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Combined effect of ozone and household air pollution on COPD in people aged less than 50 years old

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ABSTRACT:

Objectives Air pollution has been suggested as an important risk factor for chronic obstructive pulmonary disease (COPD); however, evidence of interactive effects on COPD between different factors was sparse, especially for young adults. We aimed to assess the combined effects of ambient ozone (O_3) and household air pollution on COPD in young individuals.

Methods We conducted a population-based study of residents aged 15–50 years in the low-income and middle-income regions of western China. We used multivariable logistic regression models to examine the associations between long-term ozone exposure and COPD in young individuals.

Results A total of 6537 young cases were identified among the participants, with a COPD prevalence rate of 7.8 (95% CI 7.2% to 8.5%), and most young COPD individuals were asymptomatic. Exposure to household air pollution was associated with COPD in young patients after adjustment for other confounding factors (OR 1.82, 95% CI 1.41 to 2.37). We also found positive associations of COPD with O_3 per IQR increase of 20 ppb (OR 1.92, 95% CI 1.59 to 2.32). The individual effects of household air pollution and O_3 were 1.68 (95% CI 1.18 to 2.46) and 1.55 (95% CI 0.99 to 2.43), respectively, while their joint effect was 3.28 (95% CI 2.35 to 4.69) with the relative excess risk due to interaction of 1.05 (95% CI 0.33 to 1.78).

Conclusions This study concludes that exposure to ambient O_3 and household air pollution might be important risk factors for COPD among young adults, and simultaneous exposure to high levels of the two pollutants may intensify their individual effects.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Ozone and household air pollution are considered to be major risk factors for non-smoking people with chronic obstructive pulmonary disease (COPD). Early exposure to these risk factors may be failed to achieve optimal lung function trajectories, which may contribute to younger population with COPD. We aimed to estimate the prevalence of COPD for young individuals in the low-income and middle-income regions and identify the combined effect of ozone and household air pollution on COPD for these populations.

WHAT THIS STUDY ADDS

⇒ Our findings confirmed that COPD in the young population is highly prevalent but most are asymptomatic. Simultaneous exposure to ambient ozone and household air pollution could intensify their individual effects on COPD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The prevalence of COPD in young people is no longer negligible. Enhancing prevention and control of air pollution (including ozone and household air pollution) should be considered public health priorities in low-income and middle-income regions.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in low-income and middle-income countries (LMICs), leading to substantial clinical, economic and societal burdens.[1 2] COPD has been traditionally considered a disease of old people, self-inflicted by tobacco smoking, air pollution, tuberculosis and other environmental factors. Many studies on COPD have mainly focused on older patients aged more than 40 years with established severe disease, as these cases comprise a significant proportion of the clinical consultations.[3 4] Yet, it is time for a change that attached importance to the primary prevention of COPD for young adults. It is anticipated that early diagnosis of COPD in young individuals may offer a window of opportunity for taking preventive measures and pharmacological interventions, resulting in better outcomes and slowing down disease progression.

Air pollution contributes to approximately 50% of the risk of COPD, and more so in LMICs.[5] Household air pollution (HAP) is mainly caused by the burning of solid fuel for cooking or heating and is associated with a variety of respiratory diseases. Approximately half of the world's population uses solid fuels, especially in rural areas in LMICs. The most highly exposed are women of childbearing age and young people.[6] Several epidemiological studies have reported an increased risk of COPD with HAP.[7–9] Ambient ozone (O_3), a typical secondary air pollutant, has been ranked as the fifth largest cause of COPD in recent decades. The effects of ozone exposure on COPD include contributions to COPD mortality,[10] new-onset COPD[11] and an increased

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risk of COPD hospital admission.[12] However, no evidence of the interactive effects of HAP and O_3 has been reported. Given that both air pollutants have irritated effects on COPD, we thus hypothesised that HAP and O_3 may have both independent and interactive associations with the prevalence of COPD among young individuals.

In this context, we first aimed to describe the general characteristics of people with COPD among young participants aged 15–50 years in the low-income and middle-income regions. In addition, we also investigated whether exposure to HAP and O_3 was associated with COPD and examined their combined effects on COPD in the study population.

METHODS

Study design and participants

The multistage stratified sampling was used to enrol a regionally representative sample of adults aged 15 years or older between June 2015 and August 2016, details of which have been reported elsewhere.[13 14] First, 13 districts or counties (4 cities and 9 counties) were selected in both urban and rural areas of Tibet and Xinjiang using the probability proportional to size method. Then, two streets and townships were selected with the simple random sampling method from each city and county, respectively. Third, three communities or village communities were selected using simple random sampling method from each of the street or township, respectively. Finally, participants from each of the sex/age strata from communities or villages were chosen using the simple random sampling method. Only one participant was selected from each household. The proportion of samples from each gender and age group was based on the 2010 census of Chinese population. A standardised questionnaire covering sociodemographic status, living conditions, respiratory symptoms, comorbidities, and environmental and occupational factors was administered by experienced interviewers at local community health centres. Furthermore, a range of physical measurements was taken using a standard protocol, including anthropometry, blood pressure, oxygen saturation by pulse oximetry and lung function by spirometry.

Pulmonary function tests were measured by trained technicians in all qualified study participants (spirometry) with a MasterScreenTM Pneumo PC spirometer (CareFusion, Yorba Linda, California) according to the American Thoracic Society/European Respiratory Society.[15] Each participant underwent the same procedure two times, before and after receiving a bronchodilator (BD) (400 µg of salbutamol through a 500 mL spacer). The forced expiratory manoeuvres were performed 3–8 times until the lung function results achieved acceptable repeatability, defined as the differences between the two highest forced expiratory volume in 1 s (FEV_1) values and the two highest forced vital capacity (FVC) values within 150 mL.[16] Data were uploaded daily to a database and examined for inconsistencies by the study supervisors and the principal investigator. Quality control was performed by a field supervisor at the filing centre and included analysis of flow volume curves for artefacts and appropriate techniques. We excluded those participants whose lung function results did not meet the quality control requirements.

COPD was defined as a postbronchodilator FEV_1/FVC ratio of <0.70 based on Global Initiative for Chronic Obstructive Lung Disease guidelines. Young COPD was a subpopulation of the population with COPD less than 50 years of age.[17 18] A postbronchodilator FEV_1/FVC ratio below the lower limit of normal (LLN) was used to define young COPD for the 15–50 years in a sensitivity analysis based on the reference values on GLI lung function equations for a North East Asian population. Small airway dysfunction was diagnosed when at least two of these three indicators, MMEF, FEF at 50% of vital capacity and FEF at 75% of vital capacity, were less than 65% of predicted values.[19] HAP was defined as the use of charcoal, coal, coke, wood, crop residues or dung as the primary means of cooking or heating during the previous 6 months or longer. Ever smoker, never smoker, post-tuberculosis, occupational exposure, history of asthma and respiratory symptoms have been previously reported.[13 14]

Ground maximum daily 8-hour average (MDA8) ozone concentrations were predicted by random forest models at the daily level and 1 km×1 km spatial resolution in 2013–2019 in mainland China. The detailed methodology was described in a previous study and summarised here.[20] Random forest models were developed by combining ground ozone measurements from fixed stations, ozone simulations from the Community Multiscale Air Quality modelling system, meteorological parameters, road length, elevation and population density. Overall, the tenfold cross validation R^2 and root-mean-square error values between the measured and predicted MDA8 ozone at the daily level of the random forest models were 0.80 and 20.93 $\mu g/m^3$, respectively. The monthly and annual mean ozone concentrations were calculated for each grid cell at a 1 km spatial resolution. They were assigned to participants based on the geographical coordinates, which were converted by the specific address information through geocoding.

Statistical analysis

All analyses were performed with R statistical program V.4.0.3 (www.r-project. org/). The statistically significant differences were tested by analysis of variance or Student's t-test for continuous variables and by χ^2 test for categorical variables. Multivariable logistic regression models were built to explore risk factors (sex, age, body mass index (BMI), educational level, smoking status, HAP, history of tuberculosis, occupational exposure, history of asthma and O_3 exposure) for young COPD. The variance inflation factor was used to detect collinearity between variables. It is generally believed that there is no multicollinearity when the variance inflation factor is less than 10.[21] We then examined the concentration–response relationship between exposure to O_3 and COPD in young individuals using a natural spline smoothing function.

We conducted multivariable logistic regression models to investigate associations of young COPD with ozone and risk factors (smoking status, HAP, occupational exposure, history of tuberculosis and history of asthma) with adjustment for potential confounding covariates (sex, age, education level, BMI, smoking status, HAP, occupational exposure, history of tuberculosis and history of asthma except for grouping factor). Ozone levels were categorised into quartiles according to the distribution of ozone, and the lowest quartile group of ozone combined with no exposure to related risk factors was used as the reference group in the logistic regression model. Ozone levels were divided into three groups according to the 25th and 75th percentiles of ozone exposure. Group 1 is defined as ozone lower than 58 parts per billion (ppb) (<25 percentile). And group 2 is defined as ozone between 58–77 ppb (25th–75th percentile). While group 3 is defined as ozone higher than 78 ppb (≥75th percentile).

To evaluate interaction effects between exposure variables, interactions of ozone and HAP were evaluated by using multiplicative and additive interaction terms. The multivariable logistics model fit via multiplicative interaction was assessed by including

a product term between O_3 and HAP. The product term between O_3 and HAP is the multiplicative interaction coefficient. 'exp(-multiplicative interaction coefficient)=1' means no interaction; 'exp(multiplicative interaction coefficient)>1' represents synergistic effect; 'exp(multiplicative interaction coefficient)<1' represents antagonism effect.[22] Additive interactions were examined using three indicators: relative excess risk due to interaction (RERI), attributable proportion (AP) and synergy index (SI).[23] RERI or AP more than 0 or SI greater than 1 denoted a synergetic interaction, meaning that the joint effects of O_3 and HAP were larger than the sum of their individual effects. RERI or AP less than 0 or SI smaller than 1 indicated an antagonistic interaction, meaning that with simultaneous exposure to the two pollutants, one pollutant could reduce the effect of the other.[24 25] We classified O_3 into two levels (low and high) using the median value as the cut-point, based on which we created a new variable to represent the combination of the variable. As a categorical variable, it had four categories: (1) low O_3 exposure and no exposure to HAP; (2) low O_3 exposure and exposure to HAP; (3) high O_3 exposure and no exposure to HAP and (4) high O_3 exposure and exposure to HAP. Differences with two-sided $p<0.05$ were considered statistically significant.

RESULTS

Participants were recruited between June 2015 and August 2016. Of the 12 991 subjects invited to participate in the survey, 11 747 completed the survey questionnaire. After excluding 3630 participants aged more than 50 years old, 8117 participants underwent the spirometry examination. Among them, 1056 participants were excluded from this analysis because they could not complete post-BD testing; 504 participants were excluded because they had no reliable spirometric data. The final analysis for determining COPD included 6537 individuals (3256 men and 3281 women), with an overall mean age of 33.39 (SD 10.23) years (online supplemental figure 1).

The distribution of our study population by general characteristics and risk factors is summarised in table 1. Young COPD individuals were more likely to be older, overweight, have a lower educational level and have a more frequent history of asthma. They had a higher frequency of exposure to HAP and a higher concentration level of O_3. When compared with subjects without COPD, these participants had worse pre-BD and post-BD lung function parameters. Most young people with COPD had small airway dysfunction (SAD, 84.2%), but we still found that approximately 30.3% of young adults without COPD suffered from SAD. Online supplemental table 1 presents the exposures, respiratory symptoms and spirometric results of SAD participants among young participants without COPD. These subjects with SAD had lower pre-BD and post-BD spirometric values, more recurrent wheezing symptoms, a more frequent history of asthma and TB, and more exposure to environmental factors such as HAP, ambient O_3 and occupational exposure compared with 'no SAD' participants.

The overall prevalence of COPD was 7.8% (95% CI 7.2% to 8.5%) among the young population aged less than 50 years or older (online supplemental table 2). Men had a higher prevalence (8.7%, 95% CI 7.2% to 9.1%) than women (7.6%, 95% CI 6.7% to 8.5%), but the difference for sex was not statistically significant (p=0.434). The prevalence increased with age and was 4.9% (95% CI 4.1% to 5.8%) among individuals aged 15–30 years, 7.6% (95% CI 6.5% to 8.9%) among participants aged 31–40 years and 11.8% (95% CI 10.4% to 13.3%) among those aged 41–50 years or older (p<0.001 for age difference). The overall prevalence of LLN-defined COPD was 14.0% (95% CI 13.2% to 14.9%), with 13.8% (95% CI 12.6% to 15.2%) in men and 14.3% (95% CI 13.1% to 15.5%) in women. The prevalence of LLN-defined COPD by sex and age group is shown in online supplemental figure 2. Main respiratory symptoms by COPD grades are presented in online supplemental table 3. Approximately 24.7% of COPD subjects self-reported typical respiratory symptoms, such as frequent cough, sputum, recurrent wheezing or apnoea.

In multivariable-adjusted analyses, male sex, age, underweight (BMI<18.5 kg/m²), history of asthma, exposure to HAP and O_3 were significantly associated with the risk of COPD among the young population (figure 1). In addition, we assessed the cumulative effects of O_3 exposure according to the IQR group on young COPD patients (table 2). A significant interaction was noted between O_3 exposure and HAP. Compared with those without exposure to HAP and exposed to less than 58 ppb O_3, the risk of COPD was increased (OR 3.94, 95% CI 2.53 to 6.41) among HAP-exposed people who were exposed to 78 ppb or more O_3. Figure 2 shows the concentration–response relationships of ambient O_3 with COPD among the young population in the multivariable regression models.

Table 3 depicts the interaction between HAP and O_3 on the prevalence of COPD in young people by additive interactions analysis. Using the low O_3-no HAP group as a reference, we found that the ORs in the other three groups (low-yes, high-no and high-yes) were higher than that in the reference group. In the interaction model, we found a larger joint effect than the sum of their individual effects, indicating a synergistic interaction. The individual effects of HAP and O_3 were 1.68 (95% CI 1.18 to 2.46) and 1.55 (95% CI 0.99 to 2.43), respectively, while their joint effect was 3.28 (95% CI 2.35 to 4.69) with the RERI of 1.05 (95% CI 0.33 to 1.78), the AP of 0.32 (95% CI 0.10 to 0.54) and the SI of 1.85 (95% CI 0.99 to 3.46). The multiplicative interaction analysis was presented in online supplemental table 4.

DISCUSSION

To the best of our knowledge, this is the first study to estimate the prevalence and burden of COPD among young participants in the low-income and middle-income regions of Western China. First, using a rigorous sampling design and stringent quality control process, we found the overall prevalence of COPD to be rather high (7.8%), considering the young age of the participants for the first time, and the prevalence of COPD has been reported among the Chinese population aged <20 years in China. Second, approximately one-third of young adults without COPD suffer from SAD. These people with SAD were exposed to high concentrations of ambient O_3 and had a higher proportion of HAP. Finally, ambient O_3 and HAP were identified as major preventable risk factors for COPD. In particular, there may be a synergistic interaction between O_3 and HAP on the effect of COPD in young individuals in the study population.

Many epidemiological studies have reported the prevalence of COPD among young individuals. The Epidemiological Study of COPD in Spain study on the prevalence of COPD established that the global prevalence of COPD in individuals aged <50 years was 3.8% (95% CI 2.9% to 5.0%).[26] The Global Burden of Disease study identifies a large geographical heterogeneity of COPD prevalence in those aged <50 years by country; prevalence is highest in males in Papua New Guinea (4.99%) and United Arab Emirates (4.35%) and in females in Papua New Guinea (6.16%) and Taiwan (6.01%).[5] The LEAD study found

Table 1 Characteristics of participants with chronic obstructive pulmonary disease aged less than 50 years

	Total (n=6537)	Non-COPD (n=6026)	COPD (n=511)	P value
Demographic characteristics				
Gender				
Male	3256 (49.8%)	2993 (49.7%)	263 (51.5%)	0.462
Female	3281 (50.2%)	3033 (50.3%)	248 (48.5%)	
Age, years	33.39 (10.23)	33.07 (10.22)	37.17 (9.47)	<0.001
Education attainment				
Primary school and lower	2271 (34.7%)	2060 (34.2%)	211 (41.3%)	<0.001
Middle and high school	2908 (44.5%)	2678 (44.4%)	230 (45.0%)	
College and higher	1358 (20.8%)	1288 (21.4%)	70 (13.7%)	
BMI, kg/m^2	23.92 (4.06)	23.89 (4.10)	24.28 (3.62)	0.036
City dwellers	2301 (35.2%)	2153 (35.7%)	148 (29.0%)	0.002
Exposures				
Cigarette smoking				
Never-smoker	4757 (72.8%)	4399 (73.0%)	358 (70.1%)	0.161
Ever-smoker	1777 (27.2%)	1624 (27.0%)	153 (29.9%)	
History of TB	327 (5.0%)	294 (4.9%)	33 (6.5%)	0.143
Household air pollution	4551 (69.6%)	4127 (68.5%)	424 (83.0%)	<0.001
Occupational exposure	668 (10.6%)	606 (10.4%)	62 (12.6%)	0.150
O_3 exposure, ppb	69.67 (10.92)	69.37 (10.95)	73.27 (9.83)	<0.001
Lung function parameters				
FVC pre-BD % pred	101.86 (19.90)	101.66 (19.83)	104.24 (20.54)	0.005
FVC post-BD % pred	101.64 (19.11)	101.31 (18.75)	105.56 (22.57)	<0.001
FEV_1 pre-BD % pred	97.34 (19.86)	98.85 (18.94)	79.60 (21.83)	<0.001
FEV_1 post-BD % pred	99.61 (20.07)	101.66 (18.69)	75.46 (20.02)	<0.001
FEV_1/FVC post-BD, %	83.62 (9.89)	85.60 (7.00)	60.32 (9.18)	<0.001
MMEF pre-BD % pred	73.13 (28.75)	75.64 (27.83)	43.58 (22.07)	<0.001
MMEF post-BD % pred	81.46 (60.84)	84.70 (58.40)	40.86 (74.62)	<0.001
$FEF_{50\%}$ pre-BD % pred	83.02 (28.06)	85.87 (26.59)	49.48 (22.69)	<0.001
$FEF_{50\%}$ post-BD % pred	90.25 (29.83)	94.20 (27.17)	41.67 (14.44)	<0.001
$FEF_{75\%}$ pre-BD % pred	81.42 (37.75)	83.95 (37.05)	51.49 (32.73)	<0.001
$FEF_{75\%}$ post-BD % pred	91.55 (40.84)	95.19 (39.64)	46.77 (26.42)	<0.001
Respiratory symptoms	1618 (24.8%)	1492 (24.8%)	126 (24.7%)	1.000
SAD	2233 (34.5%)	1807 (30.3%)	426 (84.2%)	<0.001
History of asthma	203 (3.1%)	179 (3.0%)	24 (4.7%)	0.043

Data are expressed as the number (%) or mean (SD). The statistically significant differences were tested by analysis of variance or Student's t test for continuous variables and by $\chi 2$ test for categorical variables.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEF, forced expiratory flow; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HAP, household air pollution; MMEF, mMaximum mid-expiratory flow; O_3, Ozone; post-BD, post-bronchodilator; ppb, parts per billion; pre-BD, pre-bronchodilator; SAD, small airway dysfunction; TB, tuberculosis.

that the prevalence of pre-BD FEV_1/FVC<LLN increased with age, from 6.6%, 8.8% to 8.6% in adolescence and early adulthood (15–30 years), adulthood (30–45 years) and late adulthood (45–60 years).[27] In a recent large epidemiological study in China, the prevalence of COPD in adults aged 20–49 years was 2.1% (95% CI 1.4% to 3.2%).[28] However, these studies included older people aged more than 40 years, did not strictly use random sampling, or incorporated no postbronchodilator testing. Furthermore, although for the data from China, this study emphasised residents in low-income and middle-income regions. This study describes that the prevalence of COPD was 4.9% (95% CI 4.1% to 5.8%) among individuals aged 15–30 years, 7.6% (95% CI 6.5% to 8.9%) among those aged 31–40 years and 11.8% (95% CI 10.4% to 13.3%) among those aged 41–50 years in the young individuals. Thus, there was a substantial disease burden in young participants with COPD among the low-income and middle-income regions.

Long-term O_3 exposure is a main cause of some chronic disease burdens and is influenced by the following underlying mechanisms. Only a limited number of studies have examined the associations between O_3 and COPD incidence. In the national UK cohort, Atkinson *et al* reported negative associations with COPD incidence, with hazard ratios (HRs) of 0.94 (95% CI 0.89 to 1.00) per 3 $\mu g/m^3$ increase in O_3 based on general practitioner records.[29] Another population-based cohort study of all Ontarians found that each IQR increase in pollution exposure yielded

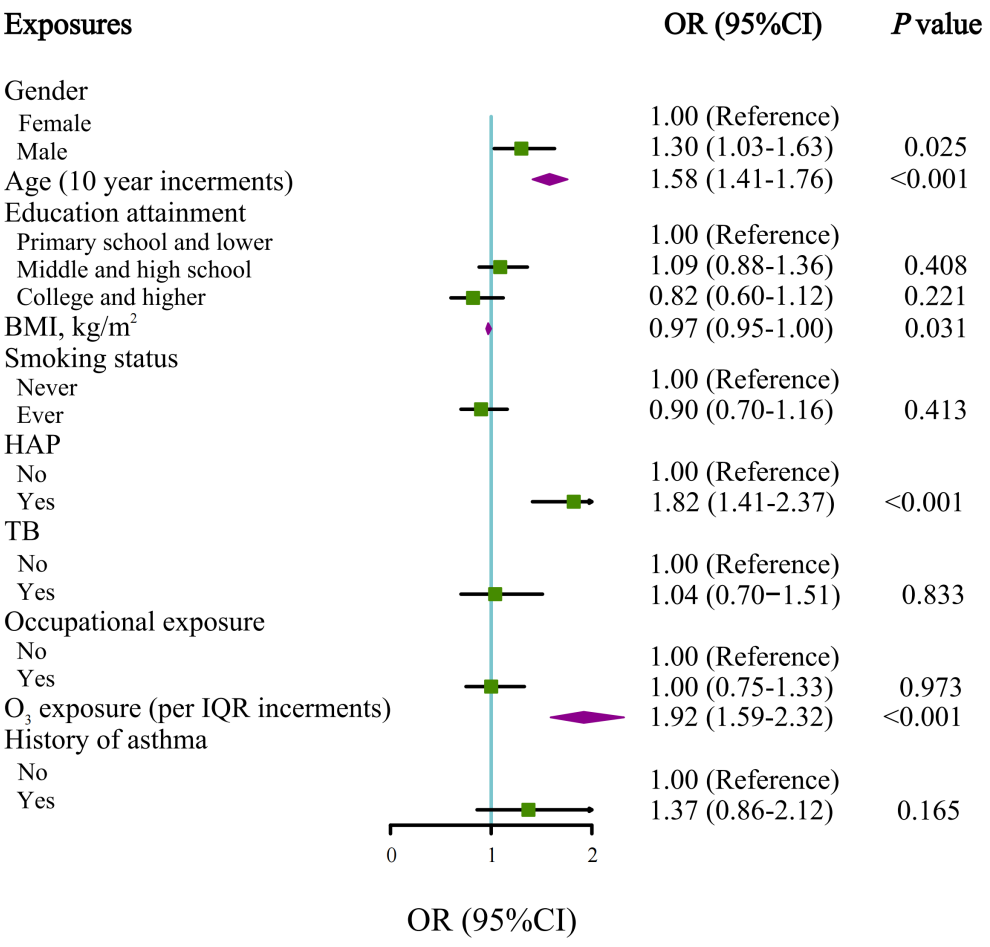

Figure 1 Forest plot showing OR for young COPD participants. Each square represents an OR. The horizontal lines indicate 95% CIs. Adjusted for age, sex, BMI and education plus history of asthma, history of TB and environmental exposures (ozone (O_3), HAP, smoking status and occupational exposure). BMI, body mass index; COPD, chronic obstructive pulmonary disease; HAP, household air pollution; TB, tuberculosis.

1.9 (1.3–2.5) excess cases of COPD per 100 000 adults for O_3.[11] The CPH study found that the association between long-term ozone exposure (warm-season average ozone concentrations of 42.1 ppb) and small airway dysfunction was consistently greater in the COPD population than in the non-COPD population.[30] In our study, we observed positive associations of COPD among young participants with a per IQR increase in O_3 (1.92, 95% CI 1.59 to 2.32) in the low-income and middle-income regions with relatively high ozone levels, suggesting that people residing in high poverty and high ozone areas have a potentially large respiratory health burden, especially COPD. Long-term exposure to ozone is associated with impaired pulmonary function,[30 31] adverse respiratory symptoms[32 33] increased hazard of COPD admissions,[12 34 35] deterioration of lung disease and increased mortality due to diseases of the respiratory system, including COPD.[10 36–38] Exposure to ozone is associated with reduced pulmonary function, increased airway inflammation and progressed emphysema. Li *et al* found that an IQR increase in ambient O_3-8 hours max (80.5 mg/m^3, 5 days) was associated with a 5.9% (95% CI −11.0% to −0.7%) reduction in FEV_1 and a 6.2% (95% CI −10.9% to −1.5%) reduction in peak expiratory flow.[31] Another study found that exposure to 0.06 ppm ozone for 6.6 hours of healthy young adults causes a significant decrement of FEV_1 and an increase in neutrophilic inflammation in the airways.[39] Niu *et al* performed the randomised, double-blind, cross-over, controlled exposure trial and revealed that inhalation of ozone could impair lung function and disturb microbiota and glucose homoeostasis in the respiratory tract.[40] The cohort study showed that ambient concentrations of O_3 were significantly associated with greater increases in percent emphysema per 10 years (O_3: 0.13 per 3 parts per billion (95% CI 0.03 to 0.24)). Ambient O_3 during follow-up was also significantly associated with greater increases in percent emphysema.[41] Overall, our findings strengthen the evidence base by adding new results to support the association between long-term exposure to ozone and risk of COPD. In addition, decisions and policies aimed at lowering the long-term O_3 concentration level are important in alleviating the public health burden associated with ambient O_3 exposures. Studies in many countries have linked solid fuel exposure to an increased risk of COPD.[7 42] HAP-related COPD showed greater small airway disease and less emphysema supported by CT scans and had more chronic bronchitis symptoms and greater bronchial hyper-responsiveness.[43] In our study, we found that the proportion of subjects exposed to HAP was fairly high (83.0% for young COPD) and COPD had an increased risk of 82% (OR 1.82, 95% CI 1.41 to 2.37) of HAP, confirming the increasingly acknowledged impact of HAP on COPD.

Table 2 Multiple-adjusted ORs of chronic obstructive pulmonary disease by ambient O_3

	O_3 exposure, ppb		
Variables*	**<58**	**58–77**	**≥78**
HAP			
No	1.00 (Reference)	1.52 (0.82–2.74)	1.71 (0.98–3.02)
Yes	1.70 (1.03–2.89)†	2.74 (1.78–4.45)§	3.94 (2.53–6.41)§
Smoking status			
Never	1.00 (Reference)	1.43 (1.04–1.98)†	2.13 (1.55–2.94)§
Ever	0.71 (0.33–1.37)	1.52 (1.04–2.24)†	1.79 (1.18–2.71)‡
History of TB			
No	1.00 (Reference)	1.53 (1.14–2.07)‡	2.15 (1.61–2.92)§
Yes	0.89 (0.26–2.24)	2.04 (1.07–3.66)†	1.99 (1.01–3.67)†
History of asthma			
No	1.00 (Reference)	1.57 (1.17–2.13)‡	2.20 (1.64–2.97)§
Yes	1.70 (0.50–4.46)	2.30 (1.10–4.43)†	2.49 (1.10–5.09)†
Occupational exposure			
No	1.00 (Reference)	1.64 (1.22–2.23)‡	2.18 (1.22–2.23)§
Yes	1.85 (0.74–4.00)	1.87 (1.22–2.84)‡	1.57 (0.84–2.76)

*First, we adjusted the common variables to be age, sex, BMI and education. Then we set grouping factor as dummy variable in combination with risk factors of COPD with adjusting for other variables. For example, when HAP as group variable, we adjusted for history of asthma, history of TB and environmental exposures (smoking status and occupational exposure).
†P<0.05.
‡P<0.01.
§P<0.001.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; HAP, household air pollution; O_3, ozone; ppb, parts per billion; TB, tuberculosis.

In this study, we did not only investigate the associations between young COPD participants and their exposure to air pollution, including ambient ozone and household environments; we also observed that ambient O_3 and HAP may have a synergistic interaction on COPD. Besides, our results found that ozone exposure level and HAP proportion were both higher in SAD

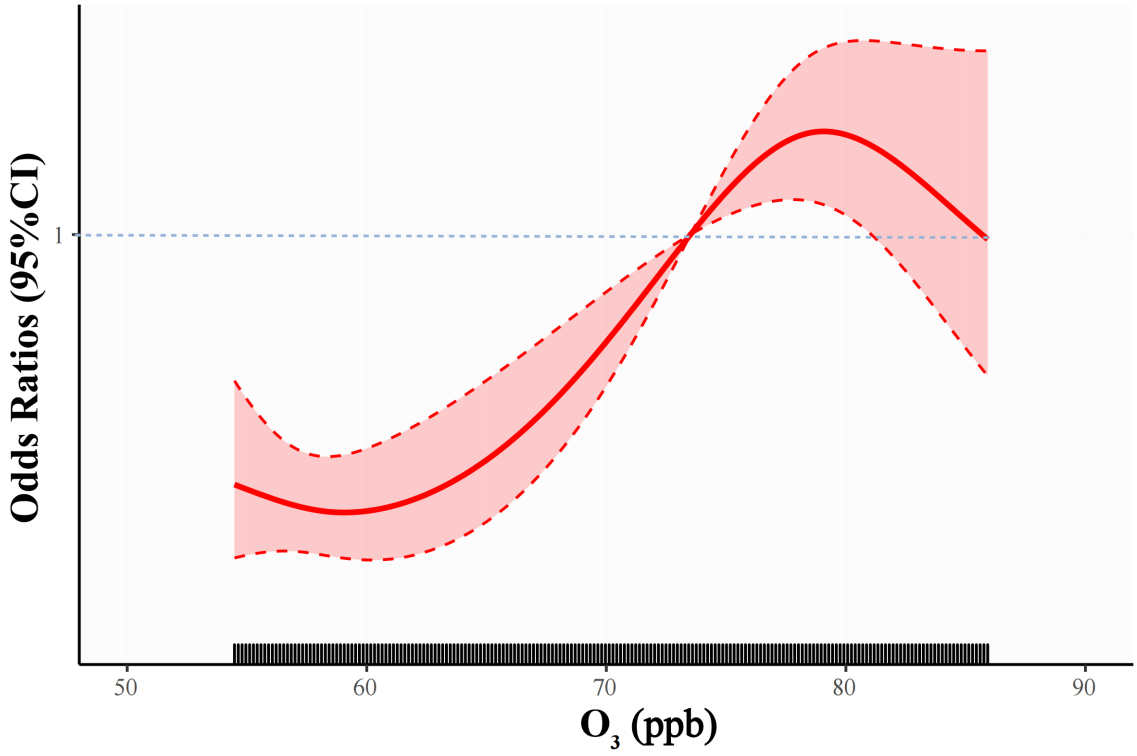

Figure 2 Concentration response curves between ozone (O_3) exposures and COPD. COPD, chronic obstructive pulmonary disease; ppb, parts per billion.

Table 3 The interactive effects between HAP and O_3 on the prevalence of COPD in the study population

Category	N	Adjusted OR* (95% CI)	P value	RERI (95% CI)	AP (95% CI)	SI (95% CI)
O_3-HAP				1.05 (0.33 to 1.78)	0.32 (0.10 to 0.54)	1.85 (0.99 to 3.46)
Low-no	1208	Reference				
Low-yes	1938	1.68 (1.18 to 2.46)	0.005			
High-no	778	1.55 (0.99 to 2.43)	0.057			
High-yes	2613	3.28 (2.35 to 4.69)	<0.001			

*We controlled for age, sex, BMI and education plus history of asthma, history of TB and environmental exposures (smoking status and occupational exposure).
AP, attributable proportion; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HAP, household air pollution; O_3, ozone; RERI, relative excess risk due to interaction; SI, synergy index.

group than in the no-SAD group among young people without COPD. The findings indicate that people exposed to HAP may be at greater risk for SAD and COPD in areas known to have higher levels of ozone exposure. Thus, addressing the threats of ambient and HAP from a range of sources will require strong public health policies such as alternatives to clean energy for heating or cooking, application of ventilation systems reducing the concentration of pollutes and avoiding exposure to multiple risk factors at the same time.

Our study findings have important public health implications. With a decline in lung function in early adulthood, a high prevalence of solid fuels, and heavy ozone pollution, the burden of COPD in young people is anticipated to continue to increase, especially in low-income and middle-income regions. Furthermore, a higher level of ozone exposure and HAP could be the most important factors for young COPD patients, as well as for SAD young individuals, providing more useful information for policymakers to consider more stringent air pollution control measures, especially in underdeveloped areas. Several limitations should be acknowledged. First, our cross-sectional research design cannot establish a causal relationship between air pollution (O_3 and HAP) and COPD. The adjustment factors involved in this study were based on the adjustment factors reported in previous studies[11 28 30] and statistical analysis. Indeed, adjustments to the cause-and-effect map may make the conclusions more accurate. Second, people with asthma were not excluded from the study population, which might cause an overestimation of COPD prevalence in younger age groups. Third, some analyses were limited by the design of the questionnaire, which was intended to be comprehensive and easy to administer, but in some cases prevented optimal detailed data collection. We were unable to quantify direct exposure to HAP caused by solid fuels beyond self-report questionnaires. Forth, the FEF_{50} predicted value was derived from the prediction equations of European Community for Steel and Coal report in 1993. The equation is more appropriate for adults aged 18–70 years, so there may be a bias for younger people.[44] Finally, ozone exposure misclassification is possible, as the ozone concentrations were estimated from the spatiotemporal models and thus may not accurately reflect individual exposure indoors. However, we believe such measurement errors should be nondifferential and so would bias the results towards the null.

CONCLUSION

In conclusion, our data document the prevalence of COPD among young residents aged 15–50 years living in the low-income and middle-income regions. Ozone exposure and HAP are major preventable risk factors for the disease, and the impact on SAD young people without COPD should also pay more attention. Moreover, it seems that simultaneous exposure to high levels of the two pollutants enhances their individual effects.

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