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RESEARCH ARTICLE

Ambient gaseous pollutant exposure and incidence of visual impairment among children and adolescents: findings from a longitudinal, two-center cohort study in China

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Abstract
Evidence on the effects of exposure to ambient gaseous pollutants on children's vision was consistently scarce. We aimed to explore the effect of ambient gaseous pollutant exposure on the incidence of visual impairment (VI) in children. From 2005 to 2018, a total of 340,313 children without VI participated in a longitudinal and two-center dynamic cohort. The logMAR acuity was used to assess visual function. The space–time extremely randomized trees model was used to estimate SO_2 and CO exposures levels. The association between SO_2 and CO and VI risks among children was assessed using a proportional hazards model with a restricted cubic spline. Subgroup analyses stratified by gender and grades were used to investigate the differences in an association of SO_2 and CO exposures with childhood VI. A total of 158381 (46.54%) children experienced an new incident VI. A ten-unit (10 μg/m^3) increase in SO_2 exposure concentrations was significantly associated with a 1.70 times higher risk of childhood VI. In addition, a 0.1-unit (0.1 mg/m^3) increase in CO exposure was significantly associated with a 1.22 times higher risk of childhood VI. The positive association between ambient gaseous pollutants (including SO_2 and CO exposures) and childhood VI risks remained even after adjusting for other environmental variables. An increase in the incidence of VI in children was positively linked to SO_2 and CO exposure. Such evidence might aid governments in developing strategies to interfere with children's eyesight by decreasing air pollution and changing school curricula.

Keywords Visual impairment · Children · Longitudinal study · SO_2 · CO

Introduction

Visual impairment (VI) has emerged as a major public health and social concern globally, with significant negative consequences for people's health, as well as economic and educational prospects (Eckert et al. 2015). VI was

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characteriszed by the loss of visual acuity, which meant that a person's eyesight could not be corrected to a "normal" level (World Health Organization 2021). It was estimated that VI affected an estimated 405 million people globally in 2015 (Bourne et al. 2017). The population of children and adolescents aged 7 to 18 with VI in China even exceeded 152 million by 2020 and was expected to increase to nearly 180 million by 2030 (Sun et al. 2015). Thus, the increasing prevalence of VI promoted many countries to implement national policies for preventing VI development, including China, which had the highest prevalence of childhood VI worldwide (Jan et al. 2019).

Given the high prevalence of VI and its explicit and adverse health effects in children and adolescents, research on its influencing factors were always a hot research topic. Many previous studies explored factors affecting VI in children and adolescents, such as physical activities, parental behaviors, genetic effects, and environmental factors (Morgan et al. 2018). Among many environmental factors, air pollution was always an important one due to its association with multiple health issues at various periods of life (Wei et al. 2019). Adverse health effects of air pollution were reported in numerous studies, such as cardiovascular diseases (Kim et al. 2017; Parker et al. 2018), cancer(Weinmayr et al. 2018), gestational hypertension (Yang et al. 2018), suicide(Min et al. 2018), and respiratory diseases (Broitman and Portnov 2020; Hendryx et al. 2019). Air pollution exposure throughout infancy and early childhood damaged the lungs, inhibited lung development, and increased the risk of asthma, pneumonia, and chronic obstructive pulmonary disease later in life (Gauderman et al. 2015; Korten et al. 2017).

Some studies explored the effects of air pollution on human eyes and found that the consequences of ambient air pollution were particularly harmful to the eyes during the early period of children and adolescents who were experiencing the eye development (Chien et al. 2014). Air pollution could irritate the eyes directly, particularly in the cornea and conjunctiva, causing dryness and inflammation (Cui et al. 2018; West et al. 2013). One direct evidence was that air pollution increased outpatient visits for nonspecific conjunctivitis (Malerbi et al. 2012; Matsuda et al. 2015), and another similar study also confirmed such evidence in Taiwan population (Wei et al. 2019). Prior animal experiments showed that fine particulate matter induced myopia in hamsters by enhancing inflammation (Wei et al. 2019). The majority of prior researches concentrated on the negative effects of NO_X and fine particulate matter on vision (Malerbi et al. 2012; Matsuda et al. 2015; Wei et al. 2019), whereas few studies explored the effects of sulfur dioxide (SO_2) and nitric oxide (CO) on vision. Thus, there was a lack of researches on the association between gaseous pollutants and VI, especially in causal demonstration researches with new incident VI in children and adolescents, which could help policymakers and individuals take relevant measures to improve visual health in children and adolescents.

Therefore, we used a longitudinal dynamic cohort study in two cities of China with 340313 children and adolescents without visual impairment at baseline to examine the following two objectives: (1) to explore the association between long-term gaseous pollutant (SO_2 and CO) exposure concentrations and the incidence of VI in children and adolescents; and (2) to examine the concentration–response relationship between gaseous pollutant concentrations and risk ratios of the incidence of VI in children and adolescents.

Methods

Study design

A longitudinal, two-center, dynamic cohort study was conducted from 2005 to 2018 in two typical cities of Beijing and Zhongshan city, China. The annual physical examination survey, which covered all school-aged children and adolescents in the two cities, was used to generate the longitudinal dynamic cohort. All students had a unique individual ID number that was used to link with annual survey data. Our research group participated in the design and implementation of these two surveys, so the comparability of their measured data could be guaranteed.

All participants from these two surveys underwent a complete medical examination to ascertain their VI status and incidence. Medical examination data in each survey year included height, weight, test date, birth date, school location, and unaided distance visual acuity. The data of students from primary, middle, and high schools from 2005 to 2018 in two cities were included in the study, and the health individual ID of each student was used to identify those who had undergone medical examinations for both academic years. Height and weight were measured while the students wore light clothing without shoes. Age was calculated using the examination date minus birthdate. Sociodemographic variables, including gender and grade level, were included in this study. Students with missing data (weight, height, birthday, and unaided distance visual acuity) were excluded. Students with VI at baseline were excluded. Finally, a total of 340313 students without VI from Beijing (266528) and Zhongshan (73785) were included in the current study (as shown in Fig. 1).

Assessment of air pollution

Two compounds include gas pollutants: SO_2 and CO. A 10-km resolution gaseous pollutants around schools were collected from the ChinaHighAirPollutants (CHAP) dataset,

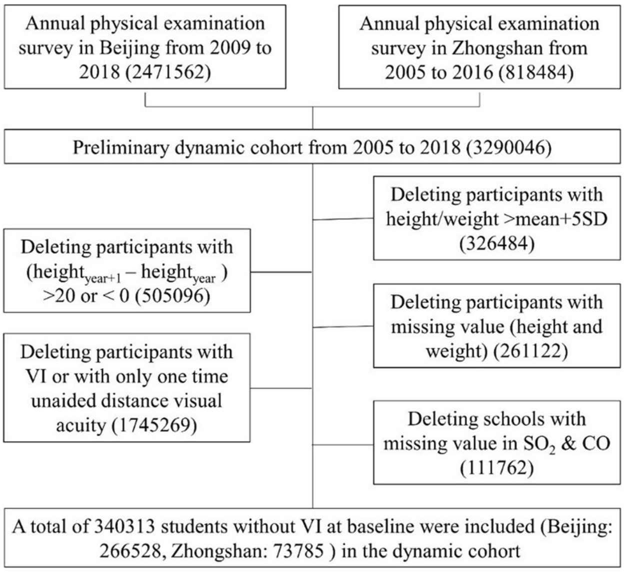

Fig. 1 Flow chart of generating dynamic cohort

which were estimated from big data utilizing the developed Space–Time Extra-Trees (STET) model (Wei et al. 2021, 2022). In short, we trained STET models individually with tenfold cross-validation in the high-resolution surface of SO_2 and CO concentrations from 2013 to 2018 with full coverage utilizing meteorological data, surface stress, satellite remote sensing products, and a multisolution emission inventory. Out-of-sample tenfold cross-validation (10-CV) approach was utilized for near-face gaseous pollutants to assess the overall performance of the model. Similarly, gaseous pollutant exposure was evaluated using the annual average gaseous pollutant concentration for each study year. The data on gas pollutants were matched to the schools' addresses. Figure 2 shows the temporal distribution and geographical distribution in Beijing and Zhongshan city.

Ascertainment of the incident of visual impairment

A retro illuminated logMAR chart with tumbling-E optotypes (Precision Vision) (Lougheed 2014) was used to measure the unaided distance visual acuity for each eye of children and adolescents. In the current study, the definition of visual impairment (VI) was based on the definitions for population surveys set by the International Council of Ophthalmology in cooperation with the World Health Organization and the International Agency for the Prevention of Blindness (Colenbrander 2002). VI was defined

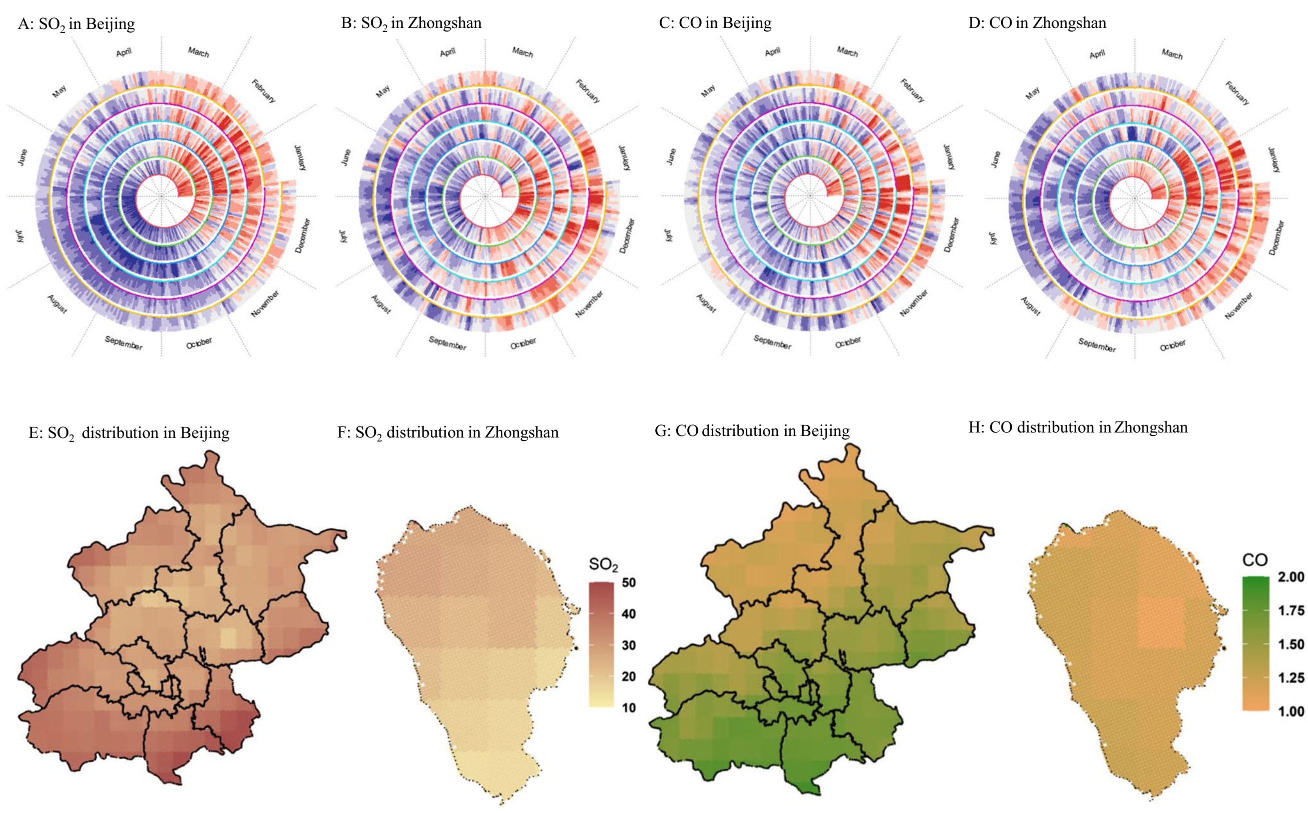

Fig. 2 Temporal and geographical distributions of gaseous pollutant concentrations in Beijing and Zhongshan. Note: Subfigures A to D represent the temporal distribution in Beijing and Zhongshan, respectively. Blue and red represent low- (< P50) and high-level (> P50) air pollutants, respectively. Subfigures E to H represents the geographical distribution in Beijing and Zhongshan, respectively

as unaided distance visual acuity (UDVA) lower than 4.9 (5/6 Snellen equivalent) in either eye (Jan et al. 2019). Considering the large sample size, it was not feasible to diagnose myopia according to its diagnostic criteria (cycloplegic refraction). A previous study indicated that logMAR has high sensitivity and specificity to diagnose myopia (O'Donoghue et al. 2012), so logMAR has been widely used in large population studies (Jan et al. 2019).

For all participants, the UDVA was measured by qualified optometry physicians for each eye. Participants who stand at a distance of 5 m from the logMAR chart were required to indicate the direction of the E optotype within 5 s in the UDVA examination. Using a staircase protocol to test the UDVA began at the fourth line from the bottom (6/6). Identifying a fourth of five optotypes was considered a correct response. The UDVA of the eye was determined by the lowest line to read correctly. The participants were advanced to 2.5 or 1 m when the top line was not read correctly. VI was defined as unaided distance visual acuity lower than 4.9 (5/6 Snellen equivalent) in either eye (Jan et al. 2019). Among all students, the student's VI was examined at the same time in each academic year.

Statistical analysis

Continuous variables were reported as the mean and standard deviation (SD), and the frequencies were calculated for categorical variables. To assess the separate association between SO_2 and CO around school and the onset of VI among children and adolescents, as well as their dose–response relationship, the restricted cubic spline (RCS) with 3 knots combined with proportional hazards model (Cox model) was applied to calculate the risks ratio (RR) with both qualitative and quantitative results after adjusting for age, grade level (primary school, junior high school, and high school), sex, height, weight, city, fine particulate matter ($PM_{2.5}$), and NO_2. We categorized the SO_2 and concentrations into four groups: Q1, first quartile (< 9.07 μg/m^3); Q2, second quartile (9.07–11.51 μg/m^3); Q3, third quartile (11.51–16.16 μg/m^3); and Q4, fourth quantile (> 16.16 μg/m^3). CO was categorized into four groups based on the quartiles of CO as follows: Q1 (< 0.88 mg/m^3); Q2 (0.88–1.07 mg/m^3); Q3 (1.07–1.28 mg/m^3); and Q4 (> 1.28 mg/m^3). To investigate these confounding effects, we utilized double-exposure models. A two-exposure model connected the health results to two environmental factors at the same time. Stratification analysis was also utilized by gender. The R software (version 4.0.3) was used to perform all analyses. The packages "survival" and "rms" were used to fit the Cox model and restrict the cubic spline model, respectively. Statistical significance was defined as a two-tailed *p* value of less than 0.05.

Results

Characteristics of participants

Characteristics of participants were shown in Table 1. A total of 340,313 participants with 144,781 (42.50%) girls and 195,532 (57.50%) boys were included in the current study. The mean (SD) age was 11.30(2.64) years. During the follow-up year, a total of 158,381 (46.54%) children and adolescents experienced a new incidence of VI.

Separate association between SO_2 and CO exposure and incidence of VI

Long-term SO_2 and CO exposure increased the risks of VI in children, and the risks increased with the quantiles of exposure to SO_2 and CO concentrations. After adjusting for confounders, compared with quartile 1 with the lowest SO_2 exposure concentrations, the adjusted RRs were 1.33 (95% CI: 1.31–1.35) in quartile 2, 1.57 (95% CI, 1.55–1.60) in quartile 3, and 2.26 (95% CI, 2.22–2.29) in quartile 4. The adjusted RRs were 1.20 (95% CI, 1.18–1.23) in quartile 2, 2.13 (95% CI, 2.10–2.17) in quartile 3, and 2.30 (95% CI, 2.26–2.35) in quartile 4, compared with quartile 1 of the lowest CO exposure (Table 2).

Dose–response relationship between SO_2 and CO exposure and incidence of VI

Data were fitted by a restricted cubic spline Cox regression model to explore the dose–response relationship between SO_2 and CO concentration and the incidence of VI. Figure 3 shows a statistically significant positive association between SO_2 and CO exposure and the incidence of VI in children and adolescents after adjustment for age, grade level, sex, weight, height, age, city, fine particulate matter, and NO_2. Because the nonlinear analysis results were close to the linear relationship between them, the quantitative results showed that a ten-unit (10 μg/m^3) increase in SO_2 exposure concentrations was significantly associated with a 1.50 times higher risk of VI among children and adolescents. In addition, a 0.1-unit (0.1 mg/m^3) increase in CO exposure was significantly associated with a 1.19 times higher risk of VI. In the double exposure model, the association between SO_2, CO, and VI was robust.

Table 1 Baseline characteristics of 340313 participants

Characteristics		Overall (N = 340,313)	Non-VI (N = 181,932)	VI (N = 158,381)
Enter year, N (%)	2005	277 (0.08)	194 (70.0)	83 (30.0)
	2006	402 (0.12)	262 (65.2)	140 (34.8)
	2007	513 (0.15)	315 (61.4)	198 (38.6)
	2008	1181 (0.35)	491 (41.6)	690 (58.4)
	2009	19,784 (5.81)	11,013 (55.7)	8771 (44.3)
	2010	23,075 (6.78)	11,556 (50.1)	11,519 (49.9)
	2011	38,261 (11.2)	18,575 (48.5)	19,686 (51.5)
	2012	48,494 (14.2)	25,660 (52.9)	22,834 (47.1)
	2013	69,178 (20.3)	33,103 (47.9)	36,075 (52.1)
	2014	54,353 (16.0)	30,222 (55.6)	24,131 (44.4)
	2015	54,868 (16.1)	33,048 (60.2)	21,820 (39.8)
	2016	29,237 (8.59)	16,987 (58.1)	12,250 (41.9)
	2017	690 (0.20)	506 (73.3)	184 (26.7)
Grade level (N,%)	Primary school	243,850 (71.7)	121,986 (50.0)	121,864 (50.0)
	Junior high school	71,434 (21.0)	43,080 (60.3)	28,354 (39.7)
	High School	25,029 (7.35)	16,866 (67.4)	8163 (32.6)
Gender (N,%)	Girls	144,781 (42.5)	69,498 (48.0)	75,283 (52.0)
	Boys	195,532 (57.5)	112,434 (57.5)	83,098 (42.5)
City, N (%)	Beijing	266,528 (78.3)	132,630 (49.8)	133,898 (50.2)
	Zhongshan	73,785 (21.7)	49,302 (66.8)	24,483 (33.2)
Age, mean (sd, year old)		11.30 (2.64)	11.70 (2.77)	10.8 (2.41)
Height, mean (sd, cm)		146 (22.6)	149 (15.8)	142 (28.0)
Weight, mean (sd, kg)		41.8 (16.4)	43.7 (16.5)	39.6 (16.0)
$PM_{2.5}$, mean (sd, μg/m^3)		60.6 (20.1)	56.6 (20.3)	65.1 (18.9)
NO_2, mean (sd, μg/m^3)		13.3 (6.69)	12.5 (6.40)	14.2 (6.90)
SO_2, mean (sd, μg/m^3)		13.3 (6.69)	12.5 (6.40)	14.2 (6.90)
CO, mean (sd, mg/m^3)		1.08 (0.22)	1.04 (0.22)	1.13 (0.21)

VI, visual impairment

Table 2 Separate association between SO_2 and CO exposure and incidence of VI with RRs (95% CI) of quartile logistic regression results

Parameter		RR	95% CI
SO_2 (crude model)	Q2 vs. Q1	1.27	1.25–1.29
	Q3 vs. Q1	1.44	1.41–1.46
	Q4 vs. Q1	2.05	2.02–2.08
SO_2 (adjusted model)	Q2 vs. Q1	1.33	1.31–1.35
	Q3 vs. Q1	1.57	1.55–1.60
	Q4 vs. Q1	2.26	2.22–2.29
CO (crude model)	Q2 vs. Q1	1.30	1.28–1.32
	Q3 vs. Q1	2.09	2.06–2.12
	Q4 vs. Q1	2.34	2.30–2.37
CO (adjusted model)	Q2 vs. Q1	1.20	1.18–1.23
	Q3 vs. Q1	2.13	2.10–2.17
	Q4 vs. Q1	2.30	2.26–2.35

all models were adjusted for gender, grade level, height, weight, age, city, fine particulate matter, and NO_2, and the results were presented as risk ratios (RRs) with 95% CIs; *Q1*, first quartile; *Q2*, second quartile; *Q3*, third quartile; *Q4*, fourth quartile

Discussion

To our knowledge, this was the first study to assess the effect of exposure to SO_2 and CO on new VI incident among Chinese school-aged children and adolescents using a longitudinal study with large sample size. We found that a significantly increased risk of VI was associated with a high concentration of SO_2 and CO exposure around school settings. Our findings were of great public health significance, supporting the urgent need and potential benefits of effective air pollution mitigation strategies for the prevention of childhood VI.

Many previous studies on the population health of air pollution focused on the association with multiple specific chronic diseases, such as cancer, cardiovascular disease, lung disease, and their mortality (Atkinson et al. 2014; Guan et al. 2016); however, only a few studies explored the associations between air pollution exposure and eye health, such as retinal vein occlusion (Zhang et al. 2019), dry eye (Mandell et al. 2020), retinal microvasculature (Louwies et al.

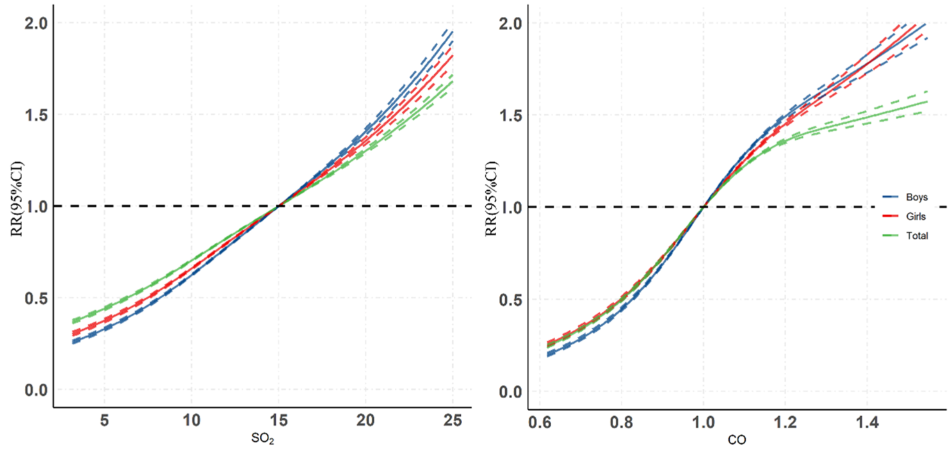

Fig. 3 The relationship between the concentration of SO_2, CO, and risk of VI in children and adolescents. Note: single exposure model included SO_2 and CO as exposure, separately; double exposure model included SO_2 and CO as the exposure simultaneously

Exposure	RR(95%CI, single exposure model)	RR(95%CI, double exposure model)
SO_2	1.50 (1.49-1.51)	1.25 (1.24-1.26)
CO	1.19 (1.19-1.20)	1.12 (1.11-1.12)

2013), nonspecific conjunctivitis (Matsuda et al. 2015; Tau et al. 2013), and myopia (Wei et al. 2019). These studies confirmed the ecological correlation between air pollution and eye health; that is, air pollution, especially fine particulate pollution, could increase the risk of some types of eye diseases. However, evidence from a longitudinal study on clear causality between ambient gaseous pollutants and eye health was lacking. Thus, the current study made up for the evidence in the effects of ambient gaseous pollutants on VI among the pediatric population.

We found that long-term SO_2 and CO exposure was associated with an increased risk of VI in children and adolescents. Some potential mechanisms could help explain such results. Usually, exposure to SO_2 and CO might affect the outdoor activity plans. For example, when children and adolescents were exposed to high levels of pollution, they might postpone or suspend plans for outdoor activities. Previous studies found that the exposure time to sunlight could partly explain the difference between SO_2 and CO exposure on the risk of VI in children and adolescents (Morgan et al. 2018). The connection between SO_2 and CO exposure and childhood VI episodes might be explained by several underlying causes and processes. SO_2- and CO-induced oxidative damage and inflammation might be key potential routes. Another possible mechanism was that air pollution lowered outdoor activities and sunshine exposure in children and adolescents.

A lack of long-term outdoor activity could reduce the exposure time to sunlight. Increases in SO_2 and CO were frequently followed by increasing other air pollutants (such as fine particulate matter and NO_X), resulting in an exacerbation of air pollution (Wang et al. 2021). Rising air pollutants concentration could reduce the amount of time spent outdoors and time exposed to sunlight, and increase the time of secondary behavior (Yu et al. 2018). Time spent outdoors was an important protective factor against VI (Wu et al. 2016). In human and animal studies on myopia, there was increasing evidence that ambient light exposure was an important factor in the regulation of eye development (Ashby et al. 2009; Backhouse et al. 2013; Cohen et al. 2011). Outdoor natural light was a kind of full-spectrum high-intensity light that was conducive to promoting the secretion of dopamine. Dopamine could mediate the inhibition of eye growth and acts upstream of the choroid, causing a temporary increase in the thickness of the choroid (Nickla and Wallman 2010). One study with 18 months of follow-up found that children without myopia received a daily quantity of illumination significantly higher than those myopic children, and the lack of light myopic eye axis in children was growing significantly faster than the average daily amount of light higher than myopia in children (Read et al. 2015). Thus, when pollutants were low, parents and teachers might consider expanding children's outside activities flexibly to support ocular axis growth and development.

The current findings had several implications in the following aspects. Firstly, our study confirmed the effects of SO_2 and CO on VI among children and adolescents. It was also helpful for the government to formulate policies to improve visual health among children and adolescents. It also suggested that families should take the effects of air pollution on visual acuity into account in addition to behavioral intervention when taking measures to prevent myopia in children and adolescents. We suggested that parents adjusted their children's outdoor activities according to the concentration of pollutants in the weather forecast. When the sun was abundant and the concentration of pollutants was low, it was recommended to take children outdoors for physical activities so that they could receive enough sunlight and avoid SO_2 and CO exposures. Secondly, the government and schools needed to pay more attention to the way children and adolescents performed physical exercise when air pollution was serious. We recommended that the Education Department should give schools a more flexible policy on physical activity. At present, the school was relatively inflexible when making the student physical education curriculum. We recommended that schools considered air pollution when formulating physical education curricula and reducing outdoor activities while increasing indoor activities when air pollution was serious. At the same time, the school would set the stadium in a position that could receive enough light according to the geographical location of the school and the situation of receiving light.

Our study had two notable strengths. Firstly, we used two longitudinal data sources to verify the effect of SO_2 and CO on VI in children and adolescents. Secondly, the current study involved many schools and a large-scale sample to verify the effects of long-term and short-term exposure to SO_2 and CO on VI in children and adolescents, which increased the credibility and extrapolation of the results. Despite these strengths, the findings from our study should be interpreted in the context of several potential limitations. Firstly, there might be bias in the determination of VI, and the classification of myopia and farsightedness could not be identified at the same time. However, visual acuity varied greatly during childhood and adolescence, and research on VI could help to guide policy-making for VI prevention. Secondly, the medical examination did not investigate detailed information in students, such as time spent on physical activity, smoking status, drinking status, parents' myopia status, and education levels, which could also be associated with students' vision health. Thirdly, although this study assessed SO_2 and CO exposure in the schools' settings, due to the lack of home addresses of students, the exposure of SO_2 and CO around school and home could not be comprehensively considered. Fourthly, pollutant exposure in the same school was assessed by the geographical location of the schools; thus, the exposure assessment was the same for every student in the same school. However, such an assessment method could not accurately assess the exposure level of SO_2 and CO for everyone, which could lead to overestimation or underestimation. This was appropriate for large studies where long-term exposure assessment was applied in our study, and long-term exposure assessment focused more on overall exposure levels over long periods.

Conclusion

In conclusion, in this large longitudinal dynamic cohort of Chinese children and adolescents, we found that an increased incidence of VI in children and adolescents was associated with SO_2 and CO exposure, which represented obvious adverse effects of SO_2 and CO on VI with potential explicit causality. This study could help governments formulate policies to intervene in students' vision by reducing air pollution, adjusting the schools' curriculum and prompting parents to adjust children's outdoor activities according to air quality.

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Author contribution LC and YHD conceived and designed the study. LC carried out the initial analyses and prepared the first draft of the manuscript. TM, DG, XJW, BW, MMC, YHL, JJ, LJW, WML, XTL, YS, JW, YHD, XHG, and JM critically reviewed and revised the manuscript. YS, YHD, and XHG conducted the research and collected the data. JW provided the data of air pollutants. All authors read and approved the final manuscript.

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Data availability Researchers should be able to have reasonable access to the data from the corresponding authors. The CHAP dataset is freely available at https://weijing-rs.github.io/product.html.

Declarations

Ethics approval This project was approved by the Medical Research Ethics Committee of Peking University Health Science Center (Reference Number: IRB00001052-20033).

Consent to participate Not applicable. The current study used data from annual medical examinations, and the Medical Research Ethics Committee allowed us to not acquire individual informed permission.

Competing interests The authors declare no competing interests.

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