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Association of long-term exposure to ambient air pollutants with blood lipids in Chinese adults: The China Multi-Ethnic Cohort study

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ABSTRACT

Background: Dyslipidemia is a crucial risk factor for cardiovascular diseases. Previous studies have suggested that air pollution is associated with blood lipids. However, little evidence exists in low- and middle-income regions. We aimed to investigate the association between air pollution and blood lipids in southwestern China.

Methods: We included 67,305 participants aged 30–79 years from the baseline data of the China Multi-Ethnic Cohort (CMEC) study. Three-year average concentrations of particles with diameters ≤1 μm (PM_1), particles with diameters ≤ 2.5 μm ($PM_{2.5}$), particles with diameters ≤ 10 μm (PM_{10}), nitrogen dioxide (NO_2), and ozone (O_3) were estimated using satellite-based spatiotemporal models. Individual serum lipids, including cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), were measured. Linear, logistic, and quantile regression models were used to evaluate the association between ambient air pollution and blood lipids.

Results: All five air pollutants in our study were associated with lipid levels. Increased air pollution exposure was associated with a high risk of dyslipidemia. Each 10 μg/m^3 increase in $PM_{2.5}$ was associated with 0.92% (95% confidence interval (CI): 0.64%, 1.20%), 2.23% (95% CI: 1.44%, 3.02%), and 3.04% (95% CI: 2.61%, 3.47%) increases in TC, TG, and LDL-C levels, respectively, and a 2.03% (95% CI: 1.69%, 2.37%) decrease in HDL-C levels, and high risks of dyslipidemia (OR = 1.14, 95% CI: 1.10, 1.18). Stronger associations of air pollution with blood lipids were found in participants with high lipid levels than in those with low lipid levels.

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Conclusion: Long-term exposure to air pollutants was associated with blood lipid levels and the risk of dyslipidemia. People with high lipid levels were more susceptible to air pollution. Therefore, air pollution prevention and control may help reduce the incidence of dyslipidemia and the burden of CVDs.

1. Introduction

Dyslipidemia refers to an abnormal level of blood lipids, involving elevated levels of total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C) (Reiner et al., 2011). Moreover, it is one of the most critical risk factors for cardiovascular diseases (CVDs) (Laslett et al., 2012), which are a leading cause of death, accounting for 18.6 million deaths per year worldwide (Roth et al., 2020).

As a major global environmental problem, ambient air pollution has been shown to promote the development of risk factors for CVDs (Brook et al., 2010, 2014; Cesaroni et al., 2014; Jiang et al., 2016) through multiple pathways, such as increased systemic inflammation and oxidative stress (Pope et al., 2004; Rajagopalan et al., 2018).

In recent years, many studies have explored the associations between ambient air pollution and lipid profile parameters or dyslipidemia, but the results from these studies have been inconsistent (Bell et al., 2017; Kim et al., 2019; Mao et al., 2020; Rajagopalan et al., 2018; Sørensen et al., 2015; Wang et al., 2018). Additionally, most studies have been conducted in high-income countries, and evidence among people in low- and middle-income countries (LMICs) is limited, where air pollution is often more severe (Murray et al., 2020; Yusuf et al., 2020). The annual average population-weighted $PM_{2.5}$ level in China was 52.7 $\mu g/m^3$ in 2017 (Yin et al., 2020), which was five times higher than the World Health Organization (WHO) air quality guideline (10 $\mu g/m^3$). Moreover, the mean total-to-HDL cholesterol ratio, a predictor of CVD risk (Lewington et al., 2007), has increased in China (Collaboration, 2020) due to dietary shifts and a lower treatment rate of dyslipidemia (Yang et al., 2012; Zhai et al., 2014). Given the severity of both dyslipidemia (Zhang et al., 2018) and ambient air pollution, it is necessary to investigate how air pollution in China affects blood lipid markers.

Previous studies focused primarily on the average lipid levels, but little is known about how the overall distribution of blood lipids is associated with ambient air pollution. Given that the occurrence and development of dyslipidemia is a continuous process, identifying whether specific individuals with different lipid levels are more susceptible to air pollution is of considerable public health significance. Koenker and Bassett introduced quantile regression as an extension of the traditional linear regression model in the 1970s (Koenker and Bassett, 1978). Quantile regression could provide more comprehensive information by revealing the relationship between the dependent and independent variables at any quantile of the dependent variable (Staffa et al., 2019). In addition, quantile regression is a distribution-free method, making up for the limitations of traditional linear regression when blood lipid data fail to satisfy the normal distribution assumption (Bind et al., 2016). Therefore, we could use quantile regression to examine the relationship of air pollution with lipid levels across its distribution and develop more effective prevention strategies for populations with different lipid levels.

This study aimed to explore the association of air pollutants (PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3) with lipid levels and dyslipidemia using baseline data from the China Multi-Ethnic Cohort (CMEC), a community population-based prospective observational study. We also applied quantile regression to explore the shape and strength of quantile-specific associations.

2. Methods

2.1. Study population

The current study used data from the baseline of the CMEC study, which was described in detail previously (Zhao et al., 2020). The CMEC study recruited a total of 99,556 participants aged 30–79 years in Southwestern China by multistage, stratified cluster sampling method. Nine ethnic groups, including the Han in Basin (Chongqing, Chengdu), Han in Yunnan, Yi in Yunnan, Bai in Yunnan, Tibetans in Aba, Tibetans in Lhasa, Miao in Guizhou, Bouyei in Guizhou, and Dong in Guizhou, involving mixed groups of urban and rural residents in five provinces were selected. We excluded 1) people who did not have available residential address information; 2) Tibetans in Aba because they lived a nomadic life, migrating with the seasons, and had no fixed residence; 3) Tibetans in Lhasa because they had different genetic backgrounds and lived at high altitudes and thus were less comparable to people living in low and middle altitudes; 4) people who lived at their current residential address for less than three years; 5) people who did not have available information on blood lipids; 6) people who had self-reported dyslipidemia so that patients detected by clinical laboratory tests during our survey were newly-diagnosed patients; 7) pregnant women; and 8) people with missing information on covariates. Ultimately, this study included 67,305 participants. Ethical approval was received from the Sichuan University Medical Ethical Review Board (K2016038).

2.2. Exposure data

The daily average concentrations of PM_1, $PM_{2.5}$, and PM_{10} at a 1-km spatial resolution were predicted by the space-time extremely randomized trees model using aerosol optical depth, meteorological, topographical, and land-use data (Wei et al., 2019a, 2019b, 2020, 2021). In addition, NO_2 and O_3 were assessed using a random forest model at a 10-km spatial resolution using ground-monitored air pollution data, aerosol optical depth data, and other spatial and temporal predictors (Li et al., 2020; Liu et al., 2019). According to geocoded residential addresses, we assigned daily PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3 concentrations to participants. We calculated the previous 3-year average exposure concentrations of PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3 before the baseline survey time as a substitute for long-term air pollution exposure.

2.3. Outcomes

The CMEC collected participants' blood samples after at least 8 h of fasting and measured levels of TC, TG, LDL-C, and HDL-C by an AU5800 Automated Chemistry Analyzer (Beckman Coulter Commercial Enterprise, Shanghai, China). Hypercholesterolemia was defined as TC $\geq$ 6.22 mmol/L, hypertriglyceridemia was defined as TG $\geq$ 2.26 mmol/L, hypoalphalipoproteinemia was defined as HDL-C $<$ 1.04 mmol/L, and hyperbetalipoproteinemia was defined as LDL-C $\geq$ 4.14 mmol/L, according to the Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults (Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults, 2007). Participants with one or more abnormities of these lipid levels above were defined as having dyslipidemia.

2.4. Covariates

A standardized questionnaire was used to collect information including age, sex, highest educational completed, annual family income, smoking status, secondary smoke, alcohol drinking status, dietary pattern, physical activity, indoor pollution, and ethnic group. Body mass index (BMI) was calculated based on measured height and weight. Temperature and relative humidity data were obtained from weather stations of China Meteorological Data Sharing Service System (http://data.cman.c/), and daily values of temperature and relative humidity were interpolated by kriging for areas not covered by weather stations (Chen et al., 2018). The dietary pattern was evaluated by the Dietary Approaches to Stop Hypertension (DASH) diet score, which assessed fruit, vegetables, nuts, sodium, low-fat dairy, red and processed meats, and whole grain intake. Participants' physical activity was estimated by the metabolic equivalent tasks (METs) considering participants' occupation, traffic, chores, and leisure time activities (Ainsworth et al., 2000). The degree of indoor air pollution was assessed as low, moderate, or high according to the frequency of cooking, cooking fuel, and the presence of smokestacks or smoke exhaust devices.

2.5. Statistical analysis

Differences in essential characteristics between men and women were tested using Student's *t*-test, the Wilcoxon rank-sum test, and the chi-square test. We applied linear regression models to assess associations between individual air pollutants (per 10 μg/m^3 increase) and blood lipid levels (TC, TG, HDL-C, and LDL-C), which were naturally log-transformed in our regression models to achieve normal distributions. Association estimates were then back-transformed from the log scale using 100 × [exp(β)-1] and are presented as percent changes with the 95% confidence intervals (95% CI) corresponding to each 10 μg/m^3 increase in ambient air pollutants. We also used logistic regression models to investigate associations of ambient air pollutants (per 10 μg/m^3 increase) with hypercholesterolemia, hypertriglyceridemia, hypoalphalipoproteinemia, hyperbetalipoproteinemia, and dyslipidemia. These results are presented as odds ratios (ORs) with corresponding 95% CIs. Additionally, we used quantile regression models to directly explore the association between air pollutants and different quantiles of blood lipid levels expressed in the original unit, as quantile regression is a distribution-free method (Koenker and Hallock, 2000) and log-transformation is not necessary. We performed subgroup analyses by sex (men, women), age (≥60 years, <60 years), BMI (≥25 kg/m^2, <25 kg/m^2), and ethnic group (Han in Basin, Han in Yunnan, Yi in Yunnan, Bai in Yunnan, Dong in Guizhou, Bouyei in Guizhou, and Miao in Guizhou). Two-pollutant models were used to compare the results of single pollutant models. Additionally, we conducted sensitivity analyses by including participants with self-reported dyslipidemia, excluding participants who had diabetes or cardiovascular diseases, and we repeated the regression analyses applying different exposure terms (1 year, 2 years, and 4 years). We subtracted the PM_1 concentrations from the $PM_{2.5}$ concentrations to obtain concentrations of $PM_{1\text{-}2.5}$. A similar method was used to obtain concentrations of $PM_{2.5\text{-}10}$. And we investigated the effects of $PM_{1\text{-}2.5}$ and $PM_{2.5\text{-}10}$. All regression models were adjusted for the variables listed in the Covariates section. Data analysis was performed using R 4.0.2 (R Foundation for Statistical Computing), with a P value < 0.05 considered statistically significant for a two-tailed test.

3. Results

3.1. General characteristics

Table 1 displays the essential characteristics of the 67,305 participants. The mean age of the study population was 51.97 years, and 26,547 participants (39.4%) were men. Moreover, 37.1% of the

Table 1
Study population characteristics (n = 67,305).

Variables	Total (n = 67,305)	Men (n = 26,528)	Women (n = 40,777)	P
Age (years), mean ± SD	51.97 ± 11.36	52.97 ± 11.66	51.33 ± 11.12	<0.001
Ethnic group, n (%)				<0.001
Han in Basin	33,194 (49.32%)	15,208 (57.33%)	17,986 (44.11%)	
Han in Yunnan	9163 (13.61%)	3184 (12.00%)	5979 (14.66%)	
Bai in Yunnan	5202 (7.73%)	1483 (5.59%)	3719 (9.12%)	
Yi in Yunnan	5046 (7.50%)	1655 (6.24%)	3391 (8.32%)	
Bouyei in Guizhou	4629 (6.88%)	1386 (5.22%)	3243 (7.95%)	
Dong in Guizhou	5750 (8.54%)	2011 (7.58%)	3739 (9.17%)	
Miao in Guizhou	4321 (6.42%)	1601 (6.04%)	2720 (6.67%)	
Highest education completed, n (%)				<0.001
Illiteracy	15,940 (23.68%)	3338 (12.58%)	12,602 (30.90%)	
Primary school	17,394 (25.84%)	6965 (26.26%)	10,429 (25.58%)	
Junior high school	18,406 (27.35%)	8738 (32.94%)	9668 (23.71%)	
High school	8092 (12.02%)	3916 (14.76%)	4176 (10.24%)	
Junior college or higher	7473 (11.10%)	3571 (13.46%)	3902 (9.57%)	
Annual family income (Yuan/year), n (%)				<0.001
<12,000	12,001 (17.83%)	4524 (17.05%)	7477 (18.34%)	
12,000–20,000	11,748 (17.45%)	4025 (15.17%)	7723 (18.94%)	
20,000–60,000	24,496 (36.40%)	9402 (35.44%)	15,094 (37.02%)	
60,000–100,000	10,033 (14.91%)	4358 (16.43%)	5675 (13.92%)	
≥100,000	9027 (13.41%)	4219 (15.90%)	4808 (11.79%)	
Smoking status, n (%)				<0.001
Never	49,975 (74.25%)	9686 (36.51%)	40,289 (98.80%)	
Former	3261 (4.85%)	3184 (12.00%)	77 (0.19%)	
Current	14,069 (20.90%)	13,658 (51.49%)	411 (1.01%)	
Secondary smoke, n (%)				<0.001
Yes	34,607 (51.42%)	12,816 (48.31%)	21,791 (53.44%)	
No	32,698 (48.58%)	13,712 (51.69%)	18,986 (46.56%)	
Alcohol drinking status, n (%)				<0.001
Never	37,513 (55.74%)	8397 (31.65%)	29,116 (71.40%)	
Occasionally	20,509 (30.47%)	9997 (37.68%)	10,512 (25.78%)	
Often	9283 (13.79%)	8134 (30.66%)	1149 (2.82%)	
DASH score, mean ± SD	20.39 ± 4.48	19.74 ± 4.45	20.81 ± 4.45	<0.001
Physical activity (METs/day), mean ± SD	27.23 ± 18.45	27.09 ± 19.04	27.33 ± 18.05	<0.001
BMI (kg/m^2), mean ± SD	23.91 ± 3.36	24.15 ± 3.29	23.75 ± 3.39	<0.001
Indoor pollution, n (%)				<0.001
Low	10,753 (15.98%)	7873 (29.68%)	2880 (7.06%)	
Moderate	53,060 (78.84%)	17,648 (66.53%)	35,412 (86.84%)	
High	3492 (5.19%)	1007 (3.80%)	2485 (6.09%)	

(continued on next page)

Table 1 (*continued*)

Variables	Total (n = 67,305)	Men (n = 26,528)	Women (n = 40,777)	P
Temperature, mean ± SD	17.14 ± 1.13	17.24 ± 1.11	17.08 ± 1.14	<0.001
Relative humidity, mean ± SD	74.72 ± 7.04	75.41 ± 6.63	74.27 ± 7.26	<0.001
Blood lipids & dyslipidemia				
TC (mmol/L), median (P_{25}, P_{75})	4.92 (4.34, 5.58)	4.94 (4.35, 5.57)	4.91 (4.33, 5.59)	0.260
TG (mmol/L), median (P_{25}, P_{75})	1.32 (0.95, 1.92)	1.41 (0.98, 2.13)	1.27 (0.93, 1.81)	<0.001
HDL-C (mmol/L), median (P_{25}, P_{75})	1.46 (1.22, 1.73)	1.34 (1.13, 1.62)	1.52 (1.30, 1.79)	<0.001
LDL-C (mmol/L), median (P_{25}, P_{75})	2.87 (2.36, 3.43)	2.91 (2.40, 3.46)	2.84 (2.34, 3.41)	<0.001
Hypercholesterolemia, n (%)	7379 (10.96%)	2779 (10.48%)	4600 (11.28%)	0.001
Hypertriglyceridemia, n (%)	11,465 (17.03%)	5789 (21.82%)	5676 (13.92%)	<0.001
Hypoalphalipoproteinemia, n (%)	5100 (7.58%)	3265 (12.31%)	1835 (4.50%)	<0.001
Hyperbetalipoproteinemia, n (%)	5649 (8.39%)	2208 (8.32%)	3441 (8.44%)	0.610
Dyslipidemia, n (%)	19,260 (28.62%)	9160 (34.53%)	10,100 (24.77%)	<0.001

Abbreviations: DASH, Dietary Approaches to Stop Hypertension; METs: metabolic equivalent tasks; BMI, body mass index; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; P_{25}, 25th percentile; P_{75}, 75th percentile.

participants were minorities. Approximately half of them had a junior high school or higher education (50.4%). Only 13.4% of the participants had more than 100,000 Yuan annual family income. Regarding smoking and drinking status, 25.7% and 44.3% were smokers and drinkers, respectively. The prevalence of hypercholesterolemia, hypertriglyceridemia, hypoalphalipoproteinemia, and hyperbetalipoproteinemia was 11.0%, 17.0%, 7.6%, and 8.4%, respectively. A total of 19,260 participants (28.6%) were classified as having dyslipidemia. The median concentrations of TC, TG, HDL-C, and LDL-C were 4.92 mmol/L, 1.32 mmol/L, 1.46 mmol/L, and 2.87 mmol/L, respectively. Differences in age, ethnic group, highest educational completed, annual family income, BMI, smoking status, secondary smoke, alcohol drinking status, DASH score, physical activity, and indoor pollution between men and women were statistically significant. The three-year average exposure concentrations of PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3 were 27.70 μg/m^3, 37.39 μg/m^3, 64.09 μg/m^3, 24.02 μg/m^3, and 83.45 μg/m^3, respectively (Table 2).

3.2. Associations between air pollutants and blood lipids

Table 3 displays the associations between air pollutants and blood lipids. For all participants, each 10 μg/m^3 increase in $PM_{2.5}$ was associated with 0.92% (95% CI: 0.64%, 1.20%) increases in TC levels, 2.23% (95% CI: 1.44%, 3.02%) increases in TG levels, 3.04% (95% CI: 2.61%, 3.47%) increases in LDL-C levels and 2.03% (95% CI: 1.69%, 2.37%) decreases in HDL-C levels. PM_{10} had similar effects on lipid levels, while high PM_1 exposure was associated with increased TG and LDL-C levels and reduced HDL-C levels but not with TC. For gaseous pollutants, each 10 μg/m^3 increase in NO_2 was associated with a 0.56% (95% CI: 0.36%, 0.76%) increase in TC levels, a 0.52% (95% CI: 0.22%, 0.83%) increase in LDL-C levels and a 0.85% (95% CI: 0.60%, 1.09%) decrease in HDL-C levels. High O_3 exposure also showed statistically significant associations with increased TC and LDL-C levels and decreased HDL-C levels but not with TG. $PM_{1\text{-}2.5}$, $PM_{2.5\text{-}10}$ were both associated with increased TC, TG, and LDL-C levels, and decreased HDL-C levels (Table A1). The results remained basically stable in sensitivity analyses where participants with self-reported dyslipidemia were included (Table A3), participants with diabetes were excluded (Table A.5), participants with cardiovascular diseases were excluded (Table A.7), and exposure data in different terms were applied (Table A.9).

3.3. Associations between air pollutants and dyslipidemia

We found that ambient air pollutants (PM_1, $PM_{2.5}$, PM_{10}, NO_2, and O_3) were associated with the risk of dyslipidemia. In detail, we detected that increased PM_1 exposure was associated with high risks of hypertriglyceridemia (OR = 1.12, 95% CI: 1.03, 1.21) and hypoalphalipoproteinemia (OR = 1.20, 95% CI: 1.09, 1.32); increased $PM_{2.5}$ exposure was associated with high risks of hypercholesterolemia (OR = 1.12, 95% CI: 1.07, 1.18), hypertriglyceridemia (OR = 1.08, 95% CI: 1.03, 1.12), hypoalphalipoproteinemia (OR = 1.14, 95% CI: 1.08, 1.20), and hyperbetalipoproteinemia (OR = 1.11, 95% CI: 1.04, 1.18); increased PM_{10} exposure was associated with high risks of hypercholesterolemia (OR = 1.08, 95% CI: 1.05, 1.12), hypertriglyceridemia (OR = 1.04, 95% CI: 1.01, 1.07), hypoalphalipoproteinemia (OR = 1.09, 95% CI: 1.06, 1.13), and hyperbetalipoproteinemia (OR = 1.10, 95% CI: 1.06, 1.14); increased NO_2 exposure was associated with high risks of hypercholesterolemia (OR = 1.04, 95% CI: 1.01, 1.08), and hypoalphalipoproteinemia (OR = 1.12, 95% CI: 1.08, 1.16); and increased O_3 exposure was associated with high risks of hypercholesterolemia (OR = 1.14, 95% CI: 1.04, 1.24) and hyperbetalipoproteinemia (OR = 1.31, 95% CI: 1.19, 1.45) (Table 4).

3.4. Quantile regression analyses

Fig. 1 shows that the association between ambient air pollution and lipid levels varied with quantiles of lipid level distribution (with breaks at the 10th, 20th, 30th, 40th, 50th, 60th, 70th, 80th, and 90th percentiles). The effects of all air pollutants in this study were strongest at the highest percentiles of HDL-C. For example, among participants with HDL-C levels in the 10th percentile, a per 10 μg/m^3 increase in PM_1 was associated with a 0.019 mmol/L (95% CI: 0.008, 0.029) decrease in HDL-C, whereas among subjects with HDL-C levels in the 90th

Table 2
Three-year average concentrations of air pollutants.

Pollutant	Summary statistics							Spearman correlation coefficients				
	Mean	SD	Minimum	P_{25}	Median	P_{75}	Maximum	PM_1	$PM_{2.5}$	PM_{10}	NO_2	O_3
PM_1 (μg/m^3)	28.22	6.65	11.09	21.56	27.70	33.58	53.57	1.00	0.95*	0.93*	0.83*	−0.19*
$PM_{2.5}$ (μg/m^3)	41.93	16.01	16.49	26.02	37.39	55.62	105.29	0.95*	1.00	0.99*	0.81*	−0.10*
PM_{10} (μg/m^3)	72.08	23.85	33.26	51.82	64.09	91.98	165.19	0.93*	0.99*	1.00	0.80*	−0.03*
NO_2 (μg/m^3)	27.66	11.11	9.99	20.10	24.02	33.09	63.32	0.83*	0.81*	0.80*	1.00	−0.21*
O_3 (μg/m^3)	83.15	3.22	73.87	80.92	83.45	85.11	97.14	−0.19*	−0.10*	−0.03*	−0.21*	1.00

Abbreviations: PM_1, particles with aerodynamic diameter ≤1.0 μm; $PM_{2.5}$; particles with aerodynamic diameter ≤2.5 μm; PM_{10}, particles with aerodynamic diameter ≤10 μm; NO_2, nitrogen dioxide; O_3, ozone; SD, standard deviation; P_{25}, 25th percentile; P_{75}, 75th percentile.
* Statistically significant correlation ($P < 0.05$).

Table 3
Associations between per 10-μg/m^3 increment in air pollutants and blood lipid levels (n = 67,305).

Pollutant	TC		TG		HDL-C		LDL-C	
	% changes (95% CI)[a]	P	% changes (95% CI)[a]	P	% changes (95% CI)[a]	P	% changes (95% CI)[a]	P
PM_1	0.48 (−0.04, 1.01)	0.069	2.63 (1.14, 4.13)	<0.001	−2.39 (−3.03, −1.75)	<0.001	2.17 (1.36, 2.98)	<0.001
$PM_{2.5}$	0.92 (0.64, 1.20)	<0.001	2.23 (1.44, 3.02)	<0.001	−2.03 (−2.37, −1.69)	<0.001	3.04 (2.61, 3.47)	<0.001
PM_{10}	0.57 (0.40, 0.75)	<0.001	1.18 (0.69, 1.68)	<0.001	−1.85 (−2.07, −1.63)	<0.001	2.62 (2.35, 2.89)	<0.001
NO_2	0.56 (0.36, 0.76)	<0.001	−0.30 (−0.86, 0.25)	0.285	−0.85 (−1.09, −0.60)	<0.001	0.52 (0.22, 0.83)	0.001
O_3	1.34 (0.81, 1.87)	<0.001	−1.28 (−2.71, 0.17)	0.083	−5.16 (−5.78, −4.53)	<0.001	9.46 (8.60, 10.33)	<0.001

Abbreviations: PM_1, particles with aerodynamic diameter ≤1.0 μm; $PM_{2.5}$; particles with aerodynamic diameter ≤2.5 μm; PM_{10}, particles with aerodynamic diameter ≤10 μm; NO_2, nitrogen dioxide; O_3, ozone; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

[a] Adjusted for age, sex, ethnic group, highest education completed, annual family income, body mass index, smoking status, secondary smoke, alcohol drinking status, DASH score, physical activity, indoor pollution, temperature, relative humidity.

Table 4
Associations between per 10-μg/m^3 increment in air pollutants and dyslipidemias (n = 67,305).

Pollutant	Hypercholesterolemia		Hypertriglyceridemia		Hypoalphalipoproteinemia		Hyperbetalipoproteinemia		Dyslipidemia	
	OR (95% CI)[a]	P	OR (95% CI)[a]	P	OR (95% CI)[a]	P	OR (95% CI)[a]	P	OR (95% CI)[a]	P
PM_1	1.03 (0.94, 1.14)	0.492	1.12 (1.03, 1.21)	0.006	1.20 (1.09, 1.32)	<0.001	1.06 (0.94, 1.19)	0.339	1.13 (1.06, 1.21)	<0.001
$PM_{2.5}$	1.12 (1.07, 1.18)	<0.001	1.08 (1.03, 1.12)	0.001	1.14 (1.08, 1.20)	<0.001	1.11 (1.04, 1.18)	0.001	1.14 (1.10, 1.18)	<0.001
PM_{10}	1.08 (1.05, 1.12)	<0.001	1.04 (1.01, 1.07)	0.003	1.09 (1.06, 1.13)	<0.001	1.10 (1.06, 1.14)	<0.001	1.09 (1.07, 1.12)	<0.001
NO_2	1.04 (1.01, 1.08)	0.020	0.99 (0.96, 1.02)	0.501	1.12 (1.08, 1.16)	<0.001	1.01 (0.97, 1.05)	0.716	1.05 (1.03, 1.08)	<0.001
O_3	1.14 (1.04, 1.24)	0.003	0.99 (0.91, 1.07)	0.768	1.10 (0.98, 1.23)	0.093	1.31 (1.19, 1.45)	<0.001	1.15 (1.08, 1.22)	<0.001

Abbreviations: PM_1, particles with aerodynamic diameter ≤1.0 μm; $PM_{2.5}$; particles with aerodynamic diameter ≤2.5 μm; PM_{10}, particles with aerodynamic diameter ≤10 μm; NO_2, nitrogen dioxide; O_3, ozone.

[a] Adjusted for age, sex, ethnic group, highest education completed, annual family income, body mass index, smoking status, secondary smoke, alcohol drinking status, DASH score, physical activity, indoor pollution, temperature, relative humidity.

percentile, the same exposure was related to a 0.061 mmol/L (95% CI: 0.041, 0.081) decrease in HDL-C. A similar increasing trend was observed in the effects of air pollutants on TC levels. The results for TG and LDL-C levels were less consistent. For example, the associations of PM_1, $PM_{2.5}$, PM_{10}, and O_3 with TG levels were greatest for individuals with TG levels between the 70th and 80th percentiles, while NO_2 showed a decreasing trend across the whole distribution. For TG levels, the associations of PM_1, $PM_{2.5}$, PM_{10}, and NO_2 with LDL-C levels were greatest for individuals with LDL-C levels in the 80th percentile, while O_3 showed a decreasing trend across the whole distribution.

3.5. Stratified analyses

In stratified analyses by age, the associations were greater among younger people (age <60 years). For example, each 10 μg/m^3 increase in PM_1 was associated with a 0.76% (95% CI: 0.16%, 1.37%) increase in TC among participants under 60 years old, while no statistically significant association was observed among participants over 60. In stratified analyses by sex, the results were mixed. For example, the associations of NO_2 with HDL-C were greater among men than among women. However, for TC, NO_2 showed a statistically significant association only among women. In stratified analyses by BMI, associations of all air pollutants with HDL-C were consistently stronger in participants who were not overweight or obese. A 10 μg/m^3 increase in $PM_{2.5}$ was related to 2.28% (95% CI: 1.82%, 2.74%) and 1.29% (95% CI: 0.74%, 1.83%) decreases in HDL-C in normal participants (BMI < 25 kg/m^2) and overweight/obese participants (BMI ≥ 25 kg/m^2), respectively. In stratified analyses by ethnic group, we observed statistically significant interactions between air pollution and ethnic group on lipid levels, but the pattern was complex. For example, the association of PM_{10} with TC was stronger among Han in Basin, while the association of PM_{10} with HDL-C was stronger among Bai in Yunnan (Table A.11).

3.6. Two-pollutant models

Fig. 2. Showed the results of the two-pollutant models. The associations between O_3 and blood lipid levels were most stable after adding the other pollutant in the models. The associations of NO_2 with blood lipid levels also remained generally consistent after the inclusion of another pollutant. The associations of PM_1 with blood lipid levels became weaker after adjusting $PM_{2.5}$ or PM_{10}. For example, PM_1 was associated with a 2.63% (1.14%, 4.13%) increase in TG in a single pollutant model, while no statistically significant association was observed after the inclusion of $PM_{2.5}$ or PM_{10}. The associations between PM_{10} and TC, TG were weaker after adjusting $PM_{2.5}$. However, The associations between PM_{10} and HDL-C and LDL-C were greater after adjusting $PM_{2.5}$.

4. Discussion

To the best of our knowledge, the current epidemiological study is the largest to explore the associations between long-term ambient air pollution exposure and blood lipid levels and dyslipidemia in LMICs. We also revealed the quantile-specific associations between air pollution and blood lipids. As similar studies were all conducted in the U.S., our findings could fill in the gap among people in LMICs.

The precise mechanism by which ambient air pollution affects lipid levels has not yet been fully characterized. One hypothesis indicated that air pollution could induce systemic inflammation and oxidative stress (Araujo et al., 2008; Chen et al., 2013b), leading to lipid metabolism disorders (Zhang et al., 2003), including reduced HDL efflux capacity. Another theory suggested that exposure to ambient air pollution would result in abnormal DNA methylation (Bind et al., 2015; Chen et al., 2016), altering specific genes related to lipid metabolism (Bind et al., 2014).

Several previous studies investigated associations between air pollution exposure and blood lipid levels or dyslipidemia. In accordance with our findings, a large nationally representative U.S. survey found that a per 11.1 μg/m^3 increase in PM_{10} exposure was associated with 1.43%, 2.42%, and 1.18% increases in TC, TG, and LDL-C levels, respectively (Shanley et al., 2016). Another cross-sectional study from China reported that high PM_1 exposure was associated with elevated TC,

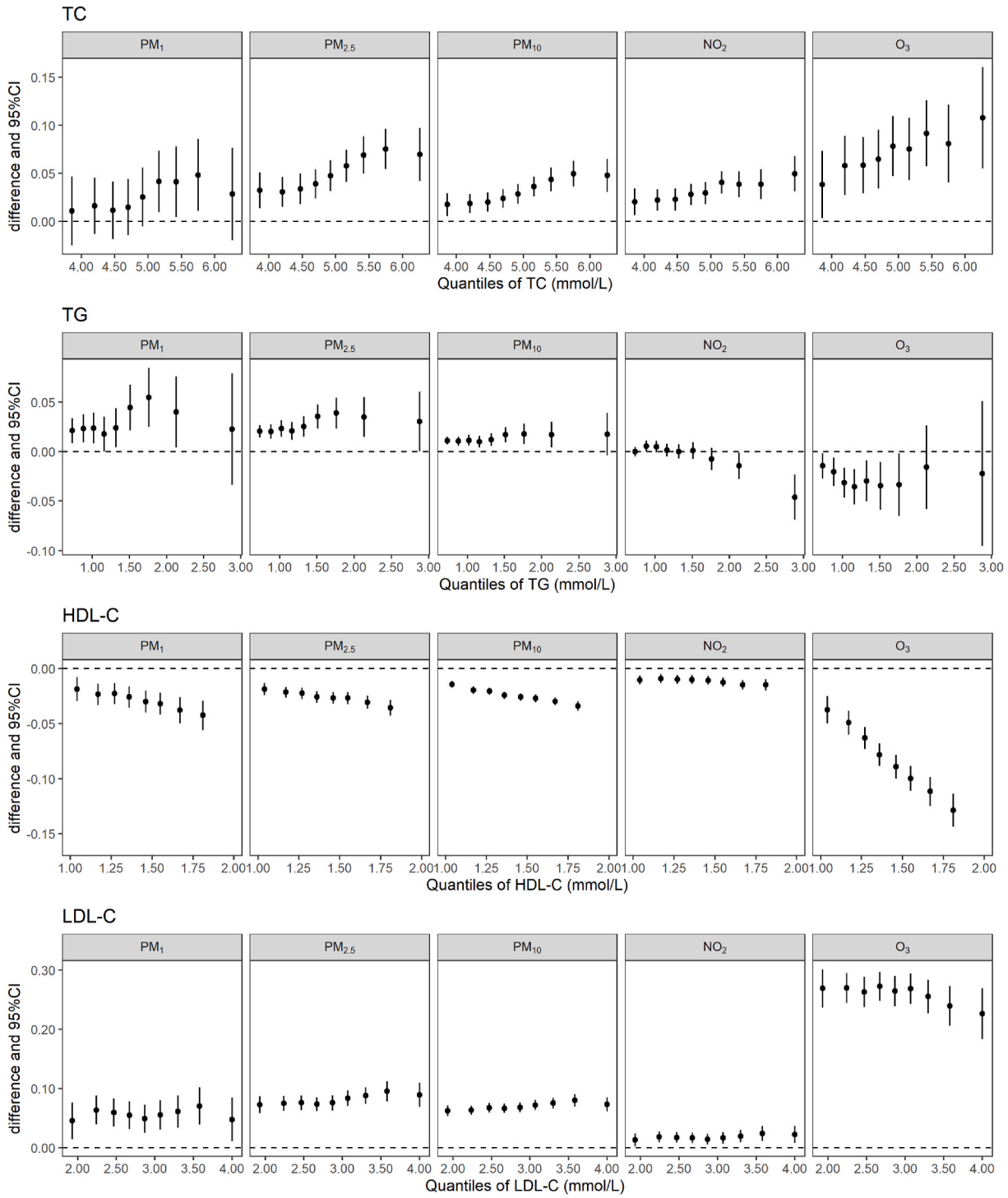

Fig. 1. Associations between per 10-μg/m^3 increment in air pollutants and quantiles of blood lipid levels
Abbreviations: PM_1, particles with aerodynamic diameter ≤1.0 μm; $PM_{2.5}$; particles with aerodynamic diameter ≤2.5 μm; PM_{10}, particles with aerodynamic diameter ≤10 μm; NO_2, nitrogen dioxide; O_3, ozone; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

TG, and LDL-C levels and decreased HDL-C levels (Yang et al., 2018). A recent study in a Chinese rural area showed a negative association between NO_2 and TG levels (Mao et al., 2020). A meta-analysis found that a 10 mg/m^3 NO_2 increase was associated with a 3.14% increase in TG levels (Gaio et al., 2019), while there was no similar statistically significant association observed in our results. The reasons underlying the inconsistent results across studies may be the differences in exposure concentration and exposure period. In addition, adjusted confounders varied across these studies, such as family income, educational attainment, race, and eating habits, leading to heterogeneity in the results.

We additionally examined the heterogeneity of the relationship between air pollution and blood lipids by applying quantile regression models. Our results showed an increasing trend for the associations of all the air pollutants with TC and HDL-C levels. An individual with high lipid levels was more susceptible to air pollutants than one with low lipid levels. Compared with the results of traditional linear models, we

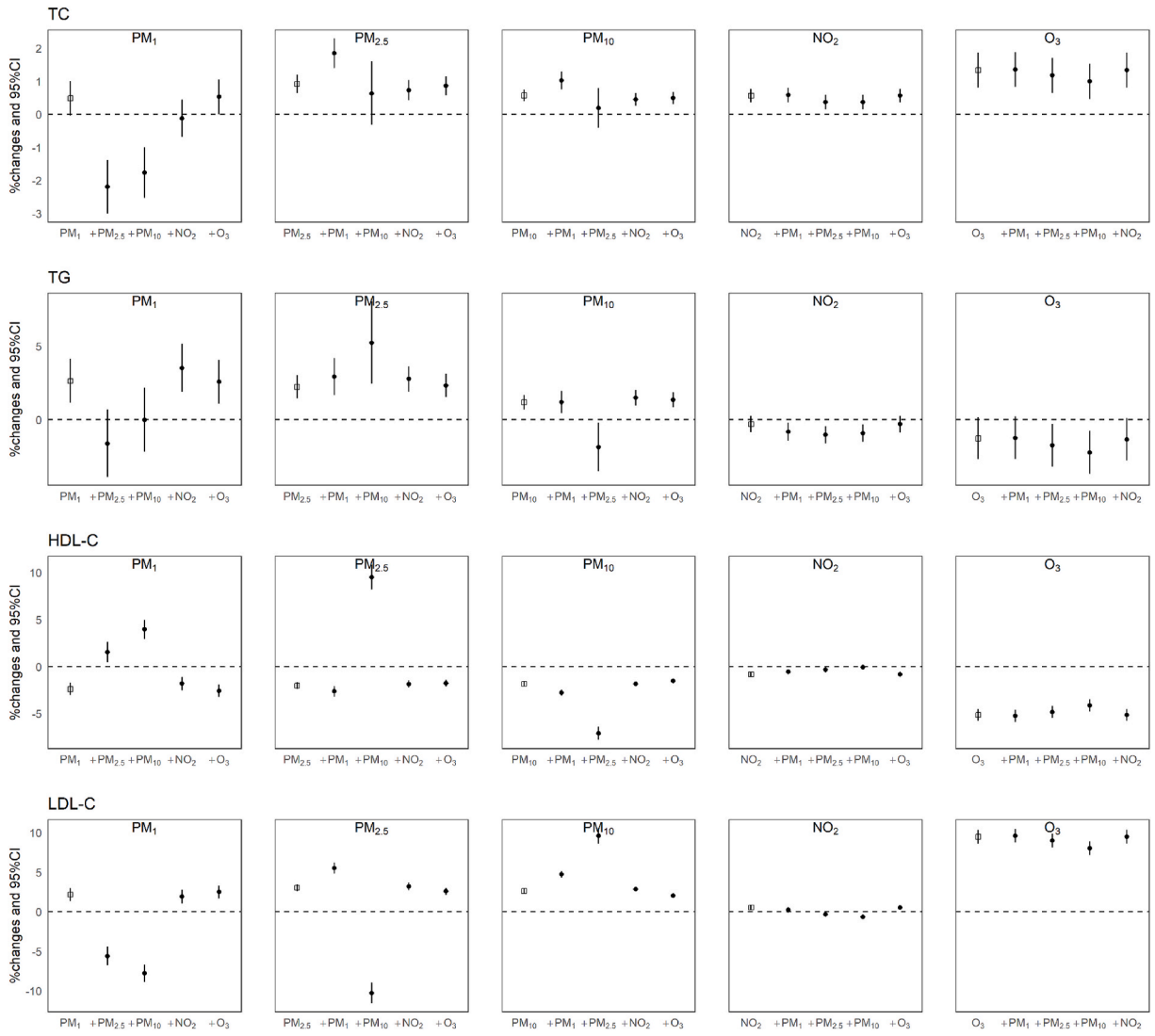

Fig. 2. Associations between per 10-μg/m^3 increment in air pollutants and blood lipid levels in single pollutant models and two-pollutant models
Abbreviations: PM_1, particles with aerodynamic diameter ≤1.0 μm; $PM_{2.5}$; particles with aerodynamic diameter ≤2.5 μm; PM_{10}, particles with aerodynamic diameter ≤10 μm; NO_2, nitrogen dioxide; O_3, ozone; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
Note: Square: % changes in the blood lipid levels in the single-pollutant models; Circles: % changes in the blood lipid levels in the two-pollutant models.

also found that quantile regression can reveal some hidden associations. For example, there was no statistically significant association between PM_1 and TC for the linear regression models, while a statistically significant association was observed in individuals in the higher quantiles of TC levels for the quantile regression models. To our knowledge, only two previous studies have investigated quantile-specific associations between air pollutants and blood lipids. A study in elderly American men revealed that the effects of $PM_{2.5}$ on TG, HDL, and LDL levels were strongest in the highest percentiles of these outcomes (Bind et al., 2016), which is consistent with our study. Another recent study in patients undergoing cardiac catheterization also found an increasing trend between $PM_{2.5}$ and TC and LDL-C (Shanley et al., 2016). Both studies were from the U.S. and focused on specific populations; to generalize the findings to broader populations, more studies conducted in different areas are warranted.

We found stronger associations between air pollutants and HDL-C levels among normal participants than among overweight or obese participants in stratified analyses. We suspected that this is because BMI might increase the risk of dyslipidemia through the same oxidative stress and inflammation pathways (Fernández-Sánchez et al., 2011). Among overweight or obese participants, BMI might dominate the main effect on blood lipids. Therefore, additional exposure to air pollutants does not further enhance the effects in these participants as much as it does among normal participants. We also found that the associations were stronger among younger people, possibly because younger people spent more time outdoors than elderly people, increasing exposure to air pollutants. The modification effects of sex in our results were mixed. A cross-sectional study in the U.S. reported a greater association between PM_{10} and TC among men (Shanley et al., 2016), while another study found that the association between $PM_{2.5}$ and HDL-C was stronger in women (Bell et al., 2017). It has been suggested that air pollution may interfere with estrogen-mediated regulation of lipid metabolism (Chen et al., 2013a; Zore et al., 2018), whereas lifestyle differences, such as smoking and drinking, are more common among men and would also affect the associations of air pollution with lipid levels. The differences between Han and other ethnic groups may be related to genetic predisposition and socioeconomic status. Besides, the sources of pollutants differed from site to site, which complicated the interaction effects of ethnic group and air pollutants on lipid levels. The results of two-pollutant models showed the associations of gaseous pollutants (O_3,

NO_2) with lipid levels were generally consistent after controlling for particulate pollutants (PM_1, $PM_{2.5}$, PM_{10}), indicating that the effects of gaseous pollutants and particulate pollutants might be independent. However, the effects of PM_1 became weaker after the inclusion of the other particulate pollutants. This finding suggests that the effects of particulate pollutants on blood lipids are mainly caused by $PM_{2.5}$ and PM_{10}.

Our study has several strengths. First, this analysis was based on a large sample from southwestern China, which could provide new evidence for the adverse effects of air pollution on blood lipids in LMICs. Second, the wide concentration range of air pollutants in our study has implications for both high- and low-pollution areas. Third, unlike most previous studies, which focused only on the average lipid levels, our study also examined the effects of air pollution on different quantiles of lipid levels to identify sensitive populations.

Our study also has some limitations. First, the cross-sectional research limited our exploration of the causal relationship between ambient air pollution and blood lipids. However, we excluded people who had lived at their current residence for less than three years and people who had self-reported dyslipidemia; thus, exposure was most likely to occur prior to the outcome. Second, we assigned exposure to participants based on residential addresses and did not consider the exposure of individuals in the workplace, leading to some exposure misclassification. Third, we used LDL-C, which reflected the cholesterol content of LDL particles, rather than the total number of LDL particles as the outcome measure. However, some researchers have suggested that LDL particle number may be a better discriminator of CVDs (Blake et al., 2002; Brunzell et al., 2008); thus, more sensitive and clinically significant biomarkers indicating CVD risk are needed in further studies to fully and accurately explore the associations of air pollution with blood lipids. Finally, although some confounders were adjusted in this research, some unmeasured or unknown confounders were not included, such as nephrotic syndrome, renal failure, systemic lupus erythematosus, and myeloma, which would affect blood lipids as well.

5. Conclusions

Our findings suggest that long-term exposure to ambient air pollution is associated with altered lipid levels and the risk of dyslipidemia. People with already high blood lipid levels should pay more attention to protective measures to reduce air pollution exposure. This study was expected to provide references for further studies on the associations between ambient air pollution and blood lipids and to provide a scientific basis for relevant departments to make policies, thus reducing the disease burden of CVDs and promoting population health through feasible and achievable targeted interventions. However, considering the limitations of our study, future population-based longitudinal studies are warranted to provide more definitive evidence on the association between ambient air pollution and blood lipids.

Credit author statement

Lei Wang, Writing – original draft. Gongbo Chen, Data curation. Yongyue Pan, Data collection. Jingjie Xia, Data collection. Liling Chen, Data collection. Xiaoqing Zhang, Data collection. Yangzong Silang, Data collection. Jiayi Chen, Data collection. Huan Xu, Software. Chunmei Zeng, Software. Jing Wei, Data collection. Shanshan Li, Data collection. Yuming Guo, Validation. Shujuan Yang, Writing- Reviewing and Editing. Feng Hong, Writing- Reviewing and Editing. Xing Zhao, Writing-Reviewing and Editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.111174.

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