (16.2)	425 555 (20.0)	
Never	4563 (59.6)	34 (26.2)		75 163 769 (59.1)	572 883 (27.0)	
Not available	6 (0.1)	0 (0.0)		64 341 (0.1)	0 (0.0)	
Passive smoking (%)						
Yes	1339 (17.5)	58 (44.6)	<0.001	20 276 302 (16.0)	944 053 (44.4)	<0.001
No	6278 (82.0)	72 (55.4)		106 138 576 (83.5)	1 180 023 (55.6)	
Not available	37 (0.5)	0 (0.00)		660 151 (0.5)	0 (0.0)	
Occupational exposure (%)						
Yes	3955 (51.7)	86 (66.2)	0.004	65 872 426 (51.8)	1 443 492 (68.0)	0.006
No	3426 (44.8)	42 (32.3)		57 146 593 (45.0)	648 803 (30.5)	
Not available	273 (3.6)	2 (1.5)		4 056 010 (3.2)	31 782 (1.5)	
Self-reported asthma (%)						
Yes	1093 (14.3)	27 (20.8)	0.009	18 573 023 (14.6)	320 395 (15.1)	0.023
No	6553 (85.6)	102 (78.5)		108 366 090 (85.3)	1 781 931 (83.9)	
Not available	8 (0.1)	1 (0.8)		135 916 (0.1)	21 751 (1.0)	
Self-reported emphysema (%)						
Yes	32 (0.4)	4 (3.1)	<0.001	695 925 (0.5)	64 197 (3.0)	<0.001
No	7621 (99.6)	125 (96.2)		126 338 246 (99.4)	2 026 371 (95.4)	
Not available	1 (0.0)	1 (0.8)		40 858 (0.0)	33 509 (1.6)	
Self-reported chronic bronchitis (%)						
Yes	286 (3.7)	10 (7.7)	0.002	5 015 364 (3.9)	141 679 (6.7)	0.063
No	7362 (96.2)	119 (91.5)		121 959 624 (96.0)	1 971 504 (92.8)	
Not available	6 (0.1)	1 (0.8)		100 042 (0.1)	10 894 (0.5)	
Self-reported cancer (%)						
Yes	202 (2.6)	6 (4.6)	0.371	4 228 071 (3.3)	175 608 (8.3)	0.148
No	7448 (97.3)	124 (95.4)		122 714 211 (96.6)	1 948 469 (91.7)	
Not available	4 (0.1)	0 (0.00)		132 747 (0.1)	0 (0.0)	
Self-reported congestive heart failure (%)						
Yes	40 (0.5)	1 (0.8)	0.875	707 293 (0.6)	37 463 (1.8)	0.288
No	7607 (99.4)	129 (99.2)		126 306 191 (99.4)	2 086 614 (98.2)	
Not available	7 (0.1)	0 (0.0)		61 545 (0.0)	0 (0.0)	

Continued

Table 1 Continued

Level	Unweighted			Weighted		
	Non-COPD	COPD	P values	Non-COPD	COPD	P values
Shortness of breath (%)						
Yes	707 (9.2)	34 (26.2)	<0.001	12 039 982 (9.5)	674 010 (31.7)	<0.001
No	1968 (25.7)	45 (34.6)		34 663 663 (27.3)	738 439 (34.8)	
Not available	4979 (65.1)	51 (39.2)		80 371 385 (63.2)	711 628 (33.5)	
Chronic cough (%)						
Yes	237 (3.1)	14 (10.8)	<0.001	4 391 558 (3.5)	227 198 (10.7)	<0.001
No	2437 (31.8)	65 (50.0)		42 279 634 (33.3)	1 185 251 (55.8)	
Not available	4980 (65.1)	51 (39.2)		80 403 837 (63.3)	711 628 (33.5)	
Chronic sputum (%)						
Yes	183 (2.4)	12 (9.2)	<0.001	3 052 669 (2.4)	231 115 (10.9)	<0.001
No	2377 (31.1)	63 (48.5)		41 296 940 (32.5)	1 128 389 (53.1)	
Not available	5094 (66.6)	55 (42.3)		82 725 420 (65.1)	764 573 (36.0)	
Wheezing or whistling (%)						
Yes	953 (12.5)	46 (35.4)	<0.001	15 988 216 (12.6)	660 146 (31.1)	<0.001
No	2203 (28.8)	50 (38.5)		37 833 946 (29.8)	929 252 (43.7)	
Not available	4498 (58.8)	34 (26.2)		73 252 867 (57.6)	534 679 (25.2)	
Dry cough at night (%)						
Yes	384 (5.0)	12 (9.2)	<0.001	6 230 646 (4.9)	231 170 (10.9)	<0.001
No	2364 (30.9)	62 (47.7)		41 123 698 (32.4)	1 068 392 (50.3)	
Not available	4906 (64.1)	56 (43.1)		79 720 685 (62.7)	824 515 (38.8)	
Pre-FEV_1 (mean (SD))	3.42 (0.81)	2.99 (0.84)	<0.001	3.54 (0.82)	3.07 (0.90)	<0.001
Pre-FEV_1/FVC (mean (SD))	0.81 (0.07)	0.62 (0.06)	<0.001	0.81 (0.07)	0.61 (0.07)	<0.001

NHANES results were estimated from statistical study weights. Data are presented as mean (SD) for continuous measures and n (%) for categorical measures. t-test was used for continuous variables, and Rao-Scott χ^2 test was used for categoric variables.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; pre-FEV_1, pre-bronchodilator forced expiratory volume in the first second; pre-FEV_1/FVC, pre-bronchodilator forced expiratory volume in the first second/forced vital capacity.

Patient and public involvement

There was no specific patient and public involvement in planning or execution of the study.

RESULTS

Characteristics of COPD in young people

A total of 30 442 participants in NHANES 2007–2012 were accessed and 7784 subjects aged 20–50 years who completed a PFT were included in the final analysis, including 130 COPD and 7654 non-COPD (online supplemental e-figure 1).

After statistical weights, there were 129 199 106 participants aged 20–50 years old in the USA, including COPD group (n=2 124 077) and non-COPD group (n=127 075 029). Demographic characteristics are shown in table 1. More than half of young patients with COPD (51.5%) exhibited at least one respiratory symptom, with 'wheezing and whistling' being the most common symptom. According to the weighted results, patients with COPD were more likely to be males (77.8%) and non-Hispanic whites (83.0%). Compared with non-COPD group, the patients with COPD were older, thinner and had a higher proportion of people with current smoking status, passive smoking, occupational exposure, self-reported asthma, self-reported emphysema and respiratory symptoms. The pre-bronchodilator FEV_1/FVC ratio and FEV_1 value in the COPD group were lower than those in the non-COPD group (0.6 vs 0.8 for FEV_1/FVC; 3.07 vs 3.54 for FEV_1).

The prevalence of COPD in young people

Among people aged 20–50 years, the unweighted and weighted prevalences of COPD were 1.67% and 1.64%, respectively. Prevalence was higher in males than females (2.59% vs 0.72%, p<0.001). The prevalence of COPD increased with age in the general population, as well as in females and males. The prevalence was 0.18% for 20–25, 0.95% for 26–30, 1.39% for 31–35, 1.66% for 36–40, 2.10% for 41–45 and 3.65% for 46–50 years, respectively. In the 45–50 age range, the prevalence reached up to 5.85% in males and 1.46% in females (figure 1).

The results of sensitivity analysis using the LLN in addition to the fixed ratio of 0.70 was shown in online supplemental e-table 1 and online supplemental e-figure 2.

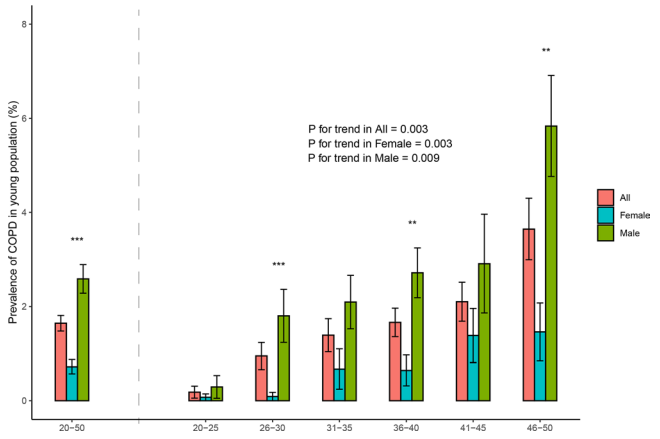

Figure 1 Prevalence of COPD in young people by sex and age. Prevalence was estimated using sample weights from NHANES. We fitted linear regression models using age groups as continuous variables to evaluate trends over time. COPD, chronic obstructive pulmonary disease; NHANES, National Health and Nutrition Examination Survey. Comparison between males and females, *p<0.05; **p<0.01; ***p<0.001.

GOLD classification, BDR and ACOS in young patients with COPD

Among young subjects with COPD, the proportions of GOLD 1–3 were 65.6%, 31.1% and 3.4%, respectively, according to the GOLD classification (figure 2A). There were 12% of young patients with COPD who had positive BDR (figure 2B). There were only 1.8% of young subjects with COPD who satisfied the definition of ACOS.

Risk factors for COPD in young people

As shown in figure 3A, males (OR=3.66; 95% CI: 2.25 to 5.95), age >35 years (OR=3.27; 95% CI: 2.01 to 5.30), non-Hispanic blacks (OR=3.78; 95% CI: 1.54 to 9.26), non-Hispanic whites (OR=6.90; 95% CI: 2.87 to 16.6), current smoking (OR=4.73; 95% CI: 2.94 to 7.60), previous smoking (OR=2.71, 95% CI: 1.44 to 5.08), passive smoking (OR=4.19, 95% CI: 2.92 to 6.00), occupational exposure (OR=1.93; 95% CI: 1.25 to 2.98), previous diagnosis of emphysema (OR=5.75; 95% CI: 1.17 to 28.32), cancer (OR=2.62; 95% CI: 1.03 to 6.63), shortness of breath (OR=2.63; 95% CI: 1.22 to 5.66), chronic cough (OR=1.85; 95% CI: 1.02 to 3.33), chronic sputum (OR=2.77; 95% CI: 1.25 to 6.17) and wheezing (OR=1.68; 95% CI: 1.01 to 2.80) were risk factors for the COPD in young people.

The results of multivariate logistic regression (figure 3B) showed that males (OR=4.56; 95% CI: 2.74 to 7.61), non-Hispanic blacks (OR=2.77; 95% CI: 1.14 to 6.75), non-Hispanic whites (OR=4.93; 95% CI: 2.16 to 11.28), current smoking (OR=2.36; 95% CI: 1.40 to 3.98), previous smoking (OR=1.92; 95% CI: 1.05 to 3.51) and passive smoking (OR=2.12; 95% CI: 1.41 to 3.20) were independent risk factors for COPD in young people.

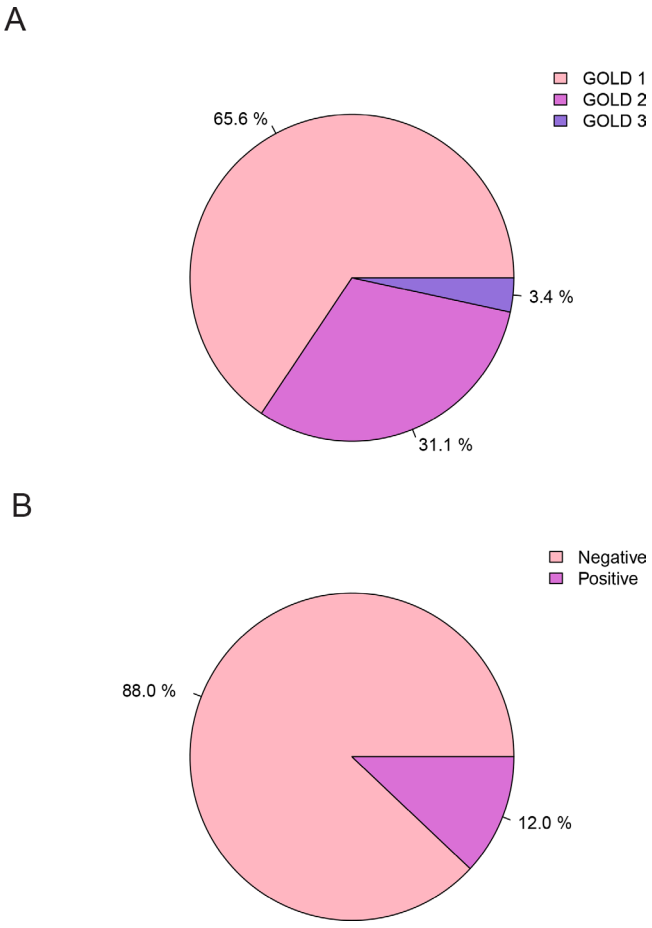

Figure 2 The GOLD classification and bronchodilator response of COPD in young people. (A) Severity of COPD in young people according to gold classification. (B) Bronchodilator response of COPD in young people. Number of patients was estimated using sample weights from NHANES. COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; NHANES, National Health and Nutrition Examination Survey.

Risk of all-cause mortality in COPD in young people

We continued with passive follow-up for survival for 7–13 years. As shown in figure 4A, compared with the gender, age and race-matched non-COPD population, a higher risk of all-cause mortality was observed in young patients with COPD (HR=3.314, p=0.0004). Meanwhile, figure 4B showed an increasing trend in the risk of mortality in young COPD compared with the gender, age, race, smoking and occupational exposure matched population, but it did not reach statistical significance (HR=1.395, p=0.269).

DISCUSSION

In our study, a retrospective population-based cohort was established to determine the prevalence, risk factors and risk of all-cause mortality of COPD in young people (20–50 years old, post-bronchodilators $FEV_1/FVC<0.7$) in the USA. To the best of our knowledge, there is a paucity

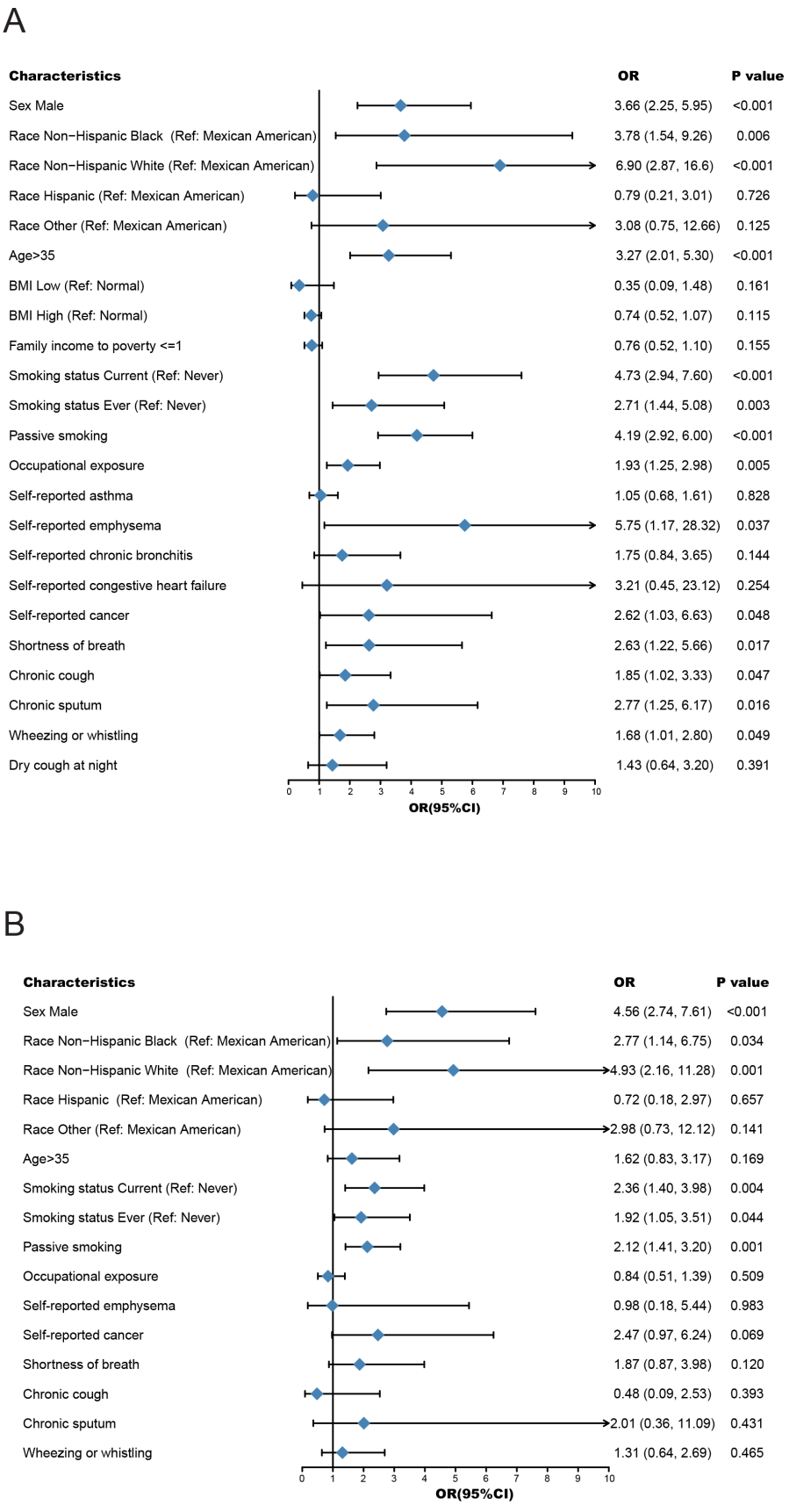

Figure 3 Logistic analysis of risk factors for COPD in young people. (A) Univariable logistic analysis of risk factors. (B) Multivariable logistic analysis of risk factors. OR and 95% CI were estimated using sample weights from NHANES. BMI<18.5 was regarded as BMI low. BMI>25 was regarded as BMI high. BMI, body mass index; COPD, chronic obstructive pulmonary disease; NHANES, National Health and Nutrition Examination Survey.

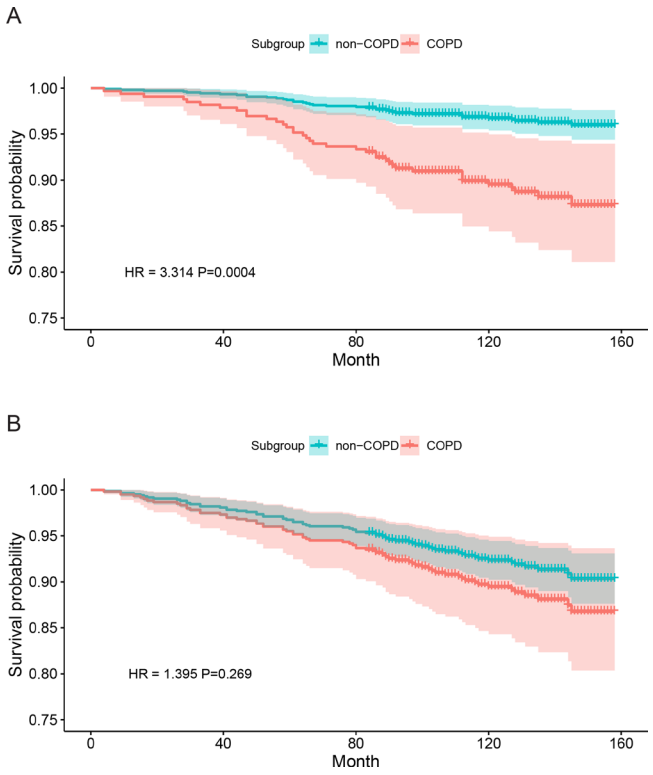

Figure 4 Risk of all-cause mortality for COPD and non-COPD in young people. (A) Survival curve for sex, age and race-matched population. (B) Survival curve for sex, age, race, smoking and occupational exposure matched population. Propensity score matching and Cox proportional hazards regression model were performed to estimate the all-cause mortality risk. COPD, chronic obstructive pulmonary disease.

of data with respect to young COPD, especially large-scale population-based studies and longitudinal observations. The main findings of the present study were shown as followings: the weighted prevalence of COPD in young people was 1.64% and it increased with age; males, non-Hispanic blacks, non-Hispanic whites, smoking and passive smoking were independent risk factors for COPD in young people; young COPD had a higher risk of all-cause mortality than the matched non-COPD (HR=3.314, p=0.0004).

Our study showed that the prevalences of COPD in young people in the USA were 0.18%, 0.95%, 1.39%, 1.66%, 2.10% and 3.65% for the 20–25, 26–30, 31–35, 36–40, 41–45 and 46–50 years, respectively. As reported previously, the China Pulmonary Health study assessed the prevalence of COPD in Chinese people aged 20–50 years, with prevalences of 1.4%, 3% and 5.1% for age 20–29, 30–39 and 40–49, years respectively.[12] Obviously, the prevalence of COPD in young people in the USA is lower than that in China. This could be attributed to the differences in smoking rates, biofuel exposure, air pollution exposure and other factors between the two countries.[13–15] In addition, we found the risk of COPD is more attentionally demanding in young males than females, which is consistent with the results observed in the population over 40 years old.[1] Apparently, this is associated with more serious smoking exposure in males. Furthermore, the high level of oestrogen in young females might be a protective factor that could reduce the occurrence of persistent airflow restriction by stimulating alveolar regeneration and maintaining alveolar structure.[16]

Similar to a multicentre study based on a population aged 20–44 years in Europe,[17] our study showed that COPD in young people was dominated by GOLD 1 and GOLD 2 (96.7%), indicating that young patients with COPD were relatively mild in the severity of airflow limitation. The mild symptom and airflow limitation might not drive patients to the hospital and may result in insufficient attention paid to COPD in young people. The positive rate of BDR in our study was 12%, significantly lower than that in another large cohort study COPDgene (32.5%).[18] This difference may be distributed to the following aspects. First, our study applied a complex sampling design to obtain a nationally representative sample, while the COPDgene study did not use a random sampling method to enrol participants. Second, since the proportion of positive BDR in patients with COPD is positively correlated with the severity of airflow limitation,[19] mild airflow limitation accounting for the majority of COPD participants in our study could result in a low proportion of positive BDR. In our study, there was 12% of young patients with COPD who had positive BDR, and only 1.8% of young subjects with COPD met the ACOS criteria. Therefore, we speculate that asthma may represent a minor proportion of young COPD.

In the present study, smoking exposures, including current smoking, previous smoking and passive smoking, were shown to be independent risk factors for COPD in young people. This result was supported by previous studies and revealed the adverse effect of smoking on young people.[12 20 21] Meanwhile, we noticed that non-Hispanic blacks and non-Hispanic whites had a higher risk for COPD, and this may be attributed to their smoking behaviour and genetic susceptibility to COPD. For instance, a high prevalence of smoking and low cessation rates were found in non-Hispanic black,[22] and family history of COPD was shown to be more common in non-Hispanic whites (37.1%). Prenatal COPD could increase the risk of COPD and exacerbations in the offspring.[23] In addition, it is somewhat surprising that self-reported asthma was not shown to be a risk factor for young COPD in the present study. This might be explained by the difference between self-reported asthma and medically diagnosed asthma because the latter determined by symptoms and examinations would be more scientific and credible than self-reported asthma. Another major interpretation is that the asthma might lead to the occurrence of spirometry-defined COPD in the older population (ie, >50 years old) rather than young population.

Our survival analysis showed that young patients with COPD had a higher risk of all-cause mortality than matched non-COPD subjects. This was supported by a recent study,

in which young COPD had a ninefold increased mortality risk compared with controls.[8] Furthermore, there were different comorbidities between young COPD and old COPD, with tuberculosis, substance use and bipolar disorders being distinct comorbidities associated with increased mortality risk in young COPD.[8] It is worthwhile comparing the mortality problem between young COPD and old COPD, but statistic analysis should be performed with caution, since age has strong confounding effect as a predictor of death. Another study showed that individuals with early COPD were associated with an increased risk of acute respiratory hospitalisations and early death.[7] These results suggest that early detection and intervention of young COPD may be of great importance and would improve the long-term outcomes of such a population. However, a substantial portion of patients with COPD remain underdiagnosed and untreated in many countries or regions. For example, a cross-sectional survey of China in 2007 showed that only 35.1% of patients with COPD were previously diagnosed with chronic bronchitis, emphysema or COPD.[24] Compared with older subjects, young people are less likely to be sent for spirometry and specialist clinic because of their milder symptoms, so early intervention of young COPD would be more difficult. As reported in a population-based cohort in Korea, only 6.3% of young subjects with COPD received inhalation therapy.[6]

The pathogenesis of COPD in young people is not yet fully understood. The latest research indicated that early-onset COPD might be related to impaired pulmonary development, epigenetic recoding of epithelial cells and changes in lung microbiota. Impaired pulmonary development is associated with smoke exposure during fetal life and adolescence, the history of low birth weight and being born preterm, which could lead to a small lung. Epigenetic recoding of distal airway basal epithelial cells is the earliest detectable histological change in COPD. Epigenetic recoding can accelerate the remodelling of bronchoalveolar stenosis and increase the risk of COPD. Nevertheless, the alteration in the lung microbiota can destroy airway cilia structure, reduce the efficacy of humoral immunity and induce airway inflammation, thus increasing the risk of COPD.[4 25 26]

The strengths of this study included the rigorous design and approach. Given the population-based, complex and long-term follow-up study design, our cohort comprised a nationally representative sample of adults aged 20–50 years. However, there are also some limitations in this study. First, data on longitudinal changes in pulmonary function in young patients with COPD could not be provided in this study. Second, due to the lack of detailed data on birth history, family history of respiratory disease and history of respiratory disease in childhood among the enrolled adults of NHANES, we failed to explore the relationship between the above risk factors and COPD in young people. Third, acute exacerbation event, an important outcome of COPD, was also not investigated in this study.

CONCLUSION

The weighted prevalence of COPD in young people was 1.64% in the USA from 2007 to 2012, and the prevalence increased with age. Most of the young subjects with COPD had mild airflow limitation. Males, non-Hispanic blacks, non-Hispanic whites and smoking are independent risk factors for COPD in young people, and this population has a higher risk of all-cause mortality than matched non-COPD participants. Therefore, early detection and intervention of COPD in young people may be of great significance and deserves further research.

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REFERENCES

1 Safiri S, Carson-Chahhoud K, Noori M, *et al*. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the global burden of disease study 2019. *BMJ* 2022;378:e069679.

2 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD: 2022 Reprot; 2022. Available: https://goldcopd.org/2022-gold-reports-2/
3 Martinez FJ, Agusti A, Celli BR, *et al*. Treatment trials in young patients with chronic obstructive pulmonary disease and pre-chronic obstructive pulmonary disease patients: time to move forward. *Am J Respir Crit Care Med* 2022;205:275–87.
4 Martinez FJ, Han MK, Allinson JP, *et al*. At the root: defining and halting progression of early chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2018;197:1540–51.
5 Cosío BG, Pascual-Guardia S, Borras-Santos A, *et al*. Phenotypic characterisation of early COPD: a prospective case-control study. *ERJ Open Res* 2020;6:00047-2020.
6 Jo YS, Kim KJ, Rhee CK, *et al*. Prevalence, characteristics, and risk of exacerbation in young patients with chronic obstructive pulmonary disease. *Respir Res* 2022;23:212.
7 Çolak Y, Afzal S, Nordestgaard BG, *et al*. Prevalence, characteristics, and prognosis of early chronic obstructive pulmonary disease. The copenhagen general population study. *Am J Respir Crit Care Med* 2020;201:671–80.
8 Divo MJ, Marin JM, Casanova C, *et al*. Comorbidities and mortality risk in adults younger than 50 years of age with chronic obstructive pulmonary disease. *Respir Res* 2022;23:267.
9 Schober P, Vetter TR. Logistic regression in medical research. *Anesth Analg* 2021;132:365–6.
10 Schober P, Vetter TR. Propensity score matching in observational research. *Anesth Analg* 2020;130:1616–7.
11 Fisher LD, Lin DY. Time-dependent covariates in the cox proportional-hazards regression model. *Annu Rev Public Health* 1999;20:145–57.
12 Bhasin S, Ellenberg SS, Storer TW, *et al*. Effect of testosterone replacement on measures of mobility in older men with mobility limitation and low testosterone concentrations: secondary analyses of the testosterone trials. *Lancet Diabetes Endocrinol* 2018;6:879–90.
13 World Health Organization. WHO global report on trends in prevalence of tobacco use 2000-2025. Available: https://www.who.int/publications/i/item/9789240039322 [Accessed 16 Nov 2021].
14 World Health Organization. WHO ambient air quality database 2022. 2022. Available: https://www.who.int/publications/m/item/who-air-quality-database-2022
15 Reitsma MB, Flor LS, Mullany EC, *et al*. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and initiation among young people in 204 countries and territories, 1990-2019. *Lancet Public Health* 2021;6:e472–81.
16 Kamil F, Pinzon I, Foreman MG. Sex and race factors in early-onset COPD. *Curr Opin Pulm Med* 2013;19:140–4.
17 de Marco R, Accordini S, Cerveri I, *et al*. An international survey of chronic obstructive pulmonary disease in young adults according to GOLD stages. *Thorax* 2004;59:120–5.
18 Bhatt SP, Fortis S, Bodduluri S. New guidelines for Bronchodilator responsiveness in COPD: a test in search of a use. *Am J Respir Crit Care Med* 2022;206:1042–4.
19 Li Y, Lin J, Wang Z, *et al*. Bronchodilator responsiveness defined by the 2005 and 2021 ERS/ATS criteria in patients with asthma as well as chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2022;17:2623–33.
20 Perez-Padilla R, Menezes AMB. Chronic obstructive pulmonary disease in Latin America. *Ann Glob Health* 2019;85:7.
21 Sutradhar I, Das Gupta R, Hasan M, *et al*. Prevalence and risk factors of chronic obstructive pulmonary disease in Bangladesh: a systematic review. *Cureus* 2019;11:e3970.
22 Ho JY, Elo IT. The contribution of smoking to black-white differences in U.S. mortality. *Demography* 2013;50:545–68.
23 Sikjær MG, Klitgaard A, Hilberg O, *et al*. Parental COPD as a risk factor for the development of COPD and disease severity in offspring: a systematic Scoping review. *Int J Chron Obstruct Pulmon Dis* 2022;17:1323–38.
24 Zhong N, Wang C, Yao W, *et al*. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med* 2007;176:753–60.
25 Martinez FD. Early-life origins of chronic obstructive pulmonary disease. *N Engl J Med* 2016;375:871–8.
26 Soriano JB, Polverino F, Cosio BG. What is early COPD and why is it important? *Eur Respir J* 2018;52:1801448.